

TRK Fusion Cancer

Some cancers are caused by specific changes in genes. Genes carry instructions for proteins in cells. An abnormal change to the genes can lead to an alteration of the proteins. As a result, these altered proteins may drive the growth and spread of tumors.



Neurotrophic tyrosine receptor kinase (NTRK) genes provide instructions for coding **TRK proteins**.¹⁻³



When an NTRK gene fusion joins, or **fuses** with an unrelated gene – it produces an altered TRK fusion protein.¹⁻³



This **tropomyosin receptor kinase (TRK) fusion protein** becomes active, triggering a signaling cascade.^{1,2} In people with TRK fusion cancer, these TRK fusion proteins are a driver of the spread and growth of tumors.⁴

Prevalence



TRK fusion cancer occurs across a broad range of tumor types with varying prevalence and in both adult and pediatric patients.

Estimated frequency of NTRK gene fusions in specific tumor types

ADULT



90% - 100%

Mammary analogue secretory^{5,6}



1.5%-14.5%

Thyroid Cancer⁷



3.6%

Intrahepatic cholangiocarcinoma⁸



0.2%-3.3%

Lung Cancer⁹



3.2%

Gastrointestinal Stromal Tumor¹⁰



1.5%

Colon Cancer¹¹



0.3%

Melanoma¹²

PEDIATRIC



91% - 100%

Infantile fibrosarcoma^{13,14}



92%

Secretory breast cancer¹⁵



83%

Congenital mesoblastic nephroma^{14,16}



7.1%

Non-brainstem high-grade glioma¹⁷



Testing



- // Only specific tests can detect TRK fusion cancer.^{1,3}
- // **Next-generation sequencing (NGS)** can identify TRK fusion cancer by recognizing the presence of an NTRK gene fusion.^{18, 19}
- // **Immunohistochemistry (IHC)** uses antibodies to detect the presence of proteins, in this case, TRK proteins, in a given sample²⁰
- // **Fluorescence *in situ* hybridization (FISH)** is a laboratory technique used to look at specific pieces of the DNA binding to fluorescent probes, lighting up when viewed under a microscope.²¹

For more information visit:
trkcancer.com

1. Vaishnavi A, et al. TRKking down an old oncogene in a new era of targeted therapy. *Cancer Discov.* 2015;5(1):25-34.
2. Amatu A, et al. *ESMO Open.* 2016;1(2):e000023.
3. Kumar-Sinha C, et al. Landscape of gene fusions in epithelial cancers: seq and ye shall find. *Genome Med.* 2015;7:129. doi:10.1186/s13073-015-0252-1
4. Okimoto RA, Bivona TG. Tracking Down Response and Resistance to TRK Inhibitors. *Cancer Discov.* 2016;6(1):14-16.
5. Bishop JA, et al. Mammary Analog Secretory Carcinoma of Salivary Glands. *Hum Pathol.* 2013;44:1982-1988.
6. Krings G, et al. Genomic profiling of breast secretory carcinomas reveals distinct genetics from other breast cancers and similarity to mammary analog secretory carcinomas. *Mod Pathol.* 2017;30:1086-99.
7. Yoshihara K, et al. The landscape and therapeutic relevance of cancer-associated transcript fusions. *Oncogene.* 2015; 34(37):4845-4854.
8. Ross JS, et al. New routes to targeted therapy of intrahepatic cholangiocarcinomas revealed by next-generation sequencing. *Oncologist.* 2014;19:235-242.
9. Vaishnavi A, et al. Oncogenic and drug sensitive NTRK1 rearrangements in lung cancer. *Nat Med.* 2013;19(11):1469-1472.
10. Shi E, et al. FGFR1 and NTRK3 actionable alterations in "Wild-Type" gastrointestinal stromal tumors. *J Transl Med.* 2016 Dec 14;14(1):339.
11. Gatalica Z, et al. Molecular characterization of cancers with NTRK gene fusions. *Mod Pathol.* 2019;32(1):147-153.
12. Okamura, et al. Analysis of NTRK Alterations in Pan-Cancer Adult and Pediatric Malignancies: Implications for NTRK-Targeted Therapeutics. *JCO Precision Oncology.* 2018 ;2, 1-20.
13. Bourgeois JM, et al. Molecular detection of the ETV6-NTRK3 gene fusion differentiates congenital fibrosarcoma from other childhood spindle cell tumors. *Am J Surg Pathol.* 2000;24(7):937-946.
14. Rubin BP, et al. Congenital Mesoblastic Nephroma t(12;15) Is Associated with ETV6-NTRK3 Gene Fusion. *Am J Pathol.* 1998;153:1451-1458.
15. Tognon C, et al. Expression of the ETV6-NTRK3 gene fusion as a primary event in human secretory breast carcinoma. *Cancer Cell.* 2002;2:367-376.
16. Argani P, et al. Detection of the ETV6-NTRK3 Chimeric RNA of Infantile Fibrosarcoma/Cellular Congenital Mesoblastic Nephroma in Paraffin-Embedded Tissue: Application to Challenging Pediatric Renal Stromal Tumors. *Mod Pathol.* 2000;13:29-36.
17. Wu G, et al. The genomic landscape of diffuse intrinsic pontine glioma and pediatric non-brainstem high-grade glioma. *Nat Genet.* 2014;46:444-450.
18. Abel HJ, et al. Detection of gene rearrangements in targeted clinical next-generation sequencing. *J Mol Diagn.* 2014;16(4):405-417.
19. Rogers T-M, et al. *Sci Rep.* 2017;7:42259. doi:10.1038/srep42259.
20. Hechtman JF, et al. Pan-trk immunohistochemistry is an efficient and reliable screen for the detection of NTRK fusions. *Am J Surg Pathol.* 2017;41(11):1547-1551.
21. Weier HU, et al. Rapid physical mapping of the human trk protooncogene (NTRK1) to human chromosome 1q21-q22 by P1 clone selection, fluorescence in situ hybridization (FISH), and computer-assisted microscopy. *Genomics* 1995;26:390-3. doi:10.1016/0888-7543(95)80226-C.