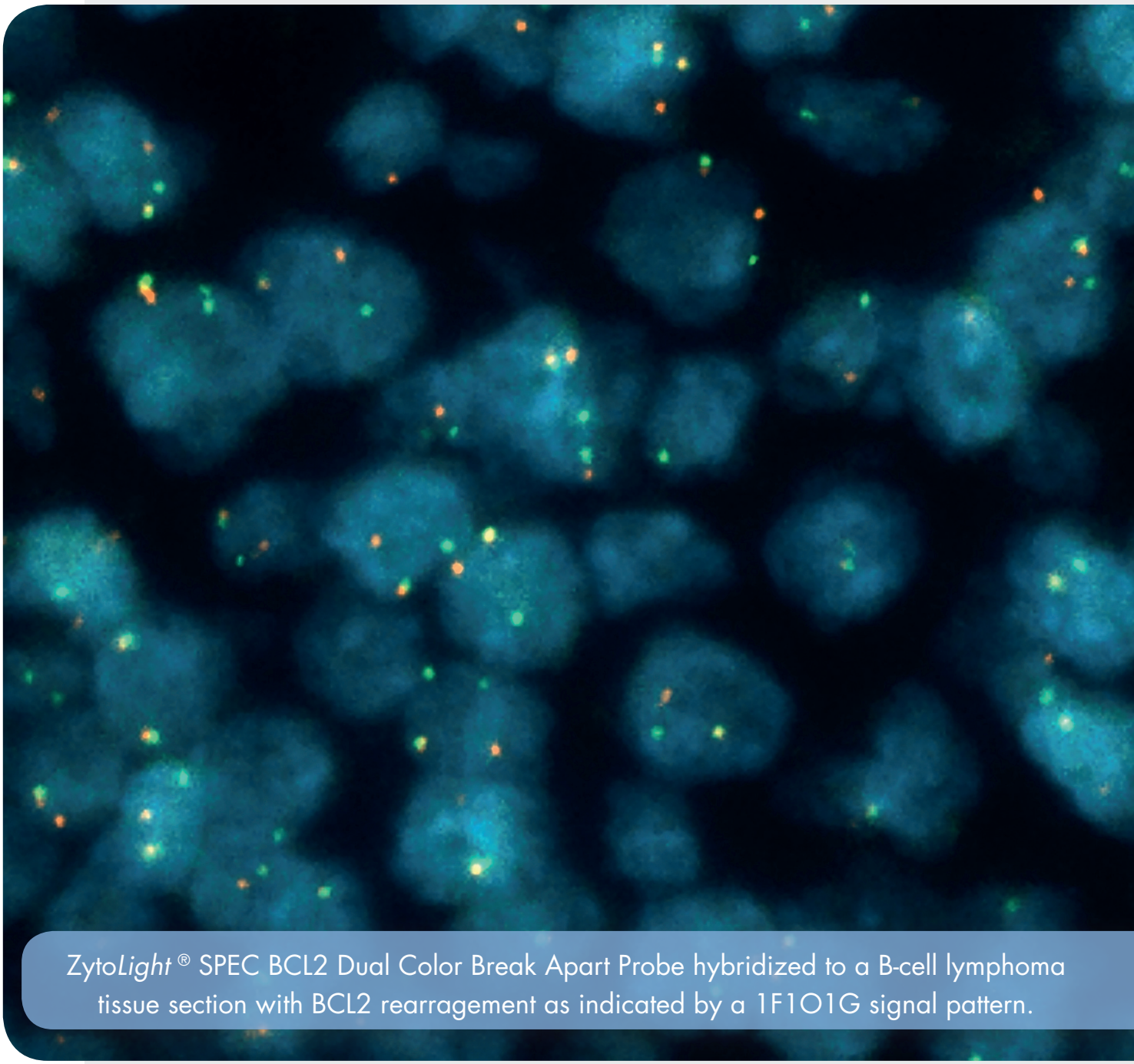
Recurrent genetic aberrations in hematologic malignancies detectable by *in situ* hybridization (ISH)



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

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Molecular diagnostics simplified

