



CytoCell



A Sysmex Group Company

Hematology FISH Probes for AML & MDS



Features

- Proven safe and effective probes—reduce the validation burden for your laboratory
- FISH probe, DAPI, detailed protocol and analysis guidelines—ensure optimal FISH test performance
- High-intensity signals with excellent contrast—reduce retest rates
- Easy-to-use, pre-mixed probes—simplify processing and minimize chance for error



CytoCell
FDA-cleared
FISH probes

Introduction

Acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) are neoplastic hematological disorders that arise from myeloid progenitor cells in the bone marrow. AML is characterized by the clonal expansion of myeloid blasts in the peripheral blood, bone marrow or other tissues, while MDS is characterized by the simultaneous proliferation and apoptosis of hemopoietic cells¹.

According to the World Health Organization (WHO), the global incidence for MDS is 3–5 cases per 100,000 (non–age corrected) with approximately 10,000 new cases of MDS diagnosed annually in the USA¹. The Surveillance Epidemiology and End Results (SEER) statistics present a similar picture for AML with a USA incidence of 4.3 per 100,000 (non–sex specific)².

Our range of FDA–cleared Class II IVD FISH probe test kits have been specifically designed to detect common chromosomal rearrangements reported in AML and MDS.

The OGT Partnership

Behind every sample is a life that can be improved through the right care decisions. The OGT partnership approach is key to providing the highest level of service, working closely with you to understand your unique challenges, customising our approach to meet your exact needs. Choose CytoCell® probes for your FISH analysis; our effective, accurate and simple to use products help clinical decision makers to reach the right decisions for each patient.

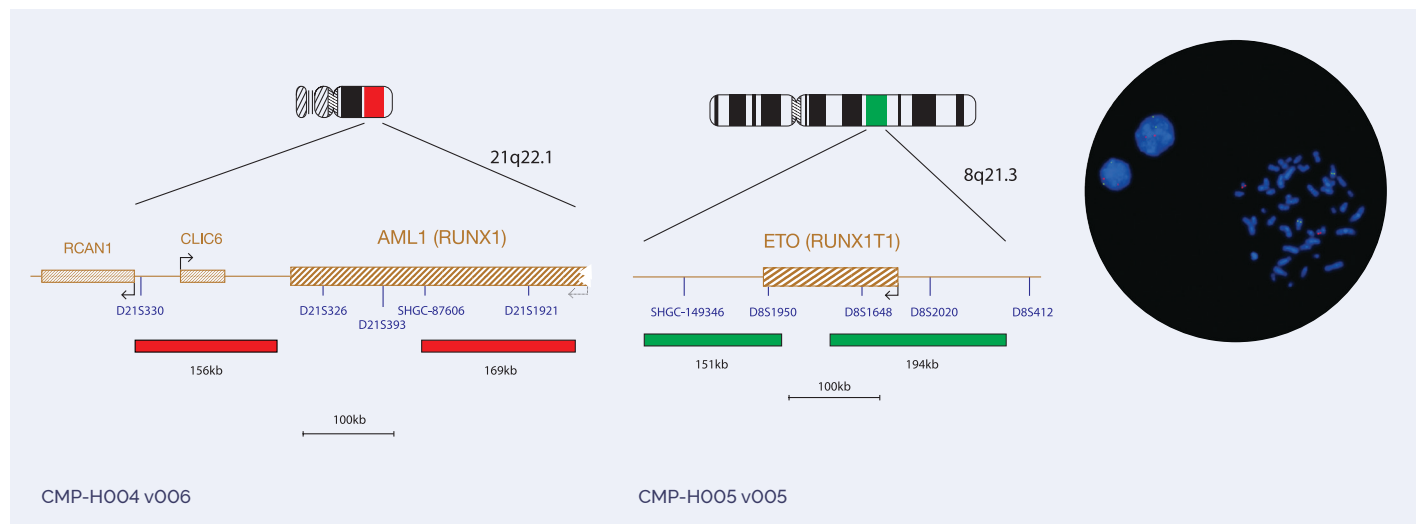
References

1. Swerdlow, *et al* (eds). WHO Classification of Tumours of Haematopoietic and Lymphoid Tissue, Lyon, France, 4th edition, IARC, 2017.
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AML1/ETO (RUNX1/RUNX1T1) Translocation, Dual Fusion FISH Probe Kit

Cat. No. USA-LPH 026 (10 tests)

AML with a RUNX1–RUNX1T1 fusion resulting from a t(8;21)(q22;q22) translocation is a recognized disease entity according to the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia¹. The translocation is commonly observed in patients with AML FAB type M2, most commonly in children and young adults² and is a good prognostic indicator^{3,4,5}. The t(8;21) breakpoint mainly occurs in the intron between exons 5 and 6, just before the transactivation domain. The fusion protein created contains the DNA-binding domain of RUNX1 fused to the transcription factor RUNX1T1². In addition to the reciprocal t(8;21) translocation creating the RUNX1–RUNX1T1 fusion, variant translocations have also been reported. These variant rearrangements may be cryptic and easily overlooked by G-banding; however, FISH can indicate the presence of such rearrangements².



