VENTANA pan-TRK (EPR17341) Assay

For patients with solid tumors, let testing be your guide

Every cancer is unique. Let's treat it that way.

To help patients with NTRK fusion-positive cancer, you must first identify them.

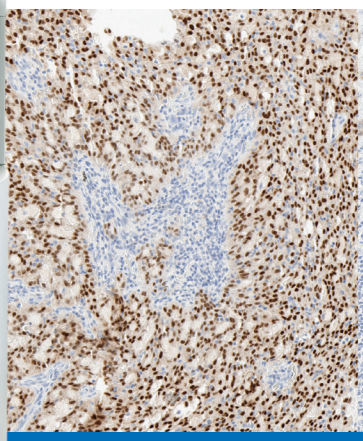
Neurotrophic tyrosine receptor kinase (NTRK) gene fusions are emerging as actionable biomarkers across a wide range of tumor types. Pan-TRK immunohistochemistry (IHC) has been shown to be a resource-efficient method to identify patients for NTRK fusion genetic testing.[1,2]

NTRK gene fusions drive cancer through aberrant signaling[1,2,9,10]

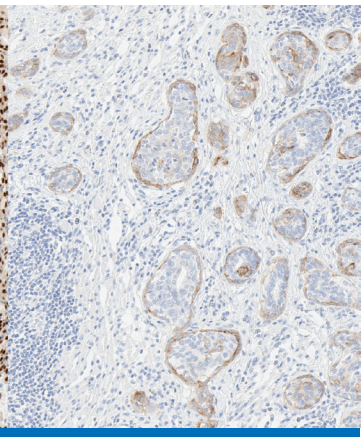
- NTRK gene fusions create an oncogenic chimeric protein that activates a signaling cascade implicated in cell proliferation, survival, and angiogenesis.[1,2]
- NTRK gene fusions may be mutually exclusive to other oncogenic drivers.[2,11]
- Each NTRK gene can combine with multiple fusion partners; at least 25 distinct NTRK gene fusions have been identified to date.[1-3,11]

VENTANA pan-TRK (EP17341) Assay

This assay enables immunohistochemical detection of the C-terminal region of the tropomyosin receptor kinase (TRK) proteins A, B and C, which is known to be conserved across wild-type and fusion proteins. The assay detects both wild-type and NTRK-fusion proteins but does not distinguish between the two. Designed for use on BenchMark IHC/ISH staining instruments, the fully automated assay offers an efficient means to assess TRK expression as part of a testing strategy to help identify patients with NTRK fusion-positive cancer.



Protein expression in mammary analogue secretory carcinoma with TRK fusion (20x)



Protein expression in head and neck squamous cell carcinoma with wild-type TRK (20x)

Incidence of NTRK gene fusions

NTRK gene fusions are most common in rare tumors, but have also been detected less frequently in more common cancers.[1] TRK fusion proteins have been identified in a wide range of commonly occurring tumors, such as lung cancer, thyroid cancer and sarcoma, but at low frequencies.[1-7] In very rare tumors, such as infantile fibrosarcoma, secretory/juvenile breast cancer and mammary analogue secretory cancers (MASC, secretory carcinoma) of the salivary glands, TRK fusion proteins are likely to be the defining genetic feature.[8-12]

NTRK gene fusions are most common in rare tumors, but have also been detected less frequently in more common cancers[1]

