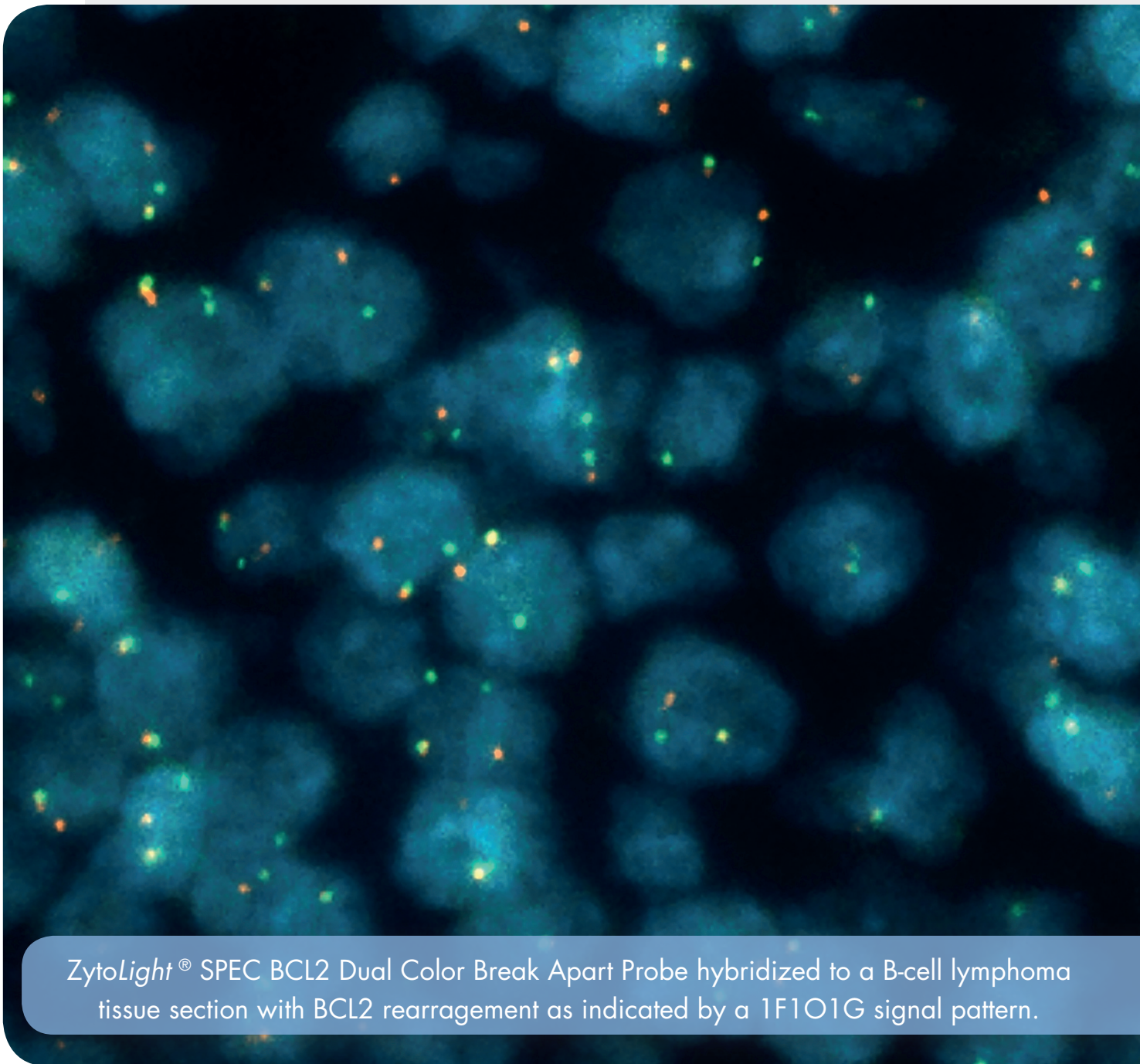


## Recurrent genetic aberrations in hematologic malignancies detectable by *in situ* hybridization (ISH)



ZytoLight® SPEC BCL2 Dual Color Break Apart Probe hybridized to a B-cell lymphoma tissue section with BCL2 rearrangement as indicated by a 1F1O1G signal pattern.

