ZYTOVISION

Molecular diagnostics simplified

CATALOGUE 2020

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ZYTOVISION

ZytoVision GmbH · Fischkai 1
27572 Bremerhaven · Germany · www.zytovision.com

Dear Valued Customer,

ZytoVision GmbH is known to be an innovative German company focused on the development and production of high quality, state-of-the-art diagnostic products of prognostic, predictive and therapeutic value. We fulfil this claim by a continuous product development process in cooperation with many international clinical partners as well as strict and thorough quality controls during our production processes.

Nowadays, more and more genetic markers need to be evaluated on a patient's sample to identify the appropriate treatment. In many cases, only small biopsy samples are available resulting in a limited number of slides on which immunohistochemistry, sequencing, PCR, and/or *in situ* Hybridization (ISH) should be performed. These diagnostic requirements led us to the development of a new and innovative DistinguISH™ probe design for the simultaneous detection of different genetic markers on only one slide.

This catalogue presents our most current product portfolio of ISH probes and associated reagents, introducing many new products especially for the diagnosis of tumors of the hematopoietic and lymphoid tissues. Moreover, it includes our recently launched product line Zyto*Mation*® for an automated FISH workflow and new F*lex*ISH® probes designed for a flexible FISH that allows choosing between a 1-day and a 2-day protocol.
In order that treatments can be tailored with the utmost precision to the clinical profile of an individual patient, ZytoVision offers clinical trial services comprising the development of companion diagnostics.

We believe in a long-lasting relationship with our customers and support you via our worldwide network of highly qualified local distributors allowing us to respond to your needs immediately.

Always to meet your expectations is one of our major strategies. We would like to thank existing customers for their partnership, and would like to give a warm welcome to those of you who are new customers.

Sincerely,

Your ZytoVision Team

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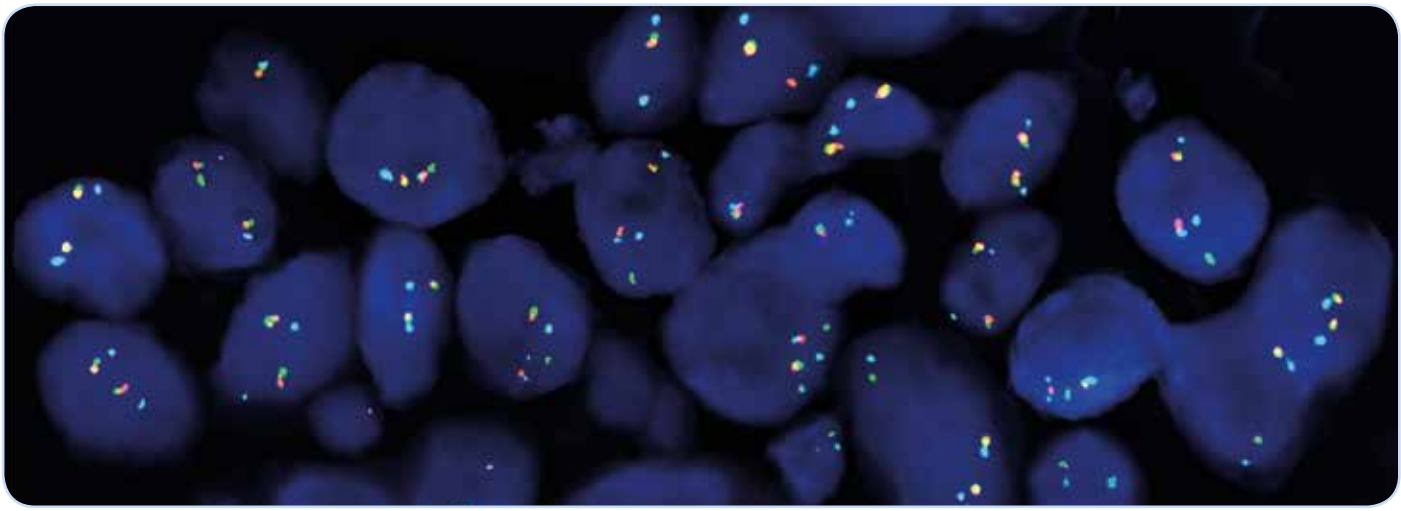
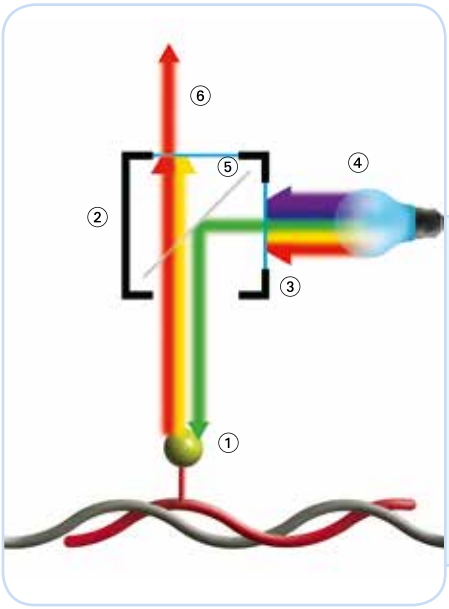
Reliable Multi-Target Detection using Fluorescence *in situ* Hybridization!



Introduction
ZytoLight® products are designed for the identification of genetic aberrations e.g. translocations, deletions, amplifications, and chromosomal aneuploidies by Fluorescence *in situ* Hybridization (FISH) in formalin-fixed, paraffin-embedded tissue sections, cell samples, blood or bone marrow smears, and metaphase chromosome spreads.

High Sensitivity and Specificity
ZytoLight® FISH probes are direct labeled using the unique ZytoLight® *Direct Label System II* providing improved signal intensity. All ZytoLight® single copy (SPEC ™) probes are processed by the unique ZytoLight® *Repeat Subtraction Technique* resulting in advanced specificity and less background. No further blocking of repetitive sequences is needed!
ZytoLight® CEN ™ probes hybridize to highly repetitive human satellite DNA sequences of chromosomes producing sharp, bright signals specific for each individual chromosome.

ZytoLight® Kits – Convenient Solutions
For making FISH analysis reliable and user-friendly, all ZytoLight® FISH probes can be combined with the ZytoLight® FISH-Tissue Implementation Kit (Z-2028-5/-20) or the ZytoLight® FISH-Cytology Implementation Kit (Z-2099-20), for FISH analyses on cytology specimens. Both Implementation Kits include all necessary pretreatment solutions, wash buffers and DAPI/DuraTect™-Solution and a detailed protocol to perform successful FISH experiments.



The ZytoLight® system uses direct labeled FISH probes ①, eliminating the need to detect the probes with fluorophore-coupled antibodies. The probes are detected by fluorescence microscopy using appropriate filter sets ②. Due to an exciter filter ③, full-spectrum light, emitted by the microscope lamp ④, is reduced to light of a defined wavelength that specifically excites the fluorophore of the probe. This light is reflected onto the specimen by a dichroic mirror ⑤. The fluorophore emits light of longer wavelengths that passes the mirror. Finally, a barrier filter ⑥ reduces the emitted light to a defined wavelength that can be detected.

Protocol Overview

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1p36.3	ZytoLight Glioma 1p/19q Probe Set CE IVD	Z-2272-20	20 tests	26
	ZytoLight SPEC 1p36/1q25 Dual Color Probe CE IVD	Z-2075-50/-200	50/200 µl	27
1p36.1	ZytoLight SPEC FOXO1/PAX7 Dual Color Single Fusion Probe CE IVD	Z-2019-50/-200	50/200 µl	128
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	ZytoLight SPEC VHL/1p12/CEN 7/17 Quadruple Color Probe CE IVD	Z-2102-200	200 µl	43
1q21	ZytoLight SPEC CKS1B/CDKN2C Dual Color Probe CE IVD	Z-2276-50	50 µl	29
	ZytoLight SPEC MCL1/1p12 Dual Color Probe CE IVD	Z-2173-200	200 µl	30
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1q23.1	ZytoLight SPEC NTRK1 Dual Color Break Apart Probe CE IVD	Z-2167-50/-200	50/200 µl	32
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4p11	ZytoLight SPEC 4p11 Probe CE IVD	Z-2083-200	200 µl	170 f.
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	10q26.1	ZytoLight SPEC FGFR2 Dual Color Break Apart Probe CE IVD	Z-2169-200	200 µl	99
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12p12.1	ZytoLight SPEC KRAS/CEN 12 Dual Color Probe CE IVD	Z-2115-200	200 µl	120
12p11.1-q11	ZytoLight CEN 12 Probe CE IVD	Z-2050-200	200 µl	170 f.
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12q13.3	ZytoLight SPEC DDIT3 Dual Color Break Apart Probe CE IVD	Z-2100-50/-200	50/200 µl	122
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	ZytoLight SPEC 13/21 Dual Color Probe CE IVD	Z-2164-200	200 µl	170 f.
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13q14.2	ZytoLight SPEC D13S319/13q34/CEN 12 Triple Color Probe CE IVD	Z-2160-50/-200	50/200 µl	113
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	ZytoLight SPEC FGFR3/IGH Dual Color Dual Fusion Probe CE IVD	Z-2282-50	50 µl	54
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		ZytoLight SPEC TP53/CEN 17 Dual Color Probe CE IVD	Z-2153-50/-200	50/200 µl	140
		ZytoLight SPEC USP6 Dual Color Break Apart Probe CE IVD	Z-2151-50	50 µl	141
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	17p11.1-q11.1	ZytoLight CEN 17 Probe CE IVD	Z-2006-200	200 µl	170 f.
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		ZytoLight SPEC ERBB2/TOP2A/CEN 17 Triple Color Probe CE IVD	Z-2093-50/-200	50/200 µl	146
	17q21.2	ZytoLight SPEC ERBB2/TOP2A/CEN 17 Triple Color Probe CE IVD	Z-2093-50/-200	50/200 µl	146
		ZytoLight SPEC PML/RARA Dual Color Dual Fusion Probe CE IVD	Z-2113-50/-200	50/200 µl	132
	17q21.3	ZytoLight SPEC COL1A1 Dual Color Break Apart Probe CE IVD	Z-2121-200	200 µl	147
		ZytoLight SPEC COL1A1/PDGFB Dual Color Dual Fusion Probe CE IVD	Z-2116-50/-200	50/200 µl	148
18	18p11.1-q11.1	ZytoLight CEN 18 Probe CE IVD	Z-2007-200	200 µl	170 f.
		ZytoLight SPEC 13/CEN 18/SPEC 21 Triple Color Probe CE IVD	Z-2095-50/-200	50/200 µl	170 f.
		ZytoLight Aneuploidy Panel 18/X/Y and 13/21 CE IVD	Z-2279-20	20 tests	172
		ZytoLight Aneuploidy Panel X/Y and 13/18/21 CE IVD	Z-2104-5/-20	5/20 tests	173
	18q11.2	ZytoLight SPEC SS18 Dual Color Break Apart Probe CE IVD	Z-2097-50/-200	50/200 µl	149
		ZytoLight SPEC SS18/SSX1 TriCheck™ Probe CE IVD	Z-2184-50	50 µl	150
	18q21.3	ZytoLight SPEC 18/CEN X/Y Triple Color Probe CE IVD	Z-2163-200	200 µl	170 f.
		ZytoLight SPEC BCL2 Dual Color Break Apart Probe CE IVD	Z-2192-50/-200	50/200 µl	151
		ZytoLight SPEC BCL2/CEN 18 Dual Color Probe CE IVD	Z-2174-50	50 µl	152
		ZytoLight SPEC BCL2/IGH Dual Color Dual Fusion Probe CE IVD	Z-2114-50/-200	50/200 µl	153
		ZytoLight SPEC BIRC3/MALT1 Dual Color Dual Fusion Probe CE IVD	Z-2146-50/-200	50/200 µl	109
		ZytoLight SPEC MALT1 Dual Color Break Apart Probe CE IVD	Z-2196-50/-200	50/200 µl	154
19	19p13.3	ZytoLight Glioma 1p/19q Probe Set CE IVD	Z-2272-20	20 tests	26
		ZytoLight SPEC 19q13/19p13 Dual Color Probe CE IVD	Z-2076-50/-200	50/200 µl	28
	19q13.2	ZytoLight SPEC CIC Dual Color Break Apart Probe CE IVD	Z-2285-50	50 µl	155
	19q13.3	ZytoLight Glioma 1p/19q Probe Set CE IVD	Z-2272-20	20 tests	26
		ZytoLight SPEC 19q13/19p13 Dual Color Probe CE IVD	Z-2076-50/-200	50/200 µl	28
	19q13.4	ZytoLight SPEC C19MC/19p13 Dual Color Probe CE IVD	Z-2274-50	50 µl	156
20	20q11.2	ZytoLight SPEC BCL2L1/CEN 20 Dual Color Probe CE IVD	Z-2171-200	200 µl	157
	20q12	ZytoLight SPEC MAFB/IGH Dual Color Dual Fusion Probe CE IVD	Z-2271-50	50 µl	138
	20q12-q13.1	ZytoLight SPEC PTPRT/20q11 Dual Color Probe CE IVD	Z-2213-50	50 µl	158

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	Chr. Band	Product Name	Product No.	Quantity	Page
21	21q22.1	ZytoLight SPEC RUNX1/RUNX1T1 Dual Color Dual Fusion Probe CE IVD	Z-2112-50/-200	50/200 µl	83
		ZytoLight SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe CE IVD	Z-2157-50/-200	50/200 µl	119
	21q22.1-q22.2	ZytoLight SPEC 21q22 Probe CE IVD	Z-2086-200	200 µl	170 f.
		ZytoLight SPEC 21/CEN X/Yq12 Triple Color Probe CE IVD	Z-2180-200	200 µl	170 f.
		ZytoLight SPEC 13/21 Dual Color Probe CE IVD	Z-2164-200	200 µl	170 f.
		ZytoLight SPEC 13/CEN 18/SPEC 21 Triple Color Probe CE IVD	Z-2095-50/-200	50/200 µl	170 f.
		ZytoLight Aneuploidy Panel 18/X/Y and 13/21 CE IVD	Z-2279-20	20 tests	172
		ZytoLight Aneuploidy Panel X/Y and 13/18/21 CE IVD	Z-2104-5/-20	5/20 tests	173
	21q22.2	ZytoLight SPEC ERG Dual Color Break Apart Probe CE IVD	Z-2138-200	200 µl	159
		ZytoLight SPEC ERG/TMPRSS2 TriCheck™ Probe CE IVD	Z-2135-200	200 µl	160
	21q22.3	ZytoLight SPEC ERG/TMPRSS2 TriCheck™ Probe CE IVD	Z-2135-200	200 µl	160
22	22q11.2	ZytoLight SPEC BCR/ABL1 Dual Color Dual Fusion Probe CE IVD	Z-2111-50/-200	50/200 µl	94
		ZytoLight SPEC DiGeorge/Phelan McDermid Dual Color Probe CE IVD NEW	Z-2299-50	50 µl	161
		ZytoLight SPEC DiGeorge Triple Color Probe CE IVD NEW	Z-2289-50	50 µl	162
		ZytoLight SPEC IGL Dual Color Break Apart Probe CE IVD	Z-2286-50	50 µl	163
		ZytoLight SPEC SMARCB1/22q12 Dual Color Probe CE IVD	Z-2178-50	50 µl	164
	22q12.2	ZytoLight SPEC EWSR1 Dual Color Break Apart Probe CE IVD	Z-2096-50/-200	50/200 µl	165
		ZytoLight SPEC EWSR1/FLI1 TriCheck™ Probe CE IVD	Z-2183-50	50 µl	166
	22q13.1	ZytoLight SPEC PDGFB Dual Color Break Apart Probe CE IVD	Z-2119-50/-200	50/200 µl	167
		ZytoLight SPEC COL1A1/PDGFB Dual Color Dual Fusion Probe CE IVD	Z-2116-50/-200	50/200 µl	148
	22q13.3	ZytoLight SPEC DiGeorge/Phelan McDermid Dual Color Probe CE IVD NEW	Z-2299-50	50 µl	161
X	Xp22.33	ZytoLight SPEC CRLF2 Dual Color Break Apart Probe CE IVD	Z-2201-50	50 µl	168
	Xp11.23	ZytoLight SPEC SS18/SSX1 TriCheck™ Probe CE IVD	Z-2184-50	50 µl	150
		ZytoLight SPEC TFE3 Dual Color Break Apart Probe CE IVD	Z-2109-50/-200	50/200 µl	169
	Xp11.1-q11.1	ZytoLight CEN X Probe CE IVD	Z-2008-200	200 µl	170 f.
		ZytoLight CEN X/Yq12 Dual Color Probe CE IVD	Z-2016-50/-200	50/200 µl	170 f.
		ZytoLight CEN X/Y Dual Color Probe CE IVD	Z-2120-200	200 µl	170 f.
		ZytoLight SPEC 18/CEN X/Y Triple Color Probe CE IVD	Z-2163-200	200 µl	170 f.
		ZytoLight SPEC 21/CEN X/Yq12 Triple Color Probe CE IVD	Z-2180-200	200 µl	170 f.
		ZytoLight Aneuploidy Panel 18/X/Y and 13/21 CE IVD	Z-2279-20	20 tests	172
		ZytoLight Aneuploidy Panel X/Y and 13/18/21 CE IVD	Z-2104-5/-20	5/20 tests	173
Y	Yp11.32	ZytoLight SPEC CRLF2 Dual Color Break Apart Probe CE IVD	Z-2201-50	50 µl	168
	Yp11.1-q11.1	ZytoLight CEN Y (DYZ3) Probe CE IVD	Z-2123-200	200 µl	170 f.
		ZytoLight CEN X/Y Dual Color Probe CE IVD	Z-2120-200	200 µl	170 f.
		ZytoLight SPEC 18/CEN X/Y Triple Color Probe CE IVD	Z-2163-200	200 µl	170 f.
	Yq12	ZytoLight CEN Yq12 Probe CE IVD	Z-2010-200	200 µl	170 f.
		ZytoLight CEN X/Yq12 Dual Color Probe CE IVD	Z-2016-50/-200	50/200 µl	170 f.
		ZytoLight SPEC 21/CEN X/Yq12 Triple Color Probe CE IVD	Z-2180-200	200 µl	170 f.
		ZytoLight Aneuploidy Panel 18/X/Y and 13/21 CE IVD	Z-2279-20	20 tests	172
		ZytoLight Aneuploidy Panel X/Y and 13/18/21 CE IVD	Z-2104-5/-20	5/20 tests	173

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HUGO Name	Synonym	Product Name	Product No.	Quantity	Page
ABL1	ABL, c-ABL	*ZytoLight* SPEC ABL1 Dual Color Break Apart Probe CE IVD	Z-2199-50	50 µl	93
		ZytoLight SPEC BCR/ABL1 Dual Color Dual Fusion Probe CE IVD	Z-2111-50/-200	50/200 µl	94
ABL2	ARG	*ZytoLight* SPEC ABL2 Dual Color Break Apart Probe CE IVD	Z-2200-50	50 µl	33
ALK	CD246	*ZytoLight* SPEC ALK/EML4 TriCheck™ Probe CE IVD	Z-2117-50/-200	50/200 µl	36
		ZytoLight SPEC ALK Dual Color Break Apart Probe CE IVD	Z-2124-50/-200	50/200 µl	37
		ZytoLight SPEC ALK/2q11 Dual Color Probe CE IVD	Z-2161-200	200 µl	38
ATM	ATA, TEL1	*ZytoLight* SPEC ATM/CEN 11 Dual Color Probe CE IVD NEW	Z-2297-50	50 µl	110
		ZytoLight SPEC ATM/CEN 12 Dual Color Probe CE IVD NEW	Z-2296-50	50 µl	111
		ZytoLight SPEC TP53/ATM Dual Color Probe CE IVD	Z-2159-50/-200	50/200 µl	112
BCL2	Bcl-2, PPP1R50	*ZytoLight* SPEC BCL2 Dual Color Break Apart Probe CE IVD	Z-2192-50/-200	50/200 µl	151
		ZytoLight SPEC BCL2/CEN 18 Dual Color Probe CE IVD	Z-2174-50	50 µl	152
		ZytoLight SPEC BCL2/IGH Dual Color Dual Fusion Probe CE IVD	Z-2114-50/-200	50/200 µl	153
BCL2L1	BCLX	*ZytoLight* SPEC BCL2L1/CEN 20 Dual Color Probe CE IVD	Z-2171-200	200 µl	157
BCL6	ZNF51, LAZ3	*ZytoLight* SPEC BCL6 Dual Color Break Apart Probe CE IVD	Z-2177-50/-200	50/200 µl	51
BCL9	-	*ZytoLight* SPEC MEF2D/BCL9 TriCheck™ Probe CE IVD	Z-2277-50	50 µl	31
BCR	ALL, BCR1	*ZytoLight* SPEC BCR/ABL1 Dual Color Dual Fusion Probe CE IVD	Z-2111-50/-200	50/200 µl	94
BIRC3	C-IAP, MALT2	*ZytoLight* SPEC BIRC3/MALT1 Dual Color Dual Fusion Probe CE IVD	Z-2146-50/-200	50/200 µl	109
BRAF	BRAF1, NS7	*ZytoLight* SPEC BRAF Dual Color Break Apart Probe CE IVD	Z-2189-200	200 µl	77
		ZytoLight SPEC BRAF/CEN 7 Dual Color Probe CE IVD	Z-2191-200	200 µl	78
C19MC	-	*ZytoLight* SPEC C19MC/19p13 Dual Color Probe CE IVD	Z-2274-50	50 µl	156
CARS	CARS1	*ZytoLight* SPEC CARS Dual Color Break Apart Probe CE IVD	Z-2137-50	50 µl	101
CBFB	PEBP2B	*ZytoLight* SPEC CBFB Dual Color Break Apart Probe CE IVD	Z-2207-50	50 µl	136
CCND1	BCL1, PRAD1	*ZytoLight* SPEC CCND1 Dual Color Break Apart Probe CE IVD	Z-2108-50/-200	50/200 µl	105
		ZytoLight SPEC CCND1 Break Apart/2q11/CEN 6 Quadruple Color Probe CE IVD	Z-2118-200	200 µl	44
		ZytoLight SPEC CCND1/CEN 11 Dual Color Probe CE IVD	Z-2071-50/-200	50/200 µl	106
		ZytoLight SPEC CCND1/IGH Dual Color Dual Fusion Probe CE IVD	Z-2125-50/-200	50/200 µl	107
CD274	PD-L1, PDL1	*ZytoLight* SPEC CD274,PDCD1LG2/CEN 9 Dual Color Probe CE IVD	Z-2179-50/-200	50/200 µl	87
CD74	-	*ZytoLight* SPEC NRG1/CD74 TriCheck™ Probe CE IVD	Z-2194-200	200 µl	79
CDK4	PSK-J3	*ZytoLight* SPEC CDK4/CEN 12 Dual Color Probe CE IVD	Z-2103-50/-200	50/200 µl	123
CDKN2A	p16, ARF, INK4	*ZytoLight* SPEC CDKN2A/CEN 9 Dual Color Probe CE IVD	Z-2063-50/-200	50/200 µl	89
		ZytoLight SPEC CDKN2A/CEN 3/7/17 Quadruple Color Probe CE IVD	Z-2081-50/-200	50/200 µl	90

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HUGO Name	Synonym	Product Name	Product No.	Quantity	Page
CDNK2C	-	ZytoLight SPEC CKS1B/CDKN2C Dual Color Probe CE IVD	Z-2276-50	50 µl	29
CIC	KIAA0306	ZytoLight SPEC CIC Dual Color Break Apart Probe CE IVD	Z-2285-50	50 µl	155
CKS1B	-	ZytoLight SPEC CKS1B/CDKN2C Dual Color Probe CE IVD	Z-2276-50	50 µl	29
COL1A1	OI4	ZytoLight SPEC COL1A1 Dual Color Break Apart Probe CE IVD ZytoLight SPEC COL1A1/PDGFB Dual Color Dual Fusion Probe CE IVD	Z-2121-200 Z-2116-50/-200	200 µl 50/200 µl	147 148
CREBBP	CBP, RTS	ZytoLight SPEC CREBBP Dual Color Break Apart Probe CE IVD	Z-2267-50	50 µl	134
CRKL	-	ZytoLight SPEC DiGeorge Triple Color Probe CE IVD NEW	Z-2289-50	50 µl	162
CRLF2	CRL2, TSLPR	ZytoLight SPEC CRLF2 Dual Color Break Apart Probe CE IVD	Z-2201-50	50 µl	168
CSF1R	FMS	ZytoLight SPEC CSF1R Dual Color Break Apart Probe CE IVD ZytoLight SPEC CSFR1/D5S23,D5S721 Dual Color Probe CE IVD	Z-2202-50 Z-2268-50	50 µl 50 µl	61 62
CUX1	CUT	ZytoLight SPEC CUX1/EZH2/CEN 7 Triple Color Probe CE IVD	Z-2214-50	50 µl	75
DDIT3	CHOP, GADD153	ZytoLight SPEC DDIT3 Dual Color Break Apart Probe CE IVD	Z-2100-50/-200	50/200 µl	122
DLEU1	BCMS1, LEU1	ZytoLight SPEC D13S319/13q34/CEN 12 Triple Color Probe CE IVD ZytoLight SPEC D13S319/13q34 Dual Color Probe CE IVD	Z-2160-50/-200 Z-2280-50	50/200 µl 50 µl	113 114
DUSP22	JKAP	ZytoLight SPEC IRF4,DUSP22 Dual Color Break Apart Probe CE IVD	Z-2210-50	50 µl	64
EGFR	HER1, ERBB1	ZytoLight SPEC EGFR/CEN 7 Dual Color Probe CE IVD	Z-2033-50/-200	50/200 µl	74
EGR1	KROX-24	ZytoLight SPEC EGR1/5p15 Dual Color Probe CE IVD ZytoLight SPEC EGR1/D5S23,D5S721 Dual Color Probe CE IVD	Z-2107-50/-200 Z-2211-50	50/200 µl 50 µl	59 60
EML4	ROPP120	ZytoLight SPEC EML4 Dual Color Break Apart Probe CE IVD ZytoLight SPEC ALK/EML4 TriCheck™ Probe CE IVD	Z-2136-50 Z-2117-50/-200	50 µl 50/200 µl	39 36
ERBB2	HER2, HER-2, NEU	ZytoLight SPEC ERBB2/CEN 17 Dual Color Probe CE IVD ZytoLight SPEC ERBB2/CEN 17 Dual Color Probe Kit CE IVD ZytoLight CEN 17/SPEC ERBB2 Dual Color Probe CE IVD ZytoLight SPEC ERBB2/D17S122 Dual Color Probe CE IVD ZytoLight SPEC ERBB2/TOP2A/CEN 17 Triple Color Probe CE IVD	Z-2015-50/-200 Z-2020-5/-20 Z-2077-50/-200 Z-2190-50/-200 Z-2093-50/-200	50/200 µl 5/20 tests 50/200 µl 50/200 µl 50/200 µl	143 143 144 145 146
ERBB3	HER3	ZytoLight SPEC ERBB3/CEN 12 Dual Color Probe CE IVD	Z-2056-200	200 µl	121
ERBB4	HER4, ALS19	ZytoLight SPEC ERBB4/2q11 Dual Color Probe CE IVD	Z-2057-200	200 µl	41
ERG	erg-3, p55	ZytoLight SPEC ERG Dual Color Break Apart Probe CE IVD ZytoLight SPEC ERG/TMPRSS2 TriCheck™ Probe CE IVD	Z-2138-200 Z-2135-200	200 µl 200 µl	159 160

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HUGO Name	Synonym	Product Name	Product No.	Quantity	Page
ESR1	Era, NR3A1	*ZytoLight* SPEC ESR1/CEN 6 Dual Color Probe CE IVD	Z-2069-50/-200	50/200 µl	72
ETV6	TEL	*ZytoLight* SPEC ETV6 Dual Color Break Apart Probe CE IVD	Z-2176-50/-200	50/200 µl	118
		ZytoLight SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe CE IVD	Z-2157-50/-200	50/200 µl	119
EWSR1	EWS	*ZytoLight* SPEC EWSR1 Dual Color Break Apart Probe CE IVD	Z-2096-50/-200	50/200 µl	165
		ZytoLight SPEC EWSR1/FLI1 TriCheck™ Probe CE IVD	Z-2183-50	50 µl	166
EZH2	KMT6A	*ZytoLight* SPEC CUX1/EZH2/CEN 7 Triple Color Probe CE IVD	Z-2214-50	50 µl	75
FGFR1	FLT2, BFGFR	*ZytoLight* SPEC FGFR1 Dual Color Break Apart Probe CE IVD	Z-2168-50/-200	50/200 µl	81
		ZytoLight SPEC FGFR1/CEN 8 Dual Color Probe CE IVD	Z-2072-50/-200	50/200 µl	82
FGFR2	BEK, CD332	*ZytoLight* SPEC FGFR2 Dual Color Break Apart Probe CE IVD	Z-2169-200	200 µl	99
		ZytoLight SPEC FGFR2/CEN 10 Dual Color Probe CE IVD	Z-2122-200	200 µl	100
FGFR3	CD333, JTK4	*ZytoLight* SPEC FGFR3 Dual Color Break Apart Probe CE IVD	Z-2170-50/-200	50/200 µl	52
		ZytoLight SPEC FGFR3/4p11 Dual Color Probe CE IVD	Z-2082-200	200 µl	53
		ZytoLight SPEC FGFR3/IGH Dual Color Dual Fusion Probe CE IVD	Z-2282-50	50 µl	54
FHIT	FRA3B	*ZytoLight* SPEC FHIT/CEN 3 Dual Color Probe CE IVD	Z-2062-200	200 µl	45
FIP1L1	FIP1	*ZytoLight* SPEC PDGFRA/FIP1L1 TriCheck™ Probe CE IVD	Z-2209-50	50 µl	55
FLI1	EWSR2	*ZytoLight* SPEC EWSR1/FLI1 TriCheck™ Probe CE IVD	Z-2183-50	50 µl	166
FOXO1	FKHR, FKH1	*ZytoLight* SPEC FOXO1 Dual Color Break Apart Probe CE IVD	Z-2139-50	50 µl	125
		ZytoLight SPEC FOXO1/PAX3 Dual Color Single Fusion Probe CE IVD	Z-2018-50/-200	50/200 µl	126
		ZytoLight SPEC FOXO1/PAX3 TriCheck™ Probe CE IVD	Z-2185-50	50 µl	127
		ZytoLight SPEC FOXO1/PAX7 Dual Color Single Fusion Probe CE IVD	Z-2019-50/-200	50/200 µl	128
FUS	FUS1	*ZytoLight* SPEC FUS Dual Color Break Apart Probe CE IVD	Z-2130-50	50 µl	135
GATA2	NFE1B	*ZytoLight* SPEC GATA2/MECOM Dual Color Dual Fusion Probe CE IVD NEW	Z-2287-50	50 µl	46
HIRA	TUPLE1, TUP1	*ZytoLight* SPEC DiGeorge/Phelan McDermid Dual Color Probe CE IVD NEW	Z-2299-50	50 µl	161
		ZytoLight SPEC DiGeorge Triple Color Probe CE IVD NEW	Z-2289-50	50 µl	162
IGH	IGH@	*ZytoLight* SPEC IGH Dual Color Break Apart Probe CE IVD	Z-2110-50/-200	50/200 µl	130
		ZytoLight SPEC BCL2/IGH Dual Color Dual Fusion Probe CE IVD	Z-2114-50/-200	50/200 µl	153
		ZytoLight SPEC CCND1/IGH Dual Color Dual Fusion Probe CE IVD	Z-2125-50/-200	50/200 µl	107
		ZytoLight SPEC FGFR3/IGH Dual Color Dual Fusion Probe CE IVD	Z-2282-50	50 µl	54
		ZytoLight SPEC MAF/IGH Dual Color Dual Fusion Probe CE IVD	Z-2270-50	50 µl	137
		ZytoLight SPEC MAFB/IGH Dual Color Dual Fusion Probe CE IVD	Z-2271-50	50 µl	138
		ZytoLight SPEC MYC/IGH Dual Color Dual Fusion Probe CE IVD	Z-2105-50/-200	50/200 µl	86
IGK	IGK@	*ZytoLight* SPEC IGK Dual Color Break Apart Probe CE IVD	Z-2288-50	50 µl	40
IGL	IGL@	*ZytoLight* SPEC IGL Dual Color Break Apart Probe CE IVD	Z-2286-50	50 µl	163

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IRF4	MUM1	*ZytoLight* SPEC IRF4,DUSP22 Dual Color Break Apart Probe CE IVD	Z-2210-50	50 µl	64
JAK2	JTK10	*ZytoLight* SPEC JAK2 Dual Color Break Apart Probe CE IVD NEW	Z-2294-50	50 µl	88
JAZF1	TIP27, ZNF802	*ZytoLight* SPEC JAZF1 Dual Color Break Apart Probe CE IVD	Z-2132-50	50 µl	73
KIF5B	KNS1	*ZytoLight* SPEC KIF5B Dual Color Break Apart Probe CE IVD	Z-2131-50	50 µl	96
KMT2A	MLL	*ZytoLight* SPEC KMT2A Dual Color Break Apart Probe CE IVD	Z-2193-50/-200	50/200 µl	116
KRAS	KRAS1	*ZytoLight* SPEC KRAS/CEN 12 Dual Color Probe CE IVD	Z-2115-200	200 µl	120
MAF	-	*ZytoLight* SPEC MAF/IGH Dual Color Dual Fusion Probe CE IVD	Z-2270-50	50 µl	137
MAFB	-	*ZytoLight* SPEC MAFB/IGH Dual Color Dual Fusion Probe CE IVD	Z-2271-50	50 µl	138
MALT1	MLT	*ZytoLight* SPEC MALT1 Dual Color Break Apart Probe CE IVD *ZytoLight* SPEC BIRC3/MALT1 Dual Color Dual Fusion Probe CE IVD	Z-2196-50/-200 Z-2146-50/-200	50/200 µl 50/200 µl	154 109
MAML2	MAM3	*ZytoLight* SPEC MAML2 Dual Color Break Apart Probe CE IVD	Z-2014-50/-200	50/200 µl	108
MAPK1	PRKM2, ERK	*ZytoLight* SPEC DiGeorge Triple Color Probe CE IVD NEW	Z-2289-50	50 µl	162
MCL1	BCL2L3	*ZytoLight* SPEC MCL1/1p12 Dual Color Probe CE IVD	Z-2173-200	200 µl	30
MDM2	HDM2	*ZytoLight* SPEC MDM2/CEN 12 Dual Color Probe CE IVD	Z-2013-50/-200	50/200 µl	124
MDM4	MDMX	*ZytoLight* SPEC MDM4/1p12 Dual Color Probe CE IVD	Z-2080-200	200 µl	34
MECOM	MDS1, EVI1	*ZytoLight* SPEC GATA2/MECOM Dual Color Dual Fusion Probe CE IVD NEW	Z-2287-50	50 µl	46
MEF2D	-	*ZytoLight* SPEC MEF2D/BCL9 TriCheck™ Probe CE IVD	Z-2277-50	50 µl	31
MET	HGFR, RCCP2	*ZytoLight* SPEC MET/CEN 7 Dual Color Probe CE IVD	Z-2087-50/-200	50/200 µl	76
MYB	c-myb	*ZytoLight* SPEC MYB Dual Color Break Apart Probe CE IVD *ZytoLight* SPEC MYB/CEN 6 Dual Color Probe CE IVD *ZytoLight* SPEC RREB1/MYB/CEN 6 Triple Color Probe CE IVD	Z-2143-50/-200 Z-2281-50 Z-2152-50/-200	50/200 µl 50 µl 50/200 µl	70 71 65
MYC	CMYC, bHLHe39, c-Myc	*ZytoLight* SPEC MYC Dual Color Break Apart Probe CE IVD *ZytoLight* SPEC MYC/CEN 8 Dual Color Probe CE IVD *ZytoLight* SPEC MYC/IGH Dual Color Dual Fusion Probe CE IVD	Z-2090-50/-200 Z-2092-50/-200 Z-2105-50/-200	50/200 µl 50/200 µl 50/200 µl	84 85 86
MYCN	NMYC, N-myc	*ZytoLight* SPEC MYCN/2q11 Dual Color Probe CE IVD	Z-2074-50/-200	50/200 µl	35
NR4A3	CHN, CSMF	*ZytoLight* SPEC NR4A3 Dual Color Break Apart Probe CE IVD	Z-2145-50	50 µl	92
NRG1	HGL, GGF	*ZytoLight* SPEC NRG1 Dual Color Break Apart Probe CE IVD *ZytoLight* SPEC NRG1/CD74 TriCheck™ Probe CE IVD	Z-2181-200 Z-2194-200	200 µl 200 µl	80 79

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HUGO Name	Synonym	Product Name	Product No.	Quantity	Page
NTRK1	MTC, TRK	*ZytoLight* SPEC NTRK1 Dual Color Break Apart Probe CE IVD	Z-2167-50/-200	50/200 µl	32
NTRK2	TRKB	*ZytoLight* SPEC NTRK2 Dual Color Break Apart Probe CE IVD	Z-2205-50/-200	50/200 µl	91
NTRK3	TRKC	*ZytoLight* SPEC NTRK3 Dual Color Break Apart Probe CE IVD	Z-2206-50/-200	50/200 µl	133
NUP98	NUP96	*ZytoLight* SPEC NUP98 Dual Color Break Apart Probe CE IVD	Z-2266-50	50 µl	102
NUP214	CAN, CAIN	*ZytoLight* SPEC NUP214 Dual Color Break Apart Probe CE IVD	Z-2265-50	50 µl	95
NUTM1	NUT	*ZytoLight* SPEC NUTM1 Dual Color Break Apart Probe CE IVD	Z-2208-200	200 µl	131
PAX3	HUP2	*ZytoLight* SPEC FOXO1/PAX3 Dual Color Single Fusion Probe CE IVD *ZytoLight* SPEC FOXO1/PAX3 TriCheck™ Probe CE IVD	Z-2018-50/-200 Z-2185-50	50/200 µl 50 µl	126 127
PAX7	HUP1	*ZytoLight* SPEC FOXO1/PAX7 Dual Color Single Fusion Probe CE IVD	Z-2019-50/-200	50/200 µl	128
PDCD1LG2	PD-L2, PDL2	*ZytoLight* SPEC CD274,PDCD1LG2/CEN 9 Dual Color Probe CE IVD	Z-2179-50/-200	50/200 µl	87
PDGFB	SIS, SSV	*ZytoLight* SPEC PDGFB Dual Color Break Apart Probe CE IVD *ZytoLight* SPEC COL1A1/PDGFB Dual Color Dual Fusion Probe CE IVD	Z-2119-50/-200 Z-2116-50/-200	50/200 µl 50/200 µl	167 148
PDGFRA	GAS9	*ZytoLight* SPEC PDGFRA/FIP1L1 TriCheck™ Probe CE IVD	Z-2209-50	50 µl	55
PDGFRB	JTK12, PDGFR1	*ZytoLight* SPEC PDGFRB Dual Color Break Apart Probe CE IVD	Z-2197-50	50 µl	63
PHF1	MTF2L2, PCL1	*ZytoLight* SPEC PHF1 Dual Color Break Apart Probe CE IVD	Z-2215-50	50 µl	66
PIK3CA	PI3K	*ZytoLight* SPEC PIK3CA/CEN 3 Dual Color Probe CE IVD	Z-2140-200	200 µl	49
PML	MYL, RNF71	*ZytoLight* SPEC PML/RARA Dual Color Dual Fusion Probe CE IVD	Z-2113-50/-200	50/200 µl	132
PTEN	MMAC1, TEP1	*ZytoLight* SPEC PTEN/CEN 10 Dual Color Probe CE IVD	Z-2078-50/-200	50/200 µl	98
PTPRT	KIAA0283	*ZytoLight* SPEC PTPRT/20q11 Dual Color Probe CE IVD	Z-2213-50	50 µl	158
RARA	NR1B1, RAR	*ZytoLight* SPEC PML/RARA Dual Color Dual Fusion Probe CE IVD	Z-2113-50/-200	50/200 µl	132
RB1	PPP1R130	*ZytoLight* SPEC RB1/13q12 Dual Color Probe CE IVD	Z-2165-50/-200	50/200 µl	129
RET	HSCR1, CDHF12	*ZytoLight* SPEC RET Dual Color Break Apart Probe CE IVD	Z-2148-50/-200	50/200 µl	97
RICTOR	AVO3, KIAA1999	*ZytoLight* SPEC RICTOR/5q31.1 Dual Color Probe CE IVD	Z-2278-200	200 µl	58
ROS1	MCF3, ROS	*ZytoLight* SPEC ROS1 Dual Color Break Apart Probe CE IVD *ZytoLight* SPEC ROS1/CEN 6 Dual Color Probe CE IVD	Z-2144-50/-200 Z-2162-200	50/200 µl 200 µl	68 69
RREB1	HNT	*ZytoLight* SPEC RREB1/MYB/CEN 6 Triple Color Probe CE IVD	Z-2152-50/-200	50/200 µl	65

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Gene Index

HUGO Name	Synonym	Product Name	Product No.	Quantity	Page
RUNX1	AML1, AMLCR1	*ZytoLight* SPEC RUNX1/RUNX1T1 Dual Color Dual Fusion Probe CE IVD	Z-2112-50/-200	50/200 µl	83
		ZytoLight SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe CE IVD	Z-2157-50/-200	50/200 µl	119
RUNX1T1	ETO, CDR, MTG8	*ZytoLight* SPEC RUNX1/RUNX1T1 Dual Color Dual Fusion Probe CE IVD	Z-2112-50/-200	50/200 µl	83
SHANK3	prosap2	*ZytoLight* SPEC DiGeorge/Phelan McDermid Dual Color Probe CE IVD NEW	Z-2299-50	50 µl	161
SMARCB1	BAF47	*ZytoLight* SPEC SMARCB1/22q12 Dual Color Probe CE IVD	Z-2178-50	50 µl	164
SOX2	ANOP3	*ZytoLight* SPEC SOX2/CEN 3 Dual Color Probe CE IVD	Z-2127-200	200 µl	50
SPI1	PU.1, SPI-A	*ZytoLight* SPEC SPI1 Dual Color Break Apart Probe CE IVD NEW	Z-2291-50	50 µl	104
SS18	SYT, SSXT	*ZytoLight* SPEC SS18 Dual Color Break Apart Probe CE IVD	Z-2097-50/-200	50/200 µl	149
		ZytoLight SPEC SS18/SSX1 TriCheck™ Probe CE IVD	Z-2184-50	50 µl	150
SSX1	-	*ZytoLight* SPEC SS18/SSX1 TriCheck™ Probe CE IVD	Z-2184-50	50 µl	150
TERC	hTERC, TRC3	*ZytoLight* SPEC TERC/CEN 3 Dual Color Probe CE IVD	Z-2284-200	200 µl	48
TERT	EST2, TCS1	*ZytoLight* SPEC TERT Dual Color Break Apart Probe CE IVD	Z-2273-50	50 µl	56
		ZytoLight SPEC TERT/5q31 Dual Color Probe CE IVD	Z-2091-50/-200	50/200 µl	57
TFE3	TFEA	*ZytoLight* SPEC TFE3 Dual Color Break Apart Probe CE IVD	Z-2109-50/-200	50/200 µl	169
TMPRSS2	PRSS10	*ZytoLight* SPEC ERG/TMPRSS2 TriCheck™ Probe CE IVD	Z-2135-200	200 µl	160
TOP2A	TOP2	*ZytoLight* SPEC ERBB2/TOP2A/CEN 17 Triple Color Probe CE IVD	Z-2093-50/-200	50/200 µl	146
TP53	LSF1, TRP53	*ZytoLight* SPEC TP53/17q22 Dual Color Probe CE IVD	Z-2198-50	50 µl	139
		ZytoLight SPEC TP53/ATM Dual Color Probe CE IVD	Z-2159-50/-200	50/200 µl	112
		ZytoLight SPEC TP53/CEN 17 Dual Color Probe CE IVD	Z-2153-50/-200	50/200 µl	140
USP6	Tre-2, TRE17	*ZytoLight* SPEC USP6 Dual Color Break Apart Probe CE IVD	Z-2151-50	50 µl	141
VEGFA	VEGF, VPF	*ZytoLight* SPEC VEGFA/CEN 6 Dual Color Probe CE IVD	Z-2195-200	200 µl	67
VHL	VHL1	*ZytoLight* SPEC VHL/CEN 3 Dual Color Probe CE IVD	Z-2084-200	200 µl	42
		ZytoLight SPEC VHL/1p12/CEN 7/17 Quadruple Color Probe CE IVD	Z-2102-200	200 µl	43
WT1	AWT1	*ZytoLight* SPEC WT1 Dual Color Break Apart Probe CE IVD	Z-2142-50	50 µl	103
WWTR1	TAZ	*ZytoLight* SPEC WWTR1 Dual Color Break Apart Probe CE IVD	Z-2212-50	50 µl	47
YWHAE	14-3-3 epsilon	*ZytoLight* SPEC YWHAE Dual Color Break Apart Probe CE IVD	Z-2175-50	50 µl	142
ZNF384	CIZ	*ZytoLight* SPEC ZNF384 Dual Color Break Apart Probe CE IVD	Z-2275-50	50 µl	117

The **Gene Index** list includes only those probes directed against DNA sequences assigned to known genes. It does not contain probes directed against other genomic sequences as e.g. repetitive satellite DNA sequences. For a complete overview of all *ZytoLight*® probes, please refer to the **Chromosome Index**.

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Indication Index

Indication	Product Name	Product No.	Quantity	Page
Solid Tumors				
Brain and Neural Tumors	ZytoLight Glioma 1p/19q Probe Set CE IVD	Z-2272-20	20 tests	**26**
	ZytoLight SPEC 1p36/1q25 Dual Color Probe CE IVD	Z-2075-50/-200	50/200 µl	27
	ZytoLight SPEC 19q13/19p13 Dual Color Probe CE IVD	Z-2076-50/-200	50/200 µl	28
	ZytoLight SPEC C19MC/19p13 Dual Color Probe CE IVD	Z-2274-50	50 µl	156
	ZytoLight SPEC CDKN2A/CEN 9 Dual Color Probe CE IVD	Z-2063-50/-200	50/200 µl	89
	ZytoLight SPEC EGFR/CEN 7 Dual Color Probe CE IVD	Z-2033-50/-200	50/200 µl	74
	ZytoLight SPEC MET/CEN 7 Dual Color Probe CE IVD	Z-2087-50/-200	50/200 µl	76
	ZytoLight SPEC MYCN/2q11 Dual Color Probe CE IVD	Z-2074-50/-200	50/200 µl	35
	ZytoLight SPEC NTRK2 Dual Color Break Apart Probe CE IVD	Z-2205-50/-200	50/200 µl	91
	ZytoLight SPEC PTEN/CEN 10 Dual Color Probe CE IVD	Z-2078-50/-200	50/200 µl	98
	ZytoLight SPEC TERT Dual Color Break Apart Probe CE IVD	Z-2273-50	50 µl	56
	ZytoLight SPEC TP53/17q22 Dual Color Probe CE IVD	Z-2198-50	50 µl	139
Breast Cancer	ZytoLight SPEC BCL2L1/CEN 20 Dual Color Probe CE IVD	Z-2171-200	200 µl	157
	ZytoLight SPEC CCND1/CEN 11 Dual Color Probe CE IVD	Z-2071-50/-200	50/200 µl	106
	ZytoLight SPEC EGFR/CEN 7 Dual Color Probe CE IVD	Z-2033-50/-200	50/200 µl	74
	ZytoLight SPEC ERBB2/CEN 17 Dual Color Probe CE IVD	Z-2015-50/-200	50/200 µl	143
	ZytoLight SPEC ERBB2/CEN 17 Dual Color Probe Kit CE IVD	Z-2020-5/-20	5/20 tests	143
	ZytoLight CEN 17/SPEC ERBB2 Dual Color Probe CE IVD	Z-2077-50/-200	50/200 µl	144
	ZytoLight SPEC ERBB2/D17S122 Dual Color Probe CE IVD	Z-2190-50/-200	50/200 µl	145
	ZytoLight SPEC ERBB2/TOP2A/CEN 17 Triple Color Probe CE IVD	Z-2093-50/-200	50/200 µl	146
	ZytoLight SPEC ERBB3/CEN 12 Dual Color Probe CE IVD	Z-2056-200	200 µl	121
	ZytoLight SPEC ERBB4/2q11 Dual Color Probe CE IVD	Z-2057-200	200 µl	41
	ZytoLight SPEC ESR1/CEN 6 Dual Color Probe CE IVD	Z-2069-50/-200	50/200 µl	72
	ZytoLight SPEC FGFR1/CEN 8 Dual Color Probe CE IVD	Z-2072-50/-200	50/200 µl	82
	ZytoLight SPEC FGFR2/CEN 10 Dual Color Probe CE IVD	Z-2122-200	200 µl	100
	ZytoLight SPEC MCL1/1p12 Dual Color Probe CE IVD	Z-2173-200	200 µl	30
	ZytoLight SPEC MYC/CEN 8 Dual Color Probe CE IVD	Z-2092-50/-200	50/200 µl	85
	ZytoLight SPEC PIK3CA/CEN 3 Dual Color Probe CE IVD	Z-2140-200	200 µl	49
	ZytoLight SPEC RREB1/MYB/CEN 6 Triple Color Probe CE IVD	Z-2152-50/-200	50/200 µl	65
	ZytoLight SPEC VEGFA/CEN 6 Dual Color Probe CE IVD	Z-2195-200	200 µl	67
Cervical Cancer	ZytoLight SPEC MYC/CEN 8 Dual Color Probe CE IVD	Z-2092-50/-200	50/200 µl	85
	ZytoLight SPEC PIK3CA/CEN 3 Dual Color Probe CE IVD	Z-2140-200	200 µl	49
	ZytoLight SPEC TERC/CEN 3 Dual Color Probe CE IVD	Z-2284-200	200 µl	48
	ZytoLight SPEC TERT/5q31 Dual Color Probe CE IVD	Z-2091-50/-200	50/200 µl	57
Gastrointestinal Cancer	ZytoLight SPEC BRAF Dual Color Break Apart Probe CE IVD	Z-2189-200	200 µl	77
	ZytoLight SPEC CCND1/CEN 11 Dual Color Probe CE IVD	Z-2071-50/-200	50/200 µl	106
	ZytoLight SPEC ERBB2/CEN 17 Dual Color Probe CE IVD	Z-2015-50/-200	50/200 µl	143
	ZytoLight SPEC ERBB2/CEN 17 Dual Color Probe Kit CE IVD	Z-2020-5/-20	5/20 tests	143
	ZytoLight CEN 17/SPEC ERBB2 Dual Color Probe CE IVD	Z-2077-50/-200	50/200 µl	144
	ZytoLight SPEC ERBB2/D17S122 Dual Color Probe CE IVD	Z-2190-50/-200	50/200 µl	145
	ZytoLight SPEC KRAS/CEN 12 Dual Color Probe CE IVD	Z-2115-200	200 µl	120
	ZytoLight SPEC MDM2/CEN 12 Dual Color Probe CE IVD	Z-2013-50/-200	50/200 µl	124
	ZytoLight SPEC RREB1/MYB/CEN 6 Triple Color Probe CE IVD	Z-2152-50/-200	50/200 µl	65

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Indication Index

Indication	Product Name	Product No.	Quantity	Page
Lung Cancer	ZytoLight SPEC ALK/EML4 TriCheck™ Probe CE IVD	Z-2117-50/-200	50/200 µl	36
	ZytoLight SPEC ALK Dual Color Break Apart Probe CE IVD	Z-2124-50/-200	50/200 µl	37
	ZytoLight SPEC ALK/2q11 Dual Color Probe CE IVD	Z-2161-200	200 µl	38
	ZytoLight SPEC BRAF/CEN 7 Dual Color Probe CE IVD	Z-2191-200	200 µl	78
	ZytoLight SPEC CARS Dual Color Break Apart Probe CE IVD	Z-2137-50	50 µl	101
	ZytoLight SPEC CD274,PDCD1LG2/CEN 9 Dual Color Probe CE IVD	Z-2179-50/-200	50/200 µl	87
	ZytoLight SPEC EGFR/CEN 7 Dual Color Probe CE IVD	Z-2033-50/-200	50/200 µl	74
	ZytoLight SPEC EML4 Dual Color Break Apart Probe CE IVD	Z-2136-50	50 µl	39
	ZytoLight SPEC ERBB2/CEN 17 Dual Color Probe CE IVD	Z-2015-50/-200	50/200 µl	143
	ZytoLight SPEC ERBB2/CEN 17 Dual Color Probe Kit CE IVD	Z-2020-5/-20	5/20 tests	143
	ZytoLight CEN 17/SPEC ERBB2 Dual Color Probe CE IVD	Z-2077-50/-200	50/200 µl	144
	ZytoLight SPEC ERBB2/D17S122 Dual Color Probe CE IVD	Z-2190-50/-200	50/200 µl	145
	ZytoLight SPEC FGFR1/CEN 8 Dual Color Probe CE IVD	Z-2072-50/-200	50/200 µl	82
	ZytoLight SPEC FGFR2 Dual Color Break Apart Probe CE IVD	Z-2169-200	200 µl	99
	ZytoLight SPEC FGFR2/CEN 10 Dual Color Probe CE IVD	Z-2122-200	200 µl	100
	ZytoLight SPEC FGFR3/4p11 Dual Color Probe CE IVD	Z-2082-200	200 µl	53
	ZytoLight SPEC KIF5B Dual Color Break Apart Probe CE IVD	Z-2131-50	50 µl	96
	ZytoLight SPEC KRAS/CEN 12 Dual Color Probe CE IVD	Z-2115-200	200 µl	120
	ZytoLight SPEC MET/CEN 7 Dual Color Probe CE IVD	Z-2087-50/-200	50/200 µl	76
	ZytoLight SPEC NRG1 Dual Color Break Apart Probe CE IVD	Z-2181-200	200 µl	80
	ZytoLight SPEC NRG1/CD74 TriCheck™ Probe CE IVD	Z-2194-200	200 µl	79
	ZytoLight SPEC NTRK1 Dual Color Break Apart Probe CE IVD	Z-2167-50/-200	50/200 µl	32
	ZytoLight SPEC NTRK2 Dual Color Break Apart Probe CE IVD	Z-2205-50/-200	50/200 µl	91
	ZytoLight SPEC NTRK3 Dual Color Break Apart Probe CE IVD	Z-2206-50/-200	50/200 µl	133
	ZytoLight SPEC PIK3CA/CEN 3 Dual Color Probe CE IVD	Z-2140-200	200 µl	49
	ZytoLight SPEC RET Dual Color Break Apart Probe CE IVD	Z-2148-50/-200	50/200 µl	97
	ZytoLight SPEC RICTOR/5q31.1 Dual Color Probe CE IVD	Z-2278-200	200 µl	58
	ZytoLight SPEC ROS1 Dual Color Break Apart Probe CE IVD	Z-2144-50/-200	50/200 µl	68
	ZytoLight SPEC ROS1/CEN 6 Dual Color Probe CE IVD	Z-2162-200	200 µl	69
	ZytoLight SPEC SOX2/CEN 3 Dual Color Probe CE IVD	Z-2127-200	200 µl	50
Prostate Cancer	ZytoLight SPEC ERG Dual Color Break Apart Probe CE IVD	Z-2138-200	200 µl	159
	ZytoLight SPEC ERG/TMPRSS2 TriCheck™ Probe CE IVD	Z-2135-200	200 µl	160
	ZytoLight SPEC PTEN/CEN 10 Dual Color Probe CE IVD	Z-2078-50/-200	50/200 µl	98
	ZytoLight SPEC RREB1/MYB/CEN 6 Triple Color Probe CE IVD	Z-2152-50/-200	50/200 µl	65
Renal Cell Carcinoma	ZytoLight SPEC CCND1 Break Apart/2q11/CEN 6 Quadruple Color Probe CE IVD	Z-2118-200	200 µl	44
	ZytoLight SPEC CDKN2A/CEN 3/7/17 Quadruple Color Probe CE IVD	Z-2081-50/-200	50/200 µl	90
	ZytoLight SPEC FHIT/CEN 3 Dual Color Probe CE IVD	Z-2062-200	200 µl	45
	ZytoLight SPEC TFE3 Dual Color Break Apart Probe CE IVD	Z-2109-50/-200	50/200 µl	169
	ZytoLight SPEC VHL/1p12/CEN 7/17 Quadruple Color Probe CE IVD	Z-2102-200	200 µl	43
	ZytoLight SPEC VHL/CEN 3 Dual Color Probe CE IVD	Z-2084-200	200 µl	42
Salivary Gland Tumors	ZytoLight SPEC ETV6 Dual Color Break Apart Probe CE IVD	Z-2176-50/-200	50/200 µl	118
	ZytoLight SPEC EWSR1 Dual Color Break Apart Probe CE IVD	Z-2096-50/-200	50/200 µl	165
	ZytoLight SPEC MAML2 Dual Color Break Apart Probe CE IVD	Z-2014-50/-200	50/200 µl	108
	ZytoLight SPEC MYB Dual Color Break Apart Probe CE IVD	Z-2143-50/-200	50/200 µl	70
	ZytoLight SPEC NTRK3 Dual Color Break Apart Probe CE IVD	Z-2206-50/-200	50/200 µl	133
	ZytoLight SPEC NUTM1 Dual Color Break Apart Probe CE IVD	Z-2208-200	200 µl	131
	ZytoLight SPEC WT1 Dual Color Break Apart Probe CE IVD	Z-2142-50	50 µl	103

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Indication	Product Name	Product No.	Quantity	Page
Sarcomas	ZytoLight SPEC ALK Dual Color Break Apart Probe CE IVD	Z-2124-50/-200	50/200 µl	37
	ZytoLight SPEC CDK4/CEN 12 Dual Color Probe CE IVD	Z-2103-50/-200	50/200 µl	123
	ZytoLight SPEC CIC Dual Color Break Apart Probe CE IVD	Z-2285-50	50 µl	155
	ZytoLight SPEC COL1A1 Dual Color Break Apart Probe CE IVD	Z-2121-200	200 µl	147
	ZytoLight SPEC COL1A1/PDGFB Dual Color Dual Fusion Probe CE IVD	Z-2116-50/-200	50/200 µl	148
	ZytoLight SPEC DDIT3 Dual Color Break Apart Probe CE IVD	Z-2100-50/-200	50/200 µl	122
	ZytoLight SPEC ETV6 Dual Color Break Apart Probe CE IVD	Z-2176-50/-200	50/200 µl	118
	ZytoLight SPEC EWSR1 Dual Color Break Apart Probe CE IVD	Z-2096-50/-200	50/200 µl	165
	ZytoLight SPEC EWSR1/FLI1 TriCheck™ Probe CE IVD	Z-2183-50	50 µl	166
	ZytoLight SPEC FOXO1 Dual Color Break Apart Probe CE IVD	Z-2139-50	50 µl	125
	ZytoLight SPEC FOXO1/PAX3 Dual Color Single Fusion Probe CE IVD	Z-2018-50/-200	50/200 µl	126
	ZytoLight SPEC FOXO1/PAX3 TriCheck™ Probe CE IVD	Z-2185-50	50 µl	127
	ZytoLight SPEC FOXO1/PAX7 Dual Color Single Fusion Probe CE IVD	Z-2019-50/-200	50/200 µl	128
	ZytoLight SPEC FUS Dual Color Break Apart Probe CE IVD	Z-2130-50	50 µl	135
	ZytoLight SPEC JAZF1 Dual Color Break Apart Probe CE IVD	Z-2132-50	50 µl	73
	ZytoLight SPEC MDM2/CEN 12 Dual Color Probe CE IVD	Z-2013-50/-200	50/200 µl	124
	ZytoLight SPEC MDM4/1p12 Dual Color Probe CE IVD	Z-2080-200	200 µl	34
	ZytoLight SPEC MYC/CEN 8 Dual Color Probe CE IVD	Z-2092-50/-200	50/200 µl	85
	ZytoLight SPEC NR4A3 Dual Color Break Apart Probe CE IVD	Z-2145-50	50 µl	92
	ZytoLight SPEC NTRK3 Dual Color Break Apart Probe CE IVD	Z-2206-50/-200	50/200 µl	133
	ZytoLight SPEC PDGFB Dual Color Break Apart Probe CE IVD	Z-2119-50/-200	50/200 µl	167
	ZytoLight SPEC PHF1 Dual Color Break Apart Probe CE IVD	Z-2215-50	50 µl	66
	ZytoLight SPEC SMARCB1/22q12 Dual Color Probe CE IVD	Z-2178-50	50 µl	164
	ZytoLight SPEC SS18 Dual Color Break Apart Probe CE IVD	Z-2097-50/-200	50/200 µl	149
	ZytoLight SPEC SS18/SSX1 TriCheck™ Probe CE IVD	Z-2184-50	50 µl	150
	ZytoLight SPEC TFE3 Dual Color Break Apart Probe CE IVD	Z-2109-50/-200	50/200 µl	169
	ZytoLight SPEC USP6 Dual Color Break Apart Probe CE IVD	Z-2151-50	50 µl	141
	ZytoLight SPEC VEGFA/CEN 6 Dual Color Probe CE IVD	Z-2195-200	200 µl	67
	ZytoLight SPEC WT1 Dual Color Break Apart Probe CE IVD	Z-2142-50	50 µl	103
	ZytoLight SPEC WWTR1 Dual Color Break Apart Probe CE IVD	Z-2212-50	50 µl	47
	ZytoLight SPEC YWHAE Dual Color Break Apart Probe CE IVD	Z-2175-50	50 µl	142
Hematology Specific Probes				
Acute Lymphoblastic Leukemia (ALL)	ZytoLight SPEC ABL1 Dual Color Break Apart Probe CE IVD	Z-2199-50	50 µl	93
	ZytoLight SPEC ABL2 Dual Color Break Apart Probe CE IVD	Z-2200-50	50 µl	33
	ZytoLight SPEC CRLF2 Dual Color Break Apart Probe CE IVD	Z-2201-50	50 µl	168
	ZytoLight SPEC CSF1R Dual Color Break Apart Probe CE IVD	Z-2202-50	50 µl	61
	ZytoLight SPEC ETV6 Dual Color Break Apart Probe CE IVD	Z-2176-50/-200	50/200 µl	118
	ZytoLight SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe CE IVD	Z-2157-50/-200	50/200 µl	119
	ZytoLight SPEC JAK2 Dual Color Break Apart Probe CE IVD NEW	Z-2294-50	50 µl	88
	ZytoLight SPEC KMT2A Dual Color Break Apart Probe CE IVD	Z-2193-50/-200	50/200 µl	116
	ZytoLight SPEC MEF2D/BCL9 TriCheck™ Probe CE IVD	Z-2277-50	50 µl	31
	ZytoLight SPEC MYB Dual Color Break Apart Probe CE IVD	Z-2143-50/-200	50/200 µl	70
	ZytoLight SPEC NUP98 Dual Color Break Apart Probe CE IVD	Z-2266-50	50 µl	102
	ZytoLight SPEC NUP214 Dual Color Break Apart Probe CE IVD	Z-2265-50	50 µl	95
	ZytoLight SPEC PDGFRA/FIP1L1 TriCheck™ Probe CE IVD	Z-2209-50	50 µl	55
	ZytoLight SPEC SPI1 Dual Color Break Apart Probe CE IVD NEW	Z-2291-50	50 µl	104
	ZytoLight SPEC ZNF384 Dual Color Break Apart Probe CE IVD	Z-2275-50	50 µl	117

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Indication	Product Name	Product No.	Quantity	Page
Acute Myelogenous Leukemia (AML)	ZytoLight CEN 8 Probe CE IVD	Z-2004-50/-200	50/200 µl	170 f.
	ZytoLight SPEC ABL2 Dual Color Break Apart Probe CE IVD	Z-2200-50	50 µl	33
	ZytoLight SPEC BCR/ABL1 Dual Color Dual Fusion Probe CE IVD	Z-2111-50/-200	50/200 µl	94
	ZytoLight SPEC CBFB Dual Color Break Apart Probe CE IVD	Z-2207-50	50 µl	136
	ZytoLight SPEC CREBBP Dual Color Break Apart Probe CE IVD	Z-2267-50	50 µl	134
	ZytoLight SPEC CSF1R/D5S23,D5S721 Dual Color Probe CE IVD	Z-2268-50	50µl	62
	ZytoLight SPEC CUX1/EZH2/CEN 7 Triple Color Probe CE IVD	Z-2214-50	50 µl	75
	ZytoLight SPEC EGR1/5p15 Dual Color Probe CE IVD	Z-2107-50/-200	50/200 µl	59
	ZytoLight SPEC EGR1/D5S23,D5S721 Dual Color Probe CE IVD	Z-2211-50	50 µl	60
	ZytoLight SPEC FGFR1 Dual Color Break Apart Probe CE IVD	Z-2168-50/-200	50/200 µl	81
	ZytoLight SPEC GATA2/MECOM Dual Color Dual Fusion Probe CE IVD NEW	Z-2287-50	50 µl	46
	ZytoLight SPEC KMT2A Dual Color Break Apart Probe CE IVD	Z-2193-50/-200	50/200 µl	116
	ZytoLight SPEC NUP98 Dual Color Break Apart Probe CE IVD	Z-2266-50	50 µl	102
	ZytoLight SPEC NUP214 Dual Color Break Apart Probe CE IVD	Z-2265-50	50 µl	95
	ZytoLight SPEC PDGFRA/FIP1L1 TriCheck™ Probe CE IVD	Z-2209-50	50 µl	55
	ZytoLight SPEC PDGFRB Dual Color Break Apart Probe CE IVD	Z-2197-50	50 µl	63
	ZytoLight SPEC PML/RARA Dual Color Dual Fusion Probe CE IVD	Z-2113-50/-200	50/200 µl	132
	ZytoLight SPEC PTPRT/20q11 Dual Color Probe CE IVD	Z-2213-50	50 µl	158
	ZytoLight SPEC RUNX1/RUNX1T1 Dual Color Dual Fusion Probe CE IVD	Z-2112-50/-200	50/200 µl	83
Chronic Lymphocytic Leukemia (CLL)	ZytoLight SPEC ATM/CEN 11 Dual Color Probe CE IVD NEW	Z-2297-50	50 µl	110
	ZytoLight SPEC ATM/CEN 12 Dual Color Probe CE IVD NEW	Z-2296-50	50 µl	111
	ZytoLight SPEC BCL2 Dual Color Break Apart Probe CE IVD	Z-2192-50/-200	50/200 µl	151
	ZytoLight SPEC CCND1 Dual Color Break Apart Probe CE IVD	Z-2108-50/-200	50/200 µl	105
	ZytoLight SPEC CCND1/CEN 11 Dual Color Probe CE IVD	Z-2071-50/-200	50/200 µl	106
	ZytoLight SPEC D13S319/13q34/CEN 12 Triple Color Probe CE IVD	Z-2160-50/-200	50/200 µl	113
	ZytoLight SPEC D13S319/13q34 Dual Color Probe CE IVD	Z-2280-50	50 µl	114
	ZytoLight SPEC MYB/CEN 6 Dual Color Probe CE IVD	Z-2281-50	50 µl	71
	ZytoLight SPEC MYC/CEN 8 Dual Color Probe CE IVD	Z-2092-50/-200	50/200 µl	85
	ZytoLight SPEC RB1/13q12 Dual Color Probe CE IVD	Z-2165-50/-200	50/200 µl	129
	ZytoLight SPEC TP53/ATM Dual Color Probe CE IVD	Z-2159-50/-200	50/200 µl	112
	ZytoLight SPEC TP53/CEN 17 Dual Color Probe CE IVD	Z-2153-50/-200	50/200 µl	140
Chronic Myelogenous Leukemia (CML)	ZytoLight CEN 8 Probe CE IVD	Z-2004-50/-200	50/200 µl	170 f.
	ZytoLight SPEC ABL1 Dual Color Break Apart Probe CE IVD	Z-2199-50	50 µl	93
	ZytoLight SPEC BCR/ABL1 Dual Color Dual Fusion Probe CE IVD	Z-2111-50/-200	50/200 µl	94
	ZytoLight SPEC JAK2 Dual Color Break Apart Probe CE IVD NEW	Z-2294-50	50 µl	88
	ZytoLight SPEC PDGFRB Dual Color Break Apart Probe CE IVD	Z-2197-50	50 µl	63
	ZytoLight SPEC TP53/17q22 Dual Color Probe CE IVD	Z-2198-50	50 µl	139

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Indication Index

Indication	Product Name	Product No.	Quantity	Page
Multiple Myeloma	ZytoLight SPEC CCND1 Dual Color Break Apart Probe CE IVD	Z-2108-50/-200	50/200 µl	105
	ZytoLight SPEC CCND1/CEN 11 Dual Color Probe CE IVD	Z-2071-50/-200	50/200 µl	106
	ZytoLight SPEC CCND1/IGH Dual Color Dual Fusion Probe CE IVD	Z-2125-50/-200	50/200 µl	107
	ZytoLight SPEC CKS1B/CDKN2C Dual Color Probe CE IVD	Z-2276-50	50 µl	29
	ZytoLight SPEC FGFR3 Dual Color Break Apart Probe CE IVD	Z-2170-50/-200	50/200 µl	52
	ZytoLight SPEC FGFR3/IGH Dual Color Dual Fusion Probe CE IVD	Z-2282-50	50µl	54
	ZytoLight SPEC IGH Dual Color Break Apart Probe CE IVD	Z-2110-50/-200	50/200 µl	130
	ZytoLight SPEC MAF/IGH Dual Color Dual Fusion Probe CE IVD	Z-2270-50	50 µl	137
	ZytoLight SPEC MAFB/IGH Dual Color Dual Fusion Probe CE IVD	Z-2271-50	50 µl	138
	ZytoLight SPEC RB1/13q12 Dual Color Probe CE IVD	Z-2165-50/-200	50/200 µl	129
	ZytoLight SPEC TP53/CEN 17 Dual Color Probe CE IVD	Z-2153-50/-200	50/200 µl	140
Myelodysplastic Syndrome (MDS)	ZytoLight CEN 8 Probe CE IVD	Z-2004-50/-200	50/200 µl	170 f.
	ZytoLight SPEC CREBBP Dual Color Break Apart Probe CE IVD	Z-2267-50	50 µl	134
	ZytoLight SPEC CSF1R/D5S23,D5S721 Dual Color Probe CE IVD	Z-2268-50	50 µl	62
	ZytoLight SPEC CUX1/EZH2/CEN 7 Triple Color Probe CE IVD	Z-2214-50	50 µl	75
	ZytoLight SPEC EGR1/5p15 Dual Color Probe CE IVD	Z-2107-50/-200	50/200 µl	59
	ZytoLight SPEC EGR1/D5S23,D5S721 Dual Color Probe CE IVD	Z-2211-50	50 µl	60
	ZytoLight SPEC ETV6 Dual Color Break Apart Probe CE IVD	Z-2176-50/-200	50/200 µl	118
	ZytoLight SPEC NUP98 Dual Color Break Apart Probe CE IVD	Z-2266-50	50 µl	102
	ZytoLight SPEC NUP214 Dual Color Break Apart Probe CE IVD	Z-2265-50	50 µl	95
	ZytoLight SPEC PDGFRB Dual Color Break Apart Probe CE IVD	Z-2197-50	50 µl	63
	ZytoLight SPEC PTPRT/20q11 Dual Color Probe CE IVD	Z-2213-50	50 µl	158
	ZytoLight SPEC TERT/5q31 Dual Color Probe CE IVD	Z-2091-50/-200	50/200 µl	57
Non-Hodgkin Lymphoma, other	ZytoLight SPEC 11q gain/loss Triple Color Probe CE IVD	Z-2216-50	50 µl	115
	ZytoLight SPEC BCL2 Dual Color Break Apart Probe CE IVD	Z-2192-50/-200	50/200 µl	151
	ZytoLight SPEC BCL2/CEN 18 Dual Color Probe CE IVD	Z-2174-50	50 µl	152
	ZytoLight SPEC BCL2/IGH Dual Color Dual Fusion Probe CE IVD	Z-2114-50/-200	50/200 µl	153
	ZytoLight SPEC BCL6 Dual Color Break Apart Probe CE IVD	Z-2177-50/-200	50/200 µl	51
	ZytoLight SPEC BIRC3/MALT1 Dual Color Dual Fusion Probe CE IVD	Z-2146-50/-200	50/200 µl	109
	ZytoLight SPEC CCND1 Dual Color Break Apart Probe CE IVD	Z-2108-50/-200	50/200 µl	105
	ZytoLight SPEC CCND1/CEN 11 Dual Color Probe CE IVD	Z-2071-50/-200	50/200 µl	106
	ZytoLight SPEC CCND1/IGH Dual Color Dual Fusion Probe CE IVD	Z-2125-50/-200	50/200 µl	107
	ZytoLight SPEC FGFR3 Dual Color Break Apart Probe CE IVD	Z-2170-50/-200	50/200 µl	52
	ZytoLight SPEC IGH Dual Color Break Apart Probe CE IVD	Z-2110-50/-200	50/200 µl	130
	ZytoLight SPEC IGK Dual Color Break Apart Probe CE IVD	Z-2288-50	50 µl	40
	ZytoLight SPEC IGL Dual Color Break Apart Probe CE IVD	Z-2286-50	50 µl	163
	ZytoLight SPEC IRF4,DUSP22 Dual Color Break Apart Probe CE IVD	Z-2210-50	50 µl	64
	ZytoLight SPEC MALT1 Dual Color Break Apart Probe CE IVD	Z-2196-50/-200	50/200 µl	154
	ZytoLight SPEC MYC Dual Color Break Apart Probe CE IVD	Z-2090-50/-200	50/200 µl	84
	ZytoLight SPEC MYC/IGH Dual Color Dual Fusion Probe CE IVD	Z-2105-50/-200	50/200 µl	86

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Indication Index

Indication	Product Name	Product No.	Quantity	Page
Genetics				
Sex Mismatched Bone-Marrow Transplantant Management	*ZytoLight* CEN X Probe CE IVD	Z-2008-200	200 µl	170 f.
	ZytoLight CEN X/Y Dual Color Probe CE IVD	Z-2120-200	200 µl	170 f.
	ZytoLight CEN X/Yq12 Dual Color Probe CE IVD	Z-2016-50/-200	50/200 µl	170 f.
	ZytoLight CEN Y (DYZ3) Probe CE IVD	Z-2123-200	200 µl	170 f.
	ZytoLight CEN Yq12 Probe CE IVD	Z-2010-200	200 µl	170 f.
Prenatal, Postnatal, and Preimplantation Genetics	*ZytoLight* Aneuploidy Panel 18/X/Y and 13/21 CE IVD	Z-2279-20	20 tests	172
	ZytoLight Aneuploidy Panel X/Y and 13/18/21 CE IVD	Z-2104-5/-20	5/20 tests	173
	ZytoLight SPEC 13q12 Probe CE IVD	Z-2085-200	200 µl	170 f.
	ZytoLight SPEC 13/CEN 18/SPEC 21 Triple Color Probe CE IVD	Z-2095-50/-200	50/200 µl	170 f.
	ZytoLight SPEC 13/21 Dual Color Probe CE IVD	Z-2164-200	200 µl	170 f.
	ZytoLight CEN 18 Probe CE IVD	Z-2007-200	200 µl	170 f.
	ZytoLight SPEC 18/CEN X/Y Triple Color Probe CE IVD	Z-2163-200	200 µl	170 f.
	ZytoLight SPEC 21q22 Probe CE IVD	Z-2086-200	200 µl	170 f.
	ZytoLight SPEC 21/CEN X/Yq12 Triple Color Probe CE IVD	Z-2180-200	200 µl	170 f.
	ZytoLight CEN X Probe CE IVD	Z-2008-200	200 µl	170 f.
	ZytoLight CEN X/Y Dual Color Probe CE IVD	Z-2120-200	200 µl	170 f.
	ZytoLight CEN X/Yq12 Dual Color Probe CE IVD	Z-2016-50/-200	50/200 µl	170 f.
	ZytoLight CEN Y (DYZ3) Probe CE IVD	Z-2123-200	200 µl	170 f.
	ZytoLight CEN Yq12 Probe CE IVD	Z-2010-200	200 µl	170 f.
	ZytoLight SPEC DiGeorge/Phelan McDermid Dual Color Probe CE IVD NEW	Z-2299-50	50 µl	161
	ZytoLight SPEC DiGeorge Triple Color Probe CE IVD NEW	Z-2289-50	50 µl	162

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ZytoLight® Glioma 1p/19q Probe Set

CE IVD

Background

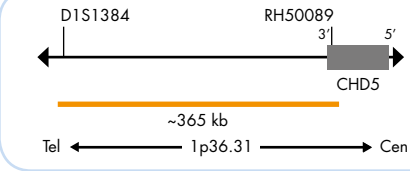
Deletions affecting the short arm of chromosome 1 (1p36) and the long arm of chromosome 19 (19q13) are frequently found in human gliomas. According to the 2016 WHO criteria for classification of tumors of the central nervous system, the detection of 1p/19q loss is required for the diagnosis of WHO grade II or III "oligodendroglioma, IDH-mutant and 1p/19q codeleted". Since both, astrocytomas and oligodendrogliomas, can exhibit IDH mutations, evaluation of 1p/19q status plays a critical role in differentiating astrocytoma from oligodendroglioma.
Oligodendroglioma morphology, IDH-mutant genotype, and 1p/19q codeletion are associated with better response to chemotherapy and improved survival. Hence, determination of 1p and 19q status may aid in therapeutic decisions and predict outcome in patients with diffuse gliomas.
Several types of tissue tend to emit intense autofluorescence including brain, liver, kidney and myocardium, making it difficult to evaluate FISH results. The ZyBlack™ Quenching Solution reduces autofluorescence without adversely affecting tissue integrity or specific fluorescence signals.

References
Barbashina V, et al. (2005) Clin Cancer Res 11: 1119-28.
Cairncross JG, et al. (1998) J Natl Cancer Inst 90: 1473-9.
Cairncross G, et al. (2013) J Clin Oncol 31: 337-43.
Griffin CA, et al. (2006) J Neuropathol Exp Neurol 65: 988-94.
Louis DN, et al. (ed.) (2016) WHO Classification of Tumours of the Central Nervous System (Revised 4th Edition).
Reifenberger G, et al. (2017) Nat Rev Clin Oncol 14: 434-52.
Rosenberg JE, et al. (1996) Oncogene 13: 2483-5.
Smith JS, et al. (1999) Oncogene 18: 4144-52.
Smith JS, et al. (2000) Genes Chromosomes Cancer 29: 16-25.

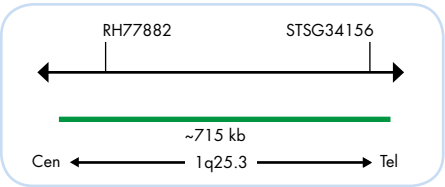
Probe Description

The ZytoLight® Glioma 1p/19q Probe Set includes the ZytoLight® SPEC 1p36/1q25 Dual Color Probe and the ZytoLight® SPEC 19q13/19p13 Dual Color Probe for the detection of both 1p36 and 19q13 loci, and the innovative ZyBlack™ Quenching Solution to reduce autofluorescence on both formalin-fixed paraffin-embedded and frozen sections.

ZytoLight® SPEC 1p36/1q25 Dual Color Probe

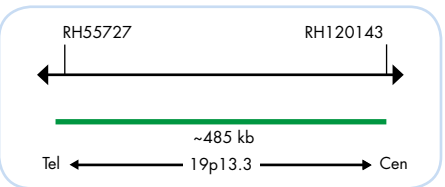


SPEC 1p36 Probe map (not to scale).

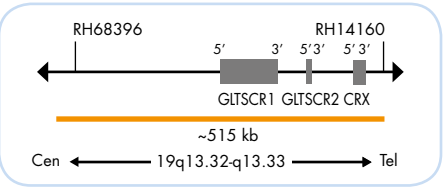


SPEC 1q25 Probe map (not to scale).

ZytoLight® SPEC 19q13/19p13 Dual Color Probe



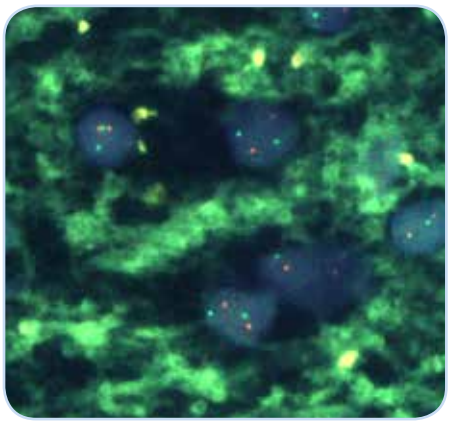
SPEC 19p13 Probe map (not to scale).



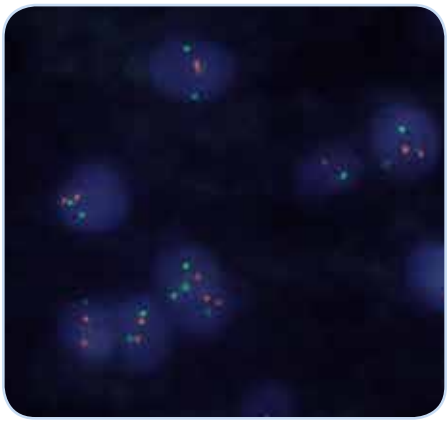
SPEC 19q13 Probe map (not to scale).

Results

Using the SPEC 1p36/1q25 Dual Color Probe or the SPEC 19q13/19p13 Dual Color Probe in a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletions affecting the 1p36 or 19q13 locus, one or no copy of the orange signal will be observed.



Brain tissue section hybridized with the ZytoLight® SPEC 1p36/1q25 Dual Color Probe without ZyBlack™ Quenching Solution.



Brain tissue section hybridized with the ZytoLight® SPEC 1p36/1q25 Dual Color Probe with ZyBlack™ Quenching Solution.

Prod. No.	Product	Label	Tests* (Volume)
Z-2272-20	ZytoLight Glioma 1p/19q Probe Set CE IVD Incl. ZytoLight SPEC 1p36/1q25 Dual Color Probe, 0.2 ml; ZytoLight SPEC 19q13/19p13 Dual Color Probe, 0.2 ml; ZyBlack Quenching Solution, 8 ml		20
Related Products			
Z-2075-200	ZytoLight SPEC 1p36/1q25 Dual Color Probe CE IVD	●/●	20 (200 µl)
Z-2076-200	ZytoLight SPEC 19q13/19p13 Dual Color Probe CE IVD	●/●	20 (200 µl)
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC 1p36/1q25 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC 1p36/1q25 Dual Color Probe is designed for the detection of 1p deletions.

Deletions affecting the short arm of chromosome 1 (1p) are frequently found in human gliomas and neuroblastomas, but also in breast, lung, endometrial, ovarian, and colorectal carcinomas.

Deletions affecting the long arm of chromosome 19 (19q) are frequently found in human malignant gliomas as well as in neuroblastomas and epithelial ovarian cancers.

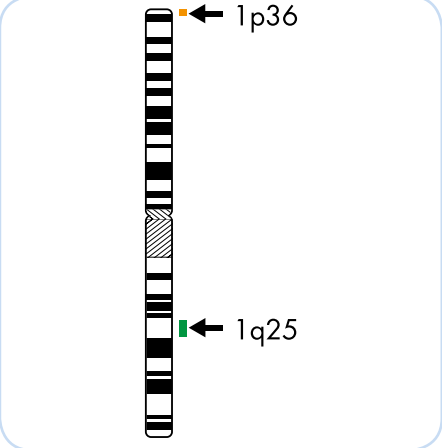
Combined loss of the complete 1p/19q chromosome arms, caused by an unbalanced t(1;19)(q10;p10) translocation, is characteristic of oligodendrogliomas.

According to the 2016 WHO criteria for classification of tumors of the central nervous system, the detection of 1p/19q loss is required for the diagnosis of WHO grade II or III "oligodendroglioma, IDH-mutant and 1p/19q codeleted". Since both, astrocytomas and oligodendrogliomas, can exhibit IDH mutations, evaluation of 1p/19q status plays a critical role in differentiating astrocytoma from oligodendroglioma.

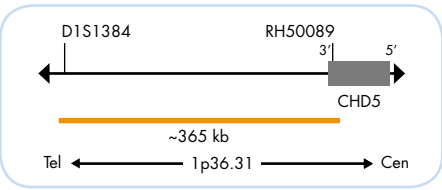
Oligodendroglioma morphology, IDH-mutant genotype, and 1p/19q codeletion are associated with better response to chemotherapy and improved survival. Hence, determination of 1p and 19q status may aid in therapeutic decisions and predict outcome in patients with diffuse gliomas.

Probe Description

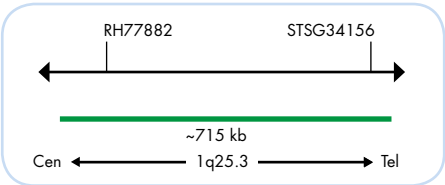
The SPEC 1p36/1q25 Dual Color Probe is a mixture of an orange fluorochrome direct labeled 1p36 probe specific for the smallest region of consistent deletion (SRD) of chromosome 1 defined in neuroblastoma at 1p36.31 and a green fluorochrome direct labeled 1q25 probe specific for 1q25.3.



Ideogram of chromosome 1 indicating the hybridization locations.



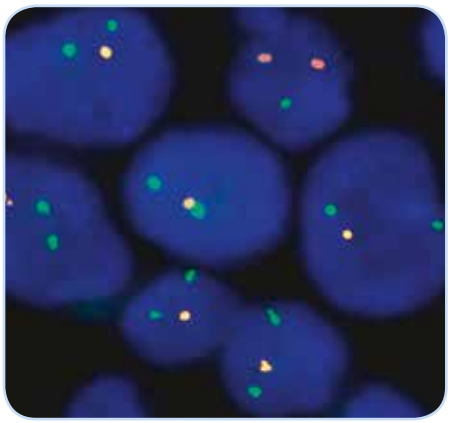
SPEC 1p36 Probe map (not to scale).



SPEC 1q25 Probe map (not to scale).

Results

Using the SPEC 1p36/1q25 Dual Color Probe in a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletions affecting the 1p36 locus, one or no copy of the orange signal will be observed.



SPEC 1p36/1q25 Dual Color Probe hybridized to a glioma tissue section with 1p36 deletion as indicated by one orange signal in each nucleus.

References

Barbashina V, et al. (2005) Clin Cancer Res 11: 1119-28.
Cairncross JG, et al. (1998) J Natl Cancer Inst 90: 1473-9.
Cairncross G, et al. (2013) J Clin Oncol 31: 337-43.
Caron H, et al. (1996) N Engl J Med 334: 225-30.
Griffin CA, et al. (2006) J Neuropathol Exp Neurol 65: 988-94.
Louis DN, et al. (ed.) (2016) WHO Classification of Tumours of the Central Nervous System (Revised 4th Edition).
Ragnarsson G, et al. (1999) Br J Cancer 79: 1468-74.
Reifenberger G, et al. (2017) Nat Rev Clin Oncol 14: 434-52.
Rosenberg JE, et al. (1996) Oncogene 13: 2483-5.
Smith JS, et al. (1999) Oncogene 18: 4144-52.
Smith JS, et al. (2000) Genes Chromosomes Cancer 29: 16-25.

Prod. No.	Product	Label	Tests* (Volume)
Z-2075-50	ZytoLight SPEC 1p36/1q25 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2075-200	ZytoLight SPEC 1p36/1q25 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2272-20	ZytoLight Glioma 1p/19q Probe Set CE IVD Incl. ZytoLight SPEC 1p36/1q25 Dual Color Probe, 0.2 ml; ZytoLight SPEC 19q13/19p13 Dual Color Probe, 0.2 ml; ZyBlack Quenching Solution, 8 ml		20
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC 19q13/19p13 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC 19q13/19p13 Dual Color Probe is designed for the detection of 19q deletions.

Deletions affecting the long arm of chromosome 19 (19q) are frequently found in human malignant gliomas as well as in neuroblastomas and epithelial ovarian cancers.

Deletions affecting the short arm of chromosome 1 (1p) are frequently found in human gliomas and neuroblastomas, but also in breast, lung, endometrial, ovarian, and colorectal carcinomas.

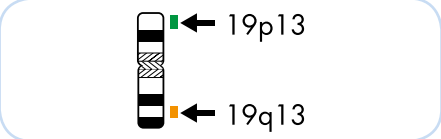
Combined loss of the complete 1p/19q chromosome arms, caused by an unbalanced t(1;19)(q10;p10) translocation, is characteristic of oligodendrogliomas.

According to the 2016 WHO criteria for classification of tumors of the central nervous system, the detection of 1p/19q loss is required for the diagnosis of WHO grade II or III "oligodendroglioma, IDH-mutant and 1p/19q codeleted". Since both, astrocytomas and oligodendrogliomas, can exhibit IDH mutations, evaluation of 1p/19q status plays a critical role in differentiating astrocytoma from oligodendroglioma.

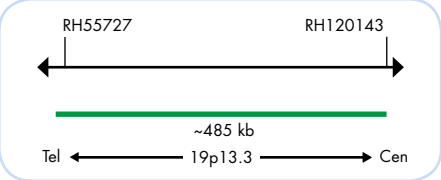
Oligodendroglioma morphology, IDH-mutant genotype, and 1p/19q codeletion are associated with better response to chemotherapy and improved survival. Hence, determination of 1p and 19q status may aid in therapeutic decisions and predict outcome in patients with diffuse gliomas.

Probe Description

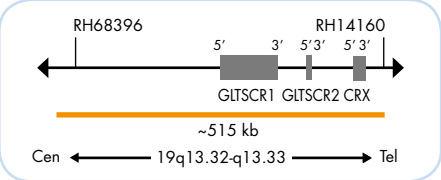
The SPEC 19q13/19p13 Dual Color Probe is a mixture of an orange fluorochrome direct labeled 19q13 probe specific for the region of common deletion in gliomas at 19q13.32-q13.33 and a green fluorochrome direct labeled 19p13 probe specific for 19p13.3.



Ideogram of chromosome 19 indicating the hybridization locations.



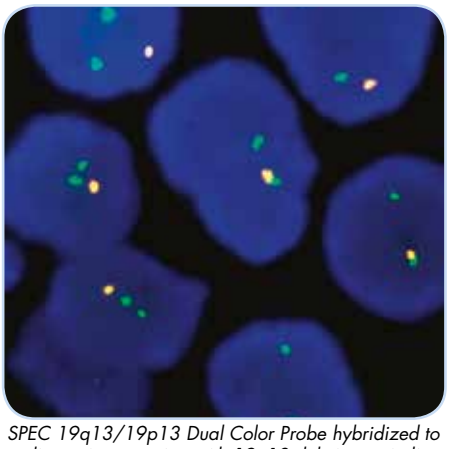
SPEC 19p13 Probe map (not to scale).



SPEC 19q13 Probe map (not to scale).

Results

Using the SPEC 19q13/19p13 Dual Color Probe in a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletions affecting the 19q13 locus, one or no copy of the orange signal will be observed.



SPEC 19q13/19p13 Dual Color Probe hybridized to a glioma tissue section with 19q13 deletion as indicated by one orange signal in each nucleus.

References

Barbashina V, et al. (2005) Clin Cancer Res 11: 1119-28.
Cairncross JG, et al. (1998) J Natl Cancer Inst 90: 1473-9.
Cairncross G, et al. (2013) J Clin Oncol 31: 337-43.
Caron H, et al. (1996) N Engl J Med 334: 225-30.
Griffin CA, et al. (2006) J Neuropathol Exp Neurol 65: 988-94.
Louis DN, et al. (ed.) (2016) WHO Classification of Tumours of the Central Nervous System (Revised 4th Edition).
Ragnarsson G, et al. (1999) Br J Cancer 79: 1468-74.
Reifenberger G, et al. (2017) Nat Rev Clin Oncol 14: 434-52.
Rosenberg JE, et al. (1996) Oncogene 13: 2483-5.
Smith JS, et al. (1999) Oncogene 18: 4144-52.
Smith JS, et al. (2000) Genes Chromosomes Cancer 29: 16-25.

Prod. No.	Product	Label	Tests* (Volume)
Z-2076-50	ZytoLight SPEC 19q13/19p13 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2076-200	ZytoLight SPEC 19q13/19p13 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2272-20	ZytoLight Glioma 1p/19q Probe Set CE IVD Incl. ZytoLight SPEC 1p36/1q25 Dual Color Probe, 0.2 ml; ZytoLight SPEC 19q13/19p13 Dual Color Probe, 0.2 ml; ZyBlack Quenching Solution, 8 ml		20
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC CKS1B/CDKN2C Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC CKS1B/CDKN2C Dual Color Probe is designed for the detection of gains/amplifications affecting the chromosomal region 1q21.3-q22 (CKS1B) and/or deletions of the chromosomal region 1p32.2 (CDKN2C).

Chromosome 1 abnormalities are among the most common cytogenetic findings in multiple myeloma (MM). This B-cell malignancy is characterized by slow proliferation of malignant plasma cells localized primarily in the bone marrow. Copy number alterations (CNA) occur frequently in this entity. The short arm of chromosome 1 is often affected by deletions whereas the long arm is mainly affected by gains/amplifications.

The CKS1B gene is located on the long arm of chromosome 1 at 1q21. Tandem duplications and jumping translocations of the 1q21 band are acquired during myeloma disease progression, and 1q amplifications have been linked to a poor prognosis in MM patients.

The CDKN2C gene maps to the chromosomal region 1p32.2 and belongs to the INK4 gene family that consists of tumor suppressor genes which play a role in the regulation of cell proliferation.

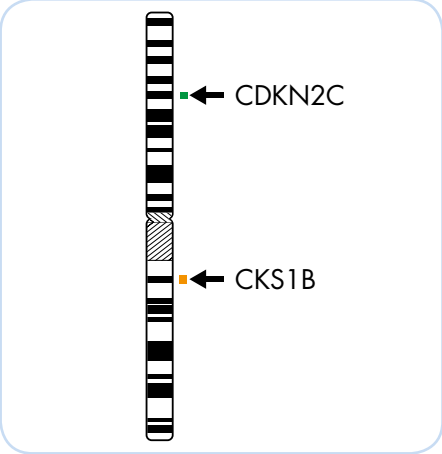
MM patients harboring a deletion of the CDKN2C gene region have a worse overall survival compared to those lacking this alteration.

Hence, Fluorescence *in situ* Hybridization may be a helpful tool for diagnosis and therapy decisions.

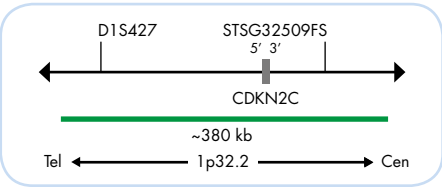
References
Chang H, et al. (2010) Bone Marrow Transplant 45: 117-21.
Kulkarni MS, et al. (2002) Leukemia 16: 127-34.
Shaughnessy J, et al. (2005) Hematology 10: 117-26.
Walker BA, et al. (2010) Blood 116: 56-65.
Zhan F, et al. (2007) Blood 109: 4995-5001.

Probe Description

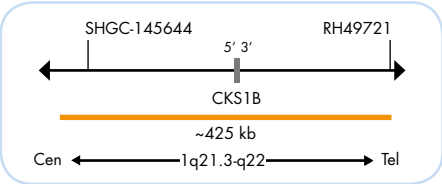
The SPEC CKS1B/CDKN2C Dual Color Probe is a mixture of an orange fluorochrome direct labeled SPEC CKS1B probe hybridizing to the chromosomal region 1q21.3-q22 and a green labeled SPEC CDKN2C probe hybridizing to the chromosomal region 1p32.2.



Ideogram of chromosome 1 indicating the hybridization locations.



SPEC CDKN2C Probe map (not to scale).



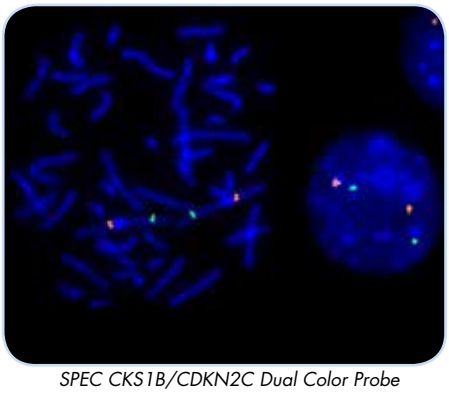
SPEC CKS1B Probe map (not to scale).

Results

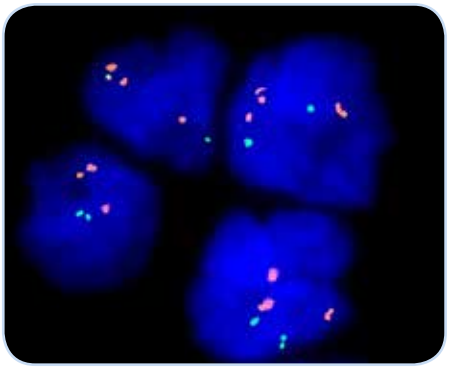
In a normal interphase nucleus, two orange and two green signals are expected.

In a cell with a gain/amplification of the CKS1B gene locus, multiple copies of the orange signal or orange signal clusters will be observed.

In a cell with deletion of the CDKN2C gene locus one or no copy of the green signal will be observed. Deletions affecting only parts of the CDKN2C locus might result in a normal signal pattern with green signals of reduced size.



SPEC CKS1B/CDKN2C Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals and to metaphase chromosomes of a normal cell.



Bone marrow smear of a pediatric ALL case with amplification affecting the CKS1B locus as indicated by three or more orange signals.

Material kindly provided by Paediatric Oncology/ Haematology, Charieté – Universitätsmedizin Berlin.

Prod. No.	Product	Label	Tests* (Volume)
Z-2276-50	ZytoLight SPEC CKS1B/CDKN2C Dual Color Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC MCL1/1p12 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC MCL1/1p12 Dual Color Probe is designed for the detection of MCL1 gene amplifications.

The MCL1 (MCL1, BCL2 family apoptosis regulator, a.k.a. BCL2L3) gene is located in the chromosomal region 1q21.3 and encodes for an anti-apoptotic protein that belongs to the BCL2 family. These genes are involved in a wide variety of cellular activities including lymphocyte development and hematopoiesis.

MCL1 amplifications have been reported in several human cancers including bladder, gastric, ovarian, lung, breast, melanoma, and hematologic malignancies.

Overexpression of MCL1 reduces MYC-induced apoptosis in immortalized bronchial epithelial cells.

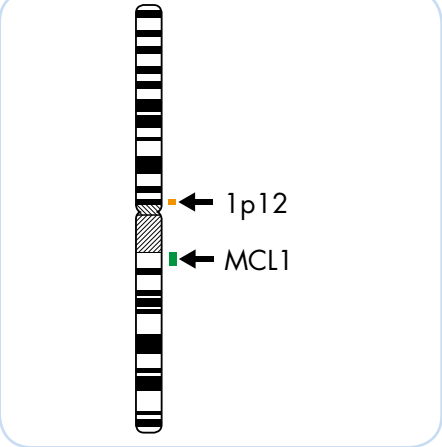
Furthermore, MCL1 amplifications are found in many tumor cell lines with resistance to chemotherapeutic agents. However, many MCL1 amplified cell lines are sensitive to treatment with the cyclin-dependent kinase (CDK) inhibitor dinaciclib. Targeting the BCL2 family proteins with small non-peptidic compounds, so called BH3-mimetics, is currently investigated in clinical trials.

Hence, the identification of MCL1 amplifications by Fluorescence *in situ* Hybridization and the inhibition of MCL1 signaling may be of therapeutic significance in various types of tumors.

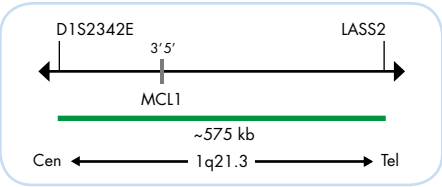
References
Beroukhim R, et al. (2010) Nature 463: 899-905.
Booher RN, et al. (2014) PloS One 9: e108371.
Sochalska M, et al. (2015) FEBS J 282: 834-49.
Yasui K, et al. (2004) Cancer Res 64: 1403-10.

Probe Description

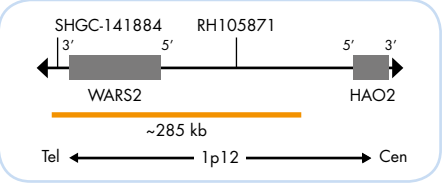
The SPEC MCL1/1p12 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC MCL1 probe hybridizing to the MCL1 gene in the chromosomal region 1q21.3 and an orange fluorochrome direct labeled SPEC 1p12 probe specific for the chromosomal region 1p12. Due to cross-hybridizations of chromosome 1 alpha satellites to other centromeric regions, probes specific for 1p12 are frequently used for chromosome 1 copy number detection.



Ideogram of chromosome 1 indicating the hybridization locations.



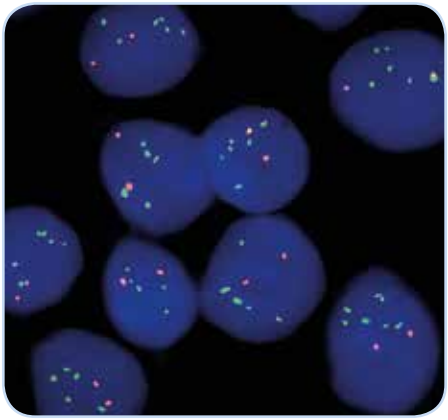
SPEC MCL1 Probe map (not to scale).



SPEC 1p12 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the MCL1 gene locus, multiple copies of the green signal or green signal clusters will be observed.



H2110 cell line with interphase cells showing amplification of the MCL1 gene locus as indicated by multiple green signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2173-200	ZytoLight SPEC MCL1/1p12 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC MEF2D/BCL9 TriCheck™ Probe

CE IVD

Background

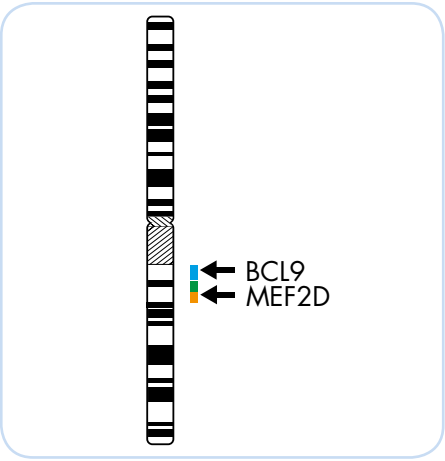
The ZytoLight® SPEC MEF2D/BCL9 TriCheck™ Probe is designed to detect inversions involving the chromosomal region 1q21.2 harboring the BCL9 gene and the chromosomal region 1q22 harboring the MEF2D gene. Moreover, using this probe it is possible to discriminate between MEF2D-BCL9 inversions and MEF2D translocations not affecting BCL9.

Rearrangements of the myocyte enhancer factor 2D (MEF2D) have been frequently found in acute lymphoblastic leukemia (ALL). Recurring rearrangements have been found in 3-4% of pediatric and up to 7% of adult ALL patients, respectively. In B-progenitor ALL cases the most common translocation partner of MEF2D is BCL9. Other known translocation partners are CSF1R (5q32), DAZAP1 (19p13.3), HNRNPUL1 (19q13.2), SS18 (18q11.2), and FOXJ2 (12p13.31). ALL cases harboring MEF2D rearrangements are often associated with copy number alterations of the aberrant locus and display an increased sensitivity to histone deacetylase inhibitor (HDAC) treatment. MEF2D gene translocation derived ALL cases show a markedly high expression of HDAC9 inducing resistance to conventional chemotherapy and in case of MEF2D-BCL9 gene fusion also a resistance to dexamethasone treatment. MEF2D-rearranged ALL represents a distinct form of high-risk leukemia; consequently MEF2D-BCL9 fusion detection by Fluorescence *in situ* Hybridization (FISH) might be of diagnostic and therapeutic relevance.

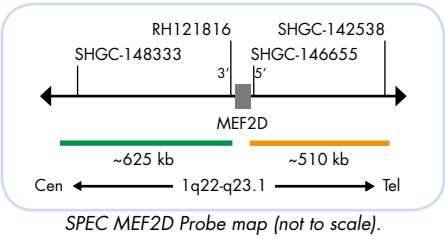
References
Gu Z, et al. (2016) Nat Commun 7: 13331.
Liu YF, et al. (2016) EBioMedicine 8: 173-83.
Suzuki K, et al. (2016) J Clin Oncol 34: 3451-9.

Probe Description

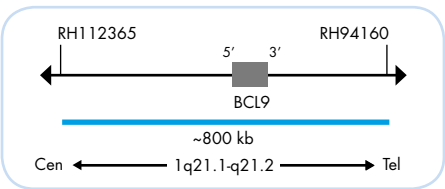
The SPEC MEF2D/BCL9 TriCheck™ Probe is a mixture of three direct labeled probes hybridizing to the long arm of chromosome 1. The green fluorochrome direct labeled probe hybridizes proximal to the MEF2D gene breakpoint region at 1q22, the orange fluorochrome direct labeled probe hybridizes distal to the MEF2D gene breakpoint region at 1q22-q23.1, and the blue fluorochrome direct labeled probe hybridizes to the BCL9 gene region at 1q21.1-q21.2.



Ideogram of chromosome 1 indicating the hybridization locations.



SPEC MEF2D Probe map (not to scale).



SPEC BCL9 Probe map (not to scale).

Results

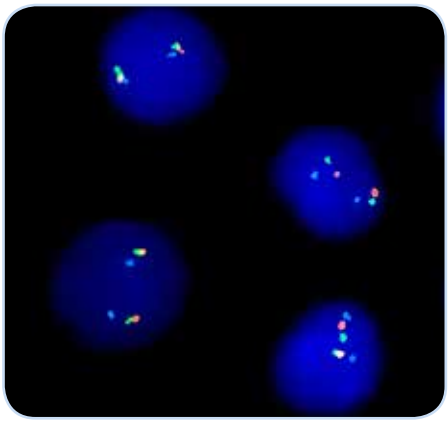
In an interphase nucleus without rearrangement of the MEF2D/BCL9 locus, two green/orange fusion signals and two blue signals are expected.

A MEF2D-BCL9 inversion is indicated by one separate green signal, one separate orange signal, and an additional blue signal.

A MEF2D translocation, without BCL9 involvement, is indicated by one separate green signal and one separate orange signal, without an additional blue signal.

Gain of the aberrant region may be observed and is indicated by multiple copies of the respective signal pattern.

Signal patterns other than those described above may indicate deviant rearrangements.



SPEC MEF2D/BCL9 TriCheck™ Probe on normal interphase cells with non-rearranged MEF2D loci (two green/orange fusion signals), and non-rearranged BCL9 loci (two blue signals).

Prod. No.	Product	Label	Tests* (Volume)
Z-2277-50	ZytoLight SPEC MEF2D/BCL9 TriCheck Probe CE IVD	●/●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC NTRK1 Dual Color Break Apart Probe

CE IVD

Background

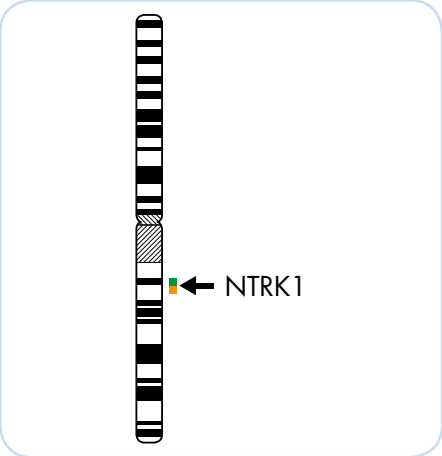
The ZytoLight® SPEC NTRK1 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 1q23.1 harboring the NTRK1 (neurotrophic receptor tyrosine kinase 1, a.k.a. TRKA or TRK) gene.

NTRK1 encodes a tyrosine kinase (TK) receptor for the nerve growth factor (NGF). The NTRK1 gene was found to be rearranged in about 12% of papillary thyroid carcinoma (PTC) cases. PTC accounts for about 80% of all thyroid cancers. NTRK1 rearrangements result in the fusion of the 3' end of the NTRK1 gene with the 5' end of different activating genes (TPM3, TPR, or TFG). All these fusion genes encode hybrid proteins comprising the TK domain of NTRK1 and the N-terminus of the partner proteins carrying coiled-coil domains. NTRK1 rearrangements were shown to be involved in thyroid carcinogenesis. Several studies showed that NTRK1 rearrangements may be associated with a worse clinical course when compared with NTRK1 rearrangement-negative PTCs. Recently, NTRK1 rearrangements were also found in lung adenocarcinomas. Various inhibitors targeting the NTRK1-derived fusion proteins were shown *in vitro* to inhibit proliferation of cells expressing the fusion genes. This indicates that these fusion genes are potential therapeutic targets.

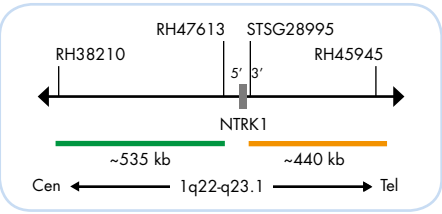
Hence, detection of NTRK1 rearrangements by Fluorescence *in situ* Hybridization represents a useful tool for studying thyroid carcinogenesis and may be of prognostic and therapeutic significance.

Probe Description

The SPEC NTRK1 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 1q22-q23.1 band. The green fluorochrome direct labeled probe hybridizes proximal and the orange fluorochrome direct labeled probe hybridizes distal to the NTRK1 gene.



Ideogram of chromosome 1 indicating the hybridization locations.

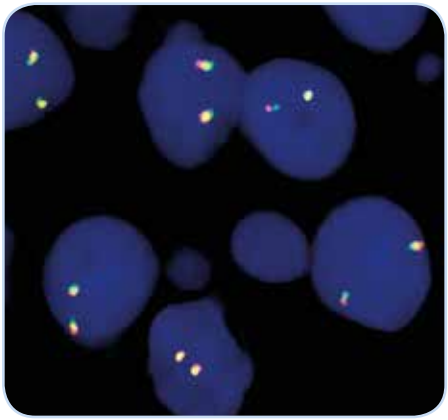


SPEC NTRK1 Probe map (not to scale).

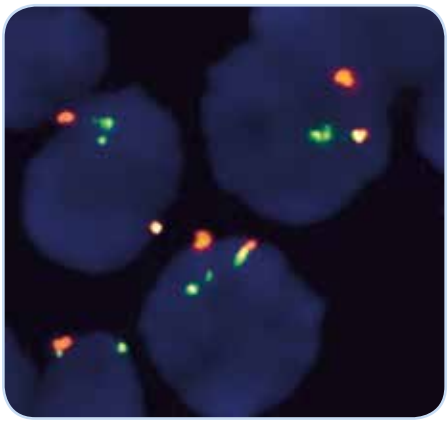
References
Alberti L, et al. (2003) J Cell Physiol 195: 168-86.
Bongarzone I, et al. (1998) Clin Cancer Res 4: 223-8.
Doebele RC, et al. (2013) J Clin Oncol 31 Suppl: Abstr. 8023.
Greco A, et al. (2010) Mol Cell Endocrinol 321: 44-9.
Musholt TJ (2000) Surgery 128: 984-93.
Russell JP, et al. (2000) Oncogene 19: 5729-35.

Results

In an interphase nucleus lacking a translocation involving the 1q22-q23.1 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 1q22-q23.1 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 1q22-q23.1 locus and one 1q22-q23.1 locus affected by a translocation.



SPEC NTRK1 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Lung cancer tissue section with translocation of the NTRK1 gene as indicated by one non-rearranged orange/green fusion signal, one orange and one separate green signal.

Image kindly provided by Prof. Büttner, Cologne, Germany.

Prod. No.	Product	Label	Tests* (Volume)
Z-2167-50	ZytoLight SPEC NTRK1 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2167-200	ZytoLight SPEC NTRK1 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ABL2 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC ABL2 Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal region 1q25.2 harboring the ABL2 (ABL proto-oncogene 2, non-receptor tyrosine kinase, a.k.a. ARG) gene.

The ABL2 gene encodes for a non-receptor tyrosine kinase (TK) with high homology to ABL1. ABL1 and ABL2 proteins belong to the Abelson family and link diverse extracellular stimuli to signaling pathways controlling cell growth, survival, invasion, and migration.

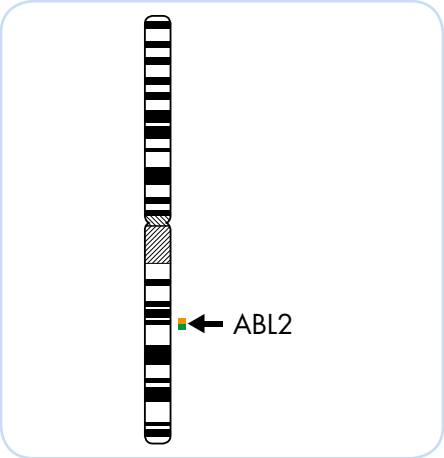
The translocation t(1;12)(q25.2;p13.2) involving ABL2 was shown to result in a chimeric protein consisting of the helix-loop-helix (HLH) domain of ETV6 and the TK domain of ABL2. The HLH domain of ETV6 is known to confer oncogenic activity to chimeric tyrosine kinase proteins by forming ligand-independent oligomers. The ETV6-ABL2 fusion gene has been detected in a patient with AML-M3 and in a T-cell ALL cell line.

Further ABL2 fusion partners have been identified in patients with Philadelphia chromosome-like ALL, including PAG1, RCSD1, and ZC3HAV1. Cell lines expressing ABL2 fusions were shown to respond to tyrosine kinase inhibitors. Moreover, a patient with B-ALL positive for RCSD1-ABL2 fusion was reported to respond to treatment with the ABL1 inhibitor imatinib. Hence, detection of ABL2 rearrangements by FISH may help in selecting patients eligible for therapy with TK inhibitors.

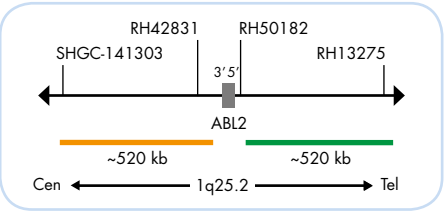
References
Cazzaniga G, et al. (1999) Blood 94: 4370-3.
De Braekeleer E, et al. (2012) Leuk Res 36: 945-61.
Greuber EK, et al. (2013) Nat Rev Cancer 13: 559-71.
Roberts KG, et al. (2014) N Engl J Med 371: 1005-15.

Probe Description

The SPEC ABL2 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 1q25.2 band. The orange fluorochrome direct labeled probe hybridizes proximal to the ABL2 gene at 1q25.2, the green fluorochrome direct labeled probe hybridizes distal to the ABL2 gene at 1q25.2



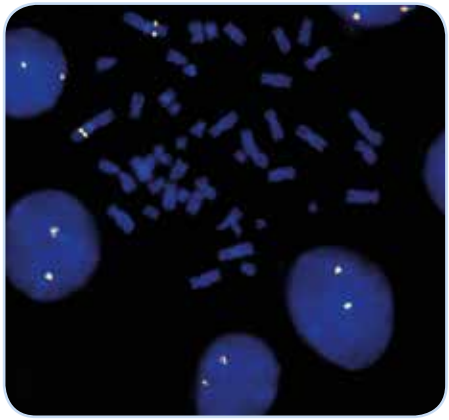
Ideogram of chromosome 1 indicating the hybridization locations.



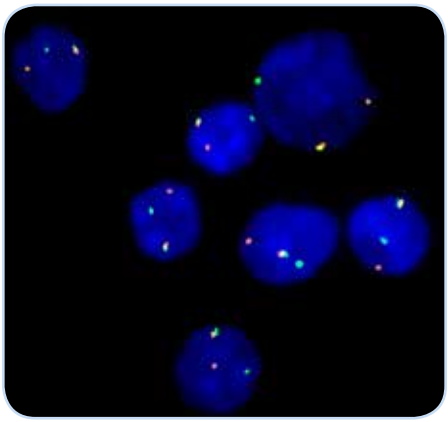
SPEC ABL2 Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 1q25.2 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 1q25.2 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 1q25.2 locus and one 1q25.2 locus affected by a translocation.



SPEC ABL2 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus and to metaphase chromosomes of a normal cell.



Blood smear with translocation of the ABL2 gene as indicated by one non-rearranged orange/green fusion signal, one orange and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2200-50	ZytoLight SPEC ABL2 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC MDM4/1p12 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC MDM4/1p12 Dual Color Probe is designed for the detection of MDM4 gene amplifications found in 10-20% of various tumors such as lung, colon, stomach, and breast cancers, as well as in 65% of retinoblastomas.

The MDM4 (MDM4, p53 regulator) gene (a.k.a. HDMX or MDMX) is located in the chromosomal region 1q32.1 and encodes a 490-amino acid protein which shows significant structural similarity to the p53-binding protein MDM2.

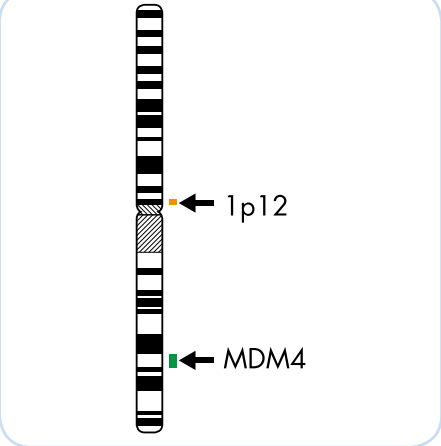
Like MDM2, the oncogene MDM4 can bind to p53 thereby inactivating the function of p53 as a transcriptional activator. In addition, MDM4 has been shown to bind to MDM2 resulting in inhibition of MDM2 degradation.

Antitumor strategies employing combined inhibitors of the two oncogenic proteins MDM2 and MDM4 may lead to an effective activation of the tumor suppressor p53.

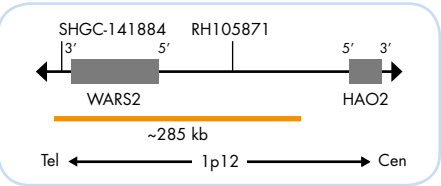
References
Duhamel LA, et al. (2012) Histopathology 60: 357-9.
Laurie NA, et al. (2006) Nature 444: 61-6.
Shvarts A, et al. (1996) EMBO J 15: 5349-57.
Shvarts A, et al. (1997) Genomics 43: 34-42.
Tanimura S et al. (1999) FEBS Lett 447: 5-9.
Toledo F & Wahl GM (2006) Nat Rev Cancer 6: 909-23.
Toledo F & Wahl GM (2007) Int J Biochem Cell Biol 39: 1476-82.

Probe Description

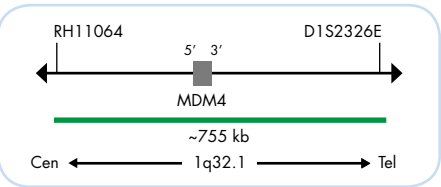
The SPEC MDM4/1p12 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC MDM4 probe hybridizing distal and proximal to the human MDM4 gene in the chromosomal region 1q32.1 and an orange fluorochrome direct labeled SPEC 1p12 probe hybridizing in close proximity to the centromere of chromosome 1 at the chromosomal region 1p12. Due to cross-hybridizations of chromosome 1 alpha satellites to other centromeric regions, probes specific for 1p12 are frequently used for chromosome 1 copy number detection.



Ideogram of chromosome 1 indicating the hybridization locations.



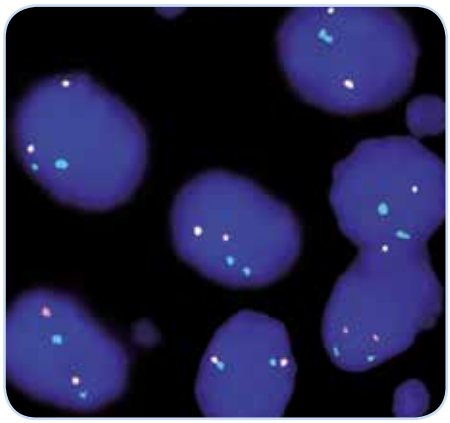
SPEC 1p12 Probe map (not to scale).



SPEC MDM4 Probe map (not to scale).

Results

In a normal interphase nucleus two orange and two green signals are expected. Nuclei with amplification of the MDM4 gene locus or aneuploidy of chromosome 1 will show multiple copies of the green signal or large green signal clusters.



SPEC MDM4/1p12 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2080-200	ZytoLight SPEC MDM4/1p12 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC MYCN/2q11 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC MYCN/2q11 Dual Color Probe is designed for the detection of MYCN amplification which represents the most powerful unfavorable prognostic factor for neuroblastoma. Less frequently amplifications are found in retinoblastoma, small cell lung cancer, astrocytoma and other tumors derived from the neuroectoderm.

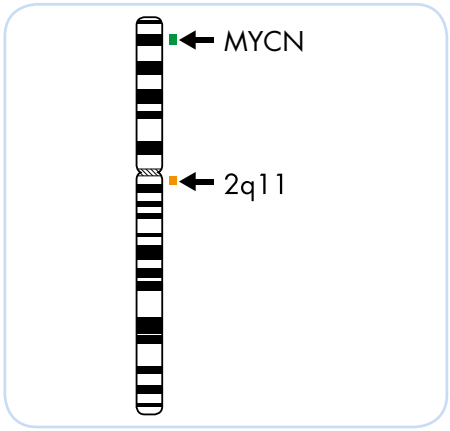
The MYCN (MYCN proto-oncogene, bHLH transcription factor, a.k.a. NMYC) gene is located in the chromosomal region 2p24.3 and encodes a 62-64 kDa transcription factor mainly expressed in the developing nervous system.

Amplification of the MYCN gene is found in about 25% of primary neuroblastomas and is strongly associated with rapid tumor progression, advanced stages of the disease, and poor prognosis. Hence, amplification status is increasingly being used for stratification of patients to different treatment protocols.

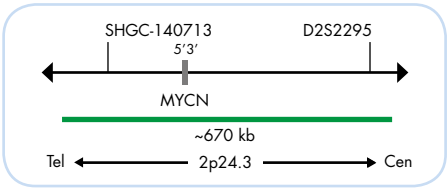
References
Gessi M, et al. (2014) Neuro Oncol 16: 924-32.
Kaneko M, et al. (1998) Med Pediatr Oncol 31: 1-7.
Lee WH, et al. (1984) Nature 309: 458-60.
Slamon DJ, et al. (1986) Science 232: 768-72.
Suita S, et al. (2007) J Pediatr Surg 42: 489-93.

Probe Description

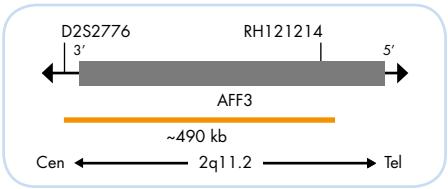
The SPEC MYCN/2q11 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC MYCN probe hybridizing to the human MYCN gene in the chromosomal region 2p24.3 and an orange fluorochrome direct labeled SPEC 2q11 probe specific for the AFF3 (AF4/FMR2 family, member 3) gene region in 2q11.2. Due to cross-hybridizations of chromosome 2 alpha satellites to other centromeric regions, probes specific for 2q11 are frequently used for chromosome 2 copy number detection.



Ideogram of chromosome 2 indicating the hybridization locations.



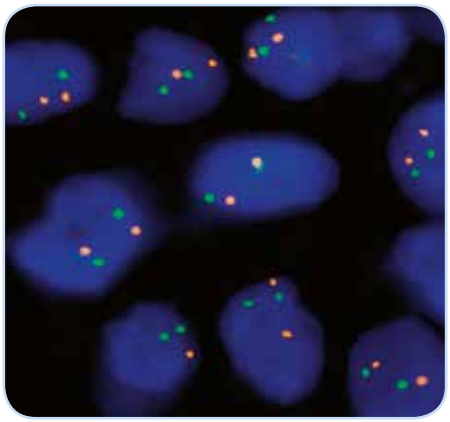
SPEC MYCN Probe map (not to scale).



SPEC 2q11 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the MYCN gene locus, multiple copies of the green signal or green signal clusters will be observed.



SPEC MYCN/2q11 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2074-50	ZytoLight SPEC MYCN/2q11 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2074-200	ZytoLight SPEC MYCN/2q11 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ALK/EML4 TriCheck™ Probe

CE IVD

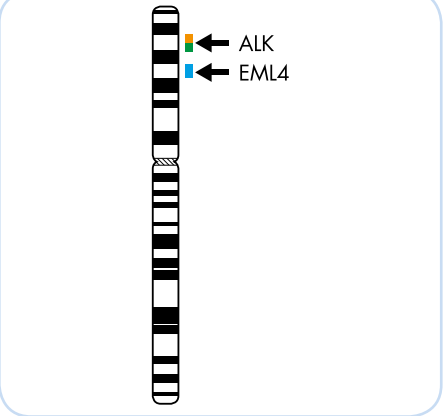
Background

The ZytoLight® SPEC ALK/EML4 TriCheck™ Probe is designed to detect inversions involving the chromosomal region 2p23.1-p23.2 harboring the ALK gene and the chromosomal region 2p21 harboring the EML4 gene. Moreover, using this probe it is possible to discriminate between EML4-ALK inversions and translocations affecting ALK, but not EML4, such as ALK-TFG or ALK-KIF5B translocations.
Inversions in the short arm of chromosome 2 [inv(2)(p21p23)] have been frequently detected in non-small cell lung cancer (NSCLC) and lead to the formation of EML4-ALK fusion transcripts. A few reports also identified EML4-ALK fusion transcripts in breast, gastric, and colorectal cancers. Many different breakpoints affecting ALK and EML4 were identified in these respective inversions.
Thus, multiple EML4-ALK transcript variants have been identified, all of which involve the intracellular kinase domain of ALK. ALK kinase targeted therapies may represent a very effective therapeutic strategy in NSCLC patients carrying EML4-ALK rearrangements. For the detection of this subset of NSCLC patients, the specific detection of EML4-ALK rearrangements using Fluorescence *in situ* Hybridization is a helpful tool for diagnosis and for selecting treatment.

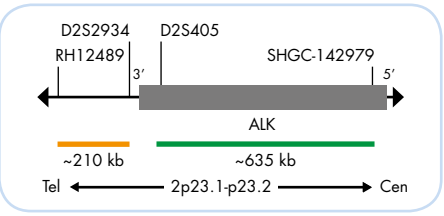
References
Inamura K, et al. (2009) Mod Pathol 22: 508-15.
Koivunen JP, et al. (2008) Clin Cancer Res 14: 4275-83.
Lawce HJ & Olson S (2013) J Assoc Genet Technol 39: 66-71.
Martelli MP, et al. (2009) Am J Pathol 174: 661-70.
Perner S, et al. (2008) Neoplasia 10: 298-302.
Preusser M, et al. (2013) Lung Cancer 80: 278-83.
Rodig SJ, et al. (2009) Clin Cancer Res 15: 5216-23.
Sasaki T, et al. (2010) Eur J Cancer 46: 1773-80.
Schildgen V, et al. (2012) Per Med 9: 801-3.
Schildhaus HU, et al. (2013) Mod Pathol 26: 1468-77.
Schoppmann SF, et al. (2013) Eur J Cancer 49: 1876-81.
Thunnissen E, et al. (2012) Virchows Arch 461: 245-57.
Von Laffert M, et al. (2013) Lung Cancer 81: 200-6.

Probe Description

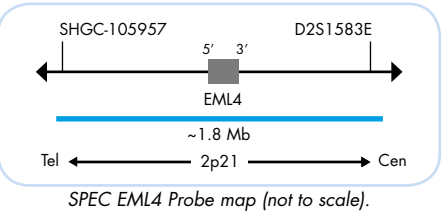
The SPEC ALK/EML4 TriCheck™ Probe is a mixture of three direct labeled probes hybridizing to the short arm of chromosome 2. The orange fluorochrome direct labeled probe hybridizes distal to the ALK gene breakpoint region at 2p23.2, the green fluorochrome direct labeled probe hybridizes proximal to the ALK gene breakpoint region at 2p23.1-p23.2, and the blue fluorochrome direct labeled probe hybridizes to the EML4 gene region at 2p21.



Ideogram of chromosome 2 indicating the hybridization locations.



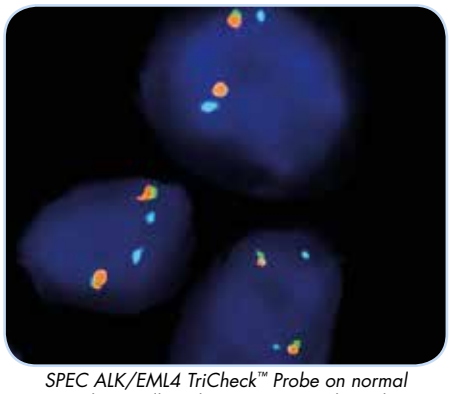
SPEC ALK Probe map (not to scale).



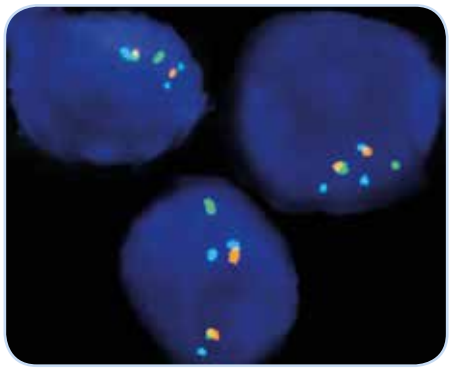
SPEC EML4 Probe map (not to scale).

Results

In an interphase nucleus without rearrangement of the EML4-ALK locus, two orange/green fusion signals and two blue signals are expected.
An EML4-ALK inversion is indicated by one separate green signal, one separate orange signal, and an additional blue signal.
An ALK translocation is indicated by separated orange and green signals without an additional blue signal.
EML4-ALK inversion with deletion of 5′-ALK sequences is indicated by loss of one green signal and co-localization of the isolated orange signal with a blue signal.



SPEC ALK/EML4 TriCheck™ Probe on normal interphase cells with non-rearranged ALK loci (two orange/green fusion signals), and non-rearranged EML4 loci (two blue signals).



NSCLC tissue section with an EML4-ALK inversion as indicated by one green, one separated orange, and one additional blue signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2117-50	ZytoLight SPEC ALK/EML4 TriCheck Probe CE IVD	●/●/●	5 (50 µl)
Z-2117-200	ZytoLight SPEC ALK/EML4 TriCheck Probe CE IVD	●/●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ALK Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC ALK Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal region 2p23.1-p23.2 harboring the ALK (ALK receptor tyrosine kinase, a.k.a. CD246) gene.

ALK encodes a transmembrane receptor tyrosine kinase. This gene exerts characteristic oncogenic activities through fusion to several gene partners or mutations both in hematopoietic and non-hematopoietic solid tumors.

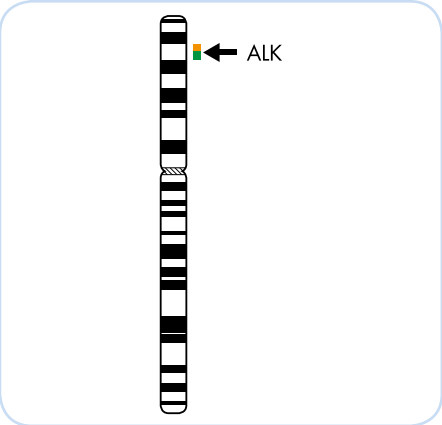
Translocations affecting the ALK gene locus are frequently found in anaplastic large cell lymphoma (ALCL), an aggressive non-Hodgkin lymphoma arising from T-cells. The most frequent translocation t(2;5) results in a fusion with the NPM1 (nucleophosmin a.k.a. nucleolar phosphoprotein B23, numatrin) gene located on chromosome 5q35. This rearrangement results in a NPM1/ALK fusion protein, which is constitutively activated through autophosphorylation, and that in turn mediates malignant cell transformation by activating downstream effectors like e.g. STAT3.

Additionally, inversions affecting the ALK gene located on the short arm of chromosome 2 [inv(2)(p21p23)] have been frequently detected in non-small cell lung cancer (NSCLC) and lead to the formation of EML4-ALK fusion transcripts.

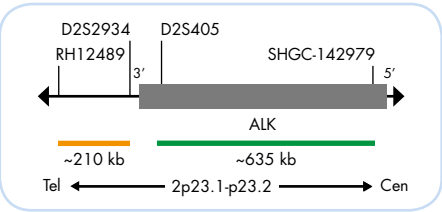
ALK kinase targeted therapies may represent a very effective therapeutic strategy in NSCLC patients carrying EML4-ALK rearrangements.

Probe Description

The SPEC ALK Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 2p23.1-p23.2 band. The orange fluorochrome direct labeled probe hybridizes distal to the ALK gene breakpoint region at 2p23.2, the green fluorochrome direct labeled probe hybridizes proximal to the ALK gene breakpoint region at 2p23.1-p23.2.



Ideogram of chromosome 2 indicating the hybridization locations.

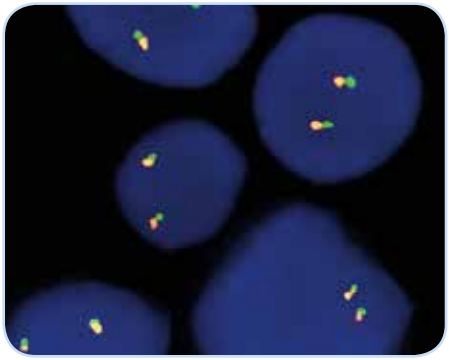


SPEC ALK Probe map (not to scale).

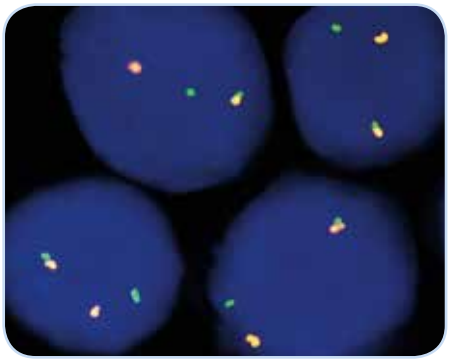
References
Inamura K, et al. (2009) Mod Pathol 22: 508-15.
Koivunen JP, et al. (2008) Clin Cancer Res 14: 4275-83.
Martelli MP, et al. (2009) Am J Pathol 174: 661-70.
Palmer RH, et al. (2009) Biochem J 420: 345-61.
Perner S, et al. (2008) Neoplasia 10: 298-302.
Rodig SJ, et al. (2009) Clin Cancer Res 15: 5216-23.
Sasaki T, et al. (2010) Eur J Cancer 46: 1773-80.
Von Laffert M, et al. (2013) Lung Cancer 81: 200-6.
Zhang Q, et al. (2007) Nat Med 11: 1341-8.

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 2p23.1-p23.2 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 2p23.1-p23.2 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 2p23.1-p23.2 locus and one 2p23.1-p23.2 locus affected by a translocation or inversion. EML4-ALK inversion with deletion of 5′-ALK sequences is indicated by one or multiple isolated orange signals.



SPEC ALK Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Lung carcinoma tissue section with translocation affecting the 2p23 locus as indicated by one orange/green fusion (non-rearranged) signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2124-50	ZytoLight SPEC ALK Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2124-200	ZytoLight SPEC ALK Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ALK/2q11 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC ALK/2q11 Dual Color Probe is designed for the detection of amplifications of the chromosomal region harboring the ALK gene.

The ALK (ALK receptor tyrosine kinase, a.k.a. CD246) gene is located on chromosome 2p23.1-p23.2 and encodes a transmembrane receptor tyrosine kinase. ALK was originally identified as a fusion partner of NPM1. This gene fusion is frequently found in anaplastic large cell lymphoma (ALCL), an aggressive non-Hodgkin lymphoma. Rearrangements affecting the ALK gene locus have also been found to play a role in carcinogenesis of a variety of hematopoietic and non-hematopoietic solid tumors, including non-small cell lung cancer (NSCLC).

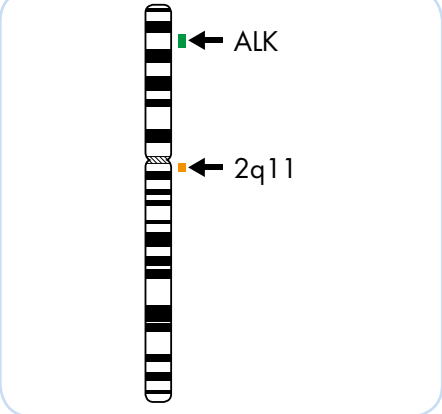
Moreover, ALK amplifications and copy number gains have been reported to occur in a variety of tumors including NSCLC and alveolar rhabdomyosarcoma (ARMS). In colorectal cancer, ALK amplification was correlated with nodal status suggesting that ALK amplified tumors have a more aggressive phenotype. ALK copy number gains and amplifications are also a frequent genetic event in the tumorigenesis of neuroblastomas and were found to result in high ALK expression correlating with an unfavorable neuroblastoma phenotype. Hence, the identification of ALK gene copy number changes by *in situ* Hybridization might be of prognostic and therapeutic relevance.

