ZytoLight® SPEC CSF1R Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC CSF1R Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal region 5q32 harboring the CSF1R (colony stimulating factor 1 receptor, a.k.a. FMS) gene.

The CSF1 receptor is activated by dimerization upon binding of its ligand CSF1 and is involved in macrophage development.

Rearrangement of the CSF1R gene was first detected in an acute megakaryoblastic leukemia (AMKL) cell line generating the RBM6-CSF1R fusion gene. A MEF2D-CSF1R fusion gene was described in a patient with primary pre-B cell acute lymphoblastic leukemia (pre-B ALL). Both fusion proteins contain the intact kinase domain of CSF1R.

Philadelphia chromosome-like ALL (Ph-like ALL) is a subgroup of B-cell precursor ALL and is associated with a high risk of treatment failure. SSBP2-CSF1R fusions were detected in some patients with Ph-like ALL. They result from either the balanced translocation t(5;5)(q14;q32) or the duplication dup(5)(q14q32). Expression of this fusion gene results in cytokine-independent growth and enhanced STAT5 activation which are inhibited by dasatinib *in vitro*. CSF1R signaling was also shown to be suppressed by the ABL1 kinase inhibitor imatinib.

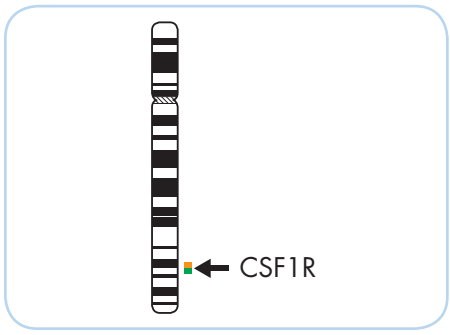
Hence, the detection of CSF1R rearrangements by FISH may help in selecting ALL patients eligible for treatment with CSF1R inhibitors.

References
Dewar AL, et al. (2005) Blood 105: 3127-32.
Gu TL, et al. (2007) Blood 110: 323-33.
Lilljebjörn H, et al. (2014) Leukemia 28: 977-9.
Roberts KG, et al. (2014) N Engl J Med 371: 1005-15.
Schwab C, et al. (2014) Blood 124: 3773.

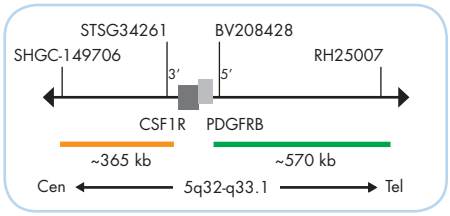
Probe Description

The ZytoLight® SPEC CSF1R Dual Color Break Apart Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10.0 ng/µl), which target sequences mapping in 5q32-q33.1** (chr5:149,548,518-150,118,449) distal to the CSF1R breakpoint region.
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 5q32** (chr5:149,058,515-149,421,081) proximal to the CSF1R breakpoint region.
- Formamide based hybridization buffer



Ideogram of chromosome 5 indicating the hybridization locations.

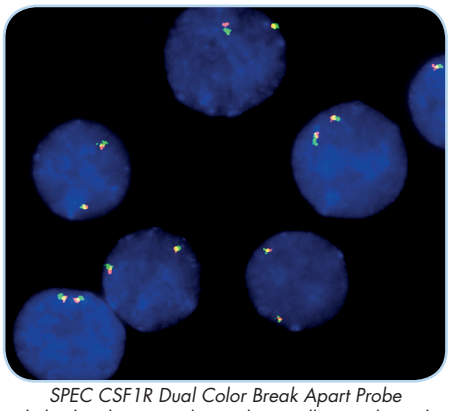


SPEC CSF1R Probe map (not to scale).

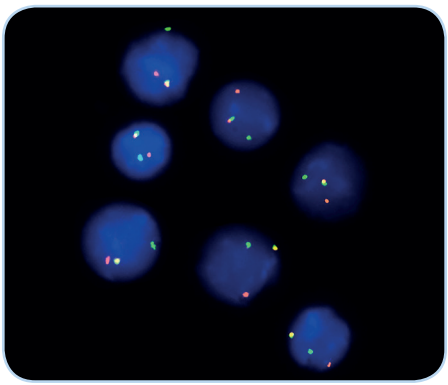
Results

In an interphase nucleus of a normal cell lacking a translocation involving the 5q32-q33.1 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 5q32-q33.1 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 5q32-q33.1 locus and one 5q32-q33.1 locus affected by a translocation.

Duplication of the 5q32 locus will result in additional orange signals.



SPEC CSF1R Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Blood smear with translocation of the CSF1R gene as indicated by one non-rearranged orange/green fusion signal, one orange and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2202-50	ZytoLight SPEC CSF1R Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. IVD labeled products are only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

***According to Human Genome Assembly GRCh37/hg19*