# Tumors of Haematopoietic and Lymphoid Tissues

Leukemia, lymphoma, and myeloma are cancer types that affect the bone marrow, blood cells, lymph nodes and other parts of the lymphatic system. Approximately 8% of the new cancer cases diagnosed worldwide in 2020 were leukemia, lymphoma, and myeloma [1].

The classifications of tumors of the hematopoietic and lymphoid tissues is based on World Health Organization (WHO) criteria, which classify these neoplasms primarily according to their lineage: myeloid, lymphoid, and histiocytic/dendritic. For the diagnosis of hematological neoplasms a complete blood count and a bone marrow examination are essential. Genetic analysis contributes to the diagnosis and/or management of nearly every form of hematologic malignancy. Chromosomal aberrations are a common cause of hematologic cancers. The *in situ* hybridization (ISH) method plays a crucial role in the determination of specific chromosomal aberrations which could otherwise not be detected by e.g. conventional karyotyping.

Apart from the immunophenotype, genotype, and clinical features, FISH and CISH are very useful, specific, and reliable tools that are helpful for differential diagnosis and may thus guide therapy management in patients with hematopoietic and lymphoid neoplasms [2].

## References

1. Global Cancer Observatory - IARC: <https://gco.iarc.fr/> (May 05, 2023).
2. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, 5th Edition (2023).

# Overview of Genetic Aberrations in Hematological Disorders detectable by ISH

## Lymphocytic Lineage

Tumor	Aberration	Gene(s) involved
<b>Acute Lymphocytic Leukemia (ALL)</b>		
	t(v;9q34.12)	ABL1
	t(v;1q25.2)	ABL2
	t(9;22)(q34.12;q11.23)	BCR-ABL1
	del(9p21.3)	CDKN2A
	Hyperploidy	Chromosomes 4, 10, 17
	t(v;Xp22.33), t(v;Yp11.32)	CRIF2
	t(v;5q32)	CSF1R
	t(v;12p13.2)	ETV6
	t(12;21)(p13.2;q22.12)	ETV6-RUNX1
	t(v;14q32.33)	IGH
	del(7p12.2)	IKZF1
	t(v;9p24.1)	JAK2
	t(v;11q23.3)	KMT2A
	del(6q)	MYB
	t(v;9q34.1)	NUP214
	t(v;11p15.4)	NUP98
	t(v;9p13.2)	PAX5
	t(v;4q12), del(4q12)	PDGFRA
	t(v;5q32)	PDGFRB
	t(v;11p11.2)	SPI1
	t(1;19)(q23.3;p13.3)	TCF3-PBX1
	t(v;12p13.31)	ZNF384
BCR-ABL1-Like ALL (Previously: Ph-Like ALL)	t(v;9q34.12)	ABL1
	t(v;1q25.2)	ABL2
	t(v;Xp22.33), t(v;Yp11.32)	CRIF2
	t(v;5q32)	CSF1R
	del(7p12.2)	IKZF1
	t(v;9p24.1)	JAK2
	t(v;5q32)	PDGFRB