References

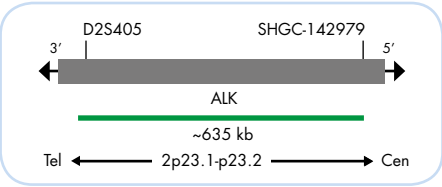
Carén H, et al. (2008) Biochem J 416: 153-9.
Corao DA, et al. (2009) Pediatr Dev Pathol 12: 275-83.
Koivunen JP, et al. (2008) Clin Cancer Res 14: 4275-83.
Montagut C, et al. (2010) J Clin Oncol 28: Suppl 10537.
Pelosi G, et al. (2012) Lung Cancer 77: 507-14.
Salido M, et al. (2011) J Thorac Oncol 6: 21-7.
Subramaniam MM, et al. (2009) Hum Pathol 40: 1638-42.

Probe Description

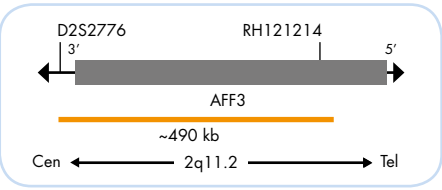
The SPEC ALK/2q11 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC ALK probe hybridizing to the human ALK gene in the chromosomal region 2p23.1-p23.2 and an orange fluorochrome direct labeled SPEC 2q11 probe. The SPEC 2q11 probe is specific for the AFF3 (AF4/FMR2 family, member 3) gene region in 2q11.2. Due to cross-hybridizations of chromosome 2 alpha satellites to other centromeric regions, probes specific for 2q11 are frequently used for chromosome 2 copy number detection.



Ideogram of chromosome 2 indicating the hybridization locations.



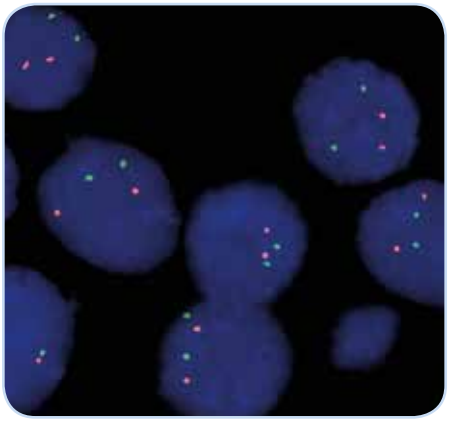
SPEC ALK Probe map (not to scale).



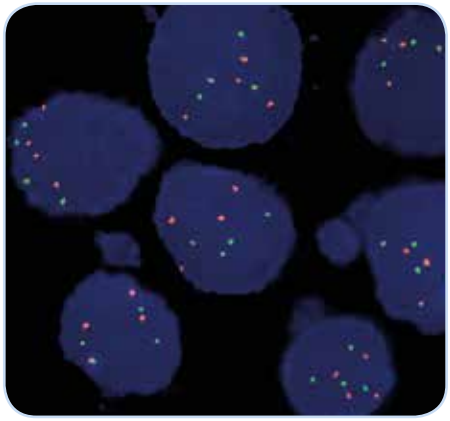
SPEC 2q11 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the ALK gene locus, multiple copies of the green signal or green signal clusters will be observed.



SPEC ALK/2q11 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Neuroblastoma tissue section with tetrasomy of chromosome 2 as indicated by four orange (2q11) and four green (ALK) signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2161-200	ZytoLight SPEC ALK/2q11 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC EML4 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC EML4 Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal region 2p21 harboring the EML4 (echinoderm microtubule-associated protein-like 4, a.k.a. ROPP120) gene.

Inversions in the short arm of chromosome 2 [inv(2)(p21p23)] have been frequently detected in non-small cell lung cancer (NSCLC) and lead to the formation of EML4-ALK fusion transcripts. A few reports also identified these fusion transcripts in breast, gastric, and colorectal cancers.

The fusion genes comprise variably truncated N-terminal portions of the EML4 gene and the intracellular signaling domain of the ALK receptor tyrosine kinase (a.k.a. CD246). It was found that EML4 mediates ligand-independent dimerization of ALK, resulting in constitutive kinase activity. EML4-ALK was shown to possess transforming activity *in vitro* and *in vivo*.

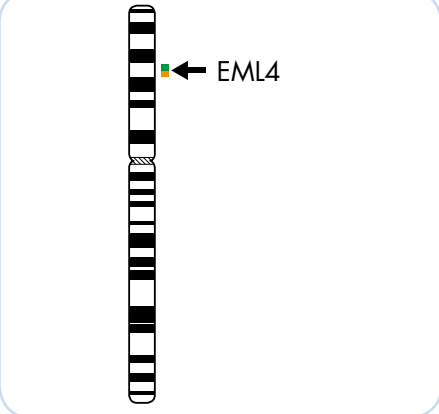
The EML4-ALK fusion transcript is found in about 5% of NSCLC, predominantly adenocarcinomas, and is considered to be mutually exclusive to EGFR or KRAS mutations. The detection of the inversion by Fluorescence *in situ* Hybridization might represent a valuable tool to identify a subpopulation of NSCLC likely to respond to ALK kinase targeting therapies.

The SPEC EML4 Dual Color Break Apart Probe can be used to subsequently confirm EML4-ALK inversion if an ALK Break Apart Probe has been used for initial diagnosis.

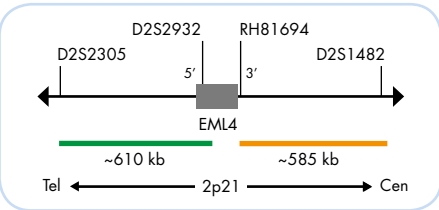
References
Choi YL, et al. (2008) Cancer Res 69: 4971-6.
Inamura K, et al. (2009) Mod Pathol 22: 508-15.
Lin E, et al. (2009) Mol Cancer Res 7: 1466-76.
Perner S, et al. (2008) Neoplasia 10: 298-302.
Rodig SJ, et al. (2009) Clin Cancer Res 15: 5216-23.
Soda M, et al. (2007) Nature 448: 561-6.
Shaw AT, et al. (2009) J Clin Oncol 27: 4247-53.

Probe Description

The SPEC EML4 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 2p21 band. The orange fluorochrome direct labeled probe hybridizes proximal, the green fluorochrome direct labeled probe hybridizes distal to the EML4 gene breakpoint region at 2p21.



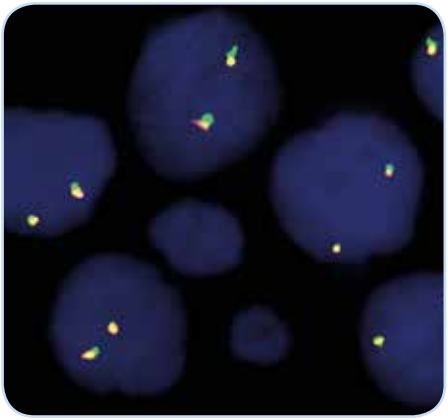
Ideogram of chromosome 2 indicating the hybridization locations.



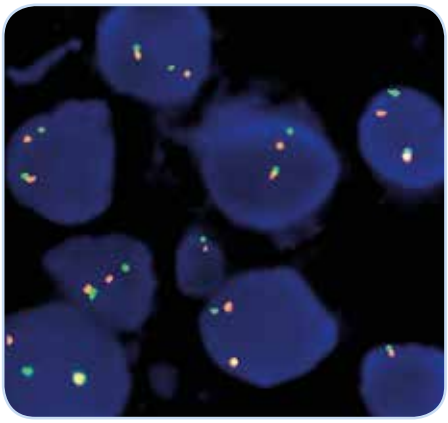
SPEC EML4 Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking an inversion involving the 2p21 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 2p21 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 2p21 locus and one 2p21 locus affected by an inversion or translocation.



SPEC EML4 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



NSCLC tissue section with inversion affecting the EML4 locus at 2p21 as indicated by one orange/green fusion (non-rearranged) signal, one green signal, and one separate orange signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2136-50	ZytoLight SPEC EML4 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC IGK Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC IGK Dual Color Break Apart Probe is designed to detect rearrangements affecting the chromosomal region 2p11.2 harboring the IGK (immunoglobulin kappa locus, a.k.a. IGK@, IGκ) gene cluster region.

Translocations involving the immunoglobulin (IG) genes are recurring events of B-cell oncogenesis. In all of these translocations, an oncogene is activated and overexpressed by juxtaposing this oncogene to IG regulatory sequences.

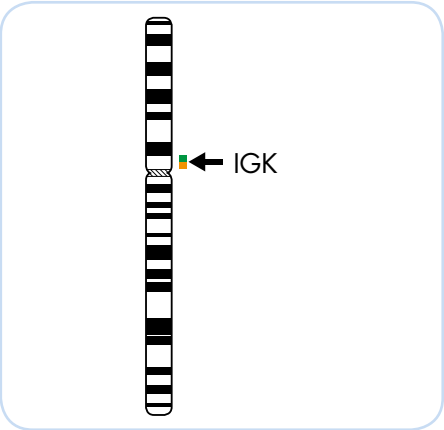
Burkitt lymphoma (BL) is characterized by reciprocal translocations involving the MYC gene and one of the IG loci. The majority of translocations involve the immunoglobulin heavy chain (IGH) locus while a minor part involves the immunoglobulin light chain loci, either the kappa light chain (IGK) or the lambda light chain (IGL). IGK and IGL rearrangements resulting from the variant translocations t(2;8)(p11.2;q24.21) and t(8;22)(q24.21;q11.2), respectively, have been detected in up to 25% of BL cases.

In non-Hodgkin lymphoma (NHL) harboring IG-MYC rearrangements, the MYC translocation partner is IGK and IGL in 8 and 22% of the cases, respectively.

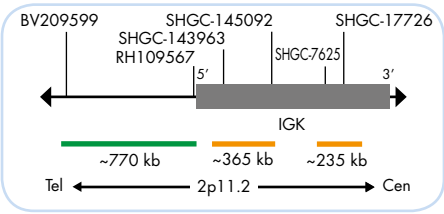
IG translocations have been reported in several B-cell lineage malignancies other than BL including atypical Burkitt/Burkitt-like lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, mantle cell lymphoma, and multiple myeloma. Other rearrangement events involve the IGK and IGL gene with the BCL2 and BCL6 oncogenes as translocation partners. The detection of IGK and IGL involvement in lymphomas by Fluorescence *in situ* Hybridization may prove a valuable diagnostic and prognostic tool.

Probe Description

The SPEC IGK Dual Color Break Apart Probe is a mixture of a green fluorochrome direct labeled probe hybridizing distal to the IGK breakpoint region at 2p11.2 and an orange fluorochrome direct labeled probe hybridizing proximal to the IGK breakpoint region. Due to homologous sequence segments proximal to the IGK breakpoint region, the orange probe has two hybridization regions in close proximity.



Ideogram of chromosome 2 indicating the hybridization locations.

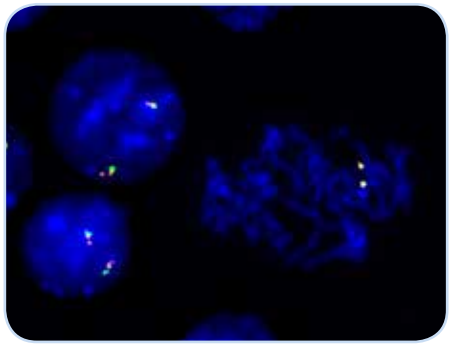


IGK Probe map (not to scale).

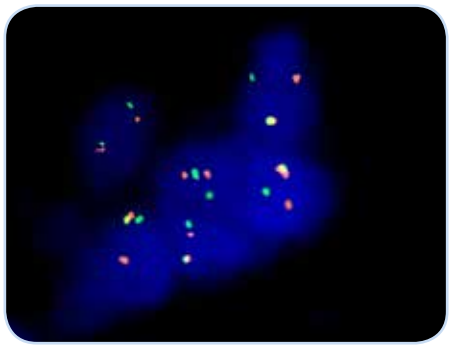
References
Cario G, et al. (2000) Br J Haematol 110: 537-46.
Einerson RR, et al. (2006) Leukemia 20: 1790-9.
Henglein B, et al. (1989) Mol Cell Biol 9: 2105-13.
Martín-Subero JI, et al. (2002) Int J Cancer 98: 470-4.
Poulsen TS, et al. (2002) Leukemia 16: 2148-55.

Results

In an interphase nucleus lacking a translocation involving the IGK locus at 2p11.2, two orange/green fusion signals are expected. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal IGK locus and one IGK locus affected by a translocation. Due to the two hybridization regions of the orange probe, orange signals may appear as paired signal dots.



SPEC IGK Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals in each nucleus and to metaphase chromosomes of a normal cell. Orange signals may appear as paired signal dots.



Burkitt lymphoma with an IGK translocation affecting the 2p11.2 locus as indicated by one non-rearranged orange/green fusion signal, one orange signal (may appear as paired signal dots), and one separate green signal.

Specimen kindly provided by Dr. Brändle, Vienna, Austria.

Prod. No.	Product	Label	Tests* (Volume)
Z-2288-50	ZytoLight SPEC IGK Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ERBB4/2q11 Dual Color Probe

CE IVD

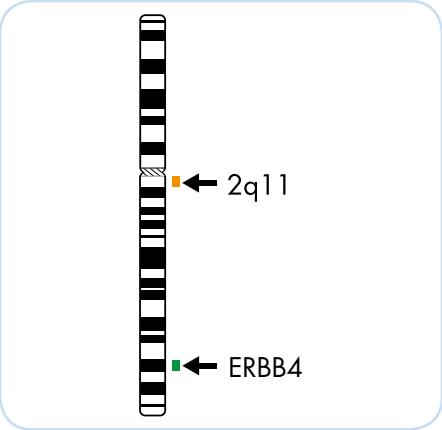
Background

The ZytoLight® SPEC ERBB4/2q11 Dual Color Probe is designed for the detection of amplifications of the chromosomal regions harboring the ERBB4 gene.
The ERBB4 (a.k.a. HER4) gene encodes a transmembrane glycoprotein acting as a cellular growth factor receptor. It belongs to the epidermal growth factor receptor subgroup of the receptor tyrosine kinase superfamily also including ERBB1 (EGFR), ERBB2, which is known to be affected by gene amplifications in a number of malignant tumors, and ERBB3.
Although EGFR and ERBB2 have been shown to represent good predictive markers and appropriate targets for therapeutic approaches, relatively less is known of comparable significance for ERBB3 and ERBB4. However, there is growing evidence that cooperation of all four members of the ERBB gene family contributes to a more aggressive tumor phenotype and influences therapeutic response.
Accordingly, it is assumed that the assessment of the combined amplification status of ERBB1 to ERBB4 may improve the diagnostic value significantly.
Recently it was shown in a retrospective study that responsiveness to Herceptin™ turned out to be more efficient if tumor cells show ERBB4 gene amplification.

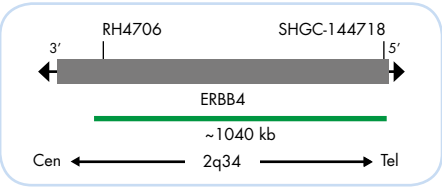
References
Alimandi M, et al. (1995) Oncogene 10: 1813-21.
Begnami MD, et al. (2011) J Clin Oncol 29: 3030-6.
Brockhoff G, et al. (2011) Acta Derm Venereol 91: 488-90.
Brunner K, et al. (2010) Anal Quant Cytol Histol 32: 78-89.
Plowman GD, et al. (1993) Proc Natl Acad Sci U S A 90: 1746-50.
Sassen A, et al. (2008) Breast Cancer Res 10: R2.
Sassen A, et al. (2009) Breast Cancer Res 11: R50.
Zaczek A, et al. (2005) Histol Histopathol 20: 1005-15.
Zimonjic DB, et al. (1995) Oncogene 10: 1235-7.

Probe Description

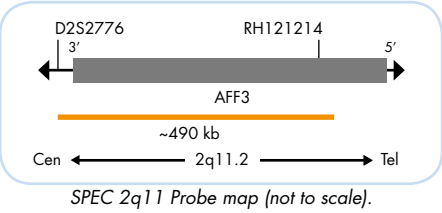
The SPEC ERBB4/2q11 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC ERBB4 probe hybridizing to intronic sequences of the human ERBB4 gene in the chromosomal region 2q34 and an orange fluorochrome direct labeled SPEC 2q11 probe. The SPEC 2q11 probe is specific for the AFF3 (AF4/FMR2 family, member 3) gene region in 2q11.2. Due to cross-hybridizations of chromosome 2 alpha satellites to other centromeric regions, probes specific for 2q11 are frequently used for chromosome 2 copy number detection.



Ideogram of chromosome 2 indicating the hybridization locations.



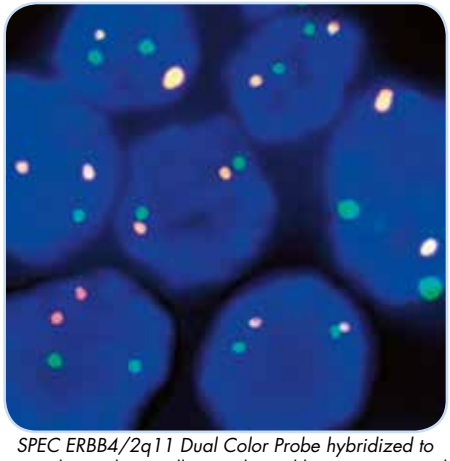
SPEC ERBB4 Probe map (not to scale).



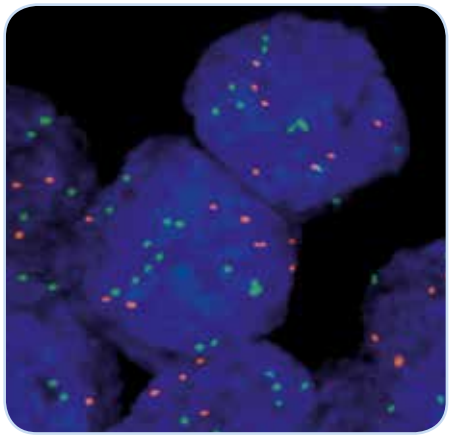
SPEC 2q11 Probe map (not to scale).

Results

Using the SPEC ERBB4/2q11 Dual Color Probe in a normal interphase nucleus, two green and two orange signals are expected. In a cell with amplification of the ERBB4 gene locus, multiple copies of the green signal or green signal clusters will be observed.



SPEC ERBB4/2q11 Dual Color Probe hybridized to normal interphase cells as indicated by two green and two orange signals in each nucleus.



Breast cancer tissue section with amplification of the ERBB4 gene (green), SPEC 2q11 (orange).

Image kindly provided by Prof. Brockhoff, Regensburg, Germany.

Prod. No.	Product	Label	Tests* (Volume)
Z-2057-200	ZytoLight SPEC ERBB4/2q11 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC VHL/CEN 3 Dual Color Probe

CE IVD

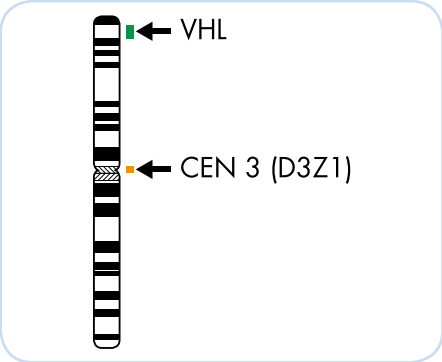
Background

The ZytoLight® SPEC VHL/CEN 3 Dual Color Probe is designed for the detection of deletions affecting the VHL gene.
The tumor suppressor gene VHL (von Hippel-Lindau tumor suppressor) is located on 3p25.3 and encodes a 30 kDa protein with ubiquitin ligase E3 activity. The protein is involved in the ubiquitination and degradation of hypoxia-inducible-factor (HIF), which is a transcription factor that plays a critical role in the regulation of gene expression by oxygen.
Loss of heterozygosity (LOH) at chromosome 3p and inactivation of the VHL gene by deletion or mutation is the most frequent genetic change in sporadic as well as VHL disease-associated conventional renal cell carcinomas (RCC) whereas alterations of this region are rarely seen in papillary and chromophobe RCC. Recent studies suggest that the determination of the VHL status by FISH can significantly improve the accuracy of kidney tumor biopsy evaluation, providing prognostic information that can guide management decisions.

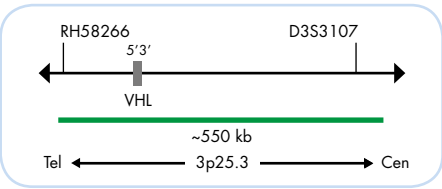
References
Barocas DA, et al. (2006) BJU Int 99: 290-5.
Broom RJ, et al. (2012) Clin Genitourin Cancer 10: 202-6.
Dagher J, et al. (2013) Hum Pathol 44: 2106-15.
Hosoe S, et al. (1990) Genomics 8: 634-40.
Latif F, et al. (1993) Science 260: 1317-20.
Sükösd F, et al. (2003) Cancer Res 63: 455-7.

Probe Description

The SPEC VHL/CEN 3 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 3 probe specific for the alpha satellite centromeric region of chromosome 3 (D3Z1) and a green fluorochrome direct labeled SPEC VHL probe spanning the VHL gene at 3p25.3.



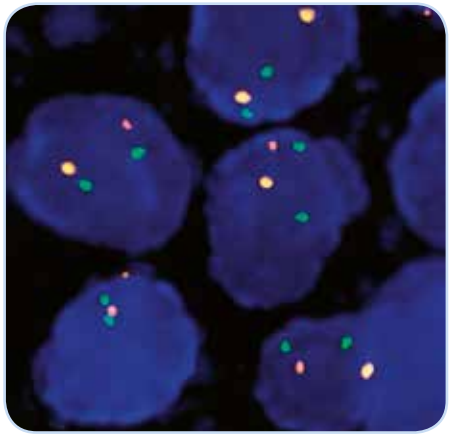
Ideogram of chromosome 3 indicating the hybridization locations.



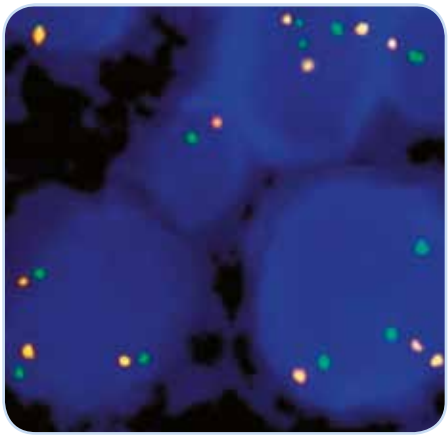
SPEC VHL Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletions affecting the VHL gene, one or no copy of the green signal will be observed.



SPEC VHL/CEN 3 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Trisomy of chromosome 3 as indicated by three orange (CEN 3) and three green (VHL) signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2084-200	ZytoLight SPEC VHL/CEN 3 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC VHL/1p12/CEN 7/17 Quadruple Color Probe

CE IVD

Background

The ZytoLight® SPEC VHL/1p12/CEN 7/17 Quadruple Color Probe is designed for an accurate identification of renal cell carcinoma (RCC) subtypes by the simultaneous detection of VHL gene status and enumeration of chromosomes 1, 7, and 17 in tumor cells.

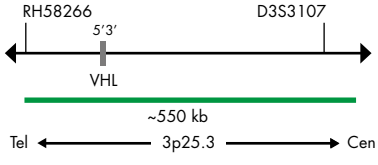
Clear cell RCC (ccRCC), papillary RCC (pRCC), chromophobe RCC (chRCC) and renal oncocytomas (ROs) are the most frequent renal cell tumor subtypes. Patients with ccRCC have a poorer prognosis than patients with pRCC and chRCC. RO is considered to be a benign neoplasm. The differentiation between RCC types may sometimes be difficult on histopathological features alone. However, the different subtypes of kidney tumors are characterized by distinct genetic patterns. Chromosome 3p deletion, including deletion of the tumor suppressor gene VHL (von Hippel-Lindau tumor suppressor) in 3p25.3, is the most typical genetic abnormality in ccRCC. pRCC is characterized by trisomy/polysomy of chromosomes 7 and 17. Combined losses of chromosomes 1, 2, 6, 10, 13, 17, and 21 (with 1, 2, 6, and 17 being affected most frequently) are the most common changes in chRCC, whereas ROs often show rearrangements involving 11q13.3 harboring the CCND1 gene or losses of chromosomes 1, 14, and sex chromosomes.

Consequently, the ZytoLight® SPEC VHL/1p12/CEN 7/17 Quadruple Color Probe is designed to differentiate between ccRCC, pRCC, and some chRCC tumors and should be used in combination with the ZytoLight® SPEC CCND1 Break Apart/2q11/CEN 6 Quadruple Color Probe which helps to especially differentiate between chRCC and ROs.

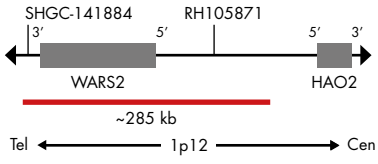
References
Brunelli M, et al. (2005) Modern Pathology 18: 161-9.
Iqbal MA, et al. (2000) Diagn Cytopathol 22: 3-6.
Jhang JS, et al. (2004) Cancer Genet Cytogenet 149: 114-9.
Mertz KD, et al. (2006) Urologe 45: 316-22.
Moch H (2013) Semin Cancer Biol 23: 3-9.
Sanjmyatav J, et al. (2013) Eur Urol 64: 689-91.
Sukov WR, et al. (2009) Hum Pathol 40: 1296-303.

Probe Description

The SPEC VHL/1p12/CEN 7/17 Quadruple Color Probe is a mixture of a green fluorochrome direct labeled SPEC VHL probe spanning the VHL gene at 3p25.3, a gold fluorochrome direct labeled CEN 7 probe specific for the alpha satellite centromeric region of chromosome 7 (D7Z1), a blue fluorochrome direct labeled CEN 17 probe specific for the alpha satellite centromeric region of chromosome 17 (D17Z1), and a red fluorochrome direct labeled SPEC 1p12 hybridizing in close proximity to the centromere of chromosome 1 at the chromosomal region 1p12. Due to cross-hybridizations of chromosome 1 alpha satellites to other centromeric regions, probes specific for 1p12 are frequently used for chromosome 1 copy number detection.



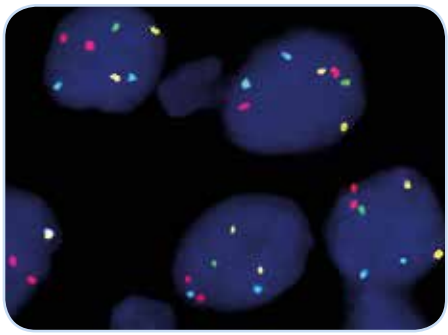
SPEC VHL Probe map (not to scale).



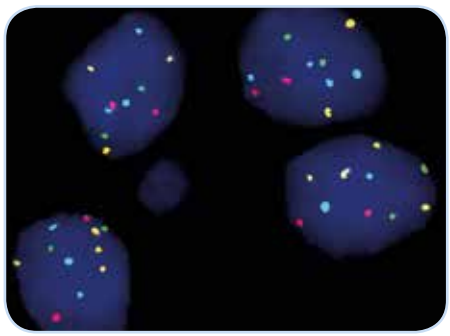
SPEC 1p12 Probe map (not to scale).

Results

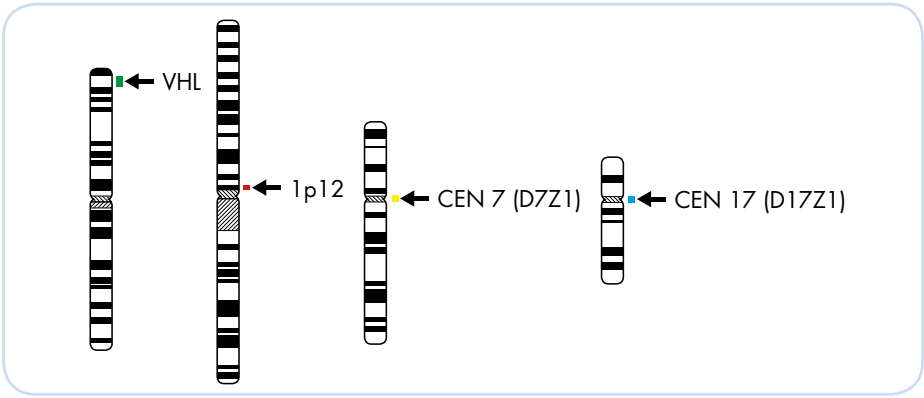
In a normal interphase nucleus, two green, two red, two gold, and two blue signals are expected. In a cell with deletion affecting the VHL gene, a reduced number of green signals will be observed. In cells with aneusomy of chromosome 1, 7, or 17, more or less signals of the respective color will be visible.



Renal cell carcinoma tissue section with deletion of the VHL gene as indicated by one green signal in each nucleus.



Renal cell carcinoma tissue section with polysomy of the chromosome 7 and 17 as indicated by multiple gold and/or blue signals in each nucleus.



Ideograms of chromosomes 3, 1, 7, and 17 indicating the hybridization locations.

Prod. No.	Product	Label	Tests* (Volume)
Z-2102-200	ZytoLight SPEC VHL/1p12/CEN 7/17 Quadruple Color Probe CE IVD	●/●/●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

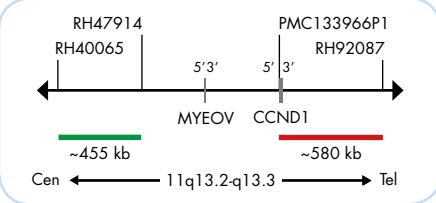
ZytoLight® SPEC CCND1 Break Apart/2q11/CEN 6 Quadruple Color Probe CE IVD

Background

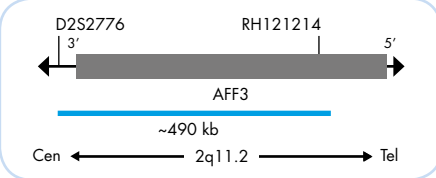
The ZytoLight® SPEC CCND1 Break Apart/2q11/CEN 6 Quadruple Color Probe is designed for an accurate identification of renal cell carcinoma (RCC) subtypes by the simultaneous detection of rearrangements affecting the CCND1 (cyclin D1, a.k.a. BCL2 or PRAD1) gene in 11q13.3 and enumeration of chromosomes 2 and 6 in tumor cells.
Clear cell RCC (ccRCC), papillary RCC (pRCC), chromophobe RCC (chRCC), and renal oncocytomas (ROs) are the most frequent renal cell tumor subtypes. Patients with ccRCC have a poorer prognosis than patients with pRCC and chRCC. RO is considered to be a benign neoplasm. The differentiation between RCC types may sometimes be difficult on histopathological features alone. However, the different subtypes of kidney tumors are characterized by distinct genetic patterns. Chromosome 3p deletion, including deletion of the tumor suppressor gene VHL (von Hippel-Lindau tumor suppressor) in 3p25.3, is the most typical genetic abnormality in ccRCC. pRCC is characterized by trisomy/polysomy of chromosomes 7 and 17. Combined losses of chromosomes 1, 2, 6, 10, 13, 17, and 21 (with 1, 2, 6, and 17 being affected most frequently) are the most common changes in chRCC, whereas ROs often show rearrangements involving 11q13.3 or losses of chromosomes 1, 14, and sex chromosomes. Consequently, the ZytoLight® SPEC CCND1 Break Apart/2q11/CEN 6 Quadruple Color Probe is designed to especially differentiate between chRCC and ROs and should be used in combination with the ZytoLight® SPEC VHL/1p12/CEN 7/17 Quadruple Color Probe which is designed for the differentiation between ccRCC, pRCC, and some chRCC tumors.

Probe Description

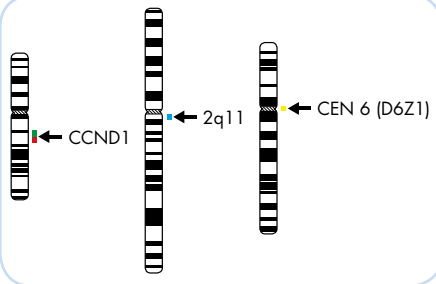
The SPEC CCND1 Break Apart/2q11/CEN 6 Quadruple Color Probe is a mixture of a green and a red fluorochrome direct labeled probe hybridizing proximal and distal to the breakpoint on 11q13.3, respectively, a gold fluorochrome direct labeled CEN 6 probe specific for the alpha satellite centromeric region of chromosome 6 (D6Z1), and a blue fluorochrome direct labeled SPEC 2q11 probe. The SPEC 2q11 probe is specific for the AFF3 (AF4/FMR2 family, member 3) gene region in 2q11.2. Due to cross-hybridizations of chromosome 2 alpha satellites to other centromeric regions, probes specific for 2q11 are frequently used for chromosome 2 copy number detection.



SPEC CCND1 Probe map (not to scale).



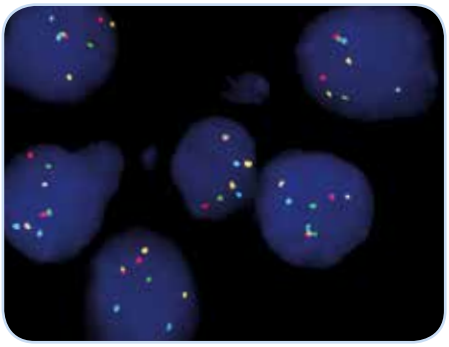
SPEC 2q11 Probe map (not to scale).



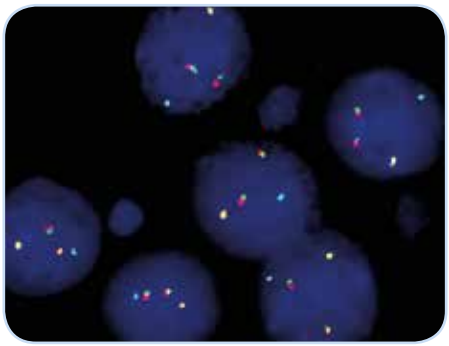
Ideograms of chromosomes 11, 2, and 6 indicating the hybridization locations.

Results

In a normal interphase nucleus, two red/green fusion signals, two blue, and two gold signals are expected. In a cell with translocation of the CCND1 gene locus, a signal pattern consisting of one red/green fusion signal, one red, and a separate green signal indicates one normal CCND1 locus and one CCND1 locus affected by an 11q13.3 translocation. In cells with aneusomy of chromosome 2 or 6, more or less signals of the respective color will be visible.



Renal cell carcinoma tissue section with translocation affecting the 11q13.3 locus as indicated by one non-rearranged red/green fusion signal, one red signal, and one separate green signal.



Renal cell carcinoma tissue section with monosomy of chromosome 2 and 6 as indicated by one blue and one gold signal in each nucleus.

References
Brunelli M, et al. (2005) Modern Pathology 18: 161-9.
Iqbal MA, et al. (2000) Diagn Cytopathol 22: 3-6.
Jhang JS, et al. (2004) Cancer Genet Cytogenet 149: 114-9.
Mertz KD, et al. (2006) Urologe 45: 316-22.
Moch H (2013) Semin Cancer Biol 23: 3-9.
Sanjmyatav J, et al. (2013) Eur Urol 64: 689-91.
Sukov WR, et al. (2009) Hum Pathol 40: 1296-303.

Prod. No.	Product	Label	Tests* (Volume)
Z-2118-200	ZytoLight SPEC CCND1 Break Apart/2q11/CEN 6 Quadruple Color Probe CE IVD	●/●/●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC FHIT/CEN 3 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC FHIT/CEN 3 Dual Color Probe is designed for the detection of FHIT gene deletions frequently observed in most of the common epithelial neoplasms.

The FHIT (fragile histidine triad) gene is located in the chromosomal region 3p14.2 and encodes a 16.8 kDa member of the HIT superfamily of nucleoside monophosphate hydrolases and transferases.

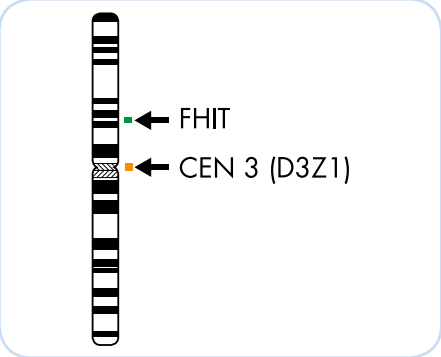
The 1.6 Mb FHIT gene encompasses the most carcinogen-sensitive common fragile region FRA3B and the t(3;8) translocation breakpoint associated with hereditary renal carcinoma.

The tumor suppressor gene FHIT is inactivated by deletions in a variety of human tumors e.g. lung, kidney, gastric, breast, pancreatic, and cervical tumors. Since loss of the FHIT locus occurs in a number of preneoplastic lesions, FHIT may represent a potential marker for the detection of tumor precursor cells.

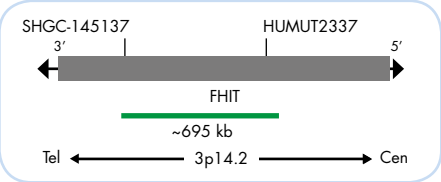
References
Broom RJ, et al. (2012) Clin Genitourin Cancer 10: 202-6.
Cirombella R, et al. (2010) Cancer Lett 291: 230-6.
Huebner K, et al. (1998) Annu Rev Genet 32: 7-31.
Ishii H, et al. (2003) J Exp Ther Oncol 3: 291-6.
Ohta M, et al. (1996) Cell 84: 587-97.
Pekarsky Y, et al. (2002) Lancet Oncol 3: 748-54.
Schwarz S, et al. (2008) Cytometry A 73: 305-11.
Vieira J, et al. (2010) Genes Chromosomes Cancer 49: 935-47.

Probe Description

The SPEC FHIT/CEN 3 Dual Color probe is a mixture of an orange fluorochrome direct labeled CEN 3 probe specific for the alpha satellite centromeric region of chromosome 3 (D3Z1) and a green fluorochrome direct labeled SPEC FHIT probe hybridizing to sequences of introns 4 and 5 of the human FHIT gene at 3p14.2.



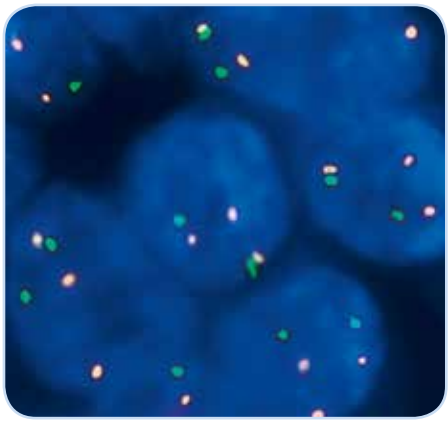
Ideogram of chromosome 3 indicating the hybridization locations.



SPEC FHIT Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletion of the FHIT gene locus, a reduced number of green signals will be observed. Deletions affecting only parts of introns 4 and/or 5 of the FHIT gene might result in a normal signal pattern with green signals of reduced size.



SPEC FHIT/CEN 3 Dual Color Probe hybridized to interphase cells each showing three orange and two green signals.

Prod. No.	Product	Label	Tests* (Volume)
Z-2062-200	ZytoLight SPEC FHIT/CEN 3 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC GATA2/MECOM Dual Color Dual Fusion Probe

CE IVD

Background

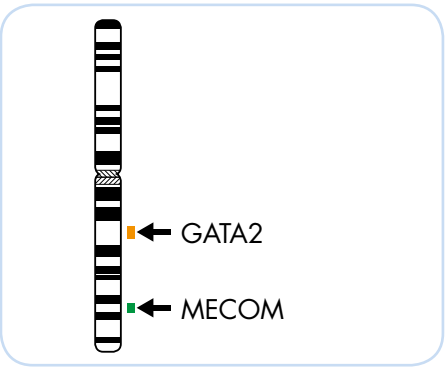
The ZytoLight® SPEC GATA2/MECOM Dual Color Dual Fusion Probe is designed to detect the inversion inv(3)(q21q26.2) and the translocation t(3;3)(q21;q26.2) both affecting the GATA2 (a.k.a. NFE1B) gene in the chromosomal region 3q21.3 and the MECOM (MDS1 and EVI1 complex locus, a.k.a. MDS1, EVI1) gene in 3q26.2. MECOM and GATA2 are transcription factors that play an essential role in the proliferation of hematopoietic stem cells. Inv(3)/t(3;3), and less commonly ins(3;3)(q26.2;q21q26.2), occur in 1-2.5% of acute myeloid leukemia (AML) and are also observed in myelodysplastic syndromes and in the blastic phase of chronic myeloid leukemia. A variety of other MECOM translocations involving other fusion partner genes have also been reported in various types of myeloid malignancies. 3q26.2 rearrangements are associated with minimal to no response to chemotherapy and poor clinical outcome.

The inv(3) and t(3;3) result in overexpression of the MECOM gene due to its juxtaposition to enhancer sequences of the GATA2 gene and simultaneously confer GATA2 haploinsufficiency, leading to leukemogenesis.

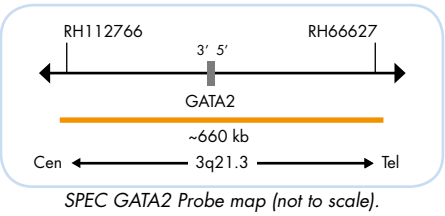
In the revised 2016 WHO classification of myeloid neoplasms and acute leukemia, "AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); GATA2, MECOM" is classified as its own entity, emphasizing the unique clinicopathologic features and poorer prognosis of this subgroup of AML patients. Chromosome 3q26.2 rearrangements may be cryptic on standard karyotype analysis. Hence, FISH may be a helpful tool to confirm the diagnosis of this distinct AML subgroup.

Probe Description

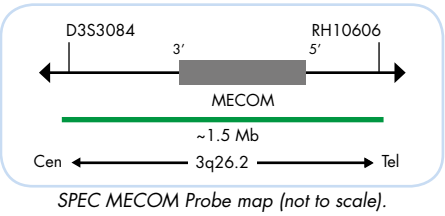
The SPEC GATA2/MECOM Dual Color Dual Fusion Probe is a mixture of an orange fluorochrome direct labeled probe spanning the GATA2 gene region at 3q21.3 and a green fluorochrome direct labeled probe spanning the MECOM gene region at 3q26.2. This probe is approved to be used with a hybridization time of 2 hours on cytological specimens.



Ideogram of chromosome 3 indicating the hybridization locations.



SPEC GATA2 Probe map (not to scale).

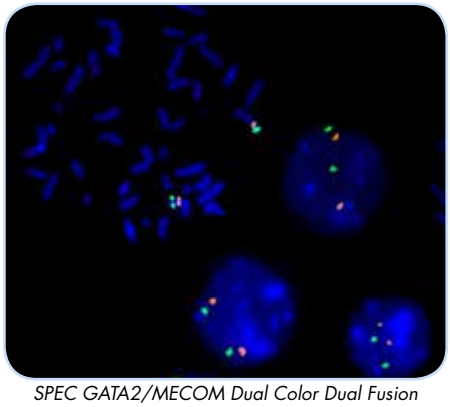


SPEC MECOM Probe map (not to scale).

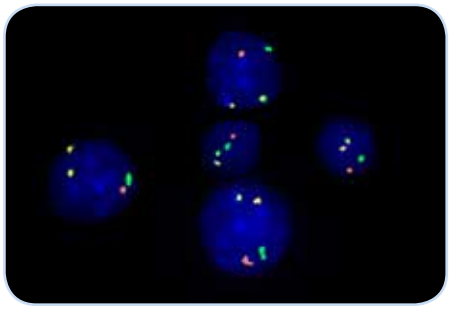
References
Arber DA, et al. (2016) Blood 127: 2391-405.
Bobadilla D, et al. (2007) Br J Haematol 136: 806-13.
De Braekeleer E, et al. (2011) Anticancer Res 31: 3441-8.
Pintado T, et al. (1985) Cancer 55: 535-41.
Tang Z, et al. (2019) Cancer Genet 233-234: 21-31.
Yamazaki H, et al. (2014) Cancer Cell 25: 415-27.

Results

In a normal interphase nucleus, two green and two orange signals are expected. An aberration involving the chromosomal regions of GATA2 and MECOM generates a fusion signal on each of the chromosomes involved in case of a t(3;3) or two fusion signals on the involved chromosome in case of an inv(3). The chromosomal regions that are not translocated are indicated by the single green and orange signal, respectively. Other relevant signal patterns may also be observed as a result of ins(3;3) or 3q26.2 rearrangements without the involvement of the GATA2 locus.



SPEC GATA2/MECOM Dual Color Dual Fusion Probe hybridized to normal interphase cells as indicated by two orange and two green signals and to metaphase chromosomes of a normal cell.



Bone marrow smear with rearrangement affecting the GATA2/MECOM loci as indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.

Prod. No.	Product	Label	Tests* (Volume)
Z-2287-50	ZytoLight SPEC GATA2/MECOM Dual Color Dual Fusion Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC WWTR1 Dual Color Break Apart Probe

CE IVD

Background

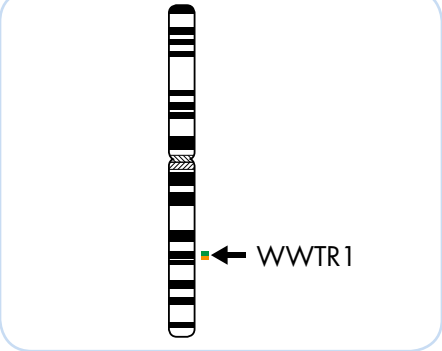
The ZytoLight® SPEC WWTR1 Dual Color Break Apart Probe is designed for the detection of translocations involving the chromosomal region 3q25.1 harboring the WWTR1 (WW domain containing transcription regulator 1, a.k.a. TAZ) gene. Epithelioid vascular tumors encompass a spectrum of diseases that includes epithelioid hemangioma (EH), a benign neoplasm, epithelioid hemangioendothelioma (EHE), a low to intermediate grade malignancy, and epithelioid angiosarcoma (EAS), a high grade malignancy. Although certain morphologic features allow to distinguish EHE from EH and EAS, the diagnosis can be challenging due to considerable morphologic overlap, particularly on small biopsies or when EAS lacks vasoformative properties. Clinical behavior and, consequently, treatment and prognosis vary significantly among vascular tumors. Therefore, it is paramount to effectively distinguish them from each other.

The recurrent translocation t(1;3)(p36.3;q25.1) was identified in approximately 90% of EHE cases, but not in other vascular tumors. t(1;3) results in the WWTR1-CAMTA1 fusion gene which encodes a putative chimeric transcription factor which is under the transcriptional control of the WWTR1 promoter. A recurrent YAP1-TFE3 gene fusion has been identified in WWTR1-CAMTA1 negative EHEs. Thus, FISH analysis for the presence of WWTR1 translocation may serve as a useful molecular tool in the differential diagnosis of challenging cases.

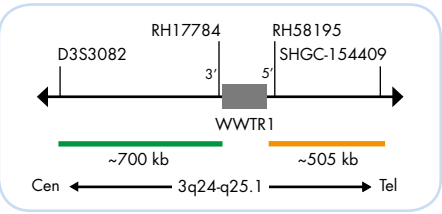
References
Anderson T, et al. (2015) Am J Surg Pathol 39: 132-9.
Errani C, et al. (2011) Genes Chromosomes Cancer 50: 644-53.
Mendlick MR, et al. (2001) Am J Surg Pathol 25: 684-7.
Puls F, et al. (2015) Virchows Arch 466: 473-8.
Tanas MR, et al. (2011) Sci Transl Med 3: 98ra82.

Probe Description

The SPEC WWTR1 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 3q24-3q25.1 band. The green fluorochrome direct labeled probe hybridizes in 3q24-3q25.1 proximal and the orange fluorochrome direct labeled probe hybridizes in 3q25.1 distal to the WWTR1 gene.



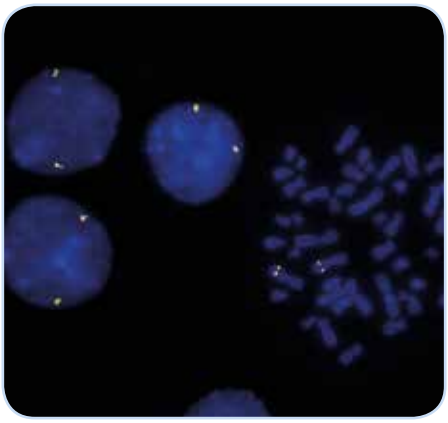
Ideogram of chromosome 3 indicating the hybridization locations.



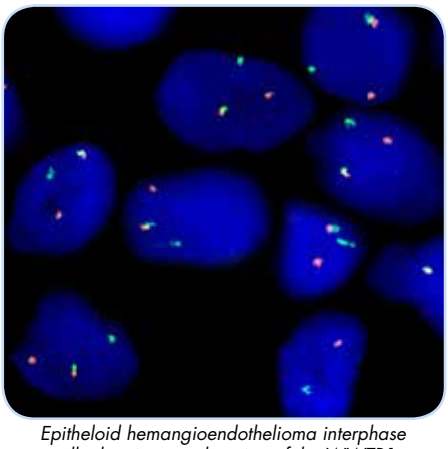
SPEC WWTR1 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 3q24-3q25.1 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 3q24-3q25.1 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 3q24-3q25.1 locus and one 3q24-3q25.1 locus affected by a translocation.



SPEC WWTR1 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus and to metaphase chromosomes of a normal cell.



Epitheloid hemangioendothelioma interphase cells showing translocation of the WWTR1 gene as indicated by one non-rearranged orange/green fusion signal, one orange signal and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2212-50	ZytoLight SPEC WWTR1 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC TERC/CEN 3 Dual Color Probe

CE IVD

Background

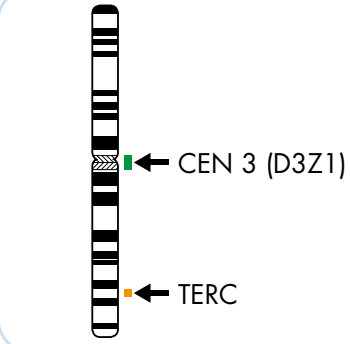
The ZytoLight® SPEC TERC/CEN 3 Dual Color Probe is designed to detect amplifications affecting the chromosomal region 3q26.2 harboring the TERC (telomerase RNA component, a.k.a. hTERC, TRC3) gene.

3q copy number gains including the TERC gene locus, have been found in several epithelial carcinomas such as cervix carcinoma, prostate cancer, non-small cell lung cancer, and lung squamous cell carcinoma. TERC amplifications are not only found in cancers but also in pre-cancerous lesions such as atypical squamous cell of undetermined significance (ASCUS). For cervical carcinoma, which is the second most common malignancy among women worldwide, TERC amplifications have become a molecular marker to distinguish between low-grade dysplasia and high-grade cervical neoplasia and invasive carcinoma. Only a minority of cases which are cytologically diagnosed as low-grade squamous intraepithelial lesion (LSIL) show a development to high-grade squamous intraepithelial lesions (HSIL). Since an increase in TERC gene copy number has been shown to be strongly associated with the progression of cervical intraepithelial neoplasia (CIN) to invasive carcinoma, TERC amplification has been proposed as prognostic marker to identify low-grade lesions with high risk to progress to high-grade disease and cancer. Fluorescence *in situ* Hybridization (FISH) may be a reliable diagnostic tool to complement Pap-testings and may be of prognostic relevance.

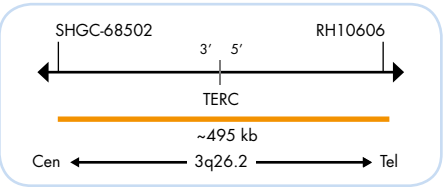
References
Andersson S, et al. (2009) Am J Pathol 175: 1831-47.
Heselmeyer-Haddad K, et al. (2005) Am J Pathol 166: 1229-38.
Heselmeyer K, et al. (1996) Proc Natl Acad Sci U S A 93: 479-84.
Pelosi G, et al. (2007) Clin Cancer Res 13: 1995-2004.
Yokoi S, et al. (2003) Clin Cancer Res 9: 4705-13.

Probe Description

The SPEC TERC/CEN 3 Dual Color Probe is a mixture of an orange fluorochrome direct labeled probe spanning the TERC gene region at 3q26.2 and a green fluorochrome direct labeled probe hybridizing to the alpha satellite centromeric region of chromosome 3 (D3Z1).



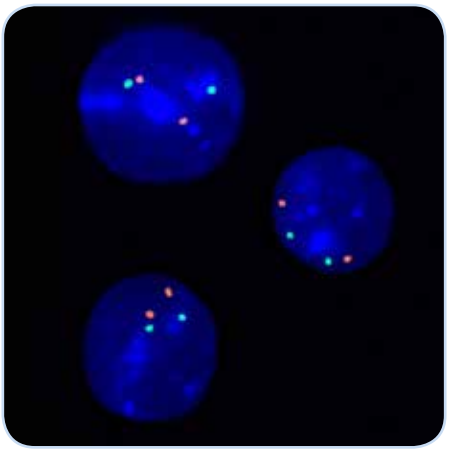
Ideogram of chromosome 3 indicating the hybridization locations.



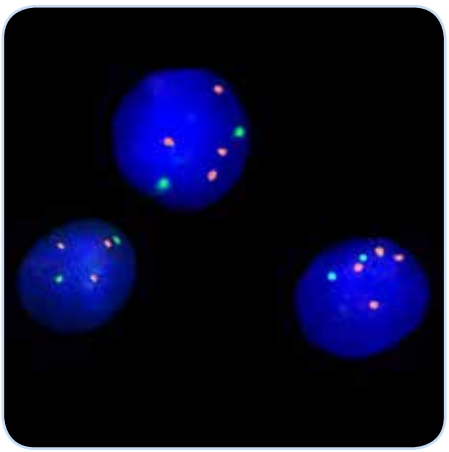
SPEC TERC Probe map (not to scale).

Results

Using the SPEC TERC/CEN 3 Dual Color Probe in a normal interphase nucleus, two orange and two green signals are expected. In a cell with gain of the TERC gene locus, multiple copies of the orange signal or orange signal clusters will be observed.



SPEC TERC/CEN 3 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals per nucleus.



SPEC TERC/CEN 3 Dual Color Probe hybridized to CaSki cells with TERC amplification as indicated by three or four orange signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2284-200	ZytoLight SPEC TERC/CEN 3 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC PIK3CA/CEN 3 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC PIK3CA/CEN 3 Dual Color Probe is designed for the detection of PIK3CA gene amplifications frequently found in a variety of human cancers.

The PIK3CA (a.k.a. PI3K-alpha) gene is located on chromosome 3q26.32 and encodes the 110 kDa catalytic subunit of the phosphatidylinositol 3-kinase (PI3K). Amplifications of PIK3CA were found e.g. in cervical, ovarian, endometrial, breast, gastric, and lung cancer.

In ovarian cancer as well as cervical cancer cells increased copy numbers were shown to be associated with increased expression of the gene product and PI3K activity. Furthermore, treatment with a PI3K inhibitor leads to decreased proliferation and increased apoptosis. It was concluded that PIK3CA is an important oncogene in these tumors.

Likewise in endometrial carcinomas detection of PIK3CA amplification is associated with tumor grade and stage.

A significant correlation between PIK3CA amplification and poor survival was found for gastric cancer patients.

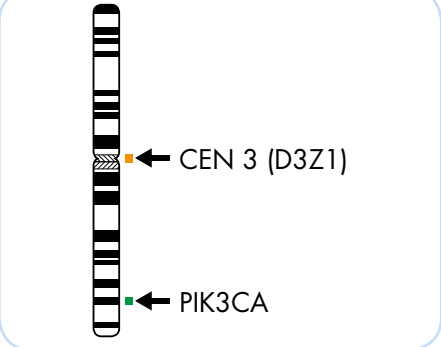
PIK3CA amplification was also frequently found in non-small cell lung cancer (NSCLC) and was shown to be associated with certain clinicopathologic features.

PIK3CA amplification seems to promote tumorigenesis through aberrant activation of the PI3K/Akt signaling pathway. Hence, this pathway might represent an effective therapeutic target in several cancer types.

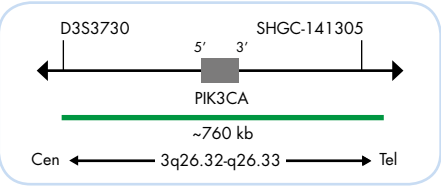
References
Ji M, et al. (2011) BMC Cancer 11: 147.
Ma YY, et al. (2000) Oncogene 19: 2739-44.
Shayesteh L, et al. (1999) Nat Genet 21: 99-102.
Shi J, et al. (2012) BMC Cancer 12: 50.
Volinia S, et al. (1994) Genomics 24: 472-7.

Probe Description

The SPEC PIK3CA/CEN 3 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 3 probe specific for the alpha satellite centromeric region of chromosome 3 (D3Z1) and a green fluorochrome direct labeled SPEC PIK3CA probe specific for the chromosomal region 3q26.32-q26.33 harboring the PIK3CA gene.



Ideogram of chromosome 3 indicating the hybridization locations.

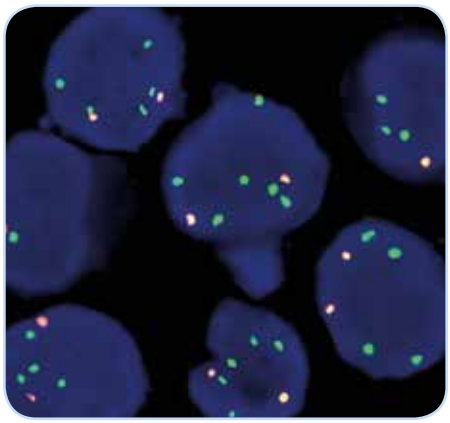


SPEC PIK3CA Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. Nuclei with amplification of the PIK3CA gene locus 3q26.32-q26.33 or aneuploidy of chromosome 3 will show multiple copies of the green signal or large green signal clusters.

SPEC PIK3CA/CEN 3 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Human breast cancer cell line with amplification of the PIK3CA gene as indicated by multiple green signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2140-200	ZytoLight SPEC PIK3CA/CEN 3 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC SOX2/CEN 3 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC SOX2/CEN 3 Dual Color Probe is designed for the detection of SOX2 gene amplifications frequently observed in squamous cell carcinoma (SCC) of the lung, the esophagus, the oral cavity, and further organ sites. In addition, amplifications and/or overexpression were found in glioma, breast cancer, and other tumor types.

The SOX2 (SRY-box 2, a.k.a. ANOP3) gene is located on chromosome 3q26.33 and encodes a High Mobility Group domain transcription factor that is a regulator of normal stem cell function in embryonic and neural stem cells.

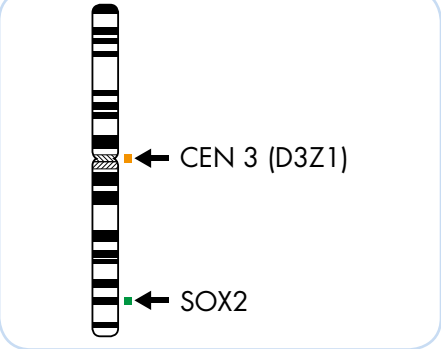
Amplification of the SOX2 gene was found in about 20% of lung SCC and 15% of esophageal SCC and results in oncogenic SOX2 overexpression. In a large series of lung SCC it was shown that amplification of SOX2 was associated with lower tumor grade and hence with favorable prognosis.

However, in glioma and glioma cell lines SOX2 expression seems to show a positive correlation with malignancy grade.

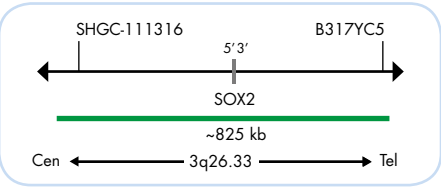
References
Alonso MM, et al. (2011) PLoS One 6: e26740.
Annovazzi L, et al. (2011) Cancer Genomics Proteomics 8: 139-47.
Bass AJ, et al. (2009) Nat Genet 41: 1238-42.
Hussenet T, et al. (2010) PLoS One 5: e8969.
Kokalj Vokac N, et al. (2014) Mol Cytogenet 7: 5.
Maier S, et al. (2011) Hum Pathol 42: 1078-88.
Wilbertz T, et al. (2011) Mod Pathol 24: 944-53.

Probe Description

The SPEC SOX2/CEN 3 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 3 probe specific for the alpha satellite centromeric region of chromosome 3 (D3Z1) and a green fluorochrome direct labeled SPEC SOX2 probe specific for the SOX2 gene at 3q26.33.



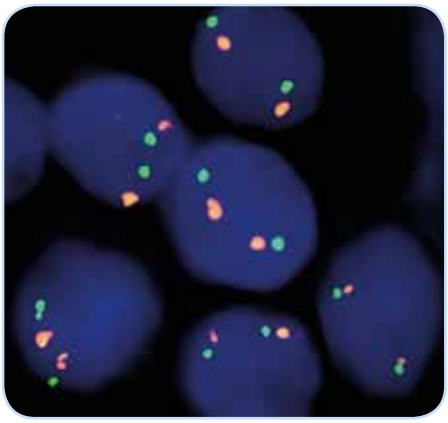
Ideogram of chromosome 3 indicating the hybridization locations.



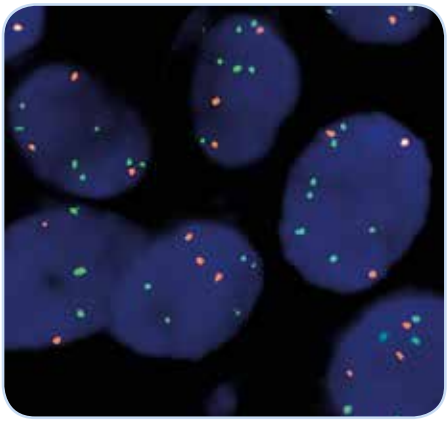
SPEC SOX2 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. Nuclei with amplification of the SOX2 gene locus 3q26.33 or aneuploidy of chromosome 3 will show multiple copies of the green signal or large green signal clusters.



SPEC SOX2/CEN 3 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Lung cancer tissue section with amplification of the SOX2 gene (green) and trisomy of chromosome 3 (orange).

Prod. No.	Product	Label	Tests* (Volume)
Z-2127-200	ZytoLight SPEC SOX2/CEN 3 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC BCL6 Dual Color Break Apart Probe

CE IVD

Background

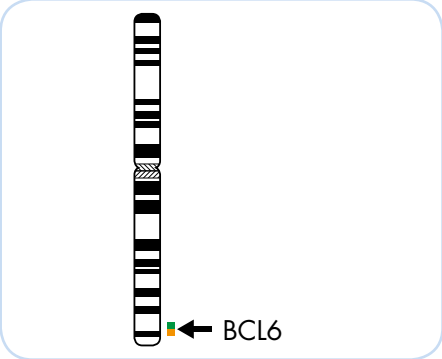
The ZytoLight® SPEC BCL6 Dual Color Break Apart Probe is designed for the detection of translocations involving the chromosomal region 3q27.3 harboring the BCL6 (BCL6 transcription repressor, a.k.a. ZNF51, LAZ3) gene.

The BCL6 protein acts as a transcriptional repressor that is involved in the regulation of lymphoid development and function. Chromosomal rearrangements of the BCL6 gene region were found to occur in different types of non-Hodgkin lymphoma (NHL), including diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL). The most common BCL6 translocation t(3;14)(q27;q32.3) results in the IGH-BCL6 gene fusion. In addition, more than 20 partner loci have been identified including immunoglobulin (Ig) genes but also a number of non-Ig genes. As a result of these translocations, the rearranged BCL6 gene comes under the control of the promoter of the partner gene leading to deregulated expression of BCL6.

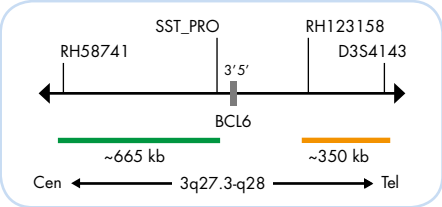
In DLBCL, the most common histologic subtype of NHL, BCL6 translocations represent one of the most frequent cytogenetic abnormality, occurring in 20% to 40% of the cases. Several studies reported a correlation of BCL6 translocation with an inferior overall survival. Moreover, DLBCL which are positive for both BCL6 and MYC rearrangements have been shown to have an extremely poor prognosis. Hence, the detection of BCL6 rearrangements by Fluorescence *in situ* Hybridization may help in predicting the clinical outcome in patients with NHL.

Probe Description

The SPEC BCL6 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 3q27.3-q28 band. The green fluorochrome direct labeled probe hybridizes at 3q27.3 proximal to the BCL6 gene, and the orange fluorochrome direct labeled probe hybridizes at 3q27.3-q28 distal to the BCL6 gene.



Ideogram of chromosome 3 indicating the hybridization locations.

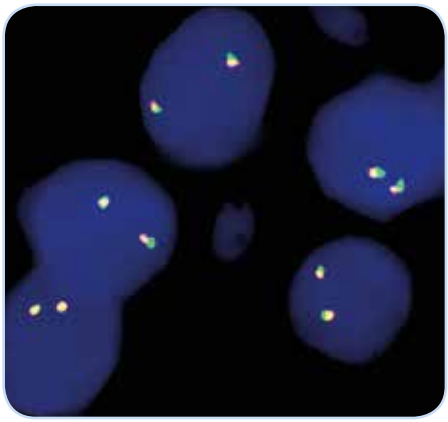


SPEC BCL6 Probe map (not to scale).

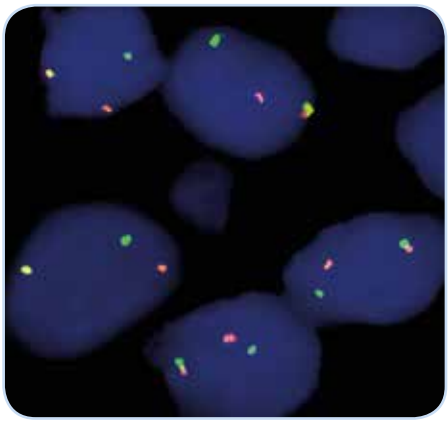
References
Akyurek N, et al. (2012) Cancer 118: 4173-83.
Cady FM, et al. (2008) J Clin Oncol 26: 4814-9.
Ohno H (2004) Histol Histopathol 19: 637-50.
Ohno H (2006) J Clin Exp Hematop 46: 43-53.

Results

In an interphase nucleus lacking a translocation involving the 3q27.3-q28 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 3q27.3-q28 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 3q27.3-q28 locus and one 3q27.3-q28 locus affected by a translocation.



SPEC BCL6 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



DLBCL tissue section with translocation of the BCL6 gene as indicated by one non-rearranged orange/green fusion signal, one orange, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2177-50	ZytoLight SPEC BCL6 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2177-200	ZytoLight SPEC BCL6 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC FGFR3 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC FGFR3 Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal region 4p16.3 harboring the FGFR3 (fibroblast growth factor receptor 3, a.k.a. JTK4) gene.

Rearrangements affecting the FGFR3 gene are frequently found in carcinomas of various types including multiple myeloma (MM), bladder cancer, glioblastoma, peripheral T-cell lymphoma, and lung squamous cell carcinoma.

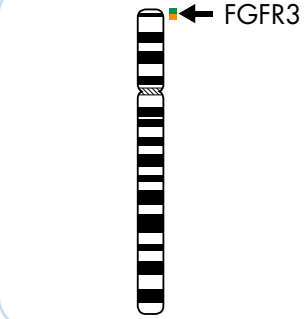
FGFR3 encodes for a transmembrane receptor tyrosine kinase which dimerizes after ligand binding leading to activation of downstream signaling cascades. This gene develops characteristic oncogenic activities after fusion to several gene partners which often leads to ligand-independent activation of the tyrosine kinase of the FGFR3 fusion protein.

Several *in vivo* and *in vitro* studies have demonstrated the therapeutic potential of FGFR inhibitors in cell lines and animal models harboring FGFR3 fusion genes. Hence, the detection of FGFR3 translocations by Fluorescence *in situ* Hybridization may be a useful predictive biomarker in the selection of patients for FGFR-targeted therapy.

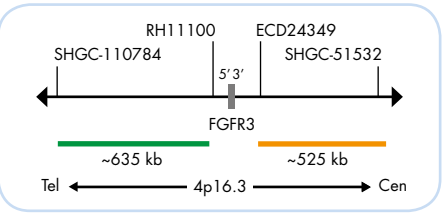
References
Cheng T, et al. (2013) PLoS One 8: e57284.
Fonseca R, et al. (2009) Leukemia 23: 2210-21.
Kang S, et al. (2009) Mol Cell Biol 29: 2105-17.
Knowles MA (2007) World J Urol 25: 581-93.
Parker BC, et al. (2014) J Pathol 232: 4-15.
Williams SV, et al. (2012) Hum Mol Genet 22: 795-803.

Probe Description

The SPEC FGFR3 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 4p16.3 band. The orange fluorochrome direct labeled probe hybridizes proximal, the green fluorochrome direct labeled probe hybridizes distal to the FGFR3 gene at 4p16.3.



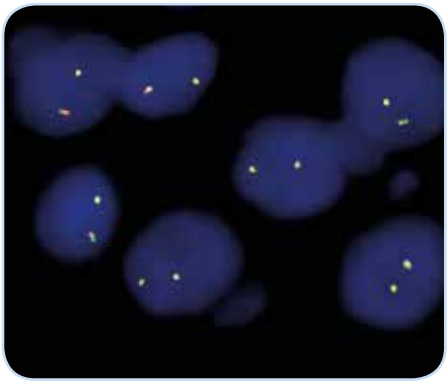
Ideogram of chromosome 4 indicating the hybridization locations.



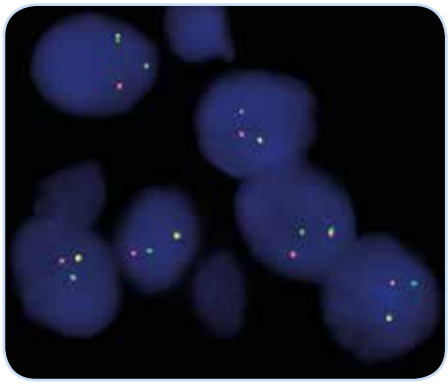
SPEC FGFR3 Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 4p16.3 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 4p16.3 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 4p16.3 locus and one 4p16.3 locus affected by a translocation.



SPEC FGFR3 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Breast cancer tissue section with translocation affecting the FGFR3 gene as indicated by one non-rearranged orange/green fusion signal, one orange, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2170-50	ZytoLight SPEC FGFR3 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2170-200	ZytoLight SPEC FGFR3 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC FGFR3/4p11 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC FGFR3/4p11 Dual Color Probe is designed for the detection of FGFR3 gene amplifications.

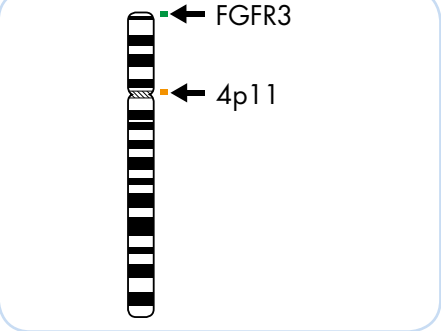
The FGFR3 (fibroblast growth factor receptor 3) gene is located in the chromosomal region 4p16.3 and encodes a receptor tyrosine kinase.

FGFR family members differ from one another in their ligand affinities and tissue distribution. The extracellular portion of the protein interacts with fibroblast growth factors, setting in motion a cascade of downstream signals, ultimately influencing mitogenesis and differentiation. The FGFR3 protein binds acidic and basic fibroblast growth hormone and plays a role in bone development and maintenance. Activating mutations are associated with multiple myeloma, cervical carcinoma, and carcinoma of the bladder. Additionally, it was found that copy number gains at 4p16.3 occurred significantly more frequently in recurred/metastasized salivary gland adenoid cystic carcinoma (ACC) compared with indolent ACC.

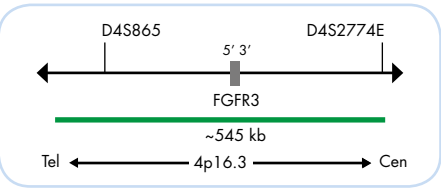
References
Keegan K, et al. (1991) Proc Natl Acad Sci U S A 88: 1095-9.
L'Hôte CG & Knowles MA (2005) Exp Cell Res 304: 417-31.
Thompson LM, et al. (1991) Genomics 11: 1133-42.
Vékony H, et al. (2007) Clin Cancer Res 13: 3133-9.

Probe Description

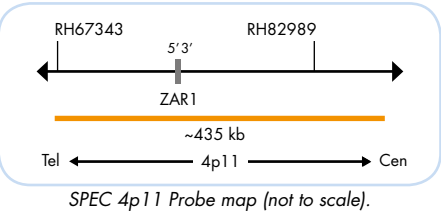
The SPEC FGFR3/4p11 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC FGFR3 probe hybridizing to the FGFR3 gene in the chromosomal region 4p16.3 and an orange fluorochrome direct labeled SPEC 4p11 probe specific for the ZAR1 (zygote arrest 1) gene region in 4p11. For an unambiguous enumeration of chromosome 4 the SPEC 4p11 is found to be more suitable.



Ideogram of chromosome 4 indicating the hybridization locations.



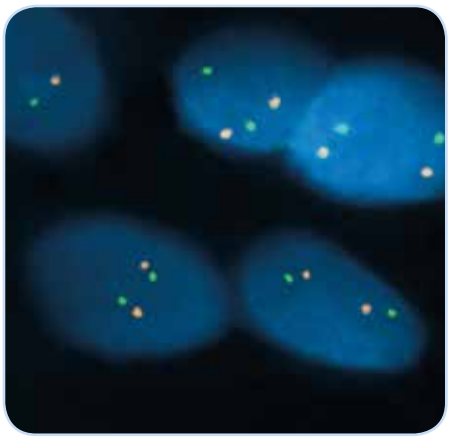
SPEC FGFR3 Probe map (not to scale).



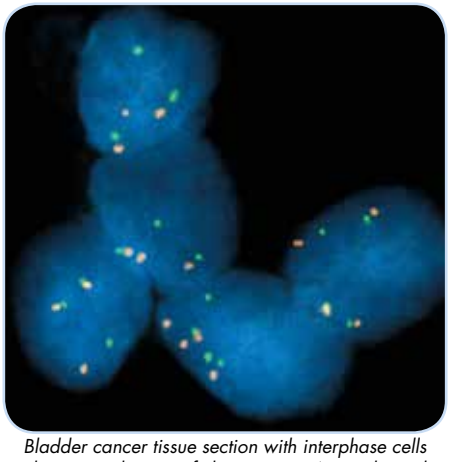
SPEC 4p11 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the FGFR3 gene locus, multiple copies of the green signal or large green signal clusters will be observed.



SPEC FGFR3/4p11 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Bladder cancer tissue section with interphase cells showing polysomy of chromosome 4 as indicated by multiple green and orange signals in the nuclei.

Prod. No.	Product	Label	Tests* (Volume)
Z-2082-200	ZytoLight SPEC FGFR3/4p11 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC FGFR3/IGH Dual Color Dual Fusion Probe

CE IVD

Background

The ZytoLight® SPEC FGFR3/IGH Dual Color Dual Fusion Probe is designed to detect the translocation t(4;14)(p16.3;q32.3) affecting the FGFR3 (fibroblast growth factor receptor 3, a.k.a. JTK4) gene in the chromosomal region 4p16.3 and the IGH (immunoglobulin heavy locus, a.k.a. IGH@) locus in 14q32.33.

FGFR3 encodes for a receptor tyrosine kinase, which regulates downstream signaling cascades after ligand binding. Fusion to several partner genes (including the IGH locus) can lead to a ligand-independent activation of the tyrosine kinase of the resulting FGFR3 fusion protein, frequently found in multiple myeloma (MM).

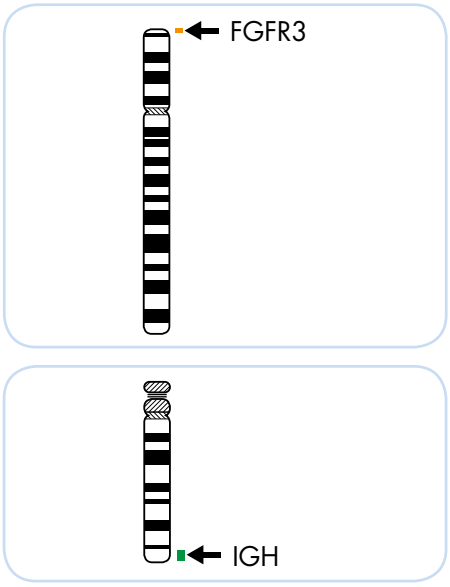
FGFR3/IGH translocations are observed in approximately 15–20% of patients with MM. The breaking points for the 4p16.3 locus are found between the FGFR3 gene and the 5′ end of the NSD2 gene. The t(4;14)(p16.3;q32.3) translocation is associated with upregulation of the FGFR3 and the myeloma NSD2 (a.k.a. MMSET) domain protein. Patients with FGFR3/IGH translocation demonstrate an overall poor prognosis that is only partially mitigated by the use of the novel agents bortezomib and lenalidomide.

With conventional cytogenetics, the t(4;14)(p16.3;q32.3) translocation is difficult to identify. Thus, the detection of FGFR3/IGH translocations by Fluorescence *in situ* Hybridization may be of diagnostic and prognostic relevance.

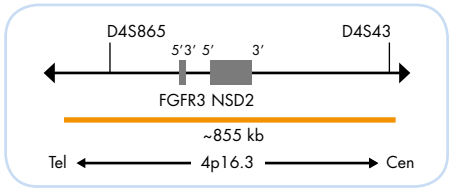
References
Bergsagel PL & Kuehl WM (2001) Oncogene 20: 5611-22.
Chesi M, et al. (1998) Blood 92: 3025-34.
Fabris S, et al. (2005) Genes Chromosomes Cancer 42: 117-27.
Fenton JA, et al. (2003) Oncogene 22: 1103-13.
Kalff A & Spencer A (2012) Blood Cancer J 7: e89.
Sonneveld P, et al. (2016) Blood 127: 2955-62.
Walker BA, et al. (2013) Blood 121: 3413-19.

Probe Description

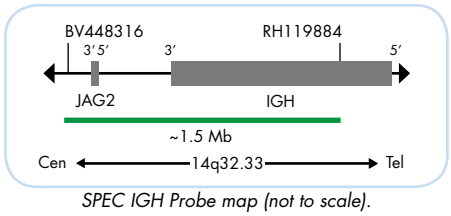
The SPEC FGFR3/IGH Dual Color Dual Fusion Probe is a mixture of an orange direct labeled probe spanning the FGFR3 gene region at 4p16.3 and a green direct labeled probe hybridizing to the IGH gene locus a 14q32.33.



Ideograms of chromosomes 4 (above) and 14 (below) indicating the hybridization locations.



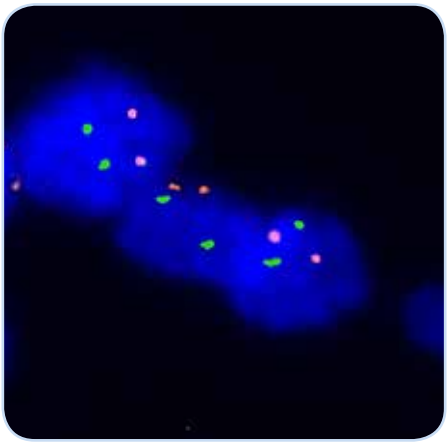
SPEC FGFR3 Probe map (not to scale).



SPEC IGH Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. A reciprocal translocation involving two breakpoints splits the two signals and generates a fusion signal on each of the chromosomes involved. The chromosomal regions which are not translocated are indicated by the single orange and green signal, respectively.



SPEC FGFR3/IGH Dual Color Dual Fusion Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2282-50	ZytoLight SPEC FGFR3/IGH Dual Color Dual Fusion Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC PDGFRA/FIP1L1 TriCheck™ Probe

CE IVD

Background

The ZytoLight® SPEC PDGFRA/FIP1L1 TriCheck™ Probe is designed to detect rearrangements involving the chromosomal region 4q12 harboring the PDGFRA gene. The PDGFRA (platelet-derived growth factor receptor alpha) gene encodes a transmembrane glycoprotein that belongs to the type III receptor tyrosine kinase family and has a key role in a variety of cellular processes.

PDGFRA gene rearrangements are rarely genetic events detected in myeloid and lymphoid neoplasms. These rearrangements most frequently occur in chronic eosinophilic leukemia (CEL), but can be also detected in acute myeloid leukemia (AML), and T-lymphoblastic leukemia/lymphoma (T-ALL).

The most common gene fusion partner for PDGFRA is the FIP1-like 1 (FIP1L1) gene caused by an 800 kb interstitial deletion on chromosome 4q12. The result of this deletion is the loss of the CHIC2 gene and the fusion of the 5' end of the FIP1L1 gene with the 3' end of the PDGFRA gene.

Although FIP1L1 is the most common fusion partner of PDGFRA, five other partner genes have been identified, including BCR, ETV6, KIF5B, STRN, and CDK5RAP2.

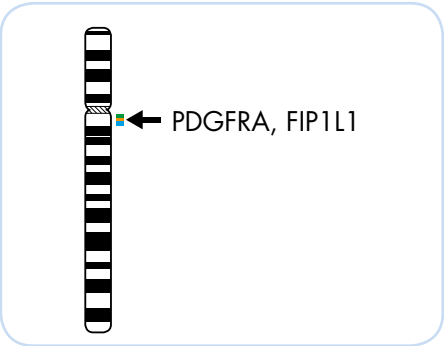
Identification of patients harboring a PDGFRA rearrangement is important as these patients respond very well to a targeted therapy with imatinib.

In CEL patients harboring a PDGFRA-FIP1L1 fusion a good response to other tyrosine kinase inhibitors like dastinib, nilotinib, sorafenib, and midostaurin could be demonstrated.

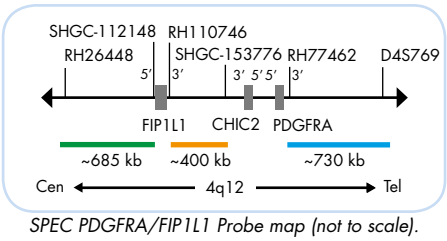
Hence, detection of PDGFRA rearrangements by Fluorescence *in situ* Hybridization (FISH) may be of diagnostic and predictive relevance.

Probe Description

The SPEC PDGFRA/FIP1L1 TriCheck™ Probe is a mixture of three direct labeled probes hybridizing to the 4q12 band. The green fluorochrome direct labeled probe hybridizes proximal to the FIP1L1 gene, the orange fluorochrome direct labeled probe hybridizes distal to the FIP1L1 gene and proximal to the PDGFRA gene, and the blue fluorochrome direct labeled probe hybridizes distal to the PDGFRA gene.



Ideogram of chromosome 4 indicating the hybridization locations.



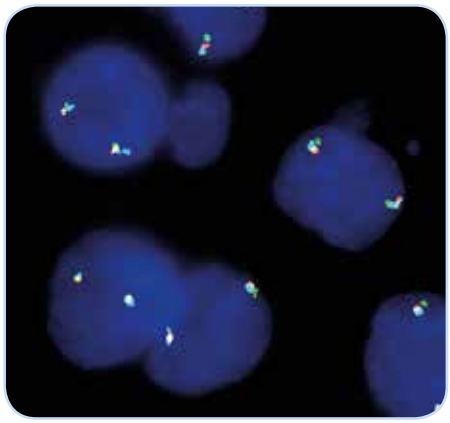
SPEC PDGFRA/FIP1L1 Probe map (not to scale).

Results

In an interphase nucleus lacking a deletion or translocation involving the 4q12 band, two tricolor orange/green/blue fusion signals are expected representing two normal 4q12 loci.

A PDGFRA-FIP1L1 fusion resulting from an interstitial DNA deletion is indicated by the loss of the orange signal leading to a separate green signal co-localizing with a blue signal.

A PDGFRA translocation without involvement of FIP1L1 is indicated by one orange/green fusion signal and one separate blue signal.



SPEC PDGFRA/FIP1L1 TriCheck™ Probe hybridized to normal interphase cells as indicated by two tricolor orange/green/blue fusion signals per nucleus.

References
Bain BJ (2010) Haematologica 95: 696-8.
Cools J, et al. (2003) N Engl J Med 348: 1201-14.
Curtis CE, et al. (2007) Br J Haematol 138: 77-81.
Gotlib J, et al. (2004) Blood 103: 2879-91.
Savage N, et al. (2013) Int J Lab Hematol 35: 491-500.
Vega F, et al. (2015) Am J Clin Pathol 144: 377-92.

Prod. No.	Product	Label	Tests* (Volume)
Z-2209-50	ZytoLight SPEC PDGFRA/FIP1L1 TriCheck Probe CE IVD	●/●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC TERT Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC TERT Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 5p15.33 harboring the TERT gene. The TERT (telomerase reverse transcriptase, a.k.a. EST2, TCS1) gene encodes the reverse transcriptase component, a catalytic domain of the enzyme telomerase. Telomerases are necessary to maintain the ends of chromosomes and are inactive in the majority of somatic cells but active in cancer cells. Remodeling of the genomic context, due to 5p15.33 rearrangements, abrogates transcriptional silencing of the TERT gene. TERT translocations are the second common aberration found in neuroblastomas. These translocations are observed either in a 50 kb region proximal or more rarely in a 40 kb region distal to the gene. Molecular genetic studies showed that rearrangements of the chromosomal region 5p15.33 occur exclusively in high-risk neuroblastomas. Therefore, TERT rearrangements are considered to define a sub-group of high-risk neuroblastomas with a poor prognosis. Rearrangements of TERT are found in chromophobe renal cell carcinomas, non-Hodgkin lymphomas, and mantle cell lymphomas.

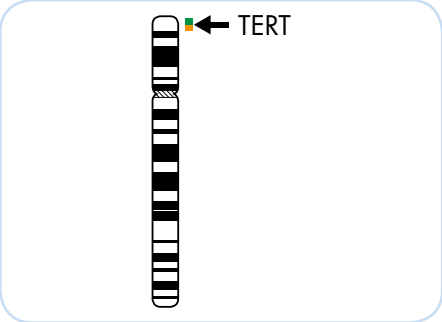
FISH is a suitable tool for the detection of these TERT rearrangements and thus may be of prognostic relevance.

References

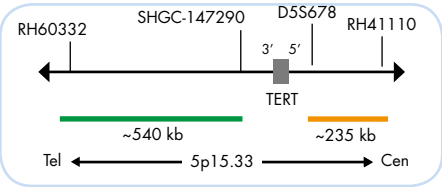
Davis CF, et al. (2014) Cancer Cell 26: 319-30.
Nagel I, et al. (2010) Blood 116: 1317-20.
Pfeifer M, et al. (2015) Nature 526: 700-4.
Schilling G, et al. (2013) Leukemia Res 37: 280-6.

Probe Description

The SPEC TERT Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 5p15.33 band. The orange fluorochrome labeled TERT probe hybridizes proximal to the TERT gene, the green fluorochrome labeled TERT probe hybridizes distal to that gene.



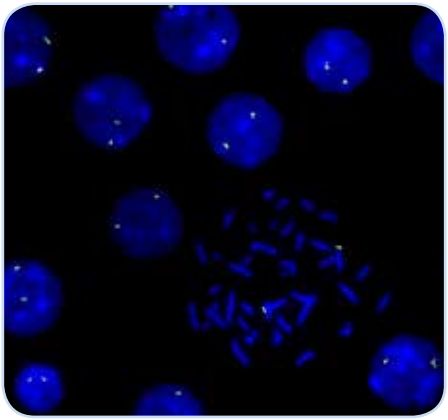
Ideogram of chromosome 5 indicating the hybridization locations.



SPEC TERT Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 5p15.33 band, two orange/green fusion signals are expected, representing two normal (non-rearranged) 5p15.33 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 5p15.33 locus and one 5p15.33 locus affected by a TERT translocation.



SPEC TERT Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals in each nucleus and to metaphase chromosomes of a normal cell.

Prod. No.	Product	Label	Tests* (Volume)
Z-2273-50	ZytoLight SPEC TERT Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC TERT/5q31 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC TERT/5q31 Dual Color Probe is designed for the detection of TERT gene amplifications and chromosomal gains found in a variety of human tumors.

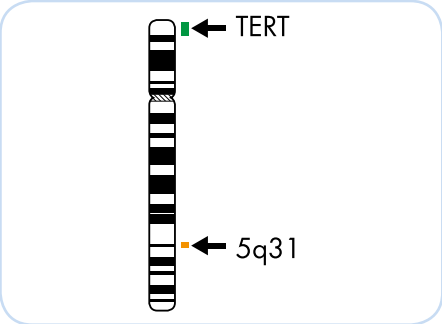
The TERT (telomerase reverse transcriptase) gene is located in the chromosomal region 5p15.33 and encodes the reverse transcriptase component of the human telomerase. Telomerase, the ribonucleoprotein enzyme complex necessary to maintain the ends of chromosomes, is absent from the majority of somatic cells but is present and active in the majority of immortal cell lines and human cancers.

Chromosomal gain or amplification of the TERT gene was found in various human tumors such as lung, cervical, bladder, breast, hepatocellular and colorectal carcinomas as well as in neuroblastoma and melanoma. It was shown that TERT amplification is a poor prognostic factor in non-small cell lung cancer (NSCLC) and is associated with poorly differentiated histopathology of hepatocellular carcinomas. Thus, detection of TERT amplification may have useful applications in cancer diagnosis and prognosis.

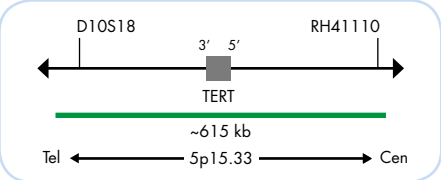
References
Bryce LA, et al. (2000) Neoplasia 2: 197-201.
Cao Y, et al. (2008) Cancer Sci 99: 1092-9.
Morin GB (1989) Nature 353: 454-6.
Takuma Y, et al. (2004) J Gastroenterol Hepatol 19: 1300-4.
Zhu C-Q, et al. (2006) Br J Cancer 94: 1452-9.

Probe Description

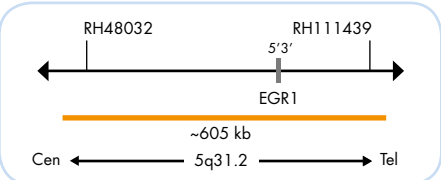
The SPEC TERT/5q31 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC TERT probe hybridizing to the TERT gene in the chromosomal region 5p15.33 and an orange fluorochrome direct labeled SPEC 5q31 probe specific for the chromosomal region 5q31.2 harboring the EGR1 gene. Since chromosomes 1, 5, and 19 share the same repetitive sequences, probes specific for 5q31.2 are commonly used for chromosome 5 copy number detection.



Ideogram of chromosome 5 indicating the hybridization locations.



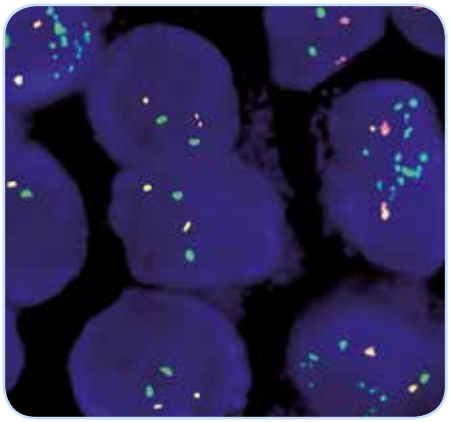
SPEC 5p15 Probe map (not to scale).



SPEC 5q31 Probe map (not to scale).

Results

In a normal interphase nucleus two orange and two green signals are expected.
In a cell with amplification of the TERT gene locus or aneuploidy of chromosome 5, multiple copies of the green signal or green signal clusters will be observed.



SPEC TERT/5q31 Dual Color Probe hybridized to melanoma tissue section showing normal cells as indicated by two green and two orange signals in each nucleus and cells with TERT gene amplification as indicated by multiple green signals per nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2091-50	ZytoLight SPEC TERT/5q31 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2091-200	ZytoLight SPEC TERT/5q31 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC RICTOR/5q31.1 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC RICTOR/5q31.1 Dual Color Probe is designed to detect amplifications affecting the chromosomal region 5p13.1 harboring the RICTOR (RPTOR independent companion of MTOR complex 2, a.k.a. AVO3, KIAA1999) gene.

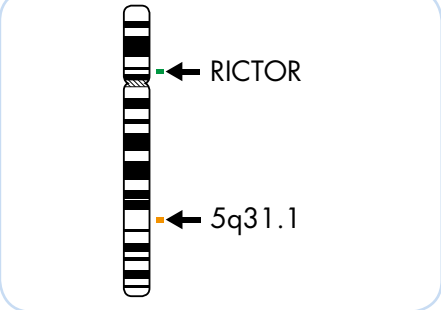
RICTOR is part of the RICTOR-mTOR protein complex which is involved in the phosphorylation and regulation of the AKT/Protein Kinase B (PKB) which in turn triggers cell proliferation and cell survival. Amplification of the RICTOR gene region leads to a dysregulation of PKB, known to be a responsible factor in tumor pathogenesis.

In 8-13% of non-small cell lung carcinomas (NSCLC) and small cell lung cancer (SCLC) an amplification of the RICTOR gene region has been demonstrated. Amplifications of the RICTOR gene region represent one of the most abundant genetic events in SCLC patients. Hence, RICTOR amplifications have been proposed as biomarker for a targeted therapy with mTOR inhibitory agents in patients diagnosed with lung cancer. Fluorescence *in situ* Hybridization may be a suitable diagnostic tool for the detection of RICTOR amplifications.

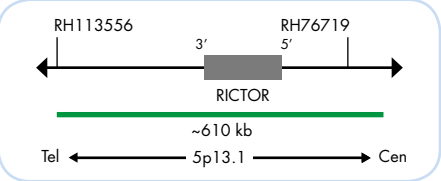
References
Cheng H, et al. (2015) Cancer Discov 5: 1262-70.
Ross JS, et al. (2014) J Clin Pathol 67: 772-6.
Sarbassov DD, et al. (2005) Science 307: 1098-101.

Probe Description

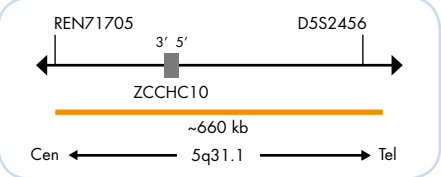
The SPEC RICTOR/5q31.1 Dual Color Probe is a mixture of a green fluorochrome direct labeled probe spanning the RICTOR gene region at 5p13.1 and an orange fluorochrome direct labeled SPEC 5q31.1 probe specific for the chromosomal region 5q31.1 harboring the ZCCHC10 gene.



Ideogram of chromosome 5 indicating the hybridization locations.



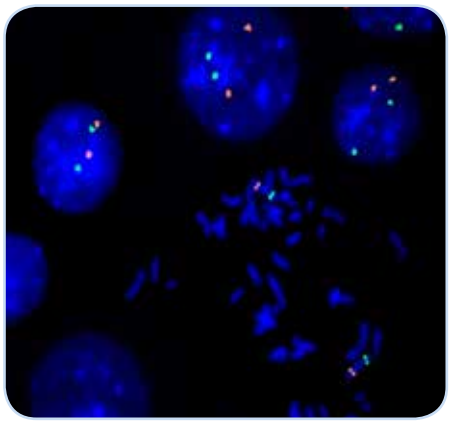
SPEC RICTOR Probe map (not to scale).



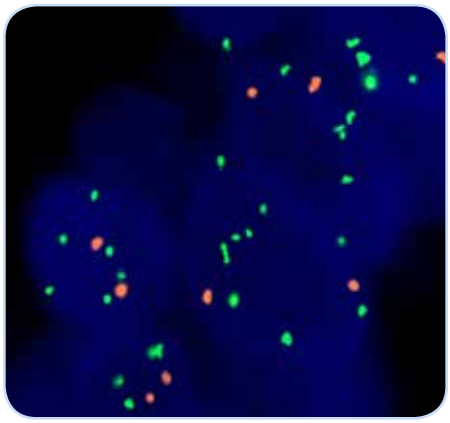
SPEC 5q31.1 Probe map (not to scale).

Results

Using the SPEC RICTOR/5q31.1 Dual Color Probe in a normal interphase nucleus, two orange and two green signals are expected. In a cell with gain of the RICTOR gene locus, multiple copies of the green signal or green signal clusters will be observed.



SPEC RICTOR/5q31.1 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus and to metaphase chromosomes of a normal cell.



Squamous cell carcinoma section with RICTOR amplification as indicated by multiple green signals in each nucleus.

Kindly provided by Prof. Dr. Schildhaus, Essen, Germany.

Prod. No.	Product	Label	Tests* (Volume)
Z-2278-200	ZytoLight SPEC RICTOR/5q31.1 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC EGR1/5p15 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC EGR1/5p15 Dual Color Probe is designed for the detection of EGR1 gene deletions.

The EGR1 (early growth response 1) gene is located in the chromosomal region 5q31.2. Deletions spanning the region 5q31.2 are among the most common reoccurring abnormalities detectable in myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML).

The EGR1 protein belongs to the EGR family of C2H2-type zinc-finger proteins. It is a nuclear protein and functions as a transcriptional regulator.

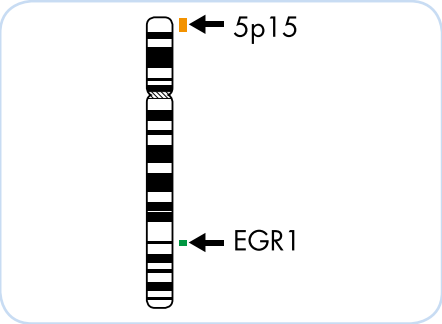
Deletion of EGR1 in estrogen receptor negative (ER-) breast carcinomas is correlated with a higher tumor grade, suggesting that loss of the EGR1 gene (and thereby loss of functioning EGR1 protein) may contribute to the pathogenesis of ER- breast carcinomas.

In patients with therapy-related MDS and AML, dicentric chromosomes have often been observed. In such conditions, many patients show a complex karyotype with several marker chromosomes unidentifiable by conventional cytogenetics. Fluorescence *in situ* Hybridization (FISH) has now made the characterization of these rearrangements much easier.

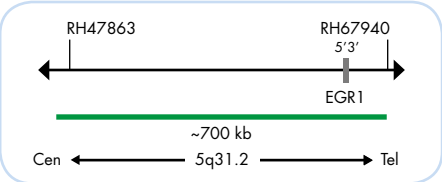
References
Graubert TA, et al. (2009) PLoS One 4: e4583.
Herry A, et al. (2007) Cancer Genet Cytogenet 175: 125-31.
Ronski K, et al. (2005) Cancer 104: 925-30.
Sun Y & Cook JR (2010) Leuk Res 34: 340-3.

Probe Description

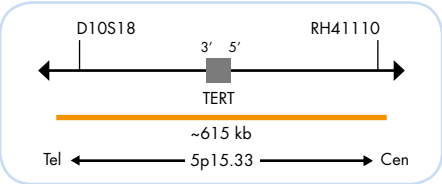
The SPEC EGR1/5p15 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC EGR1 probe hybridizing to the EGR1 gene in the chromosomal region 5q31.2 and an orange fluorochrome direct labeled SPEC 5p15 probe specific for the chromosomal region 5p15.33.



Ideogram of chromosome 5 indicating the hybridization locations.



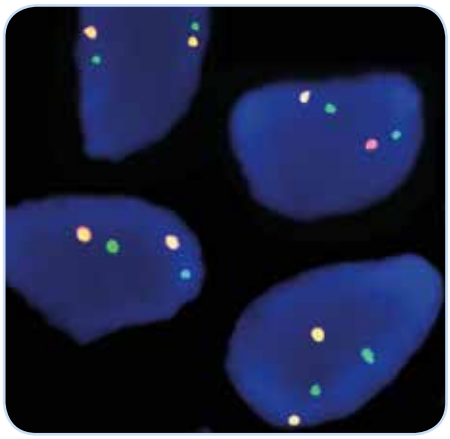
SPEC EGR1 Probe map (not to scale).



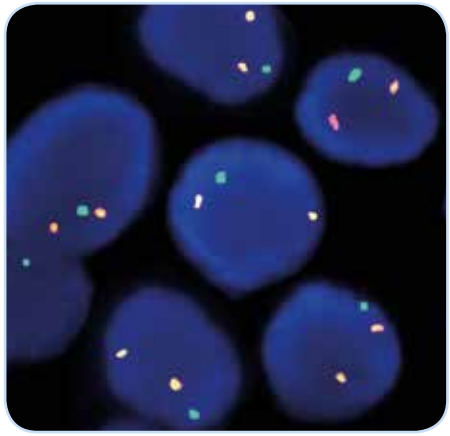
SPEC 5p15 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletions affecting the EGR1 gene locus, one or no copy of the green signal will be observed.



SPEC EGR1/5p15 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



SPEC EGR1/5p15 Dual Color Probe hybridized to bone marrow biopsy section with deletion of the EGR1 gene as indicated by one green signal and two orange signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2107-50	ZytoLight SPEC EGR1/5p15 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2107-200	ZytoLight SPEC EGR1/5p15 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC EGR1/D5S23,D5S721 Dual Color Probe

CE IVD

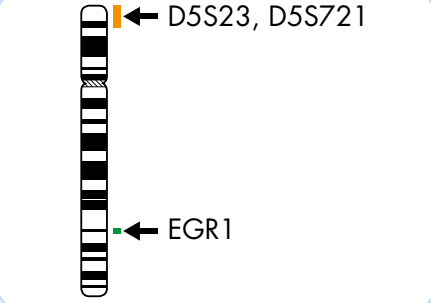
Background

The ZytoLight® SPEC EGR1/D5S23, D5S721 Dual Color Probe is designed for the detection of EGR1 gene deletions.
The EGR1 (early growth response 1) gene is located in the chromosomal region 5q31.2 and encodes a zinc finger transcription factor which is associated with cell proliferation, differentiation, and transformation.
Deletions spanning the region 5q31.2 are among the most common reoccurring abnormalities detectable in myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML). In therapy-related MDS or AML, 40% of the patients exhibit a 5q deletion.
Deletion of EGR1 in estrogen receptor negative (ER-) breast carcinomas is correlated with a higher tumor grade, suggesting that loss of the EGR1 gene may contribute to the pathogenesis of ER- breast carcinomas.
Transfusion-dependent, lower-risk MDS patients with 5q deletion are treated with the thalidomide analog lenalidomide which is approved by the FDA.
In patients with *de novo* or therapy-related MDS and AML, dicentric chromosomes, involving chromosome 5, have often been observed. These patients frequently show a complex karyotype. In such conditions the characterization of rearrangement is nearly not feasible by conventional cytogenetics. Hence, Fluorescence *in situ* Hybridization (FISH) may be a helpful tool for diagnosis and therapy decisions.

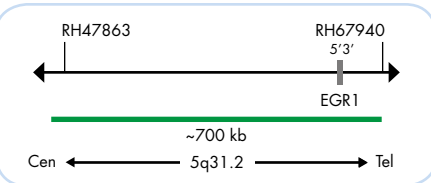
References
Boultwood J, et al. (2010) Blood 116: 5803-11.
Coleman JF, et al. (2011) Am J Clin Pathol 135: 915-20.
Herry A, et al. (2007) Cancer Genet Cytogenet 175: 125-31.
Horrigan SK, et al. (2000) Blood 95: 2372-7.
Sukhatme V, et al. (1988) Cell 53: 37-43.
Sun Y & Cook JR (2010) Leuk Res 34: 340-3.
Tian J, et al. (2016) Intractable Rare Dis Res 5: 76-82.
Wei S, et al. (2009) Proc Natl Acad Sci U S A 106: 12974-9.
Zhao N, et al. (1997) Proc Natl Acad Sci U S A 94: 6948-53.

Probe Description

The SPEC EGR1/D5S23,D5S721 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC EGR1 probe hybridizing to the EGR1 gene in the chromosomal region 5q31.2 and an orange fluorochrome direct labeled SPEC D5S23,D5S721 probe specific for the chromosomal region 5p15.2-p15.31. Since in diverse solid tumors the chromosomal region 5p15.33 is affected by amplifications, probes targeting the D5S23,D5S721 region are more suitable for the enumeration of chromosome 5.



Ideogram of chromosome 5 indicating the hybridization locations.

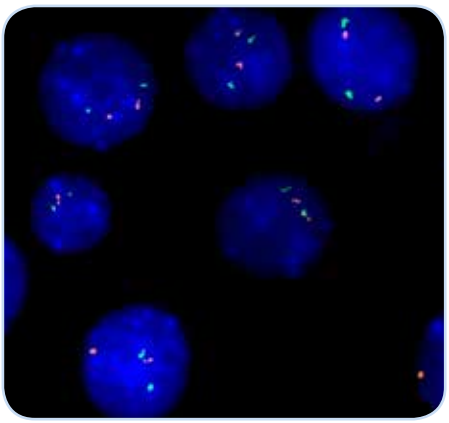


SPEC EGR1 Probe map (not to scale).

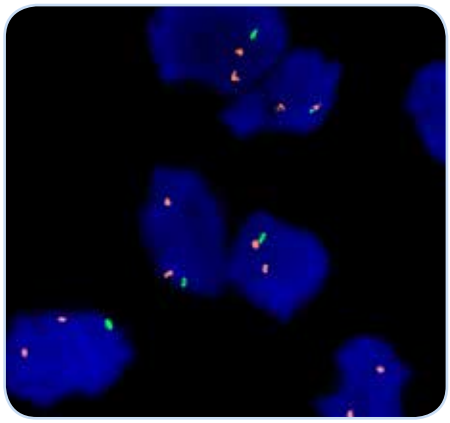
SPEC D5S23,D5S721 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletion of the EGR1 gene locus, one or no copy of the green signal will be observed.



SPEC EGR1/D5S23,D5S721 Dual Color Probe hybridized to normal interphase calls as indicated by two orange and two green signals in each nucleus.



SPEC EGR1/D5S23,D5S721 Dual Color Probe hybridized to an ALL specimen with deletion of the EGR1 gene as indicated by one green and two orange signals in each nucleus.

Specimens kindly provided by Paediatric Oncology/Haematology, Charité - Universitätsmedizin Berlin, Germany.

Prod. No.	Product	Label	Tests* (Volume)
Z-2211-50	ZytoLight SPEC EGR1/D5S23,D5S721 Dual Color Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC CSF1R Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC CSF1R Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal region 5q32 harboring the CSF1R (colony stimulating factor 1 receptor, a.k.a. FMS) gene.

The CSF1 receptor is activated by dimerization upon binding of its ligand CSF1 and is involved in macrophage development.

Rearrangement of the CSF1R gene was first detected in an acute megakaryoblastic leukemia (AMKL) cell line generating the RBM6-CSF1R fusion gene. A MEF2D-CSF1R fusion gene was described in a patient with primary pre-B cell acute lymphoblastic leukemia (pre-B ALL). Both fusion proteins contain the intact kinase domain of CSF1R.

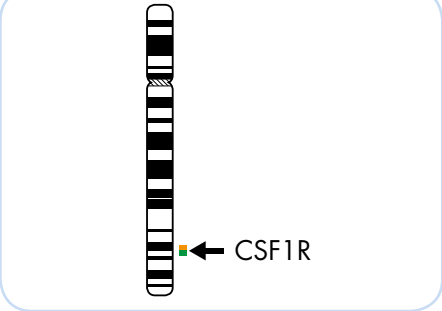
Philadelphia chromosome-like ALL (Ph-like ALL) is a subgroup of B-cell precursor ALL and is associated with a high risk of treatment failure. SSBP2-CSF1R fusions were detected in some patients with Ph-like ALL. They result from either the balanced translocation t(5;5)(q14;q32) or the duplication dup(5)(q14q32). Expression of this fusion gene results in cytokine-independent growth and enhanced STAT5 activation which are inhibited by dasatinib *in vitro*. CSF1R signaling was also shown to be suppressed by the ABL1 kinase inhibitor imatinib.

Hence, the detection of CSF1R rearrangements by FISH may help in selecting ALL patients eligible for treatment with CSF1R inhibitors.

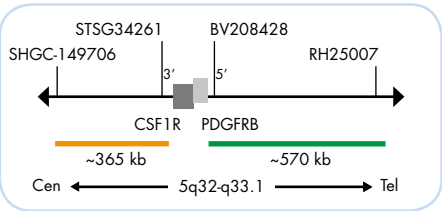
References
Dewar AL, et al. (2005) Blood 105: 3127-32.
Gu TL, et al. (2007) Blood 110: 323-33.
Lilljebjörn H, et al. (2014) Leukemia 28: 977-9.
Roberts KG, et al. (2014) N Engl J Med 371: 1005-15.
Schwab C, et al. (2014) Blood 124: 3773.

Probe Description

The SPEC CSF1R Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 5q32-q33.1 band. The orange fluorochrome direct labeled probe hybridizes proximal to the CSF1R gene at 5q32, the green fluorochrome direct labeled probe hybridizes distal to the CSF1R gene at 5q32-q33.1.



Ideogram of chromosome 5 indicating the hybridization locations.

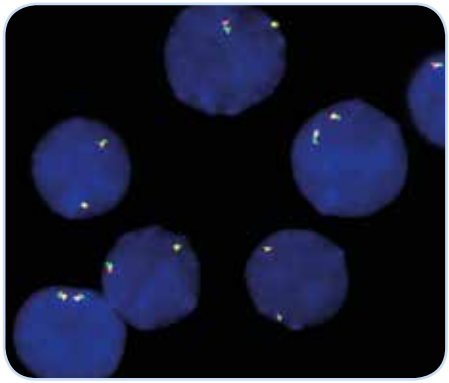


SPEC CSF1R Probe map (not to scale).

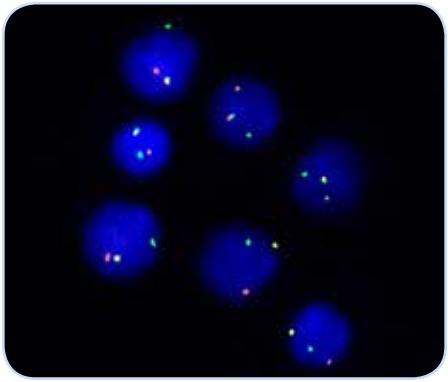
Results

In an interphase nucleus of a normal cell lacking a translocation involving the 5q32-q33.1 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 5q32-q33.1 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 5q32-q33.1 locus and one 5q32-q33.1 locus affected by a translocation.

Duplication of the 5q32 locus will result in additional orange signals.



SPEC CSF1R Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Blood smear with translocation of the CSF1R gene as indicated by one non-rearranged orange/green fusion signal, one orange and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2202-50	ZytoLight SPEC CSF1R Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC CSF1R/D5S23,D5S721 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC CSF1R/D5S23,D5S721 Dual Color Probe is designed for the detection of 5q deletions. The CSF1R (colony stimulating factor 1 receptor, a.k.a. C-FMS) gene is located in the chromosomal region 5q32.

The interstitial deletion of chromosome 5q is a characteristic hallmark of the myelodysplastic syndrome (MDS) with isolated del(5q). The size of the deletion as well as the breakpoints are variable but a commonly deleted region (CDR) has been narrowed to the approximately 1.5 Mb interval at 5q32-q33.1 flanked by the DNA marker D5S413 and the GLRA1 gene.

One candidate gene for the development of MDS in patients with 5q- syndrome is RPS14 (ribosomal protein 14), a tumor suppressor gene located in the chromosomal region 5q33.1. Haploinsufficiency (caused by hemizygous deletion) of RPS14 is the probable cause of the erythroid defect that characterizes the 5q- syndrome. Lenalidomide has been reported to overcome the pathogenic effect of 5q deletion in MDS.

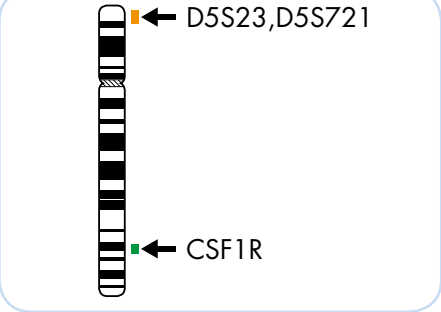
Despite the severe phenotype of the 5q- syndrome, it has a relatively low (10%) transformation risk to acute myeloid leukemia (AML). Therefore, FISH may be a helpful tool for diagnosis and therapy decision.

References

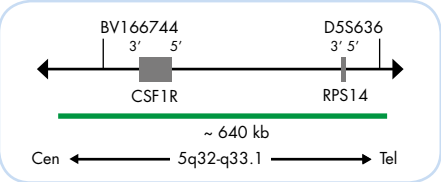
Boultwood J, et al. (1991) Proc Natl Acad Sci U S A 88: 6176-80.
Boultwood J, et al. (2010) Blood 116: 5803-11.
Giagounidis AA, et al. (2004) Clin Cancer Res 12: 5-10.
Van den Berghe H & Michaux JL (1974) Nature 251: 437-8.
Swerdlow SH, et al. (ed.) (2008) WHO classification of tumours of haematopoietic and lymphoid tissues.

Probe Description

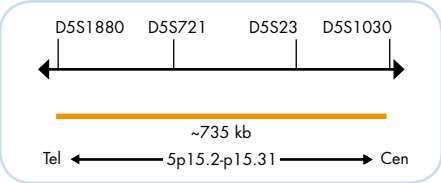
The SPEC CSF1R/D5S23,D5S721 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC CSF1R probe hybridizing to the CSF1R gene in the chromosomal region 5q32-q33.1 and an orange fluorochrome direct labeled SPEC D5S23,D5S721 probe specific for the chromosomal region 5p15.2-p15.31.



Ideogram of chromosome 5 indicating the hybridization locations.



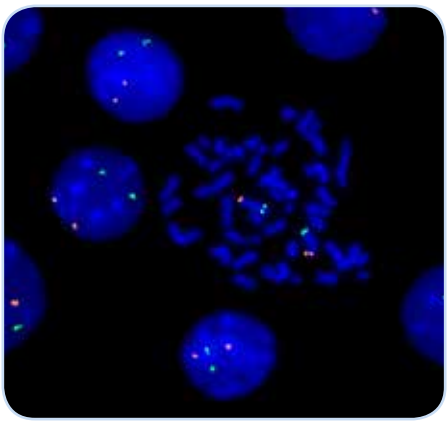
SPEC CSF1R Probe map (not to scale).



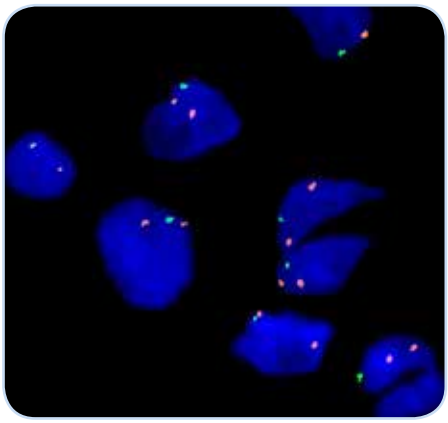
SPEC D5S23,D5S721 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletion of the CSF1R gene locus, one or no copy of the green signal will be observed.



SPEC CSF1R/D5S23,D5S721 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus and to metaphase chromosomes of a normal cell.



Bone marrow biopsy tissue section of an ALL case showing hemizygous deletion of the CSF1R gene as indicated by the loss of one green signal in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2268-50	ZytoLight SPEC CSF1R/D5S23,D5S721 Dual Color Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC PDGFRB Dual Color Break Apart Probe

CE IVD

Background

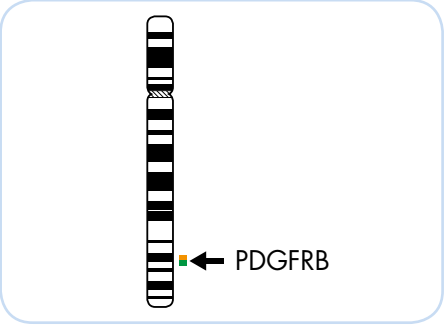
The ZytoLight® SPEC PDGFRB Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 5q32 harboring the PDGFRB gene. The PDGFRB (platelet derived growth factor receptor beta) gene encodes a transmembrane glycoprotein that belongs to the type III receptor tyrosine kinase family and has a key role in a variety of cellular processes.

Translocations involving the PDGFRB gene are rare genetic disorders and are identified in myelodysplastic/myeloproliferative neoplasms (MDS/MPNs), chronic myeloproliferative disorders (CMPD), acute myeloid leukemia (AML), and also in atypical (BCR-ABL1-negative) chronic myeloid leukemia/chronic myelomonocytic leukemia (CML/CMML)-like diseases, often with eosinophilia and splenomegaly. The most common translocation involving PDGFRB is the t(5;12)(q32;p13.2). Result of this translocation is the fusion protein ETV6-PDGFRB, in which the pointed domain of ETV6 is juxtaposed next to the transmembrane and entire tyrosine kinase domain of PDGFRB. As a result, the tyrosine kinase is constitutively activated leading to hematopoietic cell proliferation. Patients with myeloid malignancies bearing PDGFRB fusion genes were shown to achieve durable long-term remissions under imatinib treatment. Recent studies revealed that sorafenib is a further potential inhibitor of patients with ETV6-PDGFRB translocation.

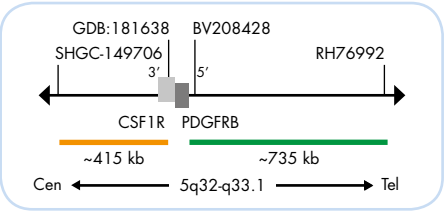
References
Bain BJ (2010) Haematologica 95: 696-8.
Cross NC & Reiter A (2008) Acta Haematol 119: 199-206.
Jones AV & Cross NC (2004) Cell Mol Life Sci 61: 2912-23.
Keene P, et al. (1987) Br J Haematol 67: 25-31.
Lierman E, et al. (2007) Haematologica 92: 27-34.
Savage N, et al. (2013) Int J Lab Hematol 35: 491-500.
Steer EJ & Cross NC (2002) Acta Haematol 107: 113-22.
Vega F, et al. (2015) Am J Clin Pathol 144: 377-92.

Probe Description

The SPEC PDGFRB Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 5q32-q33.1 band. The green fluorochrome direct labeled probe hybridizes distal to the PDGFRB gene, and the orange fluorochrome direct labeled probe hybridizes proximal to the PDGFRB locus.



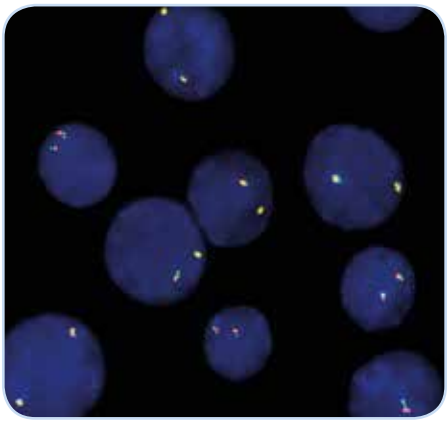
Ideogram of chromosome 5 indicating the hybridization locations.



SPEC PDGFRB Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 5q32-q33.1 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 5q32-q33.1 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 5q32-q33.1 locus and one 5q32-q33.1 locus affected by a translocation.



SPEC PDGFRB Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2197-50	ZytoLight SPEC PDGFRB Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC IRF4,DUSP22 Dual Color Break Apart Probe

CE IVD

Background

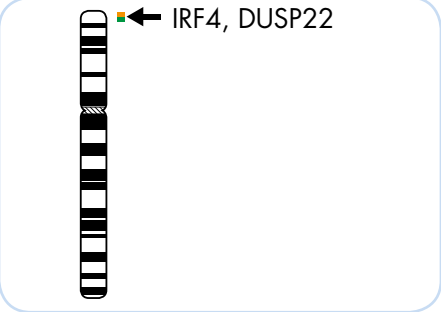
The ZytoLight® SPEC IRF4,DUSP22 Dual Color Break Apart Probe is designed for the detection of translocations involving the chromosomal region 6p25.3 harboring the DUSP22 (dual specificity phosphatase 22, a.k.a. JKAP) and IRF4 (interferon regulatory factor 4, a.k.a. MUM1) genes.

IRF4 is normally expressed in plasma cells, melanocytes, some B-cells, and in activated T-cells. The IRF4 protein is required at several stages of B-cell development, and is also critical for T-cell differentiation. Rearrangements of the IRF4/DUSP22 chromosomal region have been detected in various B-cell and T-cell lymphomas. Large B-cell lymphoma (LBCL) with IRF4 rearrangement, which occurs most commonly in children and young adults, is considered a distinct new provisional entity. These lymphomas most typically occur in Waldeyer ring and/or cervical lymph nodes. Most cases have IG/IRF4 fusions and have a favorable prognosis. Rearrangements of IRF4 and/or DUSP22 have also been described in peripheral T-cell lymphomas and in cutaneous anaplastic large cell lymphoma (ALCL). ALCL is difficult to distinguish from other CD30-positive T-cell lymphoproliferative disorders. IRF4 translocation has a high specificity for cutaneous ALCL supporting the clinical utility of FISH for IRF4 in the differential diagnosis of T-cell lymphoproliferative disorders.

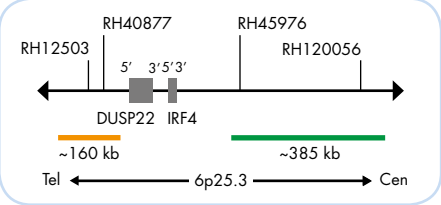
Moreover, DUSP22 rearrangement in ALK-negative ALCL is associated with a favorable outcome indicating the usefulness of DUSP22 as a predictive biomarker.

Probe Description

The SPEC IRF4,DUSP22 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 6p25.3 band. The green fluorochrome direct labeled probe hybridizes proximal and the orange fluorochrome direct labeled probe hybridizes distal to the IRF4 and DUSP22 genes.



Ideogram of chromosome 6 indicating the hybridization locations.

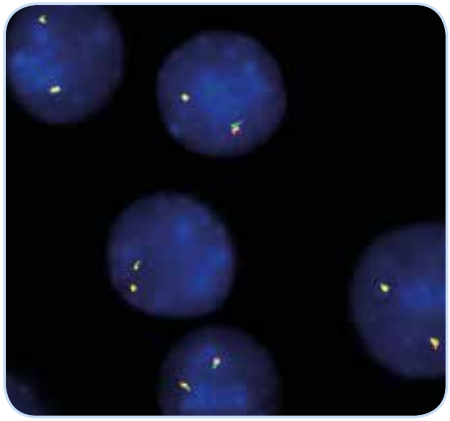


SPEC IRF4, DUSP22 Probe map (not to scale).

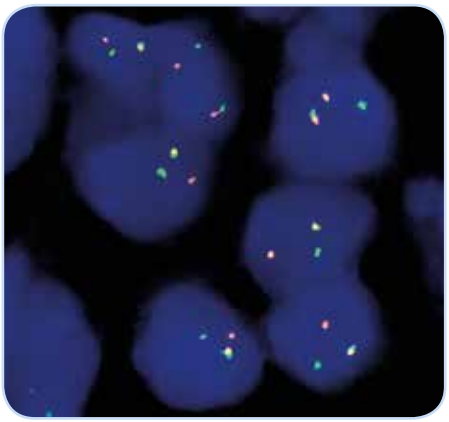
References
Iida S, et al. (1997) Nat Genet 17: 226-30.
Parrilla Castellar ER, et al. (2014) Blood 124: 1473-80.
Pham-Ledard A, et al. (2010) J Invest Dermatol 130: 816-25.
Salaverria I, et al. (2011) Blood 118: 139-47.
Swerdlow SH, et al. (2016) Blood 127: 2375-90.
Wada DA, et al. (2011) Mod Pathol 24: 596-605.

Results

In an interphase nucleus lacking a translocation involving the 6p25.3 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 6p25.3 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 6p25.3 locus and one 6p25.3 locus affected by a translocation.



SPEC IRF4, DUSP22 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



T-cell lymphoma tissue section with translocation affecting the 6p25.3 locus as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2210-50	ZytoLight SPEC IRF4,DUSP22 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC RREB1/MYB/CEN 6 Triple Color Probe

CE IVD

Background

The ZytoLight® SPEC RREB1/MYB/CEN 6 Triple Color Probe is designed for the detection of copy number changes of the chromosomal regions harboring the RREB1 and the MYB gene, respectively.

The RREB1 (ras responsive element binding protein 1, a.k.a. HNT) gene is located in 6p24.3 and encodes a zinc finger transcription factor. The MYB (MYB proto-oncogene, transcription factor, a.k.a. c-myb) gene is located in 6q23.3 and encodes a transcription factor that is implicated in proliferation, survival, and differentiation of hematopoietic progenitor cells.

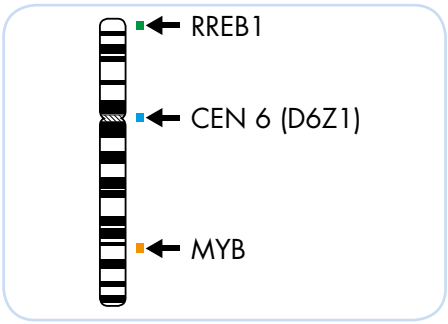
Overexpression of the RREB1 protein was detected in prostate cancer and in a medullary thyroid cancer cell line. RREB1 is suggested to play a role in Ras and Raf signal transduction in medullary thyroid cancer.

MYB has been found to be amplified in a variety of human cancers. In pancreatic cancer, MYB amplification was mainly found in advanced and metastatic tumors. In breast tumors from BRCA1 germline mutation carriers, MYB amplification was observed in 29% of the cases and resulted in overexpression of the MYB protein. Moreover, duplication of the MYB gene occurs in 8.4% of individuals with T-cell acute lymphoblastic leukemia (T-ALL).

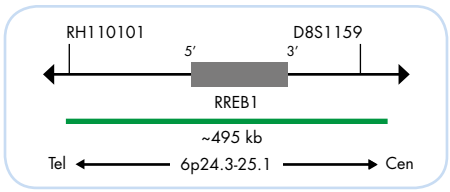
References
Kauraniemi P, et al. (2000) Cancer Res 60: 5323-8.
Lahortiga I, et al. (2007) Nat Genet 39: 593-5.
Thiagalingam A, et al. (1996) Mol Cell Biol 16: 5335-45.
Wallrapp C, et al. (1997) Cancer Res 57: 3135-9.
Zou J, et al. (2011) Prostate 71: 1518-24.

Probe Description

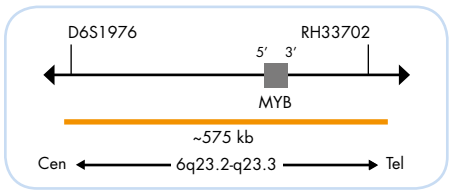
The SPEC RREB1/MYB/CEN 6 Triple Color Probe is a mixture of a green fluorochrome direct labeled SPEC RREB1 probe hybridizing to the RREB1 locus at 6p24.3-p25.1, an orange fluorochrome direct labeled SPEC MYB probe hybridizing to the MYB locus at 6q23.2-q23.3, and a blue fluorochrome direct labeled CEN 6 probe specific for the alpha satellite centromeric region of chromosome 6 (D6Z1).



Ideogram of chromosome 6 indicating the hybridization locations.



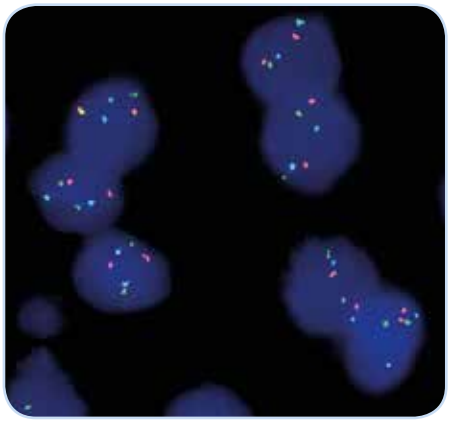
SPEC RREB1 Probe map (not to scale).



SPEC MYB Probe map (not to scale).

Results

In a normal interphase nucleus, two green, two orange, and two blue signals are expected. In a cell with amplification of the RREB1 or the MYB gene locus, multiple copies of the green or orange signal will be observed, respectively. In a cell with deletion of the RREB1 or the MYB gene locus, a reduced number of green or orange signals will be observed, respectively.



SPEC RREB1/MYB/CEN 6 Triple Color Probe hybridized to normal interphase cells as indicated by two green, two orange, and two blue signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2152-50	ZytoLight SPEC RREB1/MYB/CEN 6 Triple Color Probe CE IVD	●/●/●	5 (50 µl)
Z-2152-200	ZytoLight SPEC RREB1/MYB/CEN 6 Triple Color Probe CE IVD	●/●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC PHF1 Dual Color Break Apart Probe

CE IVD

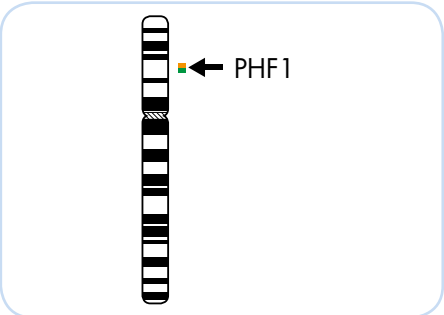
Background

The ZytoLight® SPEC PHF1 Dual Color Break Apart Probe is designed for the detection of translocations involving the chromosomal region 6p21.32 harboring the PHF1 (PHD finger protein 1, a.k.a. MTF2L2, PCL1) gene. The PHF1 protein is known to affect processes, such as development and cell proliferation, through modulation of histone H3 methylation. Endometrial stromal tumors (ESTs) are the second most common pure mesenchymal tumors of the uterus. ESTs may pose diagnostic challenges particularly when they exhibit variant histologic appearances, involve extrauterine sites, or present as metastatic disease. Several rearrangements involving the genes JAZF1, PHF1, or YWHAE have been identified in ESTs, detection of which may be helpful in the differential diagnosis of these tumors.
PHF1 rearrangements were found to occur in endometrial stromal sarcomas but not in endometrial stromal nodules or undifferentiated endometrial sarcomas.
Moreover, recurrent rearrangements of the PHF1 gene have also been detected in up to 85% of ossifying fibromyxoid tumors (OFMTs) including benign and malignant cases.
Thus, FISH analysis for the detection of PHF1 translocation may also serve as a diagnostic tool to identify OFMT cases.

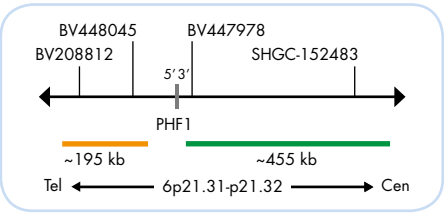
References
Antonescu CR, et al. (2014) Genes Chromosomes Cancer 53: 183-93.
D'Angelo E, et al. (2013) Am J Surg Pathol 37: 514-21.
Gebre-Medhin S, et al. (2012) Am J Pathol 181: 1069-77.
Hodge JC, et al. (2016) J Mol Diagn 18: 516-26.
Micci F, et al. (2006) Cancer Res 66: 107-12.

Probe Description

The SPEC PHF1 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 6p21.31-p21.32 band. The green fluorochrome direct labeled probe hybridizes in 6p21.31-p21.32 proximal and the orange fluorochrome direct labeled probe hybridizes in 6p21.32 distal to the PHF1 gene.



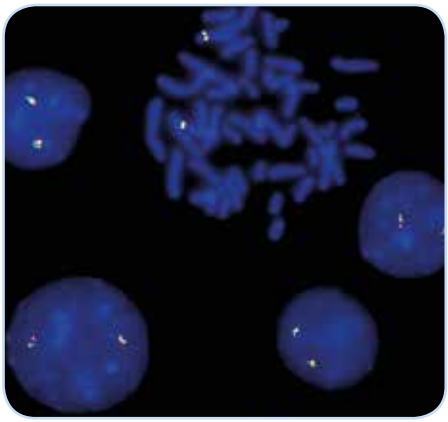
Ideogram of chromosome 6 indicating the hybridization locations.



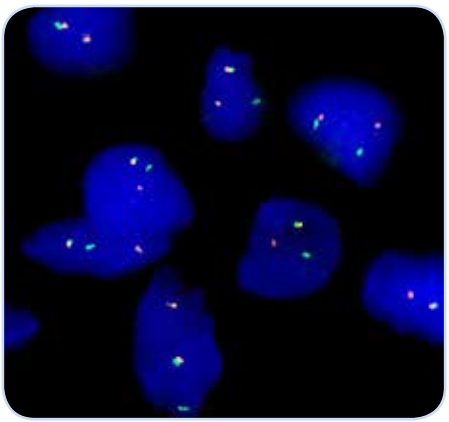
SPEC PHF1 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 6p21.31-p21.32 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 6p21.31-p21.32 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 6p21.31-p21.32 locus and one 6p21.31-p21.32 locus affected by a translocation.
Deletion of 5'-PHF1 sequences is indicated by one or multiple isolated green signals.



SPEC PHF1 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus and to metaphase chromosomes of a normal cell.



Sarcoma tissue section with translocation of the PHF1 gene as indicated by one non-rearranged orange/green fusion signal, one orange, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2215-50	ZytoLight SPEC PHF1 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC VEGFA/CEN 6 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC VEGFA/CEN 6 Dual Color Probe is designed for the detection of amplifications involving the chromosomal region 6p21.1 harboring the VEGFA gene (vascular endothelial growth factor A, a.k.a. VEGF, VPF).

The VEGFA protein is involved in vascular permeability, angiogenesis, cell migration, and inhibition of apoptosis. In addition, binding of VEGFA to its receptors activates the RAS/MEK/MAPK pathway, thus, leading to mitotic activation.

Amplification of the VEGFA gene locus was found in several types of malignancy, such as osteosarcoma, hepatocellular carcinoma (HCC), and colorectal cancers.

In patients with osteosarcoma, VEGFA gene amplification results in elevated expression of VEGFA and is associated with adverse tumor-free survival.

VEGFA amplifications occur in 3-6% of colorectal cancers and result in a highly aggressive disease.

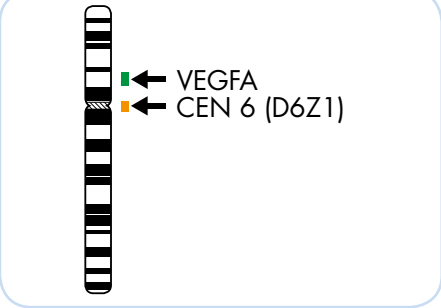
HCC patients with VEGFA gain responded better to sorafenib, a multi-kinase inhibitor that blocks, i.a., receptors of the VEGFA protein, resulting in improved survival of the patients. This suggests that VEGFA is a potential biomarker for response to sorafenib therapy in HCC.

Hence, detection of VEGFA amplifications by Fluorescence *in situ* Hybridization may help in selecting patients eligible for an anti-VEGFA therapy.

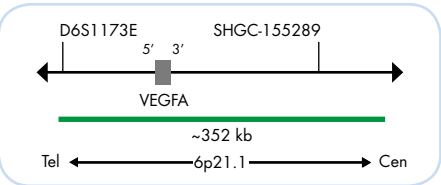
References
Horwitz E, et al. (2014) Cancer Discov 4: 730-43.
Vlajnic T, et al. (2011) Mod Pathol 24: 1404-12.
Yang J, et al. (2011) Cancer 117: 4925-38.

Probe Description

The SPEC VEGFA/CEN 6 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC VEGFA probe specific for the VEGFA gene at 6p21.1 and an orange fluorochrome direct labeled CEN 6 probe specific for the alpha satellite centromeric region of chromosome 6 (D6Z1).



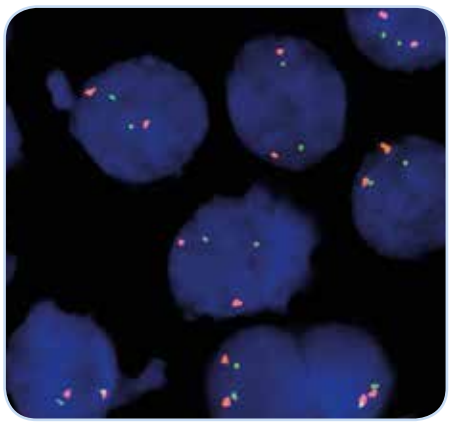
Ideogram of chromosome 6 indicating the hybridization locations.



