ZYTOMICS®

Product Catalogue

In Situ Hybridization | Arrays

EXCELLENT

PRODUCTS, SOLUTIONS AND **SYSTEMS**

FOR **CLINICAL CANCER DIAGNOSTICS**

Contact Details

We help you get in touch

Reach out to our international sales managers and they will bring you in contact with the right partner!

order-ISH-distribution@zytomics.com

We value your opinion and would be delighted to take your suggestions into account in future projects.

Please feel free to send us your feedback at: **marketing@zytomics.com**

Content

ZYTOMICS at a Glance

Founded in 2021, **ZYTOMICS** is a combination of three established and longstanding European cancer diagnostics companies: Zytomed Systems, ZytoVision and Diagomics. All original founders of these companies shared the same vision: enabling clinical pathologists to provide a precise and timely cancer diagnosis. Unified under ZYTOMICS, we proudly carry on the vision of our founders.

ZYTOMICS is a leading manufacturer and provider of products and solutions used in clinical cancer diagnostics. Our offering includes reagents, automation and analytics with a focus on immunohistochemistry, in situ hybridization and next generation sequencing diagnostics. We aim to be the partner of trust for clinical pathology laboratories by providing best-in-class product quality, regulatory compliance, clinical and scientific insights as well as supply reliability. We are certified in accordance with Regulation (EU) 2017/746 (IVDR) for a significant portion of our Class C product portfolio.

ZYTOMICS has established a leading presence in major European markets and is consistently growing beyond European borders. Operations are located across sites in Northern Germany, Switzerland, and Southern France. Our international distribution network covers more than 90 countries.

Our Mission

Be the partner of trust for clinical pathology laboratories by providing best-in-class product quality, regulatory compliance, clinical and scientific insights as well as supply reliability.

Our Vision

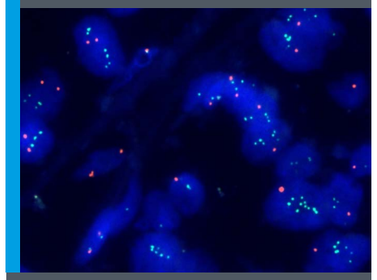
Aid clinical pathologists to provide a precise and timely cancer diagnosis.

Our Values

We believe in people empowerment to make the best decisions confidently, we embrace innovation to help our customers and staff achieving their goals in the most efficient and impactful manner, we foster collaborative diversity to come up with the most innovative ideas and solutions, and we promote continuous improvement to achieve lifelong professional growth as one team.

Product Portfolio

In Situ Hybridization



Fluorescence In Situ Hybridization
Chromogenic In Situ Hybridization

Arrays

DNA Microarray-Chips

How does the catalogue work?

The products are divided into two categories based on the technology used and —as shown above —each is identified by a specific color.

In all sections, you will find guidance on product categorization to help you navigate quickly and easily. To find a specific product, we recommend consulting the table of contents to locate the appropriate category and then navigating directly to the desired product.

A digital version of the catalog is also available. You can request this from the Marketing Communications Department (marketing@zytomics.com), our Customer Support team, or your local sales representative.

Our Brand

ZYTOVISION
Molecular diagnostics simplified

Our Product Lines

ZytoLight®
FlexISH®
ZytoMation®
ZytoFast®
ZytoDot®
VisionArray®

IVDR Certification

We are excited to share that **more than 200 products** from our portfolio are **IVDR certified**!

As a manufacturer of CE/IVD products, we consider compliance with the In Vitro Diagnostics Regulation (EU) 2017/746 (IVDR) to be of utmost importance - and not merely a challenge. We aim to meet the highest quality standards, and we are committed to make a valuable contribution to improving patient care and safety.

By following our mission, to be your partner of trust and In line with our commitment to conformity and compliance, we remain focused on extending our IVDR certified portfolio!

On our website, you will find products that are already IVDR-marked and comply with the latest and most stringent EU requirements.

Scan the QR code or visit:
www.zytomics.com/ivdr-certified-portfolio

EU-IVDR

Product Availability and Regulatory Status

Product availability and regulatory status may vary by country and are subject to change. For detailed information on availability and the applicable regulations in your region, please visit our website or contact your local sales representative.

You can find the latest product information, portfolio expansions, and changes and new additions on our website at any time. Please note that the regulatory status of our products is also subject to change. Therefore, the most up-to-date information on our website is always authoritative.

Resources Area

We are pleased to introduce the new Resources section on our website. This section provides you with convenient, centralized access to user manuals, safety data sheets, and certificates of analysis for our ZytoVision brand products.

You can find the new Resources section here:
www.zytomics.com/de/resources

Alternatively, our customer support team is always available to assist you if you need help.

Abbreviations

CE/IVD = In Vitro Diagnostics
RUO = Research Use Only

In Situ Hybridization

Based on morphology, fast and easy. Trust what you see.

In situ hybridization, ISH, is a powerful method for visualizing nucleic acid sequences - DNA and RNA - in cells and tissues. The two main techniques used are fluorescence in situ hybridization, FISH, and chromogenic in situ hybridization, CISH.

ZYTOMICS' extensive portfolio includes the outstanding Zyto*Light*®, Zyto*Dot*®, Zyto*Fast*®, *Flex*ISH® and Zyto*Mation*® probes from ZytoVision as well as the associated kits and detection systems.

In our product portfolio, you will find the following categories under in situ hybridisation:

ZytoLight®

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 (FFPE) tissue sections or cytology specimens.

ZytoVision GmbH

ZytoLight® SPEC and CEN Probes

ZytoLight® FISH probes are direct labeled FISH probes. ZytoLight® SPEC™ probes are designed for the detection of single copy human DNA sequences.

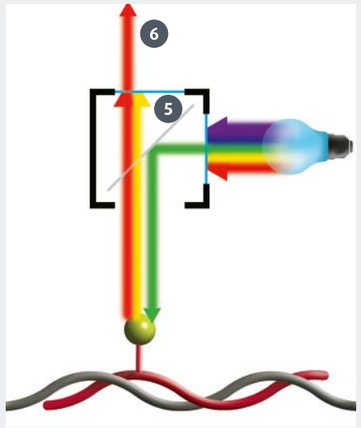
ZytoLight® CEN™ probes hybridize to highly repetitive human satellite DNA sequences of chromosomes producing signals specific for each individual chromosome.

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) for FISH anlyses on FFPE specimens and/or the ZytoLight® FISH-Cytology Implementation Kit (Z-2099-20) for FISH analyses on cytology specimens.

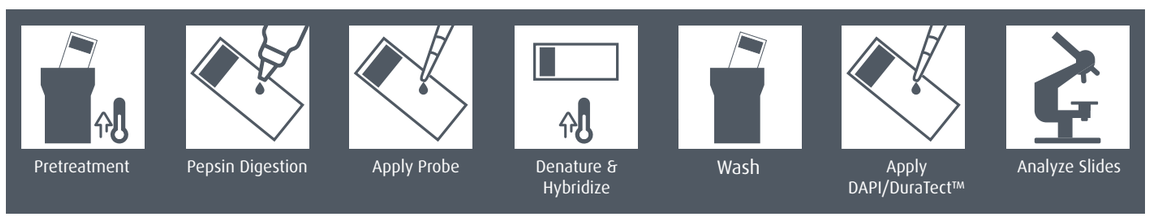
Both Implementation Kits include all necessary pretreatment solutions, wash buffers and DAPI/Dura Tect™-Solution and a detailed protocol to perform successful FISH experiments.

Method

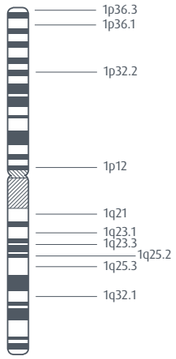


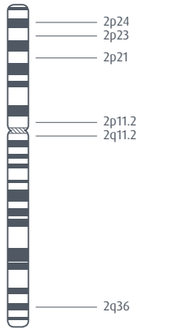
The ZytoLight® system uses direct-labeled FISH probes **[1]**, eliminating the need to detect the probes with fluorophore-coupled antibodies. The probes are detected by fluorescence microscopy using appropriate filter sets **[2]**.
Due to an exciter filter **[3]** full-spectrum light, emitted by the 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.

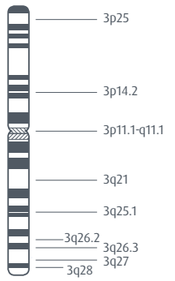
Protocol Overview



Chromosome Index







Chr. Band	Product Name	Reg. Status	Order No.	Page
1p36.3	ZytoLight Glioma 1p/19q Probe Set	CE/IVD	Z-2272-20	22
	ZytoLight SPEC 1p36/1q25 Dual Color Probe	CE/IVD	Z-2075-50/-200	23
	ZytoLight SPEC TNFRSF14/1q25 Dual Color Probe	RUO	Z-2323-50	113
1p36.1	ZytoLight SPEC FOXO1/PAX7 Dual Color Single Fusion Probe	CE/IVD	Z-2019-50/-200	80
1p32.2	ZytoLight SPEC CKS1B/CDKN2C Dual Color Probe	CE/IVD	Z-2276-50/-200	24
1p12	ZytoLight SPEC 1p12 Probe	RUO	Z-2101-200	110
	ZytoLight SPEC VHL/1p12/CEN 7/17 Quadruple Color Probe	CE/IVD	Z-2102-200	32
1q21	ZytoLight SPEC CKS1B/CDKN2C Dual Color Probe	CE/IVD	Z-2276-50/-200	24
	ZytoLight SPEC MCL1/1p12 Dual Color Probe	CE/IVD	Z-2173-200	25
1q23.1	ZytoLight SPEC NTRK1 Dual Color Break Apart Probe	CE/IVD	Z-2167-50/-200	25
1q23.3	ZytoLight SPEC NECTIN4/1p12 Dual Color Probe	CE/IVD	Z-2331-50/-200	26
	ZytoLight SPEC TCF3/PBX1 Dual Color Dual Fusion Probe	CE/IVD	Z-2308-50	27
1q25.2	ZytoLight SPEC ABL2 Dual Color Break Apart Probe	CE/IVD	Z-2200-50	26
1q25.3	ZytoLight Glioma 1p/19q Probe Set	CE/IVD	Z-2272-20	22
	ZytoLight SPEC 1p36/1q25 Dual Color Probe	CE/IVD	Z-2075-50/-200	23
1q32.1	ZytoLight SPEC MDM4/1p12 Dual Color Probe	CE/IVD	Z-2080-200	28

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2p24	ZytoLight SPEC MYCN/2q11 Dual Color Probe	CE/IVD	Z-2074-50/-200	28
2p23	ZytoLight SPEC ALK/EML4 TriCheck™ Probe	CE/IVD	Z-2117-50/-200	29
	ZytoLight SPEC ALK Dual Color Break Apart Probe	CE/IVD	Z-2124-50/-200	30
	ZytoLight SPEC ALK/2q11 Dual Color Probe	CE/IVD	Z-2161-200	30
2p21	ZytoLight SPEC EML4 Dual Color Break Apart Probe	RUO	Z-2136-50	113
	ZytoLight SPEC ALK/EML4 TriCheck™ Probe	CE/IVD	Z-2117-50/-200	29
2p11.2	ZytoLight SPEC IGK Dual Color Break Apart Probe	CE/IVD	Z-2288-50	31
2q11.2	ZytoLight SPEC 2q11 Probe	RUO	Z-2049-200	110
	ZytoLight SPEC CCND1 Break Apart/2q11/CEN 6 Quadruple Color Probe	CE/IVD	Z-2118-200	33
2q36	ZytoLight SPEC FOXO1/PAX3 Dual Color Single Fusion Probe	CE/IVD	Z-2018-50/-200	79
	ZytoLight SPEC FOXO1/PAX3 TriCheck™ Probe	CE/IVD	Z-2185-50	79

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3p25	ZytoLight SPEC VHL/CEN 3 Dual Color Probe	CE/IVD	Z-2084-200	31
	ZytoLight SPEC VHL/1p12/CEN 7/17 Quadruple Color Probe	CE/IVD	Z-2102-200	32
3p14.2	ZytoLight SPEC FHIT/CEN 3 Dual Color Probe	RUO	Z-2062-200	113
3p11.1-q11.1	ZytoLight Bladder Cancer Quadruple Color Probe	CE/IVD	Z-2305-50/-200	34
	ZytoLight CEN 3 Probe	RUO	Z-2001-200	110
	ZytoLight SPEC CDKN2A/CEN 3/7/17 Quadruple Color Probe	CE/IVD	Z-2081-50/-200	59
3q21	ZytoLight SPEC GATA2/MECOM Dual Color Dual Fusion Probe	CE/IVD	Z-2287-50	36
3q25.1	ZytoLight SPEC WWTR1 Dual Color Break Apart Probe	CE/IVD	Z-2212-50	35
3q26.2	ZytoLight SPEC GATA2/MECOM Dual Color Dual Fusion Probe	CE/IVD	Z-2287-50	36
	ZytoLight SPEC TERC/CEN 3 Dual Color Probe	RUO	Z-2284-200	113
3q26.3	ZytoLight SPEC PIK3CA/CEN 3 Dual Color Probe	CE/IVD	Z-2140-200	36
	ZytoLight SPEC SOX2/CEN 3 Dual Color Probe	RUO	Z-2127-200	113
	ZytoLight SPEC TP63/TBL1XR1 TriCheck™ Probe	CE/IVD	Z-2320-50	37
3q27	ZytoLight SPEC BCL6 Dual Color Break Apart Probe	CE/IVD	Z-2177-50/-200	37
3q28	ZytoLight SPEC TP63/TBL1XR1 TriCheck™ Probe	CE/IVD	Z-2320-50	37

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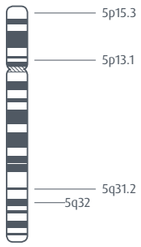
4p16.3	Zyto*Light* SPEC FGFR3 Dual Color Break Apart Probe	CE/IVD	**Z-2170-50/-200**	**38**
	Zyto*Light* SPEC FGFR3/4p11 Dual Color Probe	CE/IVD	**Z-2082-200**	**38**
	Zyto*Light* SPEC FGFR3/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2282-50**	**39**
4p11	Zyto*Light* SPEC 4p11 Probe	RUO	**Z-2083-200**	**110**
	Zyto*Light* SPEC 4p11/CEN 10/17 Triple Color Probe	CE/IVD	**Z-2307-50**	**40**
4q12	Zyto*Light* SPEC PDGFRA/FIP1L1 TriCheck™ Probe	CE/IVD	**Z-2209-50**	**40**



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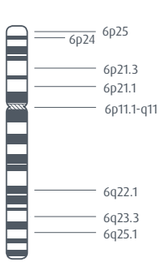
5p15.3	Zyto*Light* SPEC TERT Dual Color Break Apart Probe	CE/IVD	**Z-2273-50**	**41**
	Zyto*Light* SPEC TERT/5q31 Dual Color Probe	CE/IVD	**Z-2091-50/-200**	**41**
5p13.1	Zyto*Light* SPEC RICTOR/5q31.1 Dual Color Probe	RUO	**Z-2278-200**	**113**
5q31.2	Zyto*Light* SPEC EGR1/D5S23,D5S721 Dual Color Probe	CE/IVD	**Z-2211-50**	**42**
5q32	Zyto*Light* SPEC CSF1R Dual Color Break Apart Probe	CE/IVD	**Z-2202-50**	**42**
	Zyto*Light* SPEC CSF1R/D5S23,D5S721 Dual Color Probe	CE/IVD	**Z-2268-50**	**43**
	Zyto*Light* SPEC NRG1/CD74 TriCheck™ Probe	CE/IVD	**Z-2194-200**	**53**
	Zyto*Light* SPEC PDGFRB Dual Color Break Apart Probe	CE/IVD	**Z-2197-50**	**44**



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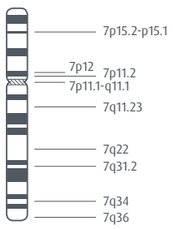
6p25	Zyto*Light* SPEC IRF4,DUSP22 Dual Color Break Apart Probe	CE/IVD	**Z-2210-50/-200**	**44**
6p24	Zyto*Light* SPEC RREB1/MYB/CEN 6 Triple Color Probe	CE/IVD	**Z-2152-50/-200**	**45**
6p21.3	Zyto*Light* SPEC PHF1 Dual Color Break Apart Probe	CE/IVD	**Z-2215-50**	**45**
6p21.1	Zyto*Light* SPEC VEGFA/CEN 6 Dual Color Probe	RUO	**Z-2195-200**	**110**
6p11.1-q11	Zyto*Light* CEN 6 Probe	RUO	**Z-2002-200**	**110**
	Zyto*Light* SPEC CCND1 Break Apart/2q11/CEN 6 Quadruple Color Probe	CE/IVD	**Z-2118-200**	**33**
6q22.1	Zyto*Light* SPEC ROS1 Dual Color Break Apart Probe	CE/IVD	**Z-2144-50/-200**	**46**
	Zyto*Light* SPEC ROS1/CEN 6 Dual Color Probe	CE/IVD	**Z-2162-200**	**47**
6q23.3	Zyto*Light* SPEC MYB Dual Color Break Apart Probe	CE/IVD	**Z-2143-50/-200**	**47**
	Zyto*Light* SPEC MYB/CEN 6 Dual Color Probe	CE/IVD	**Z-2281-50**	**48**
	Zyto*Light* SPEC RREB1/MYB/CEN 6 Triple Color Probe	CE/IVD	**Z-2152-50/-200**	**45**
6q25.1	Zyto*Light* SPEC ESR1/CEN 6 Dual Color Probe	CE/IVD	**Z-2069-50**	**48**



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7p15.2-p15.1	Zyto*Light* SPEC JAZF1 Dual Color Break Apart Probe	CE/IVD	**Z-2132-50**	**49**
7p12	Zyto*Light* SPEC IKZF1/CEN 7 Dual Color Probe	CE/IVD	**Z-2304-50**	**49**
7p11.2	Zyto*Light* SPEC EGFR/CEN 7 Dual Color Probe	CE/IVD	**Z-2033-50/-200**	**50**
7p11.1-q11.1	Zyto*Light* Bladder Cancer Quadruple Color Probe	CE/IVD	**Z-2305-50/-200**	**34**
	Zyto*Light* CEN 7 Probe	RUO	**Z-2003-200**	**110**
	Zyto*Light* SPEC CDKN2A/CEN 3/7/17 Quadruple Color Probe	CE/IVD	**Z-2081-50/-200**	**59**
	Zyto*Light* SPEC VHL/1p12/CEN 7/17 Quadruple Color Probe	CE/IVD	**Z-2102-200**	**32**
7q11.23	Zyto*Light* SPEC Williams-Beuren Dual Color Probe	CE/IVD	**Z-2302-50**	**50**

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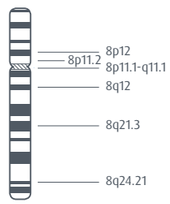
7q22	Zyto*Light* SPEC CUX1/EZH2/CEN 7 Triple Color Probe	CE/IVD	**Z-2214-50**	**51**
7q31.2	Zyto*Light* SPEC MET/CEN 7 Dual Color Probe	CE/IVD	**Z-2087-50/-200**	**51**
7q34	Zyto*Light* SPEC BRAF Dual Color Break Apart Probe	CE/IVD	**Z-2189-200**	**52**
	Zyto*Light* SPEC BRAF/CEN 7 Dual Color Probe	CE/IVD	**Z-2191-200**	**52**
7q36	Zyto*Light* SPEC CUX1/EZH2/CEN 7 Triple Color Probe	CE/IVD	**Z-2214-50**	**51**



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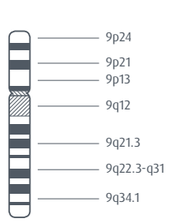
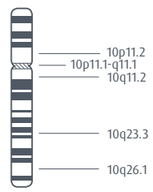
8p12	Zyto*Light* SPEC NRG1 Dual Color Break Apart Probe	CE/IVD	**Z-2181-200**	**53**
	Zyto*Light* SPEC NRG1/CD74 TriCheck™ Probe	CE/IVD	**Z-2194-200**	**53**
8p11.2	Zyto*Light* SPEC FGFR1 Dual Color Break Apart Probe	CE/IVD	**Z-2168-50/-200**	**54**
	Zyto*Light* SPEC FGFR1/CEN 8 Dual Color Probe	CE/IVD	**Z-2072-50/-200**	**54**
8p11.1-q11.1	Zyto*Light* CEN 8 Probe	CE/IVD	**Z-2004-50/-200**	**108**
8q12	Zyto*Light* SPEC PLAG1 Dual Color Break Apart Probe	RUO	**Z-2326-50**	**113**
8q21.3	Zyto*Light* SPEC RUNX1/RUNX1T1 Dual Color Dual Fusion Probe	CE/IVD	**Z-2112-50/-200**	**55**
8q24.21	Zyto*Light* SPEC MYC Dual Color Break Apart Probe	CE-IVD	**Z-2090-50/-200**	**56**
	Zyto*Light* SPEC MYC/CEN 8 Dual Color Probe	CE/IVD	**Z-2092-50/-200**	**56**
	Zyto*Light* SPEC MYC/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2105-50/-200**	**57**



Chr. Band	Product Name	Reg. Status	Order No.	Page
9p24	Zyto*Light* SPEC CD274,PDCD1LG2/CEN 9 Dual Color Probe	CE/IVD	**Z-2179-50/-200**	**57**
	Zyto*Light* SPEC JAK2 Dual Color Break Apart Probe	CE/IVD	**Z-2294-50**	**58**
9p21	Zyto*Light* Bladder Cancer Quadruple Color Probe	CE/IVD	**Z-2305-50/-200**	**34**
	Zyto*Light* SPEC CDKN2A/CEN 9 Dual Color Probe	CE/IVD	**Z-2063-50/-200**	**58**
	Zyto*Light* SPEC CDKN2A/CEN 3/7/17 Quadruple Color Probe	CE/IVD	**Z-2081-50/-200**	**59**
9p13	Zyto*Light* SPEC PAX5 Dual Color Break Apart Probe	CE/IVD	**Z-2300-50**	**60**
9q12	Zyto*Light* CEN 9 Probe	RUO	**Z-2067-200**	**110**
9q21.3	Zyto*Light* SPEC NTRK2 Dual Color Break Apart Probe	CE/IVD	**Z-2205-50/-200**	**60**
9q22.3-q31	Zyto*Light* SPEC NR4A3 Dual Color Break Apart Probe	CE/IVD	**Z-2145-50**	**61**
9q34.1	Zyto*Light* SPEC ABL1 Dual Color Break Apart Probe	CE/IVD	**Z-2199-50**	**61**
	Zyto*Light* SPEC BCR/ABL1 Dual Color Dual Fusion Probe	CE/IVD	**Z-2111-50/-200**	**63**
	Zyto*Light* SPEC NUP214 Dual Color Break Apart Probe	CE/IVD	**Z-2265-50**	**62**



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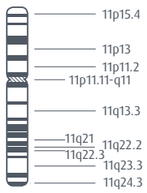
10p11.2	Zyto*Light* SPEC KIF5B Dual Color Break Apart Probe	RUO	**Z-2131-50**	**113**
10p11.1-q11.1	Zyto*Light* CEN 10 Probe	RUO	**Z-2079-200**	**110**
	Zyto*Light* SPEC 4p11/CEN 10/17 Triple Color Probe	CE/IVD	**Z-2307-50**	**40**
10q11.2	Zyto*Light* SPEC RET Dual Color Break Apart Probe	CE/IVD	**Z-2148-50/-200**	**63**
10q23.3	Zyto*Light* SPEC PTEN/CEN 10 Dual Color Probe	CE/IVD	**Z-2078-50/-200**	**64**
10q26.1	Zyto*Light* SPEC FGFR2 Dual Color Break Apart Probe	CE/IVD	**Z-2169-50/-200**	**64**
	Zyto*Light* SPEC FGFR2/CEN 10 Dual Color Probe	CE/IVD	**Z-2122-200**	**65**



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11p13	Zyto*Light* SPEC WT1 Dual Color Break Apart Probe	CE/IVD	**Z-2142-50**	**66**
11p11.2	Zyto*Light* SPEC SPI1 Dual Color Break Apart Probe	RUO	**Z-2291-50**	**67**
11p11.11-q11	Zyto*Light* CEN 11 Probe	CE/IVD	**Z-2005-200**	**108**
11q13.3	Zyto*Light* SPEC CCND1 Dual Color Break Apart Probe	CE/IVD	**Z-2108-50/-200**	**67**
	Zyto*Light* SPEC CCND1 Break Apart/2q11/CEN 6 Quadruple Color Probe	CE/IVD	**Z-2118-200**	**33**
	Zyto*Light* SPEC CCND1/CEN 11 Dual Color Probe	CE/IVD	**Z-2071-50/-200**	**68**
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	Zyto*Light* SPEC ATM/CEN 12 Dual Color Probe	CE/IVD	**Z-2296-50**	**71**
	Zyto*Light* SPEC TP53/ATM Dual Color Probe	CE/IVD	**Z-2159-50/-200**	**71**
11q23.3	Zyto*Light* SPEC 11q gain/loss Triple Color Probe	CE/IVD	**Z-2216-50**	**73**
	Zyto*Light* SPEC KMT2A Dual Color Break Apart Probe	CE/IVD	**Z-2193-50/-200**	**74**
11q24.3	Zyto*Light* SPEC 11q gain/loss Triple Color Probe	CE/IVD	**Z-2216-50**	**73**
	Zyto*Light* SPEC EWSR1/FLI1 TriCheck™ Probe	CE/IVD	**Z-2183-50**	**103**

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12p13.2	Zyto*Light* SPEC ETV6 Dual Color Break Apart Probe	CE/IVD	**Z-2176-50/-200**	**76**
	Zyto*Light* SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe	CE/IVD	**Z-2157-50/-200**	**75**
12p12.1	Zyto*Light* SPEC KRAS/CEN 12 Dual Color Probe	CE/IVD	**Z-2115-200**	**76**
12p11.1-q11	Zyto*Light* CEN 12 Probe	CE/IVD	**Z-2050-200**	**108**
	Zyto*Light* SPEC ATM/CEN 12 Dual Color Probe	CE/IVD	**Z-2296-50**	**71**
	Zyto*Light* SPEC D13S319/13q34/CEN 12 Triple Color Probe	CE/IVD	**Z-2160-50/-200**	**72**
12q13.3	Zyto*Light* SPEC DDIT3 Dual Color Break Apart Probe	CE/IVD	**Z-2100-50/-200**	**77**
12q14	Zyto*Light* SPEC CDK4/CEN 12 Dual Color Probe	CE/IVD	**Z-2103-50/-200**	**77**
12q15	Zyto*Light* SPEC MDM2/CEN 12 Dual Color Probe	CE/IVD	**Z-2013-50/-200**	**78**

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	Zyto*Light* SPEC 13/21 Dual Color Probe	CE/IVD	**Z-2164-200**	**108**
	Zyto*Light* Aneuploidy Panel 18/X/Y and 13/21	CE/IVD	**Z-2279-20**	**108**
	Zyto*Light* Aneuploidy Panel X/Y and 13/18/21	CE/IVD	**Z-2104-5/-20**	**112**
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	Zyto*Light* SPEC FOXO1/PAX3 Dual Color Single Fusion Probe	CE/IVD	**Z-2018-50/-200**	**79**
	Zyto*Light* SPEC FOXO1/PAX3 TriCheck™ Probe	CE/IVD	**Z-2185-50**	**79**
	Zyto*Light* SPEC FOXO1/PAX7 Dual Color Single Fusion Probe	CE/IVD	**Z-2019-50/-200**	**80**
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	Zyto*Light* SPEC D13S319/13q34 Dual Color Probe	CE/IVD	**Z-2280-50/-200**	**73**
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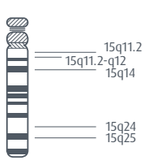
	Zyto*Light* SPEC BCL2/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2114-50/-200**	**172**
	Zyto*Light* SPEC CCND1/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2125-50/-200**	**144**
	Zyto*Light* SPEC FGFR3/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2282-50**	**115**
	Zyto*Light* SPEC MAF/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2270-50**	**162**
	Zyto*Light* SPEC MAFB/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2271-50**	**163**
	Zyto*Light* SPEC MALT1/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2325-50**	**171**
	Zyto*Light* SPEC MYC/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2105-50/-200**	**133**



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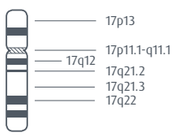

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	Zyto*Light* SPEC USP6 Dual Color Break Apart Probe	CE/IVD	**Z-2151-50/-200**	**89**
	Zyto*Light* SPEC YWHAE Dual Color Break Apart Probe	CE/IVD	**Z-2175-50**	**90**
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	Zyto*Light* CEN 17 Probe	RUO	**Z-2006-200**	**110**
	Zyto*Light* SPEC 4p11/CEN 10/17 Triple Color Probe	CE/IVD	**Z-2307-50**	**40**
	Zyto*Light* SPEC CDKN2A/CEN 3/7/17 Quadruple Color Probe	CE/IVD	**Z-2081-50/-200**	**59**
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	Zyto*Light* SPEC ERBB2/CEN 17 Dual Color Probe Kit	CE/IVD	**Z-2020-5/-20**	**90**
	Zyto*Light* CEN 17/SPEC ERBB2 Dual Color Probe	CE/IVD	**Z-2077-50/-200**	**91**
	Zyto*Light* SPEC ERBB2/D17S122 Dual Color Probe	CE/IVD	**Z-2190-50/-200**	**91**
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	Zyto*Light* SPEC PML/RARA Dual Color Dual Fusion Probe	CE/IVD	**Z-2113-50/-200**	**84**
17q21.3	Zyto*Light* SPEC COL1A1 Dual Color Break Apart Probe	CE/IVD	**Z-2121-200**	**92**
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18q11.2	Zyto*Light* SPEC SS18 Dual Color Break Apart Probe	CE/IVD	**Z-2097-50/-200**	**93**
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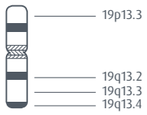
	Zyto*Light* SPEC BCL2/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2114-50/-200**	**96**
	Zyto*Light* SPEC BIRC3/MALT1 Dual Color Dual Fusion Probe	CE/IVD	**Z-2146-50/-200**	**69**
	Zyto*Light* SPEC MALT1 Dual Color Break Apart Probe	CE/IVD	**Z-2196-50/-200**	**95**
	Zyto*Light* SPEC MALT1/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2325-50**	**95**



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19p13.3	Zyto*Light* Glioma 1p/19q Probe Set	CE/IVD	**Z-2272-20**	**22**
	Zyto*Light* SPEC 19q13/19p13 Dual Color Probe	CE/IVD	**Z-2076-50/-200**	**23**
	Zyto*Light* SPEC TCF3/PBX1 Dual Color Dual Fusion Probe	CE/IVD	**Z-2308-50**	**27**
19q13.2	Zyto*Light* SPEC CIC Dual Color Break Apart Probe	CE/IVD	**Z-2285-50**	**97**
19q13.3	Zyto*Light* Glioma 1p/19q Probe Set	CE/IVD	**Z-2272-20**	**22**
	Zyto*Light* SPEC 19q13/19p13 Dual Color Probe	CE/IVD	**Z-2076-50/-200**	**23**
19q13.4	Zyto*Light* SPEC C19MC/19p13 Dual Color Probe	CE/IVD	**Z-2274-50**	**97**

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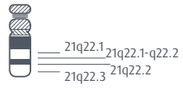
20q12-q13.1	Zyto*Light* SPEC PTPRT/20q11 Dual Color Probe	CE/IVD	**Z-2213-50**	**98**



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21q22.1	Zyto*Light* SPEC RUNX1/RUNX1T1 Dual Color Dual Fusion Probe	CE/IVD	**Z-2112-50/-200**	**55**
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21q22.1-q22.2	Zyto*Light* SPEC 21q22 Probe	RUO	**Z-2086-200**	**110**
	Zyto*Light* SPEC 21/CEN X/Yq12 Triple Color Probe	CE/IVD	**Z-2180-200**	**108**
	Zyto*Light* SPEC 13/21 Dual Color Probe	CE/IVD	**Z-2164-200**	**108**
	Zyto*Light* SPEC 13/CEN 18/SPEC 21 Triple Color Probe	CE/IVD	**Z-2095-50/-200**	**108**
	Zyto*Light* Aneuploidy Panel 18/X/Y and 13/21	CE/IVD	**Z-2279-20**	**111**
	Zyto*Light* Aneuploidy Panel X/Y and 13/18/21	CE/IVD	**Z-2104-5/-20**	**112**
21q22.2	Zyto*Light* SPEC ERG Dual Color Break Apart Probe	CE/IVD	**Z-2138-200**	**99**
	Zyto*Light* SPEC ERG/TMPRSS2 TriCheck™ Probe	CE/IVD	**Z-2135-200**	**99**
21q22.3	Zyto*Light* SPEC ERG/TMPRSS2 TriCheck™ Probe	CE/IVD	**Z-2135-200**	**99**

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	Zyto*Light* SPEC DiGeorge/Phelan McDermid Dual Color Probe	CE/IVD	**Z-2299-50**	**100**
	Zyto*Light* SPEC DiGeorge Triple Color Probe	CE/IVD	**Z-2289-50**	**101**
	Zyto*Light* SPEC IGL Dual Color Break Apart Probe	CE/IVD	**Z-2286-50**	**102**
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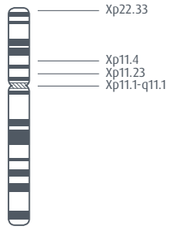
22q12.2	Zyto*Light* SPEC EWSR1 Dual Color Break Apart Probe	CE/IVD	**Z-2096-50/-200**	**103**
	Zyto*Light* SPEC EWSR1/FLI1 TriCheck™ Probe	CE/IVD	**Z-2183-50**	**103**
22q13.1	Zyto*Light* SPEC PDGFB Dual Color Break Apart Probe	CE/IVD	**Z-2119-50/-200**	**104**
	Zyto*Light* SPEC COL1A1/PDGFB Dual Color Dual Fusion Probe	CE/IVD	**Z-2116-50/-200**	**93**
22q13.3	Zyto*Light* SPEC DiGeorge/Phelan McDermid Dual Color Probe	CE/IVD	**Z-2299-50**	**100**



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Xp11.1-q11.1	Zyto*Light* CEN X Probe	RUO	**Z-2008-200**	**110**
	Zyto*Light* CEN X/Yq12 Dual Color Probe	CE/IVD	**Z-2016-50/-200**	**108**
	Zyto*Light* CEN X/Y Dual Color Probe	CE/IVD	**Z-2120-200**	**108**
	Zyto*Light* SPEC 18/CEN X/Y Triple Color Probe	CE/IVD	**Z-2163-200**	**108**
	Zyto*Light* SPEC 21/CEN X/Yq12 Triple Color Probe	CE/IVD	**Z-2180-200**	**108**
	Zyto*Light* Aneuploidy Panel 18/X/Y and 13/21	CE/IVD	**Z-2279-20**	**108**
	Zyto*Light* Aneuploidy Panel X/Y and 13/18/21	CE/IVD	**Z-2104-5/-20**	**108**

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	ZytoLight SPEC 18/CEN X/Y Triple Color Probe	CE/IVD	**Z-2163-200**	**108**
Yq12	ZytoLight CEN Yq12 Probe	RUO	**Z-2010-200**	**110**
	ZytoLight CEN X/Yq12 Dual Color Probe	CE/IVD	**Z-2016-50/-200**	**108**
	ZytoLight SPEC 21/CEN X/Yq12 Triple Color Probe	CE/IVD	**Z-2180-200**	**108**
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ABL2	ARG	ZytoLight SPEC ABL2 Dual Color Break Apart Probe	CE/IVD	**Z-2200-50**	**26**
ALK	CD246	ZytoLight SPEC ALK/EML4 TriCheck™ Probe	CE/IVD	**Z-2117-50/-200**	**29**
		ZytoLight SPEC ALK Dual Color Break Apart Probe	CE/IVD	**Z-2124-50/-200**	**30**
		ZytoLight SPEC ALK/2q11 Dual Color Probe	CE/IVD	**Z-2161-200**	**30**
ARSA	ASA, MLD	ZytoLight SPEC DiGeorge/Phelan McDermid Dual Color Probe	CE/IVD	**Z-2299-50**	**100**
ATM	ATA, TEL1	ZytoLight SPEC ATM/CEN 11 Dual Color Probe	CE/IVD	**Z-2297-50**	**70**
		ZytoLight SPEC ATM/CEN 12 Dual Color Probe	CE/IVD	**Z-2296-50**	**71**
		ZytoLight SPEC TP53/ATM Dual Color Probe	CE/IVD	**Z-2159-50/-200**	**71**
BCL2	Bcl-2, PPP1R50	ZytoLight SPEC BCL2 Dual Color Break Apart Probe	CE/IVD	**Z-2192-50/-200**	**96**
		ZytoLight SPEC BCL2/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2114-50/-200**	**96**
BCL2L1	BCLX	ZytoLight SPEC BCL2L1/CEN 20 Dual Color Probe	RUO	**Z-2171-200**	**113**
BCL6	ZNF51, LAZ3	ZytoLight SPEC BCL6 Dual Color Break Apart Probe	CE/IVD	**Z-2177-50/-200**	**37**
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BIRC3	C-IAP, MALT2	ZytoLight SPEC BIRC3/MALT1 Dual Color Dual Fusion Probe	CE/IVD	**Z-2146-50/-200**	**69**
BRAF	BRAF1, NS7	ZytoLight SPEC BRAF Dual Color Break Apart Probe	CE/IVD	**Z-2189-200**	**52**
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CBFB	PEBP2B	ZytoLight SPEC CBFB Dual Color Break Apart Probe	CE/IVD	**Z-2207-50**	**88**
CCND1	BCL1, PRAD1	ZytoLight SPEC CCND1 Dual Color Break Apart Probe	CE/IVD	**Z-2108-50/-200**	**67**
		ZytoLight SPEC CCND1 Break Apart/2q11/CEN 6 Quadruple Color Probe	CE/IVD	**Z-2118-200**	**33**
		ZytoLight SPEC CCND1/CEN 11 Dual Color Probe	CE/IVD	**Z-2071-50/-200**	**68**
		ZytoLight SPEC CCND1/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2125-50/-200**	**68**
CD274	PD-L1, PDL1	ZytoLight SPEC CD274,PDCD1LG2/CEN 9 Dual Color Probe	CE/IVD	**Z-2179-50/-200**	**57**
CD74	-	ZytoLight SPEC NRG1/CD74 TriCheck™ Probe	CE/IVD	**Z-2194-200**	**53**
CDK4	PSK-J3	ZytoLight SPEC CDK4/CEN 12 Dual Color Probe	CE/IVD	**Z-2103-50/-200**	**77**
CDKN2A	p16, ARF, INK4	ZytoLight Bladder Cancer Quadruple Color Probe	CE/IVD	**Z-2305-50/-200**	**34**
		ZytoLight SPEC CDKN2A/CEN 9 Dual Color Probe	CE/IVD	**Z-2063-50/-200**	**58**
		ZytoLight SPEC CDKN2A/CEN 3/7/17 Quadruple Color Probe	CE/IVD	**Z-2081-50/-200**	**59**
CDNK2C	-	ZytoLight SPEC CKS1B/CDKN2C Dual Color Probe	CE/IVD	**Z-2276-50/-200**	**24**
CIC	KIAA0306	ZytoLight SPEC CIC Dual Color Break Apart Probe	CE/IVD	**Z-2285-50**	**97**
CKS1B	-	ZytoLight SPEC CKS1B/CDKN2C Dual Color Probe	CE/IVD	**Z-2276-50/-200**	**24**
COL1A1	OI4	ZytoLight SPEC COL1A1 Dual Color Break Apart Probe	CE/IVD	**Z-2121-200**	**92**
		ZytoLight SPEC COL1A1/PDGFB Dual Color Dual Fusion Probe	CE/IVD	**Z-2116-50/-200**	**93**
CREBBP	CBP, RTS	ZytoLight SPEC CREBBP Dual Color Break Apart Probe	CE/IVD	**Z-2267-50**	**85**
CRKL	-	ZytoLight SPEC DiGeorge Triple Color Probe	CE/IVD	**Z-2289-50**	**101**
CRLF2	CRL2, TSLPR	ZytoLight SPEC CRLF2 Dual Color Break Apart Probe	CE/IVD	**Z-2201-50**	**105**
CSF1R	FMS	ZytoLight SPEC CSF1R Dual Color Break Apart Probe	CE/IVD	**Z-2202-50**	**42**
		ZytoLight SPEC CSF1R/D5S23,D5S721 Dual Color Probe	CE/IVD	**Z-2268-50**	**43**
CUX1	CUT	ZytoLight SPEC CUX1/EZH2/CEN 7 Triple Color Probe	CE/IVD	**Z-2214-50**	**51**
DDIT3	CHOP, GADD153	ZytoLight SPEC DDIT3 Dual Color Break Apart Probe	CE/IVD	**Z-2100-50/-200**	**77**
DLEU1	BCMS1, LEU1	ZytoLight SPEC D13S319/13q34/CEN 12 Triple Color Probe	CE/IVD	**Z-2160-50/-200**	**72**
		ZytoLight SPEC D13S319/13q34 Dual Color Probe	CE/IVD	**Z-2280-50/-200**	**73**
DUSP22	JKAP	ZytoLight SPEC IRF4,DUSP22 Dual Color Break Apart Probe	CE/IVD	**Z-2210-50/-200**	**44**
EGFR	HER1, ERBB1	ZytoLight SPEC EGFR/CEN 7 Dual Color Probe	CE/IVD	**Z-2033-50/-200**	**50**
EGR1	KROX-24	ZytoLight SPEC EGR1/D5S23,D5S721 Dual Color Probe	CE/IVD	**Z-2211-50**	**42**
ELN	WBS	ZytoLight SPEC Williams-Beuren Dual Color Probe	CE/IVD	**Z-2302-50**	**50**
EML4	ROPP120	ZytoLight SPEC EML4 Dual Color Break Apart Probe	RUO	**Z-2136-50**	**113**
		ZytoLight SPEC ALK/EML4 TriCheck™ Probe	CE/IVD	**Z-2117-50/-200**	**29**
ERBB2	HER2, HER-2, NEU	ZytoLight SPEC ERBB2/CEN 17 Dual Color Probe	CE/IVD	**Z-2015-50/-200**	**90**
		ZytoLight SPEC ERBB2/CEN 17 Dual Color Probe Kit	CE/IVD	**Z-2020-5/-20**	**90**
		ZytoLight CEN 17/SPEC ERBB2 Dual Color Probe	CE/IVD	**Z-2077-50/-200**	**91**
		ZytoLight SPEC ERBB2/D17S122 Dual Color Probe	CE/IVD	**Z-2190-50/-200**	**91**
		ZytoLight SPEC ERBB2/TOP2A/CEN 17 Triple Color Probe	CE/IVD	**Z-2093-50/-200**	**92**
ERG	erg-3, p55	ZytoLight SPEC ERG Dual Color Break Apart Probe	CE/IVD	**Z-2138-200**	**99**
		ZytoLight SPEC ERG/TMPRSS2 TriCheck™ Probe	CE/IVD	**Z-2135-200**	**99**
ESR1	Era, NR3A1	ZytoLight SPEC ESR1/CEN 6 Dual Color Probe	CE/IVD	**Z-2069-50**	**48**
ETV6	TEL	ZytoLight SPEC ETV6 Dual Color Break Apart Probe	CE/IVD	**Z-2176-50/-200**	**76**
		ZytoLight SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe	CE/IVD	**Z-2157-50/-200**	**75**
EWSR1	EWS	ZytoLight SPEC EWSR1 Dual Color Break Apart Probe	CE/IVD	**Z-2096-50/-200**	**103**
		ZytoLight SPEC EWSR1/FLI1 TriCheck™ Probe	CE/IVD	**Z-2183-50**	**103**
EZH2	KMT6A	ZytoLight SPEC CUX1/EZH2/CEN 7 Triple Color Probe	CE/IVD	**Z-2214-50**	**51**

HUGO Name	Synonym	Product Name	Reg. Status	Order No.	Page
FGFR1	FLT2, BFGFR	ZytoLight SPEC FGFR1 Dual Color Break Apart Probe	CE/IVD	**Z-2168-50/-200**	**54**
		ZytoLight SPEC FGFR1/CEN 8 Dual Color Probe	CE/IVD	**Z-2072-50/-200**	**54**
FGFR2	BEK, CD332	ZytoLight SPEC FGFR2 Dual Color Break Apart Probe	CE/IVD	**Z-2169-50/-200**	**64**
		ZytoLight SPEC FGFR2/CEN 10 Dual Color Probe	CE/IVD	**Z-2122-200**	**65**
FGFR3	CD333, JTK4	ZytoLight SPEC FGFR3 Dual Color Break Apart Probe	CE/IVD	**Z-2170-50/-200**	**38**
		ZytoLight SPEC FGFR3/4p11 Dual Color Probe	CE/IVD	**Z-2082-200**	**38**
		ZytoLight SPEC FGFR3/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2282-50**	**39**
FHIT	FRA3B	ZytoLight SPEC FHIT/CEN 3 Dual Color Probe	RUO	**Z-2062-200**	**113**
FIP1L1	FIP1	ZytoLight SPEC PDGFRA/FIP1L1 TriCheck™ Probe	CE/IVD	**Z-2209-50**	**40**
FLI1	EWSR2	ZytoLight SPEC EWSR1/FLI1 TriCheck™ Probe	CE/IVD	**Z-2183-50**	**103**
FOXO1	FKHR, FKH1	ZytoLight SPEC FOXO1 Dual Color Break Apart Probe	CE/IVD	**Z-2139-50**	**78**
		ZytoLight SPEC FOXO1/PAX3 Dual Color Single Fusion Probe	CE/IVD	**Z-2018-50/-200**	**79**
		ZytoLight SPEC FOXO1/PAX3 TriCheck™ Probe	CE/IVD	**Z-2185-50**	**79**
		ZytoLight SPEC FOXO1/PAX7 Dual Color Single Fusion Probe	CE/IVD	**Z-2019-50/-200**	**80**
FUS	FUS1	ZytoLight SPEC FUS Dual Color Break Apart Probe	CE/IVD	**Z-2130-50**	**85**
GATA2	NFE1B	ZytoLight SPEC GATA2/MECOM Dual Color Dual Fusion Probe	CE/IVD	**Z-2287-50**	**36**
HIRA	TUPLE1, TUP1	ZytoLight SPEC DiGeorge/Phelan McDermid Dual Color Probe	CE/IVD	**Z-2299-50**	**100**
		ZytoLight SPEC DiGeorge Triple Color Probe	CE/IVD	**Z-2289-50**	**101**
IGH	IGH@	ZytoLight SPEC IGH Dual Color Break Apart Probe	CE/IVD	**Z-2110-50/-200**	**81**
		ZytoLight SPEC BCL2/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2114-50/-200**	**96**
		ZytoLight SPEC CCND1/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2125-50/-200**	**68**
		ZytoLight SPEC FGFR3/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2282-50**	**39**
		ZytoLight SPEC MAF/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2270-50**	**86**
		ZytoLight SPEC MAFB/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2271-50**	**87**
		ZytoLight SPEC MALT1/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2325-50**	**95**
		ZytoLight SPEC MYC/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2105-50/-200**	**57**
IGK	IGK@	ZytoLight SPEC IGK Dual Color Break Apart Probe	CE/IVD	**Z-2288-50**	**31**
IGL	IGL@	ZytoLight SPEC IGL Dual Color Break Apart Probe	CE/IVD	**Z-2286-50**	**102**
IKZF1	IKAROS	ZytoLight SPEC IKZF1/CEN 7 Dual Color Probe	CE/IVD	**Z-2304-50**	**49**
IRF4	MUM1	ZytoLight SPEC IRF4,DUSP22 Dual Color Break Apart Probe	CE/IVD	**Z-2210-50/-200**	**44**
JAK2	JTK10	ZytoLight SPEC JAK2 Dual Color Break Apart Probe	CE/IVD	**Z-2294-50**	**58**
JAZF1	TIP27, ZNF802	ZytoLight SPEC JAZF1 Dual Color Break Apart Probe	CE/IVD	**Z-2132-50**	**49**
KIF5B	KNS1	ZytoLight SPEC KIF5B Dual Color Break Apart Probe	RUO	**Z-2131-50**	**113**
KMT2A	MLL	ZytoLight SPEC KMT2A Dual Color Break Apart Probe	CE/IVD	**Z-2193-50/-200**	**74**
KRAS	KRAS1	ZytoLight SPEC KRAS/CEN 12 Dual Color Probe	CE/IVD	**Z-2115-200**	**761**
LAMP1	CD107a	ZytoLight SPEC D13S319/13q34/CEN 12 Triple Color Probe	CE/IVD	**Z-2160-50/-200**	**72**
		ZytoLight SPEC D13S319/13q34 Dual Color Probe	CE/IVD	**Z-2280-50/-200**	**73**
MAF	-	ZytoLight SPEC MAF/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2270-50**	**86**

HUGO Name	Synonym	Product Name	Reg. Status	Order No.	Page
MAFB	-	ZytoLight SPEC MAFB/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2271-50**	**87**
MALT1	MLT	ZytoLight SPEC MALT1 Dual Color Break Apart Probe	CE/IVD	**Z-2196-50/-200**	**95**
		ZytoLight SPEC MALT1/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2325-50**	**95**
		ZytoLight SPEC BIRC3/MALT1 Dual Color Dual Fusion Probe	CE/IVD	**Z-2146-50/-200**	**69**
MAML2	MAM3	ZytoLight SPEC MAML2 Dual Color Break Apart Probe	CE/IVD	**Z-2014-50/-200**	**70**
MAPK1	PRKM2, ERK	ZytoLight SPEC DiGeorge Triple Color Probe	CE/IVD	**Z-2289-50**	**101**
MCL1	BCL2L3	ZytoLight SPEC MCL1/1p12 Dual Color Probe	CE/IVD	**Z-2173-200**	**25**
MDM2	HDM2	ZytoLight SPEC MDM2/CEN 12 Dual Color Probe	CE/IVD	**Z-2013-50/-200**	**78**
MDM4	MDMX	ZytoLight SPEC MDM4/1p12 Dual Color Probe	CE/IVD	**Z-2080-200**	**28**
MECOM	MDS1, EVI1	ZytoLight SPEC GATA2/MECOM Dual Color Dual Fusion Probe	CE/IVD	**Z-2287-50**	**36**
MET	HGFR, RCCP2	ZytoLight SPEC MET/CEN 7 Dual Color Probe	CE/IVD	**Z-2087-50/-200**	**51**
MYB	c-myb	ZytoLight SPEC MYB Dual Color Break Apart Probe	CE/IVD	**Z-2143-50/-200**	**47**
		ZytoLight SPEC MYB/CEN 6 Dual Color Probe	CE/IVD	**Z-2281-50**	**48**
		ZytoLight SPEC RREB1/MYB/CEN 6 Triple Color Probe	CE/IVD	**Z-2152-50/-200**	**45**
MYC	CMYC, bHLHe39, c-Myc	ZytoLight SPEC MYC Dual Color Break Apart Probe	CE/IVD	**Z-2090-50/-200**	**56**
		ZytoLight SPEC MYC/CEN 8 Dual Color Probe	CE/IVD	**Z-2092-50/-200**	**56**
		ZytoLight SPEC MYC/IGH Dual Color Dual Fusion Probe	CE/IVD	**Z-2105-50/-200**	**57**
MYCN	NMYC, N-myc	ZytoLight SPEC MYCN/2q11 Dual Color Probe	CE/IVD	**Z-2074-50/-200**	**28**
NECTIN4	PVRL4	ZytoLight SPEC NECTIN4/1p12 Dual Color Probe	CE/IVD	**Z-2331-50/-200**	**26**
NR4A3	CHN, CSMF	ZytoLight SPEC NR4A3 Dual Color Break Apart Probe	CE/IVD	**Z-2145-50**	**61**
NRG1	HGL, GGF	ZytoLight SPEC NRG1 Dual Color Break Apart Probe	CE/IVD	**Z-2181-200**	**53**
		ZytoLight SPEC NRG1/CD74 TriCheck™ Probe	CE/IVD	**Z-2194-200**	**53**
NTRK1	MTC, TRK	ZytoLight SPEC NTRK1 Dual Color Break Apart Probe	CE/IVD	**Z-2167-50/-200**	**25**
NTRK2	TRKB	ZytoLight SPEC NTRK2 Dual Color Break Apart Probe	CE/IVD	**Z-2205-50/-200**	**60**
NTRK3	TRKC	ZytoLight SPEC NTRK3 Dual Color Break Apart Probe	CE/IVD	**Z-2206-50/-200**	**83**
NUP98	NUP96	ZytoLight SPEC NUP98 Dual Color Break Apart Probe	CE/IVD	**Z-2266-50**	**65**
NUP214	CAN, CAIN	ZytoLight SPEC NUP214 Dual Color Break Apart Probe	CE/IVD	**Z-2265-50**	**62**
NUTM1	NUT	ZytoLight SPEC NUTM1 Dual Color Break Apart Probe	CE/IVD	**Z-2208-200**	**83**
PAX3	HUP2	ZytoLight SPEC FOXO1/PAX3 Dual Color Single Fusion Probe	CE/IVD	**Z-2018-50/-200**	**79**
		ZytoLight SPEC FOXO1/PAX3 TriCheck™ Probe	CE/IVD	**Z-2185-50**	**79**
PAX5	BSAP	ZytoLight SPEC PAX5 Dual Color Break Apart Probe	CE/IVD	**Z-2300-50**	**60**
PAX7	HUP1	ZytoLight SPEC FOXO1/PAX7 Dual Color Single Fusion Probe	CE/IVD	**Z-2019-50/-200**	**80**
PBX1	-	ZytoLight SPEC TCF3/PBX1 Dual Color Dual Fusion Probe	CE/IVD	**Z-2308-50**	**27**
PDCD1LG2	PD-L2, PDL2	ZytoLight SPEC CD274,PDCD1LG2/CEN 9 Dual Color Probe	CE/IVD	**Z-2179-50/-200**	**57**
PDGFB	SIS, SSV	ZytoLight SPEC PDGFB Dual Color Break Apart Probe	CE/IVD	**Z-2119-50/-200**	**104**
		ZytoLight SPEC COL1A1/PDGFB Dual Color Dual Fusion Probe	CE/IVD	**Z-2116-50/-200**	**93**
PDGFRA	GAS9	ZytoLight SPEC PDGFRA/FIP1L1 TriCheck™ Probe	CE/IVD	**Z-2209-50**	**40**

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PDGFRB	JTK12, PDGFR1	Zyto*Light* SPEC PDGFRB Dual Color Break Apart Probe	CE/IVD	**Z-2197-50**	**44**
PHF1	MTF2L2, PCL1	Zyto*Light* SPEC PHF1 Dual Color Break Apart Probe	CE/IVD	**Z-2215-50**	**45**
PIK3CA	PI3K	Zyto*Light* SPEC PIK3CA/CEN 3 Dual Color Probe	CE/IVD	**Z-2140-200**	**36**
PLAG1	ZNF912	Zyto*Light* SPEC PLAG1 Dual Color Break Apart Probe	RUO	**Z-2326-50**	**113**
PML	MYL, RNF71	Zyto*Light* SPEC PML/RARA Dual Color Dual Fusion Probe	CE/IVD	**Z-2113-50/-200**	**84**
PTEN	MMAC1, TEP1	Zyto*Light* SPEC PTEN/CEN 10 Dual Color Probe	CE/IVD	**Z-2078-50/-200**	**64**
PTPRT	KIAA0283	Zyto*Light* SPEC PTPRT/20q11 Dual Color Probe	CE/IVD	**Z-2213-50**	**98**
RARA	NR1B1, RAR	Zyto*Light* SPEC PML/RARA Dual Color Dual Fusion Probe	CE/IVD	**Z-2113-50/-200**	**84**
RB1	PPP1R130	Zyto*Light* SPEC RB1/13q34 Dual Color Probe	CE/IVD	**Z-2324-50/-200**	**80**
RET	HSCR1, CDHF12	Zyto*Light* SPEC RET Dual Color Break Apart Probe	CE/IVD	**Z-2148-50/-200**	**63**
RICTOR	AVO3, KIAA1999	Zyto*Light* SPEC RICTOR/5q31.1 Dual Color Probe	RUO	**Z-2278-200**	**113**
ROS1	MCF3, ROS	Zyto*Light* SPEC ROS1 Dual Color Break Apart Probe	CE/IVD	**Z-2144-50/-200**	**46**
		Zyto*Light* SPEC ROS1/CEN 6 Dual Color Probe	CE/IVD	**Z-2162-200**	**47**
RREB1	HNT	Zyto*Light* SPEC RREB1/MYB/CEN 6 Triple Color Probe	CE/IVD	**Z-2152-50/-200**	**45**
RUNX1	AML1, AMLCR1	Zyto*Light* SPEC RUNX1/RUNX1T1 Dual Color Dual Fusion Probe	CE/IVD	**Z-2112-50/-200**	**55**
		Zyto*Light* SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe	CE/IVD	**Z-2157-50/-200**	**75**
RUNX1T1	ETO, CDR, MTG8	Zyto*Light* SPEC RUNX1/RUNX1T1 Dual Color Dual Fusion Probe	CE/IVD	**Z-2112-50/-200**	**55**
SHANK3	prosap2	Zyto*Light* SPEC DiGeorge/Phelan McDermid Dual Color Probe	CE/IVD	**Z-2299-50**	**100**
SMARCB1	BAF47	Zyto*Light* SPEC SMARCB1/22q12 Dual Color Probe	CE/IVD	**Z-2178-50**	**102**
SNRPN	PWCR	Zyto*Light* SPEC Prader-Willi Dual Color Probe	CE/IVD	**Z-2318-50**	**82**
SOX2	ANOP3	Zyto*Light* SPEC SOX2/CEN 3 Dual Color Probe	RUO	**Z-2127-200**	**113**
SPI1	PU.1, SPI-A	Zyto*Light* SPEC SPI1 Dual Color Break Apart Probe	RUO	**Z-2291-50**	**110**
SS18	SYT, SSXT	Zyto*Light* SPEC SS18 Dual Color Break Apart Probe	CE/IVD	**Z-2097-50/-200**	**93**
		Zyto*Light* SPEC SS18/SSX1 TriCheck™ Probe	CE/IVD	**Z-2184-50**	**94**
SSX1	-	Zyto*Light* SPEC SS18/SSX1 TriCheck™ Probe	CE/IVD	**Z-2184-50**	**94**
TBL1XR1	IRA1	Zyto*Light* SPEC TP63/TBL1XR1 TriCheck™ Probe	CE/IVD	**Z-2320-50**	**37**
TCF3	E2A	Zyto*Light* SPEC TCF3/PBX1 Dual Color Dual Fusion Probe	CE/IVD	**Z-2308-50**	**27**
TERC	hTERC, TRC3	Zyto*Light* SPEC TERC/CEN 3 Dual Color Probe	RUO	**Z-2284-200**	**113**
TERT	EST2, TCS1	Zyto*Light* SPEC TERT Dual Color Break Apart Probe	CE/IVD	**Z-2273-50**	**41**
		Zyto*Light* SPEC TERT/5q31 Dual Color Probe	CE/IVD	**Z-2091-50/-200**	**41**
TFE3	TFEA	Zyto*Light* SPEC TFE3 Dual Color Break Apart Probe	CE/IVD	**Z-2109-50/-200**	**104**
TMPRSS2	PRSS10	Zyto*Light* SPEC ERG/TMPRSS2 TriCheck™ Probe	CE/IVD	**Z-2135-200**	**99**
TNFRSF14	HVEM	Zyto*Light* SPEC TNFRSF14/1q25 Dual Color Probe	RUO	**Z-2323-50**	**113**
TOP2A	TOP2	Zyto*Light* SPEC ERBB2/TOP2A/CEN 17 Triple Color Probe	CE/IVD	**Z-2093-50/-200**	**92**
TP53	LSF1, TRP53	Zyto*Light* SPEC TP53/17q22 Dual Color Probe	CE/IVD	**Z-2198-50**	**88**
		Zyto*Light* SPEC TP53/ATM Dual Color Probe	CE/IVD	**Z-2159-50/-200**	**71**
		Zyto*Light* SPEC TP53/CEN 17 Dual Color Probe	CE/IVD	**Z-2153-50/-200**	**89**

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TP63	TP73L	Zyto*Light* SPEC TP63/TBL1XR1 TriCheck™ Probe	CE/IVD	**Z-2320-50**	**37**
UBE3A	AS	Zyto*Light* SPEC Angelman Dual Color Probe	CE/IVD	**Z-2319-50**	**81**
USP6	Tre-2, TRE17	Zyto*Light* SPEC USP6 Dual Color Break Apart Probe	CE/IVD	**Z-2151-50/-200**	**89**
VEGFA	VEGF, VPF	Zyto*Light* SPEC VEGFA/CEN 6 Dual Color Probe	RUO	**Z-2195-200**	**46**
VHL	VHL1	Zyto*Light* SPEC VHL/CEN 3 Dual Color Probe	CE/IVD	**Z-2084-200**	**31**
		Zyto*Light* SPEC VHL/1p12/CEN 7/17 Quadruple Color Probe	CE/IVD	**Z-2102-200**	**32**
WT1	AWT1	Zyto*Light* SPEC WT1 Dual Color Break Apart Probe	CE/IVD	**Z-2142-50**	**66**
WWTR1	TAZ	Zyto*Light* SPEC WWTR1 Dual Color Break Apart Probe	CE/IVD	**Z-2212-50**	**35**
YWHAE	14-3-3 epsilon	Zyto*Light* SPEC YWHAE Dual Color Break Apart Probe	CE/IVD	**Z-2175-50**	**90**
ZNF384	CIZ	Zyto*Light* SPEC ZNF384 Dual Color Break Apart Probe	CE/IVD	**Z-2275-50**	**74**

ZytoLight® Glioma 1p/19q Probe Set

Intended Purpose

The ZytoLight Glioma 1p/19q Probe Set is intended to be used for the qualitative detection of deletions involving the human chromosomal region 1p36.31 as well as deletions involving the human chromosomal region 19q13.32-q13.33 in formalin-fixed, paraffin-embedded specimens, such as gliomas, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of gliomas and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The ZytoLight Glioma 1p/19q Probe Set is a set comprising two separate probes and a quenching solution:

- ZytoLight SPEC 1p36/1q25 Dual Color Probe (Prod. No. Z-2075-200)
- ZytoLight SPEC 19q13/19p13 Dual Color Probe (Prod. No. Z-2076-200)
- ZyBlack Quenching Solution (Prod. No. BS-0002-8)

The ZytoLight SPEC 1p36/1q25 Dual Color Probe (PL34) is composed of:

- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 1p36.31* (chr1:5,808,946-6,176,336) (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 1q25.3* (chr1:184,271,714-184,986,522) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

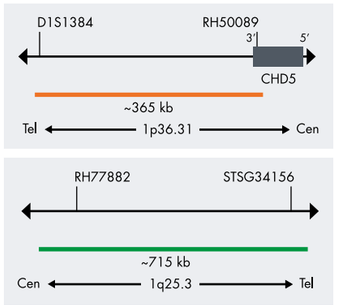
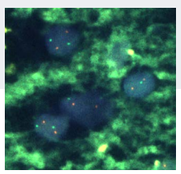


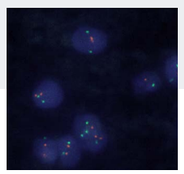
Fig. 1: Top: SPEC 1p36 Probe map; Bottom: SPEC 1q25 Probe map (not to scale)

Results

Normal situation: In interphases of normal cells or cells without a deletion involving the 1p36 locus, two green and two orange signals appear.
Aberrant situation: In a cell with deletion affecting the 1p36 locus, a reduced number of orange signals will be observed. Deletions affecting only parts of the 1p36 locus might result in a normal signal pattern with orange signals of reduced size.



