EMPIRE GENOMICS

NTRK PROBES
FOR DETECTING NTRK FUSIONS

NTRK fusions have proven to be a promising new class of potential therapeutic targets in a variety of cancers. Fusions nearly always form by the same mechanism: the 3' region of the NTRK gene, bearing its kinase domain, fuses with the 5' sequence of a partner gene, resulting in a hybrid oncogene with constitutive TRK activation. NTRK proliferation and growth pathways then go unchecked, leading to tumor development.[1]

NTRK fusions are highly promiscuous; so far, over 80 different 5' fusion partners have been discovered, including those listed below. NTRK1 partners are mostly found on chromosome 1, indicating that intrachromosomal rearrangements are the main drivers of NTRK1 fusions. NTRK2 and NTRK3 fusions, on the other hand, usually occur via interchromosomal rearrangements.[2]

NTRK GENE	FUSION PARTNER	ASSOCIATED CANCERS
NTRK1	IRF2BP2	Lung cancer, thyroid cancer, prostate cancer
	LMNA	Appendiceal cancer, breast cancer, cholangiocarcinoma, colorectal cancer, gallbladder carcinoma, soft tissue sarcoma, Spitzoid neoplasm, uterine sarcoma
	TPM3	Breast cancer, cervical cancer, cholangiocarcinoma, colorectal cancer, glioma, infantile fibrosarcoma, lung cancer, soft tissue sarcoma, thyroid cancer, uterine sarcoma
	TPR	Lung cancer, thyroid cancer, uterine sarcoma, pediatric mesenchymal tumor
NTRK2	DAP21P	Colorectal cancer
	NOS1AP	Anaplastic astrocytoma, glioma
	SQSTM1	Glioma, lung cancer
	TRAF2	Melanoma
NTRK3	EML4	Congenital mesoblastic nephroma, glioma, infantile fibrosarcoma, thyroid cancer
	ETV6	Acute lymphoblastic leukemia, acute myeloid leukemia, breast cancer, colorectal cancer, congenital mesoblastic nephroma, gastrointestinal tract stromal tumor, glioma, infantile fibrosarcoma, inflammatory myofibroblastic tumor, lung cancer, melanoma, neuroendocrine cancer, secretory breast cancer, secretory carcinoma of salivary gland, sinonasal adenocarcinoma, soft tissue sarcoma, Spitzoid neoplasm, thyroid cancer
	RBPMS	Thyroid cancer, uterine sarcoma

Although TRK inhibitors have generated impressive response, nearly one fifth of patients still develop resistance to first generation anti-TRK therapy. However, second generation inhibitors look promising. In a panel of 29 patients who'd already developed resistance to first-generation anti-TRK therapy, 10 had complete or partial response when treated with the second generation inhibitor LOXO-195.[3] The development of second and third generation TRK inhibitors will hopefully allow for the prolonged responses made possible by other fusion-targeted therapies, like those currently used against EGFR, ALK, and ROS1-positive tumors.

To View Our NTRK FISH Probes

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2. Hsiao, Susan J., et al. "Detection of tumor NTRK gene fusions to identify patients who may benefit from TRK inhibitor therapy." The Journal of Molecular Diagnostics (2019).
3. Hyman D, Kummar S, Farago A, et al. CT127 - Phase I and expanded access experience of LOXO-195 (BAY 2731954), a selective next-generation TRK inhibitor (TRKi). American Association for Cancer Research Annual Meeting 2019; 29 March–3 April 2019: Atlanta, Georgia, USA.