References

1. Swerdlow, *et al* (eds). WHO Classification of Tumours of Haematopoietic and Lymphoid Tissue, Lyon, France, 4th edition, IARC,2017.
2. Reikvam HH, *et al*. J Biomed Biotechnol. 2011;2011:1–23.
3. Grimwade D, *et al*. Blood. 2001 Sep 1;98(5):1312–20.
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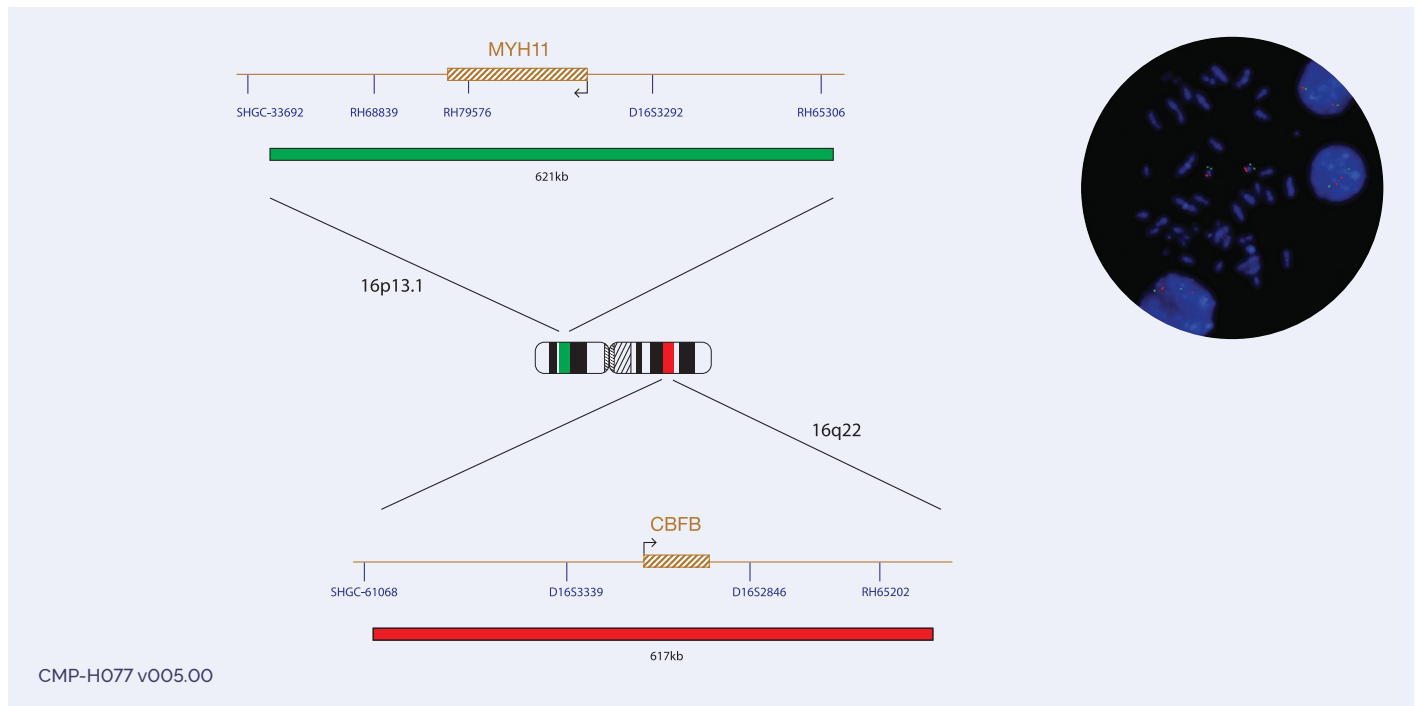
The AML1/ETO (RUNX1/RUNX1T1) Translocation, Dual Fusion FISH Probe Kit is a fluorescence *in situ* hybridization (FISH) Test used to detect rearrangement involving the AML1 (RUNX1) region on chromosome 21 at location 21q22.1 and the ETO (RUNX1T1) region on chromosome 8 at location 8q21.3 in fixed bone marrow specimens from patients with acute myeloid leukemia (AML). The test is indicated for characterization of patient specimens consistent with World Health Organization (WHO) guidelines for Classification of Tumours of Haematopoietic and Lymphoid Tissues (Revised 4th Edition) and in conjunction with other clinicopathological criteria. The assay results are intended to be interpreted by a qualified pathologist or cytogeneticist. The test is not intended for use as a stand-alone diagnostic, disease screening, or as a companion diagnostic. For *In Vitro* Diagnostic Use. Rx only.

The device has not been specifically validated in patients with <20% blast count.

CBFβ (CBFB)/MYH11 Translocation, Dual Fusion FISH Probe Kit

Cat. No. USA-LPH 022 (10 tests)

The CBFB (*core-binding factor beta subunit*) gene is located at 16q22, while the MYH11 (*myosin heavy chain 11*) gene is located at 16p13.1. The inversion *inv(16)(p13.1;q22.1)* and the translocation *t(16;16)(p13.1;q22.1)* give rise to the CBFB-MYH11 fusion gene. Acute myeloid leukemias with *inv(16)(p13.1;q22.1)* or *t(16;16)(p13.1;q22.1)* form a recognized disease entity according to the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia¹. These rearrangements are frequently found in patients with a myelomonocytic subtype with increased bone marrow eosinophils, AML FAB (French-American-British classification) type M4Eo. Cases of therapy-related AML may also have this rearrangement^{1,2}.



