XL CRLF2 BA

Break Apart Probe

Order No.:
D-5130-100-OG

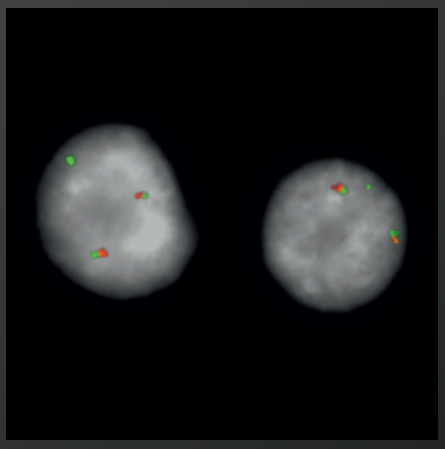
Description

XL CRLF2 BA is designed as a break apart probe. The orange labeled probe hybridizes proximal to the breakpoint in the CRLF2 gene region at Xp22.33 and Yp11.32, the green labeled probe hybridizes distal to the breakpoint at Xp22.33 and Yp11.32.

Clinical Details

Acute lymphoblastic leukemia (ALL) is the most common malignancy in children (prevalence of approximately 1:1500). Children with Down syndrome have a 10- to 20-fold increased risk of developing acute leukemia. B-Cell dependent BCR-ABL1-like ALL, also known as Philadelphia chromosome (Ph)-like ALL, is a high-risk subset with a gene expression profile that shares significant overlap with that of Ph-positive (Ph+) ALL, but lacking the BCR-ABL1 fusion. In 2017, the WHO recognized BCR-ABL1-like ALL as new entity. Chromosomal rearrangements resulting in the overexpression of cytokine receptor like factor 2 (CRLF2) can be found in up to 50% of BCR-ABL1-like ALL cases. The CRLF2 gene is located in the pseudoautosomal region 1 (PAR1) of the X and the Y chromosome. Three genetic key mechanisms regarding CRLF2 and ALL are known. First, the CRLF2 gene is placed under the control of the IGH enhancer. Translocations of the type t(X;14) or t(Y;14) are the genetic basis for this aberration. Second, fusion of CRLF2 to CSF2RA, a further PAR1 gene, has also been described. Third, cryptic interstitial deletions juxtaposing the initial non-coding exon of the purinergic receptor P2Y8 (P2RY8) and CRLF2 have been shown. The resulting P2RY8-CRLF2 fusion being under the control of the P2RY8 promoter, is strongly transcribed in lymphoid cells. CRLF2 rearrangements result in increased protein levels, which initiate significantly enhanced JAK/STAT signaling, whereby disproportionate JAK and subsequent STAT5 activation induces strongly enhanced B-cell activation and proliferation.

XL CRLF2 BA detects chromosomal aberrations resulting from CRLF2 gene rearrangements (deletions and translocations). XL P2RY8 del (D-5150-100-OG) can be used as an additional tool to detect the presence of the P2RY8-CRLF2 fusion gene.



XL CRLF2 BA hybridized to bone marrow cells. Two aberrant cells of a patient with a gonosomal constellation of XXY are shown. Two normal CRLF2 loci were observed indicated by two fusion signals. The separate green signal indicates a deletion proximal of CRLF2.

Clinical Applications

- ALL

Literature

- Roll and Reuther (2010) Cancer Res 70:7347-7352
- Yoda et al (2010) Proc Natl Acad Sci 107:252-257
- Tasian et al (2017) Blood 130:2064-2072

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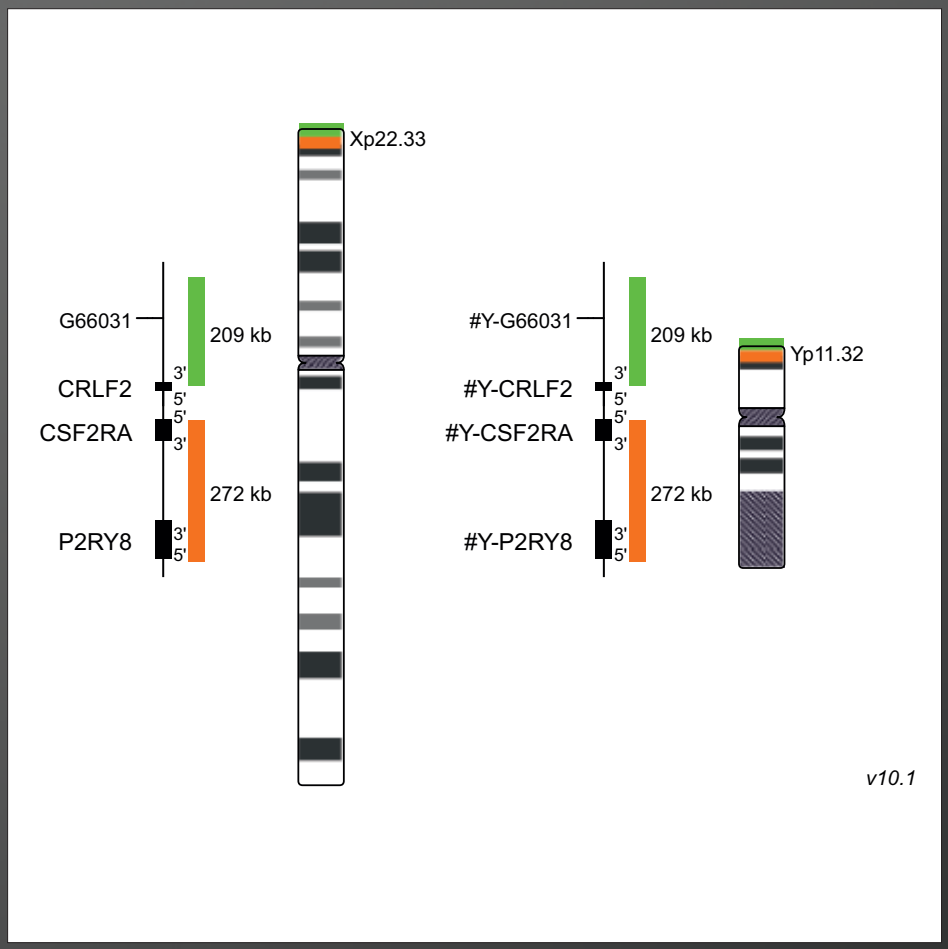
MetaSystems Probes



Normal cell: Two green-orange colocalization/fusion signals (2GO).	
Aberrant Cell (typical results): One green-orange colocalization/fusion signal (1GO), one separate green (1G) and orange (1O) signal each resulting from a chromosome break in the relevant locus.	
Aberrant Cell (typical results): One green-orange (1GO) colocalization/fusion signal and one green (1G) signal resulting from the loss of one orange signal.	

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