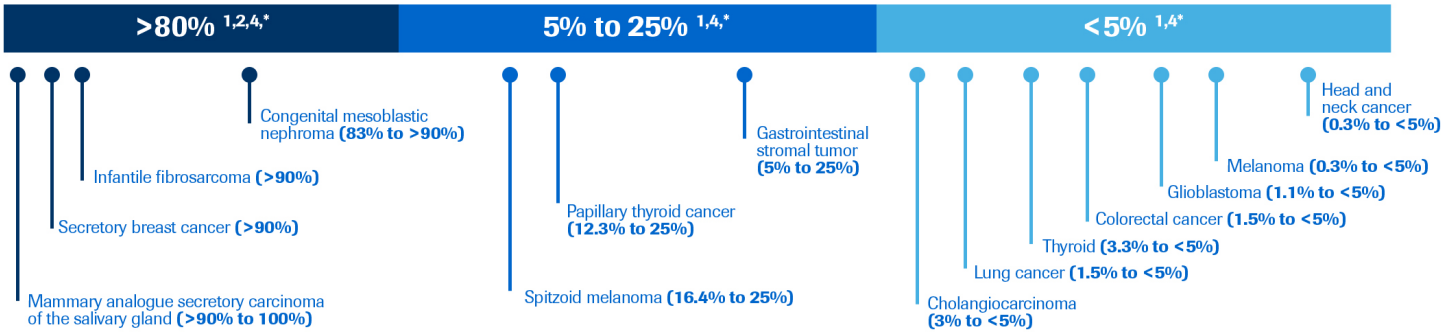


Figure 1: Incidence of NTRK gene fusions by tumor type.

Role of NTRK gene fusions in cancer

Fusions involving NTRK are oncogenic drivers across a wide range of pediatric and adult cancer types.[1-3] The TRK family comprises three proteins — TRKA, TRKB, and TRKC — which are encoded by the genes NTRK1, NTRK2, and NTRK3, respectively.[3] The TRK gene family can drive cancer progression after recombination with other genes such as ETV6, EML4, LMNA and TPM3. TRK fusion proteins are aberrantly expressed and constitutively active, independent of ligand binding.[1]