References

1. Swerdlow, et al (eds). WHO Classification of Tumours of Haematopoietic and Lymphoid Tissue, Lyon, France, 4th edition, IARC,2017.
2. Hernandez JM, et al. Haematologica. 2000 May;85(5):481-5.

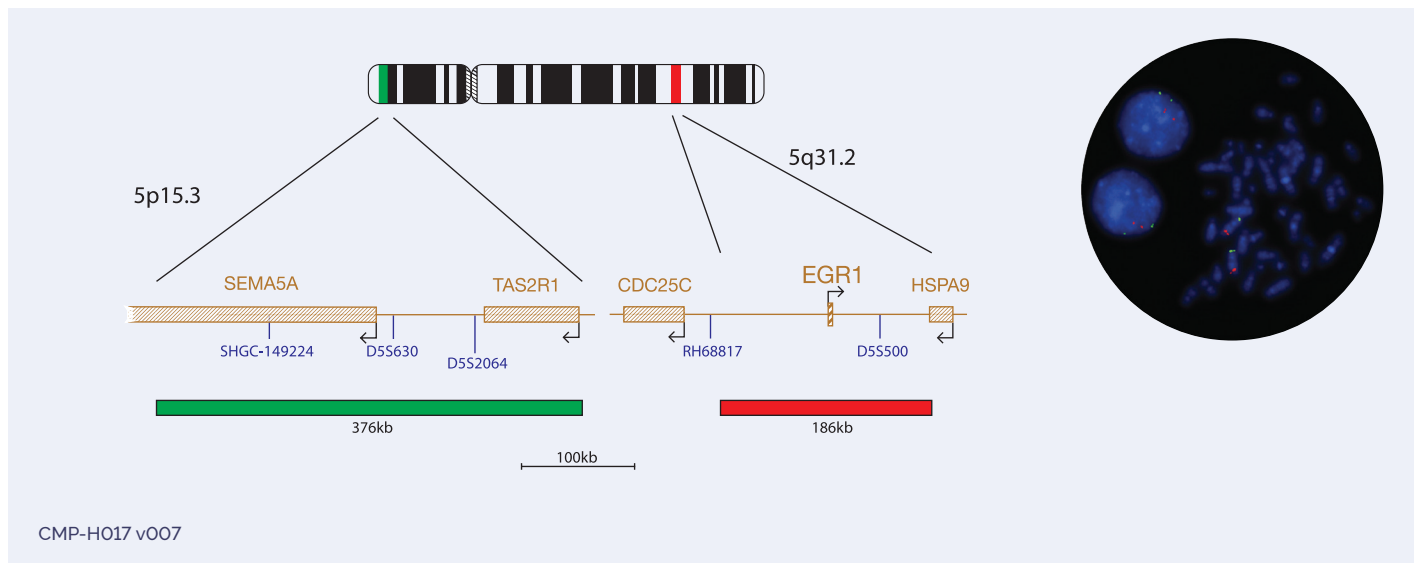
The CBFβ (CBFB)/MYH11 Translocation, Dual Fusion FISH Probe Kit is a fluorescence *in situ* hybridization (FISH) test used to detect rearrangement of the chromosome 16 causing the CBFβ-MYH11 (CBFB-MYH11) fusion in fixed bone marrow specimens from patients with acute myeloid leukemia (AML). The test is indicated for characterization of patient specimens consistent with World Health Organization (WHO) guidelines for Classification of Tumours of Haematopoietic and Lymphoid Tissues (Revised 4th Edition) and in conjunction with other clinicopathological criteria. The assay results are intended to be interpreted by a qualified pathologist or cytogeneticist. The test is not intended for use as a stand-alone diagnostic, disease screening, or as a companion diagnostic. For *In Vitro* Diagnostic Use. Rx only.

The device has not been specifically validated in patients with <20% blast count.

Del(5q) Deletion FISH Probe Kit

Cat. No. USA-LPH 024 (10 tests)

Deletions of the long arm of chromosome 5 are one of the most common karyotypic abnormalities reported in myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) with myelodysplasia related changes^{1,2}. EGR1 (*early growth response 1*), a tumor suppressor gene at 5q31.2, has been shown to act through haploinsufficiency to initiate the development of MDS/AML³. Loss of 5q31.2, the region detected by this probe set, which includes the EGR1 gene, have been linked to a more aggressive form of MDS and AML and is often accompanied by additional cytogenetic abnormalities and a poorer prognosis^{2,4,5}. This probe can also detect some deletions that are associated with 5q- syndrome². However, the probe does not cover the critical deleted region for 5q33 and is not intended for the detection of all deletions associated with 5q- syndrome.



