MetaSystems Probes

Acute Myeloid Leukemia
FISH Guide

The 2017 ´WHO Classification of Tumours of the Haematopoietic and Lymphoid Tissues´ defines six acute myeloid leukaemia (AML) categories, ´AML with recurrent genetic abnormalities´, ´AML with myelodysplasia-related changes´, ´Therapy-related myeloid neoplasms´, ´AML, NOS´, ´Myeloid sarcoma´, and ´Myeloid proliferations associated with Down syndrome´.

AML with recurrent genetic abnormalities

The WHO category ´AML with recurrent genetic abnormalities´ recognizes eight balanced translocations and inversions. Whereas a blast count of ≥20% is required for the diagnosis AML in general, the presence of t(8;21)(q22;q22.1), inv(16)(p13.1q22), t(16;16)(p13.1;q22) or t(15;17)(q24.1;q21.2) allows the diagnosis of AML without regard to cell blast count. Translocations and inversions often result in in-frame fusions between the genes involved and can be detected by appropriate DNA FISH probes. FISH is recommended if fast results are required, chromosome banding analysis has failed, if a submicroscopic rearrangement, cryptic by chromosome banding analysis, is suspected or to confirm or exclude chromosome rearrangements with prognostic implications if their presence is in doubt.

Aberration, Genes	MetaSystems FISH Probe
t(8;21)(q22;q22.1), RUNX1-RUNX1T1	XL t(8;21) plus XL RUNX1
inv(16)(p13.1q22) or t(16;16)(p13.1;q22), CBFB-MYH11	XL CBFB/MYH11 plus XL CBFB
t(15;17)(q24.1;q21.2), PML-RARA	XL t(15;17) DF XL RARA BA
t(9;11)(p21.3;q23.3), KMT2A-MLLT3	XL t(9;11) MLLT3/KMT2A DF XL KMT2A BA
t(6;9)(p23;q34.1), DEK-NUP214	XL t(6;9) DEK/NUP214
inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2), GATA2, MECOM	XL t(3;3) GATA2/MECOM DF XL MECOM 3q26
t(1;22)(p13.3;q13.1), RBM15-MKL1	-
t(9;22)(q34.1;q11.2), BCR-ABL1	XL BCR/ABL1 plus XL BCR/ABL1/ASS

FISH GUIDE

The molecular landscape in AML patients provides important prognostic and therapy relevant information. Differences in event-free and overall survival in AML patients are, to a large extent, the result of particular genetic lesions. Current risk stratification strategies combine cytogenetics, FISH and key mutations analysis in the decision-making process. Two widely-accepted stratification schemes are the recommendations of the European LeukemiaNet (ELN) 2017 and a study based on analysis of patients treated in successive United Kingdom national AML trials for younger adults. The presence, absence or combination of certain structural rearrangements and gene mutations assign patients to one of the three prognostic risk groups **favorable**, **intermediate** or **adverse**.

AML risk category ´Favorable´

ELN risk stratification[1]	**Independent prognostic risk stratification in younger adults**[2]	**MetaSystems FISH Probe**
t(8;21)(q22;q22.1); RUNX1-RUNX1T1	t(8;21)(q22;q22)/RUNX1-RUNX1T1	XL t(8;21) plus XL RUNX1
inv(16)(p13.1q22) or t(16;16)(p13.1;q22); CBFB-MYH11	inv(16)(p13q22)/t(16;16)(p13;q22)/ CBFB-MYH11	XL CBFB/MYH11 plus XL CBFB
Mutated NPM1 without FLT3-ITD or with FLT3-ITD^{low} (<0.5)	NPM1 mutation (in absence of FLT3-ITD or DNMT3A mutation)	n.a.
Biallelic mutated CEBPA	Biallelic CEBPA mutation	n.a.
-	t(15;17)(q22;q21)/PML-RARA	XL t(15;17) DF XL RARA BA

AML risk category ´Intermediate´

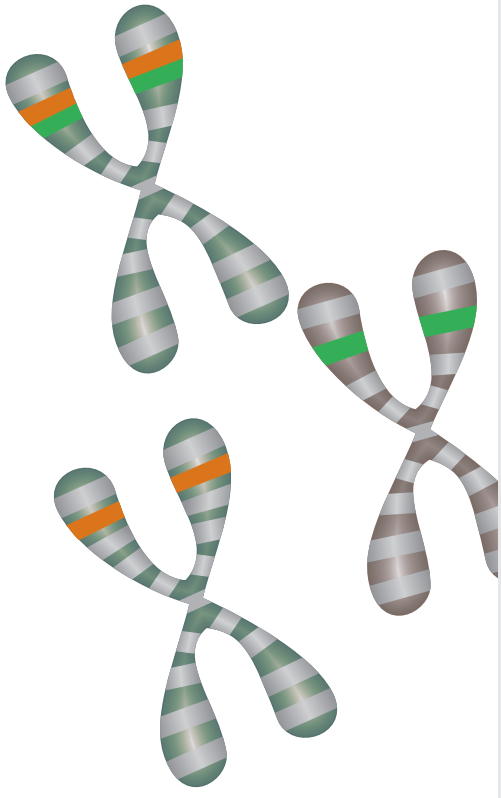
ELN risk stratification[1]	**Independent prognostic risk stratification in younger adults**[2]	**MetaSystems FISH Probe**
Mutated NPM1 and FLT3-ITD^{high} (≥0.5)	-	n.a.
Wild-type NPM1 without FLT3-ITD or with FLT3-ITD^{low} (<0.5)[3]	-	n.a.
t(9;11)(p21.3;q23.3); MLLT3-KMT2A[4]	-	XL t(9;11) MLLT3/KMT2A DF XL KMT2A BA
Cytogenetic abnormalities not classified as favorable or adverse	Cytogenetic/molecular genetic abn. not class. as favorable or adverse	n.a.