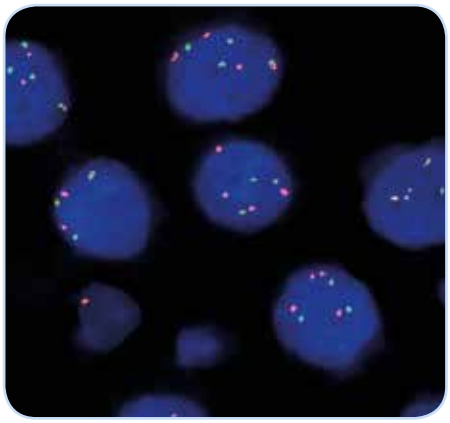
SPEC VEGFA Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the VEGFA gene locus, multiple copies of the green signal or large green signal clusters will be observed.



SPEC VEGFA/CEN 6 Dual Color Probe hybridized to normal interphase calls as indicated by two orange and two green signals in each nucleus.



HCC tissue section with interphase cells showing a polysomy of chromosome 6 as indicated by multiple green (VEGFA) and orange (CEN 6) signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2195-200	ZytoLight SPEC VEGFA/CEN 6 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ROS1 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC ROS1 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 6q22.1 harboring the ROS proto-oncogene 1, receptor tyrosine kinase (ROS1, a.k.a. MCF3) gene.

The ROS1 gene is located on 6q22.1 and encodes a receptor tyrosine kinase. Translocations affecting ROS1 have been detected in glioblastoma, cholangiocarcinoma, and non-small cell lung cancer (NSCLC).

In NSCLC several ROS1 translocation partners have been detected all of which result in the fusion of variably truncated forms of e.g. TPM3, SDC4, SLC34A2, CD74, EZR, or LRIG3 to the kinase domain of ROS1. GOPC has also been found to be fused to ROS1 in NSCLC. GOPC-ROS1 fusions result from interstitial deletion of approx. 240 kb on 6q22.1.

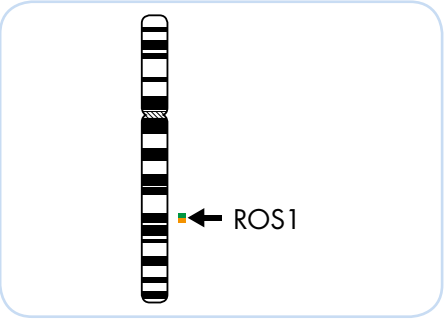
ROS1 rearrangements are thought to define a molecular subset of NSCLC with distinct clinical characteristics that are similar to those observed in patients with ALK rearranged NSCLC.

First evidence suggests that administration of ROS1 kinase inhibitors may represent a very effective therapeutic strategy in NSCLC patients harboring activating ROS1 rearrangements. Accordingly, detection of ROS1 rearrangements using Fluorescence *in situ* Hybridization might be a helpful tool for the identification of patients likely to respond to ROS1 kinase targeting therapies.

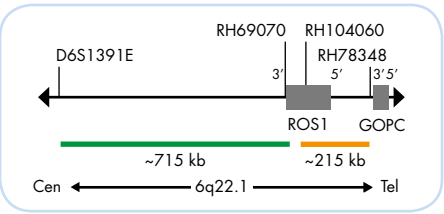
References
Bergethon K, et al. (2012) J Clin Oncol 30: 863-70.
Birchmaier C, et al. (1987) Proc Natl Acad Sci U S A 84: 9270-4.
Bos M, et al. (2013) Lung Cancer 81: 142-3.
Lee SE, et al. (2015) Mod Pathol 28: 468-79.
Rikova K, et al. (2007) Cell 131: 1190-203.
Rimkunas VM, et al. (2012) Clin Cancer Res 18: 4449-57.
Suehara Y, et al. (2012) Clin Cancer Res 18: 6599-608.
Takeuchi K, et al. (2012) Nat Med 18: 378-81.

Probe Description

The SPEC ROS1 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 6q22.1 band. The orange fluorochrome direct labeled probe hybridizes distal, the green fluorochrome direct labeled probe hybridizes proximal to the ROS1 breakpoint region at 6q22.1.



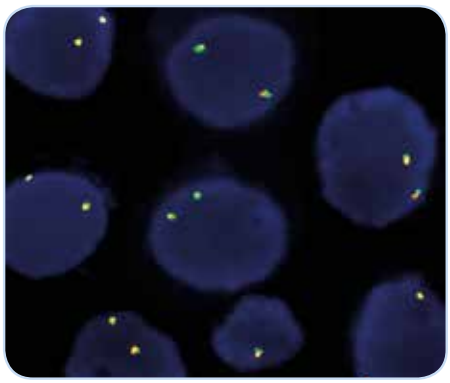
Ideogram of chromosome 6 indicating the hybridization locations.



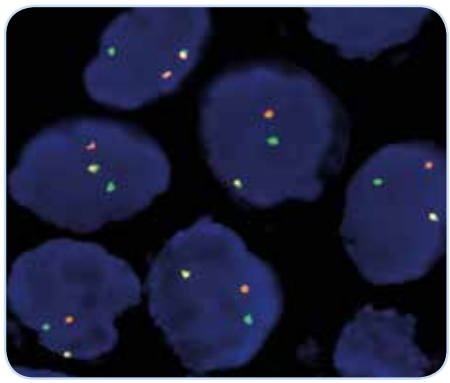
SPEC ROS1 Probe map (not to scale).

Results

In an interphase nucleus lacking an aberration involving the 6q22.1 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 6q22.1 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 6q22.1 locus and one 6q22.1 locus affected by a translocation. Isolated green signals are the result of deletions distal to the ROS1 breakpoint region or are due to unbalanced translocations affecting this chromosomal region.



SPEC ROS1 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Section of paraffin embedded NSCLC cell line with translocation affecting the 6q22.1 locus harboring ROS1 as indicated by one orange/green fusion signal (non-rearranged), one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2144-50	ZytoLight SPEC ROS1 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2144-200	ZytoLight SPEC ROS1 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ROS1/CEN 6 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC ROS1/CEN 6 Dual Color Probe is designed for the detection of amplifications of the chromosomal region harboring the ROS1 gene.

The ROS1 (ROS proto-oncogene 1, receptor tyrosine kinase, a.k.a. MCF3) gene is located on 6q22.1 and encodes a receptor tyrosine kinase of the insulin receptor family. ROS1 has been found to undergo genetic rearrangements in a variety of human cancers including glioblastoma, cholangiocarcinoma, and non-small cell lung cancer (NSCLC).

ROS1 rearrangements, detected in adenocarcinoma of the lung, are thought to define a molecular subset of NSCLC with distinct clinical characteristics that are similar to those observed in patients with ALK rearranged NSCLC. Targeting ROS1 fusion proteins with the kinase inhibitor crizotinib was shown to be a promising and effective therapy in NSCLC patients whose tumors are positive for this genetic aberration.

Recently, copy number gain of the ROS1 gene was reported to occur in NSCLC patients and to be associated with poor prognosis.

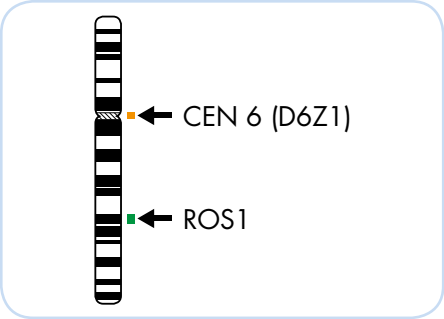
Hence, detection of ROS1 amplification by FISH could help to identify patients who might be selected for further clinical examinations with regard to potential ROS1 targeting treatments.

References

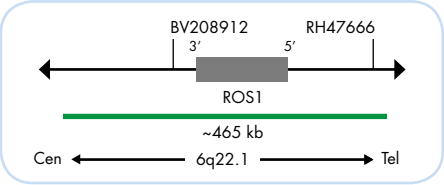
Bergethon K, et al. (2012) J Clin Oncol 30: 863-70.
Bos M, et al. (2013) Lung Cancer 81: 142-3.
Jin Y, et al. (2015) Virchows Arch 466: 45-52.
Mazières J, et al. (2015) J Clin Oncol 33: 992-9.
Takeuchi K, et al. (2012) Nat Med 18: 378-81.

Probe Description

The SPEC ROS1/CEN 6 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 6 probe specific for the alpha satellite centromeric region of chromosome 6 (D6Z1) and a green fluorochrome direct labeled SPEC ROS1 probe specific for the ROS1 gene at 6q22.1.



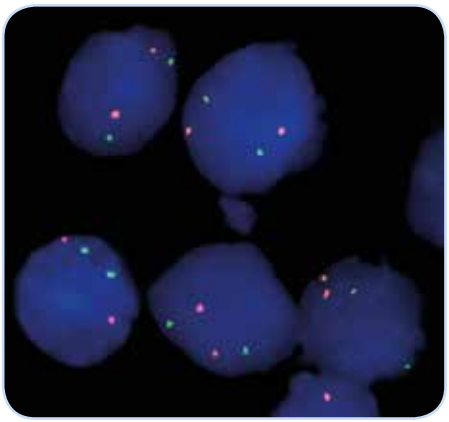
Ideogram of chromosome 6 indicating the hybridization locations.



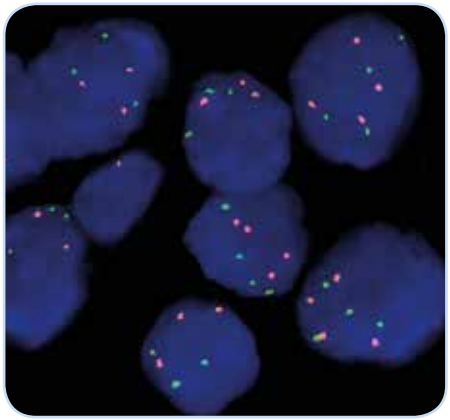
SPEC ROS1 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the ROS1 gene locus, multiple copies of the green signal or green signal clusters will be observed.



SPEC ROS1/CEN 6 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Lung cancer tissue section with interphase cells showing a polysomy of chromosome 6 as indicated by multiple orange (CEN 6) and green (ROS1) signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2162-200	ZytoLight SPEC ROS1/CEN 6 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC MYB Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC MYB Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 6q23.3 harboring the MYB (MYB proto-oncogene, transcription factor, a.k.a. c-myb) gene.

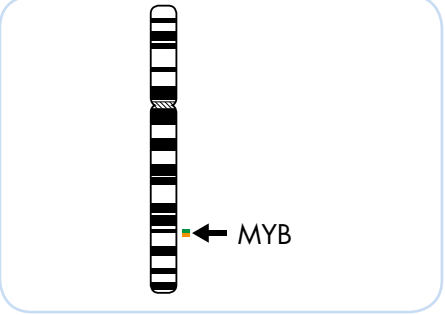
The MYB gene is expressed predominantly in immature progenitor cells of all hematopoietic lineages and is highly expressed in most leukemias and in some solid tumors. Translocations affecting MYB have been detected in T-cell acute lymphoblastic leukemia (T-ALL) and adenoid cystic carcinoma (ACC).

Recent studies have identified a subgroup of T-ALL with reciprocal translocation t(6;7)(q23.3;q34) that juxtaposes MYB and TCRB (T-cell receptor beta locus) leading to the activation of MYB expression. Since the translocation breakpoints in 6q23 map to two clusters located 5 kb and more than 50 kb telomeric of MYB, no true MYB fusion gene is generated. It is assumed that the abnormal MYB expression could confer oncogenic properties and that MYB might represent a potential target for therapeutic intervention in T-ALL.

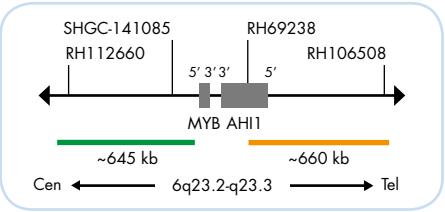
In ACC a recurrent translocation t(6;9)(q22-23;p23-24) is found in about one third of karyotypically abnormal cases. The translocation results in the fusion of the two transcription factor genes MYB and NFIB (nuclear factor I/B) which leads to enhanced expression of the MYB-NFIB fusion protein. The detection of MYB rearrangements using FISH might represent a powerful adjunctive diagnostic tool useful in the differential diagnosis of ACC.

Probe Description

The SPEC MYB Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 6q23.2-q23.3 band. The orange fluorochrome direct labeled probe hybridizes distal and the green fluorochrome direct labeled probe hybridizes proximal to the MYB breakpoint cluster region.



Ideogram of chromosome 6 indicating the hybridization locations.

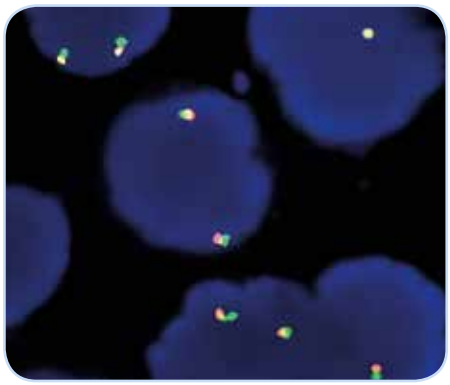


SPEC MYB Probe map (not to scale).

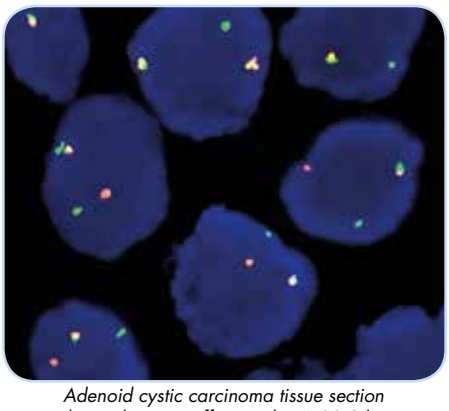
References
Clappier E, et al. (2007) Blood 110: 1251-61.
Persson M, et al. (2009) Proc Natl Acad Sci U S A 106: 18740-4.
Stenman G, et al. (2010) Cell Cycle 9: 2986-95.

Results

In an interphase nucleus lacking a translocation involving the 6q23.2-q23.3 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 6q23.2-q23.3 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 6q23.2-q23.3 locus and one 6q23.2-q23.3 locus affected by a translocation.



SPEC MYB Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Adenoid cystic carcinoma tissue section with translocation affecting the 6q23.3 locus as indicated by one orange/green fusion (non-rearranged) signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2143-50	ZytoLight SPEC MYB Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2143-200	ZytoLight SPEC MYB Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC MYB/CEN 6 Dual Color Probe

CE IVD

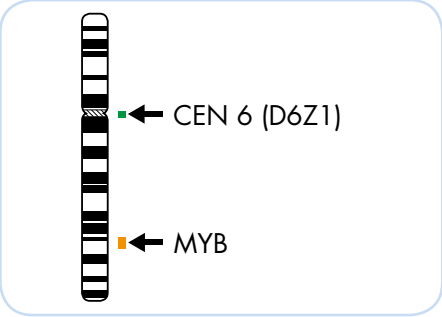
Background

The ZytoLight® SPEC MYB/CEN 6 Dual Color Probe is designed to detect deletions affecting the chromosomal region 6q23.3 harboring the MYB gene.
The MYB (MYB proto-oncogene, transcription factor, a.k.a c-myb) gene encodes for a transcription factor which is primarily expressed in premature lymphoid and myeloid T-cells. Aberrations of 6q are the most commonly found chromosomal changes for different types of lymphoid neoplasms. Several major deletion regions have been detected on the long arm of chromosome 6, one of them is 6q23.
3-10% of chronic lymphocytic leukemia (CLL) cases have been shown to harbor structural aberrations in the chromosomal region 6q. Deletions of MYB often occur as secondary changes indicating disease progression. CLL patients presenting a 6q23 deletion seem to exhibit a more favorable prognosis than patients with 11q23.3 and 17p13 deletions. However, the prognostic relevance of 6q deletions in CLL is still controversially discussed.
Since conventional cytogenetic methods often miss alterations in CLL, investigation by molecular cytogenetic methods such as Fluorescence *in situ* Hybridization (FISH) may be of diagnostic and prognostic relevance.

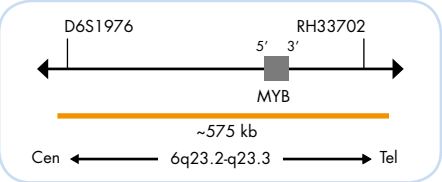
References
Döhner H, et al. (1999) J Mol Med 77: 266-81.
Johansson B, et al. (1993) Genes Chromosomes Cancer 8: 205-18.
Stilgenbauer S, et al. (1999) Leukemia 13: 1331-4.
Urbankova H, et al. (2014) Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 158: 56-64.
Wang DM, et al. (2011) Leuk Lymphoma 52: 230-7.

Probe Description

The SPEC MYB/CEN 6 Dual Color Probe is a mixture of a green fluorochrome direct labeled CEN 6 probe specific for the alpha satellite centromeric region of chromosome 6 (D6Z1) and an orange fluorochrome direct labeled SPEC MYB probe specific for the chromosomal region 6q23.2-23.3 harboring the MYB gene.



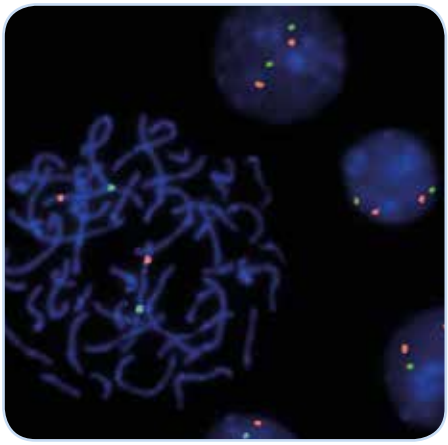
Ideogram of chromosome 6 indicating the hybridization locations.



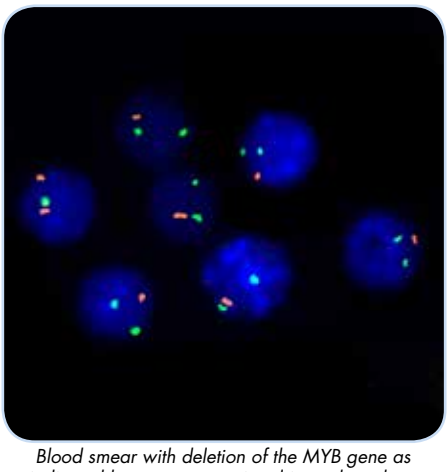
SPEC MYB Probe map (not to scale).

Results

In a normal interphase nucleus, two green and two orange signals are expected.
In a cell with deletion affecting the 6q23.3 locus, one or no copy of the orange signal will be observed.



SPEC MYB/CEN 6 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus and to metaphase chromosomes of a normal cell.



Blood smear with deletion of the MYB gene as indicated by one orange signal in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2281-50	ZytoLight SPEC MYB/CEN 6 Dual Color Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ESR1/CEN 6 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC ESR1/CEN 6 Dual Color Probe is designed for the detection of ESR1 gene amplification frequently observed in breast cancer.

The ESR1 (estrogen receptor 1) gene is located in the chromosomal region 6q25.1 and encodes estrogen receptor alpha (ER). ER expression is one of the most important known factors in the development of breast cancer, and assessing its status by immunohistochemistry is important for determining the use of anti-estrogen receptor therapies.

ESR1 gene amplification has been found frequently in ER-positive breast tumors. Additionally, it has been shown very recently for breast cancer patients receiving adjuvant tamoxifen monotherapy that survival is significantly longer in cases of ESR1 gene amplification as determined by FISH compared to immunohistochemically ER-positive cases without gene amplification. Additionally, it has been shown that response to tamoxifen is dependent on the absolute ESR1 copy number. Thus, determination of ESR1 amplification may identify a subgroup of breast cancer patients particularly likely to respond to anti-estrogen therapy.

References
Burkhardt L, et al. (2010) Breast Cancer Res Treat 123: 757-65.
Holst F, et al. (2007) Nature Genet 39: 655-60.
Lacroix M (2006) Endocr Relat Cancer 13: 1033-67.
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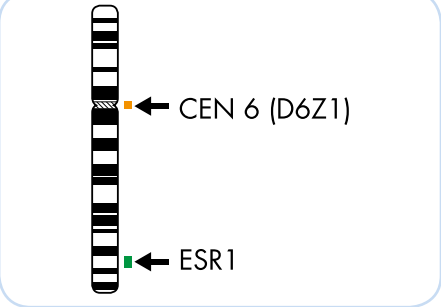
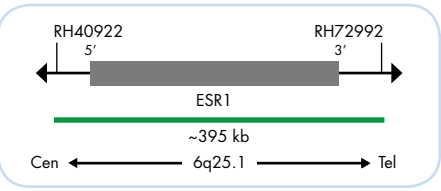
Nembrot M, et al. (1990) Biochem Biophys Res Comm 166: 601-7.
Nessling M, et al. (2005) Cancer Res 65: 439-47.
Pentheroudakis G, et al. (2013) PLoS One 8: e70634.
Rahman MT, et al. (2013) Anticancer Res 33: 3775-81.
Sassen A, et al. (2009) Breast Cancer Res 11: R50.
Tomita S, et al. (2009) Cancer Sci 100: 1012-7.

Probe Description

The SPEC ESR1/CEN 6 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 6 probe specific for the alpha satellite centromeric region of chromosome 6 (D6Z1) and a green fluorochrome direct labeled SPEC ESR1 probe hybridizing to the ESR1 locus at 6q25.1.



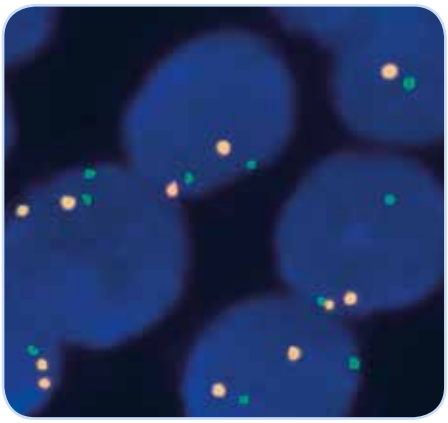
Ideogram of chromosome 6 indicating the hybridization locations.



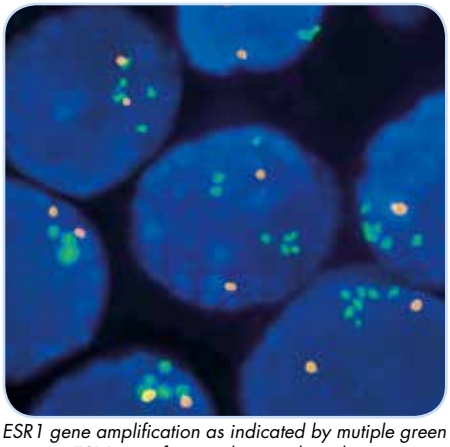
SPEC ESR1 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the ESR1 gene locus, multiple copies of the green signal or green signal clusters will be observed.



SPEC ESR1/CEN 6 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



ESR1 gene amplification as indicated by mutiple green ESR1 specific signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2069-50	ZytoLight SPEC ESR1/CEN 6 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2069-200	ZytoLight SPEC ESR1/CEN 6 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC JAZF1 Dual Color Break Apart Probe

CE IVD

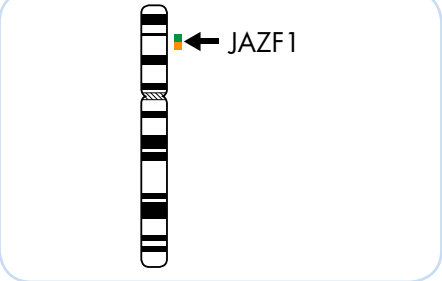
Background

The ZytoLight® SPEC JAZF1 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 7p15.1-p15.2 harboring the JAZF1 (JAZF zinc finger 1) gene.
Translocations involving the region 7p15.1-p15.2 are frequently found in endometrial stromal sarcoma (ESS). The most common cytogenetic abnormality detected in 33-80% of ESS is t(7;17)(p15.1-p15.2;q11.2) which results in the fusion of the JAZF1 gene at 7p15.1-p15.2 to the JJAZ1 (Joined to JAZF1; a.k.a. SUZ12) gene at 17q11.2. Both genes involved contain zinc finger domains characteristic for DNA binding proteins. It was shown that the fusion protein JAZF1-JJAZ1 can promote cell proliferation when the wild-type JJAZ1 is silenced as it is in ESS harboring the t(7;17).
In 25-30% of ESS the JAZF1 gene is disrupted by another translocation t(6;7) where the first zinc finger domain of JAZF1 is fused to both zinc finger domains of the PHF1 (PHD finger protein 1) gene at 6p21.32. As a result the entire coding region of PHF1 is regulated by the JAZF1 promoter.
Since the diagnosis of ESS is often difficult in cases showing diverse histological differentiation or in undifferentiated endometrial sarcoma (UES), the detection of the JAZF1 translocations can serve as a diagnostic tool to confirm the diagnosis of ESS.

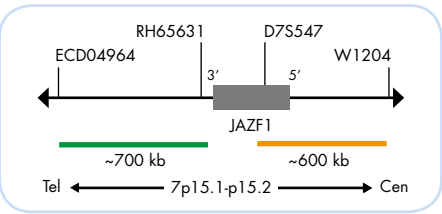
References
Hrzenjak A, et al. (2005) J Mol Diagn 7: 388-95.
Koontz JI, et al. (2001) Proc Natl Acad Sci U S A 98: 6348-53.
Li H, et al. (2007) Proc Natl Acad Sci U S A 104: 20001-6.
Micci F, et al. (2003) Cancer Genet Cytogenet 144: 119-24.

Probe Description

The SPEC JAZF1 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 7p15.1-p15.2 band. The orange fluorochrome direct labeled probe hybridizes proximal, the green fluorochrome direct labeled probe hybridizes distal to the JAZF1 breakpoint region.



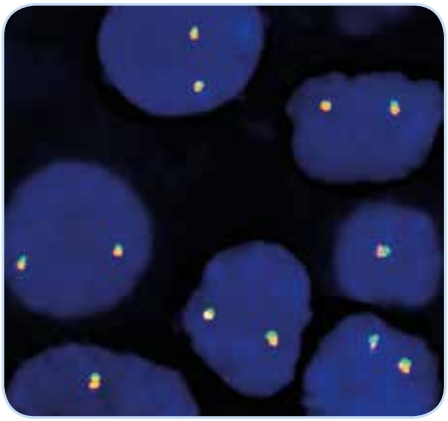
Ideogram of chromosome 7 indicating the hybridization locations.



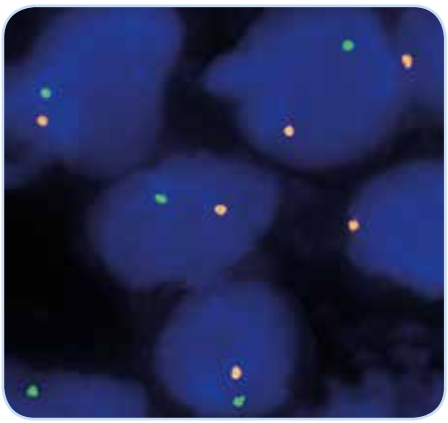
SPEC JAZF1 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 7p15.1-p15.2 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 7p15.1-p15.2 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 7p15.1-p15.2 locus and one 7p15.1-p15.2 locus affected by a translocation.



SPEC JAZF1 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Endometrial stromal sarcoma with translocation affecting JAZF1 at 7p15.1-p15.2 as well as monosomy of chromosome 7 as indicated by one orange and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2132-50	ZytoLight SPEC JAZF1 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC EGFR/CEN 7 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC EGFR/CEN 7 Dual Color Probe is designed for the detection of EGFR gene amplification frequently observed in solid neoplasms including non-small cell lung cancer (NSCLC) and glioblastoma.

The EGFR gene (a.k.a. ERBB1 and HER1) is located in the chromosomal region 7p11.2 and encodes a transmembrane glycoprotein acting as a cellular growth factor receptor. The protein belongs to the EGFR (epidermal growth factor receptor) subgroup of the RTK (receptor tyrosine kinase) superfamily also including ERBB2 (HER2), ERBB3 (HER3), and ERBB4 (HER4).

Overexpression of EGFR has been shown in a number of tumor entities and is associated with poor prognosis. EGFR copy number identified by FISH is thought to be a molecular predictor in neoplasms.

References

Ach T, et al. (2013) Virchows Arch 462: 65-72.
Balla P, et al. (2011) Histopathology 59: 376-89.
Bernardes VM, et al. (2013) BMJ Open 3: e002077.
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Cappuzzo F, et al. (2005) J Natl Cancer Inst 97: 643-55.
Ettl T, et al. (2012) Br J Cancer 106: 719-26.
Ettl T, et al. (2014) Head Neck 36: 517-23.
Gogas H, et al. (2010) Clin Breast Cancer 10: 230-7.
Gonçalves A, et al. (2008) BMC Cancer 8: 169ff.
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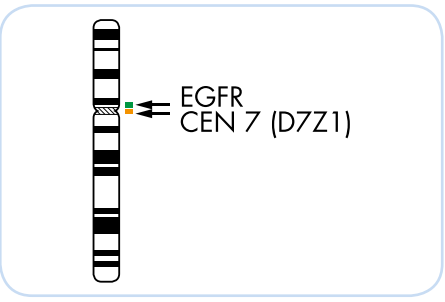
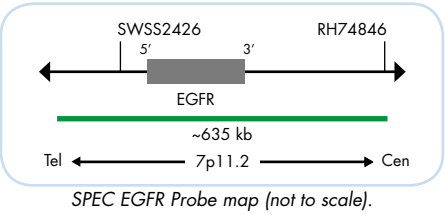
Libermann TA, et al. (1985) J Cell Sci Suppl 3: 161-72.
Merlino GT, et al. (1985) J Clin Invest 75: 1077-9.
Murray S, et al. (2012) J Exp Clin Cancer Res 31: 77.
Projetti F, et al. (2013) Human Pathology 44: 2116-25.
Sassen A, et al. (2008) Breast Cancer Res 10: R2.
Sassen A, et al. (2009) Breast Cancer Res 11: R50.
Tovey SM, et al. (2004) Breast Cancer Res 6: 246-51.

Probe Description

The SPEC EGFR/CEN 7 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 7 probe specific for the alpha satellite centromeric region of chromosome 7 (D7Z1) and a green fluorochrome direct labeled SPEC EGFR probe specific for the EGFR gene at 7p11.2



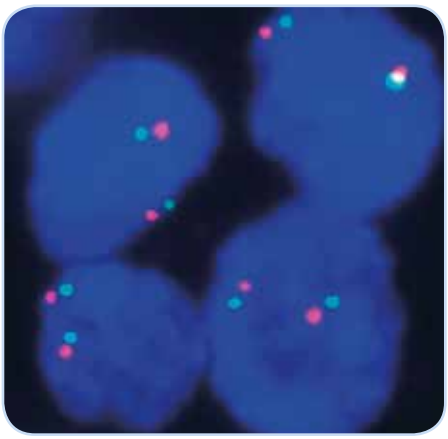
Ideogram of chromosome 7 indicating the hybridization locations.



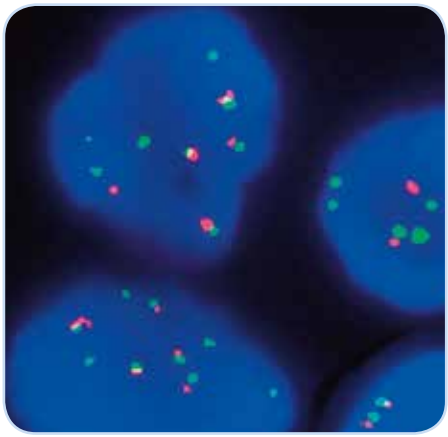
SPEC EGFR Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the EGFR gene locus, multiple copies of the green signal or green signal clusters will be observed.



SPEC EGFR/CEN 7 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Cancer cells with multiple copies of chromosome 7 and extra EGFR signals (green) in sputum sample from an NSCLC patient.

Prod. No.	Product	Label	Tests* (Volume)
Z-2033-50	ZytoLight SPEC EGFR/CEN 7 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2033-200	ZytoLight SPEC EGFR/CEN 7 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC CUX1/EZH2/CEN 7 Triple Color Probe

CE IVD

Background

The ZytoLight® SPEC CUX1/EZH2/CEN 7 Triple Color Probe is designed to detect losses of an entire chromosome 7 (monosomy 7) and deletions of the long arm of chromosome 7 (del(7q)).

In myeloid disorders, monosomy 7 or del(7q) are among the most common recurrent chromosome abnormalities. These aberrations occur in 8% of *de novo* acute myeloid leukemia (AML), in 5-10% of *de novo* patients with myelodysplastic syndrome (MDS), and in approximately 50% of therapy-related myeloid neoplasms. Myeloid malignancies with monosomy 7 or del(7q) respond poorly to chemotherapy and are associated with an unfavorable prognosis.

Several commonly deleted regions (CDRs) located on 7q have been identified in MDS and AML, including CDRs at 7q22, 7q32-33, and 7q35-36.

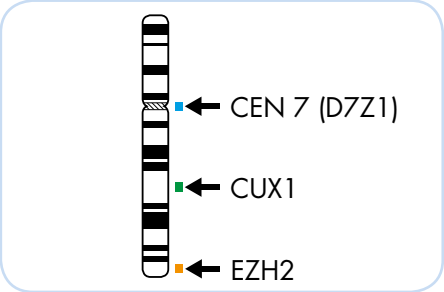
Loss of one or more yet unidentified tumor suppressor gene(s) is thought to contribute to leukemic growth in myeloid malignancies with -7/del(7q). CUX1 is a transcription factor encoded in the CDR at 7q22 that exerts tumor suppressor activity by regulating proliferative genes. Loss of CUX1 may thus contribute to disease pathogenesis.

The CDR at 7q35-36 encodes nine genes including CUL1 and EZH2 which are the most promising candidates due to known function in and association with cancer.

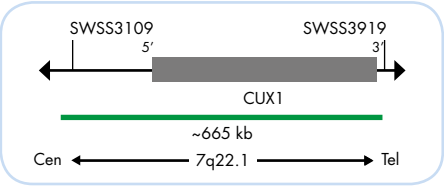
References
De Weer A, et al. (2010) PLoS One 5: e8676.
Döhner K, et al. (1998) Blood 92: 4031-5.
McNerney ME, et al. (2013) Blood 121: 975-83.
Pellagatti A & Boultwood J (2015) Eur J Haematol 95: 3-15.

Probe Description

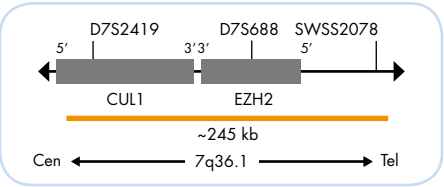
The SPEC CUX1/EZH2/CEN 7 Triple Color Probe is a mixture of a green fluorochrome direct labeled SPEC CUX1 probe hybridizing in the CDR at 7q22.1, an orange fluorochrome direct labeled SPEC EZH2 probe hybridizing in the CDR at 7q36.1, and a blue fluorochrome direct labeled CEN 7 probe specific for the alpha satellite centromeric region of chromosome 7 (D7Z1).



Ideogram of chromosome 7 indicating the hybridization locations.



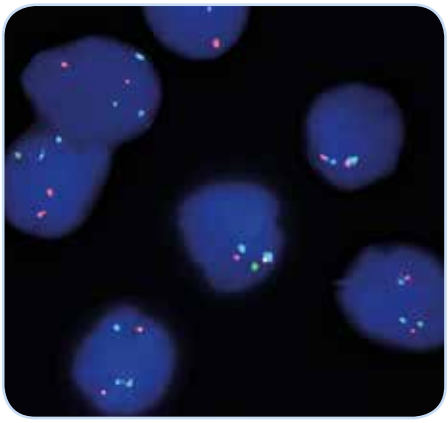
SPEC CUX1 Probe map (not to scale).



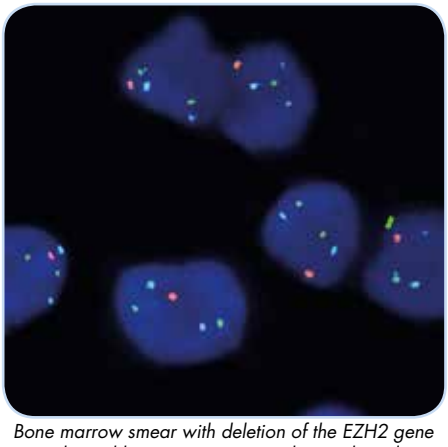
SPEC EZH2 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange, two green, and two blue signals are expected. In a cell with deletions affecting the 7q22.1 and/or 7q36.1 locus, one or no copy of the green and/or orange signal will be observed. Monosomy 7 will result in a loss of a green, orange, and blue signal.



Bone marrow smear with deletion of the CUX1 gene as indicated by one green signal in each nucleus.



Bone marrow smear with deletion of the EZH2 gene as indicated by one orange signal in each nucleus.

Specimens kindly provided by Paediatric Oncology/Haematology, Charité-Universitätsmedizin Berlin, Germany.

Prod. No.	Product	Label	Tests* (Volume)
Z-2214-50	ZytoLight SPEC CUX1/EZH2/CEN 7 Triple Color Probe CE IVD	●/●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC MET/CEN 7 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC MET/CEN 7 Dual Color Probe is designed for the detection of MET gene amplifications found in a variety of human tumors.
The MET gene (a.k.a. c-Met) is located in the chromosomal region 7q31.2 and encodes a transmembrane tyrosine kinase receptor for the hepatocyte growth factor (HGF). HGF and MET play an important role in angiogenesis and tumor growth. Activation or upregulation of MET was found in a number of carcinomas including lung, breast, colorectal, prostate, and gastric carcinomas as well as in gliomas, melanomas and some sarcomas. MET overexpression is known as a negative prognostic indicator in patients with various carcinomas, multiple myeloma, or glioma. Therefore, several inhibitors of the HGF/MET signaling pathway are being studied and developed as potent therapies to inhibit angiogenesis and tumor growth. Recently, it was shown that MET amplification leads to resistance to gefitinib or erlotinib in lung cancer by driving ERBB3-dependent activation of the PI3K pathway.

References
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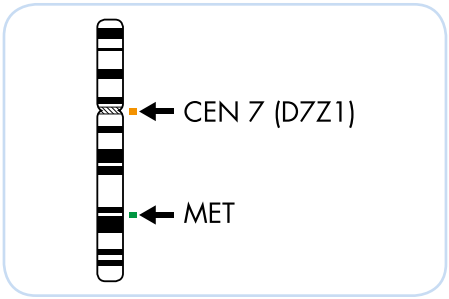
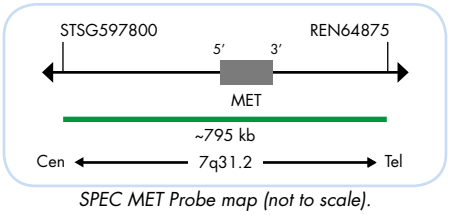
Engelman JA, et al. (2007) Science 316: 1039-43.
Ettl T, et al. (2014) Head Neck 36: 517-23.
Garcia S, et al. (2007) Int J Oncol 31: 49-58.
Hara T, et al. (1998) Lab Invest 78: 1143-53.
Lacroix L, et al. (2014) PLoS One 1: e84319.
Lee D, et al. (2015) Cancer Res Treat 47: 120-5.
Preusser M, et al. (2014) Histopathology 65: 684-92.
Schildhaus HU, et al. (2015) Clin Cancer Res 21: 907-15.

Probe Description

The SPEC MET/CEN 7 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 7 probe specific for the alpha satellite centromeric region of chromosome 7 (D7Z1) and a green fluorochrome direct labeled SPEC MET probe specific for the MET gene located at 7q31.2.



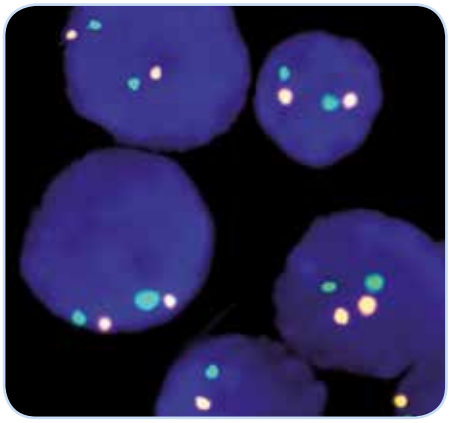
Ideogram of chromosome 7 indicating the hybridization locations.



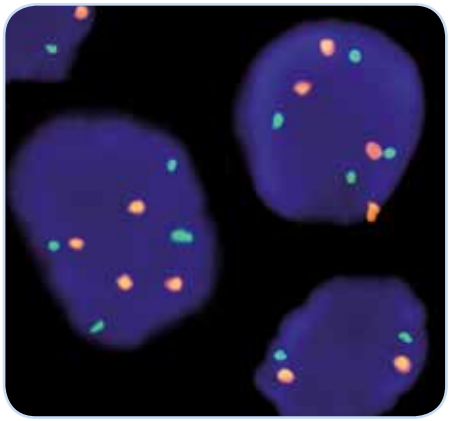
SPEC MET Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the MET gene locus, multiple copies of the green signal or green signal clusters will be observed.



SPEC MET/CEN 7 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Lung cancer cells with polysomy of chromosome 7 as indicated by four orange (CEN 7) and four green (MET) signals in the nuclei.

Prod. No.	Product	Label	Tests* (Volume)
Z-2087-50	ZytoLight SPEC MET/CEN 7 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2087-200	ZytoLight SPEC MET/CEN 7 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC BRAF Dual Color Break Apart Probe

CE IVD

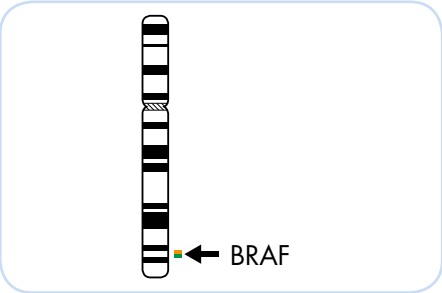
Background

The ZytoLight® SPEC BRAF Dual Color Break Apart Probe is designed for the detection of rearrangements involving the chromosomal region 7q34 harboring the BRAF (B-Raf proto-oncogene, serine/threonine kinase, a.k.a. BRAF1, NS7) gene.
The BRAF gene encodes a protein-serine/threonine kinase that participates in the MAPK cascade, which regulates a large variety of cell processes.
Various BRAF translocations were observed in melanocytic nevi, pilocytic astrocytomas, malignant melanoma, prostate and gastric cancer. The AKAP9-BRAF fusion resulting from paracentric inversion of chromosome 7q was found in radiation-induced papillary thyroid carcinomas. The fusion proteins contain the protein kinase domain but lack the autoinhibitory N-terminal portion of BRAF resulting in constitutive kinase activity.
In addition, in pilocytic astrocytoma the FAM131B-BRAF fusion has been described resulting from interstitial deletion which removes the BRAF N-terminal inhibitory domain. Moreover, pancreatic acinar cell carcinoma - a rare subtype of pancreatic cancer with poor prognosis - shows a recurrent SND1-BRAF rearrangement. SND1-BRAF-transformed cells were shown to be sensitive to treatment with a MEK inhibitor.
Hence, the detection of BRAF rearrangements by Fluorescence *in situ* Hybridization may represent a novel therapeutic target in various diseases.

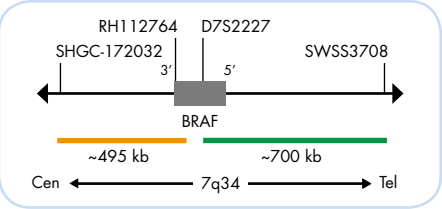
References
Chmielecki J, et al. (2014) Cancer Discov 4: 1398-405.
Ciampi R, et al. (2005) J Clin Invest 115: 94-101.
Cin H, et al. (2011) Acta Neuropathol 121: 763-74.
Dessars B, et al. (2007) J Invest Dermatol 127: 1468-70.
Dougherty MJ, et al. (2010) Neuro Oncol 12: 621-30.
Hutchinson KE, et al. (2013) Clin Cancer Res 19: 6696-702.
Jones DT, et al. (2013) Nat Genet 45: 927-32.
Miller VA, et al. (2014) J Clin Oncol 32 Suppl: Abstr. 11029.
Palanisamy N, et al. (2010) Nat Med 16: 793-8.

Probe Description

The SPEC BRAF Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 7q34 band. The orange fluorochrome direct labeled probe hybridizes proximal, and the green fluorochrome direct labeled probe hybridizes distal to the BRAF gene breakpoint region.



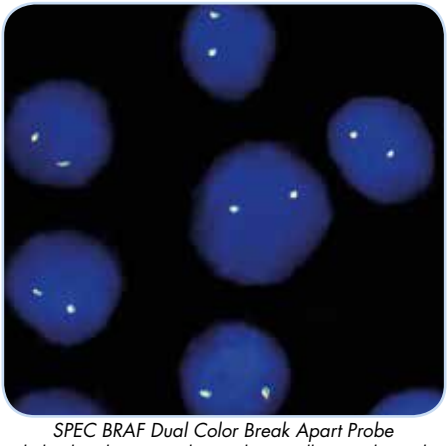
Ideogram of chromosome 7 indicating the hybridization locations.



SPEC BRAF Probe map (not to scale).

Results

In an interphase nucleus lacking a rearrangement involving the 7q34 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 7q34 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 7q34 locus and one 7q34 locus affected by a translocation or inversion. Isolated orange signals are the result of deletions distal to the BRAF breakpoint region.



SPEC BRAF Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2189-200	ZytoLight SPEC BRAF Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC BRAF/CEN 7 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC BRAF/CEN 7 Dual Color Probe is designed for the detection of amplifications involving the chromosomal region 7q34 harboring the BRAF gene (B-Raf proto-oncogene, serine/threonine kinase). The BRAF gene encodes a protein-serine/threonine kinase that participates in the MAPK cascade, which regulates a large variety of cell processes. Activating mutations in BRAF are found in many tumor types, including malignant melanoma, thyroid, colorectal, and ovarian carcinomas, lung adenocarcinoma, as well as in some sarcomas and gliomas. These mutations lead to constitutive activation of BRAF thereby promoting tumorigenesis.

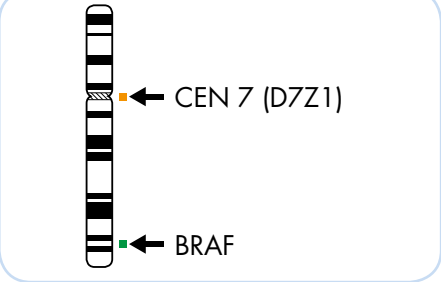
Copy number gains of mutated and non-mutated BRAF have been identified in malignant melanoma (MM), follicular thyroid tumors, astrocytoma, colorectal, and prostate cancer due to amplification of the gene or polysomy of chromosome 7. These amplifications lead to an overexpression of BRAF and to constitutive activation of the MAPK signaling pathway. Follicular carcinomas with BRAF copy number gain were observed to be more often invasive. Colorectal carcinoma or melanoma patients with BRAF V600E mutation were found to acquire resistance to MEK and BRAF inhibitors through amplification of the mutated BRAF gene.

Hence, detection of BRAF amplifications by Fluorescence *in situ* Hybridization may be of therapeutic relevance for these cancer patients.

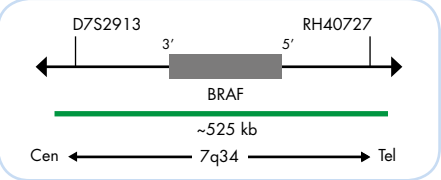
References
Ciampi R, et al. (2005) Endocr Pathol 16: 99-105.
Corcoran RB, et al. (2010) Sci Signal 3: ra84.
Dougherty MJ, et al. (2010) Neuro Oncol 12: 621-30.
Little AS, et al. (2011) Sci Signal 4: ra17.
Pfister S, et al. (2008) J Clin Invest 118: 1739-49.
Ren G, et al. (2012) Genes Chromosomes Cancer 51: 1014-23.
Roskoski R Jr. (2010) Biochem Biophys Res Commun 399: 313-7.
Spittle C, et al. (2007) J Mol Diagn 9: 464-71.
Tanami H, et al. (2004) Oncogene 23: 8796-804.
Villanueva J, et al. (2013) Cell Rep 4: 1090-9.
Willmore-Payne C, et al. (2006) Hum Pathol 37: 520-7.

Probe Description

The SPEC BRAF/CEN 7 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC BRAF probe specific for the BRAF gene at 7q34 and an orange fluorochrome direct labeled CEN 7 probe specific for the alpha satellite centromeric region of chromosome 7 (D7Z1).



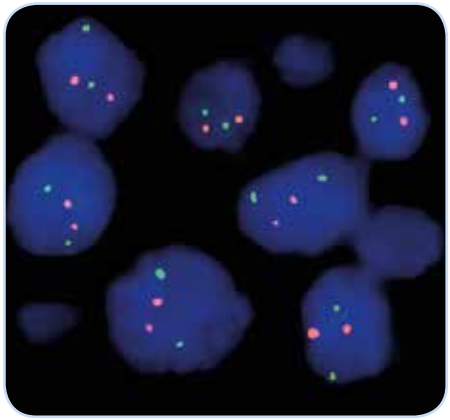
Ideogram of chromosome 7 indicating the hybridization locations.



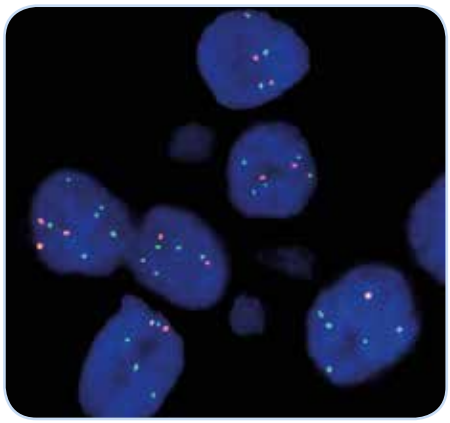
SPEC BRAF Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the BRAF gene locus or polysomy of chromosome 7, multiple copies of the green signal or large green signal clusters will be observed.



Normal interphase cells, BRAF (green), CEN 7 (orange).



NSCLC tissue section with amplification of the BRAF gene (green).

Prod. No.	Product	Label	Tests* (Volume)
Z-2191-200	ZytoLight SPEC BRAF/CEN 7 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC NRG1/CD74 TriCheck™ Probe

CE IVD

Background

The ZytoLight® SPEC NRG1/CD74 TriCheck™ Probe is designed to detect translocations involving the chromosomal region 8p12 harboring the NRG1 (neuregulin 1, a.k.a. HGL or GGF) gene and the chromosomal region 5q32 harboring the CD74 gene.

Using this probe it is possible to discriminate between CD74-NRG1 fusions and translocations affecting NRG1, but not CD74, such as SLC3A2-NRG1 or VAMP2-NRG1 fusions.

NRG1 encodes a variety of growth factors that are ligands for tyrosine kinase receptors of the ERBB family. Rearrangements of the NRG1 gene have been detected in various tumors, including breast cancer, lung cancer, and ovarian adenocarcinoma.

NRG1 translocation-positive breast tumors show a more advanced pathological stage compared with translocation-negative tumors.

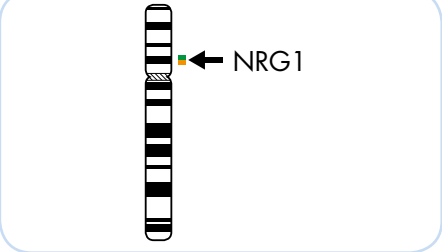
NRG1 rearrangements in lung adenocarcinoma of never smokers were found to result in, e.g., the fusion of CD74 to the EGF-like domain of NRG1and to be associated with a shorter overall and disease-free survival. Due to the involvement of NRG1 fusion proteins in oncogenesis and their association with ERBB receptors, NRG1 constitutes a good candidate for potential therapeutic applications, e.g., in relation to lung tumor subtypes with so far no effective treatment.

Hence, detection of NRG1 rearrangements and CD74-NRG1 fusions by FISH may be of prognostic and therapeutic significance.

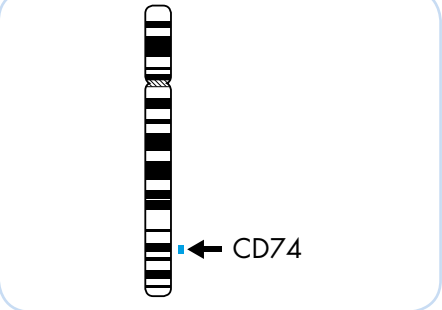
References
Adélaïde J, et al. (2003) Genes Chromosomes Cancer 37: 333-45.
Fernandez-Cuesta L, et al. (2014) Cancer Discov 4: 415-22.
Han JY, et al. (2015) Cancer Res 75: 614.
Huang HE, et al. (2004) Cancer Res 64: 6840-4.
Jung Y, et al. (2015) J Thorac Oncol 10: 1107-11.
Pole JC, et al. (2006) Oncogene 25: 5693-706.

Probe Description

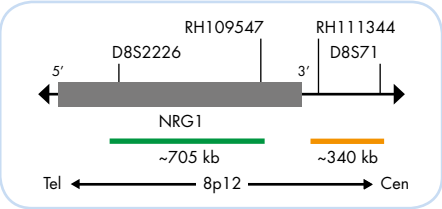
The SPEC NRG1/CD74 TriCheck™ Probe is a mixture of three direct labeled probes hybridizing to the 8p12 and 5q32-q33.1 bands. The green fluorochrome direct labeled probe hybridizes distal and the orange fluorochrome direct labeled probe hybridizes proximal to the NRG1 breakpoint region at 8p12. The blue fluorochrome direct labeled probe hybridizes to the CD74 gene region at 5q32-q33.1.



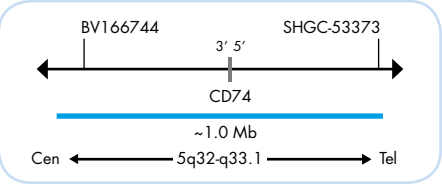
Ideogram of chromosome 8 indicating the hybridization locations.



Ideogram of chromosome 5 indicating the hybridization locations.



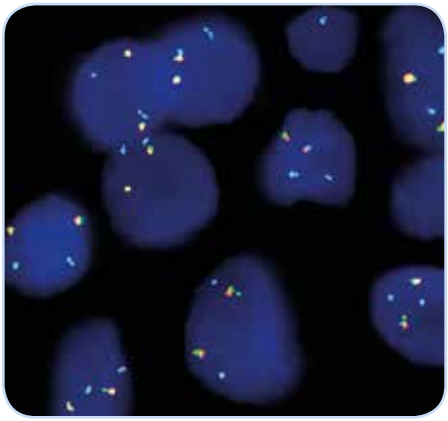
SPEC NRG1 Probe map (not to scale).



SPEC CD74 Probe map (not to scale).

Results

In an interphase nucleus lacking a rearrangement involving the 8p12 and 5q32-q33.1 bands, two orange/green fusion signals and two blue signals are expected. A CD74-NRG1 fusion is indicated by one separate green signal, one separate orange signal, and an additional blue signal which colocalizes with the separated orange signal. An NRG1 rearrangement not involving CD74 is indicated by separated orange and green signals without an additional blue signal.



SPEC NRG1/CD74 TriCheck™ Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals and two blue signals per nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2194-200	ZytoLight SPEC NRG1/CD74 TriCheck Probe CE IVD	●/●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC NRG1 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC NRG1 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 8p12 harboring the NRG1 (neuregulin 1, a.k.a. HGL or GGF) gene. NRG1 encodes a variety of growth factors that are ligands for tyrosine kinase receptors of the ERBB family. Rearrangements of the NRG1 gene have been detected in various tumors, including breast cancer, lung cancer, and ovarian adenocarcinoma. NRG1 translocation-positive breast tumors show a more advanced pathological stage compared with translocation-negative tumors.

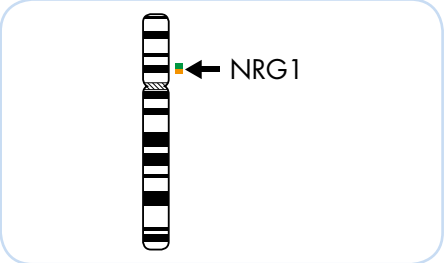
NRG1 rearrangements in lung adenocarcinomas of never smokers were found to result in the fusion of CD74 to the EGF-like domain of NRG1. Several *in vitro* studies indicate that NRG1 fusion proteins lead to an increased activation of ERBB receptors and are hence involved in tumor development.

Due to the involvement of NRG1 isoforms in oncogenesis and their association with ERBB receptors, NRG1 constitutes a good candidate for potential therapeutic applications, e.g., in relation to lung tumor subtypes with so far no effective treatment. Hence, detection of NRG1 rearrangements by Fluorescence *in situ* Hybridization represents a useful tool for studying carcinogenesis of various solid tumors and may be of prognostic and therapeutic significance.

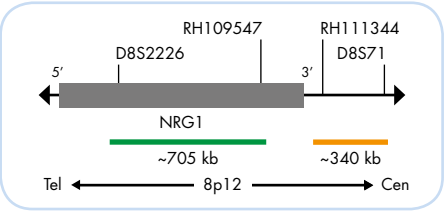
References
Adélaïde J, et al. (2003) Genes Chromosomes Cancer 37: 333-45.
Fernandez-Cuesta L, et al. (2014) Cancer Discov 4: 415-22.
Huang HE, et al. (2004) Cancer Res 64: 6840-4.
Pole JC, et al. (2006) Oncogene 25: 5693-706.

Probe Description

The SPEC NRG1 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 8p12 band. The green fluorochrome direct labeled probe hybridizes distal and the orange fluorochrome direct labeled probe hybridizes proximal to the NRG1 breakpoint region.



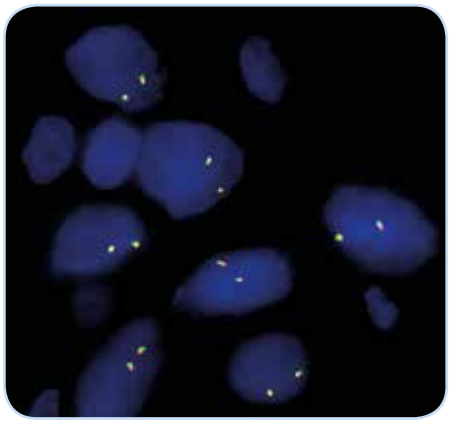
Ideogram of chromosome 8 indicating the hybridization locations.



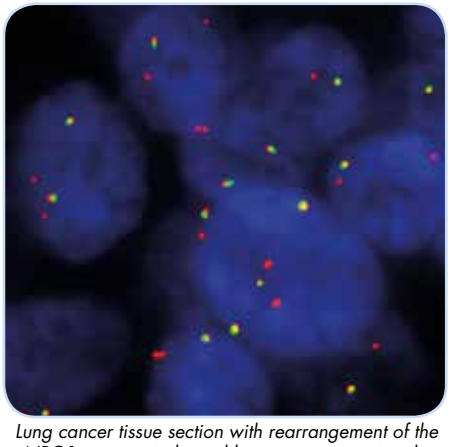
SPEC NRG1 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 8p12 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 8p12 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal in lung adenocarcinoma specimens indicates one normal 8p12 locus and one 8p12 locus affected by a translocation.



SPEC NRG1 Dual Color Break Apart Probe hybridized on normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Lung cancer tissue section with rearrangement of the NRG1 gene as indicated by extra orange signals.

Image kindly provided by Mc Leer A, Duruisseaux M, Wislez M, and colleagues, Grenoble and Paris, France.

Prod. No.	Product	Label	Tests* (Volume)
Z-2181-200	ZytoLight SPEC NRG1 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC FGFR1 Dual Color Break Apart Probe

CE IVD

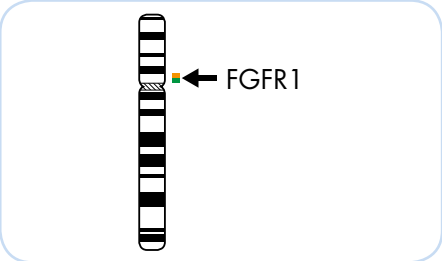
Background

The ZytoLight® SPEC FGFR1 Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal region 8p11.23-p11.22 harboring the FGFR1 (fibroblast growth factor receptor 1, a.k.a. FLT2 and FLG) gene.
Translocations affecting FGFR1 are hallmarks of the 8p11 myeloproliferative syndrome (EMS), also known as stem cell leukemia/lymphoma syndrome, an aggressive stem cell myeloproliferative neoplasm that is associated with eosinophilia, poor prognosis, T-cell lymphoma, and frequent progression to acute myeloid leukemia.
The most common translocation detected in EMS is t(8;13)(p11.2;q12.1) fusing FGFR1 to ZMYM2 (a.k.a. ZNF198). Several other rearrangements affecting the FGFR1 locus are also common in EMS, all of which result in fusion proteins comprising the tyrosine kinase domain of FGFR1 and a dimerization domain of a partner protein. Due to dimerization these fusion proteins show constitutive kinase activity. Currently, bone marrow or stem cell transplantation is the only curative treatment for patients with EMS. *In vitro* studies suggest that certain receptor tyrosine kinase inhibitors may provide a new therapeutic option.
Detection of FGFR1 rearrangements using FISH may assist in the diagnosis of patients with this aggressive stem cell disorder.

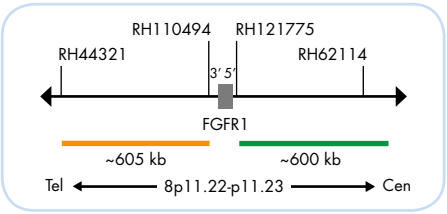
References
Chase A, et al. (2007) Blood 110: 3729-34.
Chase A, et al. (2013) Haematologica 98: 103-6.
Jackson CC, et al. (2010) Hum Pathol 41: 461-76.
Sohal J, et al. (2001) Genes Chromosomes Cancer 32: 155-63.

Probe Description

The SPEC FGFR1 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 8p11.23-p11.22 band. The orange fluorochrome direct labeled probe hybridizes distal, the green fluorochrome direct labeled probe hybridizes proximal to the FGFR1 gene breakpoint region at 8p11.23-p11.22.



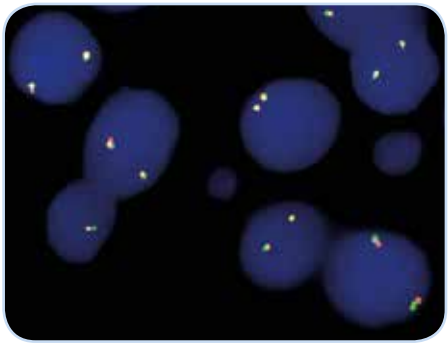
Ideogram of chromosome 8 indicating the hybridization locations.



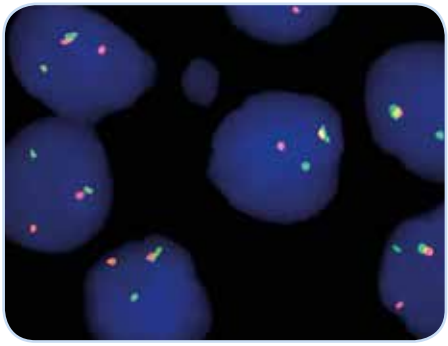
SPEC FGFR1 Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 8p11.23-p11.22 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 8p11.23-p11.22 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 8p11.23-p11.22 locus and one 8p11.23-p11.22 locus affected by a translocation.



SPEC FGFR1 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



8p11 myeloproliferative syndrome (EMS) tissue section with translocation of the FGFR1 gene as indicated by one non-rearranged orange/green fusion signal, one orange, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2168-50	ZytoLight SPEC FGFR1 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2168-200	ZytoLight SPEC FGFR1 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC FGFR1/CEN 8 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC FGFR1/CEN 8 Dual Color Probe is designed for the detection of FGFR1 gene amplification frequently observed in malignant tumors e.g. breast and prostate cancer and oral squamous cell carcinoma (OSCC).

The FGFR1 (fibroblast growth factor receptor 1) gene is located in the chromosomal region 8p11.23-p11.22 and encodes a transmembrane receptor tyrosine kinase. Amplification of the FGFR1 gene, observed in approximately 10% of all breast cancer samples, has revealed to be an independent prognostic factor for overall survival. FGFR1 is believed to emerge as a potential therapeutic target for lobular breast carcinomas.

In prostate cancer, FGFR1 gene amplification seems to be an important step during the transmission to hormone resistance.

In OSCC, FGFR1 gene amplification, observed in nearly 20% of all cases, is indicated to contribute to oral carcinogenesis at an early stage of development.

References

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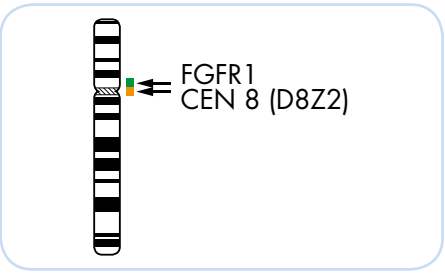
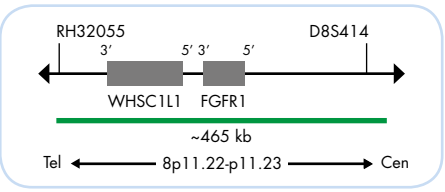
Schultheis AM, et al. (2014) Mod Pathol 27: 214-21.
Seo AN, et al. (2014) Virchows Arch 465: 547-58.
Turner N, et al. (2010) Cancer Res 70: 2085-94.
Wetterskog D, et al. (2012) J Pathol 226: 84-96.

Probe Description

The SPEC FGFR1/CEN 8 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 8 probe specific for the alpha satellite centromeric region of chromosome 8 (D8Z2) and a green fluorochrome direct labeled SPEC FGFR1 probe specific for the FGFR1 gene at 8p11.23-p11.22.



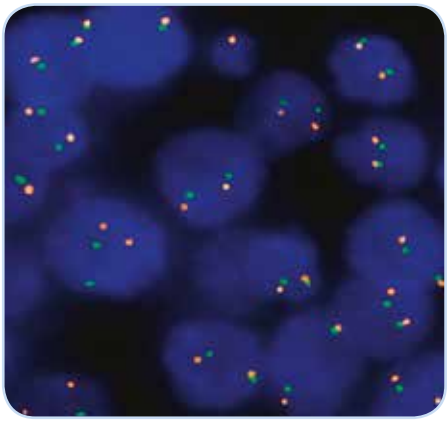
Ideogram of chromosome 8 indicating the hybridization locations.



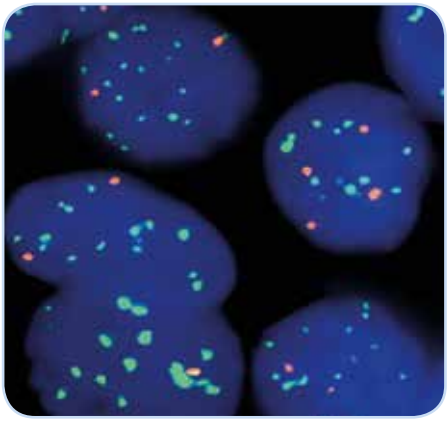
SPEC FGFR1 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the FGFR1 gene locus, multiple copies of the green signal or green signal clusters will be observed.



SPEC FGFR1/CEN 8 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Lung carcinoma tissue section with interphase cells showing amplification of the FGFR1 gene (green) and partly polysomy 8 (orange).

Prod. No.	Product	Label	Tests* (Volume)
Z-2072-50	ZytoLight SPEC FGFR1/CEN 8 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2072-200	ZytoLight SPEC FGFR1/CEN 8 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC RUNX1/RUNX1T1 Dual Color Dual Fusion Probe

CE IVD

Background

The ZytoLight® SPEC RUNX1/RUNX1T1 Dual Color Dual Fusion Probe is designed to detect the specific translocation involving the chromosomal region 21q22.12 harboring the RUNX1 (a.k.a. AML1) gene and the chromosomal region 8q21.3 harboring the RUNX1T1 (a.k.a. ETO, CBF2T1) gene.

The balanced chromosomal translocation t(8;21) is found in about 90% of acute myeloid leukemia (AML) patients. AML is a heterogeneous clonal disorder of hematopoietic progenitor cells and one of the most common malignant myeloid disorders in adults.

The runt related transcription factor 1 gene (RUNX1) and RUNX1 translocation partner 1 (RUNX1T1) gene are both involved in the transcriptional regulation of genes during normal hematopoiesis.

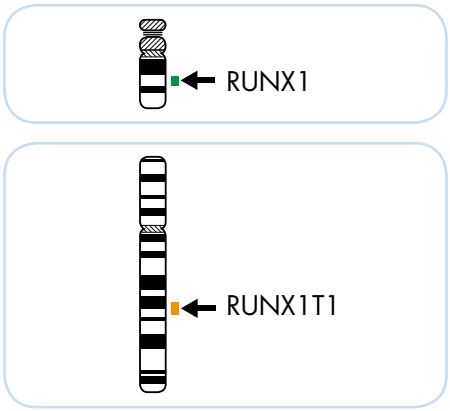
The non-random translocation t(8;21)(q21.3;q22.1) is strongly associated with the French-American-British (FAB) phenotype M2 (AML-M2) and produces a chimeric gene consisting of the 5′-region of the RUNX1 gene fused to the 3′-region of the RUNX1T1 gene. The chimeric protein is thought to be associated with the nuclear corepressor/histone deacetylase complex to block hematopoietic differentiation.

Fluorescence *in situ* Hybridization (FISH) can provide important information for the management of patients with hematologic disorders.

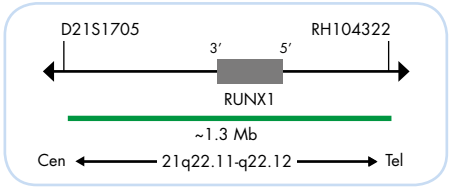
References
Dayyani F, et al. (2008) Blood 111: 4338-47.
Estey E & Döhner H (2006) Lancet 368: 1894-907.
Gmidène A, et al. (2011) Med Oncol 28 Suppl 1: 509-12.
Licht D (2001) Oncogene 20: 5560-79.
Vangala RK, et al. (2003) Blood 101: 270-7.

Probe Description

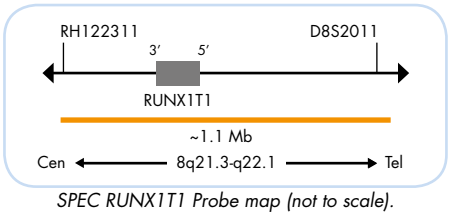
The SPEC RUNX1/RUNX1T1 Dual Color Dual Fusion Probe is a mixture of a green fluorochrome direct labeled RUNX1 probe covering the breakpoint region of the RUNX1 gene and an orange fluorochrome direct labeled RUNX1T1 probe covering the breakpoint region of the RUNX1T1 gene. This probe is approved to be used with a hybridization time of 2 hours on cytological specimens.



Ideograms of chromosomes 21 (above) and 8 (below) indicating the hybridization locations.



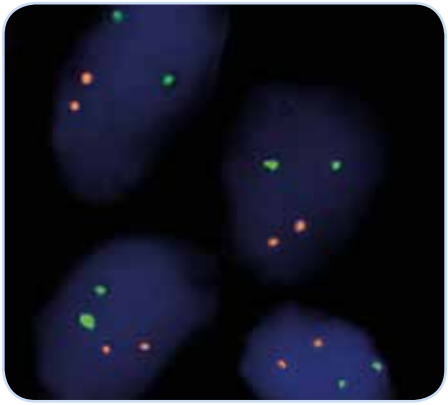
SPEC RUNX1 Probe map (not to scale).



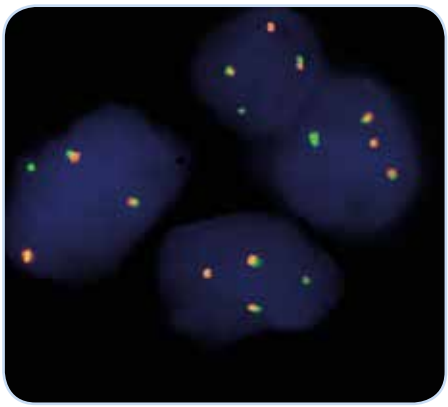
SPEC RUNX1T1 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. A reciprocal translocation involving two breakpoints splits the two signals and generates a fusion signal on each of the chromosomes involved. The chromosomal regions which are not translocated are indicated by the single orange and green signal, respectively.



SPEC RUNX1/RUNX1T1 Dual Color Dual Fusion Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Bone marrow biopsy section with translocation affecting the RUNX1/RUNX1T1 locus as indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.

Prod. No.	Product	Label	Tests* (Volume)
Z-2112-50	ZytoLight SPEC RUNX1/RUNX1T1 Dual Color Dual Fusion Probe CE IVD	●/●	5 (50 µl)
Z-2112-200	ZytoLight SPEC RUNX1/RUNX1T1 Dual Color Dual Fusion Probe CE IVD	●/●	20 (200µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC MYC Dual Color Break Apart Probe

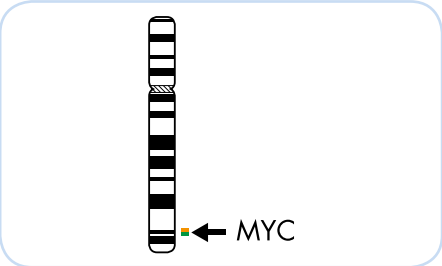
Background

The ZytoLight® SPEC MYC Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 8q24.21 harboring the MYC gene. The MYC proto-oncogene (MYC proto-oncogene, bHLH transcription factor, a.k.a. CMYC) encodes a transcription factor essential for cell growth and proliferation and is broadly implicated in tumorigenesis. Translocations involving the MYC gene are considered to be cytogenetic hallmarks for Burkitt lymphoma but are also found in other types of lymphomas.
The most frequent translocation involving the MYC gene region is t(8;14)(q24.21;q32.3) juxtaposing the MYC gene in 8q24.21 next to the IgH (immunoglobulin heavy chain) locus in 14q32.33. Further translocations affecting the MYC gene are t(8;22)(q24.21;q11.2) and t(2;8)(p11.2;q24.21), both of which involve one of the two immunoglobulin light chain loci. All three translocations bring the MYC gene under the control of a regulatory element from one of the immunoglobulin loci resulting in constitutive overexpression of MYC.

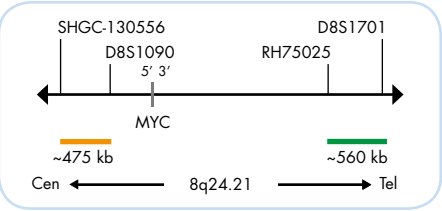
References
Boerma EG, et al. (2009) Leukemia 23: 225-34.
Dalla-Favera R, et al. (1982) Proc Natl Acad Sci U S A 79: 6497-501.
Haralambieva E, et al. (2004) Genes Chromosomes Cancer 40: 10-8.
Veronese ML, et al. (1995) Blood 85: 2132-8.

Probe Description

The SPEC MYC Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 8q24.21 band. The orange fluorochrome direct labeled probe hybridizes proximal to the MYC gene, the green fluorochrome direct labeled probe hybridizes distal to that gene. The wide gap between the two probes of approximately 2 Mb allows for the detection of the t(2;8) translocation as well as of t(8;14) and t(8;22). This probe is approved to be used with a hybridization time of 2 hours on cytological specimens.



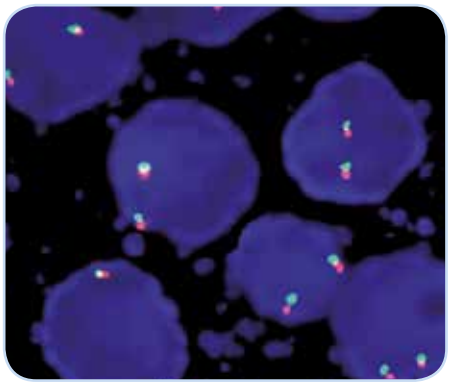
Ideogram of chromosome 8 indicating the hybridization locations.



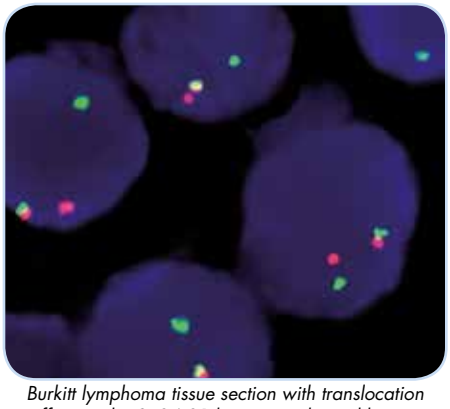
SPEC MYC Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 8q24.21 band two orange/green fusion signals are expected representing two normal (non-rearranged) 8q24.21 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 8q24.21 locus and one 8q24.21 locus affected by an 8q24.21 translocation.



SPEC MYC Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Burkitt lymphoma tissue section with translocation affecting the 8q24.21 locus as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2090-50	ZytoLight SPEC MYC Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2090-200	ZytoLight SPEC MYC Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC MYC/CEN 8 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC MYC/CEN 8 Dual Color Probe is designed for the detection of MYC gene amplifications found in a variety of human tumors.

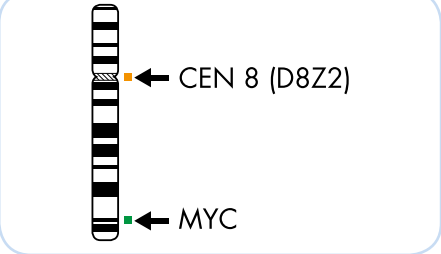
The MYC proto-oncogene (MYC proto-oncogene, bHLH transcription factor, a.k.a. CMYC) is located in the chromosomal region 8q24.21 and encodes a transcription factor that can activate and repress transcription thereby regulating expression of numerous target genes that are essential for cell growth and proliferation.

Deregulation of MYC is a common denominator in cancer. MYC amplification was found e.g. in breast, colon, kidney, lung, ovary, bladder, head and neck, and endometrial cancer. Several studies showed a correlation between gene amplification and disease progression or recurrence in breast cancer and other malignancies. Malignant cutaneous angiosarcomas, for example, but not benign and atypical vascular lesions occurring after radiotherapy of breast cancer are characterized by amplification of the MYC gene. The presence of MYC amplification is thus of considerable diagnostic importance for the distinction of malignant from atypical postradiation vascular neoplasms of the skin.

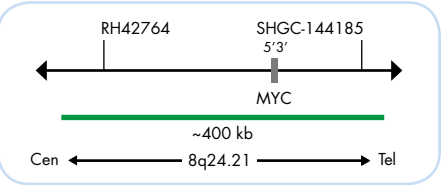
Since inactivation of MYC appears to be effective in the treatment of neoplasia MYC targeting therapies have been developed some of which have entered clinical trials.

Probe Description

The SPEC MYC/CEN 8 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 8 probe specific for the alpha satellite centromeric region of chromosome 8 (D8Z2) and a green fluorochrome direct labeled SPEC MYC probe specific for the MYC gene at 8q24.21.



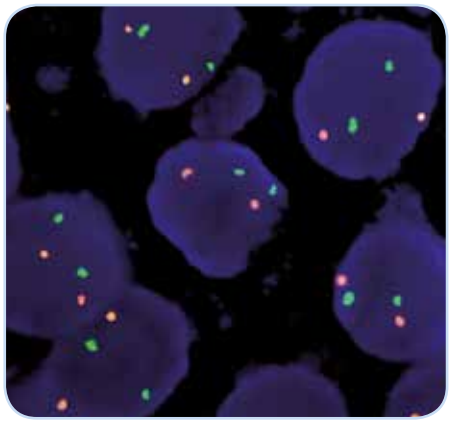
Ideogram of chromosome 8 indicating the hybridization locations.



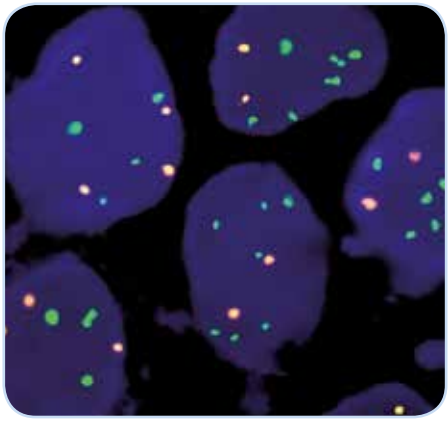
SPEC MYC Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the MYC gene locus, multiple copies of the green signal or green signal clusters will be observed.



SPEC MYC/CEN 8 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Breast cancer tissue section with interphase cells showing partly polysomy 8 and partly amplification of the MYC gene locus.

References

Dalla-Favera R, et al. (1982) Proc Natl Acad Sci U S A 79: 6497-501.
Fromont G, et al. (2013) Hum Pathol 44: 1617-23.
Mannuci S, et al. (2012) Adv Hematol 2012: 149780.
Mentzel T, et al. (2012) Mod Pathol 25: 75-95.
Nesbit CE, et al. (1999) Oncogene 18: 3004-16.
Schraml P, et al. (1999) Clin Cancer Res 5: 1966-75.
Taub R, et al. (1982) Proc Natl Acad Sci U S A 79: 7837-41.

Prod. No.	Product	Label	Tests* (Volume)
Z-2092-50	ZytoLight SPEC MYC/CEN 8 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2092-200	ZytoLight SPEC MYC/CEN 8 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC MYC/IGH Dual Color Dual Fusion Probe

CE IVD

Background

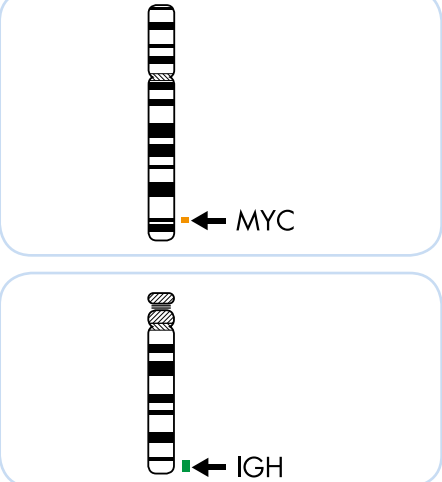
The ZytoLight® SPEC MYC/IGH Dual Color Dual Fusion Probe is designed to detect the translocation t(8;14)(q24.21;q32.3) affecting the MYC gene in the chromosomal region 8q24.21 and the IGH locus in 14q32.33. The MYC proto-oncogene (MYC proto-oncogene, bHLH transcription factor, a.k.a. CMYC) encodes a transcription factor essential for cell growth and proliferation and is broadly implicated in tumorigenesis. Translocations involving the MYC gene are considered to be cytogenetic hallmarks for Burkitt lymphoma (BL) but are also found in other types of lymphomas.

The most frequent translocation involving the MYC gene region t(8;14)(q24.21;q32.3) can be found in approx. 80% of the BL cases and juxtaposes the MYC gene next to IGH (immunoglobulin heavy locus). Further translocations affecting the MYC gene are t(8;22)(q24.21;q11.2) and t(2;8)(p11.2;q24.21), both of which involve one of the two immunoglobulin light chain loci. All three translocations bring the MYC gene under the control of a regulatory element from one of the immunoglobulin loci resulting in constitutive overexpression of MYC.

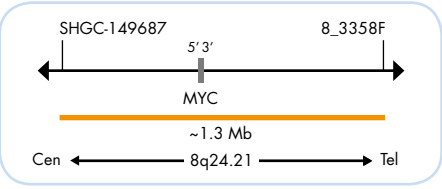
The identification of MYC specific rearrangements is a critical part of the diagnostic work-up and management of patients, identifying those who will benefit from the intensive therapeutic regimens used to treat BL. Fluorescence *in situ* Hybridization (FISH) which allows the correlation with immunochemistry can be critical to patient management and is an approach commonly used.

Probe Description

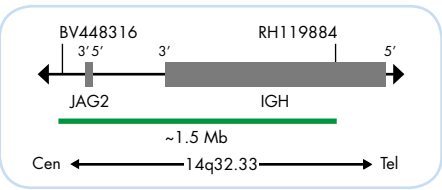
The SPEC MYC/IGH Dual Color Dual Fusion Probe is a mixture of an orange fluorochrome direct labeled MYC probe spanning the known MYC breakpoints, and a green fluorochrome direct labeled IGH probe spanning the known breakpoints of IGH.



Ideograms of chromosomes 8 (above) and 14 (below) indicating the hybridization locations.



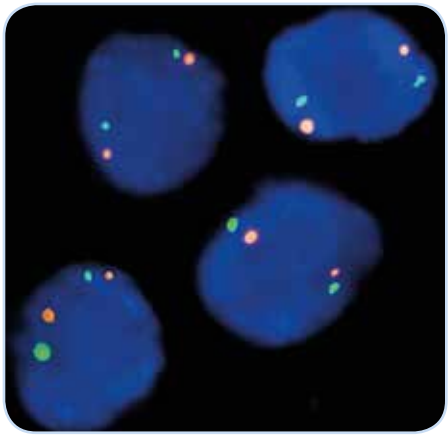
SPEC MYC Probe map (not to scale).



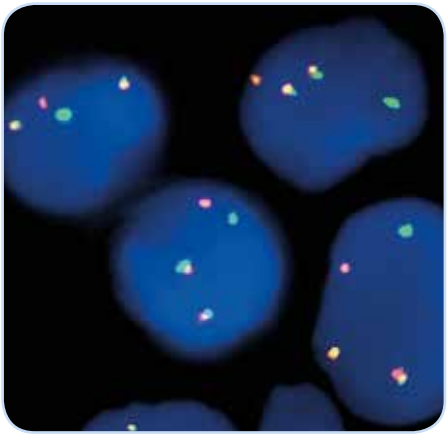
SPEC IGH Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. A reciprocal translocation involving two breakpoints splits the two signals and generates a fusion signal on each of the chromosomes involved. The chromosomal regions which are not translocated are indicated by the single orange respectively green signal.



SPEC MYC/IGH Dual Color Dual Fusion Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Burkitt lymphoma tissue section with t(8;14) as indicated by one separate orange signal, one separate green signal and two orange/green fusion signals indicating the MYC/IGH translocation.

References
May P, et al. (2010) Cancer Genet Cytogenet 198: 71-5.
Perkins AS & Friedberg JW (2008) Hematology Am Soc Hematol Educ Program: 341-8.
Veronese ML, et al. (1995) Blood 85: 2132-8.

Prod. No.	Product	Label	Tests* (Volume)
Z-2105-50	ZytoLight SPEC MYC/IGH Dual Color Dual Fusion Probe CE IVD	●/●	5 (50 µl)
Z-2105-200	ZytoLight SPEC MYC/IGH Dual Color Dual Fusion Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC CD274,PDCD1LG2/CEN 9 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC CD274,PDCD1LG2/CEN 9 Dual Color Probe is designed for the detection of CD274,PDCD1LG2 gene cluster amplifications observed in various carcinomas, e.g. classical non-Hodgkin lymphoma and mediastinal large B-cell lymphoma.

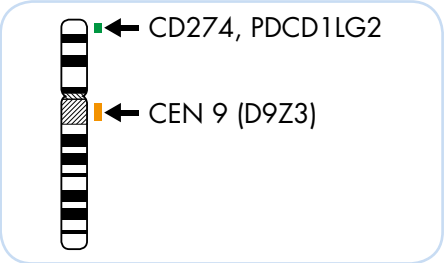
The CD274 (CD274 molecule, a.k.a. PDCD1LG1, PDL1) and PDCD1LG2 (programmed cell death 1 ligand 2, a.k.a. PDL2, CD273) genes, which are separated by 42 kilobases, are located on chromosome 9p24.1.

The genes encode ligands for the PD-1 receptor of T-cells. CD274 is expressed by cancer cells of various tumor types, including melanoma, non-small cell lung cancer (NSCLC), breast cancer, and renal cell carcinomas. It is believed that interactions between the T-cell PD-1 receptor and its ligands CD274 or PDCD1LG2 expressed by tumor cells prevent the immune system from attacking the tumor cells.

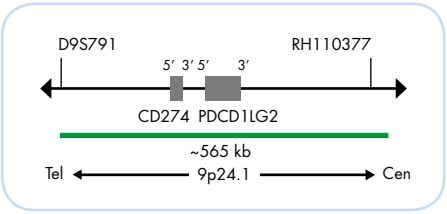
The blockade of the PD-1/CD274, PDCD1LG2 pathway has yielded promising results in clinical trials conducted on tumors that express the PD-1 receptor. In early phase clinical trials compounds blocking PD-1 and CD274 have shown to be especially effective in advanced-stage NSCLC patients positive for CD274. Hence, targeting PD-1 or CD274, PDCD1LG2 represents a promising new treatment for this cancer entity. Consequently, the identification of CD274,PDCD1LG2 gene copy number detected by Fluorescence *in situ* Hybridization might be of prognostic and predictive relevance in diverse cancers.

Probe Description

The SPEC CD274, PDCD1LG2/CEN 9 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC CD274, PDCD1LG2 probe specific for the CD274 and PDCD1LG2 genes at 9p24.1 and an orange fluorochrome direct labeled CEN 9 probe specific for the classical satellite III region of chromosome 9 (D9Z3) at 9q12.



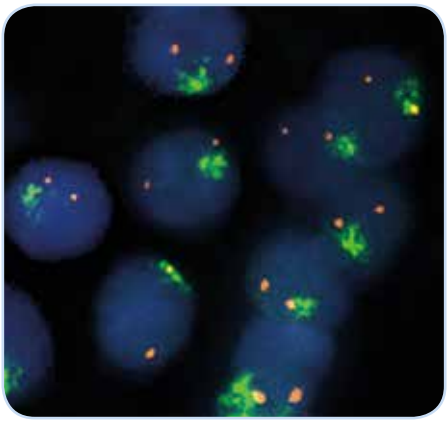
Ideogram of chromosome 9 indicating the hybridization locations.



SPEC CD274, PDCD1LG2 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the CD274,PDCD1LG2 gene cluster, multiple copies of the green signal or large green signal clusters will be observed.



Primary mediastinal large B-cell lymphoma tissue section with amplification of the CD274,PDCD1LG2 gene region as indicated by green signal clusters in each nucleus.

References
Green MR, et al. (2012) Clin Cancer Res 18: 1611-8.
Hao Y, et al. (2014) Clin Cancer Res 20: 2674-83.
Mamalis A, et al. (2014) Arch Dermatol Res 306: 511-9.
Schalper KA, at al. (2014) Clin Cancer Res 20: 2773-82.
Velcheti V, et al. (2014) Lab Invest 94: 107-16.

Prod. No.	Product	Label	Tests* (Volume)
Z-2179-50	ZytoLight SPEC CD274,PDCD1LG2/CEN 9 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2179-200	ZytoLight SPEC CD274,PDCD1LG2/CEN 9 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC JAK2 Dual Color Break Apart Probe

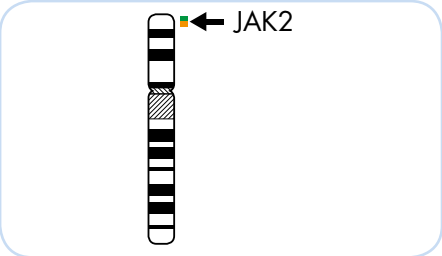
CE IVD

Background

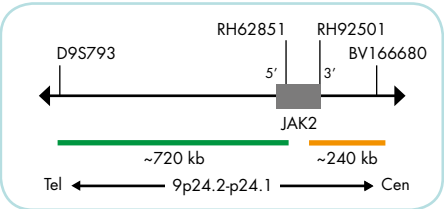
The ZytoLight® SPEC JAK2 Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal region 9p24.1 harboring the JAK2 (Janus kinase 2, a.k.a. JTK10) gene.
The JAK (Janus kinase) family proteins, which include JAK1, JAK2, JAK3, and TYK2, are cytoplasmic tyrosine kinases that are essential in maintaining normal hematopoiesis due to their involvement in the JAK-STAT signaling pathway. Gain of function mutations, translocations, and amplifications involving JAK2, which lead to constitutive activation of the JAK2 kinase, have been described in various hematologic malignancies.
JAK2 translocations are associated with a poor prognosis and have been found in myeloproliferative neoplasms (MPNs), including chronic myeloid leukemia (CML), as well as in other hematologic malignancies, e.g., in acute lymphoblastic leukemia (ALL). Ph-like ALL patients with rearrangement of JAK2 were shown to have the worst outcome compared to Ph-like ALL patients carrying other genetic aberrations. Various different JAK2 fusion partners have been identified, with PMC1, BCR, and ETV6 being most common. In the revised 2016 WHO classification of myeloid neoplasms and acute leukemia, "myeloid/lymphoid neoplasms with PCM1-JAK2" are classified as a new provisional entity.
Recent studies reported that after treatment with ruxolitinib, a JAK2 inhibitor, patients with JAK2-rearranged MPN achieved hematologic remission.
Hence, detection of JAK2 rearrangements by FISH may help in selecting patients eligible for therapy with JAK2 inhibitors.

Probe Description

The SPEC JAK2 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 9p24.2-p24.1 bands. The orange fluorochrome direct labeled probe hybridizes proximal to the JAK2 gene at 9p24.1, the green fluorochrome direct labeled probe hybridizes distal to the JAK2 gene at 9p24.2-p24.1.



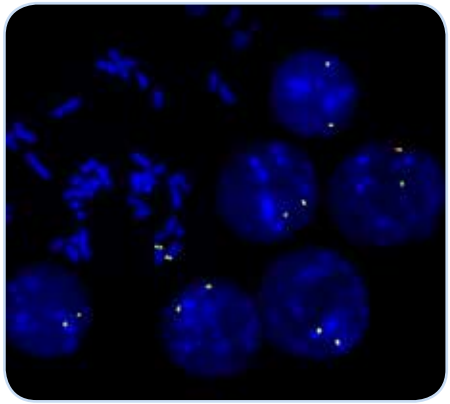
Ideogram of chromosome 9 indicating the hybridization locations.



SPEC JAK2 Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 9p24.2-p24.1 bands, two orange/green fusion signals are expected representing two normal (non-rearranged) 9p24.2-p24.1 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 9p24.2-p24.1 locus and one 9p24.2-p24.1 locus affected by a translocation.



SPEC JAK2 Break Apart Dual Color Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus and to metaphase chromosomes of a normal cell.

References
Arber DA, et al. (2016) Blood 127: 2391-405.
He R, et al. (2016) Cancer Genet 209: 223-8.
Ho K, et al. (2010) J Assoc Genet Technol 36: 107-9.
Lacronique V, et al. (1997) Science 278: 1309-12.
Levavi H, et al. (2019) Acta Haematol 142: 105-12.
Roberts KG, et al. (2014) N Engl J Med 371: 1005-15.
Rumi E, et al. (2015) Ann Hematol 94: 1927-8.

Prod. No.	Product	Label	Tests* (Volume)
Z-2294-50	ZytoLight SPEC JAK2 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC CDKN2A/CEN 9 Dual Color Probe

CE IVD

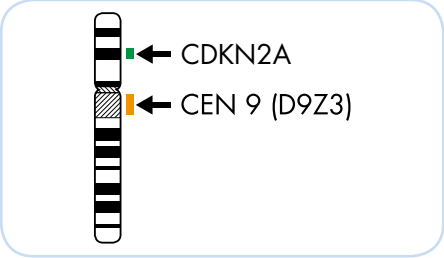
Background

The ZytoLight® SPEC CDKN2A/CEN 9 Dual Color Probe is designed for the detection of CDKN2A deletions frequently observed in most tumor cell lines as well as in primary human malignancies.
The CDKN2A gene, often referred to as p16 or INK4a/ARF, is located in the chromosomal region 9p21.3. Using alternative first exons and an alternative reading frame, the gene encodes for two distinct tumor suppressor proteins p16INK4a and p14ARF, both involved in cell cycle regulation. CDKN2A has been identified as a major susceptibility gene for melanoma. The tumor suppressor gene CDKN2A is inactivated by homozygous deletions with high frequency in a variety of human primary tumors e.g. bladder and renal cell carcinoma, prostate and ovarian adenocarcinoma, non-small cell lung cancer, sarcoma, glioma, mesothelioma, and melanoma. Furthermore, deletion of the CDKN2A gene is found in up to 80% of T-cell acute lymphoblastic leukemia cases and is associated with poor prognosis and relapse of the disease.

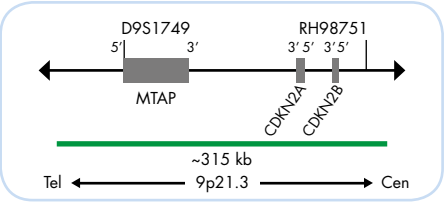
References
Cowan JM et al. (1988) J Natl Cancer Inst 80: 1159-64.
Holley T, et al. (2012) PLoS One 7: e50586.
Hussussian CJ, et al. (1994) Nat Genet 8: 15-21.
Kamb A, et al. (1994) Science 264: 436-40.
Nobori T, et al. (1994) Nature 368: 753-6.
Quelle DE, et al. (1995) Cell 83: 993-1000.
Rocco JW & Sidransky D (2001) Exp Cell Res 264: 42-55.
Schoppmeyer K, et al. (1999) Neoplasia 1: 128-37.
Schwarz S, et al. (2008) Cytometry A 73: 305-11.
Sharpless NE (2005) Mutat Res 576: 22-38.

Probe Description

The SPEC CDKN2A/CEN 9 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 9 probe specific for the classical satellite III region of chromosome 9 (D9Z3) at 9q12 and a green fluorochrome direct labeled SPEC CDKN2A probe specific for the CDKN2A gene at 9p21.3.



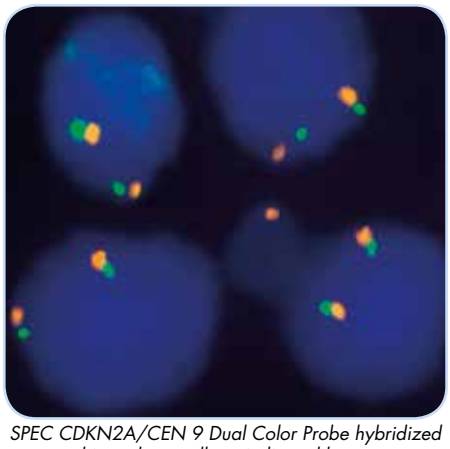
Ideogram of chromosome 9 indicating the hybridization locations.



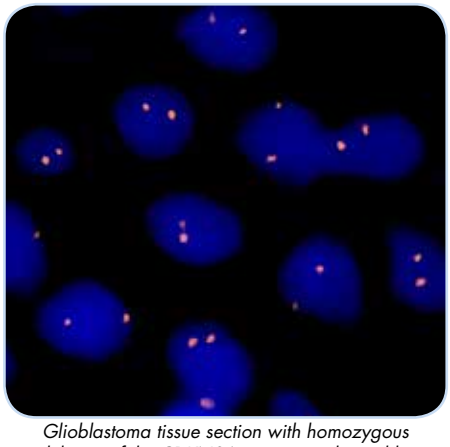
SPEC CDKN2A Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletion of the CDKN2A gene locus, a reduced number of green signals will be observed. Deletions affecting only parts of the CDKN2A gene might result in a normal signal pattern with green signals of reduced size.



SPEC CDKN2A/CEN 9 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Glioblastoma tissue section with homozygous deletion of the CDKN2A gene as indicated by the loss of both green signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2063-50	ZytoLight SPEC CDKN2A/CEN 9 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2063-200	ZytoLight SPEC CDKN2A/CEN 9 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC CDKN2A/CEN 3/7/17 Quadruple Color Probe

CE IVD

Background

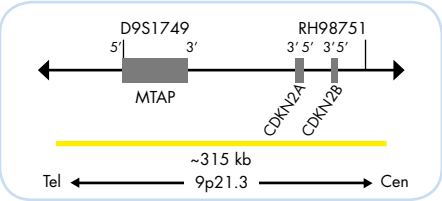
The ZytoLight® SPEC CDKN2A/CEN 3/7/17 Quadruple Color Probe is designed for the simultaneous detection of CDKN2A gene status and enumeration of chromosomes 3, 7, and 17 in tumor cells. The tumor suppressor gene CDKN2A (a.k.a. p16 or p16INK4a) is located in the chromosomal region 9p21.3 and is inactivated by homozygous deletions with high frequency in a variety of human primary tumors e.g. renal cell carcinoma, prostate and ovarian adenocarcinoma, non-small cell lung cancer, sarcoma, glioma, mesothelioma, and melanoma. Additionally, non-random numerical chromosome aberrations are frequently observed in a variety of solid tumors.

Hence, detection of these specific chromosome aberrations in tumor cells can serve as a valuable diagnostic aid in tumor classification and staging. For example, in papillary renal cell carcinoma trisomy 7 or 17 is frequently found, while chromophobic RCC is characterized by widespread chromosomal losses.

References
Barocas DA, et al. (2006) BJU Int 99: 290-5.
Gallucci M, et al. (2005) J Clin Pathol 58: 367-71.
Kamb A, et al. (1994) Science 264: 436-40.
Sharpless NE (2005) Mutat Res 576: 22-38.

Probe Description

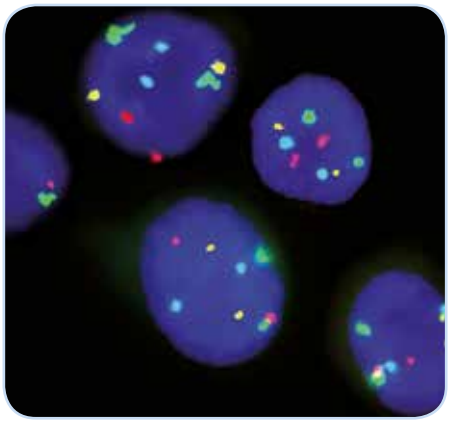
The SPEC CDKN2A/CEN 3/7/17 Quadruple Color Probe is a mixture of a gold fluorochrome direct labeled SPEC CDKN2A probe specific for the CDKN2A gene at 9p21.3, a red fluorochrome direct labeled CEN 3 probe specific for the alpha satellite centromeric region of chromosome 3 (D3Z1), a green fluorochrome direct labeled CEN 7 probe specific for the alpha satellite centromeric region of chromosome 7 (D7Z1), and a blue fluorochrome direct labeled CEN 17 probe specific for the alpha satellite centromeric region of chromosome 17 (D17Z1).



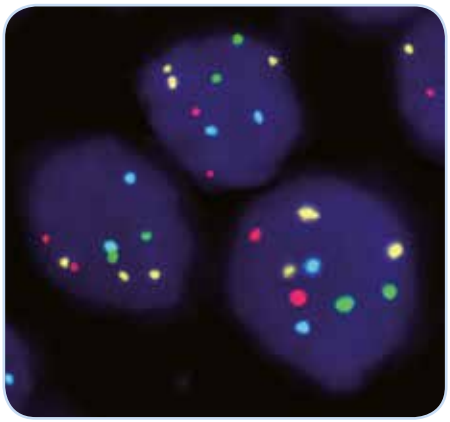
SPEC CDKN2A Probe map (not to scale).

Results

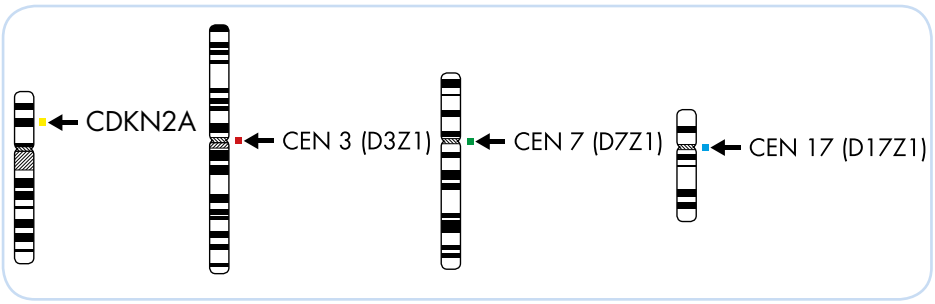
In a normal interphase nucleus, two gold, two red, two green, and two blue signals are expected. In a cell with deletion of the CDKN2A gene locus, a reduced number of gold signals will be observed. In cells with aneusomy of chromosomes 3, 7, or 17 more or less signals of the respective color will be visible.



Normal cytological specimen hybridized with SPEC CDKN2A/CEN 3/7/17 Quadruple Color Probe as indicated by two gold (CDKN2A), two red (CEN 3), two green (CEN 7), and two blue (CEN 17) signals.



SPEC CDKN2A/CEN 3/7/17 Quadruple Color Probe hybridized to tumor cells showing a trisomy 9 as indicated by three CDKN2A signals (gold) in each nucleus.



Ideograms of chromosomes 9, 3, 7, and 17 indicating the hybridization locations.

Prod. No.	Product	Label	Tests* (Volume)
Z-2081-50	ZytoLight SPEC CDKN2A/CEN 3/7/17 Quadruple Color Probe CE IVD	●/●/●/●	5 (50 µl)
Z-2081-200	ZytoLight SPEC CDKN2A/CEN 3/7/17 Quadruple Color Probe CE IVD	●/●/●/●	20 (200 µl)

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC NTRK2 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC NTRK2 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 9q21.33 harboring the NTRK2 (neurotrophic receptor tyrosine kinase 2, a.k.a. TRKB) gene.

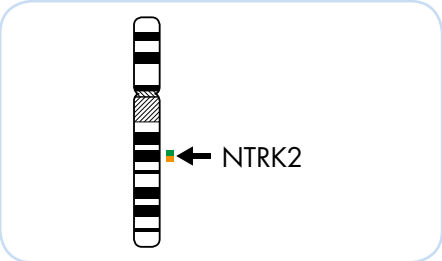
NTRK2 is a receptor tyrosine kinase (TK) that upon brain-derived growth factor (BDGF) and neurotrophin 4/5 (NT-4/5) binding phosphorylates itself and members of the MAPK pathway. It plays a key role in central and peripheral nervous system development as well as in cell survival. Translocations affecting the NTRK2 gene have been reported in several cancer types, including glioblastomas, pilocytic astrocytomas, head and neck squamous cell carcinoma, and lung adenocarcinoma. NTRK2 rearrangements result in the fusion of the 3' end of the NTRK2 gene with the 5' end of different activating genes (AGBL4, PAN3, or AFAP1). All these fusion genes encode hybrid proteins comprising the TK domain of NTRK2 and the N-terminus of the partner proteins encoding dimerization domains which results in ligand-independent TK activity.

Currently, there are several ongoing clinical trials involving drugs with known inhibitory activity of NTRK-related kinases. Entrectinib and LOXO-101 represent two of these TRK inhibitors which have shown promising activity and good tolerability in patients with advanced solid tumors or NSCLC harboring NTRK1, 2, and 3 rearrangements.

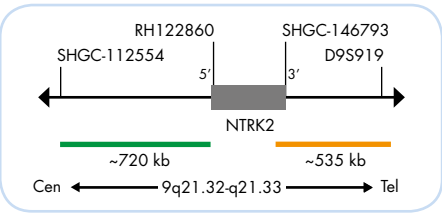
Hence, detection of NTRK2 translocations by Fluorescence *in situ* Hybridization (FISH) may be of diagnostic and therapeutic relevance.

Probe Description

The SPEC NTRK2 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 9q21.32-q21.33 band. The green fluorochrome direct labeled probe hybridizes proximal to the NTRK2 breakpoint region at 9q21.32-q21.33, the orange fluorochrome direct labeled probe hybridizes distal to the NTRK2 breakpoint region at 9q21.33.



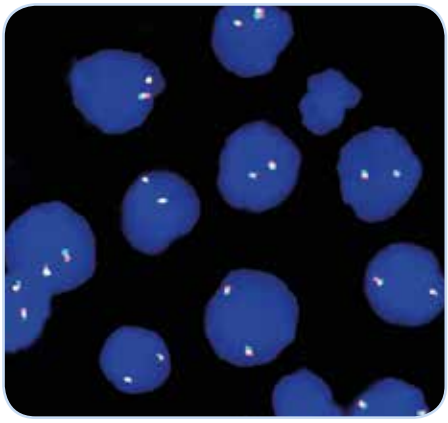
Ideogram of chromosome 9 indicating the hybridization locations.



SPEC NTRK2 Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 9q21.32-q21.33 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 9q21.32-q21.33 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 9q21.32-q21.33 locus and one 9q21.32-q21.33 locus affected by a translocation.



SPEC NTRK2 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.

References
Amatu A, et al. (2016) ESMO Open 1: e000023.
Jones DTW, et al. (2013) Nat Genet 45: 927-32.
Raez LE & Rolfo C (2016) Lung Cancer Manag 5: 1-4.
Stransky N, et al. (2014) Nat Commun 5: 4846.
Wu G, et al. (2014) Nat Genet 46: 444-50.

Prod. No.	Product	Label	Tests* (Volume)
Z-2205-50	ZytoLight SPEC NTRK2 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2205-200	ZytoLight SPEC NTRK2 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC NR4A3 Dual Color Break Apart Probe

CE IVD

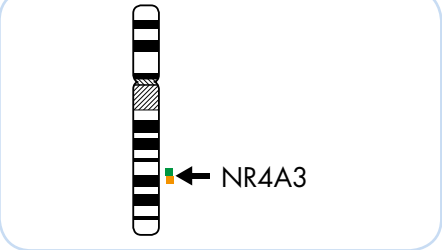
Background

The ZytoLight® SPEC NR4A3 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 9q22.33-q31.1 harboring the nuclear receptor subfamily 4, group A, member 3 (NR4A3; a.k.a. TEC, NOR1, CHN) gene.Extraskeletal myxoid chondrosarcoma (EMC) is a rare soft-tissue sarcoma of chondroblastic origin that occurs primarily in adults. The tumor is characterized by recurrent chromosomal translocations resulting in fusions of the NR4A3 gene to various N-terminal partners including EWSR1, RBP56, TCF12, and TFG. NR4A3 is a member of the steroid/thyroid receptor superfamily and acts as a transcriptional activator. The resulting chimeric proteins contain N-terminal parts of the various partners fused to the entire coding sequence of NR4A3. The most frequent reciprocal translocation is t(9;22)(q22.3-q31;q12.2) found in about 70% of EMC generating a EWSR1-NR4A3 fusion gene in which the 3'-terminal part of EWSR1 is replaced by the entire NR4A3 gene. EMC is histologically characterized by a mixture of cellular and myxoid stromal components, making it difficult to distinguish it from other benign or malignant mesenchymal tumors. Since chromosomal translocations of EWSR1 are found in several different neoplasias while NR4A3 rearrangements have been exclusively detected in EMC, assessment of NR4A3 rearrangements by Fluorescence *in situ* Hybridization might represent a helpful tool for the differential diagnosis of EMC.

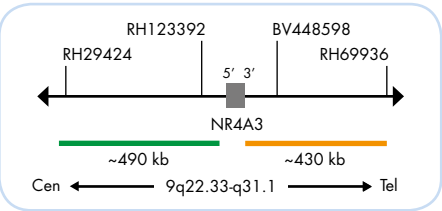
References
Benini S, et al. (2014) J Mol Diagn 16: 314-23.
Labelle Y, et al. (1995) Hum Mol Genet 4: 2219-26.
Nogushi H, et al. (2010) Hum Pathol 41: 336-42.
Ohkura N, et al. (1994) Biochem Biophys Res Commun 205: 1959-65.
Panagopoulos I, et al. (2002) Genes Chromosomes Cancer 35: 340-52.

Probe Description

The SPEC NR4A3 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 9q22.33-q31.1 band. The orange fluorochrome direct labeled probe hybridizes distal to the NR4A3 gene and the green fluorochrome direct labeled probe hybridizes proximal to that gene.



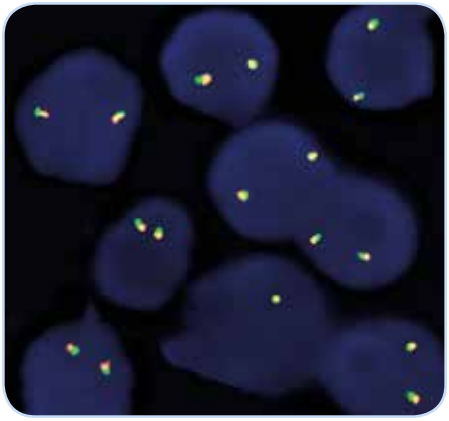
Ideogram of chromosome 9 indicating the hybridization locations.



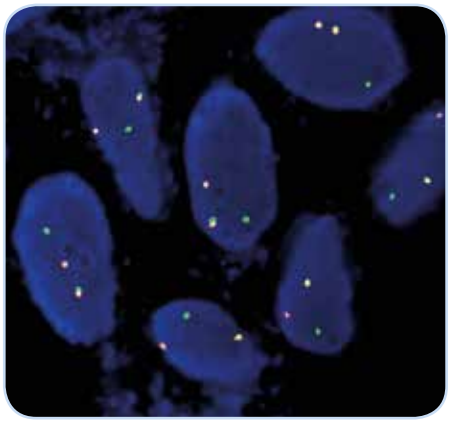
SPEC NR4A3 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 9q22.33-q31.1 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 9q22.33-q31.1 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 9q22.33-q31.1 locus and one 9q22.33-q31.1 locus affected by a translocation.



SPEC NR3A3 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signal per nucleus.



Extraskeletal myxoid chondrosarcoma tissue section with translocation affecting the 9q22.33-q31.1 locus as indicated by one orange/green fusion (non-rearranged) signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2145-50	ZytoLight SPEC NR4A3 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ABL1 Dual Color Break Apart Probe

CE IVD

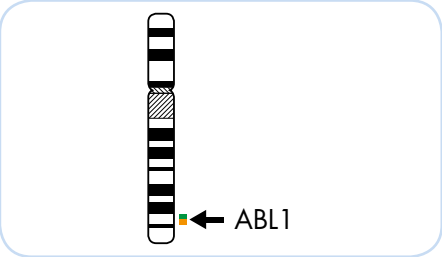
Background

The ZytoLight® SPEC ABL1 Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal region 9q34.12 harboring the ABL1 (ABL proto-oncogene 1, non-receptor tyrosine kinase, a.k.a. ABL) gene. Chromosomal rearrangements involving ABL1 occur in various hematological malignancies leading to fusions of the ABL1 gene to different fusion partners.
The translocation t(9;22)(q34.1;q11.2) results in BCR/ABL1 fusion and is observed in approx. 90% of patients with chronic myeloid leukemia (CML) and in approx. 25% of adults with acute lymphoblastic leukemia (ALL). The rearrangements are cytogenetically characterized by the presence of the Philadelphia (Ph) chromosome. Other ABL1 fusion partners include, e.g., ETV6 and NUP214. The kinase domain of ABL1 is retained in all chimeric proteins. The NUP214-ABL1 is the second most prevalent ABL1 fusion gene in malignant hemopathies, with a frequency of 5% in T-cell ALL. NUP214-ABL1 fusion genes are often found amplified on episomes. Tyrosine kinase inhibitors, such as imatinib, suppress the constitutive kinase activity of ABL1 fusion proteins. Therefore, these drugs may have potential in the treatment of patients with ABL1 fusions.

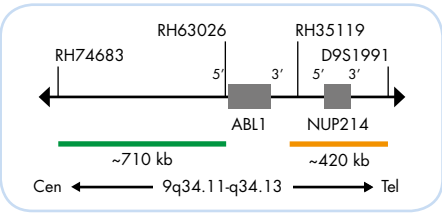
References
De Braekeleer E, et al. (2011) Eur J Haematol 86: 361-71.
De Klein A, et al. (1982) Nature 300: 765-7.
Graux C, et al. (2009) Leukemia 23: 125-33.
Lim TH, et al. (2005) Ann Acad Med Singapore 34: 533-8.
Primo D, et al. (2003) Leukemia 17: 1124-9.
Rieder H, et al. (1998) Leukemia 12: 1473-81.
Sessarego M, et al. (2000) Haematologica 85: 35-9.
Zheng X, et al. (2009) PLoS One 4: e7661.

Probe Description

The SPEC ABL1 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 9q34.11-q34.13 band. The green fluorochrome direct labeled probe hybridizes proximal to the ABL1 gene at 9q34.11-q34.12, the orange fluorochrome direct labeled probe hybridizes distal to the ABL1 gene at 9q34.12-q34.13.



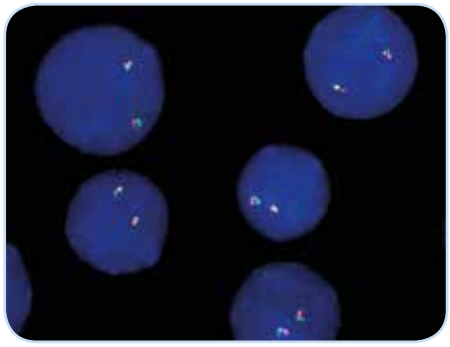
Ideogram of chromosome 9 indicating the hybridization locations.



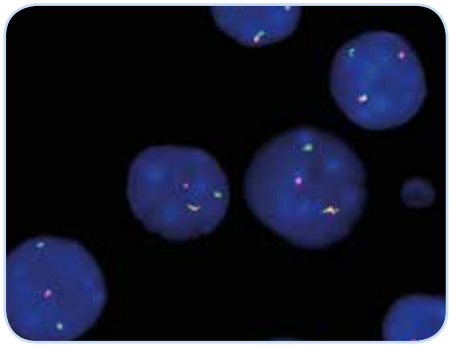
SPEC ABL1 Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 9q34.11-q34.13 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 9q34.11-q34.13 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 9q34.11-q34.13 locus and one 9q34.11-q34.13 locus affected by a translocation.
Amplifications of the NUP214-ABL1 fusion genes will result in multiple orange signals or orange signal clusters.



SPEC ABL1 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Bone marrow biopsy section with translocation affecting the 9q34.11-q34.13 locus as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2199-50	ZytoLight SPEC ABL1 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC BCR/ABL1 Dual Color Dual Fusion Probe

CE IVD

Background

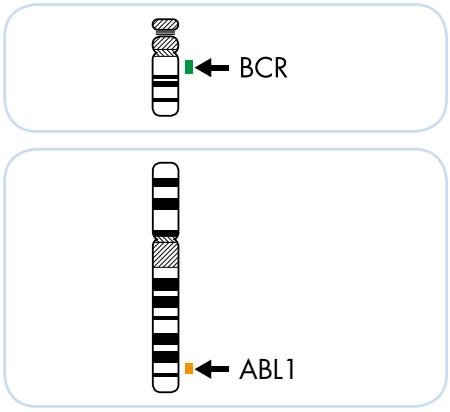
The ZytoLight® SPEC BCR/ABL1 Dual Color Dual Fusion Probe is designed for the detection of the specific translocations involving the chromosomal region 9q34.12 harboring the ABL1 (a.k.a ABL) gene, and the chromosomal region 22q11.23, harboring the BCR (a.k.a. BCR1) gene. Rearrangements involving t(9;22)(q34.1;q11.2) are observed in approx. 90% of patients with chronic myeloid leukemia (CML) and in approx. 25% of adults with acute lymphoblastic leukemia (ALL). The rearrangements are cytogenetically characterized by the presence of the Philadelphia (Ph) chromosome. The translocation frequently results in the formation of a chimeric BCR/ABL1 fusion gene on the derivative chromosome 22. The gene product is a BCR/ABL1 protein with abnormal tyrosine kinase activity. In normal cells, ABL1 kinase activity is finely regulated in response to growth factors and other stimuli. The BCR/ABL1 fusion protein leads to constitutive activation of down-stream signaling pathways, including Ras, Jak/Stat and PI-3 kinase. In rare cases the BCR/ABL1 fusion gene is located on chromosomal sites other than the Ph chromosome.

Fluorescence *in situ* Hybridization (FISH) allows for the identification of rearrangements that could otherwise not be detected by conventional karyotyping.

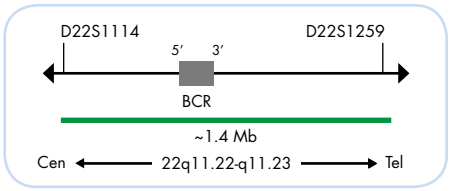
References
Hehne S, et al. (2012) Pathol Res Pract 208: 510-7.
Lim TH, et al. (2005) Ann Acad Med Singapore 34: 533-8.
Primo D, et al. (2003) Leukemia 17: 1124-9.
Rieder H, et al. (1998) Leukemia12: 1473-81.
Sessargeo M, et al. (2000) Haematologica 85: 35-9.
Zheng X, et al. (2009) PLoS One 4: e7661.

Probe Description

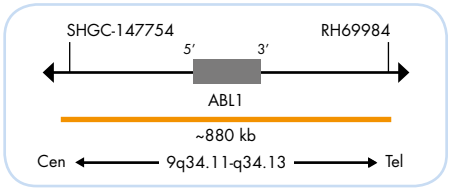
The SPEC BCR/ABL1 Dual Color Dual Fusion Probe is a mixture of a green fluorochrome direct labeled BCR probe spanning the minor and major breakpoint cluster of the BCR gene and an orange fluorochrome direct labeled ABL1 probe spanning the breakpoint region of the ABL1 gene. This probe is approved to be used with a hybridization time of 2 hours on cytological specimens.



Ideograms of chromosomes 22 (above) and 9 (below) indicating the hybridization locations.



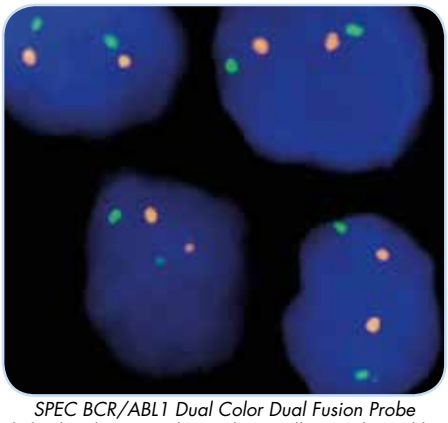
SPEC BCR Probe map (not to scale).



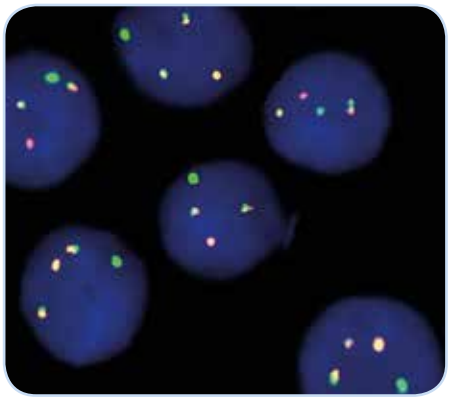
SPEC ABL1 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. A reciprocal translocation involving two breakpoints splits the two signals and generates a fusion signal on each of the chromosomes involved. The chromosomal regions which are not translocated are indicated by the single orange respectively green signal.



SPEC BCR/ABL1 Dual Color Dual Fusion Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Bone marrow biopsy tissue section with translocation affecting the BCR/ABL1 loci as indicated by one separate orange signal, one separate green signal and two orange/green fusion signals.

Prod. No.	Product	Label	Tests* (Volume)
Z-2111-50	ZytoLight SPEC BCR/ABL1 Dual Color Dual Fusion Probe CE IVD	●/●	5 (50 µl)
Z-2111-200	ZytoLight SPEC BCR/ABL1 Dual Color Dual Fusion Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC NUP214 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC NUP214 Dual Color Break Apart Probe is designed for the detection of translocations involving the chromosomal region 9q34.13 harboring the NUP214 (nucleoporin 214, a.k.a. CAN, CAIN) gene.

Rearrangements of the NUP214 gene have been implicated in the pathogenesis of several types of hematologic malignancies, including T-cell acute lymphoblastic leukemia (T-ALL), acute myeloid leukemia (AML), and also myelodysplastic syndrome (MDS). Several fusion partners have been identified for NUP214. The most common are the DEK, SET, and the tyrosine kinase encoding gene ABL1.

The translocation t(6;9)(p22.3;q34.1) results in a DEK-NUP214 fusion and defines a specific subcategory of AML according to the World Health Organization 2008 classification.

The SET-NUP214 fusion is associated with T-ALL, less frequently with AML, and acute undifferentiated leukemia and can result from either a translocation or a deletion.

NUP214-ABL1 fusions are exclusively associated with T-ALL patients. These patients may be considered for a targeted therapy with specific tyrosine kinase inhibitors. The fusion is often located on amplified episomes and is cytogenetically cryptic but can be detected by FISH.

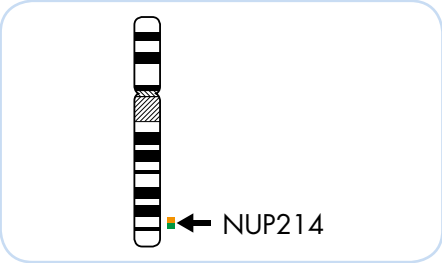
Malignancies with NUP214 rearrangements are associated with a poor prognosis indicating the usefulness of NUP214 also as a prognostic biomarker.

References

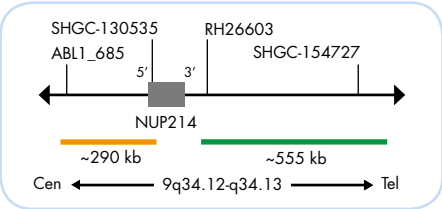
Fahrenkrog B (2014) New J Sci 2014: 468306.
Takeda A & Yaseen NR (2014) Semin Cancer Biol 27: 3-10.
von Lindern M, et al. (1992) Baillieres Clin Haematol 5: 857-79.
Zhou MH & Yang QM (2014) Oncol Lett 8: 959-62.

Probe Description

The SPEC NUP214 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 9q34.12-q34.13 band. The orange fluorochrome direct labeled probe hybridizes proximal and the green fluorochrome direct labeled probe hybridizes distal to the NUP214 gene.



Ideogram of chromosome 9 indicating the hybridization locations.

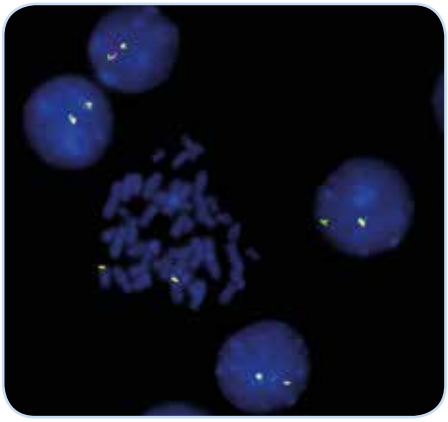


SPEC NUP214 Probe map (not to scale).

Results

In an interphase nucleus lacking a rearrangement involving the 9q34.12-q34.13 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 9q34.12-q34.13 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 9q34.12-q34.13 locus and one 9q34.12-q34.13 locus affected by a translocation.

Isolated green signals are the result of deletions proximal to the NUP214 breakpoint region.



SPEC NUP214 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus and to metaphase chromosomes of a normal cell.

Prod. No.	Product	Label	Tests* (Volume)
Z-2265-50	ZytoLight SPEC NUP214 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

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ZytoLight® SPEC KIF5B Dual Color Break Apart Probe

CE IVD

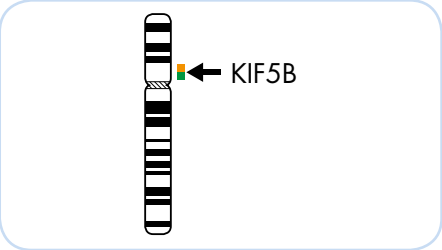
Background

The ZytoLight® SPEC KIF5B Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 10p11.22 harboring the KIF5B (kinesin family member 5B) gene.
About 5% of all non-small cell lung cancer cases are positive for the ALK-EML4 fusion as a result of an inversion in chromosome 2. However, not in all cases showing an aberration of the ALK gene the EML4-ALK fusion transcript could be detected. KIF5B was identified as a novel fusion partner for ALK in ALK-positive lung cancer.
KIF5B is a ubiquitously expressed microtubule-based motor protein involved in organelle transport. The translocation t(2;10)(p23;p11.2) results in the fusion of the first domains of KIF5B including the motor domain and the coiled-coil domain with the tyrosine kinase domain of ALK. Overexpression of the aberrant KIF5B/ALK fusion transcript can lead to enhanced cell proliferation, migration, and invasion.
A further aberration affecting the KIF5B gene is inv(10)(p11.2q11.2). This inversion was detected in adenocarcinomas of the lung and results in the fusion of KIF5B with the ret proto-oncogene (RET). The fusion transcript again comprises the coiled-coil domain of KIF5B and the tyrosine kinase domain of RET. In accordance with the EML4-ALK fusion the development of specific agents targeting KIF5B-RET might provide a new therapeutic strategy for lung adenocarcinomas.

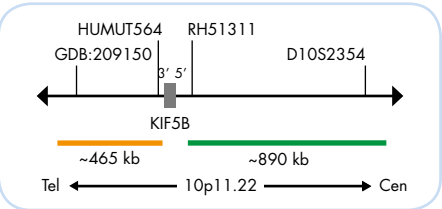
References
Gautschi O, et al. (2013) J Thorac Oncol 8: e43-4.
Ju YS, et al. (2012) Genome Res 22: 436-45.
Kohno T, et al. (2012) Nat Med 18: 375-7.
Takeuchi K, et al. (2009) Clin Cancer Res 15: 3143-9.
Takeuchi K, et al. (2012) Nat Med 18: 378-81.
Wong DW, et al. (2011) Cancer 117: 2709-18.

Probe Description

The SPEC KIF5B Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 10p11.22 band. The orange fluorochrome direct labeled probe hybridizes distal, the green fluorochrome direct labeled probe hybridizes proximal to the KIF5B gene.



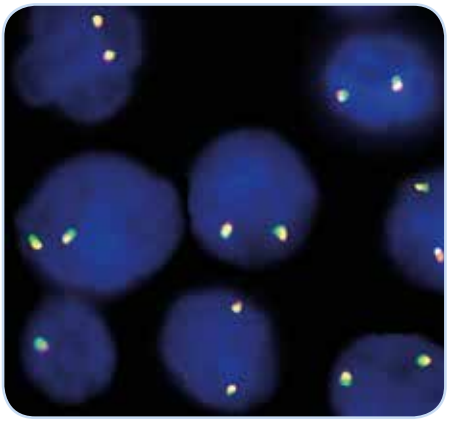
Ideogram of chromosome 10 indicating the hybridization locations.



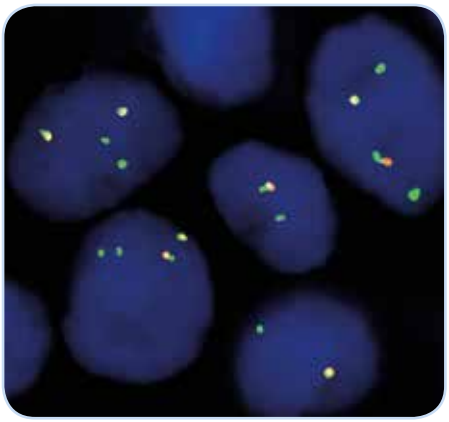
SPEC KIF5B Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 10p11.22 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 10p11.22 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 10p11.22 locus and one 10p11.22 locus affected by a translocation.



SPEC KIF5B Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



NSCLC tissue section with tetrasomy of chromosome 10 in some cells and an unbalanced translocation affecting KIF5B as indicated by one or two extra green signals.

Prod. No.	Product	Label	Tests* (Volume)
Z-2131-50	ZytoLight SPEC KIF5B Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC RET Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC RET Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 10q11.21 harboring the RET (ret proto-oncogene) gene.

RET encodes a tyrosine kinase (TK) receptor. Translocations involving RET were first described in papillary thyroid carcinoma (PTC) where somatic rearrangements result in the fusion of its TK catalytic domain with an N-terminal dimerization domain encoded by various fusion partner genes.

More recently, recurrent inversions [inv (10)(p11.2q11.2)] fusing the coiled-coil domains of the kinesin family member 5B (KIF5B) gene to the RET kinase domain have been detected in lung adenocarcinoma. The resulting KIF5B-RET fusion protein can form homodimers through the coiled-coil domains of KIF5B, causing an aberrant activation of the TK of RET, a mechanism known from KIF5B-ALK fusions which is also found in lung adenocarcinoma.

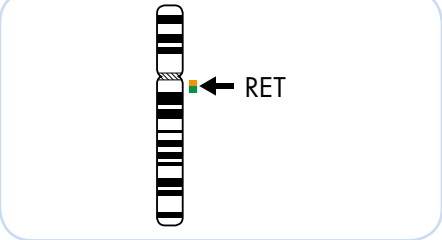
Since *in vitro* studies showed transforming activity of KIF5B-RET which could be suppressed by a TK inhibitor, it was assumed that the chimeric oncogene might be a promising molecular target for the treatment of lung cancer.

The same holds true for the very recently discovered BCR-RET and FGFR1OP-RET fusion genes in chronic myelomonocytic leukemia (CMML) generated by two balanced translocations t(10;22)(q11.2;q11.2) and t(6;10)(q27;q11.2), respectively.

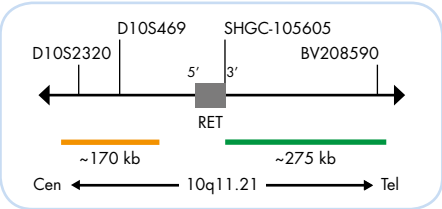
References
Ballerini P, et al. (2012) Leukemia 26: 2384-9.
Gautschi O, et al. (2013) J Thorac Oncol 8: e43-4.
Ju YS, et al. (2012) Genome Res 22: 436-45.
Kohno T, et al. (2012) Nat Med 18: 375-7.
Lee SE, et al. (2015) Mod Pathol 28: 468-79.
Nikiforov YE (2002) Endocr Pathol 13: 3-16.
Takahashi M, et al. (1985) Cell 42: 581-8.
Takeuchi K, et al. (2012) Nat Med 18: 378-81.

Probe Description

The SPEC RET Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 10q11.21 band. The orange fluorochrome direct labeled probe hybridizes proximal to the RET gene, the green fluorochrome direct labeled probe hybridizes distal to that gene.



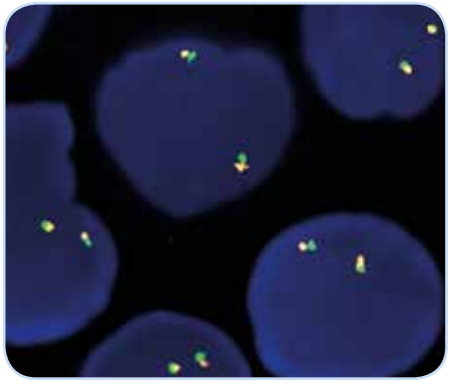
Ideogram of chromosome 10 indicating the hybridization locations.



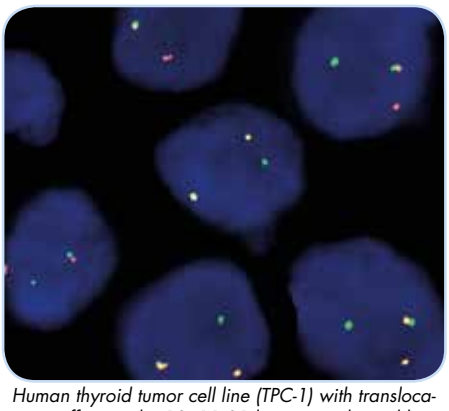
SPEC RET Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 10q11.21 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 10q11.21 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 10q11.21 locus and one 10q11.21 locus affected by a translocation or inversion. Isolated green signals are the result of deletions proximal to the RET breakpoint region.



SPEC RET Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Human thyroid tumor cell line (TPC-1) with translocation affecting the 10q11.21 locus as indicated by one orange/green fusion (non-rearranged) signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2148-50	ZytoLight SPEC RET Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2148-200	ZytoLight SPEC RET Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC PTEN/CEN 10 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC PTEN/CEN 10 Dual Color Probe is designed for the detection of PTEN deletions frequently observed in many tumor types, including renal, melanoma, endometrial, breast, prostate, lung, bladder, and thyroid cancer but also in hematological neoplasms.

The tumor suppressor gene PTEN (phosphatase and tensin homolog deleted on chromosome ten), often referred to as MMAC1 (mutated in multiple advanced cancers 1), is located on 10q23.31 and encodes a 47 kDa dual-specificity phosphatase that has both lipid and protein phosphatase activity. Its inactivation results in constitutive activation of the PI3K/AKT pathway and in subsequent increase in protein synthesis, cell cycle progression, migration, and survival.

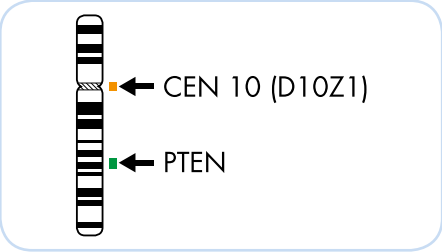
Deletions affecting the long arm of chromosome 10 have been detected in 30 to 50% of early and advanced stage sporadic melanomas and about 40 to 70% of prostate cancers. In both tumor entities loss of PTEN has been associated with poor clinical outcome. Currently, several drugs targeting the PI3K/AKT pathway for the therapy of solid tumors have entered clinical trials.