References

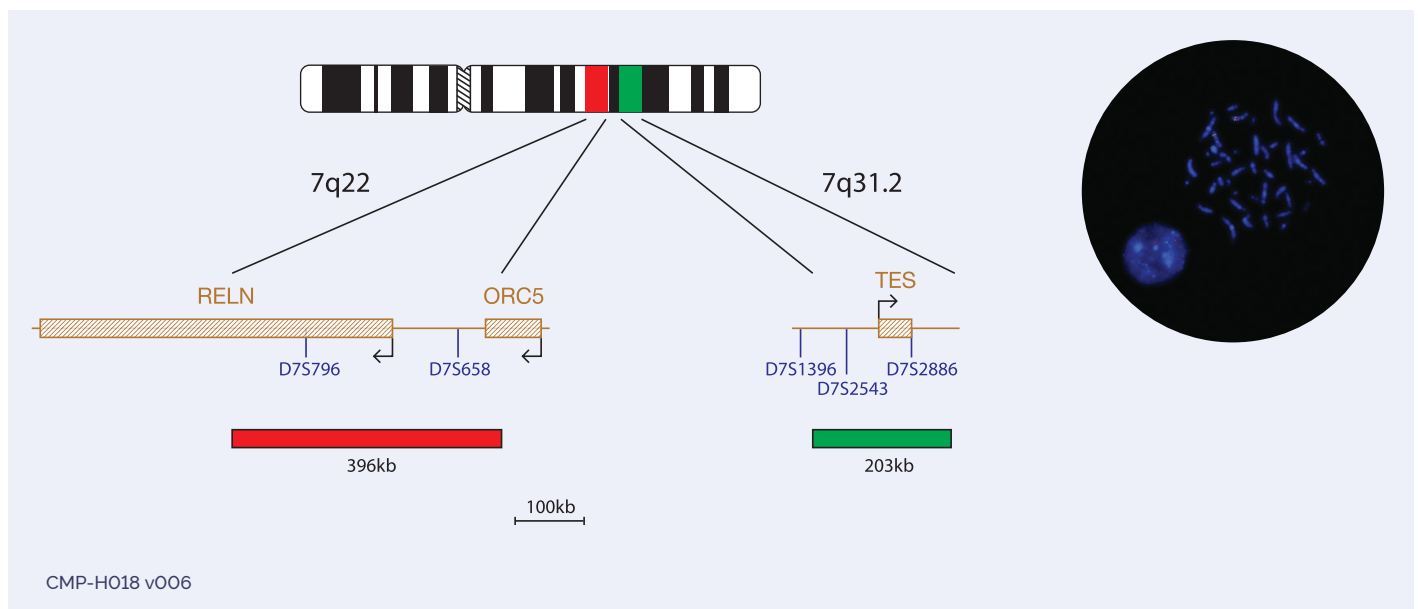
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3. Boultonwood J, et al. Blood. 2010;116(26):5803–11.
4. Joslin JM, et al. Blood. 2007 Jul 15;110(2):719–26.
5. Fang J, et al. Cell Rep. 2014;8(5):1328–38.

The Del(5q) Deletion FISH Probe Kit is a fluorescence *in situ* hybridization (FISH) test used to detect deletions within the long arm of chromosome 5 at location 5q31.2 in fixed bone marrow specimens from patients with acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS). The test is indicated for characterization of patient specimens consistent with World Health Organization (WHO) guidelines for Classification of Tumours of Haematopoietic and Lymphoid Tissues (Revised 4th Edition) and in conjunction with other clinicopathological criteria. The assay results are intended to be interpreted by a qualified pathologist or cytogeneticist. The test is not intended for use as a stand-alone diagnostic, disease screening, or as a companion diagnostic. For *In Vitro* Diagnostic Use. Rx only.

Del(7q) Deletion FISH Probe Kit

Cat. No. USA-LPH 025 (10 tests)

Monosomy of chromosome 7 and deletions of the long arm of chromosome 7 are recognized recurrent chromosomal aberrations frequently seen in myeloid disorders, including myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML)¹. Furthermore, these abnormalities occur in MDS and AML that develop in patients with constitutional disorders (e.g., Fanconi anemia, Kostmann syndrome, neurofibromatosis type 1, and familial monosomy 7)². The presence of monosomy 7 or del(7q) as karyotypic change is associated with a poorer outcome in myeloid malignancies^{1,3}. Deletions of chromosome 7 are typically large with heterogeneity in the breakpoints in myeloid diseases, making it difficult to map the common deleted regions (CDRs)⁴.



References

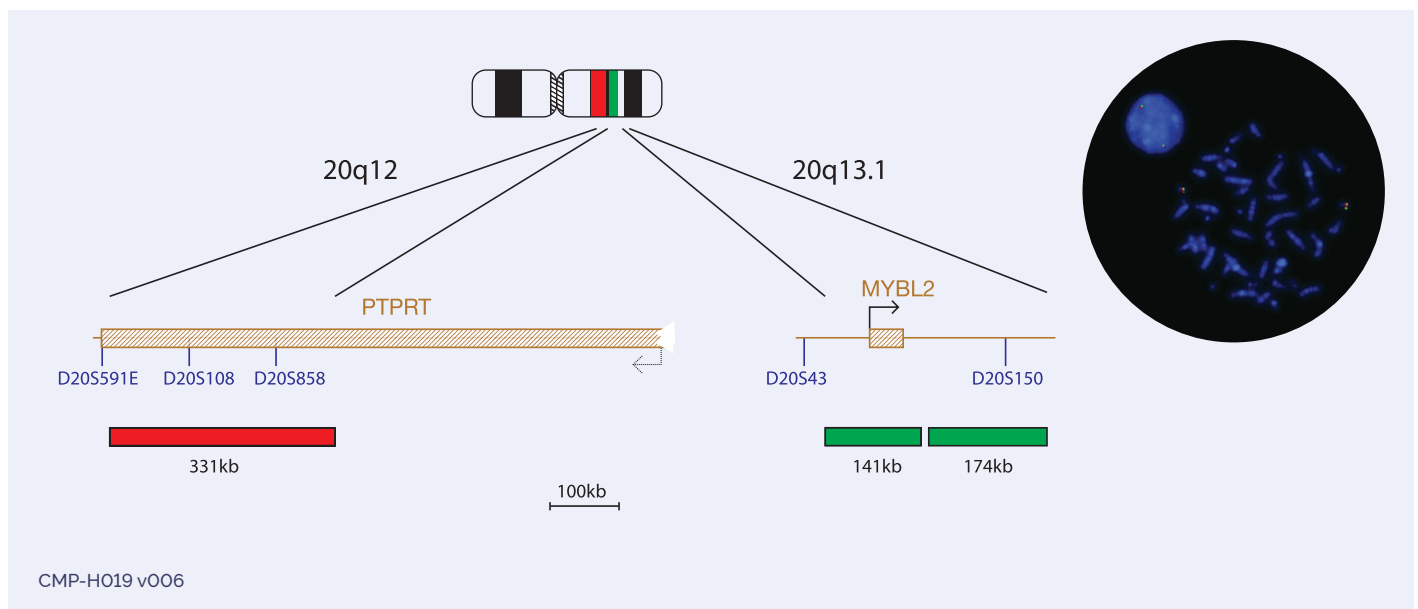
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2. Fischer K, et al. Blood. United States; 1997 Mar;89(6):2036–41.
3. Trobaugh-Lotrario a D, et al. Bone Marrow Transplant. 2005 Jan;35(2):143–9.
4. Mcnerney ME, et al. Biochem J. 2013;444(3):975–83.

