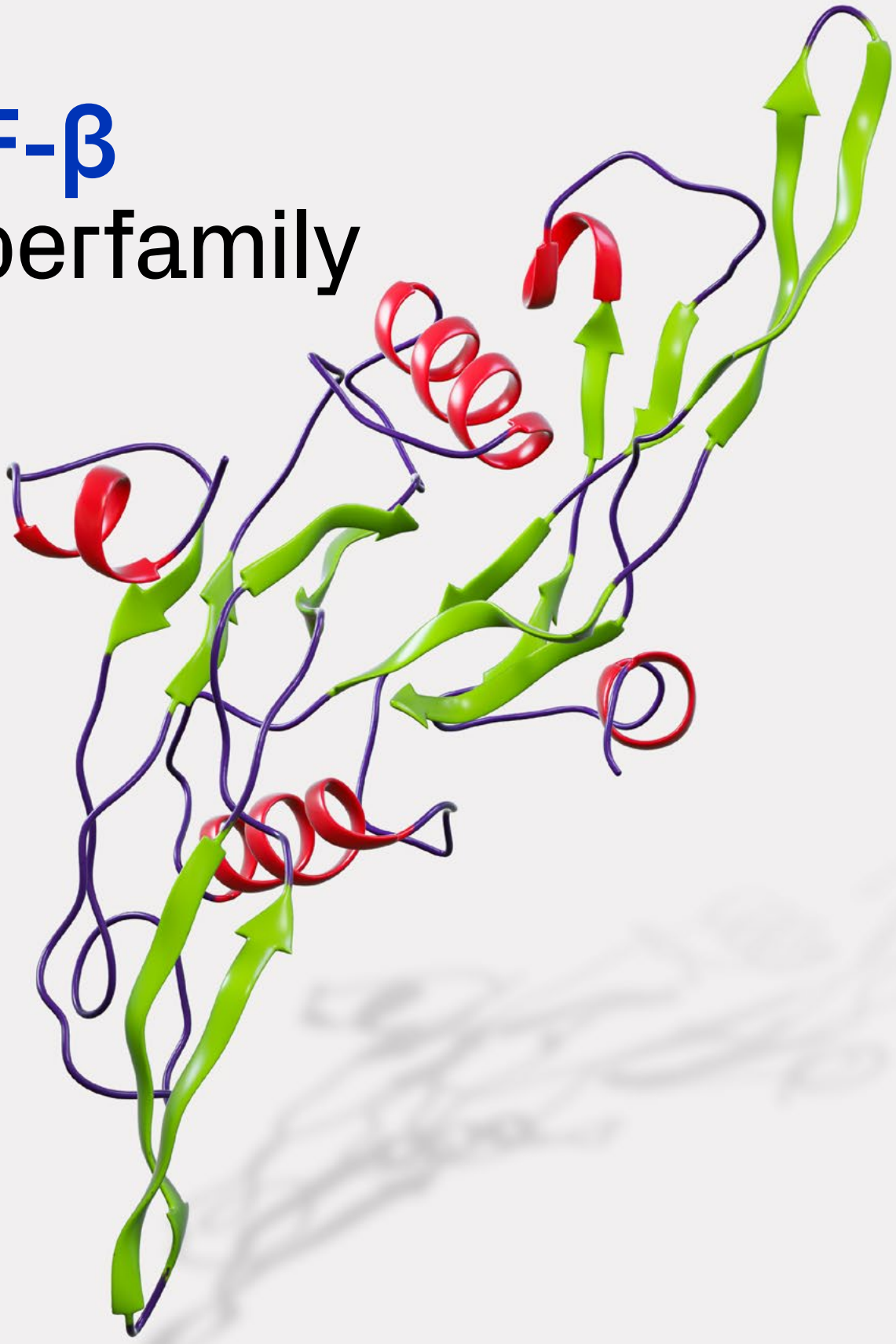
bio-techne® | R&D SYSTEMS

TGF-β Superfamily

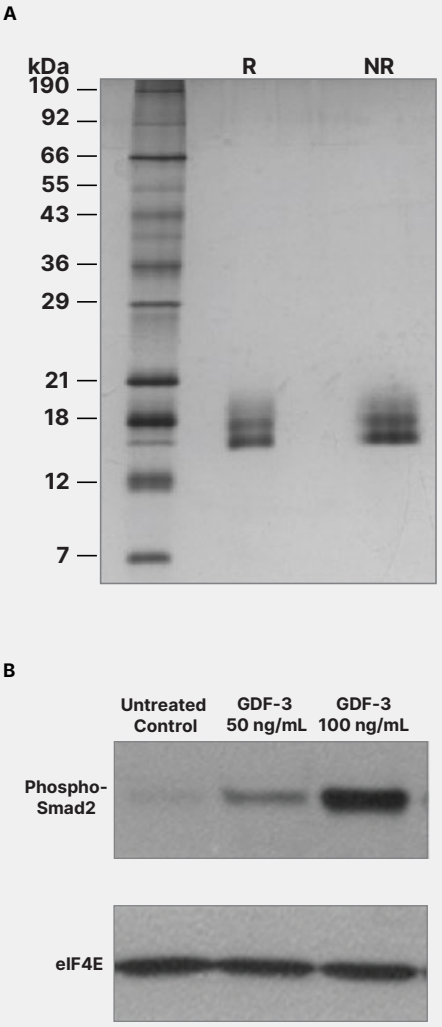


TGF-β Superfamily Proteins

R&D Systems continues to release new and exclusive bioactive TGF-β superfamily ligands and modulators, including new GDF family members, biotinylated BMP proteins, and GMP proteins suitable for cell therapy manufacturing.

New Products for TGF-β Superfamily Research

Product	Species	Source	Catalog#
Latent Activin A	Human	CHO	9129-LA
Biotinylated BMP-7 (bioactive)	Human	NSO	BT354B
Chordin-like 2	Human	NSO	9127-CH
GDF-3	Mouse	CHO	9009-GD
GDF-11/BMP-11	Human/ Mouse/Rat	*E. coli*	1958-GD
GDF-15	Mouse	*E. coli*	8944-GD
Inhibin A	Human	CHO	8506-AB
PRDC/GREM2	Human	*E. coli*	8436-PR
TGF-β1	Equine	CHO	8617-B1
TGF-β3	Human	CHO	8420-B3
USAG-1	Mouse	*E. coli*	9008-SD

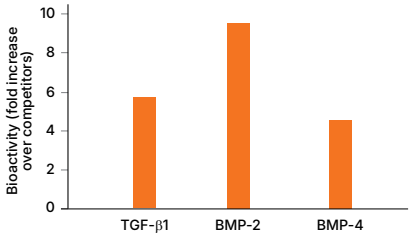


Recombinant Mouse GDF-3 Purity and Activity. **A.** To highlight purity, 1 µg/lane of Recombinant Mouse GDF-3 (Catalog # 9009-GD) was resolved with SDS-PAGE under reducing (R) and non-reducing (NR) conditions and visualized by silver staining. **B.