In format provided by M. Croft (APRIL 2009)

Table 2 | **Therapeutic targeting of TNF superfamily interactions**

Model	Interaction targeted	Mice or reagent tested	Effect on disease symptom	Refs
EAE	OX40L–OX40	Toxin-conjugated OX40-specific antibody (depleting)	Substantial inhibition	1
		OX40–immunoglobulin fusion protein (neutralizing)	Substantial inhibition	2
		OX40L-specific antibody (neutralizing)	Substantial inhibition	3
		Ox40$^{-/-}$ or *Ox40l*$^{-/-}$ mice	Substantial inhibition	4,5
	TL1A–DR3	*Dr3*$^{-/-}$ mice	Substantial inhibition	6
		Tl1a$^{-/-}$ mice	Partial inhibition	7
	CD70–CD27	CD70-specific antibody (neutralizing)	Substantial inhibition	8
	4-1BBL–4-1BB	4-1BB-specific antibody (agonist)	Substantial inhibition	9
Colitis and IBD	OX40L–OX40	OX40–immunoglobulin fusion protein (neutralizing and depleting)	Substantial inhibition	10–12
		OX40L-specific antibody (neutralizing)	Substantial inhibition	13,14
	TL1A–DR3	TL1A-specific antibody (neutralizing)	Partial inhibition	15
	4-1BBL–4-1BB	4-1BB-specific antibody (agonist)	Substantial inhibition	16
Asthma and atopy	OX40L–OX40	*Ox40*$^{-/-}$ or *Ox40l*$^{-/-}$ mice	Substantial inhibition	17,18
		OX40L-specific antibody (neutralizing)	Substantial inhibition	19–21
	TL1A–DR3	*Dr3*$^{-/-}$ mice	Substantial inhibition	6
		TL1A-specific antibody (neutralizing)	Substantial inhibition	22
	4-1BBL–4-1BB	4-1BB-specific antibody (agonist)	Substantial inhibition	23
Diabetes	OX40L–OX40	*Ox40l*$^{-/-}$ mice	Substantial inhibition	24
		OX40L-specific antibody (neutralizing)	Substantial inhibition	25
	4-1BBL–4-1BB	4-1BB-specific antibody (agonist)	Substantial inhibition	26
Arthritis	OX40L–OX40	OX40L-specific antibody (neutralizing)	Substantial inhibition	27,28
		Toxin-conjugated OX40-specific antibody (depleting)	Partial inhibition	29
	TL1A–DR3	*Dr3*$^{-/-}$ mice orTL1A-specific antibody (neutralizing)	Partial inhibition	30
	4-1BBL–4-1BB	4-1BB-specific antibody (agonist)	Substantial inhibition	31,32
		4-1BBL-specific antibody (neutralizing)	Partial inhibition	32
SLE	4-1BBL–4-1BB	4-1BB-specific antibody (agonist)	Substantial inhibition	33,34
Atherosclerosis	OX40L–OX40	*Ox40l*$^{-/-}$ mice	Substantial inhibition	35
		OX40L-specific antibody (neutralizing)	Substantial inhibition	36
Minor MHC transplant mismatch	OX40L–OX40	OX40–immunoglobulin fusion protein (neutralizing)	Substantial inhibition	37
	4-1BBL–4-1BB	4-1BB–immunoglobulin fusion protein (neutralizing)	Partial inhibition	43
Major MHC transplant mismatch	OX40L–OX40	OX40–immunoglobulin fusion protein (neutralizing)	No effect	37
		OX40L-specific antibody (neutralizing)	Substantial inhibition with CD28 or CD28 and CD40L blockade	38–41
	CD70–CD27	CD70-specific antibody (neutralizing)	No effect alone; no effect with CD28 and CD40L blockade; substantial inhibition with CD4 and CD28 blockade	40,42
	4-1BBL–4-1BB	*4-1bb*$^{-/-}$ or *4-1bbl*$^{-/-}$ mice	Varying results: no effect or inhibition	44–47
		4-1BB–immunoglobulin fusion protein (neutralizing)	Partial inhibition	48,49
GVHD	OX40L–OX40	OX40L-specific antibody (neutralising)	Substantial inhibition	50,51
		Ox40$^{-/-}$ mice	Substantial inhibition	50
	4-1BBL–4-1BB	*4-1bb*$^{-/-}$ mice	Substantial inhibition	52
		4-1BB-specific antibody (agonist)	Substantial inhibition	53

No published reports are available for the interactions that are not mentioned. 4-1BBL, 4-1BB ligand; DR3, death receptor 3; EAE, experimental autoimmune encephalomyelitis; GVHD, graft-versus-host disease; IBD, inflammatory bowel disease; OX40L, OX40 ligand; SLE, systemic lupus erythematosus.