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
Acute Lymphocytic Leukemia (ALL)		
	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)	CRLF2
	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)	CRLF2
	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
Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma		
	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	
Multiple Myeloma (MM) a.k.a. Plasma Cell Myeloma (PCM)		
	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
Acute Myeloid Leukemia (AML)		
	t(9;22)(q34.12;q11.23)	BCR-ABL1
	inv(16)(p13.11q22.1) t(16;16)(p13.11;q22.1)	CBFB
	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) inv(3)(q21.3q26.2)	GATA2-MECOM
	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
Chronic Myeloid Leukemia (CML)		
	t(9;22)(q34.12;q11.23)	BCR-ABL1
	-7/del(7q)	CUX1, EZH2
	t(3;3)(q21.3;q26.2) inv(3)(q21.3q26.2)	GATA2-MECOM
	isochromosome 17q	TP53, MPO
	Trisomy 8	
Myelodysplastic Syndrome (MDS)		
	del(11q)	ATM
	del(5q)	CSF1R, EGR1
	-7/del(7q)	CUX1, EZH2
	t(3;3)(q21.3;q26.2) inv(3)(q21.3q26.2)	GATA2-MECOM
	t(v;11p15.4)	NUP98
	del(20q)	PTPRT
	amp(5p)	TERT
	TP53 deletion	TP53
	-Y	
	Trisomy 8	
Myeloid/Lymphoid Neoplasms with Eosinophilia (MLNE)		
	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

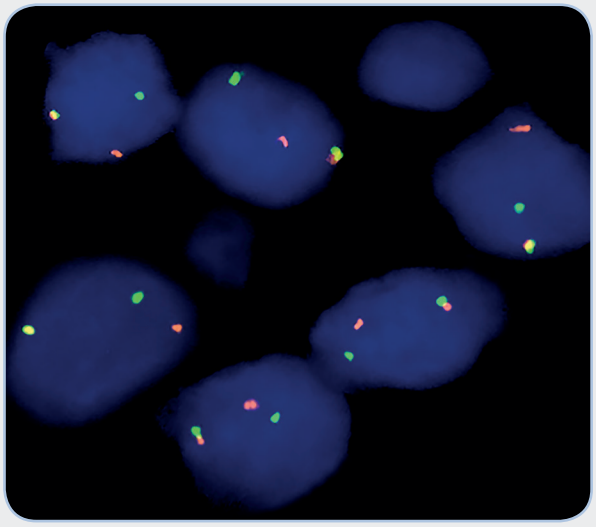
Tumor	Aberration	Gene(s) involved
Burkitt Lymphoma (BL)		
	lack of t(v;18q21.33)	BCL2
	lack of t(v;3q27.3)	BCL6
	Epstein-Barr virus (EBV) infection	EBER1 RNA
	t(v;8q24.21)	MYC
	t(8;14)(q24.21;q32.33)	MYC-IGH
	t(8;2)(q24.21;p11.2)	MYC-IGK
	t(8;22)(q24.21;q11)	MYC-IGL
	lack of 11q gain/loss	TMPRSS4

Tumor	Aberration	Gene(s) involved
Large B-cell Lymphoma (LBCL)		
	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
Follicular Lymphoma (FL)		
	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
Hodgkin Lymphoma (HL)		
	amp(9p24.1)	CD274, PDCD1LG2
	Epstein-Barr virus (EBV) infection	EBER1 RNA
Mantle Cell Lymphoma (MCL)		
	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
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (EMZL)		
	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
T-cell Lymphoma		
	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, DUPS22
	del(10q23.31)	PTEN
	del(17p13.1)	TP53
	inv(3)(q26.32q28) t(v;3q28)	TP63
	Trisomy 8	

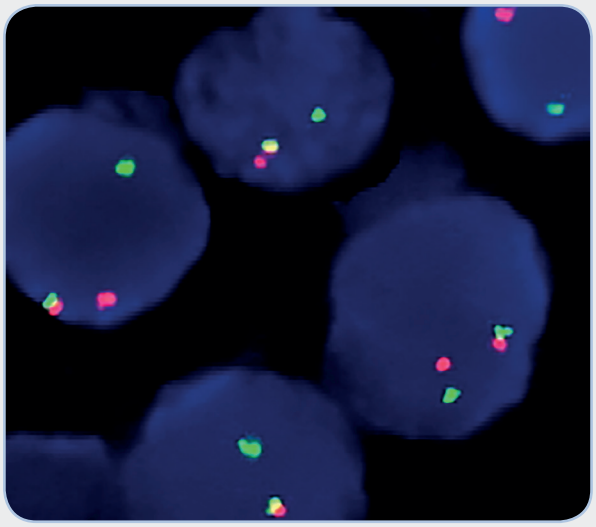
Abbreviations
amp amplification, del deletion, inv inversion, p short chromosome arm, q long chromsome arm, t translocation, v various partner

