XL t(10;11) MLLT10/ KMT2A DF

Translocation/
Dual Fusion Probe

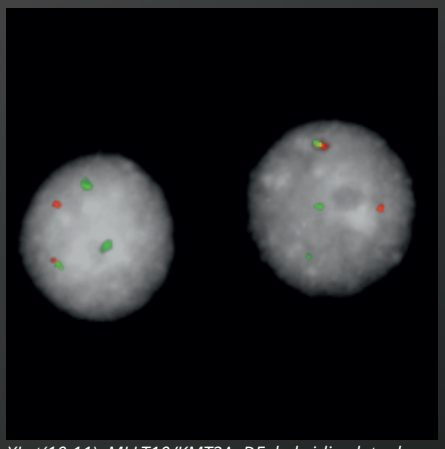
Order No.:
D-5134-100-OG

Description

XL t(10;11) MLLT10/KMT2A DF is designed as a dual fusion probe. The orange labeled probe spans the breakpoint at 10p12.3 (MLLT10), the green labeled probe spans the breakpoint at 11q23.3 (KMT2A).

Clinical Details

Chromosomal rearrangements of the KMT2A (lysine methyltransferase 2A) gene, formerly MLL (mixed lineage leukemia), are associated with various hematological disorders. Most patients suffer from acute myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL), while only a minority develops mixed lineage leukemia (MLL). Several chromosomal aberrations involving the KMT2A gene have been identified. However, the majority of leukemias result from translocations leading to KMT2A fusions. More than 90 KMT2A translocation partner genes fused to the 5´-KMT2A portion have been identified. The most common translocation partners in KMT2A associated leukemia are AFF1, MLLT3, MLLT1, MLLT10, ELL and AFDN, described here in the order of their frequency. MLLT10 (MLLT10 Histone Lysine Methyltransferase DOT1L Cofactor), previously known as AF10, is one of the most frequent fusion partners of KMT2A across all acute leukemia cases. KMT2A-MLLT10 fusions result from multiple breakpoints in both gene loci. The subsequent chromosomal rearrangements include reciprocal translocations, insertions, inversions, deletions and duplications. MLLT10 is a cofactor of the histone H3K79 methyltransferase DOT1L and mediates the interaction of AFF1, MLLT1 and MLLT3 with DOT1L. The consequence of the presence of KMT2A-AFF1, AFF1-KMT2A, KMT2A-MLLT3, KMT2A-MLLT1, and KMT2A-MLLT10 fusions is an increased and extended H3K79 methylation signature that is a requirement for the maintenance of RNA transcription. DOT1L inhibitors are promising candidates for clinical treatment which are currently being evaluated.



XL t(10;11) MLLT10/KMT2A DF hybridized to bone marrow cells, two aberrant cells are shown. An insertion of portions of the green signal into the orange signal has occured generating a pattern of 2 green, one orange and one green-orange colocalization/fusion signal.

Clinical Applications

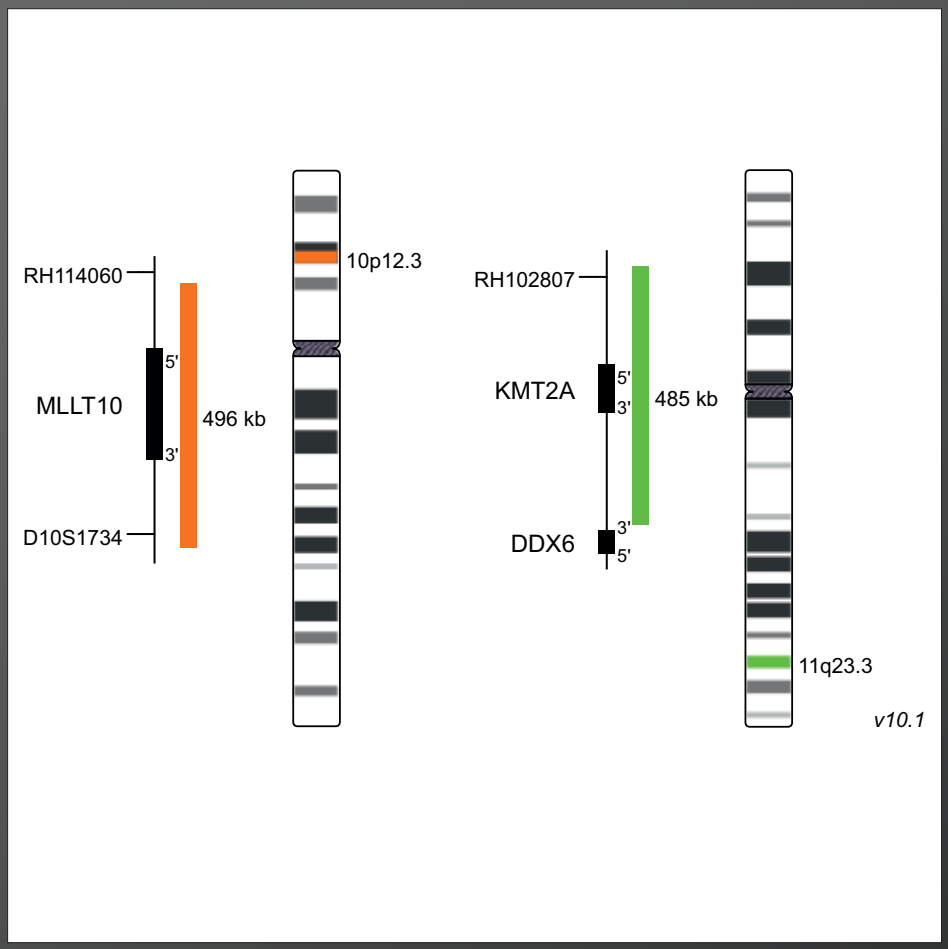
- Acute Lymphoblastic Leukemia (ALL)
- Acute Myelogenous Leukemia (AML)

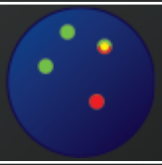
Literature

- De Braekeleer et al (2011) Mol Oncol 5: 555-563
- Meyer et al (2013) Leukemia 27:2165-2176
- Peterson et al (2019) Genes Chromosomes Cancer 58:567-577

FACTSHEET

MetaSystems
Probes



Normal Cell: Two green (2G) and two orange (2O) signals.	
Aberrant Cell (typical results): Two green (2G), one orange (1O), and one green-orange colocalization/fusion signal (1GO).	
Aberrant Cell (typical results): Two green (2G), two orange (2O), and one green-orange colocalization/fusion signals (1GO).	

Complex genomic rearrangements must occur to create an in-frame KMT2A/MLLT10 fusion gene. At least 3 chromosomal breaks are required to produce the pathogenic 5'KMT2A/3'MLLT10 fusion. The majority of cases show an abnormal karyotype; however, cryptic aberrations may occur.

FACTSHEET

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