** Recombinant Mouse GDF-3 induces dose-dependent Smad2 phosphorylation in P19 mouse embryonic carcinoma cells. eIF4E was used as a loading control.

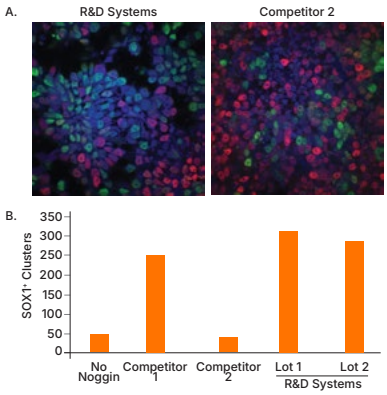
Scan the QR code or visit:
rndsystems.com/tgfbeta

Superior Bioactivity and Reproducibility

R&D Systems is dedicated to producing proteins with industry-leading bioactivity and lot-to -lot consistency. We regularly bring in reagents from competitors for side-by-side testing to ensure that our proteins remain the best in class. In addition, each new lot must meet rigorously defined analytical specifications before reaching the market.



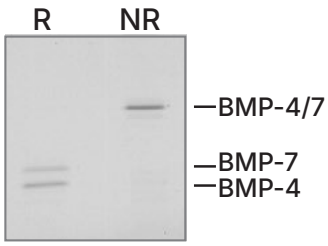
R&D Systems™ Recombinant TGF-β1, BMP-2, and BMP-4 Higher Bioactivity Compared to the Competitor. Side-by-side bioassays were performed using R&D Systems proteins and those from another manufacturer. The fold-difference in bioactivity (Competitor ED_{50}/R&D Systems ED_{50}) was determined and plotted.