References

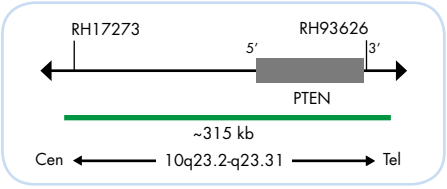
Ach T, et al. (2013) Virchows Arch 462: 65-72.
Dahia PLM, et al. (1999) Hum Mol Genet 8: 185-93.
Ettl T, et al. (2012) Br J Cancer 106: 719-26.
Ettl T, et al. (2014) Head Neck 36: 517-23.
Healy E, et al. (1998) Oncogene 16: 2213-8.
Li J, et al. (1997) Science 275: 1943-7.
Swoboda A, et al. (2011) Genes Chromosomes Cancer 50: 680-8.
Weng LP, et al. (2001) Hum Mol Genet 10: 599-604.
Yoshimoto M, et al. (2006) Cancer Genet Cytogenet 169: 128-37.
Yoshimoto M, et al. (2007) Br J Cancer 97: 678-85.

Probe Description

The SPEC PTEN/CEN 10 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 10 probe specific for the alpha satellite centromeric region of chromosome 10 (D10Z1) and a green fluorochrome direct labeled SPEC PTEN probe specific for the chromosomal region 10q23.2-q23.31 harboring the PTEN gene.



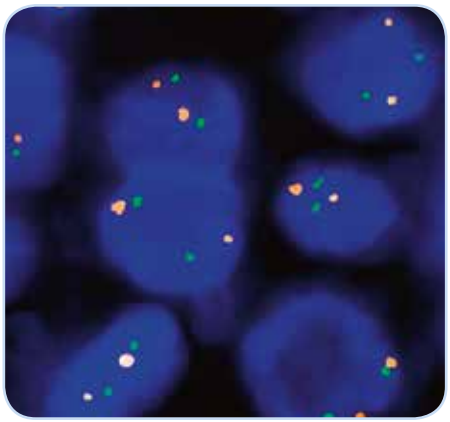
Ideogram of chromosome 10 indicating the hybridization locations.



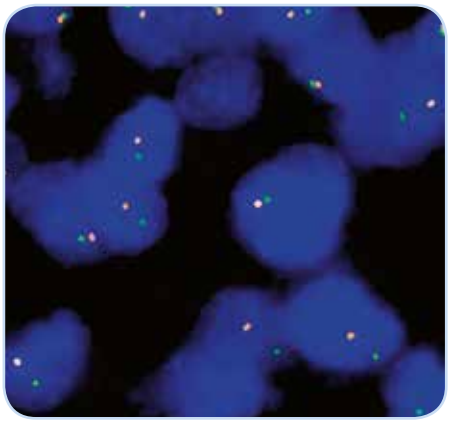
SPEC PTEN Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletions of the PTEN gene locus, a reduced number of green signals will be observed. Deletions affecting only parts of the PTEN gene might result in normal signal pattern with green signals of reduced size.



SPEC PTEN/CEN 10 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Melanoma tissue section with chromosome 10 monosomy as indicated by one orange and one green signal in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2078-50	ZytoLight SPEC PTEN/CEN 10 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2078-200	ZytoLight SPEC PTEN/CEN 10 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC FGFR2 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC FGFR2 Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal region 10q26.13 harboring the FGFR2 (fibroblast growth factor receptor 2, a.k.a. BEK) gene.

Translocations and inversions affecting FGFR2 have been detected in several solid tumors, including e.g. breast cancer, lung cancer, and the intrahepatic subtype of cholangiocarcinoma.

Several partner genes have been described to be fused to FGFR2 after rearrangement. The resulting fusion genes are predicted to encode chimeric proteins carrying the kinase domain of FGFR2. Most of the currently known FGFR2 fusion products are likely to exhibit oligomerization capability resulting in kinase activation.

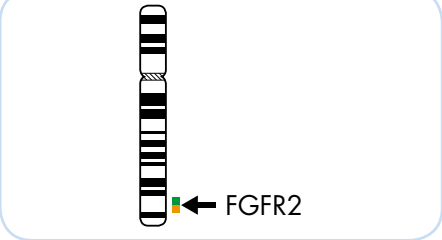
In prostate cancer FGFR2 was found to be fused to the promoter region of SLC45A3 predicted to result in signal activation by overexpression of the FGFR2 protein.

Recent studies indicate the involvement of FGFR2 fusion proteins in tumorigenesis. Moreover, *in vitro* studies suggest that certain FGFR tyrosine kinase inhibitors may provide a new therapeutic option for patients showing FGFR2 rearrangement. Hence, detection of FGFR2 rearrangements using FISH may help to identify patients which might respond to FGFR2 kinase targeting therapies.

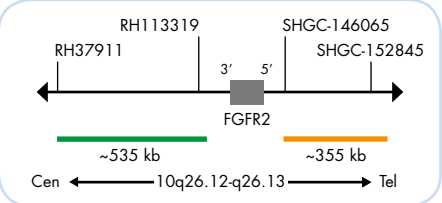
References
Arai Y, et al. (2014) Hepatology 59: 1427-34.
Seo JS, et al. (2012) Genome Res 22: 2109-19.
Wu YM, et al. (2013) Cancer Discov 3: 636-47.

Probe Description

The SPEC FGFR2 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 10q26.12-q26.13 band. The orange fluorochrome direct labeled probe hybridizes distal to the FGFR2 gene at 10q26.13, the green fluorochrome direct labeled probe hybridizes proximal to the FGFR2 gene at 10q26.12-q26.13.



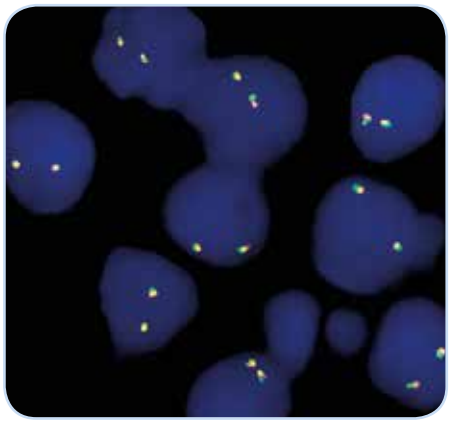
Ideogram of chromosome 10 indicating the hybridization locations.



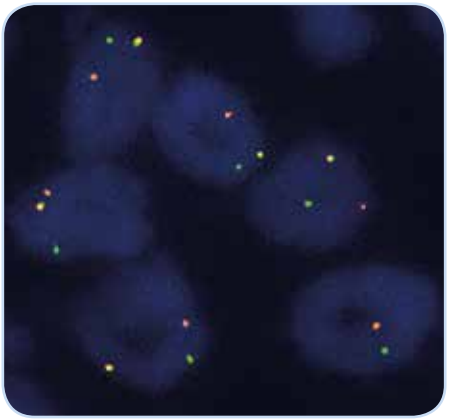
SPEC FGFR2 Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 10q26.13 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 10q26.13 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 10q26.13 locus and one 10q26.13 locus affected by a translocation.



SPEC FGFR2 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Cholangiocellular adenocarcinoma tissue section with translocation of the FGFR2 gene as indicated by one non-rearranged orange/green fusion signal, one orange, and one separate green signal.

Kindly provided by Prof. Dr. Büttner, Cologne, Germany.

Prod. No.	Product	Label	Tests* (Volume)
Z-2169-200	ZytoLight SPEC FGFR2 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC FGFR2/CEN 10 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC FGFR2/CEN 10 Dual Color Probe is designed for the detection of FGFR2 gene amplifications frequently observed in breast cancer as well as in gastric cancer.

The FGFR2 (fibroblast growth factor gene 2, a.k.a. BEK) gene is located on chromosome 10q26.13 and encodes splice variants of the receptor tyrosine kinases FGFR2b and FGFR2c.

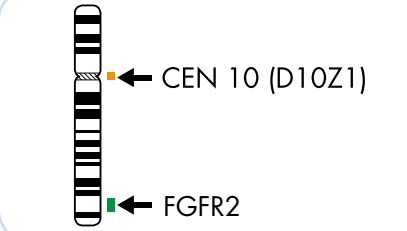
Amplification of the FGFR2 gene leads to overexpression of the FGFR2 protein and subsequently to signal activation. Additionally, during the amplification process the C-terminal deletion of FGFR2 can occur due to exclusion of the last exon from the FGFR2 amplicon. Both, overexpression and deletion of the last exon result in FGFR2 signaling activation based on constitutive phosphorylation of the FRS2 adaptor molecule.

The process of ligand independent FGFR2 signaling leads to a more severe malignant phenotype of these tumors. Moreover, high FGFR2 expression is correlated with poor overall survival (OS) and poor disease-free survival (DFS) rates in breast cancer patients. Consequently, FGFR2 gene amplification detected by Fluorescence *in situ* Hybridization might be used as a prognostic marker e.g. in breast cancer.

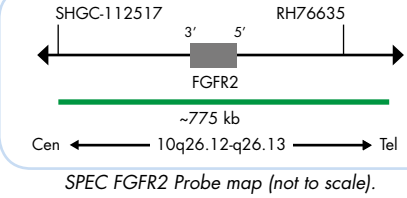
References
Azuma K, et al. (2011) Biochem Biophys Res Commun 407: 219-24.
Chang J, et al. (2015) Oncotarget 6: 2009-22.
Katoh M (2010) Expert Rev Anticancer Ther 10: 1375-9.
Katoh Y & Katoh M (2009) Int J Mol Med 23: 307-11.
Moffa AB, et al. (2004) Mol Cancer Res 2: 643-52.
Sun S, et al. (2012) J Surg Oncol 105: 773-9.

Probe Description

The SPEC FGFR2/CEN 10 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 10 probe specific for the alpha satellite centromeric region of chromosome 10 (D10Z1) and a green fluorochrome direct labeled SPEC FGFR2 probe specific for the chromosomal region 10q26.12-q26.13 harboring the FGFR2 gene.



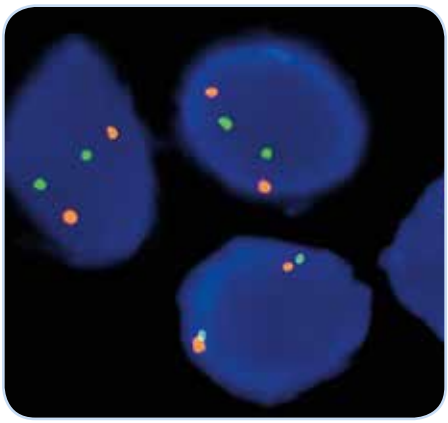
Ideogram of chromosome 10 indicating the hybridization locations.



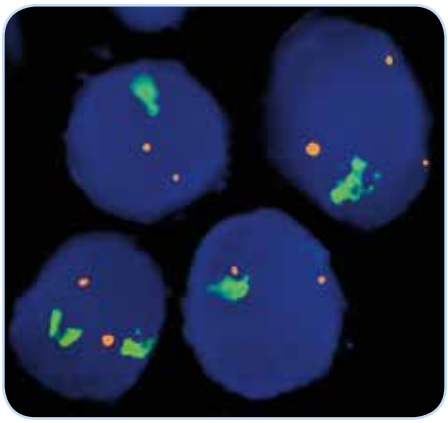
SPEC FGFR2 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. Nuclei with amplification of the FGFR2 gene locus 10q26.12-q26.13, or aneuploidy of chromosome 10 will show multiple copies of the green signal or large green signal clusters.



SPEC FGFR2/CEN 10 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Breast cancer tissue section with amplification of the FGFR2 gene as indicated by green signal clusters in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2122-200	ZytoLight SPEC FGFR2/CEN 10 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC CARS Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC CARS Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 11p15.4 harboring the CARS (cysteinyl-tRNA-synthetase) gene detected in inflammatory myofibroblastic tumors (IMT).

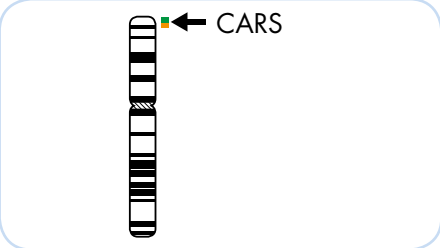
IMT are neoplastic mesenchymal proliferations that occur predominantly in children and young adults. Cytogentic studies of IMT show various complex karyotypic abnormalities, frequently involving the short arm of chromosome 2 harboring the ALK gene locus in 2p23.1-p23.2. The ALK (ALK receptor tyrosine kinase, a.k.a. CD246) gene encodes a receptor tyrosine kinase and was frequently identified as a fusion partner of various hybrid genes predominantly in anaplastic large cell lymphoma, and more recently, in non-small cell lung cancer. However, also in IMT several different ALK fusion genes have been identified including CARS-ALK. CARS encodes a class 1 aminoacyl-tRNA synthetase and is ubiquitously expressed. The translocation results in the fusion of the active promoter as well as the first domains of CARS to the receptor tyrosine kinase domain of ALK. Thus, CARS is predicted to mediate homodimerization of the chimeric product resulting in constitutive ALK kinase activation.

The detection of translocations affecting CARS and ALK by Fluorescence *in situ* Hybridization might represent a valuable tool to identify a subpopulation of IMT likely to respond to ALK kinase targeting therapies.

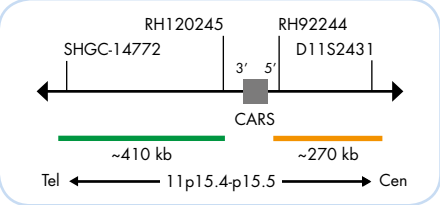
References
Butrynski JE, et al. (2010) N Engl J Med 363: 1727-33.
Cools J, et al. (2002) Genes Chromosomes Cancer 34: 354-62.
Cruzen ME, et al. (1993) Genomics 15: 692-3.
Debelenko LV, et al. (2003) Lab Invest 83: 1255-65.

Probe Description

The SPEC CARS Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 11p15.4-p15.5 band. The orange fluorochrome direct labeled probe hybridizes proximal to the CARS gene and the green fluorochrome direct labeled probe hybridizes distal to that gene.



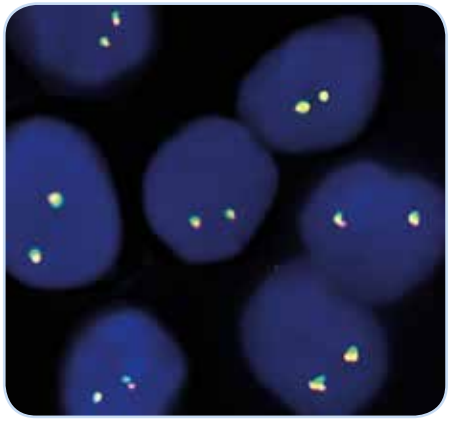
Ideogram of chromosome 11 indicating the hybridization locations.



SPEC CARS Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 11p15.4-p15.5 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 11p15.4-p15.5 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 11p15.4-p15.5 locus and one 11p15.4-p15.5 locus affected by a translocation.



SPEC CARS Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2137-50	ZytoLight SPEC CARS Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC NUP98 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC NUP98 Dual Color Break Apart Probe is designed for the detection of translocations involving the chromosomal region 11p15.4 harboring the NUP98 (nucleoporin 98, a.k.a. NUP96) gene.

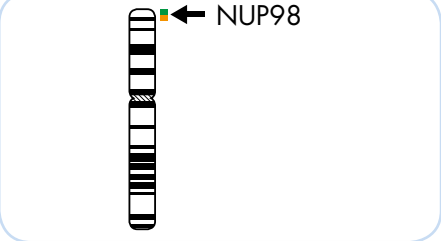
The nucleoporin NUP98, a component of the nuclear pore complex, is involved in nucleocytoplasmic transport and exhibits multiple roles in RNA export from and protein import into the nucleus. Rearrangements of the NUP98 gene have been implicated in the pathogenesis of several types of hematologic malignancies, including *de novo* and therapy-related acute myeloid leukemia (AML), and also myelodysplastic syndrome (MDS), chronic myelogenous leukemia (CML), and T-cell acute lymphoblastic leukemia (T-ALL). NUP98 rearrangements result in the fusion of the N-terminal region of NUP98, which is rich in phenylalanine-glycine (FG) repeats, to one of 29 different proteins. Many of the NUP98 fusion partners are transcription factors of the homeobox family. NUP98 fusions cause aberrant differentiation and increased proliferation when expressed in primary human hematopoietic cells.

Malignancies with NUP98 rearrangements are associated with a poor prognosis and a poor treatment outcome indicating the usefulness of NUP98 as a prognostic biomarker.

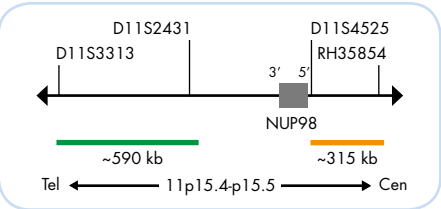
References
Borrow J, et al. (1996) Nat Genet 12: 159-67.
Fahrenkrog B (2014) New J Sci 2014: 468306.
Takeda A & Yaseen NR (2014) Semin Cancer Biol 27: 3-10.

Probe Description

The SPEC NUP98 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 11p15.4-p15.5 band. The orange fluorochrome direct labeled probe hybridizes proximal and the green fluorochrome direct labeled probe hybridizes distal to the NUP98 gene.



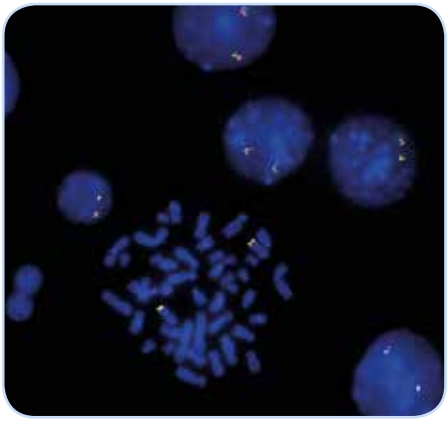
Ideogram of chromosome 11 indicating the hybridization locations.



SPEC NUP98 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 11p15.4-p15.5 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 11p15.4-p15.5 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 11p15.4-p15.5 locus and one 11p15.4-p15.5 locus affected by a translocation or inversion.



SPEC NUP98 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus and to metaphase chromosomes of a normal cell.

Prod. No.	Product	Label	Tests* (Volume)
Z-2266-50	ZytoLight SPEC NUP98 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC WT1 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC WT1 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 11p13 harboring the WT1 (Wilms tumor 1) gene.

The WT1 gene is located on 11p13 and encodes a zinc finger DNA-binding protein that acts as a transcriptional activator or repressor depending on the cellular or chromosomal context. Inactivating mutations in the tumor suppressor gene WT1 have been identified in patients with Wilms' tumor and in a subset of sporadic cancers.

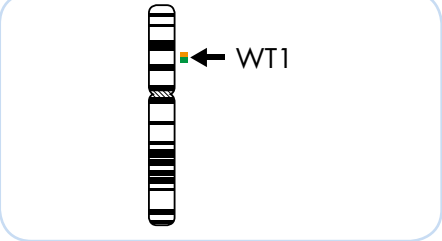
However, in desmoblastic small round cell tumors (DSRCT) recurrent translocations affecting the WT1 gene have been found. DSRCT is a highly aggressive mesenchymal tumor that primarily affects male adolescents and young adults. The translocation t(11;22)(p13;q12.2) is detectable in virtually all DSRCT tested and results in the fusion of the potent transcriptional activator domain of the EWSR1 gene and the DNA-binding zinc-finger domains of the WT1 gene. The EWSR1-WT1 chimeric protein acts as an oncogenic transcription factor as evidenced by its ability to transform cells *in vitro*.

While EWSR1 rearrangements are present in about 90% of DSRCT but are also frequently found in other small round blue cell neoplasms as e.g. Ewing sarcoma, WT1 translocations are exclusively found in DSRCT. Hence, detection of the t(11;22) by Fluorescence *in situ* Hybridization represents a valuable tool for the differential diagnosis of DSRCT.

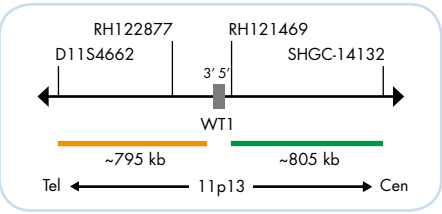
References
Gerald WL, et al. (1995) Proc Natl Acad Sci U S A 92: 1028-32.
Kim J, et al. (1998) Oncogene 16: 1973-9.
Ladanyi M & Gerald W (1994) Cancer Res 54: 2837-40.
Wang ZY, et al. (1993) J Biol Chem 268: 9172-5.

Probe Description

The SPEC WT1 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 11p13 band. The orange fluorochrome direct labeled probe hybridizes distal and the green fluorochrome direct labeled probe hybridizes proximal to the WT1 gene.



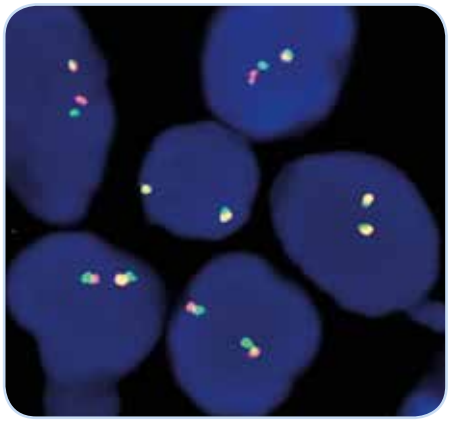
Ideogram of chromosome 11 indicating the hybridization locations.



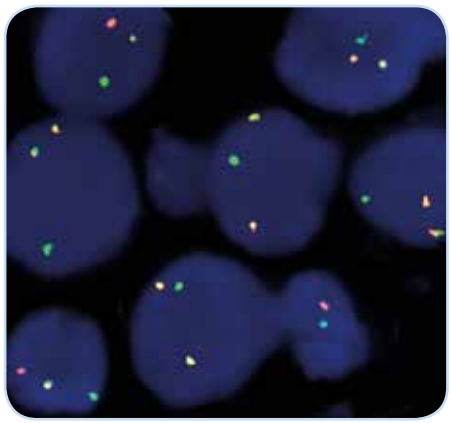
SPEC WT1 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 11p13 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 11p13 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 11p13 locus and one 11p13 locus affected by a translocation.



SPEC WT1 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Desmoblastic small round cell tumor tissue section with translocation affecting the 11p13 locus as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2142-50	ZytoLight SPEC WT1 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC SPI1 Dual Color Break Apart Probe

CE IVD

Background

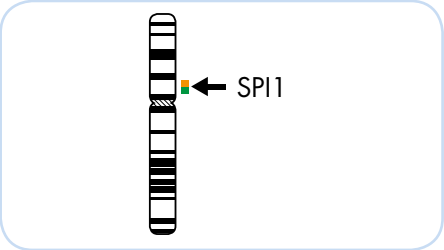
The ZytoLight® SPEC SPI1 Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal region 11p11.2 harboring the SPI1 (Spi-1 proto-oncogene, a.k.a. PU.1, SPI-A) gene.

SPI1 is a member of the ETS family of transcription factors and is essential for the normal development of hematopoietic stem cells. SPI1 rearrangements were detected in some pediatric T-cell acute lymphoblastic leukemia (T-ALL) cases resulting in the fusion of the N-terminal region of the fusion partner (STMN1, TCF7, or BCL11B) to the C-terminal DNA binding ETS domain of the SPI1 protein. Hence, the resulting fusion proteins retain the transcriptional activity inherent to SPI1. SPI1 fusion positive cases show markedly elevated SPI1 expression, most likely because the fusion gene comes under the transcriptional control of the heterologous promoter of the respective partner gene. Overexpression of SPI1 is thought to contribute to T-cell leukemogenesis. Moreover, T-ALL patients with SPI1 fusion show a uniformly poor overall survival and seem to be incurable with current standard chemotherapy. This underscores the importance of detecting this subset of patients by FISH so that they may receive more intensive or alternative therapies.

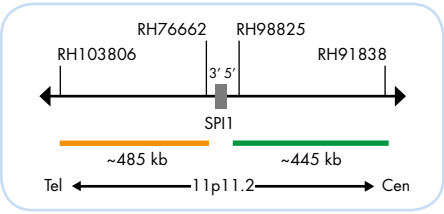
References
Homminga I, et al. (2011) Cancer Cell 19: 484-97.
Liu Y, et al. (2017) Nat Genet 49: 1211-8.
Seki M, et al. (2017) Nat Genet 49: 1274-81.

Probe Description

The SPEC SPI1 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 11p11.2 band. The green fluorochrome direct labeled probe hybridizes proximal to the SPI1 gene at 11p11.2, the orange fluorochrome direct labeled probe hybridizes distal to the SPI1 gene at 11p11.2.



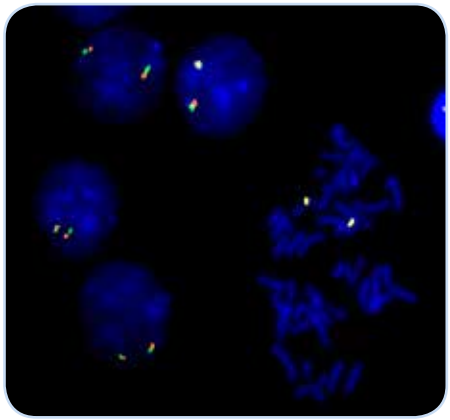
Ideogram of chromosome 11 indicating the hybridization locations.



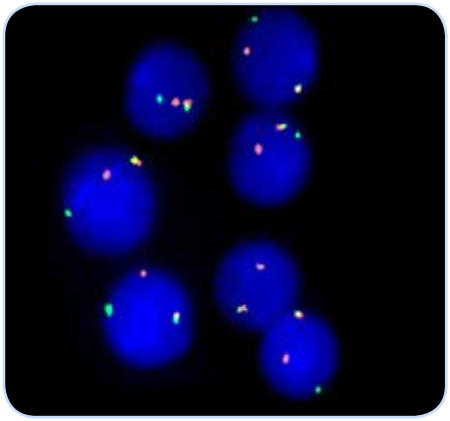
SPEC SPI1 Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 11p11.2 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 11p11.2 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 11p11.2 locus and one 11p11.2 locus affected by a translocation.



SPEC SPI1 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals in each nucleus and to metaphase chromosomes of a normal cell.



Bone marrow smear with translocation of the SPI1 gene as indicated by one non-rearranged orange/green fusion signal, one orange and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2291-50	ZytoLight SPEC SPI1 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC CCND1 Dual Color Break Apart Probe

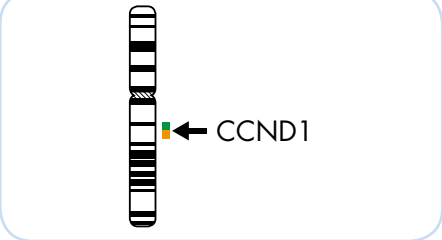
CE IVD

Background

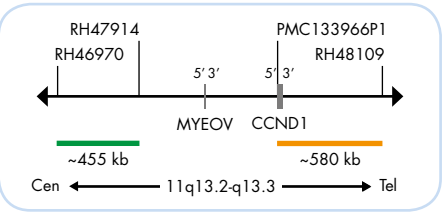
The ZytoLight® SPEC CCND1 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 11q13.3 harboring the CCND1 gene. The CCND1 gene (cyclin D1, a.k.a. BCL1 or PRAD1) encodes a regulatory subunit of cyclin-dependent kinases. Translocations involving the chromosomal region t(11;14) (q13.3;q32.3) are considered to be characteristic for mantle cell lymphomas (MCL) but have also been identified in other lymphoproliferative disorders (LPDs), such as B-prolymphocytic leukemia, and, less frequently, in plasma cell myelomas, B-cell chronic lymphocytic leukemia, and in splenic lymphomas with villous lymphocytes (SLVL).
The t(11;14) rearrangement often leads to overexpression of the CCND1 protein. Determination of translocations involving the chromosomal region 11q13.3 can also help to distinguish MCL from other chronic lymphoproliferative disorders. Since the course of MCL is aggressive, and its response to chemotherapy is poor, differential diagnosis is clinically important. Additionally, it was also shown that a renal oncocytoma (RO) specific breakpoint is located in band 11q13.3, involving the CCND1 locus. The histologic features of RO may overlap with those of chromophobe renal cell carcinoma (ChRCC). Fluorescence *in situ* Hybridization (FISH) can be used as a diagnostic tool for differentiation of RO from ChRCC.

Probe Description

The SPEC CCND1 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 11q13.2-q13.3 band. The orange fluorochrome direct labeled probe hybridizes distal to and covers the CCDN1 gene, while the green fluorochrome direct labeled probe hybridizes proximal to that gene.



Ideogram of chromosome 11 indicating the hybridization locations.

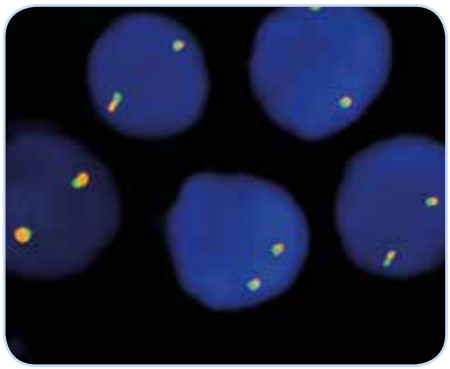


SPEC CCND1 Probe map (not to scale).

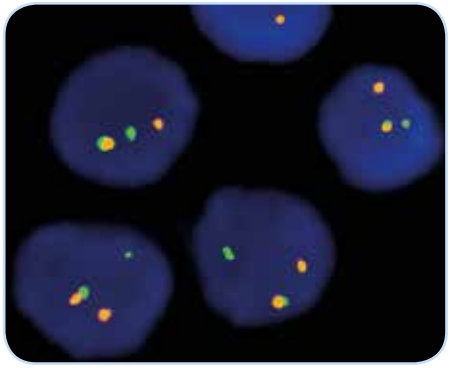
References
Bentz JS, et al. (2004) Cancer 102: 124-31.
Bosch F, et al. (1997) Cancer 82: 567-75.
Sinke RJ, et al. (1997) Cancer Genet Cytogenet 96: 95-101.
Sukov WR, et al. (2007) Hum Pathol 40: 1296-303.
Tarsitano M, et al. (2009) Cancer Genet Cytogenet 195: 164-7.
Vaandrager JW, et al. (1996) Blood 4: 1177-82.

Results

In an interphase nucleus lacking a translocation involving the 11q13.2-q13.3 band, two orange/green fusion signals are expected representing two normal (non-rearranged) CCND1 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal CCND1 locus and one CCND1 locus affected by an 11q13.2-q13.3 translocation.



SPEC CCND1 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Bone marrow biopsy section with translocation affecting the 11q13.2-q13.3 locus as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2108-50	ZytoLight SPEC CCND1 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2108-200	ZytoLight SPEC CCND1 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC CCND1/CEN 11 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC CCND1/CEN 11 Dual Color Probe is designed for the detection of CCND1 gene amplification frequently observed in breast cancer and other human tumors.

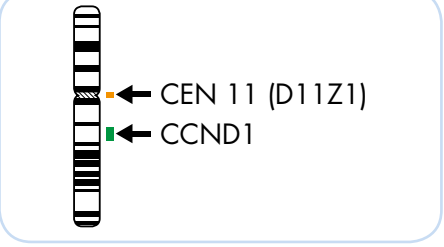
The cyclin D1 gene CCND1 (a.k.a. BCL1 or PRAD1) is located in the chromosomal region 11q13.3 and encodes a regulatory subunit of cyclin-dependent kinases that promote progression through the cell cycle.

The proto-oncogene CCND1 is amplified in a number of solid tumors including approx. 20% of all human breast cancer cases and about 30% of squamous cell carcinomas of the esophagus and the head and neck region. Amplification of chromosomal material from 11q13.3 harboring the CCND1 gene is discussed as a prognostic marker in terms of metastasis, tumor recurrence, and survival for several tumor entities. In gastrointestinal stromal tumors (GIST), CCND1 amplification was found in 16% of high-risk tumors and was absent in low- or intermediate-risk tumors indicating the prognostic relevance of this genetic alteration in GIST.

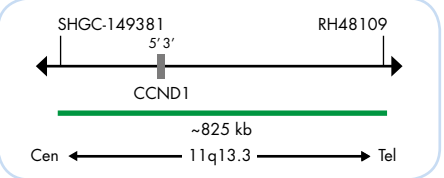
References
Al-Kuraya K, et al. (2004) Cancer Res 64: 8534-40.
Courjal F, et al. (1997) Cancer Res 57: 4360-7.
Motokura T, et al. (1991) Nature 350: 512-5.
Ormandy CJ, et al. (2003) Breast Cancer Res Treat 78: 323-35.
Schuuring E (1995) Gene 159: 83-96.
Tornillo L, et al. (2005) Lab Invest 85: 921-31.
Xiong Y, et al. (1991) Cell 65: 691-9.

Probe Description

The SPEC CCND1/CEN 11 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 11 probe specific for the alpha satellite centromeric region of chromosome 11 (D11Z1) and a green fluorochrome direct labeled SPEC CCND1 probe specific for the CCND1 gene at 11q13.3.



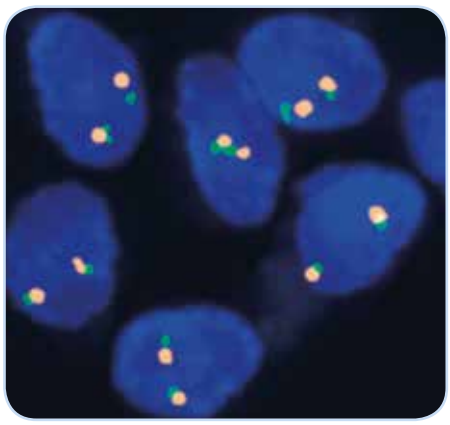
Ideogram of chromosome 11 indicating the hybridization locations.



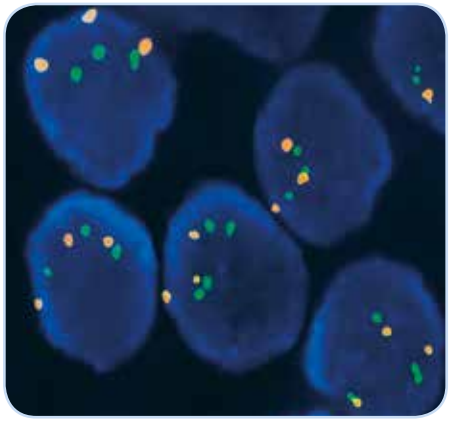
SPEC CCND1 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the CCND1 gene locus, multiple copies of the green signal or large green signal clusters will be observed.



SPEC CCND1/CEN 11 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Polysomy of chromosome 11 as indicated by three orange (CEN 11) and three green (CCND1) signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2071-50	ZytoLight SPEC CCND1/CEN 11 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2071-200	ZytoLight SPEC CCND1/CEN 11 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC CCND1/IGH Dual Color Dual Fusion Probe

CE IVD

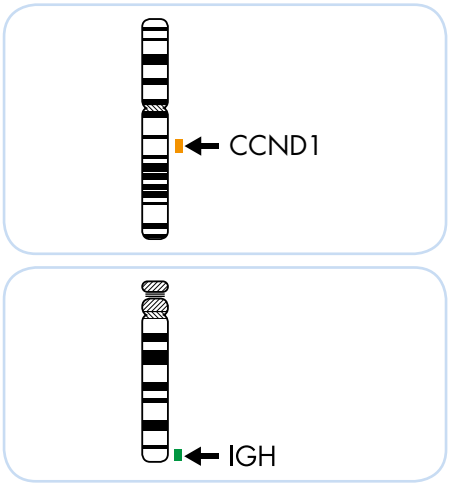
Background

The ZytoLight® SPEC CCND1/IGH Dual Color Dual Fusion Probe is designed to detect translocation t(11;14)(q13.3;q32.3) frequently found in mantle cell lymphomas. The translocation juxtaposes the CCND1 gene (cyclin D1, a.k.a. PRAD1 and BCL1) next to the IGH (immunoglobulin heavy locus, a.k.a. IGH@) locus and results in constitutive overexpression of CCND1. The translocation t(11;14)(q13.3;q32.3) that involves the CCND1 and IGH gene regions is detected in up to 95% of patients with mantle cell lymphomas (MCL) and is considered to be the genetic hallmark of this subtype of low-grade peripheral B-cell neoplasms. However, the t(11;14) has also been identified in other lymphoproliferative disorders (LPDs), such as B-prolymphocytic leukemia (PLL), and, less frequently, in plasma cell myelomas, B-cell chronic lymphocytic leukemia, and in splenic lymphomas with villous lymphocytes (SLVL).
Since the course of MCL is aggressive, and its response to standard chemotherapy is poor, differential diagnosis from other chronic lymphoproliferative disorders via detection of the t(11;14) translocation might be of great clinical importance.

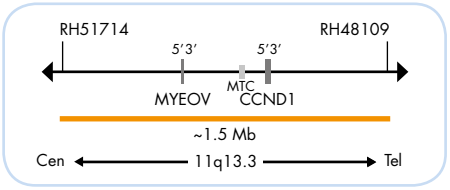
References
Bentz JS, et al. (2004) Cancer 102: 124-31.
Li JY, et al. (1999) Am J Pathol 154: 1449-52.
Siebert R, et al. (1998) Ann Oncol 9: 519-26.
Vaandrager JW, et al. (1996) Blood 88: 1177-82.

Probe Description

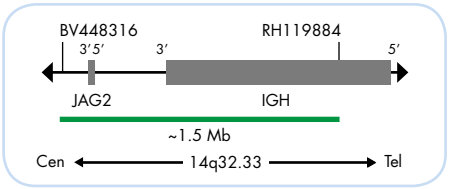
The SPEC CCND1/IGH Dual Color Dual Fusion Probe is a mixture of an orange fluorochrome direct labeled CCND1 probe spanning the major translocation cluster (MTC) region comprising about 120 kb upstream of CCND1 and a green fluorochrome direct labeled IGH probe spanning the breakpoint cluster region of IGH.



Ideograms of chromosomes 11 (above) and 14 (below) indicating the hybridization locations.



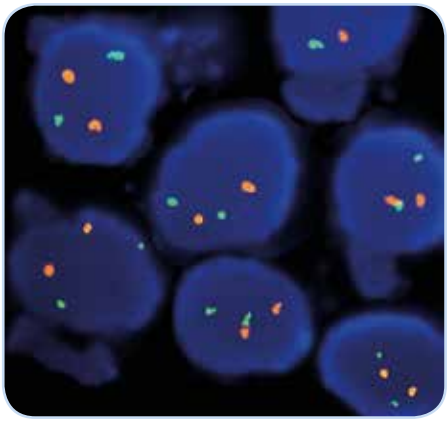
SPEC CCND1 Probe map (not to scale).



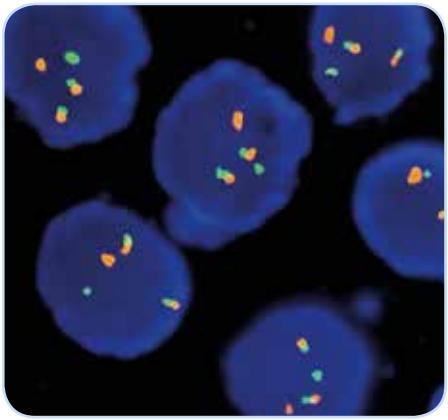
SPEC IGH Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. A reciprocal CCND1/IGH translocation leads to two orange/green fusion signals indicating both rearranged chromosomes. Additionally, the non-rearranged chromosomes are indicated by one orange signal and a separate green signal, respectively.



SPEC CCND1/IGH Dual Color Dual Fusion Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Section of an iliac crest biopsy with translocation affecting the CCND1/IGH loci as indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.

Prod. No.	Product	Label	Tests* (Volume)
Z-2125-50	ZytoLight SPEC CCND1/IGH Dual Color Dual Fusion Probe CE IVD	●/●	5 (50 µl)
Z-2125-200	ZytoLight SPEC CCND1/IGH Dual Color Dual Fusion Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC MAML2 Dual Color Break Apart Probe

CE IVD

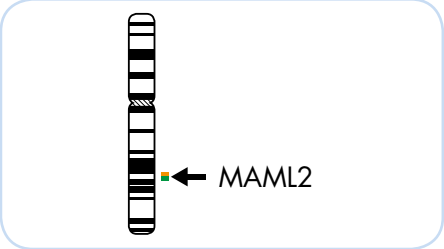
Background

The ZytoLight® SPEC MAML2 Dual Color Break Apart Probe is designed to detect the translocation t(11;19)(q21;p13.1) specific for mucoepidermoid carcinomas. The mucoepidermoid carcinoma is the most common malignant tumor of the salivary gland. With about 30-50% of all cases, the translocation t(11;19)(q21;p13.1) is the most frequent chromosomal aberration in mucoepidermoid carcinomas. In some cases the t(11;19) is the sole chromosomal anomaly and in other cases the t(11;19) was found either as a more complex translocation involving other chromosomes or together with other abnormalities.

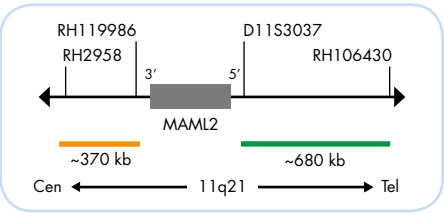
References
Bishop JA, et al. (2014) Head Neck Pathol 8: 287-90.
Camelo-Piragua SI, et al. (2009) Hum Pathol 40: 887-92.
Chiosea SI, et al. (2012) Laryngoscope 122: 1690-4.
El-Naggar A, et al. (1996) Cancer Genet Cytogenet 87: 29-33.
Jee KJ, et al. (2013) Mod Pathol 26: 213-22.
Lei Y & Chiosea SI (2012) Head Neck Pathol 6: 166-70.
Noda H, et al. (2013) Cancer Sci 104: 85-92.
Nordkvist A, et al. (1994) Cancer Genet Cytogenet 74: 77-83.
Rotellini M, et al. (2012) J Oral Pathol Med 41: 615-20.
Schwarz S, et al. (2011) Histopathology 58: 557-70.
Schwarz S, et al. (2011) Int J Clin Exp Pathol 4: 336-48.
Winnes M, et al. (2007) Genes Chromosomes Cancer 46: 559-63.
Zhu F, et al. (2014) PLoS One 9: e94399.

Probe Description

The SPEC MAML2 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 11q21 band. The green fluorochrome direct labeled probe hybridizes distal to the MAML2 gene, the orange fluorochrome direct labeled probe hybridizes proximal to that gene.



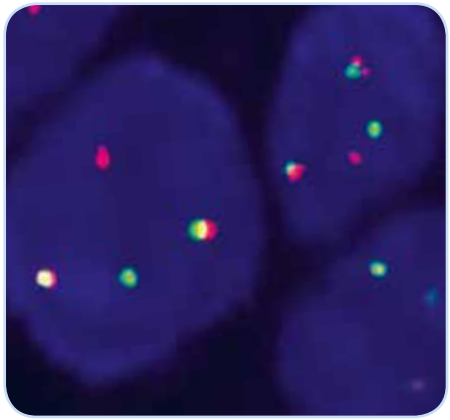
Ideogram of chromosome 11 indicating the hybridization locations.



SPEC MAML2 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 11q21 band two orange/green fusion signals are expected representing two normal (non-rearranged) 11q21 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 11q21 locus and one 11q21 locus affected by the translocation specific for mucoepidermoid carcinomas.



SPEC MAML2 Dual Color Break Apart Probe hybridized to abnormal nuclei containing two normal chromosomes 11 as indicated by two orange/green signal pairs and a derivative chromosome 11 with a translocation involving the 11q21 band as indicated by one orange and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2014-50	ZytoLight SPEC MAML2 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2014-200	ZytoLight SPEC MAML2 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC BIRC3/MALT1 Dual Color Dual Fusion Probe

CE IVD

Background

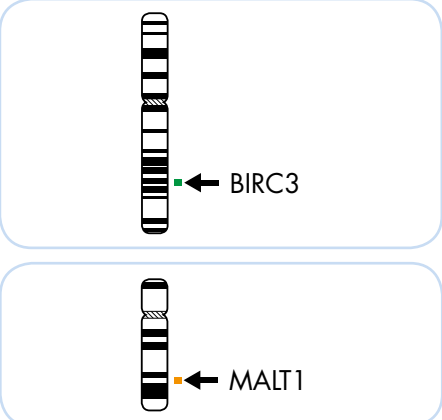
The ZytoLight® SPEC BIRC3/MALT1 Dual Color Dual Fusion Probe is designed to detect translocations involving the chromosomal region 11q22.2 harboring the BIRC3 (baculoviral IAP repeat containing 3, a.k.a. API2) gene and the chromosomal region 18q21.32 harboring the MALT1 (MALT1 paracaspase, a.k.a. MLT) gene. The recurrent translocation t(11;18)(q22.2;q21.3) is frequently found in mucosa-associated lymphoid tissue (MALT) lymphoma which represents the most common extranodal B-cell tumor and accounts for 5-10% of all non-Hodgkin lymphoma. The translocation results in the expression of chimeric fusion transcripts comprising the N-terminal end of the apoptosis inhibitor BIRC3 which is highly expressed in adult lymphoid tissue and C-terminal parts of the MALT1 protease.

The BIRC3/MALT1 fusion protein was shown to induce proteolytic cleavage of NF-kappa-B-inducing kinase (NIK) ultimately resulting in constitutive non-canonical NF-kappa-B signaling, enhanced B-cell adhesion, and apoptosis resistance. It is assumed that disruption of the BIRC3-NIK interaction and/or blocking of MALT1 protease or NIK kinase activity could represent new treatment approaches for refractory t(11;18)-positive MALT lymphoma.

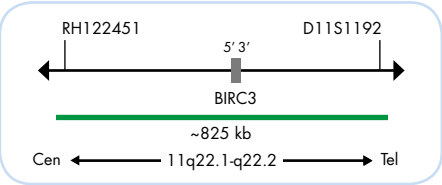
References
Dierlamm J, et al. (1999) Blood 93: 3601-9.
Dierlamm J, et al. (2000) Blood 96: 2215-8.
Morgan JA, et al. (1999) Cancer Res 59: 6205-13.
Rosebeck S, et al. (2011) Science 331: 468-72.

Probe Description

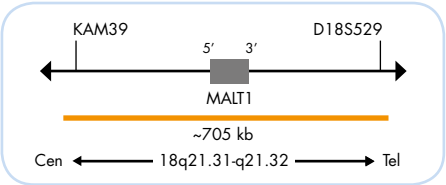
The SPEC BIRC3/MALT1 Dual Color Dual Fusion Probe is a mixture of a green direct labeled BIRC3 probe spanning the BIRC3 gene region at 11q22.1-q22.2 and an orange direct labeled MALT1 probe spanning the MALT1 gene region at 18q21.31-q21.32.



Ideograms of chromosomes 11 (above) and 18 (below) indicating the hybridization locations.



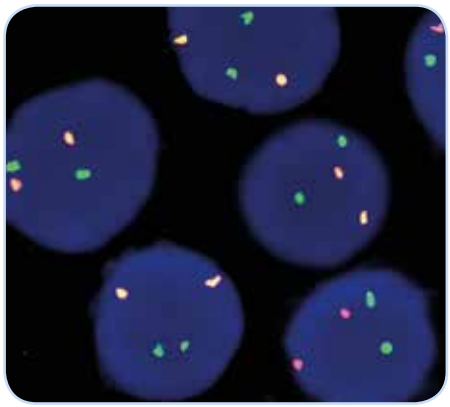
SPEC BIRC3 Probe map (not to scale).



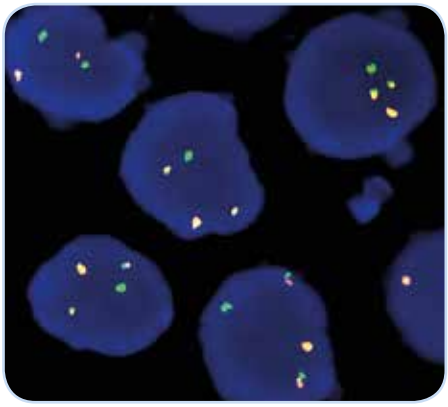
SPEC MALT1 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. A reciprocal translocation involving two breakpoints splits the two signals and generates a fusion signal on each of the chromosomes involved. The chromosomal regions which are not translocated are indicated by the single orange and green signal, respectively.



SPEC BIRC3/MALT1 Dual Color Dual Fusion Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



MALT lymphoma tissue section with translocation affecting the BIRC3/MALT1 loci as indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.

Prod. No.	Product	Label	Tests* (Volume)
Z-2146-50	ZytoLight SPEC BIRC3/MALT1 Dual Color Dual Fusion Probe CE IVD	●/●	5 (50 µl)
Z-2146-200	ZytoLight SPEC BIRC3/MALT1 Dual Color Dual Fusion Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ATM/CEN 11 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC ATM/CEN 11 Dual Color Probe is designed for the detection of deletions affecting the ATM (ATM serine/threonine kinase, a.k.a. ATA, TEL1) gene.

The ATM gene is located on 11q22.3 and encodes a protein kinase. This kinase regulates the response to DNA double strand breaks by triggering signaling, which synchronizes DNA repair, cell-cycle arrest, and apoptosis.

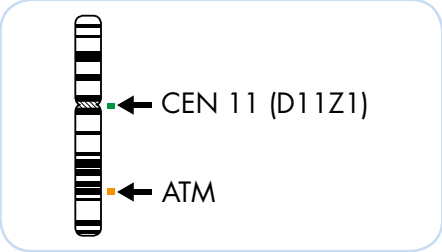
In chronic lymphocytic leukemia (CLL), recurrent alterations include deletions at chromosome 13q14, 11q22.3, 17p13 and 6q21, trisomy of chromosome 12 and IGH translocation. It was shown that compared to the absence of cytogenetic abnormalities, 17p13 deletion conferred the worst prognosis, followed by 11q22.3 deletion and trisomy 12, whereas 13q14 deletion as a sole abnormality was found to be associated with a good prognosis. Chromosome 11q22.3 deletion is detected in approximately 20% of all CLL patients at diagnosis. These patients exhibit rapid disease progression and shorter treatment-free and overall survival times. Moreover, CLL subsets with 11q deletion are associated with an elevation of gene copy number alterations representing genomic instability.

Hence, FISH can be used for the detection of 11q22.3 deletions in CLL to predict disease progression and overall survival.

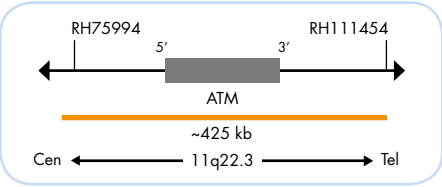
References
Döhner H, et al. (2000) N Engl J Med 343: 1910-6.
Stankovic T & Skowronska A (2014) Leuk Lymphoma 55: 1227-39.
Zenz T, et al. (2010) Best Pract Res Clin Haematol 23: 71-84.

Probe Description

The SPEC ATM/CEN 11 Dual Color Probe is a mixture of an orange fluorochrome direct labeled SPEC ATM probe specific for the ATM gene at 11q22.3 and a green fluorochrome direct labeled CEN 11 probe specific for the alpha satellite centromeric region of chromosome 11 (D11Z1).



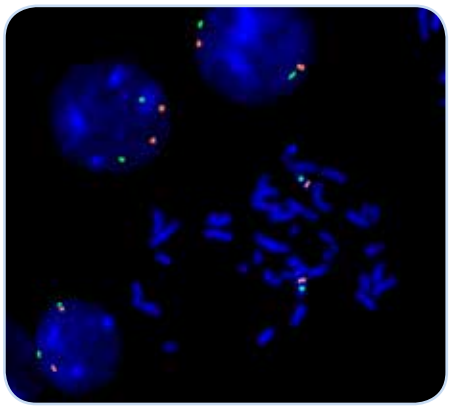
Ideogram of chromosome 11 indicating the hybridization locations.



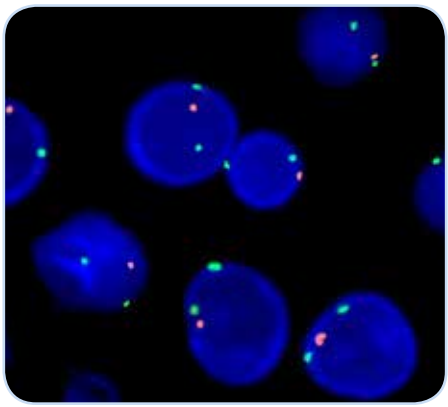
SPEC ATM Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletion of the ATM gene locus, one or no copy of the orange signal will be observed.



SPEC ATM/CEN 11 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus and to metaphase chromosomes of a normal cell.



CLL with deletion affecting the ATM locus as indicated by one orange signal in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2297-50	ZytoLight SPEC ATM/CEN 11 Dual Color Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ATM/CEN 12 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC ATM/CEN 12 Dual Color Probe is designed for the detection of deletions affecting the ATM (ATM serine/threonine kinase, a.k.a. ATA, TEL1) gene as well as for the enumeration of chromosome 12.

The ATM gene is located on 11q22.3 and encodes a protein kinase. This kinase regulates the response to DNA double strand breaks by triggering signaling, which synchronizes DNA repair, cell-cycle arrest and apoptosis.

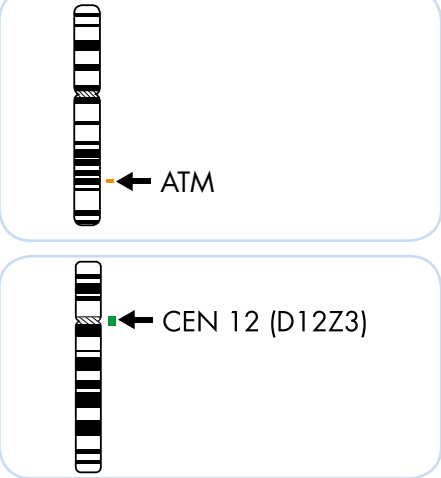
In chronic lymphocytic leukemia (CLL), recurrent alterations include deletions at chromosome 13q14, 11q22.3, 17p13 and 6q21, trisomy of chromosome 12 and IGH translocation. It was shown that compared to the absence of cytogenetic abnormalities, 17p13 deletion conferred the worst prognosis, followed by 11q22.3 deletion and trisomy 12, whereas 13q14 deletion as a sole abnormality was found to be associated with a good prognosis. Trisomy 12 and 11q22.3 deletion are both detected in about 20% of CLL cases. Patients with 11q deletion exhibit rapid disease progression and shorter treatment-free and overall survival times. Moreover, CLL subsets with 11q deletion are associated with an elevation of gene copy number alterations representing genomic instability.

Trisomy 12 is associated with a median survival and an atypical morphology. Hence, FISH can be used to predict disease progression and overall survival in CLL patients.

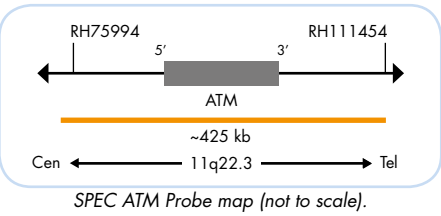
References
Döhner H, et al. (2000) N Engl J Med 343: 1910-6.
Glassman AB & Hayes KJ (2005) Cancer Genet Cytogenet 158: 88-91.
Stankovic T & Skowronska A (2014) Leuk Lymphoma 55: 1227-39.
Zenz T, et al. (2010) Best Pract Res Clin Haematol 23: 71-84.

Probe Description

The SPEC ATM/CEN 12 Dual Color Probe is a mixture of an orange fluorochrome direct labeled SPEC ATM probe specific for the ATM gene at 11q22.3 and a green fluorochrome direct labeled CEN 12 probe specific for the alpha satellite centromeric region of chromosome 12 (D12Z3).



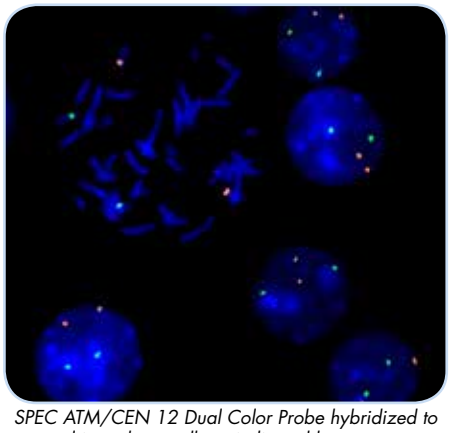
Ideograms of chromosomes 11 (above) and 12 (below) indicating the hybridization locations.



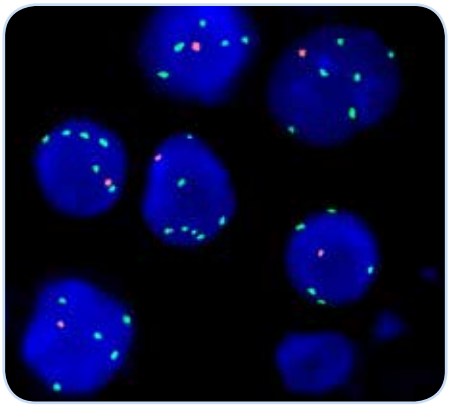
SPEC ATM Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletion of the ATM gene locus, one or no copy of the orange signal will be observed. In a cell with trisomy or polysomy 12, three or more copies of the green signal will be observed, respectively.



SPEC ATM/CEN 12 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus and to metaphase chromosomes of a normal cell.



CLL with deletion of the ATM gene and amplification affecting the centromeric region of chromosome 12 as indicated by one orange signal and five or more green signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2296-50	ZytoLight SPEC ATM/CEN 12 Dual Color Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC TP53/ATM Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC TP53/ATM Dual Color Probe is designed for the detection of deletions affecting the genes TP53 and ATM.

CLL (chronic lymphocytic leukemia) is the most common form of leukemia in Western population.

TP53 (tumor protein p53, a.k.a. p53) gene deletions have been detected in patients with CLL, multiple myeloma (MM), and acute myeloid leukemia (AML). In CLL patients, allelic loss of the short arm of chromosome 17 is associated with treatment failure with alkylating agents and short survival times.

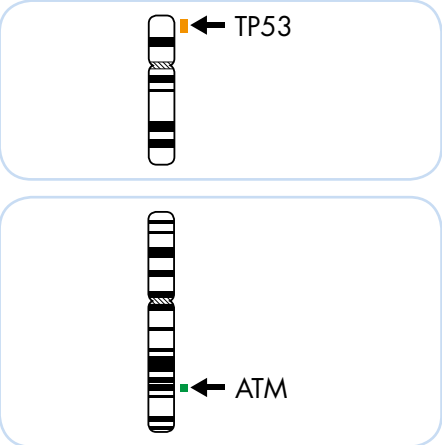
The ATM (ATM serine/threonine kinase) gene is located on 11q22.3 and encodes a protein kinase which is involved in cell cycle regulation, including TP53 activation. CLL patients with 11q deletion exhibit rapid disease progression and inferior survival.

Hence, in combination with further biological markers, morphology and clinical information FISH is a valuable tool to predict disease progression and overall survival in CLL patients.

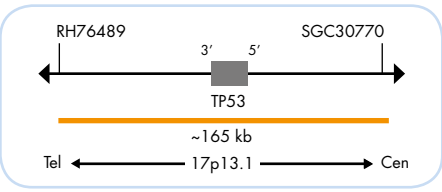
References
Pettitt AR, et al. (2001) Blood 98: 814-22.
Ripollés L, et al. (2006) Cancer Genet Cytogenet 171: 57-64.
Shanafelt TD, et al. (2006) Ann Intern Med 145: 435-47.
Stilgenbauer S, et al. (2002) Leukemia 16: 993-1007.

Probe Description

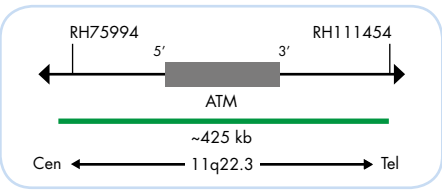
The SPEC TP53/ATM Dual Color Probe is a mixture of an orange fluorochrome direct labeled SPEC TP53 probe hybridizing to the TP53 gene in the chromosomal region 17p13.1 and a green fluorochrome direct labeled SPEC ATM probe specific for the ATM gene at 11q22.3.



Ideograms of chromosomes 17 (above) and 11 (below) indicating the hybridization locations.



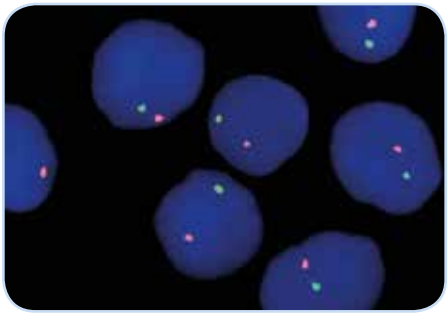
SPEC TP53 Probe map (not to scale).



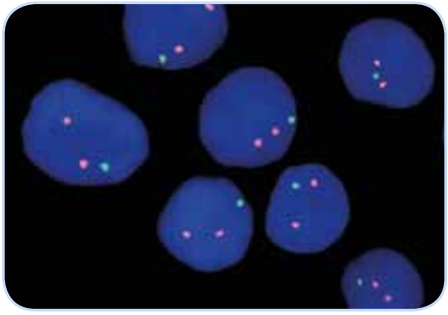
SPEC ATM Probe map (not to scale).

Results

Using the SPEC TP53/ATM Dual Color Probe in a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletions affecting the TP53 gene locus, a reduced number of orange signals will be observed. Deletions affecting only parts of the TP53 locus might result in a normal signal pattern with orange signals of reduced size. In a cell with ATM gene deletions, a reduced number of green signals will be observed. Deletions affecting only parts of the ATM locus might result in a normal signal pattern with green signals of reduced size.



SPEC TP53/ATM Dual Color Probe hybridized to bone marrow biopsy section with deletions of the ATM and the TP53 genes as indicated by one green and one orange signal in each nucleus.



SPEC TP53/ATM Dual Color Probe hybridized to bone marrow biopsy section with deletion of the ATM gene as indicated by one green signal in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2159-50	ZytoLight SPEC TP53/ATM Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2159-200	ZytoLight SPEC TP53/ATM Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

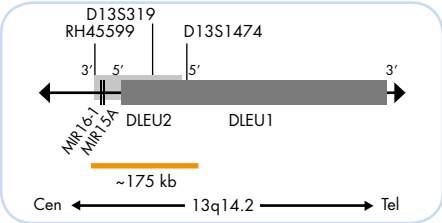
ZytoLight® SPEC D13S319/13q34/CEN 12 Triple Color Probe

CE IVD

Background

The ZytoLight® SPEC D13S319/13q34/CEN 12 Triple Color Probe is designed for the detection of D13S319 deletions as well as for the enumeration of chromosome 12.
CLL (chronic lymphocytic leukemia) is the most common form of leukemia in Western population.
The most frequent aberration in CLL is the deletion of 13q14 which involves the D13S319 locus and which is associated with a favorable prognosis if occurring as the sole genetic aberration. Deletions of the long arm of chromosome 13 are also frequently detected in patients with aggressive non-Hodgkin lymphoma (NHL) and have been found to represent an adverse prognostic factor in MM.
Trisomy 12 represents another frequent chromosomal aberration in CLL, detected in about 20% of CLL cases. Trisomy 12 as single aberration is associated with an intermediate prognostic outcome.
Hence, in combination with further biological markers, morphology and clinical information FISH is a valuable tool to predict disease progression and overall survival in CLL patients.

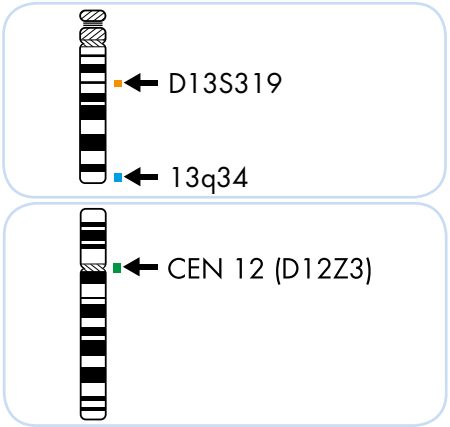
References
Chang H, et al. (1999) Leukemia 13: 105-9.
Dal Bo M, et al. (2011) Genes Chromosomes Cancer 50: 633-43.
Ouillette P, et al. (2011) Clin Cancer Res 21: 6778-90.
Ripollés L, et al. (2006) Cancer Genet Cytogenet 171: 57-64.
Shanafelt TD, et al. (2006) Ann Intern Med 145: 435-47.
Stilgenbauer S, et al. (2002) Leukemia 16: 993-1007.



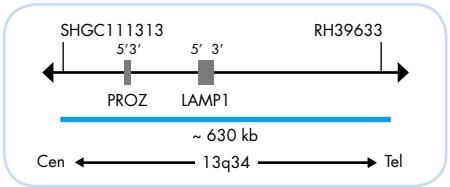
SPEC D13S319 Probe map (not to scale).

Probe Description

The SPEC D13S319/13q34/CEN 12 Triple Color Probe is a mixture of an orange fluorochrome direct labeled SPEC D13S319 probe specific for the D13S319 locus at 13q14.2, a blue fluorochrome direct labeled SPEC 13q34 probe specific for the chromosomal region 13q34 and a green fluorochrome direct labeled CEN 12 probe specific for the alpha satellite centromeric region of chromosome 12 (D12Z3).
The SPEC 13q34 probe is specific for the LAMP1 (lysomal associated membrane protein 1) gene region in 13q34. Due to cross-hybridizations of chromosome 13 alpha satellites to other centromeric regions, probes specific for 13q34 are frequently used for chromosome 13 copy number detection.



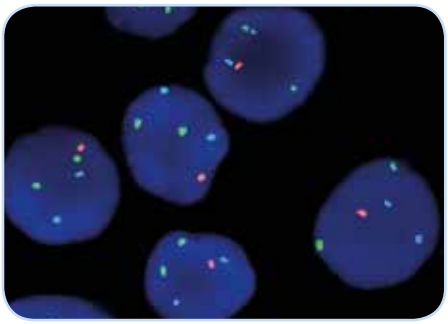
Ideograms of chromosomes 13 (above) and 12 (below) indicating the hybridization locations.



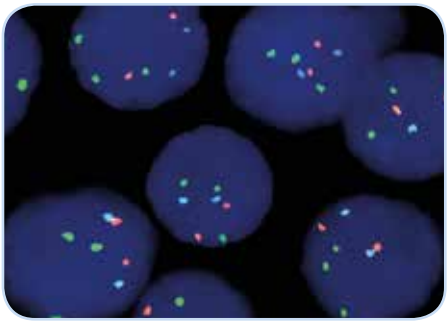
SPEC 13q34 Probe map (not to scale).

Results

Using the SPEC D13S319/13q34/CEN 12 Triple Color Probe in a normal interphase nucleus, two orange, two green, and two blue signals are expected. In a cell with deletions affecting the D13S319 locus, a reduced number of orange signals will be observed. Deletions affecting only parts of the D13S319 locus might result in a normal signal pattern with orange signals of reduced size. In a cell with trisomy or polysomy 12, three or more copies of the green signal will be observed, respectively.



SPEC D13S319/13q34/CEN 12 Triple Color Probe hybridized to bone marrow biopsy section with deletion of the D13S319 locus as indicated by one orange signal and two blue signals in each nucleus.



SPEC D13S319/13q34/CEN 12 Triple Color Probe hybridized to bone marrow biopsy section with trisomy of chromosome 12 as indicated by three green signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2160-50	ZytoLight SPEC D13S319/13q34/CEN 12 Triple Color Probe CE IVD	●/●/●	5 (50 µl)
Z-2160-200	ZytoLight SPEC D13S319/13q34/CEN 12 Triple Color Probe CE IVD	●/●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC D13S319/13q34 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC D13S319/13q34 Dual Color Probe is designed for the detection of deletions on the long arm of chromosome 13.

Chronic lymphocytic leukemia (CLL) is the most common form of leukemia in the Western population. It is characterized by a marked variable outcome, from an indolent clinical course to more aggressive forms, depending on the aberration. The most frequent aberration in CLL is the deletion of 13q14.2 which involves the D13S319 locus and which is associated with a favorable prognosis if occurring as the sole genetic aberration.

Deletions of the long arm of the chromosome 13 are also frequently detected in patients with aggressive non-Hodgkin lymphoma (NHL) and have been found to represent an adverse prognostic factor in multiple myeloma (MM). The telomeric region 13q34 is used as control region, to distinguish between an interstitial deletion and a complete loss of the 13q arm.

In combination with further biological markers, morphology, and clinical information, Fluorescence *in situ* Hybridization (FISH) can be a valuable tool to predict disease progression and overall survival in CLL patients.

References

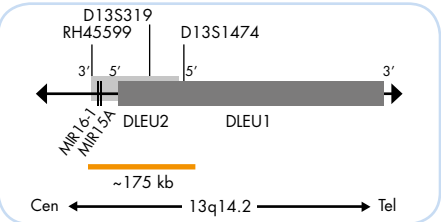
Chang H, et al. (1999) Leukemia 13: 105-9.
Dal Bo M, et al. (2011) Genes Chromosomes Cancer 50: 633-43.
Liu Y, et al. (1998) Blood 86: 1911-15.
La Starza R, et al. (2018) Mol Cytogenet 11: 6.
Ouillette P, et al. (2011) Clin Cancer Res 21: 6778-90.
Stilgenbauer S, et al. (1998) Oncogene 16: 1891-7.

Probe Description

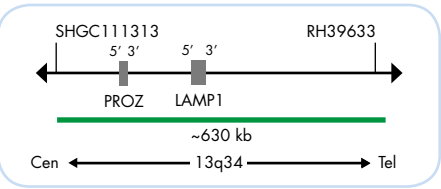
The SPEC D13S319/13q34 Dual Color Probe is a mixture of an orange fluorochrome direct labeled SPEC D13S319 probe specific for the D13S319 locus at 13q14.2 and a green fluorochrome direct labeled SPEC 13q34 probe specific for the chromosomal region 13q34.

The SPEC 13q34 probe is specific for the LAMP1 (lysosome-associated membrane protein 1) gene region in 13q34. Due to cross-hybridizations of chromosome 13 alpha satellites to other centromeric regions, probes specific for 13q34 are frequently used for chromosome 13 copy number detection.

Ideogram of chromosome 13 indicating the hybridization locations.



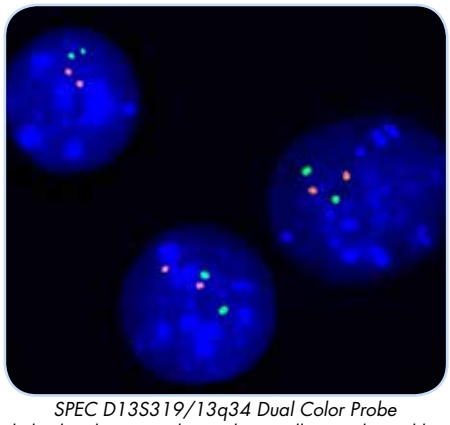
SPEC D13S319 Probe map (not to scale).



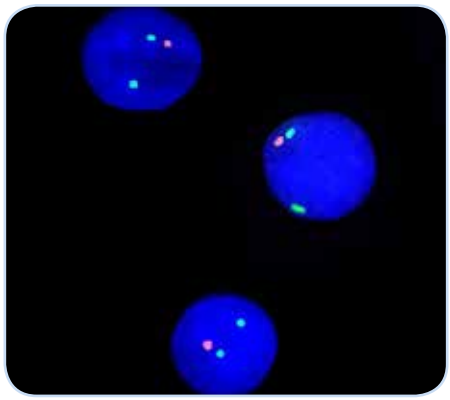
SPEC 13q34 Probe map (not to scale).

Results

Using the SPEC D13S319/13q34 Dual Color Probe in a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletions affecting the D13S319 locus, a reduced number of orange signals will be observed. Deletions affecting only parts of the D13S319 locus might result in a normal signal pattern with orange signals of reduced size. If deletions affect the D13S319 locus as well as the 13q34 locus, this might result in a reduced number of orange and green signals.



SPEC D13S319/13q34 Dual Color Probe hybridized to normal interphase cells as indicated by two green and two orange signals in each nucleus.



Bone marrow biopsy section with deletion of the D13S319 locus as indicated by one orange and two green signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2280-50	ZytoLight SPEC D13S319/13q34 Dual Color Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC 11q gain/loss Triple Color Probe

CE IVD

Background

The ZytoLight® SPEC 11q gain/loss Triple Color Probe is designed to detect 11q alterations.

A subset of lymphomas with gene expression and pathological characteristics of Burkitt lymphomas (BL) but absence of MYC translocation has been recently described which carries 11q proximal gains and telomeric losses. It is assumed that this aberration leads to co-deregulation of oncogenes and tumor suppressor genes which are located in the affected chromosomal regions. The current WHO classification introduced this new provisional entity as Burkitt-like lymphoma with 11q aberration. The minimal region of gain (MGR) and loss (MLR) was defined at 11q23.3 and at 11q24.1-q25, respectively, based on the studies by Ferreiro *et al.* (2015) and Salaverria *et al.* (2014). Potential oncogenes located in the MGR are USP2 and PAFAH1B2. The candidate tumor suppressor genes in the MLR comprise, e.g., FLI1 and ETS1.

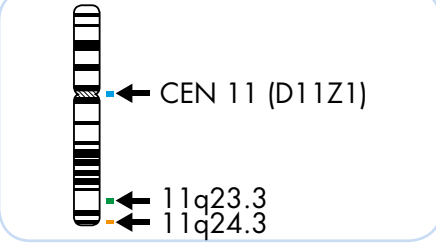
The 11q-gain/loss pattern in high-grade B-cell lymphoma is significantly more frequent in lymphoma occurring in the setting of transplantation and immunosuppression than in immunocompetent patients. This suggests that immunosuppression may favor its formation.

As identification of patients with the 11q-gain/loss aberration is clinically important but cytogenetically challenging, FISH assay is a useful diagnostic tool to evaluate both post-transplant and immunocompetent Burkitt and Burkitt-like lymphoma patients.

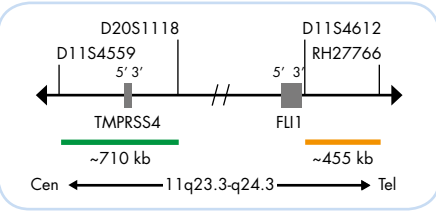
References
Ferreiro JF, et al. (2015) Haematologica 100: e275-9.
Salaverria I, et al. (2014) Blood 123: 1187-98.
Swerdlow SH, et al. (2016) Blood 127: 2375-90.

Probe Description

The SPEC 11q gain/loss Triple Color Probe is a mixture of a green fluorochrome direct labeled probe hybridizing in the MGR at 11q23.3, an orange fluorochrome direct labeled probe hybridizing in the MLR at 11q24.3, and a blue fluorochrome direct labeled CEN 11 probe specific for the alpha satellite centromeric region of chromosome 11 (D11Z1).



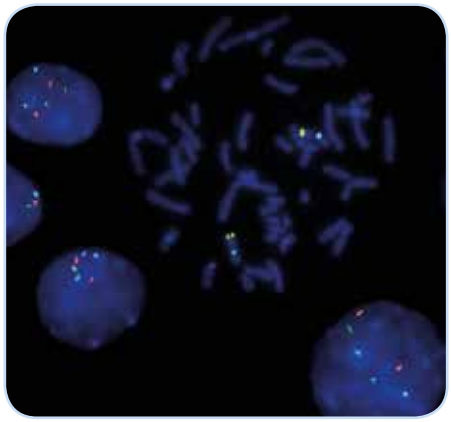
Ideogram of chromosome 11 indicating the hybridization locations.



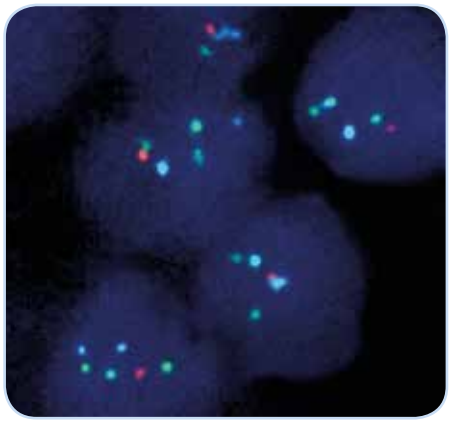
SPEC 11q Probe map (not to scale).

Results

In a normal interphase nucleus, two green, two orange, and two blue signals are expected. In a cell with amplification at 11q23.3 and deletion at 11q24.3, multiple copies of the green signals and a reduced number of orange signals will be observed.



SPEC 11q gain/loss Triple Color Probe hybridized to normal interphase cells as indicated by two green, two orange, and two blue signals per nucleus and to metaphase chromosomes of a normal cell.



Burkitt-like lymphoma tissue section with 11q aberration as indicated by three green signals and one orange signal indicating the gain and loss at 11q, respectively.

Prod. No.	Product	Label	Tests* (Volume)
Z-2216-50	ZytoLight SPEC 11q gain/loss Triple Color Probe CE IVD	●/●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC KMT2A Dual Color Break Apart Probe

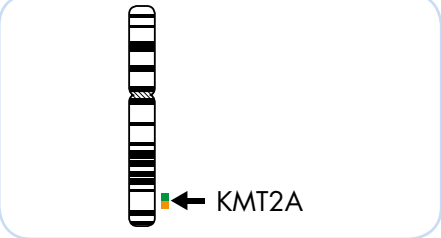
CE IVD

Background

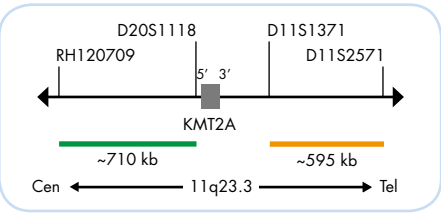
The ZytoLight® SPEC KMT2A Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 11q23.3 harboring the KMT2A gene. The KMT2A (lysine methyltransferase 2A, a.k.a. MLL) gene encodes a histone lysine N-methyltransferase and is involved in a variety of cellular processes, including hematopoiesis, DNA damage response, and cell cycle control.
Translocations involving the KMT2A gene are identified in 5-6% of all acute myeloid leukemias (AML) and 5-10% of all acute lymphoblastic leukemias (ALL). The frequency of translocations involving the KMT2A gene is significantly higher in infants with AML (50%) as well as with ALL (80%). More than 30 fusion partners are documented for KMT2A, the most common translocations are t(4;11) and t(11;19) in ALL, and t(6;11), t(9;11), and t(11;19) in AML patients.
Between 1-15% of cancer patients treated with DNA topoisomerase II inhibitor develop therapy-related leukemia (t-AML) associated with KMT2A translocations. Generally, the presence of KMT2A rearrangements in patients with acute leukemia indicates a less favorable prognosis. However, recent studies suggest that the specific KMT2A translocation partner may influence response to therapy and overall prognosis depending on the clinical context. Hence, detection of KMT2A translocations by Fluorescence *in situ* Hybridization may be of diagnostic and prognostic relevance.

Probe Description

The SPEC KMT2A Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 11q23.3 band. The green fluorochrome direct labeled probe hybridizes proximal to the KMT2A gene, and the orange fluorochrome direct labeled probe hybridizes distal to the KMT2A gene region. This probe is approved to be used with a hybridization time of 2 hours on cytological specimens.



Ideogram of chromosome 11 indicating the hybridization locations.

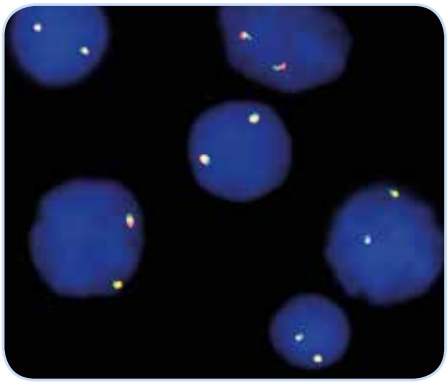


SPEC KMT2A Probe map (not to scale).

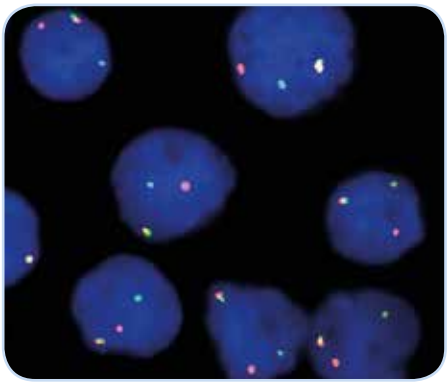
References
Broeker PL, et al. (1996) Blood 87: 1912-22.
De Braekeleer M, et al. (2005) Anticancer Res 25: 1931-44.
Ford DJ & Dingwall AK (2015) Cancer Genet 208: 178-91.
Gindin T, et al. (2015) Hematol Oncol 33: 239-46.
Keefe JG, et al. (2010) J Mol Diagn 12: 441-52.
Langer T, et al. (2003) Genes Chromosomes Cancer 36: 393-401.
Wechsler DS, et al. (2003) Genes Chromosomes Cancer 36: 26-36.

Results

In an interphase nucleus lacking a translocation involving the 11q23.3 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 11q23.3 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 11q23.3 locus and one 11q23.3 locus affected by a translocation.



SPEC KMT2A Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Bone marrow smear with translocation of the KMT2A gene as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2193-50	ZytoLight SPEC KMT2A Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2193-200	ZytoLight SPEC KMT2A Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ZNF384 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC ZNF384 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 12p13.31 harboring the ZNF384 gene.

The ZNF384 (zinc-finger protein 384, a.k.a. CIZ) gene encodes a transcription factor involved in the regulation of matrix metalloproteinases.

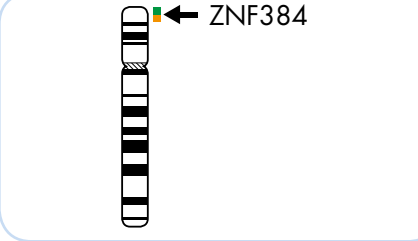
Rearrangements of the ZNF384 gene are recurrent in acute leukemia and are most frequently found in precursor B-cell acute lymphoblastic leukemia (BCP-ALL) in children and young adults with an incidence of about 3-4%. ZNF384-related fusion genes with multiple fusion partners have been found to define a distinct subgroup of pediatric BCP-ALL with a characteristic immunophenotype. Known translocation partners are TCF3 (19p13.3), EWSR1 (22q12.2), TAF15 (17q12), EP300 (22q13.2), ARID1B (6q25.3), CREBBP (16p13.3), and BMP2K (4q21.21) with TCF3 being the most prevalent. The breakpoints are located within the ZNF384 gene. However, the balanced translocations are resulting in fusion genes including the complete protein coding information.

Since ZNF384-related fusion genes are difficult to detect by common G-banding, investigation by FISH may be of diagnostic and prognostic relevance.

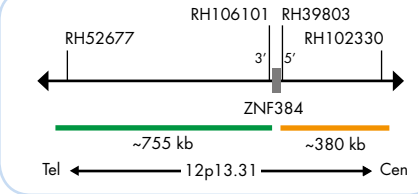
References
Hirabayashi S, et al. (2017) Haematologica 102: 118-29.
Krance RA, et al. (1992) Leukemia 6: 251-5.
La Starza R, et al. (2005) Leukemia 19: 1696-9.
Shago M, et al. (2016) Pediatr Blood Cancer 63: 1915-21.

Probe Description

The SPEC ZNF384 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 12p13.31 band. The orange fluorochrome direct labeled probe hybridizes proximal to the ZNF384 gene, the green fluorochrome direct labeled probe hybridizes distal to the ZNF384 gene.



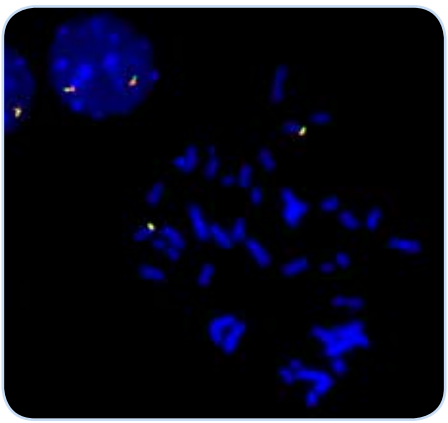
Ideogram of chromosome 12 indicating the hybridization locations.



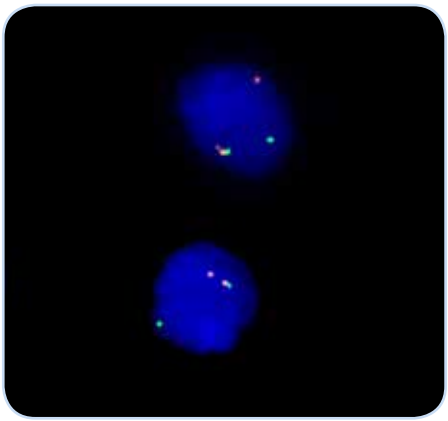
SPEC ZNF384 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 12p13.31 band, two orange/green fusion signals are expected, representing two normal (non-rearranged) 12p13.31 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 12p13.31 locus and one 12p13.31 locus affected by a ZNF384 translocation.



SPEC ZNF384 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus and to metaphase chromosomes of a normal cell.



Bone marrow smear of an ALL case with translocation of the ZNF384 gene as indicated by one orange/green fusion signal, one separate green, and one separate orange signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2275-50	ZytoLight SPEC ZNF384 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ETV6 Dual Color Break Apart Probe

CE IVD

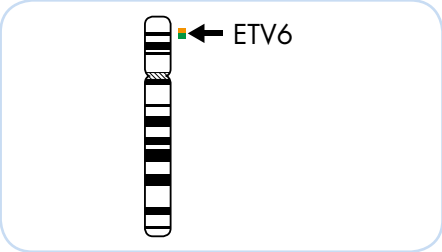
Background

The ZytoLight® SPEC ETV6 Dual Color Break Apart Probe is designed for the detection of translocations involving the chromosomal region 12p13.2 harboring the ETV6 (ETS variant 6, a.k.a. TEL) gene. ETV6 is a member of the ETS family of transcription factors. More than 40 translocations with ETV6 involvement have been reported in diverse types of hematological and non-hematological malignancies.
The balanced chromosomal translocation t(12;21)(p13.2;q22.1), which leads to ETV6-RUNX1 fusion, represents the most frequent genetic rearrangement (19-27%) in initial childhood B-cell precursor (BCP) acute lymphoblastic leukemia (ALL) and has been associated with good prognosis.
The ETV6-NTRK3 gene fusion resulting from the t(12;15)(p13.2;q25) translocation was found to be characteristic for mammary analogue secretory carcinoma (MASC) of the salivary glands. Since MASC morphologically mimics other neoplasms, the detection of ETV6 rearrangements may be helpful for the differential diagnosis of MASC.
In a subgroup of myeloproliferative disorders, the t(5;12)(q32;p13.2) translocation is a recurrent chromosome abnormality resulting in the fusion of ETV6 to the receptor tyrosine kinase PDGFRB. Patients carrying the t(5;12) translocation can be successfully treated with tyrosine kinase inhibitors.

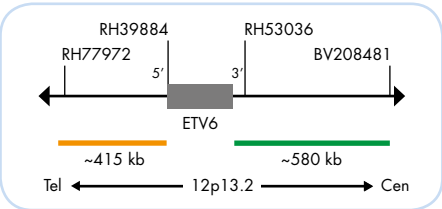
References
Bohlander SK (2005) Semin Cancer Biol 15: 162-74.
De Braekeleer E, et al. (2012) Leuk Res 36: 945-61.
Peter A, et al. (2009) Eur J Haematol 83: 420-32.
Pinto A, et al. (2014) Mod Pathol 27: 30-7.

Probe Description

The SPEC ETV6 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 12p13.2 band. The green fluorochrome direct labeled probe hybridizes proximal and the orange fluorochrome direct labeled probe hybridizes distal to the ETV6 gene.



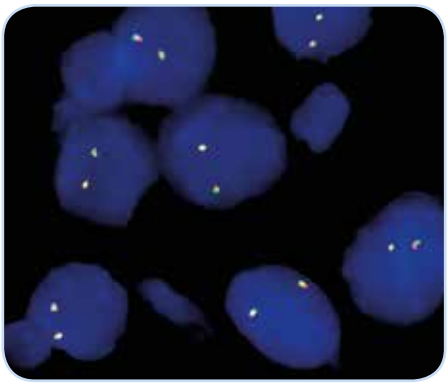
Ideogram of chromosome 12 indicating the hybridization locations.



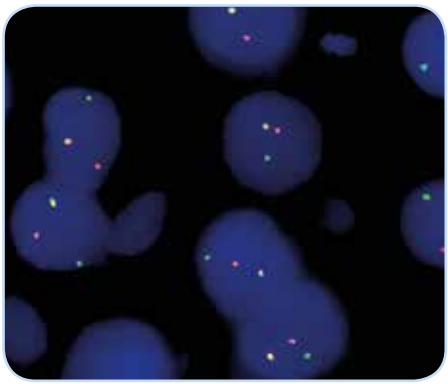
SPEC ETV6 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 12p13.2 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 12p13.2 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 12p13.2 locus and one 12p13.2 locus affected by a translocation.



SPEC ETV6 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



MASC tissue section of the salivary glands with translocation of the ETV6 gene as indicated by one non-rearranged orange/green fusion signal, one orange and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2176-50	ZytoLight SPEC ETV6 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2176-200	ZytoLight SPEC ETV6 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe

CE IVD

Background

The ZytoLight® SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe is designed for the detection of the specific translocation involving the chromosomal region 12p13.2 harboring the ETV6 (ETS variant 6, a.k.a. TEL) gene and the chromosomal region 21q22.12 harboring the RUNX1 (runt related transcription factor 1, a.k.a. AML1) gene.

The balanced chromosomal translocation t(12;21)(p13.2;q22.1), which leads to ETV6/RUNX1 fusion, represents the most frequent genetic rearrangement in initial childhood B-cell precursor (BCP) acute lymphoblastic leukemia (ALL) (19-27%) and has been associated with good prognosis.

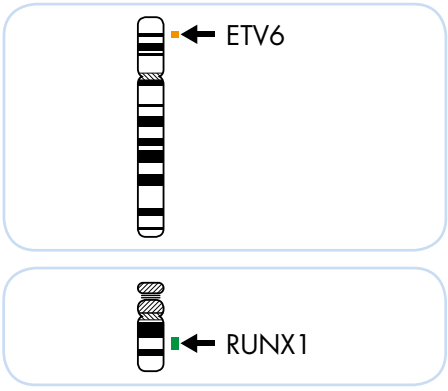
The ETV6/RUNX1 fusion protein, comprising a putative repressor domain of ETV6, a member of the ETS family of transcription factors, fused to RUNX1, the DNA-binding subunit of the RUNX1/CBF beta transcription factor complex, acts as a trans-dominant repressor of RUNX1 regulated target genes involved in hematopoiesis.

Three secondary aberrations in ETV6/RUNX1 positive ALL have been found to negatively influence the clinical course: deletion of the second non-translocated ETV6 allele, gains of the RUNX1 gene, and duplication of the derivative chromosome 21.

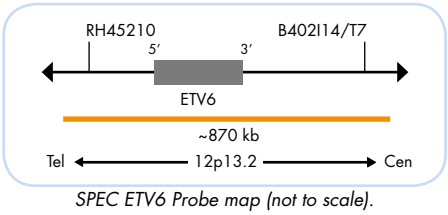
Detection of t(12;21) by Fluorescence *in situ* Hybridization enables the simultaneous identification of the most common secondary changes and thus provides additional information about the possible outcome of the disease in patients with ALL.

Probe Description

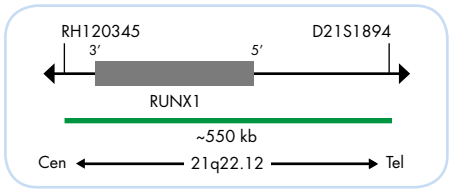
The SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe is a mixture of an orange fluorochrome direct labeled ETV6 probe spanning the known breakpoint region of the ETV6 gene and a green fluorochrome direct labeled RUNX1 probe covering the known breakpoint region of the RUNX1 gene.



Ideograms of chromosomes 12 (above) and 21 (below) indicating the hybridization locations.



SPEC ETV6 Probe map (not to scale).

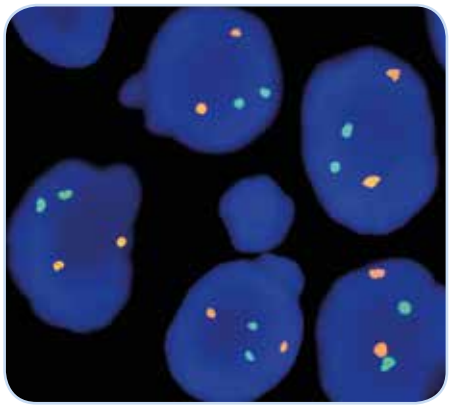


SPEC RUNX1 Probe map (not to scale).

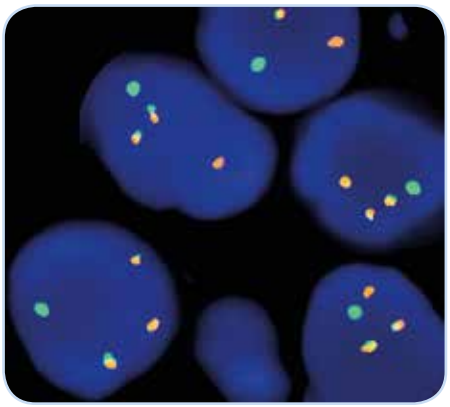
References
Fenrick R, et al. (1999) Mol Cell Biol 19: 6566-74.
Martínez-Ramírez A, et al. (2001) Haematologica 86: 1245-53.
Morrow M, et al. (2007) Oncogene 26: 4404-14.
Peter A, et al. (2009) Eur J Haematol 83: 420-32.
Shurtleff SA, et al. (1995) Leukemia 9: 1985-9.

Results

In a normal interphase nucleus, two orange and two green signals are expected. A reciprocal translocation involving two breakpoints splits the two signals and generates a fusion signal on each of the chromosomes involved. The chromosomal regions which are not translocated are indicated by the single orange and green signal, respectively.



SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Bone marrow tissue section with translocation affecting the ETV6/RUNX1 loci as indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.

Prod. No.	Product	Label	Tests* (Volume)
Z-2157-50	ZytoLight SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe CE IVD	●/●	5 (50 µl)
Z-2157-200	ZytoLight SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC KRAS/CEN 12 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC KRAS/CEN 12 Dual Color Probe is designed for the detection of KRAS gene amplifications found e.g. in lung cancer.

The KRAS (KRAS proto-oncogene, GTPase) gene located on chromosome 12p12.1 is a member of the RAS gene family comprising HRAS, KRAS, and NRAS, all of which encode a 21 kDa protein. The wildtype proteins play a pivotal role in cell proliferation, differentiation, and senescence. Mutations of KRAS are frequently found in epithelial malignancies and lead to activation of the downstream mitogen-activated protein kinase (MAPK) resulting in unchecked cellular proliferation and tumor progression.

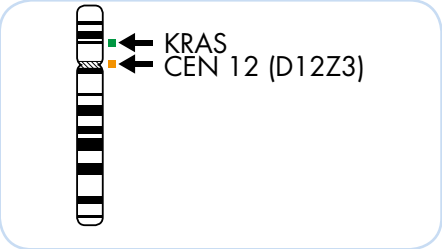
Amplifications of KRAS and the implications in tumorigenesis are not as well characterized as KRAS mutations. However, recent studies using different methods found amplification of KRAS or copy number gain of the 12p12.1 region including KRAS in various primary tumors, as e.g. in lung, colorectal, pancreatic, and gastric cancers.

For non-small cell lung cancer (NSCLC) patients KRAS amplification as assessed by Fluorescence *in situ* Hybridization (FISH) was detected in about 15% of the tumors. Amplification of KRAS was found to be correlated with poor prognosis and may act synergistically with KRAS mutations to promote tumor progression.

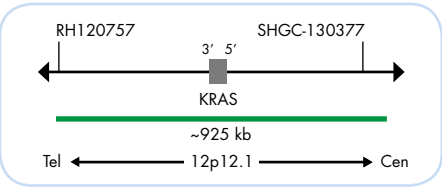
References
Little AS, et al. (2011) Sci Signal 4: er2.
Mita H, et al. (2009) BMC Cancer 9: 198.
Sasaki H, et al. (2011) J Thorac Oncol 6: 15-20.
Wagner PL, et al. (2011) Lung Cancer 74: 118-23.

Probe Description

The SPEC KRAS/CEN 12 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 12 probe specific for the alpha satellite centromeric region of chromosome 12 (D12Z3) and a green fluorochrome direct labeled SPEC KRAS probe specific for the KRAS gene at 12p12.1.



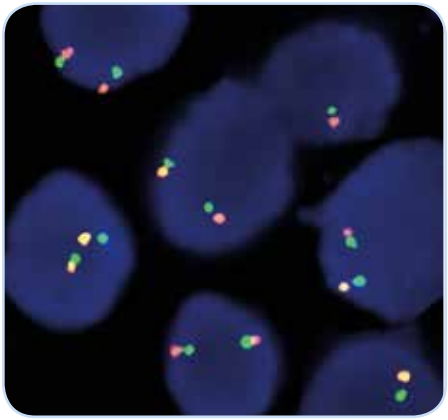
Ideogram of chromosome 12 indicating the hybridization locations.



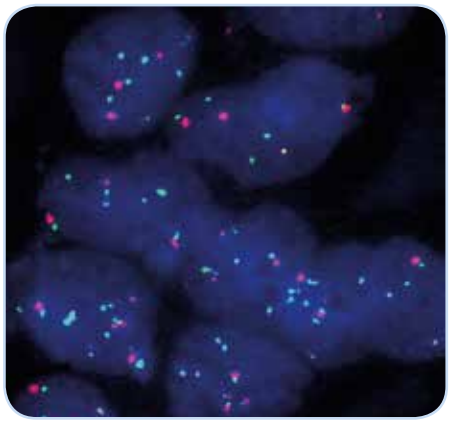
SPEC KRAS Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. Nuclei with amplification of the KRAS gene locus 12p12.1 or aneuploidy of chromosome 12 will show multiple copies of the green signal or large green signal clusters.



SPEC KRAS/CEN 12 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Lung cancer tissue section with amplification of the KRAS gene (green).

Image kindly provided by Prof. Diebold, Lucerne, Switzerland.

Prod. No.	Product	Label	Tests* (Volume)
Z-2115-200	ZytoLight SPEC KRAS/CEN 12 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ERBB3/CEN 12 Dual Color Probe

CE IVD

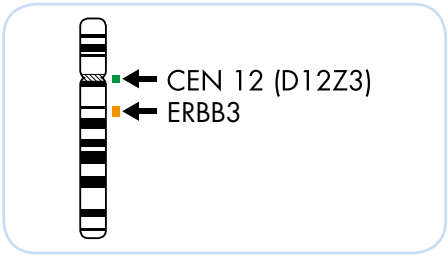
Background

The ZytoLight® SPEC ERBB3/CEN 12 Dual Color Probe is designed for the detection of amplifications of the chromosomal regions harboring the ERBB3 gene.
The ERBB3 (a.k.a. HER3) gene encodes a transmembrane glycoprotein acting as a cellular growth factor receptor. It belongs to the epidermal growth factor receptor subgroup of the receptor tyrosine kinase superfamily also including ERBB1 (EGFR), ERBB2, which is known to be affected by gene amplifications in a number of malignant tumors, and ERBB4.
Although EGFR and ERBB2 have been shown to represent good predictive markers and appropriate targets for therapeutic approaches, relatively less is known of comparable significance for ERBB3 and ERBB4. However, there is growing evidence that cooperation of all four members of the ERBB gene family contributes to a more aggressive tumor phenotype and influences therapeutic response.
Accordingly, it is assumed that the assessment of the combined amplification status of ERBB1 to ERBB4 may improve the diagnostic value significantly.

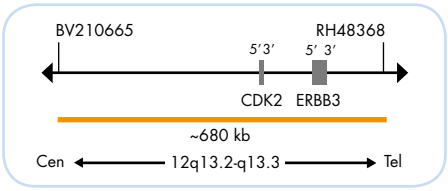
References
Alimandi M, et al. (1995) Oncogene 10: 1813-21.
Begnami MD, et al. (2011) J Clin Oncol 29: 3030-6.
Berghoff AS, et al. (2014) Breast J 23: 637-43.
Brunner K, et al. (2010) Anal Quant Cytol Histol 32: 78-89.
Kraus MH, et al. (1989) Proc Natl Acad Sci U S A 86: 9193-7.
Lédel F, et al. (2014) Eur J Cancer 50: 656-62.
Sassen A, et al. (2008) Breast Cancer Res 10: R2.
Sassen A, et al. (2009) Breast Cancer Res 11: R50.
Zaczek A, et al. (2005) Histol Histopathol 20: 1005-15.
Zimonjic DB, et al. (1995) Oncogene 10: 1235-7.

Probe Description

The SPEC ERBB3/CEN 12 Dual Color Probe is a mixture of a green fluorochrome direct labeled CEN 12 probe specific for the alpha satellite centromeric region of chromosome 12 (D12Z3) and an orange fluorochrome direct labeled SPEC ERBB3 probe hybridizing distal and proximal to the human ERBB3 gene in the chromosomal region 12q13.2-q13.3.



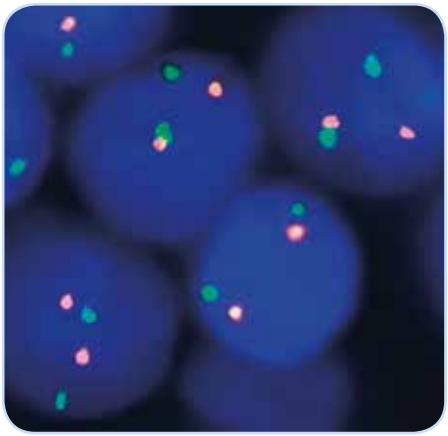
Ideogram of chromosome 12 indicating the hybridization locations.



SPEC ERBB3 Probe map (not to scale).

Results

Using the SPEC ERBB3/CEN 12 Dual Color Probe in a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the ERBB3 gene locus, multiple copies of the orange signal or orange signal clusters will be observed.



SPEC ERBB3/CEN 12 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2056-200	ZytoLight SPEC ERBB3/CEN 12 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC DDIT3 Dual Color Break Apart Probe

CE IVD

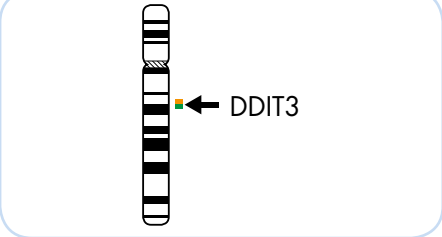
Background

The ZytoLight® SPEC DDIT3 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 12q13.3 harboring the DDIT3 (DNA damage inducible transcript 3) gene (a.k.a. CHOP, GADD153).
The DDIT3 gene encodes for a stress-induced dominant-negative inhibitor of the transcription factors C/EBP and LAP. DDIT3 is consistently rearranged in myxoid liposarcomas (MLS). The most frequent translocation involving the DDIT3 gene region is t(12;16)(q13.3;p11.2) and occurs in about 90% of patients with MLS. The rearrangement results in a fusion gene comprising the 5´ part of the FUS (fused in sarcoma) gene, located in 16p11.2, and the complete coding region of the DDIT3 gene. The FUS-DDIT3 fusion protein acts as an abnormal transcription factor and development of myxoid liposarcomas is thus regarded as a consequence of deregulated FUS-DDIT3 target genes.
Differential diagnosis of liposarcomas and accurate classification, the latter being especially important with regard to appropriate treatment and prognosis, are often problematic. Therefore, detection of DDIT3 rearrangements via FISH analysis is a valuable tool to confirm the histopathological diagnosis of myxoid liposacrcoma.

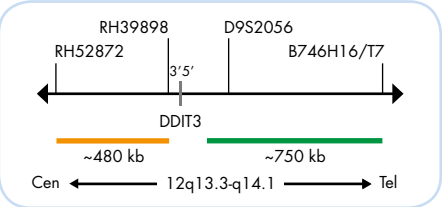
References
Aman P, et al. (1992) Genes Chromosomes Cancer 5: 278-85.
Andersson M, et al. (2010) BMC Cancer 10: 249-58.
Germano G, et al. (2010) Cancer Res 70: 2235-44.
Meis-Kindblom JM, et al. (2001) Virchows Arch 439: 141-51.
Panagopoulos I, et al. (1994) Cancer Res 54: 6500-3.
Ron D & Habener JF (1992) Genes Dev 6: 439-53.

Probe Description

The SPEC DDIT3 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 12q13.3-q14.1 band. The orange fluorochrome direct labeled probe hybridizes proximal to the DDIT3 gene and the green fluorochrome direct labeled probe hybridizes distal to that gene.



Ideogram of chromosome 12 indicating the hybridization locations.

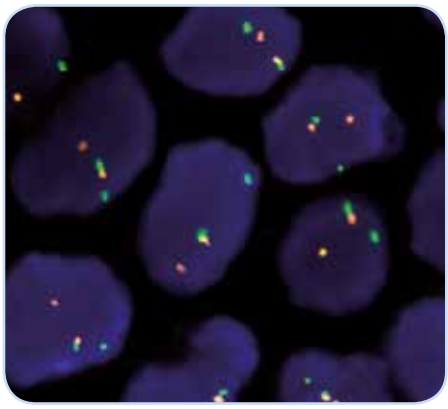


SPEC DDIT3 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 12q13.3-q14.1 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 12q13.3-q14.1 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 12q13.3-q14.1 locus and one 12q13.3-q14.1 locus affected by a 12q13.3-q14.1 translocation.

SPEC DDIT3 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Myxoid liposarcoma tissue section with translocation affecting the 12q13.3-q14.1 locus as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2100-50	ZytoLight SPEC DDIT3 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2100-200	ZytoLight SPEC DDIT3 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC CDK4/CEN 12 Dual Color Probe

CE IVD

Background

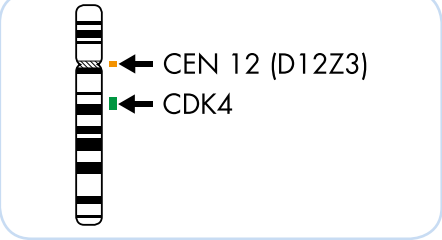
The ZytoLight® SPEC CDK4/CEN 12 Dual Color Probe is designed for the detection of CDK4 gene amplifications. The cyclin-dependent kinase 4 (CDK4) gene is located in the chromosomal region 12q14.1, ~10 Mb centromeric to the murine double minute (MDM2) gene and is frequently coamplified with MDM2 in different malignancies.

In a complex with cyclin D1 (CCND1), the CDK4 encoded serine/threonine kinase phosphorylates the retinoblastoma protein 1 (RB1) which in turn leads to the release of the EF2 transcription factor and subsequently to an upregulation of genes which are required for progression through the S-, G2-, and M-phases of the cell cycle. Due to amplification of the respective chromosomal region, CDK4 is overexpressed in many human tumors such as soft tissue sarcomas, osteosarcomas (OS), and gliomas. In glioblastomas, the lack of amplification of several genes like CDK4 was recognized to be associated with a longer survival time. In OS, coamplification of MDM2 and CDK4, located in two discontinuous regions, occurs frequently in parosteal OS and less often in classical high-grade OS.

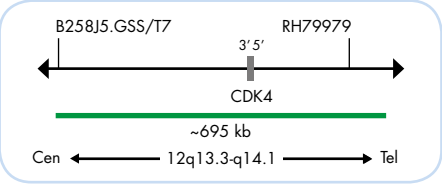
Although MDM2/CDK4 coamplification is not restricted to atypical lipomatous tumors/well-differentiated liposarcomas (ALT/WDLPS) and dedifferentiated liposarcomas (DDLPS), its detection is a strong criterion for distinguishing these tumor types from other undifferentiated sarcomas and even from carcinomas and lymphomas.

Probe Description

The SPEC CDK4/CEN 12 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 12 probe specific for the alpha satellite centromeric region of chromosome 12 (D12Z3) and a green fluorochrome direct labeled SPEC CDK4 probe specific for the chromosomal region 12q13.3-q14.1 harboring the CDK4 gene.



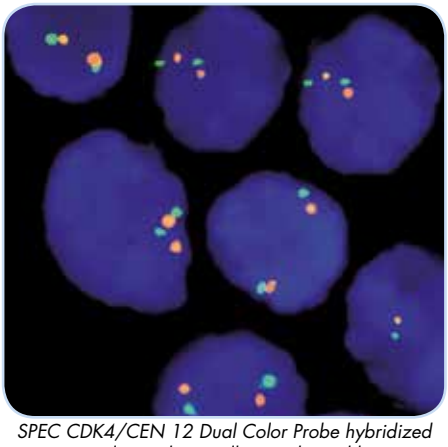
Ideogram of chromosome 12 indicating the hybridization locations.



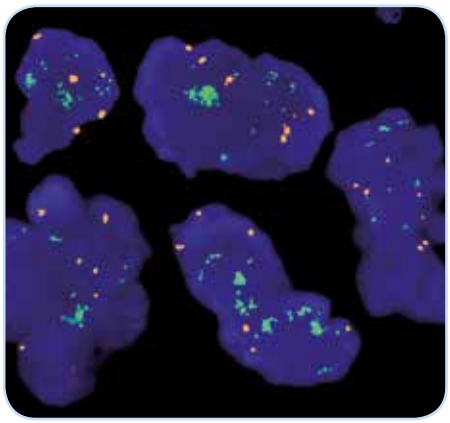
SPEC CDK4 Probe map (not to scale).

Results

In a normal interphase nucleus two orange and two green signals are expected. Nuclei with amplification of the CDK4 gene locus 12q13.3-q14.1, or polysomy of chromosome 12 will show multiple copies of the green signal or large green signal clusters.



SPEC CDK4/CEN 12 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Liposarcoma tissue section, CDK4 signal cluster (green), CEN 12 (orange).

References
Binh MB, et al. (2005) Am J Surg Pathol 29: 1340-7.
Fischer U, et al. (2010) Int J Cancer 126: 2594-602.
Lopes MA, et al. (2001) Oral Oncol 37: 566-71.
Mejia-Guerrero S, et al. (2010) Genes Chromosomes Cancer 49: 518-25.
Sirvent N, et al. (2007) Am J Surg Pathol 31: 1476-89.
Wunder JS, et al. (1999) Oncogene 18: 783-8.

Prod. No.	Product	Label	Tests* (Volume)
Z-2103-50	ZytoLight SPEC CDK4/CEN 12 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2103-200	ZytoLight SPEC CDK4/CEN 12 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC MDM2/CEN 12 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC MDM2/CEN 12 Dual Color Probe is designed for the detection of MDM2 gene amplifications found in more than 10% of human tumors. The MDM2 (MDM2 proto-oncogene) gene is located in the chromosomal region 12q15 and encodes for an E3 ubiquitin ligase which acts as a major negative regulator of the tumor suppressor p53. Due to amplification of the respective chromosomal region, MDM2 is overexpressed in many human tumors such as soft tissue sarcomas, osteosarcomas, gliomas, NSCLC, gastric and breast carcinomas. Well-differentiated liposarcomas (WDLPS), the most common soft tissue tumors in adults, are characterized by the amplification of 12q-derived chromosomal material, harboring the MDM2 oncogene while lipomas show balanced translocations involving 12q13-15. Accordingly, detection of the 12q14-15 amplification is regarded as a valuable tool for the differential diagnosis between WDLPS and lipomas. Furthermore, detection of MDM2 amplification might have prognostic relevance in gastrointestinal stromal tumors (GIST), the most common primary mesenchymal tumor of the gastrointestinal tract.

References
Brisson M, et al. (2013) Skeletal Radiol 42: 635-47.
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Flanagan AM, et al. (2010) Skeletal Radiol 39: 213-24.
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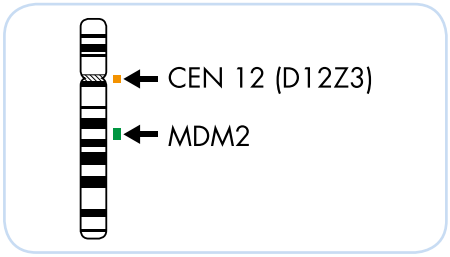
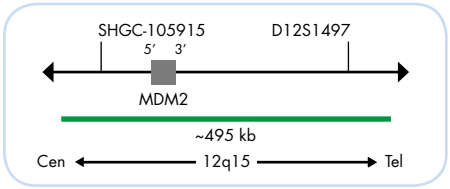
Pedeutour F, et al. (2012) Virchows Arch 461: 67-78.
Poaty H, et al. (2012) PLoS One 7: e29426.
Toledo F & Wahl GM (2006) Nat Rev Cancer 6: 909-23.
Tornillo L, et al. (2005) Lab Invest 85: 921-31.
Vassilev LT (2007) Trends Mol Med 13: 23-31.

Probe Description

The SPEC MDM2/CEN 12 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 12 probe specific for the alpha satellite centromeric region of chromosome 12 (D12Z3) and a green fluorochrome direct labeled SPEC MDM2 probe specific for the MDM2 gene at 12q15.



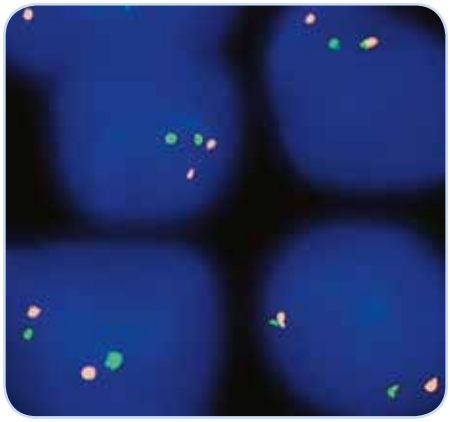
Ideogram of chromosome 12 indicating the hybridization locations.



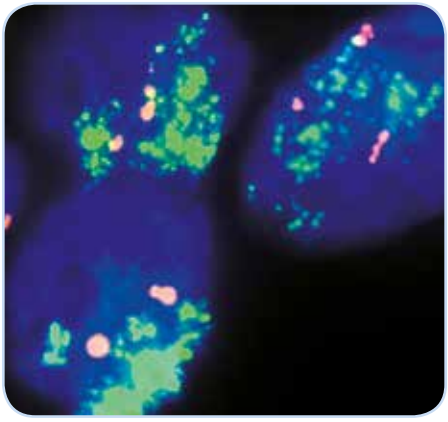
SPEC MDM2 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the MDM2 gene locus, multiple copies of the green signal or green signal clusters will be observed.



Normal interphase cells, MDM2 (green), CEN 12 (orange).



Liposarcoma tissue section with amplification of the MDM2 gene (green), CEN 12 (orange).

Prod. No.	Product	Label	Tests* (Volume)
Z-2013-50	ZytoLight SPEC MDM2/CEN 12 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2013-200	ZytoLight SPEC MDM2/CEN 12 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC FOXO1 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC FOXO1 Dual Color Break Apart Probe is designed for the detection of specific translocations involving the chromosomal region 13q14.11 harboring the FOXO1 (forkhead box O1, a.k.a. FKHR) gene characteristic for alveolar rhabdomyosarcoma.

Among solid tumors of the childhood, rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma. RMS are classified in two main categories: embryonal rhabdomyosarcoma (ERMS) and alveolar rhabdomyosarcoma (ARMS). The alveolar histology is associated with a poorer prognosis. ARMS is characterized by two tumor-specific reciprocal translocations t(2;13)(q36;q14.1) and t(1;13)(p36.1;q14.1) detectable in more than 80% of all ARMS. These translocations fuse the FOXO1 locus on 13q14.11 to either PAX3 on chromosome 2 or to PAX7 on chromosome 1. The resulting fusion transcripts encode for the chimeric proteins PAX3-FOXO1 and PAX7-FOXO1 that combine transcriptional domains from the corresponding wild-type proteins and thereby acquire oncogenic activity.

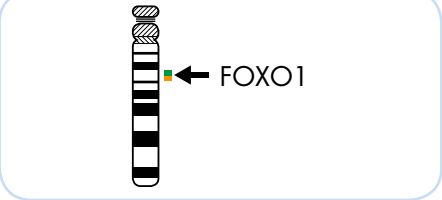
The translocations and their fusion genes represent highly specific genetic markers useful in the diagnosis of ARMS.

References

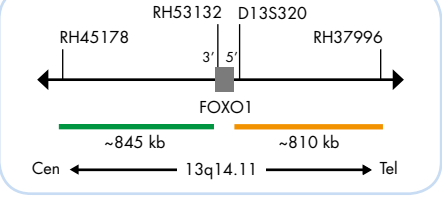
Dal Cin P, et al. (1991) Cancer Genet Cytogenet 55: 191-5.
Douglass EC, et al. (1991) Genes Chromosomes Cancer 3: 480-2.
Gunawan B, et al. (1999) Pathol Oncol Res 5: 211-3.
Seidal T, et al. (1982) Acta Pathol Microbiol Immunol Scand A 90: 345-54.
Sorensen PH, et al. (2002) J Clin Oncol 20: 2672-9.

Probe Description

The SPEC FOXO1 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 13q14.11 band. The orange fluorochrome direct labeled probe hybridizes distal, the green fluorochrome direct labeled probe hybridizes proximal to the breakpoint region of the FOXO1 gene.



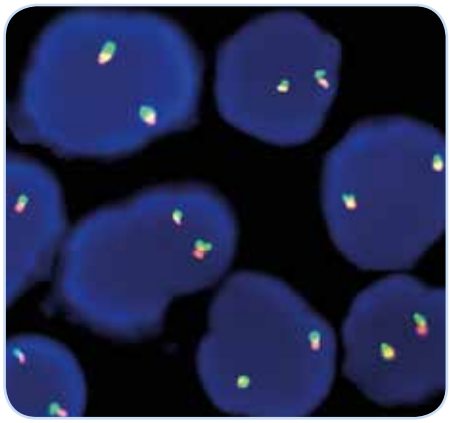
Ideogram of chromosome 13 indicating the hybridization locations.



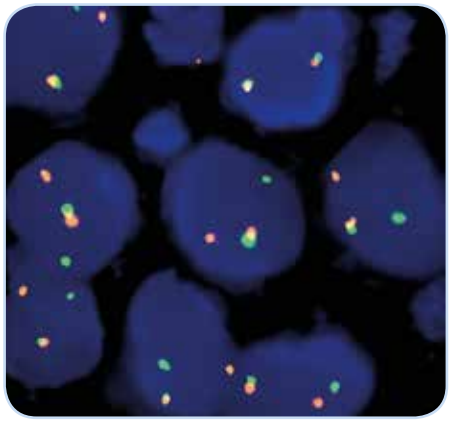
SPEC FOXO1 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 13q14.11 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 13q14.11 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 13q14.11 locus and one 13q14.11 locus affected by a translocation.



SPEC FOXO1 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Rhabdomyosarcoma tissue section with translocation affecting the 13q14.11 locus harboring FOXO1 as indicated by one orange/green fusion signal (non-rearranged), one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2139-50	ZytoLight SPEC FOXO1 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC FOXO1/PAX3 Dual Color Single Fusion Probe

CE IVD

Background

The ZytoLight® SPEC FOXO1/PAX3 Dual Color Single Fusion Probe is designed to detect the translocation t(2;13)(q36;q14.1) in alveolar rhabdomyosarcomas.

Among solid tumors of the childhood, rhabdomyosarcoma is the most common soft tissue sarcoma. Rhabdomyosarcomas are classified in two main categories: embryonal and alveolar rhabdomyosarcoma. The alveolar histology is associated with a poorer prognosis.

Alveolar rhabdomyosarcoma is characterized by two tumor-specific translocations, i.e., t(2;13)(q36;q14.1) and t(1;13)(p36.1;q14.1) which are detectable in most cases of alveolar rhabdomyosarcomas.

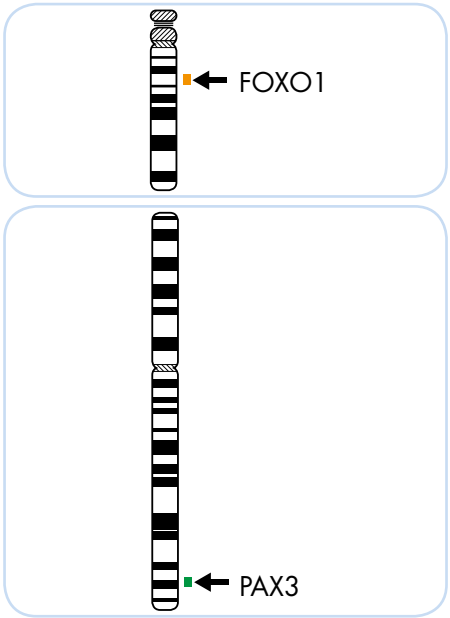
The translocations and their fusion genes represent highly specific genetic markers useful in the diagnosis of alveolar rhabdomyosarcomas.

Correlations between the type of translocation and clinical features as e.g. longer disease-free survival have been identified.

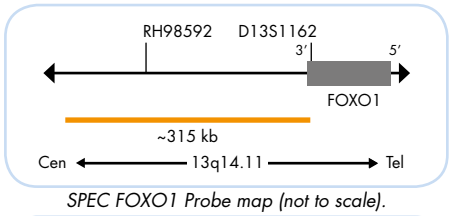
References
Dal Cin P, et al. (1991) Cancer Genet Cytogenet 55: 191-5.
Douglass EC, et al. (1991) Genes Chromosomes Cancer 3: 480-2.
Gunawan B, et al. (1999) Pathol Oncol Res 5: 211-3.
Rekhi B, et al. (2014) Pathol Res Pract 210: 328-33.
Seidal T, et al. (1982) Acta Pathol Microbiol Immunol Scand A: 345-54.

Probe Description

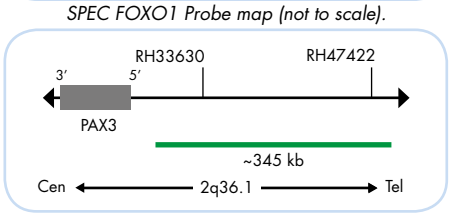
The SPEC FOXO1/PAX3 Dual Color Single Fusion Probe is a mixture of two direct labeled probes hybridizing to the 2q36.1 and 13q14.11 band. The green fluorochrome direct labeled probe hybridizes distal to the PAX3 gene at 2q36.1, the orange fluorochrome direct labeled probe hybridizes proximal to the FOXO1 gene at 13q14.11.



Ideograms of chromosomes 13 (above) and 2 (below) indicating the hybridization locations.



SPEC FOXO1 Probe map (not to scale).

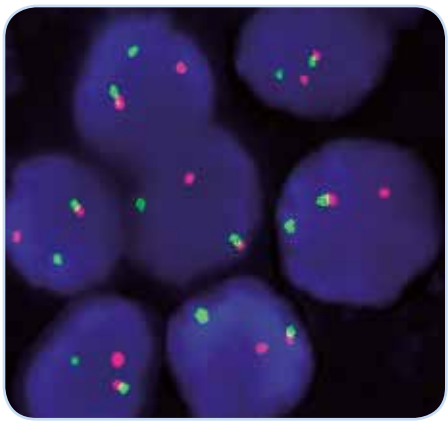


SPEC PAX3 Probe map (not to scale).

Results

In an interphase nucleus lacking the t(2;13), two orange and two green signals are expected.

In a cell harboring the t(2;13), one orange signal, one green signal, and one orange/green fusion signal will be observed.



SPEC FOXO1/PAX3 Dual Color Single Fusion Probe hybridized to abnormal nuclei harboring a t(2;13)(q35;q14) as indicated by one orange, one green, and one orange/green fusion signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2018-50	ZytoLight SPEC FOXO1/PAX3 Dual Color Single Fusion Probe CE IVD	●/●	5 (50 µl)
Z-2018-200	ZytoLight SPEC FOXO1/PAX3 Dual Color Single Fusion Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC FOXO1/PAX3 TriCheck™ Probe

CE IVD

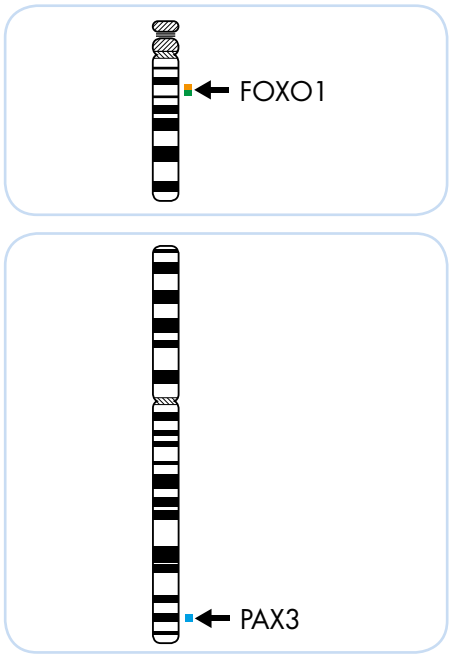
Background

The ZytoLight® SPEC FOXO1/PAX3 TriCheck™ Probe is designed to detect translocations involving the chromosomal region 13q14.11 harboring the FOXO1 (forkhead box O1, a.k.a. FKHR) gene and the chromosomal region 2q36.1 harboring the PAX3 (paired box 3, a.k.a. HUP2) gene.
Among solid tumors of the childhood, rhabdomyosarcoma is the most common soft tissue sarcoma. Rhabdomyosarcomas are classified in two main categories: embryonal and alveolar rhabdomyosarcoma. Generally, the alveolar histology is associated with a poorer prognosis.
Alveolar rhabdomyosarcoma (ARMS) is characterized by two tumor-specific translocations, i.e., t(2;13)(q36;q14.1) and t(1;13)(p36.1;q14.1) which are detectable in most cases of ARMS. The translocations involve the FOXO1 gene and either PAX7 on chromosome 1p36.13 or PAX3 on chromosome 2q36.1. PAX7-FOXO1 is less common but is associated with a better prognosis than PAX3-FOXO1 fusion.
The translocations and their fusion genes represent highly specific genetic markers useful in the diagnosis and prognosis of ARMS.

References
Dal Cin P, et al. (1991) Cancer Genet Cytogenet 55: 191-5.
Douglass EC, et al. (1991) Genes Chromosomes Cancer 3: 480-2.
Gunawan B, et al. (1999) Pathol Oncol Res 5: 211-3.
Jain S, et al. (2010) Int J Clin Exp Pathol 3: 416-28.
Seidal T, et al. (1982) Acta Pathol Microbiol Immunol Scand A 90: 345-54.

Probe Description

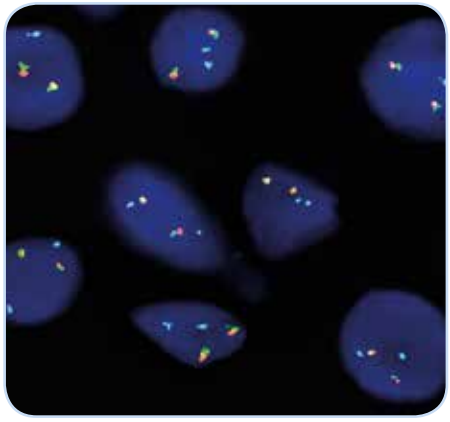
The SPEC FOXO1/PAX3 TriCheck™ Probe is a mixture of three direct labeled probes hybridizing to the 13q14.11 and 2q36.1 bands. The orange fluorochrome direct labeled probe hybridizes proximal and the green fluorochrome direct labeled probe hybridizes distal to the FOXO1 breakpoint region at 13q14.11. The blue fluorochrome direct labeled probe hybridizes distal to the PAX3 gene at 2q36.1.



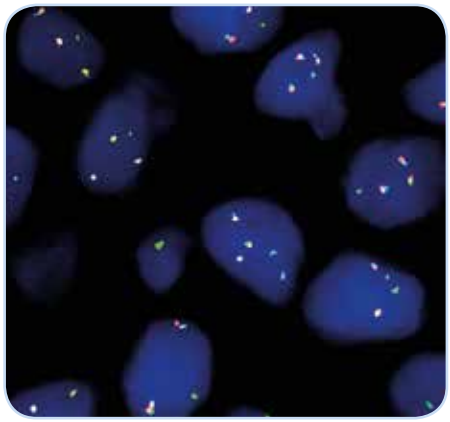
Ideograms of chromosomes 13 (above) and 2 (below) indicating the hybridization locations.

Results

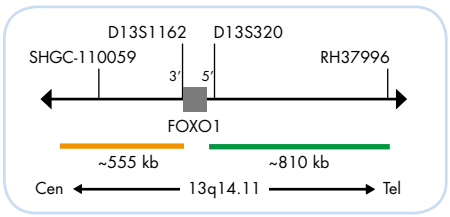
In an interphase nucleus without PAX3-FOXO1 rearrangement, two green/orange fusion signals and two blue signals are expected.
A PAX3-FOXO1 fusion is indicated by one separate orange signal co-localizing with one blue signal and one separate green signal.
A FOXO1 translocation without involvement of PAX3 is indicated by the split of one green/orange fusion signal without co-localization of the separated orange signal with one blue signal.



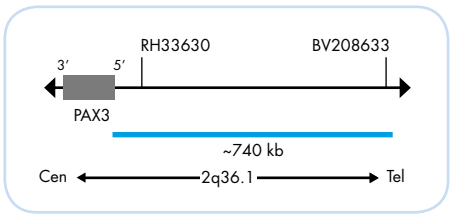
SPEC FOXO1/PAX3 TriCheck™ Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals and two blue signals per nucleus.



ARMS tissue section with PAX3-FOXO1 fusion as indicated by orange/blue fusion signals.



SPEC FOXO1 Probe map (not to scale).



SPEC PAX3 Probe map (not to scale).

Prod. No.	Product	Label	Tests* (Volume)
Z-2185-50	ZytoLight SPEC FOXO1/PAX3 TriCheck Probe CE IVD	●/●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC FOXO1/PAX7 Dual Color Single Fusion Probe

CE IVD

Background

The ZytoLight® SPEC FOXO1/PAX7 Dual Color Single Fusion Probe is designed to detect the translocation t(1;13)(p36.1;q14.1) in alveolar rhabdomyosarcomas.

Among solid tumors of the childhood, rhabdomyosarcoma is the most common soft tissue sarcoma. Rhabdomyosarcomas are classified in two main categories: embryonal and alveolar rhabdomyosarcoma. The alveolar histology is associated with a poorer prognosis.

Alveolar rhabdomyosarcoma is characterized by two tumor-specific translocations, i.e., t(2;13)(q36;q14.1) and t(1;13)(p36.1;q14.1) which are detectable in most cases of alveolar rhabdomyosarcomas.

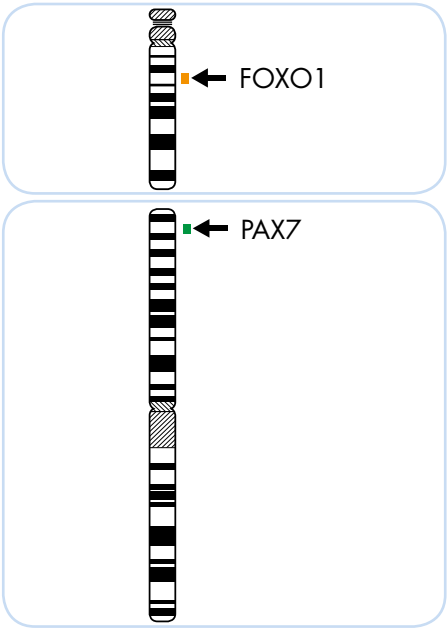
The translocations and their fusion genes represent highly specific genetic markers useful in the diagnosis of alveolar rhabdomyosarcomas.

Correlations between the type of translocation and clinical features as e.g. longer disease-free survival have been identified.

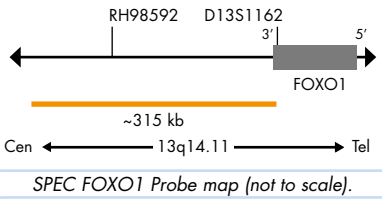
References
Dal Cin P, et al. (1991) Cancer Genet Cytogenet 55: 191-5.
Douglass EC, et al. (1991) Genes Chromosomes Cancer 3: 480-2.
Gunawan B, et al. (1999) Pathol Oncol Res 5: 211-3.
Rekhi B, et al. (2014) Pathol Res Pract 210: 328-33.
Seidal T, et al. (1982) Acta Pathol Microbiol Immunol Scand A: 345-54.

Probe Description

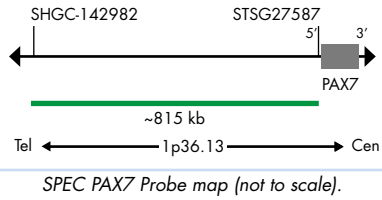
The SPEC FOXO1/PAX7 Dual Color Single Fusion Probe is a mixture of two direct labeled probes hybridizing to the 1p36.13 and 13q14.11 band. The green fluorochrome direct labeled probe hybridizes distal to the PAX7 gene at 1p36.13, the orange fluorochrome direct labeled probe hybridizes proximal to the FOXO1 gene at 13q14.11.



Ideograms of chromosomes 13 (above) and 1 (below) indicating the hybridization locations.



SPEC FOXO1 Probe map (not to scale).

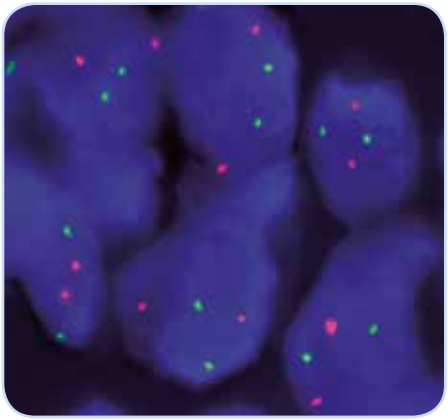


SPEC PAX7 Probe map (not to scale).

Results

In an interphase nucleus lacking the t(1;13), two orange and two green signals are expected.

In a cell harboring the t(1;13), one orange signal, one green signal, and one orange/green fusion signal will be observed.



SPEC FOXO1/PAX7 Dual Color Single Fusion Probe hybridized to normal interphase cells as indicated by two orange and two green signals.

Prod. No.	Product	Label	Tests* (Volume)
Z-2019-50	ZytoLight SPEC FOXO1/PAX7 Dual Color Single Fusion Probe CE IVD	●/●	5 (50 µl)
Z-2019-200	ZytoLight SPEC FOXO1/PAX7 Dual Color Single Fusion Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC RB1/13q12 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC RB1/13q12 Dual Color Probe is designed for the detection of deletions affecting the RB1 gene.

The RB1 (RB transcriptional corepressor 1, a.k.a. pRb) gene is located on 13q14.2 and encodes a protein which acts as a tumor suppressor playing a crucial role in cell cycle regulation and genome stability. Deletions of RB1 are frequently found in retinoblastoma.

However, either monoallelic or biallelic deletions of RB1 are also common in a wide variety of solid tumors and hematologic malignancies such as multiple myeloma (MM) and chronic lymphocytic leukemia (CLL).

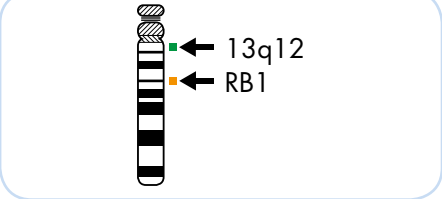
While 13q14 deletions exclusive of RB1 confer a more favorable prognosis in CLL patients, 13q14 deletions that encompass the RB1 locus (present in approx. 20% of all CLL cases) are associated with shortened survival.

Hence, Fluorescence *in situ* Hybridization is a valuable tool for the detection of RB1 gene deletions and can be used in combination with further biological markers, morphology and clinical information for the prediction of disease progression and overall survival.

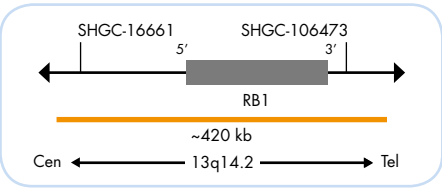
References
Dal Bo M, et al. (2011) Genes Chromosomes Cancer 50: 633-43.
Dao DD, et al. (1994) Leukemia 8: 1280-4.
Di Fiore R, et al. (2013) J Cell Physiol 228: 1676-87.
Juge-Morineau N, et al. (1997) Leuk Lymphoma 24: 229-37.
Orlandi EM, et al. (2013) Hematol Oncol 31: 136-42.
Ouillette P, et al. (2011) Clin Cancer Res 17: 6778-90.