# Overview of Genetic Aberrations in Hematological Disorders detectable by ISH

## Lymphocytic Lineage

Tumor	Aberration	Gene(s) involved
<b>Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma</b>		
	del(11q)	ATM
	t(14;18)(q32.33;q21.33)	BCL2-IGH
	lack of t(v;11q13.3)	CCND1
	lack of t(11;14)(q13.3;q32.33)	CCND1-IGH
	del(9p21.3)	CDKN2A
	del(13q)	DLEU2-mir-15-16 cluster, RB1
	Epstein-Barr virus (EBV) infection	EBER1 RNA
	t(v;14q32.33)	IGH
	del(6q)	MYB
	amp(8q24.21)	MYC
	del(17p)	TP53
	Trisomy 12	
<b>Multiple Myeloma (MM) a.k.a. Plasma Cell Myeloma (PCM)</b>		
	t(11;14)(q13.3;q32.33)	CCND1-IGH
	del(1p)	CDKN2C
	gain/amplification of 1q21	CKS1B
	del(13q)	DLEU2-mir-15-16 cluster, RB1
	t(4;14)(p16.3;q32.33)	FGFR3-IGH
	t(v;14q32.33)	IGH
	t(v;2p11.2) or clonality	IGK
	t(v;22q11) or clonality	IGL
	t(14;16)(q32.33;q23.2)	MAF-IGH
	t(14;20)(q32.33;q12)	MAFB-IGH
	t(v;8q24.21)	MYC
	del(17p)	TP53

## Myelocytic Lineage

Tumor	Aberration	Gene(s) involved
<b>Acute Myeloid Leukemia (AML)</b>		
	t(9;22)(q34.12;q11.23)	BCR-ABL1
	inv(16)(p13.11q22.1)	CBFB
	t(16;16)(p13.11;q22.1)	
	t(v;16p13.3)	CREBBP
	-5/del(5q)	CSF1R, EGR1
	-7/del(7q)	CUX1, EZH2
	t(v;12p13.2)	ETV6
	t(3;3)(q21.3;q26.2)	GATA2-MECOM
	inv(3)(q21.3q26.2)	
	t(v;11q23.3)	KMT2A
	t(v;11p15.4)	NUP98
	t(15;17)(q24.1;q21.2)	PML-RARA
	t(8;21)(q21.3;q22.12)	RUNX1-RUNX1T1
	-17/del(17p)	TP53
	Trisomy 8	

Tumor	Aberration	Gene(s) involved
<b>Chronic Myeloid Leukemia (CML)</b>		
	t(9;22)(q34.12;q11.23)	BCR-ABL1
	-7/del(7q)	CUX1, EZH2
	t(3;3)(q21.3;q26.2)	GATA2-MECOM
	inv(3)(q21.3q26.2)	GATA2-MECOM
	isochromosome 17q	TP53, MPO
	Trisomy 8	
<b>Myelodysplastic Syndrome (MDS)</b>		
	del(11q)	ATM
	del(5q)	CSF1R, EGR1
	-7/del(7q)	CUX1, EZH2
	t(3;3)(q21.3;q26.2)	GATA2-MECOM
	inv(3)(q21.3q26.2)	GATA2-MECOM
	t(v;11p15.4)	NUP98
	del(20q)	PTPRT
	amp(5p)	TERT
	TP53 deletion	TP53
	-Y	
	Trisomy 8	
<b>Myeloid/Lymphoid Neoplasms with Eosinophilia (MLNE)</b>		
	t(v;9q34.12)	ABL1
	t(v;12p13.2)	ETV6
	t(v;8p11.2)	FGFR1
	t(v;9p24.1)	JAK2
	t(v;4q12), del(4q12)	PDGFRA
	t(v;5q32)	PDGFRB

## Lymphoma

Tumor	Aberration	Gene(s) involved
<b>Burkitt Lymphoma (BL)</b>		
	lack of t(v;18q21.33)	BCL2
	lack of t(v;3q27.3)	BCL6
	Epstein-Barr virus (EBV) infection	EBER1 RNA
	t(v;8q24.21)	MYC
	t(8;14)(q24.21;q32.33)	MYC-IGH
	t(8;2)(q24.21;p11.2)	MYC-IGK
	t(8;22)(q24.21;q11)	MYC-IGL
	lack of 11q gain/loss	TMPRSS4