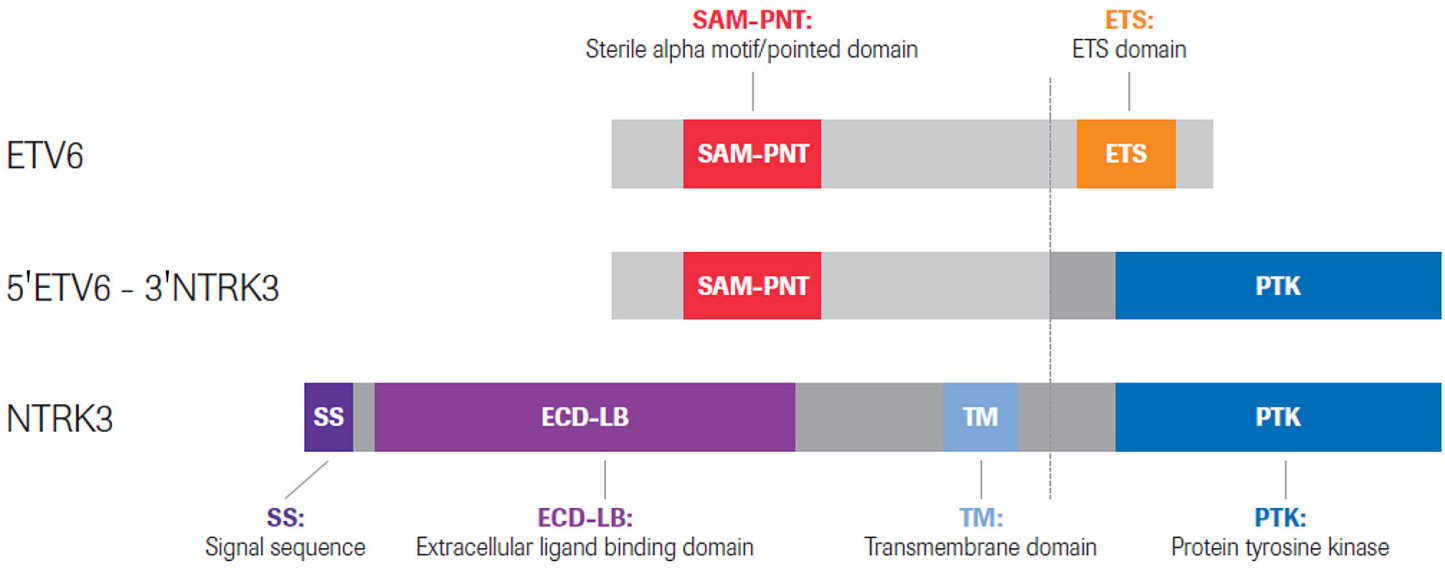


Figure 2: Schematic diagram of 5'ETV6-3'NTRK gene fusion. This rearrangement fuses the N-terminal SAM-PNT domain of ETV6 to the C-terminal PTK domain of NTRK3.

Incorporating NTRK gene-fusion testing into a diagnostic workup has the potential to help advance personalized healthcare for cancer patients.[12-16]

The European Society for Medical Oncology (ESMO) has recommended a strategy for NTRK gene-fusion testing. As part of this testing approach, the use of pan-TRK IHC to identify patients with solid tumors allows you to focus on those who may benefit from next-generation sequencing.

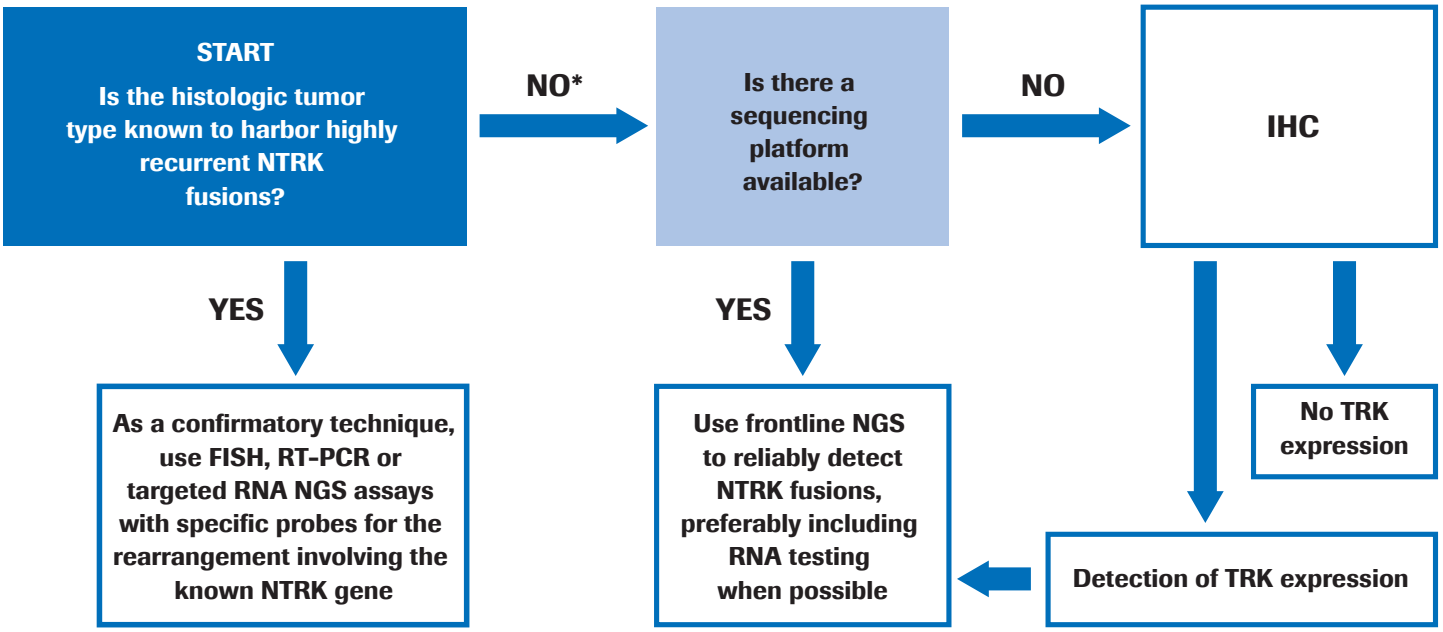
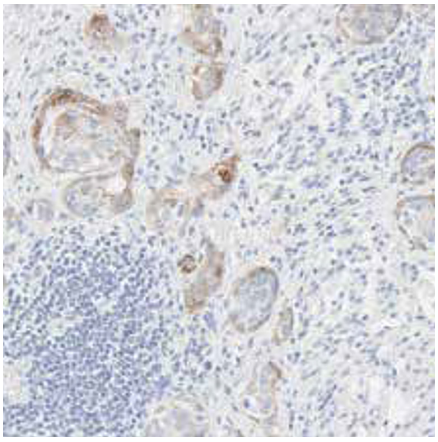