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.

The ZytoLight SPEC 19q13/19p13 Dual Color Probe (PL35) is composed of:

- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 19q13.32-q13.33* (chr19:47,857,776-48,374,564) .
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10.0 ng/µl), which target sequences mapping in 19p13.3* (chr19:658,555-1,144,465) .
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

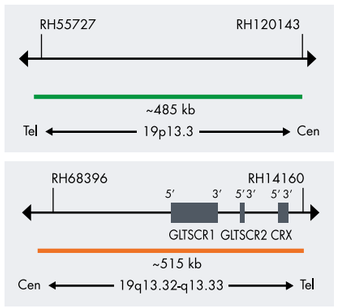


Fig. 2: Top: SPEC 19p13 Probe map; Bottom: SPEC 19q13 Probe map (not to scale)

Results

Normal situation: In interphases of normal cells or cells without a deletion involving the 19q13 locus, two green and two orange signals appear.
Aberrant situation: In a cell with deletions affecting the 19q13 locus, a reduced number of orange signals will be observed. Deletions affecting only parts of the 19q13 locus might result in a normal signal pattern with orange signals of reduced size.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	1, 19	CE/IVD	20	**Z-2272-20**

Includes 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

ZytoLight® SPEC 1p36/1q25 Dual Color Probe

Intended Purpose

The ZytoLight SPEC 1p36/1q25 Dual Color Probe (PL34) is intended to be used for the qualitative detection of deletions involving the human chromosomal region 1p36.31 as well as the detection of chromosome 1q25.3 specific sequences in formalin-fixed, paraffin-embedded specimens, such as glioma, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of glioma and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The ZytoLight SPEC 1p36/1q25 Dual Color Probe is composed of:

- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 1p36.31* (chr1:5,808,946-6,176,336) (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 1q25.3* (chr1:184,271,714-184,986,522) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

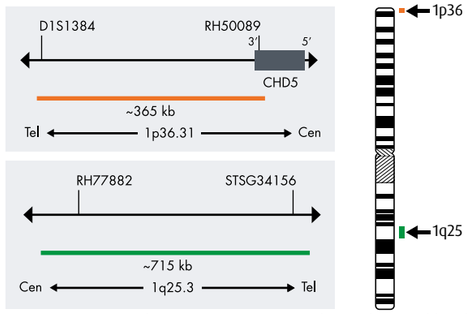
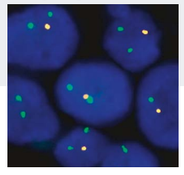


Fig. 1: Top: SPEC 1p36 Probe map; Bottom: SPEC 1q25 Probe map (not to scale); Right: Ideogram of chromosome 1 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a deletion involving the 1p36 locus, two orange signals and two green signals appear.
Aberrant situation: In a cell with deletion affecting the 1p36 locus, a reduced number of orange signals will be observed. Deletions affecting only parts of the 1p36 locus might result in a normal signal pattern with orange signals of reduced size.



Hybridized to a glioma tissue section with 1p36 deletion as indicated by one orange signal in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	1	CE/IVD	5 (50 µl)	**Z-2075-50**
			20 (200 µl)	**Z-2075-200**

ZytoLight® SPEC 19q13/19p13 Dual Color Probe

Intended Purpose

The ZytoLight SPEC 19q13/19p13 Dual Color Probe (PL35) is intended to be used for the qualitative detection of deletions involving the human chromosomal region 19q13.32-q13.33 as well as the detection of chromosome 19p13.3 specific sequences in formalin-fixed, paraffin-embedded specimens, such as glioma, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of glioma and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The ZytoLight SPEC 19q13/19p13 Dual Color Probe is composed of:

- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1.5 ng/µl), which target sequences mapping in 19q13.32-q13.33* (chr19:47,857,776-48,374,564) (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 19p13.3* (chr19:658,555-1,144,465) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

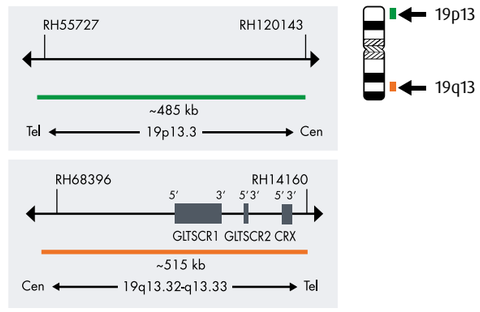
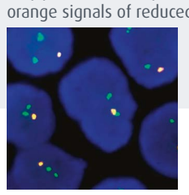


Fig. 1: Top: SPEC 19p13 Probe map; Bottom: SPEC 19q13 Probe map (not to scale); Right: Ideogram of chromosome 19 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a deletion involving the 19q13 locus, two orange signals and two green signals appear.
Aberrant situation: In a cell with deletion affecting the 19q13 locus, a reduced number of orange signals will be observed. Deletions affecting only parts of the 19q13 locus might result in a normal signal pattern with orange signals of reduced size.



Hybridized to a glioma tissue section with 19q13 deletion as indicated by one orange signal in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	19	CE/IVD	5 (50 µl)	**Z-2076-50**
			20 (200 µl)	**Z-2076-200**

ZytoLight® SPEC CKS1B/CDKN2C Dual Color Probe

Intended Purpose

The ZytoLight SPEC CKS1B/CDKN2C Dual Color Probe (PL232) is intended to be used for the qualitative detection of amplifications/gains involving the human CKS1B gene at 1q21.3-q22 and deletions involving the human CDKN2C gene at 1p32.3 in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The ZytoLight SPEC CKS1B/CDKN2C Dual Color Probe is composed of:

- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 1q21.3-q22* (chr1:154,722,168-155,144,639) harboring the CKS1B gene region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 1p32.3* (chr1:51,196,272-51,737,475) harboring the CDKN2C gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	1	CE/IVD	5 (50 µl)	**Z-2276-50**
			20 (200 µl)	**Z-2276-200**

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

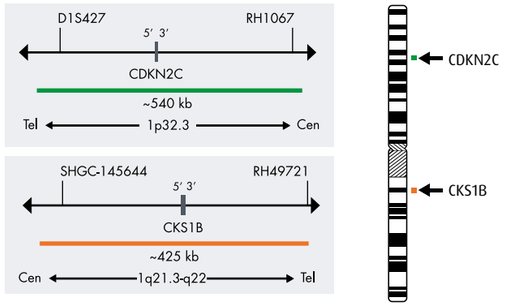
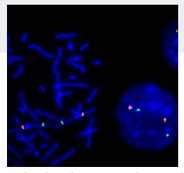


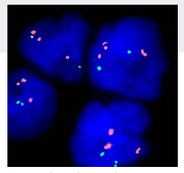
Fig. 1: Top: SPEC CDKN2C Probe map; Bottom: SPEC CKS1B Probe map (not to scale); Right: Ideogram of chromosome 1 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without an amplification/gain involving the CKS1B gene region or a deletion involving the CDKN2C gene region, two orange signals and two green signals appear.
Aberrant situation: In cells with an amplification/gain of the CKS1B gene region, an increased number of orange signals will be observed. In cells with deletion affecting the CDKN2C gene region, a reduced number of green signals will be observed. Deletions affecting only parts of the CDKN2C gene region might result in a normal signal pattern with green signals of reduced size.



Hybridized to normal interphase cells as indicated by two orange and two green signals and to metaphase chromosomes of a normal cell.



Example of an aberrant signal pattern: Bone marrow smear of a pediatric ALL case with amplification affecting the CKS1B locus as indicated by three or more orange signals.

ZytoLight® SPEC MCL1/1p12 Dual Color Probe

Intended Purpose

The ZytoLight SPEC MCL1/1p12 Dual Color Probe (PL129) is intended to be used for the qualitative detection of amplifications involving the human MCL1 gene as well as the detection of chromosome 1p12 specific sequences in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The ZytoLight MCL1/1p12 Dual Color Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 1q21.3* (chr1:150,363,209-150,940,432) harboring the MCL1 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 1p12* (chr1:119,537,102-119,823,147) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

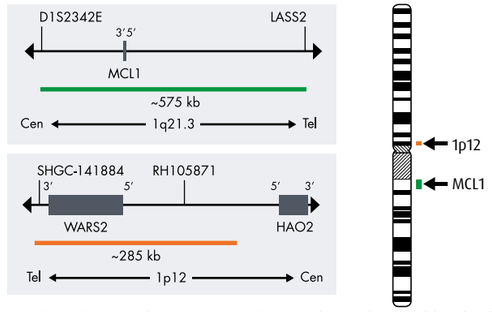


Fig. 1: Top: SPEC MCL1 Probe map; Bottom: SPEC 1p12 Probe map (not to scale); Right: Ideogram of chromosome 1 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without an amplification involving the MCL1 gene region, two green and two orange signals appear.
Aberrant situation: In cells with an amplification of the MCL1 gene region, an increased number of green signals or green signal clusters will be observed.

Example of an aberrant signal pattern: Paraffin-embedded H2110 cell line with interphase cells showing amplification of the MCL1 gene locus as indicated by multiple green signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	1	CE/IVD	20 (200 µl)	**Z-2173-200**

ZytoLight® SPEC NTRK1 Dual Color Break Apart Probe

Intended Purpose

The ZytoLight SPEC NTRK1 Dual Color Break Apart Probe (PL123) is intended to be used for the qualitative detection of translocations involving the human NTRK1 gene at 1q23.1 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The ZytoLight SPEC NTRK1 Dual Color Break Apart Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 1q22-q23.1* (chr1:156,245,849-156,781,745) proximal to the NTRK1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 1q23.1* (chr1:156,854,527-157,296,918) distal to the NTRK1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

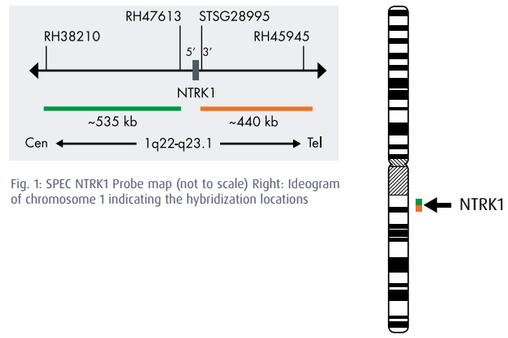
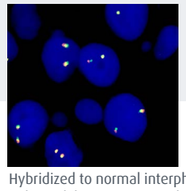


Fig. 1: SPEC NTRK1 Probe map (not to scale) Right: Ideogram of chromosome 1 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a translocation involving the NTRK1 gene region, two green/orange fusion signals appear.
Aberrant situation: One NTRK1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal. Isolated orange signals are the result of deletions proximal to the NTRK1 breakpoint region or are due to unbalanced translocations affecting this chromosomal region.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.

Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	1	CE/IVD	5 (50 µl)	**Z-2167-50**
			20 (200 µl)	**Z-2167-200**

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

ZytoLight® SPEC NECTIN4/1p12 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC NECTIN4/1p12 Dual Color Probe (PL291) is intended to be used for the qualitative detection of amplifications involving the human NECTIN4 gene as well as the detection of chromosome 1p12 specific sequences in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC NECTIN4/1p12 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 1q23.3* (Chr1:160,773,463-161,218,427) harboring the NECTIN4 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 1p12* (Chr1:119,537,102-119,823,147) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

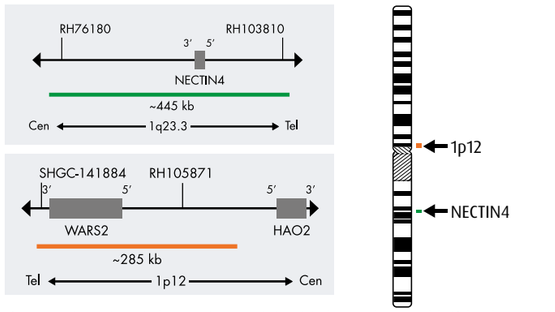
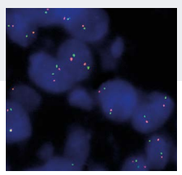
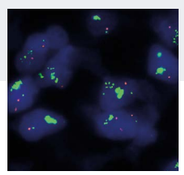


Fig. 1: Top: SPEC NECTIN4 Probe map; Bottom: SPEC 1p12 Probe map (not to scale); Right: Ideogram of chromosome 1 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the NECTIN4 gene region, two green signals and two orange signals appear.
Aberrant situation: In cells with an amplification of the NECTIN4 gene region, an increased number of green signals or green signal clusters will be observed.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Example of an aberrant signal pattern: Hybridized to urothelial carcinoma tissue section with amplification of the NECTIN4 gene as indicated by green signal clusters.

Labels	Chromosome	Reg. Status	Tests	Order No.
● | ●	1	CE/IVD	5 (50 µl)	**Z-2331-50**
			20 (200 µl)	**Z-2331-200**

ZytoLight® SPEC ABL2 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC ABL2 Dual Color Break Apart Probe (PL158) is intended to be used for the qualitative detection of translocations involving the human ABL2 gene at 1q25.2 in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC ABL2 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 1q25.2* (chr1:179,141,608-179,659,091) distal to the ABL2 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 1q25.2* (chr1:178,496,704-179,015,312) proximal to the ABL2 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

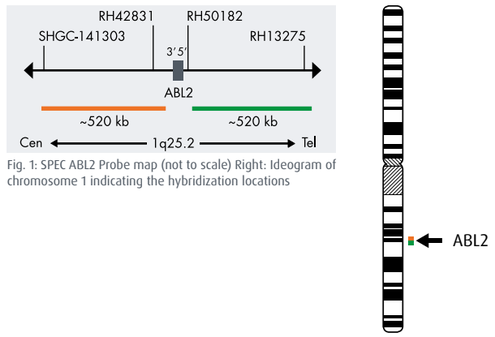
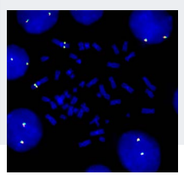
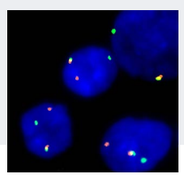


Fig. 1: SPEC ABL2 Probe map (not to scale) Right: Ideogram of chromosome 1 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the ABL2 gene region, two green/orange fusion signals appear.
Aberrant situation: One ABL2 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus and to metaphase chromosomes of a normal cell.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
● | ●	1	CE/IVD	5 (50 µl)	**Z-2200-50**

ZytoLight® SPEC TCF3/PBX1 Dual Color Dual Fusion Probe

Intended Purpose
The Zyto*Light* SPEC TCF3/PBX1 Dual Color Dual Fusion Probe is designed to detect rearrangements affecting the chromosomal region 19p13.3 harboring the TCF3 (transcription factor 3, a.k.a E2A) gene and the chromosomal region 1q23.3 harboring the PBX1 (PBX homeobox 1) gene.

TCF3 is the target of several known recurrent rearrangements in ALL that create TCF3 fusion proteins. The balanced t(1;19) (q23.3;p13.3) and the more common unbalanced der(19)t(1;19)(q23.3;p13.3), which occur in approximately 6% of pediatric B-ALL cases and in 20-25% of all pre-B-ALL cases, fuse the TCF3 gene to the PBX1 gene.

The t(17;19)(q22;p13.3) fuses TCF3 to the HLF gene in <1% of cases. TCF3-PBX1 and TCF3-HLF are chimeric transcription factors that contain the same portion of TCF3, including two transcriptional activation domains, fused to regions of PBX1 or HLF that contain unique DNA binding domains.

As a sole abnormality, t(1;19)/der(19)t(1;19) is associated with an intermediate prognosis. In the context of hyperdiploid B-ALL, this translocation is associated with a poor prognosis. TCF3-HLF fusion has an extremely poor prognosis.

In the revised 2016 WHO classification of myeloid neoplasms and acute leukemia, "B-lymphoblastic leukemia/lymphoma with t(1;19)(q23.3;p13.3);TCF3-PBX1" is classified as its own cytogenetic subgroup of ALL. Because more intensive therapy improves the outcome of patients with TCF3-PBX1 gene fusions, it is critical to identify this subset of patients so that appropriate therapy can be administered.

References
Arber DA, *et al.* (2016) Blood 127: 2391-405.
Boomer T, *et al.* (2001) Leukemia 15: 95-102.
Mellentin JD, *et al.* (1989) Science 246: 379-82.
Rowsey RA, *et al.* (2019) Blood Cancer J 9 :81.
Shearer BM, *et al.* (2005) Br J Haematol 129: 45-52.
Tirado CA, *et al.* (2015) Biomark Res 3: 4.

Probe Description
The Zyto*Light* SPEC TCF3/PBX1 Dual Color Dual Fusion Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~12.0 ng/µl), which target sequences mapping in 19p13.3* (chr19:1,152,432-2,233,487) harboring the TCF3 region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~6.0 ng/µl), which target sequences mapping in 1q23.3* (chr1:164,223,543-164,979,228) harboring the PBX1 gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

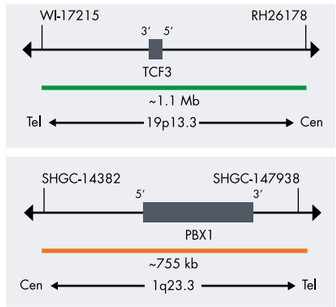
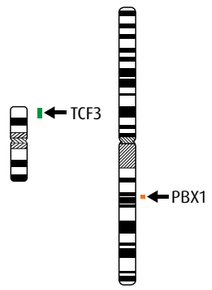


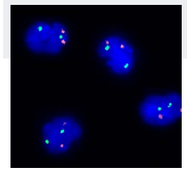
Fig. 1: Top: SPEC TCF3 Probe map; Bottom: SPEC PBX1 Probe map (not to scale)



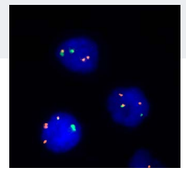
Left: Ideogram of chromosome 19 indicating the hybridization locations

Right: Ideogram of chromosome 1 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the respective gene regions, two separate green and orange signals appear.
Aberrant situation: A gene fusion is indicated by one separate green signal, one separate orange signal, and two green/orange fusion signals. A signal pattern showing one fusion signal, one separate green and two separate orange signals can occur due to an unbalanced translocation. Other relevant signal patterns may also be observed as a result of TCF3 rearrangements without the involvement of the PBX1 locus.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Bone marrow smear with rearrangement affecting the TCF3/PBX1 loci as indicated by two separate orange signals, one separate green signal, and one orange/green fusion signals.

Labels	Chromosome	Reg. Status	Tests	Order No.
● | ●	1, 19	CE/IVD	5 (50 µl)	**Z-2308-50**

ZytoLight® SPEC MDM4/1p12 Dual Color Probe

Intended Purpose

The Zyto*Light* SPEC MDM4/1p12 Dual Color Probe (PL39) is intended to be used for the qualitative detection of amplifications involving the human MDM4 gene as well as the detection of chromosome 1p12 specific sequences in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The Zyto*Light* MDM4/1p12 Dual Color Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 1q32.1* (chr1:204,126,022-204,882,307) harboring the MDM4 region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 1p12* (chr1:119,537,102-119,823,147) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

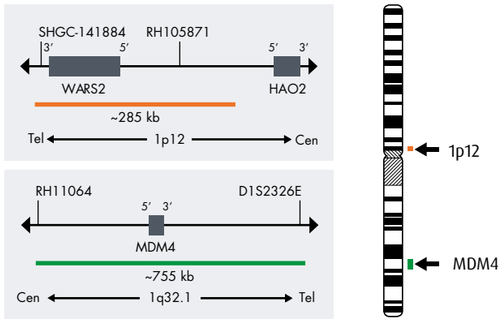
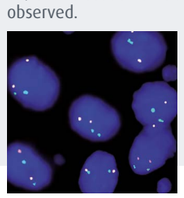


Fig. 1: Top: SPEC 1p12 Probe map; Bottom: SPEC MDM4 Probe map (not to scale) Right: Ideogram of chromosome 1 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without an amplification involving the MDM4 gene region, two green signals and two orange signals appear.
Aberrant situation: In cells with an amplification of the MDM4 gene region, an increased number of green signals or green signal clusters will be observed.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	1	CE/IVD	20 (200 µl)	**Z-2080-200**

ZytoLight® SPEC MYCN/2q11 Dual Color Probe

Intended Purpose

The Zyto*Light* SPEC MYCN/2q11 Dual Color Probe (PL33) is intended to be used for the qualitative detection of amplifications involving the human MYCN gene as well as the detection of chromosome 2q11 specific sequences in formalin-fixed, paraffin-embedded specimens, such as neuroblastoma and medulloblastoma, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of neuroblastoma and medulloblastoma and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The Zyto*Light* MYCN/2q11 Dual Color Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 2p24.3* (chr2:15,846,046-16,517,671) harboring the MYCN gene region.
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 2q11.2* (chr2:100.132,806-100,621,725).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

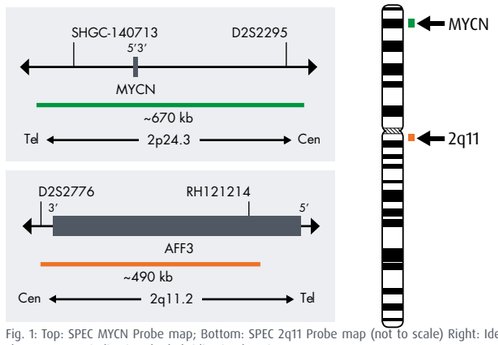


Fig. 1: Top: SPEC MYCN Probe map; Bottom: SPEC 2q11 Probe map (not to scale) Right: Ideogram of chromosome 2 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without an amplification involving the MYCN gene region, two green and two orange signals appear.
Aberrant situation: In cells with an amplification of the MYCN gene region, an increased number of green signals or green signal clusters will be observed.

Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	2	CE/IVD	5 (50 µl)	**Z-2074-50**
			20 (200 µl)	**Z-2074-200**

ZytoLight® SPEC ALK/EML4 TriCheck™ Probe

Intended Purpose

The Zyto*Light* SPEC ALK/EML4 TriCheck Probe (PL74) is intended to be used for the qualitative detection of rearrangements involving the human ALK gene at 2p23.1-p23.2 and the human EML4 gene at 2p21 in formalin-fixed, paraffin-embedded specimens, such as non-small cell lung cancer (NSCLC), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of NSCLC and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The Zyto*Light* SPEC ALK/EML4 TriCheck Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 2p23.1-p23.2* (chr2:29,460.144-30,095,822) proximal to the ALK breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 2p23.2* (chr2:29,174,204-29,383,335) distal to the ALK breakpoint region (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~37,0 ng/µl), which target sequences mapping in 2p21* (chr2:41,573,525-43,349,624) harboring the EML4 gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

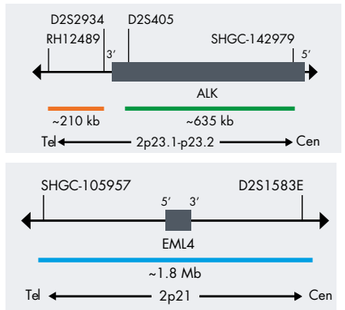
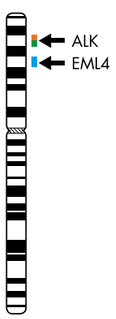


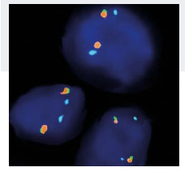
Fig. 1: Top: SPEC ALK Probe map; Bottom: SPEC EML4 Probe map (not to scale)



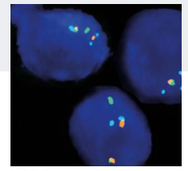
Ideogram of chromosome 2 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells without rearrangement of the EML4-ALK gene region, two orange/green fusion signals and two blue signals appear.
Aberrant situation: An EML4-ALK inversion is indicated by one separate green signal, one separate orange signal, and an additional blue signal. The separate green and orange signal each co-localize with a blue signal. An ALK translocation not affecting EML4 is indicated by separated orange and green signals without an additional blue signal. An 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 an additional 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	2	CE/IVD	5 (50 µl)	**Z-2117-50**
			20 (200 µl)	**Z-2117-200**

ZytoLight® SPEC ALK Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC ALK Dual Color Break Apart Probe (PL81) is intended to be used for the qualitative detection of translocations involving the human ALK gene at 2p23.1-p23.2 in formalin-fixed, paraffin-embedded specimens, such as non-small cell lung cancer (NSCLC), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of NSCLC and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC ALK Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 2p23.1-p23.2* (chr2:29,460.144-30,095,822) proximal to the ALK breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 2p23.2* (chr2:29,174,204-29,383,335) distal to the ALK breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

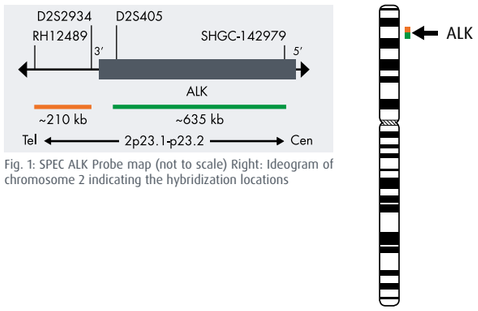
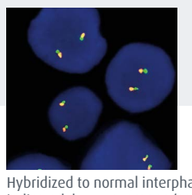
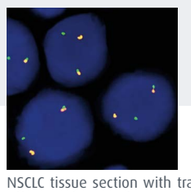


Fig. 1: SPEC ALK Probe map (not to scale) Right: Ideogram of chromosome 2 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the ALK gene region, two green/orange fusion signals appear.
Aberrant situation: One ALK gene region affected by a translocation is indicated by one separate green signal and one separate orange signal. An EML4-ALK inversion with deletion of 5′-ALK sequences is indicated by one or multiple isolated orange signals.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



NSCLC 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	2	CE/IVD	5 (50 µl)	**Z-2124-50**
			20 (200 µl)	**Z-2124-200**

ZytoLight® SPEC ALK/2q11 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC ALK/2q11 Dual Color Probe (PL117) is intended to be used for the qualitative detection of amplifications involving the human ALK gene as well as the detection of chromosome 2q11 specific sequences in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* ALK/2q11 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 2p23.1-p23.2* (chr2:29,460.144-30,095,822) harboring the ALK region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 2q11.2* (chr2:100.132,806-100,621,725) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

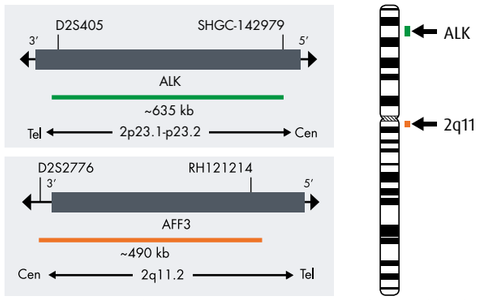
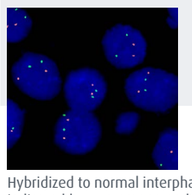
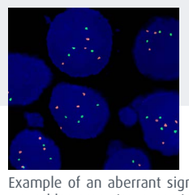


Fig. 1: Top: SPEC ALK Probe map; Bottom: SPEC 2q11 Probe map (not to scale) Right: Ideogram of chromosome 2 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the ALK gene region, two green and two orange signals appear.
Aberrant situation: In cells with an amplification of the ALK gene region, an increased number of green signals or green signal clusters will be observed.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



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

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	2	CE/IVD	20 (200 µl)	**Z-2161-200**

ZytoLight® SPEC IGK Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC IGK Dual Color Break Apart Probe (PL243) is intended to be used for the qualitative detection of translocations involving the human IGK locus at 2p11.2 in cytologic or formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with Zyto*Light* FISH Implementation Kits (Prod. No. Z-2028-5/-20, or Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC IGK Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 2p11.2* (chr2:88,382,616-89,153,517) distal to the IGK breakpoint region (see Fig.1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 2p11.2* (chr2:89,246,977-89,609,390 and chr2:89,853,315-90,089,156) proximal to the IGK breakpoint region (see Fig. 1). Due to homologous sequence segments proximal to the IGK breakpoint region, the orange probe has two hybridization regions in close proximity.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

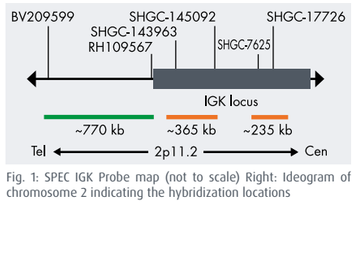


Fig. 1: SPEC IGK Probe map (not to scale) Right: Ideogram of chromosome 2 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving IGK locus, two green/orange fusion signals appear. Due to the two hybridization regions of the orange probe, orange signals may appear as paired signal dots.
Aberrant situation: One IGK locus affected by a translocation is indicated by one separate green signal and one separate orange signal. Due to the two hybridization regions of the orange probe, orange signals may appear as paired signal dots.

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.

Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	2	CE/IVD	20 (200 µl)	**Z-2288-50**

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

ZytoLight® SPEC VHL/CEN 3 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC VHL/CEN 3 Dual Color Probe (PL43) is intended to be used for the qualitative detection of deletions involving the human VHL gene and the detection of chromosome 3 alpha satellites in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC VHL/CEN 3 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 3p25.3* (chr3:10,051,220-10.598,496) harboring the VHL gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1,5 ng/µl), which target sequences mapping in 3p11.1-q11.1 specific for the alpha satellite centromeric region D3Z1 of chromosome 3.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

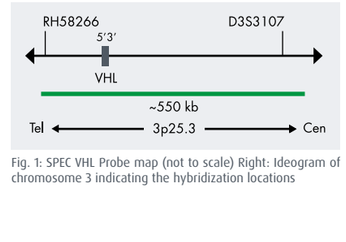
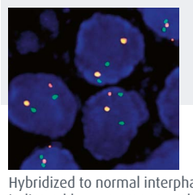
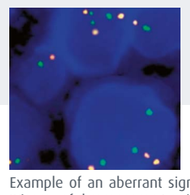


Fig. 1: SPEC VHL Probe map (not to scale) Right: Ideogram of chromosome 3 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the VHL gene region, two green and two orange signals appear.
Aberrant situation: In a cell with deletion of the VHL gene region, a reduced number of green signals will be observed. Deletions affecting only parts of the VHL gene region might result in a normal signal pattern with green signals of reduced size.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Example of an aberrant signal pattern: Trisomy of chromosome 3 as indicated by three orange (CEN3) and three green (VHL) signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	3	CE/IVD	20 (200 µl)	**Z-2084-200**

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

Intended Purpose

The Zyto*Light* SPEC VHL/1p12/CEN 7/17 Quadruple Color Probe (PL60) is intended to be used for the qualitative detection of deletions involving the human VHL gene as well as chromosome 1p12 specific sequences, and chromosome 7 and 17 alpha satellites in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description

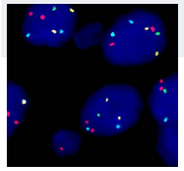
The Zyto*Light* SPEC VHL/1p12/7/17 Quadruple Color Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 3p25.3* (chr3:10,051,220-10.598,496) harboring the VHL region (see Fig. 1).
- ZyRed (excitation 580 nm/emission 599 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 1p12* (chr1:119,537,102-119,823,147).
- ZyGold (excitation 532 nm/emission 553 nm) labeled polynucleotides (~7 ng/µl), which target sequences mapping in 7p11.1-q11.1 specific for the alpha satellite centromeric region D7Z1 of chromosome 7.
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~12 ng/µl), which target sequences mapping in 17p11.1-q11.1 specific for the alpha satellite centromeric region D17Z1 of chromosome 17.
- Formamide based hybridization buffer

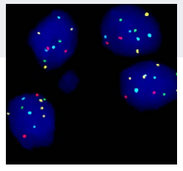
* according to Human Genome Assembly GRCh37/hg19

Results

Normal situation: In interphases of normal cells or cells without aberration involving the respective gene regions, two green, two red, two gold, and two blue signals are expected.
Aberrant situation: In a cell with deletion affecting the VHL gene region, a reduced number of green signals will be observed. Deletions affecting only parts of the VHL gene region might result in a normal signal pattern with green signals of reduced size. In cells with aneusomy of chromosome 1, 7, or 17, more or less signals of the respective color will be visible.



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



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●|●	1, 3, 7, 17	CE/IVD	20 (200 µl)	**Z-2102-200**

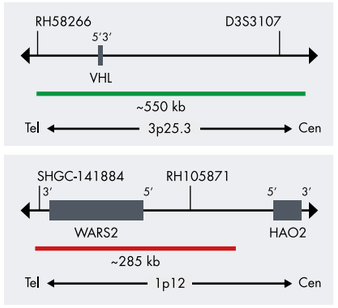
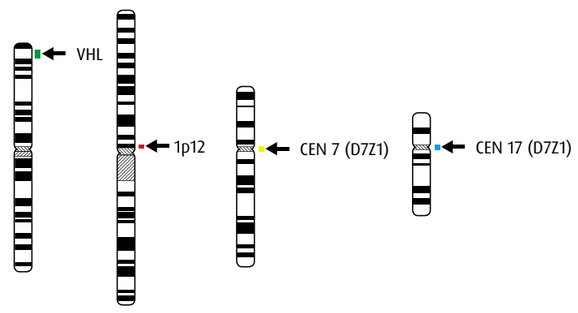


Fig. 1: Top: SPEC VHL Probe map; Bottom: SPEC 1p12 Probe map (not to scale)



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

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

Intended Purpose

The Zyto*Light* SPEC CCND1 Break Apart/2q11/CEN 6 Quadruple Color Probe (PL75) is intended to be used for the qualitative detection of translocations involving the human CCND1 gene at 11q13.3 as well as for the detection of human chromosome 2q11 specific sequences as well as chromosome 6 alpha satellites in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description

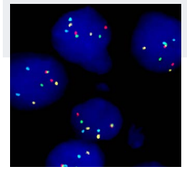
The Zyto*Light* SPEC CCND1 Break Apart/2q11/CEN 6 Quadruple Color Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 11q13.2-q13.3* (chr11:68,249,010-68,705,283) proximal to CCND1 breakpoint region (see Fig. 1).
- ZyRed (excitation 580 nm/emission 599 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 11q13.3* (chr11:69,453,301-70,031,240) distal to the CCND1 breakpoint region (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~37,0 ng/µl), which target sequences mapping in 2q11.2* (chr2:100.132,806-100,621,725) (see Fig. 1).
- ZyGold (excitation 532 nm/emission 553 nm) labeled polynucleotides (~7 ng/µl), which target sequences mapping in 6p11.1-q11 specific for the alpha satellite centromeric region D6Z1 of chromosome 6.
- Formamide based hybridization buffer

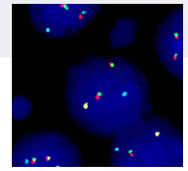
* according to Human Genome Assembly GRCh37/hg19

Results

Normal situation: In interphases of normal cells or cells without a translocation involving the CCND1 gene region, two red/green fusion signals, two blue and two gold signals appear.
Aberrant situation: In a cell with translocation of the CCND1 gene region, a signal pattern consisting of one red/green fusion signal, one red, and a separate green signal indicates one normal CCND1 gene region and one CCND1 gene region 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.



Example of an aberrant signal pattern: 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.



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

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●|●	2, 6, 11	CE/IVD	20 (200 µl)	**Z-2118-200**

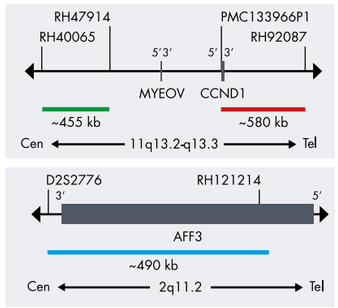
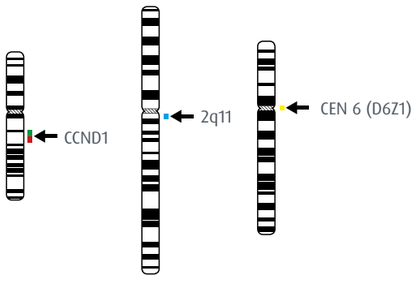


Fig. 1: Top: SPEC CCND1 Probe map; Bottom: SPEC 2q11 Probe map (not to scale)



Ideograms of chromosome 11, 2 and 6 indicating the hybridization locations

ZytoLight® Bladder Cancer Quadruple Color Probe

Intended Purpose
The Zyto*Light* Bladder Cancer Quadruple Color Probe is designed to detect CDKN2A (a.k.a. p16) deletions and aneuploidy of chromosomes 3, 7, and 17 in cytology specimens of tumors, e.g., in urine samples from patients with hematuria suspected of having bladder cancer (BC).

Moreover, it has been shown that the detection of CDKN2A deletions and/or aneusomies of chromosomes 3, 7, and/or 17 may be used for the surveillance of patients with a history of bladder cancer to early detect possible tumor recurrence.

BC represents the ninth most common cancer worldwide. About 430,000 new BC cases and 165,000 BC deaths occurred in 2012. Most of these tumors are non-invasive, well-differentiated, papillary tumors (pTa, low grade) and can be cured by endoscopic transurethral resection.

However, up to 70% of pTa and superficially invasive (pT1) tumors recur and of these, 15-30% are characterized by tumor progression. Therefore, a long-term follow-up of patients with BC is necessary.

The two standard methods used in the follow-up are either invasive (cystoscopy) or have a low sensitivity (cytology). BC cells are characterized by typical cytogenetic changes. Homozygous deletion of the CDKN2A gene at 9p21.3 and polysomy of chromosomes 3, 7, and/or 17 are common abnormalities observed in urothelial cell carcinoma, all of which can be detected by FISH. FISH on cells from urine has been shown to be highly sensitive and specific for detection of tumor cells in urine.

References
Antoni S, *et al.* (2017) Eur Urol 71: 96-108.
Dimashkieh H, *et al.* (2013) Cancer Cytopathol 121: 591-7.
Junker K, *et al.* (2006) Cytogenet Genome Res 114: 279-83.
Placer J, *et al.* (2002) Eur Urol 42: 547-52.

Probe Description
The Zyto*Light* Bladder Cancer Quadruple Color Probe is composed of:
- ZyGold (excitation 532 nm/emission 553 nm) labeled polynucleotides (~5,5 ng/µl), which target sequences mapping in 9p21.3* (chr9:21,742,619-22,056,863) harboring the CDKN2A gene region (see Fig. 1).
- ZyRed (excitation 580 nm/emission 599 nm) labeled polynucleotides (~0.5 ng/µl), which target sequences mapping in 3p11.1-q11.1 specific for the alpha satellite centromeric region D3Z1 of chromosome 3.
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 7p11.1-q11.1 specific for the alpha satellite centromeric region D7Z1 of chromosome 7.
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~12,0 ng/µl), which target sequences mapping in 17p11.1-q11.1 specific for the alpha satellite centromeric region D17Z1 of chromosome 17.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

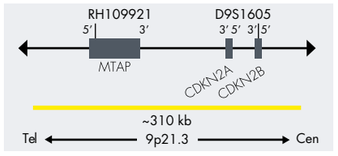
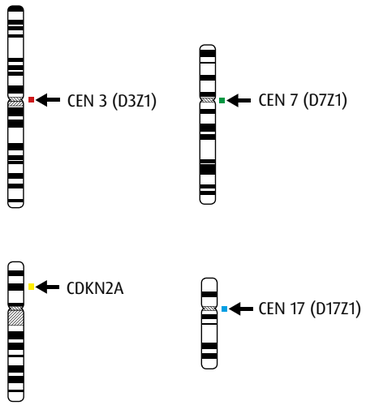
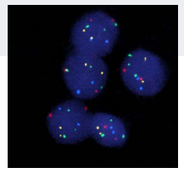


Fig. 1: SPEC CDKN2A Probe map (not to scale)



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

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the CDKN2A gene region, two gold, two red, two green, and two blue signals are expected.
Aberrant situation: In a cell with deletion of the CDKN2A gene region, a reduced number of gold signals will be observed. Deletions affecting only parts of the CDKN2A gene region might result in a normal signal pattern with gold signals of reduced size. In cells with aneusomy of chromosomes 3, 7, or 17, more or less signals of the respective color will be visible.


Interphase tumor cells with trisomy of chromosome 7 as indicated by three green signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
	3, 7, 9, 17	CE/IVD	5 (50 µl)	**Z-2305-50**
			20 (200 µl)	**Z-2305-200**

ZytoLight® SPEC WWTR1 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* 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
Underson 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 Zyto*Light* SPEC WWTR1 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 3q24-q25.1* (chr3:148,533,200-149,234,601) proximal to the WWTR1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 3q25* (chr3:149,430,325-149,933,565) distal to the WWTR1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

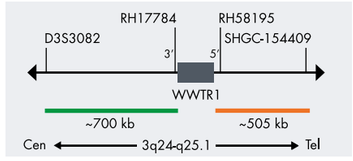
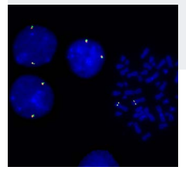
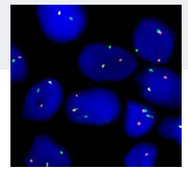


Fig. 1: SPEC WWTR1 Probe map (not to scale)

Ideogram of chromosome 3 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the WWTR1 gene region, two green/orange fusion signals appear.
Aberrant situation: One WWTR1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.


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.

Labels	Chromosome	Reg. Status	Tests	Order No.
	3	CE/IVD	5 (50 µl)	**Z-2212-50**

ZytoLight® SPEC GATA2/MECOM Dual Color Dual Fusion Probe

Intended Purpose

The Zyto*Light* SPEC GATA2/MECOM Dual Color Dual Fusion Probe (PL242) is intended to be used for the qualitative detection of the translocation t(3;3)(q21.3;q26.2) as well as the inversion inv(3)(q21.3q26.2) involving the human GATA2 and MECOM genes in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The Zyto*Light* SPEC GATA2/MECOM Dual Color Dual Fusion Probe is composed of:

- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~6,0 ng/µl), which target sequences mapping in 3q21.3* (chr3:127,902,316-128,564,215) harboring the GATA2 gene region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~12,0 ng/µl), which target sequences mapping in 3q26.2* (chr3:168,249,484-169,743,447) harboring the MECOM gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

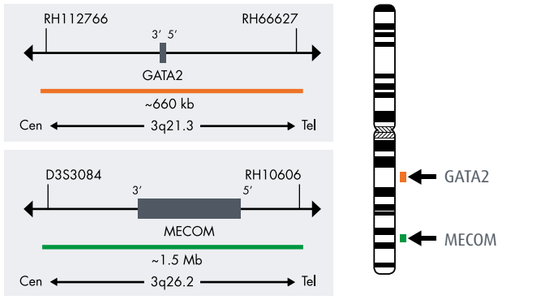
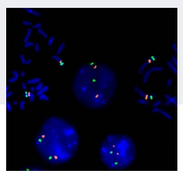


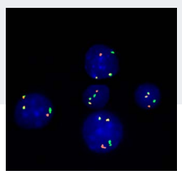
Fig. 1: Top: SPEC GATA2 Probe map; Bottom: SPEC MECOM Probe map (not to scale); Right: Ideogram of chromosome 3 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a translocation involving the respective gene regions, two separate green and orange signals appear.
Aberrant situation: A gene fusion is indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals. Three green signals and two orange signals are the result of a translocation affecting the MECOM gene region without the involvement of the GATA2 locus.



Hybridized to normal interphase cells as indicated by two orange and two green signals and to metaphase chromosomes of a normal cell.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	3	CE/IVD	5 (50 µl)	**Z-2287-50**

ZytoLight® SPEC PIK3CA/CEN 3 Dual Color Probe

Intended Purpose

The Zyto*Light* SPEC PIK3CA/CEN 3 Dual Color Probe (PL97) is intended to be used for the qualitative detection of amplifications involving the human PIK3CA gene as well as the detection of chromosome 3 alpha satellites in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The Zyto*Light* SPEC PIK3CA/CEN 3 Dual Color Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 3q26.32-q26.33* (chr3:178,535,986-179,293,464) harboring the PIK3CA gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1,5 ng/µl), which target sequences mapping in 3p11.1-q11.1 specific for the alpha satellite centromeric region D3Z1 of chromosome 3.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

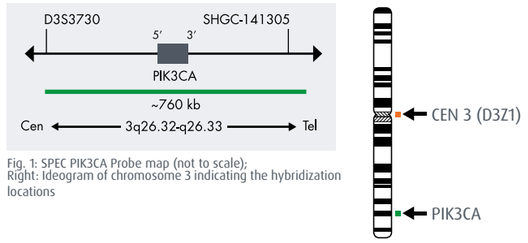
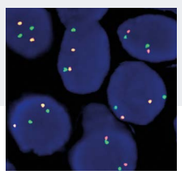


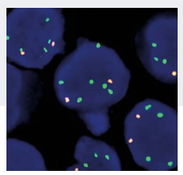
Fig. 1: SPEC PIK3CA Probe map (not to scale); Right: Ideogram of chromosome 3 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without an amplification involving the PIK3CA gene region, two green and two orange signals appear.
Aberrant situation: In cells with an amplification of the PIK3CA gene region, an increased number of green signals or green signal clusters will be observed.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Example of an aberrant signal pattern: Human breast cancer cell line with amplification of the PIK3CA gene as indicated by multiple green signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	3	CE/IVD	20 (200 µl)	**Z-2140-200**

ZytoLight® SPEC TP63/TBL1XR1 TriCheck™ Probe

Intended Purpose

The Zyto*Light* SPEC TP63/TBL1XR1 TriCheck™ Probe (PL274) is intended to be used for the qualitative detection of rearrangements involving the human TP63 gene at 3q28 and the human TBL1XR1 gene at 3q26.32 in formalin-fixed, paraffin-embedded specimens by fluorescence*in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

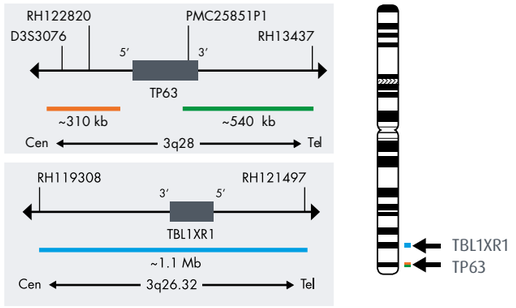
Interpretation of the results must be made within the context of the patient´s clinical history with respect to further clinical and pathologic data of the patient by a qualified pathologist.

Probe Description

The Zyto*Light* SPEC TP63/TBL1XR1 TriCheck™ Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10.0 ng/µl), which target sequences mapping in 3q28* (chr3:189,559,557-190,097,196) distal to the TP63 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 3q28* (chr3:188,995,562-189,305,431) proximal to the TP63 breakpoint region (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~37.0 ng/µl), which target sequences mapping in 3q26.32* (chr3:176,217,831-177,284,492) harboring the TBL1XR1 gene region (see Fig. 1).
- Formamide based hybridization buffer

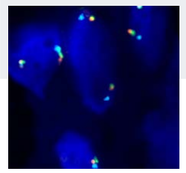
* according to Human Genome Assembly GRCh37/hg19



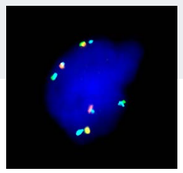
Top: SPEC TP63 Probe map; Bottom: SPEC TBL1XR1 Probe map (not to scale); Right: Ideogram of chromosome 3 indicating the hybridization locations

Results

Normal situation: In nterphases of normal cells without rearrangement of the TBL1XR1-TP63 gene region, two orange/green fusion signals and two blue signals appear.
Aberrant situation: A TBL1XR1-TP63 inversion is indicated by one separate green signal, one separate orange signal, and an additional blue signal. The separate green and orange signal each co-localize with a blue signal. A TP63 translocation not affecting TBL1XR1 is indicated by separated orange and green signals without an additional blue signal.



Hybridized to normal interphase cells with non-rearranged TP63 loci (two orange/green fusion signals), and non-rearranged TBL1XR1 loci (two blue signals).



T-cell lymphoma cell line with a TBL1XR1-TP63 inversion as indicated by separate green signals, separate orange signals, each co-localizing with a blue signal.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	3	CE/IVD	5 (50 µl)	**Z-2320-50**

ZytoLight® SPEC BCL6 Dual Color Break Apart Probe

Intended Purpose

The Zyto*Light* SPEC BCL6 Dual Color Break Apart Probe (PL136) is intended to be used for the qualitative detection of translocations involving the human BCL6 gene at 3q27.3 in formalin-fixed, paraffin-embedded specimens, such as B-cell lymphoma, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of B-cell lymphoma and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The Zyto*Light* SPEC BCL6 Dual Color Break Apart Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 3q27.3* (chr3:186,737,897-187,403,834) proximal to the BCL6 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 3q27.3-q28* (chr3:187,744,962-188,097,195) distal to the BCL6 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

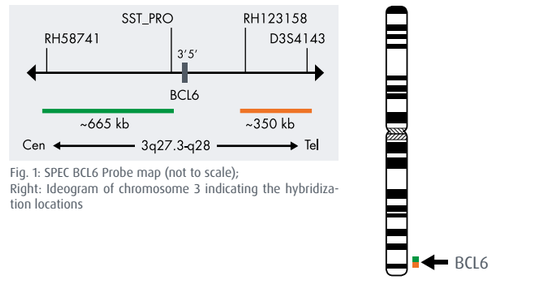
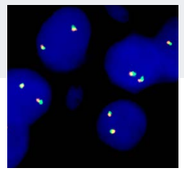


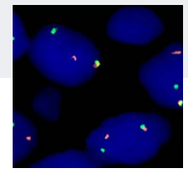
Fig. 1: SPEC BCL6 Probe map (not to scale); Right: Ideogram of chromosome 3 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a translocation involving the BCL6 gene region, two green/orange fusion signals appear.
Aberrant situation: One BCL6 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	3	CE/IVD	5 (50 µl)	**Z-2177-50**
			20 (200 µl)	**Z-2177-200**

ZytoLight® SPEC FGFR3 Dual Color Break Apart Probe

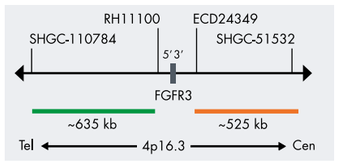
Intended Purpose
The Zyto*Light* SPEC FGFR3 Dual Color Break Apart Probe (PL126) is intended to be used for the qualitative detection of translocations involving the human FGFR3 gene at 4p16.3 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC FGFR3 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 4p16.3* (chr4:1,093,149-1,729,455) distal to the FGFR3 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 4p16.3* (chr4:1,922,997-2,446,931) proximal to the FGFR3 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



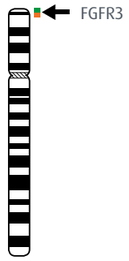
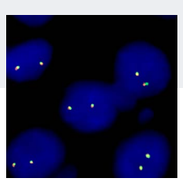


Fig. 1: SPEC FGFR3 Probe map (not to scale); Right: Ideogram of chromosome 4 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the FGFR3 gene region, two green/orange fusion signals appear.
Aberrant situation: One FGFR3 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.

Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	4	CE/IVD	5 (50 µl)	**Z-2170-50**
			20 (200 µl)	**Z-2170-200**

ZytoLight® SPEC FGFR3/4p11 Dual Color Probe

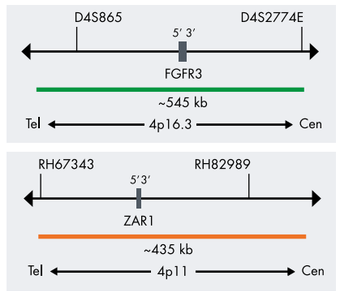
Intended Purpose
The Zyto*Light* SPEC FGFR3/4p11 Dual Color Probe (PL41) is intended to be used for the qualitative detection of amplifications involving the human FGFR3 gene as well as the detection of chromosome 4p11 specific sequences in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* FGFR3/4p11 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 4p16.3* (chr4:1,531,083-2,073,649) harboring the FGFR3 region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 4p11* (chr4:48,329,914-48,762,386) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



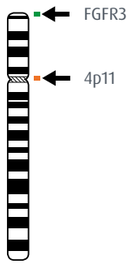
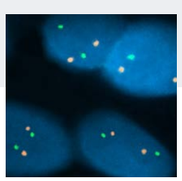
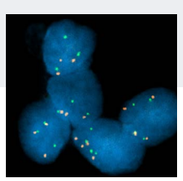


Fig. 1: Top: SPEC FGFR3 Probe map; Bottom: SPEC 4p11 Probe map (not to scale); Right: Ideogram of chromosome 4 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the FGFR3 gene region, two green signals and two orange signals appear.
Aberrant situation: In cells with an amplification of the FGFR3 gene region, an increased number of green signals or green signal clusters will be observed.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



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

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	4	CE/IVD	20 (200 µl)	**Z-2082-200**

ZytoLight® SPEC FGFR3/IGH Dual Color Dual Fusion Probe

Intended Purpose
The Zyto*Light* 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).

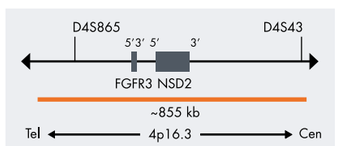
FGFR3/IGH translocations are observed in approximately 15–20% of patients with MM. The breaking points for the 4p16.3 locus are found between the FGFR3 gene and the 5′ end of the NSD2 gene. The t(4;14)(p16.3;q32.3) translocation is associated with upregulation of the FGFR3 and the myeloma NSD2 (a.k.a. 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.

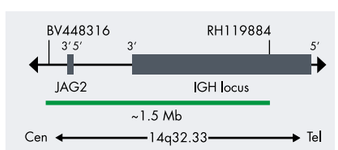
With conventional cytogenetics, the t(4;14)(p16.3;q32.3) translocation is difficult to identify. Thus, the detection of FGFR3/IGH translocations by fluorescence *in situ* hybridization may be of diagnostic and prognostic relevance.

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 Zyto*Light* SPEC FGFR3/IGH Dual Color Dual Fusion Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~6 ng/µl), which target sequences mapping in 4p16.3* (chr4:1,496,938-2,351,657) harboring the FGFR3 region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~12,0 ng/µl), which target sequences mapping in 14q32.33* (chr14:105,462,169-106,995,000) harboring the IGH locus (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19





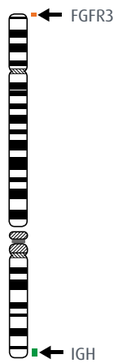
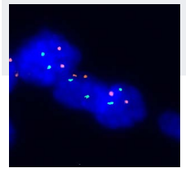


Fig. 1: Top: SPEC FGFR3 Probe map; Bottom: SPEC IGH Probe map (not to scale); Right: Ideograms of chromosome 4 and 14 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the respective gene regions, two separate orange and green signals appear.
Aberrant situation: A gene fusion is indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	4, 14	CE/IVD	5 (50 µl)	**Z-2282-50**

ZytoLight® SPEC 4p11/CEN 10/17 Triple Color Probe

Intended Purpose
The ZytoLight SPEC 4p11/CEN 10/17 Triple Color Probe (PL261) is intended to be used for the qualitative detection of human chromosome 4p11 specific sequences as well as alpha satellites of chromosomes 10 and 17 in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC 4p11/CEN 10/17 Triple Color Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 4p11* (chr4:48,329,914-48,762,386) (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 10p11.1-q11.1 specific for the alpha satellite centromeric region D10Z1 of chromosome 10.
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~12 ng/µl), which target sequences mapping in 17p11.1-q11.1 specific for the alpha satellite centromeric region D17Z1 of chromosome 17.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

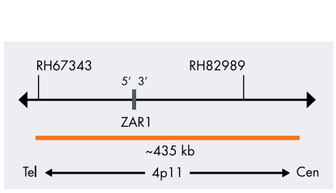
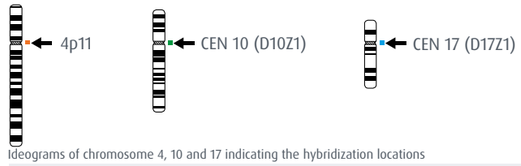


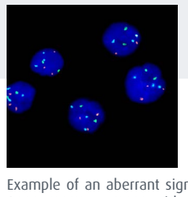
Fig. 1: SPEC 4p11 Probe map (not to scale)



Ideograms of chromosome 4, 10 and 17 indicating the hybridization locations

Results
Normal situation: In nterphases of normal cells or cells without an alteration of the respective chromosomes, two green, two orange, and two blue signals appear.
Aberrant situation: In a cell with aneusomy of the chromosomes 4, 10, and/or 17, an increased or a reduced number of signals of the respective color will be observed.

Hybridized to normal interphase cells as indicated by two orange, two green, and two blue signals in each nucleus and to metaphase chromosomes of a normal cell.



Example of an aberrant signal pattern: Bone marrow smear with trisomy of chromosome 4 and 17 as indicated by three orange and blue signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	4, 10, 17	CE/IVD	5 (50 µl)	**Z-2307-50**

ZytoLight® SPEC PDGFRA/FIP1L1 TriCheck™ Probe

Intended Purpose
The ZytoLight SPEC PDGFRA/FIP1L1 TriCheck Probe (PL167) is intended to be used for the qualitative detection of rearrangements involving the human PDGFRA gene with and without participation of the human FIP1L1 gene in cytological specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC PDGFRA/FIP1L1 TriCheck Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 4q12* (chr4:53,552,536-54,238,252) proximal to the FIP1L1 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 4q12* (chr4:54,351,156-54,749,671) proximal to the PDGFRA gene region (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~37,0 ng/µl), which target sequences mapping in 4q12* (chr4:55,185,968-55,915,442) distal to the PDGFRA gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

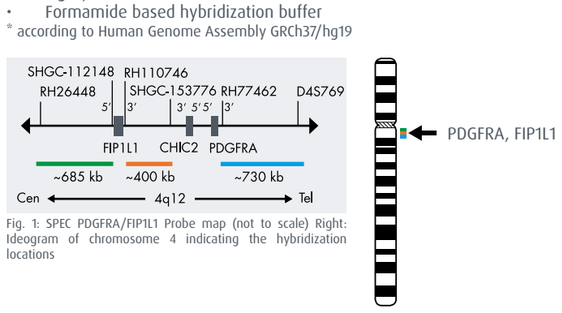
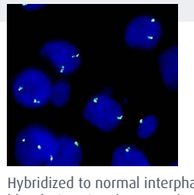


Fig. 1: SPEC PDGFRA/FIP1L1 Probe map (not to scale) Right: Ideogram of chromosome 4 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without PDGFRA-FIP1L1 rearrangements, two green/orange fusion signals appear when using an appropriate dual bandpass filter set, and two blue signals appear when using an appropriate single bandpass filter set. When using an appropriate triple color bandpass filter set, two green/orange/blue fusion signals can be observed.
Aberrant situation: A PDGFRA-FIP1L1 fusion resulting from a deletion of interstitial DNA is indicated by the loss of one orange signal leading to a separate green signal co-localizing with a blue signal. A PDGFRA translocation without involvement of FIP1L1 is indicated by a green/orange fusion signal and a separate blue signal.



