Receptor & Smad Preferences

			REGULATING MOLECULES CO-RECEPTORS	
MOLECULE		TGF-βs		
TYPE II R	Т	GF-β RII		α-Macroglobulin, BAMBI/NMA, Biglycan, BMP-1 ,Cripto, Decorin, Dermatopontin, KCP/Crim 2, LAP, LTBPE, Tollaid, Vacorin
TYPE I R	ALK-5	ALK	-1,-2	
R-SMAD	Smad2/3	Smad	1/5/8	Betaglycan, Endoglin, CD109
MOLECULE		Activins		
TYPE II R	Ad	ct RIIA/IIB		
TYPE I R	ALK-4	ALK	-1,-2	Activin AC/BC/AE/CE, BAMBI/NMA Cripto, DAN, FLRG, Endoglin,
R-SMAD	Smad2/3	Smac	11/5/8	Follistatin, Inhibin, KCP/Crim 2
MOLECULE		BMPs		RAMRI/NMA_RMD_1_Rightcom
TYPE II R	BMP RII	Act R	Caronte, Chordin-like 1,2,	
TYPE I R	ALK-2,-3,-6	ALK-4,-5	ALK-1,-2	CRIM1, Endoglin, FLRG, Follistatin
R-SMAD	Smad1/5/8	Smad2/3	Smad1/5/8	PRDC, SOST, TSK, USAG-1
				RGM-A, -B, -C
MOLECULE		GDFs		
TYPE II R	BMP RII	Act R	IIA/IIB	BMP-1, DAN, Follistatin,
TYPE I R	ALK-5 ALK-3,-6	ALK-4,-5	ALK-6	Propeptide (GDF-8, 11); GASP-1, 2, Lefty
R-SMAD	Smad2/3 Smad1/5/8	Smad2/3	Smad1/5/8	Cripto
MOLECULE	Nodal			
TYPE II R	Act RIIA/IIB			
TYPE I R	ALK-4,-7			Cerberus, DAN, Lefty, TMEFF1
R-SMAD	Smad2/3			. Cripto
MOLECULE		MIS		
TYPE II R		MIS RII		

Alternate Names for Type I Receptors

ALK-2,-3,-6

Smad1/5/8

Type T Receptor	Alternate name(s)
ALK-1	ACVLR1
ALK-2	Activin RIA
ALK-3	BMPR-IA
ALK-4	Activin RIB, ACVR1B
ALK-5	TGF-β RI
ALK-6	BMPR-IB
ALK-7	ACVR1C

TYPEIR

R-SMAD

TGF-βs

TGF- β molecules are normally secreted as an inactive, latent complex. An N-terminal latency-associated peptide (LAP) and a C-terminal mature TGF- β monomer forms disulfide-linked homodimers that are non-covalently associated after secretion, forming the small latent TGF- β 1 complex. Covalent linkage of LAP to one of three latent TGF- β binding proteins (LTBPs) creates a large latent complex that may interact with the extracellular matrix. LTBP may facilitate secretion, stability, and/or targeting of latent TGF- β . Biologically active TGF- β 1 requires release from the latent complex by the actions of proteases and integrins. Virtually all cell types secrete the three mammalian isoforms, TGF- β 1, TGF- β 2, and TGF- β 3. TGF- β 1.2 is a heterodimer of TGF- β 1 and TGF- β 2.

BMPs & GDFs

BMPs were originally identified by their ability to induce ectopic bone and cartilage formation. Further studies indicate the BMPs regulate a variety of developmental processes, including growth, differentiation, apoptosis, chemotaxis, morphogenesis, and pattern formation. BMP-1 is an exception – it is not a ligand, but a protease that regulates processing of some family members. Based on sequence homology, most of the GDFs are character-ized as part of the BMP subfamily. Many BMPs and GDFs have alternate names:

