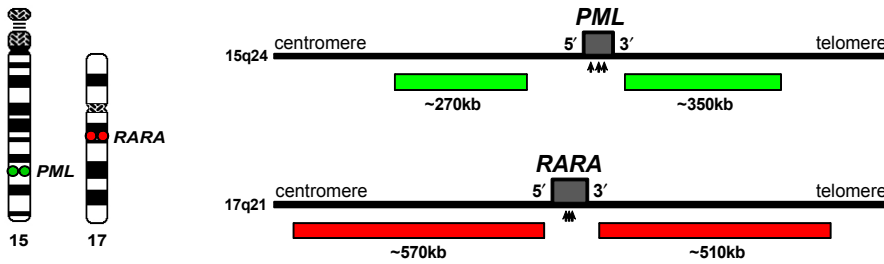


Intended Use

The ready-to-use *PML/RARA* DNA-FISH Probe is designed to detect the translocation between the *PML* gene on chromosome 15q24 (previously assigned to band 15q22) and the *RARA* gene on chromosome 17q21 by fluorescence in situ hybridization (FISH). Translocation t(15;17) is the diagnostic hallmark of acute promyelocytic leukemia and results in the fusion of the *PML* and *RARA* genes (1). The presence of a *PML-RARA* fusion predicts a favorable response to differentiation therapy with all-transretinoic acid (ATRA) and is currently the most curable subtype of acute myeloid leukemia (AML) (1-5). This translocation has also been identified in cases of chronic myeloid leukemia (CML) with promyelocytic blast crisis.



Schematic representation of the *PML/RARA* DNA-FISH Probe: Horizontal red and green bars indicate the regions covered by the probes (approximate to scale, NCBI Build 36.1/Hg18/2006). The directly labeled *PML* (green) and *RARA* (red) probes flank the common translocation breakpoints (arrows). In *PML*, the breakpoints cluster in three regions: bcr1 (exon 6-7, right arrow) (70%), bcr2 (exon 5-6, middle arrow) (10%), and bcr3 (intron 3-4, left arrow) (20%). In *RARA*, the breakpoints cluster within the approximate 17 kb intron 2.

Signal Interpretation

In normal diploid metaphase chromosomes and interphase nuclei, the *PML/RARA* DNA-FISH Probe generates two green and two red signals corresponding to the two normal chromosomes 15 and 17 (Figure 1), respectively. In cells with translocation between *PML* and *RARA*, the most commonly observed pattern is one green and one red signal, representing the normal chromosomes 15 and 17, and two fusion signals (red/green or yellow) representing the two translocated chromosomes (Figure 2). Variant, masked, or 3-way translocations resulting in other signal patterns have been reported (2-5).

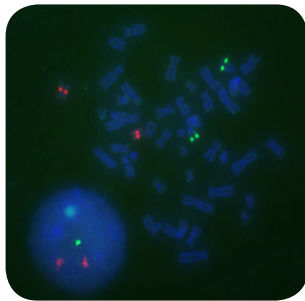


Figure 1: Normal diploid metaphase and interphase nucleus with two green (*PML*) and two red (*RARA*) signals.

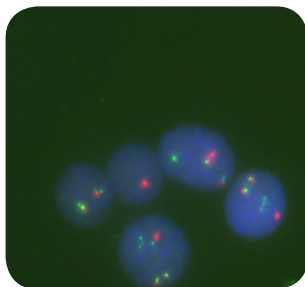


Figure 2: Tumor interphase nuclei with one green (*PML*), one red (*RARA*), and two fusion signals (red/green or yellow) signal.

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

- Melnick A, Licht JD. Blood 93:3167-3215, 1999
- Wan TS, et al. Oncol Rep 17:799-805, 2007
- Grimwade D, et al. Blood 90:4876-4885, 1997
- Brockman SR, et al. Cancer Genet Cytogenet 145:144-15, 2003
- Huret JL, Chomienne C. t(15;17)(q22;q21). Atlas Genet Cytogenet Oncol Haematol. April 1998. URL: <http://atlasgeneticsoncology.org/Anomalies/t1517ID1035.html>

For *in vitro* diagnostic use only. For professional use only.

IVD/12-008 v.05.20.10