Figure 3: European Society for Medical Oncology (ESMO) NTRK gene-fusion–detection algorithm[17]

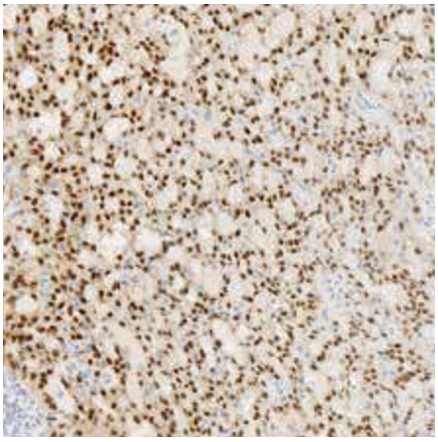
IHC = immunohistochemistry **NGS** = next-generation sequencing **FISH** = fluorescence in situ hybridization
RT-PCR = reverse transcription polymerase chain reaction

* This population would be likely represented by "any malignancy at an advanced stage, in particular if it has been proven wild type for other known genetic alterations tested in routine practice, and especially if diagnosed in young patients."

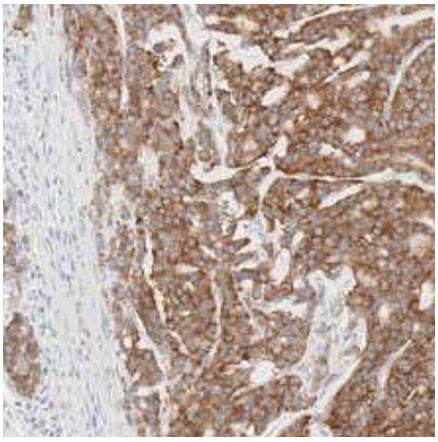
Protein expression with the VENTANA pan-TRK (EPR17341) Assay



Protein expression in head and neck squamous cell carcinoma with wild-type TRK (20x)



Protein expression in secretory carcinoma of salivary gland with TRK fusion (20x)*



Protein expression in colorectal carcinoma with TRK fusion (20x)*

* Fusion status based upon next generation sequencing reported from external laboratory developed test using Oncomine™ Focus Assay[14-17]

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The **VENTANA pan-TRK (EPR17341) Assay** is intended for the immunohistochemical (IHC) detection of the C-terminal region of the tropomyosin receptor kinase (TRK) proteins A, B and C, which is known to be conserved across wild-type and fusion proteins, in formalin-fixed, paraffin-embedded (FFPE) neoplastic tissues stained with BenchMark IHC/ISH instruments.

This product should be interpreted by a qualified pathologist in conjunction with histological examination, relevant clinical information and proper controls.

This antibody is intended for in vitro diagnostic use.

Ordering Information

VENTANA pan-TRK (EPR17341) Assay

Catalog Number	790-7026
Ordering Code	08494665001
Quantity	50 tests

Recommended Tissue Controls

Cerebellum (Positive)
Appendix (Positive)

To learn more about pan-TRK IHC testing, visit **go.roche.com/NTRKIHC** or contact your Roche representative.

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