Table 3 | **Therapeutic targeting of TNF superfamily members in cancer**

Mode of therapy	Target	Combination treatment	Tumour type	Refs
Stimulatory antibody or ligand Fc protein	OX40	NA	Sarcoma, melanoma, glioma, colon carcinoma, mammary carcinoma, thymoma and renal-cell carcinoma	54–58
		Adoptive transfer of CTLs	Sarcoma, thymoma and prostate tumour	59–61
		Administration of IL-12 and 4-1BB-specific antibody	Colon carcinoma	62
		Administration of GM-CSF	Colon and breast carcinoma	63
		Tumour transfection with CD80	B-cell lymphoma	64
		Administration of DC vaccine and 4-1BB-specific antibody	Breast carcinoma	65,66
		Administration of GM-CSF and tumour antigen vaccine	Breast tumour	67
		Administration of IL-12	Sarcoma and prostate tumor	68
	4-1BB	NA	Sarcoma, mastocytoma, glioma, colon carcinoma and B-cell lymphoma	69–75
		Administration of IL-12	Colon carcinoma and melanoma	76–78
		Adoptive transfer of CTLs	Plasmacytoma	79
		FLT3L-mediated DC mobilization	Fibrosarcoma	80
		HLA-DR- and CD40-specific antibodies	Renal carcinoma and mammary carcinoma	81
		5-fluorouracil	Renal carcinoma	82
	CD27	NA	B-cell lymphoma	8
Transfection of tumour cells	OX40L	Administration of GM-CSF	Melanoma, lung carcinomathymoma and colon carcinoma	84–86
	4-1BBL	CD80 co-transfection	Sarcoma and colon carcinoma	87,88
		CD80 and CD86 co-transfection	B-cell lymphoma	89,90
		IL-12 co-transfection	Colon carcinoma	91
		CD80	Squamous-cell carcinoma	92
		CD80, CD40L and CD48 co-transfection	T-cell lymphoma	93
		Adoptive transfer of LAK cells and NK cells	Adenocarcinoma	94
		TRANCE, CD95L and CCL21 co-transfection	T-cell lymphoma	95
		Soluble PD1 co-transfection	Hepatocarcinoma	96
	Single-chain Fv fragments specific for 4-1BB	NA	Melanoma and mammary carcinoma	97–99
	CD70	NA	Sarcoma, mastocytoma, colon carcinoma, thymoma, lymphoma, mammary adenocarcinoma and glioma	100–105
		CD80 co-transfection	Melanoma and mammary adenocarcinoma	106,107
		CD40L co-transfection	Melanoma	108
Transfection of DCs	OX40L	NA	Melanoma, thymoma and melanoma	109,110
	4-1BBL	NA	Colon carcinoma and adenocarcinoma	111
	CD70	NA	Thymoma	112
Stimulatory RNA aptamer	OX40	Administration of DC vaccine	Melanoma	113
	4-1BB	NA	Mastocytoma	114
Depleting antibody	CD70	NA	B-cell lymphoma, renal carcinoma and non-Hodgkin lymphoma	115–117

4-1BBL, 4-1BB ligand; CCL21, CC-chemokine ligand 21; CD95L, CD95 ligand; CTL, cytotoxic T lymphocyte; DC, dendritic cell; DR3, death receptor 3; FLT3, FMS-related tyrosine kinase 3; GM-CSF; granulocyte/macrophage colony-stimulating factor; IL, interleukin; LAK, lymphokine activated killer; NA, not applicable; NK, natural killer; OX40L, OX40 ligand; PD1, programmed cell death 1; TNF, tumour necrosis factor; TRANCE, TNF-related activation-induced cytokine.

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