

# FlexISH® NTRK1/NTRK3 DistinguISH™ Probe

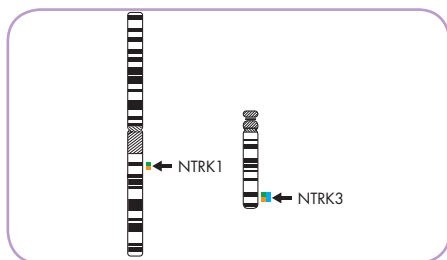


## Background

The FlexISH® NTRK1/NTRK3 DistinguISH™ Probe is designed to detect rearrangements affecting the chromosomal region 1q23.1 and 15q25.3 harboring the NTRK1 (neurotrophic receptor tyrosine kinase 1, a.k.a. TRKA, TRK) and NTRK3 (neurotrophic receptor tyrosine kinase 3, a.k.a. TRKC) gene region, respectively. The neurotrophic tyrosine receptor kinase genes (NTRK1, NTRK2, and NTRK3) encode a family of receptor tyrosine kinases that serve important roles in cell survival, proliferation, and cellular differentiation in healthy human cells. The tumor types in which NTRK gene fusions have been detected are diverse, and include, e.g., breast cancer, non-small cell lung cancer, sarcoma, melanoma, and thyroid carcinoma. The treatment of patients with NTRK fusion-positive cancers with a 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 NTRK1 and NTRK3 rearrangements by FISH may be of therapeutic significance.

### References

- Haller F, et al. (2016) J Pathol 238: 700-10.
- Hsiao SJ, et al. (2019) J Mol Diagn 21: 553-71.
- Knezevich SR, et al. (1998) Nat Genet 18: 184-7.
- Martin-Zanca D, et al. (1986) Nature 319: 743-8.
- Solomon JP & Hechtman JF (2019) Cancer Res 79: 3163-8.

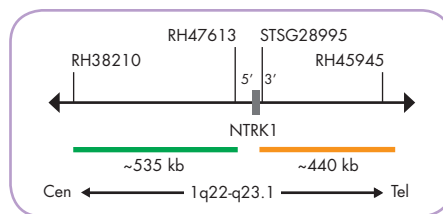


Ideograms of chromosomes 1 (left) and 15 (right) indicating the hybridization locations.

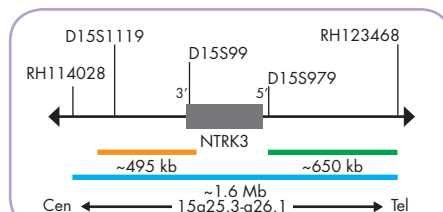
## Probe Description

The FlexISH® NTRK1/NTRK3 DistinguISH™ Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10.0 ng/µl), which target sequences mapping in 1q22-q23.1\*\* (chr1:156,245,849-156,781,745) proximal to the NTRK1 breakpoint region and in 15q25.3-q26.1\*\* (chr15:88,825,346-89,475,889) distal to the NTRK3 breakpoint region.
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~2.5 ng/µl), which target sequences mapping in 1q23.1\*\* (chr1:156,854,527-157,296,918) distal to the NTRK1 breakpoint region and in 15q25.3\*\* (chr15:87,976,717-88,471,002) proximal to the NTRK3 breakpoint region.
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides, (~70.0 ng/µl), which target sequences mapping in 15q25.3-q26.1\*\* (chr15:87,845,459-89,475,889) harboring the NTRK3 gene region.
- Formamide based hybridization buffer



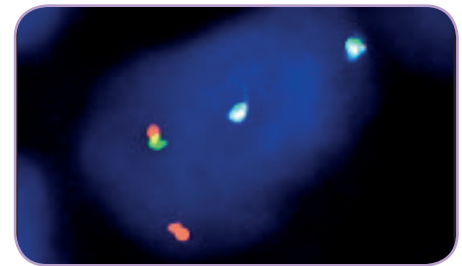
SPEC NTRK1 Probe map (not to scale).



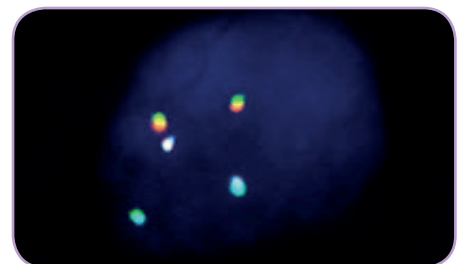
NTRK3 Probe map (not to scale).

## Results

In an interphase nucleus without NTRK1 or NTRK3 rearrangements, two NTRK1 specific green/orange fusion signals and two NTRK3 specific green/orange/blue fusion signals are expected. An NTRK1 rearrangement is indicated by one separate green and one separate orange signal, both not co-localizing with blue signals. An NTRK3 rearrangement is indicated by one separate green and one separate orange signal, both co-localizing with blue signals. Isolated orange signals and orange/blue fusion signals are the result of deletions distal to the NTRK1 and NTRK3 breakpoint region, respectively, or are due to unbalanced translocations affecting this chromosomal region.



Cell which shows two green/orange/blue fusion signals (NTRK3) and one green/orange fusion signal (NTRK1). NTRK1 rearrangement is indicated by one isolated orange signal, not co-localizing with a blue signal.



Cell which shows two green/orange fusion signals and one green/orange/blue fusion signal. NTRK3 rearrangement is indicated by one separate orange and one separate green signal, both co-localizing with blue signals.

Prod. No.	Product	Label	Tests* (Volume)
Z-2314-50	FlexISH NTRK1/NTRK3 DistinguISH Probe CE IVD	●/●/●	5 (50 µl)
Z-2314-200	FlexISH NTRK1/NTRK3 DistinguISH Probe CE IVD	●/●/●	20 (200 µl)
Related Products			
Z-2182-5	FlexISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1 ml; 5x FlexISH Wash Buffer, 150 ml; DAPI/DuraTect-Solution, 0.2 ml		5
Z-2182-20	FlexISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; 5x FlexISH Wash Buffer, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

\* 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