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NTRK Gene Fusion Cancer

Genes instruct the production of proteins to keep our bodies running.

A NTRK gene fusion in cancer, which can occur in different locations in the body, is like the accelerator getting stuck, causing cancer cells to multiply.

NTRK genes normally play an important role in our bodies. However, in NTRK gene fusion cancer, part of the NTRK gene splits and binds with a different gene, creating a ‘NTRK fusion oncogene’. NTRK fusion oncogenes produce abnormal ‘TRK fusion’ proteins, which help rewire normal cells into cancer cells and drive cancer growth.
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How NTRK* gene fusions cause cancer growth

Cancer results from a change to one or more genes inside a cell. NTRK gene fusion cancer occurs when part of the NTRK gene fuses (binds) with a different gene. This ‘fusion gene’ or ‘oncogene’ acts like a faulty recipe, producing abnormal proteins that re-wire normal cells into cancer cells.

These abnormal proteins behave like a stuck accelerator to drive cancer growth, ignoring the body’s usual controls.

Abnormal TRK fusion proteins help to drive cancer growth and spread.

(The error to the NTRK gene does not appear to be passed down through families.)

*NTRK (neurotrophic tyrosine receptor kinase) genes (NTRK 1, 2 and 3) are responsible for TRK proteins.
Brain cancers (glioma, GBM, astrocytoma)
Salivary (MASC)
Thyroid cancer
Lung cancer
Secretory breast cancer
Pancreatic
Cholangiocarcinoma
GIST
Colon
Melanoma
Sarcoma (multiple)

Gliomas
Thyroid cancer
Infantile fibrosarcoma
Congenital nephroma
Spitz nevi
Sarcoma (multiple)
NTRK gene fusions are found infrequently in common tumor types but are found frequently in certain rare tumors.

Knowledge about the frequency of NTRK gene fusions is based on small studies so we’ll find out more as NTRK testing continues

• In colorectal, breast, melanoma and lung cancer, NTRK gene fusions occur in 1-5% of cases. (In colorectal cancer, NTRK gene fusions may be more likely in tumors that are MSI-H.)

• They are found in slightly higher frequency (up to 10% of cases) in certain gastro-intestinal stromal tumors (GIST), spitzoid melanoma, and thyroid cancers. The chance of finding a NTRK gene fusion is higher in children with thyroid cancer, increasing to 26% of cases.

 Rare and unusual tumor types in which NTRK gene fusions are commonly detected include:

• Infantile Fibrosarcoma: An extremely rare childhood tumor, where NTRK gene fusions appear to be detected in 70% to 91% of cases

• Secretory Breast and Salivary Gland Carcinomas: These may harbor NTRK gene fusions in up to 90% of cases

• Congenital Mesoblastic Nephroma: A rare kidney tumor, most likely to be found in newborns and young children. Not all cases are cancerous and the chance of NTRK gene fusions vary

• Brain Tumors: NTRK gene fusions may be more likely in high-grade gliomas, particularly in younger patients
When to test?

If a cancer driver, such as a NTRK gene fusion, is suspected or the cancer has spread and/or is not responding to standard therapy, the tumor might be re-tested if cancer progresses.

Biomarker ‘genomic’ testing is the only way to identify such cancer drivers

Genomic testing involves sending a tissue sample of the tumor or a circulating blood test (cfDNA) to a laboratory for DNA sequencing.

The report from these tests can help medical teams decide upon suitable treatments or clinical trials.

Mention of finding a “NTRK gene fusion” or “NTRK gene rearrangement/alteration” is important before your medical team can decide on TRK inhibitor therapy.
There are several tests to detect genomic alterations like NTRK gene fusions. These include: (Adapted from Colorectal Cancer Alliance)

- **Immunohistochemistry (IHC)** detects NTRK (fusion) proteins in a tumor sample

- **Fluorescence In situ Hybridization (FISH)** detects gene changes (rearrangements or gene copy number changes) in a cell, but cannot indicate if an abnormal protein is being made by that mutation; these proteins are oncogenic (i.e. ‘drivers’ of cancer cells)

- **RT-PCR (Reverse-Transcriptase-Polymerase Chain Reaction)** amplifies the DNA at the point where the NTRK gene has fused with a partner gene. This method works only when NTRK is fused to a known partner gene

- **Next generation Sequencing (NGS)** looks at sequences in DNA or RNA and so can test for many different gene defects at once. NGS is also known as comprehensive biomarker testing.

If doctors find a specific cancer driver like a NTRK gene fusion and you are not responding to standard therapy, they may consider a treatment tailored to your individual cancer type – this is called precision medicine. Some precision medicines may be approved for use already or be in clinical trials for further research such as NTRK inhibitors. For more information on a list of NTRK studies, you can check the links below.

- Clinical Trials.gov (Global)
- EU clinical trials register (EU)
- Cancer Support Community Clinical Trials Matching Service (US)
THANK YOU

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