Probe Description

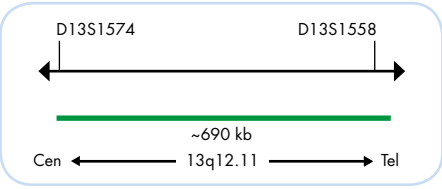
The SPEC RB1/13q12 Dual Color Probe is a mixture of an orange fluorochrome direct labeled SPEC RB1 probe specific for the RB1 gene in the chromosomal region 13q14.2 and a green fluorochrome direct labeled SPEC 13q12 probe specific for the chromosomal region 13q12.11. The SPEC 13q12 Probe is designed to hybridize in close proximity of centromere 13 at 13q12.11. Since chromosomes 13 and 21 share the same repetitive sequences, they cannot be differentiated by probes detecting centromere specific repeats.



Ideogram of chromosome 13 indicating the hybridization locations.



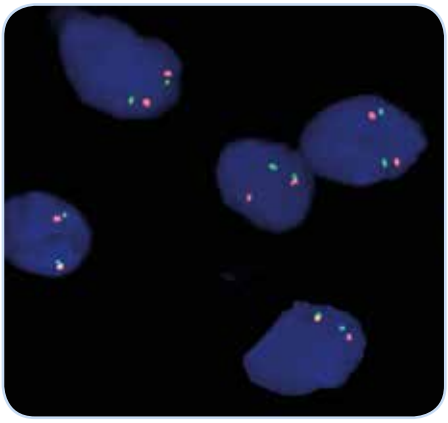
SPEC RB1 Probe map (not to scale).



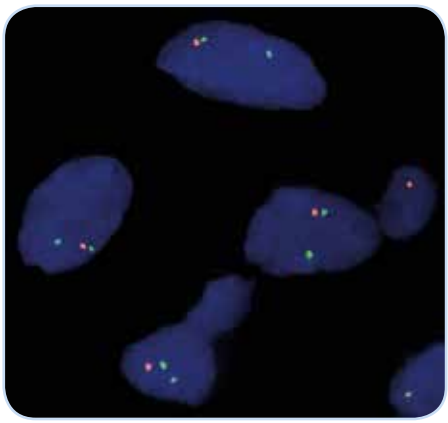
SPEC 13q12 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletions affecting the RB1 gene locus, one or no copy of the orange signal will be observed.



SPEC RB1/13q12 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



SPEC RB1/13q12 Dual Color Probe hybridized to benign spindle cell lipoma tissue section with deletion of the RB1 gene as indicated by one orange signal and two green signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2165-50	ZytoLight SPEC RB1/13q12 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2165-200	ZytoLight SPEC RB1/13q12 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC IGH Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC IGH Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 14q32.33 harboring the IGH gene.

Rearrangements involving the IGH (immunoglobulin heavy locus, a.k.a. IGH@) gene are considered to be cytogenetic hallmarks for non-Hodgkin lymphoma (NHL). NHLs represent 50% of all hematological malignancies.

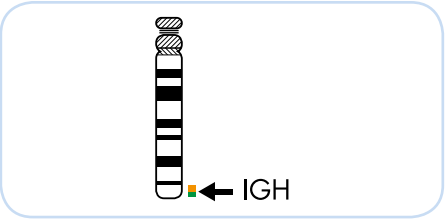
IGH gene rearrangements have been identified in about 50% of NHLs and are associated with specific subtypes of NHLs. Translocation t(11;14)(q13.3;q32.3) can be found in about in 95% of mantle cell lymphoma (MCL), t(14;18)(q32.3;q21.3) in 80% of follicular lymphoma (FL), t(3;14)(q27;q32.3) in diffuse large B-cell lymphoma (DLBCL), and t(8;14)(q24.21;q32.3) in Burkitt lymphoma. In all of these translocations an oncogene located near the breakpoint of the translocation partner is activated by juxtaposing to IGH regulatory sequences.

Rearrangements involving 14q32.33 have unique biological characteristics and correlate with clinical, morphological, and immunophenotypic features. Fluorescence *in situ* Hybridization is a helpful tool for the diagnosis, selecting treatment, and giving prognostic information.

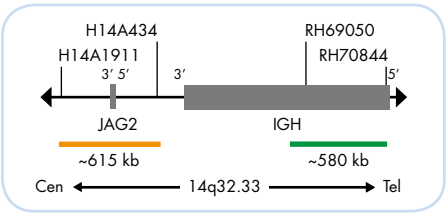
References
Bernicot I, et al. (2007) Cytogenet Genome Res 118: 345-52.
Hehne S, et al. (2012) Pathol Res Pract 208: 510-7.
Lu S, et al. (2004) Cancer Genet and Cytogenet 152: 141-5.
Nishida K, et al. (1997) Blood 90: 526-34.
Quintero-Rivera F, et al. (2009) Cancer Genet and Cytogenet 190: 33-9.

Probe Description

The SPEC IGH Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 14q32.33 band. The orange fluorochrome direct labeled probe hybridizes proximal, and the green fluorochrome direct labeled probe hybridizes distal to the constant regions of the IGH locus.



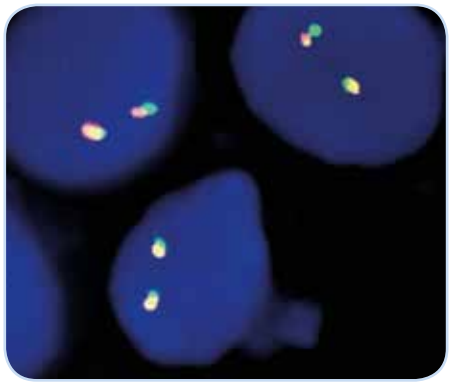
Ideogram of chromosome 14 indicating the hybridization locations.



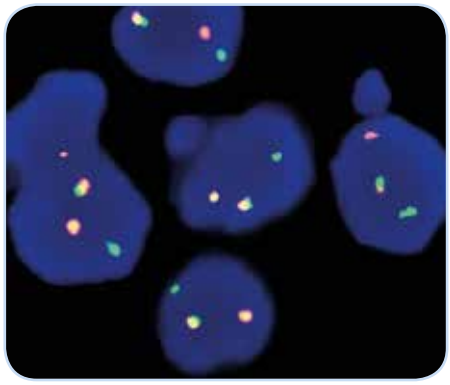
SPEC IGH Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 14q32.33 band two orange/green fusion signals are expected representing two normal (non-rearranged) 14q32.33 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 14q32.33 locus and one 14q32.33 locus affected by a translocation.



SPEC IGH Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Burkitt lymphoma tissue section with translocation affecting the 14q32.33 locus as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2110-50	ZytoLight SPEC IGH Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2110-200	ZytoLight SPEC IGH Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC NUTM1 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC NUTM1 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 15q14 harboring the NUTM1 (NUT midline carcinoma family member 1, a.k.a. NUT) gene.

NUT midline carcinoma (NMC) is a rare and aggressive form of squamous cell carcinoma that arises mainly in the head, neck, or mediastinum. NMC is genetically defined by the presence of chromosomal rearrangements involving the NUTM1 gene. Two-thirds of NMCs have t(15;19)(q14;p13.1) fusing the NUTM1 gene to the BRD4 gene. Less commonly, NMC harbors a NUTM1-variant fusion gene involving BRD3 or still-uncharacterized genes. NMCs may be indistinguishable from more common squamous cell carcinomas and are thus an underdiagnosed entity. Therefore, the diagnosis of NMC depends on the confirmation of NUTM1 rearrangement.

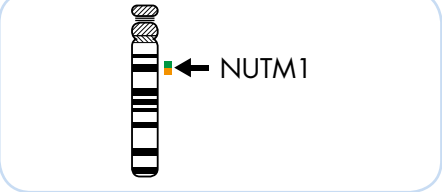
BRD3 and BRD4 belong to the bromo and extra terminal (BET) family of bromodomain proteins. BRD-NUTM1 chimeric oncoproteins repress squamous differentiation, possibly by sequestering histone acetyltransferase activity. Accordingly, histone deacetylase inhibitors or BET inhibitors were shown to reverse the effects of BRD-NUTM1 fusion proteins by inducing terminal differentiation of NMC cells *in vitro* and in xenograft models.

Hence, detection of NUTM1 rearrangements by FISH represents a useful tool in the differential diagnosis of NMC and may be of therapeutic significance.

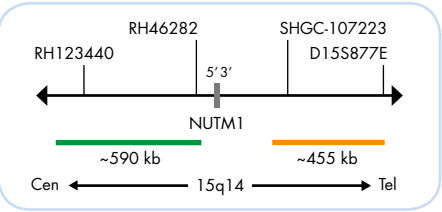
References
French CA (2012) Annu Rev Pathol 7: 247-65.
Kubonishi I, et al. (1991) Cancer Res 51: 3327-8.
Müller S & Knapp S (2014) Med Chem Commun 5: 288-96.

Probe Description

The SPEC NUTM1 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 15q14 band. The green fluorochrome direct labeled probe hybridizes proximal and the orange fluorochrome direct labeled probe hybridizes distal to the NUTM1 gene.



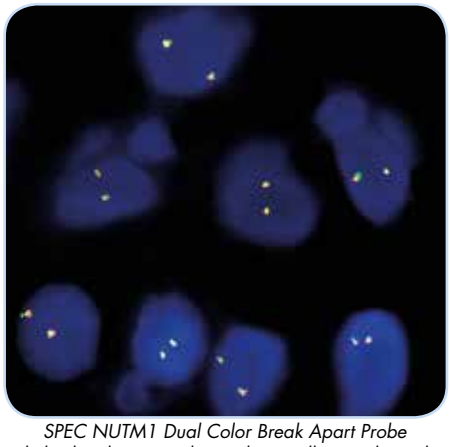
Ideogram of chromosome 15 indicating the hybridization locations.



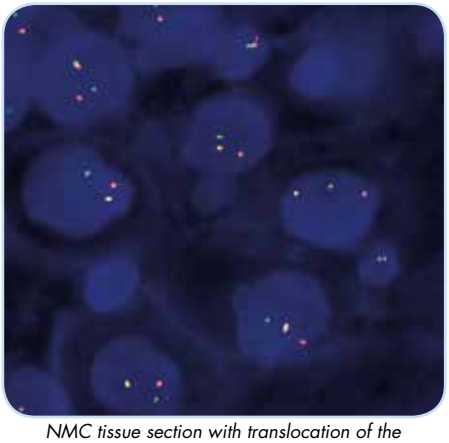
SPEC NUTM1 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 15q14 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 15q14 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 15q14 locus and one 15q14 locus affected by a translocation.



SPEC NUTM1 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



NMC tissue section with translocation of the NUTM1 gene as indicated by one non-rearranged orange/green fusion signal, one orange and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2208-200	ZytoLight SPEC NUTM1 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC PML/RARA Dual Color Dual Fusion Probe

CE IVD

Background

The ZytoLight® SPEC PML/RARA Dual Color Dual Fusion Probe is designed to detect the translocation t(15;17)(q24;q21.2) affecting the PML gene in the chromosomal region 15q24.1 and the RARA locus in 17q21.2.

Translocations involving the PML (promyelocytic leukemia, a.k.a. MYL) gene and the RARA (retinoic acid receptor alpha, a.k.a. RARα) gene are considered to be characteristic for acute promyelocytic leukemia (APL), a subtype of acute myeloid leukemia.

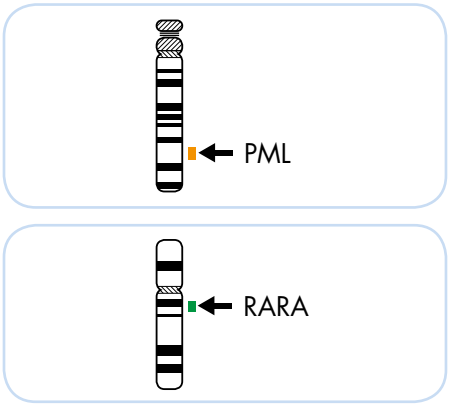
Various fusion partners of RARA have been identified, however, in 95% of all APL cases, rearrangements involving the PML gene are detectable. This translocation t(15;17)(q24;q21) leads to a gene fusion of the PML and the RARA gene. The fusion is supposed to play a fundamental role in induction, development, and progression of APL.

Since the PML/RARA fusion accounts for the response of these neoplasms to all-trans retinoic acid (ATRA) therapy and other conventional chemotherapy it is important to accurately distinguish between t(15;17) translocations and translocations involving other partners of RARA.

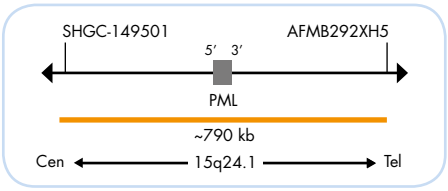
References
Abe S, et al. (2008) Cancer Genet and Cytogenet 184: 44-7.
Brockmann SR, et al. (2003) Cancer Genet and Cytogenet 145: 144-51.
Reiter A, et al. (2004) Acta Hematol 112: 55-67.
Sanz MA, et al. (2009) Blood 113: 1875-91.

Probe Description

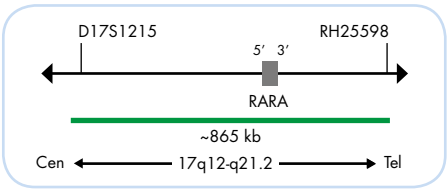
The SPEC PML/RARA Dual Color Dual Fusion Probe is a mixture of an orange fluorochrome direct labeled PML probe spanning the known PML breakpoints, and a green fluorochrome direct labeled RARA probe spanning the known breakpoints of RARA. This probe is approved to be used with a hybridization time of 2 hours on cytological specimens.



Ideograms of chromosomes 15 (above) and 17 (below) indicating the hybridization locations.



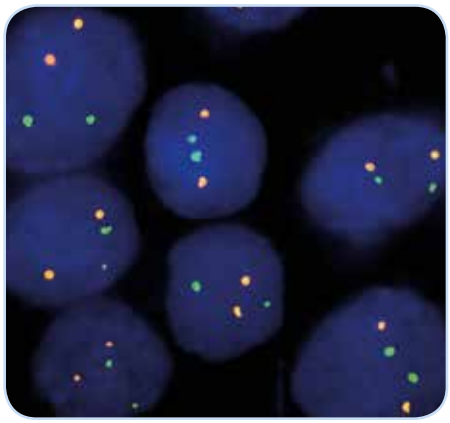
SPEC PML Probe map (not to scale).



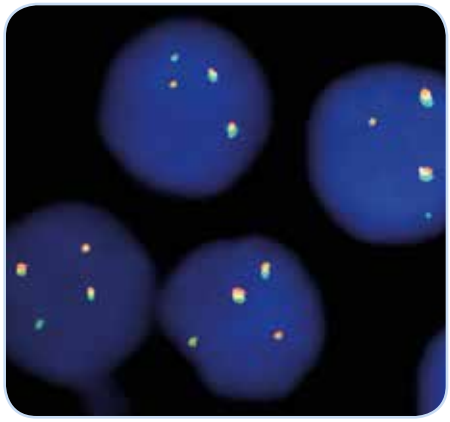
SPEC RARA Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. A reciprocal PML/RARA translocation leads to two orange/green fusion signals indicating both rearranged chromosomes. Additionally, the non-rearranged chromosomes are indicated by one orange signal and a separate green signal, respectively.



SPEC PML/RARA Dual Color Dual Fusion Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Bone marrow biopsy section with translocation affecting the PML/RARA loci as indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.

Prod. No.	Product	Label	Tests* (Volume)
Z-2113-50	ZytoLight SPEC PML/RARA Dual Color Dual Fusion Probe CE IVD	O/G	5 (50 µl)
Z-2113-200	ZytoLight SPEC PML/RARA Dual Color Dual Fusion Probe CE IVD	O/G	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC NTRK3 Dual Color Break Apart Probe

CE IVD

Background

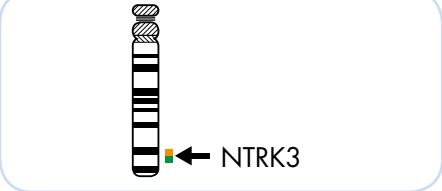
The ZytoLight® SPEC NTRK3 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 15q25.3 harboring the NTRK3 (neurotrophic receptor tyrosine kinase 3, a.k.a. TRKC) gene.

NTRK3 is a receptor tyrosine kinase (TK) for neurotrophin 3 (NT3) and plays a key role in central and peripheral nervous system development as well as in cell survival. Translocations affecting the NTRK3 gene have been reported in several cancer types, including glioblastomas, Philadelphia chromosome-like acute lymphoblastic leukemia, congenital fibrosarcomas, cellular mesoblastic nephromas, acute myeloid leukemia, radiation-associated thyroid cancer, secretory breast carcinoma, and mammary analog secretory carcinoma of the salivary gland. The most frequent rearrangement involving the NTRK3 gene is the t(12;15)(p13;q25) which results in a fusion between the 5′ part of the ETV6 gene and the 3′ part of the NTRK3 gene. This fusion gene encodes a hybrid protein comprising the TK domain of NTRK3 and the dimerization domain of ETV6 which leads to a ligand-independent TK activity.

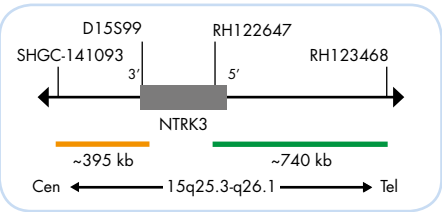
Currently, there are several ongoing clinical trials involving drugs with known inhibitory activity of NTRK-related kinases. Entrectinib and LOXO-101 represent two of these TRK inhibitors which have shown promising activity and good tolerability in patients with advanced solid tumors and NSCLC harboring NTRK1, 2, and 3 rearrangements. Hence, detection of NTRK3 translocations by Fluorescence *in situ* Hybridization (FISH) may be of diagnostic and therapeutic relevance.

Probe Description

The SPEC NTRK3 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 15q25.3-q26.1 band. The orange fluorochrome direct labeled probe hybridizes proximal to the NTRK3 breakpoint region at 15q25.3, the green fluorochrome direct labeled probe hybridizes distal to the NTRK3 breakpoint region at 15q25.3-q26.1.



Ideogram of chromosome 15 indicating the hybridization locations.



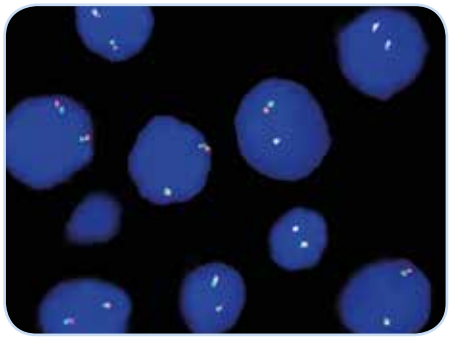
SPEC NTRK3 Probe map (not to scale).

References

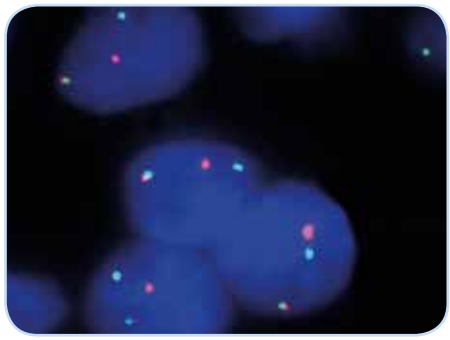
Amatu A, et al. (2016) ESMO Open 1: e000023.
Arce C, et al. (2005) World J Surg Oncol 3: 35.
Knezevich SR, et al. (1998) Nat Genet 18: 184-7.
Leeman-Neill RJ, et al. (2014) Cancer 120: 799-807.
Nagasubramanian R, et al. (2016) Pediatr Blood Cancer 63: 1468-70.
Raez LE & Rolfo C (2016) Lung Cancer Manag 5: 1-4.
Roberts KG, et al. (2014) N Engl J Med 371: 1005-15.
Skálová A, et al. (2010) Am J Surg Pathol 34: 599-608.
Tognon C, et al. (2002) Cancer Cell 2: 367-76.
Wu G, et al. (2014) Nat Genet 46: 444-50.

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 15q25.3-q26.1 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 15q25.3-q26.1 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 15q25.3-q26.1 locus and one 15q25.3-q26.1 locus affected by a translocation.



SPEC NTRK3 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Secretory breast carcinoma tissue section with translocation affecting the 15q25.3-q26.1 locus as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2206-50	ZytoLight SPEC NTRK3 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2206-200	ZytoLight SPEC NTRK3 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC CREBBP Dual Color Break Apart Probe

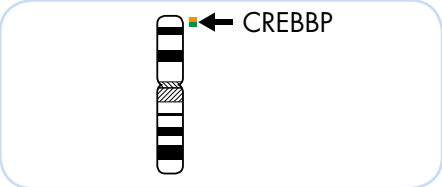
CE IVD

Background

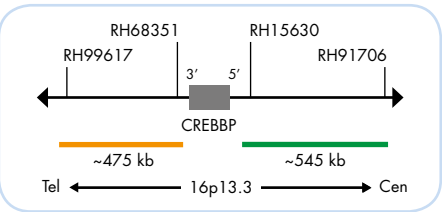
The ZytoLight® SPEC CREBBP Dual Color Break Apart Probe is designed for the detection of translocations involving the chromosomal region 16p13.3 harboring the CREBBP (CREB binding protein, a.k.a. CBP, RTS) gene. The CREBBP protein regulates transcription by means of histone acetyltransferase activity and by binding to several proteins with key cell cycle functions, such as p53 and NFκB. Rearrangements of the CREBBP gene have been observed in several hematologic malignancies. Three different fusion partners have been described so far. KMT2A (a.k.a. MLL) is fused to CREBBP in therapy-related acute myeloid (AML) or lymphoid leukemia (ALL) and myelodysplastic syndrome (MDS) with t(11;16)(q23.3;p13.3). The translocation t(10;16)(q22.2;p13.3) was reported in some AML cases and fuses KAT6B (a.k.a. MORF) to CREBBP. CREBBP is also rearranged with KAT6A (a.k.a. MOZ) in *de novo* and therapy-related AML with t(8;16)(p11.2;p13.3) after treatment with topoisomerase II inhibitors. This rearrangement is associated with an infrequent but well-defined type of AML that has characteristic morphocytochemical features. The prognosis is usually extremely poor, with a median survival of two months.
The KAT6A/CREBBP AML tends to develop within two years of adjuvant chemotherapy, especially in former breast cancer patients.
Thus, FISH analysis for the detection of CREBBP translocation may serve as a diagnostic tool to identify cases with hematologic malignancies with an aggressive presentation.

Probe Description

The SPEC CREBBP Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 16p13.3 band. The green fluorochrome direct labeled probe hybridizes proximal and the orange fluorochrome direct labeled probe hybridizes distal to the CREBBP gene.



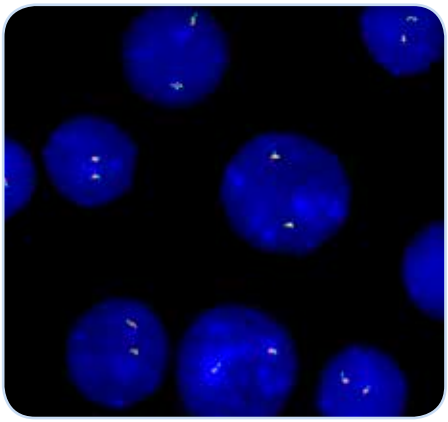
Ideogram of chromosome 16 indicating the hybridization locations.



SPEC CREBBP Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 16p13.3 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 16p13.3 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 16p13.3 locus and one 16p13.3 locus affected by a translocation.



SPEC CREBBP Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.

References
Borrow J, et al. (1996) Nat Genet 14: 33-41.
Camós M, et al. (2006) Cancer Res 66: 6947-54.
Gupta A, et al. (2014) Case Rep Oncol Med 2014: 361748.
Rozman M, et al. (2004) Genes Chromosomes Cancer 40: 140-5.
Taki T, et al. (1997) Blood 89: 3945-50.
Vizmanos JL, et al. (2003) Genes Chromosomes Cancer 36: 402-5.

Prod. No.	Product	Label	Tests* (Volume)
Z-2267-50	ZytoLight SPEC CREBBP Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC FUS Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC FUS Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 16p11.2 harboring the FUS (FUS RNA binding protein) gene (a.k.a. TLS, FUS/TLS, hnRNP P2).

The FUS gene encodes an RNA-binding protein, the C-terminal end of which is involved in protein and RNA binding and which appears to be involved in transcriptional activation with its N-terminal end. It shares distinct characteristics with EWSR1 and TAF15 which together with FUS are frequently referred to as the FET family of proteins.

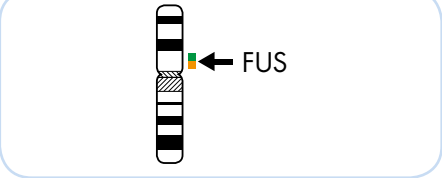
FUS gene rearrangements have been shown to be involved in both solid tumors and leukemias fusing the N-terminal end of FUS to various fusion partners. The most frequent translocation involving the FUS gene region is t(12;16)(q13.3;p11.2). Occurring in over 90% of myxoid liposarcomas, the FUS-DDIT3 fusion protein is regarded as being consequential for the development of myxoid liposarcomas by acting as an abnormal transcription factor and thus deregulating FUS-DDIT3 target genes.

Differential diagnosis of liposarcomas and accurate classification, the latter being especially important with regard to appropriate treatment and prognosis, are often problematic. Therefore, detection of FUS rearrangements via *in situ* Hybridization analysis is a valuable tool to confirm the histopathological diagnosis of myxoid liposarcoma.

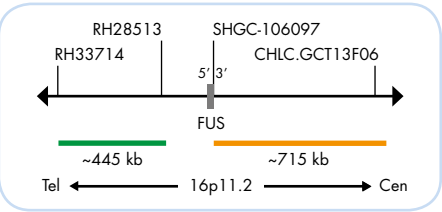
References
Andersson M, et al. (2010) BMC Cancer 10: 249-58.
Antonescu C, et al. (2000) J Mol Diagn 2: 132-8.
Germano G, et al. (2010) Cancer Res 70: 2235-44.
Kuroda M, et al. (1995) Am J Pathol 147: 1221-7.
Meis-Kindblom JM, et al. (2001) Virchows Arch 439: 141-51.
Panagopoulos I, et al. (1994) Cancer Res 54: 6500-3.
Panagopoulos I, et al. (1997) Oncogene 15: 1357-62.

Probe Description

The SPEC FUS Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 16p11.2 band. The orange fluorochrome direct labeled probe hybridizes proximal to the FUS gene, the green fluorochrome direct labeled probe hybridizes distal to that gene.



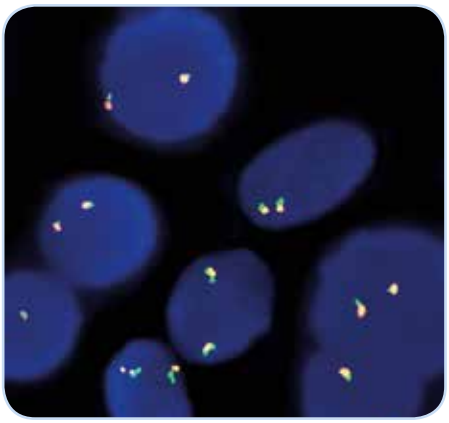
Ideogram of chromosome 16 indicating the hybridization locations.



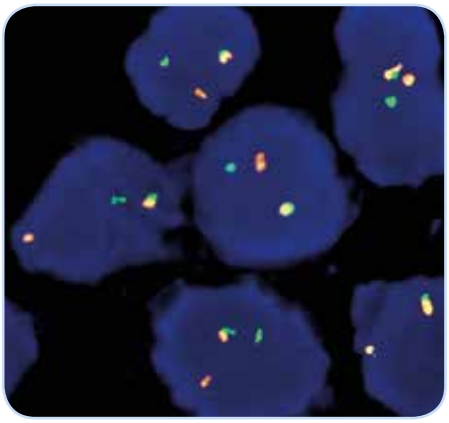
SPEC FUS Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 16p11.2 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 16p11.2 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 16p11.2 locus and one 16p11.2 locus affected by a 16p11.2 translocation.



SPEC FUS Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Myxoid liposarcoma tissue section with translocation affecting the 16p11.2 locus as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2130-50	ZytoLight SPEC FUS Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC CBFB Dual Color Break Apart Probe

CE IVD

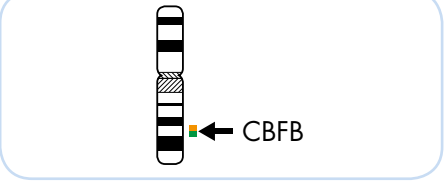
Background

The ZytoLight® SPEC CBFB Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal region 16q22.1 harboring the CBFB (core-binding factor subunit beta, a.k.a. PEBP2B) gene. CBFB encodes the beta subunit of the CBFA/CBFB transcription factor complex involved in myeloid differentiation. The chromosomal aberrations inv(16)(p13.1q22.1) and the related translocation t(16;16)(p13.1;q22.1), which have been detected in about 10% of patients with AML (acute myeloblastic leukemia), lead to the fusion of the CBFB gene with the MYH11 (myosin heavy chain 11) gene on 16p13.1. The resulting CBFB-MYH11 fusion gene is involved in a leukemic transformation. The 5′ segment of the MYH11 gene is known to be deleted occasionally as a result of the inversion event. AML patients with these genetic rearrangements have a favorable prognosis. Inv(16) may sometimes be difficult to identify using conventional cytogenetic analysis. Accordingly, Fluorescence *in situ* Hybridization proved to be a reliable method overcoming this problem and might consequently be a helpful tool to predict the prognosis of AML patients.

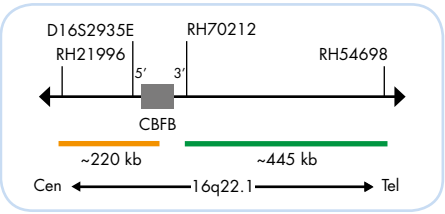
References
Aventín A, et al. (2002) Cancer Genet Cytogenet 134: 142-4.
Dawson AJ, et al. (2011) Cancer Genet 204: 344-7.
Dierlamm J, et al. (1998) Genes Chromosomes Cancer 22: 87-94.
Krauter J, et al. (2001) Genes Chromosomes Cancer 30: 342-8.
Le Beau MM, et al. (1983) N Engl J Med 309: 630-6.
Li MM, et al. (2013) Curr Genet Med Rep 1: 99-112.

Probe Description

The SPEC CBFB Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 16q22.1 band. The orange fluorochrome direct labeled probe hybridizes proximal, the green fluorochrome direct labeled probe hybridizes distal to the CBFB gene breakpoint region at 16q22.1. This probe is approved to be used with a hybridization time of 2 hours on cytological specimens.



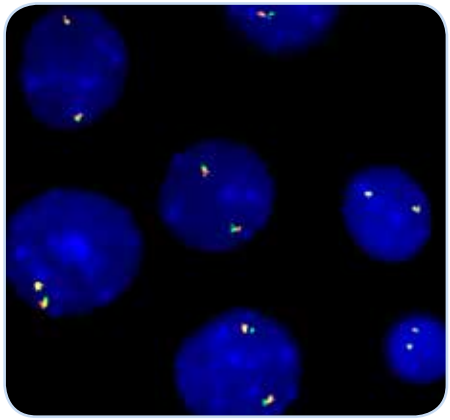
Ideogram of chromosome 16 indicating the hybridization locations.



SPEC CBFB Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 16q22.1 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 16q22.1 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 16q22.1 locus and one 16q22.1 locus affected by a translocation. In case of a deletion distal to the CBFB breakpoint region a single orange signal can be expected.



SPEC CBFB Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2207-50	ZytoLight SPEC CBFB Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC MAF/IGH Dual Color Dual Fusion Probe

CE IVD

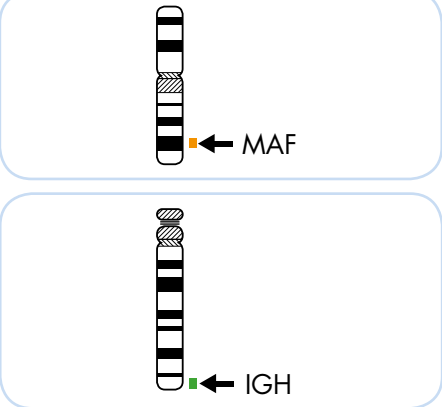
Background

The ZytoLight® SPEC MAF/IGH Dual Color Dual Fusion Probe is designed to detect the translocations affecting the MAF gene in the chromosomal region 16q23.2 and the IGH locus in 14q32.33. The translocation t(14;16)(q32.3;q23) is frequently found in multiple myeloma (MM).
MM is a malignant post-germinal center tumor of somatically-mutated, isotype-switched plasma cells that accumulate in the bone marrow. It is often preceded by a premalignant state known as monoclonal gammopathy of undetermined significance (MGUS). Five recurrent primary translocations involving the immunoglobulin heavy locus (IGH) have been identified in 40% of MGUS and MM tumors. They include t(11;14)(q13.3;q32.3), t(6;14)(p21.1;q32.3), t(4;14)(p16.3;q32.3), t(14;16)(q32.3;q23), and t(14;20)(q32.3;q12), which involve the genes CCND1, CCND3, FGFR3 and NSD2, MAF, and MAFB, respectively. All of these translocations lead to the dysregulation and overexpression of the target genes as a consequence of their juxtaposition to regulatory sequences of the IGH locus. t(14;16) occurs in approximately 5% of MM patients and is associated with a more aggressive clinical outcome. The 16q23 breakpoints have been found to be scattered 550-1280 kb centromerically to the MAF gene within the WWOX gene. Hence, detection of t(14;16) by FISH represents a useful prognostic tool and may aid in therapeutic decision making in MM.

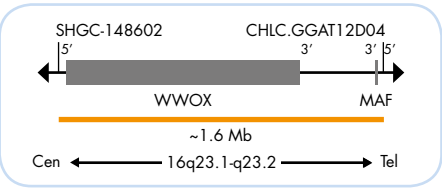
References
Chesi M, et al. (1998) Blood 91: 4457-63.
Fabris S, et al. (2005) Genes Chromosomes Cancer 42: 117-27.
Fonseca R, et al. (2009) Leukemia 23: 2210-21.
Gabrea A, et al. (2006) DNA Repair (Amst) 5: 1225-33.

Probe Description

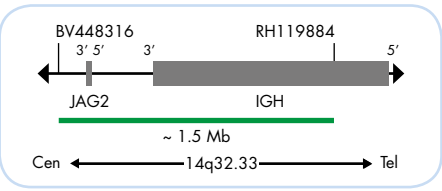
The SPEC MAF/IGH Dual Color Dual Fusion Probe is a mixture of an orange fluorochrome direct labeled MAF probe spanning the known MAF breakpoints, and a green fluorochrome direct labeled IGH probe spanning the known breakpoints of IGH.



Ideograms of chromosome 16 (above) and 14 (below) indicating the hybridization locations.



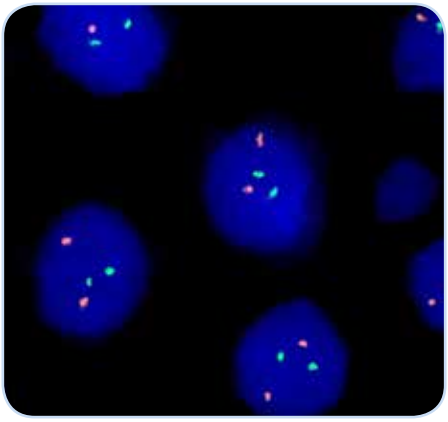
SPEC MAF Probe map (not to scale).



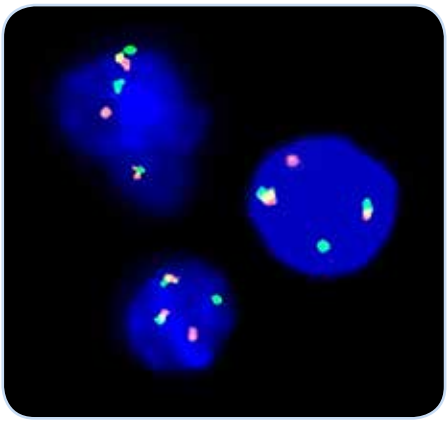
SPEC IGH Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. A reciprocal translocation involving two breakpoints splits the two signals and generates a fusion signal on each of the chromosomes involved. The chromosomal regions which are not translocated are indicated by the single orange and green signal, respectively.



SPEC MAF/IGH Dual Color Dual Fusion Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Bone marrow CD138+ cells with translocation affecting the MAF/IGH loci as indicated by two orange/green fusion signals, a single orange, and a separate green signal in each nucleus.

Kindly provided by Prof. Dr. Oskar A. Haas, Vienna, Austria.

Prod. No.	Product	Label	Tests* (Volume)
Z-2270-50	ZytoLight SPEC MAF/IGH Dual Color Dual Fusion Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC MAFB/IGH Dual Color Dual Fusion Probe

CE IVD

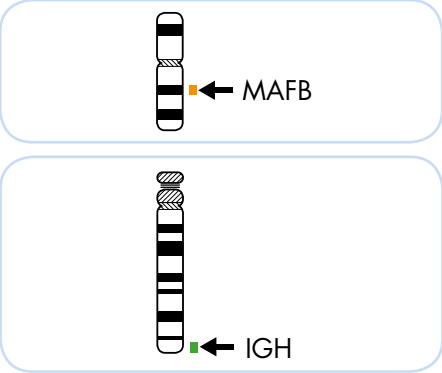
Background

The ZytoLight® SPEC MAFB/IGH Dual Color Dual Fusion Probe is designed to detect the translocations affecting the MAFB gene in the chromosomal region 20q12 and the IGH locus in 14q32.33. The translocation t(14;20)(q32.3;q12) is frequently found in multiple myeloma (MM).
MM is a low proliferative, malignant post-germinal center tumor of somatically mutated, isotype-switched plasma cells that accumulate in the bone marrow.
It is often preceded by a premalignant state known as monoclonal gammopathy of undetermined significance (MGUS).
Five recurrent primary translocations involving the immunoglobulin heavy locus (IGH) have been identified in 40% of MGUS and MM tumors. They include t(11;14)(q13.3;q32.3), t(6;14)(p21.1;q32.3), t(4;14)(p16.3;q32.3), t(14;16)(q32.3;q23), and t(14;20)(q32.3;q12), which involve the genes CCND1, CCND3, FGFR3 and NSD2, MAF, and MAFB, respectively. All of these translocations lead to the deregulation and overexpression of the target genes as a consequence of their juxtaposition to regulatory sequences of the IGH locus.
The t(14;20) occurs in approximately 1-2% of MM patients and is associated with an adverse prognosis. Thus, currently, detection of t(14;20) by FISH is a reliable prognostic tool and may sustain therapeutic decision making in MM.

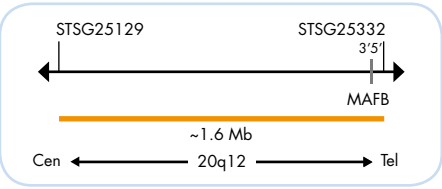
References
Boersma-Vreugdenhil GR, et al. (2004) Br J Haematol 126: 355-63.
Chesi M, et al. (1998) Blood 92: 4457-63.
Fabris S, et al. (2005) Genes Chromosomes Cancer 42: 117-27.
Fonseca R, et al. (2009) Leukemia 23: 2210-21.
Gabrea A, et al. (2006) DNA Repair (Amst) 5: 1225-33.
Hanamura I, et al. (2001) Jpn N Cancer Res 92: 638-44.

Probe Description

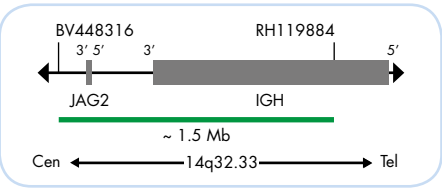
The SPEC MAFB/IGH Dual Color Dual Fusion Probe is a mixture of an orange fluorochrome direct labeled MAFB probe spanning MAFB and proximal regions known for variable breakpoints, and a green fluorochrome direct labeled IGH probe spanning the known breakpoints of the IGH locus.



Ideograms of chromosome 20 (above) and 14 (below) indicating the hybridization locations.



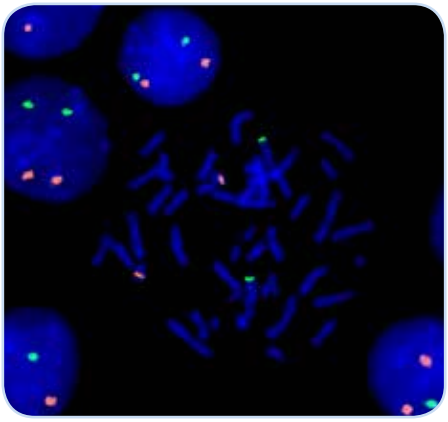
SPEC MAFB Probe map (not to scale).



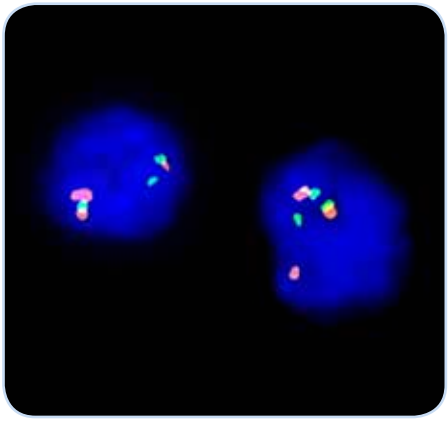
SPEC IGH Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. A reciprocal translocation involving two breakpoints splits the two signals and generates a fusion signal on each of the chromosomes involved. The chromosomal regions which are not translocated are indicated by the single orange and green signal, respectively.



SPEC MAFB/IGH Dual Color Dual Fusion Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus and to metaphase chromosomes of a normal cell.



Bone marrow CD138+ cells with translocation affecting the MAFB/IGH loci as indicated by two orange/green fusion signals, a single orange, and a separate green signal in each nucleus.

Kindly provided by Prof. Dr. Oskar A. Haas, Vienna, Austria.

Prod. No.	Product	Label	Tests* (Volume)
Z-2271-50	ZytoLight SPEC MAFB/IGH Dual Color Dual Fusion Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC TP53/17q22 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC TP53/17q22 Dual Color Probe is designed for the detection of TP53 deletions as well as for the determination of copy number changes of the chromosomal region 17q22, harboring the MPO (myeloperoxidase) gene. TP53 loss in combination with signal gain of the 17q22 chromosomal region serves as a marker for the detection of isochromosomes often found in hematologic malignancies as well as in neuroblastoma.

The TP53 gene (tumor protein p53, a.k.a. p53, BCC7, LFS1, TRP53) is located in the chromosomal region 17p13.1 and encodes a 53 kDa transcription factor. TP53 gene deletions have been detected in patients with chronic lymphocytic leukemia (CLL), multiple myeloma (MM), and acute myeloid leukemia (AML). In CLL patients, allelic loss of the short arm of chromosome 17 is associated with treatment failure with alkylating agents and short survival times.

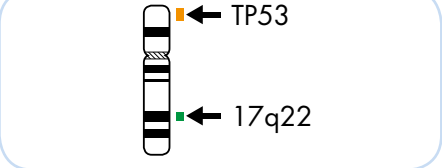
Isochromosome 17q is a frequent cytogenetic abnormality seen in hematologic malignancies including blast phase of chronic myelogenous leukemia (CML), AML, Hodgkin and non-Hodgkin lymphomas. In neuroblastoma, gain of the 17q21-qter is associated with stronger tumor progression.

Thus, the combined detection of both targets by Fluorescence *in situ* Hybridization allows for a sensitive determination of isochromosomes and may be a helpful tool for diagnosis and selecting treatment.

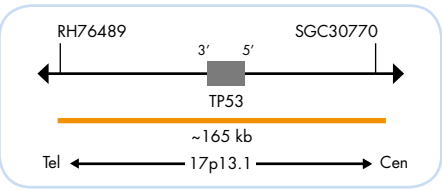
References
Becher R, et al. (1990) Blood 8: 1679-83.
Bown N, et al. (1999) N Engl J Med 340: 1954-61.
Fioretos T, et al. (1999) Blood 94: 225-32.
Pettitt AR, et al. (2001) Blood 98: 814-22.
Ripollés L, et al. (2006) Cancer Genet Cytogenet 171: 57-64.
Shanafelt TD, et al. (2006) Ann Intern Med 145: 435-47.

Probe Description

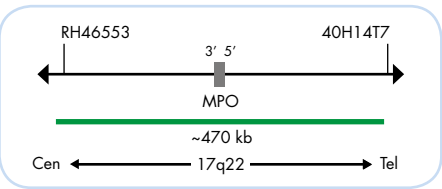
The SPEC TP53/17q22 Dual Color Probe is a mixture of an orange fluorochrome direct labeled SPEC TP53 probe hybridizing to the TP53 gene in the chromosomal region 17p13.1 and a green fluorochrome direct labeled SPEC 17q22 probe specific for the chromosomal region 17q22 harboring the MPO gene.



Ideogram of chromosome 17 indicating the hybridization locations.



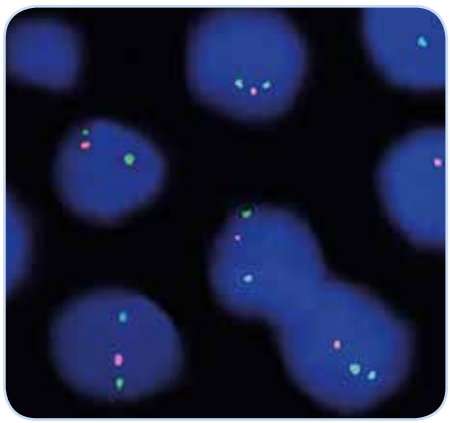
SPEC TP53 Probe map (not to scale).



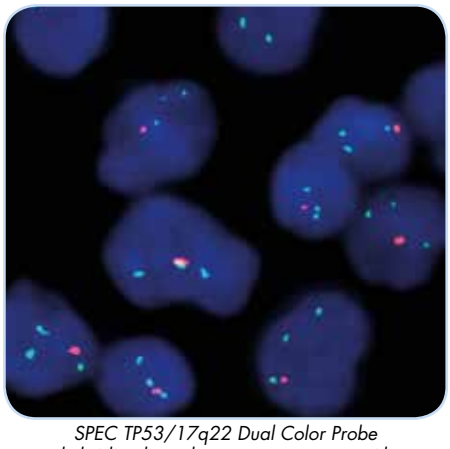
SPEC 17q22 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletion of the TP53 gene locus, one orange signal and two green signals can be detected. A gain of 17q involving the 17q22 region will result in three or more green signals and two orange signals. Isochromosome 17q is indicated by three green signals and one orange signal.



SPEC TP53/17q22 Dual Color Probe hybridized to bone marrow tissue section with deletion of the TP53 gene as indicated by one green signal and two orange signals in each nucleus.



SPEC TP53/17q22 Dual Color Probe hybridized to a bone marrow smear with isochromosome 17q as indicated by three green signals and one orange signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2198-50	ZytoLight SPEC TP53/17q22 Dual Color Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC TP53/CEN 17 Dual Color Probe

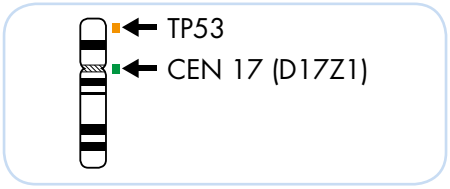
CE IVD

Background

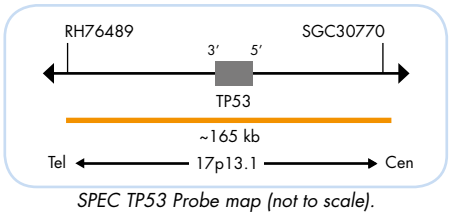
The ZytoLight® SPEC TP53/CEN 17 Dual Color Probe is designed for the detection of TP53 gene deletions observed e.g. in chronic lymphocytic leukemia (CLL).
The TP53 gene (tumor protein p53, a.k.a. p53, BCC7, LFS1, TRP53) is located in the chromosomal region 17p13.1 and encodes a 53 kDa transcription factor which regulates cell proliferation, differentiation, and apoptosis and which functions as a tumor suppressor by activating the expression of genes that inhibit cell growth. Deletions affecting the short arm of chromosome 17 (17p), the site of the TP53 gene, are often accompanied by mutations in the remaining allele, and thus result in the loss of TP53 tumor suppressor activity.
TP53 gene deletions have been detected in patients with chronic lymphocytic leukemia (CLL), multiple myeloma (MM), acute myeloid leukemia (AML), and are also very frequent in primary solid tumors of different histological origin. The presence of TP53 deletion has been shown to correlate with more aggressive disease, shortened survival, and poor response to standard treatment. CLL patients with deletion of 17p are more likely to respond to treatment with the monoclonal anti-CD52 antibody alemtuzumab than to conventional chemotherapy. FISH is an effective method to screen for deletions affecting the TP53 gene locus in order to identify patients who are candidates for alternative treatment and to avoid administration of otherwise ineffective therapy.

Probe Description

The SPEC TP53/CEN 17 Dual Color Probe is a mixture of a green fluorochrome direct labeled CEN 17 probe specific for the alpha satellite centromeric region of chromosome 17 (D17Z1) and an orange fluorochrome direct labeled SPEC TP53 probe specific for the TP53 gene at 17p13.1.



Ideogram of chromosome 17 indicating the hybridization locations.

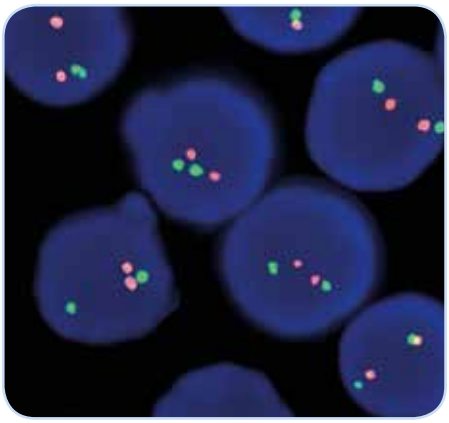


SPEC TP53 Probe map (not to scale).

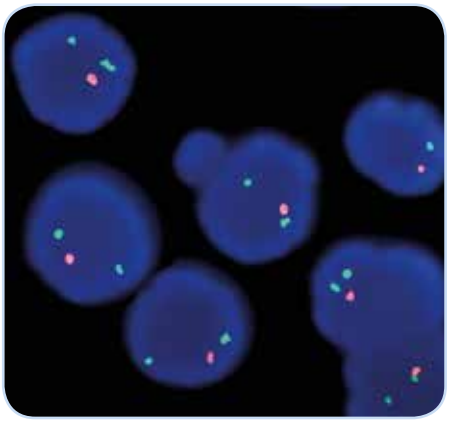
References
Amiel A, et al. (1997) Cancer Genet Cytogenet 97: 97-100.
Chang H, et al. (2005) Blood 105: 358-60.
Chang H, et al. (2010) Am J Clin Pathol 133: 70-4.
Herrera JC, et al. (2010) Biomedica 30: 390-400.
Lozanski G, et al. (2004) Blood 103: 3278-81.
Tavor S, et al. (2011) Leuk Lymphoma 52: 642-7.

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletions affecting the TP53 gene locus, one or no copy of the orange signal will be observed.



SPEC TP53/CEN 17 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



SPEC TP53/CEN 17 Dual Color Probe hybridized to bone marrow tissue section with deletion of the TP53 gene as indicated by one orange signal and two green signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2153-50	ZytoLight SPEC TP53/CEN 17 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2153-200	ZytoLight SPEC TP53/CEN 17 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC USP6 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC USP6 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 17p13.2 harboring the USP6 (Ubiquitin-specific peptidase 6, a.k.a. TRE2 or TRE17) gene.

Translocations affecting USP6 have been initially found in primary aneurysmal bone cysts (ABC), a benign, but locally aggressive bone lesion that occurs predominantly during the first two decades of life. USP6 rearrangements are restricted to spindle cells in primary ABC, indistinguishable from surrounding normal spindle cells.

The resulting fusion genes detected are formed by juxtaposition of the USP6 coding sequences to the highly active promoter sequences of several partner genes, as e.g. CDH11, COL1A1, OMD, TRAP150, and ZNF9, leading to the transcriptional upregulation of USP6. No true fusion genes are formed.

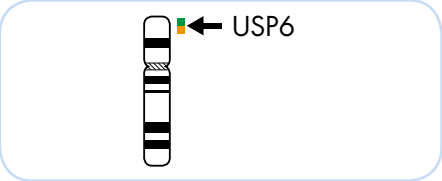
More recently, nodular fasciitis (NF), another mesenchymal lesion, has been tested positive for USP6 rearrangements. NF is a subcutaneous pseudosarcomatous myofibroblastic proliferation of unknown pathogenesis that regresses spontaneously when not surgically resected. The translocation results in the fusion of the promoter region of MYH9 located on 22q12.3 to the entire coding sequence of USP6 and subsequently in upregulated USP6 expression.

For both lesions it is assumed that the detection of USP6 rearrangements by Fluorescence *in situ* Hybridization might represent a valuable diagnostic tool.

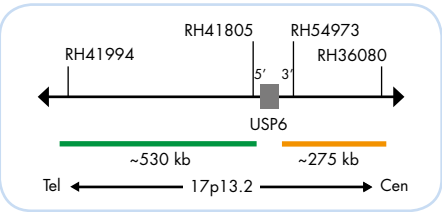
References
Erickson-Johnson MR, et al. (2011) Lab Invest 91: 1427-33.
Nakamura T, et al. (1988) Oncogene Res 2: 357-70.
Oliveira AM, et al. (2004) Cancer Res 64: 1920-3.
Oliveira AM, et al. (2005) Oncogene 24: 3419-26.

Probe Description

The SPEC USP6 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 17p13.2 band. The orange fluorochrome direct labeled probe hybridizes proximal to the USP6 gene and the green fluorochrome direct labeled probe hybridizes distal to that gene.



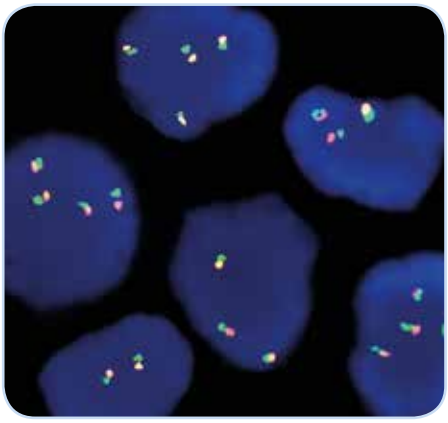
Ideogram of chromosome 17 indicating the hybridization locations.



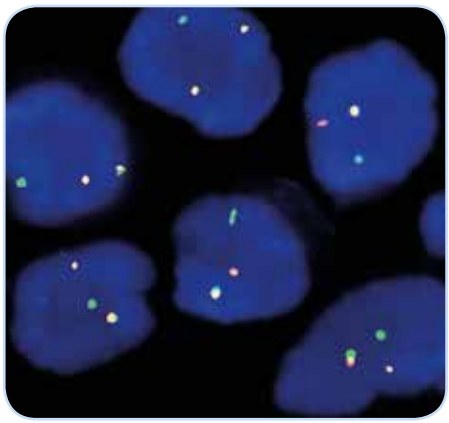
SPEC USP6 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 17p13.2 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 17p13.2 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 17p13.2 locus and one 17p13.2 locus affected by a translocation.



SPEC USP6 Break Apart Probe hybridized to aneurysmal bone cyst tissue section with polysomy of chromosome 17 but without translocation affecting the 17p13.2 locus as indicated by multiple orange/green fusion signals per nucleus.



Aneurysmal bone cyst tissue section with translocation affecting the 17p13.2 locus as indicated by one orange/green fusion (non-rearranged) signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2151-50	ZytoLight SPEC USP6 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC YWHAE Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC YWHAE Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal region 17p13.3 harboring the YWHAE (tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon a.k.a. 14-3-3 epsilon) gene. YWHAE encodes a protein of the 14-3-3 family which is involved in regulation of cellular proliferation, metabolism, and differentiation. However, altered expression of 14-3-3 family proteins is associated with development and progression of cancer.

The fusion between YWHAE and one of the FAM22 family members (FAM22A or FAM22B) caused by a t(10;17)(q22;p13) has been identified in the clinically aggressive, high-grade endometrial stromal sarcoma (ESS) as well as in clear cell sarcoma of the kidney (CCSK).

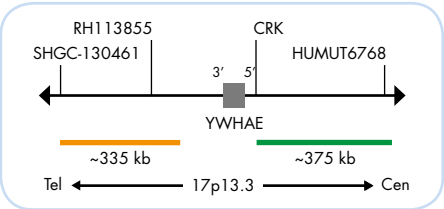
In contrast to the classic low-grade form of ESS harboring JAZF1 gene fusions, YWHAE-FAM22 ESS display high-grade histologic features and an aggressive clinical course. Moreover, due to the lack of estrogen and progesterone receptor expression in YWHAE-FAM22 ESS, the hormonal therapy used to treat low-grade ESS is likely to be ineffective. Consequently, differentiation between YWHAE-FAM22 and JAZF1 ESS by FISH is clinically relevant to support the diagnosis and may aid in therapeutic decision making.

References
Isphording A, et al. (2013) Hum Pathol 44: 837-43.
Lee CH, et al. (2012) Proc Natl Acad Sci U S A 109: 929-34.
O'Meara E, et al. (2012) J Pathol 227: 72-80.
Stewart JC, et al. (2014) Histopathology 65: 473-82.

Probe Description

The SPEC YWHAE Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 17p13.3 band. The orange fluorochrome direct labeled probe hybridizes distal to the YWHAE gene breakpoint region at 17p13.3, the green fluorochrome direct labeled probe hybridizes proximal to the YWHAE gene breakpoint region at 17p13.3.

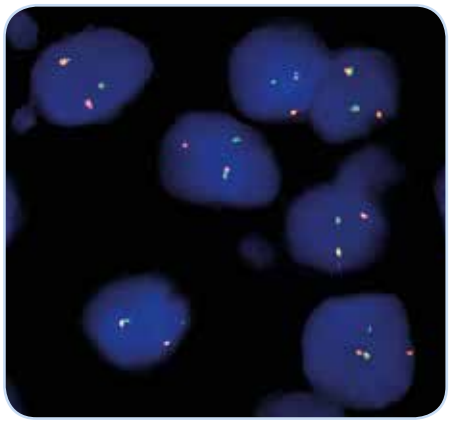
Ideogram of chromosome 17 indicating the hybridization locations.



SPEC YWHAE Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 17p13.3 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 17p13.3 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 17p13.3 locus and one 17p13.3 locus affected by a translocation.



Endometrial stromal sarcoma tissue section with translocation affecting the YWHAE gene as indicated by one non-rearranged orange/green fusion signal, one orange, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2175-50	ZytoLight SPEC YWHAE Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ERBB2/CEN 17 Dual Color Probe

CE IVD

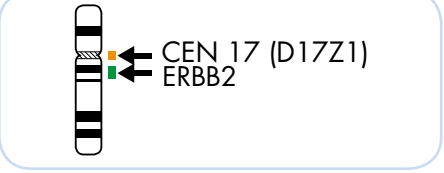
Background

The ZytoLight® SPEC ERBB2/CEN 17 Dual Color Probe is designed for the detection of ERBB2 gene amplification frequently observed in solid malignant neoplasms e.g. breast cancer samples. The ERBB2 gene (a.k.a. HER2 and NEU) is located in the chromosomal region 17q12 and encodes a 185-190 kDa transmembrane glycoprotein, p185, acting as a cellular growth factor receptor. The p185 protein belongs to the EGFR (epidermal growth factor receptor) subgroup of the RTK (receptor tyrosine kinase) superfamily also including EGFR (ERBB1, HER1), ERBB3 (HER3), and ERBB4 (HER4). Amplification of the proto-oncogene ERBB2, observed in approximately 20% of all breast cancer samples, has been correlated with a poor prognosis of the disease. Similar results have been obtained for a variety of other malignant neoplasms e.g. ovarian cancer, stomach cancer, and carcinomas of the salivary gland.

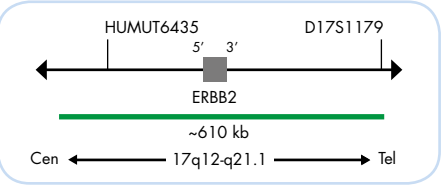
References
Baselga J, et al. (1999) Semin Oncol 26: 78-83.
Brockhoff G, et al. (2016) Histopathology 69: 635-46.
Brunello E, et al. (2012) Histopathology 60: 482-8.
Brunner K, et al. (2010) Anal Quant Cytol Histol 32: 78-89.
Coussens L, et al. (1985) Science 230: 1132-9.
Ettl T, et al. (2012) Br J Cancer 106: 719-26.
Hwang CC, et al. (2011) Histopathology 59: 984-92.
Hynes NE & Stern DF (1994) Biochim Biophys Acta 1198: 165-84.
Moelans CB, et al. (2011) Crit Rev Oncol Hematol 80: 380-92.
Park JB, et al. (1989) Cancer Res 49: 6605-9.
Popescu NC, et al. (1989) Genomics 4: 362-6.
Sassen A, et al. (2008) Breast Cancer Res 10: R2.
Slamon DJ, et al. (1987) Science 235: 177-82.
Voutsas IF, et al. (2013) Int J Radiat Biol 89: 319-25.
Wolff AC, et al. (2018) J Clin Oncol 14: 437-41.

Probe Description

The SPEC ERBB2/CEN 17 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 17 probe specific for the alpha satellite centromeric region of chromosome 17 (D17Z1) and a green fluorochrome direct labeled SPEC ERBB2 probe specific for the chromosomal region 17q12-q21.1 harboring the ERBB2 gene.



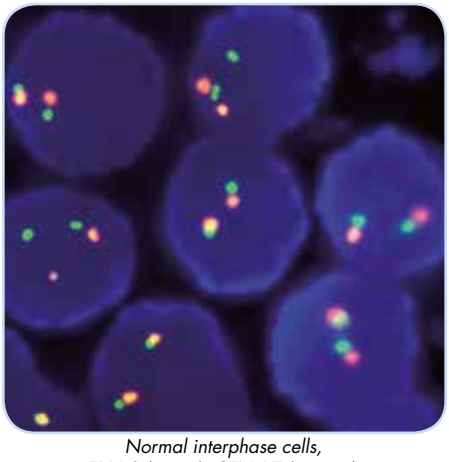
Ideogram of chromosome 17 indicating the hybridization locations.



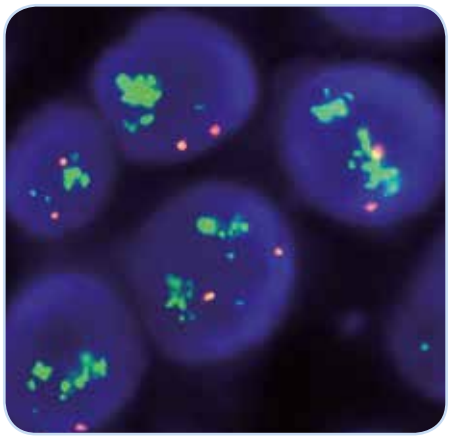
SPEC ERBB2 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the ERBB2 gene locus, multiple copies of the green signal or green signal clusters will be observed.



Normal interphase cells, ERBB2 (green), CEN 17 (orange).



Breast carcinoma tissue section, ERBB2 gene cluster (green), CEN 17 (orange).

Prod. No.	Product	Label	Tests* (Volume)
Z-2015-50	ZytoLight SPEC ERBB2/CEN 17 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2015-200	ZytoLight SPEC ERBB2/CEN 17 Dual Color Probe CE IVD	●/●	20 (200 µl)
Z-2020-5	ZytoLight SPEC ERBB2/CEN 17 Dual Color Probe Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; Probe, 0.05 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml	●/●	5
Z-2020-20	ZytoLight SPEC ERBB2/CEN 17 Dual Color Probe Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; Probe, 0.2 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml	●/●	20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® CEN 17/SPEC ERBB2 Dual Color Probe

CE IVD

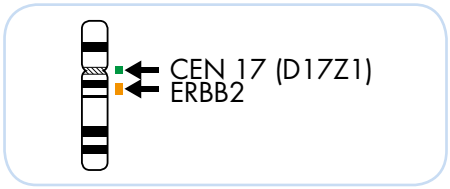
Background

The ZytoLight® CEN 17/SPEC ERBB2 Dual Color Probe is designed for the detection of ERBB2 gene amplification frequently observed in solid malignant neoplasms e.g. breast cancer samples. The ERBB2 gene (a.k.a. HER2 and NEU) is located in the chromosomal region 17q12 and encodes a 185-190 kDa transmembrane glycoprotein, p185, acting as a cellular growth factor receptor. The p185 protein belongs to the EGFR (epidermal growth factor receptor) subgroup of the RTK (receptor tyrosine kinase) superfamily also including EGFR (ERBB1, HER1), ERBB3 (HER3), and ERBB4 (HER4). Amplification of the proto-oncogene ERBB2, observed in approximately 20% of all breast cancer samples, has been correlated with a poor prognosis of the disease.
Similar results have been obtained for a variety of other malignant neoplasms e.g. ovarian cancer, stomach cancer, and carcinomas of the salivary gland.

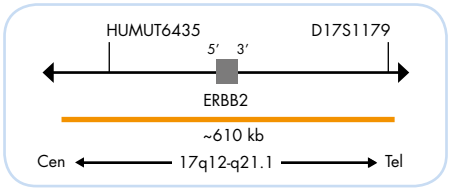
References
Baselga J, et al. (1999) Semin Oncol 26: 78-83.
Brockhoff G, et al. (2016) Histopathology 69: 635-46.
Brunello E, et al. (2012) Histopathology 60: 482-8.
Brunner K, et al. (2010) Anal Quant Cytol Histol 32: 78-89.
Coussens L, et al. (1985) Science 230: 1132-9.
Ettl T, et al. (2012) Br J Cancer 106: 719-26.
Hwang CC, et al. (2011) Histopathology 59: 984-92.
Hynes NE & Stern DF (1994) Biochim Biophys Acta 1198: 165-84.
Moelans CB, et al. (2011) Crit Rev Oncol Hematol 80: 380-92.
Park JB, et al. (1989) Cancer Res 49: 6605-9.
Popescu NC, et al. (1989) Genomics 4: 362-6.
Sassen A, et al. (2008) Breast Cancer Res 10: R2.
Slamon DJ, et al. (1987) Science 235: 177-82.
Voutsas IF, et al. (2013) Int J Radiat Biol 89: 319-25.
Wolff AC, et al. (2018) J Clin Oncol 14: 437-41.

Probe Description

The CEN 17/SPEC ERBB2 Dual Color Probe is a mixture of a green fluorochrome direct labeled CEN 17 probe specific for the alpha satellite centromeric region of chromosome 17 (D17Z1) and an orange fluorochrome direct labeled SPEC ERBB2 probe specific for the chromosomal region 17q12-q21.1 harboring the ERBB2 gene.



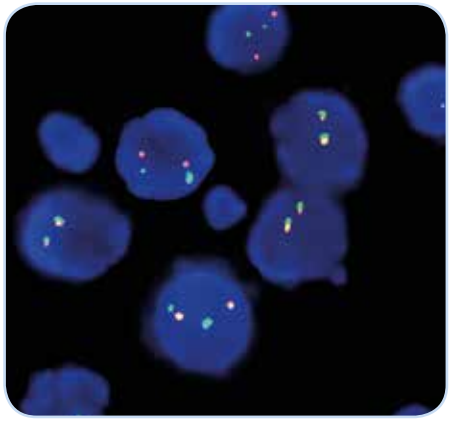
Ideogram of chromosome 17 indicating the hybridization locations.



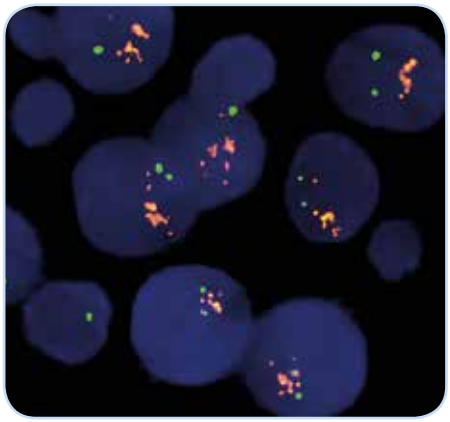
SPEC ERBB2 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the ERBB2 gene locus, multiple copies of the orange signal or orange signal clusters will be observed.



Normal interphase cells, ERBB2 (orange), CEN 17 (green).



Breast carcinoma tissue section, ERBB2 gene cluster (orange), CEN 17 (green).

Prod. No.	Product	Label	Tests* (Volume)
Z-2077-50	ZytoLight CEN 17/SPEC ERBB2 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2077-200	ZytoLight CEN 17/SPEC ERBB2 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ERBB2/D17S122 Dual Color Probe

CE IVD

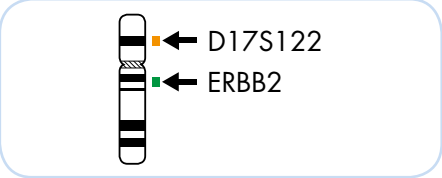
Background

The ZytoLight® SPEC ERBB2/D17S122 Dual Color Probe is designed for the detection of ERBB2 gene amplification frequently observed in solid malignant neoplasms e.g. breast cancer samples.
The ERBB2 gene (a.k.a. HER2 and NEU) is located in the chromosomal region 17q12 and encodes a 185-190 kDa transmembrane glycoprotein, p185, acting as a cellular growth factor receptor. The p185 protein belongs to the EGFR (epidermal growth factor receptor) subgroup of the RTK (receptor tyrosine kinase) superfamily also including EGFR (ERBB1, HER1), ERBB3 (HER3), and ERBB4 (HER4). Amplification of the proto-oncogene ERBB2, observed in approximately 20% of all breast cancer samples, has been correlated with a poor prognosis of the disease.
Similar results have been obtained for a variety of other malignant neoplasms e.g. ovarian cancer, stomach cancer, and carcinomas of the salivary gland.
Fluorescence *in situ* Hybridization targeting the alpha satellite centromeric regions of chromosome 17 may be misleading in some cases due to possible gains or losses of this region. For these cases, reflex testing is recommended using the SPEC ERBB2/D17S122 Dual Color Probe.

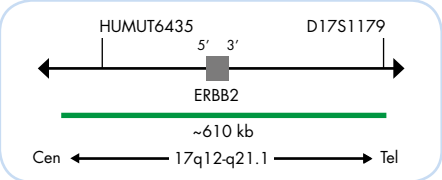
References
Baselga J, et al. (1999) Semin Oncol 26: 78-83.
Coussens L, et al. (1985) Science 230: 1132-9.
Hwang CC, et al. (2011) Histopathology 59: 984-92.
Hynes NE & Stern DF (1994) Biochim Biophys Acta 1198: 165-84.
Moelans CB, et al. (2011) Crit Rev Oncol Hematol 80: 380-92.
Park JB, et al. (1989) Cancer Res 49: 6605-9.
Popescu NC, et al. (1989) Genomics 4: 362-6.
Slamon DJ, et al. (1987) Science 235: 177-82.
Voutsas IF, et al. (2013) Int J Radiat Biol 89: 319-25.
Wolff AC, et al. (2018) J Clin Oncol 14: 437-41.

Probe Description

The SPEC ERBB2/D17S122 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC ERBB2 probe specific for the chromosomal region 17q12-q21.1 harboring the ERBB2 gene and an orange fluorochrome direct labeled SPEC D17S122 probe specific for the chromosomal region 17p12. The SPEC D17S122 probe is designed to be used for chromosome 17 copy number detection.



Ideogram of chromosome 17 indicating the hybridization locations.

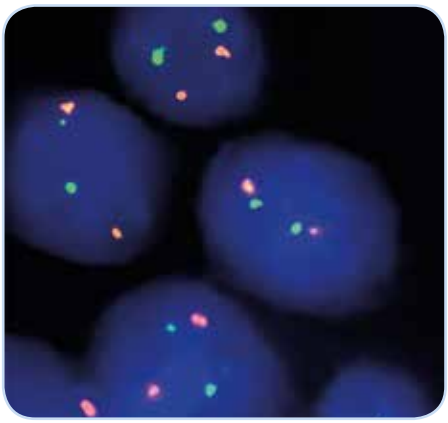


SPEC ERBB2 Probe map (not to scale).

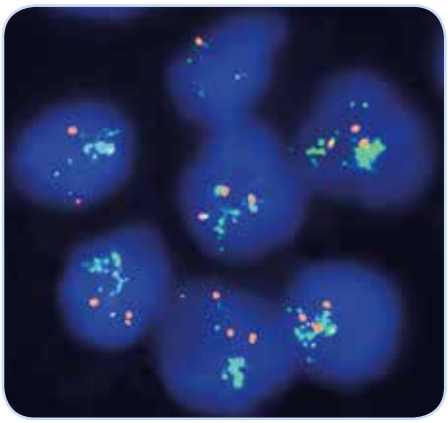
SPEC D17S122 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the ERBB2 gene locus, multiple copies of the green signal or green signal clusters will be observed.



Normal interphase cells, ERBB2 (green), D17S122 (orange).



Breast carcinoma tissue section, ERBB2 gene cluster (green), D17S122 (orange).

Prod. No.	Product	Label	Tests* (Volume)
Z-2190-50	ZytoLight SPEC ERBB2/D17S122 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2190-200	ZytoLight SPEC ERBB2/D17S122 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ERBB2/TOP2A/CEN 17 Triple Color Probe

CE IVD

Background

The ZytoLight® SPEC ERBB2/TOP2A/CEN 17 Triple Color Probe is designed for the simultaneous detection of ERBB2 and TOP2A gene status.

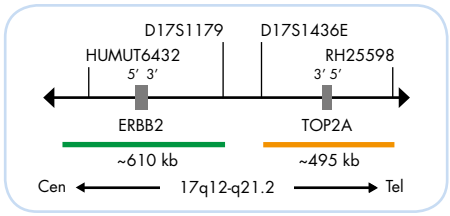
The ERBB2 gene (a.k.a. HER2 and NEU) is located in the chromosomal region 17q12 and encodes a 185 kDa transmembrane glycoprotein. The TOP2A (DNA topoisomerase II alpha) gene is located in the chromosomal region 17q21.2 and encodes a 170 kDa DNA topoisomerase. The TOP2A gene is frequently either co-amplified or deleted in ERBB2 positive breast cancer cases. TOP2A functions as the target for several anticancer agents, e.g. anthracyclines. Recent data suggests that amplification and deletion of the TOP2A gene locus may account for relative chemosensitivity or resistance to TOP2A inhibitor therapy in ERBB2 positive breast cancer. Thus, determination of the ERBB2 and TOP2A status may help to predict benefit from adjuvant anthracyclines in breast cancer treatment.

References
Arriola E, et al. (2007) Breast Cancer Res Treat 106: 181-9.
Brunello E, et al. (2012) Histopathology 60: 482–8.
Coussens L, et al. (1985) Science 230: 1132-9.
Fountzilas G, et al. (2012) J Transl Med 10: 212.
Fountzilas G, et al. (2012) PLoS One 7: e37946.
Fountzilas G, et al. (2013) BMC Cancer 13: 163.
Järvinen TA & Liu ET (2006) Curr Cancer Drug Targets 6: 579-602.
Popescu NC, et al. (1989) Genomics 4: 362-6.
Pritchard KI, et al. (2008) J Clin Oncol 26: 736-44.
Razis E, et al. (2011) Breast Cancer Res Treat 128: 447-56.
Tsai-Pflugfelder M, et al. (1988) Proc Natl Acad Sci U S A 85: 7177-81.

Probe Description

The SPEC ERBB2/TOP2A/CEN 17 Triple Color Probe is a mixture of a green fluorochrome direct labeled SPEC ERBB2 probe specific for the chromosomal region 17q12-q21.1 harboring the ERBB2 gene, an orange fluorochrome direct labeled SPEC TOP2A probe specific for the TOP2A gene at 17q21.2, and a blue fluorochrome direct labeled CEN 17 probe specific for the alpha satellite centromeric region of chromosome 17 (D17Z1).

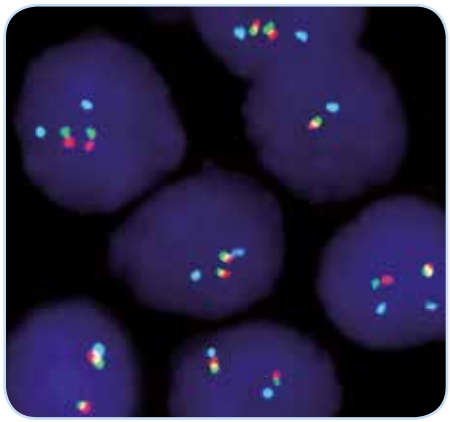
Ideogram of chromosome 17 indicating the hybridization locations.



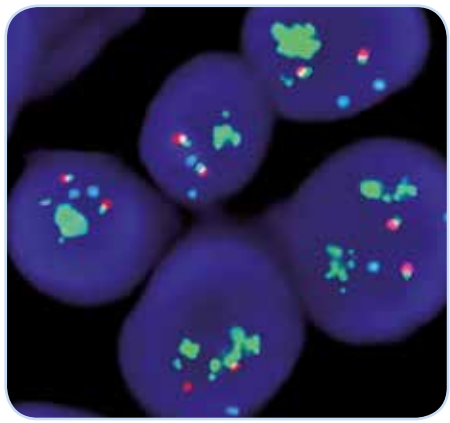
SPEC ERBB2/TOP2A Probe map (not to scale).

Results

In a normal interphase nucleus, two green, two orange, and two blue signals are expected. In a cell with amplification of the ERBB2 gene locus, multiple copies of the green signal or large green signal clusters will be observed. Amplification of TOP2A will result in multiple copies of the orange signal or large orange signal clusters. Deletion of the TOP2A gene results in a reduced number of orange signals.



SPEC ERBB2/TOP2A/CEN 17 Triple Color Probe hybridized to normal interphase cells as indicated by two green, two orange, and two blue signals per nucleus.



Breast cancer tissue section with two copies of chromosome 17 (blue) and TOP2A (orange) and ERBB2 gene clusters (green) in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2093-50	ZytoLight SPEC ERBB2/TOP2A/CEN 17 Triple Color Probe CE IVD	●/●/●	5 (50 µl)
Z-2093-200	ZytoLight SPEC ERBB2/TOP2A/CEN 17 Triple Color Probe CE IVD	●/●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC COL1A1 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC COL1A1 Dual Color Break Apart Probe is designed for the detection of the specific translocations involving the chromosomal region 17q21.33 harboring the COL1A1 (a.k.a. OI4) gene.

Reciprocal translocations involving t(17;22)(q21.3;q13.1) are characteristic for dermatofibrosarcoma protuberans (DFSP). DFSP is a highly recurrent, infiltrative skin tumor of intermediate malignancy. The rearrangements are cytogenetically characterized by the presence of supernumerary ring chromosomes containing low-level amplified sequences from chromosomes 17q21-qter and 22q10-q13.1, or unbalanced derivatives of the t(17;22)(q21.3;q13.1) translocation.

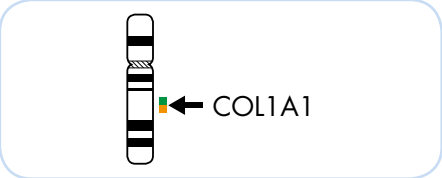
The rearrangement frequently results in formation of a COL1A1-PDGFB fusion protein which is post-transcriptionally processed to a functional platelet-derived growth factor beta chain (PDGFB) protein, and results in PDFGB-mediated autocrine and/or paracrine activation of the plateled-derived growth factor receptor-β (PDGFRB).

The accurate diagnosis of DFSP is important because of the intermediate malignant nature of the DFSP and can be facilitated by Fluorescence *in situ* Hybridization (FISH) analyses.

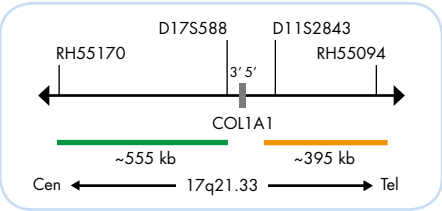
References
Labropoulos SV & Razis ED (2007) Biologics 4: 347-53.
Patel KU, et al. (2008) Human Pathol 39: 184-93.
Shimizu A, et al. (1999) Cancer Res 59: 3719-23.
Simon MP, et al. (1997) Nat Genet 15: 95-8.

Probe Description

The SPEC COL1A1 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 17q21.33 band. The orange fluorochrome direct labeled probe hybridizes distal, and the green fluorochrome direct labeled probe hybridizes proximal to the COL1A1 gene.



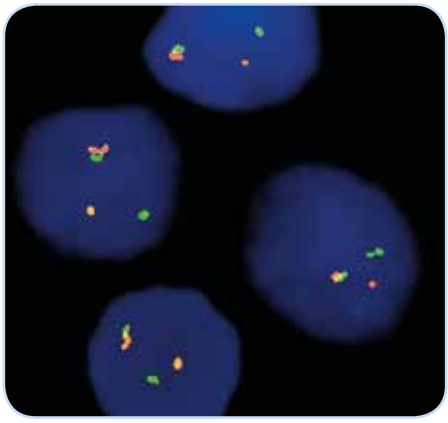
Ideograms of chromosome 17 indicating the hybridization locations.



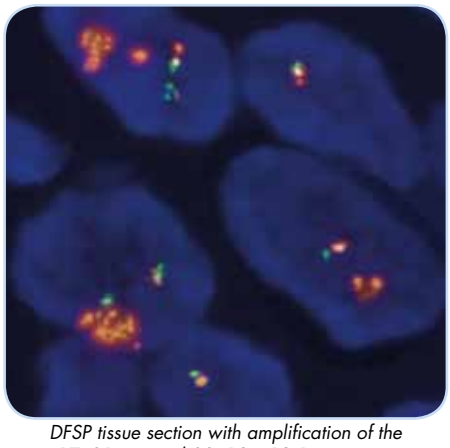
SPEC COL1A1 Probe map (not to scale).

Results

In a normal interphase nucleus lacking a translocation involving the 17q21.33 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 17q21.33 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 17q21.33 locus and one 17q21.33 locus affected by a 17q21.33 translocation.



DFSP tissue section with translocation affecting the 17q21.33 locus as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.



DFSP tissue section with amplification of the 17q21-qter and 22q10–q13.1 sequences probably due to a COL1A1-PDGFB fusion product on the ring chromosome.

Image kindly provided by Dr. Schildhaus, Essen, Germany.

Prod. No.	Product	Label	Tests* (Volume)
Z-2121-200	ZytoLight SPEC COL1A1 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC COL1A1/PDGFB Dual Color Dual Fusion Probe

CE IVD

Background

The ZytoLight® SPEC COL1A1/PDGFB Dual Color Dual Fusion Probe is designed for the detection of the specific translocations involving the chromosomal region 17q21.33 harboring the COL1A1 (a.k.a. OI4) gene, and the chromosomal region 22q13.1, harboring the PDGFB (a.k.a PDGF2, SIS) gene.

The reciprocal translocations involving t(17;22)(q21.3;q13.1) are characteristic for dermatofibrosarcoma protuberans (DFSP) patients. DFSP is a highly recurrent, infiltrative skin tumor of intermediate malignancy.

The rearrangements are cytogenetically characterized by the presence of supernumerary ring chromosomes containing low-level amplified sequences from chromosomes 17q21-qter and 22q10-q13.1, or unbalanced derivatives of the t(17;22)(q21.3;q13.1) translocation.

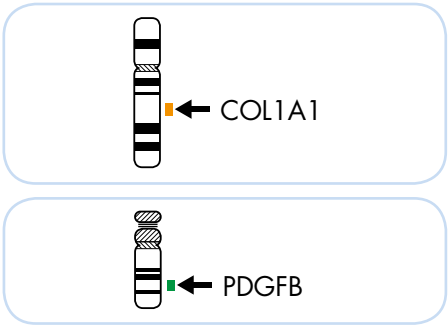
The rearrangement results in a COL1A1-PDGFB fusion protein which is post-transcriptionally processed to a functional platelet-derived growth factor beta chain (PDGFB) protein, and results in PDFGB-mediated autocrine and/or paracrine activation of the plateled-derived growth factor receptor-β (PDGFRB).

The accurate diagnosis of DFSP is important because of the intermediate malignant nature of the DFSP and can be facilitated by Fluorescence *in situ* Hybridization (FISH) analyses.

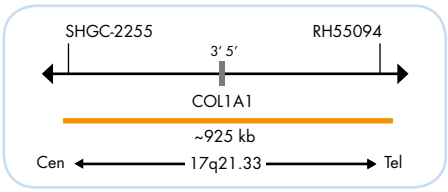
References
Labropoulos SV & Razis ED (2007) Biologics 4: 347-53.
Patel KU, et al. (2008) Human Pathol 39: 184-93.
Shimizu A, et al. (1999) Cancer Res 59: 3719-23.
Simon MP, et al. (1997) Nat Genet 15: 95-8.
Walluks K, et al. (2013) Pathol Res Pract 209: 30-5.

Probe Description

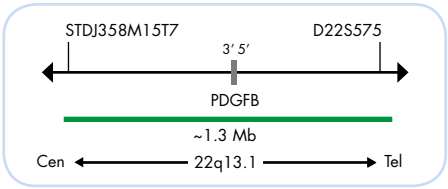
The SPEC COL1A1/PDGFB Dual Color Dual Fusion Probe is a mixture of an orange fluorochrome direct labeled COL1A1 probe covering the breakpoint region of the COL1A1 gene and a green fluorochrome direct labeled PDGFB probe covering the breakpoint region of the PDGFB gene.



Ideograms of chromosomes 17 (above) and 22 (below) indicating the hybridization locations.



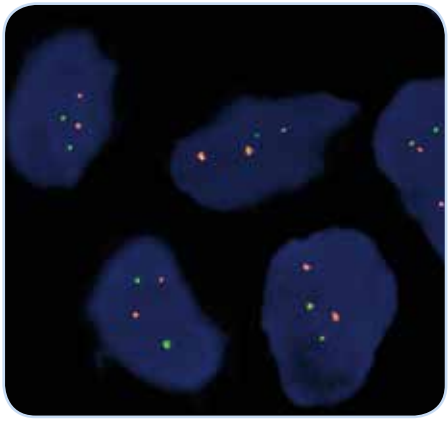
SPEC COL1A1 Probe map (not to scale).



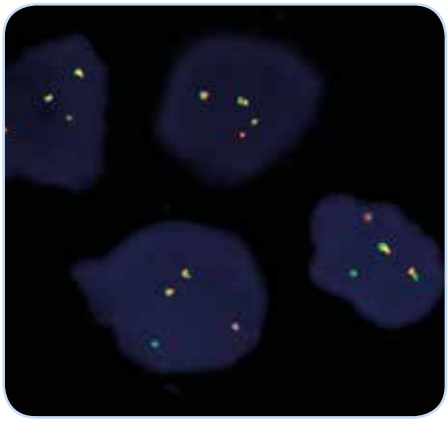
SPEC PDGFB Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. A reciprocal translocation involving two breakpoints splits the two signals and generates a fusion signal on each of the chromosomes involved. The chromosomal regions which are not translocated are indicated by the single orange and green signal, respectively.



SPEC COL1A1/PDGFB Dual Color Dual Fusion Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



DFSP tissue section with translocation affecting the COL1A1/PDGFB loci as indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.

Prod. No.	Product	Label	Tests* (Volume)
Z-2116-50	ZytoLight SPEC COL1A1/PDGFB Dual Color Dual Fusion Probe CE IVD	●/●	5 (50 µl)
Z-2116-200	ZytoLight SPEC COL1A1/PDGFB Dual Color Dual Fusion Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC SS18 Dual Color Break Apart Probe

CE IVD

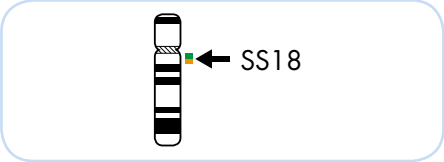
Background

The ZytoLight® SPEC SS18 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 18q11.2 harboring the SS18 (SS18, nBAF chromatin remodeling complex subunit, a.k.a. SYT) gene. Translocations involving the region 18q11.2 are found in over 90% of synovial sarcoma. Among soft tissue sarcomas, synovial sarcoma is one of the most common and classically occurs in the extremities of young adults with greater prevalence in males even though, the occurrence of synovial sarcoma has also been described in a wide variety of anatomical locations and in all ages. The most frequent translocation involving the SS18 gene region is t(X;18)(p11.23;q11.2) juxtaposing the SS18 gene in 18q11.2 either next to the SSX1 (synovial sarcoma, translocated to X chromosome) or the SSX2 gene, or very rarely to the SSX4 locus located in Xp11.23. Complex translocations involving other chromosomes are observed in less than 10% of synovial sarcomas. In combination with histopathological diagnosis, detection of SS18 rearrangements via FISH analysis is a valuable tool to confirm the diagnosis of synovial sarcoma.

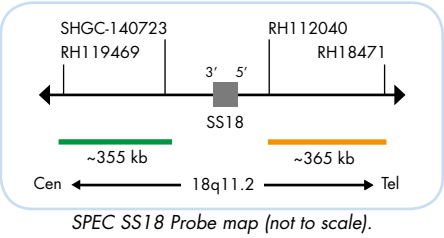
References
Amary MF, et al. (2007) Mod Pathol 20: 482-96.
Clark J, et al. (1994) Nat Genet 7: 502-8.
Ilmiawan MI, et al. (2012) Med J Indones 21: 196-202.
Kawai A, et al. (1998) N Engl J Med 338: 153-60.
Surace C, et al. (2004) Lab Invest 84: 1185-92.
Torres L, et al. (2008) Cancer Genet Cytogenet 187: 45-9.

Probe Description

The SPEC SS18 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 18q11.2 band. The orange fluorochrome direct labeled probe hybridizes distal to the SS18 gene, the green fluorochrome direct labeled probe hybridizes proximal to that gene.



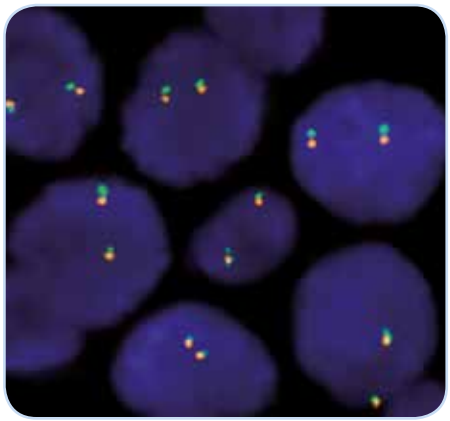
Ideogram of chromosome 18 indicating the hybridization locations.



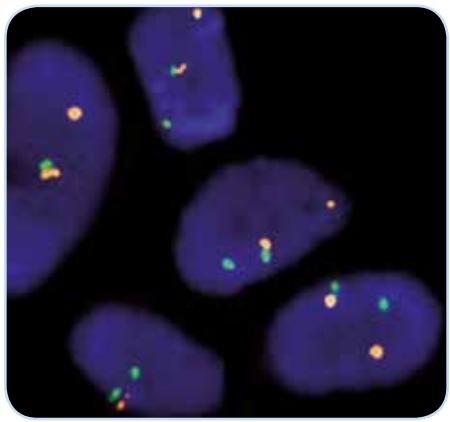
SPEC SS18 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 18q11.2 band two orange/green fusion signals are expected representing two normal (non-rearranged) 18q11.2 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 18q11.2 locus and one 18q11.2 locus affected by an 18q11.2 translocation.



SPEC SS18 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Synovial sarcoma tissue section with translocation affecting the 18q11.2 locus as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2097-50	ZytoLight SPEC SS18 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2097-200	ZytoLight SPEC SS18 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC SS18/SSX1 TriCheck™ Probe

CE IVD

Background

The ZytoLight® SPEC SS18/SSX1 TriCheck™ Probe is designed to detect translocations involving the chromosomal region 18q11.2 harboring the SS18 (SS18, nBAF chromatin remodeling complex subunit, a.k.a. SYT) gene and the chromosomal region Xp11.23 harboring the SSX1 (SSX family member 1) gene.

Synovial sarcoma is characterized by the t(X;18) found in more than 95% of these tumors and juxtaposing the SS18 gene in 18q11.2 either next to the SSX1 or the SSX2 gene, or very rarely to the SSX4 locus.

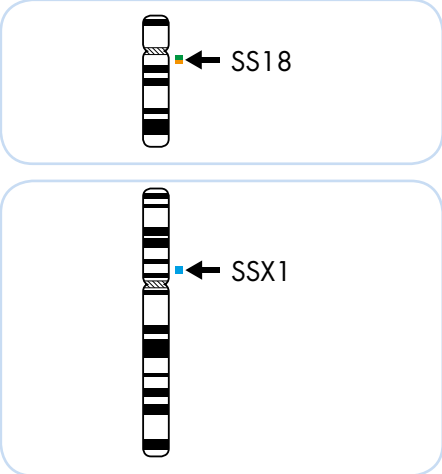
Synovial sarcoma is one of the most common soft tissue tumors that typically occurs in the extremities of young adults with greater prevalence in males, even though, the occurrence of synovial sarcoma has also been described in a wide variety of anatomical locations and in all ages.

In combination with histopathological diagnosis, detection of SS18 rearrangements via FISH is a valuable tool to confirm the diagnosis of synovial sarcoma. Moreover, patients with SS18-SSX1 fusions were shown to have a higher risk of developing metastases compared to those with SS18-SSX2 fusions. Hence, detection of the SS18 fusion gene variant by FISH may also be of prognostic significance.

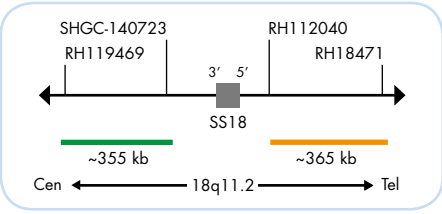
References
Amary MF, et al. (2007) Mod Pathol 20: 482-96.
Clark J, et al. (1994) Nat Genet 7: 502-8.
Kawai A, et al. (1998) N Engl J Med 338: 153-60.
Panagopoulos I, et al. (2001) Genes Chromosomes Cancer 31: 362-72.
Surace C, et al. (2004) Lab Invest 84: 1185-92.
Torres L, et al. (2008) Cancer Genet Cytogenet 187: 45-9.

Probe Description

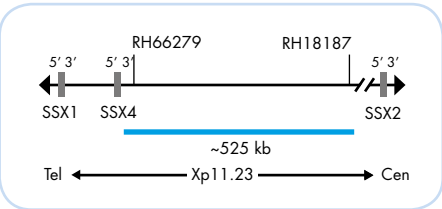
The SPEC SS18/SSX1 TriCheck™ Probe is a mixture of three direct labeled probes hybridizing to the 18q11.2 and Xp11.23 bands. The green fluorochrome direct labeled probe hybridizes proximal and the orange fluorochrome direct labeled probe hybridizes distal to the SS18 breakpoint region at 18q11.2. The blue fluorochrome direct labeled probe hybridizes proximal to the SSX1 gene at Xp11.23.



Ideograms of chromosomes 18 (above) and X (below) indicating the hybridization locations.



SPEC SS18 Probe map (not to scale).



SPEC SSX1 Probe map (not to scale).

Results

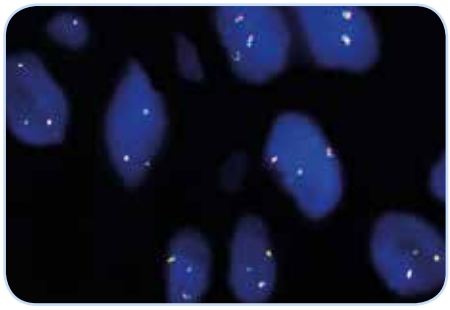
In an interphase nucleus of a normal female cell without SS18-SSX1 rearrangement, two green/orange fusion signals and two blue signals are expected.

In an interphase nucleus of a normal male cell without SS18-SSX1 rearrangement, two green/orange fusion signals and one blue signal are expected.

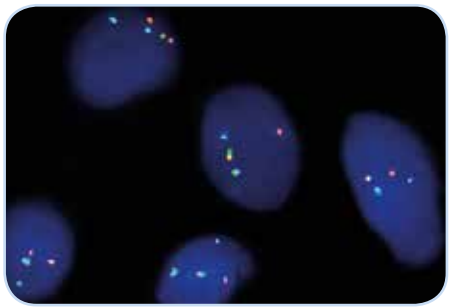
An SS18-SSX1 or an SS18-SSX4 fusion is indicated by one separate orange signal co-localizing with one blue signal and one separate green signal.

An SS18-SSX2 fusion is indicated by one separate green signal, one separate orange signal, and a blue signal in close proximity of the separated green signal.

An SS18 translocation without involvement of SSX1, SSX2, or SSX4 is indicated by the split of one green/orange fusion signal without co-localization of the separated orange or green signal with one blue signal.



Male synovial sarcoma tissue section with SS18-SSX1 or SS18-SSX4 fusion as indicated by orange/blue fusion signals.



Female synovial sarcoma tissue section with SS18-SSX2 fusion as indicated by green/blue fusion signals.

Prod. No.	Product	Label	Tests* (Volume)
Z-2184-50	ZytoLight SPEC SS18/SSX1 TriCheck Probe CE IVD	●/●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC BCL2 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC BCL2 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 18q21.33 harboring the BCL2 gene. The BCL2 (BCL2 apoptosis regulator, a.k.a. PPP1R50) gene encodes a mitochondrial membrane protein that regulates apoptosis and is expressed in B-cells.

Translocations involving the BCL2 gene are commonly identified in B-cell lymphomas. In particular, the translocation t(14;18)(q32.3;q21.3) has been identified in about 80% of follicular lymphoma (FL), in 20% to 30% of diffuse large B-cell lymphoma (DLBCL), and rarely in B-cell chronic lymphocytic leukemia (B-CLL).

In FL this translocation is considered to be a cytogenetic hallmark. As a result of this rearrangement, the BCL2 gene is juxtaposed to IGH (Immunglobulin heavy locus) at 14q32.33 which leads to overexpression of the anti-apoptotic protein BCL2, and finally to progression to lymphoma.

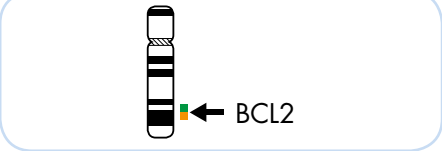
Alternative BCL2 translocations to immunoglobulin light chain genes as well as non-IG translocation events have been reported.

In DLBCL, BCL2 gene overexpression has been implicated in conferring resistance to chemotherapy and has been associated with poor prognosis.

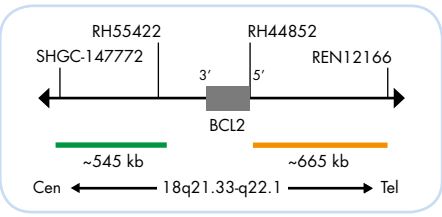
Hence, detection of BCL2 translocations by Fluorescence *in situ* Hybridization (FISH) may be of diagnostic and prognostic relevance.

Probe Description

The SPEC BCL2 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 18q21.33-q22.1 band. The green fluorochrome direct labeled probe hybridizes proximal to the BCL2 gene, and the orange fluorochrome direct labeled probe hybridizes distal to the BCL2 locus.



Ideogram of chromosome 18 indicating the hybridization locations.

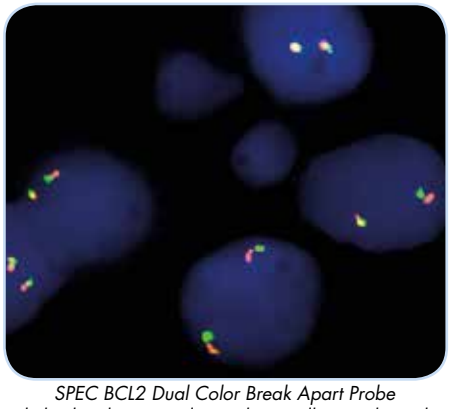


SPEC BCL2 Probe map (not to scale).

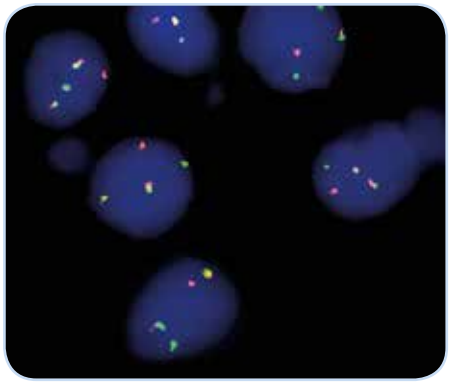
References
Da Cunha Santos G, et al. (2011) Cancer Cytopathol 119: 254-62.
Dyer MJ, et al. (1994) Blood 83: 3682-8.
Gu K, et al. (2008) Arch Pathol Lab Med 132: 1355-61.
Hockenbery D, et al. (1990) Nature 348: 334-6.
Impera L, et al. (2008) Oncogene 27: 6187-90.
López-Guillermo A, et al. (1999) Blood 93: 3081-7.
Nelson BP, et al. (2007) Am J Clin Pathol 128: 323-32.
Tibiletti MG, et al. (2009) Hum Pathol 40: 645-52.
Tomita N, et al. (2009) Haematologica 94: 935-43.
Weinberg OK, et al. (2007) J Mol Diagn 9: 530-7.

Results

In an interphase nucleus lacking a translocation involving the 18q21.33-q22.1 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 18q21.33-q22.1 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 18q21.33-q22.1 locus and one 18q21.33-q22.1 locus affected by a translocation.



SPEC BCL2 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Neck lymph node tissue section with translocation of the BCL2 gene as indicated by two non-rearranged orange/green fusion signals, one orange and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2192-50	ZytoLight SPEC BCL2 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2192-200	ZytoLight SPEC BCL2 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC BCL2/CEN 18 Dual Color Probe

CE IVD

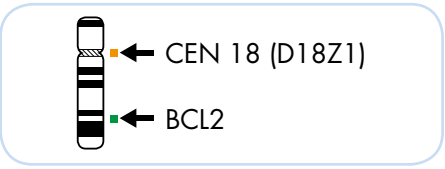
Background

The ZytoLight® SPEC BCL2/CEN 18 Dual Color Probe is designed for the detection of amplifications of the chromosomal region harboring the BCL2 gene.
The BCL2 (BCL2 apoptosis regulator, a.k.a. PPP1R50) gene is located on chromosome 18q21.33 and encodes an antiapoptosis factor involved in normal B-cell development and differentiation. The expression of BCL2 usually decreases upon B-cell differentiation. However, increased BCL2 expression has been detected in lymphomas harboring the translocation t(14;18)(q32.3;q21.3). Moreover, overexpression of BCL2 can also be caused by amplification of the BCL2 gene as detected in diffuse large B-cell lymphoma (DLBCL) and mantle cell lymphoma (MCL).
DLBCL is the most common type of non-Hodgkin lymphoma characterized by an aggressive clinical course. On the basis of their gene expression profiles, ABC (activated B-cell-like) and GCB (germinal center B-cell-like) were identified as two molecular subtypes of DLBCL. BCL2 was found to be frequently amplified in the ABC subgroup of DLBCL but rarely in the GCB subgroup. BCL2 overexpression as a result of 18q21 amplification is associated with poor survival in the ABC subgroup. Hence, the identification of BCL2 gene copy number changes by Fluorescence *in situ* Hybridization may be of prognostic significance in non-Hodgkin lymphomas.

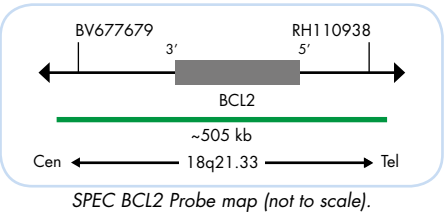
References
Alizadeh AA, et al. (2000) Nature 403: 503-11.
Beà S, et al. (2009) Blood 113: 3059-69.
Iqbal J, et al. (2006) J Clin Oncol 24: 961-8.
Monni O, et al. (1999) Leuk Lymphoma 34: 45-52.

Probe Description

The SPEC BCL2/CEN 18 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC BCL2 probe hybridizing to the human BCL2 gene in the chromosomal region 18q21.33 and an orange fluorochrome direct labeled CEN 18 probe specific for the alpha satellite centromeric region of chromosome 18 (D18Z1).



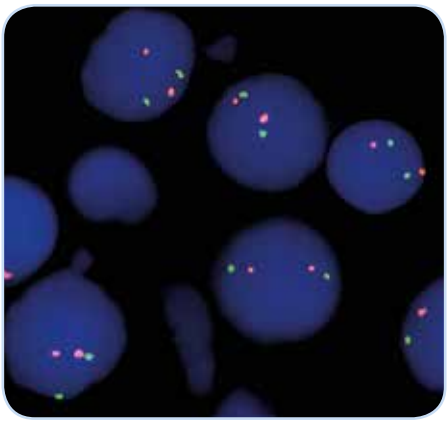
Ideogram of chromosome 18 indicating the hybridization locations.



SPEC BCL2 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the BCL2 gene locus, multiple copies of the green signal or green signal clusters will be observed.



SPEC BCL2/CEN 18 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2174-50	ZytoLight SPEC BCL2/CEN 18 Dual Color Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC BCL2/IGH Dual Color Dual Fusion Probe

CE IVD

Background

The ZytoLight® SPEC BCL2/IGH Dual Color Dual Fusion Probe is designed to detect the translocation t(14;18)(q32.3;q21.3) affecting the BCL2 gene in the chromosomal region 18q21.33 and the IGH locus in 14q32.33.

Translocations involving the BCL2 (BCL2 apoptosis regulator) gene and the IGH (immunoglobulin heavy locus, a.k.a. IGH@) gene are considered to be cytogenetic hallmarks for follicular lymphoma (FL). FL represents one of the most common non-Hodgkin lymphoma (NHL).

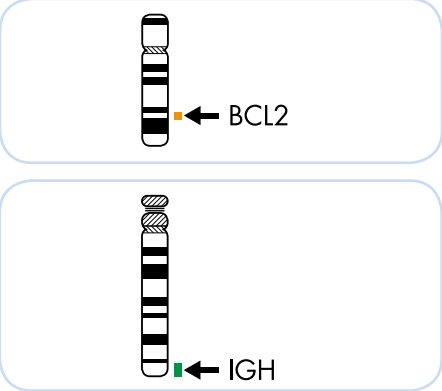
About 75% of breakpoints on chromosome 18 are clustered in the major breakpoint region (MBR) and the minor cluster region (mcr), whereas the remaining breakpoints are scattered between these clusters, or at the 5′ side (variant cluster region or vcr) of the BCL2 gene.

The translocation t(14;18)(q32.3;q21.3) has been identified in about 80% of FLs but is also observed in 20% to 30% of patients with diffuse large B-cell lymphoma (DLBCL). The rearrangement results in juxtaposition of the BCL2 gene at 18q21.33 next to the IGH (immunoglobulin heavy chain) locus at 14q32.33 and leads to overexpression of the anti-apoptotic protein BCL2. This represents most likely the initial step of malignant transformation, leading to suppression of apoptosis and progression to lymphoma.

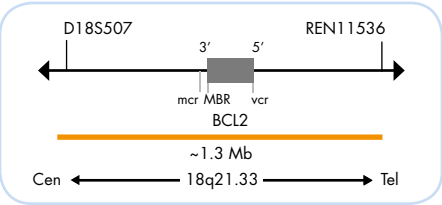
Detection of t(14;18) by Fluorescence *in situ* Hybridization (FISH) can be used to confirm the diagnosis of FL if histology is inconclusive. Additionally, this method can be used to monitor the response to therapy and detect recurrent disease.

Probe Description

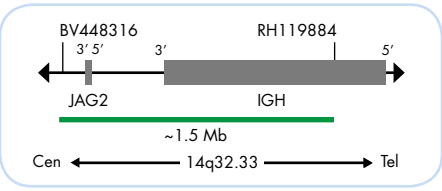
The SPEC BCL2/IGH Dual Color Dual Fusion Probe is a mixture of an orange fluorochrome direct labeled BCL2 probe spanning the known BCL2 breakpoints, and a green fluorochrome direct labeled IGH probe spanning the known breakpoints of IGH.



Ideograms of chromosomes 18 (above) and 14 (below) indicating the hybridization locations.



SPEC BCL2 Probe map (not to scale).



SPEC IGH Probe map (not to scale).

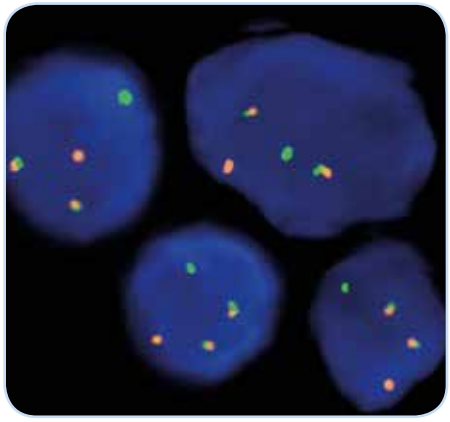
References

Baró C, et al. (2011) Leuk Res 35: 256-9.
Da Cunha Santos G, et al. (2011) Cancer Cytopathol 119: 254-62.
Einerson RR, et al. (2005) Am J Clin Pathol 124: 421-9.
Gu K, et al. (2008) Arch Pathol Lab Med 132: 1355-61.
Nguyen-Khac F, et al. (2011) Am J Blood Res 1: 13-21.
Weinberg OK, et al. (2007) J Mol Diagn 9: 530-7.

Results

In a normal interphase nucleus, two orange and two green signals are expected. A reciprocal translocation involving two breakpoints splits the two signals and generates a fusion signal on each of the chromosomes involved. The chromosomal regions which are not translocated are indicated by the single orange and green signal, respectively.

SPEC BCL2/IGH Dual Color Dual Fusion Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Bone marrow biopsy section with translocation affecting the BCL2/IGH loci as indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.

Prod. No.	Product	Label	Tests* (Volume)
Z-2114-50	ZytoLight SPEC BCL2/IGH Dual Color Dual Fusion Probe CE IVD	●/●	5 (50 µl)
Z-2114-200	ZytoLight SPEC BCL2/IGH Dual Color Dual Fusion Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC MALT1 Dual Color Break Apart Probe

CE IVD

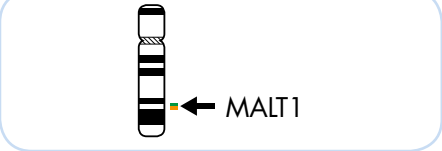
Background

The ZytoLight® SPEC MALT1 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 18q21.32 harboring the MALT1 gene. The MALT1 (MALT1 paracaspase, a.k.a. MLT) gene encodes a human paracaspase and is often rearranged in MALT lymphomas accounting for 5-10% of all B-cell non-Hodgkin lymphomas (NHL). The most common translocations affecting the MALT1 gene are t(11;18)(q22.2;q21.3) and t(14;18)(q32.3;q21.3) occurring in 50% and 15-20% of MALT lymphomas, respectively. These translocations lead to the expression of BIRC3-MALT1 (a.k.a. API2-MALT1) and IGH-MALT1 fusion proteins, resulting in constitutive activation of the NFκB signaling pathway which controls the expression of numerous anti-apoptotic and proliferation-promoting genes.
The translocation t(11;18)(q22.2;q21.3) is mainly found in pulmonary and gastric lymphomas, whereas t(14;18)(q32.3;q21.3) occurs more frequently in non-gastrointestinal MALT lymphomas, e.g., of the skin and salivary glands.
The presence of a t(11;18)(q22.2;q21.3) correlates with unresponsiveness to eradication of *Helicobacter pylori* in gastric MALT lymphomas. Hence, detection of MALT1 translocations by Fluorescence *in situ* Hybridization (FISH) may be a supportive tool to identify patients eligible for anti *H. pylori* therapy.

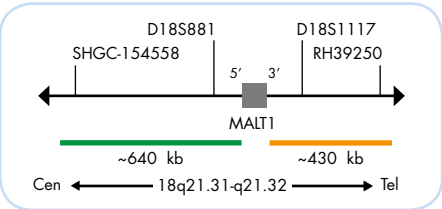
References
Afonina IS, et al. (2015) FEBS J 282: 3286-97.
Beans M, et al. (2014) PloS One 9: e103774.
Dierlamm J, et al. (1999) Blood 93: 3601-9.
Levine EG, et al. (1989) Blood 74: 1796-800.
Lucas PC, et al. (2001) J Biol Chem 276: 19012-9.
Martinelli G, et al. (2005) J Clin Oncol 23: 1979-83.
Pereira MI & Medeiros JA (2014) World J Gastroenterol 20: 684-98.
Troppan K, et al. (2015) Gastroenterol Res Pract 2015: 102656.

Probe Description

The SPEC MALT1 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 18q21.31-q21.32 band. The green fluorochrome direct labeled probe hybridizes proximal to the MALT1 gene at 18q21.31-q21.32, and the orange fluorochrome direct labeled probe hybridizes distal to the MALT1 gene region at 18q21.32.



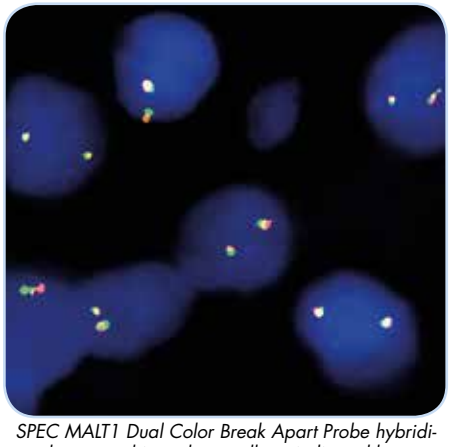
Ideogram of chromosome 18 indicating the hybridization locations.



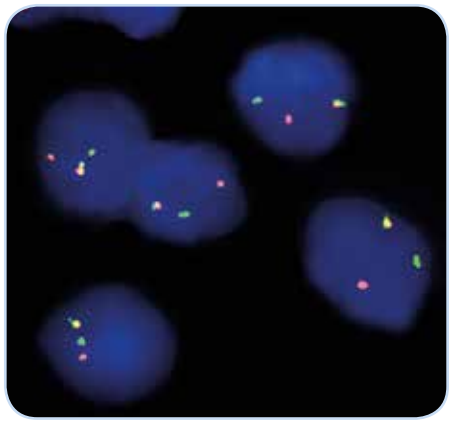
SPEC MALT1 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 18q21.31-q21.32 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 18q21.31-q21.32 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 18q21.31-q21.32 locus and one 18q21.31-q21.32 locus affected by a translocation.



SPEC MALT1 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Lymphoma tissue section with translocation of the MALT1 gene as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2196-50	ZytoLight SPEC MALT1 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2196-200	ZytoLight SPEC MALT1 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC CIC Dual Color Break Apart Probe

CE IVD

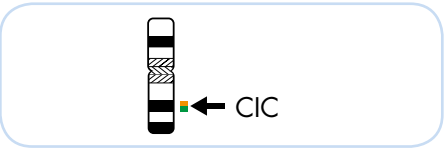
Background

The ZytoLight® SPEC CIC Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 19q13.2 harboring the CIC (capicua transcriptional repressor, a.k.a. KIAA0306) gene. The CIC gene encodes a transcriptional repressor that inhibits the expression of the PEA3 (polyoma enhancer activator 3) gene family, including ETV1, ETV4, and ETV5 and regulates receptor tyrosine kinase signaling pathways.
Rearrangements involving the CIC gene are frequently found in EWSR1-negative small blue round cell tumors (SBRCT) which arise in soft tissues of children and young adults and have been described as aggressive tumors with an inferior overall survival compared to Ewing sarcoma (EWS).
The CIC-DUX4 (double homeobox 4) gene fusion is the most frequent genetic event in EWSR1-negative SBRCT resulting from either a t(4;19)(q35;q13.2) or a t(10;19)(q26.3;q13.2).
CIC rearrangements have also been found in other tumor entities such as lung cancer and medulloblastomas and other fusion partners besides DUX4 are known (FOXO4, LEUTX).
As CIC-DUX4-positive patients do not respond well to the common forms of EWS treatment, and show a poor overall survival, novel therapy approaches are needed to treat this type of aggressive tumors. Hence, the detection of CIC translocations by Fluorescence *in situ* Hybridization (FISH) may be of prognostic and therapeutic relevance.

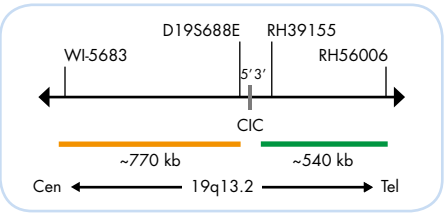
References
Antonescu R, et al. (2017) Am J Surg Pathol 7: 941-9.
Choi K, et al. (2013) Am J Surg Pathol 9: 1379-86.
Graham C, et al. (2012) Hum Pathol 2: 180-9.
Italiano A, et al. (2012) Genes Chromosomes Cancer 3: 207-18.
Kawamura-Saito M, et al. (2006) Hum Mol Genet 13: 2125-37.
Lee CJ, et al. (2005) J Neurooncol 2: 101-8.
Richkind KE, et al. (1996) Cancer Genet Cytogenet 1: 71-4.

Probe Description

The SPEC CIC Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 19q13.2 band. The orange fluorochrome direct labeled probe hybridizes proximal and the green fluorochrome direct labeled probe hybridizes distal to the CIC gene.



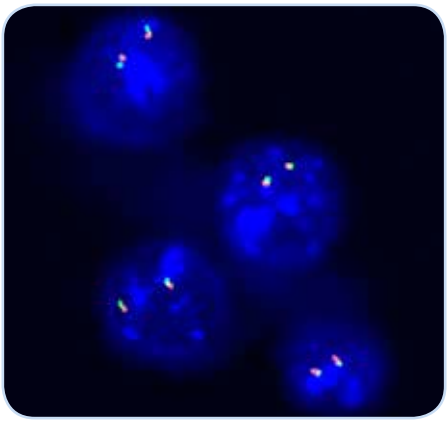
Ideogram of chromosome 19 indicating the hybridization locations.



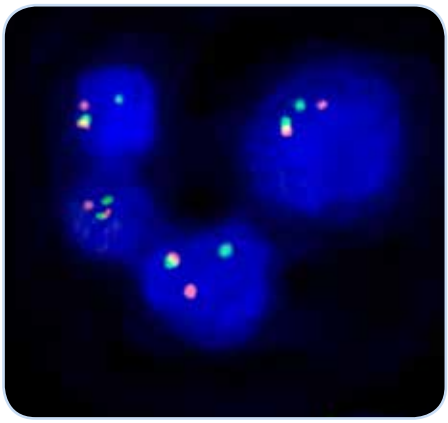
SPEC CIC Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 19q13.2 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 19q13.2 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 19q13.2 locus and one 19q13.2 locus affected by a translocation.



SPEC CIC Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Undifferentiated round cell sarcoma ‚Ewing-like' tissue section with translocation of the 19q13.2 locus as indicated by one non-rearranged orange/green fusion signal, one orange and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2285-50	ZytoLight SPEC CIC Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC C19MC/19p13 Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC C19MC/19p13 Dual Color Probe is designed for the detection of amplifications of the C19MC microRNA (miRNA) cluster region located at 19q13.42.

The C19MC miRNA cluster region comprises 46 micro RNA genes which encode for large polycistronic microRNAs. C19MC amplifications have been reported in tumor entities, such as breast cancer and parathyroid carcinomas. According to the 2016 WHO classification of tumors of the central nervous system, amplification of this region defines a new entity of embryonal tumors with multilayered rosettes (ETMR), C19MC-altered. Amplification of C19MC leads to an overexpression of miRNAs in this cluster region that drive cell proliferation, promote cell survival, and increase carcinogenicity of cells providing functional evidence that C19MC miRNAs act as oncogenes.

ETMR with C19MC miRNA cluster amplification are rare brain tumors which occur primarily in infants and young children showing a poor overall survival.

Hence, detection of C19MC miRNA cluster amplification by Fluorescence *in situ* Hybridization may be of diagnostic and prognostic relevance.

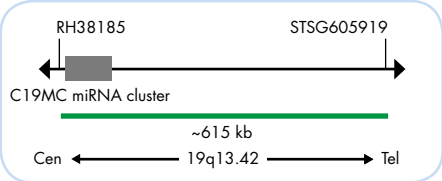
References

Chhabda S, et al. (2016) Quant Imaging Med Surg 6: 486-9.
Li M, et al. (2009) Cancer Cell 16: 533-46.
Louis DN, et al. (2016) Acta Neuropathol 131: 803-20.
Spence T, et al. (2014) Neuro Oncol 16: 62-71.
Spence T, et al. (2014) Acta Neuropathol 128: 291-303.
Vaira V, et al. (2012) J Mol Endocrinol 49: 115-24.

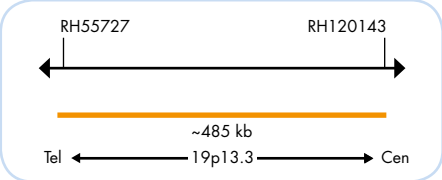
Probe Description

The SPEC C19MC/19p13 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC C19MC probe hybridizing to the C19MC region in the chromosomal region 19q13.42 and an orange fluorochrome direct labeled SPEC 19p13 probe specific for 19p13.3. Since chromosomes 1, 5, and 19 share the same repetitive sequences, probes specific for 19p13.3 are commonly used for chromosome 19 copy number detection.

Ideogram of chromosome 19 indicating the hybridization locations.



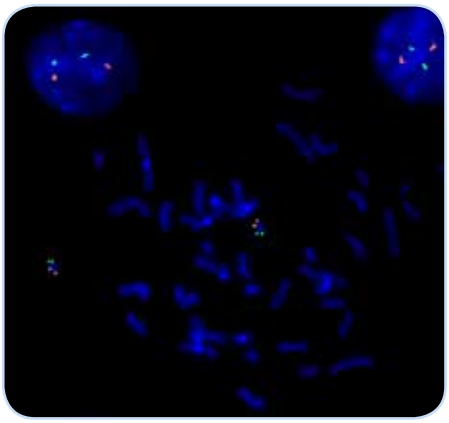
SPEC C19MC Probe map (not to scale).



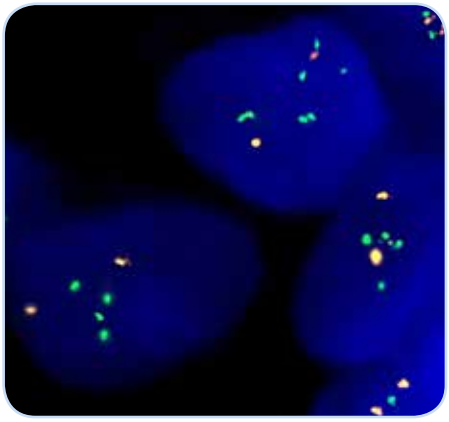
SPEC 19p13 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the C19MC region, multiple copies of the green signal or green signal clusters will be observed.



SPEC C19MC/19p13 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals per nucleus and to metaphase chromosomes of a normal cell.



Primitive neuroectodermal tumor tissue section with amplification of the C19MC miRNA cluster as indicated by multiple green signals.

Specimen kindly provided by Hannu Haapasalo, MD, PhD, Fimlab Laboratories, Finland.

Prod. No.	Product	Label	Tests* (Volume)
Z-2274-50	ZytoLight SPEC C19MC/19p13 Dual Color Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC BCL2L1/CEN 20 Dual Color Probe

CE IVD

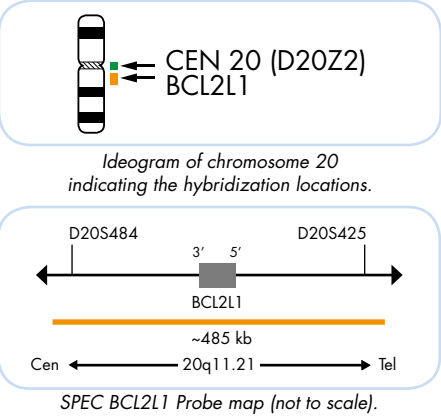
Background

The ZytoLight® SPEC BCL2L1/CEN 20 Dual Color Probe is designed for the detection of BCL2L1 gene amplifications.
The BCL2L1 (BCL2-like 1, a.k.a. BCLX) gene is located in the chromosomal region 20q11.21 and encodes for an anti-apoptotic protein that belongs to the BCL2 family. These genes are involved in a wide variety of cellular activities including lymphocyte development and hematopoiesis.
BCL2L1 amplifications have been reported in several human cancers including lung, ovarian breast, melanoma, and hematologic malignancies.
Overexpression of BCL2L1 reduces MYC-induced apoptosis in immortalized bronchial epithelial cells.
Furthermore, BCL2L1 amplifications are found in many tumor cell lines with resistance to chemotherapeutic agents.
Targeting the BCL2 family proteins with small non-peptidic compounds, so called BH3-mimetics, is currently investigated in clinical trials.
Hence, the identification of BCL2L1 amplifications by Fluorescence *in situ* Hybridization and the inhibition of BCL2L1 signaling may be of therapeutic significance in various types of tumors.

References
Beroukhim R, et al. (2010) Nature 463: 899-905.
Booher RN, et al. (2014) PloS One 9: e108371.
Sochalska M, et al. (2015) FEBS J 282: 834-49.
Yasui K, et al. (2004) Cancer Res 64: 1403-10.

Probe Description

The SPEC BCL2L1/CEN 20 Dual Color Probe is a mixture of an orange fluorochrome direct labeled SPEC BCL2L1 probe hybridizing to the BCL2L1 gene in the chromosomal region 20q11.21 and a green fluorochrome direct labeled CEN 20 probe specific for the alpha satellite centromeric region of chromosome 20 (D20Z2).

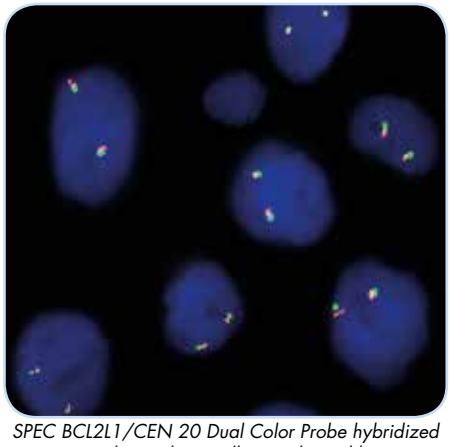


Ideogram of chromosome 20 indicating the hybridization locations.

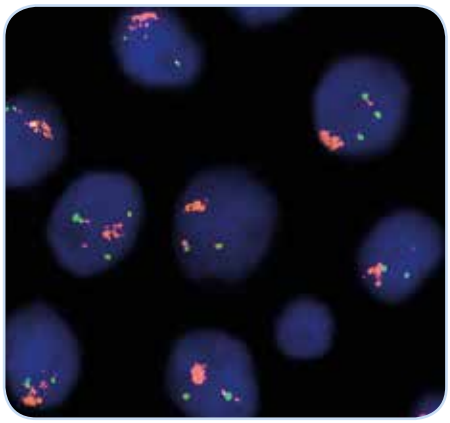
SPEC BCL2L1 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the BCL2L1 gene locus, multiple copies of the orange signal or orange signal clusters will be observed.



SPEC BCL2L1/CEN 20 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



SK-LU-1 cell line with interphase cells showing amplification of the BCL2L1 gene locus as indicated by orange signal clusters in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2171-200	ZytoLight SPEC BCL2L1/CEN 20 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC PTPRT/20q11 Dual Color Probe

CE IVD

Background

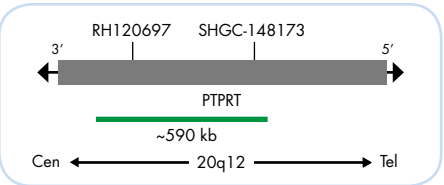
The ZytoLight® SPEC PTPRT/20q11 Dual Color Probe is designed to detect deletions of the long arm of chromosome 20.
20q deletions can occur in various myeloid disorders, e.g., myelodysplastic syndromes (MDS), acute myeloid leukemia (AML), and myeloproliferative neoplasms (MPNs).
In MDS, del(20q) as the sole cytogenetic abnormality, is associated with a favorable prognosis, with better survival, and a lower risk for transformation to AML. Del(20q) occurring with additional cytogenetic aberrations predicts a poor prognosis.
The breakpoints of the 20q deletion were identified to be heterogeneous in several studies. The minimal common deleted region (CDR) was defined to be flanked by the genes PTPRT (20q12) and EYA2 (20q13.12).
It has been suggested that one or more tumor suppressor genes could be located in the CDR, the deletion or inactivation of which may play a role in malignant growth. However, the target gene(s) remain unknown.

References
Bacher U, et al. (2014) Br J Haematol 164: 822-33.
Brezinová J, et al. (2005) Cancer Genet Cytogenet 160: 188-92.
Okada M, et al. (2012) Cancer Genet 205: 18-24.
Testa JR, et al. (1978) Blood 52: 868-77.

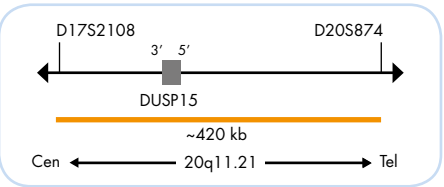
Probe Description

The SPEC PTPRT/20q11 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC PTPRT probe hybridizing in the CDR at 20q12, an orange fluorochrome direct labeled SPEC 20q11 probe specific for the chromosomal region 20q11.21 harboring the DUSP15 gene. For an unambigous enumeration of chromosome 20, the SPEC 20q11 is found to be suitable.

Ideogram of chromosome 20 indicating the hybridization locations.



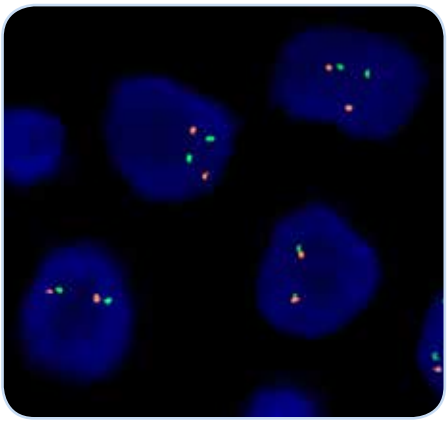
SPEC PTPRT Probe map (not to scale).



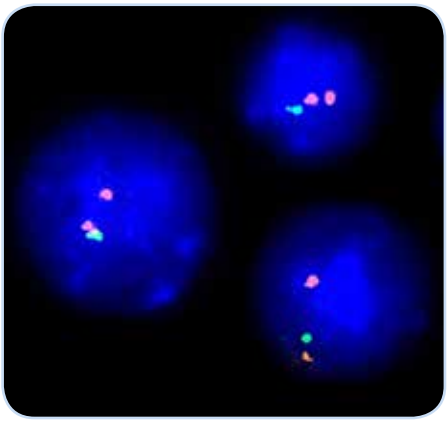
SPEC 20q11 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletions affecting the 20q12 locus, one or no copy of the green signal will be observed.



SPEC PTPRT/20q11 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Lymphocytes of a myelodysplastic syndrome showing a 20q deletion indicated by one single green and two orange signals in each nucleus.

Material kindly provided from Dr. Saurabh Bhattacharya, Lal PathLabs, India.

Prod. No.	Product	Label	Tests* (Volume)
Z-2213-50	ZytoLight SPEC PTPRT/20q11 Dual Color Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ERG Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC ERG Dual Color Break Apart Probe is designed to detect aberrations involving the ERG gene at 21q22.2 frequently detected in prostate cancers.

ERG (ETS transcription factor ERG) rearrangements have been observed in 40-60% of prostate cancers identified via prostate-specific antigen (PSA) screening. The most common aberration affecting ERG is the interstitial deletion of about 3 Mb at the chromosomal region 21q22 found in 90% of the cases. This deletion leads to the fusion of the hormonally regulated promoter of the TMPRSS2 (transmembrane serine protease 2) gene to the coding region of ERG, resulting in overexpression of the ERG transcription factor. However, about 10% of the ERG rearranged prostate cancer cases show alternative fusions, as e.g. SLC45A3-ERG or NDRG1-ERG.

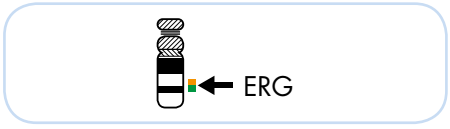
Several studies detected associations of ERG rearrangements with histomorphologic features as well as characteristic chromosomal copy number changes and gene expression signatures, defining a distinct sub-class of prostate cancers with unfavorable prognosis. Hence, the evaluation of the ERG rearrangement status in tissue or urine samples by FISH might be of diagnostic and prognostic relevance.

EWSR1-ERG gene fusions present in about 10% of patients with Ewing sarcoma may result from complex genomic rearrangements and may therefore not be detected by FISH analysis or may result in a non-classical translocation signal pattern.

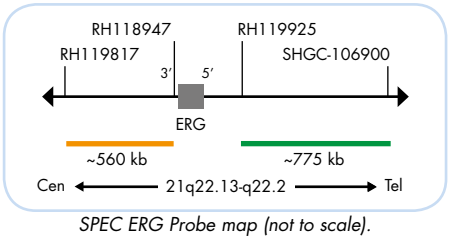
References
Esgueva R, et al. (2010) Mod Pathol 23: 539-46.
Maire G, et al. (2008) Cancer Genet Cytogenet 181: 81-92.
Nam RK, et al. (2007) Br J Cancer 97: 1690-5.
Perner S, et al. (2006) Cancer Res 66: 8337-41.
Pflueger D, et al. (2009) Neoplasia 11: 804-11.
Tomlins SA, et al. (2005) Science 310: 644-8.

Probe Description

The SPEC ERG Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the long arm of chromosome 21. The orange fluorochrome direct labeled probe hybridizes at 21q22.13-q22.2 proximal to the ERG gene breakpoint region, the green direct labeled probe hybridizes at 21q22.2 distal to the ERG gene breakpoint region.



Ideogram of chromosome 21 indicating the hybridization locations.



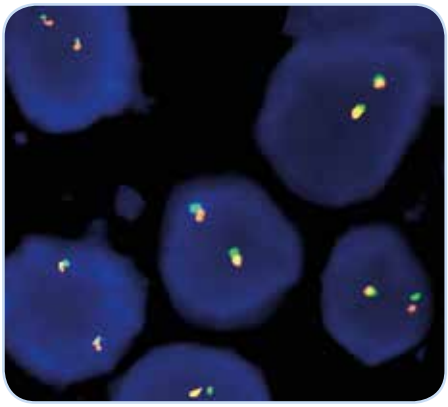
SPEC ERG Probe map (not to scale).

Results

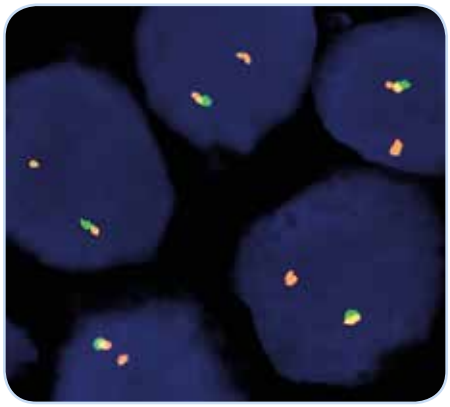
In an interphase nucleus of a normal cell lacking an aberration involving the 21q22.13-q22.2 band, two orange/green fusion signals are expected representing the two normal (non-rearranged) 21q22.13-q22.2 loci.

One 21q22.13-q22.2 locus affected by a 21q22.2 deletion resulting in the TMPRSS2-ERG fusion is indicated by the loss of one green signal.

A signal pattern consisting of one orange/green fusion signal, a separate green, and a separate orange signal indicates an ERG translocation without involvement of TMPRSS2 (e.g. SLC45A3-ERG).



SPEC ERG Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Prostate cancer tissue section with interstitial deletion of the chromosomal region 21q22.2 resulting in the TMPRSS2-ERG fusion as indicated by the loss of one green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2138-200	ZytoLight SPEC ERG Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC ERG/TMPRSS2 TriCheck™ Probe

CE IVD

Background

The ZytoLight® SPEC ERG/TMPRSS2 TriCheck™ Probe is designed to detect deletions between the ERG and the TMPRSS2 gene at 21q22 resulting in the TMPRSS2-ERG fusion. Furthermore, the triple color approach allows the detection of other translocations affecting either of these genes.

ERG (ETS transcription factor ERG) rearrangements have been observed in 40-60% of prostate cancers identified via prostate-specific antigen (PSA) screening. The most common aberration affecting ERG is the interstitial deletion of about 3 Mb at the chromosomal region 21q22 found in 90% of the cases. This deletion leads to the fusion of the hormonally regulated promoter of the TMPRSS2 (transmembrane serine protease 2) gene to the coding region of ERG, resulting in overexpression of the ERG transcription factor. The deleted fragment is sometimes observed as insertion on other chromosomes. However, about 10% of the ERG rearranged prostate cancer cases show alternative fusions, as e.g. SLC45A3-ERG. On the other hand non-ERG translocations fusing TMPRSS2 to other ETS family members, as e.g. TMPRSS2-ETV1, have been found in a few percent of these malignancies.