Ligand	Alternate Name(s)	Ligand	Alternate name(s)	Ligand	Alternate name(s)
BMP-2	BMP-2a	BMP-8	Op-2, BMP-8b	BMP-15	GDF-9b
BMP-3	Osteogenin	BMP-9	GDF-2	BMP-16	Nodal
BMP-3b	GDF-10	BMP-11	GDF-11	GDF-3	Vgr-1
BMP-4	BMP-2b	BMP-12	GDF-7, CDMP-3	GDF-8	Myostatin
BMP-6	Vgr-1	BMP-13	GDF-6, CDMP-2	GDF-15	Myc-1
BMP-7	Op-1	BMP-14	GDF-5, CDMP-1		

Activins & Inhibins

Activins and Inhibins were originally purified from gonadal fluids as proteins that stimulated or inhibited, respectively, follicle stimulating hormone (FSH) release. Activins are homodimers or heterodimers of the various β subunit isoforms, while inhibins are heterodimers of a unique α subunit and one of the various β subunits. Four mammalian beta subunits (β_A , β_B , β_C , and β_E) have been cloned to date. The activin/inhibin nomenclature reflects the subunit composition of the proteins: Activin A (β_A - β_A), Activin B (β_B - β_B), Activin AB (β_A - β_B), Inhibin A (α - β_A), etc.

GDNFs

The GDNF subfamily consists of GDNF, persephin, artemin, and neurturin. Members of this subfamily promote the survival of various neuronal populations in both the central and peripheral nervous systems at different stages of their development. Most signaling of the GDNF subfamily is mediated by a receptor complex composed of a high affinity ligand binding component, GFR α 1-4, and a common signaling receptor tyrosine kinase, RET. Other RET-independent signaling pathways include the use of neural cell adhesion molecule (NCAM), via a direct interaction with GFR α 1, or indirect activation of the receptor tyrosine kinase, MET.

Ligand/receptor preferences for the GDNF subfamily.

GDNF	GFR α 1-RET, GFR α 2-RET, GFR α 1-NCAM
Neuturin	GFR α 2-RET, GFR α 1-RET
Artemin	GFR α 3-RET, GFR α 1-RET
Persephin	GFRα4-RET

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The TGF- β **Superfamily**

The transforming growth factor beta (TGF-β) superfamily contains highly pleiotropic molecules that encompass diverse functions during embryogenesis and adult tissue homeostasis. Mammalian members of the TGF- β superfamily include TGF- β 1,- β 2,- β 3, Activins, Inhibins, BMPs (bone morphogenetic proteins), GDFs (growth differentiation factors), GDNFs (glial derived neurotrophic factors), Nodal, Lefty, and MIS (Müllerian inhibiting substance). Sequence profile analysis of the TGF- β superfamily members indicate that they have a close structural similarity, sharing approximately 25-40% amino acid sequence identity. TGF- β ligands are initially synthesized as precursor proteins that undergo proteolytic cleavage. The mature segments form active ligand dimers via a disulfide-rich core consisting of the characteristic "cysteine knot". Although homodimers are considered the standard form, there are natural heterodimers with biological activity as well.



TGF-β ligands bind to heteromeric receptor complexes with serine/threonine kinase domains. Upon ligand binding, the type II receptor activates the type I receptor by phosphorylation of the GS region. The type I receptor phosphorylates a receptor-activated Smad (R-Smad) protein. Phosphorylated R-Smads form a trimeric complex with the common Smad4, and this complex moves into the nucleus to interact with transcriptional co-activators or co-repressors. This signaling cascade that ultimately alters gene transcription and cellular responses is regulated at several levels. Co-receptors may associate with ligands and act as obligate cofactors (such as TGF-β RIII for TGF-β2) enabling signal transduction, or act to enhance signaling by increasing sensitivity to low ligand concentrations (such as RGM for BMP signaling). The particular type II-type II receptor combination, the activated Smad pathway, and the cell-specific transcription factors also offer diversity in responses. Contributions of accessory proteins such as soluble or membrane-bound regulators, and the use of Smad-independent signaling pathways further fine-tune TGF-β superfamily signaling and allow for disparate activities observed in response to TGF- β ligands in different contexts.

