FlexISH® RET/KIF5B TriCheck™ Probe

CE IVD

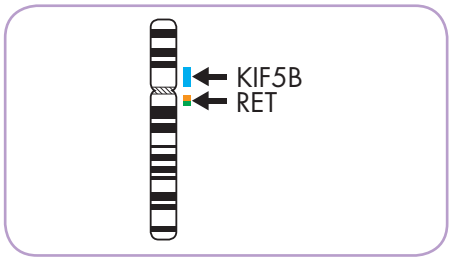
Background

The FlexISH® RET/KIF5B TriCheck™ Probe is designed to detect inversions involving the chromosomal region 10q11.21 harboring the rearranged during transfection (RET) gene and the chromosomal region 10p11.22 harboring the kinase family member 5B (KIF5B) gene. Moreover, using this probe it is possible to discriminate between KIF5B-RET inversions and RET translocations involving fusion partners other than KIF5B (e.g., BCR, FGFR1OP, and PTC). RET rearrangements, including inversions and translocations, are found in non-small cell lung cancer (NSCLC) with an incidence of 1-2%. The pericentric inversion of chromosome 10 [inv(10)(p11.2q11.2)] leads to a fusion transcript of the KIF5B gene and the RET proto-oncogene and, thus, forms a chimeric protein. The resulting homo-dimerization of the coiled-coil domains of KIF5B causes an aberrant activation of the receptor tyrosine kinase (RTK) of RET, a mechanism known from KIF5B-ALK fusion which is also found in non-small cell lung adenocarcinoma (LADC). LADC patients with KIF5B-RET fusions are commonly tested negative for LADC common driver mutations in the EGFR, KRAS, and ALK genes.
Since *in vitro* studies have shown that NSCLC patients presenting a KIF5B-RET fusion are less sensitive to vandetanib treatment compared to patients with KIF5B independent RET-fusions, FISH analysis can sustain the treatment decision.

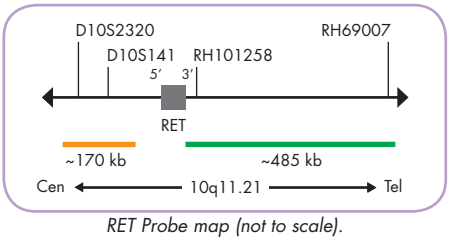
References
Gautschi O, et al. (2013) J Thorac Oncol 8: e43-4.
Ju YS, et al. (2012) Genome Res 22: 436-45.
Kohno T, et al. (2012) Nat Med 18: 375-7.
Tsuta K, et al. (2014) Br H Cancer 110: 1571-8.
Yoh K, et al. (2017) Lancet Respir Med 5: 42-50.

Probe Description

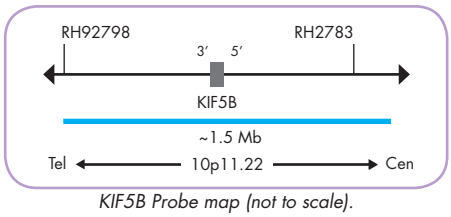
The FlexISH® RET/KIF5B TriCheck™ Probe is a mixture of three direct labeled probes hybridizing to the 10q11.21 and 10p11.22 bands. The green fluorochrome direct labeled probe hybridizes distal to the RET gene region, and the orange fluorochrome direct labeled probe hybridizes proximal to the RET gene region. The blue fluorochrome direct labeled probe spans the KIF5B gene region.



Ideogram of chromosome 10 indicating the hybridization locations.



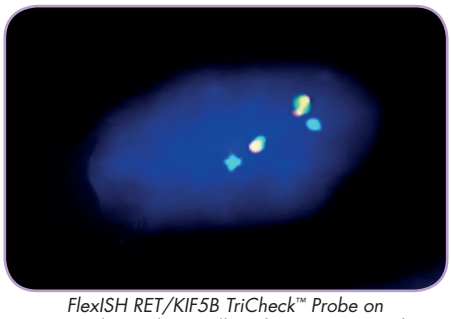
RET Probe map (not to scale).



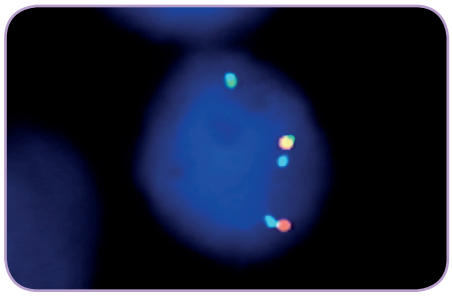
KIF5B Probe map (not to scale).

Results

In an interphase nucleus without rearrangements of the KIF5B/RET locus, two green/orange fusion signals and two blue signals are expected.
A KIF5B-RET inversion is indicated by one separate green signal, one separate orange signal, and an additional blue signal.
A RET translocation is indicated by separated orange and green signals without an additional blue signal.
KIF5B-RET inversion with deletion of the 5′-RET sequences is indicated by loss of one orange signal and co-localization of the isolated green signal with a blue signal.



FlexISH RET/KIF5B TriCheck™ Probe on normal interphase cells with non-rearranged RET loci (two green/orange fusion signals), and non-rearranged KIF5B loci (two blue signals).



NSCLC tissue section with a KIF5B-RET inversion as indicated by one green, one separated orange, and an additional blue signal.

Specimen kindly provided by Dr. Schildhaus, Essen, Germany.

Prod. No.	Product	Label	Tests* (Volume)
Z-2269-50	FlexISH RET/KIF5B TriCheck Probe CE IVD	●/●/●	5 (50 µl)
Z-2269-200	FlexISH RET/KIF5B TriCheck 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. CE IVD only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*