The Del(7q) Deletion FISH Probe Kit is a fluorescence *in situ* hybridization (FISH) test used to detect deletions within the long arm of chromosome 7 at locations 7q22 and 7q31.2 in fixed bone marrow specimens from patients with acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS). The test is indicated for characterization of patient specimens consistent with World Health Organization (WHO) guidelines for Classification of Tumours of Haematopoietic and Lymphoid Tissues (Revised 4th Edition) and in conjunction with other clinicopathological criteria. The assay results are intended to be interpreted by a qualified pathologist or cytogeneticist. The test is not intended for use as a stand-alone diagnostic, disease screening, or as a companion diagnostic. For *In Vitro* Diagnostic Use. Rx only.

Del(20q) Deletion FISH Probe Kit

Cat. No. USA-LPH 020 (10 tests)

Deletions of the long arm of chromosome 20 are recognized as recurrent chromosomal abnormalities associated with myelodysplastic syndromes (MDS)¹. The prognosis for MDS where del(20q) is the sole abnormality is good; however, the presence of secondary abnormalities may be indicative of disease progression².



References

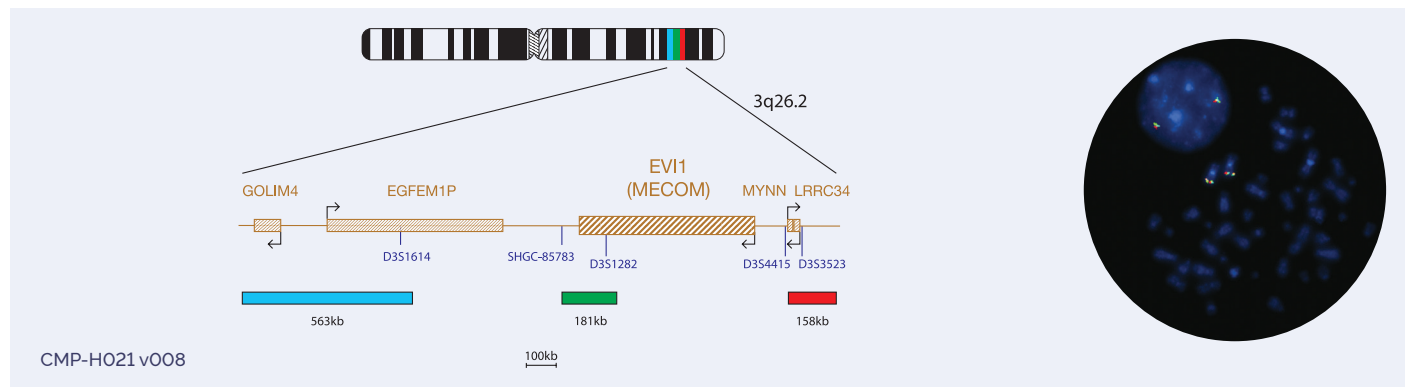
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2. Liu Y-C, et al. Cancer Genet Cytogenet. 2006 Nov;171(1):9–16.

The Del(20q) Deletion FISH Probe Kit is a fluorescence *in situ* hybridization (FISH) test used to detect deletion within the long arm of chromosome 20 at locations 20q12 and 20q13.1 in fixed bone marrow specimens from patients with myelodysplastic syndrome (MDS). The test is indicated for characterization of patient specimens consistent with World Health Organization (WHO) guidelines for Classification of Tumours of Haematopoietic and Lymphoid Tissues (Revised 4th Edition) and in conjunction with other clinicopathological criteria. The assay results are intended to be interpreted by a qualified pathologist or cytogeneticist. The test is not intended for use as a stand-alone diagnostic, disease screening, or as a companion diagnostic. For *In Vitro* Diagnostic Use. Rx only.

