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.

*NTRK (neurotrophic tyrosine receptor kinase) genes (NTRK 1, 2 and 3) are responsible for TRK proteins

Who should be tested for NTRK Gene Fusions?

NTRK gene fusions are rare but can occur in many different tumor types. Testing the tumor for genetic changes known to drive cancer, like NTRK gene fusions, can help to identify treatment options or clinical trials.

1. Some tumor types, including salivary, secretory breast and infantile fibrosarcoma, are likely to be growing because of a NTRK gene fusion.

   - Brain cancers (glioma, GBM, astrocytoma)
   - Salivary (MASC)
   - Thyroid cancer
   - Lung cancer
   - Secretory breast cancer
   - Pancreatic cancer
   - Cholangiocarcinoma
   - GIST
   - Colon cancer
   - Melanoma
   - Sarcoma (multiple)

2. For children, testing soft tissue sarcomas and glioma, particularly if high-grade, may be recommended.

   - Gliomas
   - Thyroid cancer
   - Infantile fibrosarcoma
   - Congenital nephroma
   - Spitz nevi
   - Sarcoma (multiple)

3. In more common cancers, NTRK gene fusions are found in only a small number of cases but they can be more likely in childhood cancers and in Gastrointestinal stromal tumor (GIST), spitzoid melanoma, some thyroid cancers and MSI-H colorectal cancer.

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, 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.

For more information, visit www.NTRKers.org