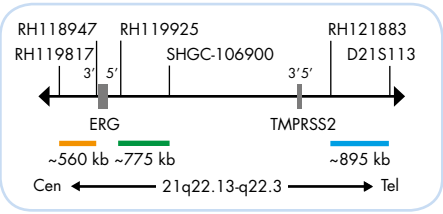
Several studies detected associations of ERG rearrangements with histomorphologic features as well as characteristic chromosomal copy number changes and gene expression signatures defining a distinct sub-class of prostate cancers with unfavorable prognosis. Hence, the evaluation of the TMPRSS2-ERG rearrangement status in tissue or urine samples by FISH might be of diagnostic and prognostic relevance.

References
Esgueva R, et al. (2010) Mod Pathol 23: 539-46.
Nam RK, et al. (2007) Br J Cancer 97: 1690-5.
Perner S, et al. (2006) Cancer Res 66: 8337-41.
Tomlins SA, et al. (2005) Science 310: 644-8.

Probe Description

The SPEC ERG/TMPRSS2 TriCheck™ Probe is a mixture of three direct labeled probes hybridizing to the chromosomal regions 21q22.13-q22.3. The orange fluorochrome direct labeled probe hybridizes at 21q22.13-q22.2 proximal to the ERG gene breakpoint region, the green fluorochrome direct labeled probe hybridizes at 21q22.2 distal to that region, and the blue fluorochrome direct labeled probe hybridizes at 21q22.3 distal to the TMPRSS2 gene region.

Ideogram of chromosome 21 indicating the hybridization locations.



SPEC ERG/TMPRSS2 TriCheck™ Probe map (not to scale).

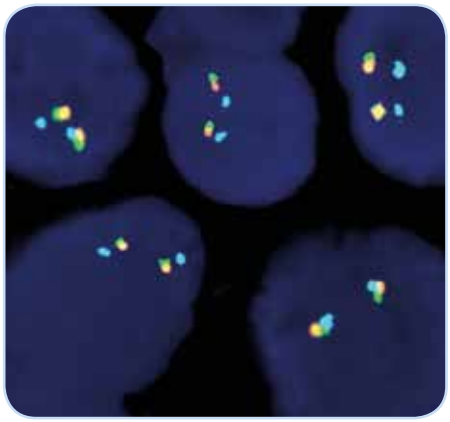
Results

In a normal interphase nucleus, two orange/green fusion signals and two blue signals in close proximity of the respective fusion signals are expected representing two normal (non-rearranged) 21q22.13-q22.3 loci.

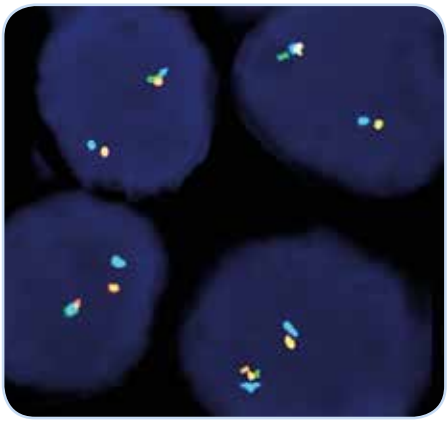
One 21q22 locus affected by a 21q22.2 deletion resulting in the TMPRSS2-ERG fusion is indicated by one separate orange signal co-localizing with one blue signal, and the loss of one green signal.

An ERG translocation without involvement of TMPRSS2 is indicated by a separated orange signal and a blue signal co-localizing with the separate green signal.

A non-ERG translocation affecting TMPRSS2 is indicated by a separated blue signal not co-localizing with the ERG fusion signal.



SPEC ERG/TMPRSS2 TriCheck™ Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals and two blue signals in close proximity of the respective fusion signals.



Prostate cancer tissue section with one 21q22 locus affected by an interstitial deletion of the chromosomal region 21q22.2 resulting in the TMPRSS2-ERG fusion as indicated by one separate orange signal co-localizing with one blue signal, and the loss of one green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2135-200	ZytoLight SPEC ERG/TMPRSS2 TriCheck Probe CE IVD	●/●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC DiGeorge/Phelan McDermid Dual Color Probe

CE IVD

Background

The ZytoLight® SPEC DiGeorge/Phelan McDermid Dual Color Probe is designed to detect deletions affecting the chromosomal regions 22q11.21 harboring the HIRA (a.k.a. TUPLE1) gene and 22q13.33 harboring the SHANK3 (a.k.a. prosap2) gene, respectively..

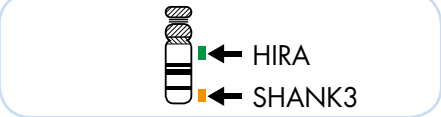
The 22q11.2 deletion syndrome (22q11.2DS), also known as velocardiofacial syndrome (VCFS) and DiGeorge syndrome, is a genetic disorder caused by hemizygous microdeletions on chromosome 22q11.2, with population prevalence of about 1 to 4,000 births. The characteristic phenotype of 22q11.2DS includes cardiac defects, velopharyngeal insufficiency, immune deficiency due to thymic aplasia, growth restriction, and deficits in cognitive abilities.

The 22q11.2 deletion usually occurs by meiotic non-allelic homologous recombination events between low copy repeats on chromosome 22q11.2 termed LCR22. There are eight LCR22s that span the 22q11.2 region termed LCR22A through LCR22H. The majority (90%) of 22q11.2DS patients show a recurrent 3 Mb deletion between LCR22A and LCR22D harboring the HIRA gene.

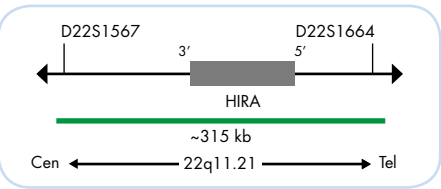
The 22q13.3 deletion syndrome (Phelan-McDermid syndrome) typically results from deletions of 100 kb to 9 Mb involving the distal long arm of chromosome 22. Almost all of these deletions include the gene SHANK3 that encodes a scaffold protein in the postsynaptic densities of excitatory synapses, connecting membrane-bound receptors to the actin cytoskeleton. This syndrome is characterized by neurological deficits, which include global developmental delay, moderate to severe intellectual impairment, absent or severely delayed speech, and neonatal hypotonia.

Probe Description

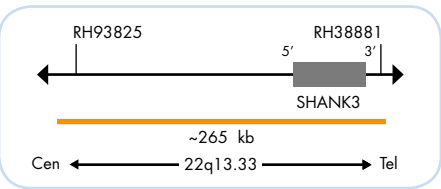
The SPEC DiGeorge/Phelan McDermid Dual Color Probe is a mixture of an orange fluorochrome direct labeled probe spanning the HIRA gene region at 22q11.21 and a green fluorochrome direct labeled probe spanning the SHANK3 gene region at 22q13.33.



Ideogram of chromosome 22 indicating the hybridization locations.



SPEC HIRA Probe map (not to scale).

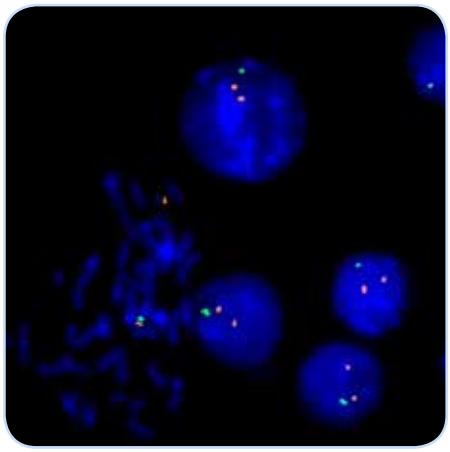


SPEC SHANK3 Probe map (not to scale).

References
Burnside RD (2015) Cytogenet Genome Res 146: 89-99.
Morrow BE, et al. (2018) Am J Med Genet A 176: 2070-81.
Phelan K & McDermid HE (2012) Mol Syndromol 2: 186-201.
Scambler PJ, et al. (1991) Genomics 10: 201-6.
Watt JL, et al. (1985) J Med Genet 22: 283-7.

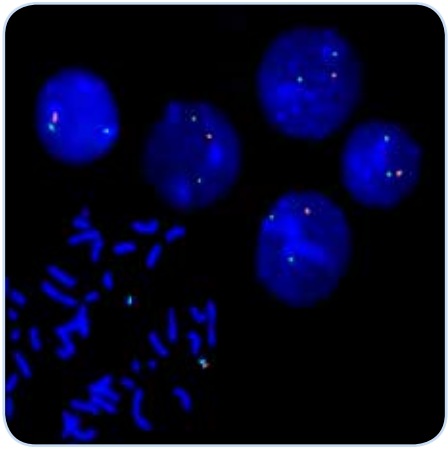
Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletion of the HIRA gene locus, a reduced number of orange signals will be observed. In a cell with deletion of the SHANK3 gene locus, a reduced number of green signals will be observed.



Lymphocytes and metaphase chromosomes from a DiGeorge syndrome case showing a HIRA deletion as indicated by the loss of one green signal.

Kindly provided by Dr. Liehr, Jena, Germany.



Lymphocytes and metaphase chromosomes from a Phelan-McDermid syndrome case showing a SHANK3 deletion as indicated by the loss of one orange signal.

Kindly provided by Dr. Kazmierczak, Bremen, Germany.

Prod. No.	Product	Label	Tests* (Volume)
Z-2299-50	ZytoLight SPEC DiGeorge/Phelan McDermid Dual Color Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC DiGeorge Triple Color Probe

CE IVD

Background

The ZytoLight® SPEC DiGeorge Triple Color Probe is designed to detect deletions affecting the chromosomal regions 22q11.21 harboring the genes HIRA (a.k.a. TUPLE1) and CRKL as well as 22q11.21-q11.22 harboring the MAPK1 (a.k.a. PRKM2, ERK) gene.

The 22q11.2 deletion syndrome (22q11.2DS), also known as velocardiofacial syndrome (VCFS) and DiGeorge syndrome, is a genetic disorder caused by hemizygous microdeletions on chromosome 22q11.2, with population prevalence of about 1 in 4,000 births. The characteristic phenotype of 22q11.2DS includes cardiac defects, immune deficiency, growth restriction, and deficits in cognitive abilities.

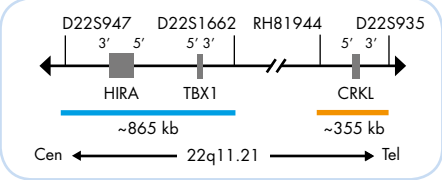
The 22q11.2 deletion usually occurs by meiotic non-allelic homologous recombination events between low copy repeats on chromosome 22q11.2 termed LCR22. There are eight LCR22s that span the 22q11.2 region termed LCR22A through LCR22H. The majority (90%) of 22q11.2DS patients show a recurrent 3 Mb deletion between LCR22A and LCR22D while 8% harbor a nested 1.5 Mb deletion (LCR22A-B). Some rare atypical deletions of shorter size and in variable locations have also been reported (e.g., LCR22B-D and LCR22C-D). Classic FISH probes for the detection of 22q11.2DS target the HIRA gene mapping to the LCR22A-B region, and thus, miss deletions that occur outside this region. The DiGeorge Triple Color Probe additionally targets CRKL that maps to the LCR22C-D region allowing the detection of rare deletions.

Various deletions of more distal regions (between LCR22D-H) have also been reported and result in phenotypic features similar to 22q11.2DS. FISH probes targeting MAPK1, which maps to the LCR22D-E region, can be used for the detection of this 22q11.2 distal deletion syndrome.

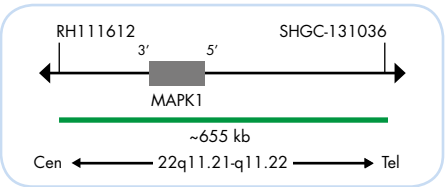
Probe Description

The SPEC DiGeorge Triple Color Probe is a mixture of a blue fluorochrome direct labeled probe spanning the HIRA gene region at 22q11.21, an orange fluorochrome direct labeled probe spanning the CRKL gene region at 22q11.21, and a green fluorochrome direct labeled probe spanning the MAPK1 gene region at 22q11.21-q11.22. The MAPK1 targeting probe additionally serves as a reference in case of a deletion of the HIRA and CRKL gene loci (LCR22A-D).

Ideogram of chromosome 22 indicating the hybridization locations.



SPEC HIRA/SPEC CRKL Probe map (not to scale).



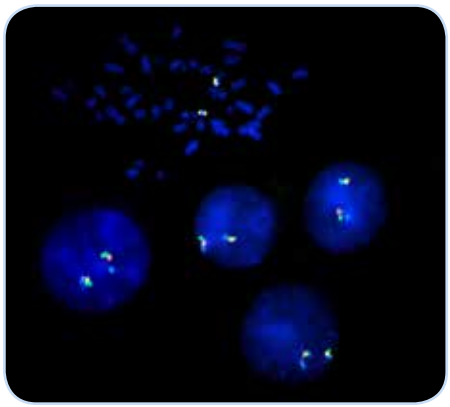
SPEC MAPK1 Probe map (not to scale).

References

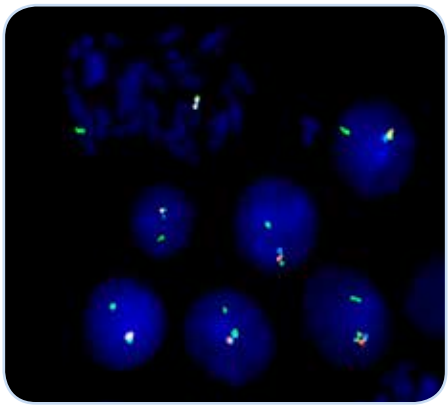
Ben-Shachar S, et al. (2008) Am J Hum Genet 82: 214-21.
Burnside RD (2015) Cytogenet Genome Res 146: 89-99.
Michaelovsky E, et al. (2012) BMC Med Genet 13: 122.
Morrow BE, et al. (2018) Am J Med Genet A 176: 2070-81.
Scambler PJ, et al. (1991) Genomics 10: 201-6.

Results

In a normal interphase nucleus, two blue, two orange, and two green signals are expected. In a cell with deletion of the HIRA and/or the CRKL gene locus, a reduced number of blue and/or orange signals will be observed, respectively. In a cell with deletion of the MAPK1 gene locus, a reduced number of green signals will be observed.



SPEC DiGeorge Triple Color Probe hybridized to normal interphase cells as indicated by two orange, two green, and two blue signals and to metaphase chromosomes of a normal cell.



Lymphocytes and metaphase chromosomes from a DiGeorge syndrome case showing a HIRA/CRKL deletion as indicated by the loss of one blue and one orange signal.

Kindly provided by Dr. Liehr, Jena, Germany.

Prod. No.	Product	Label	Tests* (Volume)
Z-2289-50	ZytoLight SPEC DiGeorge Triple Color Probe CE IVD	●/●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC IGL Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC IGL Dual Color Break Apart Probe is designed to detect rearrangements affecting the chromosomal region 22q11.22 harboring the IGL (immunoglobulin lambda locus, a.k.a., IGλ) gene cluster region.

Translocations involving the immunoglobulin (IG) genes are recurring events of B-cell oncogenesis. In all of these translocations, an oncogene is activated and overexpressed by juxtaposing this oncogene to IG regulatory sequences.

Burkitt lymphoma (BL) is characterized by reciprocal translocations involving the MYC gene and one of the IG loci. The majority of translocations involve the immunoglobulin heavy chain (IGH) locus while a minor part involves the immunoglobulin light chain loci, either the kappa light chain (IGK) or the lambda light chain (IGL). IGK and IGL rearrangements resulting from the variant translocations t(2;8)(p11.2;q24.21) and t(8;22)(q24.21;q11.2), respectively, have been detected in up to 25% of BL cases.

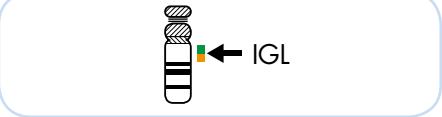
In non-Hodgkin lymphoma (NHL) harboring IG-MYC rearrangements, the MYC translocation partner is IGK and IGL in 8 and 22% of the cases, respectively.

IG translocations have been reported in several B-cell lineage malignancies other than BL including atypical Burkitt/Burkitt-like lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, mantle cell lymphoma, and multiple myeloma. The detection of IGK and IGL involvement in lymphomas by Fluorescence *in situ* Hybridization may prove a valuable diagnostic and prognostic tool.

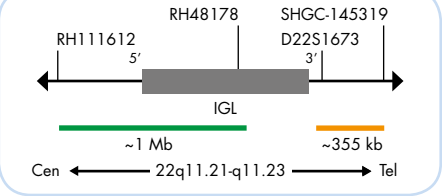
References
Cario G, et al. (2000) Br J Haematol 110: 537-46.
Einerson RR, et al. (2006) Leukemia 20: 1790-9.
Martín-Subero JI, et al. (2002) Int J Cancer 98: 470-4.
Poulsen TS, et al. (2002) Leukemia 16: 2148-55.

Probe Description

The SPEC IGL Dual Color Break Apart Probe is a mixture of a green fluorochrome direct labeled probe hybridizing proximal to the IGL breakpoint region at 22q11.21-q11.22 and an orange fluorochrome direct labeled probe hybridizing distal to the IGL breakpoint region at 22q11.22-q11.23.



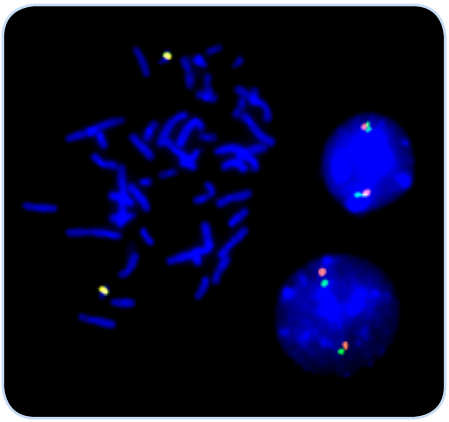
Ideogram of chromosome 22 indicating the hybridization locations.



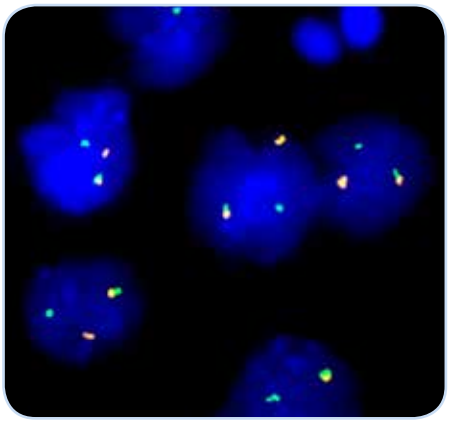
SPEC IGL Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the IGL locus at 22q11.22, two orange/green fusion signals are expected. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal IGL locus and one IGL locus affected by a translocation.



SPEC IGL Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals in each nucleus and to metaphase chromosomes of a normal cell.



Cell line with an IGL translocation affecting the 22q11.21-q11.23 locus as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2286-50	ZytoLight SPEC IGL Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC SMARCB1/22q12 Dual Color Probe

CE IVD

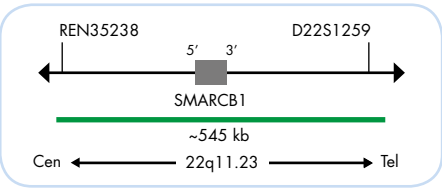
Background

The ZytoLight® SPEC SMARCB1/22q12 Dual Color Probe is designed for the detection of deletions of the chromosomal region harboring the SMARCB1 gene.
The SMARCB1 (SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily b, member 1, a.k.a. INI1, SNF5, or BAF47) gene is located on chromosome 22q11.23 and encodes a tumor suppressor.
Rhabdoid tumors are highly malignant neoplasms that typically arise in infancy and early childhood. They are classified as atypical teratoid/rhabdoid tumors (AT/RT) when they occur in the CNS or as malignant rhabdoid tumors (MRT) when they are found in renal or extra-renal sites. The vast majority of AT/RTs and MRTs are characterized by loss of function of the SMARCB1 gene due to deletions or mutations. The molecular alterations are often bi-allelic resulting in complete loss of this tumor suppressor gene, and thus in cell cycle progression.
Patients with germline alterations of SMARCB1, including deletions, duplications, and mutations, were found to be predisposed to malignant rhabdoid tumors and schwannomatosis.
Moreover, deletions of the SMARCB1 gene were found to occur in patients with highly aggressive renal medullary carcinoma (RMC), epithelioid sarcoma, and poorly differentiated sarcoma.
The identification of SMARCB1 deletions by FISH may represent a powerful adjunctive diagnostic tool useful in the differential diagnosis of rhabdoid tumors. Moreover, prenatal testing should be performed in situations where alterations of SMARCB1 have been documented in the family.

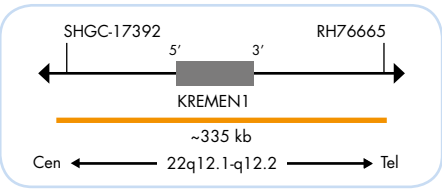
Probe Description

The SPEC SMARCB1/22q12 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC SMARCB1 probe hybridizing to the human SMARCB1 gene in the chromosomal region 22q11.23 and an orange fluorochrome direct labeled SPEC 22q12 probe specific for the KREMEN1 (kringle containing transmembrane protein 1) gene region in 22q12.1-q12.2. Due to cross-hybridizations of chromosome 22 alpha satellites to other centromeric regions, probes specific for 22q12 are frequently used for chromosome 22 copy number detection.

Ideogram of chromosome 22 indicating the hybridization locations.



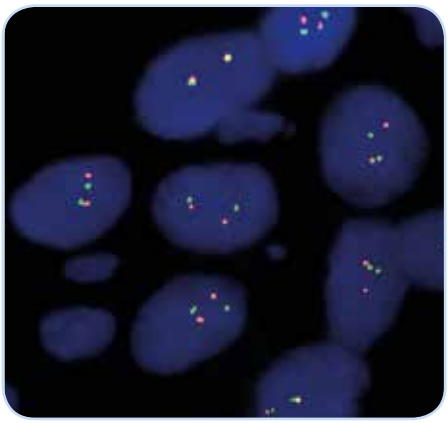
SPEC SMARCB1 Probe map (not to scale).



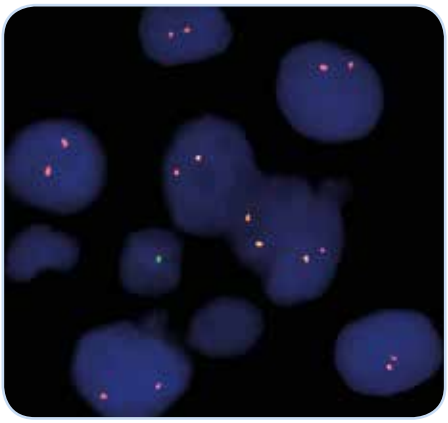
SPEC 22q12 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletion of the SMARCB1 gene locus, a reduced number of green signals will be observed. Deletions affecting only parts of the SMARCB1 gene might result in a normal signal pattern with green signals of reduced size.



SPEC SMARCB1/22q12 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals per nucleus.



SPEC SMARCB1/22q12 Dual Color Probe hybridized to epithelioid sarcoma tissue section with biallelic deletion of the SMARCB1 gene as indicated by missing green signals in the nuclei.

References
Calderaro J, et al. (2012) Histopathology 61: 428-35.
Eaton KW, et al. (2011) Pediatr Blood Cancer 56: 7-15.
Mobley BC, et al. (2010) Acta Neuropathol 120: 745-53.
Roberts CW & Biegel JA (2009) Cancer Biol Ther 8: 412-6.
Sullivan LM, et al. (2013) Mod Pathol 26: 385-92.

Prod. No.	Product	Label	Tests* (Volume)
Z-2178-50	ZytoLight SPEC SMARCB1/22q12 Dual Color Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC EWSR1 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC EWSR1 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 22q12.2 harboring the EWSR1 (EWS RNA binding protein 1, a.k.a. EWS) gene.

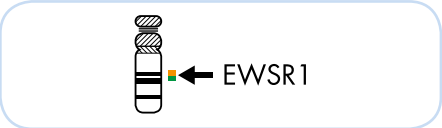
Translocations involving the chromosomal region 22q12.2 are found in 90-95% of patients with Ewing sarcoma or peripheral primitive neuroectodermal tumors (PNET). Ewing sarcoma is the second most common, highly malignant bone tumor in children and young adults. The most frequent translocation involving the EWSR1 gene region is t(11;22)(q24.3;q12.2) juxtaposing the EWSR1 gene in 22q12.2 next to the FLI-1 (friend leukemia virus integration 1) locus in 11q24.3. FLI-1 is a member of the ETS family of transcription factors. Less frequently, EWSR1 can also be fused to ERG, a transcription factor closely related to FLI-1 but located in 21q22.2.

For prognosis and appropriate treatment it is important to differentiate Ewing sarcoma/PNET from classic neuroblastoma, Wilms tumor, and rhabdomyosarcoma. In combination with the histopathological diagnosis, detection of the EWSR1 rearrangements by FISH can be used to confirm the diagnosis of Ewing sarcoma/PNET.

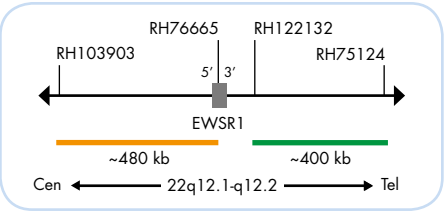
References
Bridge RS, et al. (2006) Mod Pathol 19: 1-8.
Delattre O, et al. (1992) Nature 359: 162-5.
Lee J, et al. (2005) Cancer Genet Cytogenet 159: 177-80.
Rekhi B, et al. (2012) Virchows Arch 461: 687-97.
Romeo S & Dei Tos AP (2010) Virchows Arch 456: 219-34.
Sandberg AA & Bridge JA (2000) Cancer Genet Cytogenet 123: 1-26.
Yang L, et al. (2012) Hum Pathol 43: 1463-70.
Zucman J, et al. (1993) EMBO J 12: 4481-7.

Probe Description

The SPEC EWSR1 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 22q12.1-q12.2 band. The orange fluorochrome direct labeled probe hybridizes proximal and extends inward into intron 4 of the EWSR1 gene, the green fluorochrome direct labeled probe hybridizes distal to that gene.



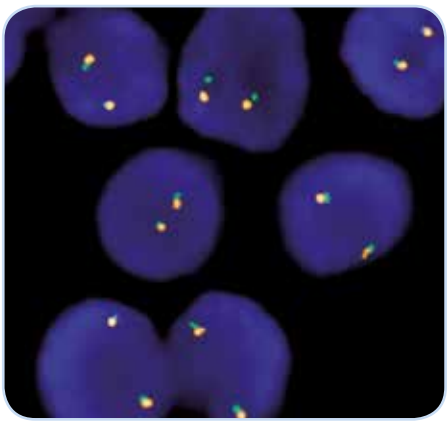
Ideogram of chromosome 22 indicating the hybridization locations.



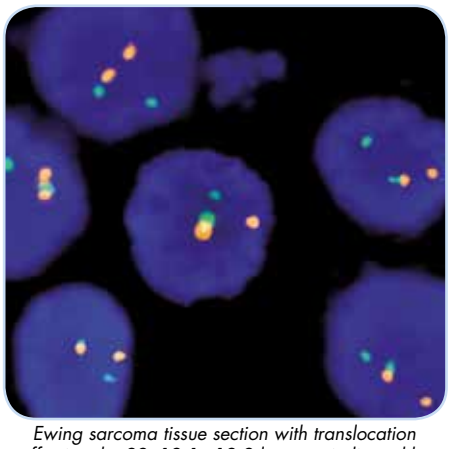
SPEC EWSR1 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 22q12.1-q12.2 band two orange/green fusion signals are expected representing two normal (non-rearranged) 22q12.1-q12.2 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 22q12.1-q12.2 locus and one 22q12.1-q12.2 locus affected by a 22q12.1-q12.2 translocation.



SPEC EWSR1 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Ewing sarcoma tissue section with translocation affecting the 22q12.1-q12.2 locus as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2096-50	ZytoLight SPEC EWSR1 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2096-200	ZytoLight SPEC EWSR1 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC EWSR1/FLI1 TriCheck™ Probe

CE IVD

Background

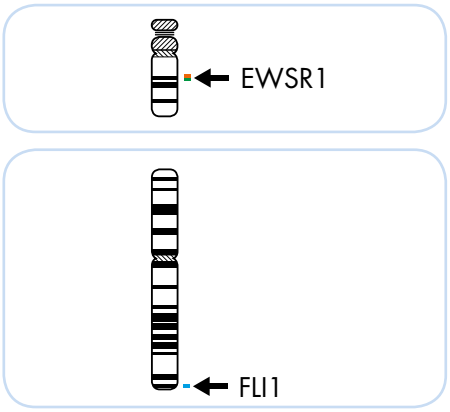
The ZytoLight® SPEC EWSR1/FLI1 TriCheck™ Probe is designed to detect translocations involving the chromosomal region 22q12.2 harboring the EWSR1 (EWS RNA binding protein 1, a.k.a. EWS) gene and the chromosomal region 11q24.3 harboring the FLI1 (Fli-1 proto-oncogene, ETS transcription factor, a.k.a. EWSR2) gene. Translocations involving the chromosomal region 22q12.2 are found in 90-95% of patients with Ewing sarcoma or peripheral primitive neuroectodermal tumors (PNET). Ewing sarcoma is the second most common, highly malignant bone tumor in children and young adults. The most frequent translocation involving the EWSR1 gene region is t(11;22)(q24.3;q12.2) juxtaposing the EWSR1 gene in 22q12.2 next to the FLI1 locus. FLI1 is a member of the ETS family of transcription factors. Less frequently, EWSR1 can also be fused to ERG, a transcription factor closely related to FLI1 but located in 21q22.2.

For prognosis and appropriate treatment it is important to differentiate Ewing sarcoma/PNET from classic neuroblastoma, Wilms tumor, and rhabdomyosarcoma. In combination with the histopathological diagnosis, detection of the EWSR1 rearrangements by FISH can be used to confirm the diagnosis of Ewing sarcoma/PNET.

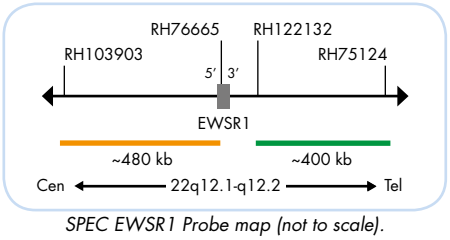
References
Bridge RS, et al. (2006) Mod Pathol 19: 1-8.
Delattre O, et al. (1992) Nature 359: 162-5.
Lee J, et al. (2005) Cancer Genet Cytogenet 159: 177-80.
Romeo S & Dei Tos AP (2010) Virchows Arch 456: 219-34.
Sandberg AA & Bridge JA (2000) Cancer Genet Cytogenet 123: 1-26.
Zucman J, et al. (1993) EMBO J 12: 4481-7.

Probe Description

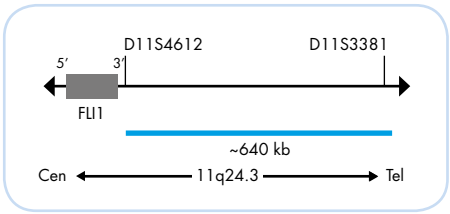
The SPEC EWSR1/FLI1 TriCheck™ Probe is a mixture of three direct labeled probes hybridizing to the 22q12.1-q12.2 and 11q24.3 bands. The orange fluorochrome direct labeled probe hybridizes proximal to the EWSR1 breakpoint region at 22q12.1-q12.2 and the green fluorochrome direct labeled probe hybridizes distal to the EWSR1 breakpoint region at 22q12.2. The blue fluorochrome direct labeled probe hybridizes distal to the FLI1 gene at 11q24.3.



Ideograms of chromosomes 22 (above) and 11 (below) indicating the hybridization locations.



SPEC EWSR1 Probe map (not to scale).



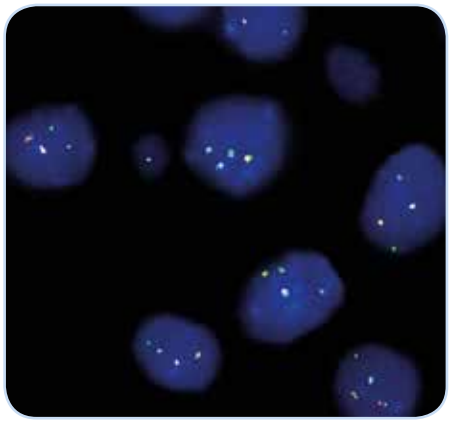
SPEC FLI1 Probe map (not to scale).

Results

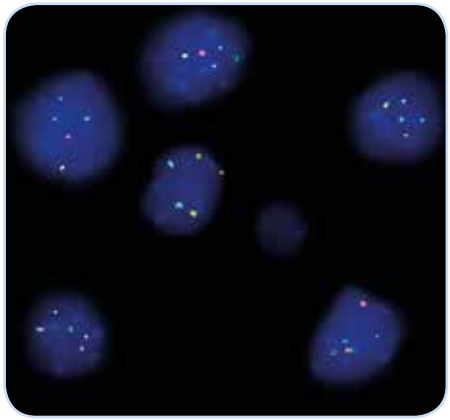
In an interphase nucleus without FLI1-EWSR1 rearrangement, two green/orange fusion signals and two blue signals are expected.

A FLI1-EWSR1 fusion is indicated by one separate orange signal co-localizing with one blue signal and one separate green signal.

An EWSR1 translocation without involvement of FLI1 is indicated by the split of one green/orange fusion signal without co-localization of the separated orange signal with one blue signal.



Ewing sarcoma tissue section with FLI1-EWSR1 fusion as indicated by orange/blue fusion signals.



Ewing sarcoma tissue section with a non-FLI1 EWSR1 rearrangement as indicated by the lack of co-localization of the separated orange signal with one blue signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2183-50	ZytoLight SPEC EWSR1/FLI1 TriCheck Probe CE IVD	●/●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC PDGFB Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC PDGFB Dual Color Break Apart Probe is designed for the detection of specific translocations involving the chromosomal region 22q13.1 harboring the PDGFB (a.k.a. SIS) gene.

The PDGFB gene (platelet derived growth factor receptor beta) belongs to the platelet-derived growth factor family and encodes a protein which acts as a receptor tyrosine kinase.

The most frequent translocation involving the PDGFB gene is t(17;22)(q21.3;q13.1) juxtaposing the PDGFB gene next to the COL1A1 gene in 17q22. Reciprocal translocations involving t(17;22)(q21.3;q13.1) are characteristic for dermatofibrosarcoma protuberans (DFSP) patients. DFSP is a highly recurrent, infiltrative skin tumor of intermediate malignancy.

The rearrangements are cytogenetically characterized by the presence of supernumerary ring chromosomes containing low-level amplified sequences from chromosomes 17q22-qter and 22q10-q13.1, or unbalanced derivatives of the t(17;22)(q21.3;q13.1) translocation.

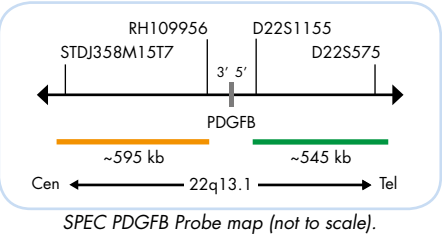
The rearrangement results in a COL1A1-PDGFB fusion protein which is post-transcriptionally processed to a functional platelet-derived growth factor beta chain (PDGFB) protein.

The importance of accurately diagnosing DFSP lies in its intermediate malignant nature and the availability of a therapy with significant anti-neoplastic activity but relatively minor adverse effects for cases not amenable to surgical excision.

Probe Description

The SPEC PDGFB Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 22q13.1 band. The orange fluorochrome direct labeled probe hybridizes proximal to the breakpoint region of the PDGFB gene, and the green fluorochrome direct labeled probe hybridizes distal to the breakpoint region of the PDGFB gene.

Ideogram of chromosome 22 indicating the hybridization locations.

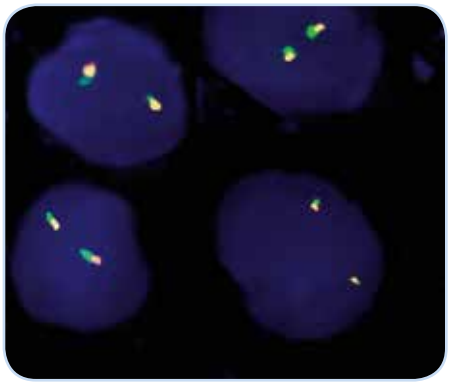


SPEC PDGFB Probe map (not to scale).

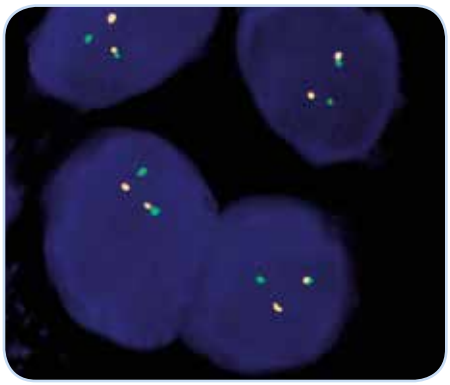
References
Broom RJ, et al. (2012) Clin Genitourin Cancer 10: 202-6.
Labropoulos SV & Razis ED (2007) Biologics 4: 347-53.
Patel KU, et al. (2008) Human Pathol 39: 184-93.
Shimizu A, et al. (1999) Cancer Res 59: 3719-23.
Simon MP, et al. (1997) Nat Genet 15: 95-8.
Sirvent N, et al. (2003) Genes Chromosomes Cancer 37: 1-19.

Results

In an interphase nucleus lacking a translocation involving the 22q13.1 band two orange/green fusion signals are expected representing two normal (non-rearranged) 22q13.1 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 22q13.1 locus and one 22q13.1 locus affected by a 22q13.1 translocation.



SPEC PDGFB Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Dermatofibrosarcoma protuberans tissue section with translocation affecting the 22q13.1 locus as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2119-50	ZytoLight SPEC PDGFB Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2119-200	ZytoLight SPEC PDGFB Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC CRLF2 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC CRLF2 Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal regions Xp22.33 and Yp11.32 harboring the CRLF2 (cytokine receptor-like factor 2, a.k.a. CRL2, TSLPR) gene.

The CRLF2 protein interacts with IL7R to form a receptor for TSLP, binding of which activates cell signaling through JAK/STAT pathways.

Approximately 7% of patients with B-cell precursor ALL (B-ALL) and more than 50% of B-ALL in children with Down syndrome harbor alterations involving the CRLF2 gene. These include the translocations t(X;14)(p22.33;q32.3) or t(Y;14)(p11.32;q32.3) which fuse the entire CRLF2 gene to the immunoglobulin heavy chain enhancer region (IGH-CRLF2).

Another common alteration is an interstitial deletion involving the pseudoautosomal region (PAR1) of the sex chromosomes upstream of CRLF2, juxtaposing the first non-coding exon of P2RY8 to the entire coding region of CRLF2 (P2RY8-CRLF2).

These rearrangements, which are often accompanied by JAK mutations, result in overexpression of CRLF2 and were shown to contribute to lymphoid transformation.

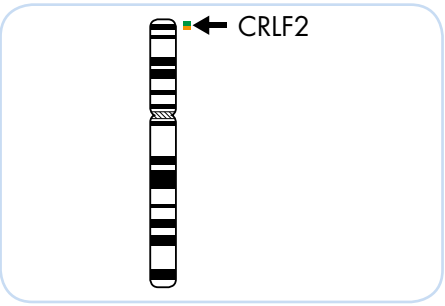
Patients with CRLF2 rearrangements and JAK mutations have a poor event-free and overall survival.

Moreover, the detection of CRLF2 rearrangements by FISH may help in selecting B-ALL patients eligible for therapy with inhibitors of the JAK/STAT pathway.

References
Harvey RC, et al. (2010) Blood 115: 5312-21.
Mullighan CG, et al. (2009) Nat Genet 41: 1243-6.
Roberts KG, et al. (2014) N Engl J Med 371: 1005-15.
Russell LJ, et al. (2009) Blood 114: 2688-98.
Tasian SK, et al. (2012) Blood 120: 833-42.

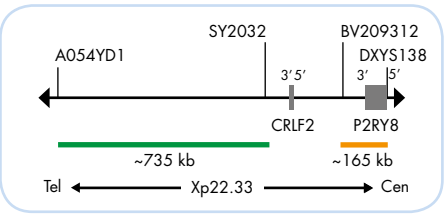
Probe Description

The SPEC CRLF2 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the Xp22.33 and Yp11.32 band, respectively. The orange fluorochrome direct labeled probe hybridizes proximal to the CRLF2 gene at Xp22.33 and Yp11.32, the green fluorochrome direct labeled probe hybridizes distal to the CRLF2 gene at Xp22.33 and Yp11.32.

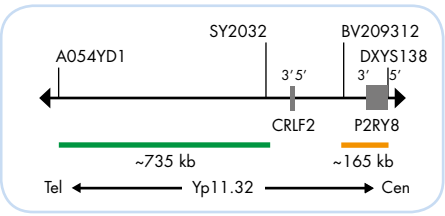


Ideogram of chromosome X indicating the hybridization locations.

Ideogram of chromosome Y indicating the hybridization locations.



SPEC CRLF2 Probe map (not to scale).



SPEC CRLF2 Probe map (not to scale).

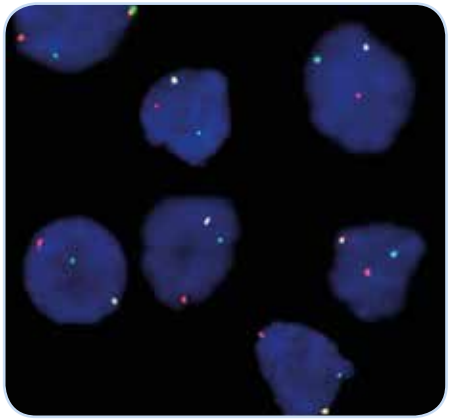
Results

In an interphase nucleus of a normal female cell lacking a translocation involving the Xp22.33 band, two orange/green fusion signals are expected representing normal (non-rearranged) Xp22.33 loci.

In an interphase nucleus of a normal male cell lacking a translocation involving the Xp22.33 or Yp11.32 band, two orange/green fusion signals are expected representing normal (non-rearranged) Xp22.33 and Yp11.32 loci.

A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal Xp22.33 or Yp11.32 locus and one Xp22.33 or Yp11.32 locus affected by a translocation.

Loss of the orange signals or orange signals of reduced size are the result of deletions proximal to the CRLF2 breakpoint region.



Bone marrow smear with translocation affecting the CRLF2 gene locus as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2201-50	ZytoLight SPEC CRLF2 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® SPEC TFE3 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC TFE3 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region Xp11.23 harboring the TFE3 (transcription factor binding to IGHM enhancer 3, a.k.a. TFEA) gene.

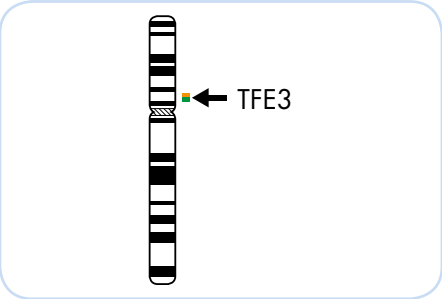
Translocations involving the chromosomal region Xp11.2 are frequently detected in renal cell carcinomas (RCCs) which usually affect children and adolescents. The Xp11.2 translocation RCCs represent a predominant and aggressive subtype in the pediatric age group but can also occur in adults. Macroscopically, Xp11.2 translocation RCCs may mimic conventional clear cell RCCs and thus, differential diagnosis of Xp11.2 translocation RCCs is clinically important.

Additionally, the unbalanced chromosomal translocation of der(17)t(X;17)(p11.23;q25) is cytogenetically characteristic for alveolar soft part sarcoma (ASPS). ASPS is a rare high grade mesenchymal malignancy affecting mainly adolescents. This translocation fuses the TFE3 gene at Xp11.23 to the ASPSCR1 (alveolar soft part sarcoma chromosome region, candidate 1, a.k.a ASPL) gene on 17q25.3. Diagnosis of ASPS is often difficult due to histologic overlap with other tumors, particularly in small biopsies. Thus, FISH analysis can improve accuracy of ASPS diagnosis.

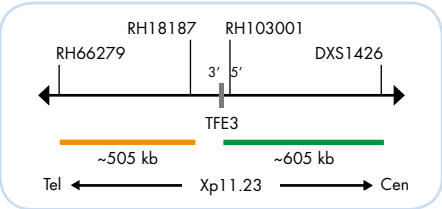
References
Argani P, et al. (2001) Am J Pathol 159: 179-92.
Armah HB, et al. (2009) Diagn Pathol 4: 15.
Dijkhuizen T, et al. (1995) Genes Chromosomes Cancer 14: 43-50.
Ladanyi M, et al. (2001) Oncogene 20: 48-57.
Llamas-Velasco M, et al. (2013) Histopathology 63: 122-9.
Pflueger D, et al. (2013) Neoplasia 15: 1231-40.
Wiliams A, et al. (2011) Virchows Arch 458: 291-300.
Wu A, et al. (2008) Histopathology 53: 533-44.
Yan BC, et al. (2009) Arch Pathol Lab Med 133: 1026-32.

Probe Description

The SPEC TFE3 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the Xp11.23 band. The orange fluorochrome direct labeled probe hybridizes distal to the TFE3 gene, the green fluorochrome direct labeled probe hybridizes proximal to that gene.



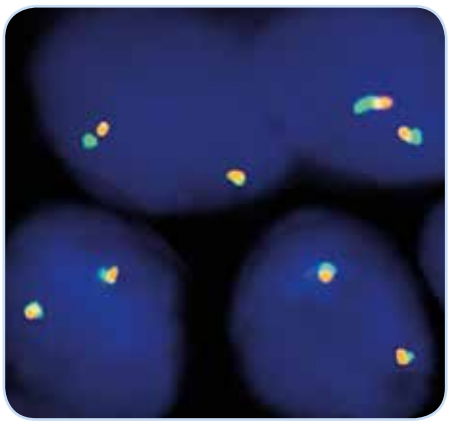
Ideogram of chromosome X indicating the hybridization locations.



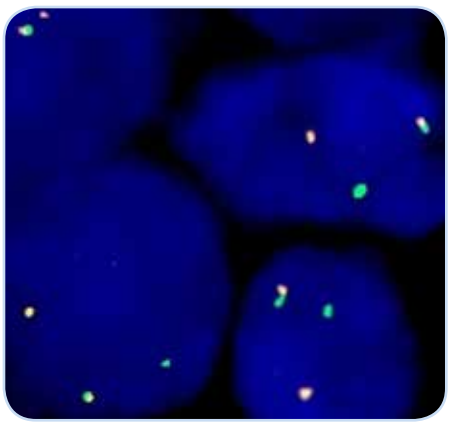
SPEC TFE3 Probe map (not to scale).

Results

In a female interphase nucleus lacking a translocation involving the Xp11.23 band two orange/green fusion signals are expected representing two normal (non-rearranged) Xp11.23 loci. In a normal male interphase nucleus one orange/green fusion signal is expected representing one normal (non-rearranged) Xp11.23 locus. One separate green and separate orange signal indicate one Xp11.23 locus affected by a translocation.



SPEC TFE3 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Renal cell carcinoma section with translocation affecting the Xp11.23 locus as indicated by one non-rearranged green/orange fusion signal, one separate green signal, and one separate orange signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2109-50	ZytoLight SPEC TFE3 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2109-200	ZytoLight SPEC TFE3 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® Probes for Chromosome Enumeration

CE IVD

Background

The ZytoLight® Chromosome Enumeration Probes are designed for identification and enumeration of human chromosomes in interphase cells and as an adjunct to standard karyotyping in metaphases. These probes will produce sharp, bright signals specific for each individual chromosome.

CEN Probe Description

For most chromosomes, direct labeled ZytoLight® CEN™ Probes hybridizing to highly repetitive human satellite DNA sequences mainly located at the centromeric regions of chromosomes are applicable.

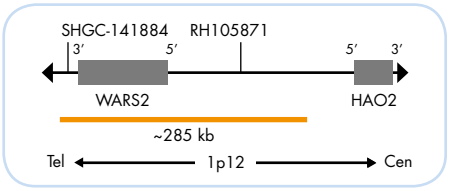
SPEC Probe Description

As several chromosomes share the same repetitive sequences resulting in cross-hybridization signals, they cannot be differentiated by centromere specific probes. Instead, these chromosomes can be identified by direct labeled ZytoLight® SPEC™ Probes hybridizing in close proximity to the respective satellite DNA sequences or to other chromosome specific loci.

Results

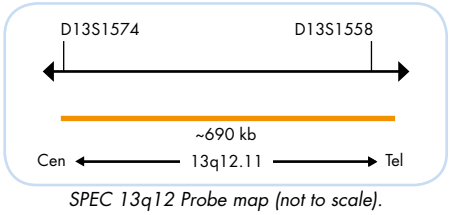
In a normal interphase nucleus, two signals are expected using Chromosome Enumeration Probes specific for autosomes. Using chromosome Y specific probes will result in normal male cells in one signal and in normal female cells in no signal. Using chromosome X specific probes will result in normal male cells in one signal and in normal female cells in two signals per nucleus. Other signal patterns indicate numerical aberrations of the respective chromosome.

ZytoLight® SPEC Probe Maps



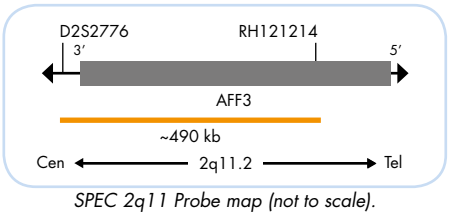
SPEC 1p12 Probe map (not to scale).

The ZytoLight® SPEC 1p12 Probe is designed to hybridize in close proximity of centromere 1 at 1p12 harboring WARS2 and HA02. Since chromosomes 1, 5, and 19 share the same repetitive sequences, they cannot be differentiated by probes detecting centromere specific repeats.



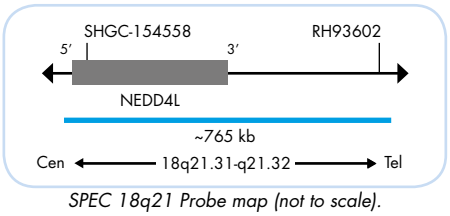
SPEC 13q12 Probe map (not to scale).

The ZytoLight® SPEC 13q12 Probe is designed to hybridize in close proximity of centromere 13 at 13q12.11. Since chromosomes 13 and 21 share the same repetitive sequences, they cannot be differentiated by probes detecting centromere specific repeats.



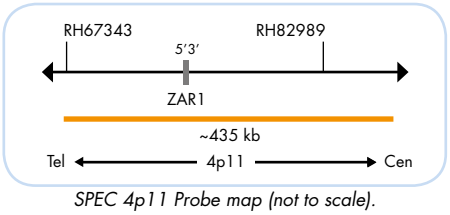
SPEC 2q11 Probe map (not to scale).

The ZytoLight® SPEC 2q11 Probe is specific for the AFF3 (AF4/FMR2 family, member 3) gene region in 2q11.2. Due to cross-hybridizations of chromosome 2 alpha satellites to other centromeric regions, probes specific for 2q11 are frequently used for chromosome 2 copy number detection.



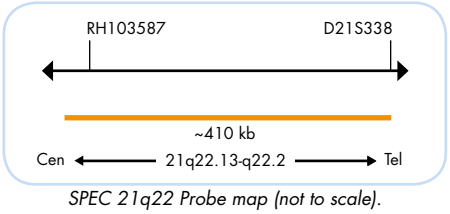
SPEC 18q21 Probe map (not to scale).

The SPEC 18q21 Probe, included in the ZytoLight® SPEC 18/CEN X/Y Triple Color Probe, is specific for NEDD4L (NEDD4 like E3 ubiquitin protein ligase) gene region in 18q21.31-q21.32.



SPEC 4p11 Probe map (not to scale).

The ZytoLight® SPEC 4p11 Probe is designed to hybridize in close proximity of centromere 4 at 4p11 harboring the ZAR1 (zygote arrest 1) gene. For an unambiguous enumeration of chromosome 4 the SPEC 4p11 is found to be more suitable.



SPEC 21q22 Probe map (not to scale).

The ZytoLight® SPEC 21q22 Probe hybridizes to the so-called Down Syndrome Critical Region on 21q22.13-q22.2 commonly duplicated in cases with partial trisomy 21. Since chromosomes 13 and 21 share the same repetitive sequences, they cannot be differentiated by probes detecting centromere specific repeats.

CE IVD

Prod. No.	Product	Alpha/Class. Sat.	Chr. Band	Label	Tests* (Volume)
Z-2101-200	ZytoLight SPEC 1p12 Probe CE IVD	-	1p12	●	20 (200 µl)
Z-2049-200	ZytoLight SPEC 2q11 Probe CE IVD	-	2q11.2	●	20 (200 µl)
Z-2001-200	ZytoLight CEN 3 Probe CE IVD	D3Z1	3p11.1-q11.1	●	20 (200 µl)
Z-2083-200	ZytoLight SPEC 4p11 Probe CE IVD	-	4p11	●	20 (200 µl)
Z-2002-200	ZytoLight CEN 6 Probe CE IVD	D6Z1	6p11.1-q11	●	20 (200 µl)
Z-2003-200	ZytoLight CEN 7 Probe CE IVD	D7Z1	7p11.1-q11.1	●	20 (200 µl)
Z-2004-50/-200	ZytoLight CEN 8 Probe CE IVD	D8Z2	8p11.1-q11.1	●	5/20 (50/200 µl)
Z-2067-200	ZytoLight CEN 9 Probe CE IVD	III D9Z3	9q12	●	20 (200 µl)
Z-2079-200	ZytoLight CEN 10 Probe CE IVD	D10Z1	10p11.1-q11.1	●	20 (200 µl)
Z-2005-200	ZytoLight CEN 11 Probe CE IVD	D11Z1	11p11.11-q11	●	20 (200 µl)
Z-2050-200	ZytoLight CEN 12 Probe CE IVD	D12Z3	12p11.1-q11	●	20 (200 µl)
Z-2085-200	ZytoLight SPEC 13q12 Probe CE IVD	-	13q12.11	●	20 (200 µl)
Z-2095-50/-200	ZytoLight SPEC 13/CEN 18/SPEC 21 Triple Color Probe CE IVD	D18Z1	13q12.11/18p11.1/21q22.13-q22.2	●/●/●	5/20 (50/200 µl)
Z-2164-200	ZytoLight SPEC 13/21 Dual Color Probe CE IVD	-	13q12.11/21q22.13-q22.2	●/●	20 (200 µl)
Z-2006-200	ZytoLight CEN 17 Probe CE IVD	D17Z1	17p11.1-q11.1	●	20 (200 µl)
Z-2007-200	ZytoLight CEN 18 Probe CE IVD	D18Z1	18p11.1-q11.1	●	20 (200 µl)
Z-2163-200	ZytoLight SPEC 18/CEN X/Y Triple Color Probe CE IVD	DXZ1/DYZ3	18q21.31-q21.32/Xp11.1-q11.1/Yp11.1-q11.1	●/●/●	20 (200 µl)
Z-2086-200	ZytoLight SPEC 21q22 Probe CE IVD	-	21q22.13-q22.2	●	20 (200 µl)
Z-2180-200	ZytoLight SPEC 21/CEN X/Yq12 Triple Color Probe CE IVD	DXZ1/ III DYZ1	21q22.13-q22.2/Xp11.1-q11.1/Yq12	●/●/●	20 (200 µl)
Z-2008-200	ZytoLight CEN X Probe CE IVD	DXZ1	Xp11.1-q11.1	●	20 (200 µl)
Z-2010-200	ZytoLight CEN Yq12 Probe CE IVD	III DYZ1	Yq12	●	20 (200 µl)
Z-2123-200	ZytoLight CEN Y (DYZ3) Probe CE IVD	DYZ3	Yp11.1-q11.1	●	20 (200 µl)
Z-2016-50/-200	ZytoLight CEN X/Yq12 Dual Color Probe CE IVD	DXZ1/III DYZ1	Xp11.1-q11.1/Yq12	●/●	5/20 (50/200 µl)
Z-2120-200	ZytoLight CEN X/Y Dual Color Probe CE IVD	DXZ1/ DYZ3	Xp11.1-q11.1/Yp11.1-q11.1	●/●	20 (200 µl)
Related Products					
Z-2279-20	ZytoLight Aneuploidy Panel 18/X/Y and 13/21 CE IVD Incl. ZytoLight SPEC 18/CEN X/Y Triple Color Probe, 0.2 ml (Z-2163-200); ZytoLight SPEC 13/21 Dual Color Probe, 0.2 ml (Z-2164-200)				20
Z-2104-5	ZytoLight Aneuploidy Panel X/Y and 13/18/21 CE IVD Incl. ZytoLight CEN X/Yq12 Dual Color Probe, 0.05 ml (Z-2016-50); ZytoLight SPEC 13/CEN 18/SPEC 21 Triple Color Probe, 0.05 ml (Z-2095-50)				5
Z-2104-20	ZytoLight Aneuploidy Panel X/Y and 13/18/21 CE IVD Incl. ZytoLight CEN X/Yq12 Dual Color Probe, 0.2 ml (Z-2016-200); ZytoLight SPEC 13/CEN 18/SPEC 21 Triple Color Probe, 0.2 ml (Z-2095-200)				20
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml				5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml				20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml				20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® Aneuploidy Panel 18/X/Y and 13/21

CE IVD

Background

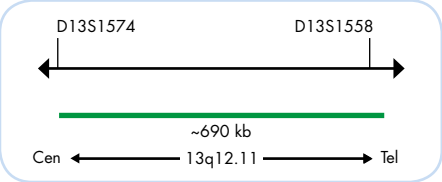
The ZytoLight® Aneuploidy Panel 18/X/Y and 13/21 is designed for chromosome enumeration of the chromosomes 13, 18, 21, X, and Y.

Trisomies of the autosomes 13, 18, or 21 (Down Syndrome) are common genomic aberrations. Aberrant numbers of the gonosomes X and Y are resulting in disorders of sex development (DSD). Diseases such as Ulrich-Turner-Syndrome (45, X) or Triple X Syndrome (47, XXX) may cause severe developmental and metabolic disorders. The prevalence of chromosomal abnormalities detectable in the newborn, including chromosome 13, 18, 21, X, and Y, is about 0.92%.

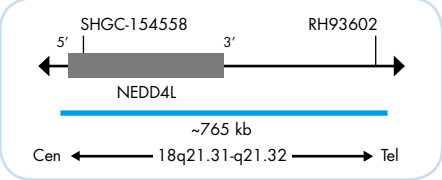
References
Gillenberg C, (1998) J Autism Dev Disord 28: 415-25.
Jacobs PA, et al. (1992) J Med Genet 29: 103-8.

Probe Description

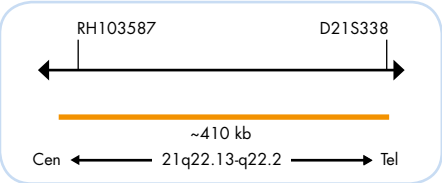
The ZytoLight® Aneuploidy Panel 18/X/Y and 13/21 is comprised of the ZytoLight® SPEC 18/CEN X/Y Triple Color Probe hybridizing to chromosome 18 specific sequences at 18q21.31-q21.32 and to the alpha satellites of the chromosomes X (DYZ1) and Y (DYZ3), and of the ZytoLight® SPEC 13/21 Dual Color Probe hybridizing to chromosome 13 and 21 specific sequences at 13q12.11 and 21q22.13-q22.2, respectively. Both probes are approved to be used with a hybridization time of 2 hours on cytological specimens.



SPEC 13q12 Probe map (not to scale).



SPEC 18q21 Probe map (not to scale).



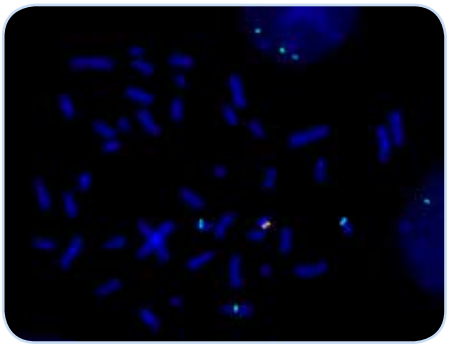
SPEC 21q22 Probe map (not to scale).

Results

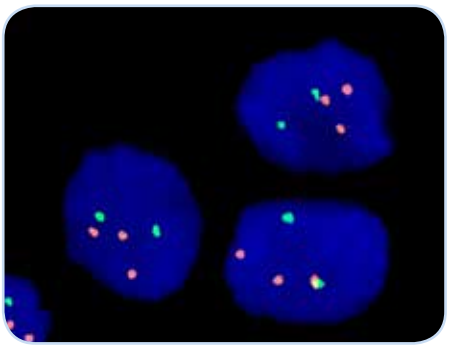
In an interphase nucleus of a normal cell using the ZytoLight® SPEC 13/21 Dual Color Probe, two green and two orange signals are expected.

In an interphase nucleus of a normal cell, using the ZytoLight® SPEC 18/CEN X/Y Triple Color Probe, two blue signals are expected. Two green signals are expected in a normal female cell, or one single green and one single orange signal is expected in a normal male cell.

Other signal patterns indicate numerical aberration of the respective chromosomes.



SPEC 18/CEN X/Y Triple Color Probe hybridized to interphase nuclei of normal male cells and to chromosomes of a metaphase spread.



SPEC 13/21 Dual Color Probe hybridized to interphase cells with trisomy of chromosome 21.

Prod. No.	Product	Label	Tests* (Volume)
Z-2279-20	ZytoLight Aneuploidy Panel 18/X/Y and 13/21 CE IVD		20 (200 µl)
Related Products			
Z-2164-200	ZytoLight SPEC 13/21 Dual Color Probe CE IVD	●/●	20 (200 µl)
Z-2163-200	ZytoLight SPEC 18/CEN X/Y Triple Color Probe CE IVD	●/●/●	20 (200 µl)
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoLight® Aneuploidy Panel X/Y and 13/18/21

CE IVD

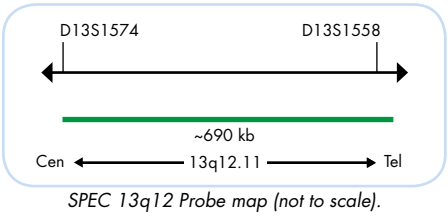
Background

The ZytoLight® Aneuploidy Panel X/Y and 13/18/21 is designed for enumeration of the chromosomes 13, 18, 21, X, and Y. Trisomies of the autosomes 13, 18, or 21 (Down Syndrome) are common genomic aberrations. Aberrant numbers of the gonosomes X and Y are resulting in disorders of sex development (DSD). Diseases such as Ulrich-Turner-Syndrome (45, X) or Triple X Syndrome (47, XXX) may cause severe developmental and metabolic disorders. The prevalence of chromosomal abnormalities detectable in the newborn including chromosomes 13, 18, 21, X, and Y, is about 0.92%.

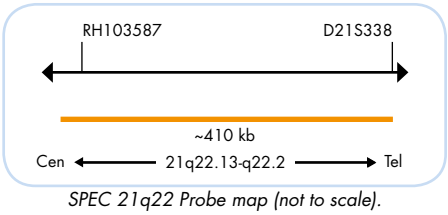
References
Gillenberg C, (1998) J Autism Dev Disord 28: 415-25.
Jacobs PA, et al. (1992) J Med Genet 29: 103-8.

Probe Description

The ZytoLight® Aneuploidy Panel X/Y and 13/18/21 is comprised of the ZytoLight® CEN X/Yq12 Dual Color Probe hybridizing to the alpha satellites of chromosome X (DYZ1) and to the classical satellite III of chromosome Y (DYZ1), and of the ZytoLight® SPEC 13/CEN 18/SPEC 21 Triple Color Probe hybridizing to the chromosome 13 and 21 specific sequences at 13q12.11 and 21q22.13-q22.2, respectively, and to the alpha satellites of chromosome 18. Both probes are approved to be used with a hybridization time of 2 hours on cytological specimens.



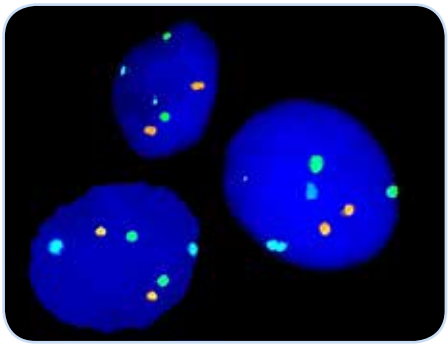
SPEC 13q12 Probe map (not to scale).



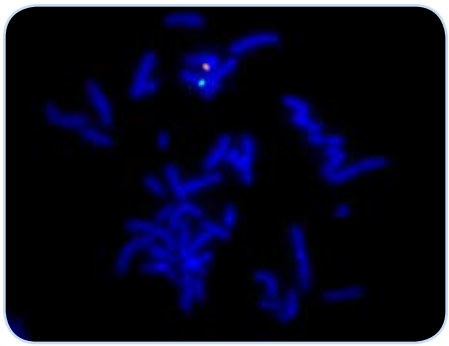
SPEC 21q22 Probe map (not to scale).

Results

In an interphase nucleus, using the ZytoLight® CEN X/Yq12 Dual Color Probe, two orange signals are expected in a normal female cell whereas one single orange and one single green signal is expected in a normal male cell.
In an interphase nucleus of a normal cell, using the ZytoLight® SPEC 13/CEN 18/SPEC 21 Triple Color Probe, two green, two blue, and two orange signals are expected.
Other signal patterns indicate numerical aberrations of the respective chromosomes.



SPEC 13/CEN 18/ SPEC 21 Triple Color Probe hybridized to normal interphase cells.



CEN X/Yq12 Dual Color Probe hybridized to metaphase chromosomes of a normal male cell.

Prod. No.	Product	Label	Tests* (Volume)
Z-2104-5/20	ZytoLight Aneuploidy Panel X/Y and 13/18/21 CE IVD		5/20 (50/200 µl)
Related Products			
Z-2095-50/-200	ZytoLight SPEC 13/CEN 18/ SPEC 21 Triple Color Probe CE IVD	●/●/●	5/20 (50/200 µl)
Z-2016-50/-200	ZytoLight CEN X/Yq12 Dual Color Probe CE IVD	●/●	5/20 (50/200 µl)
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

FlexISH®

Products for flexible FISH

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Simply Adapt the Hybridization Time to your Needs!

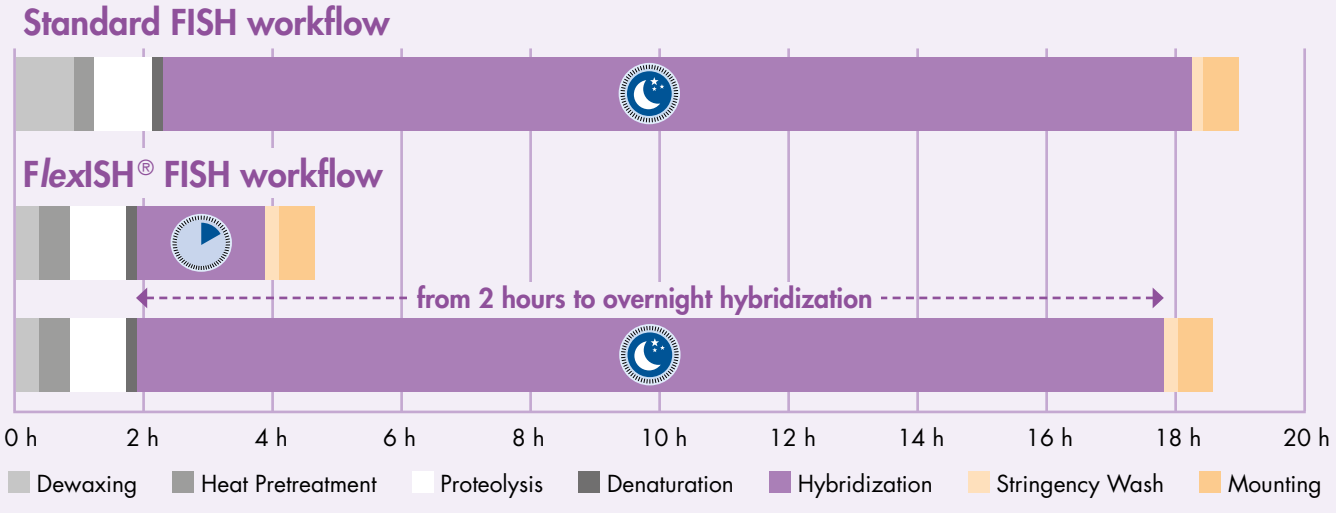
Introduction
F*lex*ISH® products are designed for identification of chromosomal aberrations on various specimens by FISH. Using the F*lex*ISH® products gives you the flexibility to choose between a 1-day (2 h hybridization) or a 2-day (overnight hybridization) protocol by adapting the hybridization time just according to your individual needs!

Advantages of F*lex*ISH®
- Hybridization time can be varied between 2 hours and overnight.
- With a hybridization temperature of 37°C the F*lex*ISH® protocol is fully compatible with routine workflows in pathology laboratories.
- Short hybridization time does not negatively affect the performance, specimen quality or diagnostic result[1].

F*lex*ISH® Kit - Convenient Solution
All F*lex*ISH® probes can be combined with the F*lex*ISH®-Tissue Implementation Kit to obtain reliable results already within 4.5 hours.
The F*lex*ISH® protocol can also be incorporated into the routine workflow with overnight hybridization providing the highest flexibility.

High-Quality FISH Results with flexible Hybridization Time

There is an excellent correlation between the FISH results obtained after overnight and short hybridization periods with regard to signal brightness, signal-to-noise ratio, and the diagnostic result[1].



References
[1] Brockhoff G, et al. (2016) Histopathology 69: 635-46.

Chromosome Index

Chr.	Band	Product Name	Product No.	Quantity	Page
1		no probes available yet			
2	2p23	FlexISH ALK/ROS1 DistinguISH™ Probe CE IVD	Z-2203-50/-200	50/200 µl	179
3	3q27	FlexISH BCL2/BCL6 DistinguISH™ Probe CE IVD	Z-2283-50/-200	50/200 µl	180
4-5		no probes available yet			
6	6q22.1	FlexISH ALK/ROS1 DistinguISH™ Probe CE IVD	Z-2203-50/-200	50/200 µl	179
7		no probes available yet			
8	8q24.21	FlexISH MYC/IGH TriCheck™ Probe CE IVD NEW	Z-2293-50	50 µl	181

CE IVD *only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

Chromosome Index

	Chr. Band	Product Name	Product No.	Quantity	Page
9		no probes available yet			
10	10p11.2	FlexISH RET/KIF5B TriCheck™ Probe CE IVD NEW	Z-2269-50/-200	50/200 µl	182
	10q11.2	FlexISH RET/KIF5B TriCheck™ Probe CE IVD NEW	Z-2269-50/-200	50/200 µl	182
11-13		no probes available yet			
14	14q32.3	FlexISH MYC/IGH TriCheck™ Probe CE IVD NEW	Z-2293-50	50 µl	181
15-16		no probes available yet			
17	17q12	FlexISH ERBB2/CEN 17 Dual Color Probe CE IVD	Z-2166-50/-200	50/200 µl	183
18	18q21.3	FlexISH BCL2/BCL6 DistinguISH™ Probe CE IVD	Z-2283-50/-200	50/200 µl	180
19-22		no probes available yet			
X, Y		no probes available yet			

CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.

Gene Index

HUGO Name	Synonym	Product Name	Product No.	Quantity	Page
ALK	CD246	FlexISH ALK/ROS1 DistinguISH™ Probe CE IVD	Z-2203-50/-200	50/200 µl	179
BCL2	Bcl-2, PPP1R50	FlexISH BCL2/BCL6 DistinguISH™ Probe CE IVD	Z-2283-50/-200	50/200 µl	180
BCL6	ZNF51, LAZ3	FlexISH BCL2/BCL6 DistinguISH™ Probe CE IVD	Z-2283-50/-200	50/200 µl	180
ERBB2	HER2, HER-2, NEU	FlexISH ERBB2/CEN 17 Dual Color Probe CE IVD	Z-2166-50/-200	50/200 µl	183
IGH	IGH@	FlexISH MYC/IGH TriCheck™ Probe CE IVD NEW	Z-2293-50	50 µl	181
KIF5B	KNS1	FlexISH RET/KIF5B TriCheck™ Probe CE IVD NEW	Z-2269-50/-200	50/200 µl	182
MYC	CMYC, bHLHe39, c-Myc	FlexISH MYC/IGH TriCheck™ Probe CE IVD NEW	Z-2293-50	50 µl	181
RET	HSCR1, CDHF12	FlexISH RET/KIF5B TriCheck™ Probe CE IVD NEW	Z-2269-50/-200	50/200 µl	182
ROS1	MCF3, ROS	FlexISH ALK/ROS1 DistinguISH™ Probe CE IVD	Z-2203-50/-200	50/200 µl	179

Indication Index

Indication	Product Name	Product No.	Quantity	Page
Solid Tumors				
Breast Cancer	FlexISH ERBB2/CEN 17 Dual Color Probe CE IVD	Z-2166-50/-200	50/200 µl	183
Gastrointestinal Cancer	FlexISH ERBB2/CEN 17 Dual Color Probe CE IVD	Z-2166-50/-200	50/200 µl	183
Lung Cancer	FlexISH ALK/ROS1 DistinguISH™ Probe CE IVD	Z-2203-50/-200	50/200 µl	179
	FlexISH RET/KIF5B TriCheck™ Probe CE IVD NEW	Z-2269-50/-200	50/200 µl	182
	FlexISH ERBB2/CEN 17 Dual Color Probe CE IVD	Z-2166-50/-200	50/200 µl	183
Hematology Specific Probes				
Non-Hodgkin Lymphoma, other	FlexISH BCL2/BCL6 DistinguISH™ Probe CE IVD	Z-2283-50/-200	50/200 µl	180
	FlexISH MYC/IGH TriCheck™ Probe CE IVD NEW	Z-2293-50	50 µl	181

CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.

FlexISH® ALK/ROS1 DistinguISH™ Probe

CE IVD

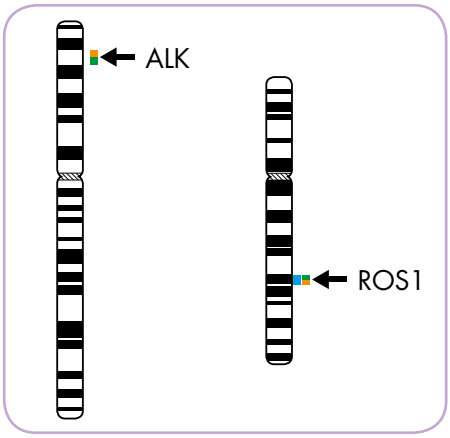
Background

The FlexISH® ALK/ROS1 DistinguISH™ Probe is designed to detect rearrangements involving the chromosomal region 2p23.1-p23.2 and 6q22.1 harboring the ALK (ALK receptor tyrosine kinase, a.k.a. CD246) and ROS1 (ROS proto-oncogene 1, receptor tyrosine kinase) gene, respectively. Using this probe, it is possible to simultaneously detect ALK and ROS1 rearrangements and, additionally, to discriminate between possible aberrations affecting these chromosomal regions.
Both, the ALK as well as the ROS1 gene, encode for transmembrane receptor tyrosine kinases. Rearrangements affecting the ALK or the ROS1 gene locus are frequently found in non-small cell lung cancer (NSCLC). The most frequent ALK rearrangement in NSCLC is the inversion [inv(2)(p21p23)] affecting the genes ALK and EML4, both located on chromosome 2. The ROS1 gene is evolutionary closely related to the ALK family which forms part of the scientific basis of using inhibitors of ALK as inhibitors of ROS1. ALK and ROS1 positive NSCLC patients benefit from a tyrosine kinase targeted therapy, like, e.g., crizotinib.

References
Birchmaier C, et al. (1987) Proc Natl Acad Sci U S A 84: 9270-4.
Bos M, et al. (2013) Lung Cancer 81: 142-3.
Sasaki T, et al. (2010) Eur J Cancer 46: 1773-80.
Shaw AT, et al. (2014) N Engl J Med 371: 1963-71.

Probe Description

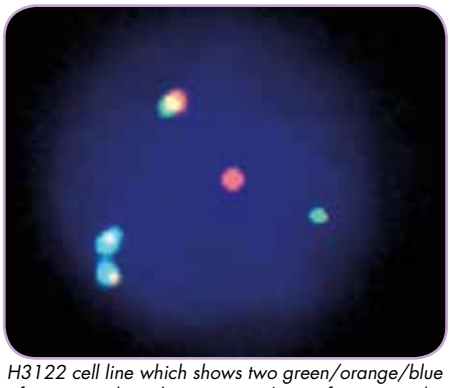
The FlexISH® ALK/ROS1 DistinguISH™ Probe is a mixture of five direct labeled probes hybridizing to the 2p23.1-p23.2 and 6q22.1-q22.2 bands. The orange fluorochrome direct labeled probe fractions hybridize distal to the ALK and ROS1 breakpoint regions, the green direct labeled probe fractions hybridize proximal to the ALK and ROS1 breakpoint regions. The blue fluorochrome direct labeled probe hybridizes distal and proximal to the ROS1 breakpoint region.



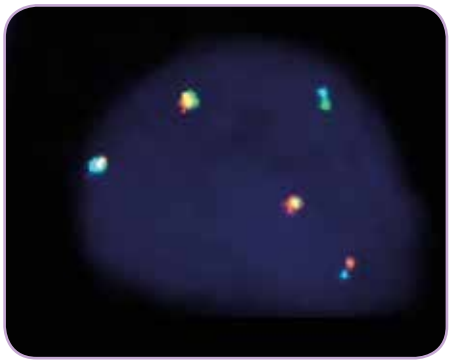
Ideograms of chromosomes 2 (left) and 6 (right) indicating the hybridization locations.

Results

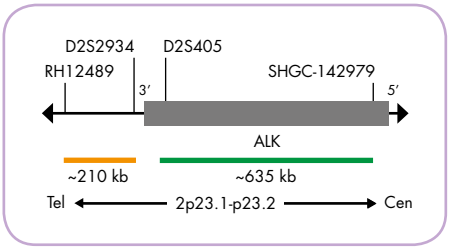
In an interphase nucleus without ALK or ROS1 rearrangements, two ALK specific green/orange fusion signals and two ROS1 specific green/orange/blue fusion signals are expected. An ALK rearrangement is indicated by one separate orange signal and/or one separate green signal, both not co-localizing with blue signals. A ROS1 rearrangement is indicated by one separate green signal, and/or one separate orange signal both co-localizing with blue signals.



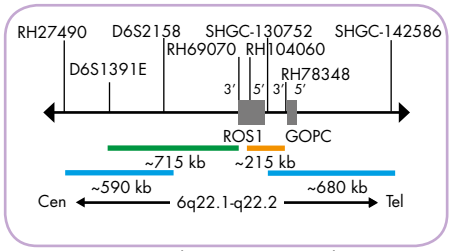
H3122 cell line which shows two green/orange/blue fusion signals and one orange/green fusion signal. An ALK rearrangement is indicated by one separate orange and one separate green signal, both not co-localizing with blue signals.



HCC78 cell line which shows two green/orange fusion signals and one green/orange/blue fusion signal. ROS1 rearrangement is indicated by one separate orange and one separate green signal, both co-localizing with blue signals.



ALK Probe map (not to scale).



ROS1 Probe map (not to scale).

Prod. No.	Product	Label	Tests* (Volume)
Z-2203-50	FlexISH ALK/ROS1 DistinguISH Probe CE IVD	●/●/●	5 (50 µl)
Z-2203-200	FlexISH ALK/ROS1 DistinguISH Probe CE IVD	●/●/●	20 (200 µl)
Related Products			
Z-2182-5	FlexISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; 5x FlexISH Wash Buffer, 150 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2182-20	FlexISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; 5x FlexISH Wash Buffer, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

FlexISH® BCL2/BCL6 DistinguISH™ Probe

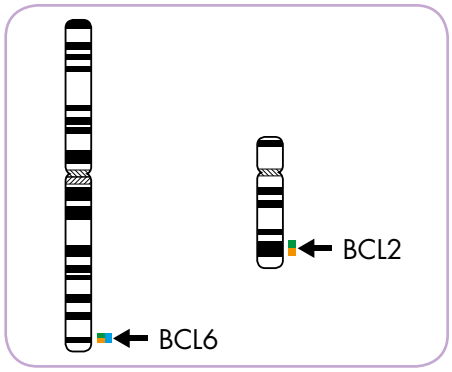
CE IVD

Background

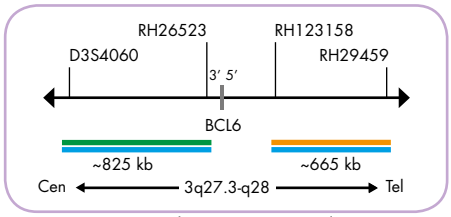
The FlexISH® BCL2/BCL6 DistinguISH™ Probe is designed to detect rearrangements involving the chromosomal regions 18q21.33 and 3q27.3 harboring the BCL2 (BCL2 apoptosis regulator, a.k.a. PPP1R50) gene and the BCL6 (BCL6 transcription repressor, a.k.a. ZNF51, LAZ3) gene, respectively. Using this probe, it is possible to simultaneously detect BCL2 and BCL6 rearrangements and, additionally, to discriminate between possible aberrations affecting these chromosomal regions, individually.
BCL2 encodes for a mitochondrial membrane protein that regulates apoptosis and is expressed in B-cells. BCL6 encodes for a protein that acts as a transcriptional repressor involved in the regulation of lymphoid development and function. BCL2 and BCL6 rearrangements are frequently found in various Non-Hodgkin lymphomas. Additionally, BCL2 and BCL6 rearrangements are known to be concurrent with MYC rearrangements. MYC rearrangements with either BCL2 or BCL6 co-aberration are so-called double-hit B-cell lymphomas (DHL) known to be highly aggressive with poor prognosis. Rarely, triple-hit B-cell lymphomas (THL) showing simultaneous rearrangements of MYC, BCL2, and BCL6 occur. According to the revised 4th edition of the WHO classification of tumors of haematopoietic and lymphoid tissues (2017) DHL and THL are classified as high-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements. Hence, detection of BCL2 and/or BCL6 rearrangements using Fluorescence *in situ* Hybridization (FISH) may be of diagnostic and prognostic relevance.

Probe Description

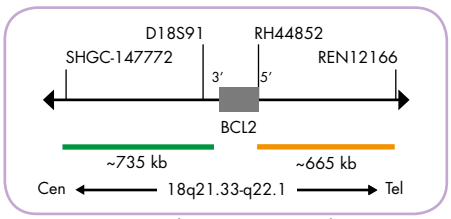
The FlexISH® BCL2/BCL6 DistinguISH™ Probe is a mixture of five direct labeled probes hybridizing to the 18q21.33-q22.1 and 3q27.3-q28 bands. The green fluorochrome direct labeled probes hybridize proximal to the BCL2 and BCL6 breakpoint regions, and the orange fluorochrome direct labeled probes hybridize distal to the BCL2 and BCL6 breakpoint regions. The blue fluorochrome direct labeled probe hybridizes distal and proximal to the BCL6 breakpoint region.



Ideograms of chromosomes 3 (left) and 18 (right) indicating the hybridization locations.



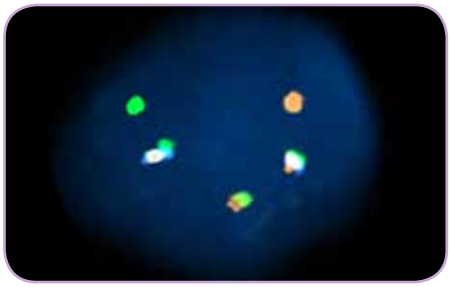
BCL6 Probe map (not to scale).



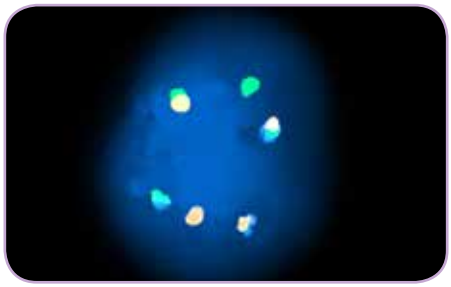
BCL2 Probe map (not to scale).

Results

In an interphase nucleus without BCL2 or BCL6 rearrangements, two BCL2 specific green/orange fusion signals and two BCL6 specific green/orange/blue fusion signals are expected. A BCL2 rearrangement is indicated by one separate green and one separate orange signal, both not co-localizing with blue signals. A BCL6 rearrangement is indicated by one separate green and one separate orange signal, both co-localizing with blue signals.



Lymphoma tissue which shows two green/orange/blue fusion signals and one green/orange fusion signal. BCL2 rearrangement is indicated by one separate green and one separate orange signal, both not co-localizing with blue signals.
Specimen kindly provided by Dr. Rontogianni, Athens, Greece.



DLBCL tissue which shows one green/orange/blue fusion signal and one green/orange fusion signal. BCL6 rearrangement is indicated by one separate green and one separate orange signal, both colocalizing with blue signals. Additionally, one separate orange and one separate green signal indicate a further BCL2 positivity, confirming a BCL2/BCL6 co-rearrangement.

References

Swerdlow SH, et al. (ed.) (2017) WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues (Revised 4th Edition).

Prod. No.	Product	Label	Tests* (Volume)
Z-2283-50	FlexISH BCL2/BCL6 DistinguISH Probe CE IVD	●/●/●	5 (50 µl)
Z-2283-200	FlexISH BCL2/BCL6 DistinguISH Probe CE IVD	●/●/●	20 (200 µl)
Related Products			
Z-2182-5	FlexISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; 5x FlexISH Wash Buffer, 150 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2182-20	FlexISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; 5x FlexISH Wash Buffer, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

FlexISH® MYC/IGH TriCheck™ Probe

CE IVD

Background

The FlexISH® MYC/IGH TriCheck™ Probe is designed to detect the translocation t(8;14)(q24.21;q32.3) affecting the MYC gene in the chromosomal region 8q24.21 and the IGH locus in 14q32.33. Moreover, using this probe it is possible to discriminate between MYC-IGH translocations and MYC translocations involving fusion partners other than IGH.

The MYC proto-oncogene (a.k.a. CMYC) encodes a transcription factor essential for cell growth and proliferation and is broadly implicated in tumorigenesis. Translocations involving the MYC gene are considered to be cytogenetic hallmarks for Burkitt lymphoma (BL) but are also found in other types of lymphomas.

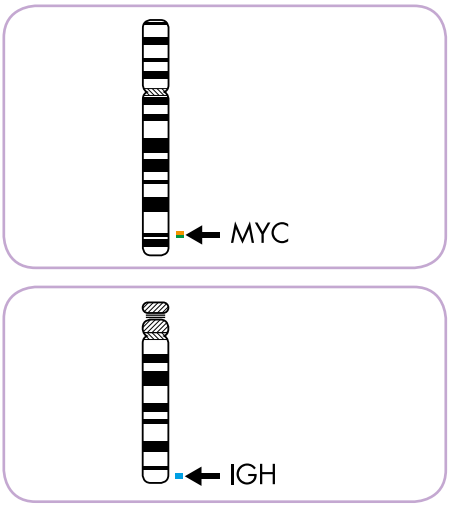
The most frequent translocation involving the MYC gene region t(8;14)(q24.21;q32.3) can be found in approx. 80% of the BL cases and juxtaposes the MYC gene next to IGH (immunoglobulin heavy locus). Further translocations affecting the MYC gene are t(8;22)(q24.21;q11.2) and t(2;8)(p11.2;q24.21), both of which involve one of the two immunoglobulin light chain loci. All three translocations bring the MYC gene under the control of a regulatory element from one of the immunoglobulin loci resulting in constitutive overexpression of MYC.

Large B-cell lymphoma patients with MYC-IG have shorter overall survival compared with both MYC translocation with non-IG translocation partner gene as well as absence of MYC translocation. Thus, the detection of MYC translocation partner by FISH may prove a valuable diagnostic and prognostic tool.

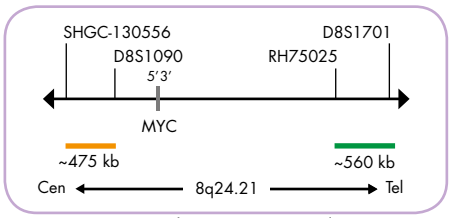
References
May P, et al. (2010) Cancer Genet Cytogenet 198: 71-5.
Pedersen MØ, et al. (2014) Eur J Haematol 92: 42-8.
Perkins AS & Friedberg JW (2008) Hematology Am Soc Hematol Educ Program: 341-8.
Veronese ML, et al. (1995) Blood 85: 2132-8.

Probe Description

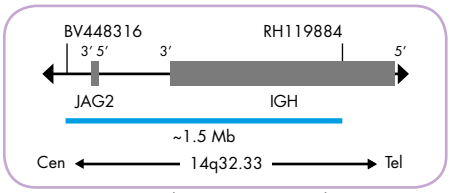
The FlexISH® MYC/IGH TriCheck™ Probe is a mixture of three direct labeled probes hybridizing to the 8q24.21 and 14q32.33 bands. The orange fluorochrome direct labeled probe hybridizes proximal to the MYC gene region, and the green fluorochrome direct labeled probe hybridizes distal to the MYC gene region. The blue fluorochrome direct labeled probe spans the known breakpoints of IGH.



Ideograms of chromosomes 8 (above) and 14 (below) indicating the hybridization locations.



MYC Probe map (not to scale).

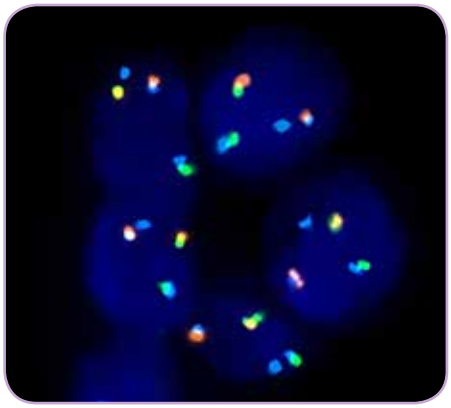


IGH Probe map (not to scale).

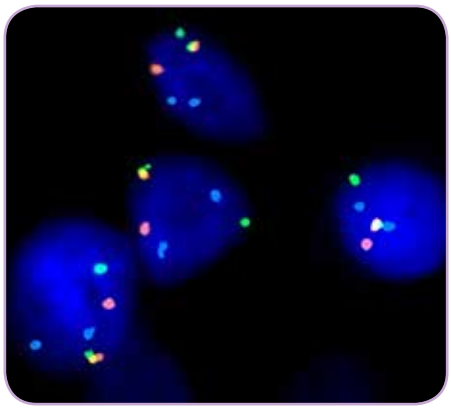
Results

In an interphase nucleus without rearrangements of the MYC/IGH loci, two green/orange fusion signals and two blue signals are expected.

A MYC-IGH fusion is indicated by one separate green signal and one separate orange signal, both co-localizing with blue signals. A MYC translocation without involvement of IGH is indicated by separated orange and green signals without co-localization of the separated signals with blue signals.



Non-Hodgkin lymphoma tissue section with t(8;14) as indicated by one separate green and one separate orange signal, and one additional blue signal.



Non-Hodgkin lymphoma tissue section with translocation of the MYC gene without IGH involvement as indicated by one separate green and one separate orange signal, without an additional blue signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2293-50	FlexISH MYC/IGH TriCheck Probe CE IVD	●/●/●	5 (50 µl)
Related Products			
Z-2182-5	FlexISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; 5x FlexISH Wash Buffer, 150 ml; DAPI/DuraTect-Solution, 0.2 ml		5

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

FlexISH® RET/KIF5B TriCheck™ Probe

CE IVD

Background

The FlexISH® RET/KIF5B TriCheck™ Probe is designed to detect inversions involving the chromosomal region 10q11.21 harboring the rearranged during transfection (RET) gene and the chromosomal region 10p11.22 harboring the kinase family member 5B (KIF5B) gene. Moreover, using this probe it is possible to discriminate between KIF5B-RET inversions and RET translocations involving fusion partners other than KIF5B (e.g., BCR, FGFR1OP, and PTC). RET rearrangements, including inversions and translocations, are found in non-small cell lung cancer (NSCLC) with an incidence of 1-2%. The pericentric inversion of chromosome 10 [inv(10)(p11.2q11.2)] leads to a fusion transcript of the KIF5B gene and the RET proto-oncogene and, thus, forms a chimeric protein. The resulting homo-dimerization of the coiled-coil domains of KIF5B causes an aberrant activation of the receptor tyrosine kinase (RTK) of RET, a mechanism known from KIF5B-ALK fusion which is also found in non-small cell lung adenocarcinoma (LADC). LADC patients with KIF5B-RET fusions are commonly tested negative for LADC common driver mutations in the EGFR, KRAS, and ALK genes.
Since *in vitro* studies have shown that NSCLC patients presenting a KIF5B-RET fusion are less sensitive to vandetanib treatment compared to patients with KIF5B independent RET-fusions, FISH analysis can sustain the treatment decision.

References
Gautschi O, et al. (2013) J Thorac Oncol 8: e43-4.
Ju YS, et al. (2012) Genome Res 22: 436-45.
Kohno T, et al. (2012) Nat Med 18: 375-7.
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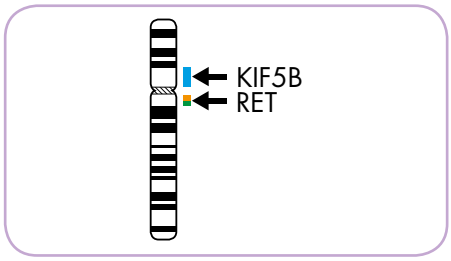
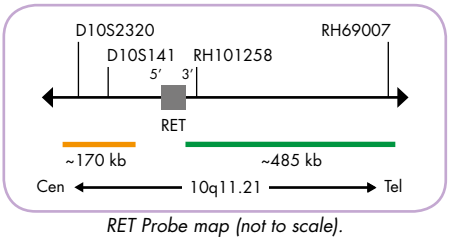
Probe Description

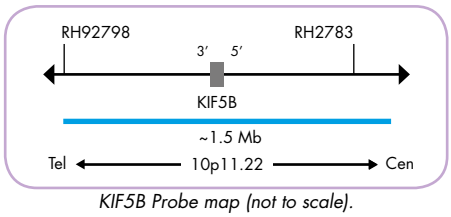
The FlexISH® RET/KIF5B TriCheck™ Probe is a mixture of three direct labeled probes hybridizing to the 10q11.21 and 10p11.22 bands. The green fluorochrome direct labeled probe hybridizes distal to the RET gene region, and the orange fluorochrome direct labeled probe hybridizes proximal to the RET gene region. The blue fluorochrome direct labeled probe spans the KIF5B gene region.



Ideogram of chromosome 10 indicating the hybridization locations.



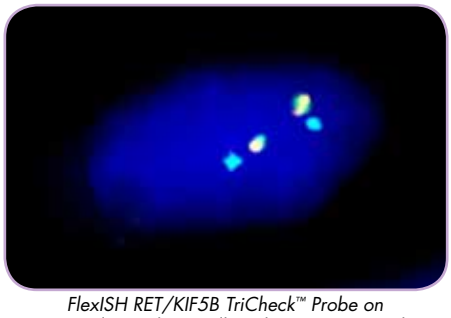
RET Probe map (not to scale).



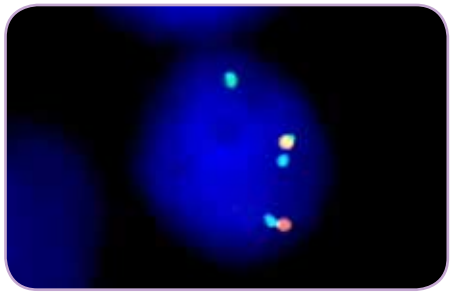
KIF5B Probe map (not to scale).

Results

In an interphase nucleus without rearrangements of the KIF5B/RET locus, two green/orange fusion signals and two blue signals are expected.
A KIF5B-RET inversion is indicated by one separate green signal, one separate orange signal, and an additional blue signal.
A RET translocation is indicated by separated orange and green signals without an additional blue signal.
KIF5B-RET inversion with deletion of the 5′-RET sequences is indicated by loss of one orange signal and co-localization of the isolated green signal with a blue signal.



FlexISH RET/KIF5B TriCheck™ Probe on normal interphase cells with non-rearranged RET loci (two green/orange fusion signals), and non-rearranged KIF5B loci (two blue signals).



NSCLC tissue section with a KIF5B-RET inversion as indicated by one green, one separated orange, and an additional blue signal.

Specimen kindly provided by Dr. Schildhaus, Essen, Germany.

Prod. No.	Product	Label	Tests* (Volume)
Z-2269-50	FlexISH RET/KIF5B TriCheck Probe CE IVD	●/●/●	5 (50 µl)
Z-2269-200	FlexISH RET/KIF5B TriCheck Probe CE IVD	●/●/●	20 (200 µl)
Related Products			
Z-2182-5	FlexISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; 5x FlexISH Wash Buffer, 150 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2182-20	FlexISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; 5x FlexISH Wash Buffer, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

FlexISH® ERBB2/CEN 17 Dual Color Probe

CE IVD

Background

The FlexISH® ERBB2/CEN 17 Dual Color Probe is designed for the detection of ERBB2 gene amplification frequently observed in solid malignant neoplasms, e.g., breast cancer samples.

The ERBB2 gene (a.k.a. HER2 and NEU) is located in the chromosomal region 17q12 and encodes a 185-190 kDa transmembrane glycoprotein, p185, acting as a cellular growth factor receptor. The p185 protein belongs to the EGFR (epidermal growth factor receptor) subgroup of the RTK (receptor tyrosine kinase) superfamily also including EGFR (ERBB1), ERBB3 (HER3), and ERBB4 (HER4).

Amplification of the proto-oncogene ERBB2, observed in approximately 20% of all breast cancer samples, has been correlated with a poor prognosis of the disease. Similar results have been obtained for a variety of other malignant neoplasms, e.g., ovarian cancer, stomach cancer, and carcinomas of the salivary gland.

References

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Brockhoff G, et al. (2016) Histopathology 69: 635-46.
Brunello E, et al. (2012) Histopathology 60: 482-8.
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Popescu NC, et al. (1989) Genomics 4: 362-6.
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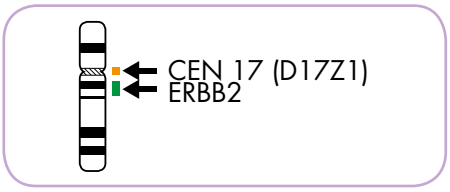
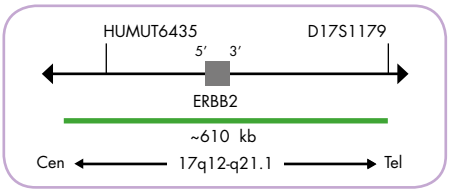
Probe Description

The ERBB2/CEN 17 Dual Color Probe is a mixture of a green fluorochrome direct labeled ERBB2 probe specific for the chromosomal region 17q12-q21.1 harboring the ERBB2 gene and an orange fluorochrome direct labeled CEN 17 probe specific for the alpha satellite centromeric region of chromosome 17 (D17Z1).



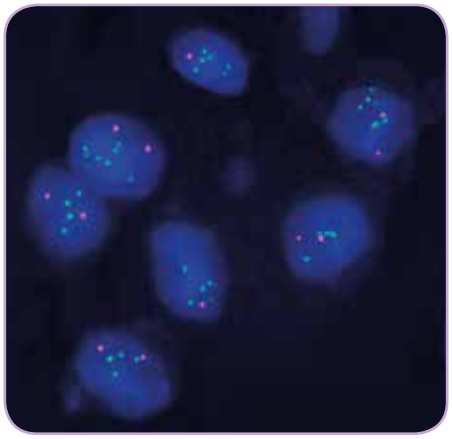
Ideogram of chromosome 17 indicating the hybridization locations.



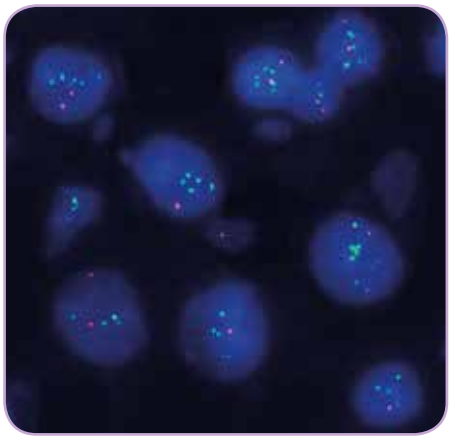
ERBB2 Probe map (not to scale).

Results

In a normal interphase nucleus, two green and two orange signals are expected. In a cell with amplification of the ERBB2 gene locus, multiple copies of the green signal or green signal clusters will be observed.



FlexISH ERBB2/CEN 17 Dual Color Probe hybridized for 2 hours on an endometrial carcinoma tissue section with ERBB2 (green) amplification.



FlexISH ERBB2/CEN 17 Dual Color Probe hybridized overnight on an endometrial carcinoma tissue section with ERBB2 (green) amplification.

Prod. No.	Product	Label	Tests* (Volume)
Z-2166-50	FlexISH ERBB2/CEN 17 Dual Color Probe CE IVD	●/●	5 (50 µl)
Z-2166-200	FlexISH ERBB2/CEN 17 Dual Color Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2182-5	FlexISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; 5x FlexISH Wash Buffer, 150 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2182-20	FlexISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; 5x FlexISH Wash Buffer, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

FISH Accessories

ZytoLight® Products for FISH analysis

ZytoLight® Implementation Kits

For the detection of ZytoLight® Probes

Prod. No.	Product	Tests
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml	5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml	20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8ml	20

ZytoLight® Wash Buffers

Prod. No.	Product
WB-0001-560	Wash Buffer SSC, 560 ml CE IVD
WB-0002-50	25x Wash Buffer A, 50 ml CE IVD
WB-0003-50	20x SSC Solution, 50 ml
WB-0005-50	20x Wash Buffer TBS, 50 ml CE IVD
WB-0007-500	Cytology Stringency Wash Buffer SSC, 500 ml CE IVD
WB-0008-500	Cytology Wash Buffer SSC, 500 ml CE IVD

FlexISH® Products for flexible FISH

FlexISH® Implementation Kits

For the detection of FlexISH® Probes

Prod. No.	Product	Tests
Z-2182-5	FlexISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; 5x FlexISH Wash Buffer, 150 ml; DAPI/DuraTect-Solution, 0.2 ml	5
Z-2182-20	FlexISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; 5x FlexISH Wash Buffer, 500 ml; DAPI/DuraTect-Solution, 0.8 ml	20
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml	20

The FlexISH®-Tissue Implementation Kit can be used for FFPE samples and the ZytoLight® FISH-Cytology Implementation Kit for cytology specimens in combination with any FlexISH® FISH probe.

FlexISH® Wash Buffers

Prod. No.	Product
WB-0007-500	Cytology Stringency Wash Buffer SSC, 500 ml CE IVD
WB-0008-500	Cytology Wash Buffer SSC, 500 ml CE IVD
WB-0010-500	5x FlexISH Wash Buffer, 500 ml CE IVD

CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.

FISH Accessories

FISH Pretreatment Reagents

Prod. No.	Product
ES-0001-4	Pepsin Solution, 4 ml CE IVD
ES-0001-8	Pepsin Solution Set, 2x 4 ml CE IVD
ES-0001-50	Pepsin Solution, 50 ml CE IVD
ES-0001-1000	Pepsin Solution, 1000 ml CE IVD
ES-0002-4	Cytology Pepsin Solution, 4 ml CE IVD
ES-0002-50	Cytology Pepsin Solution, 50 ml CE IVD
PT-0001-1000	Heat Pretreatment Solution Citric, 1000 ml CE IVD
PT-0006-100	Formaldehyde Dilution Buffer Set CE IVD Incl. 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml

Ancillary Reagents

Prod. No.	Product
E-4005-50	Fixogum Rubber Cement, 50 g
E-4005-125	Fixogum Rubber Cement, 125 g

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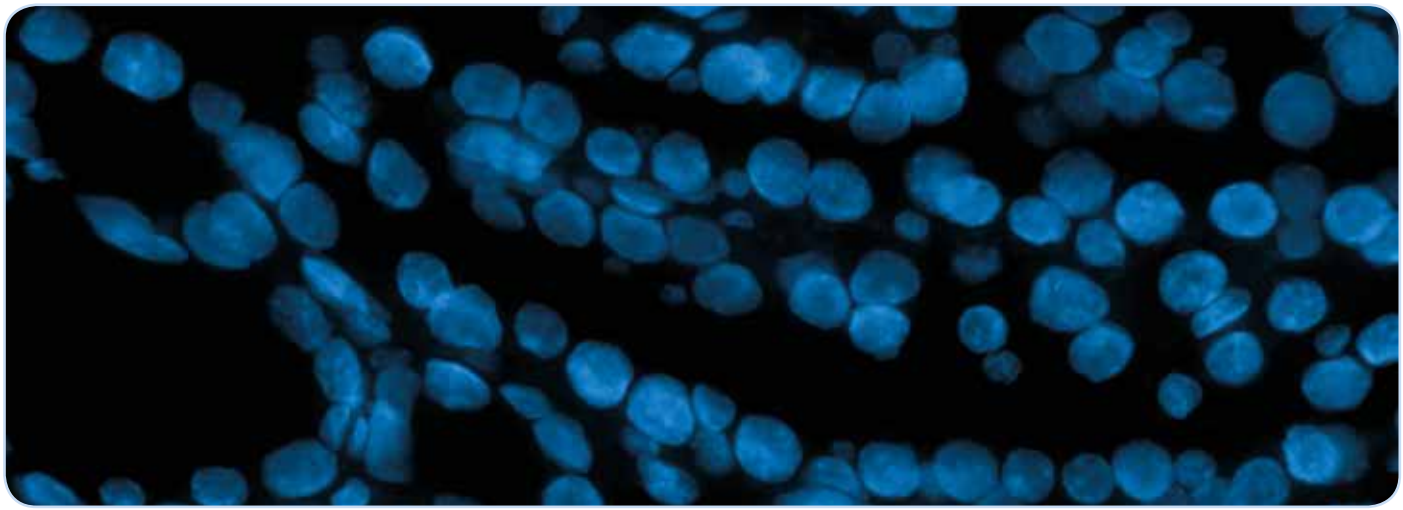
DAPI/DuraTect™ Solutions



Product Description

ZytoVision's DAPI/Antifade Mounting Solutions are ready-to-use mounting media that are applied directly to fluorescently labeled tissue or cell specimens on microscope slides. They contain the nuclear counterstain DAPI (4', 6-diamidino-2-phenylindole) which produces a blue fluorescence when bound to DNA.

ZytoVision's DAPI/Antifade Mounting Solutions are optimized to be used on tissue or cell specimens that have been hybridized with any available Zyto*Light* ®, F*lex*ISH ®, or Zyto*Mation* ® FISH Probe. They are all particularly compatible with the ZytoVision fluorochromes ZyGreen™, ZyOrange™, ZyBlue™, ZyGold™ and ZyRed™.

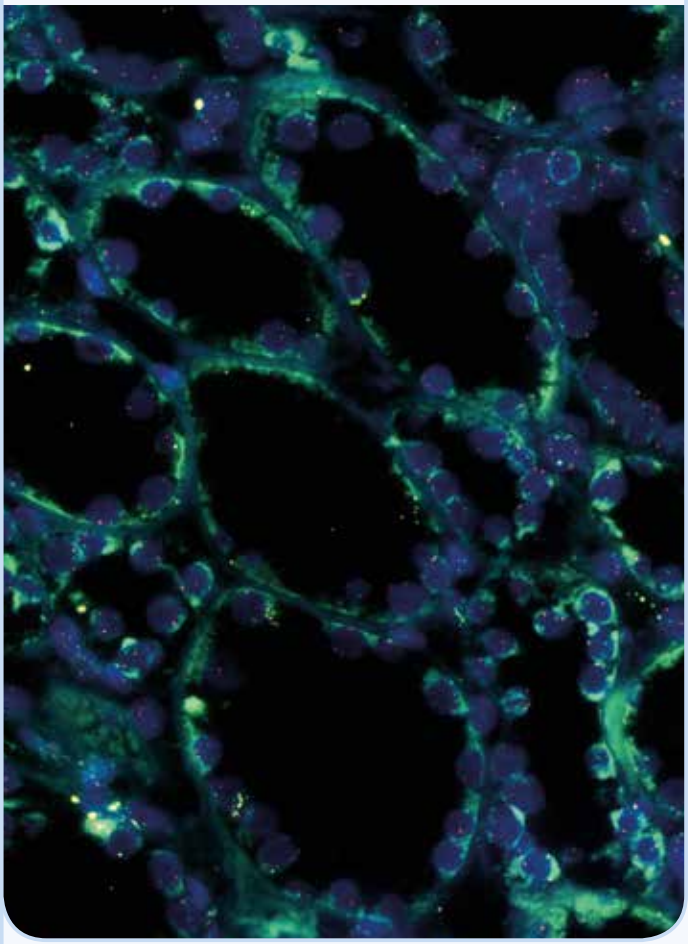
ZytoVision's DAPI/Antifade Mounting Solutions prevent permanent loss of fluorescence and protect fluorescent dyes from photobleaching during fluorescence microscopy.

Prod. No.	Product	Concentration	Storage Temperature	Description
MT-0007-0.8	DAPI/DuraTect-Solution, 0.8 ml CE IVD	150 ng DAPI/ml	2...8°C	· Best overall signal protection · Superior signal stability of mounted tissue sections (≤3 months at 2...21°C)
MT-0008-0.8	DAPI/DuraTect-Solution (ultra), 0.8 ml CE IVD	1360 ng DAPI/ml	2...8°C	· Best overall signal protection · Superior signal stability of mounted tissue sections (≤3 months at 2...21°C) · Recommended when a more intense DAPI stain is desired

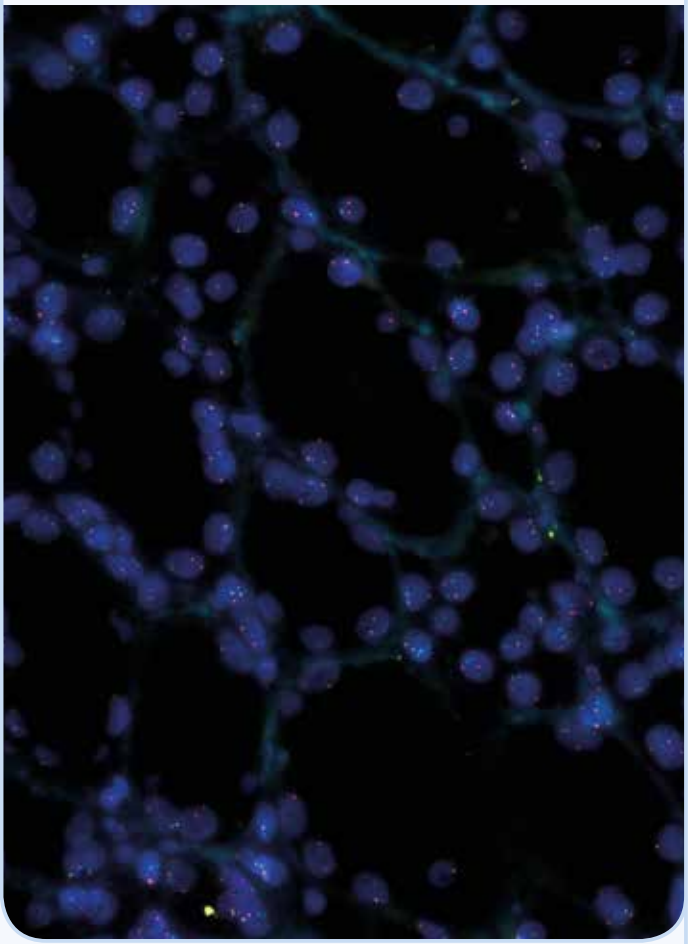
CE IVD *only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZyBlack™ Quenching Solution

Without ZyBlack™ Quenching Solution



With ZyBlack™ Quenching Solution



Kidney tissue section hybridized with the Zyto*Light* ® SPEC PTEN/CEN 10 Dual Color Probe.

Product Description

ZyBlack™ Quenching Solution is a ready-to-use solution to reduce autofluorescence on both formalin-fixed paraffin-embedded and frozen sections.
It can be easily incorporated into the manual FISH protocol by applying it after the proteolytic pretreatment.

One of the major concerns of Fluorescence *in situ* Hybridization (FISH)-based diagnostic assays is the interference by autofluorescence. Several types of tissue tend to emit intense autofluorescence, including brain, liver, kidney and myocardium, making it difficult to evaluate FISH results.

ZyBlack™ Quenching Solution reduces autofluorescence without adversely affecting tissue integrity or specific fluorescence signals.

Prod. No.	Product	Volume
BS-0002-8	ZyBlack Quenching Solution CE IVD	8 ml

CE IVD *only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoVision Fluorochromes and Filter Recommendations

ZytoVision Fluorochromes
Two factors that mainly influence FISH analyses:
- **Fluorochromes of the FISH probes**
- **Appropriate filter sets**

Fluorochrome	Excitation	Emission	Equivalent to
ZyBlue™	418 nm	467 nm	DEAC
ZyGreen™	503 nm	528 nm	FITC
ZyGold™	532 nm	553 nm	Rhodamine 6G
ZyOrange™	547 nm	572 nm	Rhodamine
ZyRed™	580 nm	599 nm	TexasRed®

Recommended Filter Sets
All filter sets are produced by well known manufacturers and have a **superior-signal-to-noise ratio!**

Prod. No	Product	Detected Fluorochrome
E-4030-1	DAPI Single Bandpass Filter Set v2	DAPI
E-4026-1	ZyBlue™ Single Bandpass Filter Set v2	●
E-4012-1	ZyGreen™ Single Bandpass Filter Set v2	●
E-4027-1	ZyGold™ Single Bandpass Filter Set v2	●
E-4013-1	ZyOrange™ Single Bandpass Filter Set v2	●
E-4017-1	ZyRed™ Single Bandpass Filter Set v2	●
E-4016-1	ZyGreen™/ZyOrange™ Dual Bandpass Filter Set v2	●/●
E-4010-1	DAPI/ZyGreen™/ZyOrange™ Triple Bandpass Filter Set	DAPI/●/●
E-4028-1	ZyBlue™/ZyGreen™/ZyOrange™ Triple Bandpass Filter Set	●/●/●

Fluorescence Filter Holder
The filter sets need to be assembled in fluorescence filter holder specific for the respective microscope.

Prod. No	Product	Compatible for Microscopes e.g.*
E-4111-1	ZEISS Fluorescence Filter Holder „FL EC P&C“	Zeiss: Axio Imager, Axiostar plus, Axioskop 40
E-4113-1	ZEISS Fluorescence Filter Holder „FL“	Zeiss: Axioplan 2, Axioskop 2, Axiophot 2
E-4121-1	OLYMPUS Fluorescence Filter Holder „U-MF 2“	Olympus: AX, AX70, BX41, BX50, BX51
E-4122-1	OLYMPUS Fluorescence Filter Holder „U-FF“	Olympus: BX43, BX53, BX63
E-4131-1	LEICA Fluorescence Filter Holder „DM K“	Leica: DM4000-6000, DMI4000-6000
E-4141-1	NIKON Fluorescence Filter Holder „C-FL“	Nikon: Eclipse 50i, Eclipse 80i, Eclipse TI

*If your model is not listed, please contact helptech@zytovision.com

Microscope Specifications
In order to provide you with the best possible service, please provide us with the following details:
- **Microscope manufacturer**
- **Type or model of microscope**
- **Approx. age of microscope**

These filter sets, optimized for Zyto*Light*® and F*lex*ISH® FISH probes, will significantly increase brightness and quality of your FISH results!

ZytoMation® Products for automated FISH

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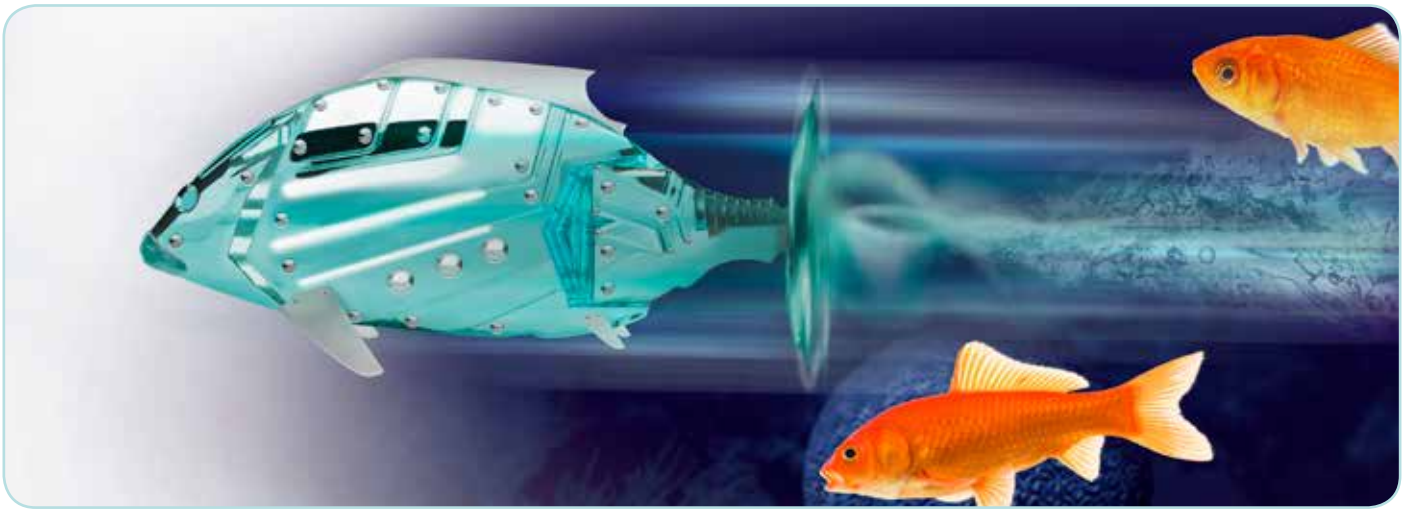
Fully automated Probes for the BOND™ Systems!



Introduction

The Zyto*Mation*® probes combine the known high quality of the ZytoVision probes for Fluorescence *in situ* Hybridization (FISH) with an automated workflow. They are designed for fully automated FISH to detect genetic aberrations such as translocations and amplifications in formalin-fixed, paraffin-embedded tissue sections on the Leica BOND™ Systems.

Advantages of Zyto*Mation*®

- High sensitivity and specificity on fully automated Leica BOND™ Systems
- Ready-to-use probes
- Reduced hands-on time
- Fully automated 5 h protocol

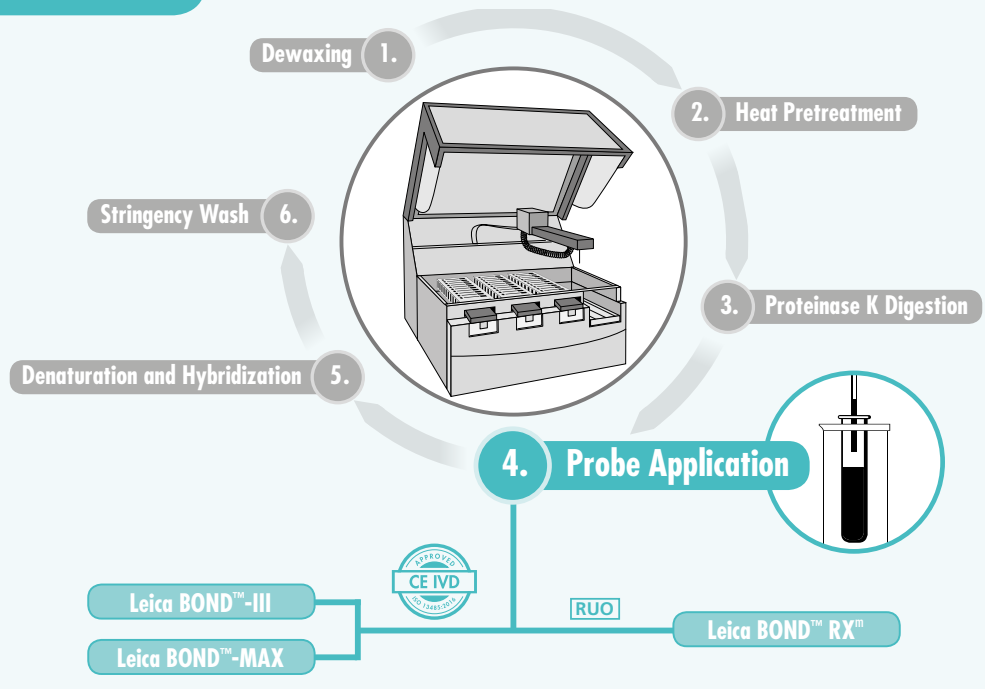
Compatible BOND™ Systems

- Leica BOND™-III
- Leica BOND™-MAX
- Leica BOND™ RX^m

Workflow

To successfully use the Zyto*Mation*® probes, the Leica BOND™ FISH Kit (DS9636) is required.
Before starting the Leica BOND™ System, the Leica BOND™ FISH Kit has to be complemented with the BOND™ Enzyme Pretreatment Kit and the ready-to-use Zyto*Mation*® FISH probe, transferred to the BOND™ Titration Kit. Prior to evaluation, the hybridized slides should be mounted using a DAPI/DuraTect™-Solution (MT-0007-0.8/MT-0008-0.8).

Workflow Schedule



Chromosome Index

Chr.	Band	Product Name	Product No.	Quantity	Page
1-5		no probes available yet			
6	6q22.1	ZytoMation ROS1 Dual Color Break Apart FISH Probe CE IVD NEW	Z-2298-5.1ML	5.1 ml	193
7-16		no probes available yet			
17	17q12	ZytoMation ERBB2/CEN 17 Dual Color FISH Probe CE IVD NEW	Z-2292-5.1ML	5.1 ml	194
18-22		no probes available yet			
X, Y		no probes available yet			

CE IVD *only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

Gene Index

HUGO Name	Synonym	Product Name	Product No.	Quantity	Page
ERBB2	HER2, HER-2, NEU	*ZytoMation* ERBB2/CEN 17 Dual Color FISH Probe CE IVD NEW	Z-2292-5.1ML	5.1 ml	194
ROS1	MCF3, ROS	*ZytoMation* ROS1 Dual Color Break Apart FISH Probe CE IVD NEW	Z-2298-5.1ML	5.1 ml	193

Indication Index

Indication	Product Name	Product No.	Quantity	Page
Solid Tumors				
Breast Cancer	*ZytoMation* ERBB2/CEN 17 Dual Color FISH Probe CE IVD NEW	Z-2292-5.1ML	5.1 ml	194
Gastrointestinal Cancer	*ZytoMation* ERBB2/CEN 17 Dual Color FISH Probe CE IVD NEW	Z-2292-5.1ML	5.1 ml	194
Lung Cancer	*ZytoMation* ERBB2/CEN 17 Dual Color FISH Probe CE IVD NEW *ZytoMation* ROS1 Dual Color Break Apart FISH Probe CE IVD NEW	Z-2292-5.1ML Z-2298-5.1ML	5.1 ml 5.1 ml	194 193

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ZytoMation® ROS1 Dual Color Break Apart FISH Probe

CE IVD

Background

The ZytoMation® ROS1 Dual Color Break Apart FISH Probe is designed to detect translocations involving the chromosomal region 6q22.1 harboring the ROS proto-oncogene 1, receptor tyrosine kinase (ROS1, a.k.a. MCF3) gene.

The ROS1 gene is located on 6q22.1 and encodes a receptor tyrosine kinase. Translocations affecting ROS1 have been detected in glioblastoma, cholangiocarcinoma, and non-small cell lung cancer (NSCLC).

In NSCLC several ROS1 translocation partners have been detected all of which result in the fusion of variably truncated forms of e.g. TPM3, SDC4, SLC34A2, CD74, EZR, or LRIG3 to the kinase domain of ROS1. GOPC has also been found to be fused to ROS1 in NSCLC. GOPC-ROS1 fusions result from interstitial deletion of approx. 240 kb on 6q22.1. ROS1 rearrangements are thought to define a molecular subset of NSCLC with distinct clinical characteristics that are similar to those observed in patients with ALK rearranged NSCLC.

First evidence suggests that administration of ROS1 kinase inhibitors may represent a very effective therapeutic strategy in NSCLC patients harboring activating ROS1 rearrangements. Accordingly, detection of ROS1 rearrangements using Fluorescence *in situ* Hybridization might be a helpful tool for the identification of patients likely to respond to ROS1 kinase targeting therapies.

References
Bergethon K, et al. (2012) J Clin Oncol 30: 863-70.
Birchmaier C, et al. (1987) Proc Natl Acad Sci U S A 84: 9270-74.
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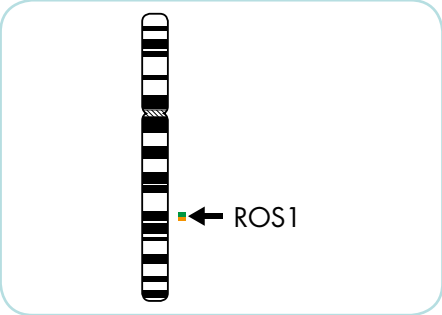
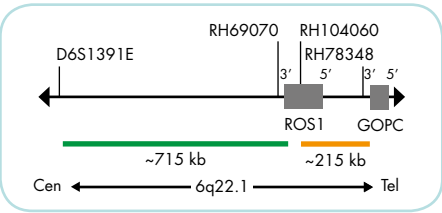
Rimkunas VM, et al. (2012) Clin Cancer Res 18: 4449-57.
Suehara Y, et al. (2012) Clin Cancer Res 18: 6599-608.
Takeuchi K, et al. (2012) Nat Med 18: 378-81.

Probe Description

The ROS1 Dual Color Break Apart FISH Probe is a mixture of two direct labeled probes hybridizing to the 6q22.1 band. The orange fluorochrome direct labeled probe hybridizes distal, the green fluorochrome direct labeled probe hybridizes proximal to the ROS1 breakpoint region at 6q22.1.



Ideogram of chromosome 6 indicating the hybridization locations.

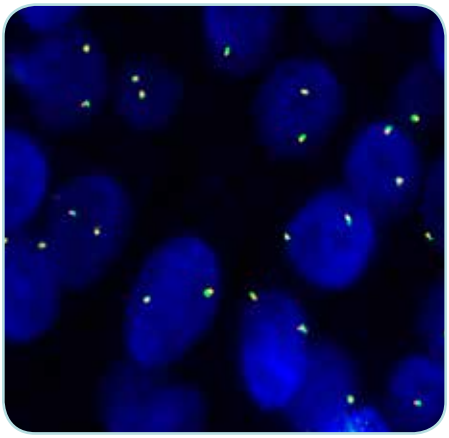


ROS1 Probe map (not to scale).

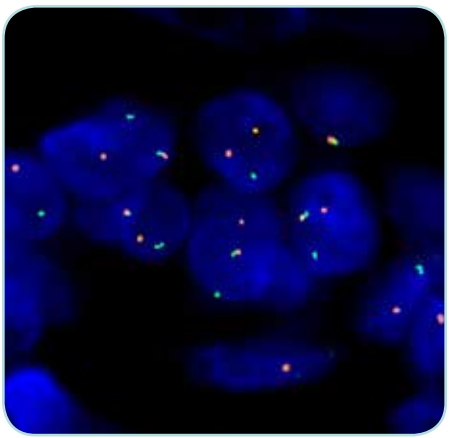
Results

In an interphase nucleus lacking an aberration involving the 6q22.1 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 6q22.1 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 6q22.1 locus and one 6q22.1 locus affected by a translocation.

Isolated green signals are the result of deletions distal to the ROS1 breakpoint region or are due to unbalanced translocations affecting this chromosomal region.



ROS1 Dual Color Break Apart FISH Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Lung cancer tissue section with translocation of the ROS1 gene as indicated by one non-rearranged orange/green fusion signal, one orange and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2298-5.1ML	ZytoMation ROS1 Dual Color Break Apart FISH Probe CE IVD	●/●	up to 20 (5.1 ml)

** Using 240 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoMation® ERBB2/CEN 17 Dual Color FISH Probe

CE IVD

Background

The ZytoMation ® ERBB2/CEN 17 Dual Color FISH Probe is designed for the detection of ERBB2 gene amplification frequently observed in solid malignant neoplasms e.g. breast cancer samples. The ERBB2 gene (a.k.a. HER2 and NEU) is located in the chromosomal region 17q12 and encodes a 185-190 kDa transmembrane glycoprotein, p185, acting as a cellular growth factor receptor. ERBB2 is a member of the Erb-b2 receptor tyrosine kinase (RTK) family, also including EGFR (ERBB1, HER1), ERBB3 (HER3), and ERBB4 (HER4).

Amplification of the proto-oncogene ERBB2, observed in approximately 20% of all breast cancer samples, has been correlated with a poor prognosis of the disease.

Similar results have been obtained for a variety of other malignant neoplasms e.g. ovarian cancer, stomach cancer, and carcinomas of the salivary gland.

References

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Brunner K, et al. (2010) Anal Quant Cytol Histol 32: 78-89.
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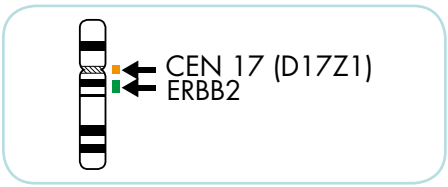
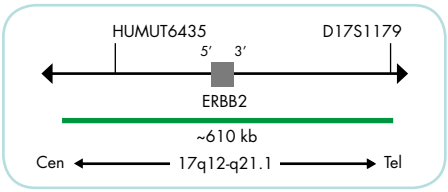
Wolff AC, et al. (2013) J Clin Oncol 31: 3997-4013.

Probe Description

The ERBB2/CEN 17 Dual Color FISH Probe is a mixture of an orange fluorochrome direct labeled CEN 17 probe specific for the alpha satellite centromeric region of chromosome 17 (D17Z1) and a green fluorochrome direct labeled ERBB2 probe specific for the chromosomal region 17q12-q21.1 harboring the ERBB2 gene.



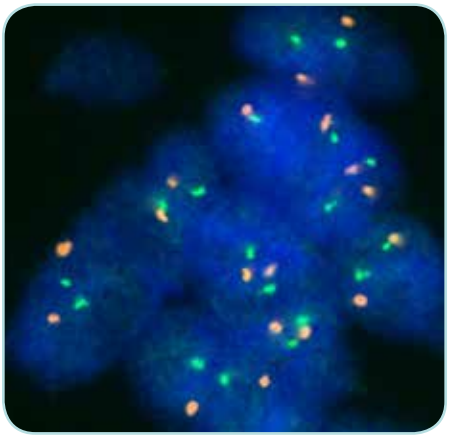
Ideogram of chromosome 17 indicating the hybridization locations.



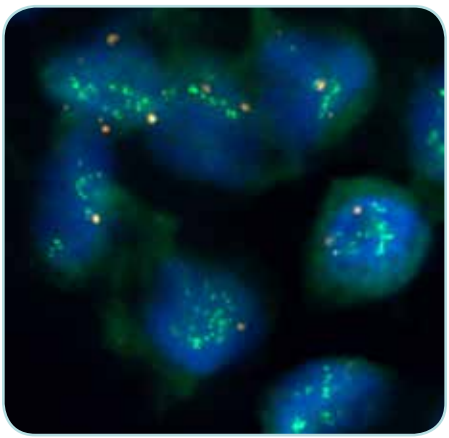
ERBB2 Probe map (not to scale).

Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the ERBB2 gene locus, multiple copies of the green signal or green signal clusters will be observed.



ERBB2/CEN 17 Dual Color FISH Probe hybridized to normal interphase cells as indicated by two green and two orange signals in each nucleus.



Breast cancer tissue section with amplification of the ERBB2 gene locus as indicated by multiple copies of the green signal in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2292-5.1ML	ZytoMation ERBB2/CEN 17 Dual Color FISH Probe CE IVD	●/●	up to 20 (5.1 ml)

** Using 240 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot ® Products for CISH analysis

ZytoDot ® 2C Products for CISH analysis

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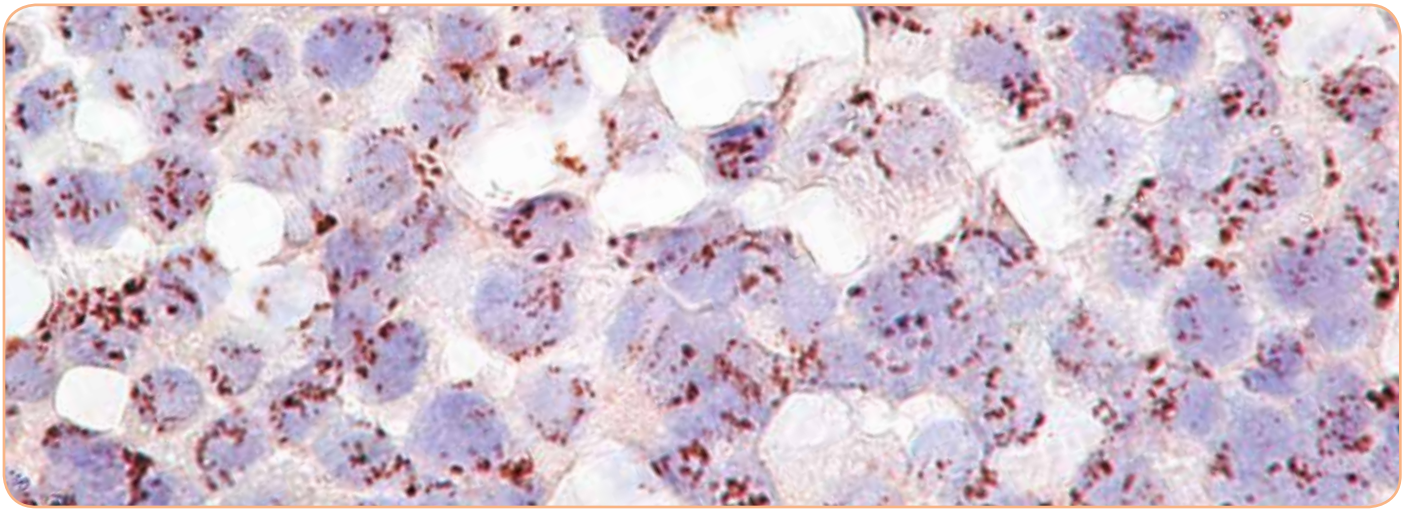
Reliable and Simple Detection of Genomic Alterations using Light Microscopy!



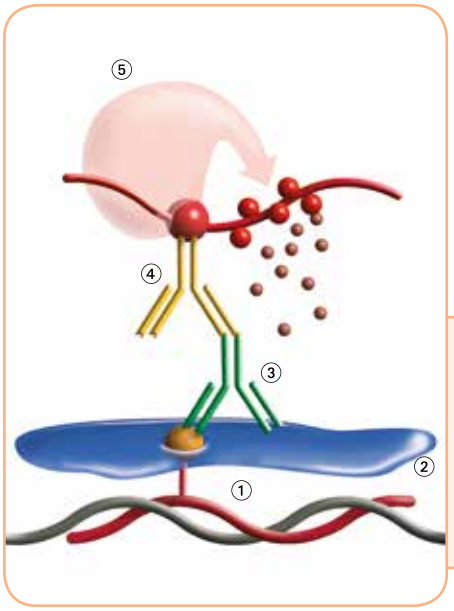
Introduction
The Zyto*Dot* ® products are designed for the detection of aneuploidies and gene amplifications by Chromogenic *in situ* Hybridization (CISH) in formalin-fixed, paraffin-embedded tissue sections, cell samples, blood or bone marrow smears, and metaphase chromosome spreads.

CISH: A reliable Alternative to FISH
High concordance between CISH and FISH ranging from 92-100% has been shown by numerous international studies for ERBB2 amplification.