AML risk category ´Adverse´

ELN risk stratification[1]	**Independent prognostic risk stratification in younger adults**[2] In the absence of favorable risk cytogenetic/molecular genetic abnormalities.	**MetaSystems FISH Probe**
t(6;9)(p23;q34.1); DEK-NUP214	t(6;9)(p23;q34)/DEK-NUP214	XL t(6;9) DEK/NUP214
t(v;11q23.3); KMT2A rearranged	t(11q23) [excluding t(9;11)(p21~22;q23) and t(11;19)(q23;p13)]	XL KMT2A BA, XL t(9;11) MLLT3/KMT2A DF, XL t(11;19) KMT2A/ELL DF *****, XL t(11;19) KMT2A/MLLT1 DF
t(9;22)(q34.1;q11.2); BCR-ABL1	t(9;22)(q34;q11)/BCR-ABL	XL BCR/ABL1 plus, XL BCR/ABL1/ASS
inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); GATA2,MECOM(EVI1)	inv(3)(q21q26)/t(3;3)(q21;q26)/GATA2/EVI1	XL MECOM 3q26 XL t(3;3) GATA2/MECOM DF
-5 or del(5q)	add(5q)/del(5q), -5	XL 5q31/5q33, XL 5q31/5q33/5p15, XL Del(5)(q31), XL Del(5)(q33)
-7	add(7q)/del(7q), -7	XL 7q22/7q36, XL del(7)(q22q31)
-17/abn(17p)	-17/abn(17p)	XL TP53/17cen, XL TP53/NF1
Complex karyotype, three or more unrelated chromosome abnormalities in the absence of 1 of the WHO-designated recurring translocations or inversions[5]	Complex karyotype (≥4 unrelated abnormalities)	24XCyte (Human Multicolor FISH)
Monosomal karyotype[6]	-	n.a.
Wild-type NPM1 and FLT3-ITD^{high} (≥0.5)	FLT3-ITD	n.a.
Mutated RUNX1[7], ASXL1[7], TP53[8]	Mutated RUNX1, ASXL1, DNMT3A, TP53 and MLL-PTD	n.a.
-	abn(3q) [excluding t(3;5)(q21~25;q31~35)/NPM1-MLF1]	n.a.
-	t(5;11)(q35;p15.5)/ NUP98-NSD1	XL t(5;11) NSD1/NUP98 DF *****, XL NUP98

1. Döhner et al, 2017; 2. Grimwade et al, 2016; 3. Without adverse-risk genetic lesions; 4. The presence of t(9;11)(p21.3;q23.3) takes precedence over rare, concurrent adverse-risk gene mutations.; 5. t(8;21), inv(16) or t(16;16), t(9;11), t(v;11)(v;q23.3), t(6;9), inv(3) or t(3;3); AML with BCR-ABL1; 6. Defined by the presence of 1 single monosomy (excluding loss of X or Y) in association with at least 1 additional monosomy or structural chromosome abnormality (excluding core-binding factor AML).; 7. These markers should not be used as an adverse prognostic marker if they co-occur with favorable-risk AML subtypes.; 8. TP53 mutations are significantly associated with AML with complex and monosomal karyotype.

***** The highlighted probes are not yet available, but will be offered soon.



Ordering Information

Product	Size	Order No.
XL MECOM 3q26	100µl	D-5059-100-OG
XL t(3;3) GATA2/MECOM DF	100µl	D-5124-100-OG
XL Del(5)(q31)	100µl	D-5085-100-OG
XL Del(5)(q33)	100µl	D-5091-100-OG
XL 5q31/5q33	100 µl	D-5042-100-OG
XL 5q31/5q33/5p15	100µl	D-5081-100-TC
XL t(5;11) NSD1/NUP98 DF	100µl	D-5141-100-OG*
XL t(6;9) DEK/NUP214	100µl	D-5097-100-OG
XL 7q22/7q36	100µl	D-5043-100-TC
XL del(7)(q22q31)	100µl	D-5068-100-TC
XL t(8;21) plus	100µl	D-5114-100-OG
XL BCR/ABL1 plus	100µl	D-5052-100-OG
XL BCR/ABL1/ASS	100µl	D-5082-100-TC
XL t(9;11) MLLT3/KMT2A DF	100µl	D-5133-100-OG
XL NUP98	100µl	D-5077-100-OG
XL KMT2A BA	100µl	D-5090-100-OG
XL t(11;19) KMT2A/ELL DF	100µl	D-5135-100-OG*
XL t(11;19) KMT2A/MLLT1 DF	100µl	D-5136-100-OG
XL t(15;17) DF	100µl	D-5086-100-OG
XL CBFB	100µl	D-5092-100-OG
XL CBFB/MYH11 plus	100µl	D-5126-100-OG
XL RARA BA	100µl	D-5087-100-OG
XL TP53/17cen	100µl	D-5103-100-OG
XL TP53/NF1	100µl	D-5089-100-OG
XL RUNX1	100µl	D-5096-100-OG
24XCyte (mFISH)	120µl	D-0125-120-DI*