TGF-β**-Related Products**

	PROTEINS		FLISAs		
MOLECULE		POLYCLONAL	MONOCLONAL	LABELED	ASSAY
Activin A	H M R	HMR	H M R	H M R	Н
Activin AB, AC	Н				
Activin B	Н		Н		
Activin C		НМ	Н	М	
Activin RIA/ALK-2	Н	Н	Н	Н	
Activin RIB/ALK-4	НМ	НМ	НМ	Н	
Activin RIIA	Н	Н	Н	Н	
Activin RIIB	НМ	Н	Н	Н	
ALK-1	НМ	НМ	НМ	НМ	М
ALK-7	R	R	R	R	
Artemin	НМ	НМ	НМ	НM	
BAMBI/NMA		НМ		НМ	
BMP-1/PCP	Н	Н	Н		
BMP-2	ΗZ	Н	ΗZ	Н	HMR
BMP-3	Н	Н	Н	Н	
BMP-3b/GDF-10	Н	Н			
BMP-4	H M Z	Н	ΗZ	Н	Н
BMP-5	Н	Н	Н	Н	Н
BMP-6	Н	Н	Н	Н	Н
BMP-7	Н	Н	Н	Н	Н
BMP-8, 9	Н	Н	Н	Н	
BMP-10	Н	Н		Н	
BMP-15/GDF-9B	Н	Н	Н	Н	
BMPR-IA/ALK-3	НМ	Н	Н	Н	
BMPR-IB/ALK-6	НМ	н	НМ	Н	
BMPR-II	Н	Н	Н	Н	
Caronte	Ch	Ch	Ch	Ch	
CD109	Н	Н		Н	
Cerberus		НМ	НМ	НМ	
Chordin	М	М	М	М	м
Chordin-Like 1	Н	Н	Н	Н	
Chordin-Like 2	М	НМ	НМ	НМ	
C0C0	НМ	М	НМ	М	
CRIM1		Н	Н	н	

For a complete & up-to-date listing, visit www.RnDSystems.com/go/TGFbeta

	DEATEINIC		ELISAs/		
MOLECULE	PROTEINS	POLYCLONAL	MONOCLONAL	LABELED	ASSAYS
Cripto	НМ	НМ	НМ	НМ	Н
Cryptic	Н	нм	НМ	НМ	
CV-2	нм нм нм		НМ		
DAN	НМ	нм	НМ	НМ	Н
Decapentaplegic	D	D	D		
Decorin	НМ	НМ	НМ	НМ	НМ
Dermatopontin	Н				
Endoglin/CD105	НМ	НМ	НМ	НМ	НМ
FLRG	НМ	нм	НМ	НМ	Н
Follistatin	НМ	Н	Н	Н	Н
Follistatin-like 1		НМ	H M R	НМ	
Follistatin-like 4	Н				
GASP-1/ WFIKKNRP	Н	Н	Н	Н	
GASP-2/WFIKKN	Н	Н	Н	Н	Н
GDF-1		м		М	
GDF-3	М	M M		М	
GDF-5	F-5 M M M		М	М	
GDF-6	М				
GDF-7/BMP-12	М	м		м	
GDF-8	М	м	М	м	
GDF-9		м		м	
GDF-11	Н				
GDF-15	Н	Н	Н	Н	Н
GDNF	HR	Н	Н	Н	Н
GFRα-1	H R	HR	H R	H R	
GFR α-2	НМ	НМ	Н	НМ	
GFR α-3	НМ	НМ	Н	НМ	
GFRα-4		НМ	НМ	НМ	
Gremlin M M			М		
Lefty	НМ	нм	НМ	НМ	
MIS/AMH	Н	HR	H M R		
MIS RII	HR	R			
Neurturin	НМ	нм	Н	НМ	
Nodal	НМ	М	М		