Advantages of CISH
- Quick and easy interpretation of results comparable to IHC
- Simultaneous observation of tissue morphology and CISH signals
- Storage of slides at room temperature - CISH signals are permanent
- No costly fluorescent microscope needed

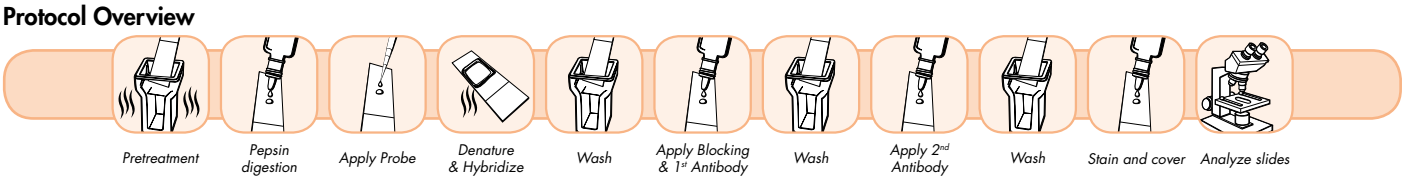
High Signal-to-Noise Ratio
The Zyto*Dot* ® probes are processed by the unique ZytoVision ® *Repeat Subtraction Technique* resulting in advanced specificity and less background. No further blocking of repetitive sequences is needed!

Zyto*Dot* ® Kits – Convenient Solutions
For making CISH analysis reliable and user-friendly, all Zyto*Dot* ® CISH probes can be combined with the Zyto*Dot* ® CISH Implementation Kit (C-3018-40) which includes all necessary pretreatment solutions, wash buffers, antibodies, chromogenic substrates, counterstaining solution, mounting solution and a detailed protocol to perform successful CISH experiments. Additionally, for ERBB2 a complete kit including the probe and all necessary reagents is available.

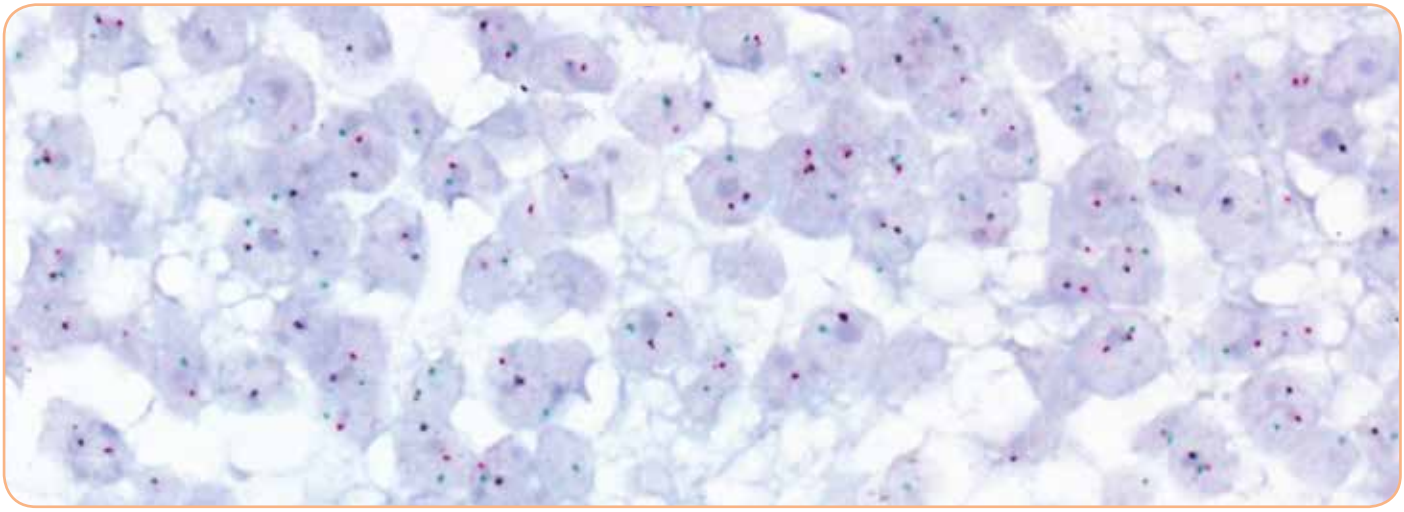


The Zyto*Dot* ® system uses Digoxigenin (DIG)-labeled probes ① which are, after blocking ②, detected using a Mouse-anti-DIG antibody ③. This antibody is detected by a polymerized HRP-Goat-anti-Mouse antibody ④. The enzymatic reaction of DAB ⑤ leads to the formation of strong permanent brown signals that can be visualized by light microscopy using a 40x objective.

Protocol Overview



ZytoDot® 2C™ – 2-Color CISH for the Detection of Genomic Alterations



Introduction

The ZytoDot® 2C™ products are designed for the simultaneous detection of two different genomic targets by Chromogenic *in situ* Hybridization (CISH) in formalin-fixed, paraffin-embedded tissue sections, cell samples, and blood or bone marrow smears. This two color system is especially useful for the differentiation of aneuploidies from gene amplifications, and the detection of deletions and translocations.

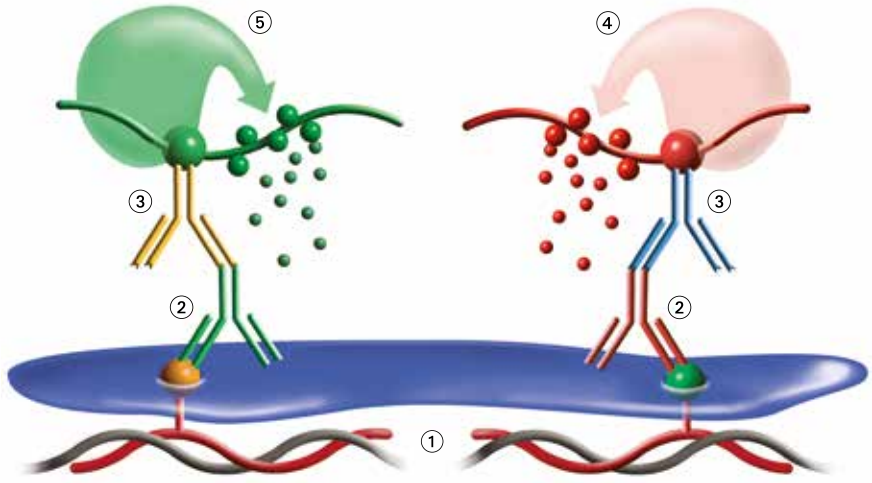
Advantages of ZytoDot® 2C™

- Simultaneous observation of tissue morphology and CISH signals at 40x using light microscopy
- Two targets detected simultaneously
- High contrasting distinct red and green signals
- Quick and easy interpretation of results comparable to IHC
- Standardized and complete kits
- No costly fluorescent microscope needed

ZytoDot® 2C™ Kits – Standardized Solutions

For making CISH analysis reliable and user-friendly, a complete ZytoDot® 2C™ kit is available for the detection of ERBB2 amplification. This kit includes the probe, all necessary pretreatment solutions, wash buffers, antibodies, chromogenic substrates, counterstaining and mounting solution, and a detailed protocol.

For other targets, any separately available ZytoDot® 2C™ probe can be combined with the ZytoDot® 2C™ CISH Implementation Kit resulting in target specific kit solutions.



The ZytoDot® 2C™ system uses DIG- and DNP-labeled probe cocktails targeting different genomic sections ① which are detected using a Mouse-anti-DIG/Rabbit-anti-DNP cocktail ②. These antibodies are detected by a unique cocktail of polymerized HRP-Goat-anti-Mouse/AP-Goat-anti-Rabbit antibodies ③. The enzymatic reaction of AP-Red ④ and HRP-Green ⑤ leads to the formation of strong permanent red respectively green signals that can be visualized by light microscopy using a 40x objective.

Protocol Overview

Chromosome Index

Chr. Band	Product Name	Product No.	Quantity	Page
1				
1p36.3	ZytoDot 2C Glioma 1p/19q Probe Set CE IVD	C-3076-10/-40	10/40 tests	206
	ZytoDot 2C SPEC 1p36/1q25 Probe CE IVD	C-3036-100/-400	100/400 µl	207
1p12	ZytoDot SPEC 1p12 Probe CE IVD	C-3035-400	400 µl	242 f.
1q25.3	ZytoDot 2C Glioma 1p/19q Probe Set CE IVD	C-3076-10/-40	10/40 tests	206
	ZytoDot 2C SPEC 1p36/1q25 Probe CE IVD	C-3036-100/-400	100/400 µl	207
2				
2p24	ZytoDot SPEC MYCN Probe CE IVD	C-3029-400	400 µl	209
2p23	ZytoDot 2C SPEC ALK Break Apart Probe CE IVD	C-3055-100/-400	100/400 µl	210
2p21	ZytoDot 2C SPEC EML4 Break Apart Probe CE IVD	C-3059-400	400 µl	211
2q11.2	ZytoDot SPEC 2q11 Probe CE IVD	C-3051-400	400 µl	242 f.
3				
3p11.1-q11.1	ZytoDot CEN 3 Probe CE IVD	C-3045-400	400 µl	242 f.
3q27	ZytoDot 2C SPEC BCL6 Break Apart Probe CE IVD	C-3074-100	100 µl	212
4-5	no probes available yet			
6				
6p11.1-q11	ZytoDot CEN 6 Probe CE IVD	C-3002-400	400 µl	242 f.
6q22.1	ZytoDot 2C SPEC ROS1 Break Apart Probe CE IVD	C-3063-100/-400	100/400 µl	213

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Chromosome Index

Chr. Band	Product Name	Product No.	Quantity	Page
7				
7p11.2	ZytoDot SPEC EGFR Probe CE IVD	C-3007-400	400 µl	214
	ZytoDot 2C SPEC EGFR/CEN 7 Probe CE IVD	C-3033-100/-400	100/400 µl	215
7p11.1-q11.1	ZytoDot CEN 7 Probe CE IVD	C-3008-400	400 µl	242 f.
7q31.2	ZytoDot 2C SPEC MET/CEN 7 Probe CE IVD	C-3057-400	400 µl	216
8				
8p11.2	ZytoDot 2C SPEC FGFR1/CEN 8 Probe CE IVD	C-3050-400	400 µl	217
8p11.1-q11.1	ZytoDot CEN 8 Probe CE IVD	C-3016-400	400 µl	242 f.
8q24.21	ZytoDot SPEC MYC Probe CE IVD	C-3013-400	400 µl	218
	ZytoDot 2C SPEC MYC Break Apart Probe CE IVD	C-3066-400	400 µl	219
9				
9p21	ZytoDot 2C SPEC CDKN2A/CEN 9 Probe CE IVD	C-3067-400	400 µl	220
10				
10q11.2	ZytoDot 2C SPEC RET Break Apart Probe CE IVD	C-3064-100/-400	100/400 µl	221
10q23.3	ZytoDot 2C SPEC PTEN/CEN 10 Probe CE IVD	C-3053-400	400 µl	222
10q26.1	ZytoDot 2C SPEC FGFR2/CEN 10 Probe CE IVD	C-3056-400	400 µl	223
11				
11q13.3	ZytoDot 2C SPEC CCND1 Break Apart Probe CE IVD	C-3075-100	100 µl	224
12				
12p11.1-q11	ZytoDot CEN 12 Probe CE IVD	C-3014-400	400 µl	242 f.
12q13.3	ZytoDot 2C SPEC DDIT3 Break Apart Probe CE IVD	C-3047-100	100 µl	225
12q14	ZytoDot 2C SPEC CDK4/CEN 12 Probe CE IVD	C-3062-400	400 µl	226
12q15	ZytoDot SPEC MDM2 Probe CE IVD	C-3012-400	400 µl	227
	ZytoDot 2C SPEC MDM2/CEN 12 Probe CE IVD	C-3049-100/-400	100/400 µl	228

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Chromosome Index

		Chr. Band	Product Name	Product No.	Quantity	Page
13		13q12.1	ZytoDot SPEC 13q12 Probe CE IVD	C-3052-400	400 µl	242 f.
		13q14.1	ZytoDot 2C SPEC FOXO1 Break Apart Probe CE IVD	C-3065-100	100 µl	229
14		14q32.3	ZytoDot 2C SPEC IGH Break Apart Probe CE IVD	C-3071-100	100 µl	230
15			no probes available yet			
16		16p11.2	ZytoDot 2C SPEC FUS Break Apart Probe CE IVD	C-3054-100	100 µl	231
17		17p13	ZytoDot 2C SPEC USP6 Break Apart Probe CE IVD NEW	C-3077-100	100 µl	232
		17p11.1-q11.1	ZytoDot CEN 17 Probe CE IVD	C-3006-400	400 µl	242 f.
		17q12	ZytoDot SPEC ERBB2 Probe CE IVD	C-3001-400	400 µl	233
			ZytoDot SPEC ERBB2 Probe Kit CE IVD	C-3003-40	40 tests	233
			ZytoDot 2C SPEC ERBB2/CEN 17 Probe CE IVD	C-3032-100/-400	100/400 µl	234
			ZytoDot 2C SPEC ERBB2/CEN 17 Probe Kit CE IVD	C-3022-10/-40	10/40 tests	234
			ZytoDot 2C SPEC ERBB2/D17S122 Probe CE IVD	C-3068-100	100 µl	235
		17q21.2	ZytoDot 2C SPEC TOP2A/CEN 17 Probe CE IVD	C-3040-400	400 µl	236
18		18q11.2	ZytoDot 2C SPEC SS18 Break Apart Probe CE IVD	C-3046-100	100 µl	237
		18q21.3	ZytoDot 2C SPEC BCL2 Break Apart Probe CE IVD	C-3073-100	100 µl	238
			ZytoDot 2C SPEC MALT1 Break Apart Probe CE IVD	C-3072-100	100 µl	239
19		19p13.3	ZytoDot 2C Glioma 1p/19q Probe Set CE IVD	C-3076-10/-40	10/40 tests	206
			ZytoDot 2C SPEC 19q13/19p13 Probe CE IVD	C-3037-100/-400	100/400 µl	208
		19q13.3	ZytoDot 2C Glioma 1p/19q Probe Set CE IVD	C-3076-10/-40	10/40 tests	206
			ZytoDot 2C SPEC 19q13/19p13 Probe CE IVD	C-3037-100/-400	100/400 µl	208
20			no probes available yet			

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Chromosome Index

		Chr. Band	Product Name	Product No.	Quantity	Page
21		21q22.1-q22.2	ZytoDot SPEC 21q22 Probe CE IVD	C-3026-400	400 µl	242 f.
		21q22.2	ZytoDot 2C SPEC ERG Break Apart Probe CE IVD	C-3058-400	400 µl	240
22		22q12.2	ZytoDot 2C SPEC EWSR1 Break Apart Probe CE IVD	C-3043-100	100 µl	241
X		Xp11.1-q11.1	ZytoDot CEN X Probe CE IVD	C-3025-400	400 µl	242 f.
			ZytoDot 2C CEN X/Y Probe CE IVD	C-3048-400	400 µl	242 f.
Y		Yp11.1-q11.1	ZytoDot 2C CEN X/Y Probe CE IVD	C-3048-400	400 µl	242 f.
		Yq12	ZytoDot CEN Yq12 Probe CE IVD	C-3020-400	400 µl	242 f.

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Gene Index

HUGO Name	Synonym	Product Name	Product No.	Quantity	Page
ALK	CD246	ZytoDot 2C SPEC ALK Break Apart Probe CE IVD	C-3055-100/-400	100/400 µl	210
BCL2	Bcl-2, PPP1R50	ZytoDot 2C SPEC BCL2 Break Apart Probe CE IVD	C-3073-100	100 µl	238
BCL6	ZNF51, LAZ3	ZytoDot 2C SPEC BCL6 Break Apart Probe CE IVD	C-3074-100	100 µl	212
CCND1	BCL1, PRAD1	ZytoDot 2C SPEC CCND1 Break Apart Probe CE IVD	C-3075-100	100 µl	224
CDK4	PSK-J3	ZytoDot 2C SPEC CDK4/CEN 12 Probe CE IVD	C-3062-400	400 µl	226
CDKN2A	p16, ARF, INK4	ZytoDot 2C SPEC CDKN2A/CEN 9 Probe CE IVD	C-3067-400	400 µl	220
DDIT3	CHOP, GADD153	ZytoDot 2C SPEC DDIT3 Break Apart Probe CE IVD	C-3047-100	100 µl	225
EGFR	HER1, ERBB1	ZytoDot SPEC EGFR Probe CE IVD ZytoDot 2C SPEC EGFR/CEN 7 Probe CE IVD	C-3007-400 C-3033-100/-400	400 µl 100/400 µl	214 215
EML4	ROPP120	ZytoDot 2C SPEC EML4 Break Apart Probe CE IVD	C-3059-400	400 µl	211
ERBB2	HER2, HER-2, NEU	ZytoDot SPEC ERBB2 Probe CE IVD ZytoDot SPEC ERBB2 Probe Kit CE IVD ZytoDot 2C SPEC ERBB2/CEN 17 Probe CE IVD ZytoDot 2C SPEC ERBB2/CEN 17 Probe Kit CE IVD ZytoDot 2C SPEC ERBB2/D17S122 Probe CE IVD	C-3001-400 C-3003-40 C-3032-100/-400 C-3022-10/-40 C-3068-100	400 µl 40 tests 100/400 µl 10/40 tests 100 µl	233 233 234 234 235
ERG	erg-3, p55	ZytoDot 2C SPEC ERG Break Apart Probe CE IVD	C-3058-400	400 µl	240
EWSR1	EWS	ZytoDot 2C SPEC EWSR1 Break Apart Probe CE IVD	C-3043-100	100 µl	241
FGFR1	FLT2, BFGFR	ZytoDot 2C SPEC FGFR1/CEN 8 Probe CE IVD	C-3050-400	400 µl	217
FGFR2	BEK, CD332	ZytoDot 2C SPEC FGFR2/CEN 10 Probe CE IVD	C-3056-400	400 µl	223
FOXO1	FKHR, FKH1	ZytoDot 2C SPEC FOXO1 Break Apart Probe CE IVD	C-3065-100	100 µl	229
FUS	FUS1	ZytoDot 2C SPEC FUS Break Apart Probe CE IVD	C-3054-100	100 µl	231
IGH	IGH@	ZytoDot 2C SPEC IGH Break Apart Probe CE IVD	C-3071-100	100 µl	230
MALT1	MLT	ZytoDot 2C SPEC MALT1 Break Apart Probe CE IVD	C-3072-100	100 µl	239
MDM2	HDM2	ZytoDot SPEC MDM2 Probe CE IVD ZytoDot 2C SPEC MDM2/CEN 12 Probe CE IVD	C-3012-400 C-3049-100/-400	400 µl 100/400 µl	227 228
MET	HGFR, RCCP2	ZytoDot 2C SPEC MET/CEN 7 Probe CE IVD	C-3057-400	400 µl	216
MYC	CMYC, bHLHe39, c-Myc	ZytoDot SPEC MYC Probe CE IVD ZytoDot 2C SPEC MYC Break Apart Probe CE IVD	C-3013-400 C-3066-400	400 µl 400 µl	218 219

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Gene Index

HUGO Name	Synonym	Product Name	Product No.	Quantity	Page
MYCN	NMYC, N-myc	*ZytoDot* SPEC MYCN Probe CE IVD	C-3029-400	400 µl	209
PTEN	MMAC1, TEP1	*ZytoDot* 2C SPEC PTEN/CEN 10 Probe CE IVD	C-3053-400	400 µl	222
RET	HSCR1, CDHF12	*ZytoDot* 2C SPEC RET Break Apart Probe CE IVD	C-3064-100/-400	100/400 µl	221
ROS1	MCF3, ROS	*ZytoDot* 2C SPEC ROS1 Break Apart Probe CE IVD	C-3063-100/-400	100/400 µl	213
SS18	SYT, SSXT	*ZytoDot* 2C SPEC SS18 Break Apart Probe CE IVD	C-3046-100	100 µl	237
TOP2A	TOP2	*ZytoDot* 2C SPEC TOP2A/CEN 17 Probe CE IVD	C-3040-400	400 µl	236
USP6	Tre-2, TRE17	*ZytoDot* 2C SPEC USP6 Break Apart Probe CE IVD NEW	C-3077-100	100 µl	232

The **Gene Index** list includes only those probes directed against DNA sequences assigned to known genes. It does not contain probes directed against other genomic sequences as e.g. repetitive satellite DNA sequences. For a complete overview of all *ZytoDot* ® probes, please refer to the **Chromosome Index**.

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Indication Index

Indication	Product Name	Product No.	Quantity	Page
Solid Tumors				
Brain and Neural Tumors	ZytoDot 2C Glioma 1p/19q Probe Set CE IVD	C-3076-10/-40	10/40 tests	206
	ZytoDot 2C SPEC 1p36/1q25 Probe CE IVD	C-3036-100/-400	100/400 µl	207
	ZytoDot 2C SPEC 19q13/19p13 Probe CE IVD	C-3037-100/-400	100/400 µl	208
	ZytoDot 2C SPEC CDKN2A/CEN 9 Probe CE IVD	C-3067-400	400 µl	220
	ZytoDot SPEC EGFR Probe CE IVD	C-3007-400	400 µl	214
	ZytoDot 2C SPEC EGFR/CEN 7 Probe CE IVD	C-3033-100/-400	100/400 µl	215
	ZytoDot 2C SPEC MET/CEN 7 Probe CE IVD	C-3057-400	400 µl	216
	ZytoDot SPEC MYCN Probe CE IVD	C-3029-400	400 µl	209
	ZytoDot 2C SPEC PTEN/CEN 10 Probe CE IVD	C-3053-400	400 µl	222
Breast Cancer	ZytoDot SPEC EGFR Probe CE IVD	C-3007-400	400 µl	214
	ZytoDot 2C SPEC EGFR/CEN 7 Probe CE IVD	C-3033-100/-400	100/400 µl	215
	ZytoDot SPEC ERBB2 Probe CE IVD	C-3001-400	400 µl	233
	ZytoDot SPEC ERBB2 Probe Kit CE IVD	C-3003-40	40 tests	233
	ZytoDot 2C SPEC ERBB2/CEN 17 Probe CE IVD	C-3032-100/-400	100/400 µl	234
	ZytoDot 2C SPEC ERBB2/CEN 17 Probe Kit CE IVD	C-3022-10/-40	10/40 tests	234
	ZytoDot 2C SPEC ERBB2/D17S122 Probe CE IVD	C-3068-100	100 µl	235
	ZytoDot 2C SPEC FGFR1/CEN 8 Probe CE IVD	C-3050-400	400 µl	217
	ZytoDot 2C SPEC FGFR2/CEN 10 Probe CE IVD	C-3056-400	400 µl	223
	ZytoDot SPEC MYC Probe CE IVD	C-3013-400	400 µl	218
	ZytoDot 2C SPEC TOP2A/CEN 17 Probe CE IVD	C-3040-400	400 µl	236
Cervical Cancer	ZytoDot SPEC MYC Probe CE IVD	C-3013-400	400 µl	218
Gastrointestinal Cancer	ZytoDot SPEC ERBB2 Probe CE IVD	C-3001-400	400 µl	233
	ZytoDot SPEC ERBB2 Probe Kit CE IVD	C-3003-40	40 tests	233
	ZytoDot 2C SPEC ERBB2/CEN 17 Probe CE IVD	C-3032-100/-400	100/400 µl	234
	ZytoDot 2C SPEC ERBB2/CEN 17 Probe Kit CE IVD	C-3022-10/-40	10/40 tests	234
	ZytoDot 2C SPEC ERBB2/D17S122 Probe CE IVD	C-3068-100	100 µl	235
	ZytoDot SPEC MDM2 Probe CE IVD	C-3012-400	400 µl	227
	ZytoDot 2C SPEC MDM2/CEN 12 Probe CE IVD	C-3049-100/-400	100/400 µl	228
Lung Cancer	ZytoDot 2C SPEC ALK Break Apart Probe CE IVD	C-3055-100/-400	100/400 µl	210
	ZytoDot 2C SPEC EML4 Break Apart Probe CE IVD	C-3059-400	400 µl	211
	ZytoDot SPEC EGFR Probe CE IVD	C-3007-400	400 µl	214
	ZytoDot 2C SPEC EGFR/CEN 7 Probe CE IVD	C-3033-100/-400	100/400 µl	215
	ZytoDot SPEC ERBB2 Probe CE IVD	C-3001-400	400 µl	233
	ZytoDot SPEC ERBB2 Probe Kit CE IVD	C-3003-40	40 tests	233
	ZytoDot 2C SPEC ERBB2/CEN 17 Probe CE IVD	C-3032-100/-400	100/400 µl	234
	ZytoDot 2C SPEC ERBB2/CEN 17 Probe Kit CE IVD	C-3022-10/-40	10/40 tests	234
	ZytoDot 2C SPEC ERBB2/D17S122 Probe CE IVD	C-3068-100	100 µl	235
	ZytoDot 2C SPEC FGFR1/CEN 8 Probe CE IVD	C-3050-400	400 µl	217
	ZytoDot 2C SPEC FGFR2/CEN 10 Probe CE IVD	C-3056-400	400 µl	223
	ZytoDot 2C SPEC MET/CEN 7 Probe CE IVD	C-3057-400	400 µl	216
	ZytoDot 2C SPEC RET Break Apart Probe CE IVD	C-3064-100/-400	100/400 µl	221
	ZytoDot 2C SPEC ROS1 Break Apart Probe CE IVD	C-3063-100/-400	100/400 µl	213

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Indication Index

Indication	Product Name	Product No.	Quantity	Page
Prostate Cancer	ZytoDot 2C SPEC ERG Break Apart Probe CE IVD	C-3058-400	400 µl	240
	ZytoDot 2C SPEC PTEN/CEN 10 Probe CE IVD	C-3053-400	400 µl	222
Salivary Gland Tumors	ZytoDot 2C SPEC EWSR1 Break Apart Probe CE IVD	C-3043-100	100 µl	241
Sarcomas	ZytoDot 2C SPEC ALK Break Apart Probe CE IVD	C-3055-100/-400	100/400 µl	210
	ZytoDot 2C SPEC CDK4/CEN 12 Probe CE IVD	C-3062-400	400 µl	226
	ZytoDot 2C SPEC DDIT3 Break Apart Probe CE IVD	C-3047-100	100 µl	225
	ZytoDot 2C SPEC EWSR1 Break Apart Probe CE IVD	C-3043-100	100 µl	241
	ZytoDot 2C SPEC FOXO1 Break Apart Probe CE IVD	C-3065-100	100 µl	229
	ZytoDot 2C SPEC FUS Break Apart Probe CE IVD	C-3054-100	100 µl	231
	ZytoDot SPEC MDM2 Probe CE IVD	C-3012-400	400 µl	227
	ZytoDot 2C SPEC MDM2/CEN 12 Probe CE IVD	C-3049-100/-400	100/400 µl	228
	ZytoDot SPEC MYC Probe CE IVD	C-3013-400	400 µl	218
	ZytoDot 2C SPEC SS18 Break Apart Probe CE IVD	C-3046-100	100 µl	237
	ZytoDot 2C SPEC USP6 Break Apart Probe CE IVD NEW	C-3077-100	100 µl	232
Hematology Specific Probes				
Acute Myelogenous Leukemia (AML)	ZytoDot CEN 8 Probe CE IVD	C-3016-400	400 µl	242 f.
Chronic Lymphocytic Leukemia (CLL)	ZytoDot 2C SPEC BCL2 Break Apart Probe CE IVD	C-3073-100	100 µl	238
	ZytoDot 2C SPEC CCND1 Break Apart Probe CE IVD	C-3075-100	100 µl	224
	ZytoDot SPEC MYC Probe CE IVD	C-3013-400	400 µl	218
Chronic Myelogenous Leukemia (CML)	ZytoDot CEN 8 Probe CE IVD	C-3016-400	400 µl	242 f.
Multiple Myeloma	ZytoDot 2C SPEC CCND1 Break Apart Probe CE IVD	C-3075-100	100 µl	224
	ZytoDot 2C SPEC IGH Break Apart Probe CE IVD	C-3071-100	100 µl	230
Myelodysplastic Syndrome (MDS)	ZytoDot CEN 8 Probe CE IVD	C-3016-400	400 µl	242 f.
Non-Hodgkin Lymphoma, other	ZytoDot 2C SPEC BCL2 Break Apart Probe CE IVD	C-3073-100	100 µl	238
	ZytoDot 2C SPEC BCL6 Break Apart Probe CE IVD	C-3074-100	100 µl	212
	ZytoDot 2C SPEC CCND1 Break Apart Probe CE IVD	C-3075-100	100 µl	224
	ZytoDot 2C SPEC IGH Break Apart Probe CE IVD	C-3071-100	100 µl	230
	ZytoDot 2C SPEC MALT1 Break Apart Probe CE IVD	C-3072-100	100 µl	239
	ZytoDot 2C SPEC MYC Break Apart Probe CE IVD	C-3066-400	400 µl	219
Genetics				
Sex Mismatched Bone-Marrow Transplantant Management	ZytoDot CEN X Probe CE IVD	C-3025-400	400 µl	242 f.
	ZytoDot CEN Yq12 Probe CE IVD	C-3020-400	400 µl	242 f.
	ZytoDot 2C CEN X/Y Probe CE IVD	C-3048-400	400 µl	242 f.
Prenatal, Postnatal, and Preimplantation Genetics	ZytoDot SPEC 21q22 Probe CE IVD	C-3026-400	400 µl	242 f.
	ZytoDot CEN X Probe CE IVD	C-3025-400	400 µl	242 f.
	ZytoDot CEN Yq12 Probe CE IVD	C-3020-400	400 µl	242 f.
	ZytoDot 2C CEN X/Y Probe CE IVD	C-3048-400	400 µl	242 f.

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ZytoDot® 2C Glioma 1p/19q Probe Set

CE IVD

Background

Deletions affecting the short arm of chromosome 1 (1p36) and the long arm of chromosome 19 (19q13) are frequently found in human gliomas.
According to the 2016 WHO criteria for classification of tumors of the central nervous system, the detection of 1p/19q loss is required for the diagnosis of WHO grade II or III "oligodendroglioma, IDH-mutant and 1p/19q codeleted". Since both, astrocytomas and oligodendrogliomas, can exhibit IDH mutations, evaluation of 1p/19q status plays a critical role in differentiating astrocytoma from oligodendroglioma.
Oligodendroglioma morphology, IDH-mutant genotype, and 1p/19q codeletion are associated with better response to chemotherapy and improved survival. Hence, determination of 1p and 19q status may aid in therapeutic decisions and predict outcome in patients with diffuse gliomas.

References
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Louis DN, et al. (ed.) (2016) WHO Classification of Tumours of the Central Nervous System (Revised 4th Edition).
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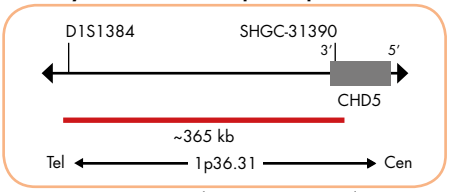
Smith JS, et al. (2000) Genes Chromosomes Cancer 29: 16-25.

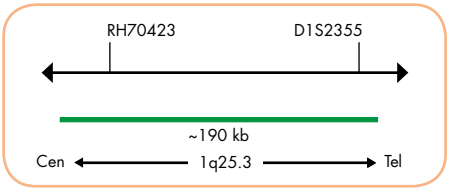
Probe Description

The ZytoDot® 2C Glioma 1p/19q Probe Set includes the ZytoDot® 2C SPEC 1p36/1q25 Probe and the ZytoDot® 2C SPEC 19q13/19p13 Probe for the detection of both 1p36 and 19q13 loci.

ZytoDot® 2C SPEC 1p36/1q25 Probe

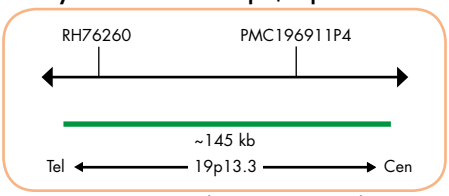


SPEC 1p36 Probe map (not to scale).

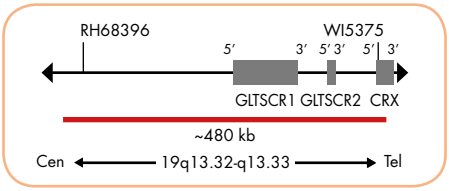


SPEC 1q25 Probe map (not to scale).

ZytoDot® 2C SPEC 19q13/19p13 Probe



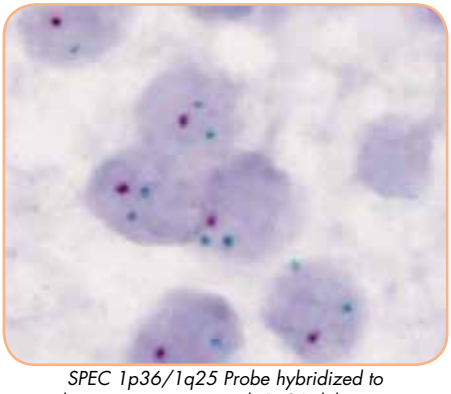
SPEC 19p13 Probe map (not to scale).



SPEC 19q13 Probe map (not to scale).

Results

Using the SPEC 1p36/1q25 Probe or the SPEC 19q13/19p13 Probe in a normal interphase nucleus, two red and two green signals are expected. In a cell with deletions affecting the 1p36 or 19q13 locus, one or no copy of the red signal will be observed.



SPEC 1p36/1q25 Probe hybridized to glioma tissue section with 1p36 deletion as indicated by one red signal in each nucleus.

SPEC 19q13/19p13 Dual Color Probe hybridized to glioma tissue section with 19q13 deletion as indicated by one red signal in each nucleus.

Images kindly provided by Prof. W. Müller, University Leipzig, Germany.

Prod. No.	Product	Label	Tests* (Volume)
C-3076-10	ZytoDot 2C Glioma 1p/19q Probe Set CE IVD Incl. ZytoDot 2C SPEC 1p36/1q25 Probe, 0.1 ml; ZytoDot 2C SPEC 19q13/19p13 Probe, 0.1 ml		10
C-3076-40	ZytoDot 2C Glioma 1p/19q Probe Set CE IVD Incl. ZytoDot 2C SPEC 1p36/1q25 Probe, 0.4 ml; ZytoDot 2C SPEC 19q13/19p13 Probe, 0.4 ml		40
Related Products			
C-3036-100/-400	ZytoDot 2C SPEC 1p36/1q25 Probe CE IVD	DNP/DIG	10/40 (100 µl/400 µl)
C-3037-100/-400	ZytoDot 2C SPEC 19q13/19p13 Probe CE IVD	DNP/DIG	10/40 (100 µl/400 µl)
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC 1p36/1q25 Probe

CE IVD

Background

The ZytoDot® 2C SPEC 1p36/1q25 Probe is designed for the detection of 1p deletions.

Deletions affecting the short arm of chromosome 1 (1p) are frequently found in human gliomas and neuroblastomas, but also in breast, lung, endometrial, ovarian, and colorectal carcinomas.

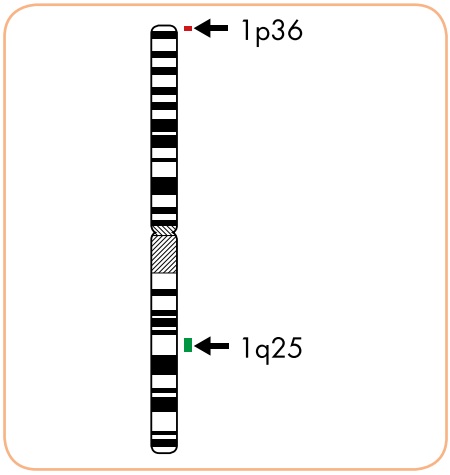
Deletions affecting the long arm of chromosome 19 (19q) are frequently found in human malignant gliomas as well as in neuroblastomas and epithelial ovarian cancers.

Combined loss of the complete 1p/19q chromosome arms, caused by an unbalanced t(1;19)(q10;p10) translocation, is characteristic of oligodendrogliomas. According to the 2016 WHO criteria for classification of tumors of the central nervous system, the detection of 1p/19q loss is required for the diagnosis of WHO grade II or III "oligodendroglioma, IDH-mutant and 1p/19q codeleted". Since both, astrocytomas and oligodendrogliomas, can exhibit IDH mutations, evaluation of 1p/19q status plays a critical role in differentiating astrocytoma from oligodendroglioma.

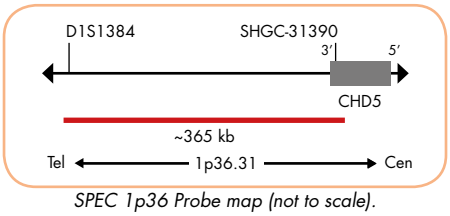
Oligodendroglioma morphology, IDH-mutant genotype, and 1p/19q codeletion are associated with better response to chemotherapy and improved survival. Hence, determination of 1p and 19q status may aid in therapeutic decisions and predict outcome in patients with diffuse gliomas.

Probe Description

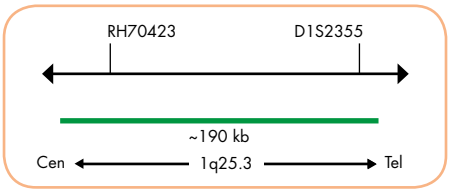
The ZytoDot® 2C SPEC 1p36/1q25 Probe is a mixture of a Dinitrophenyl-labeled 1p36 probe specific for the smallest region of consistent deletion (SRD) of chromosome 1 defined in neuroblastoma at 1p36.31 and a Digoxigenin-labeled 1q25 probe specific for 1q25.3.



Ideogram of chromosome 1 indicating the hybridization locations.



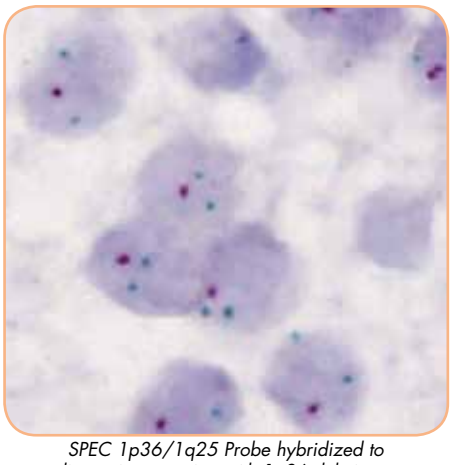
SPEC 1p36 Probe map (not to scale).



SPEC 1q25 Probe map (not to scale).

Results

In a normal interphase nucleus, using the ZytoDot® 2C SPEC 1p36/1q25 Probe in combination with ZytoDot® 2C CISH Implementation Kit, two red (1p) and two green (1q) signals are expected. In a cell with deletions affecting the 1p36 locus, one or no copy of the red signal will be observed.



SPEC 1p36/1q25 Probe hybridized to glioma tissue section with 1p36 deletion as indicated by one red signal in each nucleus.

Image kindly provided by Prof. W. Müller, University Leipzig, Germany.

References

Barbashina V, et al. (2005) Clin Cancer Res 11: 1119-28.
Cairncross JG, et al. (1998) J Natl Cancer Inst 90: 1473-9.
Cairncross G, et al. (2013) J Clin Oncol 31: 337-43.
Caron H, et al. (1996) N Engl J Med 334: 225-30.
Griffin CA, et al. (2006) J Neuropathol Exp Neurol 65: 988-94.
Louis DN, et al. (ed.) (2016) WHO Classification of Tumours of the Central Nervous System (Revised 4th Edition).
Lass U, et al. (2013) Brain Pathol 23: 311-8.
Ragnarsson G, et al. (1999) Br J Cancer 79: 1468-74.
Reifenberger G, et al. (2017) Nat Rev Clin Oncol 14: 434-52.
Rosenberg JE, et al. (1996) Oncogene 13: 2483-5.
Smith JS, et al. (1999) Oncogene 18: 4144-52.
Smith JS, et al. (2000) Genes Chromosomes Cancer 29: 16-25.

Prod. No.	Product	Label	Tests* (Volume)
C-3036-100	ZytoDot 2C SPEC 1p36/1q25 Probe CE IVD	DNP/DIG	10 (100 µl)
C-3036-400	ZytoDot 2C SPEC 1p36/1q25 Probe CE IVD	DNP/DIG	40 (400 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC 19q13/19p13 Probe

CE IVD

Background

The ZytoDot® 2C SPEC 19q13/19p13 Probe is designed for the detection of 19q deletions.

Deletions affecting the short arm of chromosome 1 (1p) are frequently found in human gliomas and neuroblastomas, but also in breast, lung, endometrial, ovarian, and colorectal carcinomas.

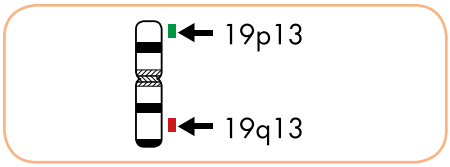
Deletions affecting the long arm of chromosome 19 (19q) are frequently found in human malignant gliomas as well as in neuroblastomas and epithelial ovarian cancers.

Combined loss of the complete 1p/19q chromosome arms, caused by an unbalanced t(1;19)(q10;p10) translocation, is characteristic of oligodendrogliomas. According to the 2016 WHO criteria for classification of tumors of the central nervous system, the detection of 1p/19q loss is required for the diagnosis of WHO grade II or III "oligodendroglioma, IDH-mutant and 1p/19q codeleted". Since both, astrocytomas and oligodendrogliomas, can exhibit IDH mutations, evaluation of 1p/19q status plays a critical role in differentiating astrocytoma from oligodendroglioma.

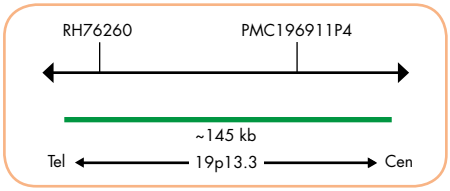
Oligodendroglioma morphology, IDH-mutant genotype, and 1p/19q codeletion are associated with better response to chemotherapy and improved survival. Hence, determination of 1p and 19q status may aid in therapeutic decisions and predict outcome in patients with diffuse gliomas.

Probe Description

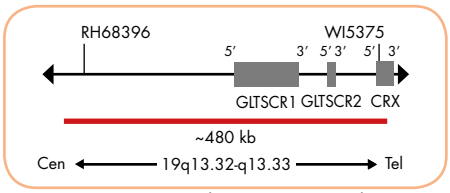
The ZytoDot® 2C SPEC 19q13/19p13 Probe is a mixture of a Dinitrophenyl-labeled 19q13 probe specific for the region of common deletion in gliomas at 19q13.32-q13.33 and a Digoxigenin-labeled 19p13 probe specific for 19p13.3.



Ideogram of chromosome 19 indicating the hybridization locations.



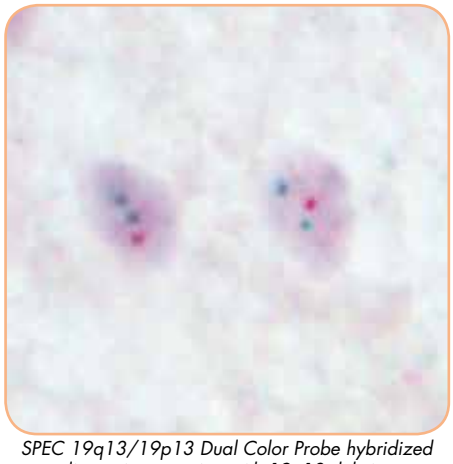
SPEC 19p13 Probe map (not to scale).



SPEC 19q13 Probe map (not to scale).

Results

Using the ZytoDot® 2C SPEC 19q13/19p13 Probe in combination with the ZytoDot® 2C CISH Implementation Kit, two red (19q) and two green (19p) signals are expected in a normal interphase nucleus. In a cell with deletions affecting the 19q13 locus, one or no copy of the red signal will be observed.



SPEC 19q13/19p13 Dual Color Probe hybridized to glioma tissue section with 19q13 deletion as indicated by one red signal in each nucleus.

Image kindly provided by Prof. W. Müller, University Leipzig, Germany.

References

Barbashina V, et al. (2005) Clin Cancer Res 11: 1119-28.
Cairncross JG, et al. (1998) J Natl Cancer Inst 90: 1473-9.
Cairncross G, et al. (2013) J Clin Oncol 31: 337-43.
Caron H, et al. (1996) N Engl J Med 334: 225-30.
Griffin CA, et al. (2006) J Neuropathol Exp Neurol 65: 988-94.
Louis DN, et al. (ed.) (2016) WHO Classification of Tumours of the Central Nervous System (Revised 4th Edition).
Lass U, et al. (2013) Brain Pathol 23: 311-8.
Ragnarsson G, et al. (1999) Br J Cancer 79: 1468-74.
Reifenberger G, et al. (2017) Nat Rev Clin Oncol 14: 434-52.
Rosenberg JE, et al. (1996) Oncogene 13: 2483-5.
Smith JS, et al. (1999) Oncogene 18: 4144-52.
Smith JS, et al. (2000) Genes Chromosomes Cancer 29: 16-25.

Prod. No.	Product	Label	Tests* (Volume)
C-3037-100	ZytoDot 2C SPEC 19q13/19p13 Probe CE IVD	DNP/DIG	10 (100 µl)
C-3037-400	ZytoDot 2C SPEC 19q13/19p13 Probe CE IVD	DNP/DIG	40 (400 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot ® SPEC MYCN Probe

CE IVD

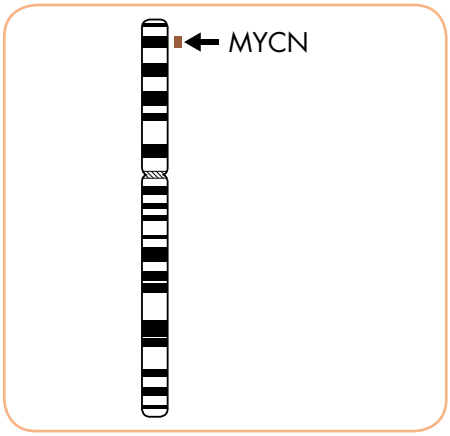
Background

The ZytoDot ® SPEC MYCN Probe is designed for the detection of MYCN amplification which represents the most powerful unfavorable prognostic factor for neuroblastoma. Less frequently amplifications are found in retinoblastoma, small cell lung cancer, astrocytoma and other tumors derived from the neuroectoderm.
The MYCN (MYCN proto-oncogene, bHLH transcription factor, a.k.a. NMYC) gene is located in the chromosomal region 2p24.3 and encodes a 62-64 kDa transcription factor normally expressed in the developing nervous system and other selected tissues.
The MYCN oncogene is amplified in about 25% of primary neuroblastomas and 90% of tumor-derived cell lines. Additional copies are rarely located at the normal locus but are detected as double minute chromosomes or homogeneously staining regions.
Amplification of the MYCN gene is strongly associated with rapid tumor progression, advanced stages of the disease, and poor prognosis. Hence, amplification status is increasingly being used for stratification of patients to different treatment protocols.

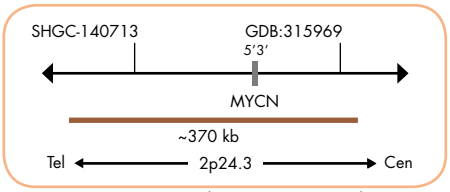
References
Kaneko M, et al. (1998) Med Pediatr Oncol 31: 1-7.
Lee WH, et al. (1984) Nature 309: 458-60.
Maris JM, et al. (2007) Lancet 369: 2106-20.
Slamon DJ, et al. (1986) Science 232: 768-72.
Suita S, et al. (2007) J Pediatr Surg 42: 489-93.
Thorner PS, et al. (2006) Am J Surg Pathol 30: 635-42.

Probe Description

The ZytoDot ® SPEC MYCN Probe is a Digoxigenin-labeled probe specific for the MYCN gene at 2p24.3, processed by the unique *ZytoVision® Repeat Subtraction Technique* resulting in advanced specificity and less background.



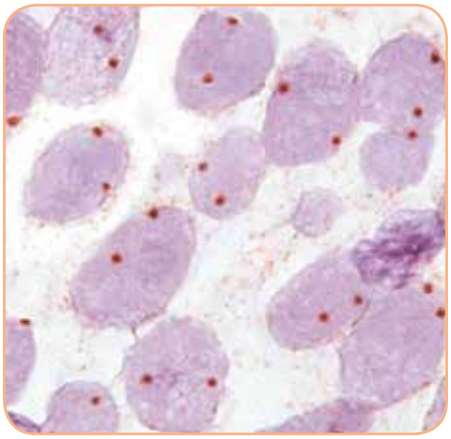
Ideogram of chromosome 2 indicating the hybridization locations.



SPEC MYCN Probe map (not to scale).

Results

In normal cells, two distinct dot-shaped signals per nucleus will be observed. Nuclei with amplification of the MYCN gene locus or aneuploidy of chromosome 2 will show multiple dots or large signal clusters.



Normal nuclei each with two MYCN signals.

Prod. No.	Product	Label	Tests* (Volume)
C-3029-400	ZytoDot SPEC MYCN Probe CE IVD	DIG	40 (400 µl)
Related Products			
C-3018-40	ZytoDot CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; PBS/Tween, good for 2000 ml; Blocking Solution, 4 ml; Mouse-anti-DIG, 4 ml; Anti-Mouse-HRP-Polymer, 4 ml; DAB Solution A, 0.3 ml; DAB Solution B, 10 ml; Mayer's Hematoxylin Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC ALK Break Apart Probe

CE IVD

Background

The ZytoDot® 2C SPEC ALK Break Apart Probe is designed to detect rearrangements involving the chromosomal region 2p23.2 harboring the ALK (ALK receptor tyrosine kinase, a.k.a. CD246) gene.

ALK encodes a transmembrane receptor tyrosine kinase. This gene exerts characteristic oncogenic activities through fusion to several gene partners or mutations both in hematopoietic and non-hematopoietic solid tumors.

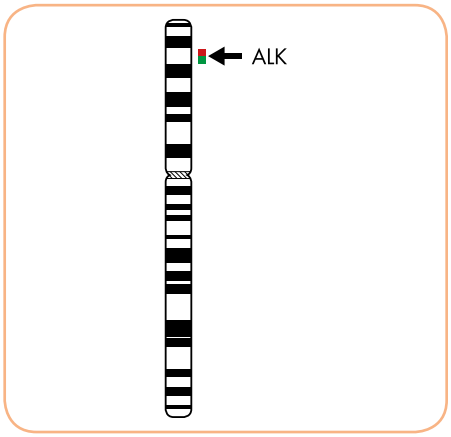
Translocations affecting the ALK gene locus are frequently found in anaplastic large cell lymphoma (ALCL), an aggressive non-Hodgkin lymphoma arising from T-cells. The most frequent translocation t(2;5) results in a fusion with the NPM1 (nucleophosmin a.k.a. nucleolar phosphoprotein B23, numatrin) gene located on chromosome 5q35. This rearrangement results in a NPM1/ALK fusion protein, which is constitutively activated through autophosphorylation, and that in turn mediates malignant cell transformation by activating downstream effectors like e.g. STAT3.

Additionally, inversions affecting the ALK gene located on the short arm of chromosome 2 [inv(2)(p21p23)] have been frequently detected in non-small cell lung cancer (NSCLC) and lead to the formation of EML4-ALK fusion transcripts.

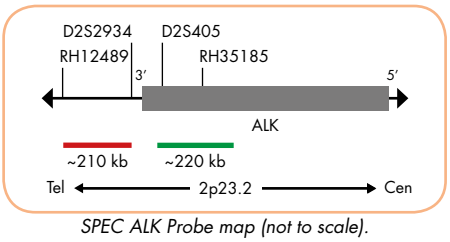
ALK kinase targeted therapies may represent a very effective therapeutic strategy in NSCLC patients carrying EML4-ALK rearrangements.

Probe Description

The ZytoDot® 2C SPEC ALK Break Apart Probe is a mixture of a Digoxigenin-labeled probe and a Dinitrophenyl-labeled probe hybridizing to the 2p23.2 band. The Digoxigenin-labeled probe hybridizes proximal to the ALK gene breakpoint region at 2p23.2, the Dinitrophenyl-labeled probe hybridizes distal to the ALK gene breakpoint region at 2p23.2.



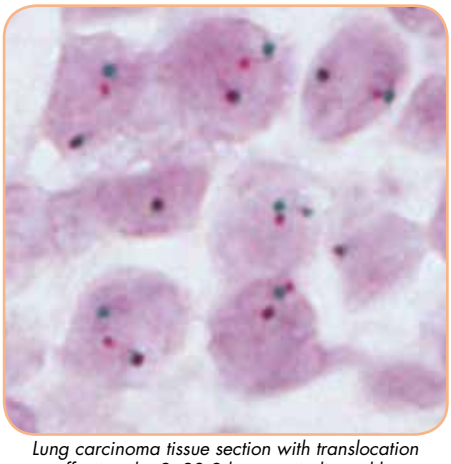
Ideogram of chromosome 2 indicating the hybridization locations.



SPEC ALK Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 2p23.2 band, using the ZytoDot® 2C CISH Implementation Kit, two red/green fusion signals are expected representing two normal (non-rearranged) 2p23.2 loci. A signal pattern consisting of one red/green fusion signal, one red signal, and a separate green signal indicates one normal 2p23.2 locus and one 2p23.2 locus affected by a translocation or inversion. EML4-ALK inversion with deletion of 5′-ALK sequences is indicated by one or multiple isolated red signals.



Lung carcinoma tissue section with translocation affecting the 2p23.2 locus as indicated by one red/green fusion (non-rearranged) signal, one red signal, and one separate green signal.

References
Inamura K, et al. (2009) Mod Pathol 22: 508-15.
Koivunen JP, et al. (2008) Clin Cancer Res 14: 4275-83.
Martelli MP, et al. (2009) Am J Pathol 174: 661-70.
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Perner S, et al. (2008) Neoplasia 10: 298-302.
Rodig SJ, et al. (2009) Clin Cancer Res 15: 5216-23.
Sasaki T, et al. (2010) Eur J Cancer 46: 1773-80.
Schildhaus HU, et al. (2013) Mod Pathol 26: 1468-77.
von Laffert M, et al. (2014) J Thorac Oncol 9: 1464-9.
Wagner F, et al. (2014) J Clin Pathol 67: 403-7.
Zhang Q, et al. (2007) Nat Med 11: 1341-8.

Prod. No.	Product	Label	Tests* (Volume)
C-3055-100	ZytoDot 2C SPEC ALK Break Apart Probe CE IVD	DIG/DNP	10 (100 µl)
C-3055-400	ZytoDot 2C SPEC ALK Break Apart Probe CE IVD	DIG/DNP	40 (400 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC EML4 Break Apart Probe

CE IVD

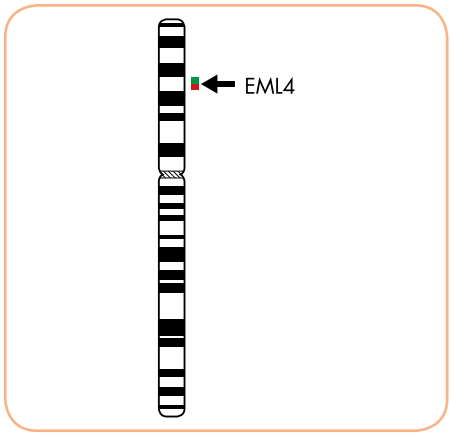
Background

The ZytoDot® 2C SPEC EML4 Break Apart Probe is designed to detect rearrangements involving the chromosomal region 2p21 harboring the EML4 (echinoderm microtubule-associated protein-like 4, a.k.a. ROPP120) gene.
Inversions in the short arm of chromosome 2 [inv(2)(p21p23)] have been frequently detected in non-small cell lung cancer (NSCLC) and lead to the formation of EML4-ALK fusion transcripts. A few reports also identified these fusion transcripts in breast, gastric, and colorectal cancers. EML4 belongs to the family of echinoderm microtubule-associated protein-like proteins. The EML4-ALK fusion transcripts comprise variably truncated N-terminal portions of the EML4 gene and the intracellular signaling domain of the ALK receptor tyrosine kinase (a.k.a. CD246). It was found that EML4 mediates ligand-independent dimerization of ALK, resulting in constitutive kinase activity. EML4-ALK was demonstrated to possess transforming activity *in vitro* and *in vivo*.
The EML4-ALK fusion transcript is found in about 5% of NSCLC, predominantly adenocarcinomas, and is considered to be mutually exclusive to EGFR or KRAS mutations. The detection of the inversion by *in situ* Hybridization might represent a valuable tool to identify a subpopulation of NSCLC likely to respond to ALK kinase targeting therapies.

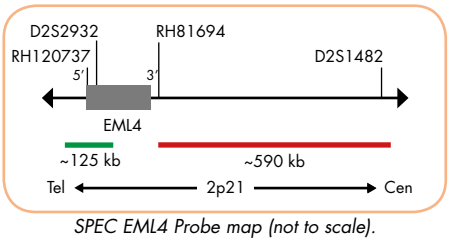
References
Choi YL, et al. (2008) Cancer Res 69: 4971-6.
Inamura K, et al. (2009) Mod Pathol 22: 508-15.
Lin E, et al. (2009) Mol Cancer Res 7: 1466-76.
Perner S, et al. (2008) Neoplasia 10: 298-302.
Rodig SJ, et al. (2009) Clin Cancer Res 15: 5216-23.
Schildhaus HU, et al. (2013) Mod Pathol 26: 1468-77.
Shaw AT, et al. (2009) J Clin Oncol 27: 4247-53.
Soda M, et al. (2007) Nature 448: 561-6.

Probe Description

The ZytoDot® 2C SPEC EML4 Break Apart Probe is a mixture of a Digoxigenin-labeled and a Dinitrophenyl-labeled probe hybridizing to the 2p21 band. The DNP-labeled probe hybridizes proximal to the EML4 gene breakpoint region at 2p21, the DIG-labeled probe hybridizes distal to the EML4 gene breakpoint region.



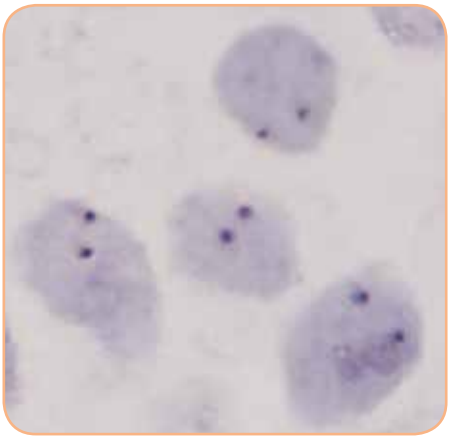
Ideogram of chromosome 2 indicating the hybridization locations.



SPEC EML4 Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 2p21 band, using the ZytoDot® 2C CISH Implementation Kit, two red/green fusion signals are expected representing two normal (non-rearranged) 2p21 loci. A signal pattern consisting of one red/green fusion signal, one red signal, and a separate green signal indicates one normal 2p21 locus and one 2p21 locus affected by a translocation or inversion.



SPEC EML4 Break Apart Probe hybridized to normal interphase cells as indicated by two red/green fusion signals pert nucleus.

Prod. No.	Product	Label	Tests* (Volume)
C-3059-400	ZytoDot 2C SPEC EML4 Break Apart Probe CE IVD	DIG/DNP	40 (400 µl)
Related Products			
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC BCL6 Break Apart Probe

CE IVD

Background

The ZytoDot® 2C SPEC BCL6 Break Apart Probe is designed for the detection of translocations involving the chromosomal region 3q27.3 harboring the BCL6 (BCL6 transcription repressor, a.k.a. ZNF51, LAZ3) gene.

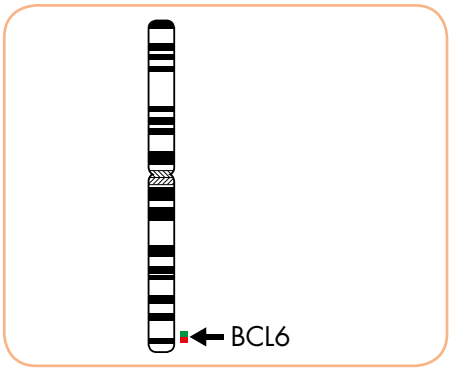
The BCL6 protein acts as a transcriptional repressor that is involved in the regulation of lymphoid development and function. Chromosomal rearrangements of the BCL6 gene region were found to occur in different types of non-Hodgkin lymphoma (NHL), including diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL). The most common BCL6 translocation t(3;14)(q27;q32.3) results in the IGH-BCL6 gene fusion. In addition, more than 20 partner loci have been identified including immunoglobulin (Ig) genes but also a number of non-Ig genes. As a result of these translocations, the rearranged BCL6 gene comes under the control of the promoter of the partner gene leading to deregulated expression of BCL6.

In DLBCL, the most common histologic subtype of NHL, BCL6 translocations represent one of the most frequent cytogenetic abnormality, occurring in 20% to 40% of the cases. Several studies reported a correlation of BCL6 translocation with an inferior overall survival. Moreover, DLBCL which are positive for both BCL6 and MYC rearrangements have been shown to have an extremely poor prognosis. Hence, the detection of BCL6 rearrangements by CISH may help in predicting the clinical outcome in patients with NHL.

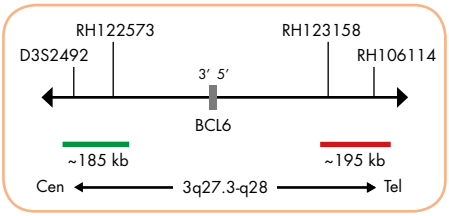
References
Akyurek N, et al. (2012) Cancer 118: 4173-83.
Cady FM, et al. (2008) J Clin Oncol 26: 4814-9.
Ohno H (2004) Histol Histopathol 19: 637-50.
Ohno H (2006) J Clin Exp Hematop 46: 43-53.

Probe Description

The ZytoDot® 2C SPEC BCL6 Break Apart Probe is a mixture of a Digoxigenin-labeled and a Dinitrophenyl-labeled probe hybridizing to the 3q27.3-q28 band. The DNP-labeled probe hybridizes distal to the BCL6 gene at 3q27.3-q28, the DIG-labeled probe hybridizes proximal to the BLC6 gene at 3q27.3.



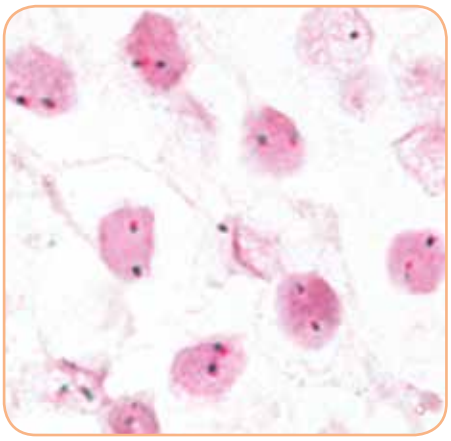
Ideogram of chromosome 3 indicating the hybridization locations.



SPEC BCL6 Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 3q27.3-q28 band, using the ZytoDot® 2C CISH Implementation Kit, two red/green fusion signals are expected representing two normal (non-rearranged) 3q27.3-q28 loci. A signal pattern consisting of one red/green fusion signal, one red signal, and a separate green signal indicates one normal 3q27.3-q28 locus and one 3q27.3-q28 locus affected by a translocation.



SPEC BCL6 Break Apart Probe hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.

Prod. No.	Product	Label	Tests* (Volume)
C-3074-100	ZytoDot 2C SPEC BCL6 Break Apart Probe CE IVD	DIG/DNP	10 (100 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC ROS1 Break Apart Probe

CE IVD

Background

The ZytoDot® 2C SPEC ROS1 Break Apart Probe is designed to detect translocations involving the chromosomal region 6q22.1 harboring the ROS proto-oncogene 1, receptor tyrosine kinase (ROS1, a.k.a. MCF3) gene.

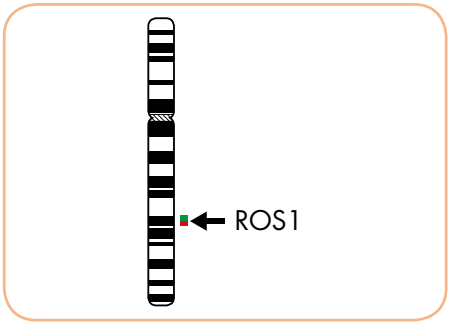
The ROS1 gene is located on 6q22.1 and encodes a receptor tyrosine kinase. Translocations affecting ROS1 have been detected in glioblastoma, cholangiocarcinoma, and non-small cell lung cancer (NSCLC).

In NSCLC several ROS1 translocation partners have been detected all of which result in the fusion of variably truncated forms of e.g. TPM3, SDC4, SLC34A2, CD74, EZR, or LRIG3 to the kinase domain of ROS1. GOPC has also been found to be fused to ROS1 in NSCLC. GOPC-ROS1 fusions result from interstitial deletion of approx. 240 kb on 6q22.1. ROS1 rearrangements have been exclusively detected in adenocarcinoma of the lung and are thought to define a molecular subset of NSCLC with distinct clinical characteristics that are similar to those observed in patients with ALK rearranged NSCLC.

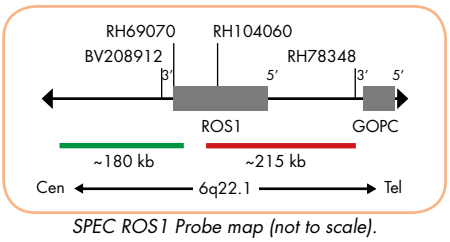
First evidence suggests that administration of ROS1 kinase inhibitors may represent a very effective therapeutic strategy in NSCLC patients harboring activating ROS1 rearrangements. Accordingly, detection of ROS1 rearrangements using Chromogenic *in situ* Hybridization might be a helpful tool for the identification of patients likely to respond to ROS1 kinase targeting therapies.

Probe Description

The ZytoDot® 2C SPEC ROS1 Break Apart Probe is a mixture of a Digoxigenin-labeled and a Dinitrophenyl-labeled probe hybridizing to the 6q22.1 band. The DNP-labeled probe hybridizes distal to the ROS1 gene breakpoint region at 6q22.1, the DIG-labeled probe hybridizes proximal to the ROS1 gene breakpoint region.



Ideogram of chromosome 6 indicating the hybridization locations.



SPEC ROS1 Probe map (not to scale).

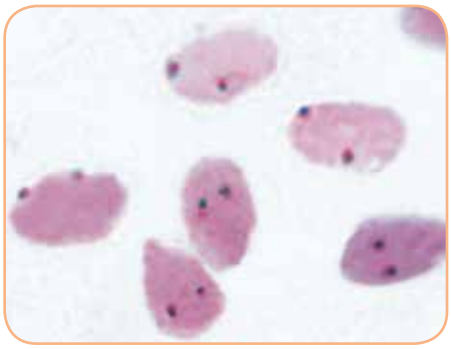
References

Bergethon K, et al. (2012) J Clin Oncol 30: 863-70.
Bos M, et al. (2013) Lung Cancer 81: 142-3.
Rikova K, et al. (2007) Cell 131: 1190-203.
Rimkunas VM, et al. (2012) Clin Cancer Res 18: 4449-57.
Suehara Y, et al. (2012) Clin Cancer Res 18: 6599-608.
Takeuchi K, et al. (2012) Nat Med 18: 378-81.

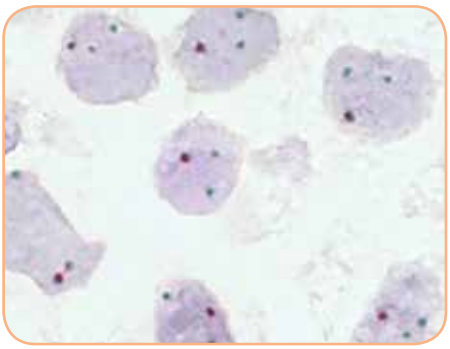
Results

In an interphase nucleus of a normal cell lacking an aberration involving the 6q22.1 band, using the ZytoDot® 2C CISH Implementation Kit, two red/green fusion signals are expected representing two normal (non-rearranged) 6q22.1 loci. A signal pattern consisting of one red/green fusion signal, one red signal, and a separate green signal indicates one normal 6q22.1 locus and one 6q22.1 locus affected by a translocation.

Isolated green signals are the result of deletions distal to the ROS1 breakpoint region or are due to unbalanced translocations affecting this chromosomal region.



SPEC ROS1 Break Apart Probe hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.



Lung cancer tissue section with rearrangement of the ROS1 gene as indicated by isolated green signals.

Prod. No.	Product	Label	Tests* (Volume)
C-3063-100	ZytoDot 2C SPEC ROS1 Break Apart Probe CE IVD	DIG/DNP	40 (400 µl)
C-3063-400	ZytoDot 2C SPEC ROS1 Break Apart Probe CE IVD	DIG/DNP	40 (400 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot ® SPEC EGFR Probe

CE IVD

Background

The ZytoDot ® SPEC EGFR Probe is designed for the detection of EGFR gene amplification frequently observed in solid neoplasms including non-small cell lung cancer (NSCLC) and glioblastoma. The EGFR gene (a.k.a. ERBB1 and HER1) is located in the chromosomal region 7p11.2 and encodes a transmembrane glycoprotein acting as a cellular growth factor receptor.

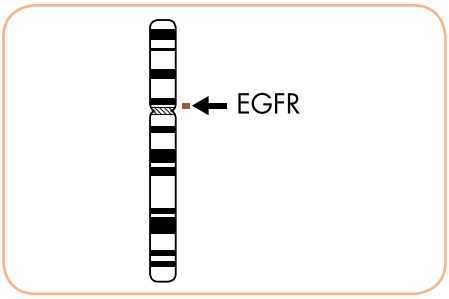
Overexpression of EGFR has been shown in a number of tumor entities and is associated with poor prognosis. EGFR copy number identified by *in situ* Hybridization is thought to be a molecular predictor in neoplasms.

References

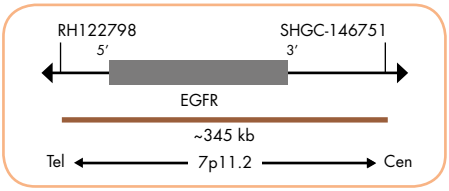
Balla P, et al. (2011) Histopathology 59: 376-89.
Brunner K, et al. (2010) Anal Quant Cytol Histol 32: 78-89.
Ettl T, et al. (2012) Hum Pathol 43: 921-31.
Gont A, et al. (2013) Oncotarget 4: 1266-79.
Isola J & Tanner M (2004) Methods Mol Med 97: 133-44.
Kondo I & Shimizu N (1983) Cytogenet Cell Genet 35: 9-14.
Laurent-Puig P, et al. (2009) J Clin Oncol 27: 5924-30.
Marquez A, et al. (2004) Diagn Mol Pathol 13: 1-8.
Miyazawa H, et al. (2008) Cancer Sci 99: 595-600.
Oikawa M, et al. (2013) J Oral Pathol Med 42: 424-34.
Thomas F, et al. (2007) Clin Cancer Res 13: 7086-92.
Tsukamoto T, et al. (1991) Int J Dev Biol 35: 25-32.
Walker F, et al. (2009) Hum Pathol 40: 1517-27.
Yoo SB, et al. (2010) Lung Cancer 67: 301-5.
Zaczek A, et al. (2005) Histol Histopathol 20: 1005-15.

Probe Description

The ZytoDot ® SPEC EGFR Probe is a Digoxigenin-labeled probe specific for the EGFR gene at 7p11.2, processed by the unique *ZytoVision® Repeat Subtraction Technique* resulting in advanced specificity and less background.



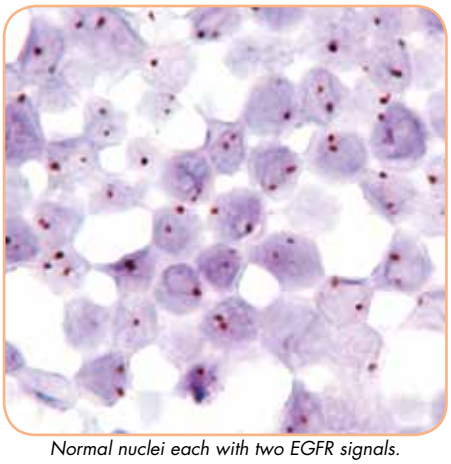
Ideogram of chromosome 7 indicating the hybridization locations.



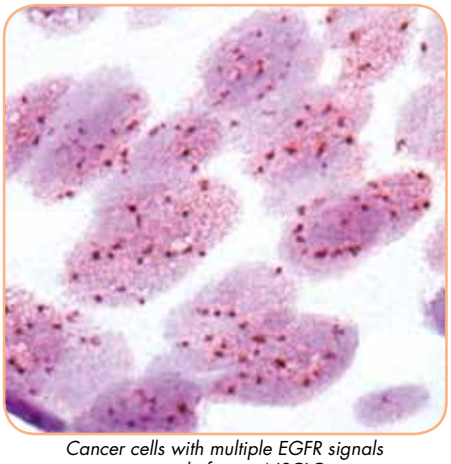
SPEC EGFR Probe map (not to scale).

Results

In normal cells, two distinct dot-shaped signals per nucleus will be observed. Nuclei with amplification of the EGFR gene locus or aneuploidy of chromosome 7 will show multiple dots or large signal clusters.



Normal nuclei each with two EGFR signals.



Cancer cells with multiple EGFR signals in sputum sample from a NSCLC patient.

Prod. No.	Product	Label	Tests* (Volume)
C-3007-400	ZytoDot SPEC EGFR Probe CE IVD	DIG	40 (400 µl)
Related Products			
C-3018-40	ZytoDot CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; PBS/Tween, good for 2000 ml; Blocking Solution, 4 ml; Mouse-anti-DIG, 4 ml; Anti-Mouse-HRP-Polymer, 4 ml; DAB Solution A, 0.3 ml; DAB Solution B, 10 ml; Mayer's Hematoxylin Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot ® 2C SPEC EGFR/CEN 7 Probe

CE IVD

Background

The ZytoDot ® 2C SPEC EGFR/CEN 7 Probe is designed for the simultaneous detection of EGFR and centromere 7 in formalin-fixed, paraffin-embedded tissue sections and cell samples.

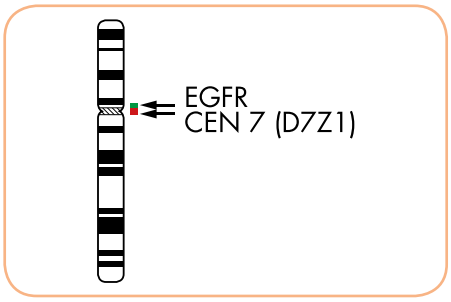
The EGFR gene (a.k.a. ERBB1 and HER1) is located in the chromosomal region 7p11.2 and encodes a transmembrane glycoprotein acting as a cellular growth factor receptor.

Overexpression of EGFR has been shown in a number of tumor entities and is associated with poor prognosis. EGFR copy number identified by *in situ* Hybridization is thought to be a molecular predictor in neoplasms.

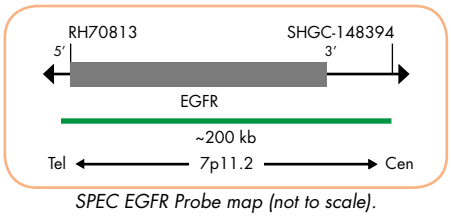
References
Balla P, et al. (2011) Histopathology 59: 376-89.
Brunner K, et al. (2010) Anal Quant Cytol Histol 32: 78-89.
Ettl T, et al. (2012) Hum Pathol 43: 921-31.
Isola J & Tanner M (2004) Methods Mol Med 97: 133-44.
Kondo I & Shimizu N (1983) Cytogenet Cell Genet 35: 9-14.
Marquez A, et al. (2004) Diagn Mol Pathol 13: 1-8.
Tsukamoto T, et al. (1991) Int J Dev Biol 35: 25-32.
Zaczek A, et al. (2005) Histol Histopathol 20: 1005-15.

Probe Description

The ZytoDot ® 2C SPEC EGFR/CEN 7 Probe is a mixture of a Digoxigenin-labeled probe specific for the EGFR gene at 7p11.2 and a Dinitrophenyl-labeled CEN 7 probe specific for the alpha satellite centromeric region of chromosome 7 (D7Z1).



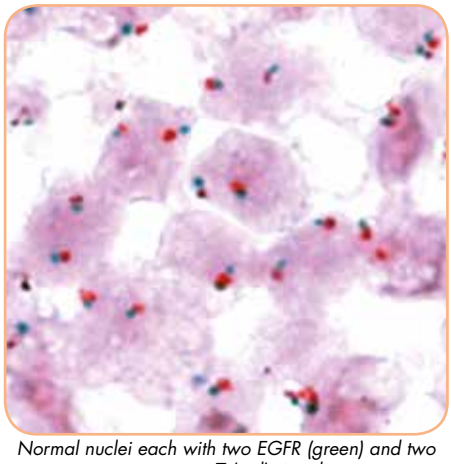
Ideogram of chromosome 7 indicating the hybridization locations.



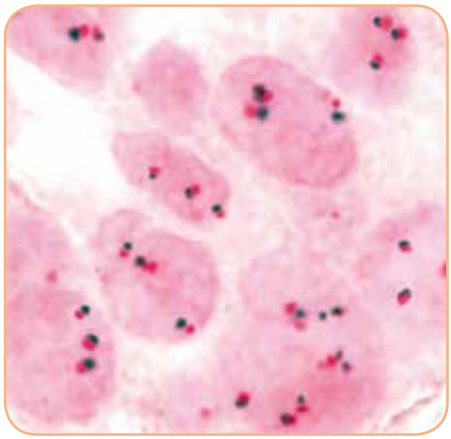
SPEC EGFR Probe map (not to scale).

Results

In a normal interphase nucleus, using the ZytoDot ® 2C CISH Implementation Kit two green and two red signals are expected. In a cell with amplification of the EGFR gene locus, multiple copies of the green signal or green signal clusters will be observed.



Normal nuclei each with two EGFR (green) and two centromere 7 (red) signals.



Trisomy of chromosome 7 as indicated by three EGFR (green) and three CEN 7 (red) signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
C-3033-100	ZytoDot 2C SPEC EGFR/CEN 7 Probe CE IVD	DIG/DNP	10 (100 µl)
C-3033-400	ZytoDot 2C SPEC EGFR/CEN 7 Probe CE IVD	DIG/DNP	40 (400 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot ® 2C SPEC MET/CEN 7 Probe

CE IVD

Background

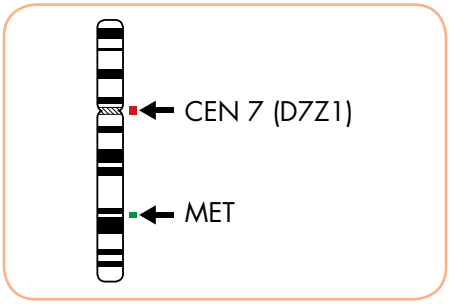
The ZytoDot ® 2C SPEC MET/CEN 7 Probe is designed for the detection of MET gene amplifications found in a variety of human tumors.

The MET gene (a. k. a. c-Met) is located in the chromosomal region 7q31.2 and encodes a transmembrane tyrosine kinase receptor for the hepatocyte growth factor (HGF). HGF and MET play an important role in angiogenesis and tumor growth. Activation or upregulation of MET was found in a number of carcinomas including lung, breast, colorectal, prostate, and gastric carcinomas as well as in gliomas, melanomas and some sarcomas. MET overexpression is known as a negative prognostic indicator in patients with various carcinomas, multiple myeloma, or glioma. Therefore, several inhibitors of the HGF/MET signaling pathway are being studied and developed as potent therapies to inhibit angiogenesis and tumor growth. Recently, it was shown that MET amplification leads to resistance to gefitinib or erlotinib in lung cancer by driving ERBB3-dependent activation of the PI3K pathway.

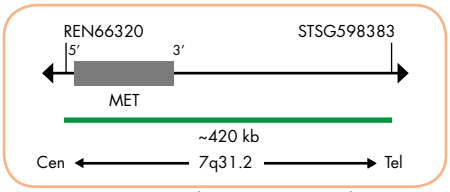
References
Cooper CS, et al. (1984) Nature 311: 29-32.
Engelman JA, et al. (2007) Science 316: 1039-43.
Garcia S, et al. (2007) Int J Oncol 31: 49-58.
Hara T, et al. (1998) Lab Invest 78: 1143-53.

Probe Description

The ZytoDot ® 2C SPEC MET/CEN 7 Probe is a mixture of a Dinitrophenyl-labeled CEN 7 probe specific for the alpha satellite centromeric region of chromosome 7 (D7Z1) and a Digoxigenin-labeled probe specific for the chromosomal region 7q31.2 harboring the MET gene.



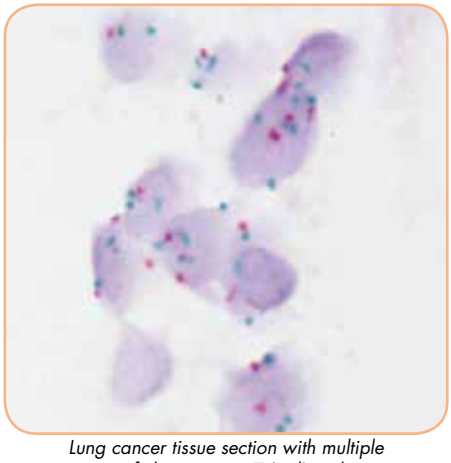
Ideogram of chromosome 7 indicating the hybridization locations.



SPEC MET Probe map (not to scale).

Results

In a normal interphase nucleus, using the ZytoDot ® 2C CISH Implementation Kit two red (CEN 7) and two green (MET) signals are expected. In a cell with amplification of the MET gene locus, multiple copies of the green signal or green signal clusters will be observed.



Lung cancer tissue section with multiple copies of chromosome 7 (red) and extra MET signals (green) in the nuclei.

Prod. No.	Product	Label	Tests* (Volume)
C-3057-400	ZytoDot 2C SPEC MET/CEN 7 Probe CE IVD	DIG/DNP	40 (400 µl)
Related Products			
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC FGFR1/CEN 8 Probe

CE IVD

Background

The ZytoDot® 2C SPEC FGFR1/CEN 8 Probe is designed for the detection of FGFR1 gene amplification frequently observed in malignant tumors e.g. breast and prostate cancer and oral squamous cell carcinoma (OSCC).

The FGFR1 (fibroblast growth factor receptor 1) gene is located in the chromosomal region 8p11.23-p11.22 and encodes a transmembrane receptor tyrosine kinase. Amplification of the FGFR1 gene, observed in approximately 10% of all breast cancer samples, has revealed to be an independent prognostic factor for overall survival. FGFR1 is believed to emerge as a potential therapeutic target for lobular breast carcinomas.

In prostate cancer, FGFR1 gene amplification seems to be an important step during the transmission to hormone resistance.

In OSCC, FGFR1 gene amplification, observed in nearly 20% of all cases, is indicated to contribute to oral carcinogenesis at an early stage of development.

References
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Elbauomy Elsheikh S, et al. (2007) Breast Cancer Res 9: R23.
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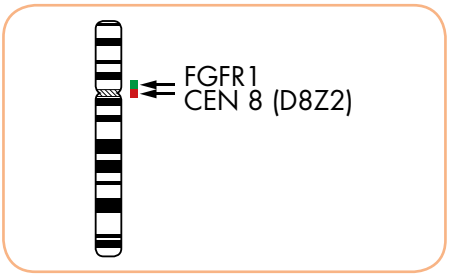
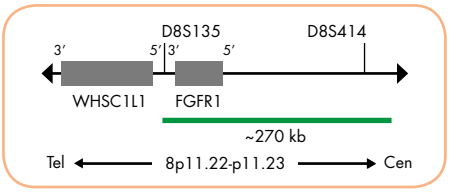
Lee PL, et al. (1989) Science 245: 57-60.
Lacroix-Triki M, et al. (2010) J Pathol 222: 282-98.
Swoboda A, et al. (2011) Genes Chromosomes Cancer 50: 680-8.
Turner N, et al. (2010) Cancer Res 70: 2085-94.
Wetterskog D, et al. (2012) J Pathol 226: 84-96.

Probe Description

The ZytoDot® 2C SPEC FGFR1/CEN 8 Probe is a mixture of a Digoxigenin-labeled probe specific for the FGFR1 gene at 8p11.23-p11.22 and a Dinitrophenyl-labeled CEN 8 probe specific for the alpha satellite centromeric region of chromosome 8 (D8Z2).



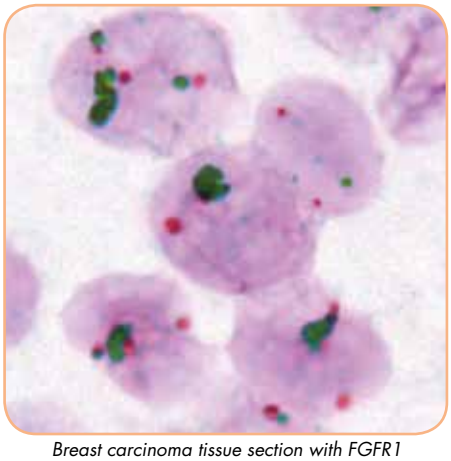
Ideogram of chromosome 8 indicating the hybridization locations.



SPEC FGFR1 Probe map (not to scale).

Results

In a normal interphase nucleus, using the ZytoDot® 2C CISH Implementation Kit two green (FGFR1) and two red (CEN 8) signals are expected. In a cell with an amplification of the FGFR1 gene locus, multiple copies of the green signal or green signal clusters will be observed.



Breast carcinoma tissue section with FGFR1 amplification as indicated by large green clusters.

Prod. No.	Product	Label	Tests* (Volume)
C-3050-400	ZytoDot 2C SPEC FGFR1/CEN 8 Probe CE IVD	DIG/DNP	40 (400 µl)
Related Products			
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® SPEC MYC Probe

CE IVD

Background

The ZytoDot® SPEC MYC Probe is designed for the detection of MYC gene amplification frequently observed in malignant tumors e.g. breast and endometrial cancer.

The proto-oncogene MYC (a.k.a. CMYC) is located in the chromosomal region 8q24.21 and encodes a nuclear transcription factor displaying high-affinity, site specific DNA-binding capacity when complexed with its cellular partners. Thus, the MYC protein is involved in proliferation, growth, differentiation, and apoptosis. Amplification of the chromosomal MYC gene region has been detected in many types of malignant neoplasms e.g. breast, lung, head, colon, kidney, neck, ovary, bladder, and endometrial cancers. It was shown that MYC amplification occurs in advanced, widespread tumors or in aggressive, primary tumors. In non-small cell lung cancer (NSCLC) and breast cancer, for example, MYC amplification was strongly associated with lymph node status. Accordingly, the MYC gene can be considered as a powerful prognostic marker.

Additionally, malignant cutaneous angiosarcomas but not benign and atypical vascular lesions occurring after radiotherapy of breast cancer are characterized by amplification of the MYC gene. The presence of MYC amplification is thus of considerable diagnostic importance for the distinction of malignant from atypical postradiation vascular neoplasms of the skin.

References
Alves Rde C, et al. (2014) J Cancer Res Clin Oncol 140: 2021-5.
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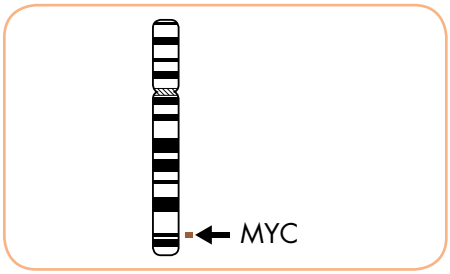
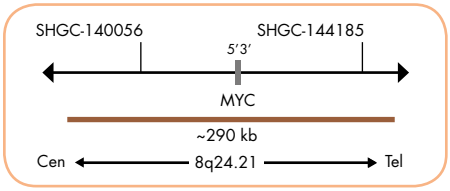
Mentzel T, et al. (2012) Mod Pathol 25: 75-95.
Rummukainen JK, et al. (2001) Lab Invest 81: 1445-51.
Schraml P, et al. (1999) Clin Cancer Res 5: 1966-75.
Yokota J, et al. (1986) Science 231: 261-5.

Probe Description

The ZytoDot® SPEC MYC Probe is a Digoxigenin-labeled probe specific for the MYC gene region at 8q24.21, processed by the unique *ZytoVision® Repeat Subtraction Technique* resulting in advanced specificity and less background.



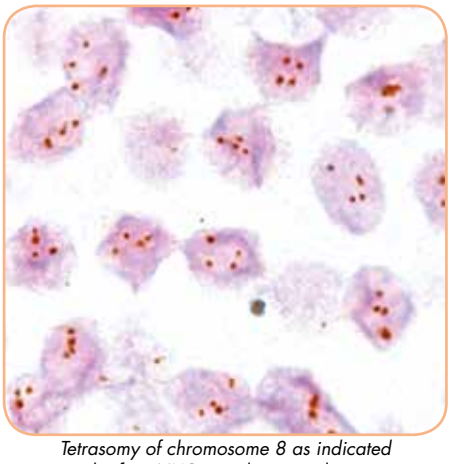
Ideogram of chromosome 8 indicating the hybridization locations.



SPEC MYC Probe map (not to scale).

Results

In normal cells, two distinct dot-shaped signals per nucleus will be observed. Nuclei with amplification of the MYC gene locus or polysomy of chromosome 8 will show multiple dots or large signal clusters.



Tetrasomy of chromosome 8 as indicated by four MYC signals per nucleus.

Prod. No.	Product	Label	Tests* (Volume)
C-3013-400	ZytoDot SPEC MYC Probe CE IVD	DIG	40 (400 µl)
Related Products			
C-3018-40	ZytoDot CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; PBS/Tween, good for 2000 ml; Blocking Solution, 4 ml; Mouse-anti-DIG, 4 ml; Anti-Mouse-HRP-Polymer, 4 ml; DAB Solution A, 0.3 ml; DAB Solution B, 10 ml; Mayer's Hematoxylin Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC MYC Break Apart Probe

CE IVD

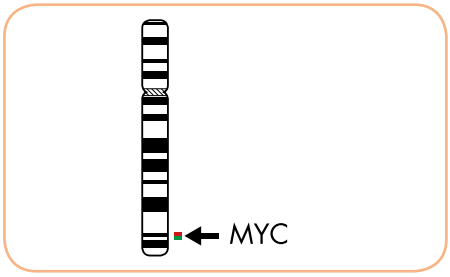
Background

The ZytoDot® 2C SPEC MYC Break Apart Probe is designed to detect translocations involving the chromosomal region 8q24.21 harboring the MYC gene.
The MYC proto-oncogene (MYC proto-oncogene, bHLH transcription factor, a.k.a. CMYC) encodes a transcription factor essential for cell growth and proliferation and is broadly implicated in tumorigenesis. Translocations involving the MYC gene are considered to be cytogenetic hallmarks for Burkitt lymphoma but are also found in other types of lymphomas. The most frequent translocation involving the MYC gene region is t(8;14)(q24.21;q32.3) juxtaposing the MYC gene in 8q24.21 next to the IGH (immunoglobulin heavy chain) locus in 14q32.33. Further translocations affecting the MYC gene are t(8;22)(q24.21;q11.2) and t(2;8)(p11.2;q24.21), both of which involve one of the two immunoglobulin light chain loci. All three translocations bring the MYC gene under the control of a regulatory element from one of the immunoglobulin loci resulting in constitutive overexpression of MYC.

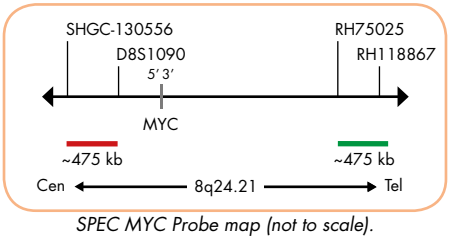
References
Boerma EG, et al. (2009) Leukemia 23: 225-34.
Dalla-Favera R, et al. (1982) Proc Natl Acad Sci U S A 79: 6497-501.
Haralambieva E, et al. (2004) Genes Chromosomes Cancer 40: 10-8.
Veronese ML, et al. (1995) Blood 85: 2132-8.
Walker BA, et al. (2014) Blood Cancer J 4: e191.

Probe Description

The ZytoDot® 2C SPEC MYC Break Apart Probe is a mixture of a Digoxigenin-labeled and a Dinitrophenyl-labeled probe hybridizing to the 8q24.21 band. The DNP-labeled probe hybridizes proximal to the MYC gene breakpoint region at 8q24.21, the DIG-labeled probe hybridizes distal to the MYC gene breakpoint region.



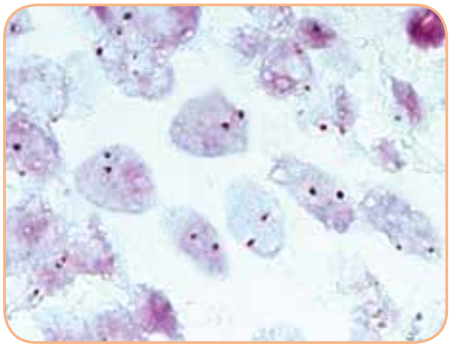
Ideogram of chromosome 8 indicating the hybridization locations.



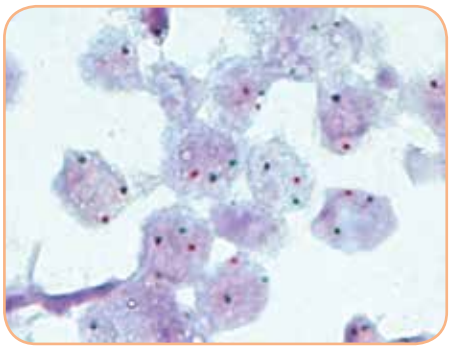
SPEC MYC Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 8q24.21 band, using the ZytoDot® 2C CISH Implementation Kit, two red/green fusion signals are expected representing two normal (non-rearranged) 8q24.21 loci. A signal pattern consisting of one red/green fusion signal, one red signal, and a separate green signal indicates one normal 8q24.21 locus and one 8q24.21 locus affected by a translocation. Alternative break points particularly observed in variant MYC translocations t(8;22) and t(2;8) might result in different signal patterns.



SPEC MYC Break Apart Probe hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.



Non-Hodgkin lymphoma tissue section with translocation affecting the 8q24.21 locus as indicated by one red/green fusion (non-rearranged) signal, one red signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
C-3066-400	ZytoDot 2C SPEC MYC Break Apart Probe CE IVD	DIG/DNP	40 (400 µl)
Related Products			
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC CDKN2A/CEN 9 Probe

CE IVD

Background

The ZytoDot® 2C SPEC CDKN2A/CEN 9 Probe is designed for the detection of CDKN2A deletions frequently observed in most tumor cell lines as well as in primary human malignancies.

The CDKN2A gene, often referred to as p16 or INK4a/ARF, is located in the chromosomal region 9p21.3. Using alternative first exons and an alternative reading frame, the gene encodes for two distinct tumor suppressor proteins p16INK4a and p14ARF, both involved in cell cycle regulation. CDKN2A has been identified as a major susceptibility gene for melanoma. The tumor suppressor gene CDKN2A is inactivated by homozygous deletions with high frequency in a variety of human primary tumors e.g. bladder and renal cell carcinoma, prostate and ovarian adenocarcinoma, non-small cell lung cancer, sarcoma, glioma, mesothelioma, and melanoma. Furthermore, deletion of the CDKN2A gene is found in up to 80% of T-cell acute lymphoblastic leukemia cases and is associated with poor prognosis and relapse of the disease.

References
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Kamb A, et al. (1994) Science 264: 436-40.
Nobori T, et al. (1994) Nature 368: 753-6.
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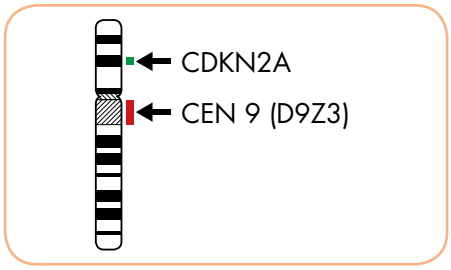
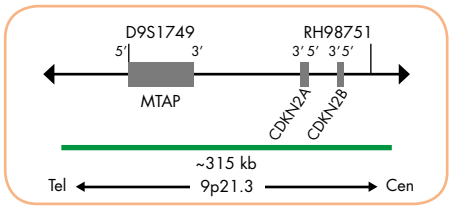
Schopmeyer K, et al. (1999) Neoplasia 1: 128-37.
Schwarz S, et al. (2008) Cytometry A 73: 305-11.
Sharpless NE (2005) Mutat Res 576: 22-38.

Probe Description

The ZytoDot® 2C SPEC CDKN2A/CEN 9 Probe is a mixture of a Digoxigenin-labeled probe specific for the CDKN2A gene at 9p21.3 and a Dinitrophenyl-labeled CEN 9 probe specific for the classical satellite III region of chromosome 9 (D9Z3) at 9q12.



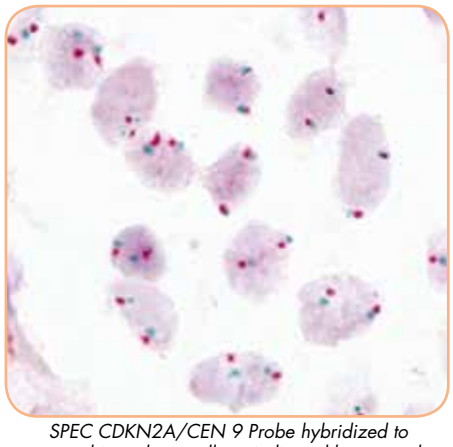
Ideogram of chromosome 9 indicating the hybridization locations.



SPEC CDKN2A Probe map (not to scale).

Results

In a normal interphase nucleus, using the ZytoDot® 2C CISH Implementation Kit two green (CDKN2A) and two red (CEN 9) signals are expected. In a cell with deletion of the CDKN2A gene locus, a reduced number of green signals will be observed. Deletions affecting only parts of the CDKN2A gene might result in a normal signal pattern with green signals of reduced size.



SPEC CDKN2A/CEN 9 Probe hybridized to normal interphase cells as indicated by two red and two green signals per nucleus.

Prod. No.	Product	Label	Tests* (Volume)
C-3067-400	ZytoDot 2C SPEC CDKN2A/CEN 9 Probe CE IVD	DIG/DNP	40 (400 µl)
Related Products			
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC RET Break Apart Probe

CE IVD

Background

The ZytoDot® 2C SPEC RET Break Apart Probe is designed to detect translocations involving the chromosomal region 10q11.21 harboring the RET (ret proto-oncogene) gene. RET encodes a tyrosine kinase (TK) receptor.

Translocations involving RET were first described in papillary thyroid carcinoma (PTC) where somatic rearrangements result in the fusion of its TK catalytic domain with an N-terminal dimerization domain encoded by various fusion partner genes.

More recently, recurrent inversions [inv(10)(p11.2q11.2)] fusing the coiled-coil domains of the kinesin family member 5B (KIF5B) gene to the RET kinase domain have been detected in lung adenocarcinoma.

The resulting KIF5B-RET fusion protein can form homodimers through the coiled-coil domains of KIF5B, causing an aberrant activation of the TK of RET, a mechanism known from KIF5B-ALK fusions which is also found in lung adenocarcinoma.

Since *in vitro* studies showed transforming activity of KIF5B-RET which could be suppressed by a TK inhibitor, it was assumed that the chimeric oncogene might be a promising molecular target for the treatment of lung cancer.

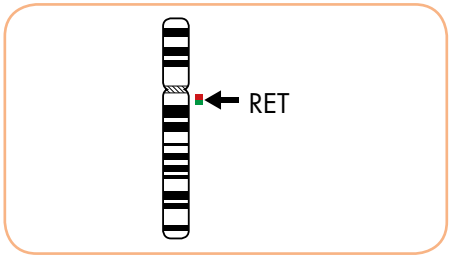
The same holds true for the BCR-RET and FGFR1OP-RET fusion genes in chronic myelomonocytic leukemia (CMML) generated by two balanced translocations t(10;22)(q11.2;q11.2) and t(6;10)(q27;q11.2), respectively.

References

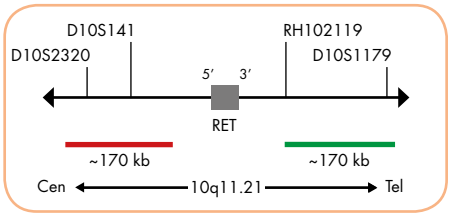
Ballerini P, et al. (2012) Leukemia 26: 2384-9.
Gautschi O, et al. (2013) J Thorac Oncol 8: e43-4.
Ju YS, et al. (2012) Genome Res 22: 436-45.
Kohno T, et al. (2012) Nat Med 18: 375-7.
Nikiforov YE (2002) Endocr Pathol 13: 3-16.
Takahashi M, et al. (1985) Cell 42: 581-8.
Takeuchi K, et al. (2012) Nat Med 18: 378-81.

Probe Description

The ZytoDot® 2C SPEC RET Break Apart Probe is a mixture of a Digoxigenin-labeled and a Dinitrophenyl-labeled probe hybridizing to the 10q11.21 band. The DNP-labeled probe hybridizes proximal to the RET gene breakpoint region at 10q11.21, the DIG-labeled probe hybridizes distal to the RET gene breakpoint region.



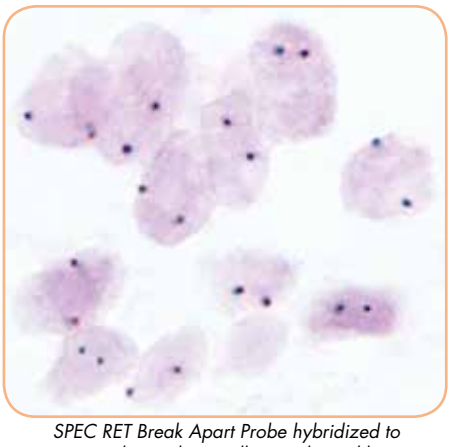
Ideogram of chromosome 10 indicating the hybridization locations.



SPEC RET Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 10q11.21 band, using the ZytoDot® 2C CISH Implementation Kit, two red/green fusion signals are expected representing two normal (non-rearranged) 10q11.21 loci. A signal pattern consisting of one red/green fusion signal, one red signal, and a separate green signal indicates one normal 10q11.21 locus and one 10q11.21 locus affected by a translocation or inversion.



SPEC RET Break Apart Probe hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.

Prod. No.	Product	Label	Tests* (Volume)
C-3064-100	ZytoDot 2C SPEC RET Break Apart Probe CE IVD	DIG/DNP	10 (100 µl)
C-3064-400	ZytoDot 2C SPEC RET Break Apart Probe CE IVD	DIG/DNP	40 (400 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot ® 2C SPEC PTEN/CEN 10 Probe

CE IVD

Background

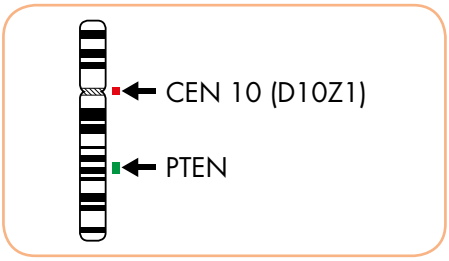
The ZytoDot ® 2C SPEC PTEN/CEN 10 Probe is designed for the detection of PTEN deletions frequently observed in many tumor types, including renal, melanoma, endometrial, breast, prostate, lung, bladder, and thyroid cancer but also in hematological neoplasms.

The tumor suppressor gene PTEN (phosphatase and tensin homolog), often referred to as MMAC1 (mutated in multiple advanced cancers 1), is located on 10q23.31 and encodes a 47 kDa dual-specificity phosphatase that has both lipid and protein phosphatase activity. Its inactivation results in constitutive activation of the PI3K/AKT pathway and in subsequent increase in protein synthesis, cell cycle progression, migration, and survival. Deletions affecting the long arm of chromosome 10 have been detected in 30 to 50% of early and advanced stage sporadic melanomas and about 40 to 70% of prostate cancers. In both tumor entities loss of PTEN has been associated with poor clinical outcome. Currently, several drugs targeting the PI3K/AKT pathway for the therapy of solid tumors have entered clinical trials.

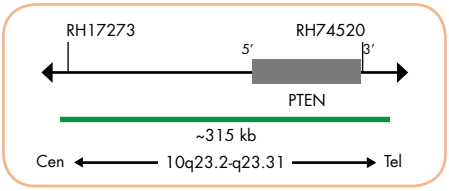
References
Dahia PLM, et al. (1999) Hum Mol Genet 8: 185-93.
Healy E, et al. (1998) Oncogene 16: 2213-8.
Li J, et al. (1997) Science 275: 1943-7.
Swoboda A, et al. (2011) Genes Chromosomes Cancer 50: 680-8.
Weng LP, et al. (2001) Hum Mol Genet 10: 599-604.
Yoshimoto M, et al. (2006) Cancer Genet Cytogenet 169: 128-37.
Yoshimoto M, et al. (2007) Br J Cancer 97: 678-85.

Probe Description

The ZytoDot ® 2C SPEC PTEN/CEN 10 Probe is a mixture of a Dinitrophenyl-labeled CEN 10 probe specific for the alpha satellite centromeric region of chromosome 10 (D10Z1) and a Digoxigenin-labeled probe specific for the chromosomal region 10q23.2-q23.31 harboring the PTEN gene.



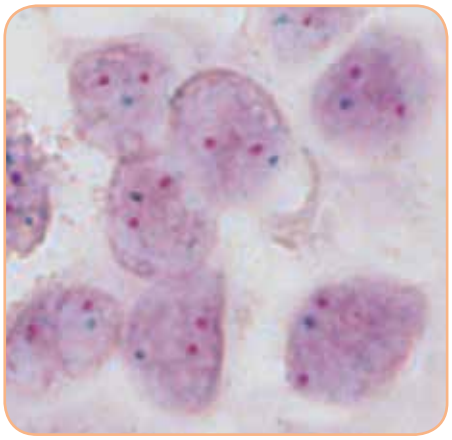
Ideogram of chromosome 10 indicating the hybridization locations.



SPEC PTEN Probe map (not to scale).

Results

In a normal interphase nucleus, using the ZytoDot ® 2C CISH Implementation Kit two red (CEN 10) and two green (PTEN) signals are expected. In a cell with a deletion of the PTEN gene locus a reduced number of green signals will be observed. Deletions affecting only parts of the PTEN gene might result in normal signal pattern with green signals of reduced size.



Prostate cancer tissue section with deletion of the PTEN gene as indicated by one green signal.

Prod. No.	Product	Label	Tests* (Volume)
C-3053-400	ZytoDot 2C SPEC PTEN/CEN 10 Probe CE IVD	DIG/DNP	40 (400 µl)
Related Products			
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC FGFR2/CEN 10 Probe

CE IVD

Background

The ZytoDot® 2C SPEC FGFR2/CEN 10 Probe is designed for the detection of FGFR2 gene amplifications frequently observed in breast cancer as well as in gastric cancer.

The FGFR2 (fibroblast growth factor receptor 2, a.k.a. BEK) gene is located on chromosome 10q26.13 and encodes splice variants of the receptor tyrosine kinases FGFR2b and FGFR2c.

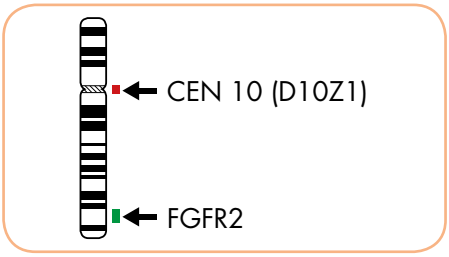
Amplification of the FGFR2 gene leads to overexpression of the FGFR2 protein and subsequently to signal activation. Additionally, during the amplification process the C-terminal deletion of FGFR2 can occur due to exclusion of the last exon from the FGFR2 amplicon. Both, overexpression and deletion of the last exon result in FGFR2 signaling activation based on constitutive phosphorylation of the FRS2 adaptor molecule.

The process of ligand independent FGFR2 signaling leads to a more severe malignant phenotype of these tumors. Moreover, high FGFR2 expression is correlated with poor overall survival (OS) and poor disease-free survival (DFS) rates in breast cancer patients. Consequently, FGFR2 gene amplification detected by Chromogenic *in situ* Hybridization might be used as a prognostic marker in breast cancer.

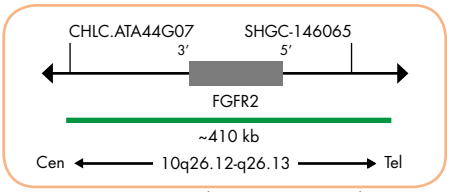
References
Azuma K, et al. (2011) Biochem Biophys Res Commun 407: 219-24.
Katoh M (2010) Expert Rev Anticancer Ther 10: 1375-9.
Katoh Y & Katoh M (2009) Int J Mol Med 23: 307-11.
Moffa AB, et al. (2004) Mol Cancer Res 2: 643-52.
Sun S, et al. (2012) J Surg Oncol 105: 773-9

Probe Description

The ZytoDot® 2C SPEC FGFR2/CEN 10 Probe is a mixture of a Dinitrophenyl-labeled CEN 10 probe specific for the alpha satellite centromeric region of chromosome 10 (D10Z1) and a Digoxigenin-labeled probe specific for the chromosomal region 10q26.12-q26.13 harboring the FGFR2 gene.



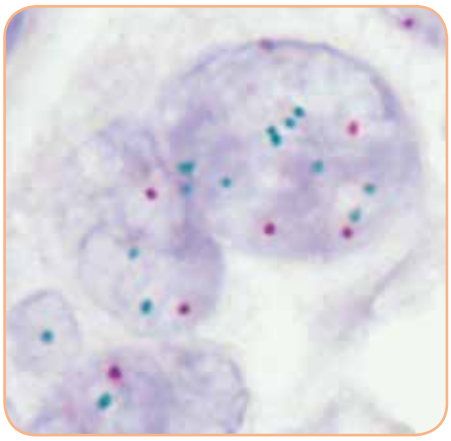
Ideogram of chromosome 10 indicating the hybridization locations.



SPEC FGFR2 Probe map (not to scale).

Results

In a normal interphase nucleus, using the ZytoDot® 2C CISH Implementation Kit two red (CEN 10) and two green (FGFR2) signals are expected. Nuclei with amplification of the FGFR2 gene locus at 10q26.12-q26.13 or polysomy of chromosome 10 will show multiple copies of the green signal or large green signal clusters.



Breast carcinoma tissue section with FGFR2 (green) amplification.

Prod. No.	Product	Label	Tests* (Volume)
C-3056-400	ZytoDot 2C SPEC FGFR2/CEN 10 Probe CE IVD	DIG/DNP	40 (400 µl)
Related Products			
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC CCND1 Break Apart Probe

CE IVD

Background

The ZytoDot® 2C SPEC CCND1 Break Apart Probe is designed to detect translocations involving the chromosomal region 11q13.3 harboring the CCND1 gene. The CCND1 gene (cyclin D1, a.k.a. PRAD1) encodes a regulatory subunit of cyclin-dependent kinases.

Translocations involving the chromosomal region t(11;14)(q13.3;q32.3) are considered to be characteristic for mantle cell lymphomas (MCL) but have also been identified in other lymphoproliferative disorders (LPDs), such as B-prolymphocytic leukemia, and, less frequently, in plasma cell myelomas, B-cell chronic lymphocytic leukemia, and in splenic lymphomas with villous lymphocytes (SLVL).

The t(11;14) rearrangement often leads to overexpression of the CCND1 protein. Determination of translocations involving the chromosomal region 11q13.3 can also help to distinguish MCL from other chronic lymphoproliferative disorders. Since the course of MCL is aggressive, and its response to chemotherapy is poor, differential diagnosis is clinically important.

Additionally, it was also shown that a renal oncocytoma (RO) specific breakpoint is located in band 11q13.3, involving the CCND1 locus. The histologic features of RO may overlap with those of chromophobe renal cell carcinoma (ChRCC).

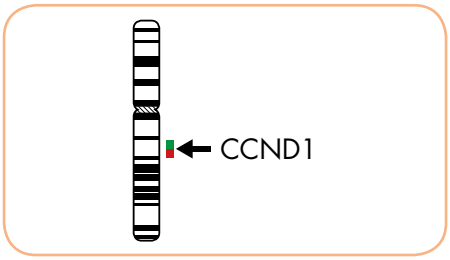
CISH can be used as a diagnostic tool for differentiation of RO from ChRCC.

References

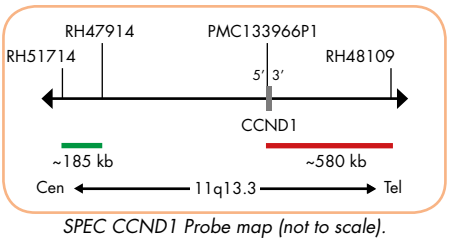
Bentz JS, et al. (2004) Cancer 102: 124-31.
Bosch F, et al. (1997) Cancer 82: 567-75.
Sinke RJ, et al. (1997) Cancer Genet Cytogenet 96: 95-101.
Sukov WR, et al. (2007) Hum Pathol 40: 1296-303.
Tarsitano M, et al. (2009) Cancer Genet Cytogenet 195: 164-7.
Tsujimoto Y, et al. (1984) Science 224: 1403-6.
Vaandrager JW, et al. (1996) Blood 4: 1177-82.

Probe Description

The ZytoDot® 2C SPEC CCND1 Break Apart Probe is a mixture of a Digoxigenin-labeled and a Dinitrophenyl-labeled probe hybridizing to the 11q13.3 band. The DNP-labeled probe hybridizes distal to the CCND1 gene breakpoint region at 11q13.3, the DIG-labeled probe hybridizes proximal to the CCND1 gene breakpoint region.



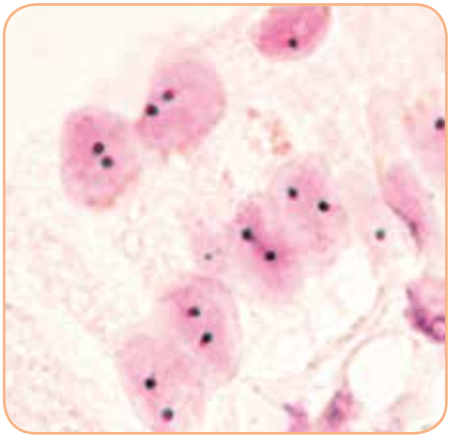
Ideogram of chromosome 11 indicating the hybridization locations.



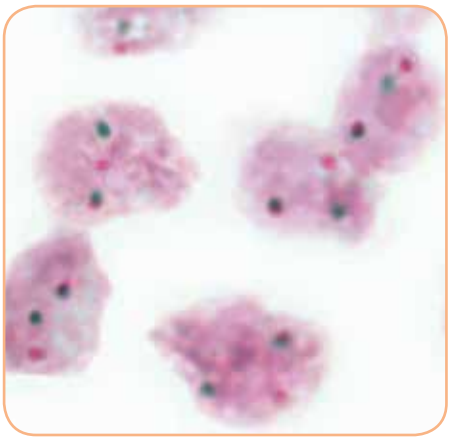
SPEC CCND1 Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 11q13.3 band, using the ZytoDot® 2C CISH Implementation Kit, two red/green fusion signals are expected representing two normal (non-rearranged) 11q13.3 loci. A signal pattern consisting of one red/green fusion signal, one red signal, and a separate green signal indicates one normal 11q13.3 locus and one 11q13.3 locus affected by a translocation.



SPEC CCND1 Break Apart Probe hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.



Mantle cell lymphoma tissue section with translocation affecting the 11q13.3 locus as indicated by one non-rearranged red/green fusion signal, one red signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
C-3075-100	ZytoDot 2C SPEC CCND1 Break Apart Probe CE IVD	DIG/DNP	10 (100 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC DDIT3 Break Apart Probe

CE IVD

Background

The ZytoDot® 2C SPEC DDIT3 Break Apart Probe is designed to detect translocations involving the chromosomal region 12q13.3 harboring the DDIT3 (DNA damage inducible transcript 3) gene (a.k.a. CHOP, GADD153) in formalin-fixed, paraffin-embedded tissue sections or cell samples.

The DDIT3 gene encodes for a stress-induced dominant-negative inhibitor of the transcription factors C/EBP and LAP. DDIT3 is consistently rearranged in myxoid liposarcomas (MLS). The most frequent translocation involving the DDIT3 gene region is t(12;16)(q13.3;p11.2) and occurs in about 90% of patients with MLS. The rearrangement results in a fusion gene comprising the 5´ part of the FUS (fused in sarcoma) gene, located in 16p11.2, and the complete coding region of the DDIT3 gene. The FUS-DDIT3 fusion protein acts as an abnormal transcription factor and development of myxoid liposarcomas is thus regarded as a consequence of deregulated FUS-DDIT3 target genes.

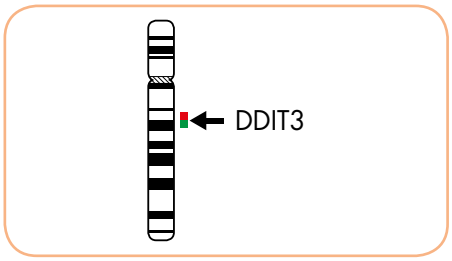
Differential diagnosis of liposarcomas and accurate classification, the latter being especially important with regard to appropriate treatment and prognosis, are often problematic. Therefore, detection of DDIT3 rearrangements via ISH analysis is a valuable tool to confirm the histopathological diagnosis of myxoid liposarcoma.

References

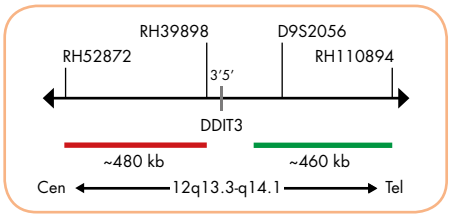
Åman P, et al. (1992) Genes Chromosomes Cancer 5: 278-85.
Andersson M, et al. (2010) BMC Cancer 10: 249-58.
Germano G, et al. (2010) Cancer Res 70: 2235-44.
Meis-Kindblom JM, et al. (2001) Virchows Arch 439: 141-51.
Panagopoulos I, et al. (1994) Cancer Res 54: 6500-3.
Ron D & Habener JF (1992) Genes Dev 6: 439-53.

Probe Description

The ZytoDot® 2C SPEC DDIT3 Break Apart Probe is a mixture of a Digoxigenin-labeled and a Dinitrophenyl-labeled probe hybridizing to the 12q13.3-q14.1 band. The DNP-labeled probe hybridizes proximal to the DDIT3 gene and the DIG-labeled probe hybridizes distal to that gene.



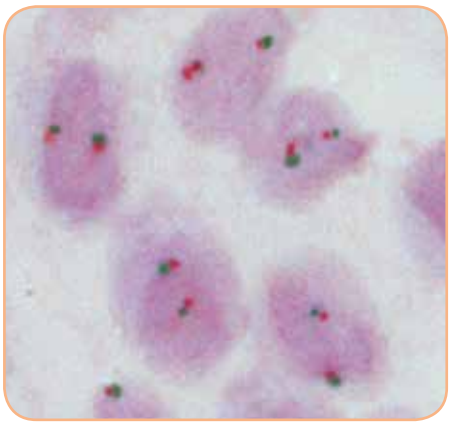
Ideogram of chromosome 12 indicating the hybridization locations.



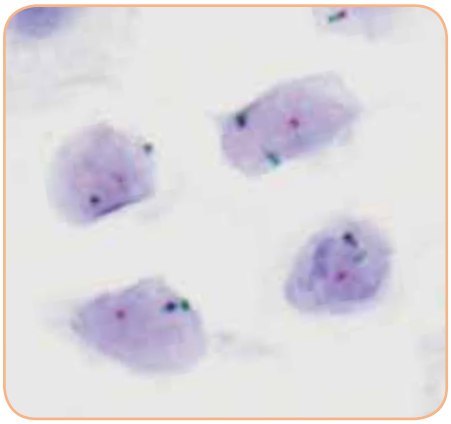
SPEC DDIT3 Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 12q13.3-q14.1 band, using the ZytoDot® 2C CISH Implementation Kit, two red/green fusion signals are expected representing two normal (non-rearranged) 12q13.3-q14.1 loci. A signal pattern consisting of one red/green fusion signal, one red signal, and a separate green signal indicates one normal 12q13.3-q14.1 locus and one 12q13.3-q14.1 locus affected by a translocation or inversion.



SPEC DDIT3 Break Apart Probe hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.



Myxoid liposarcoma tissue section with translocation affecting the 12q13.3-q14.1 locus as indicated by one non-rearranged red/green fusion signal, one red signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
C-3047-100	ZytoDot 2C SPEC DDIT3 Break Apart Probe CE IVD	DIG/DNP	10 (100 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC CDK4/CEN 12 Probe

CE IVD

Background

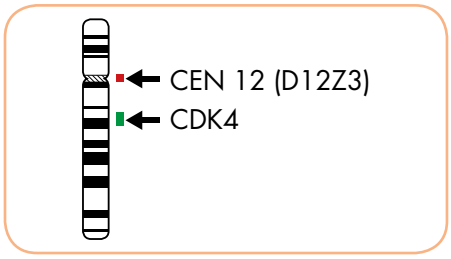
The ZytoDot® 2C SPEC CDK4/CEN 12 Probe is designed for the detection of CDK4 gene amplifications. The cyclin-dependent kinase 4 (CDK4) gene is located in the chromosomal region 12q14.1, ~10 Mb centromeric to the murine double minute (MDM2) gene and is frequently coamplified with MDM2 in different malignancies.

In a complex with cyclin D1 (CCND1), the CDK4 encoded serine/threonine kinase phosphorylates the retinoblastoma protein 1 (RB1) which in turn leads to the release of the EF2 transcription factor and subsequently to an upregulation of genes which are required for progression through the S-, G2-, and M-phases of the cell cycle. Due to amplification of the respective chromosomal region, CDK4 is overexpressed in many human tumors such as soft tissue sarcomas, osteosarcomas (OS), and gliomas. In glioblastomas, the lack of amplification of several genes like CDK4 was recognized to be associated with a longer survival time. In OS, coamplification of MDM2 and CDK4, located in two discontinuous regions, occurs frequently in parosteal OS and less often in classical high-grade OS.

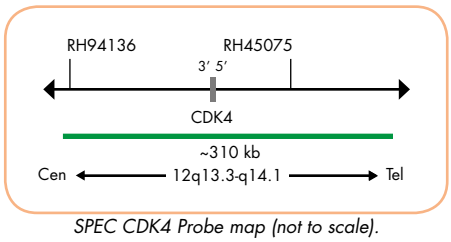
Although MDM2/CDK4 coamplification is not restricted to atypical lipomatous tumors/well-differentiated liposarcomas (ALT/WDLPS) and dedifferentiated liposarcomas (DDLPS), its detection is a strong criterion for distinguishing these tumor types from other undifferentiated sarcomas and even from carcinomas and lymphomas. Moreover, CDK4 amplification is a poor prognostic factor in WDLPS and DDLPS.

Probe Description

The ZytoDot® 2C SPEC CDK4/CEN 12 Probe is a mixture of a Digoxigenin-labeled probe specific for the chromosomal region 12q13.3-q14.1 harboring the CDK4 gene and a Dinitrophenyl-labeled CEN 12 probe specific for the alpha satellite centromeric region of chromosome 12 (D12Z3).



Ideogram of chromosome 12 indicating the hybridization locations.



SPEC CDK4 Probe map (not to scale).

Results

In a normal interphase nucleus, using the ZytoDot® 2C CISH Implementation Kit, two green (CDK4) and two red (CEN 12) signals are expected. In a cell with amplification of the CDK4 gene locus or polysomy of chromosome 12, multiple copies of the green signal or green signal clusters will be observed.

Liposarcoma tissue section with CDK4 amplification as indicated by large green clusters.

References
Binh MB, et al. (2005) Am J Surg Pathol 29: 1340-7.
Fischer U, et al. (2010) Int J Cancer 126: 2594-602.
Lee SE, et al. (2014) Histol Histopathol 29: 127-38.
Lopes MA, et al. (2001) Oral Oncol 37: 566-71.
Mejia-Guerrero S, et al. (2010) Genes Chromosomes Cancer 49: 518-25.
Sirvent A, et al. (2007) Am J Surg Pathol 31: 1476-89.
Wunder JS, et al. (1999) Oncogene 18: 783-8.

Prod. No.	Product	Label	Tests* (Volume)
C-3062-400	ZytoDot 2C SPEC CDK4/CEN 12 Probe CE IVD	DIG/DNP	40 (400 µl)
Related Products			
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® SPEC MDM2 Probe

CE IVD

Background

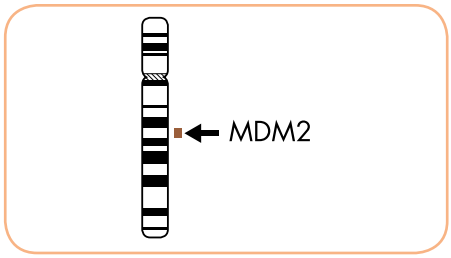
The ZytoDot® SPEC MDM2 Probe is designed for the detection of MDM2 gene amplifications found in more than 10% of human tumors.

The MDM2 (MDM2 proto-oncogene) gene is located in the chromosomal region 12q15 and encodes for an E3 ubiquitin ligase which acts as a major negative regulator of the tumor suppressor p53. Due to the amplification of the respective chromosomal region, MDM2 is overexpressed in many human tumors such as soft tissue sarcomas, osteosarcomas, gliomas, NSCLC, gastric and breast carcinomas. Well-differentiated liposarcomas (WDLPS), the most common soft tissue tumors in adults, are characterized by the amplification of 12q-derived chromosomal material, harboring the MDM2 oncogene while lipomas show balanced translocations involving 12q13-15. Accordingly, detection of the 12q14-15 amplification is regarded as a valuable tool for the differential diagnosis between well-differentiated liposarcomas and lipomas. Furthermore, detection of the MDM2 amplification might have prognostic relevance in gastrointestinal stromal tumors (GIST), the most common primary mesenchymal tumor of the gastrointestinal tract.

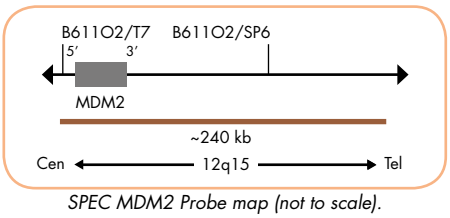
References
Korcheva VB, et al. (2011) Appl Immunhistochem Mol Morphol 19: 119-25.
Larousserie F, et al. (2013) Eur J Radiol 82: 2149-53.
Luan SL, et al. (2010) J Pathol 222: 166-79.
Momand J, et al. (1992) Cell 69: 1237-45.
Oliner JD, et al. (1992) Nature 358: 80-3.
Pedeutour F, et al. (1994) Genes Chromosomes Cancer 10: 85-94.
Pedeutour F, et al. (2004) Bull Cancer 91: 317-23.
Poaty H, et al. (2012) PLoS One 7: e29426.
Toledo F & Wahl GM (2006) Nat Rev Cancer 6: 909-23.
Tornillo L, et al. (2005) Lab Invest 85: 921-31.
Vassilev LT (2007) Trends Mol Med 13: 23-31.

Probe Description

The ZytoDot® SPEC MDM2 Probe is a Digoxigenin-labeled probe specific for the MDM2 gene region at 12q15, processed by the the unique *ZytoVision® Repeat Subtraction Technique* resulting in advanced specificity and less background.



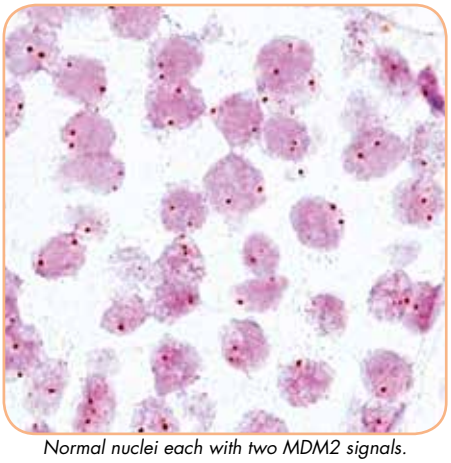
Ideogram of chromosome 12 indicating the hybridization locations.



SPEC MDM2 Probe map (not to scale).

Results

In normal cells, two distinct dot-shaped signals per nucleus will be observed. Nuclei with amplification of the MDM2 gene locus or polysomy of chromosome 12 will show multiple dots or large signal clusters.



Normal nuclei each with two MDM2 signals.

Prod. No.	Product	Label	Tests* (Volume)
C-3012-400	ZytoDot SPEC MDM2 Probe CE IVD	DIG	40 (400 µl)
Related Products			
C-3018-40	ZytoDot CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; PBS/Tween, good for 2000 ml; Blocking Solution, 4 ml; Mouse-anti-DIG, 4 ml; Anti-Mouse-HRP-Polymer, 4 ml; DAB Solution A, 0.3 ml; DAB Solution B, 10 ml; Mayer's Hematoxylin Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC MDM2/CEN 12 Probe

CE IVD

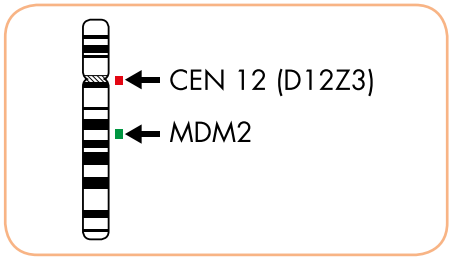
Background

The ZytoDot® 2C SPEC MDM2/CEN 12 Probe is designed for the simultaneous detection of MDM2 and centromere 12 in formalin-fixed, paraffin-embedded tissue sections or cell samples.

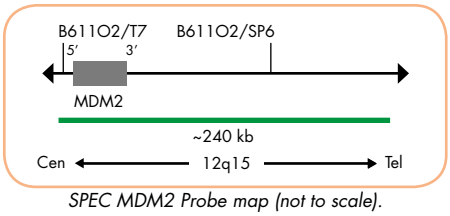
The MDM2 (MDM2 proto-oncogene) gene is located in the chromosomal region 12q15 and encodes for an E3 ubiquitin ligase which acts as a major negative regulator of the tumor suppressor p53. MDM2 gene amplifications are found in more than 10% of human tumors. Due to the amplification of the respective chromosomal region, MDM2 is overexpressed in many human tumors such as soft tissue sarcomas, osteosarcomas, gliomas, NSCLC, gastric and breast carcinomas. Well-differentiated liposarcomas (WDLPS), the most common soft tissue tumors in adults, are characterized by the amplification of 12q-derived chromosomal material, harboring the MDM2 oncogene while lipomas show balanced translocations involving 12q13-15. Accordingly, detection of the 12q14-15 amplification is regarded as a valuable tool for the differential diagnosis between well-differentiated liposarcomas and lipomas. Furthermore, detection of the MDM2 amplification might have prognostic relevance in gastrointestinal stromal tumors (GIST), the most common primary mesenchymal tumor of the gastrointestinal tract.

Probe Description

The ZytoDot® 2C SPEC MDM2/CEN 12 Probe is a mixture of a Digoxigenin-labeled probe specific for MDM2 gene at 12q15 and a Dinitrophenyl-labeled CEN 12 probe specific for the alpha satellite centromeric region of chromosome 12 (D12Z3).



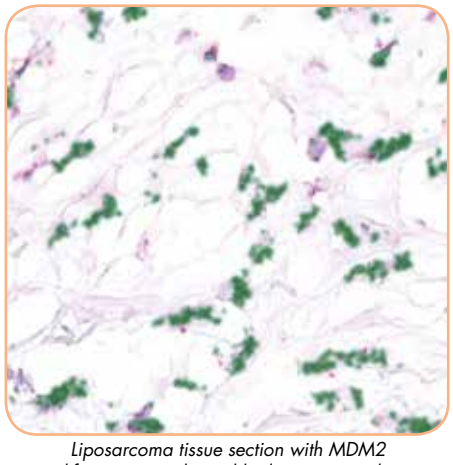
Ideogram of chromosome 12 indicating the hybridization locations.



SPEC MDM2 Probe map (not to scale).

Results

In a normal interphase nucleus,using the ZytoDot® 2C CISH Implementation Kit two red and two green signals are expected. In a cell with amplification of the MDM2 gene locus, multiple copies of the green signal or green signal clusters will be observed.



Liposarcoma tissue section with MDM2 amplification as indicated by large green clusters.

References

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Luan SL, et al. (2010) J Pathol 222: 166-79.
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Poaty H, et al. (2012) PLoS One 7: e29426.
Toledo F & Wahl GM (2006) Nat Rev Cancer 6: 909-23.
Tornillo L, et al. (2005) Lab Invest 85: 921-31.
Vassilev LT (2007) Trends Mol Med 13: 23-31.

Prod. No.	Product	Label	Tests* (Volume)
C-3049-100	ZytoDot 2C SPEC MDM2/CEN 12 Probe CE IVD	DIG/DNP	10 (100 µl)
C-3049-400	ZytoDot 2C SPEC MDM2/CEN 12 Probe CE IVD	DIG/DNP	40 (400 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC FOXO1 Break Apart Probe

CE IVD

Background

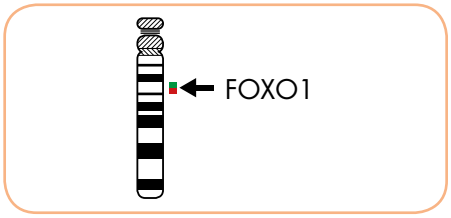
The ZytoDot® 2C SPEC FOXO1 Break Apart Probe is designed for the detection of specific translocations involving the chromosomal region 13q14.11 harboring the FOXO1 (forkhead box O1, a.k.a. FKHR) gene characteristic for alveolar rhabdomyosarcoma.

Among solid tumors of the childhood, rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma. RMS are classified in two main categories: embryonal rhabdomyosarcoma (ERMS) and alveolar rhabdomyosarcoma (ARMS). The alveolar histology is associated with a poorer prognosis. ARMS is characterized by two tumor-specific reciprocal translocations t(2;13)(q36;q14.1) and t(1;13)(p36.1;q14.1) detectable in more than 80% of all ARMS. These translocations fuse the FOXO1 locus on 13q14.11 to either PAX3 on chromosome 2 or to PAX7 on chromosome 1. The resulting fusion transcripts encode for the chimeric proteins PAX3-FOXO1 and PAX7-FOXO1 that combine transcriptional domains from the corresponding wild-type proteins and thereby acquire oncogenic activity. The translocations and their fusion genes represent highly specific genetic markers useful in the diagnosis of ARMS.

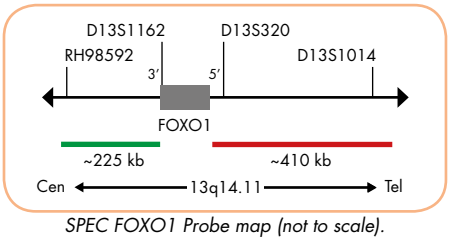
References
Dal Cin P, et al. (1991) Cancer Genet Cytogenet 55: 191-5.
Douglass EC, et al. (1991) Genes Chromosomes Cancer 3: 480-2.
Gunawan B, et al. (1999) Pathol Oncol Res 5: 211-3.
Seidal T, et al. (1982) Acta Pathol Microbiol Immunol Scand A 90: 345-54.
Sorensen PH, et al. (2002) J Clin Oncol 20: 2672-9.

Probe Description

The ZytoDot® 2C SPEC FOXO1 Break Apart Probe is a mixture of a Digoxigenin-labeled and a Dinitrophenyl-labeled probe hybridizing to the 13q14.11 band. The DNP-labeled probe hybridizes distal to the FOXO1 gene breakpoint region at 13q14.11, the DIG-labeled probe hybridizes proximal to the FOXO1 gene breakpoint region.



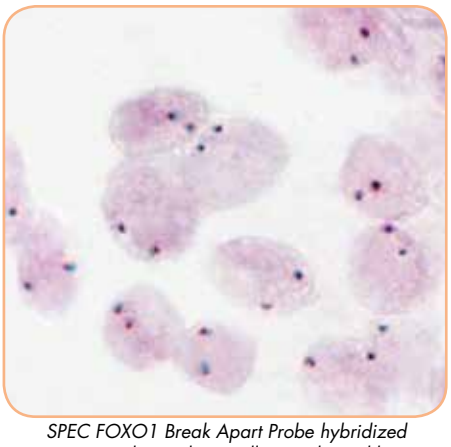
Ideogram of chromosome 13 indicating the hybridization locations.



SPEC FOXO1 Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 13q14.11 band, using the ZytoDot® 2C CISH Implementation Kit, two red/green fusion signals are expected representing two normal (non-rearranged) 13q14.11 loci. A signal pattern consisting of one red/green fusion signal, one red signal, and a separate green signal indicates one normal 13q14.11 locus and one 13q14.11 locus affected by a translocation.



SPEC FOXO1 Break Apart Probe hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.

