

ZytoDot® 2C SPEC NTRK3 Break Apart Probe



Background

The ZytoDot® 2C SPEC NTRK3 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.

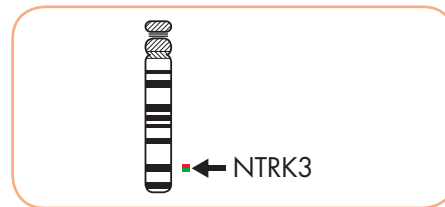
The most frequent rearrangement involving the NTRK3 gene is the t(12;15)(p13.2;q25) which results in a fusion between the 5' part of the ETV6 gene and the 3' part of the NTRK3 gene. This fusion gene encodes a hybrid protein comprising the TK domain of NTRK3 and the dimerization domain of ETV6, which 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 CISH may be of diagnostic and therapeutic relevance.

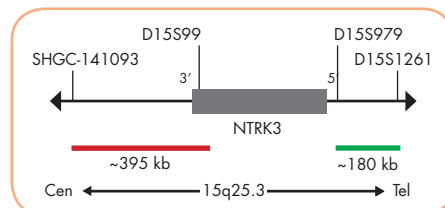
Probe Description

The ZytoDot® 2C SPEC NTRK3 Break Apart Probe is composed of:

- Digoxigenin-labeled polynucleotides (~0.50 ng/μl), which target sequences mapping in 15q25.3** (chr15:88,825,346-89,007,107) distal to the NTRK3 breakpoint region.
- Dinitrophenyl-labeled polynucleotides (~0.75 ng/μl), which target sequences mapping in 15q25.3** (chr15:88,077,591-88,471,002) proximal to the NTRK3 breakpoint region.
- Formamide based hybridization buffer



Ideogram of chromosome 15 indicating the hybridization locations.



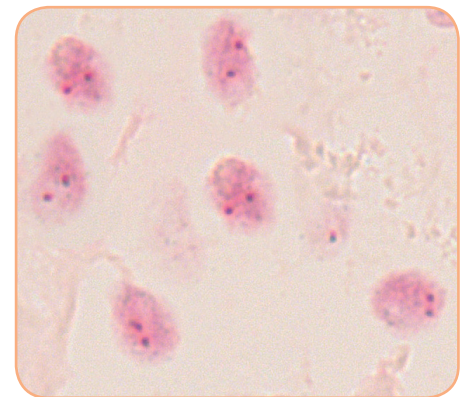
SPEC NTRK3 Probe map (not to scale).

References

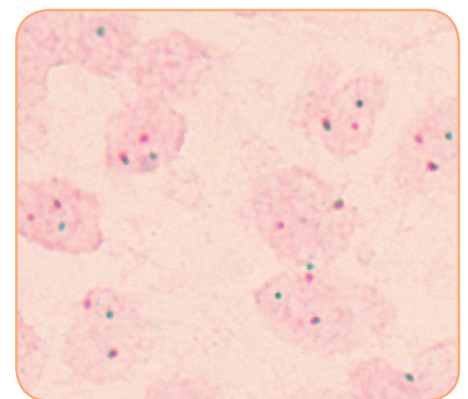
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Results

In an interphase nucleus of a normal cell lacking a translocation involving the 15q25.3 band, using the ZytoDot® 2C CISH Implementation Kit, two red/green fusion signals are expected representing two normal (non-rearranged) 15q25.3 loci. A signal pattern consisting of one red/green fusion signal, one red signal, and a separate green signal indicates one normal 15q25.3 locus and one 15q25.3 locus affected by a translocation. Isolated red signals are the result of deletions distal to the NTRK3 breakpoint region or are due to unbalanced translocations affecting this chromosomal region.



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



Mesoblastic nephroma tissue section with rearrangement of the NTRK3 gene as indicated by one red/green fusion (non-rearranged) signal, one red signal, and one separate green signal.

Prod. No.	Product	Label	Tests* (Volume)
C-3079-100	ZytoDot 2C SPEC NTRK3 Break Apart Probe CE IVD	DIG/DNP	10 (100 μl)
Related Products			
C-3044-10	ZytoDot 2C CISH Implementation Kit CE IVD		10
Incl. Heat Pretreatment Solution EDTA, 150 ml; Pepsin Solution, 1 ml; Wash Buffer SSC, 210 ml; 20x Wash Buffer TBS, 50 ml; Anti-DIG/DNP-Mix, 1 ml; HRP/AP-Polymer-Mix, 1 ml; AP-Red Solution A, 0.2 ml; AP-Red Solution B, 4 ml; HRP-Green Solution A, 0.2 ml; HRP-Green Solution B, 4 ml; Nuclear Blue Solution, 4 ml; Mounting Solution (alcoholic), 1 ml			

* Using 10 μl probe solution per test. IVD labeled products are only available in certain countries. All other countries research use only! Please contact your local dealer for more information.

**According to Human Genome Assembly GRCh37/hg19