Hybridized to normal interphase cells as indicated by two tricolor orange/green/blue fusion signals per nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	4	CE/IVD	5 (50 µl)	**Z-2209-50**

ZytoLight® SPEC TERT Dual Color Break Apart Probe

Intended Purpose
The ZytoLight SPEC TERT Dual Color Break Apart Probe (PL229) is intended to be used for the qualitative detection of translocations involving the human TERT gene in 5p15.33 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC TERT Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 5p15.33* (chr5:620.184-1,161,456) distal to the TERT breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 5p15.33* (chr5:1,353,007-1,588,209) proximal to the TERT breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

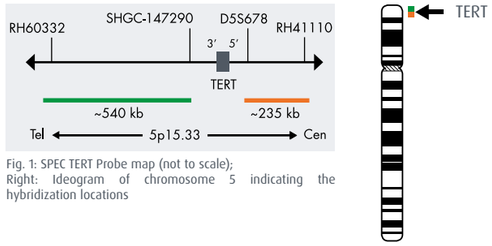
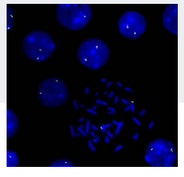


Fig. 1: SPEC TERT Probe map (not to scale); Right: Ideogram of chromosome 5 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the TERT gene region, two green/orange fusion signals appear.
Aberrant situation: One TERT gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals in each nucleus and to metaphase chromosomes of a normal cell.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	5	CE/IVD	5 (50 µl)	**Z-2273-50**

ZytoLight® SPEC TERT/5q31 Dual Color Probe

Intended Purpose
The ZytoLight SPEC TERT/5q31 Dual Color Probe (PL50) is intended to be used for the qualitative detection of amplifications involving the human TERT gene as well as the detection of chromosome 5q31 specific sequences in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight TERT/5q31 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 5p15.33* (chr5:974,089-1,588,209) harboring the TERT region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 5q31.2* (chr5:137,394,637-137,999,163) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

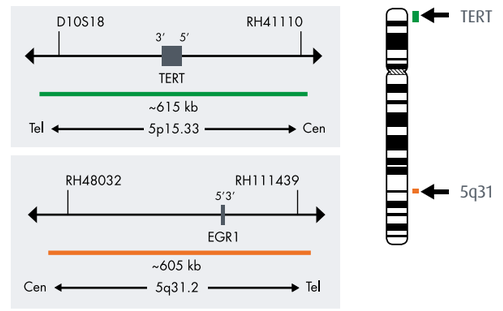
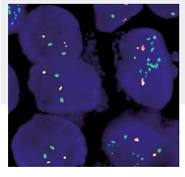


Fig. 1: Top: SPEC TERT Probe map; Bottom: SPEC 5q31 Probe map (not to scale); Right: Ideogram of chromosome 5 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the TERT gene region, two green signals and two orange signals appear.
Aberrant situation: In cells with an amplification of the TERT gene region, an increased number of green signals or green signal clusters will be observed.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	5	CE/IVD	5 (50 µl)	**Z-2091-50**
			20 (200 µl)	**Z-2091-200**

ZytoLight® SPEC EGR1/D5S23,D5S721 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC EGR1/D5S23,D5S721 Dual Color Probe (PL169) is intended to be used for the qualitative detection of deletions involving the human EGR1 gene as well as the detection of the human D5S23,D5S721 control region at 5p15.2-p15.31 in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC EGR1/D5S23,D5S721 Dual Color Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 5q31.2* (chr5:137,667,079-137,897,109) harboring the EGR1 region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 5p15.2-p15.31* (chr5:9,233,775-9,967,465) harboring the D5S23,D5S721 locus.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

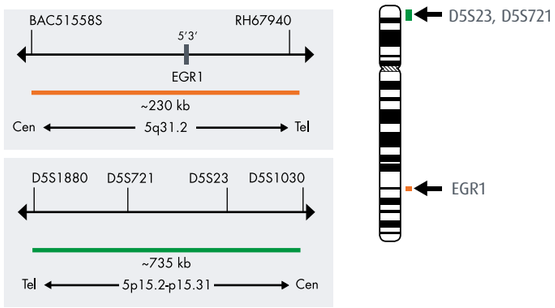
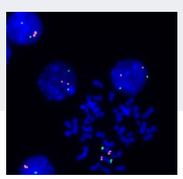
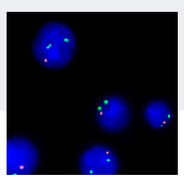


Fig. 1: Top: SPEC EGR1 Probe map; Bottom: SPEC D5S23,D5S721 Probe map (not to scale); Right: Ideogram of chromosome 5 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the EGR1 gene region, two green and two orange signals appear.
Aberrant situation: In a cell with deletion affecting the EGR1 gene region, a reduced number of orange signals will be observed. Deletions affecting only parts of the EGR1 gene region might result in a normal signal pattern with orange signals of reduced size.



Hybridized to normal interphase calls as indicated by two orange and two green signals and to metaphase chromosomes of a normal cell.



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

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	5	CE/IVD	5 (50 µl)	**Z-2211-50**

ZytoLight® SPEC CSF1R Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* 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 Zyto*Light* SPEC CSF1R Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 5q32-q33.1* (chr5:149,548,518-150.118,449) distal to the CSF1R breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 5q32* (chr5:149,058,515-149,421,081) proximal to the CSF1R breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

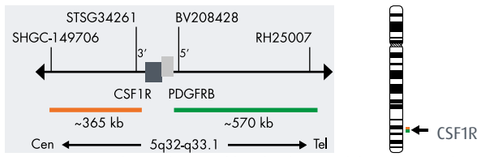
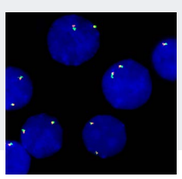
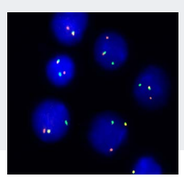


Fig. 1: SPEC CSF1R Probe map (not to scale); Right: Ideogram of chromosome 5 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the CSF1R gene region, two green/orange fusion signals appear.
Aberrant situation: One CSF1R gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	5	CE/IVD	5 (50 µl)	**Z-2202-50**

ZytoLight® SPEC CSF1R/D5S23,D5S721 Dual Color Probe

Intended Purpose
The Zyto*Light* 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.

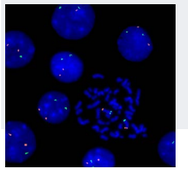
One candidate gene for the development of MDS in patients with 5q-syndrome is RPS14 (ribosomal protein 14), a tumor suppressor gene located in the chromosomal region 5q33.1. Haploinsufficiency (caused by hemizygous deletion) of RPS14 is the probable cause of the erythroid defect that characterizes the 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%) transfor*mation* risk to acute myeloid leukemia (AML). Therefore, FISH may be a helpful tool for diagnosis and therapy decision.

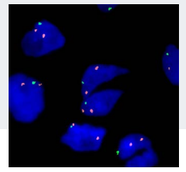
References
Boultwood J, *et al.* (1991) Proc Natl Acad Sci U S A 88: 6176-80.
Boultwood J, *et al.* (2010) Blood 116: 5803-11.
Giagounidis AA, *et al.* (2004) Clin Cancer Res 12: 5-10.
Van den Berghe H & Michaux JL (1974) Nature 251: 437-8.
Swerdlow SH, *et al.* (ed.) (2008) WHO classification of tumours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

Probe Description
The Zyto*Light* SPEC CSF1R/D5S23,D5S721 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 5q32-q33.1* (chr5:149,274,320-149,913,159) harboring the CSF1R region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 5p15.2-p15.31* (chr5:9,233,775-9,967,465) harboring the D5S23,D5S721 locus (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	5	CE/IVD	5 (50 µl)	**Z-2268-50**

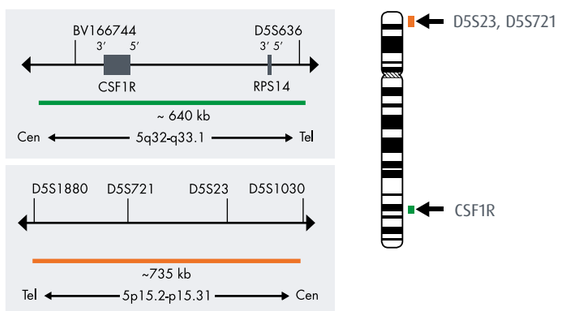


Fig. 1: Top: SPEC CSF1R Probe map; Bottom: SPEC D5S23,D5S721 Probe map (not to scale); Right: Ideogram of chromosome 5 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the CSF1R gene region, two green and two orange signals appear.
Aberrant situation: In a cell with deletion affecting the CSF1R gene region, a reduced number of green signals will be observed. Deletions affecting only parts of the CSF1R gene region might result in a normal signal pattern with green signals of reduced size.

ZytoLight® SPEC PDGFRB Dual Color Break Apart Probe

Intended Purpose
The ZytoLight SPEC PDGFRB Dual Color Break Apart Probe (PL155) is intended to be used for the qualitative detection of translocations involving the human PDGFRB gene at 5q32 in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC PDGFRB Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 5q32-q33.1* (chr5:149,548,518-150,285,722) distal to the PDGFRB breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 5q32* (chr5:149,058,515-149,471,369) proximal to the PDGFRB breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

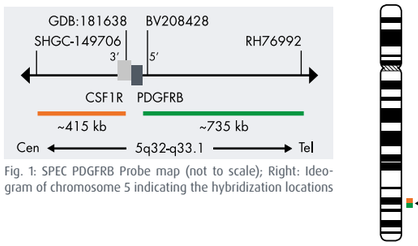
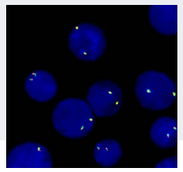


Fig. 1: SPEC PDGFRB Probe map (not to scale); Right: Ideogram of chromosome 5 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the PDGFRB gene region, two green/orange fusion signals appear.
Aberrant situation: One PDGFRB gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	5	CE/IVD	5 (50 µl)	**Z-2197-50**

ZytoLight® SPEC IRF4,DUSP22 Dual Color Break Apart Probe

Intended Purpose
The ZytoLight SPEC IRF4,DUSP22 Dual Color Break Apart Probe (PL168) is intended to be used for the qualitative detection of translocations involving the human IRF4,DUSP22 gene region at 6p25.3 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC IRF4,DUSP22 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 6p25.3* (chr6:557,233-940,968) proximal to the IRF4,DUSP22 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 6p25.3* (chr6:114,722-273,908) distal to the IRF4,DUSP22 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

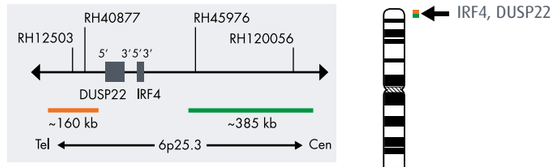
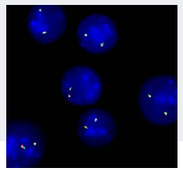
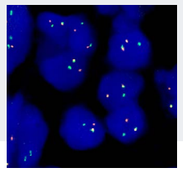


Fig. 1: SPEC IRF4,DUSP22 Probe map (not to scale); Right: Ideogram of chromosome 6 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the IRF4,DUSP22 gene region, two green/orange fusion signals appear.
Aberrant situation: One IRF4,DUSP22 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	6	CE/IVD	5 (50 µl)	**Z-2210-50**
			20 (200 µl)	**Z-2210-200**

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

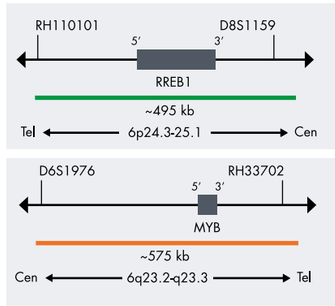
Intended Purpose
The ZytoLight SPEC RREB1/MYB/CEN 6 Triple Color Probe (PL108) is intended to be used for the qualitative detection of amplifications involving the human RREB1 gene as well as the human MYB gene and the detection of chromosome 6 alpha satellites in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC RREB1/MYB/CEN 6 Triple Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 6p24.3-p25.1* (chr6:6,913,938-7,406,653) harboring the RREB1 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 6q23.2-q23.3* (chr6:135,141,227-135,715,246) harboring the MYB region (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~12,0 ng/µl), which target sequences mapping in 6p11.1-q11 specific for the alpha satellite centromeric region D6Z1 of chromosome 6.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



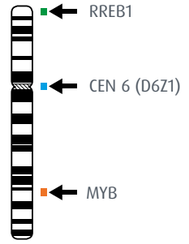
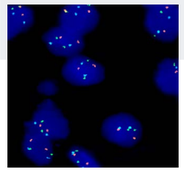


Fig. 1: Top: SPEC RREB1 Probe map; Bottom: SPEC MYB Probe map (not to scale); Right: Ideogram of chromosome 6 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the respective gene regions, two green, two orange, and two blue signals are expected.
Aberrant situation: In cells with an amplification of the RREB1 gene region or the MYB gene region, an increased number of green or orange signals will be observed, respectively. In a cell with deletions of the RREB1 gene region or the MYB gene region, a reduced number of green or orange signals will be observed, respectively. Deletions affecting only parts of the gene regions might result in a normal signal pattern with signals of reduced size.



Hybridized to normal interphase cells as indicated by two green, two orange, and two blue signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	6	CE/IVD	5 (50 µl)	**Z-2152-50**
			20 (200 µl)	**Z-2152-200**

ZytoLight® SPEC PHF1 Dual Color Break Apart Probe

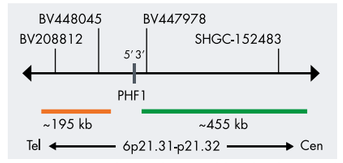
Intended Purpose
The ZytoLight SPEC PHF1 Dual Color Break Apart Probe (PL173) is intended to be used for the qualitative detection of translocations involving the human PHF1 gene at 6p21.32 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC PHF1 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 6p21.31-p21.32* (chr6:33,406,580-33,863,564) proximal to the PHF1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 6p21.32* (chr6:33,121,529-33,317,357) distal to the PHF1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



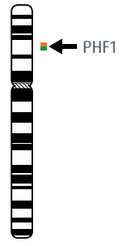
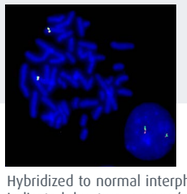


Fig. 1: SPEC PHF1 Probe map (not to scale); Right: Ideogram of chromosome 6 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the PHF1 gene region, two green/orange fusion signals appear.
Aberrant situation: One PHF1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus and to metaphase chromosomes of a normal cell.

Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	6	CE/IVD	5 (50 µl)	**Z-2215-50**

ZytoLight® SPEC VEGFA/CEN 6 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC VEGFA/CEN 6 Dual Color Probe (PL153) is intended to be used for the qualitative detection of amplifications involving the human VEGFA gene as well as the detection of chromosome 6 alpha satellites in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

Probe Description
The Zyto*Light* SPEC VEGFA/CEN 6 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 6p21.1* (chr6:43,633,271-43,985,142) harboring the VEGFA gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1,5 ng/µl), which target sequences mapping in 6p11.1-q11 specific for the alpha satellite centromeric region D6Z1 of chromosome 6.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

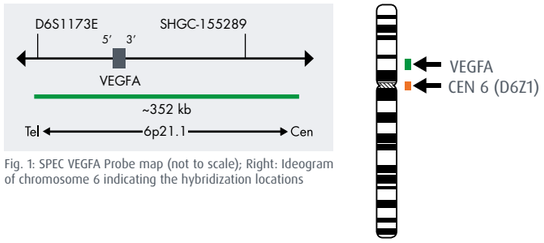
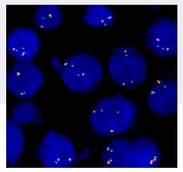
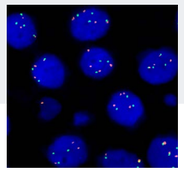


Fig. 1: SPEC VEGFA Probe map (not to scale); Right: Ideogram of chromosome 6 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the VEGFA gene region, two green and two orange signals appear.
Aberrant situation: In cells with an amplification of the VEGFA gene region, an increased number of green signals or green signal clusters will be observed.



Hybridized to normal interphase calls as indicated by two orange and two green signals in each nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	6	RUO	20 (200 µl)	**Z-2195-200**

ZytoLight® SPEC ROS1 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC ROS1 Dual Color Break Apart Probe (PL101) is intended to be used for the qualitative detection of translocations involving the human ROS1 gene at 6q22.1 in formalin-fixed, paraffin-embedded specimens, such as non-small cell lung cancer (NSCLC), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of NSCLC and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC ROS1 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 6q22.1* (chr6:116,912,298-117,627,255) proximal to the ROS1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 6q22.1* (chr6:117,659,135-117,871,701) distal to the ROS1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

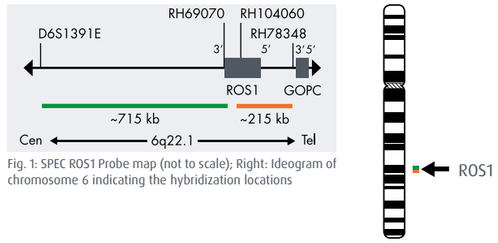
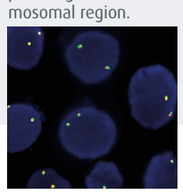
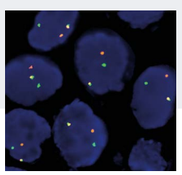


Fig. 1: SPEC ROS1 Probe map (not to scale); Right: Ideogram of chromosome 6 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the ROS1 gene region, two green/orange fusion signals appear.
Aberrant situation: One ROS1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal. Isolated green signals are the result of deletions distal to the ROS1 breakpoint region or are due to unbalanced translocations affecting this chromosomal region.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	6	CE/IVD	5 (50 µl)	**Z-2144-50**
			20 (200 µl)	**Z-2144-200**

ZytoLight® SPEC ROS1/CEN 6 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC ROS1/CEN 6 Dual Color Probe (PL118) is intended to be used for the qualitative detection of amplifications involving the human ROS1 gene as well as the detection of chromosome 6 alpha satellites in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC ROS1/CEN 6 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 6q22.1* (chr6:117,431,278-117,894,830) harboring the ROS1 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1,5 ng/µl), which target sequences mapping in 6p11.1-q11 specific for the alpha satellite centromeric region D6Z1 of chromosome 6.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

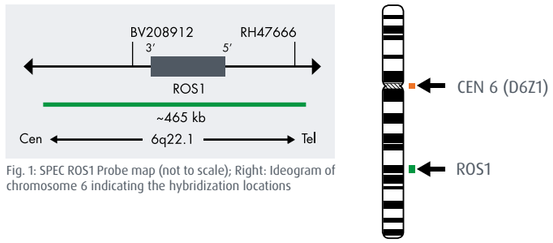
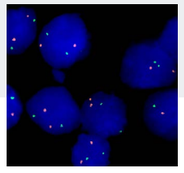
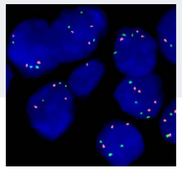


Fig. 1: SPEC ROS1 Probe map (not to scale); Right: Ideogram of chromosome 6 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the ROS1 gene region, two green and two orange signals appear.
Aberrant situation: In cells with an amplification of the ROS1 gene region, an increased number of green signals or green signal clusters will be observed.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	6	CE/IVD	20 (200 µl)	**Z-2162-50**

ZytoLight® SPEC MYB Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC MYB Dual Color Break Apart Probe (PL100) is intended to be used for the qualitative detection of translocations involving the human MYB gene at 6q23.3 in cytologic or formalin-fixed, paraffin-embedded specimens, such as adenoid cystic carcinoma (ACC), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with Zyto*Light* FISH Implementation Kits (Prod. No. Z-2028-5/-20, or Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of ACC and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC MYB Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 6q23.2-q23.3* (chr6:134,840,690-135,483,752) proximal to the MYB breakpoint region (see Fig.1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 6q23.3* (chr6:135,728,667-136,390.142) distal to the MYB breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

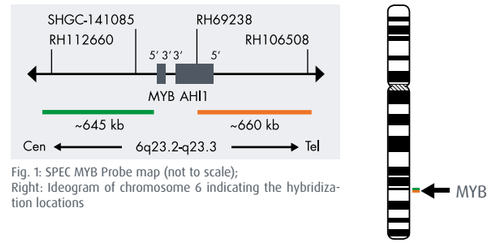
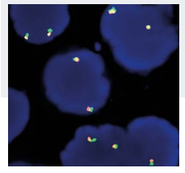
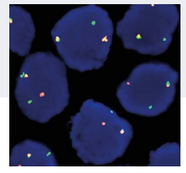


Fig. 1: SPEC MYB Probe map (not to scale);
Right: Ideogram of chromosome 6 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the MYB gene region, two green/orange fusion signals appear.
Aberrant situation: One MYB gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	6	CE/IVD	5 (50 µl)	**Z-2143-50**
			20 (200 µl)	**Z-2143-200**

ZytoLight® SPEC MYB/CEN 6 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC MYB/CEN 6 Dual Color Probe (PL236) is intended to be used for the qualitative detection of deletions involving the human MYB gene and the detection of chromosome 6 alpha satellites in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC MYB/CEN 6 Dual Color Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 6q23.2-q23.3* (chr6:135,141,227-135,715,246) harboring the MYB gene region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 6p11.1-q11 specific for the alpha satellite centromeric region D6Z1 of chromosome 6.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

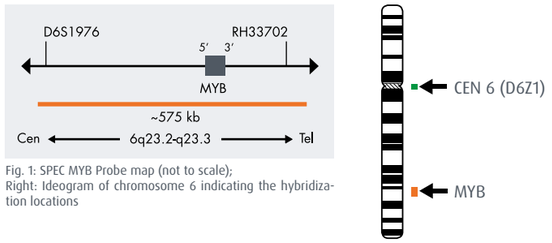
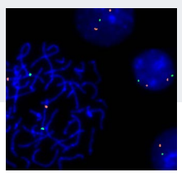
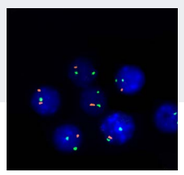


Fig. 1: SPEC MYB Probe map (not to scale); Right: Ideogram of chromosome 6 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the MYB gene region, two green and two orange signals appear.
Aberrant situation: In a cell with deletions affecting the MYB gene region, a reduced number of orange signals will be observed. Deletions affecting only parts of the MYB gene region might result in a normal signal pattern with orange signals of reduced size.



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.



Example of an aberrant signal pattern: Blood smear with deletion of the MYB gene as indicated by one orange signal in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	6	CE/IVD	5 (50 µl)	**Z-2281-50**

ZytoLight® SPEC ESR1/CEN 6 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC ESR1/CEN 6 Dual Color Probe (PL27) is intended to be used for the qualitative detection of amplifications involving the human ESR1 gene as well as the detection of chromosome 6 alpha satellites in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* ESR1/CEN 6 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 6q25.1* (chr6:152,083,365-152,478,947) harboring the ESR1 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1,5 ng/µl), which target sequences mapping in 6p11.1-q11 specific for the alpha satellite centromeric region D6Z1 of chromosome 6.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

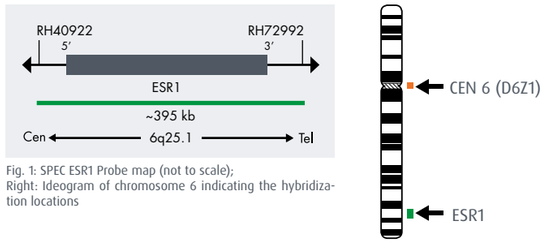
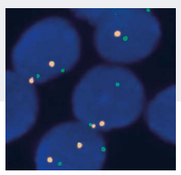
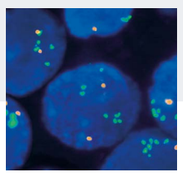


Fig. 1: SPEC ESR1 Probe map (not to scale); Right: Ideogram of chromosome 6 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the ESR1 gene region, two green and two orange signals appear.
Aberrant situation: In cells with an amplification of the ESR1 gene region, an increased number of green signals or green signal clusters will be observed.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Example of an aberrant signal pattern: ESR1 gene amplification as indicated by mutiple green ESR1 specific signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	6	CE/IVD	5 (50 µl)	**Z-2069-50**

ZytoLight® SPEC JAZF1 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC JAZF1 Dual Color Break Apart Probe (PL89) is intended to be used for the qualitative detection of translocations involving the human JAZF1 gene at 7p15.1-p15.2 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC JAZF1 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 7p15.2* (chr7:27,146,601-27,846,497) distal to the JAZF1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 7p15.1* (chr7:28,059,911-28,661,819) proximal to the JAZF1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

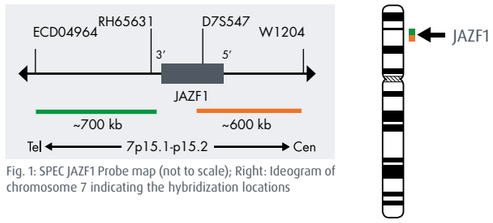
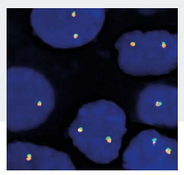
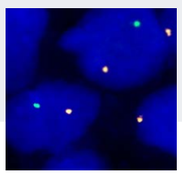


Fig. 1: SPEC JAZF1 Probe map (not to scale); Right: Ideogram of chromosome 7 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the JAZF1 gene region, two green/orange fusion signals appear.
Aberrant situation: One JAZF1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	7	CE/IVD	5 (50 µl)	**Z-2132-50**

ZytoLight® SPEC IKZF1/CEN 7 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC IKZF1/CEN 7 Dual Color Probe is designed for the detection of deletions affecting the IKZF1 (IKAROS family zinc finger 1, a.k.a. ZNFN1A1, IKAROS) gene.

The IKZF1 gene is located on 7p12.2 and encodes a zinc finger transcription factor, which is required for normal hematopoietic differentiation and proliferation, particularly in lymphoid lineages.

Genomic deletions affecting the IKZF1 gene are found in approximately 15% of pediatric and ~40% of adult B-cell precursor acute lymphoblastic leukemia (B-ALL) cases. The frequency is remarkably high in BCR-ABL1-positive (~70%) and BCR-ABL1-like (~40%) pediatric B-ALL. IKZF1 deletions were also identified in the progression of chronic myeloid leukemia to lymphoid blast crisis.

The most frequent deletions in B-ALL affect the whole gene or exons 4 to 7. Deletions affecting other exons (i.e., exons 2 to 7, exons 2 to 8, and exons 4 to 8) were also observed. IKZF1 deletions are associated with poor prognosis and high risk of relapse in cases of B-ALL. Hence, the detection of IKZF1 deletions by FISH may help in predicting the clinical outcome in patients with B-ALL.

References
Boer JM, *et al.* (2016) Leukemia 30: 32-8.
Hashiguchi J, *et al.* (2018) J Mol Diagn 20: 446-54.
Iacobucci I, *et al.* (2009) Blood 114: 2159-67.
Meyer C, *et al.* (2013) Am J Blood Res 3: 165-73.
Mullighan CG, *et al.* (2008) Nature 453: 110-4.

Probe Description
The Zyto*Light* SPEC IKZF1/CEN 7 Dual Color Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 7p12.2* (chr7:50,412,912-50,463,612) harboring the IKZF1 gene region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 7p11.1-q11.1 specific for the alpha satellite centromeric region D7Z1 of chromosome 7.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

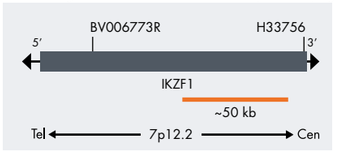
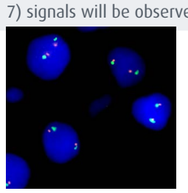


Fig. 1: SPEC IKZF1 Probe map (not to scale); Right: Ideogram of chromosome 7 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the IKZF1 gene region, two orange signals and two green signals appear.
Aberrant situation: In a cell with deletion affecting the IKZF1 gene region, a reduced number of orange signals will be observed. Deletions affecting only parts of the IKZF1 gene region might result in a normal signal pattern with orange signals of reduced size. In a cell with monosomy 7, a reduced number of both, the orange (IKZF1 gene region) and green (CEN 7) signals will be observed.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	7	CE/IVD	5 (50 µl)	**Z-2304-50**

ZytoLight® SPEC EGFR/CEN 7 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC EGFR/CEN 7 Dual Color Probe (PL15) is intended to be used for the qualitative detection of amplifications involving the human EGFR gene as well as the detection of chromosome 7 alpha satellites in formalin-fixed, paraffin-embedded specimens, such as non-small cell lung cancer (NSCLC) and glioma, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of NSCLC and glioma and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC EGFR/CEN 7 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 7p11.2* (chr7:54,912,555-55,548,375) harboring the EGFR gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1,5 ng/µl), which target sequences mapping in 7p11.1-q11.1 specific for the alpha satellite centromeric region D7Z1 of chromosome 7.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

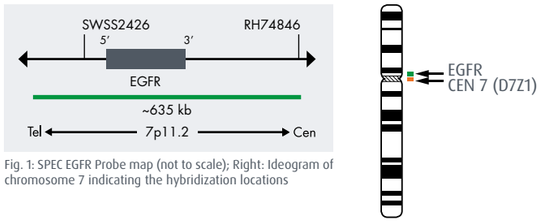
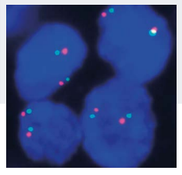
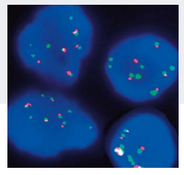


Fig. 1: SPEC EGFR Probe map (not to scale); Right: Ideogram of chromosome 7 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the EGFR gene region, two green and two orange signals appear.
Aberrant situation: In cells with an amplification of the EGFR gene region, multiple copies of the green signal or green signal clusters will be observed.



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 a sample from an NSCLC patient.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	7	CE/IVD	5 (50 µl)	**Z-2033-50**
			20 (200 µl)	**Z-2033-200**

ZytoLight® SPEC Williams-Beuren Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC Williams-Beuren Dual Color Probe is designed to detect deletions affecting the chromosomal region 7q11.23 harboring the ELN (elastin, a.k.a. WBS) gene.

The Williams-Beuren syndrome (WBS) is a genetic disorder caused by a hemizygous contiguous gene deletion on chromosome 7q11.23. The estimated prevalence of the disease ranges between 1/7,500 and 1/20,000 newborns. The WBS deletion region (~1.5-1.8 Mb) consists of a single copy gene region containing app. 28 genes, including the ELN gene that is flanked by repetitive sequences known as low-copy repeats (LCRs).

The deletions arise as a consequence of misalignment of these repetitive sequences during meiosis and a following unequal crossing over due to high similarity of LCRs. Usually, WBS occurs sporadically, but some parents of WBS patients were shown to carry a paracentric inversion of the WBS locus. Presence of this inversion predisposes to chromosomal mispairing in meiosis. WBS patients clinically display a characteristic pattern of symptoms including vascular stenosis, weakness of connective tissue, a typical face, short stature, overfriendliness, and mental retardation.

FISH analysis can be performed to confirm WBS diagnosis in patients with vascular stenosis together with mental retardation.

References
Bayés M, *et al.* (2003) Am J Hum Genet 73: 131-51.
Beuren AJ, *et al.* (1964) Am J Cardiol 13: 471-83.
Schubert C (2009) Cell Mol Life Sci 66: 1178-97.
Sugayama SM, *et al.* (2003) Arq Bras Cardiol 81: 462-73.
Williams JC, *et al.* (1961) Circulation 24: 1311-8.

Probe Description
The Zyto*Light* SPEC Williams-Beuren Dual Color Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 7q11.23* (chr7:73,408,390-73,899,599) harboring the ELN region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 7p11.1-q11.1 specific for the alpha satellite centromeric region D7Z1 of chromosome 7.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

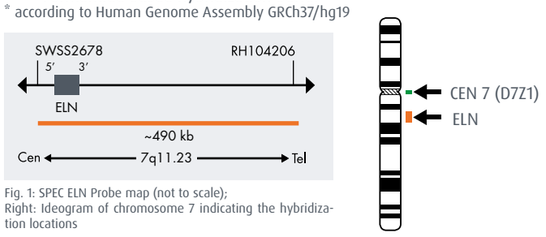
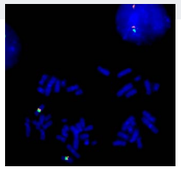
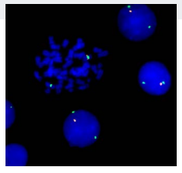


Fig. 1: SPEC ELN Probe map (not to scale);
Right: Ideogram of chromosome 7 indicating the hybridization locations

Results
Normal situation: In Interphases of normal cells or cells without a deletion involving the ELN gene region, two orange signals and two green signals appear.
Aberrant situation: In a cell with deletion affecting the ELN gene region, a reduced number of orange signals will be observed. Deletions affecting only parts of the ELN gene region might result in a normal signal pattern with orange signals of reduced size.



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.



Lymphocytes and metaphase chromosomes from a Williams-Beuren syndrome case showing an ELN deletion as indicated by the loss of one orange signal.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	7	CE/IVD	5 (50 µl)	**Z-2302-50**

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

Intended Purpose
The Zyto*Light* SPEC CUX1/EZH2/CEN 7 Triple Color Probe (PL172) is intended to be used for the qualitative detection of deletions involving the human CUX1 gene and the human EZH2 gene as well as the detection of chromosome 7 alpha satellites in cytological specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC CUX1/EZH2/CEN 7 Triple Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10.0 ng/µl), which target sequences mapping in 7q22.1* (chr7:101,270,255-101,934,924) harboring the CUX1 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 7q36.1* (chr7:148,402,839-148,647,927) harboring the EZH2 gene region (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~12.0 ng/µl), which target sequences mapping in 7p11.1-q11 specific for the alpha satellite centromeric region D7Z1 of chromosome 7.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

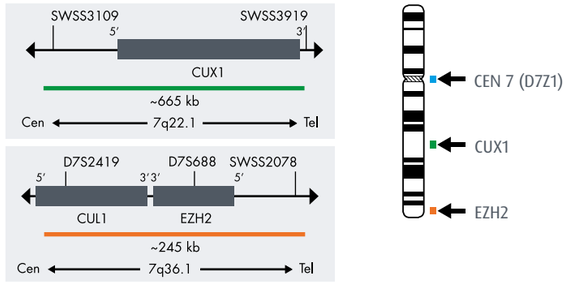
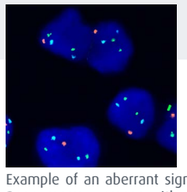


Fig. 1: Top: SPEC CUX1 Probe map; Bottom: SPEC EZH2 Probe map (not to scale); Right: Ideogram of chromosome 7 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the respective gene regions, two green, two orange, and two blue signals appear.
Aberrant situation: In a cell with deletion affecting the CUX1 gene region and/or the EZH2 gene region, a reduced number of green and/or orange signals will be observed. Deletions affecting only parts of the respective gene regions might result in a normal signal pattern with signals of reduced size. Monosomy 7 will result in a loss of one green, one orange, and one blue signal.

Example of an aberrant signal pattern: Bone marrow smear with deletion of the CUX1 gene as indicated by one green signal in each nucleus.



Example of an aberrant signal pattern: Bone marrow smear with deletion of the EZH2 gene as indicated by one orange signal in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	7	CE/IVD	5 (50 µl)	**Z-2214-50**

ZytoLight® SPEC MET/CEN 7 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC MET/CEN 7 Dual Color Probe (PL46) is intended to be used for the qualitative detection of amplifications involving the human MET gene as well as the detection of chromosome 7 alpha satellites in formalin-fixed, paraffin-embedded specimens, such as non-small cell lung cancer (NSCLC), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of NSCLC and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC MET/CEN 7 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 7q31.2* (chr7:115,925,700-116,718,699) harboring the MET gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1,5 ng/µl), which target sequences mapping in 7p11.1-q11.1 specific for the alpha satellite centromeric region D7Z1 of chromosome 7.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

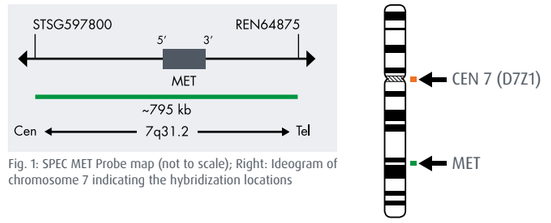
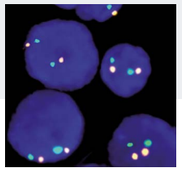
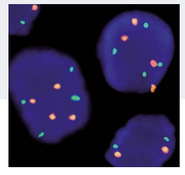


Fig. 1: SPEC MET Probe map (not to scale); Right: Ideogram of chromosome 7 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the MET gene region, two green and two orange signals appear.
Aberrant situation: In cells with an amplification of the MET gene region, an increased number of green signals or green signal clusters will be observed.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



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

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	7	CE/IVD	5 (50 µl)	**Z-2087-50**
			20 (200 µl)	**Z-2087-200**

ZytoLight® SPEC BRAF Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC BRAF Dual Color Break Apart Probe (PL147) is intended to be used for the qualitative detection of translocations involving the human BRAF gene at 7q34 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC BRAF Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 7q34* (chr7:140.535,100-141,233,856) distal to the BRAF breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 7q34* (chr7:139,972,721-140,469,362) proximal to the BRAF breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

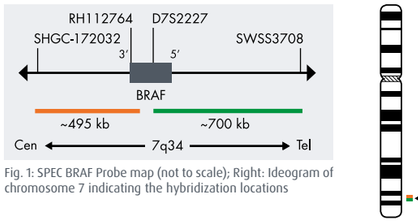
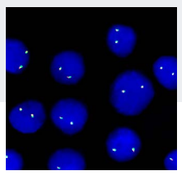


Fig. 1: SPEC BRAF Probe map (not to scale); Right: Ideogram of chromosome 7 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the BRAF gene region, two green/orange fusion signals appear.
Aberrant situation: One BRAF gene region affected by a translocation is indicated by one separate green signal and one separate orange signal. A deletion of 5′ BRAF sequences resulting in a FAM131B-BRAF fusion is indicated by the loss of one green signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	7	CE/IVD	20 (200 µl)	**Z-2189-200**

ZytoLight® SPEC BRAF/CEN 7 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC BRAF/CEN 7 Dual Color Probe (PL149) is intended to be used for the qualitative detection of amplifications involving the human BRAF gene as well as the detection of chromosome 7 alpha satellites in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC BRAF/CEN 7 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 7q34* (chr7:140,266,210-140,792,511) harboring the BRAF gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1,5 ng/µl), which target sequences mapping in 7p11.1-q11.1 specific for the alpha satellite centromeric region D7Z1 of chromosome 7.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

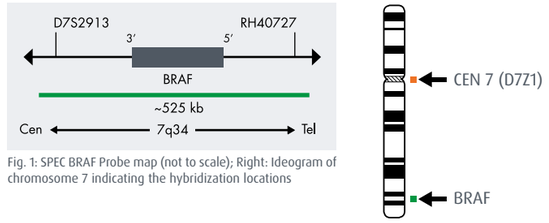
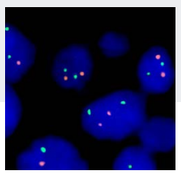
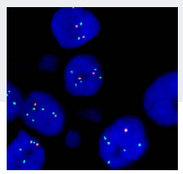


Fig. 1: SPEC BRAF Probe map (not to scale); Right: Ideogram of chromosome 7 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the BRAF gene region, two green and two orange signals appear.
Aberrant situation: In cells with an amplification of the BRAF gene region, an increased number of green signals or green signal clusters will be observed.



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



Example of an aberrant signal pattern: NSCLC tissue section with amplification of the BRAF gene (green).

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	7	CE/IVD	20 (200 µl)	**Z-2191-200**

ZytoLight® SPEC NRG1/CD74 TriCheck™ Probe

Intended Purpose
The Zyto*Light* SPEC NRG1/CD74 TriCheck Probe (PL152) is intended to be used for the qualitative detection of human NRG1 rearrangements with and without participation of the human CD74 gene in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC NRG1/CD74 TriCheck Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 8p12* (chr8:31,730,448-32,433,429) distal to the NRG1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 8p12* (chr8:32,644,505-32,985,279) proximal to the NRG1 breakpoint region (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~37,0 ng/µl), which target sequences mapping in 5q32-q33.1* (chr5:149,274,320-150,285,722) harboring the CD74 gene (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

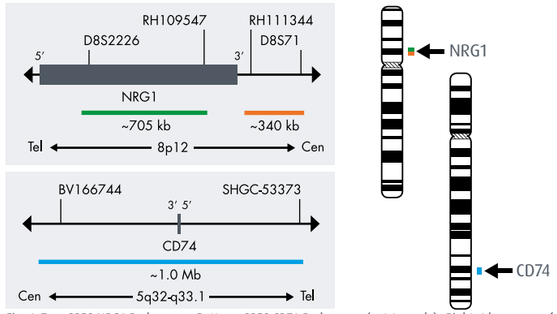
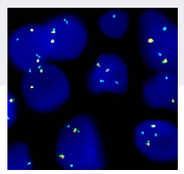


Fig. 1: Top: SPEC NRG1 Probe map; Bottom: SPEC CD74 Probe map (not to scale); Right: Ideograms of chromosome 8 and 5 indicating the hybridization locations

Results
Normal situation: In Interphases of normal cells or cells without NRG1 rearrangement, two green, two orange, and two blue signals appear.
Aberrant situation: 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. Isolated orange signals are the result of deletions distal to the NRG1 breakpoint region.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals and two blue signals per nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	5, 8	CE/IVD	20 (200 µl)	**Z-2194-200**

ZytoLight® SPEC NRG1 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC NRG1 Dual Color Break Apart Probe (PL140) is intended to be used for the qualitative detection of translocations involving the human NRG1 gene at 8p12 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC NRG1 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 8p12* (chr8:31,730,448-32,433,429) distal to the NRG1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 8p12* (chr8:32,644,505-32,985,279) proximal to the NRG1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

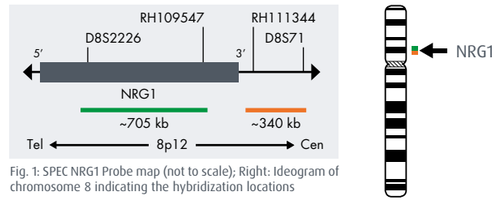
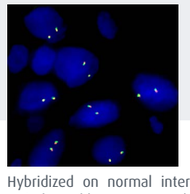
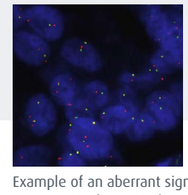


Fig. 1: SPEC NRG1 Probe map (not to scale); Right: Ideogram of chromosome 8 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the NRG1 gene region, two green/orange fusion signals appear.
Aberrant situation: One NRG1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal. Isolated orange signals are the result of deletions distal to the NRG1 breakpoint region.



Hybridized on normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Example of an aberrant signal pattern: Lung cancer tissue section with rearrangement of the NRG1 gene as indicated by extra orange signals.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	8	CE/IVD	20 (200 µl)	**Z-2181-200**

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

ZytoLight® SPEC FGFR1 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC FGFR1 Dual Color Break Apart Probe (PL124) is intended to be used for the qualitative detection of translocations involving the human FGFR1 gene at 8p11.22-p11.23 in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

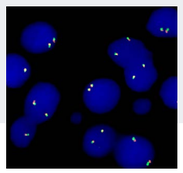
The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC FGFR1 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 8p11.22* (chr8:38,352,117-38,951,783) proximal to the FGFR1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 8p11.23* (chr8:37,635,912-38,239,669) distal to the FGFR1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

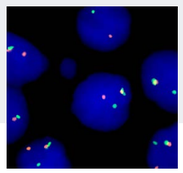
* according to Human Genome Assembly GRCh37/hg19

Fig. 1: SPEC FGFR1 Probe map (not to scale); Right: Ideogram of chromosome 8 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the FGFR1 gene region, two green/orange fusion signals appear.
Aberrant situation: One FGFR1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	8	CE/IVD	5 (50 µl)	**Z-2168-50**
			20 (200 µl)	**Z-2168-200**

ZytoLight® SPEC FGFR1/CEN 8 Dual Color Probe

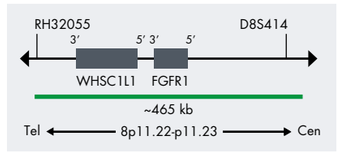
Intended Purpose
The Zyto*Light* SPEC FGFR1/CEN 8 Dual Color Probe (PL29) is intended to be used for the qualitative detection of amplifications involving the human FGFR1 gene as well as the detection of chromosome 8 alpha satellites in formalin-fixed, paraffin-embedded specimens, such as breast cancer and squamous cell lung cancer, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of breast cancer and squamous cell lung cancer and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC FGFR1/CEN 8 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 8p11.22-p11.23* (chr8:38,063,906-38,527,745) harboring the FGFR1 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1.5 ng/µl), which target sequences mapping in 8p11.1-q11.1 specific for the alpha satellite centromeric region D8Z2 of chromosome 8.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



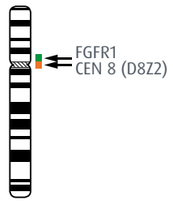
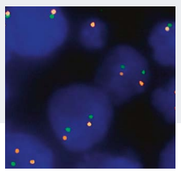
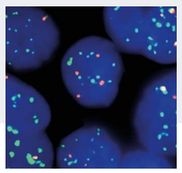


Fig. 1: SPEC FGFR1 Probe map (not to scale); Right: Ideogram of chromosome 8 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the FGFR1 gene region, two green signals and two orange signals appear.
Aberrant situation: In cells with an amplification of the FGFR1 gene region an increased number of green signals or green signal clusters will be observed.



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).

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	8	CE/IVD	5 (50 µl)	**Z-2072-50**
			20 (200 µl)	**Z-2072-200**

ZytoLight® SPEC RUNX1/RUNX1T1 Dual Color Dual Fusion Probe

Intended Purpose
The Zyto*Light* 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.

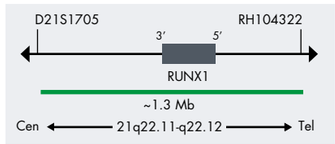
The runt related transcription factor 1 gene (RUNX1) and RUNX1 translocation partner 1 (RUNX1T1) gene are both involved in the transcriptional regulation of genes during normal hematopoiesis. The non-random translocation t(8;21) (q21.3;q22.1) is strongly associated with the French-American-British (FAB) 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 infor*Mation* 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 Zyto*Light* SPEC RUNX1/RUNX1T1 Dual Color Dual Fusion Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~12,0 ng/µl), which target sequences mapping in 21q22.11-q22.12* (chr21:35,530,283-36,855,548) harboring the RUNX1 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~6 ng/µl), which target sequences mapping in 8q21.3-q22.1* (chr8:92,632,490-93,746,043) harboring the RUNX1T1 region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



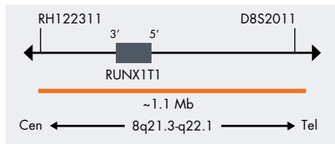
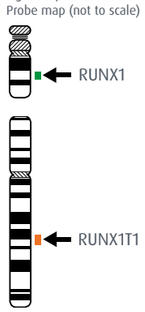
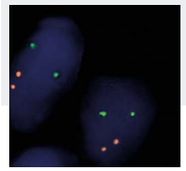


Fig. 1: Top: SPEC RUNX1 Probe map; Bottom: SPEC RUNX1T1 Probe map (not to scale)

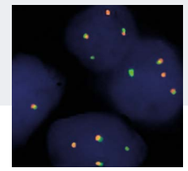


Ideograms of chromosome 21 and 8 indicating the hybridization locations

Results
Normal situation: In Interphases of normal cells or cells without a translocation involving the respective gene regions, two separate green and orange signals appear.
Aberrant situation: A gene fusion is indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	8,21	CE/IVD	5 (50 µl)	**Z-2112-50**
			20 (200 µl)	**Z-2112-200**

ZytoLight® SPEC MYC Dual Color Break Apart Probe

Intended Purpose
The ZytoLight SPEC MYC Dual Color Break Apart Probe (PL49) is intended to be used for the qualitative detection of translocations involving the human MYC gene at 8q24.21 in cytologic or formalin-fixed, paraffin-embedded specimens, such as diffuse large B-cell lymphoma (DLBCL) or Burkitt lymphoma (BL), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH Implementation Kits (Prod. No. Z-2028-5/-20, or Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of DLBCL or BL and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC MYC Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 8q24.21* (chr8:130,373,051-130,930,673) distal to the MYC breakpoint region (see Fig.1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 8q24.21* (chr8:127,888,765-128,363,281) proximal to the MYC breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

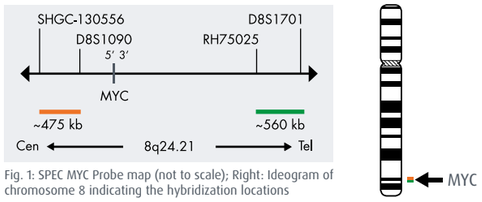
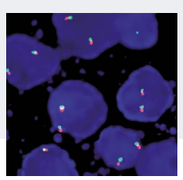
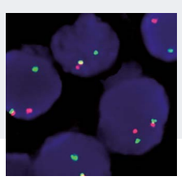


Fig. 1: SPEC MYC Probe map (not to scale); Right: Ideogram of chromosome 8 indicating the hybridization locations

Results
Normal situation: In Interphases of normal cells or cells without a translocation involving the MYC gene region, two green/orange fusion signals appear.
Aberrant situation: One MYC gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	8	CE/IVD	5 (50 µl)	**Z-2090-50**
			20 (200 µl)	**Z-2090-200**

ZytoLight® SPEC MYC/CEN 8 Dual Color Probe

Intended Purpose
The ZytoLight SPEC MYC/CEN 8 Dual Color Probe (PL51) is intended to be used for the qualitative detection of amplifications involving the human MYC gene as well as the detection of chromosome 8 alpha satellites in formalin-fixed, paraffin-embedded specimens, such as breast cancer, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of breast cancer and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight MYC/CEN 8 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 8q24.21* (chr8:128,487,995-128,887,929) harboring the MYC gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1,5 ng/µl), which target sequences mapping in 8p11.1-q11.1 specific for the alpha satellite centromeric region D8Z2 of chromosome 8.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

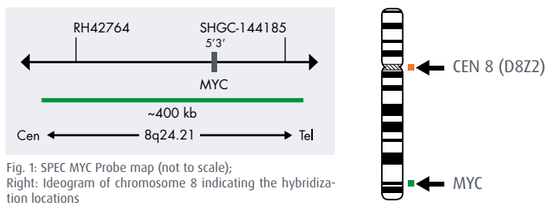
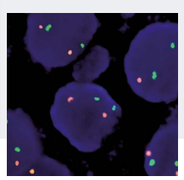
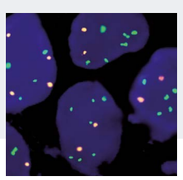


Fig. 1: SPEC MYC Probe map (not to scale);
Right: Ideogram of chromosome 8 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the MYC gene region, two green signals and two orange signals appear.
Aberrant situation: In In cells with an amplification of the MYC gene region, an increased number of green signals or green signal clusters will be observed.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	8	CE/IVD	5 (50 µl)	**Z-2092-50**
			20 (200 µl)	**Z-2092-200**

ZytoLight® SPEC MYC/IGH Dual Color Dual Fusion Probe

Intended Purpose
The ZytoLight SPEC MYC/IGH Dual Color Dual Fusion Probe (PL62) is intended to be used for the qualitative detection of the translocation t(8;14)(q24.21;q32.3) involving the human IGH and MYC genes in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC MYC/IGH Dual Color Dual Fusion Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~12 ng/µl), which target sequences mapping in 14q32.33* (chr14:105,462,169-106,995,000) harboring the IGH locus (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~6 ng/µl), which target sequences mapping in 8q24.21* (chr8:128,171,178-129,517,468) harboring the MYC gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

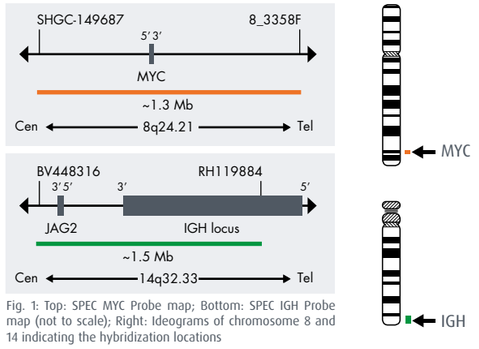
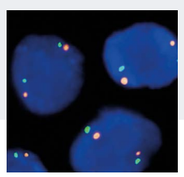
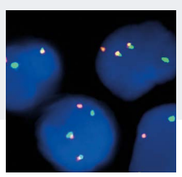


Fig. 1: Top: SPEC MYC Probe map; Bottom: SPEC IGH Probe map (not to scale); Right: Ideograms of chromosome 8 and 14 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the respective bands, two separate green/orange signals appear.
Aberrant situation: A gene fusion is indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	8, 14	CE/IVD	5 (50 µl)	**Z-2105-50**
			20 (200 µl)	**Z-2105-200**

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

Intended Purpose
The ZytoLight SPEC CD274,PDCD1LG2/CEN 9 Dual Color Probe (PL138) is intended to be used for the qualitative detection of amplifications involving the human CD274,PDCD1LG2 gene cluster as well as the detection of the classical satellite III region of chromosome 9 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC CD274,PDCD1LG2/CEN 9 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 9p24.1* (chr9:5,253,553-5,819,972) harboring the CD274, PDCD1LG2 gene cluster (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1,5 ng/µl), which target sequences mapping in 9q12 specific for the classical satellite III centromeric region D9Z3 of chromosome 9.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

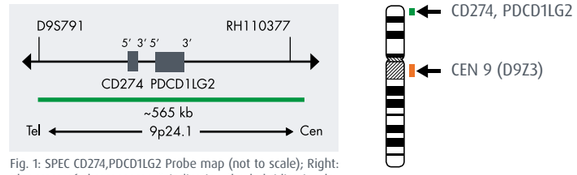
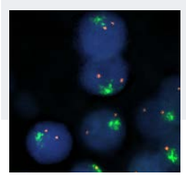


Fig. 1: SPEC CD274,PDCD1LG2 Probe map (not to scale); Right: Ideogram of chromosome 9 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the CD274,PDCD1LG2 gene cluster, two green and two orange signals appear.
Aberrant situation: In cells with an amplification of the CD274,PDCD1LG2 gene cluster, an increased number of green signals or green signal clusters will be observed.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	9	CE/IVD	5 (50 µl)	**Z-2179-50**
			20 (200 µl)	**Z-2179-200**

ZytoLight® SPEC JAK2 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC JAK2 Dual Color Break Apart Probe (PL248) is intended to be used for the qualitative detection of translocations involving the human JAK2 gene at 9p24.1 in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC JAK2 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 9p24.1-24.2* (chr9:4,311,843-5,031,620) distal to the JAK2 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 9p24.1* (chr9:5,088,700-5,328,239) proximal to the JAK2 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

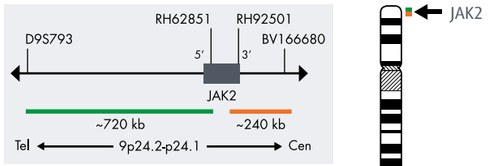
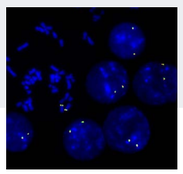
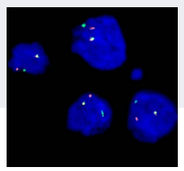


Fig. 1: SPEC JAK2 Probe map (not to scale) Right: Ideogram of chromosome 9 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the JAK2 gene region, two green/orange fusion signals appear.
Aberrant situation: One JAK2 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus and to metaphase chromosomes of a normal cell.



Example of an aberrant signal pattern: Bone marrow smear with translocation of the JAK2 gene as indicated by one non-rearranged orange/green fusion signal, one orange and one separate green signal.

Labels	Chromosome	Reg. Status	Tests	Order No.
	9	CE/IVD	5 (50 µl)	**Z-2294-50**

ZytoLight® SPEC CDKN2A/CEN 9 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC CDKN2A/CEN 9 Dual Color Probe (PL22) is intended to be used for the qualitative detection of deletions involving the human CDKN2A gene as well as the detection of the classical satellite III region of chromosome 9 in cytologic or formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with Zyto*Light* FISH Implementation Kits (Prod. No. Z-2028-5/-20, or Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC CDKN2A/CEN 9 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 9p21.3* (chr9:21,742,629-22,056,853) harboring the CDKN2A gene region (see Fig.1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1.5 ng/µl), which target sequences mapping in 9q12 specific for the classical satellite III region D9Z3 of chromosome 9.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

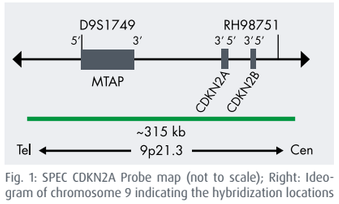
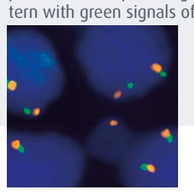
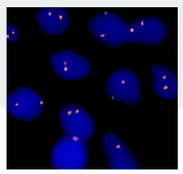


Fig. 1: SPEC CDKN2A Probe map (not to scale); Right: Ideogram of chromosome 9 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the respective gene region (CDKN2A, CDKN2B, MTAP), two green and two orange signals appear.
Aberrant situation: In a cell with deletion affecting the respective gene region, a reduced number of green signals will be observed. Please check localization of the probe (see Fig. 1) carefully. Deletions affecting only parts of the respective gene region might result in a normal signal pattern with green signals of reduced size.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Example of an aberrant signal pattern: Glioblastoma tissue section with homozygous deletion of the CDKN2A gene as indicated by the loss of both green signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
	9	CE/IVD	5 (50 µl)	**Z-2063-50**
			20 (200 µl)	**Z-2063-200**

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

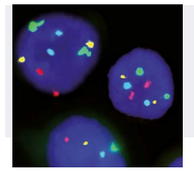
Intended Purpose
The Zyto*Light* SPEC CDKN2A/CEN 3/7/17 Quadruple Color Probe (PL40) is intended to be used for the qualitative detection of the human CDKN2A gene as well as alpha-satellites of chromosomes 3, 7, and 17 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

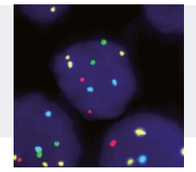
The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC CDKN2A/CEN 3/7/17 Quadruple Color Probe is composed of:
- ZyGold (excitation 532 nm/emission 553 nm) labeled polynucleotides (~5,5 ng/µl), which target sequences mapping in 9p21.3* (chr9:21,742,629-22,056,853) harboring the CDKN2A gene region (see Fig. 1).
- ZyRed (excitation 580 nm/emission 599 nm) labeled polynucleotides (~0.5 ng/µl), which target sequences mapping in 3p11.1-q11.1 specific for the alpha satellite centromeric region D3Z1 of chromosome 3.
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 7p11.1-q11.1 specific for the alpha satellite centromeric region D7Z1 of chromosome 7.
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~12,0 ng/µl), which target sequences mapping in 17p11.1-q11.1 specific for the alpha satellite centromeric region D17Z1 of chromosome 17.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



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.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
	3, 7, 9, 17	CE/IVD	5 (50 µl)	**Z-2081-50**
			20 (200 µl)	**Z-2081-200**

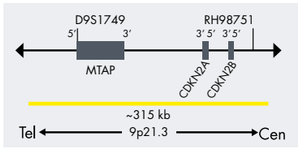


Fig. 1: SPEC CDKN2A Probe map (not to scale)

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

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the CDKN2A gene region, two gold, two red, two green, and two blue signals are expected.
Aberrant situation: In a cell with deletion of the CDKN2A gene region, a reduced number of gold signals will be observed. Deletions affecting only parts of the CDKN2A gene region might result in a normal signal pattern with gold signals of reduced size. In cells with aneusomy of chromosomes 3, 7, or 17, more or less signals of the respective color will be visible.

ZytoLight® SPEC PAX5 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC PAX5 Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal region 9p13.2 harboring the PAX5 (paired box 5, a.k.a. BSAP) gene.

The transcription factor PAX5 activates crucial genes for B-cell lineage differentiation and represses genes that play an important role in other hematopoietic lineages. PAX5 is also implicated in human B-cell malignancies, as it is deregulated by chromosomal translocations in a subset of acute lymphoblastic leukemias (ALL).

B-progenitor ALL (B-ALL), a common pediatric malignancy, is characterized by the participation of PAX5 in specific chromosomal rearrangements that generate novel fusion proteins. All PAX5 fusion proteins contain the PAX5 DNA-binding domain and thus are predicted to retain the ability to bind to PAX5 transcriptional targets, but no longer provide normal transcriptional regulatory functions. The fusion proteins contribute to B-ALL for*Mation* by competitively inhibiting the transcriptional activation of wildtype PAX5.
PAX5 rearranged ALL patients were shown to respond well to treatment with prednisone. Hence, the identification of PAX5 rearrangements by FISH may be of therapeutic significance in ALL.

References
Busslinger M, *et al.* (1996) Proc Natl Acad Sci U S A 93: 6129-34.
Cobaleda C, *et al.* (2007) Nat Immunol 8: 463-70.
Coyaud E, *et al.* (2010) Blood 115: 3089-97.
Mullighan CG, *et al.* (2007) Nature 446: 758-64.
Nebral K, *et al.* (2009) Leukemia 23: 134-43.
Offit K, *et al.* (1992) Blood 80: 2594-9.

Probe Description
The Zyto*Light* SPEC PAX5 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 9p13.2* (chr9:36,331,787-36,837,502) distal to the PAX5 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 9p13.2* (chr9:37,043,219-37,336,413) proximal to the PAX5 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

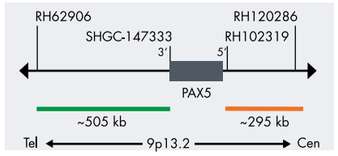
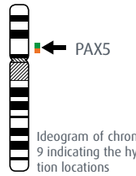


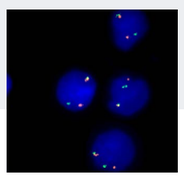
Fig. 1: SPEC PAX5 Probe map (not to scale)



Ideogram of chromosome 9 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an intragenic translocation involving the PAX5 gene region, two green/orange fusion signals appear.
Aberrant situation: One PAX5 gene region affected by an intragenic translocation is indicated by one separate green signal and one separate orange signal. In a cell with an unbalanced translocation resulting in a 3′ deletion, one separate orange signal and one orange/green fusion signal will be observed.


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 with rearrangement affecting the PAX5 gene as indicated by one non-rearranged orange/green fusion signal, one orange and one separate green signal.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	9	CE/IVD	5 (50 µl)	**Z-2300-50**

ZytoLight® SPEC NTRK2 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC NTRK2 Dual Color Break Apart Probe (PL163) is intended to be used for the qualitative detection of translocations involving the human NTRK2 gene at 9q21.33 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC NTRK2 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 9q21.32-q21.33* (chr9:86,569,621-87,287,312) proximal to the NTRK2 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 9q21.33* (chr9:87,589,037-88,124,082) distal to the NTRK2 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

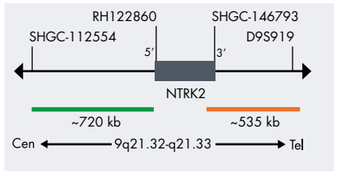
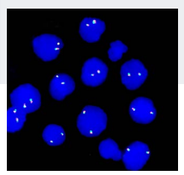
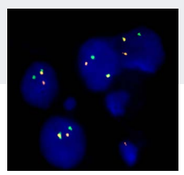


Fig. 1: SPEC NTRK2 Probe map (not to scale); Right: Ideogram of chromosome 9 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the NTRK2 gene region, two green/orange fusion signals appear.
Aberrant situation: One NTRK2 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal. Isolated orange signals are the result of deletions proximal to the NTRK2 breakpoint region or are due to unbalanced translocations affecting this chromosomal region.


Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.


Example of an aberrant signal pattern: Peritoneal carcinoma tissue section with rearrangement of the NTRK2 gene as indicated by one non-rearranged orange/green fusion signal, one orange, and one separate green signal. Kindly provided by the Institute of Pathology, University Medical Center Göttingen, Germany.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	9	CE/IVD	5 (50 µl)	**Z-2205-50**
			20 (200 µl)	**Z-2205-200**

ZytoLight® SPEC NR4A3 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC NR4A3 Dual Color Break Apart Probe (PL102) is intended to be used for the qualitative detection of translocations involving the human NR4A3 gene at 9q22.33-q31.1 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC NR4A3 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 9q22.33* (chr9:102,070,916-102,561,593) proximal to the NR4A3 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 9q31.1* (chr9:102,636,487-103,065,504) distal to the NR4A3 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

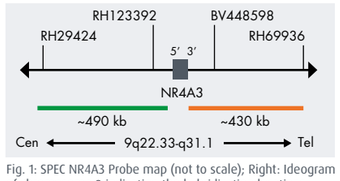
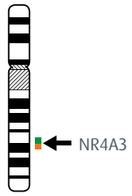
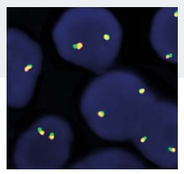
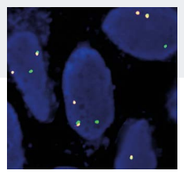


Fig. 1: SPEC NR4A3 Probe map (not to scale); Right: Ideogram of chromosome 9 indicating the hybridization locations



Results
Normal situation: In interphases of normal cells or cells without a translocation involving the NR4A3 gene region, two green/orange fusion signals appear.
Aberrant situation: One NR4A3 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.


Hybridized to normal interphase cells as indicated by two orange/green fusion signal per nucleus.


Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	9	CE/IVD	5 (50 µl)	**Z-2145-50**

ZytoLight® SPEC ABL1 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC ABL1 Dual Color Break Apart Probe (PL157) is intended to be used for the qualitative detection of translocations involving the human ABL1 gene at 9q34.12 in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC ABL1 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 9q34.11-q34.12* (chr9:132,872,357-133,580,236) proximal to the ABL1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 9q34.12-q34.13* (chr9:133,851,960-134,273,097) distal to the ABL1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

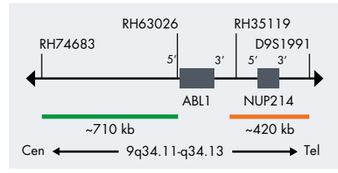
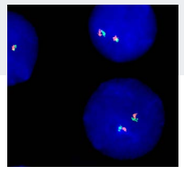
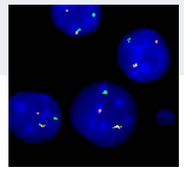


Fig. 1: SPEC ABL1 Probe map (not to scale);
Right: Ideogram of chromosome 9 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the ABL1 gene region, two green/orange fusion signals appear.
Aberrant situation: One ABL1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal. One ABL1 gene region affected by a NUP214-ABL1 fusion associated with amplified episomes is indicated by one separate green signal and multiple orange signals or an orange signal cluster.


Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.


Example of an aberrant signal pattern: Bone marrow smear 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	9	CE/IVD	5 (50 µl)	**Z-2199-50**

ZytoLight® SPEC NUP214 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* 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 Zyto*Light* SPEC NUP214 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 9q34.13* (chr9:134,153,663-134,706,700) distal to the NUP214 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 9q34.12-q34.13* (chr9:133,739,333-134,028,546) proximal to the NUP214 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

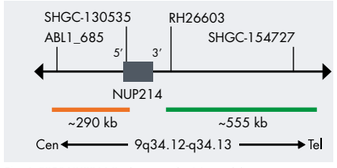
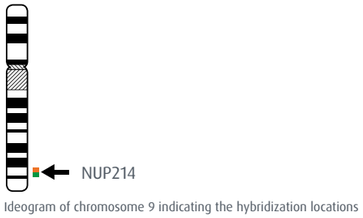
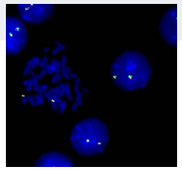


Fig. 1: SPEC NUP214 Probe map (not to scale)



Ideogram of chromosome 9 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the NUP214 gene region, two green/orange fusion signals appear.
Aberrant situation: One NUP214 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal. One locus affected by a NUP214-ABL1 fusion associated with amplified episomes is indicated by one separate green signal and multiple orange signals or an orange signal cluster. A deletion affecting the 9q34.12-q34.13 locus is indicated by one green/orange fusion signal and one separate green signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus and to metaphase chromosomes of a normal cell.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	9	CE/IVD	5 (50 µl)	**Z-2265-50**

ZytoLight® SPEC BCR/ABL1 Dual Color Dual Fusion Probe

Intended Purpose
The Zyto*Light* SPEC BCR/ABL1 Dual Color Dual Fusion Probe (PL68) is intended to be used for the qualitative detection of the translocation t(9;22)(q34.1;q11.2) involving the human BCR and ABL1 genes in cytologic specimens, such as chronic myeloid leukemia (CML), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of CML and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC BCR/ABL1 Dual Color Dual Fusion Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~12,0 ng/µl), which target sequences mapping in 22q11.22-q11.23* (chr22:23,000,029-24,431,064) harboring the BCR gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~6 ng/µl), which target sequences mapping in 9q34.11-q34.13* (chr9:133,223,081-134,103,849) harboring the ABL1 gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

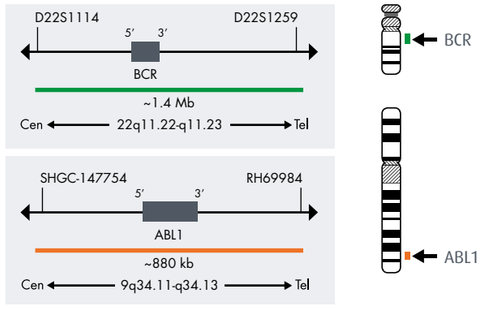
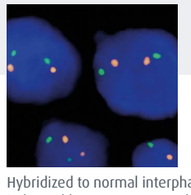


Fig. 1: Top: SPEC BCR Probe map; Bottom: SPEC ABL1 Probe map (not to scale); Right: Ideograms of chromosome 22 and 9 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the respective gene regions, two separate green and orange signals appear.
Aberrant situation: A gene fusion is indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.

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

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	9, 22	CE/IVD	5 (50 µl)	**Z-2111-50**
			20 (200 µl)	**Z-2111-200**

ZytoLight® SPEC RET Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC RET Dual Color Break Apart Probe (PL105) is intended to be used for the qualitative detection of translocations involving the human RET gene at 10q11.21 in formalin-fixed, paraffin-embedded specimens, such as non-small cell lung cancer (NSCLC) or papillary thyroid carcinoma (PTC), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of NSCLC or PTC and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC RET Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 10q11.21* (chr10:43,626,274-43,902,346) distal to the RET breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 10q11.21* (chr10:43,340,888-43,510.171) proximal to the RET breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

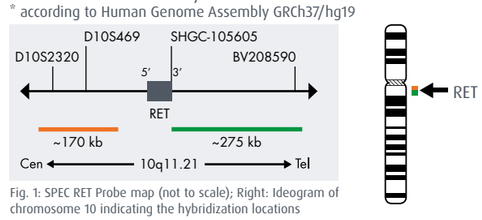
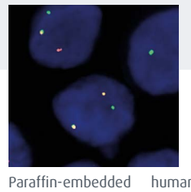


Fig. 1: SPEC RET Probe map (not to scale); Right: Ideogram of chromosome 10 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the RET gene region, two green/orange fusion signals appear.
Aberrant situation: One RET gene region affected by a translocation is indicated by one separate green signal and one separate orange signal. Isolated green signals are the result of deletions proximal to the RET breakpoint region. Inversions involving genes in close proximity such as CCDC6 might not be observable due to just subtle signal separation.

Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Paraffin-embedded 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	10	CE/IVD	5 (50 µl)	**Z-2148-50**
			20 (200 µl)	**Z-2148-200**

ZytoLight® SPEC PTEN/CEN 10 Dual Color Probe

Intended Purpose
The ZytoLight SPEC PTEN/CEN 10 Dual Color Probe (PL37) is intended to be used for the qualitative detection of deletions involving the human PTEN gene as well as the detection of chromosome 10 alpha satellites in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC PTEN/CEN 10 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 10q23.2-q23.31* (chr10:89,440,649-89,755,790) harboring the PTEN gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1,5 ng/µl), which target sequences mapping in 10p11.1-q11.1 specific for the alpha satellite centromeric region D10Z1 of chromosome 10.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

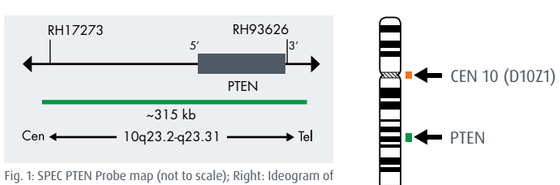
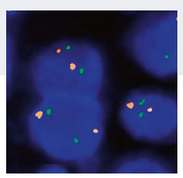
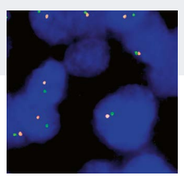


Fig. 1: SPEC PTEN Probe map (not to scale); Right: Ideogram of chromosome 10 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the PTEN gene region, two green and two orange signals appear.
Aberrant situation: In a cell with deletion affecting the PTEN gene region, a reduced number of green signals will be observed. Deletions affecting only parts of the PTEN gene region might result in normal signal pattern with green signals of reduced size.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Example of an aberrant signal pattern: Melanoma tissue section with chromosome 10 monosomy as indicated by one orange and one green signal in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	10	CE/IVD	5 (50 µl)	**Z-2078-50**
			20 (200 µl)	**Z-2078-200**

ZytoLight® SPEC FGFR2 Dual Color Break Apart Probe

Intended Purpose
The ZytoLight SPEC FGFR2 Dual Color Break Apart Probe (PL125) is intended to be used for the qualitative detection of translocations involving the human FGFR2 gene at 10q26.13 in formalin-fixed, paraffin-embedded specimens, such as intrahepatic cholangiosarcoma, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of intrahepatic cholangiosarcoma and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC FGFR2 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 10q26.12-q26.13* (chr10:122,632,462-123,166,030) proximal to the FGFR2 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 10q26.13* (chr10:123,436,230-123,791,279) distal to the FGFR2 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

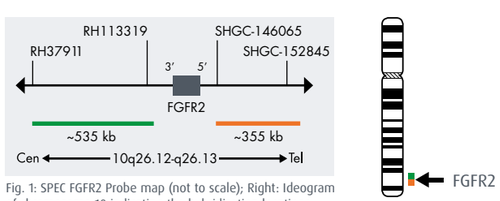
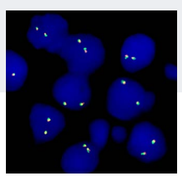
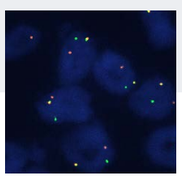


Fig. 1: SPEC FGFR2 Probe map (not to scale); Right: Ideogram of chromosome 10 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the FGFR2 gene region, two green/orange fusion signals appear.
Aberrant situation: One FGFR2 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	10	CE/IVD	5 (50 µl)	**Z-2169-50**
			20 (200 µl)	**Z-2169-200**

Kindly provided by Prof. Dr. Büttner, Cologne, Germany.

ZytoLight® SPEC FGFR2/CEN 10 Dual Color Probe

Intended Purpose
The ZytoLight SPEC FGFR2/CEN 10 Dual Color Probe (PL79) is intended to be used for the qualitative detection of amplifications involving the human FGFR2 gene as well as chromosome 10 alpha satellites in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC FGFR2/CEN 10 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 10q26.12-q26.13* (chr10:122,908,224-123,682,373) harboring the FGFR2 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1.5 ng/µl), which target sequences mapping in 10p11.1-q11.1 specific for the alpha satellite centromeric region D10Z1 of chromosome 10.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

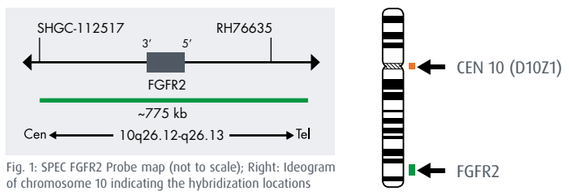
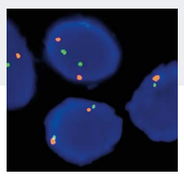
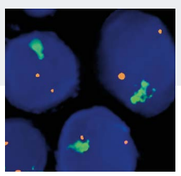


Fig. 1: SPEC FGFR2 Probe map (not to scale); Right: Ideogram of chromosome 10 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the FGFR2 gene region, two green signals and two orange signals appear.
Aberrant situation: In cells with an amplification of the FGFR2 gene region an increased number of green signals or green signal clusters will be observed.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Example of an aberrant signal pattern: Breast cancer tissue section with amplification of the FGFR2 gene as indicated by green signal clusters in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	10	CE/IVD	20 (200 µl)	**Z-2122-200**

ZytoLight® SPEC NUP98 Dual Color Break Apart Probe

Intended Purpose
The ZytoLight SPEC NUP98 Dual Color Break Apart Probe (PL223) is intended to be used for the qualitative detection of translocations involving the human NUP98 gene at 11p15.4 in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC NUP98 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 11p15.4-p15.5* (chr11:2,773,748-3,363,120) distal to the NUP98 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 11p15.4* (chr11:3,829,054-4,142,792) proximal to the NUP98 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

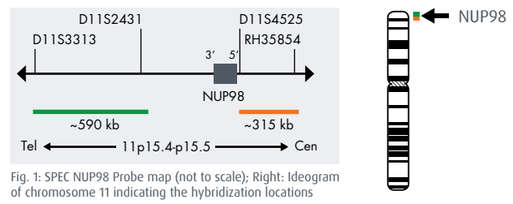
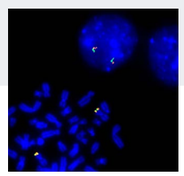


Fig. 1: SPEC NUP98 Probe map (not to scale); Right: Ideogram of chromosome 11 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the NUP98 gene region, two green/orange fusion signals appear. In specimens from normal tissue split signals have occasionally been observed. It is therefore important to define cut-off specifications carefully in order to avoid false positive results.
Aberrant situation: One NUP98 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus and to metaphase chromosomes of a normal cell.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	11	CE/IVD	5 (50 µl)	**Z-2266-50**

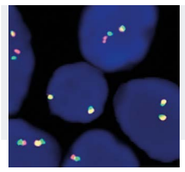
ZytoLight® SPEC WT1 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC WT1 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 11p13 harboring the WT1 (Wilms tumor 1) gene.

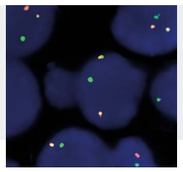
The WT1 gene is located on 11p13 and encodes a zinc finger DNA-binding protein that acts as a transcriptional activator or repressor depending on the cellular or chromosomal context. Inactivating mutations in the tumor suppressor gene WT1 have been identified in patients with Wilms' tumor and in a subset 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.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Desmoblastic small roand 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	11	CE/IVD	5 (50 µl)	**Z-2142-50**

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 Zyto*Light* SPEC WT1 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 11p13* (chr11:32,492,523-33,297,615) proximal to the WT1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 11p13* (chr11:31,590,767-32,388,208) distal to the WT1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

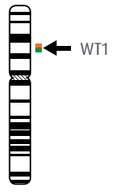


Fig. 1: SPEC WT1 Probe map (not to scale); Right: Ideogram of chromosome 11 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the WT1 gene region, two green/orange fusion signals appear.
Aberrant situation: One WT1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.

ZytoLight® SPEC SPI1 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC SPI1 Dual Color Break Apart Probe (PL245) is intended to be used for the qualitative detection of translocations involving the human SPI1 gene at 11p11.2 in cytologic specimens by fluorescence in situ hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20)

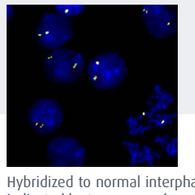
Probe Description
The Zyto*Light* SPEC SPI1 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 11p11.2* (chr11:47,424,117-47,867,019) proximal to the SPI1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 11p11.2* (chr11:46,871,411-47,354,083) distal to the SPI1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

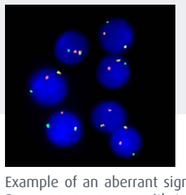
Fig. 1: SPEC SPI1 Probe map (not to scale)

Ideogram of chromosome 11 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the SPI1 gene region, two green/orange fusion signals appear.
Aberrant situation: One SPI1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals in each nucleus and to metaphase chromosomes of a normal cell.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	11	RUO	5 (50 µl)	**Z-2291-50**

ZytoLight® SPEC CCND1 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC CCND1 Dual Color Break Apart Probe (PL65) is intended to be used for the qualitative detection of translocations involving the human CCND1 gene at 11q13.3 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC CCND1 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 11q13.2-q13.3* (chr11:68,249,010-68,705,283) proximal to the CCND1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 11q13.3* (chr11:69,453,301-70,031,240) distal to the CCND1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

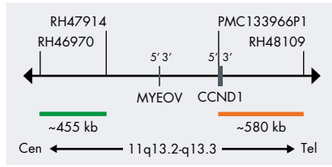
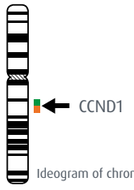
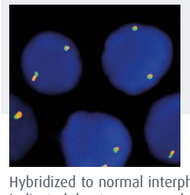


Fig. 1: SPEC CCND1 Probe map (not to scale)



Ideogram of chromosome 11 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the CCND1 gene region, two green/orange fusion signals appear.
Aberrant situation: One CCND1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.

Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	11	CE/IVD	5 (50 µl)	**Z-2108-50**
			20 (200 µl)	**Z-2108-200**

ZytoLight® SPEC CCND1/CEN 11 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC CCND1/CEN 11 Dual Color Probe (PL28) is intended to be used for the qualitative detection of amplifications involving the human CCND1 gene as well as the detection of chromosome 11 alpha satellites in formalin-fixed, paraffin-embedded specimens, such as breast cancer, by fluorescence in situ hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of breast cancer and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* CCND1/CEN 11 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 11q13.3* (chr11:69,203,885-70,031,240) harboring the CCND1 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1,5 ng/µl), which target sequences mapping in 11p11.11-q11 specific for the alpha satellite centromeric region D11Z1 of chromosome 11.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

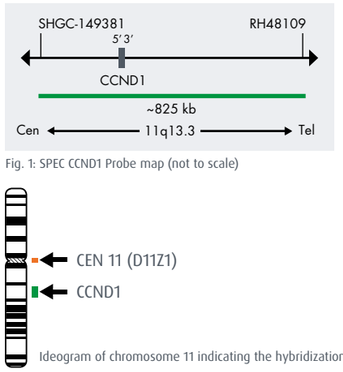
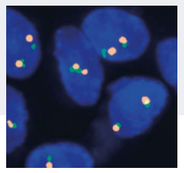


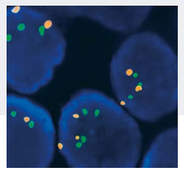
Fig. 1: SPEC CCND1 Probe map (not to scale)

Ideogram of chromosome 11 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the CCND1 gene region, two green signals and two orange signals appear.
Aberrant situation: In cells with an amplification of the CCND1 gene region, an increased number of green signals or green signal clusters are visible.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Example of an aberrant signal pattern: Polysomy of chromosome 11 as indicated by three orange (CEN 11) and three green (CCND1) signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	11	CE/IVD	5 (50 µl)	**Z-2071-50**
			20 (200 µl)	**Z-2071-200**

ZytoLight® SPEC CCND1/IGH Dual Color Dual Fusion Probe

Intended Purpose
The Zyto*Light* SPEC CCND1/IGH Dual Color Dual Fusion Probe (PL82) is intended to be used for the qualitative detection of the translocation t(11;14)(q13.3;q32.3) in cytologic or formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with Zyto*Light* FISH Implementation Kits (Prod. No. Z-2028-5/-20, or Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC CCND1/IGH Dual Color Dual Fusion Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~6 ng/µl), which target sequences mapping in 11q13.3* (chr11:68,522,105-70,031,240) harboring the CCND1 gene region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~12 ng/µl), which target sequences mapping in 14q32.33* (chr14:105,462,169-106,995,000) harboring the IGH locus (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

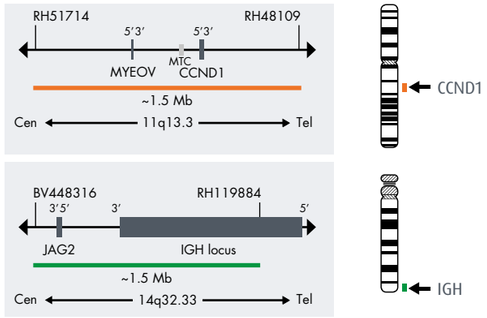
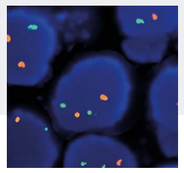
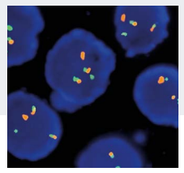


Fig. 1: Top: SPEC CCND1 Probe map; Bottom: SPEC IGH Probe map (not to scale); Right: Ideograms of chromosome 11 and 14 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the respective loci, two separate green and orange signals appear.
Aberrant situation: A gene fusion is indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	11, 14	CE/IVD	5 (50 µl)	**Z-2125-50**
			20 (200 µl)	**Z-2125-200**

ZytoLight® SPEC BIRC3/MALT1 Dual Color Dual Fusion Probe

Intended Purpose
The Zyto*Light* 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 Zyto*Light* SPEC BIRC3/MALT1 Dual Color Dual Fusion Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~12 ng/µl), which target sequences mapping in 11q22.1-q22.2* (chr11:101,756,072-102,581,817) harboring the BIRC3 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~6 ng/µl), which target sequences mapping in 18q21.31-q21.32* (chr18:56,021,766-56,724,408) harboring the MALT1 gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

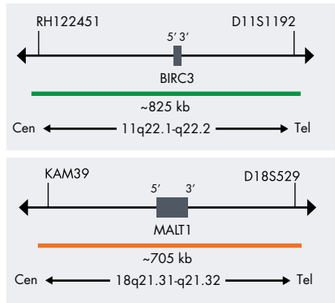
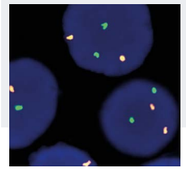


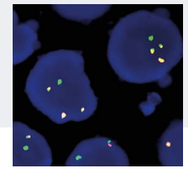
Fig. 1: Top: SPEC BIRC3 Probe map; Bottom: SPEC MALT1 Probe map (not to scale)

Ideograms of chromosome 11 and 18 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the respective gene regions, two separate green and orange signals appear.
Aberrant situation: A gene fusion is indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	11, 18	CE/IVD	5 (50 µl)	**Z-2146-50**
			20 (200 µl)	**Z-2146-200**

ZytoLight® SPEC MAML2 Dual Color Break Apart Probe

Intended Purpose

The Zyto*Light* SPEC MAML2 Dual Color Break Apart Probe (PL5) is intended to be used for the qualitative detection of translocations involving the human MAML2 gene at 11q21 in formalin-fixed, paraffin-embedded mucoepidermoid carcinoma (MEC) specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

This product is for non-automated and for laboratory professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel. This product is neither a device for near-patient testing nor a companion diagnostic.

This product is a FISH probe with ZyGreen- and ZyOrange-labeled polynucleotides intended to be used as an aid to the differential diagnosis of MEC in patients with confirmed or suspected MEC. Therapeutic measures should not be initiated based on the test result alone.

Probe Description

The Zyto*Light* SPEC MAML2 Dual Color Break Apart Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 11q21* (chr11:96,115,829-96,797,136) distal to the MAML2 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 11q21* (chr11:95,296,828-95,668,215) proximal to the MAML2 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

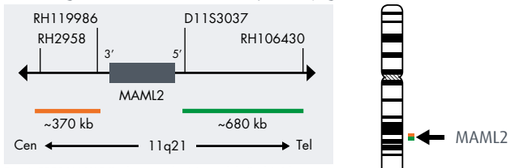
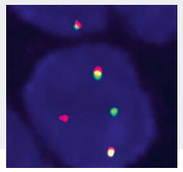


Fig. 1: SPEC MAML2 Probe map (not to scale); Right: Ideogram of chromosome 11 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a translocation involving the MAML2 gene region, two green/orange fusion signals appear.
Aberrant situation: One MAML2 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Mucoepidermoid carcinoma section with translocation affecting the 11q21 locus as indicated by one separate orange and one separate green signal.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	11	CE/IVD	5 (50 µl)	**Z-2014-50**
			20 (200 µl)	**Z-2014-200**

ZytoLight® SPEC ATM/CEN 11 Dual Color Probe

Intended Purpose

The Zyto*Light* SPEC ATM/CEN 11 Dual Color Probe (PL254) is intended to be used for the qualitative detection of deletions involving the human ATM gene as well as the detection of chromosome 11 alpha satellites in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The Zyto*Light* SPEC ATM/CEN 11 Dual Color Probe is composed of:

- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 11q22.3* (chr11:107,957,618-108,380,921) harboring the ATM gene region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 11p11.11-q11 specific for the alpha satellite centromeric region D11Z1 of chromosome 11.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

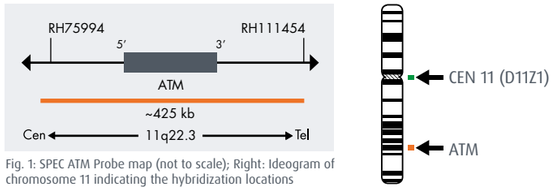
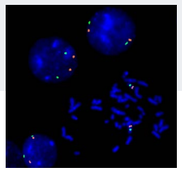


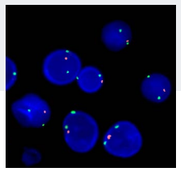
Fig. 1: SPEC ATM Probe map (not to scale); Right: Ideogram of chromosome 11 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a deletion involving the ATM gene region, two green and two orange signals appear.
Aberrant situation: In a cell with deletions affecting the ATM gene region, a reduced number of orange signals will be observed. Deletions affecting only parts of the ATM gene region might result in a normal signal pattern with orange signals of reduced size.



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.



Example of an aberrant signal pattern: CLL with deletion affecting the ATM locus as indicated by one orange signal in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	11	CE/IVD	5 (50 µl)	**Z-2297-50**

ZytoLight® SPEC ATM/CEN 12 Dual Color Probe

Intended Purpose

The Zyto*Light* SPEC ATM/CEN 12 Dual Color Probe (PL250) is intended to be used for the qualitative detection of deletions involving the human ATM gene as well as the detection of chromosome 12 alpha satellites in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The Zyto*Light* SPEC ATM/CEN 12 Dual Color Probe is composed of:

- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 11q22.3* (chr11:107,957,618-108,380,921) harboring the ATM gene region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 12p11.1-q11 specific for the alpha satellite centromeric region D12Z3 of chromosome 12.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

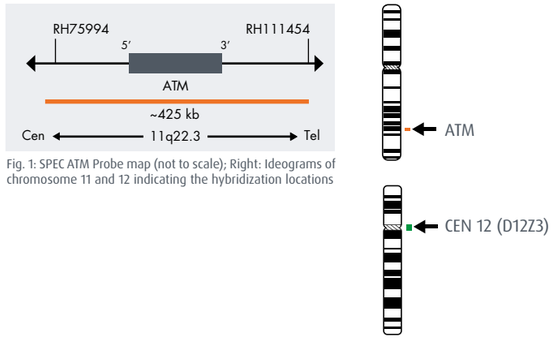
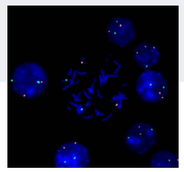


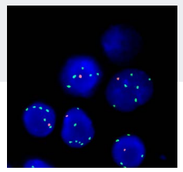
Fig. 1: SPEC ATM Probe map (not to scale); Right: Ideograms of chromosome 11 and 12 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a deletion involving the ATM gene region and without aneusomy of chromosomes 12, two orange and two green signals appear.
Aberrant situation: In a cell with deletions affecting the ATM gene region, a reduced number of orange signals will be observed. Deletions affecting only parts of the ATM gene region might result in a normal signal pattern with orange signals of reduced size. In a cell with aneusomy 12, three or more copies of the green signal will be observed, respectively.



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.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	11, 12	CE/IVD	5 (50 µl)	**Z-2296-50**

ZytoLight® SPEC TP53/ATM Dual Color Probe

Intended Purpose

The Zyto*Light* SPEC TP53/ATM Dual Color Probe (PL115) is intended to be used for the qualitative detection of deletions involving the human TP53 gene as well as the human ATM gene in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The Zyto*Light* SPEC TP53/ATM Dual Color Probe is composed of:

- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 17p13.1* (chr17:7,495,749-7,663,022) harboring the TP53 gene region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 11q22.3* (chr11:107,957,618-108,380,921) harboring the ATM gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

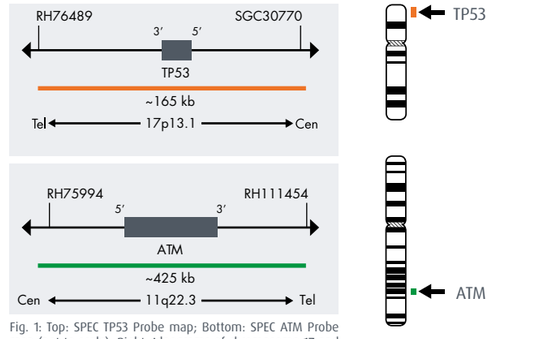
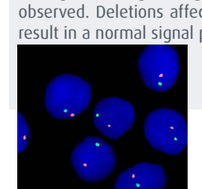


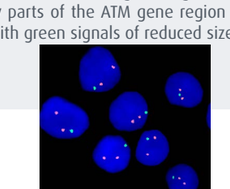
Fig. 1: Top: SPEC TP53 Probe map; Bottom: SPEC ATM Probe map (not to scale); Right: Ideograms of chromosome 17 and 11 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a deletion involving the respective gene regions, two green and two orange signals appear.
Aberrant situation: In a cell with deletions affecting the TP53 gene region, 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 deletions affecting the ATM gene region, a reduced number of green signals will be observed. Deletions affecting only parts of the ATM gene region might result in a normal signal pattern with green signals of reduced size.



Example of an aberrant signal pattern: Hybridized to bone marrow biopsy with deletions of the ATM and the TP53 genes as indicated by one green and one orange signal in each nucleus.



Example of an aberrant signal pattern: SPEC TP53/ATM Dual Color Probe hybridized to bone marrow smear with deletion of the ATM gene as indicated by one green signal in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	11, 17	CE/IVD	5 (50 µl)	**Z-2159-50**
			20 (200 µl)	**Z-2159-200**

ZytoLight® SPEC D13S319/13q34/CEN 12 Triple Color Probe

Intended Purpose
The Zyto*Light* SPEC D13S319/13q34/CEN 12 Triple Color Probe (PL116) is intended to be used for the qualitative detection of deletions involving the human D13S319 region as well as the detection of chromosome 13q34 specific sequences and chromosome 12 alpha satellites in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

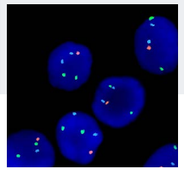
The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

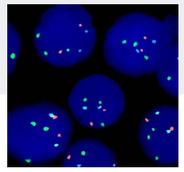
Probe Description
The Zyto*Light* SPEC D13S319/13q34/CEN 12 Triple Color Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 13q14.2* (chr13:50,607,438-50,781,256) harboring the D13S319 locus (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~37 ng/µl), which target sequences mapping in 13q34* (chr13:113,691,216-114,323,467) harboring the LAMP1 gene region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 12p11.1-q11 specific for the alpha satellite centromeric region D12Z3 of chromosome 12.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the D13S319 locus and without aneusomy of chromosomes 12 and 13, two orange, two blue, and two green signals appear.
Aberrant situation: 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 monosomy 13, a reduced number of both, the orange (D13S319 locus) and blue (13q34 locus) signals will be observed. In a cell with trisomy or polysomy 12, three or more copies of the green signal will be observed, respectively.



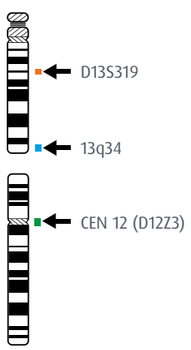
Example of an aberrant signal pattern: SPEC D13S319/13q34/CEN 12 Triple Color Probe hybridized to bone marrow biopsy section with deletion of the D13S319 locus as indicated by one orange signal and two blue signals in each nucleus.



Example of an aberrant signal pattern: SPEC D13S319/13q34/CEN 12 Triple Color Probe hybridized to bone marrow smear with trisomy of chromosome 12 as indicated by three green signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	12, 13	CE/IVD	5 (50 µl)	**Z-2160-50**
			20 (200 µl)	**Z-2160-200**

Fig. 1: Top: SPEC D13S319 Probe map; Bottom: SPEC 13q34 Probe map (not to scale)



Ideograms of chromosome 13 and 12 indicating the hybridization locations

ZytoLight® SPEC D13S319/13q34 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC D13S319/13q34 Dual Color Probe (PL235) is intended to be used for the qualitative detection of deletions involving the human D13S319 region and chromosome 13q34 specific sequences in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC D13S319/13q34 Dual Color Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 13q14.2* (chr13:50,607,438-50,781,256) harboring the D13S319 locus (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 13q34 (chr13:113,691,216-114,323,467) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

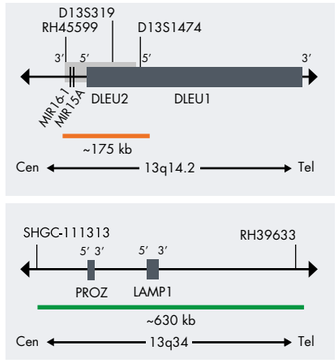
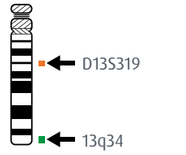
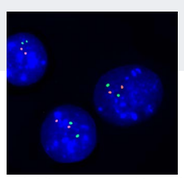


Fig. 1: Top: SPEC D13S319 Probe map; Bottom: SPEC 13q34 Probe map (not to scale)

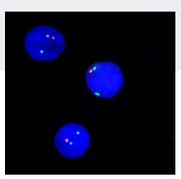


Ideogram of chromosome 13 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the D13S319 locus, two orange signals and two green signals appear.
Aberrant situation: In a cell with deletion 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 deletions affecting the 13q34 locus, a reduced number of green signals will be observed.



Hybridized to normal interphase cells as indicated by two green and two orange signals in each nucleus.



Example of an aberrant signal pattern: Bone marrow smear with deletion of the D13S319 locus as indicated by one orange and two green signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	13	CE/IVD	5 (50 µl)	**Z-2280-50**
			20 (200 µl)	**Z-2280-200**

ZytoLight® SPEC 11q gain/loss Triple Color Probe

Intended Purpose
The Zyto*Light* SPEC 11q gain/loss Triple Color Probe (PL174) is intended to be used for the qualitative detection of human 11q alterations involving human 11q23.3 and 11q24.1-q25 specific sequences in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

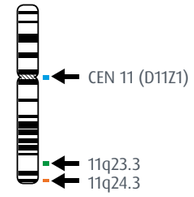
The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

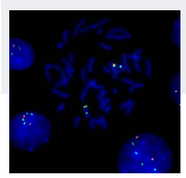
Probe Description
The Zyto*Light* SPEC 11q gain/loss Triple Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in the minimal gained region (MGR) at 11q23.3* (chr11:117,574,074-118,284,029) (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in the minimal loss region (MLR) at 11q24.3* (chr11:128,707,454-129,161,227) (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~12,0 ng/µl), which target sequences mapping in 11p11.11-q11 specific for the alpha satellite centromeric region D11Z1 of chromosome 11.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

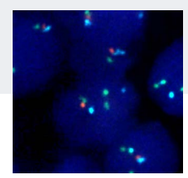
Fig. 1: SPEC 11q Probe map (not to scale);
Right: Ideogram of chromosome 11 indicating the hybridization locations



Results
Normal situation: In interphases of normal cells or cells without an 11q alteration, two green, two orange, and two blue signals appear.
Aberrant situation: In interphases of cells affected by an 11q-gain/loss alteration, one green and one orange signal is expected for the unaffected chromosome, and a gain of green signals and loss of one orange signal is expected for the chromosome affected by an 11q-gain/loss alteration. Deletions affecting only parts of the 11q loss region might result in a normal signal pattern with orange signals of reduced size.



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.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	11	CE/IVD	5 (50 µl)	**Z-2216-50**

ZytoLight® SPEC KMT2A Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC KMT2A Dual Color Break Apart Probe (PL151) is intended to be used for the qualitative detection of translocations involving the human KMT2A gene at 11q23.3 in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC KMT2A Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 11q23.3* (chr11:117,574,074-118,284,029) proximal to the KMT2A breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 11q23.3* (chr11:118,399,293-119,237,675) distal to the KMT2A breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

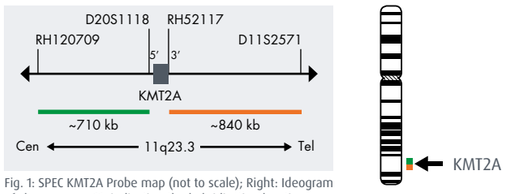
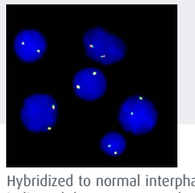
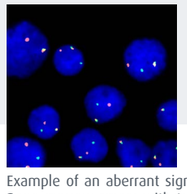


Fig. 1: SPEC KMT2A Probe map (not to scale); Right: Ideogram of chromosome 11 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the KMT2A gene region, two green/orange fusion signals appear.
Aberrant situation: One KMT2A gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	11	CE/IVD	5 (50 µl)	**Z-2193-50**
			20 (200 µl)	**Z-2193-200**

ZytoLight® SPEC ZNF384 Dual Color Break Apart Probe

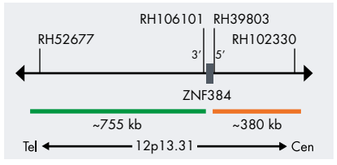
Intended Purpose
The Zyto*Light* SPEC ZNF384 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 12p13.31 harboring the ZNF384 gene.

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 infor*Mation*. 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 Zyto*Light* SPEC ZNF384 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 12p13.31* (chr12:6,016,809-6,771,300) distal to the ZNF384 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 12p13.31* (chr12:6,799,546-7,175,222) proximal to the ZNF384 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



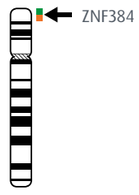


Fig. 1: SPEC ZNF384 Probe map (not to scale); Right: Ideogram of chromosome 12 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the ZNF384 gene region, two green/orange fusion signals appear.
Aberrant situation: One ZNF384 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.

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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	12	CE/IVD	5 (50 µl)	**Z-2275-50**

ZytoLight® SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe

Intended Purpose
The Zyto*Light* 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.

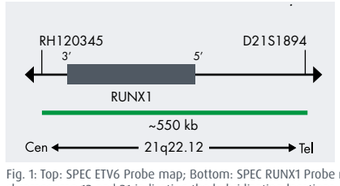
Three secondary aberrations in ETV6/RUNX1 positive ALL have been found to negatively influence the clinical course: deletion of the second non-translocated ETV6 allele, gains of the RUNX1 gene, and duplication of the derivative chromosome 21.

Detection of t(12;21) by Fluorescence *in situ* Hybridization enables the simultaneous identification of the most common secondary changes and thus provides additional infor*Mation* about the possible outcome of the disease in patients with ALL.

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.

Probe Description
The Zyto*Light* SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~6 ng/µl), which target sequences mapping in 12p13.2* (chr12:11,586,400-12,454,330) harboring the ETV6 region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~12,0 ng/µl), which target sequences mapping in 21q22.12* (chr21:36,106,492-36,657,941) harboring the RUNX1 gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



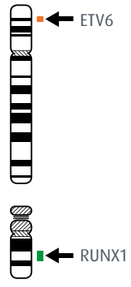
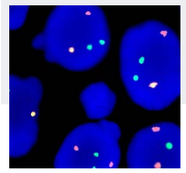
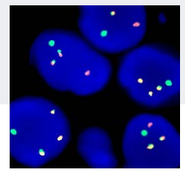


Fig. 1: Top: SPEC ETV6 Probe map; Bottom: SPEC RUNX1 Probe map (not to scale); Right: Ideograms of chromosome 12 and 21 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the respective gene regions, two separate green and orange signals appear.
Aberrant situation: A gene fusion is indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	12, 21	CE/IVD	5 (50 µl)	**Z-2157-50**
			20 (200 µl)	**Z-2157-200**

ISH

ZytoLight® SPEC ETV6 Dual Color Break Apart Probe

Intended Purpose
The ZytoLight SPEC ETV6 Dual Color Break Apart Probe (PL135) is intended to be used for the qualitative detection of translocations involving the human ETV6 gene at 12p13.2 in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC ETV6 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 12p13.2* (chr12:12,054,737-12,634,328) proximal to the ETV6 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 12p13.2* (chr12:11,393,774-11,808,608) distal to the ETV6 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

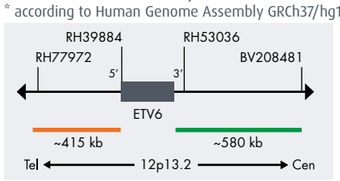
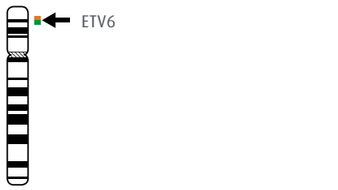
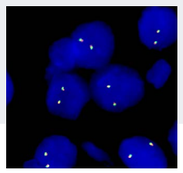


Fig. 1: SPEC ETV6 Probe map (not to scale)

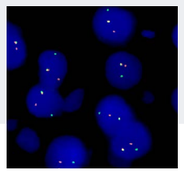


Ideogram of chromosome 12 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the ETV6 gene region, two green/orange fusion signals appear.
Aberrant situation: One ETV6 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	12	CE/IVD	5 (50 µl)	**Z-2176-50**
			20 (200 µl)	**Z-2176-200**

ZytoLight® SPEC KRAS/CEN 12 Dual Color Probe

Intended Purpose
The ZytoLight SPEC KRAS/CEN 12 Dual Color Probe (PL72) is intended to be used for the qualitative detection of amplifications involving the human KRAS gene as well as chromosome 12 alpha satellites in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC KRAS/CEN 12 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 12p12.1* (chr12:24,916,728-25,839,353) harboring the KRAS gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1,5 ng/µl), which target sequences mapping in 12p11.1-q11 specific for the alpha satellite centromeric region D12Z3 of chromosome 12.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

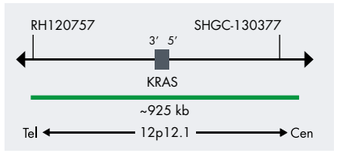
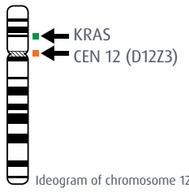
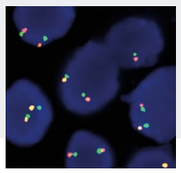


Fig. 1: SPEC KRAS Probe map (not to scale)

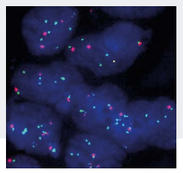


Ideogram of chromosome 12 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the KRAS gene region, two green and two orange signals appear.
Aberrant situation: In cells with an amplification of the KRAS gene region, an increased number of green signals or green signal clusters will be observed.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Example of an aberrant signal pattern: Lung cancer tissue section with amplification of the KRAS gene (green).

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	12	CE/IVD	20 (200 µl)	**Z-2115-200**

Image kindly provided by Prof. Diebold, Lucerne, Switzerland.

ZytoLight® SPEC DDIT3 Dual Color Break Apart Probe

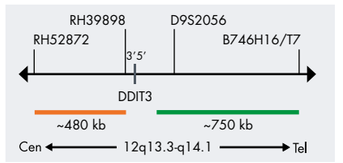
Intended Purpose
The ZytoLight SPEC DDIT3 Dual Color Break Apart Probe (PL58) is intended to be used for the qualitative detection of translocations involving the human DDIT3 gene at 12q13.3 in formalin-fixed, paraffin-embedded specimens, such as myxoid liposarcomas (MLPS), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of MLPS and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC DDIT3 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 12q13.3-14.1* (chr12:58,024,366-58,775,832) distal to the DDIT3 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 12q13.3* (chr12:57,386,312-57,865,800) proximal to the DDIT3 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



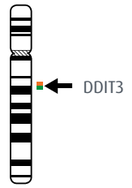
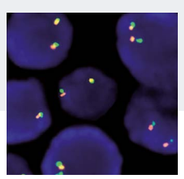
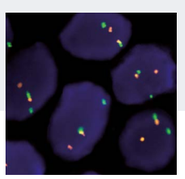


Fig. 1: SPEC DDIT3 Probe map (not to scale); Right: Ideogram of chromosome 12 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the DDIT3 gene region, two green/orange fusion signals appear.
Aberrant situation: One DDIT3 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	12	CE/IVD	5 (50 µl)	**Z-2100-50**
			20 (200 µl)	**Z-2100-200**

ZytoLight® SPEC CDK4/CEN 12 Dual Color Break Apart Probe

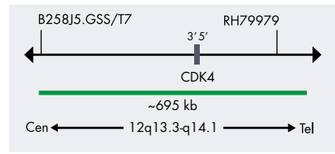
Intended Purpose
The ZytoLight SPEC CDK4/CEN 12 Dual Color Probe (PL61) is intended to be used for the qualitative detection of amplifications involving the human CDK4 gene as well as the detection of chromosome 12 alpha satellites in formalin-fixed, paraffin-embedded specimens, such as atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDLPS) and dedifferentiated liposarcoma (DDLPS), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of ALT/WDLPS and DDLPS and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC CDK4/CEN 12 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 12q13.3-q14.1* (chr12:57,740,440-58,435,534) harboring the CDK4 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1,5 ng/µl), which target sequences mapping in 12p11.1-q11 specific for the alpha satellite centromeric region D12Z3 of chromosome 12.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



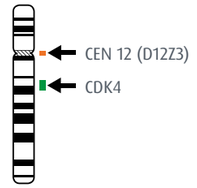
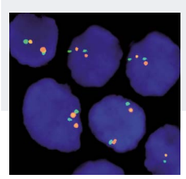
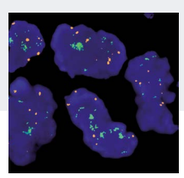


Fig. 1: SPEC CDK4 Probe map (not to scale); Right: Ideogram of chromosome 12 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the CDK4 gene, two green and two orange signals appear.
Aberrant situation: In cells with an amplification of the CDK4 gene region, an increased number of green signals or green signal clusters will be observed.



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).

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	12	CE/IVD	5 (50 µl)	**Z-2103-50**
			20 (200 µl)	**Z-2103-200**

ZytoLight® SPEC MDM2/CEN 12 Dual Color Probe

Intended Purpose
The ZytoLight SPEC MDM2/CEN 12 Dual Color Probe (PL18) is intended to be used for the qualitative detection of amplifications involving the human MDM2 gene as well as the detection of chromosome 12 alpha satellites in formalin-fixed, paraffin-embedded specimens, such as atypical lipomatous tumor/well differentiated liposarcoma (ALT/WDLPS) and dedifferentiated liposarcoma (DDLPS), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

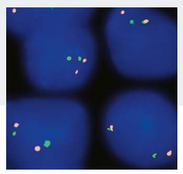
The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

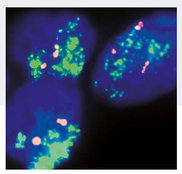
The probe is intended to be used as an aid to the differential diagnosis of ALT/WDLPS and DDLPS and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC MDM2/CEN 12 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 12q15* (chr12:69,071,802-69,565,421) harboring the MDM2 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1.5 ng/µl), which target sequences mapping in 12p11.1-q11 specific for the alpha satellite centromeric region D12Z3 of chromosome 12.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the MDM2 gene region, two green signals and two orange signals appear.
Aberrant situation: In cells with an amplification of the MDM2 gene region an increased number of green signals 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).

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	12	CE/IVD	5 (50 µl)	Z-2013-50
			20 (200 µl)	Z-2013-200

ZytoLight® SPEC FOXO1 Dual Color Break Apart Probe

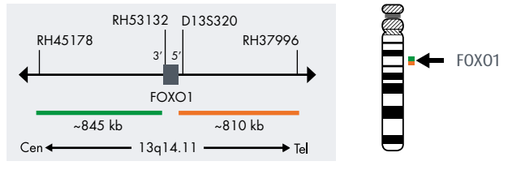
Intended Purpose
The ZytoLight SPEC FOXO1 Dual Color Break Apart Probe (PL96) is intended to be used for the qualitative detection of translocations involving the human FOXO1 gene at 13q14.11 in formalin-fixed, paraffin-embedded specimens, such as alveolar rhabdomyosarcoma (ARMS), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

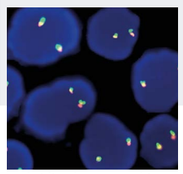
The probe is intended to be used as an aid to the differential diagnosis of ARMS and therapeutic measures should not be initiated based on the test result alone.

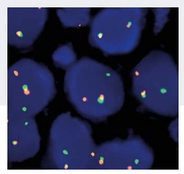
Probe Description
The ZytoLight SPEC FOXO1 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 13q14.11* (chr13:40,285,558-41,132,595) proximal to the FOXO1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 13q14.11* (chr13:41,246,917-42,054,781) distal to the FOXO1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



Results
Normal situation: In interphases of normal cells or cells without a translocation involving the FOXO1 gene region, two green/orange fusion signals appear.
Aberrant situation: One FOXO1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.


Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	13	CE/IVD	5 (50 µl)	Z-2139-50

ZytoLight® SPEC FOXO1/PAX3 Dual Color Single Fusion Probe

Intended Purpose
The ZytoLight SPEC FOXO1/PAX3 Dual Color Single Fusion Probe (PL16) is intended to be used for the qualitative detection of translocation t(2;13)(q36;q14.1) involving the human FOXO1 and PAX3 genes in formalin-fixed, paraffin-embedded specimens, such as alveolar rhabdomyosarcoma (ARMS), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of ARMS and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC FOXO1/PAX3 Dual Color Single Fusion Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 13q14.11* (chr13:40,816,168-41,132,595) proximal to the FOXO1 breakpoint region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 2q36.1* (chr2:223,196,078-223,539,352) distal to the PAX3 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

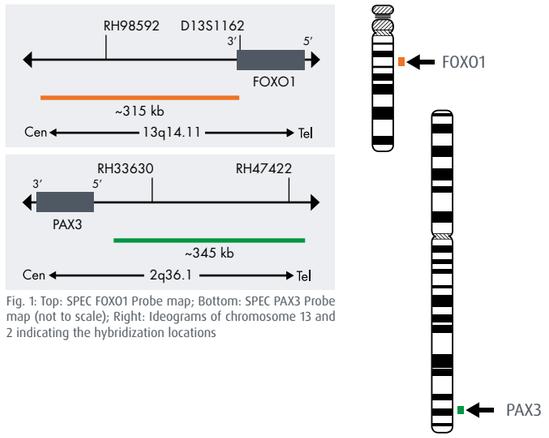
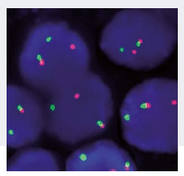


Fig. 1: Top: SPEC FOXO1 Probe map; Bottom: SPEC PAX3 Probe map (not to scale); Right: Ideograms of chromosome 13 and 2 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the respective gene regions, two separate green and orange signals appear.
Aberrant situation: A gene fusion is indicated by one separate orange signal, one separate green signal, and one orange/green fusion signal.



Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	2, 13	CE/IVD	5 (50 µl)	Z-2018-50
			20 (200 µl)	Z-2018-200

ZytoLight® SPEC FOXO1/PAX3 TriCheck™ Probe

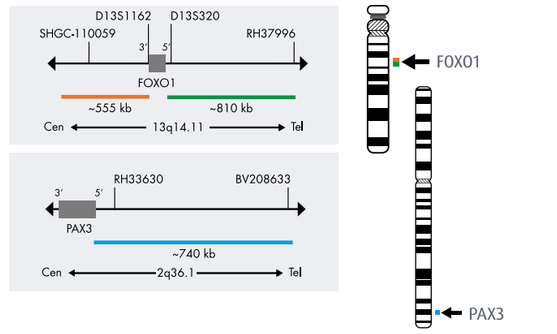
Intended Purpose
The ZytoLight SPEC FOXO1/PAX3 TriCheck Probe (PL143) is intended to be used for the qualitative detection of rearrangements involving the human FOXO1 gene at 13q14.11 and the human PAX3 gene at 2q36.1 in formalin-fixed, paraffin-embedded specimens, such as alveolar rhabdomyosarcoma (ARMS), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

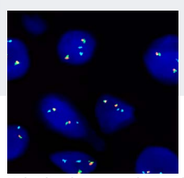
The probe is intended to be used as an aid to the differential diagnosis of ARMS and therapeutic measures should not be initiated based on the test result alone.

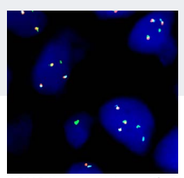
Probe Description
The ZytoLight SPEC FOXO1/PAX3 TriCheck Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 13q14.11* (chr13:41,246,917-42,054,781) distal to the FOXO1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 13q14.11* (chr13:40.578,036-41,132,595) proximal to the FOXO1 breakpoint region (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~37,0 ng/µl), which target sequences mapping in 2q36.1* (chr2:223,196,078-223,936,825) distal to the PAX3 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



Results
Normal situation: In interphases of normal cells or cells without PAX3-FOXO1 rearrangement, green/orange fusion signals and two blue signals appear.
Aberrant situation: 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.


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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	2, 13	CE/IVD	5 (50 µl)	Z-2185-50

ZytoLight® SPEC FOXO1/PAX7 Dual Color Single Fusion Probe

Intended Purpose

The Zyto*Light* SPEC FOXO1/PAX7 Dual Color Single Fusion Probe (PL17) is intended to be used for the qualitative detection of translocation t(1;13)(p36.1;q14.1) involving the human FOXO1 and PAX7 genes in formalin-fixed, paraffin-embedded specimens, such as alveolar rhabdomyosarcoma (ARMS), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of ARMS and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The Zyto*Light* SPEC FOXO1/PAX7 Dual Color Single Fusion Probe is composed of:

- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 13q14.11* (chr13:40,816,168-41,132,595) proximal to the FOXO1 breakpoint region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 1p36.13* (chr1:18,139,970-18,956,785) distal to the PAX7 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

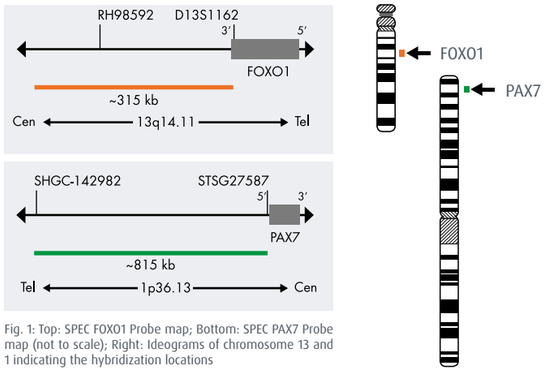
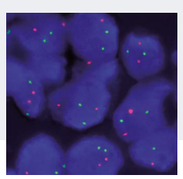


Fig. 1: Top: SPEC FOXO1 Probe map; Bottom: SPEC PAX7 Probe map (not to scale); Right: Ideograms of chromosome 13 and 1 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a translocation involving the respective gene regions, two separate green and orange signals appear.
Aberrant situation: A gene fusion is indicated by one separate orange signal, one separate green signal, and one orange/green fusion signal.



Hybridized to normal interphase cells as indicated by two orange and two green signals.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	1, 13	CE/IVD	5 (50 µl)	**Z-2019-50**
			20 (200 µl)	**Z-2019-200**

ZytoLight® SPEC RB1/13q34 Dual Color Probe

Intended Purpose

The Zyto*Light* SPEC RB1/13q34 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, FISH is a valuable tool for the detection of RB1 gene deletions and can be used in combination with further biological markers, morphology and clinical infor*Mation* for the prediction of disease progression and overall survival.

References

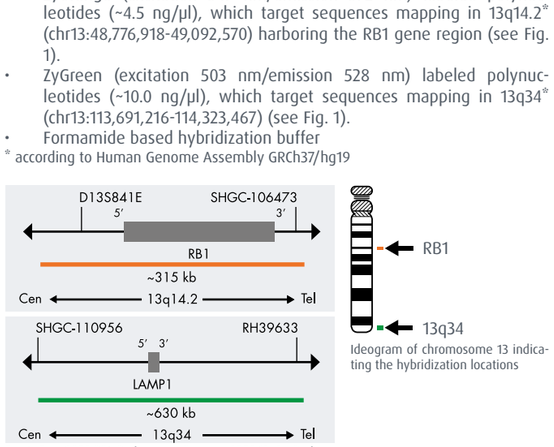
Dal Bo M, *et al.* (2011) Genes Chromosomes Cancer 50: 633-43.
Dao DD, *et al.* (1994) Leukemia 8: 1280-4.
Di Fiore R, *et al.* (2013) J Cell Physiol 228: 1676-87.
Juge-Morineau N, *et al.* (1997) Leuk Lymphoma 24: 229-37.
Orlandi EM, *et al.* (2013) Hematol Oncol 31: 136-42.
Ouillette P, *et al.* (2011) Clin Cancer Res 17: 6778-90.

Probe Description

The Zyto*Light* SPEC RB1/13q34 Dual Color Probe is composed of:

- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 13q14.2* (chr13:48,776,918-49,092,570) harboring the RB1 gene region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10.0 ng/µl), which target sequences mapping in 13q34* (chr13:113,691,216-114,323,467) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

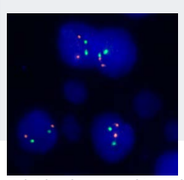


Ideogram of chromosome 13 indicating the hybridization locations

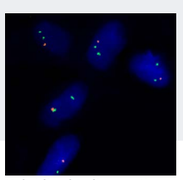
Fig. 1: Top: SPEC RB1 Probe map; Bottom: SPEC 13q34 Probe map

Results

Normal situation: In interphases of normal cells or cells without a deletion involving the RB1 gene region, two orange signals and two green signals appear.
Aberrant situation: In a cell with deletion affecting the RB1 gene region, a reduced number of the orange signals will be observed.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Hybridized to lipoma tissue section with deletion of the RB1 gene as indicated by one orange signal and two green signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	13	CE/IVD	5 (50 µl)	**Z-2324-50**
			20 (200 µl)	**Z-2324-200**

ZytoLight® SPEC IGH Dual Color Break Apart Probe

Intended Purpose

The Zyto*Light* SPEC IGH Dual Color Break Apart Probe (PL67) is intended to be used for the qualitative detection of translocations involving the human IGH locus at 14q32.33 in cytologic or formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with Zyto*Light* FISH Implementation Kits (Prod. No. Z-2028-5/-20, or Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The Zyto*Light* SPEC IGH Dual Color Break Apart Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 14q32.33* (chr14:106,690,778-107,268,412) distal to the IGH breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 14q32.33* (chr14:105,296,741-105,909,611) proximal to the IGH breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

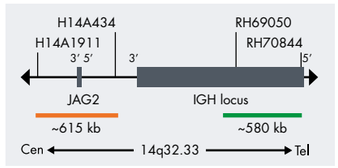
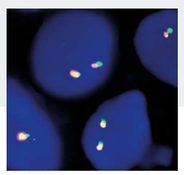


Fig. 1: SPEC IGH Probe map (not to scale)

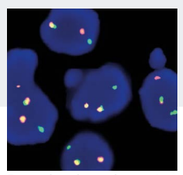
Ideogram of chromosome 14 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a translocation involving the IGH locus, two green/orange fusion signals appear.
Aberrant situation: One IGH locus affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	14	CE/IVD	5 (50 µl)	**Z-2110-50**
			20 (200 µl)	**Z-2110-200**

ZytoLight® SPEC Angelman Dual Color Probe

Intended Purpose

The Zyto*Light* SPEC Angelman Dual Color Probe (PL273) is intended to be used for the qualitative detection of human UBE3A gene deletions as well as the detection of the human PML gene in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the above mentioned product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

Interpretation of the results must be made within the context of the patient´s clinical history with respect to further clinical and pathologic data of the patient by a qualified pathologist/human geneticist.

Probe Description

The Zyto*Light* SPEC Angelmann Dual Color Probe is composed of:

- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 15q11.2-q12* (chr15:25,550,004-25,748,900) harboring the UBE3A gene region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10.0 ng/µl), which target sequences mapping in 15q24.1* (chr15:73,910,690-74,699,298) harboring the PML gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

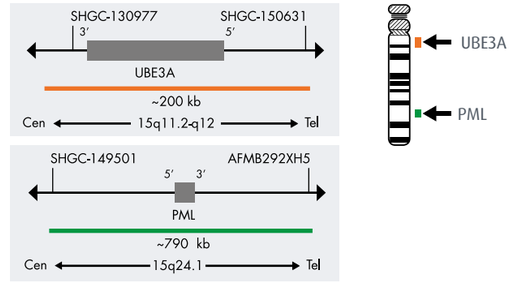
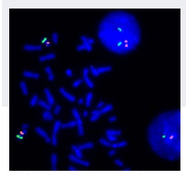


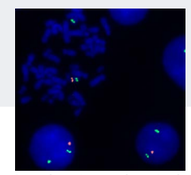
Fig. 1: Top: SPEC UBE3A Probe map; Bottom: SPEC PML Probe map (not to scale); Right: Ideogram of chromosome 15 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a deletion involving the UBE3A gene region, two green and two orange signals appear.
Aberrant situation: In a cell with deletion affecting the UBE3A gene region, a reduced number of orange signals will be observed. Deletions affecting only parts of the UBE3A gene region might result in normal signal pattern with orange signals of reduced size.



