Tumour necrosis factor (TNF) family

Overview: The TNF receptor superfamily (TNFRSF, provisional nomenclature) displays limited homology beyond an extracellular domain rich in cysteine residues and is activated by at least 18 different human homologues of TNF referred to as the TNF superfamily (TNFSF). Some homologues lacking transmembrane and cytoplasmic domains function as decoy receptors binding ligand without inducing cell signalling. Many of these receptors and ligands function as multimeric entities. Signalling through these receptors is complex and involves interaction with cytoplasmic adaptor proteins (such as TRADD and TRAF1). Several of these receptors contain cytoplasmic motifs known as 'death domains', which upon activation serve to recruit death domain- and death effector domain-containing proteins crucial for the initiation of an apoptotic response. Additional signalling pathways include the regulation of the nuclear factor κB or mitogen-activated protein kinase pathways. Pharmacological manipulation of these receptors is mainly enacted through chelating the endogenous agonists with humanized monoclonal antibodies (e.g. infliximab or adalimumab) or recombinant fusion proteins of IgG and soluble receptors (e.g. etanercept). Some mutated forms of TNF ligands are capable of selecting for different receptor subtypes.

Nomenclature	Other names	Ensembl ID	Adaptor proteins	Endogenous ligands
TNFRSF1A	TNFR1, CD120a, p55TNFR, TNFAR, TNFR60	ENSG00000067182	TRADD	TNFSF1, TNFSF2
TNFRSF1B	TNFR2, CD120b, p75TNFR, p80, TNFBR	ENSG00000028137	TRAF1, 2, 5	TNFSF1, TNFSF2
TNFRSF3	TNFR III, LTBR, TNFCR, TNFR-RP, TNFR2-RP, CD18	ENSG00000111321	TRAF3, 4, 5	TNFSF3, TNFSF14
TNFRSF4	OX-40, ACT35, TXGP1L, CD134	ENSG00000186827	TRAF1, 2, 3, 5	TNFSF4
TNFRSF5	CD40, Bp50, p50	ENSG00000101017	TRAF1, 2, 3, 5, 6	TNFSF5
TNFRSF6	Fas, CD95, APO-1, APT1, TNFRSF6A	ENSG00000026103	FADD	TNFSF6
TNFRSF7	CD27, S152, Tp55, T14	ENSG00000139193	TRAF2, SIVA	TNFSF7
TNFRSF8	CD30, Ki-1	ENSG00000120949	TRAF1, 2, 3, 5	TNFSF8
TNFRSF9	4-1BB, CDw137, ILA	ENSG00000049249	TRAF1, 2, 3	TNFSF9
TNFRSF10A	DR4, TNF-related apoptosis-inducing ligand receptor 1, TRAIL-R1, APO-2, CD261	ENSG00000104689	FADD	TNFSF10
TNFRSF10B	DR5, TNF-related apoptosis-inducing ligand receptor 2, TRAIL-R2, KILLER, CD262, TRICK2A, TRICKB	ENSG00000120889	FADD	TNFSF10
TNFRSF11A	Receptor activator of NF-κB, RANK, osteoclast differentiation factor receptor, ODFR, TRANCE-R, CD265	ENSG00000141655	TRAF1, 2, 3, 5, 6	TNFSF11
TNFRSF11B	Osteoprotegerin, OPG, osteoclastogenesis inhibitory factor, OCIF, TR1	ENSG00000164761	–	TNFSF11
TNFRSF12	TRS, WSL-1, LARD, WSL-LR, apoptosis-mediating receptor DR3, apoptosis-mediating receptor TRAMP, death domain receptor 3	ENSG00000171680	TRADD	TNFSF15, TNFSF12
TNFRSF12A	TWEAK-R, Fn14, FGF-inducible 14, CD266 antigen	ENSG00000006327	TRAF1, 2, 3, 5	TNFSF12
TNFRSF13B	Transmembrane activator and CAML interactor, TACI, CD267	ENSG00000108516	TRAF2, 5, 6	TNFSF13B
TNFRSF13C	B cell-activating factor receptor, BAFF-R, CD268, BR3	ENSG00000159958	TRAF3	TNFSF13B
TNFRSF14	Herpesvirus entry mediator A, HVEM, tumour necrosis factor receptor-like 2, TR2, LIGHT-R, ATAR, HVEA	ENSG00000157873	TRAF1,2,3,5	TNFSF14, TNFSF1, BTLA
TNFRSF16	Low affinity nerve growth factor receptor, NGF receptor, Gp80-LNGFR, p75, $p75^{NTR}$, NGF-R, NTR, CD271	ENSG00000064300	TRAF2, 4, 6	NGF, BDNF, NT-3, NT-4

