

DESCRIPTION

Source	Mouse myeloma cell line, NS0-derived mouse TrkA protein		
	Mouse TrkA (Ala34 - Pro418) Accession # Q3UFB7	IEGRMDP	Mouse IgG _{2a} (Glu98 - Lys330)
	N-terminus		C-terminus
N-terminal Sequence	Ala34		
Analysis			
Structure / Form	Disulfide-linked homodimer		
Predicted Molecular Mass	69 kDa		

SPECIFICATIONS

SDS-PAGE	100 - 125 kDa
Activity	Measured by its ability to inhibit NGF-induced proliferation of TF-1 human erythroleukemic cells. The ED ₅₀ for this effect is 4-24 ng/mL in the presence of 2 ng/mL of Recombinant Mouse β-NGF (Catalog # 1156-NG).
Endotoxin Level	<0.10 EU per 1 µg of the protein by the LAL method.
Purity	>95%, by SDS-PAGE visualized with Silver Staining and quantitative densitometry by Coomassie® Blue Staining.
Formulation	Lyophilized from a 0.2 µm filtered solution in PBS. See Certificate of Analysis for details.

PREPARATION AND STORAGE

Reconstitution	Reconstitute at 500 µg/mL in PBS.
Shipping	The product is shipped with polar packs. Upon receipt, store it immediately at the temperature recommended below.
Stability & Storage	<p>Use a manual defrost freezer and avoid repeated freeze-thaw cycles.</p> <ul style="list-style-type: none"> • 12 months from date of receipt, -20 to -70 °C as supplied. • 1 month, 2 to 8 °C under sterile conditions after reconstitution. • 3 months, -20 to -70 °C under sterile conditions after reconstitution.

DATA

<p>Bioactivity</p> <p>Mean RFU</p> <p>Recombinant Mouse TrkA (ng/mL)</p> <p>Recombinant Mouse TrkA Fc Chimera (Catalog # 10235-TK) inhibits NGF-induced proliferation of TF-1 human erythroleukemic cells. The ED₅₀ for this effect is 4-24 ng/mL in the presence of 2 ng/mL of Recombinant Mouse β-NGF (Catalog # 1156-NG).</p>	<p>SDS-PAGE</p> <p>2 µg/lane of Recombinant Mouse TrkA Fc Chimera (Catalog # 10235-TK) was resolved with SDS-PAGE under reducing (R) and non-reducing (NR) conditions and visualized by Coomassie® Blue staining, showing bands at 100-125 kDa and 200-250 kDa, respectively.</p>
--	--

BACKGROUND

Tropomyocin receptor kinase A (TrkA), also named Neurotrophic tyrosine kinase receptor type 1 (NTRK3) is a member of a nerve growth factor tyrosine kinase receptor family. There are three members of the Trk family, TrkA, TrkB and TrkC, and they bind a group of structurally related, secreted proteins termed neurotrophins, which play an important role in the development and function of the nervous system. The Trk family shares a conserved structural motif consisting of two cysteine-rich domains, a cluster of three leucine-rich motifs, and two immunoglobulin-like domains in the extracellular region, a single transmembrane domain and an intracellular tyrosine kinase domain (3). Natural splice variants of the different Trks, lacking the first cysteine-rich domain, the first and second or all three of the leucine-rich motifs, or the tyrosine kinase domain, have been described (4). Mature mouse TrkA consists of a 383 amino acid (aa) extracellular domain (ECD) which shares 79% and 93% aa identity with human and rat TrkA, respectively. Each Trk family member exhibits different ligand specificities: TrkA binds NGF and NT-3, TrkB binds BDNF, NT-3 and NT-4/5, and TrkC only binds NT-3 (1, 2). The biological activities of the neurotrophins are mediated by binding to and activating two unrelated receptor types: the p75 neurotrophin receptor (p75NTR) and the Trk family receptors (1, 2). P75NTR is a member of the tumor necrosis factor receptor superfamily (TNFRSF) and has been designated TNFRSF16. It binds all neurotrophins with low-affinity to transduce cellular signaling pathways that synergize or antagonize those activated by the Trk receptors. Several TrkA isoforms exist, two of which differ only by a 6-amino acid insertion in their extracellular domain (3). The longer TrkA isoform is the only isoform expressed within neuronal tissues whereas the shorter TrkA is expressed mainly in non-neuronal tissues (3). Trk receptor interactions with NGF play major roles in the development of the sympathetic nervous system, and TrkA, specifically, is essential to the survival of sympathetic neurons in vivo (4). NGF activates retrograde transport of TrkA endosomes for association with actin-modulatory proteins to promote F-actin disassembly, enabling their maturation into transport-competent signaling endosomes (1). Inhibition of the Trk receptors may have several therapeutic implications (5). Injection of a TrkA inhibitor in patients with knee osteoarthritis resulted in sustained pain improvement in a single center trial (6). Another inhibitor showed a significant reduction in psoriatic pruritus, which occurs via a TrkA-dependent mechanism (7).

References:

1. Harrington, A. *et al.* (2011) *Cell*. **146(3)**:421.
2. Smeyne, R. *et al.* (1994) **368(6468)**:246.
3. Barker, P. *et al.* (1992) **268(20)**:15150.
4. Fagan, A. *et al.* (1996) *J Neurosci*. **16(19)**:6208.
5. Yan, W. *et al.* (2019) *J Med. Chem.* **62(4)**:1731.
6. Krupka, E. *et al.* (2019) *Osteoarthr Cartil.* DOI: **10**:1016.
7. Yosipovitch, R. *et al.* (2015) *Acta Derm Venereol.* **95**.