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.



Lymphocytes and metaphase chromosomes from an Angelman syndrome case showing deletion affecting the chromosomal region 15q11.2-q12 as indicated by the loss of one orange signal.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	15	CE/IVD	5 (50 µl)	**Z-2319-50**

ISH

ZytoLight® SPEC Prader-Willi Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC Prader-Willi Dual Color Probe is designed to detect deletions affecting the chromosomal region 15q11.2 harboring the SNRPN (small nuclear ribonucleoprotein polypeptide N, a.k.a. PWCR) gene.

The Prader-Willi syndrome (PWS) is a sporadic genetic disorder caused by genomic errors that inactivate paternally-inherited genes in the PWS critical region on chromosome 15q11-q13. The absence of expression of one or more of these genes contributes to different phenotypes of PWS. There are three main genetic causes: paternal 5-7 Mb deletion of the 15q11-q13 region, maternal uniparental disomy 15, or imprinting defects in the PWS critical region.

The SNRPN gene is located within the PWS region and has an important regulatory role over the imprinted genes located in chromosome 15. The estimated prevalence of the disease ranges between 1/15,000 and 1/30,000 newborns. PWS patients clinically display a characteristic pattern of symptoms including hypotonia with poor suck and poor weight gain in infancy, mild mental retardation, hypogonadism, growth hormone insufficiency causing short stature, early childhood-onset hyperphagia and obesity, characteristic appearance, and behavioral and sometimes psychiatric disturbance.

Early diagnosis offers the opportunity to significantly improve health and quality of life of people with PWS. FISH analysis can be performed to detect deletions within the PWS critical region and can help to confirm PWS diagnosis in patients with clinical features characteristic for PWS.

References
Cassidy AB & Driscoll DJ (2009) Eur J Hum Genet 17: 3-13.
Costa RA, *et al.* (2019) Front Endocrinol (Lausanne) 10: 864.

Probe Description
The Zyto*Light* SPEC Prader-Willi Dual Color Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 15q11.2* (chr15:25,097,811-25,270,969) harboring the SNRPN gene region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10.0 ng/µl), which target sequences mapping in 15q24.1* (chr15:73,910,690-74,699,298) harboring the PML gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

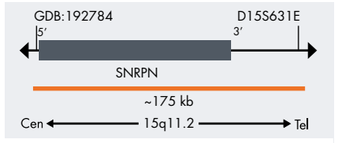
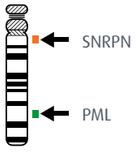
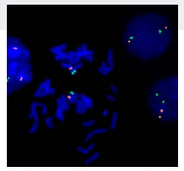


Fig. 1: Top: SPEC SNRPN Probe map; Bottom: SPEC PML Probe map (not to scale)

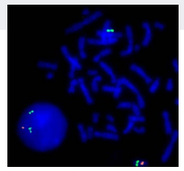


Ideogram of chromosome 15 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the SNRPN gene region, two green and two orange signals appear.
Aberrant situation: In a cell with deletion affecting the SNRPN gene region, a reduced number of orange signals will be observed. Deletions affecting only parts of the SNRPN gene region might result in normal signal pattern with orange signals of reduced size.



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.



Lymphocytes and metaphase chromosomes from a Prader-Willi syndrome case showing deletion affecting the chromosomal region 15q11.2 as indicated by the loss of one orange signal.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	15	CE/IVD	5 (50 µl)	**Z-2318-50**

ISH

ZytoLight® SPEC NUTM1 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC NUTM1 Dual Color Break Apart Probe (PL166) is intended to be used for the qualitative detection of translocations involving the human NUTM1 gene at 15q14 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC NUTM1 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 15q14* (chr15:33,999,791-34,587,649) proximal to the NUTM1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 15q14* (chr15:34,873,659-35,326,986) distal to the NUTM1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

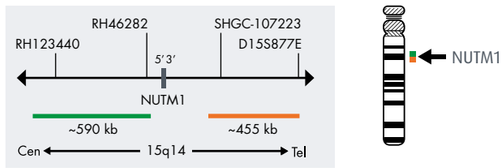
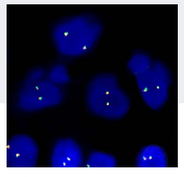
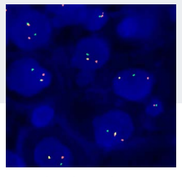


Fig. 1: SPEC NUTM1 Probe map (not to scale); Right: Ideogram of chromosome 15 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the NUTM1 gene region, two green/orange fusion signals appear.
Aberrant situation: One NUTM1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	15	CE/IVD	20 (200 µl)	**Z-2208-200**

ZytoLight® SPEC NTRK3 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC NTRK3 Dual Color Break Apart Probe (PL164) is intended to be used for the qualitative detection of translocations involving the human NTRK3 gene at 15q25.3 in cytologic or formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with Zyto*Light* FISH Implementation Kits (Prod. No. Z-2028-5/-20, or Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC NTRK3 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 15q25.3-q26.1* (chr15:88,825,346-89,475,889) distal to the NTRK3 breakpoint region (see Fig.1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 15q25.3* (chr15:87,976,717-88,471,002) proximal to the NTRK3 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

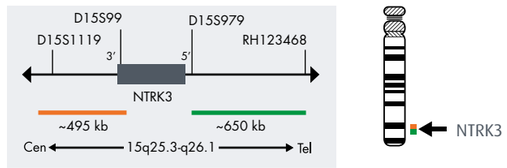
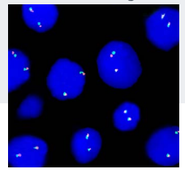
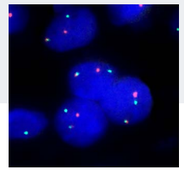


Fig. 1: SPEC NTRK3 Probe map (not to scale): Right: Ideogram of chromosome 15 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the NTRK3 gene region, two green/orange fusion signals appear.
Aberrant situation: One NTRK3 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal. Isolated orange signals are the result of deletions distal to the NTRK3 breakpoint region or are due to unbalanced translocations affecting this chromosomal region.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	15	CE/IVD	5 (50 µl)	**Z-2206-50**
			20 (200 µl)	**Z-2206-200**

ZytoLight® SPEC PML/RARA Dual Color Dual Fusion Probe

Intended Purpose
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 ZytoLight SPEC PML/RARA Dual Color Dual Fusion Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~12,0 ng/µl), which target sequences mapping in 17q12-q21.2* (chr17:37,953,503-38,818,030) (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~6 ng/µl), which target sequences mapping in 15q24.1* (chr15:73,910,690-74,699,298) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

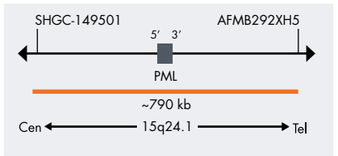
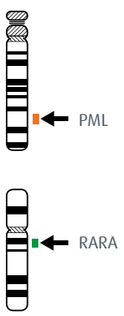
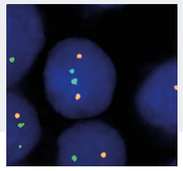


Fig. 1: Top: SPEC PML Probe map; Bottom: SPEC RARA Probe map (not to scale)

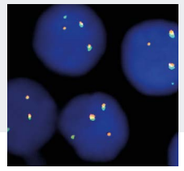


Ideograms of chromosome 15 and 17 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the respective gene regions, two separate green and orange signals appear.
Aberrant situation: A gene fusion is indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	15, 17	CE/IVD	5 (50 µl)	**Z-2113-50**
			20 (200 µl)	**Z-2113-200**

ZytoLight® SPEC CREBBP Dual Color Break Apart Probe

Intended Purpose
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.

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.

Probe Description
The ZytoLight SPEC CREBBP Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 16p13.3* (chr16:3,978,217-4,521,684) proximal to the CREBBP breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 16p13.3* (chr16:3,287,067-3,762,188) distal to the CREBBP breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

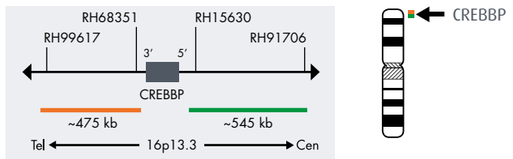
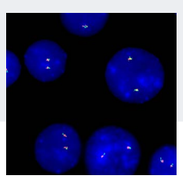


Fig. 1: SPEC CREBBP Probe map (not to scale); Right: Ideogram of chromosome 16 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the CREBBP gene region, two green/orange fusion signals appear.
Aberrant situation: One CREBBP gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	16	CE/IVD	5 (50 µl)	**Z-2267-50**

ZytoLight® SPEC FUS Dual Color Break Apart Probe

Intended Purpose
The ZytoLight SPEC FUS Dual Color Break Apart Probe (PL87) is intended to be used for the qualitative detection of translocations involving the human FUS gene at 16p11.2 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC FUS Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 16p11.2* (chr16:30,383,304-31,007,836) distal to the FUS breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 16p11.2* (chr16:31,213,259-31,927,155) proximal to the FUS breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

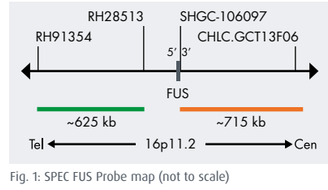
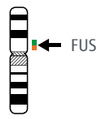
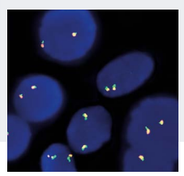


Fig. 1: SPEC FUS Probe map (not to scale)

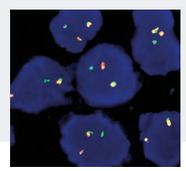


Ideogram of chromosome 16 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the FUS gene region, two green/orange fusion signals appear.
Aberrant situation: One FUS gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	16	CE/IVD	5 (50 µl)	**Z-2130-50**

ZytoLight® SPEC MAF/IGH Dual Color Dual Fusion Probe

Intended Purpose
The Zyto*Light* 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 550-1280kb 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 Zyto*Light* SPEC MAF/IGH Dual Color Dual Fusion Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~6 ng/µl), which target sequences mapping in 16q23.1-q23.2* (chr16:78,089,697-79,657,277) harboring the MAF gene region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~12,0 ng/µl), which target sequences mapping in 14q32.33* (chr14:105,462,169-106,995,000) harboring the IGH locus (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

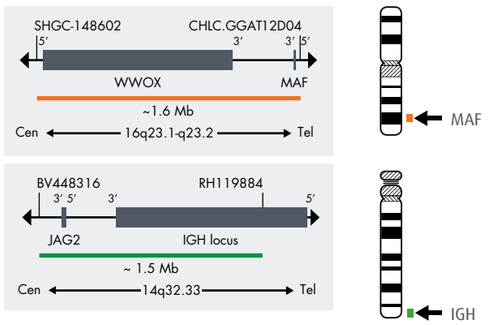
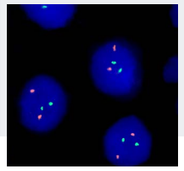
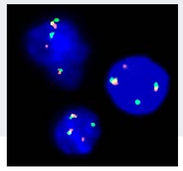


Fig. 1: Top: SPEC MAF Probe map; Bottom: SPEC IGH Probe map (not to scale); Right: Ideograms of chromosome 16 and 14 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the respective bands, two separate green and orange signals appear.
Aberrant situation: A gene fusion is indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	14, 16	CE/IVD	5 (50 µl)	**Z-2270-50**

Kindly provided by Prof. Dr. Oskar A. Haas, Vienna, Austria.

ZytoLight® SPEC MAFB/IGH Dual Color Dual Fusion Probe

Intended Purpose
The Zyto*Light* SPEC MAFB/IGH Dual Color Dual Fusion Probe is designed to detect the translocations affecting the MAFB gene in the chromosomal region on 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 dysregulation 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 Zyto*Light* SPEC MAFB/IGH Dual Color Dual Fusion Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~6 ng/µl), which target sequences mapping in 20q12* (chr20:37,782,012-39,385,613) harboring the MAFB gene region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~12,0 ng/µl), which target sequences mapping in 14q32.33* (chr14:105,462,169-106,995,000) harboring the IGH locus (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

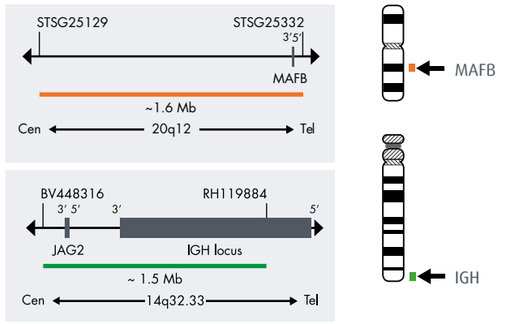
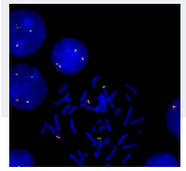
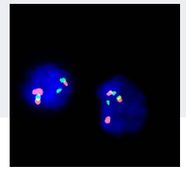


Fig. 1: Top: SPEC MAFB Probe map; Bottom: SPEC IGH Probe map (not to scale); Right: Ideograms of chromosome 20 and 14 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the respective loci, two separate green and orange signals appear.
Aberrant situation: A gene fusion is indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	14, 20	CE/IVD	5 (50 µl)	**Z-2271-50**

Kindly provided by Prof. Dr. Oskar A. Haas, Vienna, Austria.

ZytoLight® SPEC CBFB Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC CBFB Dual Color Break Apart Probe (PL165) is intended to be used for the qualitative detection of translocations involving the human CBFB gene at 16q22.1 in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

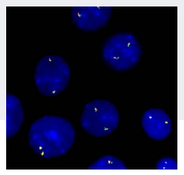
The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC CBFB Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 16q22.1* (chr16:67,161,347-67,605,304) distal to the CBFB breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 16q22.1* (chr16:66,882,262-67,102,895) proximal to the CBFB breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

Fig. 1: SPEC CBFB Probe map (not to scale); Right: Ideogram of chromosome 16 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the CBFB gene region, two green/orange fusion signals appear.
Aberrant situation: One CBFB gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	16	CE/IVD	5 (50 µl)	**Z-2207-50**

ZytoLight® SPEC TP53/17q22 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC TP53/17q22 Dual Color Probe (PL156) is intended to be used for the qualitative detection of deletions involving the human TP53 gene as well as the detection of gains of chromosome 17q22 specific sequences in cytologic or formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with Zyto*Light* FISH Implementation Kits (Prod. No. Z-2028-5/-20, or Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC TP53/17q22 Dual Color Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 17p13.1* (chr17:7,495,749-7,663,022) harboring the TP53 gene region (see Fig.1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 17q22* (chr17:56,124,338-56,594,220) (see Fig.1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

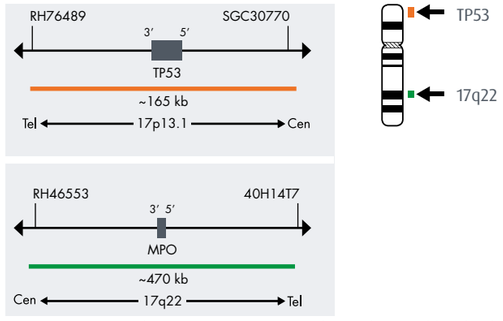
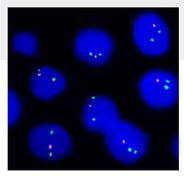
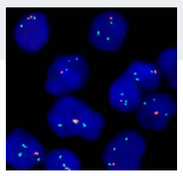


Fig. 1: Top: SPEC TP53 Probe map; Bottom: SPEC 17q22 Probe map (not to scale); Right: Ideogram of chromosome 17 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the TP53 gene region, two green and two orange signals appear.
Aberrant situation: In a cell with deletion affecting the TP53 gene region, a reduced number of orange signals will be detected. Deletions affecting only parts of the TP53 gene region might result in a normal signal pattern with orange signals of reduced size. A gain of 17q involving the 17q22 region will result in an increased number of green signals. Isochromosome 17q is indicated by three green signals and one orange signal.



Example of an aberrant signal pattern: SPEC TP53/17q22 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.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	17	CE/IVD	5 (50 µl)	**Z-2198-50**

ZytoLight® SPEC TP53/CEN 17 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC TP53/CEN 17 Dual Color Probe (PL109) is intended to be used for the qualitative detection of deletions involving the human TP53 gene as well as the detection of chromosome 17 alpha satellites in cytologic or formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with Zyto*Light* FISH Implementation Kits (Prod. No. Z-2028-5/-20, or Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC TP53/CEN 17 Dual Color Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 17p13.1* (chr17:7,495,749-7,663,022) harboring the TP53 gene region (see Fig.1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 17p11.1-q11.1 specific for the alpha satellite centromeric region D17Z1 of chromosome 17.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

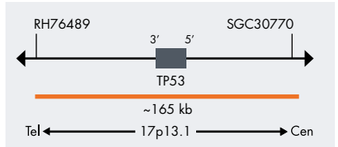
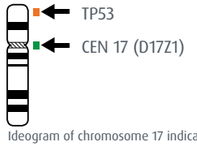
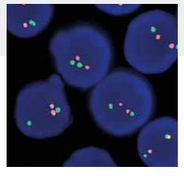


Fig. 1: SPEC TP53 Probe map (not to scale)

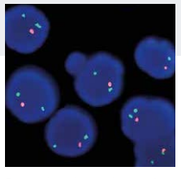


Ideogram of chromosome 17 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the TP53 gene region, two orange signals and two green signals appear.
Aberrant situation: In a cell with deletion affecting the TP53 gene region, a reduced number of orange signals will be observed. Deletions affecting only parts of the TP53 gene region might result in a normal signal pattern with orange signals of reduced size.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	17	CE/IVD	5 (50 µl)	**Z-2153-50**
			20 (200 µl)	**Z-2153-200**

ZytoLight® SPEC USP6 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC USP6 Dual Color Break Apart Probe (PL107) is intended to be used for the qualitative detection of translocations involving the human USP6 gene at 17p13.2 in formalin-fixed, paraffin-embedded specimens, such as aneurysmal bone cyst (ABC) or nodular fasciitis (NF), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20)

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of ABC or NF and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC USP6 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 17p13.2* (chr17:4,489,889-5,017,582) distal to the USP6 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 17p13.2* (chr17:5,087,046-5,361,104) proximal to the USP6 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

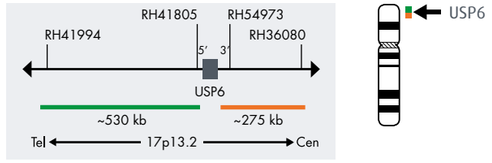
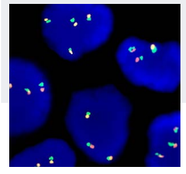
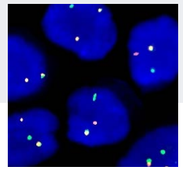


Fig. 1: SPEC USP6 Probe map (not to scale); Right: Ideogram of chromosome 17 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the USP6 gene region, two green/orange fusion signals appear.
Aberrant situation: One USP6 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	17	CE/IVD	5 (50 µl)	**Z-2151-50**
			20 (200 µl)	**Z-2151-200**

ZytoLight® SPEC YWHAE Dual Color Break Apart Probe

Intended Purpose
The ZytoLight SPEC YWHAE Dual Color Break Apart Probe (PL134) is intended to be used for the qualitative detection of translocations involving the human YWHAE gene at 17p13.3 in formalin-fixed, paraffin-embedded specimens, such as endometrial stromal sarcoma (ESS), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of ESS and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC YWHAE Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 17p13.3* (chr17:1,339,752-1,716,668) proximal to the YWHAE breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 17p13.3* (chr17:791,171-1,124,746) distal to the YWHAE breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

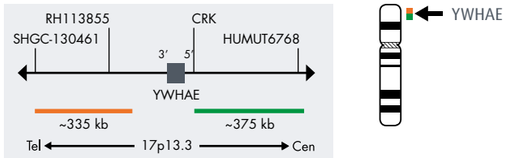
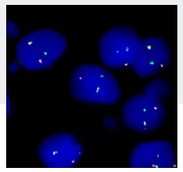


Fig. 1: SPEC YWHAE Probe map (not to scale); Right: Ideogram of chromosome 17 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the YWHAE gene region, two green/orange fusion signals appear.
Aberrant situation: One YWHAE gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	17	CE/IVD	5 (50 µl)	**Z-2175-50**

ZytoLight® SPEC ERBB2/CEN 17 Dual Color Probe

Intended Purpose
The ZytoLight SPEC ERBB2/CEN 17 Dual Color Probe (PL8) is intended to be used for the qualitative detection of amplifications involving the human ERBB2 gene as well as the detection of chromosome 17 alpha satellites in formalin-fixed, paraffin-embedded specimens, such as breast cancer and gastric/gastroesophageal junction cancer, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of breast cancer and gastric/gastroesophageal junction cancer and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC ERBB2/CEN 17 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 17q12-q21.1* (chr17:37,572,531-38,181,308) harboring the ERBB2 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1.5 ng/µl), which target sequences mapping in 17p11.1-q11.1 specific for the alpha satellite centromeric region D17Z1 of chromosome 17.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

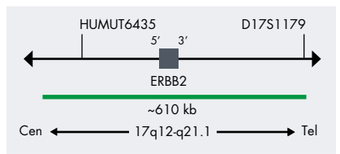
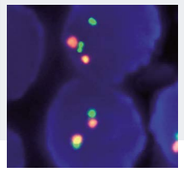
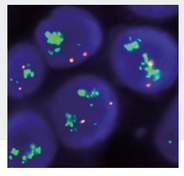


Fig. 1: SPEC ERBB2 Probe map (not to scale); Right: Ideogram of chromosome 17 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the ERBB2 gene region, two green signals and two orange signals appear.
Aberrant situation: In cells with an amplification of the ERBB2 gene region an increased number of green signals 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).

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	17	CE/IVD	5 (50 µl)	**Z-2015-50**
			20 (200 µl)	**Z-2015-200**

The product is also available as a kit in two different sizes.

ZytoLight SPEC ERBB2/CEN 17 Dual Color Probe Kit	Tests	Order No.
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-2020-5**
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	**Z-2020-20**

ZytoLight® CEN 17/SPEC ERBB2 Dual Color Probe

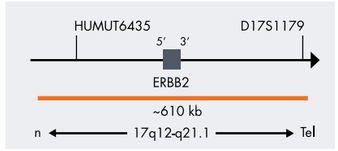
Intended Purpose
The ZytoLight CEN 17/SPEC ERBB2 Dual Color Probe (PL36) is intended to be used for the qualitative detection of amplifications involving the human ERBB2 gene as well as the detection of chromosome 17 alpha satellites in formalin-fixed, paraffin-embedded specimens, such as breast cancer and gastric/gastroesophageal junction cancer, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of breast cancer and gastric/gastroesophageal junction cancer and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight CEN 17/SPEC ERBB2 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 17p11.1-q11.1 specific for the alpha satellite centromeric region D17Z1 of chromosome 17.
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 17q12-q21.1* (chr17:37,572,531-38,181,308) harboring the ERBB2 gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



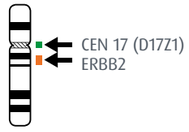
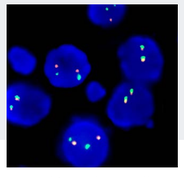
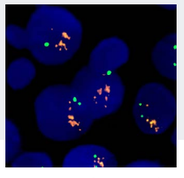


Fig. 1: SPEC ERBB2 Probe map (not to scale); Right: Ideogram of chromosome 17 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the ERBB2 gene region, two green and two orange signals appear.
Aberrant situation: In cells with an amplification of the ERBB2 gene region, an increased number of orange signals 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).

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	17	CE/IVD	5 (50 µl)	**Z-2077-50**
			20 (200 µl)	**Z-2077-200**

ZytoLight® SPEC ERBB2/D17S122 Dual Color Probe

Intended Purpose
The ZytoLight SPEC ERBB2/D17S122 Dual Color Probe (PL148) is intended to be used for the qualitative detection of amplifications involving the human ERBB2 gene as well as the detection of the D17S122 locus in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC ERBB2/D17S122 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 17q12-q21.1* (chr17:37,572,531-38,181,308) harboring the ERBB2 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 17p12* (chr17:14,954,785-15,434,017) harboring the D17S122 locus (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

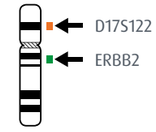
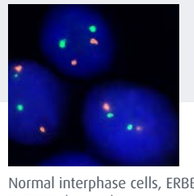
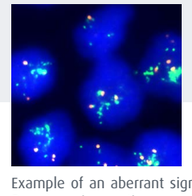


Fig. 1: Top: SPEC ERBB2 Probe map; Bottom: SPEC D17S122 Probe map (not to scale); Right: Ideogram of chromosome 17 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the ERBB2 gene region, two green signals and two orange signals appear.
Aberrant situation: In cells with an amplification of the ERBB2 gene region an increased number of green signals or green signal clusters will be observed.



Normal interphase cells, ERBB2 (green), D17S122 (orange).



Example of an aberrant signal pattern: Breast carcinoma tissue section, ERBB2 gene cluster (green), D17S122 (orange).

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	17	CE/IVD	5 (50 µl)	**Z-2190-50**
			20 (200 µl)	**Z-2190-200**

ZytoLight® SPEC ERBB2/TOP2A/CEN 17 Triple Color Probe

Intended Purpose
The Zyto*Light* SPEC ERBB2/TOP2A/CEN 17 Triple Color Probe (PL52) is intended to be used for the qualitative detection of amplifications involving the human ERBB2 gene and the human TOP2A gene as well as the detection of chromosome 17 alpha satellites in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

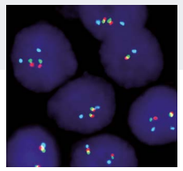
The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC ERBB2/TOP2A/CEN 17 Triple Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 17q12-q21.1* (chr17:37,572,531-38,181,308) harboring the ERBB2 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 17q21.1-q21.2* (chr17:38,323,741-38,818,030) harboring the TOP2A gene region (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~12.0 ng/µl), which target sequences mapping in 17p11.1-q11.1 specific for the alpha satellite centromeric region D17Z1 of chromosome 17.
- Formamide based hybridization buffer

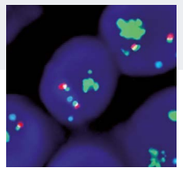
* according to Human Genome Assembly GRCh37/hg19

Fig. 1: SPEC ERBB2/TOP2A Probe map (not to scale); Right: Ideogram of chromosome 17 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the respective gene regions, two green, two orange and two blue signals appear.
Aberrant situation: In cells with an amplification of the ERBB2 gene region an increased number of green signals or green signal clusters will be observed. In cells with an amplification of the TOP2A gene region an increased number of orange signals or orange signal clusters will be observed. Deletions affecting the TOP2A gene region result in a reduced number of orange signals.



Hybridized to normal interphase cells as indicated by two green, two orange, and two blue signals per nucleus.



Example of an aberrant signal pattern: Breast cancer tissue section with two copies of chromosome 17 (blue) and TOP2A (orange) and ERBB2 gene clusters (green) in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	17	CE/IVD	5 (50 µl)	**Z-2093-50**
			20 (200 µl)	**Z-2093-200**

ZytoLight® SPEC COL1A1 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC COL1A1 Dual Color Break Apart Probe (PL78) is intended to be used for the qualitative detection of translocations involving the human COL1A1 gene at 17q21.33 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC COL1A1 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 17q21.33* (chr17:47,669,218-48,223,465) distal to the COL1A1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 17q21.33* (chr17:48,347,800-48,744,021) distal to the COL1A1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

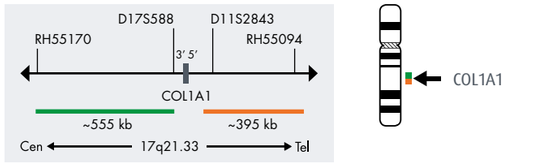
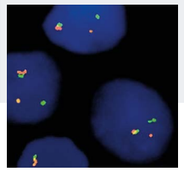
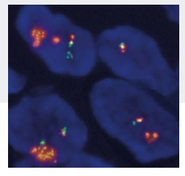


Fig. 1: SPEC COL1A1 Probe map (not to scale); Right: Ideogram of chromosome 17 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the COL1A1 gene region, two green/orange fusion signals appear.
Aberrant situation: One COL1A1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Example of an aberrant signal pattern: 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.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	17	CE/IVD	20 (200 µl)	**Z-2121-200**

Image kindly provided by Dr. Schildhaus, Essen, Germany.

ZytoLight® SPEC COL1A1/PDGFB Dual Color Dual Fusion Probe

Intended Purpose
The Zyto*Light* SPEC COL1A1/PDGFB Dual Color Dual Fusion Probe (PL73) is intended to be used for the qualitative detection of the translocation t(17;22)(q21.3;q13.1) involving the human COL1A1 and PDGFB genes in formalin-fixed, paraffin-embedded specimens, such as dermatofibrosarcoma protuberans (DFSP), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of DFSP and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC COL1A1/PDGFB Dual Color Dual Fusion Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~6 ng/µl), which target sequences mapping in 17q21.33* (chr17:47,820,343-48,744,021) harboring the COL1A1 gene region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~12 ng/µl), which target sequences mapping in 22q13.1* (chr22:38,928,973-40,267,687) harboring the PDGFB gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

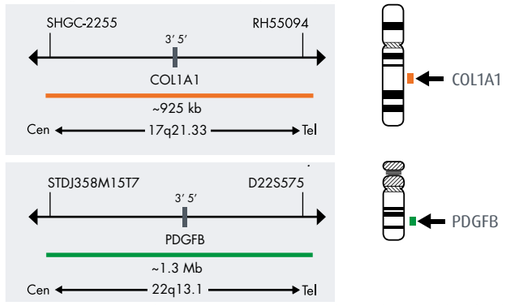
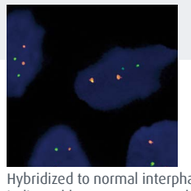


Fig. 1: Top: SPEC COL1A1 Probe map; Bottom: SPEC PDGFB Probe map (not to scale); Right: Ideograms of chromosome 17 and 22 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the respective gene regions, two separate green and orange signals appear.
Aberrant situation: A reciprocal translocation is indicated by one separate orange signal, one separate green signal, and two orange/green fusions signals. A signal pattern showing one fusion signal and variable numbers of separate green and orange signals can occur due to unbalanced translocations. Multiple copies of orange/green fusion signals indicate the presence of supernumerary ring chromosomes comprising low-level amplified COL1A1-PDGFB fusion sequences.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	17, 22	CE/IVD	5 (50 µl)	**Z-2116-50**
			20 (200 µl)	**Z-2116-200**

ZytoLight® SPEC SS18 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC SS18 Dual Color Break Apart Probe (PL56) is intended to be used for the qualitative detection of translocations involving the human SS18 gene at 18q11.2 in formalin-fixed, paraffin-embedded specimens, such as synovial sarcoma, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of synovial sarcoma and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC SS18 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 18q11.2* (chr18:23,109,942-23,466,217) proximal to the SS18 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 18q11.2* (chr18:23,772,255-24,137,169) distal to the SS18 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

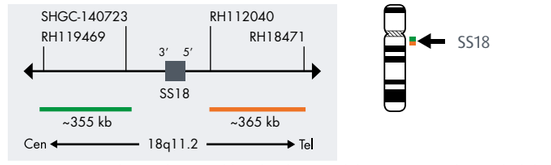
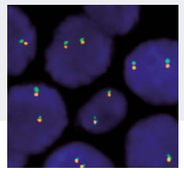
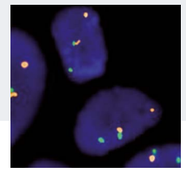


Fig. 1: SPEC SS18 Probe map (not to scale); Right: Ideogram of chromosome 18 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the SS18 gene region, two green/orange fusion signals appear.
Aberrant situation: One SS18 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	18	CE/IVD	5 (50 µl)	**Z-2097-50**
			20 (200 µl)	**Z-2097-200**

ISH

ZytoLight® SPEC SS18/SSX1 TriCheck™ Probe

Intended Purpose
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 ZytoLight SPEC SS18/SSX1 TriCheck Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 18q11.2* (chr18:23,109,942-23,466,217) proximal to the SS18 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 18q11.2* (chr18:23,772,255-24,137,169) distal to the SS18 breakpoint region (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~37,0 ng/µl), which target sequences mapping in Xp11.23* (chrX:48,265,856-48,792,674) proximal to the SSX1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

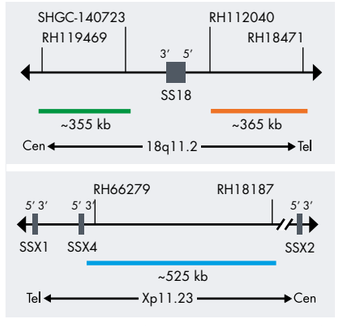
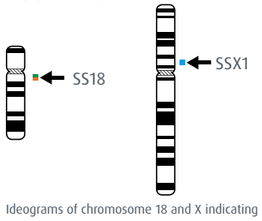
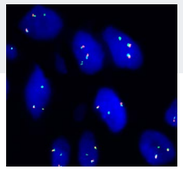


Fig. 1: Top: SPEC SS18 Probe map; Bottom: SPEC SSX1 Probe map (not to scale)

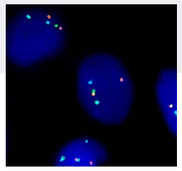


Ideograms of chromosome 18 and X indicating the hybridization locations

Results
Normal situation: In nterphases of normal female cells or female cells without SS18-SSX1 rearrangement, two green/orange fusion signals and two blue signals appear. In interphases of normal male cells or male cells without SS18-SSX1 rearrangement, two green/orange fusion signals and one blue signal appear.
Aberrant situation: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	18, X	CE/IVD	5 (50 µl)	**Z-2184-50**

ZytoLight® SPEC MALT1 Dual Color Break Apart Probe

Intended Purpose
The ZytoLight SPEC MALT1 Dual Color Break Apart Probe (PL154) is intended to be used for the qualitative detection of translocations involving the human MALT1 gene at 18q21.32 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC MALT1 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 18q21.31-q21.32* (chr18:55,690,725-56,330.582) proximal to the MALT1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 18q21.32* (chr18:56,427,386-56,859,755) distal to the MALT1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

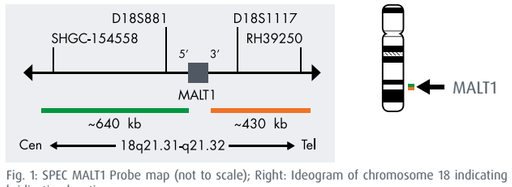
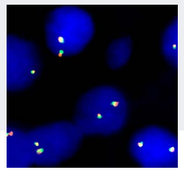
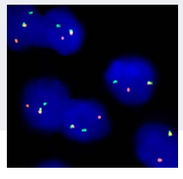


Fig. 1: SPEC MALT1 Probe map (not to scale); Right: Ideogram of chromosome 18 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the MALT1 gene region, two green/orange fusion signals appear.
Aberrant situation: One MALT1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	18	CE/IVD	5 (50 µl)	**Z-2196-50**
			20 (200 µl)	**Z-2196-200**

ISH

ZytoLight® SPEC MALT1/IGH Dual Color Dual Fusion Probe

Intended Purpose
The ZytoLight SPEC MALT1/IGH Dual Color Dual Fusion Probe (PL279) is intended to be used for the qualitative detection of the translocation t(14;18)(q32.3;q21.3) involving the human MALT1 gene at 18q21.32 and the human IGH locus at 14q32.33 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC MALT1/IGH Dual Color Dual Fusion Probe is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~6 ng/µl), which target sequences mapping in 18q21.31-q21.32* (18:56,021,766-56,724,408) harboring the MALT1 gene region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~12 ng/µl), which target sequences mapping in 14q32.33* (chr14:105,462,169-106,995,000) harboring the IGH gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

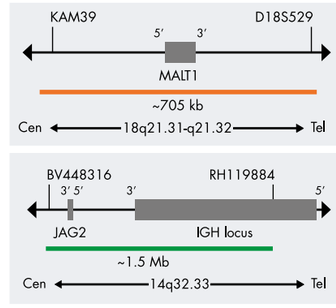
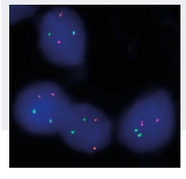
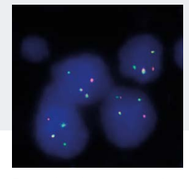


Fig. 1: Top: SPEC MALT1 Probe map; Bottom: SPEC IGH Probe map (not to scale); Right: Ideograms of chromosome 18 and 14 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the respective gene regions, two separate orange and green signals appear.
Aberrant situation: A gene fusion is indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Example of an aberrant signal pattern: SPEC MALT1/IGH Dual Color Dual Fusion Probe hybridized to MALT lymphoma tissue section with t(14;18) as indicated by one separate orange signal, one separate green signal and two orange/green fusion signals indicating the MALT1/IGH translocation.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	14, 18	CE/IVD	5 (50 µl)	**Z-2325-50**

ISH

ZytoLight® SPEC BCL2 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC BCL2 Dual Color Break Apart Probe (PL150) is intended to be used for the qualitative detection of translocations involving the human BCL2 gene at 18q21.33 in formalin-fixed, paraffin-embedded specimens, such as B-cell lymphoma, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of B-cell lymphoma and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC BCL2 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 18q21.33* (chr18:60,046,152-60.589,273) proximal to the BCL2 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 18q21.33-q22.1* (chr18:60,994,528-61,658,503) distal to the BCL2 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

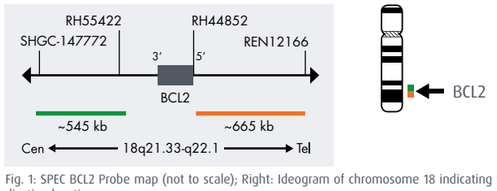
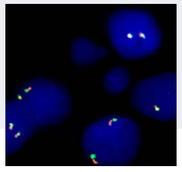
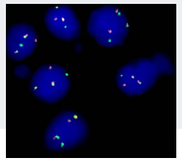


Fig. 1: SPEC BCL2 Probe map (not to scale); Right: Ideogram of chromosome 18 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the BCL2 gene region, two green/orange fusion signals appear.
Aberrant situation: One BCL2 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	18	CE/IVD	5 (50 µl)	**Z-2192-50**
			20 (200 µl)	**Z-2192-200**

ZytoLight® SPEC BCL2/IGH Dual Color Dual Fusion Probe

Intended Purpose
The Zyto*Light* SPEC BCL2/IGH Dual Color Dual Fusion Probe (PL71) is intended to be used for the qualitative detection of the translocation t(14;18)(q32.3;q21.3) involving the human IGH and BCL2 genes in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC BCL2/IGH Dual Color Dual Fusion Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~12 ng/µl), which target sequences mapping in 14q32.33* (chr14:105,462,169-106,995,000) harboring the IGH gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~6 ng/µl), which target sequences mapping in 18q21.33* (chr18:60.180,078-61,507,691) harboring the BCL2 gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

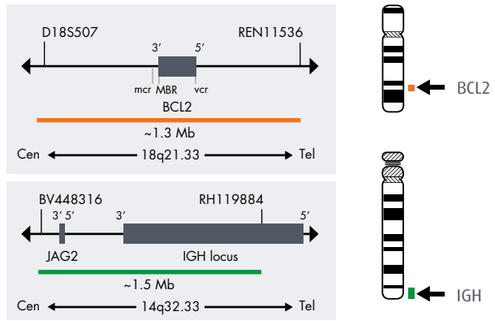
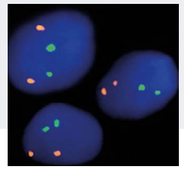
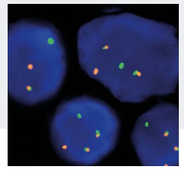


Fig. 1: Top: SPEC BCL2 Probe map; Bottom: IGH Probe map (not to scale); Right: Ideograms of chromosome 18 and 14 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the respective gene regions, two separate green and orange signals appear.
Aberrant situation: A gene fusion is indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	14, 18	CE/IVD	5 (50 µl)	**Z-2114-50**
			20 (200 µl)	**Z-2114-200**

ZytoLight® SPEC CIC Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC CIC Dual Color Break Apart Probe (PL240) is intended to be used for the qualitative detection of translocations involving the human CIC gene at 19q13.2 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC CIC Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 19q13.2* (chr19:42,835,047-43,374,575) distal to the CIC breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 19q13.2* (chr19:41,980,301-42,751,339) proximal to the CIC breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

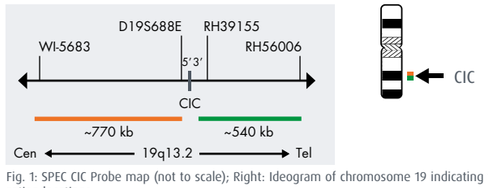
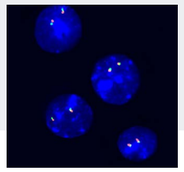
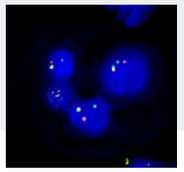


Fig. 1: SPEC CIC Probe map (not to scale); Right: Ideogram of chromosome 19 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the CIC gene region, two green/orange fusion signals appear.
Aberrant situation: One CIC gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Example of an aberrant signal pattern: Undifferentiated roand 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	19	CE/IVD	5 (50 µl)	**Z-2285-50**

ZytoLight® SPEC C19MC/19p13 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC C19MC/19p13 Dual Color Probe (PL230) is intended to be used for the qualitative detection of amplifications involving the C19MC locus as well as the detection of chromosome 19p13 specific sequences in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* C19MC/19p13 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 19q13.42* (chr19:54,156,239-54,768,983) harboring the C19MC locus (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 19p13.3* (chr19:658,555-1,144,465) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

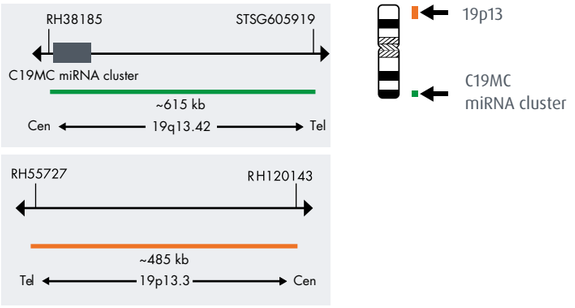
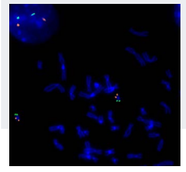
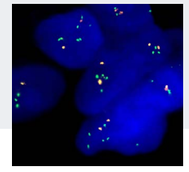


Fig. 1: Top: SPEC C19MC Probe map; Bottom: SPEC 19p13 Probe map (not to scale); Right: Ideogram of chromosome 19 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the C19MC locus, two green signals and two orange signals appear.
Aberrant situation: In cells with an amplification of the C19MC locus, an increased number of green signals or green signal clusters will be observed.



Hybridized to normal interphase cells as indicated by two orange and two green signals per nucleus and to metaphase chromosomes of a normal cell.



Example of an aberrant signal pattern: Primitive neuroectodermal tumor tissue section with amplification of the C19MC miRNA cluster.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	19	CE/IVD	5 (50 µl)	**Z-2274-50**

Specimen kindly provided by Hannu Haapasalo, MD, PhD, Fimlab Laboratories, Finland.

ZytoLight® SPEC PTPRT/20q11 Dual Color Probe

Intended Purpose
The ZytoLight SPEC PTPRT/20q11 Dual Color Probe (PL171) is intended to be used for the detection of deletions involving the human PTPRT gene as well as the detection of chromosome 20q11 specific sequences in cytologic specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Cytology Implementation Kit (Prod. No. Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC PTPRT/20q11 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 20q12* (chr20:40,807,040-41,419,634) harboring the PTPRT gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 20q11.21* (chr20:30,301,019-30,719,110) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

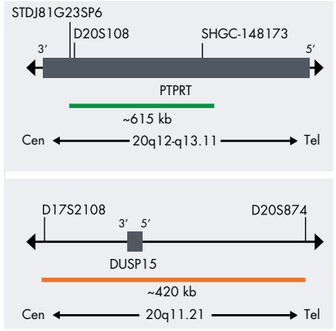
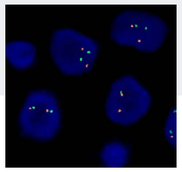


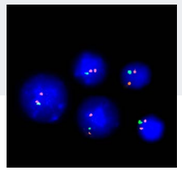
Fig. 1: Top: SPEC PTPRT Probe map; Bottom: SPEC 20q11 Probe map (not to scale)

Ideogram of chromosome 20 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the PTPRT gene region, two green and two orange signals appear.
Aberrant situation: In a cell with deletion affecting the PTPRT gene region, a reduced number of green signals will be observed. Deletions affecting only parts of the PTPRT gene region might result in a normal signal pattern with green signals of reduced size.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Example of an aberrant signal pattern: Lymphocytes of a myelodysplastic syndrome showing a 20q deletion indicated by one single green and two orange signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	20	CE/IVD	5 (50 µl)	**Z-2213-50**

Material kindly provided from Dr. Saurabh Bhattacharya, Lal PathLabs, India.

ZytoLight® SPEC ERG Dual Color Break Apart Probe

Intended Purpose
The ZytoLight SPEC ERG Dual Color Break Apart Probe (PL95) is intended to be used for the qualitative detection of translocations involving the human ERG gene at 21q22.2 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC ERG Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 21q22.2* (chr21:40,078,039-40,850.582) distal to the ERG breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 21q22.13-q22.2* (chr21:39,171,790-39,733,849) proximal to the ERG breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

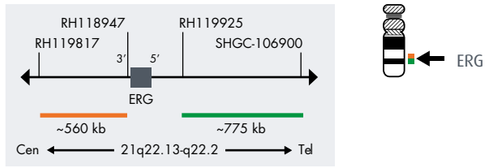
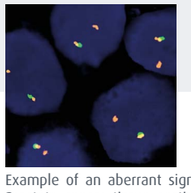


Fig. 1: SPEC ERG Probe map (not to scale); Right: Ideogram of chromosome 21 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the ERG gene region, two orange/green fusion signals appear.
Aberrant situation: One ERG gene region affected by a deletion resulting in the TMPRSS2-ERG fusion is indicated by the loss of one green signal. Deletions affecting only parts of the ERG gene region might result in a normal signal pattern with green signals of reduced size. 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).

Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	21	CE/IVD	20 (200 µl)	**Z-2138-200**

ZytoLight® SPEC ERG/TMPRSS2 TriCheck™ Probe

Intended Purpose
The ZytoLight SPEC ERG/TMPRSS2 TriCheck Probe (PL92) is intended to be used for the qualitative detection of rearrangements involving the human ERG gene at 21q22.2 and the human TMPRSS2 gene at 21q22.3 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC ERG/TMPRSS2 TriCheck Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 21q22.2* (chr21:40,078,039-40,850.582) distal to the ERG breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 21q22.13-q22.2* (chr21:39,171,790-39,733,849) proximal to the ERG breakpoint region (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~37,0 ng/µl), which target sequences mapping in 21q22.3* (chr21:43,301,411-44,195,531) distal to the TMPRSS2 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

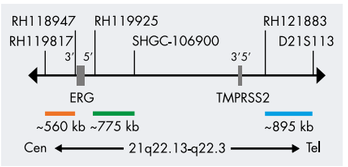
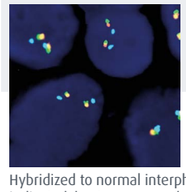
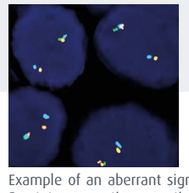


Fig. 1: SPEC ERG/TMPRSS2 Probe map (not to scale); Right: Ideogram of chromosome 21 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without rearrangements affecting the respective gene regions, two orange/green fusion signals and two blue signals in close proximity of the respective fusion signals appear.
Aberrant situation: 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.



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.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	21	CE/IVD	20 (200 µl)	**Z-2135-200**

ZytoLight® SPEC DiGeorge/Phelan McDermid Dual Color Probe

Intended Purpose

The Zyto*Light* 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.

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.

Probe Description

The Zyto*Light* SPEC DiGeorge/Phelan McDermid Dual Color Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 22q11.21* (chr22:19,191,435-19,506,869) harboring the HIRA gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 22q13.33* (chr22:50,924,766-51,188,029) harboring the SHANK3 gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

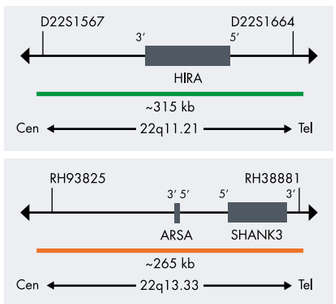
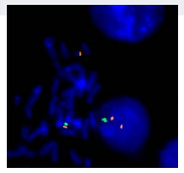


Fig. 1: Top: SPEC HIRA Probe map; Bottom: SPEC SHANK3 Probe map (not to scale)

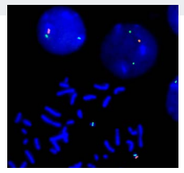
Ideogram of chromosome 22 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a deletion involving the respective gene regions, two green and two orange signals appear.
Aberrant situation: In a cell with deletions affecting the HIRA gene region, a reduced number of green signals will be observed. Deletions affecting only parts of the HIRA gene region might result in a normal signal pattern with green signals of reduced size. In a cell with deletions affecting the SHANK3 gene region, a reduced number of orange signals will be observed. Deletions affecting only parts of the SHANK3 gene region might result in a normal signal pattern with orange signals of reduced size



Lymphocytes and metaphase chromosomes from a DiGeorge syndrome case showing a HIRA deletion as indicated by the loss of one green signal.*



Lymphocytes and metaphase chromosomes from a Phelan-McDermid syndrome case showing a SHANK3 deletion as indicated by the loss of one orange signal. **

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	22	CE/IVD	5 (50 µl)	**Z-2299-50**

*Kindly provided by Dr. Liehr, Jena, Germany.

**Kindly provided by Dr. Kazmierczak, Bremen, Germany.

ZytoLight® SPEC DiGeorge Triple Color Probe

Intended Purpose

The Zyto*Light* 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.

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.

Probe Description

The Zyto*Light* SPEC DiGeorge Triple Color Probe is composed of:

- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~37 ng/µl), which target sequences mapping in 22q11.21* (chr22:19,191,435-19,932,689) harboring the HIRA gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 22q11.21* (chr22:21,096,895-21,454,102) harboring the CRKL gene region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 22q11.21-q11.22* (chr22:21,931,816-22,587,439) harboring the MAPK1 gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

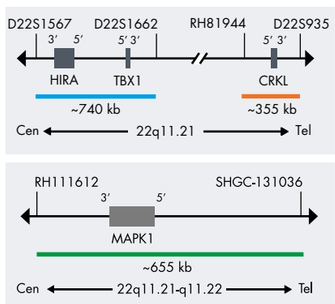
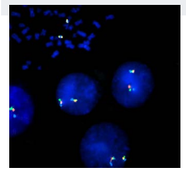


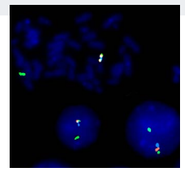
Fig. 1: Top: SPEC HIRA/SPEC CRKL Probe map; Bottom: SPEC MAPK1 Probe map (not to scale); Right: Ideogram of chromosome 22 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a deletion involving the respective gene regions, two blue, two orange, and two green signals appear.
Aberrant situation: In a cell with deletion affecting the HIRA gene region, a reduced number of blue signals will be detected. Deletions affecting both the HIRA and CRKL gene regions will result in a reduced number of blue and orange signals. A reduced number of green signals indicates deletion affecting the MAPK1 gene region. Deletions affecting only parts of the respective gene region might result in a normal signal pattern with signals of reduced size.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	22	CE/IVD	5 (50 µl)	**Z-2289-50**

Kindly provided by Dr. Liehr, Jena, Germany.

ZytoLight® SPEC IGL Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC IGL Dual Color Break Apart Probe (PL241) is intended to be used for the qualitative detection of translocations involving the human IGL locus at 22q11.22 in cytologic or formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with Zyto*Light* FISH Implementation Kits (Prod. No. Z-2028-5/-20, or Z-2099-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC IGL Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 22q11.21-q11.22* (chr22:21,931,816-22,942,402) proximal to the IGL breakpoint region (see Fig.1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 22q11.22-q11.23* (chr22:23,324,781-23,679,042) distal to the IGL breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

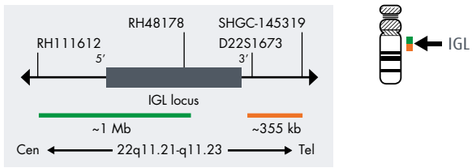
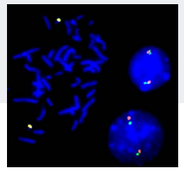
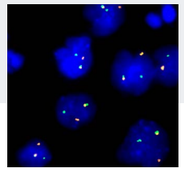


Fig. 1: SPEC IGL Probe map (not to scale); Right: Ideogram of chromosome 22 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the IGL locus, two green/orange fusion signals appear.
Aberrant situation: One IGL locus affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals in each nucleus and to metaphase chromosomes of a normal cell.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	22	CE/IVD	5 (50 µl)	**Z-2286-50**

ZytoLight® SPEC SMARCB1/22q12 Dual Color Probe

Intended Purpose
The Zyto*Light* SPEC SMARCB1/22q12 Dual Color Probe (PL137) is intended to be used for the qualitative detection of deletions involving the human SMARCB1 gene as well as the detection of chromosome 22q12 specific sequences in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC SMARCB1/22q12 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 22q11.23* (chr22:23,887,951-24,431,064) harboring the SMARCB1 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 22q12.1-22q12.2* (chr22:29,340,078-29,673,440) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

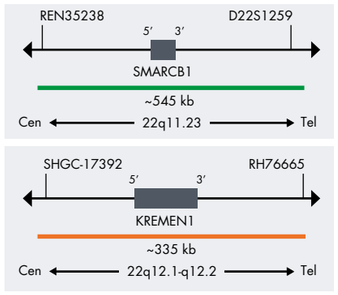
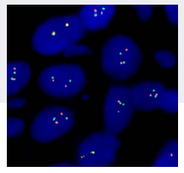
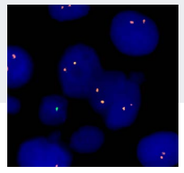


Fig. 1: Top: SPEC SMARCB1 Probe map; Bottom: SPEC 22q12 Probe map (not to scale); Right: Ideogram of chromosome 22 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the SMARCB1 gene region, two green and two orange signals appear.
Aberrant situation: In a cell with deletion affecting the SMARCB1 gene region, a reduced number of green signals will be observed. Deletions affecting only parts of the SMARCB1 gene region might result in a normal signal pattern with green signals of reduced size.



Hybridized to normal interphase cells as indicated by two orange and two green signals per nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	22	CE/IVD	5 (50 µl)	**Z-2178-50**

ZytoLight® SPEC EWSR1 Dual Color Break Apart Probe

Intended Purpose
The Zyto*Light* SPEC EWSR1 Dual Color Break Apart Probe (PL55) is intended to be used for the qualitative detection of translocations involving the human EWSR1 gene at 22q12.2 in formalin-fixed, paraffin-embedded specimens, such as Ewing sarcoma, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of Ewing sarcoma and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC EWSR1 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 22q12.2* (chr22:29,779,841-30.179,900) distal to the EWSR1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 22q12.1-q12.2* (chr22:29,191,431-29,673,440) proximal to the EWSR1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

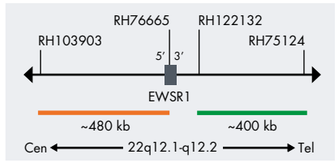
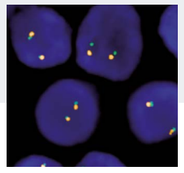
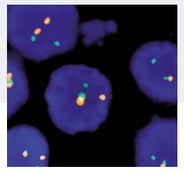


Fig. 1: SPEC EWSR1 Probe map (not to scale); Right: Ideogram of chromosome 22 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the EWSR1 gene region, two green/orange fusion signals appear.
Aberrant situation: One EWSR1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	22	CE/IVD	5 (50 µl)	**Z-2096-50**
			20 (200 µl)	**Z-2096-200**

ZytoLight® SPEC EWSR1/FLI1 TriCheck™ Probe

Intended Purpose
The Zyto*Light* SPEC EWSR1/FLI1 TriCheck Probe (PL141) is intended to be used for the qualitative detection of rearrangements involving the human EWSR1 gene at 22q12.2 and the human FLI1 gene at 11q24.3 in formalin-fixed, paraffin-embedded specimens, such as Ewing sarcoma, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Zyto*Light* FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of Ewing sarcoma and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Light* SPEC EWSR1/FLI1 TriCheck Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 22q12.2* (chr22:29,779,841-30.179,900) distal to the EWSR1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 22q12.1-q12.2* (chr22:29,191,431-29,673,440) proximal to the EWSR1 breakpoint region (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~37,0 ng/µl), which target sequences mapping in 11q24.3* (chr11:128,707,454-129,346,602) distal to the FLI1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

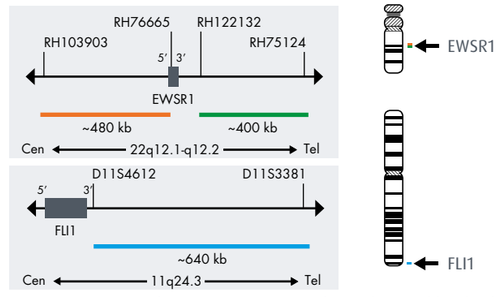
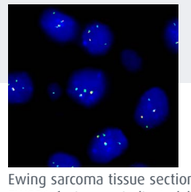
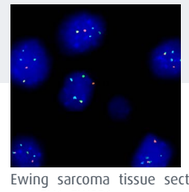


Fig. 1: Top: SPEC EWSR1 Probe map; Bottom: SPEC FLI1 Probe map (not to scale); Right: Ideograms of chromosome 22 and 11 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without FLI1-EWSR1 rearrangement, two green/orange fusion signals and two blue signals are expected.
Aberrant situation: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	11, 22	CE/IVD	5 (50 µl)	**Z-2183-50**

ZytoLight® SPEC PDGFB Dual Color Break Apart Probe

Intended Purpose
The ZytoLight SPEC PDGFB Dual Color Break Apart Probe (PL76) is intended to be used for the qualitative detection of translocations involving the human PDGFB gene at 22q13.1 in formalin-fixed, paraffin-embedded specimens, such as dermatofibrosarcoma protuberans (DFSP), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of DFSP and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC PDGFB Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 22q13.1* (chr22:39,720,415-40,267,687) distal to the PDGFB breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 22q13.1* (chr22:38,928,973-39,526,228) proximal to the PDGFB breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

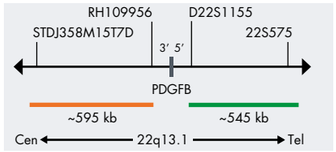
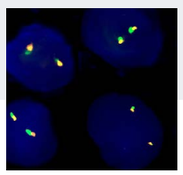


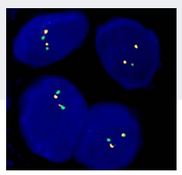
Fig. 1: SPEC PDGFB Probe map (not to scale)

Ideogram of chromosome 22 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the PDGFB gene region, two green/orange fusion signals appear.
Aberrant situation: One PDGFB gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	22	CE/IVD	5 (50 µl)	**Z-2119-50**
			20 (200 µl)	**Z-2119-200**

ZytoLight® SPEC TFE3 Dual Color Break Apart Probe

Intended Purpose
The ZytoLight SPEC TFE3 Dual Color Break Apart Probe (PL66) is intended to be used for the qualitative detection of translocations involving the human TFE3 gene at Xp11.23 in formalin-fixed, paraffin-embedded specimens, such as renal cell carcinomas (RCC), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of RCC and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoLight SPEC TFE3 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in Xp11.23* (chrX:48,906,685-49,509,699) proximal to the TFE3 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in Xp11.23* (chrX:48,287,169-48,792,674) distal to the TFE3 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

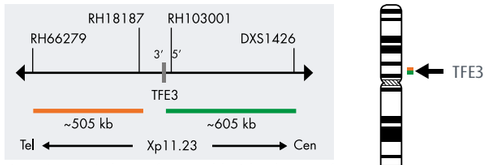
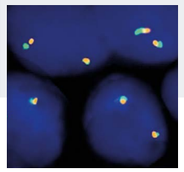
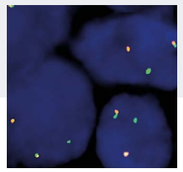


Fig. 1: SPEC TFE3 Probe map (not to scale); Right: Ideogram of chromosome X indicating the hybridization locations

Results
Normal situation: In interphases of normal female cells or cells without a translocation involving the TFE3 gene region, two green/orange fusion signals appear. In interphases of normal male cells or cells without a translocation involving the TFE3 gene region one orange/green fusion signal appears.
Aberrant situation: One TFE3 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	X	CE/IVD	5 (50 µl)	**Z-2109-50**
			20 (200 µl)	**Z-2109-200**

ZytoLight® SPEC CRLF2 Dual Color Break Apart Probe

Intended Purpose
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).

