NTRK

NTRK, or neurotrophic receptor tyrosine kinase, refers to a family of genes that encode receptor proteins involved in the regulation of neuronal development and function. These genes play a crucial role in the growth, differentiation, and survival of nerve cells (neurons) in the nervous system. Dysregulation of NTRK genes is associated with various neurological disorders and cancers.

The NTRK family includes three genes:

NTRK1 (TRKA): This gene encodes the TRKA receptor, which binds to nerve growth factor (NGF). The TRKA receptor is primarily expressed in neurons and plays a key role in promoting the survival and differentiation of sensory and sympathetic neurons.

NTRK2 (TRKB): NTRK2 encodes the TRKB receptor, which binds to brain-derived neurotrophic factor (BDNF) and neurotrophin-4 (NT-4). TRKB is also expressed in neurons and is involved in neuronal survival, synaptic plasticity, and learning and memory.

NTRK3 (TRKC): The NTRK3 gene codes for the TRKC receptor, which binds to neurotrophin-3 (NT-3). TRKC is expressed in various types of neurons and plays a role in the development and maintenance of the nervous system.

Abnormalities in NTRK genes, such as gene fusions or mutations, can have significant clinical implications:

Cancer: NTRK gene fusions are known oncogenic drivers in a subset of various cancer types, including certain pediatric cancers and rare adult cancers. These fusions result in constitutive activation of the NTRK kinase domain, leading to uncontrolled cell growth and tumor formation. Targeted therapies that inhibit NTRK kinase activity, such as larotrectinib and entrectinib, have shown promising results in treating NTRK fusion-positive cancers.

Neurological Disorders: Dysregulation of NTRK signaling has been implicated in neurological disorders, including Alzheimer's disease, Huntington's disease, and neurodevelopmental disorders. Understanding NTRK function is essential for exploring potential therapeutic interventions for these conditions.

Neurological Development: In normal development, NTRK genes play a critical role in shaping the nervous system by regulating neuronal survival, differentiation, and connectivity. Disruptions in NTRK signaling can lead to developmental abnormalities in the nervous system.

Research into the NTRK family continues to uncover their roles in both health and disease. In the context of cancer, identifying NTRK gene fusions through molecular testing is essential for selecting appropriate targeted therapies. In neurological research, understanding NTRK function can lead to insights into neurodevelopmental processes and potential strategies for neuroprotection and repair in neurological disorders.

A 5-month-old infant developed left upper limb weakness and torticollis at 3 months of age. Magnetic resonance imaging revealed T2 hyperintensity from the medulla oblongata to the upper cervical cord. She underwent a biopsy for the lesion and pathological examination findings confirmed the presence of a high-grade astrocytoma with IDH wildtype-, H3K27M wildtype-, BRAF wildtype-, and ETV-NTRK3

fusion-positivity. Postoperatively, she underwent chemoradiotherapy, but she had marked tumor growth during the treatment. According to the new World Health Organization classification, the patient's tumor is an infantile “hemispheric” glioma.

Conclusion: The characteristics and prognosis of NTRK-fused glioma are not fully understood, it is noteworthy that these tumors commonly occur in the brainstem. Further studies are needed to determine the prognosis of each tumor type and its sensitivity to treatment. This information will help in the reclassification of the tumors and identification of the precise treatment of this rare type of tumor [1].

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Yamada E, Muroi A, Suzuki R, Kino H, Sakamoto N, Tsurubuchi T, Ishikawa E. Infant-type hemispheric glioma occurring at the cervicomedullary region in a 5-month-old infant: A case report with a special emphasis on molecular classification. Surg Neurol Int. 2023 Aug 25;14:299. doi: 10.25259/SNI_405_2023. PMID: 37680912; PMCID: PMC10481863.