EVI1 (MECOM) Breakapart FISH Probe Kit

Cat. No. USA-LPH 036 (10 tests)

The MECOM (*MDS1 and EVI1 complex locus*) oncogene at 3q26.2 is often rearranged in hematological malignancies of myeloid origin. MECOM encodes a zinc finger protein that is inappropriately expressed in the leukemic cells of AML and MDS patients¹. This deregulated expression is often due to a chromosomal rearrangement involving 3q26.2, with the two most common aberrations being the t(3;3)(q21;q26.2) and inv(3)(q21q26.2)¹. The breakpoints for the translocations and inversions vary considerably. Inversion breakpoints are found centromeric to, and include the MECOM gene, covering about 600kb. The majority of breakpoints in 3q26.2 translocations are telomeric to the MECOM gene and cover a region including the telomeric end of the *MDS1* gene and the *MYNN* gene². Chromosome rearrangements involving the 3q26.2 region are associated with myeloid malignancies, aberrant expression of MECOM gene and an unfavorable prognosis². AML with inv(3)(q21q26.2) or t(3;3)(q21;q26.2) is a recognized disease entity according to the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia. This is a transformed or *de novo* AML with a very aggressive clinical course and aberrations that involve MECOM at 3q26.2 and RPN1 (ribophorin I) at 3q21³. MECOM has also been shown to be rearranged in therapy-related disease via the t(3;21)(q26.2;q22) translocation, resulting in a MECOM-RUNX1 fusion^{3,4}. MECOM rearrangements are very heterogeneous and may be difficult to detect by conventional cytogenetics, making FISH a useful tool for their detection.



References

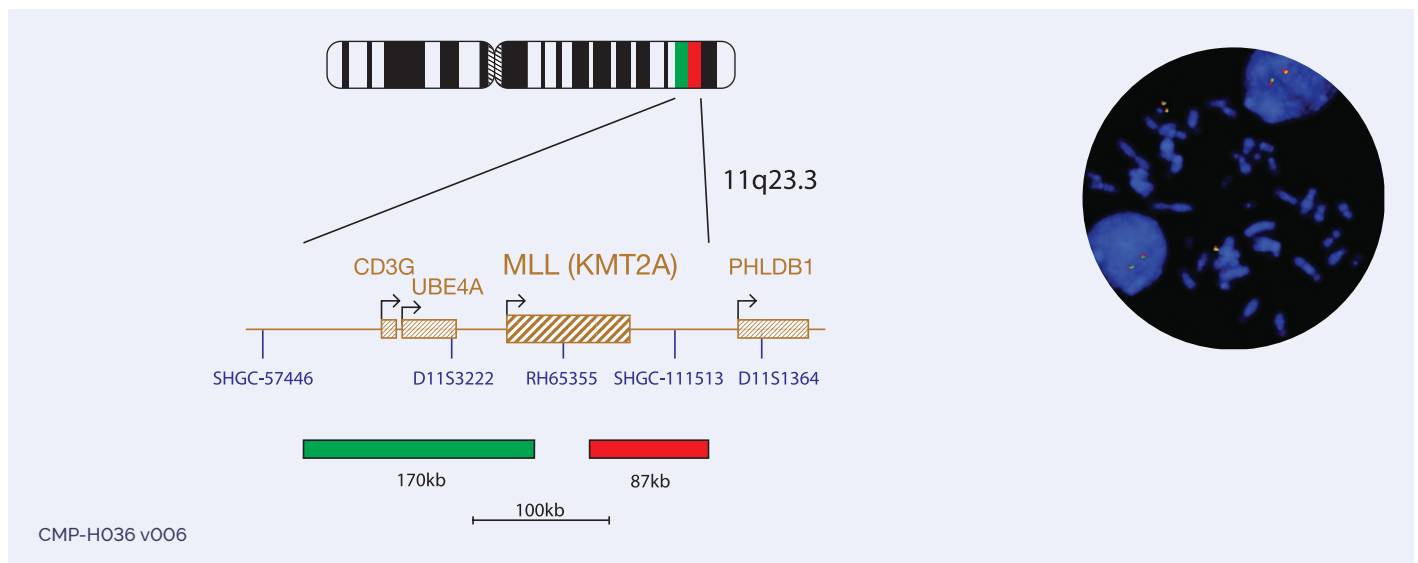
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3. Swerdlow, et al (eds). WHO Classification of Tumours of Haematopoietic and Lymphoid Tissue, Lyon, France, 4th edition, IARC,2017.
4. Pedersen-Bjergaard J, et al. *Leukemia*. England; 2008 Feb;22(2):240–8.

The EVI1 (MECOM) Breakapart FISH Probe Kit is a fluorescence *in situ* hybridization (FISH) test used to detect rearrangement involving the EVI1 (MECOM) region on chromosome 3 at location 3q26.2, in fixed bone marrow specimens from patients with acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS). The test is indicated for characterization of patient specimens consistent with World Health Organization (WHO) guidelines for Classification of Tumours of Haematopoietic and Lymphoid Tissues (Revised 4th Edition) and in conjunction with other clinicopathological criteria. The assay results are intended to be interpreted by a qualified pathologist or cytogeneticist. The test is not intended for use as a stand-alone diagnostic, disease screening, or as a companion diagnostic. For *In Vitro* Diagnostic Use. Rx only.