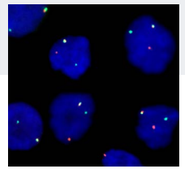
These rearrangements, which are often accompanied by JAK mutations, result in overexpression of CRLF2 and were shown to contribute to lymphoid transformation. Patients with CRLF2 rearrangements and JAK mutations have a poor event-free and overall survival. Moreover, the detection of CRLF2 rearrangements 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 ZytoLight SPEC CRLF2 Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in Xp22.33 (chrX:513,125-1,245,395) and Yp11.32* (chrY:463,125-1,195,395) distal to the CRLF2 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in Xp22.33 (chrX:1,497,976-1,660,328) and Yp11.32* (chrY:1,498,976-1,657,328) proximal to the CRLF2 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

Results
Normal situation: In interphases of normal female cells or cells without a translocation involving the CRLF2 gene region, two orange/green fusions signals appear. In interphases of normal male cells or cells without a translocation involving the CRLF2 gene region, two orange/green fusion signals appear.
Aberrant situation: A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal CRLF2 gene region and one CRLF2 gene region affected by a translocation.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	X,Y	CE/IVD	5 (50 µl)	**Z-2201-50**

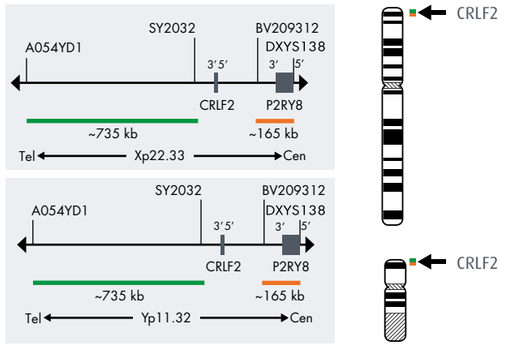


Fig. 1: Top: chromosome X SPEC CRLF2 Probe map; Bottom: chromosome Y SPEC CRLF2 Probe map (not to scale); Right: Ideograms of chromosome X and Y indicating the hybridization locations

ZytoLight® SPEC BCOR Dual Color Break Apart Probe

Intended Purpose
The ZytoLight SPEC BCOR Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal region Xp11.4 harboring the BCOR (BCL6 corepressor, a.k.a. KIAA1575) gene. In the 2020 WHO classification of soft tissue and bone tumors, BCOR-rearranged sarcoma is recognized as a distinct entity due to particular morphological, immunohistochemical, and molecular features and differing clinical outcomes compared to other undifferentiated sarcomas.

A fusion between BCOR and CCNB3 can be found in about 60% of all BCOR-rearranged sarcomas. The BCOR-CCNB3 fusion results from an X-chromosomal paracentric inversion. In vitro studies suggest that the BCOR-CCNB3 fusion protein is oncogenic and drives proliferation in these sarcomas. In addition, alternative fusion partners have been identified, including MAML3 and ZC3H7B.

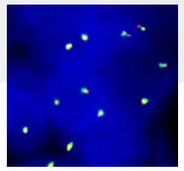
BCOR-rearranged sarcoma usually occurs in bone or soft tissue of predominantly male children with a median age in the second decade of life. There are considerable overlapping morphological and immunohistochemical features with classical Ewing sarcoma, other subtypes of small round cell tumors, as well as lymphomas and carcinomas. Therefore, the evaluation of the BCOR rearrangement status by FISH may be of diagnostic relevance.

References
Antonescu CR, *et al.* (ed.) (2020) WHO Classification of Tumours Soft Tissue and Bone Tumours (5th Edition).
Pierron G, *et al.* (2012) Nat Genet 44: 461-6.
Renzi S, *et al.* (2019) J Cell Physiol 234: 7999-8007.
Sirisena UDN, *et al.* (2021) Skeletal Radiol 50: 1291-301.
Specht K, *et al.* (2016) Am J Surg Pathol 40: 433-42.

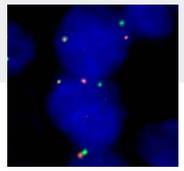
Probe Description
The ZytoLight SPEC BCOR Dual Color Break Apart Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in Xp11.4* (chrX:39,262,996-39,850,787) distal to the BCOR breakpoint region.
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in Xp11.4* (chrX:39,998,508-40,345,270) proximal to the BCOR breakpoint region.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

Results
Normal situation: In interphases of normal female cells or cells without a translocation involving the BCOR gene region, two green/orange fusion signals appear. In interphases of normal male cells or cells without a translocation involving the BCOR gene region, one green/orange fusion signal appears.
Aberrant situation: One BCOR gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



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

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	X	CE/IVD	5 (50 µl)	**Z-2310-50**

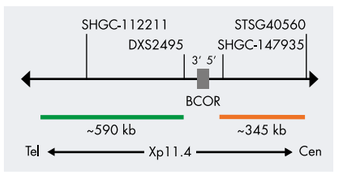
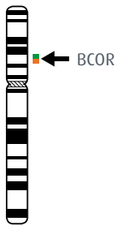


Fig. 1: SPEC BCOR Probe map (not to scale)



Ideogram of chromosome X indicating the hybridization locations

ZytoLight® Probes for Chromosome Enumeration - CE/IVD

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

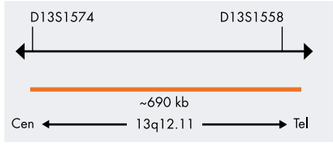
For most chromosomes, direct labeled ZytoLight® CEN™ Probes hybridizing to highly repetitive human satellite DNA sequences mainly located at the centromeric regions of chromosomes are applicable.

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.

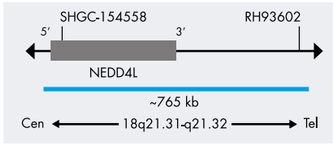
ZytoLight® SPEC Probe maps

The **ZytoLight SPEC 13q12 Probe** is composed of:
- ZyOrange (excitation 547 nm/emission 467 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 13q12.11* (chr13:20,200,365-20,892,494).
- Formamide based hybridization buffer



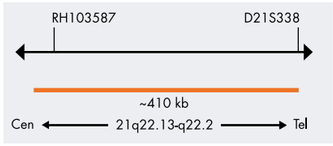
SPEC 13q12 Probe map (not to scale)

The SPEC 18q21 Probe, included in the **ZytoLight SPEC 18/CEN X/Y Triple Color Probe**, is composed of:
- ZyBlue (excitation 418 nm, Emission 467 nm) labeled polynucleotides (~37 ng/µl), which target sequences mapping in 18q21.31-q21.32* (chr18:55,690,725–56,455,119).



SPEC 18q21 Probe map (not to scale)

The **ZytoLight SPEC 21q22 Probe** is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 21q22.13-q22.2* (chr21:39,372,983-39,784,773).
- Formamide based hybridization buffer



SPEC 21q22 Probe map (not to scale)

* according to Human Genome Assembly GRCh37/hg19

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.

CE/IVD Probes

Product Name	Alpha/Class. Sat.	Chromosome band	Reg. Status	Labels	Tests	Order No.
Zyto*Light* CEN 8 Probe	D8Z2	8p11.1-q11.1	CE/IVD		5/20 (50/200 µl)	**Z-2004-50/-200**
Zyto*Light* CEN 11 Probe	D11Z1	11p11.11-q11			20 (200 µl)	**Z-2005-200**
Zyto*Light* CEN 12 Probe	D12Z3	12p11.1-q11			20 (200 µl)	**Z-2050-200**
Zyto*Light* SPEC 13/CEN 18/SPEC 21 Triple Color Probe	D18Z1	13q12.11/18p11.1/21q22.13-q22.2			5/20 (50/200 µl)	**Z-2095-50/-200**
Zyto*Light* SPEC 13/21 Dual Color Probe	-	13q12.11/21q22.13-q22.2			20 (200 µl)	**Z-2164-200**
Zyto*Light* SPEC 18/CEN X/Y Triple Color Probe	DXZ1/DYZ3	18q21.31-q21.32/Xp11.1-q11.1/Yp11.1-q11.1			20 (200 µl)	**Z-2163-200**
Zyto*Light* SPEC 21/CEN X/Yq12 Triple Color Probe	DXZ1/ III DYZ1	21q22.13-q22.2/Xp11.1-q11.1/Yq12			20 (200 µl)	**Z-2180-200**
Zyto*Light* CEN X/Yq12 Dual Color Probe	DXZ1/III DYZ1	Xp11.1-q11.1/Yq12			5/20 (50/200 µl)	**Z-2016-50/-200**
Zyto*Light* CEN X/Y Dual Color Probe	DXZ1/ DYZ3	Xp11.1-q11.1/Yp11.1-q11.1			20 (200 µl)	**Z-2120-200**

Related Products

Zyto*Light* Aneuploidy Panel 18/X/Y and 13/21 Incl. Zyto*Light* SPEC 18/CEN X/Y Triple Color Probe, 0.2 ml (Z-2163-200); Zyto*Light* SPEC 13/21 Dual Color Probe, 0.2 ml (Z-2164-200)	CE/IVD	-	20	**Z-2279-20**
Zyto*Light* Aneuploidy Panel X/Y and 13/18/21 Incl. Zyto*Light* CEN X/Yq12 Dual Color Probe, 0.05 ml (Z-2016-50); Zyto*Light* SPEC 13/CEN 18/ SPEC 21 Triple Color Probe, 0.05 ml (Z-2095-50)			5	**Z-2104-5**
Zyto*Light* Aneuploidy Panel X/Y and 13/18/21 Incl. Zyto*Light* CEN X/Yq12 Dual Color Probe, 0.2 ml (Z-2016-200); Zyto*Light* SPEC 13/CEN 18/ SPEC 21 Triple Color Probe, 0.2 ml (Z-2095-200)			20	**Z-2104-20**
Zyto*Light* FISH-Tissue Implementation Kit 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-2028-5**
Zyto*Light* FISH-Tissue Implementation Kit 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-2028-20**
Zyto*Light* FISH-Cytology Implementation Kit 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	**Z-2099-20**

Zyto*Light*® Probes for Chromosome Enumeration - RUO

The Zyto*Light*® 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

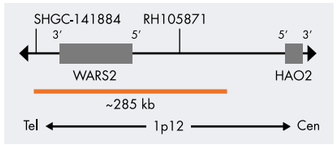
For most chromosomes, direct labeled Zyto*Light*® CEN™ Probes hybridizing to highly repetitive human satellite DNA sequences mainly located at the centromeric regions of chromosomes are applicable.

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 Zyto*Light*® SPEC™ Probes hybridizing in close proximity to the respective satellite DNA sequences or to other chromosome specific loci.

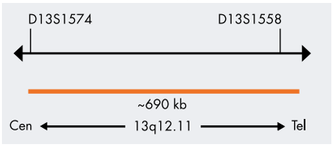
Zyto*Light*® SPEC Probe maps

The **Zyto*Light* SPEC 1p12 Probe** is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 1p12* (chr1:119,537,102-119,823,147).
- Formamide based hybridization buffer



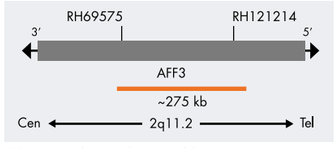
SPEC 1p12 Probe map (not to scale)

The **Zyto*Light* SPEC 13q12 Probe** is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 13q12.11* (chr13:20,200,365-20,892,494).
- Formamide based hybridization buffer



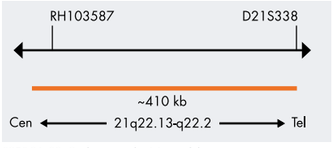
SPEC 13q12 Probe map (not to scale)

The **Zyto*Light* SPEC 2q11 Probe** is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 2q11.2* (chr2:100.132,806-100,621,725).
- Formamide based hybridization buffer



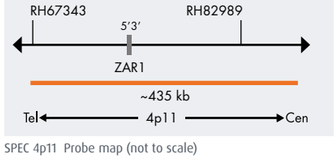
SPEC 2q11 Probe map (not to scale)

The **Zyto*Light* SPEC 21q22 Probe** is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 21q22.13-q22.2* (chr21:39,372,983-39,784,773).
- Formamide based hybridization buffer



SPEC 21q22 Probe map (not to scale)

The **Zyto*Light* SPEC 4p11 Probe** is composed of:
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 4p11* (chr4:48,329,914- 48,762,386).
- Formamide based hybridization buffer



SPEC 4p11 Probe map (not to scale)

* according to Human Genome Assembly GRCh37/hg19

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.

RUO Probes

Product Name	Alpha/Class. Sat.	Chromosome band	Reg. Status	Labels	Tests	Order No.
ZytoLight SPEC 1p12 Probe	-	1p12		●	20 (200 µl)	**Z-2101-200**
ZytoLight SPEC 2q11 Probe	-	2q11.2		●	20 (200 µl)	**Z-2049-200**
ZytoLight CEN 3 Probe	D3Z1	3p11.1-q11.1		●	20 (200 µl)	**Z-2001-200**
ZytoLight SPEC 4p11 Probe	-	4p11		●	20 (200 µl)	**Z-2083-200**
ZytoLight CEN 6 Probe	D6Z1	6p11.1-q11		●	20 (200 µl)	**Z-2002-200**
ZytoLight CEN 7 Probe	D7Z1	7p11.1-q11.1		●	20 (200 µl)	**Z-2003-200**
ZytoLight CEN 9 Probe	III D9Z3	9q12	RUO	●	20 (200 µl)	**Z-2067-200**
ZytoLight CEN 10 Probe	D10Z1	10p11.1-q11.1		●	20 (200 µl)	**Z-2079-200**
ZytoLight CEN 17 Probe	D17Z1	17p11.1-q11.1		●	20 (200 µl)	**Z-2006-200**
ZytoLight CEN 18 Probe	D18Z1	18p11.1-q11.1		●	20 (200 µl)	**Z-2007-200**
ZytoLight SPEC 21q22 Probe	-	21q22.13-q22.2		●	20 (200 µl)	**Z-2086-200**
ZytoLight CEN X Probe	DXZ1	Xp11.1-q11.1		●	20 (200 µl)	**Z-2008-200**
ZytoLight CEN Yq12 Probe	III DYZ1	Yq12		●	20 (200 µl)	**Z-2010-200**

ZytoLight® Aneuploidy Panel 18/X/Y and 13/21

Intended Purpose
The ZytoLight Aneuploidy Panel 18/X/Y and 13/21 is intended to be used for the qualitative detection of human chromosome 13 and 21 specific sequences as well as human chromosome 18 specific sequences and alpha satellites of chromosome X and Y in cytologic or formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH).

The probes are intended to be used in combination with ZytoLight FISH Implementation Kits (Prod. No. Z-2028-5/-20, or Z-2099-20). Interpretation of the results must be made within the context of the patient's clinical history with respect to further clinical and pathologic data of the patient by a qualified pathologist.

Probe Description
The ZytoLight Aneuploidy Panel 18/X/Y and 13/21 is a set comprising two separate probes:
- ZytoLight SPEC 18/CEN X/Y Triple Color Probe (Prod. No. Z-2163-200)
- ZytoLight SPEC 13/21 Dual Color Probe (Prod. No. Z-2164-200)

The ZytoLight SPEC 18/CEN X/Y Triple Color Probe (PL119) is composed of:
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~37,0 ng/µl), which target sequences mapping in 18q21.31-q21.32* (chr18:55,690,725-56,455,119) (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in Xp11.1-q11.1 specific for the alpha satellite centromeric region DXZ1 of chromosome X.
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1,5 ng/µl), which target sequences mapping in Yp11.1-q11.1 specific for the alpha satellite centromeric region DYZ3 of chromosome Y.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

The ZytoLight SPEC 13/21 Dual Color Probe (PL120) is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 13q12.11* (chr13:20,200,365-20,892,494) (see Fig. 2).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 21q22.13-q22.2* (chr21:39,372,983-39,784,773) (see Fig. 2).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

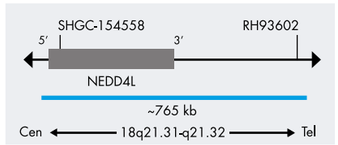
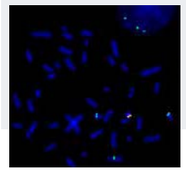


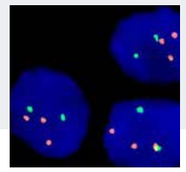
Fig. 1: SPEC 18q21 Probe map (not to scale)

Fig. 2: Top: SPEC 13q12 Probe map; Bottom: SPEC 21q22 Probe map (not to scale)

Results
Normal situation: 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.
Aberrant situation: 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.

ZytoLight Aneuploidy Panel 18/X/Y and 13/21
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)

Reg. Status	Tests	Order No.
CE/IVD	2 x 200 µl (20 Tests)	**Z-2279-20**

ZytoLight® Aneuploidy Panel X/Y and 13/18/21

Intended Purpose
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%.

Probe Description
The ZytoLight Aneuploidy Panel X/Y and 13/18/21 is a set comprising two separate probes:
- ZytoLight CEN X/Yq12 Dual Color Probe (Prod. No. Z-2016-50/200)
- ZytoLight SPEC 13/CEN 18/SPEC 21 Triple Color Probe (Prod. No. Z-2095-50/200)

The ZytoLight CEN X/Yq12 Dual Color Probe (PL3) is composed of:
- ZyOrange (excitation 547 nm /Emission 572 nm) labeled polynucleotides (~1,5 ng/µl), which target sequences mapping in Xp11.1-q11.1 specific for the alpha satellite centromeric region DXZ1 of chromosome X.
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in Yq12, specific in the classical satellite III centromeric region DYZ1 of chromosome Y.
- Formamide based hybridization buffer

The ZytoLight SPEC 13/CEN 18/SPEC 21 Triple Color Probe (PL54) is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10,0 ng/µl), which target sequences mapping in 13q12.11* (chr13:20,200,365-20,892,494) (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~12,0 ng/µl), which target sequences mapping in 18p11.1-q11.1 specific for the alpha satellite centromeric region D18Z1 of chromosome 18.
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 21q22.13-q22.2* (chr21:39,372,983-39,784,773) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

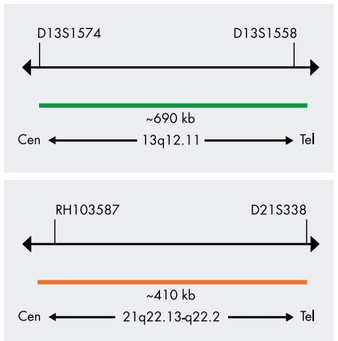
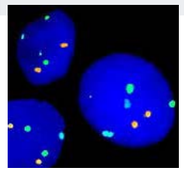
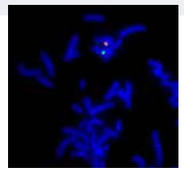


Fig. 1: Top: SPEC 13q12 Probe map; Bottom: SPEC 21q22 Probe map (not to scale)

Results
Normal situation: 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.
Aberrant situation: 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.

ZytoLight Aneuploidy Panel X/Y and 13/18/21
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)

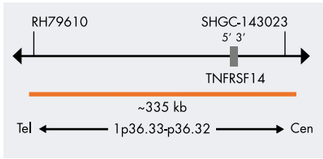
ZytoLight Aneuploidy Panel X/Y and 13/18/21
Incl. ZytoLight CEN X/Yq12 Dual Color Probe, 0.2 ml (Z-2016-200); ZytoLight SPEC 13/CEN 18/SPEC 21 Triple Color Probe, 0.2 ml (Z-2095-200)

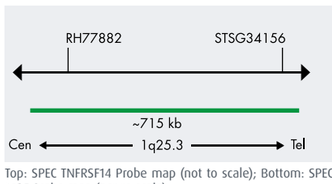
Reg. Status	Tests	Order No.
CE/IVD	2 x 50 µl (5 Tests)	Z-2104-5
	2 x 200 µl (20 Tests)	Z-2104-20

Additional ZytoLight® RUO Probes

Product Name	Chromosomenbande	Reg. Status	Labels	Tests	Order No.
ZytoLight SPEC TNFRSF14/1q25 Dual Color Probe	1p36.3	RUO	o|g	5 (50 µl)	Z-2323-50
ZytoLight SPEC EML4 Dual Color Break Apart Probe	2p21		g|o	5 (50 µl)	Z-2136-50
ZytoLight SPEC FHIT/CEN 3 Dual Color Probe	3p14.2		g|o	20 (200 µl)	Z-2062-200
ZytoLight SPEC TERC/CEN 3 Dual Color Probe	3q26.2		g|o	20 (200 µl)	Z-2284-200
ZytoLight SPEC SOX2/CEN 3 Dual Color Probe	3q26.3		g|o	20 (200 µl)	Z-2127-200
ZytoLight SPEC RICTOR/5q31.1 Dual Color Probe	5p13.1		g|o	20 (200 µl)	Z-2278-200
ZytoLight SPEC PLAG1 Dual Color Break Apart Probe	8q12		g|o	5 (50 µl)	Z-2326-50
ZytoLight SPEC KIF5B Dual Color Break Apart Probe	10p11.2		g|o	5 (50 µl)	Z-2131-50
ZytoLight SPEC BCL2L1/CEN 20 Dual Color Probe	20q11.2		o|g	20 (200 µl)	Z-2171-200

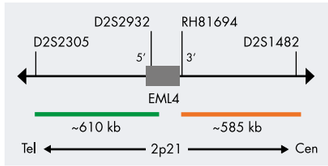
Z-2323-50





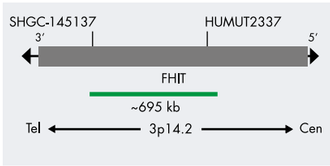
Top: SPEC TNFRSF14 Probe map (not to scale); Bottom: SPEC 1q25 Probe map (not to scale)

Z-2136-50



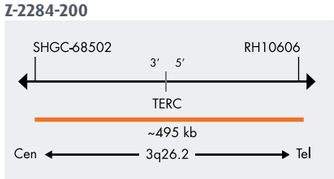
SPEC EML4 Probe map (not to scale)

Z-2062-200



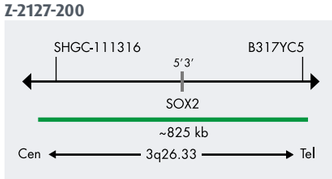
SPEC FHIT Probe map (not to scale)

Z-2284-200



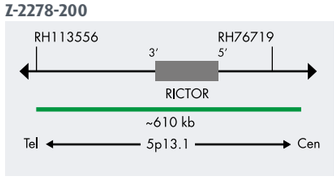
SPEC TERC Probe map (not to scale)

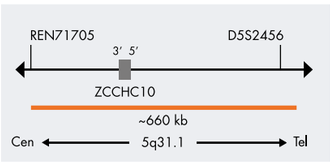
Z-2127-200



SPEC SOX2 Probe map (not to scale)

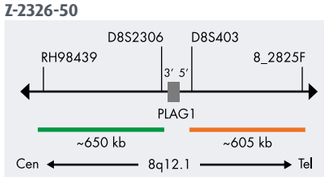
Z-2278-200





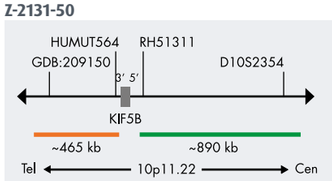
Top: SPEC RICTOR Probe map (not to scale); Bottom: SPEC 5q31.1 Probe map (not to scale)

Z-2326-50



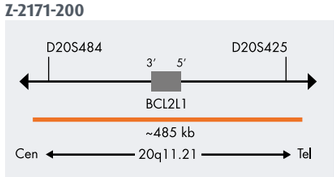
SPEC PLAG1 Probe map (not to scale)

Z-2131-50



SPEC KIF5B Probe map (not to scale)

Z-2171-200



SPEC BCL2L1 Probe map (not to scale)

Accessories

ZytoLight® Implementation Kits

For the detection of ZytoLight probes

Product	Manufacturer	Tests	Reg. Status	Order No.
ZytoLight FISH-Tissue Implementation Kit 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	ZytoVision GmbH	5	CE/IVD	**Z-2028-5**
ZytoLight FISH-Tissue Implementation Kit 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	ZytoVision GmbH	20	CE/IVD	**Z-2028-20**
ZytoLight FISH-Cytology Implementation Kit 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	ZytoVision GmbH	20	CE/IVD	**Z-2099-20**

ZytoLight® Pretreatment Reagents

Product	Manufacturer	Amount	Reg. Status	Order No.
Pepsin Solution	ZytoVision GmbH	4 ml	CE/IVD	**ES-0001-4**
Pepsin Solution	ZytoVision GmbH	50 ml	CE/IVD	**ES-0001-50**
Pepsin Solution	ZytoVision GmbH	1000 ml	CE/IVD	**ES-0001-1000**
Cytology Pepsin Solution	ZytoVision GmbH	4 ml	CE/IVD	**ES-0002-4**
Cytology Pepsin Solution	ZytoVision GmbH	50 ml	CE/IVD	**ES-0002-50**
Heat Pretreatment Solution Citric	ZytoVision GmbH	2 x 500 ml	CE/IVD	**PT-0001-1000**
Formaldehyde Dilution Buffer Set Incl.: 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml	ZytoVision GmbH	2 x 50 ml	CE/IVD	**PT-0006-100**

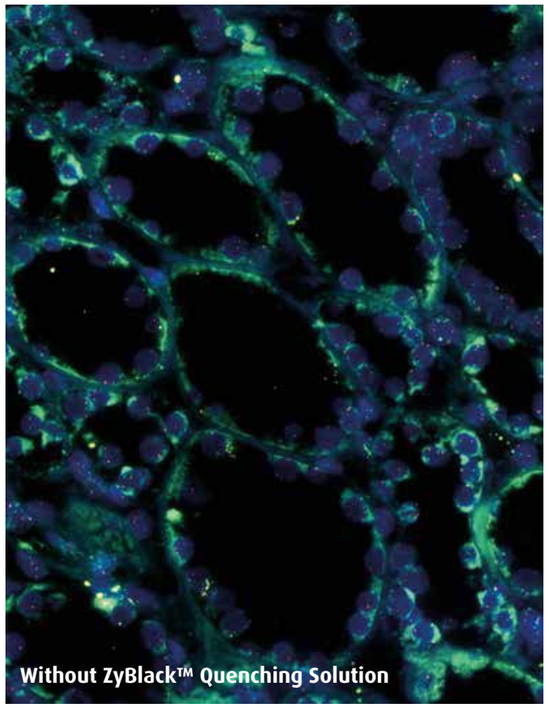
ZytoLight® Wash Buffers & Ancillary Reagents

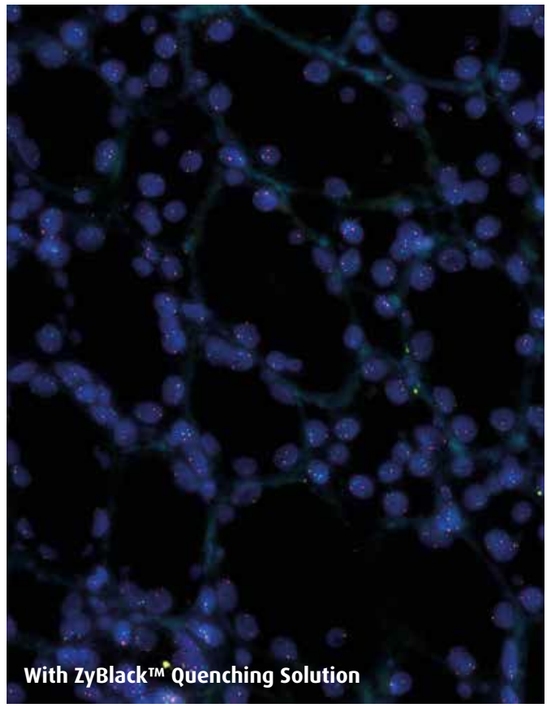
Product	Manufacturer	Amount	Reg. Status	Order No.
DAPI/DuraTect™-Solution	ZytoVision GmbH	150 ng DAPI/ml, 0.8 ml	CE/IVD	**MT-0007-0.8**
DAPI/DuraTect™-Solution (ultra)	ZytoVision GmbH	1360 ng DAPI/ml, 0.8 ml	CE/IVD	**MT-0008-0.8**
Wash Buffer SSC	ZytoVision GmbH	560 ml	CE/IVD	**WB-0001-560**
25x Wash Buffer A	ZytoVision GmbH	50 ml	CE/IVD	**WB-0002-50**
20x Wash Buffer TBS	ZytoVision GmbH	50 ml	CE/IVD	**WB-0005-50**
Cytology Stringency Wash Buffer SSC	ZytoVision GmbH	500 ml	CE/IVD	**WB-0007-500**
Cytology Wash Buffer SSC	ZytoVision GmbH	500 ml	CE/IVD	**WB-0008-500**

RUO ZytoLight® Wash Buffers & Ancillary Reagents

Product	Manufacturer	Amount	Reg. Status	Order No.
20x SSC Solution	ZytoVision GmbH	50 ml	RUO	**WB-0003-50**

ZyBlack™ Quenching Solution





Kidney tissue section hybridized with the ZytoLight SPEC PTEN/CEN 10 Dual Color Probe.

Product Description

ZyBlack™ Quenching Solution is a ready-to-use solution to reduce autofluorescence on formalin-fixed paraffin-embedded specimens. 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.

Product	Manufacturer	Amount	Reg. Status	Order No.
ZyBlack Quenching Solution	ZytoVision GmbH	8 ml		**BS-0002-8**

F*lex*ISH®

F*lex*ISH® products are designed for identification of chromosomal aberrations on formalin-fixed, paraffin-embedded (FFPE) 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!

ZytoVision GmbH

Advantages of F*lex*ISH®

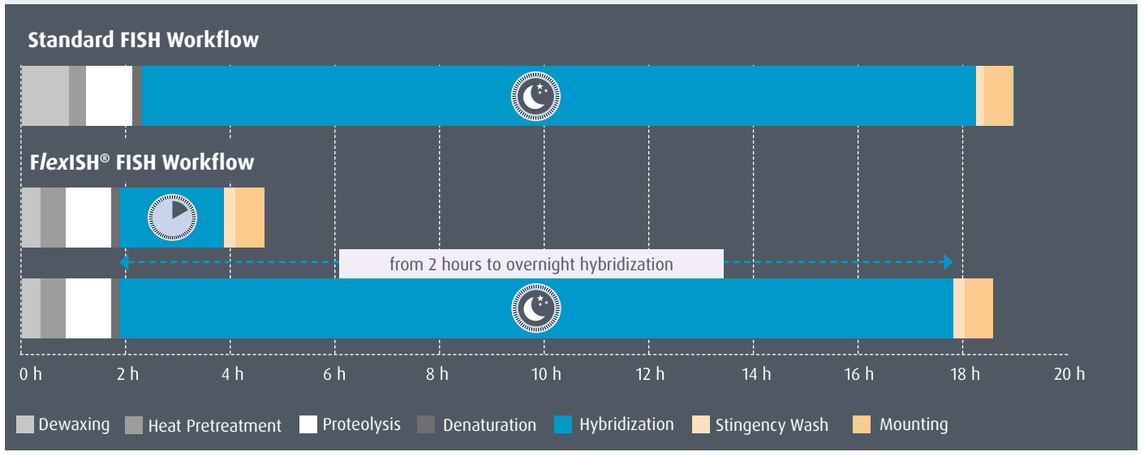
- Hybridization time can be varied between 2 hours and overnight.
- With a hybridization temperature of 37°C, the F*lex*ISH® protocol is fully compatible with routine workflows in pathology laboratories.

F*lex*ISH®-Kit – Convenient Solution

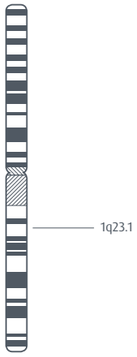
- F*lex*ISH® probes can be combined with the F*lex*ISH®-Tissue Implementation Kit to obtain reliable results already within 4.5 hours.
- The F*lex*ISH® protocol can also be incorporated into the routine workflow with overnight hybridization providing the highest flexibility.

High-Quality FISH Results with flexible Hybridization Time

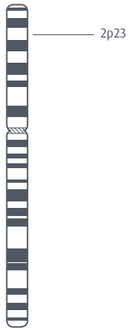
The hybridization time can be varied freely between 2 hours and overnight.



Chromosome Index

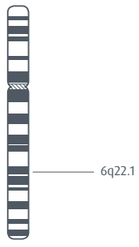


Chr. Band	Product Name	Reg. Status	Order No.	Page
1q23.1	F*lex*ISH NTRK1/NTRK3 DistinguISH™ Probe	CE/IVD	**Z-2314-50/-200**	**119**



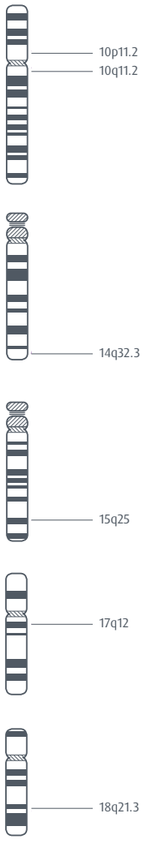
Chr. Band	Product Name	Reg. Status	Order No.	Page
2p23	F*lex*ISH ALK/ROS1 DistinguISH™ Probe	CE/IVD	**Z-2203-50/-200**	**120**

Chr. Band	Product Name	Reg. Status	Order No.	Page
3q27	F*lex*ISH BCL2/BCL6 DistinguISH™ Probe	CE/IVD	**Z-2283-50/-200**	**121**



Chr. Band	Product Name	Reg. Status	Order No.	Page
6q22.1	F*lex*ISH ALK/ROS1 DistinguISH™ Probe	CE/IVD	**Z-2203-50/-200**	**120**

Chr. Band	Product Name	Reg. Status	Order No.	Page
8q24.21	F*lex*ISH MYC/IGH TriCheck™ Probe	CE/IVD	**Z-2293-50**	**122**



Chr. Band	Product Name	Reg. Status	Order No.	Page
10p11.2	F*lex*ISH RET/KIF5B TriCheck™ Probe	CE/IVD	**Z-2269-200**	**123**
10q11.2	F*lex*ISH RET/KIF5B TriCheck™ Probe	CE/IVD	**Z-2269-200**	**123**

Chr. Band	Product Name	Reg. Status	Order No.	Page
14q32.3	F*lex*ISH MYC/IGH TriCheck™ Probe	CE/IVD	**Z-2293-50**	**122**

Chr. Band	Product Name	Reg. Status	Order No.	Page
15q25	F*lex*ISH NTRK1/NTRK3 DistinguISH™ Probe	CE/IVD	**Z-2314-50/-200**	**119**

Chr. Band	Product Name	Reg. Status	Order No.	Page
17q12	F*lex*ISH ERBB2/CEN 17 Dual Color Probe	CE/IVD	**Z-2166-50/-200**	**124**

Chr. Band	Product Name	Reg. Status	Order No.	Page
18q21.3	F*lex*ISH BCL2/BCL6 DistinguISH™ Probe	CE/IVD	**Z-2283-50/-200**	**121**

Gene Index

HUGO Name	Synonym	Product Name	Reg. Status	Order No.	Page
ALK	CD246	F*lex*ISH ALK/ROS1 DistinguISH™ Probe	CE/IVD	**Z-2203-50/-200**	**120**
BCL2	Bcl-2, PPP1R50	F*lex*ISH BCL2/BCL6 DistinguISH™ Probe	CE/IVD	**Z-2283-50/-200**	**121**
BCL6	ZNF51, LAZ3	F*lex*ISH BCL2/BCL6 DistinguISH™ Probe	CE/IVD	**Z-2283-50/-200**	**121**
ERBB2	HER2, HER-2, NEU	F*lex*ISH ERBB2/CEN 17 Dual Color Probe	CE/IVD	**Z-2166-50/-200**	**124**
IGH	IGH@	F*lex*ISH MYC/IGH TriCheck™ Probe	CE/IVD	**Z-2293-50**	**122**
KIF5B	KNS1	F*lex*ISH RET/KIF5B TriCheck™ Probe	CE/IVD	**Z-2269-200**	**123**
MYC	CMYC, bHLHe39, c-Myc	F*lex*ISH MYC/IGH TriCheck™ Probe	CE/IVD	**Z-2293-50**	**122**
NTRK1	MTC, TRK	F*lex*ISH NTRK1/NTRK3 DistinguISH™ Probe	CE/IVD	**Z-2314-50/-200**	**119**
NTRK3	TRKC	F*lex*ISH NTRK1/NTRK3 DistinguISH™ Probe	CE/IVD	**Z-2314-50/-200**	**119**
RET	HSCR1, CDHF12	F*lex*ISH RET/KIF5B TriCheck™ Probe	CE/IVD	**Z-2269-200**	**123**
ROS1	MCF3, ROS	F*lex*ISH ALK/ROS1 DistinguISH™ Probe	CE/IVD	**Z-2203-50/-200**	**120**

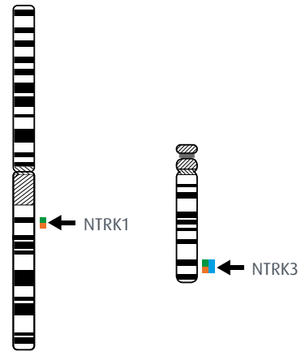
F*lex*ISH® NTRK1/NTRK3 DistinguISH™ Probe

Intended Purpose

The F*lex*ISH NTRK1/NTRK3 DistinguISH™ Probe is designed to detect rearrangements affecting the chromosomal region 1q23.1 and 15q25.3 harboring the NTRK1 (neurotrophic receptor tyrosine kinase 1, a.k.a. TRKA, TRK) and NTRK3 (neurotrophic receptor tyrosine kinase 3, a.k.a. TRKC) gene region, respectively.

The neurotrophic tyrosine receptor kinase genes (NTRK1, NTRK2, and NTRK3) encode a family of receptor tyrosine kinases that serve important roles in cell survival, proliferation, and cellular differentiation in healthy human cells. The tumor types in which NTRK gene fusions have been detected are diverse, and include, e.g., breast cancer, non-small cell lung cancer, sarcoma, melanoma, and thyroid carcinoma. The treatment of patients with NTRK fusion-positive cancers with a NTRK inhibitor, such as the FDA-approved drugs larotrectinib or entrectinib, is associated with high response rates, regardless of NTRK gene, fusion partner, and tumor type.

Hence, detection of NTRK1 and NTRK3 rearrangements by FISH may be of therapeutic significance.



Ideograms of chromosome 1 and 15 indicating the hybridization locations

References

Haller F, *et al.* (2016) J Pathol 238: 700-10.
Hsiao SJ, *et al.* (2019) J Mol Diagn 21: 553-71.
Knezevich SR, *et al.* (1998) Nat Genet 18: 184-7.
Martin-Zanca D, *et al.* (1986) Nature 319: 743-8.
Solomon JP & Hechtman JF (2019) Cancer Res 79: 3163-8.

Probe Description

The F*lex*ISH NTRK1/NTRK3 DistinguISH Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 1q22-q23.1* (chr1:156,245,849-156,781,745), proximal to the NTRK1 breakpoint region, and in 15q25.3-q26.1* (chr15:88,825,346-89,475,889), distal to the NTRK3 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~2,5 ng/µl), which target sequences mapping in 1q23.1* (chr1:156,854,527-157,296,918), distal to the NTRK1 breakpoint region, and in 15q25.3* (chr15:87,976,717-88,471,002), proximal to the NTRK3 breakpoint region (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~70,0 ng/µl), which target sequences mapping in 15q25.3-q26.1* (chr15:87,845,459-89,475,889) harboring the NTRK3 gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

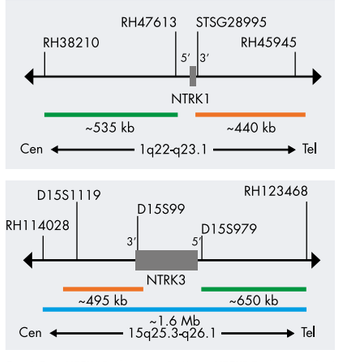
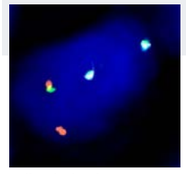


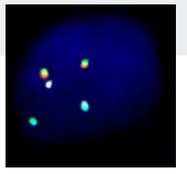
Fig. 1: Top: NRTK1 Probe map; Bottom: NRTK3 Probe map (not to scale)

Results

Normal situation: In interphases of normal cells or cells without a rearrangement involving the NTRK1 or NTRK3 gene region, four green/orange fusion signals appear when using an appropriate dual bandpass filter set, and two blue signals appear when using an appropriate single bandpass filter set.
Aberrant situation: One NTRK1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal not co-localizing with blue signals. Loss of one green signal resulting in an isolated orange signal is the result of a deletion proximal to the NTRK1 breakpoint region. One NTRK3 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal, each co-localizing with a blue signal. Loss of one green signal resulting in an isolated orange signal co-localizing with a blue signal is the result of a deletion distal to the NTRK3 breakpoint region.



Cell which shows two green/orange/blue fusion signals (NTRK3) and one green/orange fusion signal (NTRK1). NTRK1 rearrangement is indicated by one isolated orange signal, not co-localizing with a blue signal.



Cell which shows two green/orange fusion signals and one green/orange/blue fusion signal. NTRK3 rearrangement is indicated by one separate orange and one separate green signal, both co-localizing with blue signals.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	1, 15	CE/IVD	5 (50 µl)	**Z-2314-50**
			20 (200 µl)	**Z-2314-200**

*Flex*ISH® ALK/ROS1 DistinguISH™ Probe

Intended Purpose

The F*lex*ISH ALK/ROS1 DistinguISH Probe (PL161) is intended to be used for the qualitative detection of translocations involving the human ALK gene at 2p23.1-p23.2 and the human ROS1 gene at 6q22.1 in formalin-fixed, paraffin-embedded specimens, such as non-small cell lung cancer (NSCLC), by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the F*lex*ISH-Tissue Implementation Kit (Prod. No. Z-2182-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

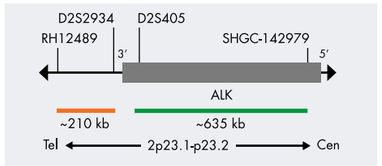
The probe is intended to be used as an aid to the differential diagnosis of NSCLC and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The F*lex*ISH ALK/ROS1 DistinguISH Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 2p23.1-p23.2* (chr2:29,460.144-30,095,822), proximal to the ALK breakpoint region, and in 6q22.1* (chr6:116,912,298-117,627,255), proximal to the ROS1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~2,5 ng/µl), which target sequences mapping in 2p23.2* (chr2:29,174,204-29,383,335), distal to the ALK breakpoint region, and in 6q22.1* (chr6:117,659,135-117,871,701), distal to the ROS1 breakpoint region (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides, (~70.0 ng/µl), which target sequences mapping in 6q22.1* (chr6:116,671,642-117,260,761) proximal to the ROS1 breakpoint region co-localizing with the green-labeled ROS1 polynucleotides and in 6q22.1-q22.2* (chr6:117,765,211-118,444,005) distal to the ROS1 breakpoint region co-localizing with the orange-labeled ROS1 polynucleotides (see Fig. 1.)
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



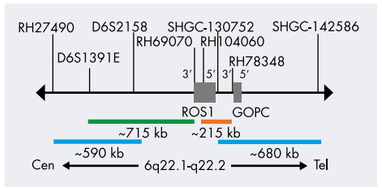


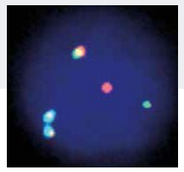
Fig. 1: Top: ALK Probe map; Bottom: ROS1 Probe map (not to scale)

Ideograms of chromosome 2 and 6 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a rearrangement involving the ALK or ROS1 gene region, four green/orange fusion signals appear when using an appropriate dual bandpass filter set, and two blue signals appear when using an appropriate single bandpass filter set.

Aberrant situation: One ALK gene region affected by a translocation is indicated by one separate green signal and one separate orange signal not co-localizing with blue signals. Loss of one green signal resulting in an isolated orange signal is the result of a deletion of 5′-ALK sequences. One ROS1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal, each co-localizing with a blue signal. Loss of one orange signal resulting in an isolated green signal co-localizing with a blue signal is the result of a deletion distal to the ROS1 breakpoint region or due to an unbalanced translocation affecting this chromosomal region.



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.

Paraffin-embedded 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	2, 6	CE/IVD	5 (50 µl)	**Z-2203-50**
			20 (200 µl)	**Z-2203-200**

*Flex*ISH® BCL2/BCL6 DistinguISH™ Probe

Intended Purpose

The F*lex*ISH BCL2/BCL6 DistinguISH Probe (PL238) is intended to be used for the qualitative detection of translocations involving the human BCL2 gene at 18q21.33 and the human BCL6 gene at 3q27.3 in formalin-fixed, paraffinembedded specimens, such as B-cell lymphoma, by fluorescence in situ hybridization (FISH). The probe is intended to be used in combination with the F*lex*ISH-Tissue Implementation Kit (Prod. No. Z-2182-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

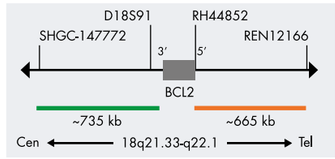
The probe is intended to be used as an aid to the differential diagnosis of B-cell lymphoma and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The F*lex*ISH BCL2/BCL6 DistinguISH Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 18q21.33* (chr18:60,046,152-60,779,138), proximal to the BCL2 breakpoint region, and in 3q27.3* (chr3:186,578,337-187,403,834), proximal to the BCL6 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~2,5 ng/µl), which target sequences mapping in 18q21.33-q22.1* (chr18:60,994,528-61,658,503), distal to the BCL2 breakpoint region, and in 3q27.3-q28* (chr3:187,744,962-188,411,425), distal to the BCL6 breakpoint region (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides, (~70.0 ng/µl), which target sequences mapping in 3q27.3* (chr3:186,578,337-187,403,834) proximal to the BCL6 breakpoint region co-localizing with the green-labeled BCL6 polynucleotides and in 3q27.3-q28* (chr3:187,744,962-188,411,425) distal to the BCL6 breakpoint region co-localizing with the orange-labeled BCL6 polynucleotides (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



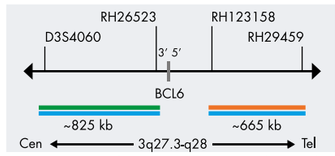
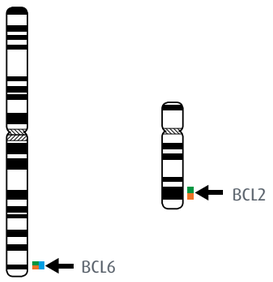


Fig. 1: Top: BCL2 Probe map; Bottom: BCL6 Probe map (not to scale)

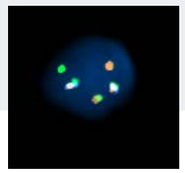


Ideograms of chromosome 3 and 18 indicating the hybridization locations

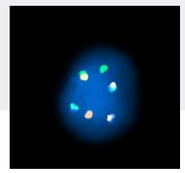
Results

Normal situation: In interphases of normal cells or cells without a rearrangement involving the BCL2 or BCL6 gene region, four green/orange fusion signals appear when using an appropriate dual bandpass filter set, and two blue signals appear when using an appropriate single bandpass filter set.

Aberrant situation: One 18q21.33-q22.1 locus affected by a BCL2 translocation is indicated by one separate green signal and one separate orange signal not co-localizing with blue signals. One 3q27.3-q28 locus affected by a BCL6 translocation is indicated by one separate green signal and one separate orange signal, each co-localizing with a blue signal**.**



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 colocalizing with blue signals.



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 co-localizing with blue signals. Additionally, one separate orange and one separate green signal indicate a further BCL2 positivity, confirming a BCL2/BCL6 co-rearrangement.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	3, 18	CE/IVD	5 (50 µl)	**Z-2283-50**
			20 (200 µl)	**Z-2283-200**

Specimen kindly provided by Dr. Rontogianni, Athens, Greece.

*Flex*ISH® MYC/IGH TriCheck™ Probe

Intended Purpose

The F*lex*ISH MYC/IGH TriCheck Probe (PL247) is intended to be used for the qualitative detection of human MYC rearrangements with and without participation of the human IGH locus in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the F*lex*ISH-Tissue Implementation Kit (Prod. No. Z-2182-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The F*lex*ISH MYC/IGH TriCheck Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 8q24.21* (chr8:130,373,051-130,930,673) distal to the MYC breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~2,5 ng/µl), which target sequences mapping in 8q24.21* (chr8:127,888,765-128,363,281) proximal to the MYC breakpoint region (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~70,0 ng/µl), which target sequences mapping in 14q32.33* (chr14:105,462,169-106,995,000) harboring the IGH locus. (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

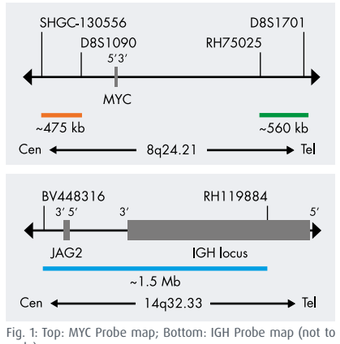
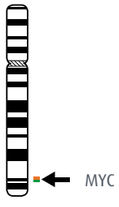
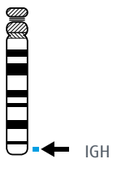


Fig. 1: Top: MYC Probe map; Bottom: IGH Probe map (not to scale)



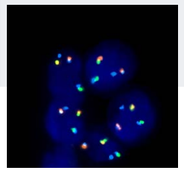


Ideograms of chromosome 8 and 14 indicating the hybridization locations

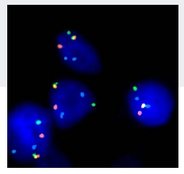
Results

Normal situation: In interphases of normal cells or cells without MYC rearrangements, two green/orange fusion signals appear when using an appropriate dual bandpass filter set and two blue signals appear when using an appropriate single bandpass filter set. When using an appropriate triple color bandpass filter set, two green/orange fusion signals and two blue signals can be observed.

Aberrant situation: A rearrangement of the MYC gene region not involving the IGH locus is indicated by a green/orange fusion signal, separated single green and orange signals and two blue signals. A MYC rearrangement involving the IGH locus is indicated by one green/orange fusion signal, one separate blue signal and one green/blue fusion signal as well as one orange/blue fusion signal. In a cell with a rearrangement of the IGH locus not involving the MYC gene or a trisomy of chromosome 14, two green/orange fusion signals and three blue signals can be observed.



Example of an aberrant signal pattern: 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.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	8, 14	CE/IVD	5 (50 µl)	**Z-2293-50**

*Flex*ISH® RET/KIF5B TriCheck™ Probe

Intended Purpose

The F*lex*ISH RET/KIF5B TriCheck Probe (PL226) is intended to be used for the qualitative detection of rearrangements involving the human RET gene with and without participation of the human KIF5B gene in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the F*lex*ISH-Tissue Implementation Kit (Prod. No. Z-2182-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

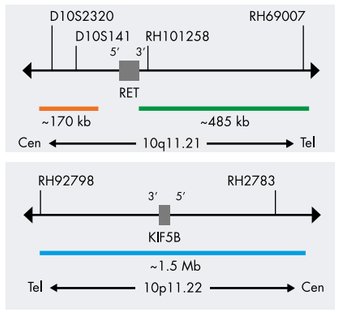
The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The F*lex*ISH RET/KIF5B TriCheck Probe is composed of:

- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~2,5 ng/µl), which target sequences mapping in 10q11.21* (chr10:43,340,888-43,510.171) proximal to the RET breakpoint region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 10q11.21* (chr10:43,626,274-44,112,146) distal to the RET breakpoint region (see Fig. 1).
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~70 ng/µl), which target sequences mapping in 10p11.22* (chr10:31,640,467-33,085,804) harboring the KIF5B gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



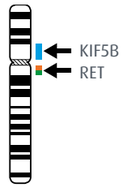
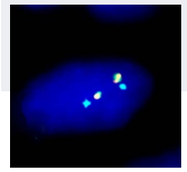


Fig. 1: Top: RET Probe map; Bottom: KIF5B Probe map (not to scale); Right: Ideogram of chromosome 10 indicating the hybridization locations

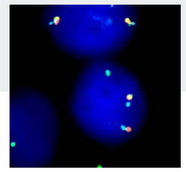
Results

Normal situation: In interphases of normal cells or cells without RET-KIF5B rearrangements, two green/orange fusion signals appear when using an appropriate dual bandpass filter set, and two blue signals appear when using an appropriate single bandpass filter set. When using an appropriate triple color bandpass filter set, two green/orange fusion signals, each in close proximity to a blue signal, can be observed, indicating the normal chromosomes 10.

Aberrant situation: A KIF5B-RET fusion caused by a RET-KIF5B inversion is indicated by a green/blue fusion signal and an orange/blue fusion signal in close proximity. A RET translocation without involvement of KIF5B is indicated by an orange and a blue signal in close proximity and a separate green signal. Isolated green signals are the result of deletions proximal to the RET breakpoint region.



F*lex*ISH 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).



Example of an aberrant signal pattern: NSCLC tissue section with a KIF5B-RET inversion as indicated by one green, one separated orange, and an additional blue signal.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●|●	10	CE/IVD	20 (200 µl)	**Z-2269-200**

Specimen kindly provided by Dr. Schildhaus, Essen, Germany.

*Flex*ISH® ERBB2/CEN 17 Dual Color Probe

Intended Purpose
The *Flex*ISH ERBB2/CEN 17 Dual Color Probe (PL122) is intended to be used for the qualitative detection of amplifications involving the human ERBB2 gene as well as the detection of chromosome 17 alpha satellites in formalin-fixed, paraffin-embedded specimens, such as breast cancer and gastric/gastroesophageal junction cancer, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the *Flex*ISH-Tissue Implementation Kit (Prod. No. Z-2182-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of breast cancer and gastric/gastroesophageal junction cancer and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The *Flex*ISH ERBB2/CEN 17 Dual Color Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 17q12-q21.1* (chr17:37,572,531-38,181,308) harboring the ERBB2 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~1.0 ng/µl), which target sequences mapping in 17p11.1-q11.1 specific for the alpha satellite centromeric region D17Z1 of chromosome 17.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

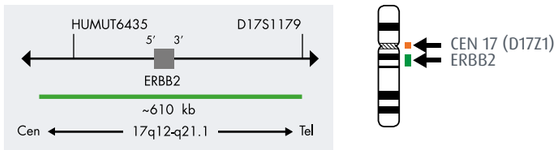


Fig. 1: ERBB2 Probe map (not to scale); Right: Ideogram of chromosome 17 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the ERBB2 gene region, two green and two orange signals appear.
Aberrant situation: In cells with an amplification of the ERBB2 gene region, an increased number of green signals or green signal clusters will be observed.

Hybridized for 2 hours on a breast cancer tissue section with ERBB2 (green) amplification.

Hybridized overnight on a breast cancer tissue section with ERBB2 (green) amplification.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	17	CE/IVD	5 (50 µl)	**Z-2166-50**
			20 (200 µl)	**Z-2166-200**

Accessories

*Flex*ISH® Implementation Kits
For the detection *Flex*ISH® probes

Product	Manufacturer	Tests	Reg. Status	Order No.
***Flex*ISH-Tissue Implementation Kit** Incl.: Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; 5x *Flex*ISH Wash Buffer, 150 ml; DAPI/DuraTect-Solution, 0.2 ml	ZytoVision GmbH	5	CE/IVD	**Z-2182-5**
***Flex*ISH-Tissue Implementation Kit** Incl.: Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; 5x *Flex*ISH Wash Buffer, 500 ml; DAPI/DuraTect-Solution, 0.8 ml	ZytoVision GmbH	10	CE/IVD	**Z-2182-20**

*Flex*ISH® Pretreatment Reagents

Product	Manufacturer	Amount	Reg. Status	Order No.
Pepsin Solution	ZytoVision GmbH	4 ml	CE/IVD	**ES-0001-4**
Pepsin Solution	ZytoVision GmbH	50 ml	CE/IVD	**ES-0001-50**
Pepsin Solution	ZytoVision GmbH	1000 ml	CE/IVD	**ES-0001-1000**
Heat Pretreatment Solution Citric	ZytoVision GmbH	2 x 500 ml	CE/IVD	**PT-0001-1000**

*Flex*ISH® Wash Buffers & Ancillary Reagents

Product	Manufacturer	Amount	Reg. Status	Order No.
DAPI/DuraTect™-Solution	ZytoVision GmbH	150 ng DAPI/ml, 0.8 ml	CE/IVD	**MT-0007-0.8**
DAPI/DuraTect™-Solution (ultra)	ZytoVision GmbH	1360 ng DAPI/ml, 0.8 ml	CE/IVD	**MT-0008-0.8**
5 x *Flex*ISH Wash Buffer	ZytoVision GmbH	500 ml	CE/IVD	**WB-0010-500**

ZytoMation®

The **ZytoMation® probes** combine the 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 (FFPE) tissue sections on the BOND™ fully automated systems (BOND™-III, BOND™-MAX, and BOND™ RXm (RUO)) by Leica Biosystems (ZytoVision is not affiliated or associated with Leica Biosystems).

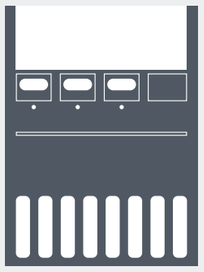
ZytoVision GmbH

Advantages of ZytoMation®

- 5 h protocol on fully automated BOND™ systems
- Ready-to-use probes
- Reduced hands-on time

Workflow

To successfully use the ZytoMation® probes, the BOND™ FISH Kit (DS9636) is required.
Prior to evaluation, the hybridized slides should be mounted using a DAPI/DuraTect™-Solution (MT-0007-0.8/MT-0008-0.8).



1. Dewaxing
2. Heat Pretreatment
3. Proteinase K Digestion
4. Probe Application
5. Denaturation and Hybridization
6. Stringency Wash

BOND™-III **CE/IVD**
BOND™-MAX **CE/IVD**

BOND™ RXm **RUO**

Chromosome Index

Chr. Band	Product Name	Reg. Status	Order No.	Page
2p23	ZytoMation ALK Dual Color Break Apart FISH Probe	CE/IVD	**Z-2315-5.1ML**	**129**

Chr. Band	Product Name	Reg. Status	Order No.	Page
3q27	ZytoMation BCL6 Dual Color Break Apart FISH Probe	CE/IVD	**Z-2313-5.1ML**	**130**

Chr. Band	Product Name	Reg. Status	Order No.	Page
6q22.1	ZytoMation ROS1 Dual Color Break Apart FISH Probe	CE/IVD	**Z-2298-5.1ML**	**131**

Chr. Band	Product Name	Reg. Status	Order No.	Page
7q31.2	ZytoMation MET/CEN 7 Dual Color FISH Probe	CE/IVD	**Z-2321-5.1ML**	**131**

Chr. Band	Product Name	Reg. Status	Order No.	Page
8q24.21	ZytoMation MYC Dual Color Break Apart FISH Probe	CE/IVD	**Z-2312-5.1ML**	**132**

ISH

Chr. Band	Product Name	Reg. Status	Order No.	Page
10q11.2	Zyto*Mation* RET Dual Color Break Apart FISH Probe	CE/IVD	**Z-2316-5.1ML**	**133**

Chr. Band	Product Name	Reg. Status	Order No.	Page
14q32.3	Zyto*Mation* IGH Dual Color Break Apart FISH Probe	CE/IVD	**Z-2317-5.1ML**	**134**

Chr. Band	Product Name	Reg. Status	Order No.	Page
17q12	Zyto*Mation* ERBB2/CEN 17 Dual Color FISH Probe	CE/IVD	**Z-2292-5.1ML**	**134**

Chr. Band	Product Name	Reg. Status	Order No.	Page
18q21.3	Zyto*Mation* BCL2 Dual Color Break Apart FISH Probe	CE/IVD	**Z-2306-5.1ML**	**135**

Gene Index

HUGO Name	Synonym	Product Name	Reg. Status	Order No.	Page
ALK	CD246	Zyto*Mation* ALK Dual Color Break Apart FISH Probe	CE/IVD	**Z-2315-5.1ML**	**129**
BCL2	Bcl-2, PPP1R50	Zyto*Mation* BCL2 Dual Color Break Apart FISH Probe	CE/IVD	**Z-2306-5.1ML**	**135**
BCL6	ZNF51, LAZ3	Zyto*Mation* BCL6 Dual Color Break Apart FISH Probe	CE/IVD	**Z-2313-5.1ML**	**130**
ERBB2	HER2, HER-2, NEU	Zyto*Mation* ERBB2/CEN 17 Dual Color FISH Probe	CE/IVD	**Z-2292-5.1ML**	**134**
IGH	IGH@	Zyto*Mation* IGH Dual Color Break Apart FISH Probe	CE/IVD	**Z-2317-5.1ML**	**134**
MET	HGFR, RCCP2	Zyto*Mation* MET/CEN 7 Dual Color FISH Probe	CE/IVD	**Z-2321-5.1ML**	**131**
MYC	CMYC, bHLHe39, c-Myc	Zyto*Mation* MYC Dual Color Break Apart FISH Probe	CE/IVD	**Z-2312-5.1ML**	**132**
RET	HSCR1, CDHF12	Zyto*Mation* RET Dual Color Break Apart FISH Probe	CE/IVD	**Z-2316-5.1ML**	**133**
ROS1	MCF3, ROS	Zyto*Mation* ROS1 Dual Color Break Apart FISH Probe	CE/IVD	**Z-2298-5.1ML**	**131**

ZytoMation® ALK Dual Color Break Apart FISH Probe

Intended Purpose

The Zyto*Mation* ALK Dual Color Break Apart FISH 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 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 formation 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.

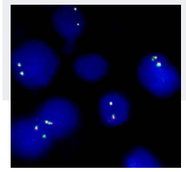
ALK kinase targeted therapies may represent a very effective therapeutic strategy in NSCLC patients carrying EML4-ALK rearrangements.

References

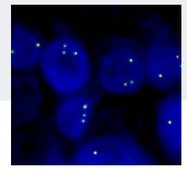
Ach T, *et al.* (2013) Virchows Arch 462: 65-72.
Cooper CS, *et al.* (1984) Nature 311: 29-32.
Engelman JA, *et al.* (2007) Science 316: 1039-43.
Ettl T, *et al.* (2014) Head Neck 36: 517-23.
Garcia S, *et al.*(2007) Int J Oncol 31: 49-58.
Hara T, *et al.* (1998) Lab Invest 78: 1143-53.
Lacroix L, *et 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.