Prod. No.	Product	Label	Tests* (Volume)
C-3065-100	ZytoDot 2C SPEC FOXO1 Break Apart Probe CE IVD	DIG/DNP	10 (100 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC IGH Break Apart Probe

IVD

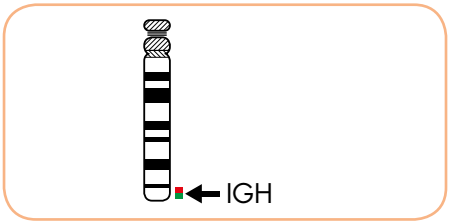
Background

The ZytoDot® 2C SPEC IGH Break Apart Probe is designed to detect translocations involving the chromosomal region 14q32.33 harboring the IGH gene. Rearrangements involving the IGH (immunoglobulin heavy locus, a.k.a. IGH@) gene are considered to be cytogenetic hallmarks for non-Hodgkin lymphoma (NHL). NHLs represent 50% of all hematological malignancies. IGH gene rearrangements have been identified in about 50% of NHLs and are associated with specific subtypes of NHLs. Translocation t(11;14)(q13.3;q32.3) can be found in about in 95% of mantle cell lymphoma (MCL), t(14;18)(q32.3;q21.3) in 80% of follicular lymphoma (FL), t(3;14)(q27;q32.3) in diffuse large B-cell lymphoma (DLBCL), and t(8;14)(q24.21;q32.3) in Burkitt lymphoma. In all of these translocations an oncogene located near the breakpoint of the translocation partner is activated by juxtaposing to IGH regulatory sequences.
Rearrangements involving 14q32.33 have unique biological characteristics and correlate with clinical, morphological, and immunophenotypic features. CISH is a helpful tool for the diagnosis, selecting treatment, and giving prognostic information.

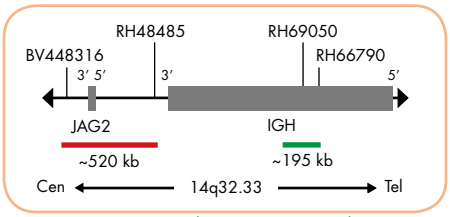
References
Bernicot I, et al. (2007) Cytogenet Genome Res 118: 345-52.
Hehne S, et al. (2012) Pathol Res Pract 208: 510-7.
Kazuhiro N, et al. (1997) Blood 90: 526-34.
Lu S, et al. (2004) Cancer Genet and Cytogenet 152: 141-5.
Nishida K, et al. (1989) Cancer Res 49: 1275-81.
Quintero-Rivera F, et al. (2009) Cancer Genet Cytogenet 190: 33-9.

Probe Description

The ZytoDot® 2C SPEC IGH Break Apart Probe is a mixture of a Digoxigenin-labeled and a Dinitrophenyl-labeled probe hybridizing to the 14q32.33 band. The DNP-labeled probe hybridizes proximal and the DIG-labeled probe hybridizes distal to the constant regions of the IGH locus at 14q32.33.



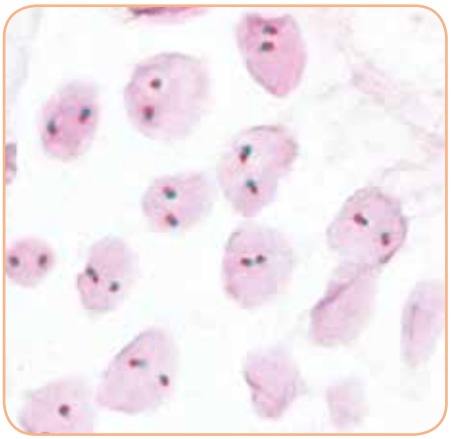
Ideogram of chromosome 14 indicating the hybridization locations.



SPEC IGH Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 14q32.33 band, using the ZytoDot® 2C CISH Implementation Kit, two red/green fusion signals are expected representing two normal (non-rearranged) 14q32.33 loci. A signal pattern consisting of one red/green fusion signal, one red signal, and a separate green signal indicates one normal 14q32.33 locus and one 14q32.33 locus affected by a translocation.



SPEC IGH Break Apart Probe hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.

Prod. No.	Product	Label	Tests* (Volume)
C-3071-100	ZytoDot 2C SPEC IGH Break Apart Probe CE IVD	DIG/DNP	10 (100 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC FUS Break Apart Probe

CE IVD

Background

The ZytoDot® 2C SPEC FUS Break Apart Probe is designed to detect translocations involving the chromosomal region 16p11.2 harboring the FUS (FUS RNA binding protein, a.k.a. TLS, FUS/TLS, hnRNP P2) gene.

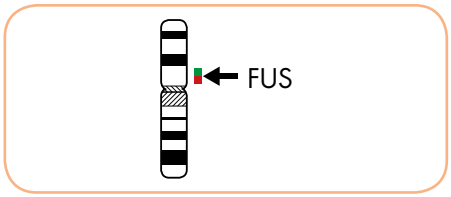
The FUS gene encodes an RNA-binding protein, the C-terminal end of which is involved in protein and RNA binding and which appears to be involved in transcriptional activation with its N-terminal end. It shares distinct characteristics with EWS and TAF15 which together with FUS are frequently referred to as the FET family of proteins.

FUS gene rearrangements have been shown to be involved in both solid tumors and leukemias fusing the N-terminal end of FUS to various fusion partners. The most frequent translocation involving the FUS gene region is t(12;16)(q13.3;p11.2). Occurring in over 90% of myxoid liposarcomas, the FUS-DDIT3 fusion protein is regarded as being consequential for the development of myxoid liposarcomas by acting as an abnormal transcription factor and thus deregulating FUS-DDIT3 target genes. Differential diagnosis of liposarcomas and accurate classification, the latter being especially important with regard to appropriate treatment and prognosis, are often problematic. Therefore, detection of FUS rearrangements via *in situ* Hybridization analysis is a valuable tool to confirm the histopathological diagnosis of myxoid liposarcoma.

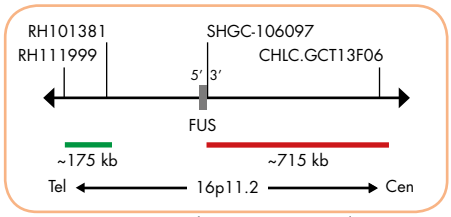
References
Andersson M, et al. (2010) BMC Cancer 10: 249-58.
Antonescu C, et al. (2000) J Mol Diagn 2: 132-8.
Germano G, et al. (2010) Cancer Res 70: 2235-44.
Kuroda M, et al. (1995) Am J Pathol 147: 1221-7.
Meis-Kindblom JM, et al. (2001) Virchows Arch 439: 141-51.
Panagopoulos I, et al. (1994) Cancer Res 54: 6500-3.
Panagopoulos I, et al. (1997) Oncogene 15: 1357-62.

Probe Description

The ZytoDot® 2C SPEC FUS Break Apart Probe is a mixture of a Digoxigenin-labeled and a Dinitrophenyl-labeled probe hybridizing to the 16p11.2 band. The DNP-labeled probe hybridizes proximal to the FUS gene, the DIG-labeled probe hybridizes distal to that gene.



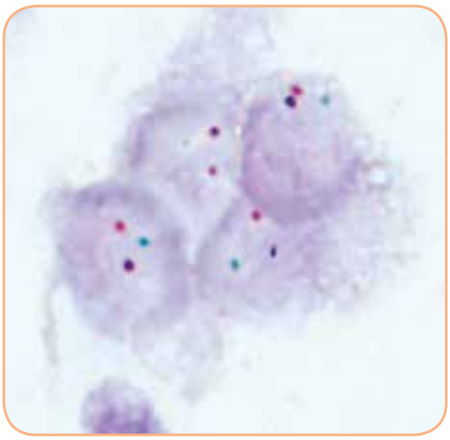
Ideogram of chromosome 16 indicating the hybridization locations.



SPEC FUS Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 16p11.2 band, using the ZytoDot® 2C CISH Implementation Kit two red/green fusion signals are expected representing two normal (non-rearranged) 16p11.2 loci. A signal pattern consisting of one red/green fusion signal, one red signal, and a separate green signal indicates one normal 16p11.2 locus and one 16p11.2 locus affected by a 16p11.2 translocation.



Myxoid liposarcoma tissue section with translocation affecting the 16p11.2 locus as indicated by one non-rearranged red/green fusion signal, one red signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
C-3054-100	ZytoDot 2C SPEC FUS Break Apart Probe CE IVD	DIG/DNP	10 (100 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC USP6 Break Apart Probe

CE IVD

Background

The ZytoDot® 2C SPEC USP6 Break Apart Probe is designed to detect translocations involving the chromosomal region 17p13.2 harboring the USP6 (ubiquitin specific peptidase 6, a.k.a. Tre-2 or TRE17) gene.

Translocations affecting USP6 have been initially found in primary aneurysmal bone cysts (ABC), a benign, but locally aggressive bone lesion that occurs predominantly during the first two decades of life. USP6 rearrangements are restricted to spindle cells in primary ABC, indistinguishable from surrounding normal spindle cells. The resulting fusion genes detected are formed by juxtaposition of the USP6 coding sequences to the highly active promoter sequences of several partner genes, as e.g. CDH11, COL1A1, OMD, TRAP150, and ZNF9, leading to the transcriptional upregulation of USP6. No true fusion genes are formed.

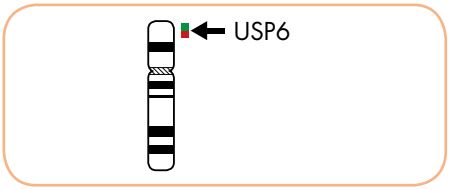
More recently, nodular fasciitis (NF), another mesenchymal lesion, has been tested positive for USP6 rearrangements. NF is a subcutaneous pseudosarcomatous myofibroblastic proliferation of unknown pathogenesis that regresses spontaneously when not surgically resected. The translocation results in the fusion of the promoter region of MYH9 located on 22q12.3 to the entire coding sequence of USP6 and subsequently in upregulated USP6 expression.

For both lesions, it is assumed that the detection of USP6 rearrangements by CISH might represent a valuable diagnostic tool.

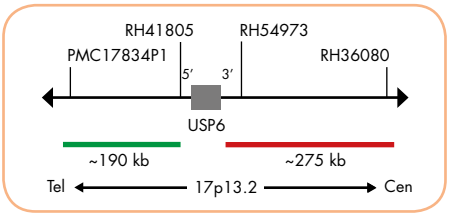
References
Erickson-Johnson MR, et al. (2011) Lab Invest 91: 1427-33.
Nakamura T, et al. (1988) Oncogene Res 2: 357-70.
Oliveira AM, et al. (2004) Cancer Res 64: 1920-3.
Oliveira AM, et al. (2005) Oncogene 24: 3419-26.

Probe Description

The ZytoDot® 2C SPEC USP6 Break Apart Probe is a mixture of a Digoxigenin-labeled and a Dinitrophenyl-labeled probe hybridizing to the 17p13.2 band. The DNP-labeled probe hybridizes proximal to the USP6 breakpoint region at 17p13.2, the DIG-labeled probe hybridizes distal to the USP6 breakpoint region.



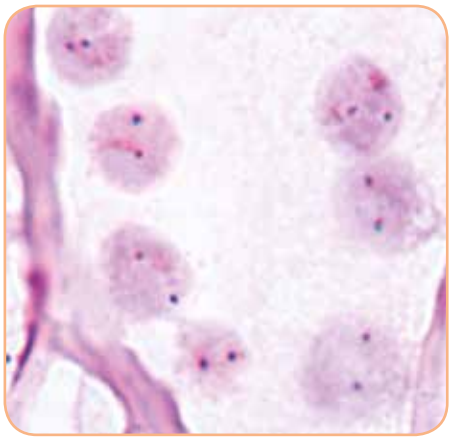
Ideogram of chromosome 17 indicating the hybridization locations.



SPEC USP6 Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 17p13.2 band, using the ZytoDot® 2C CISH Implementation Kit, two red/green fusion signals are expected representing two normal (non-rearranged) 17p13.2 loci. A signal pattern consisting of one red/green fusion signal, one red signal, and a separate green signal indicates one normal 17p13.2 locus and one 17p13.2 locus affected by a translocation.



SPEC USP6 Break Apart Probe hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.

Prod. No.	Product	Label	Tests* (Volume)
C-3077-100	ZytoDot 2C SPEC USP6 Break Apart Probe CE IVD	DIG/DNP	10 (100 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® SPEC ERBB2 Probe

CE IVD

Background

The ZytoDot® SPEC ERBB2 Probe is designed for the detection of ERBB2 gene amplification, frequently observed in solid malignant neoplasms, in formalin-fixed, paraffin-embedded tissue sections or cell samples.

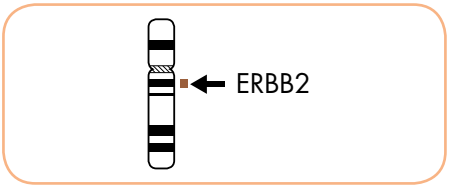
The ERBB2 gene (a.k.a. HER2 and NEU) is located in the chromosomal region 17q12 and encodes the cellular growth factor receptor p185.

Amplification of the proto-oncogene ERBB2, observed in approximately 20% of all breast cancer samples, has been correlated with a poor prognosis of the disease. Similar results have been obtained for a variety of other malignant neoplasms e.g. ovarian cancer, stomach cancer, and carcinomas of the salivary gland.

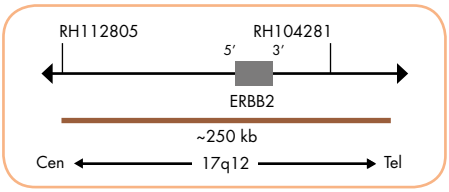
References
Baselga J, et al. (1999) Semin Oncol 26: 78-83.
Brockhoff G, et al. (2016) Histopathology 69: 635-46.
Brunello E, et al. (2012) Histopathology 60: 482-8.
Brunner K, et al. (2010) Anal Quant Cytol Histol 32: 78-89.
Coussens L, et al. (1985) Science 230: 1132-9.
Ettl T, et al. (2012) Br J Cancer 106: 719-26.
Hwang CC, et al. (2011) Histopathology 59: 984-92.
Hynes NE & Stern DF (1994) Biochim Biophys Acta 1198: 165-84.
Moelans CB, et al. (2011) Crit Rev Oncol Hematol 80: 380-92.
Park JB, et al. (1989) Cancer Res 49: 6605-9.
Popescu NC, et al. (1989) Genomics 4: 362-6.
Sassen A, et al. (2008) Breast Cancer Res 10: R2.
Slamon DJ, et al. (1987) Science 235: 177-82.
Voutsas IF, et al. (2013) Int J Radiat Biol 89: 319-25.
Wolff AC, et al. (2018) J Clin Oncol 14: 437-41.

Probe Description

The ZytoDot® SPEC ERBB2 Probe is a Digoxigenin-labeled probe specific for the ERBB2 gene at 17q12, processed by the unique *ZytoVision® Repeat Subtraction Technique* resulting in advanced specificity and less background.



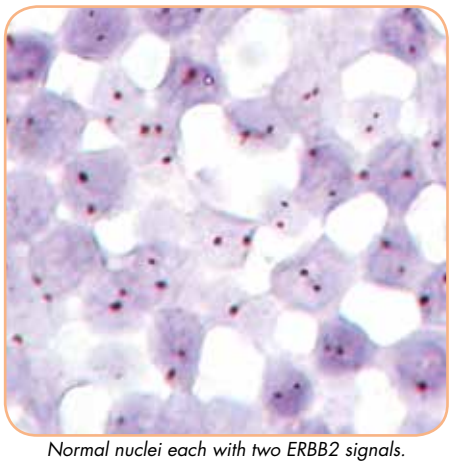
Ideogram of chromosome 17 indicating the hybridization locations.



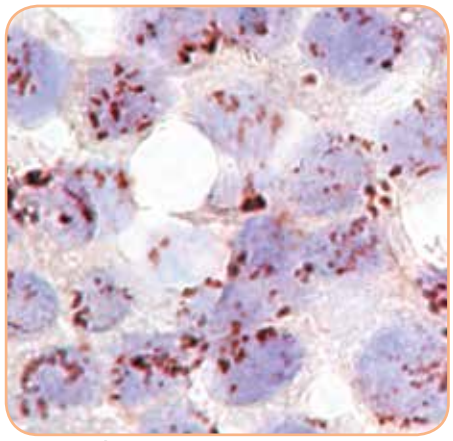
SPEC ERBB2 Probe map (not to scale).

Results

In normal cells, two distinct dot-shaped signals per nucleus will be observed. Nuclei with amplification of the ERBB2 gene locus or polysomy of chromosome 17 will show multiple dots or large signal clusters.



Normal nuclei each with two ERBB2 signals.



Breast carcinoma tissue section with ERBB2 amplification.

Prod. No.	Product	Label	Tests* (Volume)
C-3001-400	ZytoDot SPEC ERBB2 Probe CE IVD	DIG	40 (400 µl)
C-3003-40	ZytoDot SPEC ERBB2 Probe Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Probe, 0.4 ml; Wash Buffer SSC, 560 ml; PBS/Tween, good for 2000 ml; Blocking Solution, 4 ml; Mouse-anti-DIG, 4 ml; Anti-Mouse-HRP-Polymer, 4 ml; DAB Solution A, 0.3 ml; DAB Solution B, 10 ml; Mayer's Hematoxylin Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	DIG	40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC ERBB2/CEN 17 Probe

CE IVD

Background

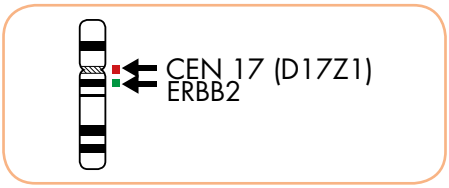
The ZytoDot® 2C SPEC ERBB2/CEN 17 Probe is designed for the simultaneous detection of ERBB2 and centromere 17 in formalin-fixed, paraffin-embedded tissue sections or cell samples.

The ERBB2 gene (a.k.a. HER2 and NEU) is located in the chromosomal region 17q12 and encodes the cellular growth factor receptor p185. Amplification of the proto-oncogene ERBB2, observed in approximately 20% of all breast cancer samples, has been correlated with a poor prognosis of the disease. Similar results have been obtained for a variety of other malignant neoplasms e.g. ovarian cancer, stomach cancer, and carcinomas of the salivary gland.

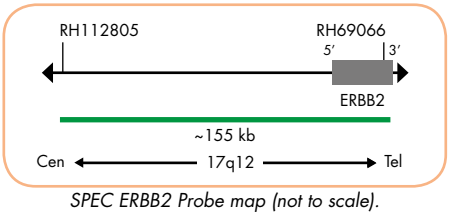
References
Baselga J, et al. (1999) Semin Oncol 26: 78-83.
Brockhoff G, et al. (2016) Histopathology 69: 635-46.
Brunello E, et al. (2012) Histopathology 60: 482-8.
Brunner K, et al. (2010) Anal Quant Cytol Histol 32: 78-89.
Coussens L, et al. (1985) Science 230: 1132-9.
Ettl T, et al. (2012) Br J Cancer 106: 719-26.
Hwang CC, et al. (2011) Histopathology 59: 984-92.
Hynes NE & Stern DF (1994) Biochim Biophys Acta 1198: 165-84.
Moelans CB, et al. (2011) Crit Rev Oncol Hematol 80: 380-92.
Park JB, et al. (1989) Cancer Res 49: 6605-9.
Popescu NC, et al. (1989) Genomics 4: 362-6.
Sassen A, et al. (2008) Breast Cancer Res 10: R2.
Slamon DJ, et al. (1987) Science 235: 177-82.
Voutsas IF, et al. (2013) Int J Radiat Biol 89: 319-25.
Wolff AC, et al. (2018) J Clin Oncol 14: 437-41.

Probe Description

The ZytoDot® 2C SPEC ERBB2/CEN 17 Probe is a mixture of a Digoxigenin-labeled probe specific for the ERBB2 gene at 17q12 and a Dinitrophenyl-labeled CEN 17 probe specific for the alpha satellite centromeric region of chromosome 17 (D17Z1).



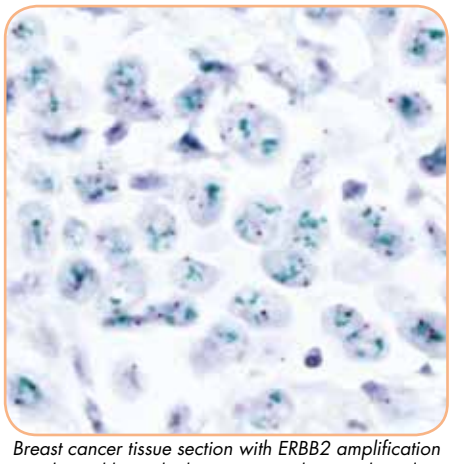
Ideogram of chromosome 17 indicating the hybridization locations.



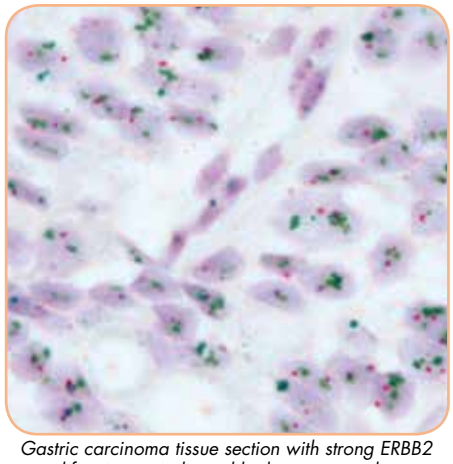
SPEC ERBB2 Probe map (not to scale).

Results

Using the ZytoDot® 2C SPEC ERBB2/CEN 17 Probe Kit, two green (ERBB2) and two red (CEN 17) signals are expected in a normal interphase nucleus. In a cell with amplification of the ERBB2 gene locus, multiple copies of the green signal or green signal clusters will be observed.



Breast cancer tissue section with ERBB2 amplification as indicated by multiple green signals in each nucleus.



Gastric carcinoma tissue section with strong ERBB2 amplification as indicated by large green clusters.

Prod. No.	Product	Label	Tests* (Volume)
C-3032-100	ZytoDot 2C SPEC ERBB2/CEN 17 Probe CE IVD	DIG/DNP	10 (100 µl)
C-3032-400	ZytoDot 2C SPEC ERBB2/CEN 17 Probe CE IVD	DIG/DNP	40 (400 µl)
C-3022-10	ZytoDot 2C SPEC ERBB2/CEN 17 Probe Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Probe, 0.1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml	DIG/DNP	10
C-3022-40	ZytoDot 2C SPEC ERBB2/CEN 17 Probe Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Probe, 0.4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	DIG/DNP	40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC ERBB2/D17S122 Probe

CE IVD

Background

The ZytoDot® 2C SPEC ERBB2/D17S122 Probe is designed for the detection of ERBB2 gene amplification frequently observed in solid malignant neoplasms e.g. breast cancer samples.

The ERBB2 gene (a.k.a. HER2 and NEU) is located in the chromosomal region 17q12 and encodes a 185-190 kDa transmembrane glycoprotein, p185, acting as a cellular growth factor receptor. The p185 protein belongs to the EGFR (epidermal growth factor receptor) subgroup of the RTK (receptor tyrosine kinase) superfamily also including ERBB1 (HER1), ERBB3 (HER3), and ERBB4 (HER4). Amplification of the proto-oncogene ERBB2, observed in approximately 20% of all breast cancer samples, has been correlated with a poor prognosis of the disease.

Similar results have been obtained for a variety of other malignant neoplasms e.g. ovarian cancer, stomach cancer, and carcinomas of the salivary gland. Chromogenic *in situ* Hybridization targeting the alpha satellite centromeric regions of chromosome 17 may be misleading in some cases due to possible gains or losses of this region. For these cases, reflex testing is recommended using the SPEC ERBB2/D17S122 Probe.

References

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Coussens L, et al. (1985) Science 230: 1132-9.
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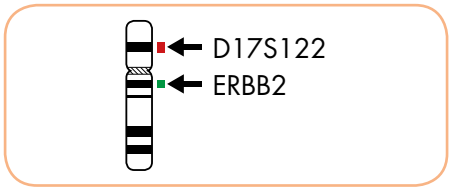
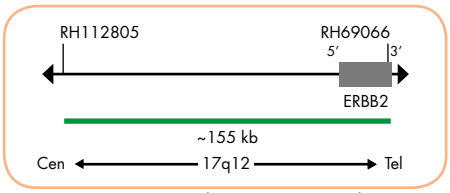
Park JB, et al. (1989) Cancer Res 49: 6605-9.
Popescu NC, et al. (1989) Genomics 4: 362-6.
Slamon DJ, et al. (1987) Science 235: 177-82.
Voutsas IF, et al. (2013) Int J Radiat Biol 89: 319-25.
Wolff AC, et al. (2018) J Clin Oncol 14: 437-41.

Probe Description

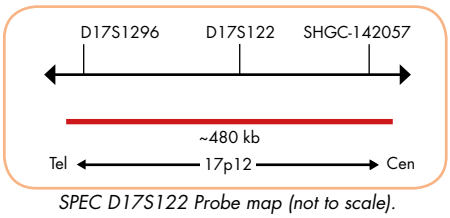
The ZytoDot® 2C SPEC ERBB2/D17S122 Probe is a mixture of a Digoxigenin-labeled probe specific for the chromosomal region 17q12 harboring the ERBB2 gene and a Dinitrophenyl-labeled SPEC D17S122 probe specific for the chromosomal region 17p12. The SPEC D17S122 probe is designed to be used for chromosome 17 copy number detection.



Ideogram of chromosome 17 indicating the hybridization locations.



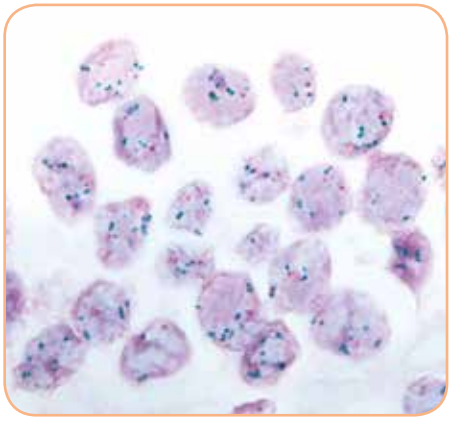
SPEC ERBB2 Probe map (not to scale).



SPEC D17S122 Probe map (not to scale).

Results

In a normal interphase nucleus, using the ZytoDot® 2C CISH Implementation Kit, two green (ERBB2) and two red (D17S122) signals are expected. In a cell with amplification of the ERBB2 gene locus or polysomy of chromosome 17, multiple copies of the green signal or green signal clusters will be observed.



Breast carcinoma tissue section with amplification of the ERBB2 gene as indicated by multiple green signals in relation to red (D17S122) signals in each nucleus.

Prod. No.	Product	Label	Tests* (Volume)
C-3068-100	ZytoDot 2C SPEC ERBB2/D17S122 Probe CE IVD	DIG/DNP	10 (100 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot ® 2C SPEC TOP2A/CEN 17 Probe

CE IVD

Background

The ZytoDot ® 2C SPEC TOP2A/CEN 17 Probe is designed for the detection of TOP2A deletions and gene amplifications in formalin-fixed, paraffin-embedded tissue sections or cell samples.

The TOP2A (DNA topoisomerase II alpha) gene is located in the chromosomal region 17q21.2 and encodes for a 170 kDa DNA topoisomerase which controls and alters the topologic state of DNA during replication, transcription, and chromosome segregation.

TOP2A gene copy number changes are frequently observed in the majority of ERBB2 amplified primary breast tumors as well as in other human malignancies without simultaneous ERBB2 amplification e.g. acute lymphoblastic leukemias, gastric and bladder carcinomas. Recent data suggests that amplification and deletion of the TOP2A gene locus may account for relative chemosensitivity or resistance to TOP2A inhibitor therapy, respectively. Thus, determination of the TOP2A status may predict benefit from adjuvant anthracyclines in ERBB2 positive breast cancer.

References

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Brunello E, et al. (2012) Histopathology 60: 482-8.
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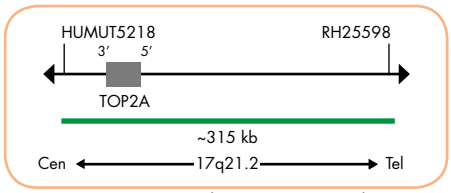
Tsai-Pflugfelder M, et al. (1988) Proc Natl Acad Sci U S A 85: 7177-81.
Wang JC (1996) Annu Rev Biochem 65: 635-92.

Probe Description

The ZytoDot ® 2C SPEC TOP2A/CEN 17 Probe is a mixture of a Digoxigenin-labeled probe specific for the TOP2A gene at 17q21.2 and a Dinitrophenyl-labeled CEN 17 probe specific for the alpha satellite centromeric region of chromosome 17 (D17Z1).

Ideogram of chromosome 17 indicating the hybridization locations.



SPEC TOP2A Probe map (not to scale).

Results

In a normal interphase nucleus, using the ZytoDot ® 2C CISH Implementation Kit two green and two red signals are expected. In a cell with amplification of the TOP2A gene locus, multiple copies of the green signal or green signal clusters will be observed.

Breast carcinoma tissue section with TOP2A amplification as indicated by multiple green signals per nucleus.

Prod. No.	Product	Label	Tests* (Volume)
C-3040-400	ZytoDot 2C SPEC TOP2A/CEN 17 Probe CE IVD	DIG/DNP	40 (400 µl)
Related Products			
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC SS18 Break Apart Probe

CE IVD

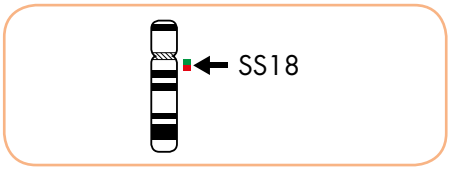
Background

The ZytoDot® 2C SPEC SS18 Break Apart Probe is designed to detect translocations involving the chromosomal region 18q11.2 harboring the SS18 (SS18, nBAF chromatin remodeling complex subunit, a.k.a. SYT) gene.
Translocations involving the region 18q11.2 are found in over 90% of synovial sarcoma. Among soft tissue sarcomas, synovial sarcoma is one of the most common and classically occurs in the extremities of young adults with greater prevalence in males even though, the occurrence of synovial sarcoma has also been described in a wide variety of anatomical locations and in all ages.
The most frequent translocation involving the SS18 gene region is t(X;18)(p11.23;q11.2) juxtaposing the SS18 gene in 18q11.2 either next to the SSX1 (synovial sarcoma, translocated to X chromosome) or the SSX2 gene, or very rarely to the SSX4 locus located in Xp11.23. Complex translocations involving other chromosomes are observed in less than 10% of synovial sarcomas. In combination with histopathological diagnosis, detection of SS18 rearrangements via *in situ* Hybridization (ISH) analysis is a valuable tool to confirm the diagnosis of synovial sarcoma.

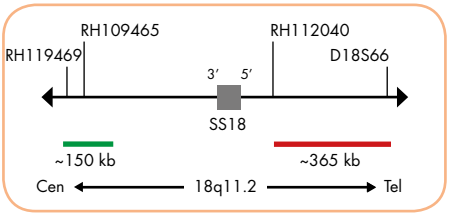
References
Amary MF, et al. (2007) Mod Pathol 20: 482-96.
Clark J, et al. (1994) Nat Genet 7: 502-8.
Kawai A, et al. (1998) N Engl J Med 338: 153-60.
Surace C, et al. (2004) Lab Invest 84: 1185-92.
Torres L, et al. (2008) Cancer Genet Cytogenet 187: 45-9.

Probe Description

The ZytoDot® 2C SPEC SS18 Break Apart Probe is a mixture of a Digoxigenin-labeled probe and a Dinitrophenyl-labeled probe hybridizing to the 18q11.2 band. The DNP-labeled probe hybridizes distal to the SS18 gene and the DIG-labeled probe hybridizes proximal to that gene.



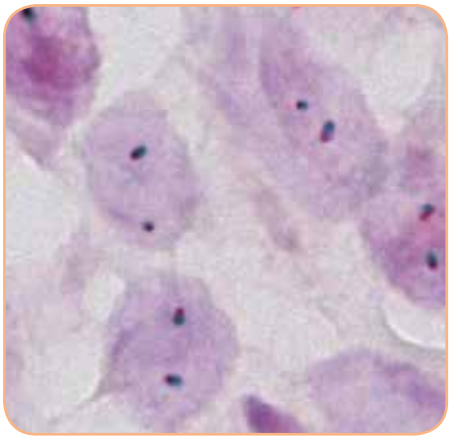
Ideogram of chromosome 18 indicating the hybridization locations.



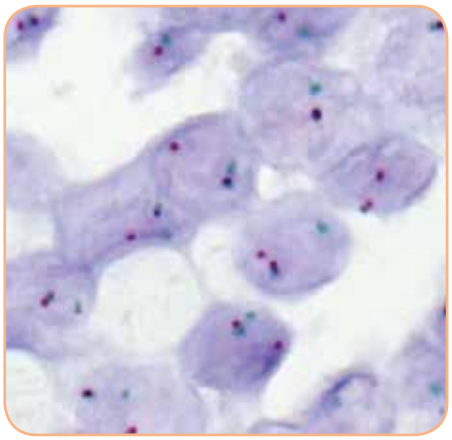
SPEC SS18 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 18q11.2 band, using the ZytoDot® 2C CISH Implementation Kit two red/green fusion signals are expected representing two normal (non-rearranged) 18q11.2 loci. A signal pattern consisting of one red/green fusion signal, one red signal, and a separate green signal indicates one normal 18q11.2 locus and one 18q11.2 locus affected by an 18q11.2 translocation.



SPEC SS18 Break Apart Probe hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.



Synovial sarcoma tissue section with translocation affecting the 18q11.2 locus as indicated by one non-rearranged red/green fusion signal, one red signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
C-3046-100	ZytoDot 2C SPEC SS18 Break Apart Probe CE IVD	DIG/DNP	10 (100 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC BCL2 Break Apart Probe

CE IVD

Background

The ZytoDot® 2C SPEC BCL2 Break Apart Probe is designed to detect translocations involving the chromosomal region 18q21.33 harboring the BCL2 gene. The BCL2 (BCL2 apoptosis regulator, a.k.a. PPP1R50) gene encodes a mitochondrial membrane protein that regulates apoptosis and is expressed in B-cells.

Translocations involving the BCL2 gene are commonly identified in B-cell lymphomas. In particular, the translocation t(14;18)(q32.3;q21.3) has been identified in about 80% of follicular lymphoma (FL), in 20% to 30% of diffuse large B-cell lymphoma (DLBCL), and rarely in B-cell chronic lymphocytic leukemia (B-CLL).

In FL this translocation is considered to be a cytogenetic hallmark. As a result of this rearrangement, the BCL2 gene is juxtaposed to the IGH (Immunglobulin heavy chain) locus at 14q32.33 which leads to overexpression of the anti-apoptotic protein BCL2, and finally to progression to lymphoma.

Alternative BCL2 translocations to immunoglobulin light chain genes as well as non-IG translocation events have been reported.

In DLBCL, BCL2 gene overexpression has been implicated in conferring resistance to chemotherapy and has been associated with poor prognosis.

Hence, detection of BCL2 translocations by CISH may be of diagnostic and prognostic relevance.

References

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Gu K, et al. (2008) Arch Pathol Lab Med 132: 1355-61.
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Impera L, et al. (2008) Oncogene 27: 6187-90.
López-Guillermo A, et al. (1999) Blood 93: 3081-7.
Nelson BP, et al. (2007) Am J Clin Pathol 128: 323-32.
Tibiletti MG, et al. (2009) Hum Pathol 40: 645-52.
Tomita N, et al. (2009) Haematologica 94: 935-43.
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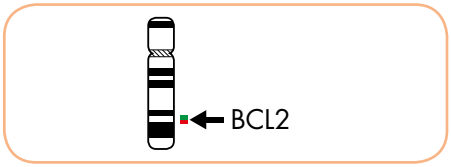
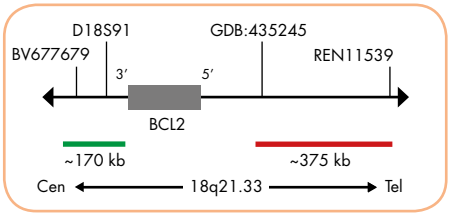
Probe Description

The ZytoDot® 2C SPEC BCL2 Break Apart Probe is a mixture of a Digoxigenin-labeled and a Dinitrophenyl-labeled probe hybridizing to the 18q21.33 band. The DNP-labeled probe hybridizes distal to the BCL2 gene at 18q21.33, the DIG-labeled probe hybridizes proximal to the BLC2 gene at 18q21.33.



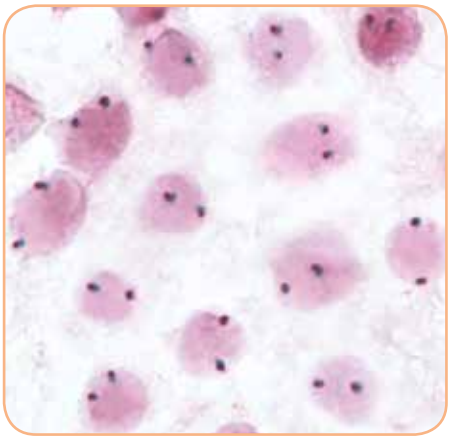
Ideogram of chromosome 18 indicating the hybridization locations.



SPEC BCL2 Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 18q21.33 band, using the ZytoDot® 2C CISH Implementation Kit, two red/green fusion signals are expected representing two normal (non-rearranged) 18q21.33 loci. A signal pattern consisting of one red/green fusion signal, one red signal, and a separate green signal indicates one normal 18q21.33 locus and one 18q21.33 locus affected by a translocation.



SPEC BCL2 Break Apart Probe hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.

Prod. No.	Product	Label	Tests* (Volume)
C-3073-100	ZytoDot 2C SPEC BCL2 Break Apart Probe CE IVD	DIG/DNP	10 (100 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC MALT1 Break Apart Probe

CE IVD

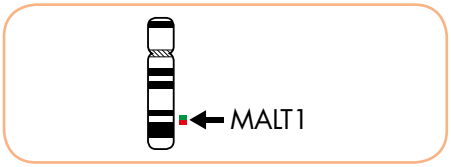
Background

The ZytoDot® 2C SPEC MALT1 Break Apart Probe is designed to detect translocations involving the chromosomal region 18q21.32 harboring the MALT1 gene.
The MALT1 (MALT1 paracaspase, a.k.a. MLT) gene encodes a human paracaspase and is often rearranged in MALT lymphomas accounting for 5-10% of all B-cell non-Hodgkin lymphomas (NHL). The most common translocations affecting the MALT1 gene are t(11;18)(q22.2;q21.3) and t(14;18)(q32.3;q21.3) occurring in 50% and 15-20% of MALT lymphomas, respectively.
These translocations lead to the expression of BIRC3-MALT1 (a.k.a. API2-MALT1) and IGH-MALT1 fusion proteins, resulting in constitutive activation of the NF-κB signaling pathway which controls the expression of numerous anti-apoptotic and proliferation-promoting genes.
The translocation t(11;18)(q22.2;q21.3) is mainly found in pulmonary and gastric lymphomas, whereas t(14;18)(q32.3;q21.3) occurs more frequently in non-gastrointestinal MALT lymphomas, e.g., of the skin and salivary glands.
The presence of a t(11;18)(q22.2;q21.3) correlates with unresponsiveness to eradication of *Helicobacter pylori* in gastric MALT lymphomas. Hence, detection of MALT1 translocations by CISH may be a supportive tool to identify patients eligible for an anti-*H. pylori* therapy.

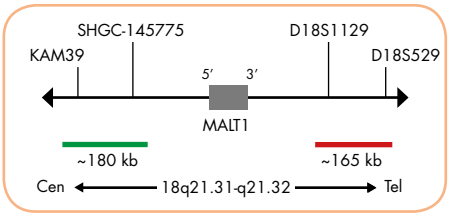
References
Afonina IS, et al. (2015) FEBS J 282: 3286-97.
Beans M, et al. (2014) PLoS One 9: e103774.
Dierlamm J, et al. (1999) Blood 93: 3601-9.
Levine EG, et al. (1989) Blood 74: 1796-800.
Lucas PC, et al. (2001) J Biol Chem 276: 19012-9.
Martinelli G, et al. (2005) J Clin Oncol 23: 1979-83.
Pereira MI & Medeiros JA (2014) World J Gastroenterol 20: 684-98.
Troppan K, et al. (2015) Gastroenterol Res Pract 2015: 102656.

Probe Description

The ZytoDot® 2C SPEC MALT1 Break Apart Probe is a mixture of a Digoxigenin-labeled and a Dinitrophenyl-labeled probe hybridizing to the 18q21.31-q21.32 band. The DNP-labeled probe hybridizes distal to the MALT1 gene at 18q21.32, the DIG-labeled probe hybridizes proximal to the MALT1 gene at 18q21.31-q21.32.



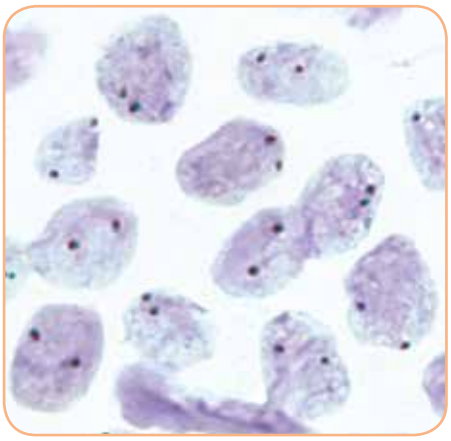
Ideogram of chromosome 18 indicating the hybridization locations.



SPEC MALT1 Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 18q21.31-q21.32 band, using the ZytoDot® 2C CISH Implementation Kit, two red/green fusion signals are expected representing two normal (non-rearranged) 18q21.31-q21.32 loci. A signal pattern consisting of one red/green fusion signal, one red signal, and a separate green signal indicates one normal 18q21.31-q21.32 locus and one 18q21.31-q21.32 locus affected by a translocation.



SPEC MALT1 Break Apart Probe hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.

Prod. No.	Product	Label	Tests* (Volume)
C-3072-100	ZytoDot 2C SPEC MALT1 Break Apart Probe CE IVD	DIG/DNP	10 (100 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC ERG Break Apart Probe

CE IVD

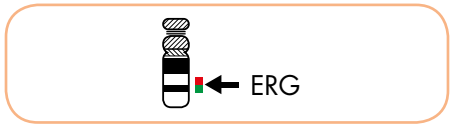
Background

The ZytoDot® 2C SPEC ERG Break Apart Probe is designed to detect aberrations involving the ERG gene at 21q22.2 frequently found in prostate cancers.
ERG (ETS transcription factor ERG) rearrangements have been observed in 40-60% of prostate cancers identified via prostate-specific antigen (PSA) screening. The most common aberration affecting ERG is the interstitial deletion of about 3 Mb at the chromosomal region 21q22 found in 90% of the cases. This deletion leads to the fusion of the hormonally regulated promoter of the TMPRSS2 (transmembrane serine protease 2) gene to the coding region of ERG, resulting in overexpression of the ERG transcription factor. However, about 10% of the ERG rearranged prostate cancer cases show alternative fusions, as e.g. SLC45A3-ERG or NDRG1-ERG.
Several studies detected associations of ERG rearrangements with histomorphologic features as well as characteristic chromosomal copy number changes and gene expression signatures, defining a distinct sub-class of prostate cancers with unfavorable prognosis. Hence, the evaluation of the ERG rearrangement status in tissue or urine samples by CISH might be of diagnostic and prognostic relevance.
EWSR1-ERG gene fusions present in about 10% of patients with Ewing sarcoma may result from complex genomic rearrangements and may therefore not be detected by CISH analysis or may result in a non-classical translocation signal pattern.

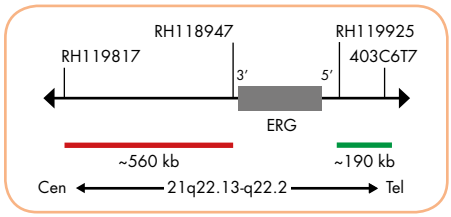
References
Esgueva R, et al. (2010) Mod Pathol 23: 539-46.
Maire G, et al. (2008) Cancer Genet Cytogenet 181: 81-92.
Nam RK, et al. (2007) Br J Cancer 97: 1690-5.
Perner S, et al. (2006) Cancer Res 66: 8337-41.
Pflueger D, et al. (2009) Neoplasia 11: 804-11.
Tomlins SA, et al. (2005) Science 310: 644-8.

Probe Description

The ZytoDot® 2C SPEC ERG Break Apart Probe is a mixture of a Digoxigenin-labeled and a Dinitrophenyl-labeled probe hybridizing to the long arm of chromosome 21. The DNP-labeled probe hybridizes proximal to the ERG gene breakpoint region at 21q22.13-q22.2, the DIG-labeled probe hybridizes distal to the ERG gene breakpoint region at 21q22.2.



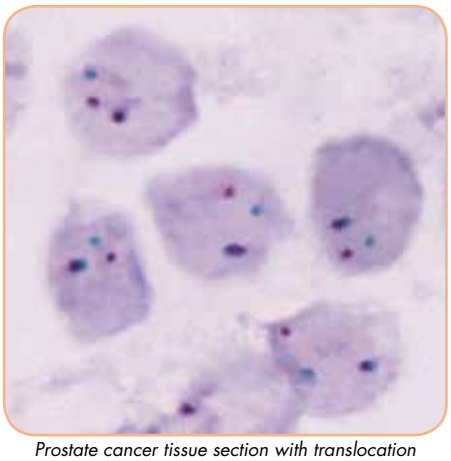
Ideogram of chromosome 21 indicating the hybridization locations.



SPEC ERG Probe map (not to scale).

Results

In an interphase nucleus of a normal cell lacking an aberration involving the 21q22.13-q22.2 band, using the ZytoDot® 2C CISH Implementation Kit, two red/green fusion signals are expected representing the two normal (non-rearranged) 21q22.13-q22.2 loci.
A 21q22.13-q22.2 locus affected by a 21q22.2 deletion resulting in the TMPRSS2-ERG fusion is indicated by the loss of one green signal.
A signal pattern consisting of one red/green fusion signal, a separate green, and a separate red signal indicates an ERG translocation without involvement of TMPRSS2 (e.g. SLC45A3-ERG).



Prostate cancer tissue section with translocation affecting the 21q22.13-q22.2 locus as indicated by one non-rearranged red/green fusion signal, one red signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
C-3058-400	ZytoDot 2C SPEC ERG Break Apart Probe CE IVD	DIG/DNP	40 (400 µl)
Related Products			
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml		40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot® 2C SPEC EWSR1 Break Apart Probe

CE IVD

Background

The ZytoDot® 2C SPEC EWSR1 Break Apart Probe is designed to detect translocations involving the chromosomal region 22q12.2 harboring the EWSR1 (EWS RNA binding protein 1, a.k.a. EWS) gene).

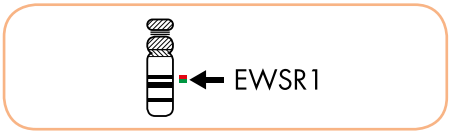
Translocations involving the chromosomal region 22q12.2 are found in 90-95% of patients with Ewing sarcoma or peripheral primitive neuroectodermal tumors (PNET). Ewing sarcoma is the second most common, highly malignant bone tumor in children and young adults. The most frequent translocation involving the EWSR1 gene region is t(11;22)(q24.3;q12.2) juxtaposing the EWSR1 gene in 22q12.2 next to the FLI-1 (friend leukemia virus integration 1) locus in 11q24.3. FLI-1 is a member of the ETS family of transcription factors. Less frequently, EWSR1 can also be fused to ERG, a transcription factor closely related to FLI-1 but located in 21q22.2.

For prognosis and appropriate treatment it is important to differentiate Ewing sarcoma/PNET from classic neuroblastoma, Wilms tumor, and rhabdomyosarcoma. In combination with the histopathological diagnosis, detection of EWSR1 rearrangements by using *in situ* Hybridization can be used to confirm the diagnosis of Ewing sarcoma/PNET.

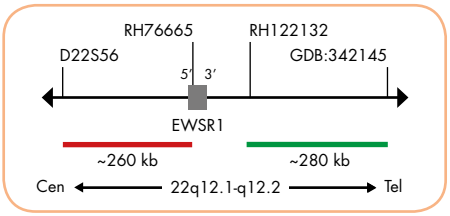
References
Bridge RS, et al. (2006) Mod Pathol 19: 1-8.
Delattre O, et al. (1992) Nature 359: 162-5.
Lee J, et al. (2005) Cancer Genet Cytogenet 159: 177-80.
Romeo S & Dei Tos AP (2010) Virchows Arch 456: 219-34.
Sandberg AA & Bridge JA (2000) Cancer Genet Cytogenet 123: 1-26.
Zucman J, et al. (1993) EMBO J 12: 4481-7.

Probe Description

The ZytoDot® 2C SPEC EWSR1 Break Apart Probe is a mixture of a Digoxigenin-labeled probe and a Dinitrophenyl-labeled probe hybridizing to the 22q12.1-q12.2 band. The DNP-labeled probe hybridizes proximal and extends inward intron 4 of the EWSR1 gene, the DIG-labeled probe hybridizes distal to that gene.



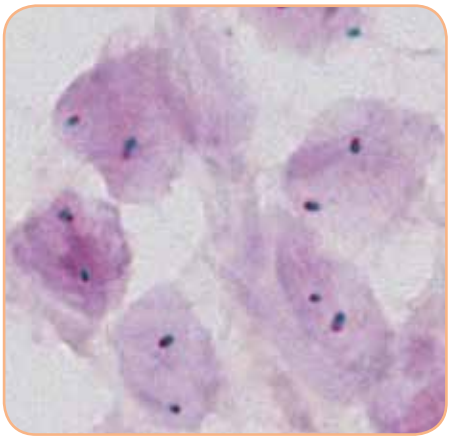
Ideogram of chromosome 22 indicating the hybridization locations.



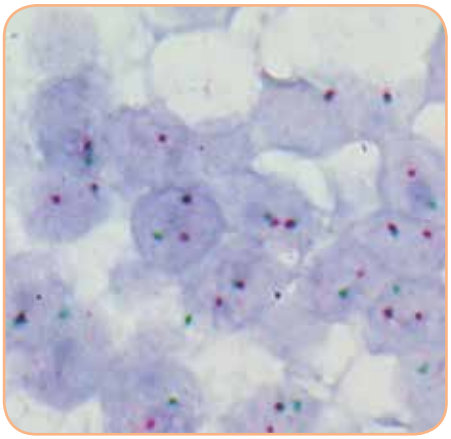
SPEC EWSR1 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 22q12.1-q12.2 band, using the ZytoDot® 2C CISH Implementation Kit two red/green fusion signals are expected representing two normal (non-rearranged) 22q12.1-q12.2 loci. A signal pattern consisting of one red/green fusion signal, one red signal, and a separate green signal indicates one normal 22q12.1-q12.2 locus and one 22q12.1-q12.2 locus affected by a 22q12.1-q12.2 translocation.



SPEC EWSR1 Break Apart Probe hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.



Ewing sarcoma tissue section with translocation affecting the 22q12.1-q12.2 locus as indicated by one non-rearranged red/green fusion signal, one red signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
C-3043-100	ZytoDot 2C SPEC EWSR1 Break Apart Probe CE IVD	DIG/DNP	10 (100 µl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml		10

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoDot ® Probes for Chromosome Enumeration

CE IVD

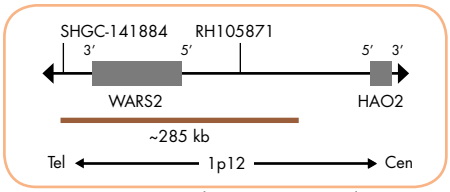
Background
The ZytoDot ® Chromosome Enumeration Probes are designed for identification and enumeration of human chromosomes in interphase cells and as an adjunct to standard karyotyping in metaphases. These probes will produce sharp, bright signals specific for each individual chromosome.

CEN Probe Description
For most chromosomes, direct labeled ZytoDot ® CEN™ Probes hybridizing to highly repetitive human satellite DNA sequences mainly located at the centromeric regions of chromosomes are applicable.

SPEC Probe Description
As several chromosomes share the same repetitive sequences resulting in cross-hybridization signals, they cannot be differentiated by centromere specific probes. Instead these chromosomes can be identified by direct labeled ZytoDot ® SPEC™ Probes hybridizing in close proximity to the respective satellite DNA sequences or to other chromosome specific loci.

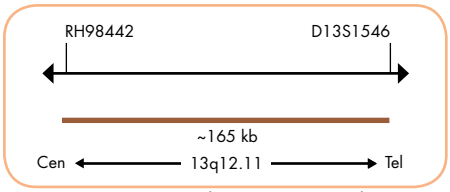
Results
In a normal interphase nucleus, two signals are expected using Chromosome Enumeration Probes specific for autosomes. Using chromosome Y specific probes will result in normal male cells in one signal and in normal female cells in no signal. Using chromosome X specific probes will result in normal male cells in one signal and in normal female cells in two signals per nucleus. Other signal patterns indicate numerical aberrations of the respective chromosome.

ZytoDot ® SPEC Probe Maps



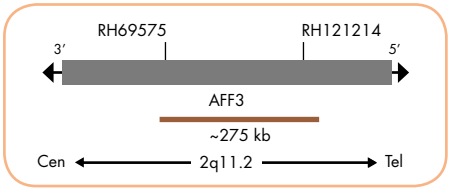
SPEC 1p12 Probe map (not to scale).

The ZytoDot ® SPEC 1p12 Probe is designed to hybridize in close proximity of centromere 1 at 1p12 harboring the WARS2 gene. Since chromosomes 1, 5, and 19 share the same repetitive sequences, they cannot be differentiated by probes detecting centromere specific repeats.



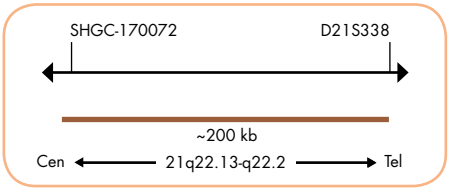
SPEC 13q12 Probe map (not to scale).

The ZytoDot ® SPEC 13q12 Probe is designed to hybridize in close proximity of centromere 13 at 13q12.11. Since chromosomes 13 and 21 share the same repetitive sequences, they cannot be differentiated by probes detecting centromere specific repeats.



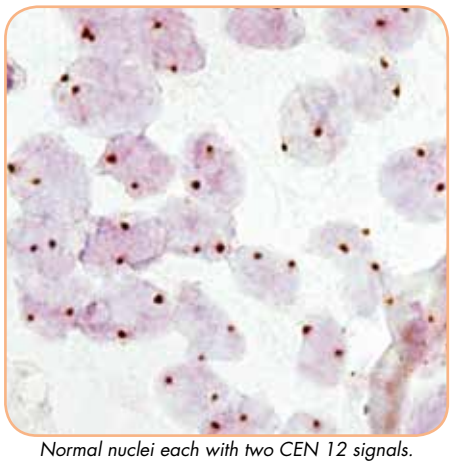
SPEC 2q11 Probe map (not to scale).

The ZytoDot ® SPEC 2q11 Probe is specific for the AFF3 (AF4/FMR2 family, member 3) gene region in 2q11.2. Due to cross-hybridizations of chromosome 2 alpha satellites to other centromeric regions, probes specific for 2q11 are frequently used for chromosome 2 copy number detection.

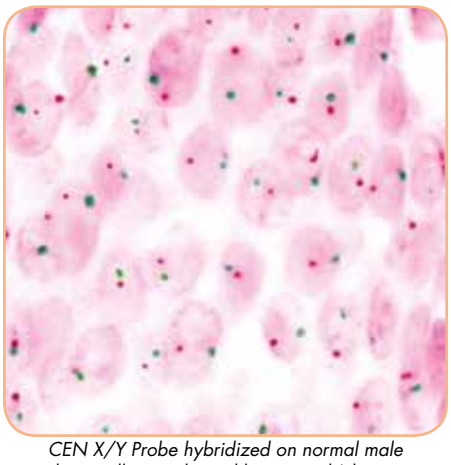


SPEC 21q22 Probe map (not to scale).

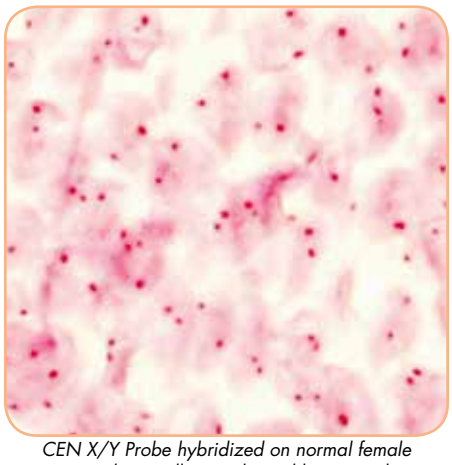
The ZytoDot ® SPEC 21q22 Probe hybridizes to the so-called Down Syndrome Critical Region on 21q22.13-q22.2 commonly duplicated in cases with partial trisomy 21. Since chromosomes 13 and 21 share the same repetitive sequences, they cannot be differentiated by probes detecting centromere specific repeats.



Normal nuclei each with two CEN 12 signals.



CEN X/Y Probe hybridized on normal male interphase cells as indicated by one red (chromosome X) and one green (chromosome Y) signal per nucleus.



CEN X/Y Probe hybridized on normal female interphase cells as indicated by two red (chromosome X) signals per nucleus.

Prod. No.	Product	Alpha/Class. Sat.	Chr. Band	Label	Tests* (Volume)
C-3035-400	ZytoDot SPEC 1p12 Probe CE IVD	-	1p12	DIG	40 (400 µl)
C-3051-400	ZytoDot SPEC 2q11 Probe CE IVD	-	2q11.2	DIG	40 (400 µl)
C-3045-400	ZytoDot CEN 3 Probe CE IVD	D3Z1	3p11.1-q11.1	DIG	40 (400 µl)
C-3002-400	ZytoDot CEN 6 Probe CE IVD	D6Z1	6p11.1-q11	DIG	40 (400 µl)
C-3008-400	ZytoDot CEN 7 Probe CE IVD	D7Z1	7p11.1-q11.1	DIG	40 (400 µl)
C-3016-400	ZytoDot CEN 8 Probe CE IVD	D8Z2	8p11.1-q11.1	DIG	40 (400 µl)
C-3014-400	ZytoDot CEN 12 Probe CE IVD	D12Z3	12p11.1-q11	DIG	40 (400 µl)
C-3052-400	ZytoDot SPEC 13q12 Probe CE IVD	-	13q12.11	DIG	40 (400 µl)
C-3006-400	ZytoDot CEN 17 Probe CE IVD	D17Z1	17p11.1-q11.1	DIG	40 (400 µl)
C-3026-400	ZytoDot SPEC 21q22 Probe CE IVD	-	21q22.13-q22.2	DIG	40 (400 µl)
C-3025-400	ZytoDot CEN X Probe CE IVD	DXZ1	Xp11.1-q11.1	DIG	40 (400 µl)
C-3020-400	ZytoDot CEN Yq12 Probe CE IVD	III DYZ1	Yq12	DIG	40 (400 µl)
C-3048-400	ZytoDot 2C CEN X/Y Probe CE IVD	DXZ1/DYZ3	Xp11.1-q11.1/Yp11.1-q11.1	DNP/DIG	40 (400 µl)
Related Products					
C-3018-40	ZytoDot CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; PBS/Tween, good for 2000 ml; Blocking Solution, 4 ml; Mouse-anti-DIG, 4 ml; Anti-Mouse-HRP-Polymer, 4 ml; DAB Solution A, 0.3 ml; DAB Solution B, 10 ml; Mayer's Hematoxylin Solution, 20 ml; Mounting Solution (alcoholic), 4 ml				40
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml				40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

Accessories

ZytoDot® Kits

For the detection of Digoxigenin-labeled ZytoDot® Probes

Prod. No.	Product	Tests
C-3005-40	ZytoDot CISH Polymer Detection Kit CE IVD Incl. Blocking Solution, 4 ml; Mouse-anti-DIG, 4 ml; Anti-Mouse-HRP-Polymer, 4 ml; DAB Solution A, 0.3 ml; DAB Solution B, 10 ml; Mayer's Hematoxylin Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40
C-3018-40	ZytoDot CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; PBS/Tween, good for 2000 ml; Blocking Solution, 4 ml; Mouse-anti-DIG, 4 ml; Anti-Mouse-HRP-Polymer, 4 ml; DAB Solution A, 0.3 ml; DAB Solution B, 10 ml; Mayer's Hematoxylin Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40

ZytoDot® 2C Kits

For the detection of Digoxigenin/Dinitrophenyl-labeled ZytoDot® 2C Probes

Prod. No.	Product	Tests
C-3028-40	ZytoDot 2C CISH Polymer Detection Kit CE IVD Incl. 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix,1 ml; AP-Red Solution A, 0.1 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml	10
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40

ZytoDot® Pretreatment Reagents

Prod. No.	Product
C-3004-40	ZytoDot Pretreatment Kit CE IVD Incl. Pepsin Solution, 4 ml; Heat Pretreatment Solution EDTA, 500 ml
ES-0001-4	Pepsin Solution, 4 ml CE IVD
ES-0001-8	Pepsin Solution Set, 2x 4 ml CE IVD
ES-0001-50	Pepsin Solution, 50 ml CE IVD
ES-0001-1000	Pepsin Solution, 1000 ml CE IVD
PT-0002-500	Heat Pretreatment Solution EDTA, 500 ml CE IVD

CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.

Accessories

ZytoDot® Wash Buffers & Ancillary Reagents

Prod. No.	Product
AB-0001-4	Mouse-anti-DIG, 4 ml CE IVD
AB-0001-30	Mouse-anti-DIG, 30 ml CE IVD
AB-0002-4	Anti-Mouse-HRP-Polymer, 4 ml CE IVD
AB-0013-4	HRP/AP-Polymer-Mix, 4 ml CE IVD
AB-0014-4	Anti-DIG/DNP-Mix, 4 ml CE IVD
BS-0001-4	Blocking Solution, 4 ml CE IVD
C-3011-40	ZytoDot Wash Buffer Set CE IVD Incl. Wash Buffer SSC, 500 ml; PBS/Tween, good for 2000 ml
C-3015-100	DAB Solution Set CE IVD Incl. DAB Solution A, 0.3 ml; DAB Solution B, 10 ml; good for 10 ml DAB Solution
C-3038-100	ZytoDot AP-Red Solution Set CE IVD Incl. AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; good for 15 ml AP-Red Solution
C-3039-100	ZytoDot HRP-Green Solution Set CE IVD Incl. HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; good for 15 ml HRP-Green Solution
CS-0001-20	Mayer's Hematoxylin Solution, 20 ml CE IVD
CS-0002-20	Nuclear Blue Solution, 20 ml CE IVD
E-4005-50	Fixogum Rubber Cement, 50 g
E-4005-125	Fixogum Rubber Cement, 125 g
E-4007-2	ERBB2 Control Slide Set, 2 pcs. CE IVD
MT-0004-4	Mounting Solution (alcoholic), 4 ml CE IVD NEW
WB-0001-560	Wash Buffer SSC, 560 ml CE IVD
WB-0004-1000	PBS/Tween, good for 1000 ml CE IVD
WB-0005-50	20x Wash Buffer TBS, 50 ml CE IVD

CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.

ZytoFast®

Products for CISH analysis

ZytoFast® PLUS

Products for CISH analysis

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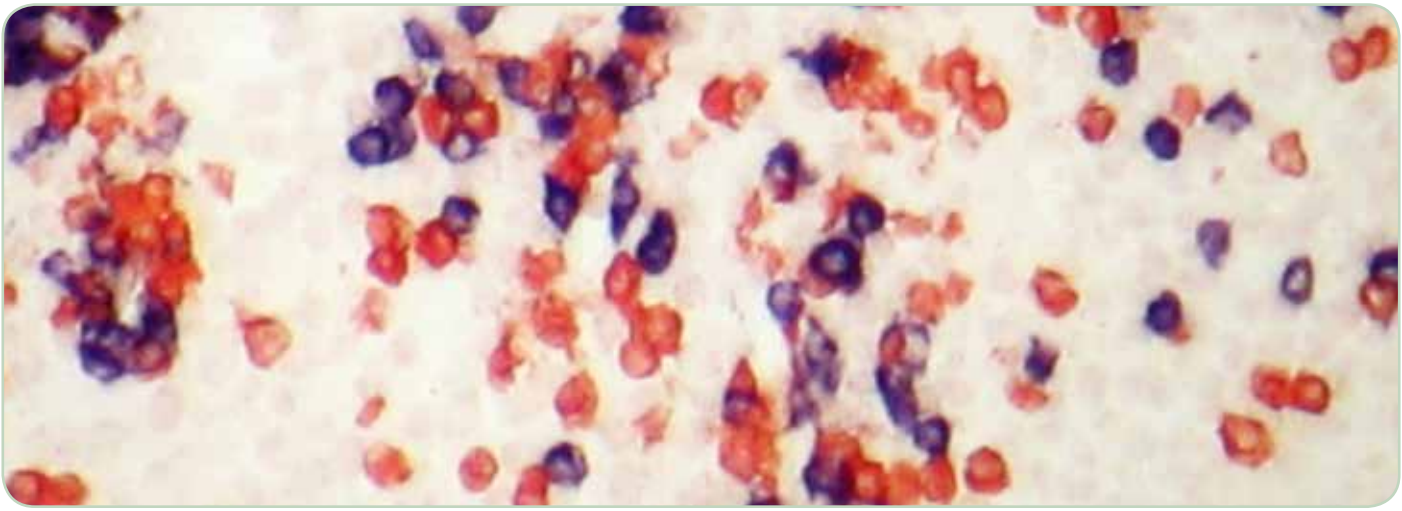
Achieving Chromogenic *in situ* Hybridization Results in just 4 Hours!

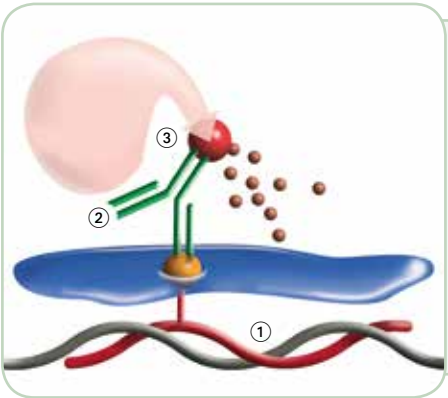


Introduction
The Zyto*Fast* ® products are designed for outstandingly fast detection and determination of lymphocyte clonality by detecting IGK and IGL light chain RNA by Chromogenic *in situ* Hybridization (CISH) in formalin-fixed, paraffin-embedded tissue sections and cell samples.

Zyto*Fast* ®: Outstandingly fast CISH
Optimized protocols and faster tissue penetration due to short oligonucleotide probes of the Zyto*Fast* ® system, make the Zyto*Fast* ® CISH procedure outstandingly fast.
Single color results can be achieved within just 5 hours, hands-on time is about 3 hours!

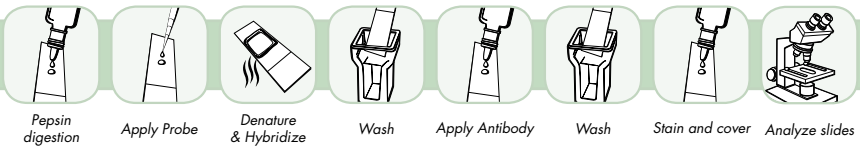
High Sensitivity and Specificity
All Zyto*Fast* ® probes are tagged using the unique Zyto*Fast* ® *HighTag System* providing improved signal intensity! High specificity without risk of cross-hybridizations is obtained due to optimized oligonucleotide probes.

Advantages of CISH
- Simultaneous observation of tissue morphology and CISH signals
- No risk of false positives due to mispriming or contamination as with PCR
- Easy method comparable to IHC
- No costly equipment needed
- Ability to test archival specimens
- High sensitivity and specificity

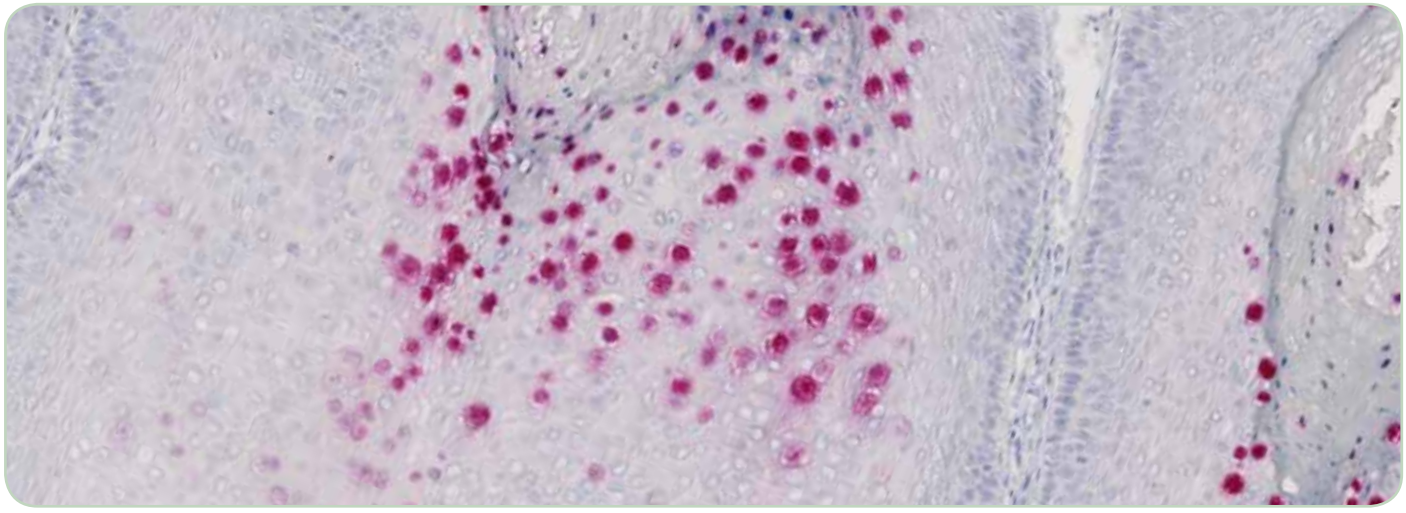


The Zyto*Fast* ® system uses oligonucleotide probes tagged with Biotin and Digoxigenin ① which are detected using HRP-conjugated antibodies and AP-conjugated streptavidin targeting the tags ②. The enzymatic reaction of chromogenic substrates ③, e.g. BCIP/NBT and AEC, leads to the formation of strong color precipitates that can be visualized by light microscopy.

Protocol Overview



ZytoFast® PLUS for Increased Sensitivity!



Introduction

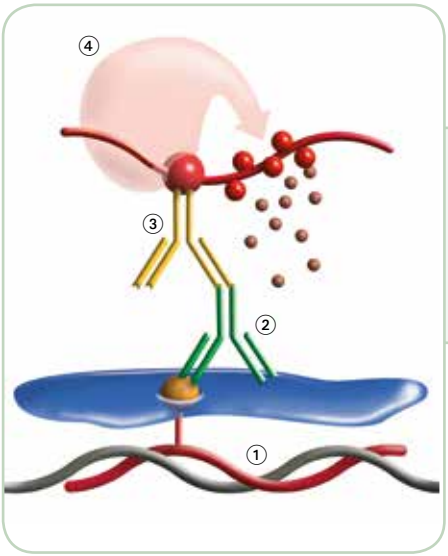
The ZytoFast® PLUS products are designed for outstandingly fast and sensitive detection and discrimination of human pathogen viruses, e.g. HPV, EBV, CMV, and the determination of lymphocyte clonality by detecting IGK and IGL light chain RNA by Chromogenic *in situ* Hybridization (CISH) in formalin-fixed, paraffin-embedded tissue sections and cell samples. The signal intensity of ZytoFast® probes is increased even more when using the ZytoFast® PLUS Implementation Kits.

ZytoFast® PLUS – Outstandingly fast and sensitive CISH

Depending on the time required for dewaxing and pretreatment of tissue sections, ZytoFast® PLUS protocols can be performed within approx. 4 hours! Thus, due to optimized protocols, the ZytoFast® PLUS method takes only slightly more time compared to ZytoFast® protocols while being much more sensitive!

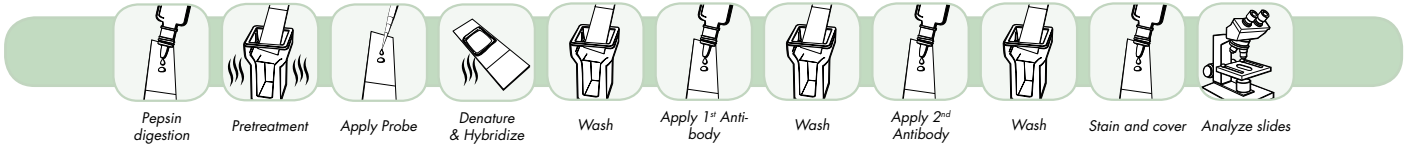
ZytoFast® PLUS – Flexibility that meets your Needs

Several ZytoFast® PLUS CISH Implementation Kits using different enzyme/substrate combinations can be combined with any separately available Digoxigenin-labeled ZytoFast® probe to meet your preferences concerning the detection chemistry, counterstaining, and embedding. Each ZytoFast® PLUS CISH Implementation Kit includes a detailed protocol, all necessary reagents as well as positive and negative control probes for versatile use in DNA as well as RNA *in situ* hybridizations.



The ZytoFast® PLUS system uses Digoxigenin-labeled probes ① which are detected using primary antibodies ②. These antibodies are detected by polymerized enzyme-conjugated secondary antibodies ③. The enzymatic reaction of chromogenic substrates ④, e.g. NBT/BCIP or DAB, leads to the formation of strong color precipitates that can be visualized by light microscopy.

Protocol Overview



Virus Index

Virus Index	Product Name	Label	Product No.	Quantity	Page
HPV	ZytoFast HPV type 6/11 Probe CE IVD	DIG	T-1055-400	400 µl	251
	ZytoFast HPV type 16/18 Probe CE IVD	DIG	T-1056-400	400 µl	251
	ZytoFast HPV type 31/33 Probe CE IVD	DIG	T-1057-400	400 µl	251
	ZytoFast HPV High-Risk (HR) Types Probe CE IVD (specific for HPV type 16/18/31/33/35/39/45/51/52/56/58/59/66/68/82)	DIG	T-1140-400	400 µl	251
	ZytoFast HPV Screening Probe CE IVD (specific for HPV type 6/11/16/18/31/33/35/39/45/51/52/56/58/59/66/68/82)	DIG	T-1144-400	400 µl	251
EBV (a.k.a. HHV-4)	ZytoFast EBV Probe CE IVD	DIG	T-1114-400	400 µl	252
CMV	ZytoFast CMV Probe	DIG	T-1113-400	400 µl	253

mRNA Index

mRNA Index	Product Name	Label	Product No.	Quantity	Page
Ig-kappa	ZytoFast human Ig-kappa Probe CE IVD	DIG	T-1115-400	400 µl	254 f.
	ZytoFast human Ig-kappa/Ig-lambda Probe CE IVD	DIG/Biotin	T-1017-400	400 µl	254 f.
	ZytoFast human Ig-kappa/Ig-lambda CISH Kit CE IVD	DIG/Biotin	T-1005-40	40 tests	254 f.
	ZytoFast human Ig-kappa/Ig-lambda Permanent CISH Kit CE IVD	DIG/Biotin	T-1105-40	40 tests	254 f.
Ig-lambda	ZytoFast human Ig-lambda Probe CE IVD	DIG	T-1116-400	400 µl	254 f.
	ZytoFast human Ig-kappa/Ig-lambda Probe CE IVD	DIG/Biotin	T-1017-400	400 µl	254 f.
	ZytoFast human Ig-kappa/Ig-lambda CISH Kit CE IVD	DIG/Biotin	T-1005-40	40 tests	254 f.
	ZytoFast human Ig-kappa/Ig-lambda Permanent CISH Kit CE IVD	DIG/Biotin	T-1105-40	40 tests	254 f.

CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.

Indication Index

Indication	Product Name	Label	Product No.	Quantity	Page
Solid Tumors					
Cervical Cancer	ZytoFast HPV type 6/11 Probe CE IVD	DIG	T-1055-400	400 µl	251
	ZytoFast HPV type 16/18 Probe CE IVD	DIG	T-1056-400	400 µl	251
	ZytoFast HPV type 31/33 Probe CE IVD	DIG	T-1057-400	400 µl	251
	ZytoFast HPV High-Risk (HR) Types Probe CE IVD (specific for HPV type 16/18/31/33/35/39/45/51/52/56/58/59/66/68/82)	DIG	T-1140-400	400 µl	251
	ZytoFast HPV Screening Probe CE IVD (specific for HPV type 6/11/16/18/31/33/35/39/45/51/52/56/58/59/66/68/82)	DIG	T-1144-400	400 µl	251
Hematology Specific Probes					
Lymphoma	ZytoFast EBV Probe CE IVD	DIG	T-1114-400	400 µl	252
	ZytoFast human Ig-kappa Probe CE IVD	DIG	T-1115-400	400 µl	254 f.
	ZytoFast human Ig-lambda Probe CE IVD	DIG	T-1116-400	400 µl	254 f.
	ZytoFast human Ig-kappa/Ig-lambda Probe CE IVD	DIG/Biotin	T-1017-400	400 µl	254 f.
	ZytoFast human Ig-kappa/Ig-lambda CISH Kit CE IVD	DIG/Biotin	T-1005-40	40 tests	254 f.
	ZytoFast human Ig-kappa/Ig-lambda Permanent CISH Kit CE IVD	DIG/Biotin	T-1105-40	40 tests	254 f.

CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.

ZytoFast® HPV-CISH System

CE IVD

Background

The ZytoFast® HPV-CISH System is designed for the detection and discrimination of human papillomavirus (HPV) DNA in paraffin-embedded tissue sections or cell samples.

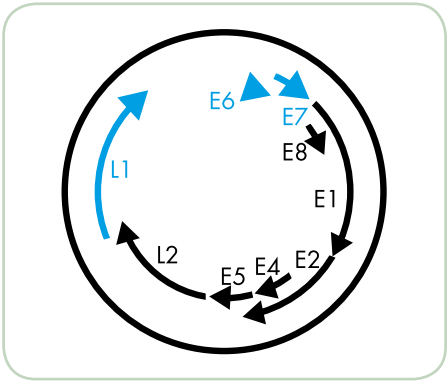
At least 50 percent of sexually active men and women acquire some form of genital HPV infection at some point in their lives. Most of the approx. 30 identified genital HPV types, predominantly types 6 and 11, are called "low-risk" types, and may cause mild Pap test abnormalities or genital warts. Until now, approximately 10–15 HPV types are associated with lesions that can progress to cancer. Among those are the HPV types 16/18/31/33/35/39/45/51/52/56/58/59/66/68/82.

These cancer-associated HPV types are designated as high-risk HPV (hr-HPV) types. The infection with the HPV hr-types can lead to development of cancer of the cervix, vulva, vagina, anus, or penis. The majority of malignant cervical carcinomas (approx. 70%) occur as a result of infections with HPV types 16 or 18.

References
Cothran MM & White JP (2002) Health Care Women Int 23: 306-19.
Cubie HA & Norval M (1988) J Virol Methods 20: 239-49.
Faulkner-Jones BE, et al. (1993) J Virol Methods 41: 277-96.
Francis IM, et al. (2013) Sultan Qaboos Univ Med J 13: 527-33.
Grundmeier N, et al. (2011) Dermatology 223: 293-300.
Kaspersen MD, et al. (2011) PLoS One 6: e18095.
Mirasoli M, et al. (2009) Anal Bioanal Chem 394: 981-7.
Montag M, et al. (2011) Arch Gynecol Obstet 284: 999-1005.
Poljak M & Kocjan BJ (2010) Expert Rev Anti Infect Ther 8: 1139-62.
Reinholz M, et al. (2013) Arch Dermatol Res 305: 723-32.
Walboomers JMM, et al. (1999) J Pathol 189: 12-9.

Probe Description

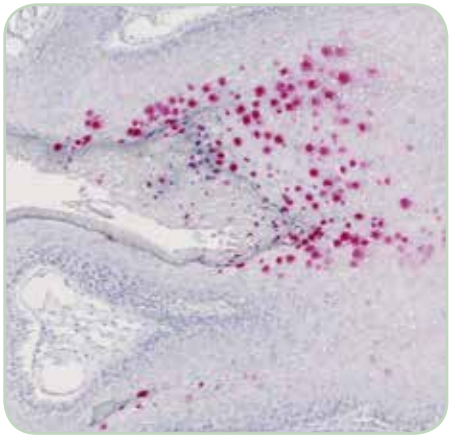
ZytoFast® HPV specific probes are directed against DNA sequences which encode the HPV proteins E6, E7 and/or L1. The probes consist of HPV-type-specific oligonucleotides, Digoxigenin-labeled by using the unique ZytoFast® *HighTag System* providing improved signal intensity. In addition to the detection of HPV at the DNA level, HPV probes will also allow detection of E6, E7, and/or L1 RNAs, which are expressed during some stages of infection.



Schematic representation of the HPV genome with E and L open reading frames. Genomic regions targeted by ZytoFast® HPV specific oligonucleotides are indicated in blue.

Results

A positive reactivity for HPV DNA in epithelial cells is indicated by a distinctly stained nucleus. Due to the detection of HPV DNA as well as E6, E7, and/or L1 RNAs, depending on the infection stage, cytoplasmic staining might be observed additionally. Depending on the detection chemistry that is used, colored precipitates, which can be clearly distinguished from the background, will be dark violet-blue when using NBT/BCIP as substrate, dark brown when using DAB, or strong red when using Permanent Red.



HPV infected cervix tissue hybridized with the ZytoFast® HPV type 6/11 Probe, detected with the ZytoFast® PLUS CISH Implementation Kit AP-Permanent Red.

Digoxigenin-labeled

Prod. No.	Product	Tests* (Volume)
T-1055-400	ZytoFast HPV type 6/11 Probe CE IVD	40 (400 µl)
T-1056-400	ZytoFast HPV type 16/18 Probe CE IVD	40 (400 µl)
T-1057-400	ZytoFast HPV type 31/33 Probe CE IVD	40 (400 µl)
T-1140-400	ZytoFast HPV High-Risk (HR) Types Probe (specific for HPV type 16/18/31/33/35/39/45/51/52/56/58/59/66/68/82) CE IVD	40 (400 µl)
T-1144-400	ZytoFast HPV Screening Probe (specific for HPV type 6/11/16/18/31/33/35/39/45/51/52/56/58/59/66/68/82) CE IVD	40 (400 µl)
Related Products		
T-1061-40	ZytoFast PLUS CISH Implementation Kit AP-NBT/BCIP CE IVD Incl. DNA (+) Control Probe, 0.1 ml; DNA (-) Control Probe, 0.1 ml; 28S rRNA (+) Control Probe, 0.1 ml; RNA (-) Control Probe, 0.1 ml; Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 4x50 ml; Rabbit-anti-DIG, 4 ml; Anti-Rabbit-AP-Polymer, 4 ml; NBT/BCIP Solution, 4ml; Nuclear Red Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40
T-1063-40	ZytoFast PLUS CISH Implementation Kit HRP-DAB CE IVD Incl. DNA (+) Control Probe, 0.1 ml; DNA (-) Control Probe, 0.1 ml; 28S rRNA (+) Control Probe, 0.1 ml; RNA (-) Control Probe, 0.1 ml; Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 4x 50 ml; Mouse-anti-DIG, 4 ml; Anti-Mouse-HRP-Polymer, 4 ml; DAB Solution A, 0.3 ml; DAB Solution B, 10 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40
T-1151-40	ZytoFast PLUS CISH Implementation Kit AP-Permanent Red CE IVD Incl. DNA (+) Control Probe, 0.1 ml; DNA (-) Control Probe, 0.1 ml; 28S rRNA (+) Control Probe, 0.1 ml; RNA (-) Control Probe, 0.1 ml; Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 4x50 ml; Rabbit-anti-DIG, 4 ml; Anti-Rabbit-AP-Polymer, 4 ml; Permanent Red Solution A, 0.25 ml; Permanent Red Solution B, 15 ml; Mayer's Hematoxylin Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoFast® EBV-CISH System

CE IVD

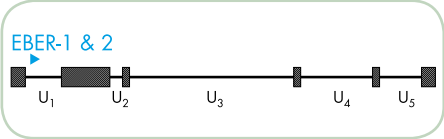
Background

The ZytoFast® EBV-CISH System is designed for the detection of Epstein-Barr virus (EBV) EBER RNA in paraffin-embedded tissue sections or cell samples.
EBV (a.k.a. human herpesvirus-4, HHV-4) is a member of the gamma-herpesvirus group and one of the most common viruses in humans.
Transmission of EBV requires close, intimate contact with a person excreting the virus in its saliva. EBV has two major target tissues *in vivo*, B lymphocytes and squamous pharyngeal epithelium. Infection of B lymphocytes with EBV results in persistant latent infection, immortalization of the cells, and perpetual proliferation. EBV, the first virus to be identified as an oncovirus, is the etiological agent of infectious mononucleosis and has been implicated in the pathogenesis of an increasing number of human malignancies such as Burkitt lymphoma, nasopharyngeal carcinoma, and polyclonal lymphomas in immunocompromised individuals. CISH-based diagnosis of EBV infection has the advantage over other methods in that it permits unequivocal localization of EBV genomes in cells and thereby obviates the risk of false positive results due to laboratory or clinical contamination.

References
Agaimy A & Wünsch PH (2006) Pathol Res Pract 202: 541-8.
Fuchs S, et al. (2012) J Immunol 188: 1523-33.
Gaiser T, et al. (2012) Diagn Pathol 7: 38.
Greifenegger N, et al. (1998) J Virol 72: 9323-8.
Khan G, et al. (1992) J Clin Pathol 45: 616-20.
Kim DN, et al. (2013) J Gen Virol 94: 497-506.
Murphy JK, et al. (1990) J Clin Pathol 43: 220-3.
Rosa MD, et al. (1981) Mol Cell Biol 1: 785-96.
Sides MD, et al. (2013) Virol J 10: 152.
Thorley-Lawson DA (2001) Nat Rev Immunol 1: 75-82.

Probe Description

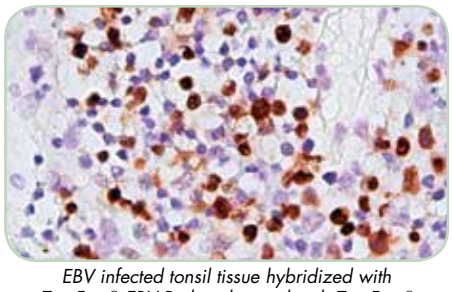
The ZytoFast® EBV Probe is directed against EBER-1 and EBER-2 RNA sequences that were found to be transcribed in every latently infected cell. Due to the large number (up to 10^7) of copies per cell, these RNAs are the most abundant transcripts in latently EBV-infected cells.
The probe consists of EBV-specific oligonucleotides, Digoxigenin-labeled by using the unique ZytoFast® *High Tag System* providing improved signal intensity.



Schematic representation of the EBV genome with the EBER-1 and EBER-2 encoding region indicated in blue. U1-U5 indicate unique nucleotide sequences, hatched boxes represent terminal and internal repeats.

Results

A positive reactivity for Epstein-Barr-virus (EBV) EBER RNA in the target cells is indicated by a distinctly stained nucleus. Depending on the detection chemistry that is used, colored precipitates, which can be clearly distinguished from the background, will be dark violet-blue when using NBT/BCIP as substrate, dark brown when using DAB, or strong red when using Permanent Red.



EBV infected tonsil tissue hybridized with ZytoFast® EBV Probe, detected with ZytoFast® PLUS CISH Implementation Kit HRP-DAB.

Digoxigenin-labeled

Prod. No.	Product	Tests* (Volume)
T-1114-400	ZytoFast EBV Probe CE IVD	40 (400 µl)
Related Products		
T-1061-40	ZytoFast PLUS CISH Implementation Kit AP-NBT/BCIP CE IVD Incl. DNA (+) Control Probe, 0.1 ml; DNA (-) Control Probe, 0.1 ml; 28S rRNA (+) Control Probe, 0.1 ml; RNA (-) Control Probe, 0.1 ml; Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 4x 50 ml; Rabbit-anti-DIG, 4 ml; Anti-Rabbit-AP-Polymer, 4 ml; NBT/BCIP Solution, 4ml; Nuclear Red Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40
T-1063-40	ZytoFast PLUS CISH Implementation Kit HRP-DAB CE IVD Incl. DNA (+) Control Probe, 0.1 ml; DNA (-) Control Probe, 0.1 ml; 28S rRNA (+) Control Probe, 0.1 ml; RNA (-) Control Probe, 0.1 ml; Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 4x 50 ml; Mouse-anti-DIG, 4 ml; Anti-Mouse-HRP-Polymer, 4 ml; DAB Solution A, 0.3 ml; DAB Solution B, 10 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40
T-1151-40	ZytoFast PLUS CISH Implementation Kit AP-Permanent Red CE IVD Incl. DNA (+) Control Probe, 0.1 ml; DNA (-) Control Probe, 0.1 ml; 28S rRNA (+) Control Probe, 0.1 ml; RNA (-) Control Probe, 0.1 ml; Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 4x50 ml; Rabbit-anti-DIG, 4 ml; Anti-Rabbit-AP-Polymer, 4 ml; Permanent Red Solution A, 0.25 ml; Permanent Red Solution B, 15 ml; Mayer's Hematoxylin Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoFast® CMV-CISH System

Background

The ZytoFast® CMV-CISH System is designed for the detection of cytomegalovirus (CMV) DNA in paraffin-embedded tissue sections or cell samples. CMV (a.k.a. human herpesvirus-5, HHV-5) is a member of the beta-herpesvirus group and may be found in 40-100% of people. CMV can be transmitted sexually as well as via breast milk, transplanted organs, and rarely from blood transfusions.

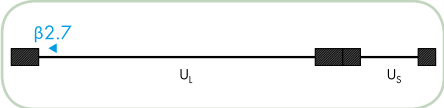
Following primary CMV infection in the normal host, the virus remains in a latent state and can be found in multiple body sites as it is, unlike other herpesviruses, not restricted to certain body areas. Among immunosuppressed patients, such as recipients of solid organ or haematopoietic stem cell allografts, CMV infections are common causes of morbidity and mortality.

In histology, the hallmark of CMV infection is the finding of intranuclear inclusions consistent with the virus. CISH-based diagnosis of CMV infection has the advantage over other methods in that it permits unequivocal localization of CMV genomes in cells and thereby obviates the risk of false positive results due to laboratory or clinical contamination.

References
Cobbs CS, et al. (2002) Cancer Res 62: 3347-50.
Chen HP, et al. (2012) J Clin Virol 54: 240-4.
Greenaway PJ & Wilkinson GWG (1987) Virus Res 7: 17-31.
Spector SA (1990) Semin Hematol 27 (2 Suppl 1): 11-6; 28-9.
Wu TC, et al. (1992) Am J Pathol 141: 1247-54.

Probe Description

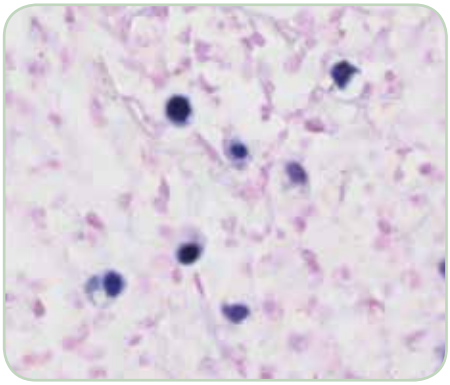
The ZytoFast® CMV Probe is directed against the sequence of the β2.7 gene, the most abundantly transcribed early CMV gene. The probe consists of CMV-specific oligonucleotides, Digoxigenin-labeled by using the unique ZytoFast® *HighTag System* providing improved signal intensity. In addition to the detection of CMV at the DNA level, the CMV Probe will also allow detection of the β2.7 RNA, which is expressed during all stages of infection.



Schematic representation of the CMV genome with the β2.7 encoding region indicated in blue. UL and US indicate unique nucleotide sequences, hatched boxes represent terminal and internal repeats.

Results

Due to the detection of CMV DNA as well as of the abundantly transcribed β2.7 RNA, a positive reactivity for cytomegalovirus (CMV) in the target cells is indicated by a cytoplasmic and/or nuclear staining pattern. Depending on the detection chemistry that is used, colored precipitates, which can be clearly distinguished from the background, will be dark violet-blue when using NBT/BCIP as substrate, dark brown when using DAB, or strong red when using Permanent Red.



CISH analysis of paraffin-embedded adrenal gland tissue using the ZytoFast® CMV Probe, detected with ZytoFast® PLUS CISH Implementation Kit AP-NBT/BCIP.

Digoxigenin-labeled

Prod. No.	Product	Tests* (Volume)
T-1113-400	ZytoFast CMV Probe	40 (400 µl)
Related Products		
T-1061-40	ZytoFast PLUS CISH Implementation Kit AP-NBT/BCIP CE IVD Incl. DNA (+) Control Probe, 0.1 ml; DNA (-) Control Probe, 0.1 ml; 28S rRNA (+) Control Probe, 0.1 ml; RNA (-) Control Probe, 0.1 ml; Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 4x 50 ml; Rabbit-anti-DIG, 4 ml; Anti-Rabbit-AP-Polymer, 4 ml; NBT/BCIP Solution, 4ml; Nuclear Red Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40
T-1063-40	ZytoFast PLUS CISH Implementation Kit HRP-DAB CE IVD Incl. DNA (+) Control Probe, 0.1 ml; DNA (-) Control Probe, 0.1 ml; 28S rRNA (+) Control Probe, 0.1 ml; RNA (-) Control Probe, 0.1 ml; Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 4x 50 ml; Mouse-anti-DIG, 4 ml; Anti-Mouse-HRP-Polymer, 4 ml; DAB Solution A, 0.3 ml; DAB Solution B, 10 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40
T-1151-40	ZytoFast PLUS CISH Implementation Kit AP-Permanent Red CE IVD Incl. DNA (+) Control Probe, 0.1 ml; DNA (-) Control Probe, 0.1 ml; 28S rRNA (+) Control Probe, 0.1 ml; RNA (-) Control Probe, 0.1 ml; Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 4x50 ml; Rabbit-anti-DIG, 4 ml; Anti-Rabbit-AP-Polymer, 4 ml; Permanent Red Solution A, 0.25 ml; Permanent Red Solution B, 15 ml; Mayer's Hematoxylin Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

ZytoFast® Ig-kappa/Ig-lambda-CISH System

CE IVD

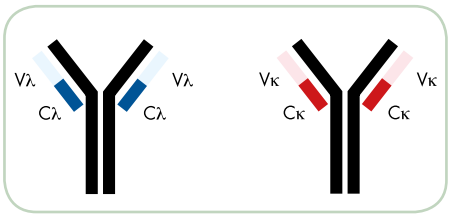
Background

The ZytoFast® Ig-kappa/Ig-lambda-CISH System is designed for the detection of immunglobulin kappa locus (Ig–κ, IGK) and/or immunglobulin lamda locus (Ig-λ, IGL) light chain mRNA in paraffin-embedded tissue sections or cell samples.
B-cells (a.k.a. B lymphocytes) develop from lymphoid stem cells in the bone marrow. Each clone of B-cells expresses a unique antibody molecule, composed of 2 identical heavy and 2 identical light chains, the latter either of κ or λ type. Determination of kappa-to-lambda ratio is useful to distinguish between neoplastic and reactive lymphoid proliferations. Polyclonal expression of κ or λ light chains is considered to reflect a reactive hyperplasia in contrast to the monoclonal expression in malignant lymphoma, the most common hematologic malignancy encountered in the Western world. Whereas detection of IGK and IGL by immunohistochemistry often results in excessive background staining, *in situ* Hybridization has the advantage of a virtually background-free signal, allowing a safe and simple analysis of the clonality of a given lymphocyte population.

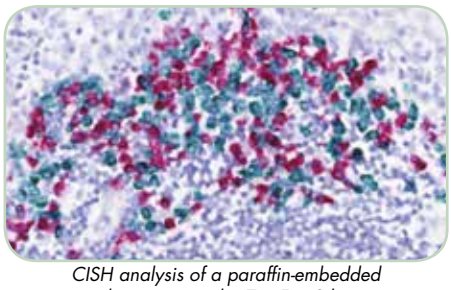
References
Erber WN, et al. (1993) Pathology 25: 63-7.
Ke L, et al. (2011) Int J Clin Exp Pathol 4: 190-6.
McElroy MK, et al. (2011) Hum Pathol 42: 1813-8.
McNicol AM & Farquharson MA (1997) J Pathol 182: 250-61.
Pringle JH, et al. (1990) J Pathol 162: 197-207.

Probe Description

ZytoFast® human Ig-kappa Probe is directed against mRNA sequences encoding κ light chain constant regions of human immunoglobulins.
The ZytoFast® human Ig-lambda Probe is directed against mRNA sequences encoding λ light chain constant regions of human immunoglobulins.
The ZytoFast® human Ig-kappa/Ig-lambda Probe is a probe mixture consisting of a Digoxigenin-labeled IGK mRNA specific probe and a Biotin-labeled IGL mRNA specific probe. All probes are tagged by using the unique ZytoFast® *HighTag System* providing improved signal intensity.



Basic immunoglobulin structure indicating the heavy chains (black), λ (blue) and κ (red) lights chains. The light chain constant regions (C) whose encoding mRNA sequences are targeted by ZytoFast® Ig-lambda and Ig-kappa probes are indicated in dark blue and red respectively, the variable regions (V) in light blue and red.



CISH analysis of a paraffin-embedded tonsil tissue using the ZytoFast® human Ig-kappa/Ig-lambda Permanent CISH Kit.

Results

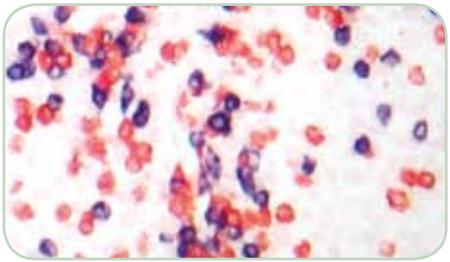
A positive reactivity in the target cells is indicated by cytoplasmic staining. Depending on the detection chemistry that is used, colored precipitates, which can be clearly distinguished from the background, will be dark violet-blue when using NBT/BCIP as substrate, strong red when using AEC, dark brown when using DAB, green when using HRP-Green, or strong red when using Permanent Red.

Using the ZytoFast® human Ig-kappa Probe, B-cells expressing antibodies with κ light chains will result in cytoplasmic staining whereas IGL expressing B-cells are not stained.

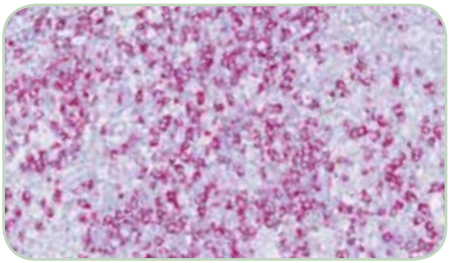
Using the ZytoFast® human Ig-lambda Probe, B-cells expressing antibodies with λ light chains will result in cytoplasmic staining whereas IGK expressing B-cells are not stained.

Using the ZytoFast® human Ig-kappa/Ig-lambda CISH Kit, B-cells expressing antibodies with κ light chains will result in a red cytoplasmic staining and simultaneously IGL expressing B-cells will result in a dark violet-blue cytoplasmic staining.

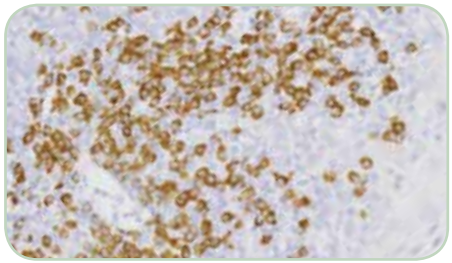
Using the ZytoFast® human Ig-kappa/Ig-lambda Permanent CISH Kit, B-cells expressing antibodies with κ light chains will result in a green cytoplasmic staining and simultaneously IGL expressing B-cells will result in permanent red cytoplasmic staining.



CISH analysis of a paraffin-embedded bone marrow biopsy specimen using the ZytoFast® human Ig-kappa/Ig-lambda CISH Kit.



Tonsil tissue with B-cells expressing Ig-kappa hybridized with ZytoFast® human Ig-kappa Probe, detected with ZytoFast® PLUS CISH Implementation Kit AP-Permanent Red.



Tonsil tissue with B-cells expressing Ig-kappa hybridized with ZytoFast® human Ig-kappa Probe, detected with ZytoFast® PLUS CISH Implementation Kit HRP-DAB.

ZytoFast® Ig-kappa/Ig-lambda Probes

Digoxigenin-labeled

Prod. No.	Product	Tests* (Volume)
T-1115-400	ZytoFast human Ig-kappa Probe CE IVD	40 (400 µl)
T-1116-400	ZytoFast human Ig-lambda Probe CE IVD	40 (400 µl)
Related Products		
T-1061-40	ZytoFast PLUS CISH Implementation Kit AP-NBT/BCIP CE IVD Incl. DNA (+) Control Probe, 0.1 ml; DNA (-) Control Probe, 0.1 ml; 28S rRNA (+) Control Probe, 0.1 ml; RNA (-) Control Probe, 0.1 ml; Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 4x 50 ml; Rabbit-anti-DIG, 4 ml; Anti-Rabbit-AP-Polymer, 4 ml; NBT/BCIP Solution, 4ml; Nuclear Red Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40
T-1063-40	ZytoFast PLUS CISH Implementation Kit HRP-DAB CE IVD Incl. DNA (+) Control Probe, 0.1 ml; DNA (-) Control Probe, 0.1 ml; 28S rRNA (+) Control Probe, 0.1 ml; RNA (-) Control Probe, 0.1 ml; Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 4x 50 ml; Mouse-anti-DIG, 4 ml; Anti-Mouse-HRP-Polymer, 4 ml; DAB Solution A, 0.3 ml; DAB Solution B, 10 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40
T-1151-40	ZytoFast PLUS CISH Implementation Kit AP-Permanent Red CE IVD Incl. DNA (+) Control Probe, 0.1 ml; DNA (-) Control Probe, 0.1 ml; 28S rRNA (+) Control Probe, 0.1 ml; RNA (-) Control Probe, 0.1 ml; Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 4x50 ml; Rabbit-anti-DIG, 4 ml; Anti-Rabbit-AP-Polymer, 4 ml; Permanent Red Solution A, 0.25 ml; Permanent Red Solution B, 15 ml; Mayer's Hematoxylin Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40

ZytoFast® Ig-kappa/Ig-lambda Probe

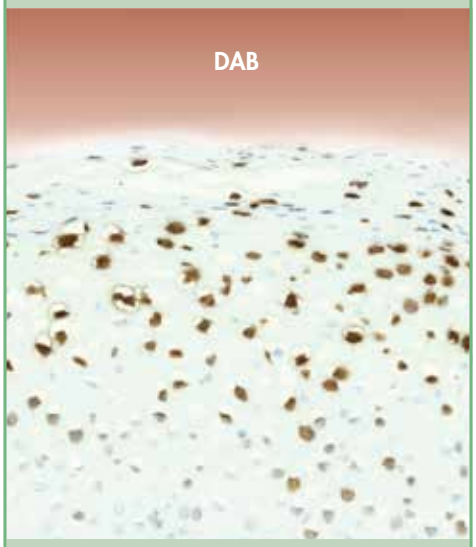
Biotin/Digoxigenin-labeled

Prod. No.	Product	Tests* (Volume)
T-1017-400	ZytoFast human Ig-kappa/Ig-lambda Probe CE IVD	40 (400 µl)
Related Products		
T-1005-40	ZytoFast human Ig-kappa/Ig-lambda CISH Kit CE IVD Incl. Ig-kappa/Ig-lambda Probe (DIG/Biotin-labeled), 0.4 ml; 28S rRNA (+) Control Probe (DIG-labeled), 0.1 ml; RNA (-) Control Probe (DIG-labeled), 0.1 ml; Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-Biotin/DIG-Mix, 4 ml; AEC Solution, 4 ml; NBT/BCIP Solution, 4 ml; Nuclear Green Solution, 20 ml; Mounting Solution (aqueous), 4 ml	40
T-1105-40	ZytoFast human Ig-kappa/Ig-lambda Permanent CISH Kit CE IVD Incl. Ig-kappa/Ig-lambda Probe (DIG/Biotin-labeled), 0.4 ml; 28S rRNA (+) Control Probe (DIG-labeled), 0.1 ml; RNA (-) Control Probe (DIG-labeled), 0.1 ml; Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-Biotin/DIG-Mix, 4 ml; HRP-Green-Solution A, 0.8 ml; HRP-Green-Solution B, 15 ml; Permanent Red Solution A, 0.25 ml; Permanent Red Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

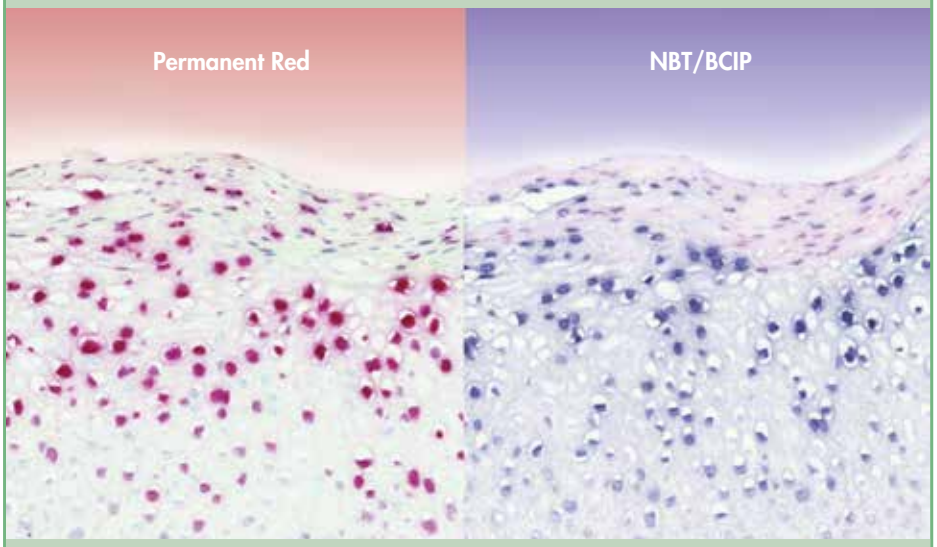
Accessories

Peroxidase (HRP)



T-1063

Alkaline Phosphatase (AP)



T-1151 T-1061

ZytoFast® PLUS Implementation Kits

For the detection of Digoxigenin-labeled ZytoFast® Probes

Prod. No.	Product	Tests
T-1061-40	ZytoFast PLUS CISH Implementation Kit AP-NBT/BCIP CE IVD Incl. DNA (+) Control Probe, 0.1 ml; DNA (-) Control Probe, 0.1 ml; 28S rRNA (+) Control Probe, 0.1 ml; RNA (-) Control Probe, 0.1 ml; Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 4x 50 ml; Rabbit-anti-DIG, 4 ml; Anti-Rabbit-AP-Polymer, 4 ml; NBT/BCIP Solution, 4ml; Nuclear Red Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40
T-1063-40	ZytoFast PLUS CISH Implementation Kit HRP-DAB CE IVD Incl. DNA (+) Control Probe, 0.1 ml; DNA (-) Control Probe, 0.1 ml; 28S rRNA (+) Control Probe, 0.1 ml; RNA (-) Control Probe, 0.1 ml; Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 4x 50 ml; Mouse-anti-DIG, 4 ml; Anti-Mouse-HRP-Polymer, 4 ml; DAB Solution A, 0.3 ml; DAB Solution B, 10 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40
T-1151-40	ZytoFast PLUS CISH Implementation Kit AP-Permanent Red CE IVD Incl. DNA (+) Control Probe, 0.1 ml; DNA (-) Control Probe, 0.1 ml; 28S rRNA (+) Control Probe, 0.1 ml; RNA (-) Control Probe, 0.1 ml; Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 4x50 ml; Rabbit-anti-DIG, 4 ml; Anti-Rabbit-AP-Polymer, 4 ml; Permanent Red Solution A, 0.25 ml; Permanent Red Solution B, 15 ml; Mayer's Hematoxylin Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	40

CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.

Accessories

ZytoFast® Pretreatment Reagents

Prod. No.	Product
ES-0001-4	Pepsin Solution, 4 ml CE IVD
ES-0001-8	Pepsin Solution Set, 2x 4 ml CE IVD
ES-0001-50	Pepsin Solution, 50 ml CE IVD
ES-0001-1000	Pepsin Solution, 1000 ml CE IVD
PT-0002-500	Heat Pretreatment Solution EDTA, 500 ml CE IVD

ZytoFast® Wash Buffers & Ancillary Reagents

Prod. No.	Product
AB-0001-4	Mouse-anti-DIG, 4 ml CE IVD
AB-0001-30	Mouse-anti-DIG, 30 ml CE IVD
AB-0002-4	Anti-Mouse-HRP-Polymer, 4 ml CE IVD
AB-0011-4	Rabbit-anti-DIG, 4 ml CE IVD
AB-0012-4	Anti-Rabbit-AP-Polymer, 4 ml CE IVD
AB-0015-4	Anti-Biotin/DIG-Mix, 4 ml CE IVD
C-3015-100	DAB Solution Set CE IVD Incl. DAB Solution A, 0.3 ml; DAB Solution B, 10 ml; good for 10 ml DAB Solution
C-3039-100	ZytoDot HRP-Green Solution Set CE IVD Incl. HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; good for 15 ml HRP-Green Solution
CS-0001-20	Mayer's Hematoxylin Solution, 20 ml CE IVD
CS-0002-20	Nuclear Blue Solution, 20 ml CE IVD
CS-0003-20	Nuclear Red Solution, 20 ml CE IVD
CS-0004-20	Nuclear Green Solution, 20 ml CE IVD
E-4005-50	Fixogum Rubber Cement, 50 g
E-4005-125	Fixogum Rubber Cement, 125 g
MT-0004-4	Mounting Solution (alcoholic), 4 ml CE IVD NEW
SB-0004-4	NBT/BCIP Solution, 4 ml CE IVD
SB-0005-4	AEC Solution, 4 ml CE IVD
WB-0005-50	20x Wash Buffer TBS, 50 ml CE IVD

ZytoFast® Control Probes

Digoxigenin-labeled

Prod. No.	Product	Tests* (Volume)
T-1053-400	ZytoFast DNA (+) Control Probe CE IVD	40 (400 µl)
T-1054-400	ZytoFast DNA (–) Control Probe CE IVD	40 (400 µl)
T-1120-400	ZytoFast 28S rRNA (+) Control Probe CE IVD	40 (400 µl)
T-1119-400	ZytoFast RNA (–) Control Probe CE IVD	40 (400 µl)

** Using 10 µl probe solution per test. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

VisionArray® *Arrays for DNA analysis*

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VisionArray® Chip - Fast and Reliable Detection of DNA Sequences!

Introduction

The VisionArray® products are designed for the qualitative detection of specific DNA sequences by DNA/DNA hybridization on immobilized catcher molecules which are arranged on a glass chip. All capture sequences and positive controls are set up on the VisionArray® Chips as duplicates.

Advantages of VisionArray®

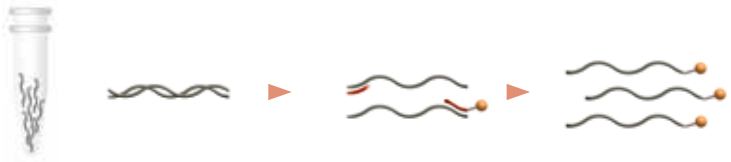
- High sensitivity and specificity
- Quick & easy 1 hour protocol
- Automated evaluation using a VisionArray® Analyzer Software – simple visualization & quick analysis in just a few minutes

Sample Collection

For the detection of DNA sequences with the VisionArray® system, the following raw material can be used for DNA extraction; depending on the VisionArray® Chip used:

- Formalin-fixed, paraffin-embedded (FFPE) tissue or cell samples
- Liquid based cytology specimens (e.g. ThinPrep®, swab/brush specimen, sputum)

Step 1: Amplification and Labeling in a PCR

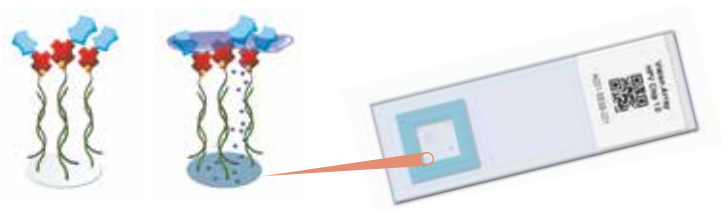


The DNA is extracted from, e.g., FFPE samples and is used as a template for PCR. Biotinylated primers are used to amplify and label different sections of the target sequences. The human HLA-DQA1 gene is also amplified and serves as a PCR positive control and as a genomic control.

Step 2: Hybridization on the Glass Chip

After amplification, the biotinylated sequences hybridize to complementary DNA capture sequences on the glass chip.

Step 3: Detection and Visualization



Specifically bound and biotinylated sequences are visualized by secondary marking with a streptavidin-peroxidase conjugate and a staining with tetramethylbenzidine. After color development, evaluation is performed using a VisionArray® Analyzer Software.

VisionArray® HPV Chip 1.0

CE IVD

Introduction

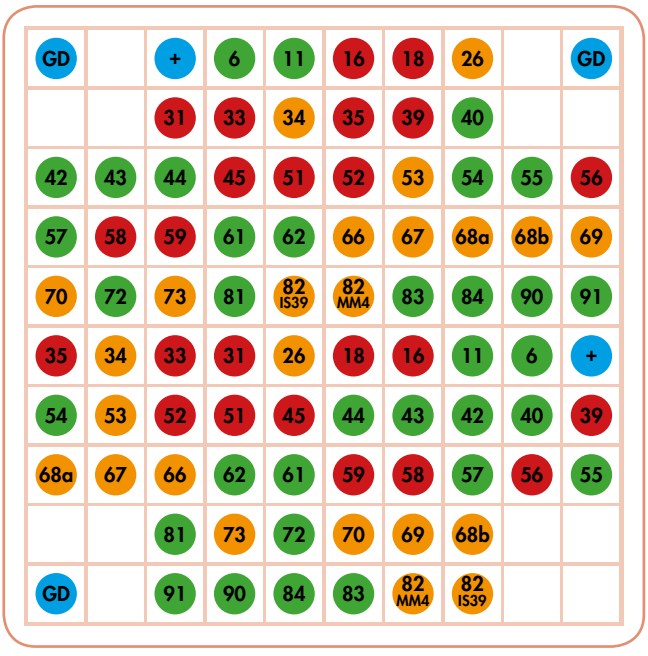
The VisionArray® HPV Chip 1.0 is intended to be used for the qualitative detection and genotyping of PCR amplificates of 41 clinically relevant human papillomavirus (HPV) genotypes that have been produced with the help of the VisionArray® HPV Primer Kit 2.0 and the VisionArray® Detection Kit.

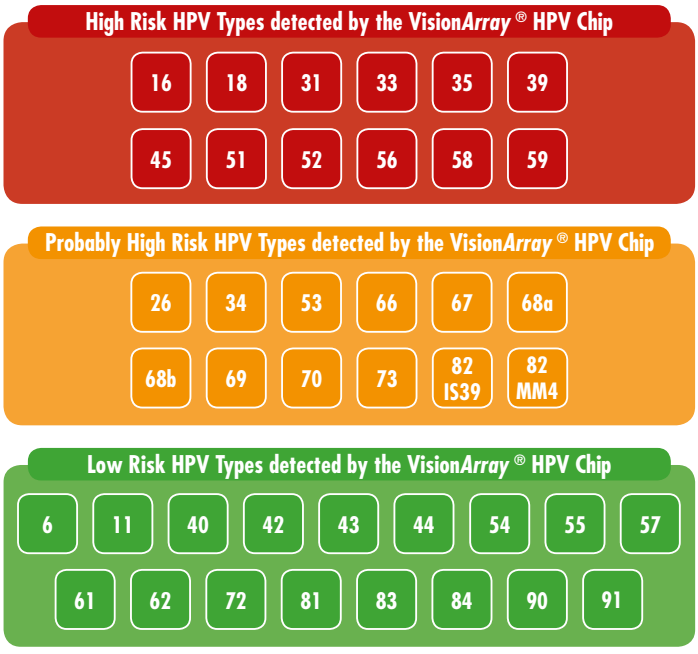
HPV has been conclusively identified as the major risk factor for cervical cancer. It is the third most common cancer in women worldwide, with an estimated number of 530,000 new cases and 280,000 deaths each year. Over the last years, the relevance of HPV in the history of oropharyngeal cancers has become more and more important which is indicated by a dramatically risen number of cancers of the oral cavity and pharynx linked to HPV.

At present, there are more than 150 different HPV types described. Depending on their risk to induce cancer, they are divided into Low Risk (LR), Probably High Risk, and High Risk (HR) types.

Chip Description

The VisionArray® HPV Chip 1.0 is designed to detect 41 clinically relevant HPV genotypes. All capture sequences and the positive control are set up on the Chip as duplicates and the guide dots as triplicates. The signals are visible on the Chip as dark blue areas. The automated evaluation of the results is performed by a VisionArray® Analyzer Software.





References
Colombo N, et al. (2012) Ann Oncol 23 Suppl 7: vii27-32.
Crow JM, et al. (2012) Nature 488: S2-S3.
IARC (2012) Biological Agents. IARC Monogr Eval Carcinog Risks Hum, 100B: 1-441.
Poljak M, et al. (2016) J Clin Virol 76 Suppl 1: S3-S13.

Prod. No.	Product	Tests
VA-0001-10	VisionArray HPV Chip 1.0 Incl. 10 pieces CE IVD	10
VA-0001-50	VisionArray HPV Chip 1.0 Incl. 5x 10 pieces CE IVD	50

CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.

VisionArray® HPV High Risk Chip 1.0

CE IVD

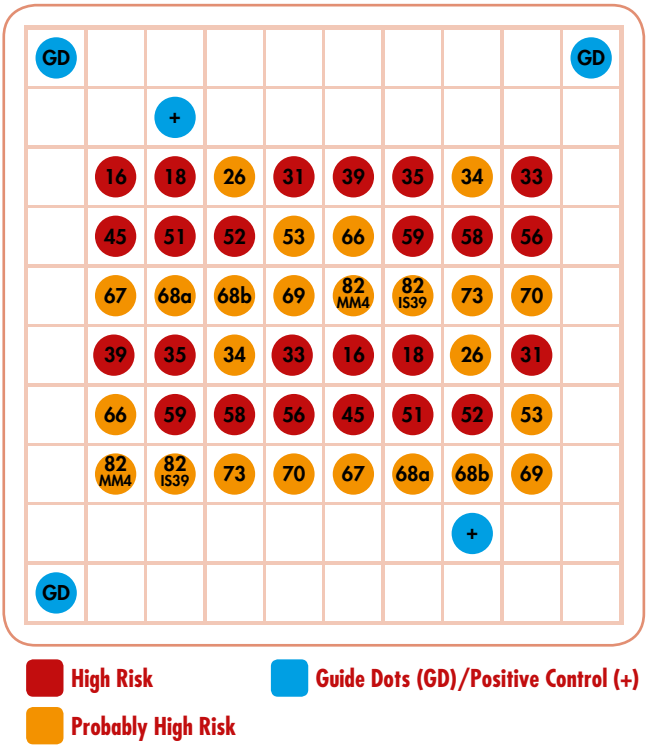
Introduction

The VisionArray® HPV High Risk Chip 1.0 is intended to be used for the qualitative detection and genotyping of PCR amplificates of 24 clinically relevant human papillomavirus (HPV) genotypes that have been produced with the help of the VisionArray HPV Primer Kit 2.0 and the VisionArray Detection Kit.
HPV has been conclusively identified as the major risk factor for cervical cancer. It is the third most common cancer in women worldwide, with an estimated number of 530,000 new cases and 280,000 deaths each year. Over the last years, the relevance of HPV in the history of oropharyngeal cancers has become more and more important which is indicated by a dramatically risen number of cancers of the oral cavity and pharynx linked to HPV.

At present, there are more than 150 different HPV types described. Several HPV types were classified as High Risk and Probably High Risk types based on their association with cervical cancer.

Chip Description

The VisionArray® HPV High Risk Chip 1.0 is designed to detect 24 clinically relevant HPV genotypes. All capture sequences and the positive control are set up on the Chip as duplicates and the guide dots as triplicates. The signals are visible on the Chip as dark blue areas. The automated evaluation of the results is performed by a VisionArray® Analyzer Software.



High Risk
Guide Dots (GD)/Positive Control (+)
Probably High Risk

High Risk HPV Types detected by the HPV High Risk Chip

16 18 31 33 35 39
45 51 52 56 58 59

Probably High Risk HPV Types detected by the HPV High Risk Chip

26 34 53 66 67 68a
68b 69 70 73 82 IS39 82 MM4

References
Colombo N, et al. (2012) Ann Oncol 23 Suppl 7: vii27-32.
Crow JM, et al. (2012) Nature 488: S2-S3.
IARC (2012) Biological Agents. IARC Monogr Eval Carcinog Risks Hum, 100B: 1-441.
Poljak M, et al. (2016) J Clin Virol 76 Suppl 1: S3-S13.

Prod. No.	Product	Tests
VA-0002-10	VisionArray HPV High Risk Chip 1.0 Incl. 10 pieces CE IVD	10
VA-0002-50	VisionArray HPV High Risk Chip 1.0 Incl. 5x 10 pieces CE IVD	50

CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.

VisionArray® MYCO Chip 1.0

CE IVD

Introduction

The VisionArray® MYCO Chip 1.0 is intended to be used with a VisionArray® Analysis Package for the qualitative detection and identification of PCR amplificates of the genera *Mycobacterium, Mycobacteroides, Mycolicibacillus, Mycolicibacter,* and *Mycolicibacterium* as well as several clinically relevant mycobacterial species that have been produced with the help of the VisionArray® MYCO Primer Kit 1.0 or the VisionArray® MYCO PreCise Master Mix.

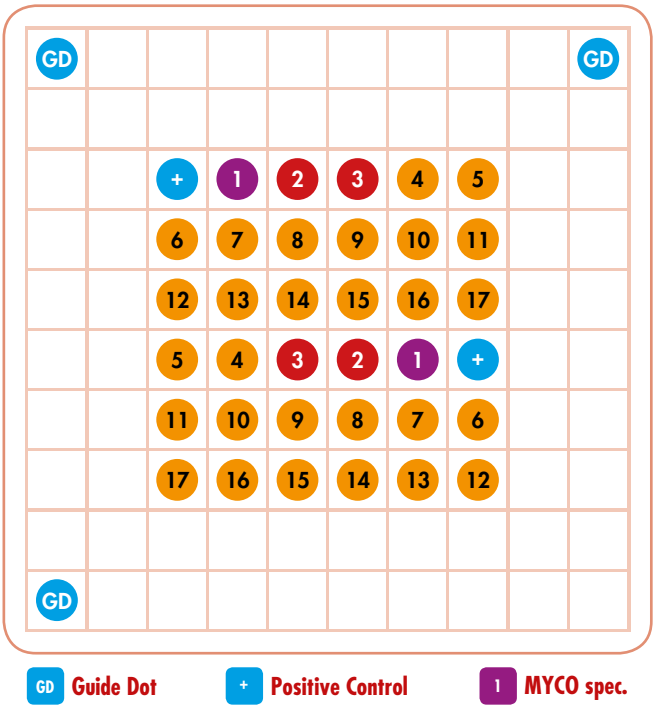
The mycobacterial genera comprise more than 140 species, which, for the purpose of diagnosis and treatment, have been grouped into three categories: *M. tuberculosis complex* (MTC), *M. leprae*, and non-tuberculous mycobacteria (NTM).

The majority of the *Mycobacterium* species belongs to the NTM group and can be found in different environments. Many of these bacteria cause life-threatening infections in humans and in recent years, the mortality and morbidity associated with NTMs has increased especially in immunocompromised patients worldwide. Treatment of NTMs is specific to each species and therefore a clear distinction between the present species is of extreme importance.

Reliable and rapid molecular diagnostics are the basis of an adequate therapy that is given by the VisionArray® MYCO Chip 1.0.

Chip Description

The VisionArray® MYCO Chip 1.0 is designed to detect several clinically relevant mycobacterial species. All capture sequences and the positive control are set up on the Chip as duplicates and the guide dots as triplicates. The signals are visible on the Chip as dark blue areas. The automated evaluation of the results is performed by a VisionArray® Analyzer Software.



M. tuberculosis (MTC) complex

2	M. tuberculosis complex (ITS Region)
3	M. tuberculosis complex (IS6110 Region)

Nontuberculous Mycobacteria (NTM)

4	M. abscessus	11	M. malmoense
5	M. avium / M. intracellulare complex	12	M. marinum / M. ulcerans
6	M. chelonae	13	M. scrofulaceum / M. parascrofulaceum
7	M. fortuitum	14	M. simiae
8	M. genavense	15	M. smegmatis
9	M. haemophilum	16	M. szulgai
10	M. kansasii	17	M. xenopi

References
Griffith DE, et al. (2007) Am J Respir Crit Core Med 175: 367-416.
Gupta RS, et al. (2018) Front Microbiol 9: 67.
Oren A & Carrity GM (2019) Int J Syst Evol Microbiol 69: 597-9.
Perez-Martinez I, et al. (2013) BMC Res Notes 6: 531.
Simons S, et al. (2011) Emerg Infect Dis 17: 343-9.
Tortoli E (2009) Clin Microbiol Infect 15: 906-10.

Prod. No.	Product	Tests
VA-0003-10	VisionArray MYCO Chip 1.0 Incl. 10 pieces CE IVD NEW	10
VA-0003-50	VisionArray MYCO Chip 1.0 Incl. 5x 10 pieces CE IVD NEW	50

CE IVD *only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

VisionArray® DNA Extraction, PCR, and Detection

VisionArray® Detection Kit

For hybridization and detection of PCR products on VisionArray® Chips

Prod. No.	Product	Tests
VK-0003-50	VisionArray Detection Kit CE IVD Incl. Hybridization Solution, 1 ml; Detection Solution, 5 ml; Blue Spot Solution, 5 ml; 100x Wash Buffer, 250 ml	50

VisionArray® DNA Extraction Kits

For isolation of genomic DNA from FFPE as well as liquid based cytology specimens

Prod. No.	Product	Tests
VI-0001-50	VisionArray FFPE DNA Extraction Kit Incl. Paraffin Dissolver; Tissue Lysis Buffer; Decrosslink Buffer; DNA Wash Buffer; Proteinase K; Proteinase K Buffer; Elution Buffer; Columns; Collection Tubes	50
VI-0002-50	VisionArray Cytology DNA Extraction Kit Incl. Pre-Lysis Buffer; Cell Lysis Buffer; DNA Wash Buffer; Proteinase K; Proteinase K Buffer; Elution Buffer; Columns; Collection Tubes	50

VisionArray® PCR Reagents

For contamination-free amplification and biotinylation of target sequences with a high quality heat stable Taq polymerase

Prod. No.	Product	Tests
VP-0001-50	VisionArray HPV Primer Kit 2.0 CE IVD Incl. HPV Primer Mix 2.0; dNTP/dUTP Solution	50
VP-0002-50	VisionArray MYCO Primer Kit 1.0 CE IVD NEW Incl. MYCO Primer Mix 1.0; dNTP/dUTP Solution	50
VE-0001-100	VisionArray PreCise Taq DNA Polymerase CE IVD Incl. VisionArray PreCise Taq DNA Polymerase; PreCise Reaction Buffer, 10x; PreCise $MgCl_2$, 25 mM	100
VE-0002-100	VisionArray Uracil-DNA Glycosylase CE IVD	100
ES-0007-50	VisionArray HPV PreCise Master Mix CE IVD Containing HPV Primer Mix 2.0; dNTP/dUTP Solution; VisionArray PreCise Taq DNA Polymerase; PCR-Buffer; $MgCl_2$; VisionArray Uracil-DNA Glycosylase	50
ES-0008-50	VisionArray MYCO PreCise Master Mix CE IVD NEW Containing MYCO Primer Mix 1.0; dNTP/dUTP Solution; VisionArray PreCise Taq DNA Polymerase; PCR-Buffer; $MgCl_2$; VisionArray Uracil-DNA Glycosylase	50

Slide Centrifuge

Prod. No.	Product
E-4051-1	Mini Slide Centrifuge Incl. 2 place slide rotor; two slide holders

CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.

VisionArray® Analysis Package SingleScan

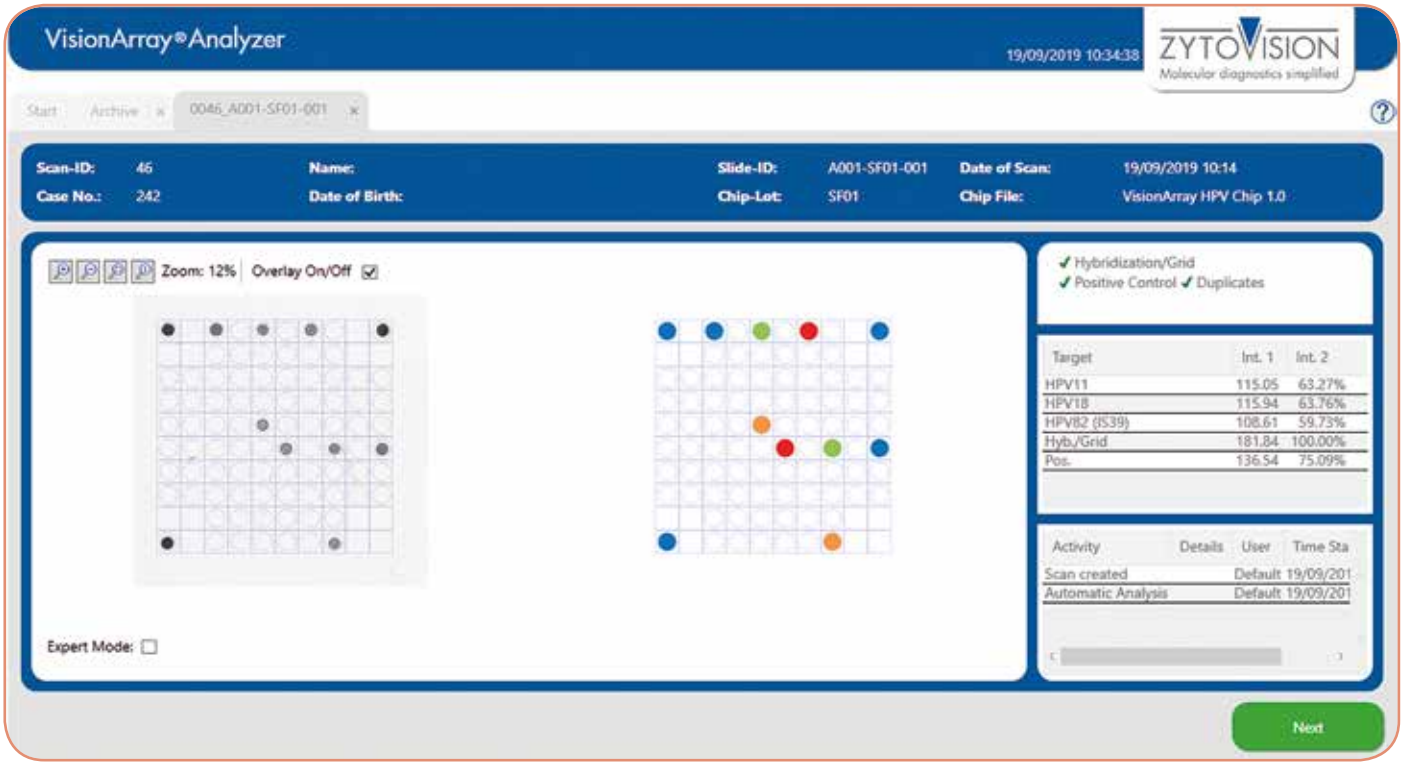
For visualization and quick analysis of the VisionArray® Chips data

Legend
1. Scanner 8100
2. Hand Scanner
3. Slide Holder
4. Laptop
5. USB-Hub
6. External Hard Drive
7. Computer Mouse

Prod. No.	Product
E-4060-1	VisionArray Analysis Package SingleScan CE IVD Incl. Scanner 8100; Slide Holder SingleScan; Hand Scanner; PC with preinstalled VisionArray Analyzer Software SingleScan; USB-Hub; External Hard Drive; Computer Mouse

VisionArray® Analyzer Software SingleScan

- Simple visualization and quick analysis of the VisionArray® Chip data
- Analysis of a Chip and the report of the results can be achieved in just a few minutes
- Program navigation is easy and intuitive for the user
- Scans are stored including all sample and Chip data in an integrated database on the enclosed external hard drive



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VisionArray® Analysis Package MultiScan

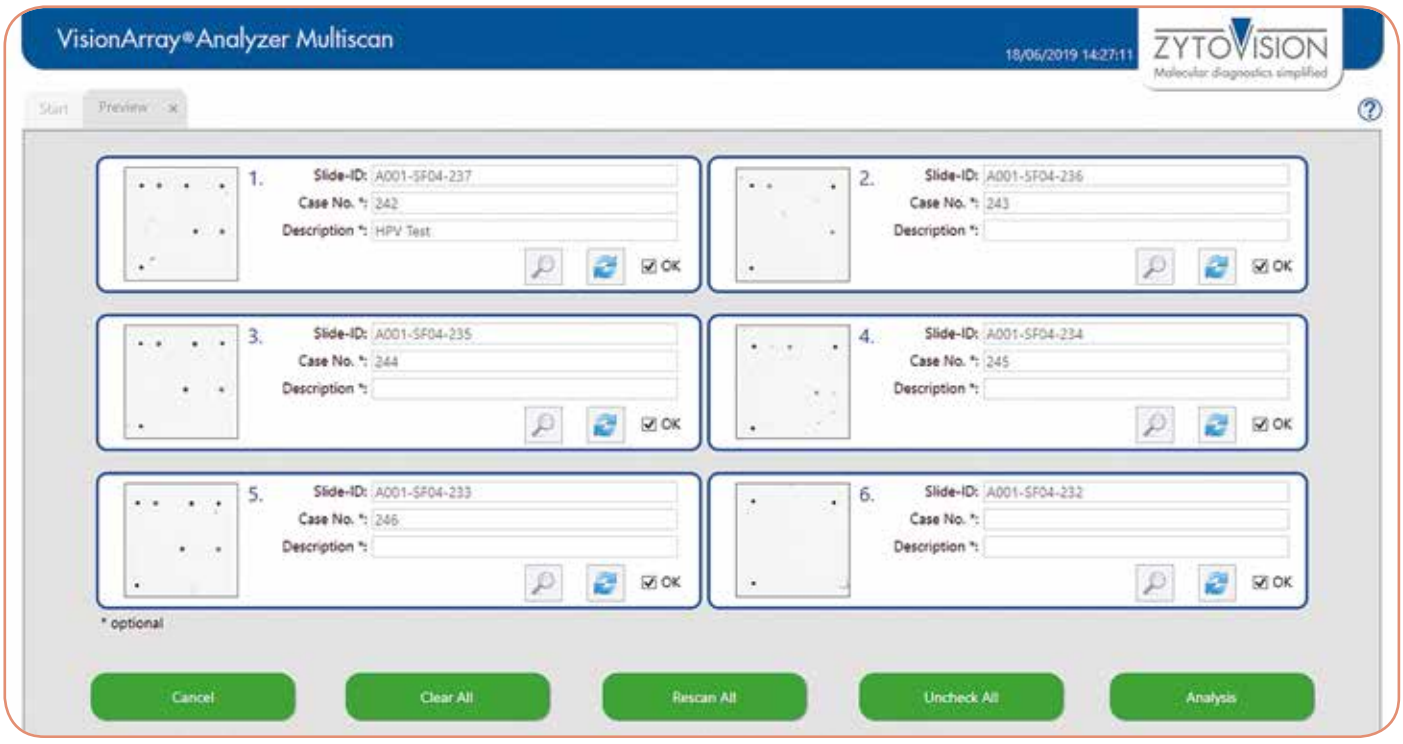
For visualization and quick analysis of up to 6 VisionArray® Chips simultaneously

Legend
1. Scanner V600 Photo
2. Laptop
3. USB-Hub
4. External Hard Drive
5. Computer Mouse

Prod. No.	Product
E-4070-1	VisionArray Analysis Package MultiScan CE IVD NEW Incl. Scanner V600 Photo; Slide Holder MultiScan; PC with preinstalled VisionArray Analyzer Software MultiScan; USB-Hub; External Hard Drive; Computer Mouse

VisionArray® Analyzer Software MultiScan

- Simple visualization and quick analysis of up to 6 VisionArray® Chips simultaneously
- All available VisionArray® Chips can be combined using the Scanner V600 Photo and are automatically detected by the software offering maximum flexibility
- Analysis of the Chips and the report of the results can be achieved in just a few minutes
- Scans are stored including all sample and Chip data in an integrated database on the enclosed external hard drive



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Product Use

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