ZytoLight® SPEC NTRK3 Dual Color Break Apart Probe

CE IVD

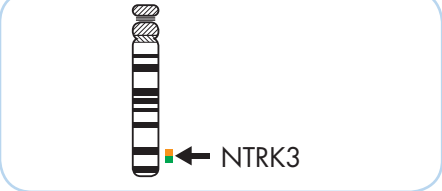
Background

The ZytoLight® SPEC NTRK3 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 15q25.3 harboring the NTRK3 (neurotrophic receptor tyrosine kinase 3, a.k.a. TRKC) gene.

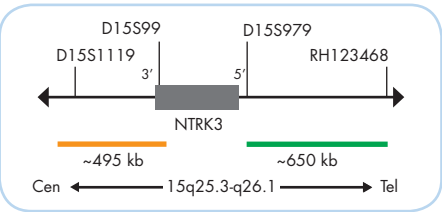
NTRK3 is a receptor tyrosine kinase (TK) for neurotrophin 3 (NT3) and plays a key role in central and peripheral nervous system development as well as in cell survival. Translocations affecting the NTRK3 gene have been reported in several cancer types, including glioblastomas, Philadelphia chromosome-like acute lymphoblastic leukemia, congenital fibrosarcomas, cellular mesoblastic nephromas, acute myeloid leukemia, radiation-associated thyroid cancer, secretory breast carcinoma, and mammary analog secretory carcinoma of the salivary gland. The most frequent rearrangement involving the NTRK3 gene is the t(12;15)(p13.2;q25) which results in a fusion between the 5′ part of the ETV6 gene and the 3′ part of the NTRK3 gene. This fusion gene encodes a hybrid protein comprising the TK domain of NTRK3 and the dimerization domain of ETV6 which leads to a ligand-independent TK activity. The treatment of patients with NTRK1, 2, or 3 fusion-positive cancers with an NTRK inhibitor, such as the FDA-approved drugs larotrectinib or entrectinib, is associated with high response rates, regardless of NTRK gene, fusion partner, and tumor type. Hence, detection of NTRK3 translocations by Fluorescence *in situ* Hybridization (FISH) may be of diagnostic and therapeutic relevance.

Probe Description

The SPEC NTRK3 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 15q25.3-q26.1 band. The orange fluorochrome direct labeled probe hybridizes proximal to the NTRK3 breakpoint region at 15q25.3, the green fluorochrome direct labeled probe hybridizes distal to the NTRK3 breakpoint region at 15q25.3-q26.1.



Ideogram of chromosome 15 indicating the hybridization locations.



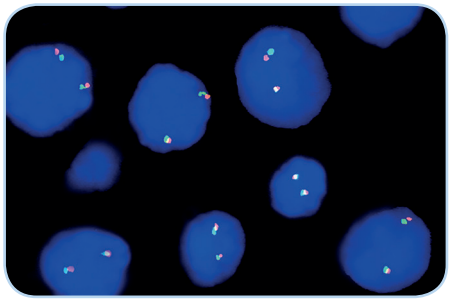
SPEC NTRK3 Probe map (not to scale).

References

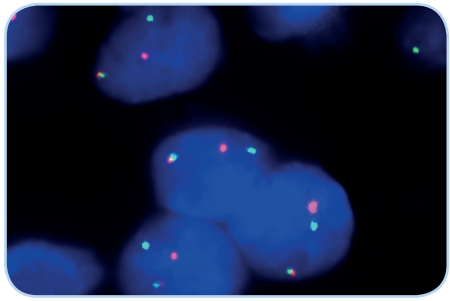
Amatu A, et al. (2016) ESMO Open 1: e000023.
Arce C, et al. (2005) World J Surg Oncol 3: 35.
Cocco E, et al. (2018) Nat Rev Clin Oncol 15: 731-47.
Knezevich SR, et al. (1998) Nat Genet 18: 184-7.
Leeman-Neill RJ, et al. (2014) Cancer 120: 799-807.
Nagasubramanian R, et al. (2016) Pediatr Blood Cancer 63: 1468-70.
Raez LE & Rolfo C (2016) Lung Cancer Manag 5: 1-4.
Roberts KG, et al. (2014) N Engl J Med 371: 1005-15.
Skálová A, et al. (2010) Am J Surg Pathol 34: 599-608.
Solomon JP & Hechtman JF (2019) Cancer Res 79: 3163-8.
Tognon C, et al. (2002) Cancer Cell 2: 367-76.
Wang L, et al. (2017) J Mol Diagn 19: 387-96.
Wu G, et al. (2014) Nat Genet 46: 444-50.

Results

In an interphase nucleus of a normal cell lacking a translocation involving the 15q25.3-q26.1 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 15q25.3-q26.1 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 15q25.3-q26.1 locus and one 15q25.3-q26.1 locus affected by a translocation. Isolated orange signals are the result of deletions distal to the NTRK3 breakpoint region or are due to unbalanced translocations affecting this chromosomal region.



SPEC NTRK3 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



Secretory breast carcinoma tissue section with translocation affecting the 15q25.3-q26.1 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-2206-50	ZytoLight SPEC NTRK3 Dual Color Break Apart Probe CE IVD	●/●	5 (50 µl)
Z-2206-200	ZytoLight SPEC NTRK3 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-5	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 560 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.*