* The highlighted probes are not yet available, but will be offered soon. * This kit is also offered in 60µl and 600 µl sizes.

Notes

All MetaSystems human FISH probes are classified as IVD products in the EU according to the In-Vitro Diagnostic Medical Device Directive 98/79/EC and are CE labeled, unless otherwise indicated in the product description. Use all MetaSystems Probes products only within the scope of the intended use! FISH analysis is used as an adjunct test to other diagnostic investigations and not to be used as sole base for diagnosis or therapy decisions. Some products may not be available in all markets.

Literature

- Grimwade et al (2016) Blood 127:29-41
- Döhner et al (2017) Blood 129:424-447
- Swerdlow et al (2017) WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues (Revised 4th edition)
- Rack et al (2019) Leukemia 33:1851-1867

MetaSystems Probes

XCyting DNA FISH Probes

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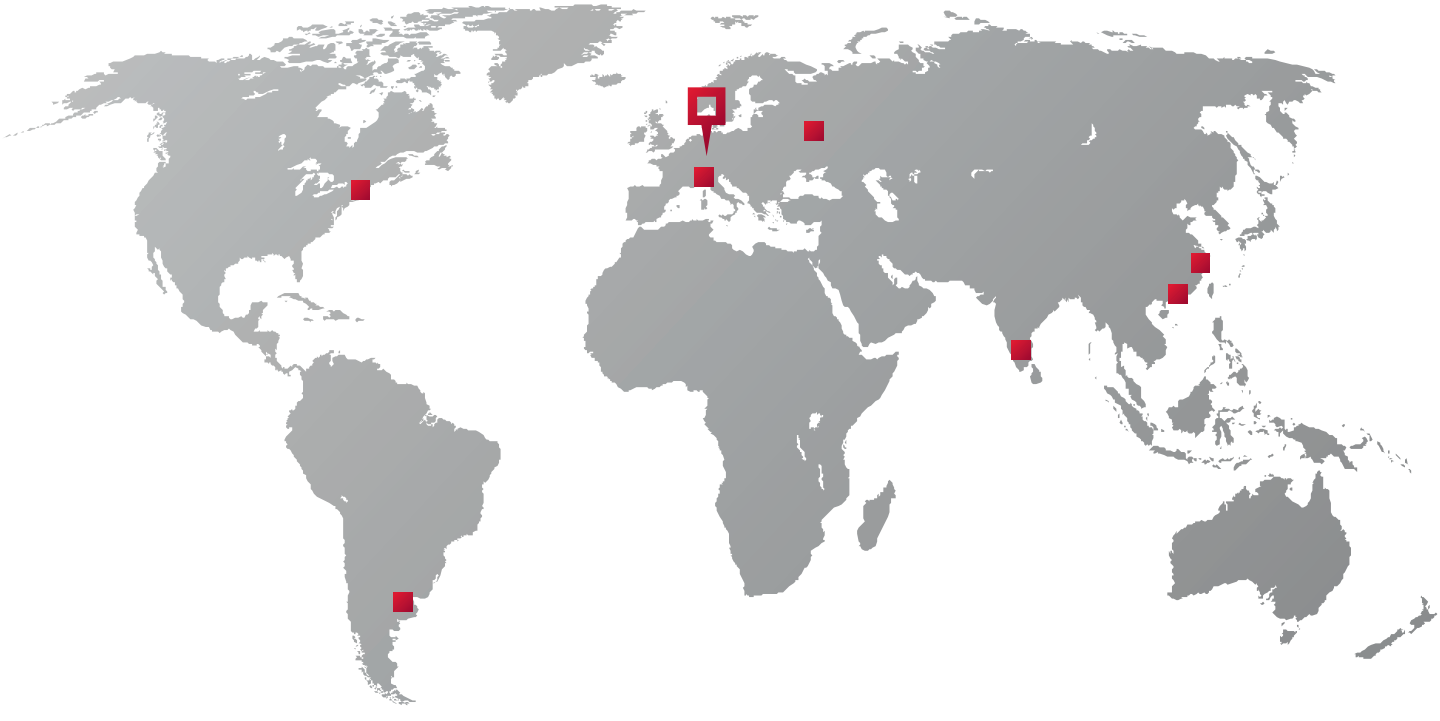

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