ZytoLight® SPEC CRLF2 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC CRLF2 Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal regions Xp22.33 and Yp11.32 harboring the CRLF2 (cytokine receptor-like factor 2, a.k.a. CRL2, TSLPR) gene.

The CRLF2 protein interacts with IL7R to form a receptor for TSLP, binding of which activates cell signaling through JAK/STAT pathways.

Approximately 7% of patients with B-cell precursor ALL (B-ALL) and more than 50% of B-ALL in children with Down syndrome harbor alterations involving the CRLF2 gene. These include the translocations t(X;14)(p22.33;q32.3) or t(Y;14)(p11.32;q32.3) which fuse the entire CRLF2 gene to the immunoglobulin heavy chain enhancer region (IGH-CRLF2).

Another common alteration is an interstitial deletion involving the pseudoautosomal region (PAR1) of the sex chromosomes upstream of CRLF2, juxtaposing the first non-coding exon of P2RY8 to the entire coding region of CRLF2 (P2RY8-CRLF2).

These rearrangements, which are often accompanied by JAK mutations, result in overexpression of CRLF2 and were shown to contribute to lymphoid transformation.

Patients with CRLF2 rearrangements and JAK mutations have a poor event-free and overall survival.

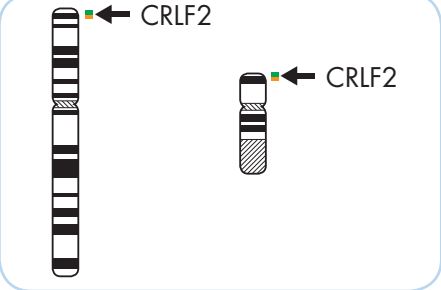
Moreover, the detection of CRLF2 rearrangements by FISH may help in selecting B-ALL patients eligible for therapy with inhibitors of the JAK/STAT pathway.

References
Harvey RC, et al. (2010) Blood 115: 5312-21.
Mullighan CG, et al. (2009) Nat Genet 41: 1243-6.
Roberts KG, et al. (2014) N Engl J Med 371: 1005-15.
Russell LJ, et al. (2009) Blood 114: 2688-98.
Tasian SK, et al. (2012) Blood 120: 833-42.

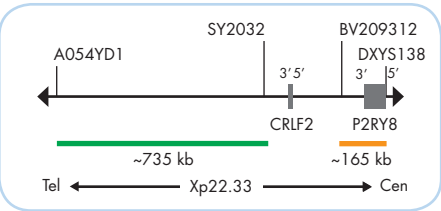
Probe Description

The ZytoLight® SPEC CRLF2 Dual Color Break Apart Probe is composed of:

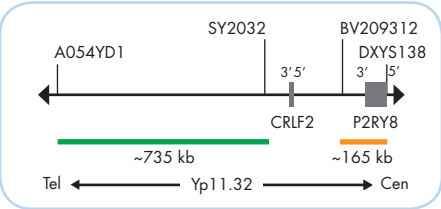
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10.0 ng/µl), which target sequences mapping in Xp22.33 (chrX:513,125-1,245,395), and Yp11.32** (chrY:463,125-1,195,395) distal to the CRLF2 breakpoint region.
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in Xp22.33 (chrX:1,497,976-1,660,328), and Yp11.32** (chrY:1,498,976-1,657,328) proximal to the CRLF2 breakpoint region.
- Formamide based hybridization buffer



Ideogram of chromosome X (left) and X (right) indicating the hybridization locations.



SPEC CRLF2 Probe map (not to scale).



SPEC CRLF2 Probe map (not to scale).

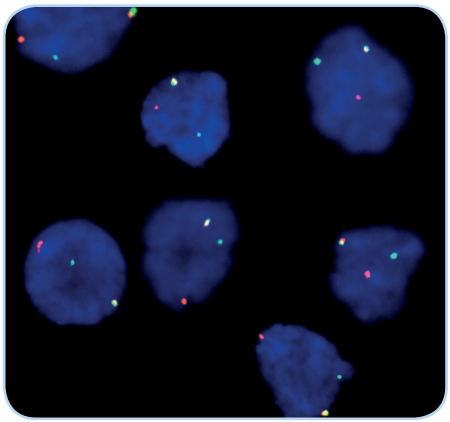
Results

In an interphase nucleus of a normal female cell lacking a translocation involving the Xp22.33 band, two orange/green fusion signals are expected representing normal (non-rearranged) Xp22.33 loci.

In an interphase nucleus of a normal male cell lacking a translocation involving the Xp22.33 or Yp11.32 band, two orange/green fusion signals are expected representing normal (non-rearranged) Xp22.33 and Yp11.32 loci.

A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal Xp22.33 or Yp11.32 locus and one Xp22.33 or Yp11.32 locus affected by a translocation.

Loss of the orange signals or orange signals of reduced size are the result of deletions proximal to the CRLF2 breakpoint region.



Bone marrow smear with translocation affecting the CRLF2 gene locus as indicated by one non-rearranged orange/green fusion signal, one orange signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
Z-2201-50	ZytoLight SPEC CRLF2 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
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*