**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 receptor type 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 (12;15) (p13;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.

Currently, there are several ongoing clinical trials involving drugs with known inhibitory activity of NTRK-related kinases. Entrectinib and LOXO-101 represent two of these TK inhibitors which have shown promising activity and good tolerability in patients with advanced solid tumors and NSCLC harboring NTRK1, 2, and 3 rearrangements. 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.

**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.

**References**