Results

Normal situation: In interphases of normal cells or cells without a translocation involving the ALK gene region, two green/orange fusion signals appear.
Aberrant situation: One ALK gene region affected by a translocation is indicated by one separate green signal and one separate orange signal. An EML4-ALK inversion with deletion of 5'-ALK sequences is indicated by one or multiple isolated orange signals.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



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

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	2	CE/IVD	Up to 20 (5.1 ml)	**Z-2315-5.1ML**

Probe Description

The Zyto*Mation* ALK Dual Color Break Apart FISH Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~6 ng/µl), which target sequences mapping in 2p23.1-p23.2* (chr2:29,460.144-30,095,822) proximal to the ALK breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,0 ng/µl), which target sequences mapping in 2p23.2* (chr2:29,174,204-29,383,335) distal to the ALK breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

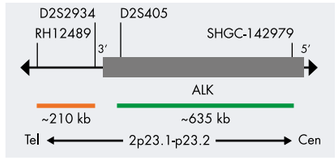
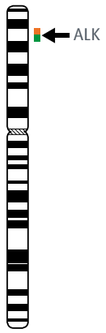


Fig. 1: ALK Probe map (not to scale)



Ideogram of chromosome 2 indicating the hybridization locations

ZytoMation® BCL6 Dual Color Break Apart FISH Probe

Intended Purpose
The Zyto*Mation* BCL6 Dual Color Break Apart FISH 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 FISH 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 Zyto*Mation* BCL6 Dual Color Break Apart FISH Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~6.0 ng/µl), which target sequences mapping in 3q27.3* (chr3:186,737,897-187,403,834) proximal to the BCL6 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~2,5 ng/µl), which target sequences mapping in 3q27.3-q28*(chr3:187,744,962-188,097,195) distal to the BCL6 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

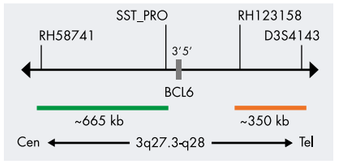
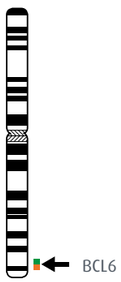
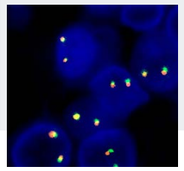


Fig. 1: BCL6 Probe map (not to scale)

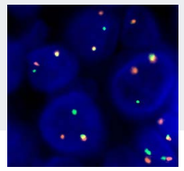


Ideogram of chromosome 3 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the BCL6 gene region, two green/orange fusion signals appear.
Aberrant situation: One BCL6 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Lymphoma 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	3	CE/IVD	Up to 20 (5.1 ml)	**Z-2313-5.1ML**

ZytoMation® ROS1 Dual Color Break Apart FISH Probe

Intended Purpose
The Zyto*Mation* ROS1 Dual Color Break Apart FISH Probe (PL251) is intended to be used for the qualitative detection of translocations involving the human ROS1 gene at 6q22.1 in formalin-fixed, paraffin-embedded specimens, such as non-small cell lung cancer (NSCLC), by fluorescence *in situ* hybridization (FISH).

The probe is intended to be used in combination with the Bond FISH Kit (DS9636) on the automated Bond-MAX or Bond III system by Leica Biosystems.

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of NSCLC and therapeutic measures should not be initiated based on the test result alone

Probe Description
The Zyto*Mation* ROS1 Dual Color Break Apart FISH Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~6,0 ng/µl), which target sequences mapping in 6q22.1* (chr6:116,912,298-117,627,255) proximal to the ROS1 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~2,5 ng/µl), which target sequences mapping in 6q22.1* (chr6:117,659,135-117,871,701) distal to the ROS1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

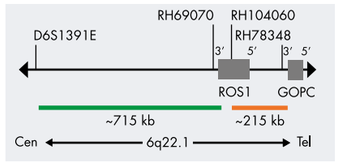
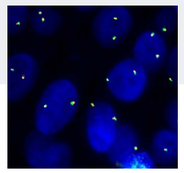
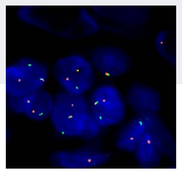


Fig. 1: ROS1 Probe map (not to scale); Right: Ideogram of chromosome 6 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the ROS1 gene region, two green/orange fusion signals appear.
Aberrant situation: One ROS1 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal. Isolated green signals are the result of deletions distal to the ROS1 breakpoint region or are due to unbalanced translocations affecting this chromosomal region.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	6	CE/IVD	Up to 20 (5.1 ml)	**Z-2298-5.1ML**

ZytoMation® MET/CEN 7 Dual Color FISH Probe

Intended Purpose
The Zyto*Mation* MET/CEN 7 Dual Color FISH 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.

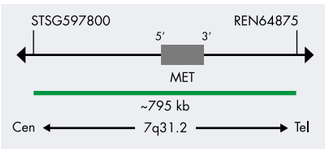
Activation or upregulation of MET was found in a number of carcinomas including lung, breast, colorectal, prostate, and gastric carcinomas as well as in gliomas, melanomas and some sarcomas. MET overexpression is known as a negative prognostic indicator in patients with various carcinomas, multiple myeloma, 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.

In addition, 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
Ach T, *et al.* (2013) Virchows Arch 462: 65-72.
Cooper CS, *et al.* (1984) Nature 311: 29-32.
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 Zyto*Mation* MET/CEN 7 Dual Color FISH Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~5 ng/µl), which target sequences mapping in 7q31.2* (chr7:115,925,700-116,718,699) harboring the MET region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~0,2 ng/µl), which target sequences mapping in 7p11.1-q11.1 specific for the alpha satellite centromeric region D7Z1 of chromosome 7.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



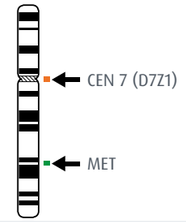
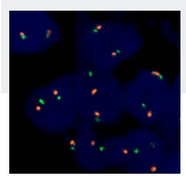
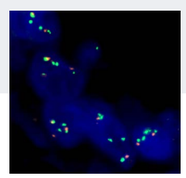


Fig. 1: MET Probe map (not to scale); Right: Ideogram of chromosome 7 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the MET gene region, two green signals and two orange signals appear.
Aberrant situation: In cells with an amplification of the MET gene region an increased number of green signals or green signal clusters will be observed.



Hybridized to normal interphase cells as indicated by two green and two orange signals in each nucleus.



Lung adenocarcinoma tissue section with amplification of the MET gene locus as indicated by multiple copies of the green signal in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	7	CE/IVD	Up to 20 (5.1 ml)	**Z-2321-5.1ML**

ZytoMation® MYC Dual Color Break Apart FISH Probe

Intended Purpose
The Zyto*Mation* MYC Dual Color Break Apart FISH 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 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) gene in 14q32.33.

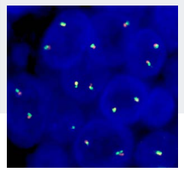
Further translocations affecting the MYC gene are t(8;22)(q24.21;q11.2) and t(2;8)(p11.2;q24.21), both of which involve one of the two immunoglobulin light chain loci. All three translocations bring the MYC gene under the control of a regulatory element from one of the immunoglobulin loci resulting in 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.

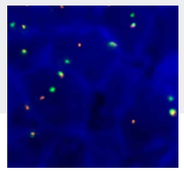
Probe Description
The Zyto*Mation* MYC Dual Color Break Apart FISH Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~6.0 ng/µl), which target sequences mapping in 8q24.21* (chr8:130,373,051-130,930,673) distal to the MYC breakpoint region (see Fig.1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~2.5 ng/µl), which target sequences mapping in 8q24.21* (chr8:127,888,765-128,363,281) proximal to the MYC breakpoint region (see Fig. 1).
- Hybridisierungsbuffer auf Basis von Formamid

* according to Human Genome Assembly GRCh37/hg19

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the MYC gene region, two green/orange fusion signals appear.
Aberrant situation: One MYC gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



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

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	8	CE/IVD	Up to 20 (5.1 ml)	**Z-2312-5.1ML**

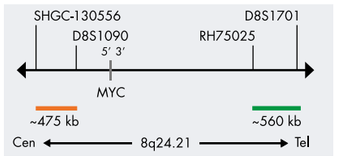
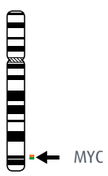


Fig. 1: MYC Probe map (not to scale)



Ideogram of chromosome 8 indicating the hybridization locations

ZytoMation® RET Dual Color Break Apart FISH Probe

Intended Purpose
The Zyto*Mation* RET Dual Color Break Apart FISH Probe is designed to detect translocations involving the chromosomal region 10q11.21 harboring the RET (retproto-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.

In addition, 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.

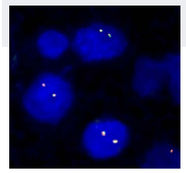
RET translocations are responsible for 1-2% of non-squamous NSCLCs. Similarly to ALK and ROS1, they are more characteristic for young non-smokers and females. This category of cancers is known to be responsive to treatment with RET tyrosine kinase inhibitors.

References
Gautschi O, *et al.* (2013) J Thorac Oncol 8: e43-4.
Imyanitov EN, *et al.* (2021) Crit Rev Oncol Hematol 157: 103194.
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.

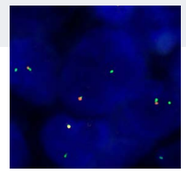
Probe Description
The Zyto*Mation* RET Dual Color Break Apart FISH Probe is composed of:
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~6.0 ng/µl), which target sequences mapping in 10q11.21* (chr10:43,626,274-43,902,346) distal to the RET breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,0 ng/µl), which target sequences mapping in 10q11.21* (chr10:43,340,888-43,510.171) proximal to the RET breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the RET gene region, two green/orange fusion signals appear.
Aberrant situation: One RET gene region affected by a translocation is indicated by one separate green signal and one separate orange signal. Isolated green signals are the result of deletions proximal to the RET breakpoint region. Inversions involving genes in close proximity such as CCDC6 might not be observable due to just subtle signal separation.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Lung adenocarcinoma tissue section with rearrangement of the RET gene as indicated by isolated green signals.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	10	CE/IVD	Up to 20 (5.1 ml)	**Z-2316-5.1ML**

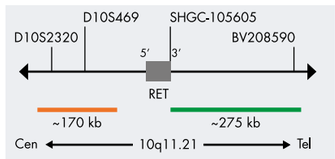


Fig. 1: RET Probe map (not to scale)

Ideogram of chromosome 10 indicating the hybridization locations

ZytoMation® IGH Dual Color Break Apart FISH Probe

Intended Purpose

The Zyto*Mation* IGH Dual Color Break Apart FISH Probe is designed to detect translocations involving the chromosomal region 14q32.33 harboring the IGH locus. Rearrangements involving the IGH (immunoglobulin heavy locus, a.k.a. IGH@) gene locus are considered to be cytogenetic hallmarks for non-Hodgkin lymphoma (NHL). NHLs represent 50% of all hematological malignancies. IGH locus 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 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 Zyto*Mation* IGH Dual Color Break Apart FISH Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~6.0 ng/µl), which target sequences mapping in 14q32.33* (chr14:106,690,778-107,268,412) distal to the IGH breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.0 ng/µl), which target sequences mapping in 14q32.33* (chr14:105,296,741-105,909,611) proximal to the IGH breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

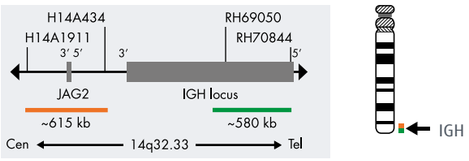
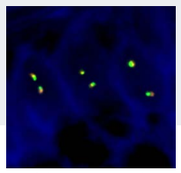


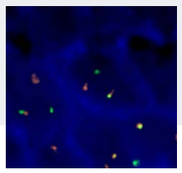
Fig. 1: IGH Probe map (not to scale); Right: Ideogram of chromosome 14 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a translocation involving the IGH locus, two green/orange fusion signals appear.
Aberrant situation: One IGH locus affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



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

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	14	CE/IVD	Up to 20 (5.1 ml)	**Z-2317-5.1ML**

ZytoMation® ERBB2/CEN 17 Dual Color FISH Probe

Intended Purpose

The Zyto*Mation* ERBB2/CEN 17 Dual Color FISH Probe (PL246) is intended to be used for the qualitative detection of amplifications involving the human ERBB2 gene as well as the detection of chromosome 17 alpha satellites in formalin-fixed, paraffin-embedded specimens, such as breast cancer and gastric/gastroesophageal junction cancer, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Bond FISH Kit (DS9636) on the automated Bond-MAX or Bond III system by Leica Biosystems.

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of breast cancer and gastric/gastroesophageal junction cancer and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The Zyto*Mation* ERBB2/CEN 17 Dual Color FISH Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 17q12-q21.1* (chr17:37,572,531-38,181,308) harboring the ERBB2 gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~0,2 ng/µl), which target sequences mapping in 17p11.1-q11.1 specific for the alpha satellite centromeric region D17Z1 of chromosome 17.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

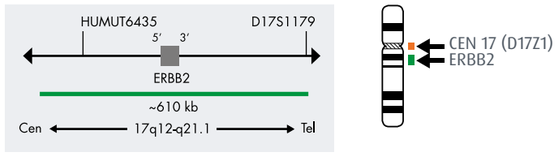
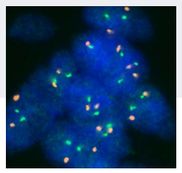


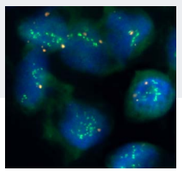
Fig. 1: ERBB2 Probe map (not to scale); Right: Ideogram of chromosome 17 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without an amplification involving the ERBB2 gene region, two green signals and two orange signals appear.
Aberrant situation: In cells with an amplification of the ERBB2 gene region an increased number of green signals or green signal clusters will be observed.



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.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	17	CE/IVD	Up to 20 (5.1 ml)	**Z-2292-5.1ML**

ZytoMation® BCL2 Dual Color Break Apart FISH Probe

Intended Purpose

The Zyto*Mation* BCL2 Dual Color Break Apart FISH Probe (PL260) is intended to be used for the qualitative detection of translocations involving the human BCL2 gene at 18q21.33 in formalin-fixed, paraffin-embedded specimens, such as B-cell lymphoma, by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the Bond FISH Kit (DS9636) on the automated Bond-MAX or Bond III system by Leica Biosystems.

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of B-cell lymphoma and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The Zyto*Mation* BCL2 Dual Color Break Apart FISH Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~6,0 ng/µl), which target sequences mapping in 18q21.33* (chr18:60,046,152-60.589,273) proximal to the BCL2 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~2,5 ng/µl), which target sequences mapping in 18q21.33-q22.1* (chr18:60,994,528-61,658,503) distal to the BCL2 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

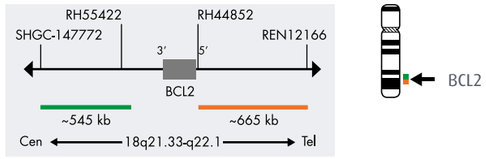
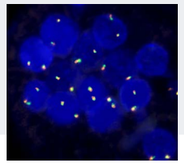


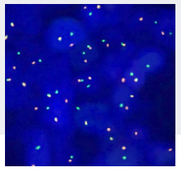
Fig. 1: BCL2 Probe map (not to scale); Right: Ideogram of chromosome 18 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a translocation involving the BCL2 gene region, two green/orange fusion signals appear.
Aberrant situation: One BCL2 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Follicular lymphoma tissue section with translocation of the BCL2 gene as indicated by one non-rearranged orange/green fusion signal, one orange and one separate green signal.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	18	CE/IVD	Up to 20 (5.1 ml)	**Z-2306-5.1ML**

ZytoDot®

Reliable and Simple Detection of Genomic Alterations using Light Microscopy!

The **ZytoDot® products** are designed for the detection of aneuploidies and gene amplifications by Chromogenic *in situ* Hybridization (CISH) in formalin-fixed, paraffin-embedded (FFPE) tissue sections.

ZytoVision GmbH

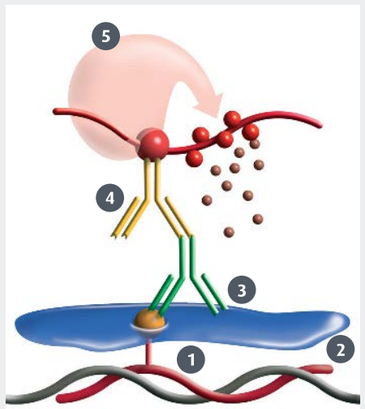
Advantages of CISH

- Simultaneous observation of tissue morphology and CISH signals
- Storage of slides at room temperature - CISH signals are permanent
- No costly fluorescent microscope needed

ZytoDot® Kits – Convenient Solutions

For making CISH analysis reliable and user-friendly, all ZytoDot® CISH probes can be combined with the ZytoDot® 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.

Method



The ZytoDot® 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

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 (FFPE) tissue sections.
This two color system is especially useful for the differentiation of aneuploidies from gene amplifications, and the detection of deletions and translocations.

ZytoVision GmbH

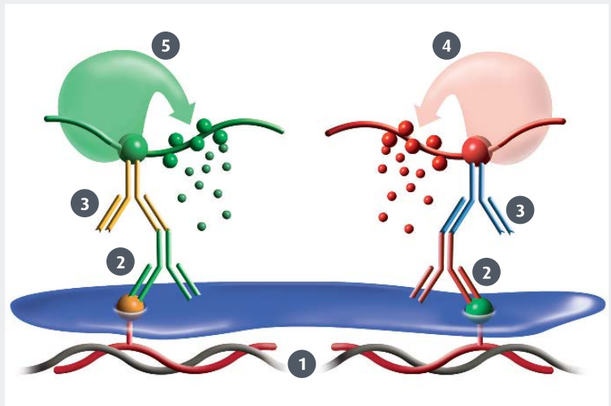
Advantages of ZytoDot® 2C™

- Simultaneous observation of tissue morphology and CISH signals at 40x using light microscopy
- Two targets detected simultaneously
- High contrasting distinct red and green signals
- Standardized and complete kits
- No costly fluorescent microscope needed

ZytoDot® 2C™ Kits – Standardized Solutions

For making CISH analysis reliable and user-friendly, any ZytoDot® 2C™ probe can be combined with the ZytoDot® 2C™ CISH Implementation Kit resulting in target specific kit solutions.
The ZytoDot® 2C™ CISH Implementation Kit includes all necessary pretreatment solutions, wash buffers, antibodies, chromogenic substrates, counterstaining and mounting solution, and a detailed protocol.

Method



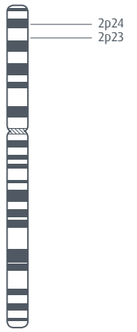
The ZytoDot® 2C™ system uses DIG-and DNP-labeled probe cocktails targeting different genomic sections **[1]** which are detected using a Mouse-anti-DIG/Rabbit-anti-DNP cocktail **[2]**. These antibodies are detected by a unique cocktail of polymerized HRP-Goat-anti-Mouse/AP-Goat-anti-Rabbit antibodies **[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

ISH

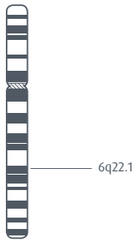
Chromosome Index

Chr. Band	Product Name	Reg. Status	Order No.	Page
1p36.3	ZytoDot 2C Glioma 1p/19q Probe Set	CE/IVD	C-3076-10/-40	142
	ZytoDot 2C SPEC 1p36/1q25 Probe	CE/IVD	C-3036-100/-400	143
1q25.3	ZytoDot 2C Glioma 1p/19q Probe Set	CE/IVD	C-3076-10/-40	142
	ZytoDot 2C SPEC 1p36/1q25 Probe	CE/IVD	C-3036-100/-400	143



Chr. Band	Product Name	Reg. Status	Order No.	Page
2p24	ZytoDot SPEC MYCN Probe	CE/IVD	C-3029-400	144
2p23	ZytoDot 2C SPEC ALK Break Apart Probe	CE/IVD	C-3055-100/-400	144

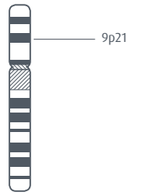
Chr. Band	Product Name	Reg. Status	Order No.	Page
3q27	ZytoDot 2C SPEC BCL6 Break Apart Probe	CE/IVD	C-3074-100	145



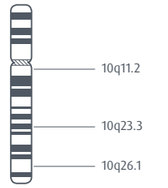
Chr. Band	Product Name	Reg. Status	Order No.	Page
6q22.1	ZytoDot 2C SPEC ROS1 Break Apart Probe	CE/IVD	C-3063-100/-400	145

Chr. Band	Product Name	Reg. Status	Order No.	Page
7p11.2	ZytoDot SPEC EGFR Probe	RUO	C-3007-400	155
	ZytoDot 2C SPEC EGFR/CEN 7 Probe	CE/IVD	C-3033-100/-400	146
7p11.1-q11.1	ZytoDot CEN 7 Probe	RUO	C-3008-400	156
7q31.2	ZytoDot 2C SPEC MET/CEN 7 Probe	CE/IVD	C-3057-400	146

Chr. Band	Product Name	Reg. Status	Order No.	Page
8p11.1-q11.1	ZytoDot CEN 8 Probe	RUO	C-3016-400	156
8q24.21	ZytoDot SPEC MYC Probe	RUO	C-3013-400	155
	ZytoDot 2C SPEC MYC Break Apart Probe	CE/IVD	C-3066-400	147

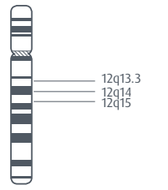


Chr. Band	Product Name	Reg. Status	Order No.	Page
9p21	ZytoDot 2C SPEC CDKN2A/CEN 9 Probe	CE/IVD	C-3067-400	147

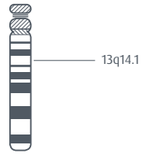


Chr. Band	Product Name	Reg. Status	Order No.	Page
10q11.2	ZytoDot 2C SPEC RET Break Apart Probe	CE/IVD	C-3064-100	148
10q23.3	ZytoDot 2C SPEC PTEN/CEN 10 Probe	RUO	C-3053-400	155
10q26.1	ZytoDot 2C SPEC FGFR2/CEN 10 Probe	CE/IVD	C-3056-400	148

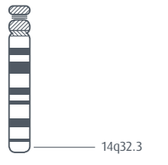
Chr. Band	Product Name	Reg. Status	Order No.	Page
11q13.3	ZytoDot 2C SPEC CCND1 Break Apart Probe	RUO	C-3075-100	149



Chr. Band	Product Name	Reg. Status	Order No.	Page
12q13.3	ZytoDot 2C SPEC DDIT3 Break Apart Probe	CE/IVD	C-3047-100	149
12q14	ZytoDot 2C SPEC CDK4/CEN 12 Probe	CE/IVD	C-3062-400	150
12q15	ZytoDot SPEC MDM2 Probe	CE/IVD	C-3012-400	150
	ZytoDot 2C SPEC MDM2/CEN 12 Probe	CE/IVD	C-3049-100/-400	151



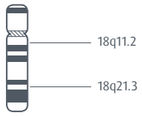
Chr. Band	Product Name	Reg. Status	Order No.	Page
13q14.1	ZytoDot 2C SPEC FOXO1 Break Apart Probe	RUO	C-3065-100	155



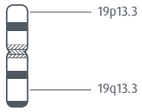
Chr. Band	Product Name	Reg. Status	Order No.	Page
14q32.3	ZytoDot 2C SPEC IGH Break Apart Probe	CE/IVD	C-3071-100	139

ISH

Chr. Band	Product Name	Reg. Status	Order No.	Page
17p13	Zyto*Dot* 2C SPEC USP6 Break Apart Probe	CE/IVD	**C-3077-100**	**152**
17q12	Zyto*Dot* SPEC ERBB2 Probe	CE/IVD	**C-3001-400**	**152**
	Zyto*Dot* SPEC ERBB2 Probe Kit	CE/IVD	**C-3003-40**	**152**
	Zyto*Dot* 2C SPEC ERBB2/CEN 17 Probe	CE/IVD	**C-3032-100/-400**	**153**
	Zyto*Dot* 2C SPEC ERBB2/CEN 17 Probe Kit	CE/IVD	**C-3022-10/-40**	**153**



Chr. Band	Product Name	Reg. Status	Order No.	Page
18q11.2	Zyto*Dot* 2C SPEC SS18 Break Apart Probe	CE/IVD	**C-3046-100**	**153**
18q21.3	Zyto*Dot* 2C SPEC BCL2 Break Apart Probe	CE/IVD	**C-3073-100**	**154**
	Zyto*Dot* 2C SPEC MALT1 Break Apart Probe	RUO	**C-3072-100**	**154**



Chr. Band	Product Name	Reg. Status	Order No.	Page
19p13.3	Zyto*Dot* 2C Glioma 1p/19q Probe Set	CE/IVD	**C-3076-10/-40**	**142**
	Zyto*Dot* 2C SPEC 19q13/19p13 Probe	CE/IVD	**C-3037-100/-400**	**143**
19q13.3	Zyto*Dot* 2C Glioma 1p/19q Probe Set	CE/IVD	**C-3076-10/-40**	**142**
	Zyto*Dot* 2C SPEC 19q13/19p13 Probe	CE/IVD	**C-3037-100/-400**	**143**

Chr. Band	Product Name	Reg. Status	Order No.	Page
22q12.2	Zyto*Dot* 2C SPEC EWSR1 Break Apart Probe	CE/IVD	**C-3043-100**	**154**

Chr. Band	Product Name	Reg. Status	Order No.	Page
Xp11.1-q11.1	Zyto*Dot* CEN X Probe	RUO	**C-3025-400**	**156**
	Zyto*Dot* 2C CEN X/Y Probe	RUO	**C-3048-400**	**156**

Chr. Band	Product Name	Reg. Status	Order No.	Page
Yp11.1-q11.1	Zyto*Dot* 2C CEN X/Y Probe	RUO	**C-3048-400**	**156**
Yq12	Zyto*Dot* CEN Yq12 Probe	RUO	**C-3020-400**	**156**

Gene Index

HUGO Name	Synonym	Product Name	Reg. Status	Order No.	Page
ALK	CD246	Zyto*Dot* 2C SPEC ALK Break Apart Probe	CE/IVD	**C-3055-100/-400**	**144**
BCL2	Bcl-2, PPP1R50	Zyto*Dot* 2C SPEC BCL2 Break Apart Probe	CE/IVD	**C-3073-100**	**154**
BCL6	ZNF51, LAZ3	Zyto*Dot* 2C SPEC BCL6 Break Apart Probe	CE/IVD	**C-3074-100**	**145**
CCND1	BCL1, PRAD1	Zyto*Dot* 2C SPEC CCND1 Break Apart Probe	RUO	**C-3075-100**	**149**
CDK4	PSK-J3	Zyto*Dot* 2C SPEC CDK4/CEN 12 Probe	CE/IVD	**C-3062-400**	**150**
CDKN2A	p16, ARF, INK4	Zyto*Dot* 2C SPEC CDKN2A/CEN 9 Probe	CE/IVD	**C-3067-400**	**147**
DDIT3	CHOP, GADD153	Zyto*Dot* 2C SPEC DDIT3 Break Apart Probe	CE/IVD	**C-3047-100**	**149**
EGFR	HER1, ERBB1	Zyto*Dot* SPEC EGFR Probe	RUO	**C-3007-400**	**152**
		Zyto*Dot* 2C SPEC EGFR/CEN 7 Probe	CE/IVD	**C-3033-100/-400**	**138**
ERBB2	HER2, HER-2, NEU	Zyto*Dot* SPEC ERBB2 Probe	CE/IVD	**C-3001-400**	**152**
		Zyto*Dot* SPEC ERBB2 Probe Kit	CE/IVD	**C-3003-40**	**152**
		Zyto*Dot* 2C SPEC ERBB2/CEN 17 Probe	CE/IVD	**C-3032-100/-400**	**153**
		Zyto*Dot* 2C SPEC ERBB2/CEN 17 Probe Kit	CE/IVD	**C-3022-10/-40**	**153**
EWSR1	EWS	Zyto*Dot* 2C SPEC EWSR1 Break Apart Probe	CE/IVD	**C-3043-100**	**154**
FGFR2	BEK, CD332	Zyto*Dot* 2C SPEC FGFR2/CEN 10 Probe	CE/IVD	**C-3056-400**	**148**
FOXO1	FKHR, FKH1	Zyto*Dot* 2C SPEC FOXO1 Break Apart Probe	RUO	**C-3065-100**	**155**
IGH	IGH@	Zyto*Dot* 2C SPEC IGH Break Apart Probe	CE/IVD	**C-3071-100**	**151**
MALT1	MLT	Zyto*Dot* 2C SPEC MALT1 Break Apart Probe	RUO	**C-3072-100**	**155**
MDM2	HDM2	Zyto*Dot* SPEC MDM2 Probe	CE/IVD	**C-3012-400**	**150**
		Zyto*Dot* 2C SPEC MDM2/CEN 12 Probe	CE/IVD	**C-3049-100/-400**	**151**
MET	HGFR, RCCP2	Zyto*Dot* 2C SPEC MET/CEN 7 Probe	CE/IVD	**C-3057-400**	**146**
MYC	CMYC, bHLHe39, c-Myc	Zyto*Dot* SPEC MYC Probe	RUO	**C-3013-400**	**155**
		Zyto*Dot* 2C SPEC MYC Break Apart Probe	CE/IVD	**C-3066-400**	**147**
MYCN	NMYC, N-myc	Zyto*Dot* SPEC MYCN Probe	CE/IVD	**C-3029-400**	**144**
PTEN	MMAC1, TEP1	Zyto*Dot* 2C SPEC PTEN/CEN 10 Probe	RUO	**C-3053-400**	**155**
RET	HSCR1, CDHF12	Zyto*Dot* 2C SPEC RET Break Apart Probe	CE/IVD	**C-3064-100**	**148**
ROS1	MCF3, ROS	Zyto*Dot* 2C SPEC ROS1 Break Apart Probe	CE/IVD	**C-3063-100/-400**	**145**
SS18	SYT, SSXT	Zyto*Dot* 2C SPEC SS18 Break Apart Probe	CE/IVD	**C-3046-100**	**153**
USP6	Tre-2, TRE17	Zyto*Dot* 2C SPEC USP6 Break Apart Probe	CE/IVD	**C-3077-100**	**152**

ISH

ZytoDot® 2C Glioma 1p/19q Probe Set

Intended Purpose

The Zyto*Dot* 2C Glioma 1p/19q Probe Set is intended to be used for the qualitative detection of deletions involving the human chromosomal region 1p36.31 as well as deletions involving the human chromosomal region 19q13.32-q13.33 in formalin-fixed, paraffin-embedded specimens, such as glioma, by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the Zyto*Dot* 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of glioma and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The Zyto*Dot* 2C Glioma 1p/19q Probe Set is a set comprising two separate probes:

- Zyto*Dot* 2C SPEC 1p36/1q25 Probe (Prod. No. C-3036-100/-400)
- Zyto*Dot* 2C SPEC 19q13/19p13 Probe (Prod. No. C-3037-100/-400)

The Zyto*Dot* 2C SPEC 1p36/1q25 Probe (PD21) is composed of:

- Digoxigenin-labeled polynucleotides (~1.7 ng/µl), which target sequences mapping in 1q25.3* (chr1:184,562,510-184,752,938) (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~1.7 ng/µl), which target sequences mapping in 1p36.31* (chr1:5,808,946-6,176,336) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

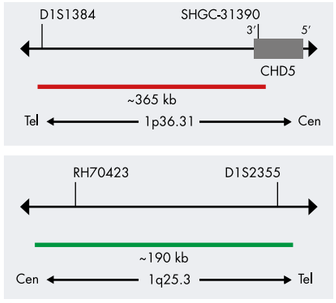


Fig. 1: Top: SPEC 1p36 Probe map; Bottom: SPEC 1q25 Probe map (not to scale)

The Zyto*Dot* 2C SPEC 19q13/19p13 Probe (PD22) is composed of:

- Digoxigenin-labeled polynucleotides (~1.7 ng/µl), which target sequences mapping in 19p13.3* (chr19:815,938-962,244) (see Fig. 2).
- Dinitrophenyl-labeled polynucleotides (~1.7 ng/µl), which target sequences mapping in 19q13.32-q13.33* (chr19:47,857,776-48,339,398) (see Fig. 2).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

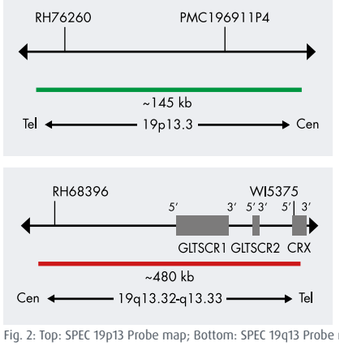
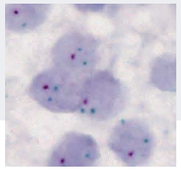


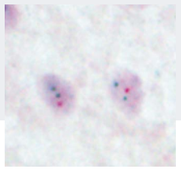
Fig. 2: Top: SPEC 19p13 Probe map; Bottom: SPEC 19q13 Probe map (not to scale)

Results

Normal situation: 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.
Aberrant situation: 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.

Labels	Contents	Reg. Status	Tests	Order No.
DNP/DIG	Zyto*Dot* 2C SPEC 1p36/1q25 Probe, 0.1 ml; Zyto*Dot* 2C SPEC 19q13/19p13 Probe, 0.1 ml	CE/IVD	10	**C-3076-10**
	Zyto*Dot* 2C SPEC 1p36/1q25 Probe, 0.4 ml; Zyto*Dot* 2C SPEC 19q13/19p13 Probe, 0.4 ml		40	**C-3076-40**

Images kindly provided by Prof. W. Müller, University Leipzig, Germany.

ISH

ZytoDot® 2C SPEC 1p36/1q25 Probe

Intended Purpose

The Zyto*Dot* 2C SPEC 1p36/1q25 Probe (PD21) is intended to be used for the qualitative detection of deletions involving the human chromosomal region 1p36.31 as well as chromosome 1q25.3 specific sequences in formalin-fixed, paraffin-embedded specimens, such as glioma, by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the Zyto*Dot* 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of glioma and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The Zyto*Dot* 2C SPEC 1p36/1q25 Probe is composed of:

- Digoxigenin-labeled polynucleotides (~1.7 ng/µl), which target sequences mapping in 1q25.3* (chr1:184,562,510-184,752,938) (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~1.7 ng/µl), which target sequences mapping in 1p36.31* (chr1:5,808,946-6,176,336) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

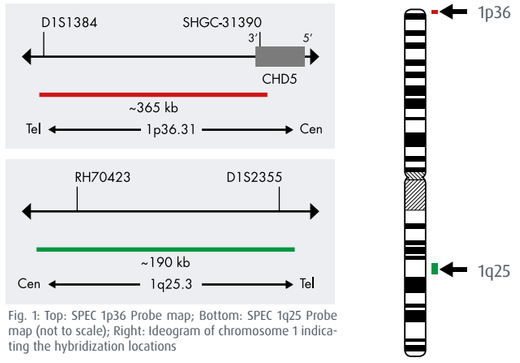


Fig. 1: Top: SPEC 1p36 Probe map; Bottom: SPEC 1q25 Probe map (not to scale); Right: Ideogram of chromosome 1 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without deletion involving the 1p36 locus, two distinct dot-shaped red and two distinct dot-shaped green signals appear.
Aberrant situation: In a cell with deletion affecting the 1p36 locus, a reduced number of red signals will be observed. Deletions affecting only parts of the 1p36 locus might result in a normal signal pattern with red signals of reduced size.

Hybridized to glioma tissue section with 1p36 deletion as indicated by one red signal in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
DNP/DIG	1	CE/IVD	10 (100 µl)	**C-3036-100**
			40 (400 µl)	**C-3036-400**

Image kindly provided by Prof. W. Müller, University Leipzig, Germany.

ISH

ZytoDot® 2C SPEC 19q13/19p13 Probe

Intended Purpose

The Zyto*Dot* 2C SPEC 19q13/19p13 Probe (PD22) is intended to be used for the qualitative detection of deletions involving the human chromosomal region 19q13.32-q13.33 as well as chromosome 19p13.3 specific sequences in formalin-fixed, paraffin-embedded specimens, such as glioma, by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the Zyto*Dot* 2C CISH Implementation Kit (Prod. No. C-3044 10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The product is intended to be used as an aid to the differential diagnosis of glioma and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The Zyto*Dot* 2C SPEC 19q13/19p13 Probe is composed of:

- Digoxigenin-labeled polynucleotides (~1.7 ng/µl), which target sequences mapping in 19p13.3* (chr19:815,938-962,244) (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~1.7 ng/µl), which target sequences mapping in 19q13.32-q13.33* (chr19:47,857,776-48,339,398) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

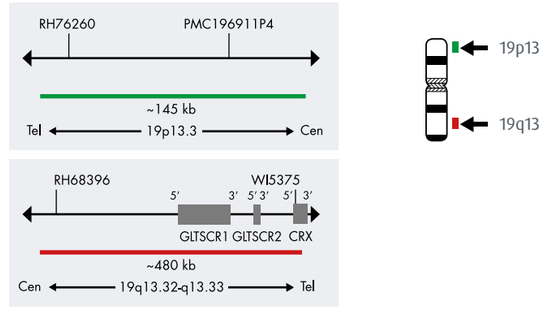


Fig. 1: Top: SPEC 19p13 Probe map; Bottom: SPEC 19q13 Probe map (not to scale); Right: Ideogram of chromosome 19 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without deletion involving the 19q13 locus, two distinct dot-shaped red and two distinct dot-shaped green signals appear.
Aberrant situation: In a cell with deletion affecting the 19q13 locus, a reduced number of red signals will be observed. Deletions affecting only parts of the 19q13 locus might result in a normal signal pattern with red signals of reduced size.

Hybridized to glioma tissue section with 19q13 deletion as indicated by one red signal in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
DNP/DIG	19	CE/IVD	10 (100 µl)	**C-3037-100**
			40 (400 µl)	**C-3037-400**

Image kindly provided by Prof. W. Müller, University Leipzig, Germany.

ZytoDot® SPEC MYCN Probe

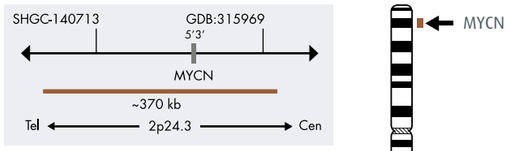
Intended Purpose
The ZytoDot SPEC MYCN Probe (PD17) is intended to be used for the qualitative detection of amplifications involving the human MYCN gene in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the ZytoDot CISH Implementation Kit (Prod. No. C-3018-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoDot SPEC MYCN Probe is composed of:
- Digoxigenin-labeled polynucleotides (~1,8 ng/µl), which target sequences mapping in 2p24.3* (chr2:15,846,046-16,213,717) harboring the MYCN gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



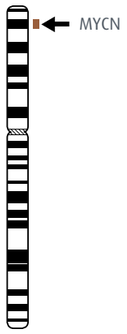
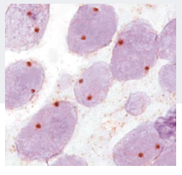


Fig. 1: SPEC MYCN Probe map (not to scale); Right: Ideogram of chromosome 2 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the MYCN gene region, two distinct dot-shaped brown signals appear.
Aberrant situation: In cells with an amplification of the MYCN gene region or polyploidy of chromosome 2, an increased number of brown signals or brown signal clusters will be observed.



Normal nuclei each with two MYCN signals.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG	2	CE/IVD	40 (400 µl)	**C-3029-400**

ZytoDot® 2C SPEC ALK Break Apart Probe

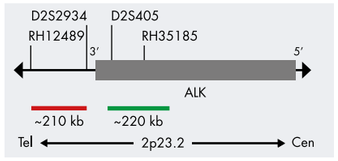
Intended Purpose
The ZytoDot 2C SPEC ALK Break Apart Probe (PD35) is intended to be used for the qualitative detection of translocations involving the human ALK gene at 2p23.2 in formalin-fixed, paraffin-embedded specimens, such as non-small cell lung cancer (NSCLC), by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the ZytoDot 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of NSCLC and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoDot 2C SPEC ALK Break Apart Probe is composed of:
- Digoxigenin-labeled polynucleotides (~0.50 ng/µl), which target sequences mapping in 2p23.2* (chr2:29,460.144-29,681,581) proximal to theALK breakpoint region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~0,75 ng/µl), which target sequences mapping in 2p23.2* (chr2:29,174,204-29,383,335) distal to the ALK breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



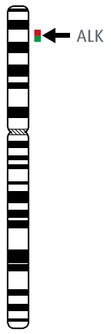
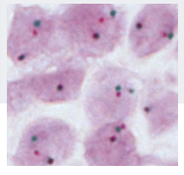


Fig. 1: SPEC ALK Probe map (not to scale); Right: Ideogram of chromosome 2 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the ALK gene region, two red/green fusion signals appear.
Aberrant situation: One ALK gene region affected by a translocation is indicated by one separate green signal and one separate red signal. 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	2	CE/IVD	10 (100 µl)	**C-3055-100**
			40 (400 µl)	**C-3055-400**

ZytoDot® 2C SPEC BCL6 Break Apart Probe

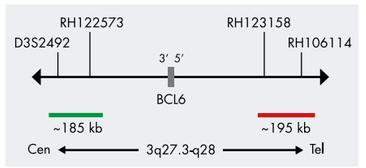
Intended Purpose
The ZytoDot 2C SPEC BCL6 Break Apart Probe (PD54) is intended to be used for the qualitative detection of translocations involving the human BCL6 gene at 3q27.3 in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the ZytoDot 2C CISH Implementation Kit (Prod. No. C-3044-10/-40)

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoDot 2C SPEC BCL6 Break Apart Probe is composed of:
- Digoxigenin-labeled polynucleotides (~0.50 ng/µl), which target sequences mapping in 3q27.3* (chr3:187,028,236-187,403,834) proximal to the BCL6 breakpoint region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~0,75 ng/µl), which target sequences mapping in 3q27.3-q28* (chr3:187,744,962-188,097,195) distal to the BCL6 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



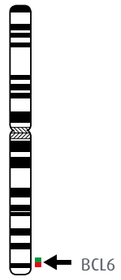
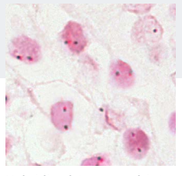


Fig. 1: SPEC BCL6 Probe map (not to scale); Right: Ideogram of chromosome 3 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the BCL6 gene region, two red/green fusion signals appear.
Aberrant situation: One BCL6 gene region affected by a translocation is indicated by one separate green signal and one separate red signal.



Hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	3	CE/IVD	10 (100 µl)	**C-3074-100**

ZytoDot® 2C SPEC ROS1 Break Apart Probe

Intended Purpose
The ZytoDot 2C SPEC ROS1 Break Apart Probe (PD43) is intended to be used for the qualitative detection of translocations involving the human ROS1 gene at 6q22.1 in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the ZytoDot 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoDot 2C SPEC ROS1 Break Apart Probe is composed of:
- Digoxigenin-labeled polynucleotides (~0.50 ng/µl), which target sequences mapping in 6q22.1* (chr6:117,448,964-117,627,255) proximal to the ROS1 breakpoint region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~0,75 ng/µl), which target sequences mapping in 6q22.1* (chr6:117,659,135-117,871,701) distal to the ROS1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

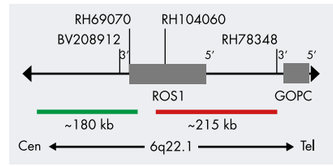
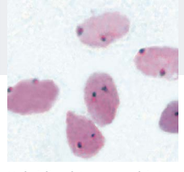
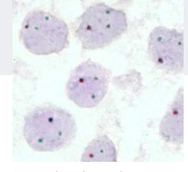


Fig. 1: SPEC ROS1 Probe map (not to scale); Right: Ideogram of chromosome 6 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the ROS1 gene region, two red/green fusion signals appear.
Aberrant situation: One ROS1 gene region affected by a translocation is indicated by one separate green signal and one separate red signal. Isolated green signals are the result of deletions distal to the ROS1 breakpoint region or are due to unbalanced translocations affecting this chromosomal region.



Hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.



Example of an aberrant signal pattern: Lung cancer tissue section with rearrangement of the ROS1 gene as indicated by isolated green signals.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	6	CE/IVD	10 (100 µl)	**C-3063-100**
			40 (400 µl)	**C-3063-400**

ZytoDot® 2C SPEC EGFR/CEN 7 Probe

Intended Purpose
The ZytoDot 2C SPEC EGFR/CEN 7 Probe (PD18) is intended to be used for the qualitative detection of amplifications involving the human EGFR gene as well as the detection of chromosome 7 alpha satellites in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the ZytoDot 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoDot 2C SPEC EGFR/CEN 7 Probe is composed of:
- Digoxigenin-labeled polynucleotides (~1,1 ng/µl), which target sequences mapping in 7p11.2* (chr7:55,082,262-55,278,647) harboring the EGFR region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~1,1 ng/µl), which target sequences mapping in 7p11.1-q11.1 specific for the alpha satellite centromeric region D7Z1 of chromosome 7.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

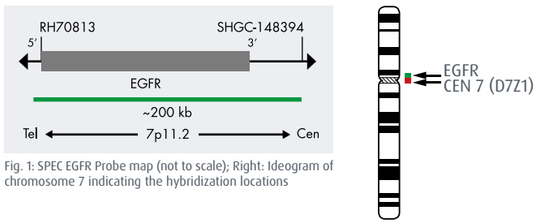
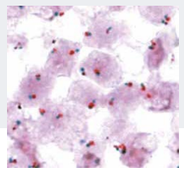
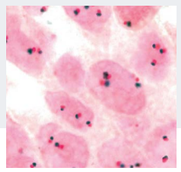


Fig. 1: SPEC EGFR Probe map (not to scale); Right: Ideogram of chromosome 7 indicating the hybridization locations

Results
Normal situation: In Interphases of normal cells or cells without an amplification involving the EGFR gene region, two distinct dot-shaped green and two distinct dot-shaped red signals appear.
Aberrant situation: In cells with an amplification of the EGFR gene region, an increased number of green signals 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	7	CE/IVD	10 (100 µl)	**C-3033-100**
			40 (400 µl)	**C-3033-400**

ZytoDot® 2C SPEC MET/CEN 7 Probe

Intended Purpose
The ZytoDot 2C SPEC MET/CEN 7 Probe (PD37) is intended to be used for the qualitative detection of amplifications involving the human MET gene as well as the detection of chromosome 7 alpha satellites in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the ZytoDot 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoDot 2C SPEC MET/CEN 7 Probe is composed of:
- Digoxigenin-labeled polynucleotides (~1.1 ng/µl), which target sequences mapping in 7q31.2* (chr7:116,298,989-116,718,699) harboring the MET region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~1.1 ng/µl), which target sequences mapping in 7p11.1-q11.1 specific for the alpha satellite centromeric region D7Z1 of chromosome 7.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

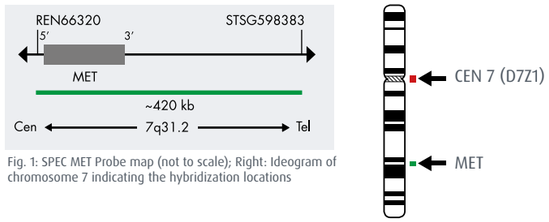
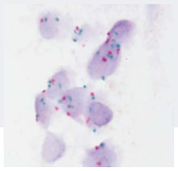


Fig. 1: SPEC MET Probe map (not to scale); Right: Ideogram of chromosome 7 indicating the hybridization locations

Results
Normal situation: In Interphases of normal cells or cells without an amplification involving the MET gene region, two distinct dot-shaped green and two distinct dot-shaped red signals appear.
Aberrant situation: In cells with an amplification of the MET gene region, an increased number of green signals or green signal clusters will be observed.



Example of an aberrant signal pattern: Lung cancer tissue section with multiple copies of chromosome 7 (red) and extra MET signals (green) in the nuclei.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	7	CE/IVD	40 (400 µl)	**C-3057-400**

ZytoDot® 2C SPEC MYC Break Apart Probe

Intended Purpose
The ZytoDot 2C SPEC MYC Break Apart Probe (PD46) is intended to be used for the qualitative detection of translocations involving the human MYC gene at 8q24.21 in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the ZytoDot 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoDot 2C SPEC MYC Break Apart Probe is composed of:
- Digoxigenin-labeled polynucleotides (~0.50 ng/µl), which target sequences mapping in 8q24.21* (chr8:130,373,051-130,847,951) distal to the MYC breakpoint region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~0,75 ng/µl), which target sequences mapping in 8q24.21* (chr8:127,888,765-128,363,281) proximal to the MYC breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

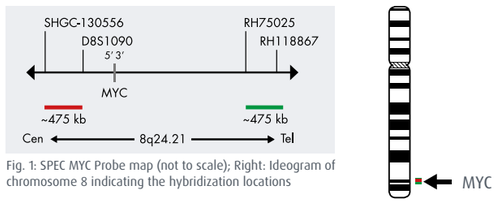
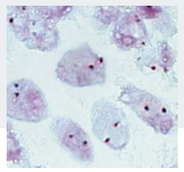
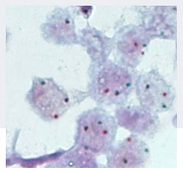


Fig. 1: SPEC MYC Probe map (not to scale); Right: Ideogram of chromosome 8 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the MYC gene region, two red/green fusion signals appear.
Aberrant situation: One MYC gene region affected by a translocation is indicated by one separate distinct dot-shaped green signal and one separate distinct dot-shaped red signal.



Hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	8	CE/IVD	40 (400 µl)	**C-3066-400**

ZytoDot® 2C SPEC CDKN2A/CEN 9 Probe

Intended Purpose
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.

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Sharpless NE (2005) Mutat Res 576: 22-38.

Probe Description
The ZytoDot 2C SPEC CDKN2A/CEN 9 Probe is composed of:
- Digoxigenin-labeled polynucleotides (~1,1 ng/µl), which target sequences mapping in 9p21.3* (chr9:21,742,629-22,056,853) harboring the CDKN2A gene region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~1.1 ng/µl), which target sequences mapping in chromosomal region 9q12 specific for the classical satellite III region D9Z3 of chromosome 9.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

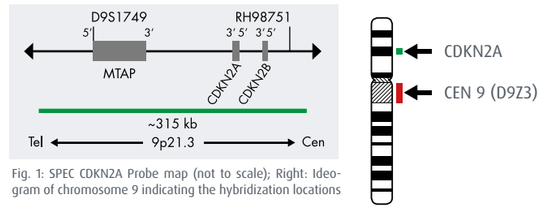
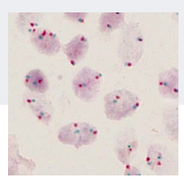


Fig. 1: SPEC CDKN2A Probe map (not to scale); Right: Ideogram of chromosome 9 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a deletion involving the CDKN2A gene region, two distinct dot-shaped green and two distinct dot-shaped red signals appear.
Aberrant situation: In a cell with deletion affecting the CDKN2A gene region, a reduced number of green signals will be observed. Deletions affecting only parts of the CDKN2A gene region might result in a normal signal pattern with green signals of reduced size.



Hybridized to normal interphase cells as indicated by two red and two green signals per nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	9	CE/IVD	40 (400 µl)	**C-3067-400**

ZytoDot® 2C SPEC RET Break Apart Probe

Intended Purpose
The ZytoDot 2C SPEC RET Break Apart Probe (PD44) is intended to be used for the qualitative detection of translocations involving the human RET gene at 10q11.21 in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the ZytoDot 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoDot 2C SPEC RET Break Apart Probe is composed of:
- Digoxigenin-labeled polynucleotides (~0.5 ng/µl), which target sequences mapping in 10q11.21* (chr10:43,687,278-43,856,587) distal to the RET breakpoint region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~0,75 ng/µl), which target sequences mapping in 10q11.21* (chr10:43,340,888-43,510.171) proximal to the RET breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

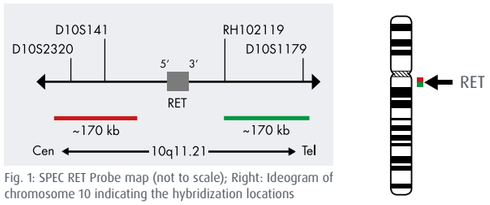
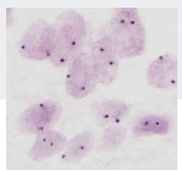


Fig. 1: SPEC RET Probe map (not to scale); Right: Ideogram of chromosome 10 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the RET gene region, two red/green fusion signals appear.
Aberrant situation: One RET gene region affected by a translocation is indicated by one separate green signal and one separate red signal. Isolated green signals are the result of deletions proximal to the RET breakpoint region.



Hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	10	CE/IVD	10 (100 µl)	**C-3064-100**

ZytoDot® 2C SPEC FGFR2/CEN 10 Probe

Intended Purpose
The ZytoDot 2C SPEC FGFR2/CEN 10 Probe (PD36) is intended to be used for the qualitative detection of amplifications involving the human FGFR2 gene as well as the detection of chromosome 10 alpha satellites in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the ZytoDot 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoDot 2C SPEC FGFR2/CEN 10 Probe is composed of:
- Digoxigenin-labeled polynucleotides (~1,1 ng/µl), which target sequences mapping in 10q26.12-10q26.13* (chr10:123,080,085-123,492,398) harboring the FGFR2 region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~1,1 ng/µl), which target sequences mapping in 10p11.1-q11.1 specific for the alpha satellite centromeric region D10Z1 of chromosome 10.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

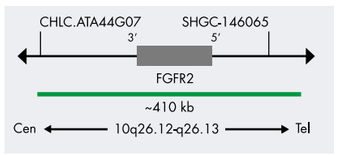
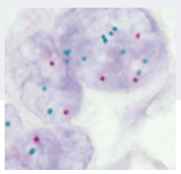


Fig. 1: SPEC FGFR2 Probe map (not to scale); Right: Ideogram of Chromosome 10 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the FGFR2 gene region, two distinct dot-shaped green and two distinct dot-shaped red signals appear.
Aberrant situation: In cells with an amplification of the FGFR2 gene region, an increased number of green signals or green signal clusters will be observed.



Example of an aberrant signal pattern: Breast carcinoma tissue section with FGFR2 (green) amplification.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	10	CE/IVD	40 (400 µl)	**C-3056-400**

ZytoDot® 2C SPEC CCND1 Break Apart Probe

Intended Purpose
The ZytoDot 2C SPEC CCND1 Break Apart Probe (PD55) is intended to be used for the qualitative detection of translocations involving the human CCND1 gene at 11q13.3 in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the ZytoDot 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

Probe Description
The ZytoDot 2C SPEC CCDN1 Break Apart Probe is composed of:
- Digoxigenin-labeled polynucleotides (~0.50 ng/µl), which target sequences mapping in 11q13.3* (chr11:68,522,105-68,705,283) proximal to the CCDN1 breakpoint region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~0,75 ng/µl), which target sequences mapping in 11q13.3* (chr11:69,453,301-70,031,240) distal to the CCND1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

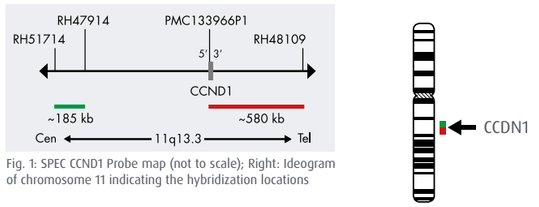
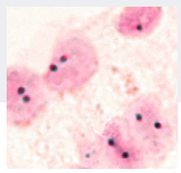
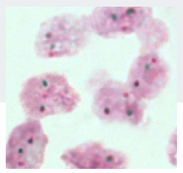


Fig. 1: SPEC CCND1 Probe map (not to scale); Right: Ideogram of chromosome 11 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the CCND1 gene region, two red/green fusion signals appear.
Aberrant situation: One CCND1 gene region affected by a translocation is indicated by one separate green signal and one separate red signal.



Hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	11	RUO	10 (100 µl)	**C-3075-100**

ZytoDot® 2C SPEC DDIT3 Break Apart Probe

Intended Purpose
The ZytoDot 2C SPEC DDIT3 Break Apart Probe (PD27) is intended to be used for the qualitative detection of translocations involving the human DDIT3 gene at 12q13.3 in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the ZytoDot 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoDot 2C SPEC DDIT3 Break Apart Probe is composed of:
- Digoxigenin-labeled polynucleotides (~0.50 ng/µl), which target sequences mapping in 12q13.3-q14.1* (chr12:58,024,366-58,486,511) distal to the DDIT3 breakpoint region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~0,75 ng/µl), which target sequences mapping in 12q13.3* (chr12:57,386,302-57,865,800) proximal to the DDIT3 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

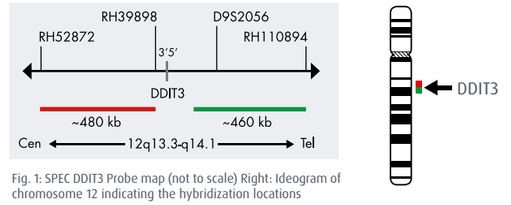
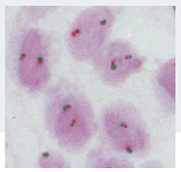
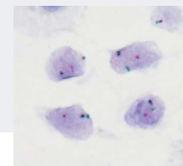


Fig. 1: SPEC DDIT3 Probe map (not to scale) Right: Ideogram of chromosome 12 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the DDIT3 gene region, two red/green fusion signals appear.
Aberrant situation: One DDIT3 gene region affected by a translocation is indicated by one separate distinct dot-shaped green signal and one separate distinct dot-shaped red signal.



Hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	12	CE/IVD	10 (100 µl)	**C-3047-100**

ZytoDot® 2C SPEC CDK4/CEN 12 Probe

Intended Purpose
The Zyto*Dot* 2C SPEC CDK4/CEN 12 Probe (PD42) is intended to be used for the qualitative detection of amplifications involving the human CDK4 gene as well as the detection of chromosome 12 alpha satellites in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the Zyto*Dot* 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Dot* 2C SPEC CDK4/CEN 12 Probe is composed of:
- Digoxigenin-labeled polynucleotides (~1,1 ng/µl), which target sequences mapping in 12q13.3-q14.1* (chr12:58,004,553-58,313,271) harboring the CDK4 region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~1,1 ng/µl), which target sequences mapping in 12p11.1-q11 specific for the alpha satellite centromeric region D12Z3 of chromosome 12.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

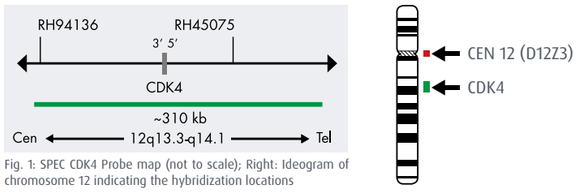
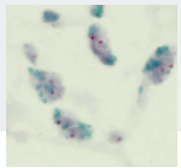


Fig. 1: SPEC CDK4 Probe map (not to scale); Right: Ideogram of chromosome 12 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the CDK4 gene region, two distinct dot-shaped green and two distinct dot-shaped red signals appear.
Aberrant situation: In cells with an amplification of the CDK4 gene region, an increased number of green signals or green signal clusters will be observed.



Example of an aberrant signal pattern: Liposarcoma tissue section with CDK4 amplification as indicated by large green clusters.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	12	CE/IVD	40 (400 µl)	**C-3062-400**

ZytoDot® SPEC MDM2 Probe

Intended Purpose
The Zyto*Dot* SPEC MDM2 Probe (PD9) is intended to be used for the qualitative detection of amplifications involving the human MDM2 gene in formalin-fixed, paraffin-embedded specimens, such as atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDLPS) and dedifferentiated liposarcoma (DDLPS), by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the Zyto*Dot* CISH Implementation Kit (Prod. No. C-3018-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of ALT/WDLPS and DDLPS and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Dot* MDM2 Probe is composed of:
- Digoxigenin-labeled polynucleotides (~1,8 ng/µl), which target sequences mapping in 12q15* (chr12:69,190,708-69,430.185) (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

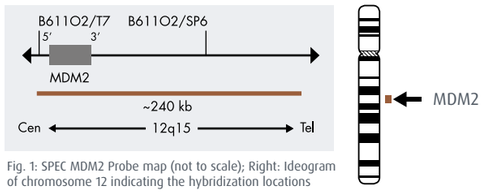
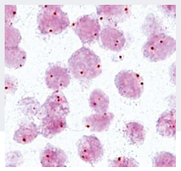


Fig. 1: SPEC MDM2 Probe map (not to scale); Right: Ideogram of chromosome 12 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the MDM2 gene region, two distinct dot-shaped brown signals appear.
Aberrant situation: In cells with an amplification of the MDM2 gene region or aneuploidy of chromosome 12, an increased number of the brown signal or brown signal clusters will be observed.



Normal nuclei each with two MDM2 signals.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG	12	CE/IVD	40 (400 µl)	**C-3012-400**

ZytoDot® 2C SPEC MDM2/CEN 12 Probe

Intended Purpose
The Zyto*Dot* 2C SPEC MDM2/CEN 12 Probe (PD29) is intended to be used for the qualitative detection of amplifications involving the human MDM2 gene as well as the detection of chromosome 12 alpha satellites in formalin-fixed, paraffin-embedded specimens, such as atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDLPS) and dedifferentiated liposarcoma (DDLPS), by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the Zyto*Dot* 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of ALT/WDLPS and DDLPS and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Dot* 2C SPEC MDM2/CEN 12 Probe is composed of:
- Digoxigenin-labeled polynucleotides (~1.1 ng/µl), which target sequences mapping in 12q15* (chr12:69,190,708-69,430.185) harboring the MDM2 region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~1.1 ng/µl), which target sequences mapping in 12p11.1-q11 specific for the alpha satellite centromeric region D12Z3 of chromosome 12.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

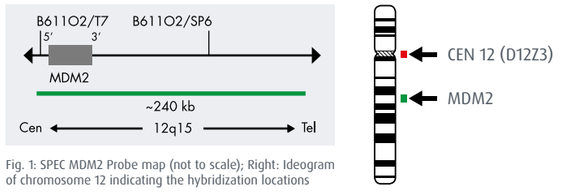
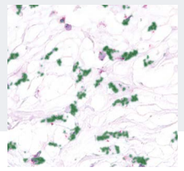


Fig. 1: SPEC MDM2 Probe map (not to scale); Right: Ideogram of chromosome 12 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the MDM2 gene region, two distinct dot-shaped green and two distinct dot-shaped red signals appear.
Aberrant situation: In cells with an amplification of the MDM2 gene region, an increased number of green signals or green signal clusters will be observed.