MOLECIUE	DDOTEINS	ANTIBODIES		ELISAs/	MADE BY DE	
MOLECULE	PROTEINS	POLYCLONAL	MONOCLONAL	LABELED	ASSAYS	
Noggin	НМ	М	М	М		
NOMO		Н				2 State Constant
Persephin	НМ	НМ	НМ	Н		
PP2Ca/PPM1A	Н					Carlos and a second
PRDC	М	М	М	М		Smad3 Expression in Human Pancreatic Cancer. Smad3 was detected in paraffin-
Ret	НМ	НМ	НМ	НM		embedded human pancreatic cancer tissue sections using anti-human Smad3 poly-
RGM-A	НМ	H M Ch	H M Ch	H M Ch		clonal antibody (Catalog # MAB4038). Tis- sue was stained using the anti-rat HRP-DAB
RGM-B	НМ	НМ	Н	М		Cell and Tissue Staining Kit (Catalog # CTS017: brown) and counterstained with
RGM-C	НМ	НМ		Н		hematoxylin (blue).
SKI		Н				
Smad1, 5, 8		Н				GDNF Antibody (μg/mL) .01 0.1 1 0.32
Smad2, 3		нм	Н			per per
Smad4		Н	Н	Н	Н	0.28 -
Smad7			H M R			e .24-
SOST/Sclerostin	НМ	НМ	НМ	НМ		Rela
TGF- β 1	ΗΡ	Ms	Ms	Ms	H M R Ca P	0.20 +
LAP (TGF- β 1)	Н	Н	Н	Н		GDNF-induced Neuronal Survival and
Latent TGF- β 1	Н					Antibody Neutralization. Chick DRG neuron survival increases in response to human
TGF -β 1.2	Н	Ms				GDNF (Catalog # 212-GD) in a dose-depen- dent manner (blue line) as measured with
TGF- β 2	НР	Ms	Ms	Ms	Н	the MTT Viability Assay (Catalog # TA5355).
TGF- β 3	Н	Ms	Ms	Ms	Н	GDNF is neutralized (green line) by increas-
TGF- β 5	A	Ms				polyclonal antibody (Catalog # AF-212-NA).
Latent TGF- β bp1			Н			
Latent TGF- β bp2			Н			M.W. Reduced Non-Reduced
Latent TGF- β bp4		м				
TGF-β RI/ALK-5	М	НМ	НМ	М		29 BMP-2/7 Heterodimer
TGF- β RII	НМ	нм	НМ	НМ		21
TGF- β RIIb	Н	Н				18.4 < BMP-7
TGF- β RIII	Н	Н	Н	Н		12.4 < BMP-2
TMEFF1/ Tomoregulin-1		НМ	Н	М		
TSG	М	М	М	М		Recombinant BMP Heterodimer. Recom- binant human BMP-2/BMP-7 protein (Cata-
TSK	Н					log # 3229-BM) is a refolded disulfide-linked heterodimer. Under reducing conditions
Vasorin/ SLIT-like 2		Н	Н	H		the heterodimer separates into monomers as revealed by SDS-PAGE.

B: Bovine Ca: Canine Ch: Chicken D: Drosophil Ms: Multi-species P: Porcine Z: Zebrafish





Twisted Gastrulation (TSG) Expression in Embryonic Mouse Ribs. Detection of TSG in a cryostat tissue section of mouse embryonic (15 d.p.c.) rib cartilage primordium using anti-mouse TSG polyclonal antibody (Catalog # AF756). Tissues were stained using donkey anti-goat Rhodamine Red™ X-conjugated secondary antibody (red) and counterstained with Fluoro Nissl Green (green).



Activin A Expression in Human Prostate Cancer Tissue Activin A was detected human prostate cancer tissue using antihuman Activin A monoclonal antibody (Catalog # MAB3381). Tissues were stained using ABC-HRP with NovaRed[™] substrate (red) and counterstained with hematoxylin (blue)



Detection of TGF- β in PC-3 cells using Flow Cytometry. Intracellular staining of human PC-3 prostate cancer cells with APCconjugated anti-human TGF- β 1, - β 2, - β 3 monoclonal antibody (Catalog # IC1835A, filled histogram) or APC-conjugated mouse IgG, isotype control (Catalog # IC002A, open histogram)

NovaRed is a trademark of Vector Labs. Rhodamine Red is a trademark of Invitrogen.