MLL (KMT2A) Breakapart FISH Probe Kit

Cat. No. USA-LPH 013 (10 tests)

The KMT2A (*lysine methyltransferase 2A*) gene at 11q23.3 encodes for a histone methyltransferase, which functions as an epigenetic regulator of transcription¹. KMT2A rearrangements are reported frequently in patients with AML and have also been reported in patients with therapy related MDS, albeit at a lower frequency^{2,3,4,5,6}. Historically, KMT2A rearrangements in acute leukemia were associated with a poorer outcome, but recent studies have shown that the prognosis is highly dependent on the fusion partner and may differ between children and adults⁷. Because this is a breakapart probe, it cannot be used to determine the fusion partner.



References

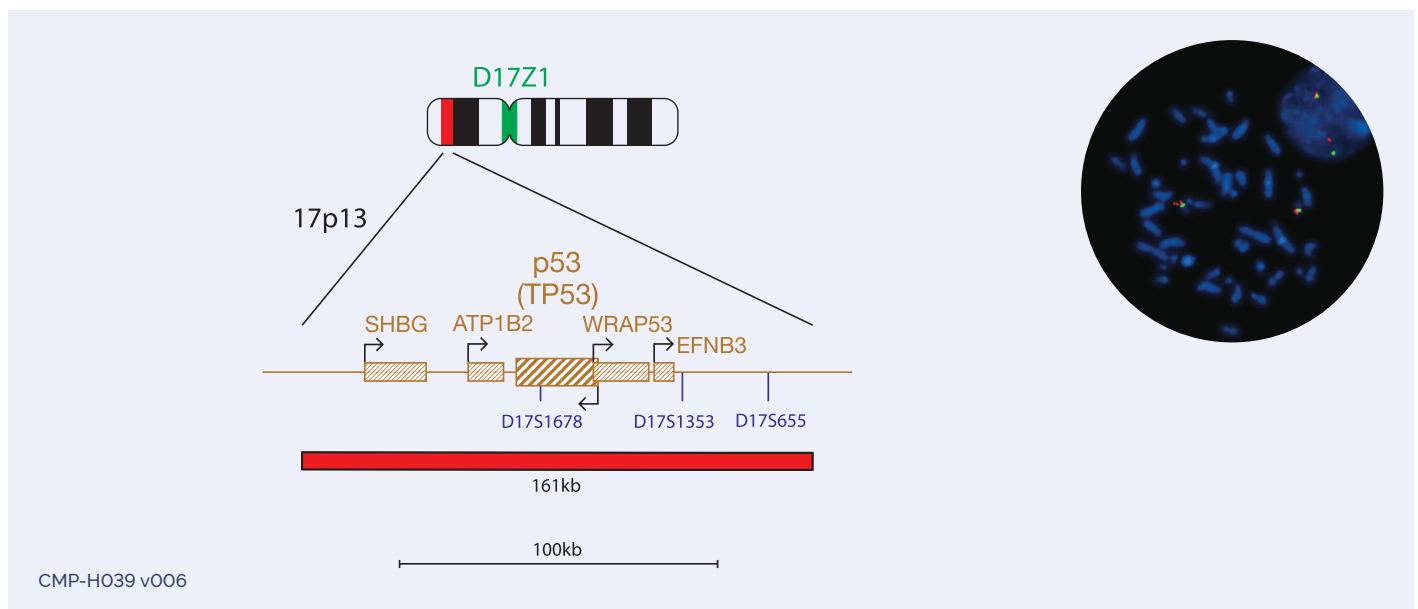
1. Tomizawa D. *Pediatr Int.* 2015;4:811–9.
2. Wright RL, *et al.* *Crit Rev Oncol Hematol.* 2014;91(3):283–91.
3. van der Burg M, *et al.* *Leuk Off J Leuk Soc Am Leuk Res Fund, UK.* 2004;18(5):895–908.
4. Grossmann V, *et al.* *Leukemia.* England; 2013. p. 1933–6.
5. Super HJ, *et al.* *Blood.* United States; 1993 Dec;82(12):3705–11.
6. Schanz J, *et al.* *J Clin Oncol.* 2012;30(8):820–9.
7. Tamai H, *et al.* *J Clin Exp Hematop.* 2010;50(2):91–8.

The MLL (KMT2A) Breakapart FISH Probe Kit is a fluorescence *in situ* hybridization (FISH) test used to detect rearrangement of the MLL (KMT2A) region on chromosome 11 at location 11q23.3 in fixed bone marrow specimens from patients with acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS). The test is indicated for characterization of patient specimens consistent with World Health Organization (WHO) guidelines for Classification of Tumours of Haematopoietic and Lymphoid Tissues (Revised 4th Edition) and in conjunction with other clinicopathological criteria. The assay results are intended to be interpreted by a qualified pathologist or cytogeneticist. The test is not intended for use as a stand-alone diagnostic, disease screening, or as a companion diagnostic. For *In Vitro* Diagnostic Use. Rx only.

P53 (TP53) Deletion FISH Probe Kit

Cat. No. USA-LPH 017 (10 tests)

The TP53 (*tumor protein p53*) gene at 17p13 is a tumor suppressor gene that has been shown to be deleted in a wide range of human malignancies. In acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS), TP53 loss is associated with a poor outcome and is often seen as a marker of disease progression or secondary disease^{1,2}.



