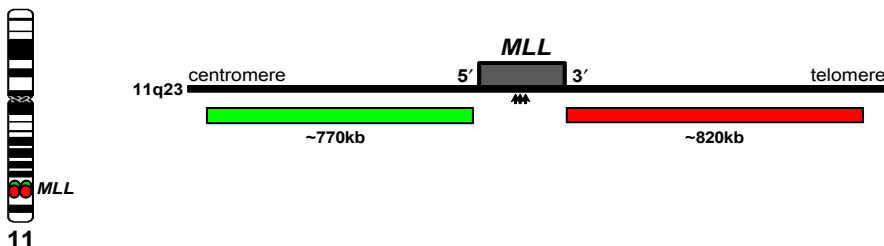


Intended Use

The ready-to-use *MLL* break apart probe is designed to detect translocations involving the *MLL* gene on chromosome 11q23 by fluorescence in situ hybridization (FISH). At least 54 translocation partner genes have been described (1). Translocations of *MLL* are found in both acute lymphoblastic leukemia (ALL) (3-10%) and acute myeloid leukemia (AML) (8-10%) and are clinically relevant (2,3). The prognostic implication, however, depends on the age and phenotype of the leukemia. Infant ALL with *MLL* rearrangement (~80%) are at high risk and require aggressive treatment. In AML, the prognosis is intermediate regardless of age. *MLL* translocations are also found in ~25% of patients with therapy-related leukemias, particularly following treatment with DNA topoisomerase II inhibitors and the prognosis in such patients is poor (2,3). In addition to translocations, deletions of 3' *MLL* and amplification of *MLL* also occur in a subset of ALL and AML (4,5).



Schematic representation of the *MLL* Break Apart translocation probe. Horizontal red and green bars indicate the region covered by the probe (approximate to scale, NCBI Build 36.1/Hg18/2006). Breakpoints in *MLL* span an 8 kb region between exons 5 to 11 (arrows). The directly labeled 5' *MLL* (green) and 3' *MLL* (red) probes flank the *MLL* gene and can detect translocations, amplifications and 3' *MLL* deletions.

Signal Interpretation

In normal diploid metaphase chromosomes and interphase nuclei, the probe generates two fusion signals (red/green or yellow) corresponding to the two normal chromosomes 11 (Figure 1). In cells with chromosomal rearrangement involving *MLL*, the most commonly observed pattern is one fusion representing the normal chromosome 11, and one red and one green signal, representing the derivative chromosomes (Figure 2). Amplifications, 3' *MLL* deletions, additional copies of chromosome 11, unbalanced translocations or multiple copies of derivatives may result in variant signal patterns and these should be confirmed by metaphase chromosome analysis whenever possible (4,5).

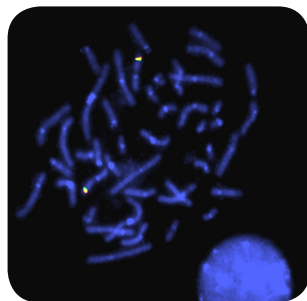


Figure 1: Normal diploid metaphase and interphase nucleus with two fusion (red/green or yellow) signals of *MLL* at 11q23.

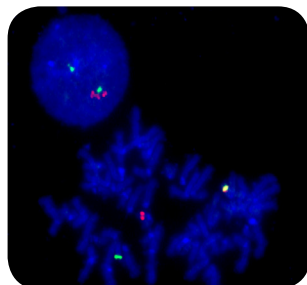


Figure 2: Tumor interphase nucleus and metaphase with one fusion (yellow, normal 11), and break apart of the *MLL* gene: one red (3' *MLL*), and one green (5' *MLL*) signal.

Filter Requirements for Fluorescence Microscopy

Fluorophore	Excitation max	Emission max
Green	496 nm	520 nm
Red	580 nm	603 nm
DAPI	360 nm	460 nm

References

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2. Raimondi SC. 11q23 rearrangements in childhood acute lymphoblastic leukemia. *Atlas Genet Cytogenet Oncol Haematol*. February 2004. URL: <http://atlasgeneticsoncology.org//Anomalies/11q23ChildALLID1321.html>
3. Chowdhury T, Brady HJ. *Blood Cells Mol Dis* 40:192-199, 2008
4. Barber KE, et al. *Genes Chromosomes Cancer* 41:226-271, 2001
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