

ZytoLight® SPEC CRLF2 Dual Color Break Apart Probe

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.

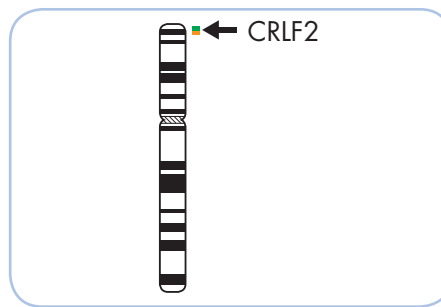
Moreover, the detection of CRLF2 rearrangements by FISH may help in selecting B-ALL patients eligible for therapy with inhibitors of the JAK/STAT pathway.

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

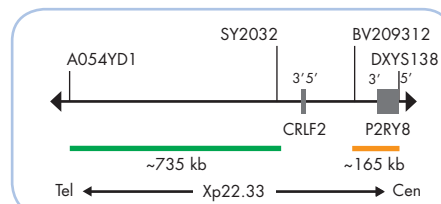
The SPEC CRLF2 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the Xp22.33 and Yp11.32 band, respectively. The orange fluorochrome direct labeled probe hybridizes proximal to the CRLF2 gene at Xp22.33 and Yp11.32, the green fluorochrome direct labeled probe hybridizes distal to the CRLF2 gene at Xp22.33 and Yp11.32.



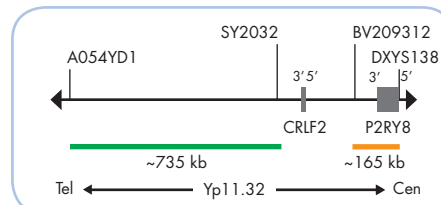
Ideogram of chromosome X indicating the hybridization locations.



Ideogram of chromosome Y indicating the hybridization locations.



SPEC CRLF2 Probe map (not to scale).



SPEC CRLF2 Probe map (not to scale).

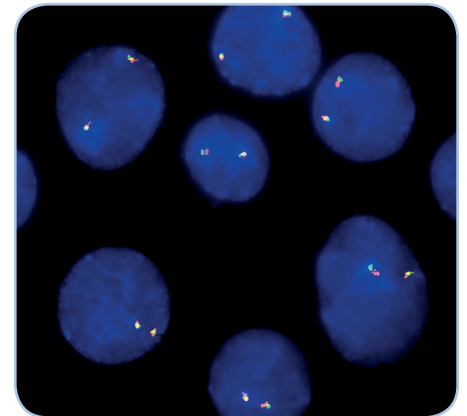
Results

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.



SPEC CRLF2 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.

Prod. No.	Product	Label	Tests* (Volume)
Z-2201-200	ZytoLight SPEC CRLF2 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 500 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20
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. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.