References

1. Grimwade D, et al. *Blood*. 2010;116(3):354–65.
2. Seifert H, et al. *Leukaemia*. 2009;23(4):656–63.

The P53 (TP53) Deletion FISH Probe Kit is a fluorescence *in situ* hybridization (FISH) Test used to detect deletion of the P53 (TP53) region on chromosome 17 at location 17p13 in fixed bone marrow specimens from patients with acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS). The test is indicated for characterization of patient specimens consistent with World Health Organization (WHO) guidelines for Classification of Tumours of Haematopoietic and Lymphoid Tissues (Revised 4th Edition) and in conjunction with other clinicopathological criteria. The assay results are intended to be interpreted by a qualified pathologist or cytogeneticist. The test is not intended for use as a stand-alone diagnostic, disease screening, or as a companion diagnostic. For *In Vitro* Diagnostic Use. Rx only.

Recommended Protocol and Sample Preparation for CytoCell AML and MDS FISH Probe Kits

Step 1		Sample and slide preparation	<ul style="list-style-type: none"> • The FISH probes for AML/MDS are designed for use on bone marrow cells fixed in Carnoy's solution (3:1 methanol/ acetic acid) that are prepared according to the laboratory or institution guidelines. • Spot the cell sample onto a glass microscope slide. Allow to dry. • Immerse the slide in 2x Saline Sodium Citrate (SSC) for 2 minutes at room temperature (RT) without agitation. • Dehydrate in an ethanol series (70%, 85% and 100%), each for 2 minutes at RT. • Allow to dry.
Step 2		Pre-denaturation	<ul style="list-style-type: none"> • Remove the probe from the freezer and allow it to warm to RT. Briefly centrifuge tubes before use. • Ensure that the probe solution is sufficiently mixed with a pipette or a vortex mixer. • Remove 10µl of probe per test, and transfer it to a microcentrifuge tube. Quickly return the remaining probe to -20°C. • Place the probe and the sample slide to prewarm on a 37°C (+/- 1°C) hotplate for 5 minutes. • Spot 10µl of probe mixture onto the cell sample and carefully apply a 24x24mm coverslip. Seal with rubber solution glue and allow the glue to dry completely.
Step 3		Denaturation	<ul style="list-style-type: none"> • Denature the sample and probe simultaneously by heating the slide on a hotplate at 75°C (+/- 1°C) for 2 minutes.
Step 4		Hybridization	<ul style="list-style-type: none"> • Place the slide in a humid, lightproof container at 37°C (+/- 1°C) overnight.
Step 5		Post-hybridization washes	<ul style="list-style-type: none"> • Remove the DAPI from the freezer and allow it to warm to RT. • Remove the coverslip and all traces of glue carefully. • Immerse the slide in 0.4x Saline Sodium Citrate (SSC) (pH 7.0) at 72°C (+/- 1°C) for 2 minutes without agitation. • Drain the slide and immerse it in 2xSSC + 0.05% Tween-20 at RT (pH 7.0) for 30 seconds without agitation. • Drain the slide and apply 10µl of DAPI antifade onto each sample. • Cover with a 24x24mm coverslip, remove any bubbles. • Edge the slide with clear nail varnish to seal. • Allow the color to develop in the dark for 10 minutes.
Step 6		Analyze	<ul style="list-style-type: none"> • View with a fluorescence microscope. • For optimal visualization of the probes, a 100-Watt mercury lamp (or equivalent) is recommended with plan apochromat objectives 63x or 100x. • Filters designed specifically for detection of DAPI, FITC, Texas Red®, and Aqua or DEAC fluorophores individually or in combination (e.g. dual or triple filters) are optimal for best results. • The final hybridized slides are analyzable for up to 1 month when stored in darkness and at 2-8°C.

Please refer to the CytoCell FDA cleared test kit IFU for more detailed information. This can be found in the product packaging and using the Resources section of the OGT website (ogt.com).

General inquiries

US +1 914 467 5285
 contact@ogt.com
 ogt.com



Ordering information

US +1 833 208 4648
 OGTorders@sysmex.com
 ogt.com

Probe Name	Supported Disease	Cat. No.*	Package Insert
AML1/ETO (RUNX1/RUNX1T1) Translocation, Dual Fusion FISH Probe Kit	AML	USA-LPH 026	DS059/USA
CBFB (CBFB)/MYH11 Translocation, Dual Fusion FISH Probe Kit	AML	USA-LPH 022	DS060/USA
Del(5q) Deletion FISH Probe Kit	AML, MDS	USA-LPH 024	DS061/USA
Del(7q) Deletion FISH Probe Kit	AML, MDS	USA-LPH 025	DS062/USA
Del(20q) Deletion FISH Probe Kit	MDS	USA-LPH 020	DS076/USA
EVI1 (MECOM) Breakapart FISH Probe Kit	AML, MDS	USA-LPH 036	DS106/USA
MLL (KMT2A) Breakapart FISH Probe Kit	AML, MDS	USA-LPH 013	DS083/USA
P53 (TP53) Deletion FISH Probe Kit	AML, MDS	USA-LPH 017	DS086/USA

*Kit includes FISH probe and DAPI. For sale in the US only. This product has not been licensed in accordance with Canadian law.



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What binds us, makes us.

Oxford Gene Technology Inc., 520 White Plains Road, Suite 500, Tarrytown, NY 10591, USA

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Refer to individual test kit Package Insert for the specific intended use and limitations

The CytoCell AML/MDS range of FISH probe test kits are for sale in the US only. These products have not been licensed in accordance with Canadian law.