TNFRSF17	BCMA, BCM, TNFRSF13, TNFRSF13a, CD269	ENSG00000048462	TRAF1,2,3,5,6	TNFSF13B, TNFSF13
TNFRSF18	Glucocorticoid-induced TNFR-related protein, GITR, activation-inducible TNFR family receptor, AITR	ENSG00000186891	TRAF1, 2, 3	TNFSF18
TNFRSF19	Toxicity and JNK inducer, TAJ, TROY, TAJ-α, TRADE	ENSG00000127863	TRAF1,2,3,5	
TNFRSF19L	Receptor expressed in lymphoid tissues, RELT	ENSG00000054967	TRAF1	
TNFRSF21	Death receptor 6, DR6	ENSG00000146072	TRADD	
TNFRSF22	SOBa; Tnfrh2, Tnfrsf1al2, mDcTrailr2	ENSMUSG00000010751	–	
TNFRSF23	mSOB, Tnfrh1, mDcTrailr1	ENSMUSG00000037613	–	
TNFRSF27	X-linked ectodysplasin-A2 receptor, EDA-A2 receptor	ENSG00000131080	–	

TNFRSF1A is preferentially activated by the shed form of TNF ligand, whereas the membrane-bound form of TNF serves to activate TNFRSF1A and TNFRSF1B equally.

TNFRSF6B (ENSG00000026036, also known as the decoy receptor for Fas ligand (DcR3), TR6, M68) acts as a non-functional target for TNFSF14, TNFSF15 and TNFSF6. TNFRSF10C (ENSG00000173535, also known as decoy receptor 1, DcR1, decoy TRAIL receptor without death domain, TNF- related apoptosis-inducing ligand receptor 3, TRAIL-R3, LIT, TRID, CD263) and TNFRSF10D (ENSG00000173530, also known as decoy receptor 2, DcR2, TNF-related apoptosis-inducing ligand receptor 4, TRAIL-R4, TRUNDD, CD264) act as non-functional targets for TNFSF10.

The tumour necrosis factor ligand superfamily includes TNFSF1 (ENSG00000204496, TNF*β*, lymphotoxin-*α*, LT*α*), TNFSF2 (ENSG00000204490, TNF, TNF*α*, cachectin, necrosin, cytotoxin, DIF), TNFSF3 (ENSG00000206327 TNFC, LTB, lymphotoxin-*β*, LT*β*), TNFSF4 (ENSG00000117586, OX-40 ligand, CD252, glycoprotein Gp34, TAX transcriptionally-activated glycoprotein 1, TXGP-1), TNFSF5 (ENSG00000102245, CD40 ligand, CD154, gp39, TNF-related activation protein, TRAP), TNFSF6 (ENSG00000117560, Fas ligand, CD95L, CD178, ApoI L, Apoptosis antigen ligand), TNFSF7 (ENSG00000125726, CD70, CD27 ligand, Ki-24), TNFSF8 (ENSG00000106952, CD30 ligand, CD153), TNFSF9 (ENSG00000125657, 4-1BB ligand, CDw137L), TNFSF10 (ENSG00000121858, TRAIL, Apo-2 ligand (Apo-2L), TL2, CD253), TNFSF11 (ENSG00000120659, Receptor activator of nuclear factor κB ligand, RANKL, TNF-related activation-induced cytokine, TRANCE, osteoprotegerin ligand, OPGL, osteoclast differentiation factor, ODF, CD254 antigen), TNFSF12 (TNF-related weak inducer of apoptosis, TWEAK, Apo-3 ligand, Apo3L, CD255), TNFSF13 (ENSG00000161955, APRIL, TALL2, TRDL-1, ZTNF2, TNFSF13A, CD256), TNFSF13B (ENSG00000102524, zTNF4, THANK, TNF- and APOL-related leukocyte expressed ligand 1, TALL-1, B lymphocyte stimulator, BLyS, B cell-activating factor, BAFF, dendritic cell-derived TNF-like molecule, DTL, CD257 antigen), TNFSF14 (ENSG00000125735, LIGHT, LTg, TR2, Herpesvirus entry mediator-ligand, CD258), TNFSF15 (ENSG00000181634, TL1,TL1A,VEGI, vascular endothelial cell growth inhibitor, TNF ligand-related molecule 1), and TNFSF18 (ENSG00000120337, TL6, glucocorticoid- induced TNF-related ligand, activation-inducible TNF-related ligand).

Abbreviations: **BDNF**, brain-derived neurotrophic factor (ENSG00000176697); **BTLA**, B- and T-lymphocyte attenuator (ENSG00000186265); **FADD**, Fas-associated death domain (ENSG00000168040); **NT-3**, neurotrophin-3 (ENSG00000185652); **NT-4**, neurotrophin-4 (ENSG00000167744); **SIVA**, ENSG00000184990; **TRADD**, TNF receptor-associated death domain (ENSG00000102871); **TRAF**, TNF receptor-associated factor (ENSF00000000597)

Further reading

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