Liposarcoma tissue section with MDM2 amplification as indicated by large green clusters.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	12	CE/IVD	10 (100 µl)	**C-3049-100**
			40 (400 µl)	**C-3049-400**

ZytoDot® 2C SPEC IGH Break Apart Probe

Intended Purpose
The Zyto*Dot* 2C SPEC IGH Break Apart Probe (PD51) is intended to be used for the qualitative detection of translocations involving the human IGH locus at 14q32.33 in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the Zyto*Dot* 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Dot* 2C SPEC IGH Break Apart Probe is composed of:
- Digoxigenin-labeled polynucleotides (~0.50 ng/µl), which target sequences mapping in 14q32.33* (chr14:106,690,778-106,883,535) distal to the IGH breakpoint region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~0,75 ng/µl), which target sequences mapping in 14q32.33* (chr14:105,462,169-105,909,611) proximal to the IGH breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

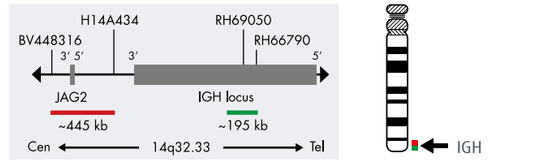
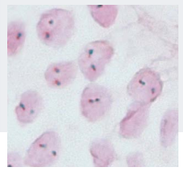
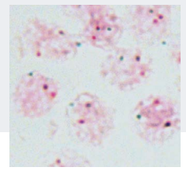


Fig. 1: SPEC IGH Probe map (not to scale); Right: Ideogram of chromosome 14 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the IGH gene region, two red/green fusion signals appear.
Aberrant situation: One IGH gene region affected by a translocation is indicated by one separate distinct dot-shaped green signal and one separate distinct dot-shaped red signal.



Hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.



Example of an aberrant signal pattern: Burkitt lymphoma tissue section with translocation affecting the 14q32.33 locus as indicated by one red/green fusion (non-rearranged) signal, one red signal, and one separate green signal.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	14	CE/IVD	10 (100 µl)	**C-3071-100**

ZytoDot® 2C SPEC USP6 Break Apart Probe

Intended Purpose
The ZytoDot 2C SPEC USP6 Break Apart Probe (PD56) is intended to be used for the qualitative detection of translocations involving the human USP6 gene at 17p13.2 in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the ZytoDot 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoDot 2C SPEC USP6 Break Apart Probe is composed of:
- Digoxigenin-labeled polynucleotides (~0.50 ng/µl), which target sequences mapping in 17p13.2* (chr17:4,825,753-5,017,582) distal to the USP6 breakpoint region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~0,75 ng/µl), which target sequences mapping in 17p13.2* (chr17:5,087,046-5,361,104) proximal to the USP6 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

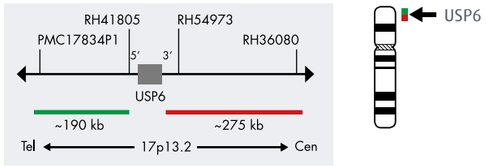
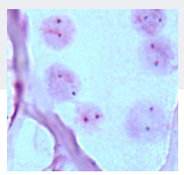


Fig. 1: SPEC USP6 Probe map (not to scale); Right: Ideogram of chromosome 17 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the USP6 gene region, two red/green fusion signals appear.
Aberrant situation: One USP6 gene region affected by a translocation is indicated by one separate green signal and one separate red signal.



Hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	17	CE/IVD	10 (100 µl)	**C-3077-100**

ZytoDot® 2C SPEC ERBB2 Probe

Intended Purpose
The ZytoDot SPEC ERBB2 Probe (PD1) is intended to be used for the qualitative detection of amplifications involving the human ERBB2 gene in formalin-fixed, paraffin-embedded specimens, such as breast cancer, by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the ZytoDot CISH Implementation Kit (Prod. No. C-3018-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of breast cancer and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoDot ERBB2 Probe is composed of:
- Digoxigenin-labeled polynucleotides (~1,8 ng/µl), which target sequences mapping in 17q12* (chr17:37,725,661-37,973,541) harboring the ERBB2 gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

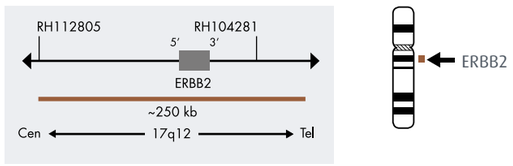
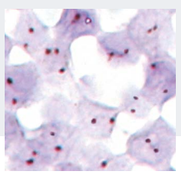
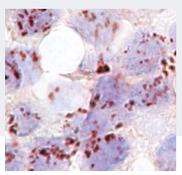


Fig. 1: SPEC ERBB2 Probe map (not to scale); Right: Ideogram of chromosome 17 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the ERBB2 gene region, two distinct dot-shaped brown signals appear.
Aberrant situation: In cells with an amplification of the ERBB2 gene region or polysomy of chromosome 17, an increased number of the brown signal or brown signal clusters will be observed.



Normal nuclei each with two ERBB2 signals.



Breast cancer tissue section with ERBB2 amplification.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG	17	CE/IVD	40 (400 µl)	**C-3001-400**

The product is also available as a kit.

ZytoDot® SPEC ERBB2 Probe Kit	Tests	Order No.
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	40	**C-3003-40**

ZytoDot® 2C SPEC ERBB2/CEN 17 Probe

Intended Purpose
The ZytoDot 2C SPEC ERBB2/CEN 17 Probe (PD12) is intended to be used for the qualitative detection of amplifications involving the human ERBB2 gene as well as the detection of chromosome 17 alpha satellites in formalin-fixed, paraffin-embedded specimens, such as breast cancer, by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the ZytoDot 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of breast cancer and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoDot 2C SPEC ERBB2/CEN 17 Probe is composed of:
- Digoxigenin-labeled polynucleotides (~1.1 ng/µl), which target sequences mapping in 17q12* (chr17:37,725,661-37,973,541) harboring the ERBB2 region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~1.1 ng/µl), which target sequences mapping in 17p11.1-q11.1 specific for the alpha satellite centromeric region D17Z1 of chromosome 17.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

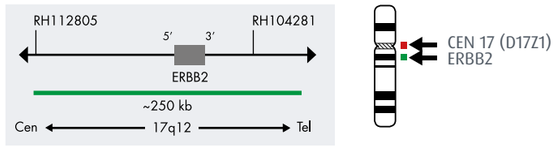
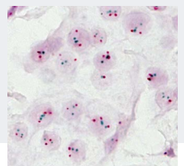
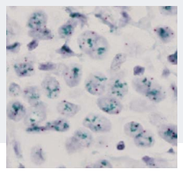


Fig. 1: SPEC ERBB2 Probe map (not to scale); Right: Ideogram of chromosome 17 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without an amplification involving the ERBB2 gene region, two distinct dot-shaped green and two distinct dot-shaped red signals appear.
Aberrant situation: In cells with an amplification of the ERBB2 gene region, an increased number of green signals or green signal clusters will be observed.



Hybridized to normal interphase cells as indicated by two red and two green signals per nucleus.



Breast cancer tissue section with ERBB2 amplification as indicated by multiple green signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	17	CE/IVD	10 (100 µl)	**C-3032-100**
			40 (400 µl)	**C-3032-400**

The product is also available as a kit in two different sizes.

ZytoDot® 2C SPEC ERBB2/CEN 17 Probe Kit	Tests	Order No.
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	10	**C-3022-10**
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	40	**C-3022-40**

ZytoDot® 2C SPEC SS18 Break Apart Probe

Intended Purpose
The ZytoDot 2C SPEC SS18 Break Apart Probe (PD26) is intended to be used for the qualitative detection of translocations involving the human SS18 gene at 18q11.2 in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the ZytoDot 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The ZytoDot 2C SPEC SS18 Break Apart Probe is composed of:
- Digoxigenin-labeled polynucleotides (~0.5 ng/µl), which target sequences mapping in 18q11.2* (chr18:23,109,942-23,262,464) proximal to the SS18 breakpoint region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~0,75 ng/µl), which target sequences mapping in 18q11.2* (chr18:23,772,255-24,137,169) distal to the SS18 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

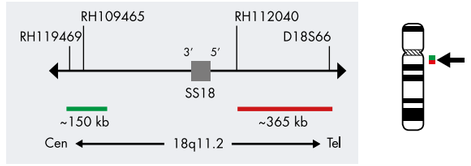
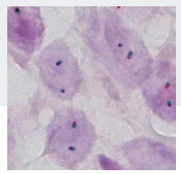
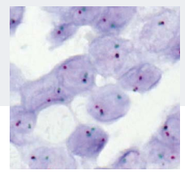


Fig. 1: SPEC SS18 Probe map (not to scale); Right: Ideogram of chromosome 18 indicating the hybridization locations

Results
Normal situation: In interphases of normal cells or cells without a translocation involving the SS18 gene region, two red/green fusion signals appear.
Aberrant situation: One SS18 gene region affected by a translocation is indicated by one separate distinct dot-shaped green signal and one separate distinct dot-shaped red signal.



Hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.



Example of an aberrant signal pattern: 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.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	18	CE/IVD	10 (100 µl)	**C-3046-100**

ZytoDot® 2C SPEC BCL2 Break Apart Probe

Intended Purpose

The ZytoDot 2C SPEC BCL2 Break Apart Probe (PD53) is intended to be used for the qualitative detection of translocations involving the human BCL2 gene at 18q21.33 in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the ZytoDot 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The ZytoDot 2C SPEC BCL2 Break Apart Probe is composed of:

- Digoxigenin-labeled polynucleotides (~0.50 ng/µl), which target sequences mapping in 18q21.33* (chr18:60,415,418-60.589,273) proximal to the BCL2 breakpoint region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~0,75 ng/µl), which target sequences mapping in 18q21.33* (chr18:60,994,528-61,507,691) distal to the BCL2 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

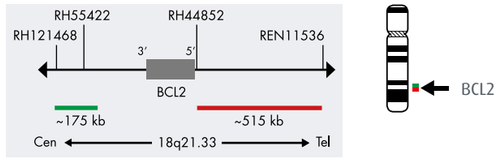
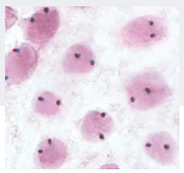


Fig. 1: SPEC BCL2 Probe map (not to scale); Right: Ideogram of chromosome 18 indicating the hybridization locations

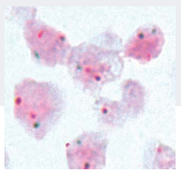
Results

Normal situation: In interphases of normal cells or cells without a translocation involving the BCL2 gene region, two red/green fusion signals appear.

Aberrant situation: One BCL2 gene region affected by a translocation is indicated by one separate distinct dot-shaped green signal and one separate distinct dot-shaped red signal.



Hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.



Example of an aberrant signal pattern: Lymphoma tissue section with translocation affecting the 18q21.33 locus as indicated by one red/green fusion (non-rearranged) signal, one red signal, and one separate green signal.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	18	CE/IVD	10 (100 µl)	**C-3073-100**

ZytoDot® 2C SPEC EWSR1 Break Apart Probe

Intended Purpose

The ZytoDot 2C SPEC EWSR1 Break Apart Probe (PD24) is intended to be used for the qualitative detection of translocations involving the human EWSR1 gene at 22q12.2 in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the ZytoDot 2C CISH Implementation Kit (Prod. No. C-3044-10/-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The ZytoDot 2C SPEC EWSR1 Break Apart Probe is composed of:

- Digoxigenin-labeled polynucleotides (~0.50 ng/µl), which target sequences mapping in 22q12.2* (chr22:29,779,841-30,057,928) distal to the EWSR1 breakpoint region (see Fig. 1).
- Dinitrophenyl-labeled polynucleotides (~0,75 ng/µl), which target sequences mapping in 22q12.1-22q12.2* (chr22:29,413,831-29,673,440) proximal to the EWSR1 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

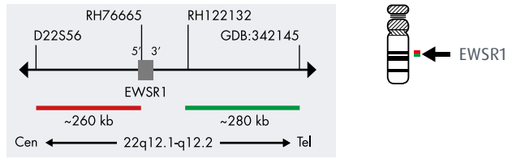
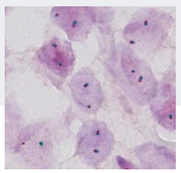


Fig. 1: SPEC EWSR1 Probe map (not to scale); Right: Ideogram of chromosome 22 indicating the hybridization locations

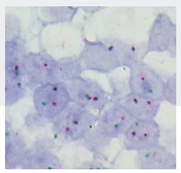
Results

Normal situation: In interphases of normal cells or cells without a translocation involving the EWSR1 gene region, two red/green fusion signals appear.

Aberrant situation: One EWSR1 gene region affected by a translocation is indicated by one separate distinct dot-shaped green signal and one separate distinct dot-shaped red signal.



Hybridized to normal interphase cells as indicated by two red/green fusion signals per nucleus.



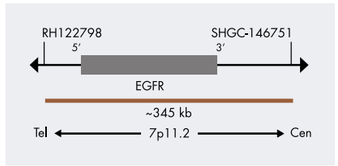
Example of an aberrant signal pattern: Ewing sarcoma tissue section with translocation affecting the 22q12.1-q12.2 locus as indicated by one non-rearranged red/green fusion signal, one red signal, and one separate green signal.

Labels	Chromosome	Reg. Status	Tests	Order No.
DIG/DNP	22	CE/IVD	10 (100 µl)	**C-3043-100**

ZytoDot® RUO Probes

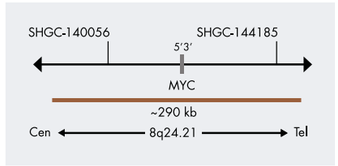
Product Name	Chr.band	Reg. Status	Labels	Tests	Order No.
ZytoDot SPEC EGFR Probe	7p11.2	RUO	DIG	40 (400 µl)	**C-3007-400**
ZytoDot SPEC MYC Probe	8q24.21		DIG	40 (400 µl)	**C-3013-400**
ZytoDot 2C SPEC PTEN/CEN 10 Probe	10q23.3		DIG/DNP	40 (400 µl)	**C-3053-400**
ZytoDot 2C SPEC FOXO1 Break Apart Probe	13q14.1		DIG/DNP	10 (100 µl)	**C-3065-100**
ZytoDot 2C SPEC MALT1 Break Apart Probe	18q21.3		DIG/DNP	10 (100 µl)	**C-3072-100**

C-3007-400



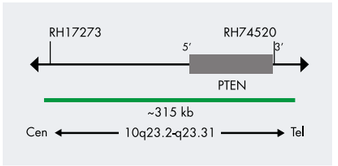
SPEC EGFR Probe map (not to scale)

C-3013-400



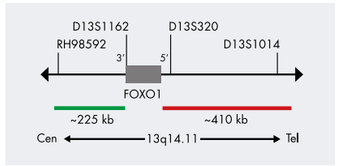
SPEC MYC Probe map (not to scale)

C-3053-400



SPEC PTEN Probe map (not to scale)

C-3065-100



SPEC FOXO1 Probe map (not to scale)

C-3072-100

SPEC MALT1 Probe map (not to scale)

ZytoDot® Probes for Chromosome Enumeration - RUO

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

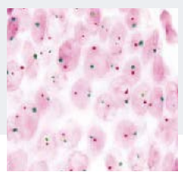
For most chromosomes, direct labeled ZytoDot® CEN™ Probes hybridizing to highly repetitive human satellite DNA sequences mainly located at the centromeric regions of chromosomes are applicable.

Results

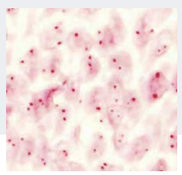
In a normal interphase nucleus, two signals are expected using Chromosome Enumeration Probes specific for autosomes.

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.



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.

RUO Probes

Product Name	Alpha/Class. Sat.	Chr.band	Reg. Status	Labels	Tests	Order No.
ZytoDot CEN 7 Probe	D7Z1	7p11.1-q11.1	RUO	DIG	40 (400 µl)	**C-3008-400**
ZytoDot CEN 8 Probe	D8Z2	8p11.1-q11.1		DIG	40 (400 µl)	**C-3016-400**
ZytoDot CEN X Probe	DXZ1	Xp11.1-q11.1		DIG	40 (400 µl)	**C-3025-400**
ZytoDot CEN Yq12 Probe	III DYZ1	Yq12		DIG	40 (400 µl)	**C-3020-400**
ZytoDot 2C CEN X/Y Probe	DXZ1/DYZ3	Xp11.1-q11.1/Yp11.1-q11.1		DNP/DIG	40 (400 µl)	**C-3048-400**

Accessories

ZytoDot® Implementation Kits

For the detection of ZytoDot® probes

Product	Manufacturer	Tests	Reg. Status	Order No.
ZytoDot CISH Implementation Kit **For the detection of Digoxigenin-labeled ZytoDot Probes** Incl.: Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 ml; PBS/Tween, ausreichend für 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	ZytoVision GmbH	40	CE/IVD	**C-3018-40**
ZytoDot 2C CISH Implementation Kit **For the detection of Digoxigenin/Dinitrophenyl-labeled ZytoDot 2C Probes** 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, 0.2 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	ZytoVision GmbH	10	CE/IVD	**C-3044-10**
ZytoDot 2C CISH Implementation Kit **For the detection of Digoxigenin/Dinitrophenyl-labeled ZytoDot 2C Probes** 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, 0.5 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	ZytoVision GmbH	40	CE/IVD	**C-3044-40**

ZytoDot® Pretreatment Reagents

Product	Manufacturer	Amount	Reg. Status	Order No.
Pepsin Solution	ZytoVision GmbH	4 ml	CE/IVD	**ES-0001-4**
Pepsin Solution	ZytoVision GmbH	50 ml	CE/IVD	**ES-0001-50**
Pepsin Solution	ZytoVision GmbH	1000 ml	CE/IVD	**ES-0001-1000**
Heat Pretreatment Solution EDTA	ZytoVision GmbH	500 ml	CE/IVD	**PT-0002-500**

ZytoDot® Wash Buffers & Ancillary Reagents

Product	Manufacturer	Amount	Reg. Status	Order No.
Mouse-anti-DIG	ZytoVision GmbH	4 ml	CE/IVD	**AB-0001-4**
Anti-Mouse-HRP-Polymer	ZytoVision GmbH	4 ml	CE/IVD	**AB-0002-4**
HRP/AP-Polymer-Mix	ZytoVision GmbH	4 ml	CE/IVD	**AB-0013-4**
Anti-DIG/DNP-Mix	ZytoVision GmbH	4 ml	CE/IVD	**AB-0014-4**
Blocking Solution	ZytoVision GmbH	4 ml	CE/IVD	**BS-0001-4**
DAB Solution Set Incl.: DAB Solution A, 0.3 ml; DAB Solution B, 10 ml; good for 10 ml DAB Solution	ZytoVision GmbH	-	CE/IVD	**C-3015-100**
ZytoDot AP-Red Solution Set Incl.: AP-Red Solution A, 0.5 ml; AP-Red Solution B, 15 ml; good for 15 ml AP-Red Solution	ZytoVision GmbH	-	CE/IVD	**C-3038-100**
ZytoDot HRP-Green Solution Set Incl.: HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; good for 15 ml HRP-Green Solution	ZytoVision GmbH	-	CE/IVD	**C-3039-100**
Mayer's Hematoxylin Solution	ZytoVision GmbH	20 ml	CE/IVD	**CS-0001-20**
Nuclear Blue Solution	ZytoVision GmbH	20 ml	CE/IVD	**CS-0002-20**
Mounting Solution (alcoholic)	ZytoVision GmbH	4 ml	CE/IVD	**MT-0004-4**
Wash Buffer SSC	ZytoVision GmbH	560 ml	CE/IVD	**WB-0001-560**
PBS/Tween	ZytoVision GmbH	good for 1000 ml	CE/IVD	**WB-0004-1000**
20x Wash Buffer TBS	ZytoVision GmbH	50 ml	CE/IVD	**WB-0005-50**

RUO ZytoDot® Accessories

Product	Manufacturer	Amount	Reg. Status	Order No.
ERBB2 Control Slide Set	ZytoVision GmbH	2 pcs.	RUO	**E-4007-2**

ZytoFast®

The **ZytoFast® 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 (FFPE) specimens.

ZytoVision GmbH

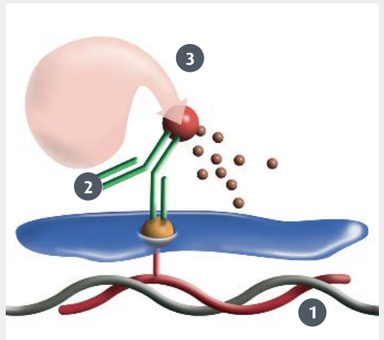
ZytoFast®
Outstandingly fast CISH

- Optimized protocols and faster tissue penetration due to short oligonucleotide probes of the ZytoFast® system, make the ZytoFast® CISH procedure outstandingly fast.
- Results can be achieved within just 5 hours, hands-on time is about 3 hours!

Advantages of CISH

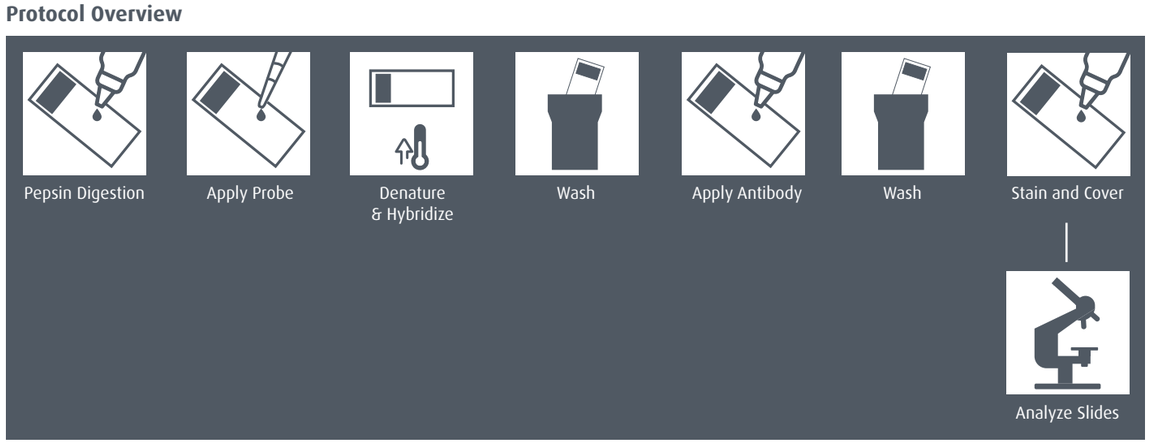
- ✚ Simultaneous observation of tissue morphology and CISH signals
- ✚ No risk of false positives due to mispriming or contamination as with PCR
- ✚ Easy method comparable to IHC
- ✚ No costly equipment needed
- ✚ Ability to test archival specimens

Method



The ZytoFast® 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

The **ZytoFast® PLUS products** are designed for outstandingly fast detection and discrimination of human pathogen viruses, e.g. HPV and EBV 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 (FFPE) specimens.
The signal intensity of ZytoFast® probes is increased even more when using the ZytoFast® PLUS Implementation Kits.

ISH

ZytoVision GmbH

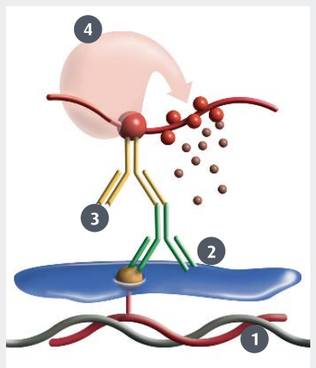
ZytoFast® PLUS
Outstandingly fast and sensitive CISH

- 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

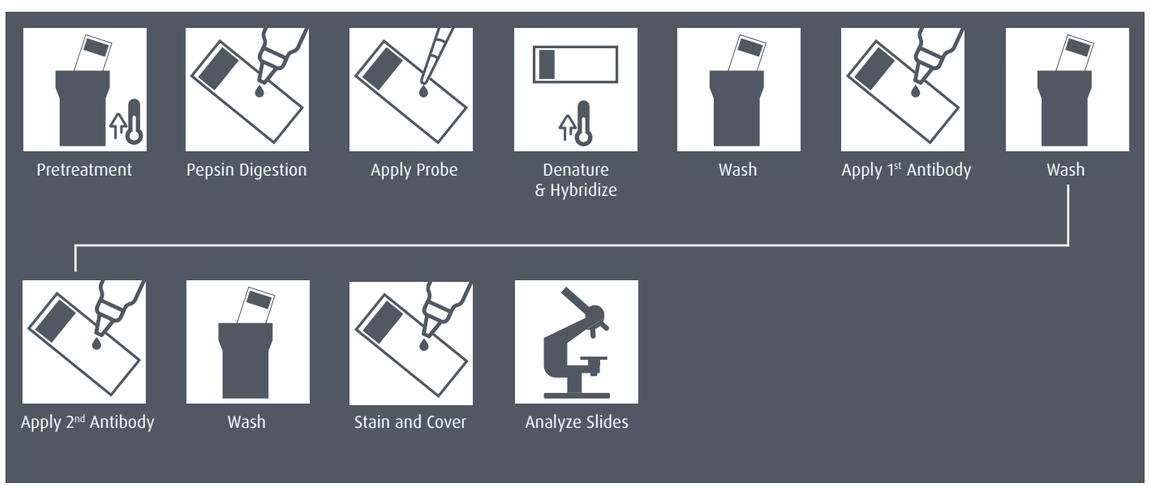
- Several ZytoFast® PLUS CISH Implementation Kits using different enzyme/substrate combinations can be combined with any separately available Digoxigenin-labeled ZytoFast® probe to meet your preferences concerning the detection chemistry and counterstaining.
- Each ZytoFast® PLUS CISH Implementation Kit includes a detailed protocol and all necessary reagents for versatile use in DNA as well as RNA *in situ* hybridizations.

Method



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. DAB, leads to the formation of strong color precipitates that can be visualized by light microscopy.

Protocol Overview



Virus Index

Virus	Product	Label	Amount	Reg. Status	Order No.	Page
HPV	Zyto*Fast* HPV type 6/11 Probe	DIG	400 µl	CE/IVD	**T-1055-400**	**161**
	Zyto*Fast* HPV type 16/18 Probe	DIG	400 µl	CE/IVD	**T-1056-400**	**161**
	Zyto*Fast* HPV type 31/33 Probe	DIG	400 µl	CE/IVD	**T-1057-400**	**161**
	Zyto*Fast* 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)	DIG	400 µl	CE/IVD	**T-1140-400**	**162**
	Zyto*Fast* HPV Screening Probe (specific for HPV type 6/11/16/18/31/33/35/39/45/51/52/56/58/59/66/68/82)	DIG	400 µl	CE/IVD	**T-1144-400**	**162**
EBV	Zyto*Fast* EBV Probe	DIG	400 µl	CE/IVD	**T-1114-400**	**162**
CMV	Zyto*Fast* CMV Probe	DIG	400 µl	RUO	**T-1113-400**	**163**

mRNA Index

mRNA	Product	Label	Amount	Reg. Status	Order No.	Page
Ig-kappa	Zyto*Fast* human Ig-kappa Probe	DIG	400 µl	CE/IVD	**T-1115-400**	**164**
	Zyto*Fast* human Ig-kappa/Ig-lambda Probe	DIG/Biotin	400 µl	CE/IVD	**T-1017-400**	**164**
	Zyto*Fast* human Ig-kappa/Ig-lambda CISH Kit	DIG/Biotin	40 tests	CE/IVD	**T-1005-40**	**164**
	Zyto*Fast* human Ig-kappa/Ig-lambda Permanent CISH Kit	DIG/Biotin	40 tests	CE/IVD	**T-1105-40**	**164**
Ig-lambda	Zyto*Fast* human Ig-lambda Probe	DIG	400 µl	CE/IVD	**T-1116-400**	**164**
	Zyto*Fast* human Ig-kappa/Ig-lambda Probe	DIG/Biotin	400 µl	CE/IVD	**T-1017-400**	**164**
	Zyto*Fast* human Ig-kappa/Ig-lambda CISH Kit	DIG/Biotin	40 tests	CE/IVD	**T-1005-40**	**164**
	Zyto*Fast* human Ig-kappa/Ig-lambda Permanent CISH Kit	DIG/Biotin	40 tests	CE/IVD	**T-1105-40**	**164**

Zyto*Fast*® HPV-CISH System

Intended Purpose
The Zyto*Fast* HPV type 6/11 Probe (PF25) is intended to be used for the qualitative detection of human papillomavirus (HPV) type 6/11 DNA in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH).

The Zyto*Fast* HPV type 16/18 Probe (PF26) is intended to be used for the qualitative detection of human papillomavirus (HPV) type 16/18 DNA in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH).

The Zyto*Fast* HPV type 31/33 Probe (PF27) is intended to be used for the qualitative detection of human papillomavirus (HPV) type 31/33 DNA in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH).

The probes are intended to be used in combination with the Zyto*Fast* PLUS CISH Implementation Kit HRP-DAB (Prod. No. T-1063-40).

The products are intended for professional use only. All tests using these products should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probes are intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Fast* HPV type 6/11 Probe is composed of:
- Digoxigenin-labeled oligonucleotides (~0.6 ng/µl) specific for HPV type 6/11, which target DNA sequences encoding for HPV 6/11 proteins E6, E7, and/or L1.
- The probe also targets the respective RNA sequences of E6, E7, and/or L1 proteins, which are expressed during some stages of infection.
- Formamide based hybridization buffer

The Zyto*Fast* HPV type 16/18 Probe is composed of:
- Digoxigenin-labeled oligonucleotides (~0.6 ng/µl) specific for HPV type 16/18, which target DNA sequences encoding for the HPV 16/18 proteins E6, E7, and/or L1.
- The probe also targets the respective RNA sequences of E6, E7, and/or L1 proteins, which are expressed during some stages of infection.
- Formamide based hybridization buffer

The Zyto*Fast* HPV type 31/33 Probe is composed of:
- Digoxigenin-labeled oligonucleotides (~0.6 ng/µl) specific for HPV type 31/33, which target DNA sequences encoding for HPV 31/33 proteins E6, E7, and/or L1.
- The probe also targets the respective RNA sequences of E6, E7, and/or L1 proteins, which are expressed during some stages of infection.
- Formamide based hybridization buffer

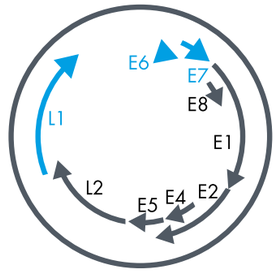
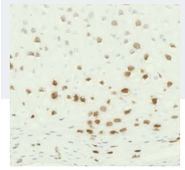


Fig. 1: Schematic representation of the HPV genome with E and L open reading frames. Genomic regions targeted by Zyto*Fast* HPV specific oligonucleotides are indicated in blue.

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. Colored precipitates, which can be clearly distinguished from the background, will be dark brown when using DAB as substrate for the detection.



Example of an HPV positive signal pattern: HPV infected cervix tissue hybridized with the Zyto*Fast* HPV type 6/11 Probe, detected with the Zyto*Fast* PLUS CISH Implementation Kit HRP-DAB.

Product Name	Labels	Reg. Status	Tests	Order No.
Zyto*Fast* HPV type 6/11 Probe	DIG	CE/IVD	40 (400 µl)	**T-1055-400**
Zyto*Fast* HPV type 16/18 Probe	DIG	CE/IVD	40 (400 µl)	**T-1056-400**
Zyto*Fast* HPV type 31/33 Probe	DIG	CE/IVD	40 (400 µl)	**T-1057-400**

ZytoFast® HPV High-Risk (HR) Types Probe

Intended Purpose
The Zyto*Fast* HPV High-Risk (HR) Types Probe (PF46) is intended to be used for the qualitative detection of human papillomavirus (HPV) type 16/18/31/33/35/39/45/51/52/56/58/59/66/68/82 DNA in formalin-fixed, paraffin-embedded specimens, such as cervical carcinoma and oropharyngeal squamous cell cancer (OSCC), by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the Zyto*Fast* PLUS CISH Implementation Kit HRP-DAB (Prod. No. T-1063-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of cervical carcinoma and OSCC and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Fast* HPV High-Risk (HR) Types Probe is composed of:
- Digoxigenin-labeled oligonucleotides (~ 2.2 ng/µl) specific for HPV type 16/18/31/33/35/39/45/51/52/56/58/59/66/68/82, which target DNA sequences encoding for HPV 16/18/31/33/ 35/39/45/51/52/56/58/59/66/68/82 proteins E6, E7, and/or L1.
- The probe also targets the respective RNA sequences of E6, E7, and/or L1 proteins, which are expressed during some stages of infection.
- Formamide based hybridization buffer

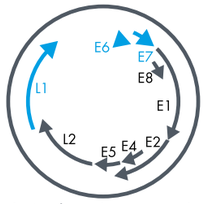
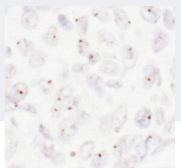


Fig. 1: Schematic representation of the HPV genome with E and L open reading frames. Genomic regions targeted by Zyto*Fast* HPV specific oligonucleotides are indicated in blue.

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. Colored precipitates, which can be clearly distinguished from the background, will be dark brown when using DAB as substrate for the detection.



HPV infected cervix tissue hybridized with the Zyto*Fast* HPV High-Risk (HR) Types Probe, detected with the Zyto*Fast* PLUS CISH Implementation Kit HRP-DAB.

Labels	Reg. Status	Tests	Order No.
DIG	CE/IVD	40 (400 µl)	**T-1140-400**

ZytoFast® HPV Screening Probe

Intended Purpose
The Zyto*Fast* HPV Screening Probe 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
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Cubie HA & Norval M (1988) J Virol Methods 20: 239-49.
Faulkner-Jones BE, *et al.* (1993) J Virol Methods 41: 277-96.
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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
The Zyto*Fast* HPV Screening Probe is composed of:
- Digoxigenin-labeled oligonucleotides (~2.6 ng/µl) specific for HPV type 6/11/16/18/31/33/35/39/45/51/52/56/58/59/66/68/82, which target DNA sequences encoding for HPV 6/11/16/18/31/33/35/39/45/51/52/56/58/59/66/68/82 proteins E6, E7, and/or L1.
- The probe also targets the respective RNA sequences of E6, E7, and/or L1 proteins, which are expressed during some stages of infection.
- Formamide based hybridization buffer

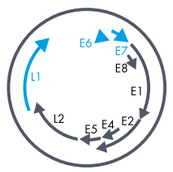
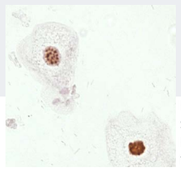


Fig. 1: Schematic representation of the HPV genome with E and L open reading frames. Genomic regions targeted by Zyto*Fast* HPV specific oligonucleotides are indicated in blue.

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 brown when using DAB as substrate for the detection.



HPV infected cells with signals from integrated and episomal HPV hybridized with the Zyto*Fast* HPV Screening Probe, detected with the Zyto*Fast* PLUS CISH Implementation Kit HRP-DAB.

Labels	Reg. Status	Tests	Order No.
DIG	CE/IVD	40 (400 µl)	**T-1144-400**

ZytoFast® EBV Probe

Intended Purpose
The Zyto*Fast* EBV Probe (PF29) is intended to be used for the qualitative detection of human Epstein-Barr virus (EBV) EBER RNA in formalin-fixed, paraffin-embedded specimens, such as diffuse large B-cell lymphomas (DLBCL) or Hodgkin lymphomas, by chromogenic *in situ* hybridization (CISH). The probe is intended to be used in combination with the Zyto*Fast* PLUS CISH Implementation Kit HRP-DAB (Prod. No. T-1063-40).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The probe is intended to be used as an aid to the differential diagnosis of DLBCL or Hodgkin lymphomas and therapeutic action should not be initiated on the basis of the test result alone.

Probe Description
The Zyto*Fast* EBV Probe is composed of:
- Digoxigenin-labeled oligonucleotides (~ 0.2 ng/µl), which target mRNA sequences encoding EBER-1 and EBER-2 regions.

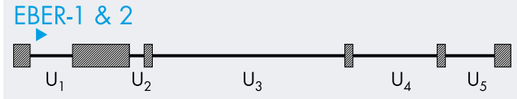
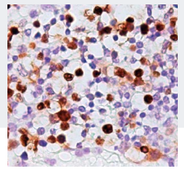


Fig. 1: Schematic representation of the EBV genome with the EBER-1 and EBER-2 encoding region indicated in blue.
U1-U5 indicate unique nucleotide sequences, hatched boxes represent terminal and internal repeats.

Results
A positive reactivity for Epstein-Barr-virus (EBV) EBER RNA in the target cells is indicated by a distinctly stained nucleus. Colored precipitates, which can be clearly distinguished from the background, will be dark brown when using DAB for detection.



EBV infected tonsil tissue hybridized with Zyto*Fast* EBV Probe, detected with Zyto*Fast* PLUS CISH Implementation Kit HRP-DAB.

Labels	Reg. Status	Tests	Order No.
DIG	CE/IVD	40 (400 µl)	**T-1114-400**

ZytoFast® CMV Probe

Intended Purpose
The Zyto*Fast* CMV Probe (PF28) is intended to be used for the qualitative detection of human cytomegalovirus (CMV (a.k.a. human herpesvirus-5, HHV-5)) DNA in formalin-fixed, paraffin-embedded specimens by chromogenic *in situ* hybridization (CISH).

The Zyto*Fast* CMV Probe is intended to be used in combination with one of the Zyto*Fast* PLUS CISH Implementation Kits, either the Zyto*Fast* PLUS CISH Implementation Kit AP-NBT/BCIP (Prod. No. T-1061-40), the Zyto*Fast* PLUS CISH Implementation Kit HRP-DAB (Prod. No. T-1063-40), or the Zyto*Fast* PLUS CISH Implementation Kit AP-Permanent Red (Prod. No. T-1151-40).

Probe Description
The Zyto*Fast* CMV Probe is composed of:
- Digoxigenin-labeled oligonucleotides (~ 0.2 ng/µl), which target DNA sequences encoding the β2.7 gene, the most abundantly transcripted early CMV gene.
- Formamide based hybridization buffer

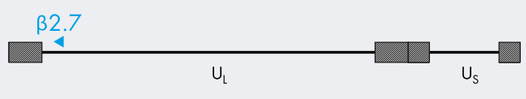
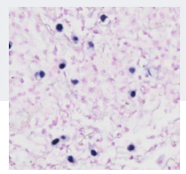


Fig. 1: Schematic representation of the CMV genome with the b2.7 encoding region indicated in blue. UL and US indicate unique nucleotide sequences, hatched boxes represent terminal and internal repeats.

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, or strong red when using Permanent Red.



CISH analysis of paraffin-embedded adrenal gland tissue using the Zyto*Fast* CMV Probe, detected with Zyto*Fast* PLUS CISH Implementation Kit AP-NBT/BCIP.

Labels	Reg. Status	Tests	Order No.
DIG	RUO	40 (400 µl)	**T-1113-400**

ZytoFast® Ig-kappa/Ig-lambda CISH System

Intended Purpose
The Zyto*Fast* Ig-kappa/Ig-lambda-CISH System is intended to be used for the qualitative detection of human Ig-kappa (κ) and Ig-lambda (λ) light chain mRNA in formalin-fixed, paraffin-embedded specimens, such as multiple myeloma, by chromogenic *in situ* hybridization (CISH).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The product is intended to be used as an aid to the differential diagnosis of multiple myeloma and therapeutic measures should not be initiated based on the test result alone.

Probe Description
The Zyto*Fast* human Ig-kappa Probe (PF30) is composed of:
- Digoxigenin-labeled oligonucleotides (~ 0.2 ng/µl), which target mRNA sequences encoding Ig-kappa light chain constant regions.

The Zyto*Fast* human Ig-lambda Probe (PF31) is composed of:
- Digoxigenin-labeled oligonucleotides (~ 0.2 ng/µl), which target mRNA sequences encoding Ig-lambda light chain constant regions.

The Zyto*Fast* human Ig-kappa/Ig-lambda Probe (PF22) is composed of:
- Digoxigenin-labeled oligonucleotides (~ 1 ng/µl), which target mRNA sequences encoding Ig-kappa light chain constant regions.
- Biotin-labeled oligonucleotides (~ 1ng/µl), which target mRNA sequences encoding Ig-lambda light chain constant regions.

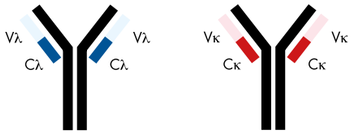


Fig. 1: Basic immunoglobulin structure indicating the heavy chains (black), l (blue) and k (red) lights chains. The light chain constant regions (C) whose encoding mRNA sequences are targeted by Zyto*Fast* lg-lambda and lg-kappa probes are indicated in dark blue and red respectively, the variable regions (V) in light blue and red.

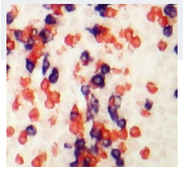
Results
A positive reactivity in the target cells is indicated by cytoplasmic staining. Depending on the detection chemistry that is used, colored precipitates, which can be clearly distinguished from the background, will be dark violet-blue when using NBT/BCIP as substrate, strong red when using AEC, dark brown when using DAB, green when using HRP-Green, or strong red when using Permanent Red.

Using the Zyto*Fast* 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.

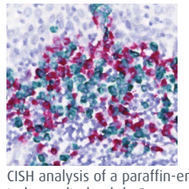
Using the Zyto*Fast* human Ig-lambda Probe, B-cells expressing antibodies with λ light chains will result in cytoplasmic staining whereas IGK expressing B-cells are not stained.

Using the Zyto*Fast* 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.

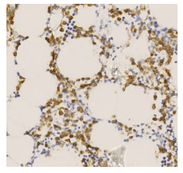
Using the Zyto*Fast* human Ig-kappa/Ig-lambda Permanent CISH Kit, B-cells expressing antibodies with κ light chains will result in a green cytoplasmic staining and simultaneously IGL expressing B-cells will result in permanent red cytoplasmic staining.



CISH analysis of a paraffin-embedded bone marrow biopsy specimen using the Zyto*Fast* human Ig-kappa/Ig-lambda CISH Kit.



CISH analysis of a paraffin-embedded tonsil tissue using the Zyto*Fast* human Ig-kappa/Ig-lambda Permanent CISH Kit.



Multiple myeloma tissue with B-cells expressing Ig-kappa hybridized with Zyto*Fast* human Ig-kappa Probe, detected with Zyto*Fast* PLUS CISH Implementation Kit HRP-DAB.

Digoxigenin-labeled Probes

Product Name	Reg. Status	Tests	Order No.
Zyto*Fast* human Ig-kappa Probe	CE/IVD	40 (400 µl)	**T-1115-400**
Zyto*Fast* human Ig-lambda Probe	CE/IVD	40 (400 µl)	**T-1116-400**

Biotin-/Digoxigenin-labeled Probes and Probe Kits

Product Name	Reg. Status	Tests	Order No.
Zyto*Fast* human Ig-kappa/Ig-lambda Probe	CE/IVD	40 (400 µl)	**T-1017-400**
Zyto*Fast* human Ig-kappa/Ig-lambda CISH Kit Incl.: Ig-kappa/Ig-lambda Probe (DIG/Biotin-labeled), 0.4 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	CE/IVD	40	**T-1005-400**
Zyto*Fast* human Ig-kappa/Ig-lambda Permanent CISH Kit Incl: Ig-kappa/Ig-lambda Probe (DIG/Biotin-labeled), 0.4 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	CE/IVD	40	**T-1105-400**

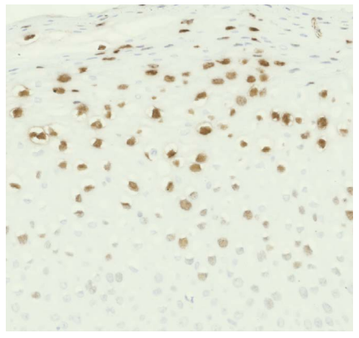
Accessories

ZytoFast® PLUS Implementation Kits for Use in Diagnostic Procedures

For the detection of Digoxigenin-labeled Zyto*Fast*® probes

Product	Manufacturer	Tests	Reg. Status	Order No.
Zyto*Fast* PLUS CISH Implementation Kit HRP-DAB Incl.: 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	ZytoVision GmbH	40	CE/IVD	**T-1063-40**

Peroxidase (HRP)



ZytoFast® Pretreatment Reagents

Product	Manufacturer	Amount	Reg. Status	Order No.
Pepsin Solution	ZytoVision GmbH	4 ml	CE/IVD	**ES-0001-4**
Pepsin Solution	ZytoVision GmbH	50 ml	CE/IVD	**ES-0001-50**
Pepsin Solution	ZytoVision GmbH	1000 ml	CE/IVD	**ES-0001-1000**
Heat Pretreatment Solution EDTA	ZytoVision GmbH	500 ml	CE/IVD	**PT-0002-500**

ZytoFast® Wash Buffers & Ancillary Reagents

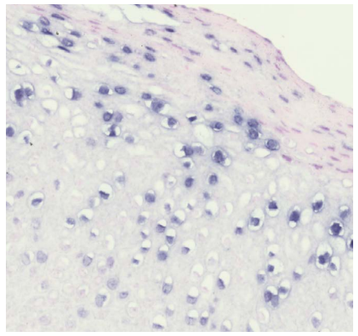
Product	Manufacturer	Amount	Reg. Status	Order No.
Mouse-anti-DIG	ZytoVision GmbH	4 ml	CE/IVD	**AB-0001-4**
Anti-Mouse-HRP-Polymer	ZytoVision GmbH	4 ml	CE/IVD	**AB-0002-4**
Anti-Biotin/DIG-Mix	ZytoVision GmbH	4 ml	CE/IVD	**AB-0015-4**
DAB Solution Set Incl.: DAB Solution A, 0.3 ml; DAB Solution B, 10 ml; good for 10 ml DAB Solution	ZytoVision GmbH	-	CE/IVD	**C-3015-100**
Zyto*Dot* HRP-Green Solution Set Incl: HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; good for 15 ml HRP-Green Solution	ZytoVision GmbH	-	CE/IVD	**C-3039-100**
Mayer's Hematoxylin Solution	ZytoVision GmbH	20 ml	CE/IVD	**CS-0001-20**
Nuclear Blue Solution	ZytoVision GmbH	20 ml	CE/IVD	**CS-0002-20**
Nuclear Green Solution	ZytoVision GmbH	20 ml	CE/IVD	**CS-0004-20**
Mounting Solution (alcoholic)	ZytoVision GmbH	4 ml	CE/IVD	**MT-0004-4**
NBT/BCIP Solution	ZytoVision GmbH	4 ml	CE/IVD	**SB-0004-4**
AEC Solution	ZytoVision GmbH	4 ml	CE/IVD	**SB-0005-4**
20x Wash Buffer TBS	ZytoVision GmbH	50 ml	CE/IVD	**WB-0005-50**

ZytoFast® PLUS Implementation Kits for Research Use Only

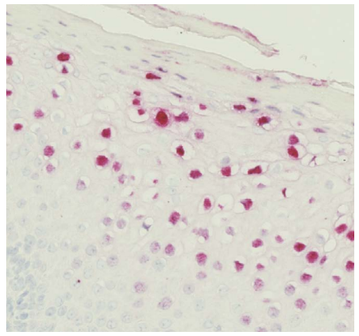
For the detection of Digoxigenin-labeled ZytoFast® probes

Product	Manufacturer	Tests	Reg. Status	Order No.
ZytoFast PLUS CISH Implementation Kit AP-NBT/BCIP Incl.: 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, 4 ml; Nuclear Red Solution, 20 ml; Mounting Solution (alcoholic), 4 ml	ZytoVision GmbH	40	RUO	**T-1061-40**
ZytoFast PLUS CISH Implementation Kit AP-Permanent Red Incl: 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	ZytoVision GmbH	40	RUO	**T-1151-40**

Alkaline Phosphatase (AP)



T-1061-40



T-1151-40

ZytoFast® Wash Buffers & Ancillary Reagents for Research Use Only

Product	Manufacturer	Amount	Reg. Status	Order No.
Rabbit-anti-DIG	ZytoVision GmbH	4 ml	RUO	**AB-0011-4**
Anti-Rabbit-AP-Polymer	ZytoVision GmbH	4 ml	RUO	**AB-0012-4**
Nuclear Red Solution	ZytoVision GmbH	20 ml	RUO	**CS-0003-20**

ZytoFast® Control Probes

Product	Labels	Manufacturer	Tests	Reg. Status	Order No.
ZytoFast DNA (+) Control Probe	DIG	ZytoVision GmbH	10 (100 µl)	RUO	**T-1053-100**
ZytoFast DNA (–) Control Probe	DIG	ZytoVision GmbH	10 (100 µl)	RUO	**T-1054-100**
ZytoFast 28S rRNA (+) Control Probe	DIG	ZytoVision GmbH	10 (100 µl)	RUO	**T-1120-100**
ZytoFast RNA (–) Control Probe	DIG	ZytoVision GmbH	10 (100 µl)	RUO	**T-1119-100**

Arrays

DNA arrays: modern technologies for reliable results

Our diverse product portfolio is fully aligned with the current standards of molecular pathology diagnostics and research. The sensitive VisionArray® system enables the reliable detection of various pathogens in infected tissues.

VisionArray®

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.

ZytoVision GmbH

Advantages of VisionArray®

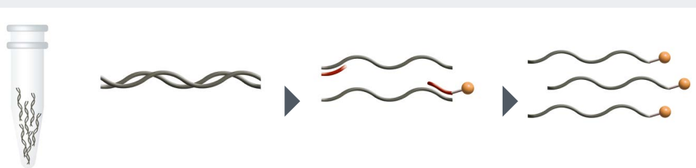
- Quick & easy 1 hour protocol
- Automated evaluation using a VisionArray® Analyzer Software – simple visualization & quick analysis in just a few minutes

Sample Collection

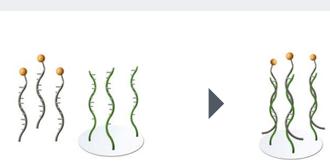
For the detection of DNA sequences with the VisionArray® system, the following raw material can be used for DNA extraction; depending on the VisionArray® Chip used:
Formalin-fixed, paraffin-embedded (FFPE) tissue or cell samples

Method

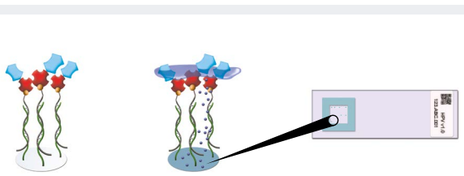
Step 1: Amplification and Labeling in a PCR
The DNA is extracted from, e.g., FFPE samples and is used as a template for PCR. Biotinylated primers are used to amplify and label different sections of the target sequences. The human HLA-DQA1 gene is also amplified and serves as a PCR positive control and 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

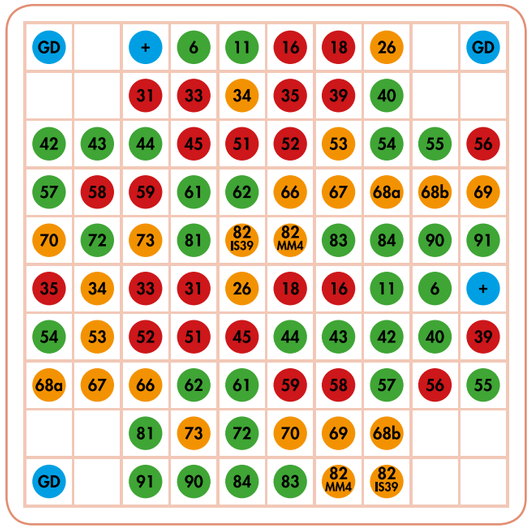
Intended Purpose
The VisionArray® HPV Chip 1.0 is intended to be used for the qualitative detection and genotyping of PCR-amplificates of 41 clinically relevant human papilloma virus (HPV) genotypes that have been produced with the help of the VisionArray® HPV PreCise Master Mix (Prod. No. ES-0007-50) from formalin-fixed, paraffin-embedded specimens, such as cervical carcinoma or head and neck squamous cell carcinoma. The chip is intended to be used in combination with a VisionArray® Software.

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

The product is intended to be used as an aid to the differential diagnosis of cervical carcinoma or head and neck squamous cell carcinoma and therapeutic measures should not be initiated based on the test result alone.

Chip Description
The components of the product are the chip as well as the VisionArray® HPV Chip File 1.0.

Positioning of the capture sequences on the chip:



High Risk HPV Types
16 18 31 33 35 39 45 51 52 56 58 59

Probably High Risk HPV Types
26 34 53 66 67 68a 68b 69 70 73 82 IS39 82 MM4

Low Risk HPV Types
6 11 40 42 43 44 54 55 57 61 62 72 81 83 84 90 91

*HPV 55 is classified by now as subtype of HPV 44, but is still labeled HPV 55 for consistency reasons.

High Risk
Probably High Risk
Low Risk
Guide Dots (GD)/Positive Control (+)

Product	Manufacturer	Amount	Reg. Status	Order No.
VisionArray® HPV Chip 1.0	ZytoVision GmbH	10 Arrays (10 Tests)	CE/IVD	**VA-0001-10**

VisionArray® Myco Chip 2.0

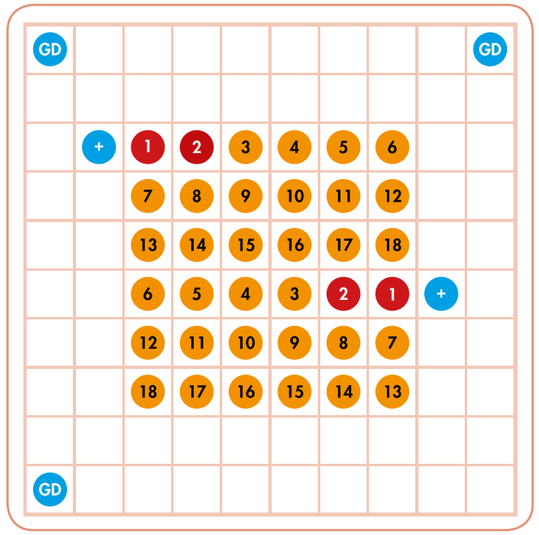
Intended Purpose
The VisionArray® MYCO Chip 2.0 is intended to be used with a VisionArray® Analysis Package for the qualitative detection and identification of PCR amplificates of the genera Mycobacterium, Mycobacteroides, Mycolicibacillus, Mycolicibacter, and Mycolicibacterium as well as several clinically relevant mycobacterial species that have been produced with the help of the VisionArray® MYCO PreCise Master Mix 2.0.

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 2.0.

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.

Chip Description
The VisionArray® MYCO Chip 2.0 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® Software.



GD Guide Dot + Positive Control

M. tuberculosis (MTC) complex

1	M. tuberculosis complex (ITS Region)
2	M. tuberculosis complex (IS6110 Region)

Nontuberculous Mycobacteria (NTM)

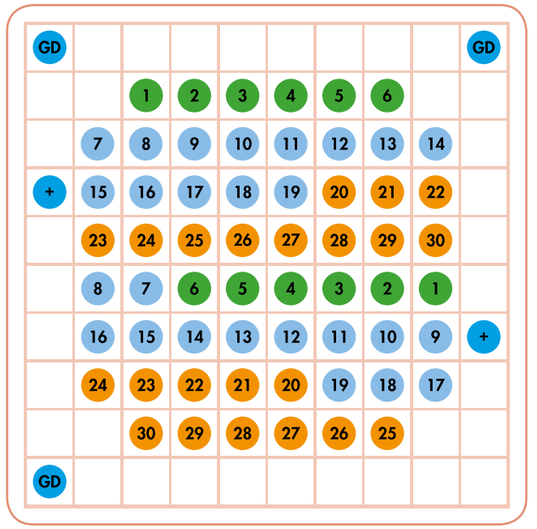
3	M. abscessus	11	M. kansasii
4	M. avium / M. intracellulare complex	12	M. malmoense
5	M. chelonae	13	M. marinum / M. ulcerans
6	M. chimaera	14	M. scrofulaceum / M. parascrofulaceum
7	M. fortuitum	15	M. simiae
8	M. genavense	16	M. smegmatis
9	M. gordonae	17	M. szulgai
10	M. haemophilum	18	M. xenopi

Product	Manufacturer	Amount	Reg. Status	Order No.
VisionArray® MYCO Chip 2.0	ZytoVision GmbH	10 Arrays (10 Tests)	CE/IVD	**VA-0005-10**

VisionArray® FUNGI Chip 1.0

Intended Purpose
The VisionArray® FUNGI Chip 1.0 is intended to be used for the qualitative detection and genotyping of PCR-amplificates of 30 clinically relevant fungi genotypes that have been produced with the help of the VisionArray® FUNGI PreCise Master Mix 1.0 (Prod. No. ES-0009-50) from formalin-fixed, paraffin-embedded specimens. The chip is intended to be used in combination with a VisionArray® Software.

Chip Description
The components of the product are the chip as well as the VisionArray® FUNGI Chip File 1.0.
Positioning of the capture sequences on the chip:



GD Guide Dot + Positive Control

Aspergillus

1	Aspergillus flavus	4	Aspergillus niger
2	Aspergillus fumigatus	5	Aspergillus terreus
3	Aspergillus nidulans / quadrilineatus	6	Aspergillus versicolor

Candida

7	Candida albicans	14	Meyerozyma guilliermondii
8	Candida auris	15	Nakaseomyces glabratus
9	Candida dubliniensis	16	Pichia fermentans
10	Candida parapsilosis	17	Pichia kudriavzevii
11	Candida tropicalis	18	Pichia norvegensis
12	Clavispora lusitaniae	19	Wickerhamomyces anomalus
13	Kluyveromyces marxianus		

Other

20	Cryptococcus neoformans	26	Purpureocillium lilacinum
21	Fusarium spp.	27	Rhizomucor pusillus
22	Lichtheimia corymbifera	28	Rhizopus spp.
23	Mucor spp.	29	Scedosporium spp.
24	Paecilomyces variotii	30	Trichophyton/Microsporum
25	Pneumocystis jirovecii		

Product	Manufacturer	Amount	Reg. Status	Order No.
VisionArray® FUNGI Chip 1.0	ZytoVision GmbH	10 Arrays (10 Tests)	RUO	**VA-0006-10**

Vision*Array*® PCR and Detection

Vision*Array*® Detection Kit

For hybridization and detection of PCR products on Vision*Array*® Chips

Product	Manufacturer	Amount	Reg. Status	Order No.
Vision*Array*® Detection Kit Incl.: Hybridization Solution, 1 ml; Detection Solution, 5 ml; Blue Spot Solution, 5 ml; 100x Wash Buffer, 250 ml	ZytoVision GmbH	1 Kit (50 Tests)	CE/IVD	**VK-0003-50**

Vision*Array*® PCR Reagents

For contamination-free amplification and biotinylation of target sequences with a high quality heat stable Taq polymerase

Product	Manufacturer	Amount	Reg. Status	Order No.
Vision*Array*® HPV PreCise Master Mix Incl.: Vision*Array*® HPV Primer; dNTP/dUTP Solution; PreCise Taq DNA Polymerase; PCR-Buffer; $MgCl_2$; Uracil-DNA Glycosylase	ZytoVision GmbH	1 Kit (50 Tests)	CE/IVD	**ES-0007-50**
Vision*Array*® MYCO PreCise Master Mix 2.0 Incl.: Vision*Array*® MYCO Primer; dNTP/dUTP Solution; PreCise Taq DNA Polymerase; PCR-Buffer; $MgCl_2$; Uracil-DNA Glycosylase	ZytoVision GmbH	1 Kit (50 Tests)	CE/IVD	**ES-0008-50**

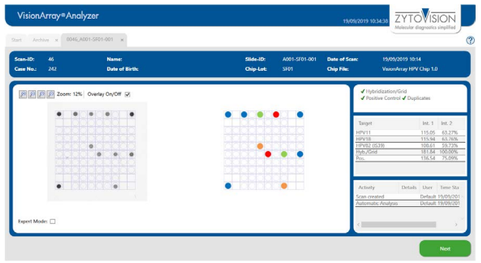
Vision*Array*® PCR Reagents for Research Use Only

For contamination-free amplification and biotinylation of target sequences with a high quality heat stable Taq polymerase

Product	Manufacturer	Amount	Reg. Status	Order No.
Vision*Array*® FUNGI PreCise Master Mix 1.0 Incl.: Vision*Array*® FUNGI Primer; dNTP/dUTP Solution; PreCise Taq DNA Polymerase; PCR-Buffer; $MgCl_2$; Uracil-DNA Glycosylase	ZytoVision GmbH	1 Kit (50 Tests)	CE/IVD	**ES-0009-50**

Vision*Array*® SingleScan Software

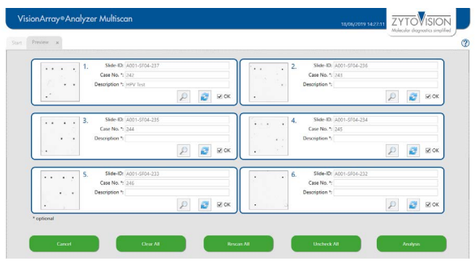
- Simple visualization and quick analysis of the Vision*Array*® Chip data
- Analysis of a Chip and the report of the results can be achieved in just a few minutes
- Program navigation is easy and intuitive for the user



Product	Reg. Status	Order No.
Vision*Array*® SingleScan Software	CE/IVD	**E-4301-1**

Vision*Array*® MultiScan Software

- Simple visualization and quick analysis of up to 6 Vision*Array*® Chips simultaneously
- All available Vision*Array*® Chips can be 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



Product	Reg. Status	Order No.
Vision*Array*® MultiScan Software	CE/IVD	**E-4302-1**

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