

Neurotrophin and collagen family

Overview: The neurotrophin and collagen receptors (provisional nomenclature) exhibit a single TM domain, with an intracellular tyrosine kinase catalytic domain (E.C. 2.7.10.1). Various isoforms of neurotrophin receptors exist, including truncated forms of trkB and trkC, which lack catalytic domains.

The endogenous ligands of neurotrophin receptors are small proteins (ca. 120 aa) and include nerve growth factor (NGF, ENSG00000134259), neurotrophin (NT) 3 (ENSG00000185652), NT4/5 (ENSG00000167744) and brain-derived neurotrophic factor (BDNF, ENSG00000176697). p75, which has homologies with tumour necrosis factor receptor, lacks a tyrosine kinase domain, but can signal *via* ceramide release and nuclear factor κ B (NF- κ B) activation. Both trkA and trkB contain two leucine-rich regions and can exist in monomeric or dimeric forms.

Nomenclature	trkA	trkB	trkC	p75
Other names	gp140 ^{trk} , high-affinity, slow-dissociating NGF receptor	gp145 ^{trkB}	gp145 ^{trkC}	p75 ^{NTR} , low-affinity neurotrophin receptor, NGFR
Ensembl ID	ENSG00000198400	ENSG00000148053	ENSG00000140538	ENSG00000064300
Potency order	NGF > NT3	BDNF, NT4/5 > NT3	NT3	NGF, BDNF, NT3, NT4/5
Probes	[¹²⁵ I]-NGF	[¹²⁵ I]-BDNF	–	–

The selectivity of small molecule peptide mimetics of NGF has not been ascertained (Massa *et al.*, 2003). There are, as yet, no selective antagonists, but activation can be blocked using anti-neurotrophin antisera or selective immunoadhesins that sequester neurotrophins (Shelton *et al.*, 1995). p75 influences the binding of NGF and NT3 to trkA. The ligand selectivity of p75 appears to be dependent on the cell type; for example, in sympathetic neurones, it binds NT3 with comparable affinity to trkC (Dechant *et al.*, 1997).

The intracellular tyrosine kinase activity of the trkA receptor can be inhibited by GW441756 (8.7, Wood *et al.*, 2004) and tyrphostin AG879 (Ohmichi *et al.*, 1993).

Collagen receptors (ENSM00260000050411) are structurally-related membrane protein tyrosine kinase activated by collagen. Collagen is probably the most abundant protein in man, with at least 29 families of genes encoding proteins, which undergo splice variation and post-translational processing, and may exist in monomeric or polymeric forms, producing a triple-stranded, twine-like structure. In man, principal family members include COL1A1 (ENSG00000108821), COL2A1 (ENSG00000139219), COL3A1 (ENSG00000168542) and COL4A1 (ENSG00000187498).

Nomenclature	DDR1	DDR2
Other names	Epithelial discoidin domain-containing receptor 1, epithelial discoidin domain receptor 1, neuroepithelial tyrosine kinase, cell adhesion kinase, TRK E, protein-tyrosine kinase RTK 6, HGK2, CD167 antigen-like family member A, CD167a antigen	Discoidin domain receptor 2, receptor protein-tyrosine kinase TKT, tyrosine-protein kinase TYRO10, neurotrophic tyrosine kinase, receptor-related 3, CD167 antigen-like family member B, CD167b antigen
Ensembl ID	ENSG00000204580	ENSG00000162733

Abbreviations: BDNF, brain-derived neurotrophic factor; GW441756, 1,3-dihydro-3-[(1-methyl-1H-indol-3-yl)methylene]-2H-pyrrolo[3,2-b]pyridin-2-one hydrochloride; NGF, nerve growth factor; tyrphostin AG879, α -cyano-(3,5-di-*t*-butyl-4-hydroxy)thiocinnamide

Further Reading

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