Tumor	Aberration	Gene(s) involved
<b>Large B-cell Lymphoma (LBCL)</b>		
	t(v;2p23.2) or inv(2)(p23.2v)	ALK
	t(v;18q21.33)	BCL2
	t(14;18)(q32.33;q21.33)	BCL2-IGH
	t(v;3q27.3)	BCL6
	amp(9p24.1)	CD274, PDCD1LG2
	Epstein-Barr virus (EBV) infection	EBER1 RNA
	t(v;14q32.33)	IGH
	t(v;2p11.2)	IGK
	t(v;22q11)	IGL
	t(v;6p25.3)	IRF4, DUSP22
	t(v;8q24.21)	MYC
	t(8;14)(q24.21;q32.33)	MYC-IGH
	11q gain/loss	TMPRSS4
<b>Follicular Lymphoma (FL)</b>		
	t(v;18q21.33)	BCL2
	t(14;18)(q32.33;q21.33)	BCL2-IGH
	t(v;3q27.3)	BCL6
	lack of t(v;6p25.3)	IRF4, DUSP22
<b>Hodgkin Lymphoma (HL)</b>		
	amp(9p24.1)	CD274, PDCD1LG2
	Epstein-Barr virus (EBV) infection	EBER1 RNA
<b>Mantle Cell Lymphoma (MCL)</b>		
	del(11q22.3)	ATM
	amp(18q21.33)	BCL2
	t(v;11q13.3)	CCND1
	t(11;14)(q13.3;q32.33)	CCND1-IGH
	del(9p21.3)	CDKN2A
	del(6q)	MYB
	amp(8q24.21)	MYC
	del(13q14.2)	RB1
	amp(3q)	PIK3CA
	del(17p)	TP53
<b>Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (EMZL)</b>		
	lack of t(v;18q21.33)	BCL2
	t(11;18)(q22;q21.32)	BIRC3-MALT1
	t(v;14q32.33)	IGH
	t(v;18q21.32)	MALT1
<b>T-cell Lymphoma</b>		
	t(v;2p23.2-p23.1)	ALK
	del(11q22.3)	ATM
	del(9p21.3)	CDKN2A
	Epstein-Barr virus (EBV) infection	EBER1 RNA
	t(v;6p25.3)	IRF4, DUSP22
	del(10q23.31)	PTEN
	del(17p13.1)	TP53
	inv(3)(q26.32q28)	TP63
	t(v;3q28)	
	Trisomy 8	

Abbreviations

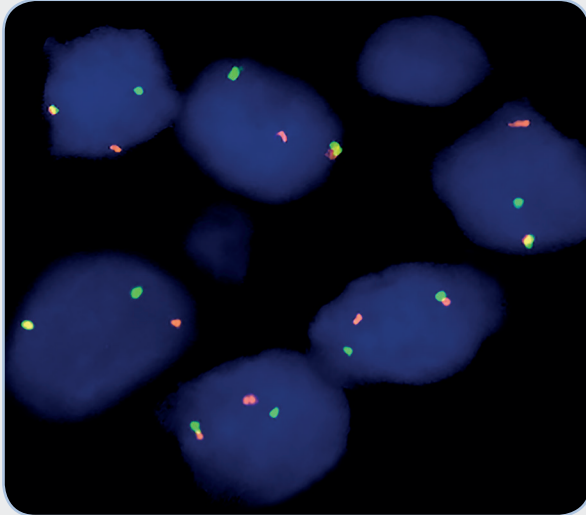
amp amplification, del deletion, inv inversion, p short chromosome arm, q long chromosome arm, t translocation, v various partner

# ISH Probes for Diagnosis of Hematological Malignancies

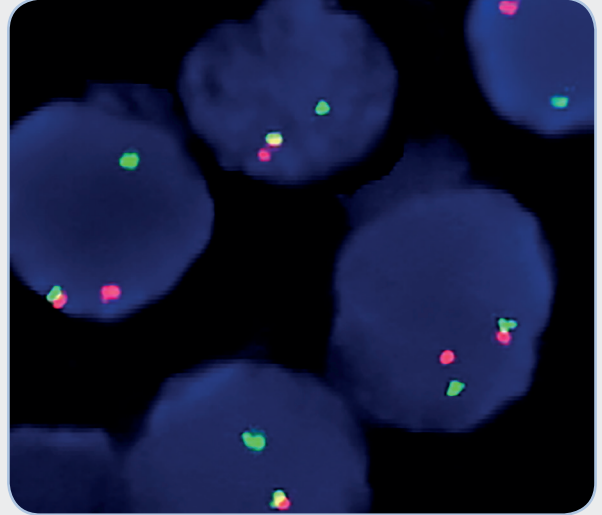
FISH is a very useful, highly sensitive and specific tool in the diagnosis of hematological malignancies which harbor consistent chromosomal alterations including translocations, deletions, and amplifications of gene regions. It can be used to distinguish between entities with similar histological appearances and overlapping immunohistochemical profiles.

