ZytoLight® SPEC PAX5 Dual Color Break Apart Probe

Intended Purpose

The ZytoLight SPEC PAX5 Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal region 9p13.2 harboring the PAX5 (paired box 5, a.k.a. BSAP) gene.

The transcription factor PAX5 activates crucial genes for B-cell lineage differentiation and represses genes that play an important role in other hematopoietic lineages. PAX5 is also implicated in human B-cell malignancies, as it is deregulated by chromosomal translocations in a subset of acute lymphoblastic leukemias (ALL).

B-progenitor ALL (B-ALL), a common pediatric malignancy, is characterized by the participation of PAX5 in specific chromosomal rearrangements that generate novel fusion proteins. All PAX5 fusion proteins contain the PAX5 DNA-binding domain and thus are predicted to retain the ability to bind to PAX5 transcriptional targets, but no longer provide normal transcriptional regulatory functions. The fusion proteins contribute to B-ALL for*Mation* by competitively inhibiting the transcriptional activation of wildtype PAX5. PAX5 rearranged ALL patients were shown to respond well to treatment with prednisone. Hence, the identification of PAX5 rearrangements by FISH may be of therapeutic significance in ALL.

References

Busslinger M, *et al.* (1996) Proc Natl Acad Sci U S A 93: 6129-34.
Cobaleda C, *et al.* (2007) Nat Immunol 8: 463-70.
Coyaud E, *et al.* (2010) Blood 115: 3089-97.
Mullighan CG, *et al.* (2007) Nature 446: 758-64.
Nebral K, *et al.* (2009) Leukemia 23: 134-43.
Offit K, *et al.* (1992) Blood 80: 2594-9.

Probe Description

The ZytoLight SPEC PAX5 Dual Color Break Apart Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 9p13.2* (chr9:36,331,787-36,837,502) distal to the PAX5 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 9p13.2* (chr9:37,043,219-37,336,413) proximal to the PAX5 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

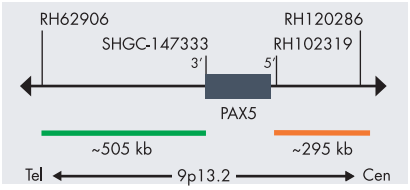


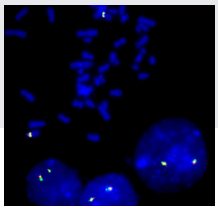
Fig. 1: SPEC PAX5 Probe map (not to scale)

Ideogram of chromosome 9 indicating the hybridization locations

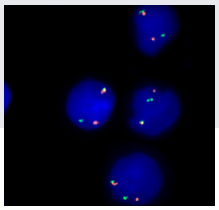
Results

Normal situation: In interphases of normal cells or cells without an intragenic translocation involving the PAX5 gene region, two green/orange fusion signals appear.

Aberrant situation: One PAX5 gene region affected by an intragenic translocation is indicated by one separate green signal and one separate orange signal. In a cell with an unbalanced translocation resulting in a 3′ deletion, one separate orange signal and one orange/green fusion signal will be observed.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus and to metaphase chromosomes of a normal cell.



Bone marrow smear with rearrangement affecting the PAX5 gene as indicated by one non-rearranged orange/green fusion signal, one orange and one separate green signal.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	9	CE/IVD	5 (50 µl)	**Z-2300-50**

ZytoLight® SPEC NTRK2 Dual Color Break Apart Probe

Intended Purpose

The ZytoLight SPEC NTRK2 Dual Color Break Apart Probe (PL163) is intended to be used for the qualitative detection of translocations involving the human NTRK2 gene at 9q21.33 in formalin-fixed, paraffin-embedded specimens by fluorescence *in situ* hybridization (FISH). The probe is intended to be used in combination with the ZytoLight FISH-Tissue Implementation Kit (Prod. No. Z-2028-5/-20).

The product is intended for professional use only. All tests using the product should be performed in a certified, licensed anatomic pathology laboratory under the supervision of a pathologist/human geneticist by qualified personnel.

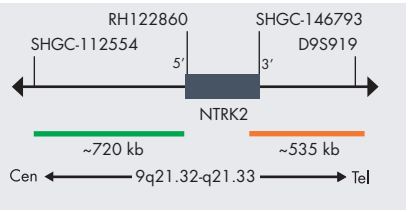
The probe is intended to be used as an aid to the differential diagnosis of various cancers and therapeutic measures should not be initiated based on the test result alone.

Probe Description

The ZytoLight SPEC NTRK2 Dual Color Break Apart Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 9q21.32-q21.33* (chr9:86,569,621-87,287,312) proximal to the NTRK2 breakpoint region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.5 ng/µl), which target sequences mapping in 9q21.33* (chr9:87,589,037-88,124,082) distal to the NTRK2 breakpoint region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19



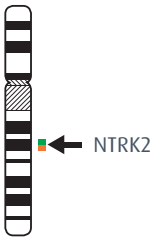
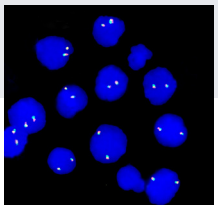


Fig. 1: SPEC NTRK2 Probe map (not to scale); Right: Ideogram of chromosome 9 indicating the hybridization locations

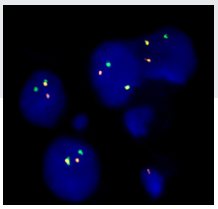
Results

Normal situation: In interphases of normal cells or cells without a translocation involving the NTRK2 gene region, two green/orange fusion signals appear.

Aberrant situation: One NTRK2 gene region affected by a translocation is indicated by one separate green signal and one separate orange signal. Isolated orange signals are the result of deletions proximal to the NTRK2 breakpoint region or are due to unbalanced translocations affecting this chromosomal region.



Hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Example of an aberrant signal pattern: Peritoneal carcinoma tissue section with rearrangement of the NTRK2 gene as indicated by one non-rearranged orange/green fusion signal, one orange, and one separate green signal. Kindly provided by the Institute of Pathology, University Medical Center Göttingen, Germany.

Labels	Chromosome	Reg. Status	Tests	Order No.
●|●	9	CE/IVD	5 (50 µl)	**Z-2205-50**
			20 (200 µl)	**Z-2205-200**