ZytoLight® SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe

Intended Purpose

The Zyto*Light* SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe is designed for the detection of the specific translocation involving the chromosomal region 12p13.2 harboring the ETV6 (ETS variant 6, a.k.a. TEL) gene and the chromosomal region 21q22.12 harboring the RUNX1 (runt related transcription factor 1, a.k.a. AML1) gene. The balanced chromosomal translocation t(12;21)(p13.2;q22.1), which leads to ETV6/RUNX1 fusion, represents the most frequent genetic rearrangement in initial childhood B-cell precursor (BCP) acute lymphoblastic leukemia (ALL) (19-27%) and has been associated with good prognosis.

The ETV6/RUNX1 fusion protein, comprising a putative repressor domain of ETV6, a member of the ETS family of transcription factors, fused to RUNX1, the DNA-binding subunit of the RUNX1/CBF beta transcription factor complex, acts as a trans-dominant repressor of RUNX1 regulated target genes involved in hematopoiesis.

Three secondary aberrations in ETV6/RUNX1 positive ALL have been found to negatively influence the clinical course: deletion of the second non-translocated ETV6 allele, gains of the RUNX1 gene, and duplication of the derivative chromosome 21.

Detection of t(12;21) by Fluorescence *in situ* Hybridization enables the simultaneous identification of the most common secondary changes and thus provides additional infor*Mation* about the possible outcome of the disease in patients with ALL.

References

Fenrick R, *et al.* (1999) Mol Cell Biol 19: 6566-74.
Martínez-Ramírez A, *et al.* (2001) Haematologica 86: 1245-53.
Morrow M, *et al.* (2007) Oncogene 26: 4404-14.
Peter A, *et al.* (2009) Eur J Haematol 83: 420-32.
Shurtleff SA, *et al.* (1995) Leukemia 9: 1985-9.

Probe Description

The Zyto*Light* SPEC ETV6/RUNX1 Dual Color Dual Fusion Probe is composed of:

- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~6 ng/µl), which target sequences mapping in 12p13.2* (chr12:11,586,400-12,454,330) harboring the ETV6 region (see Fig. 1).
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~12,0 ng/µl), which target sequences mapping in 21q22.12* (chr21:36,106,492-36,657,941) harboring the RUNX1 gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

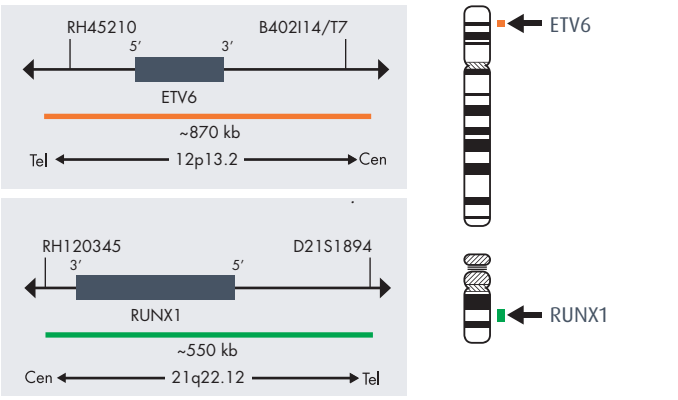
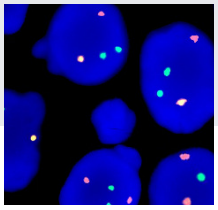


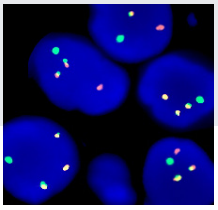
Fig. 1: Top: SPEC ETV6 Probe map; Bottom: SPEC RUNX1 Probe map (not to scale); Right: Ideograms of chromosome 12 and 21 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a translocation involving the respective gene regions, two separate green and orange signals appear.
Aberrant situation: A gene fusion is indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.



Hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Bone marrow tissue section with translocation affecting the ETV6/RUNX1 loci as indicated by one separate orange signal, one separate green signal, and two orange/green fusion signals.

Labels	Chromosome	Reg. Status	Tests	Order No.
	12, 21	CE/IVD	5 (50 µl)	**Z-2157-50**
			20 (200 µl)	**Z-2157-200**