ISH Probes for Diagnosis of Hematological Malignancies

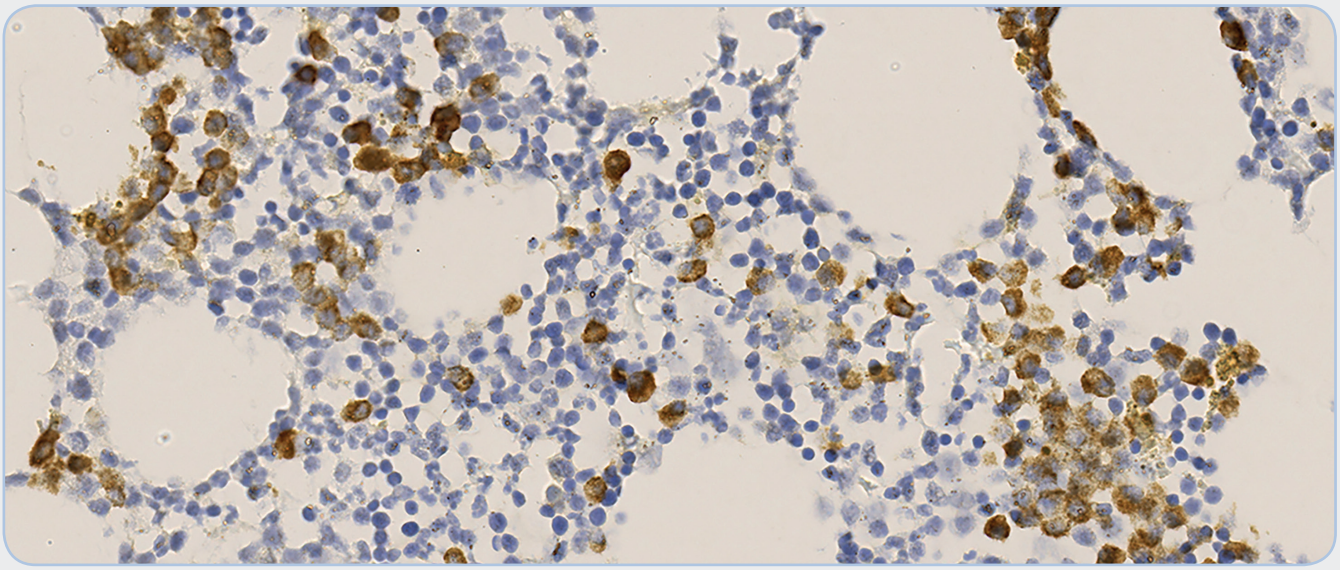
FISH is a very useful, highly sensitive and specific tool in the diagnosis of hematological malignancies which harbor consistent chromosomal alterations including translocations, deletions, and amplifications of gene regions. It can be used to distinguish between entities with similar histological appearances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

References
Kojima K, et al. (2003) Brit J Haematol 120: 271-273.
Lam DH and Aplan PD (2001) Leukemia 15, 1689–1695.
NCCN Acute Lymphoblastic Leukemia Version 1.2022 - April 4, 2022.
NCCN Acute Myeloid Leukemia Version 3.2022 - January 13, 2023.
NCCN B-Cell Lymphomas Version 1.2023 - January 25, 2023.
NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 2.2023 - January 25, 2023.
NCCN Chronic Myeloid Leukemia Version 1.2023 - August 5, 2022.
NCCN Hodgkin Lymphoma Version 2.2023 - November 8, 2022.
NCCN Multiple Myeloma Version 3.2023 - December 8, 2022.
NCCN Myelodysplastic Syndromes Version 1.2023 - September 12, 2022.
NCCN Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes Version 2.2022 - October 18, 2022.
NCCN Myeloproliferative Neoplasms Version 3.2022 - August 11, 2022.
NCCN Pediatric Acute Lymphoblastic Leukemia Version 1.2023 - November 9, 2022.
NCCN T-Cell Lymphomas Version 1.2023 - January 5, 2023.
Seki M, et al. (2017) Nat Genet 49: 1274-1281.
Swerdlow SH, et al. (2016) Blood 127: 20.
WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, 5th Edition (2023).

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