**ZytoVision offers a large number of Fluorescence and Chromogenic *in situ* Hybridization probes for the detection of genetic aberrations commonly present in leukemia and lymphomas.**

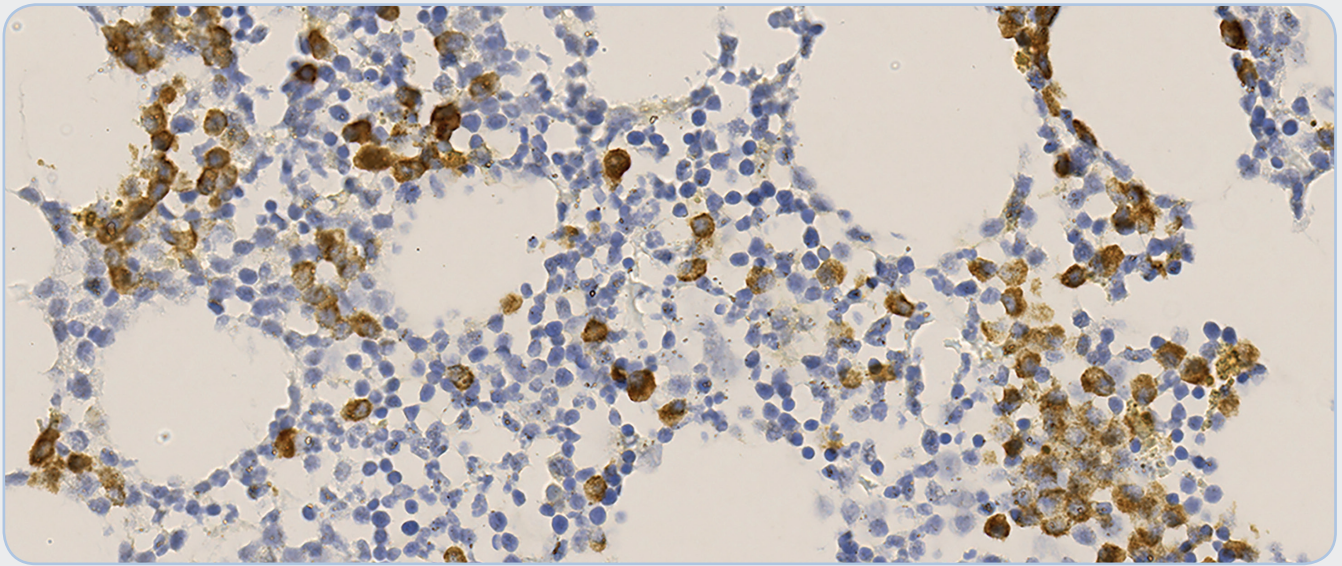
For more product information please visit [www.zytovision.com](http://www.zytovision.com) or contact [info@zytovision.com](mailto:info@zytovision.com) or your local distributor.



ZytoLight® SPEC BCL6 Dual Color Break Apart Probe hybridized on a DLBCL tissue section with translocation of the BCL6 gene.



ZytoLight® SPEC MYC Dual Color Break Apart Probe hybridized on a Burkitt lymphoma tissue section with translocation of the MYC gene.



ZytoFast® human Ig-kappa Probe hybridized on a multiple myeloma tissue section with monoclonal gammopathy, type kappa.

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- NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 2.2023 - January 25, 2023.
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- NCCN Hodgkin Lymphoma Version 2.2023 - November 8, 2022.
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- NCCN Myelodysplastic Syndromes Version 1.2023 - September 12, 2022.
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