Superior and Consistent Pluripotent Stem Cell Differentiation with R&D Systems® Recombinant Human Noggin. BG01V human embryonic stem cells were cultured in Mouse Embryonic Fibroblast Conditioned Media supplemented with FGF basic (5 ng/mL; Catalog # 233-FB). Stem cells were driven into early cells of the neuroectoderm using a 3 day incubation in recombinant human Noggin (25 µg/mL) from either R&D Systems (Lot 1, Lot 2; Catalog # 6057-NG) or from two separate competitors (Competitor 1, Competitor 2). Control cells were not incubated in Noggin (No Noggin). The cells were stained for the early ectoderm marker, Otx2, and the neuroectoderm marker, SOX1. **A.** Representative images of SOX1 (green), Otx2 (red), and DAPI (blue) staining in embryonic stem cells differentiated with Noggin. **B.** SOX1+ clusters were quantified. Cells treated with R&D Systems® Noggin showed an increase in SOX1+ cells compared to both untreated and competitor-treated cells. R&D Systems Noggin showed consistent differentiation across the lots tested.

Heterodimeric Proteins Exclusively from R&D Systems

Heterodimers of the TGF-β superfamily may exhibit different biological properties than their respective homodimeric forms. R&D Systems is the only source for these proteins.



Heterodimer Visualized by SDS-PAGE. BMP-4/7 Heterodimer formation is confirmed with SDS-PAGE. Under reducing (R) conditions the heterodimers separate into monomers.

Molecule	BMP-2/7	BMP-4/7	BMP-2/6	Activin AC
Species	Human	Human	Human	Human
ED_{50}	10-40 ng/mL	15-75 ng/mL	4-20 ng/mL	0.8-4 nM
Catalog #	3229-BM	3727-BP	7145-BP	4879-AC

GMP-Grade Proteins for Regenerative Medicine and Cell Therapies

GMP-grade proteins are manufactured under guidelines that allow for their use as ancillary materials in cell therapy manufacturing processes. They undergo extensive quality control testing and come with comprehensive documentation and full transparency and traceability of source and manufacturing system. This allows cell therapy manufacturers to be confident that they are using a consistent, safe, and traceable supply of reagents.

Documentation

GMP products manufactured, tested, and released under an ISO 9001:2015 and ISO 13485:2016 certified quality management system, lot-to-lot consistency, materials traceability, employee training and documentation, equipment maintenance and monitoring records, Drug Master Files, and more.

Regulatory Guidelines Followed

GMP proteins are manufactured in compliance of the applicable sections of the World Health Organization:

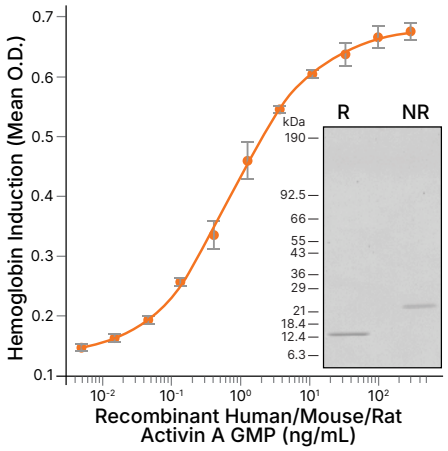
1. USP Chapter <1043>, Ancillary Materials for Cell, Gene, and Tissue-Engineered Products.
2. Ph. Eur. General Chapter 5.2.12, Raw Materials of Biological Origin for the Production of Cell-base and Gene Therapy Medicinal Products

Quality Control Testing

Mass spectrometry, HPLC, SDS-PAGE, endotoxin, presence of host cell content, adventitious agents, and more.

Satisfied Clients

Clients include more than 300 pharmaceutical and biotech companies and we regularly welcome audits of our facilities.



GMP Human Activin A Purity and Activity. Recombinant Human/Mouse/Rat Activin A (Catalog # 338-GMP) induces hemoglobin expression in K562 human chronic myelogenous leukemia cells in a dose-dependent manner. The ED_{50} specification is 0.2–1.2 ng/ml. Purity is highlighted by silver-stained SDS-PAGE (inset).

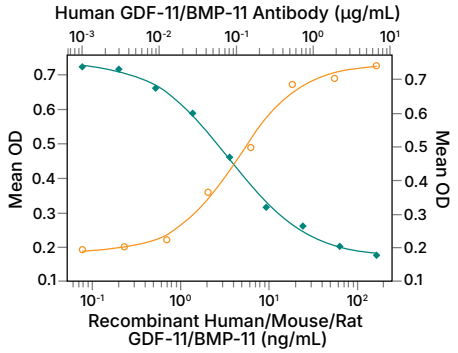
Proteins	Species	Source	GMP-grade Protein
Activin A	Human/Mouse/Rat	CHO	338-GMP
BMP-2	Human	CHO	355-GMP
BMP-4	Human	*E. coli*	314E-GMP
GDF-8/Myostatin	Human/Mouse/Rat	NS0	788-GMP
GDNF	Human	NS0	212-GMP
Noggin	Human	NS0	3344-GMP
TGF-β1	Human	CHO	240-GMP

R&D Systems GMP-grade proteins are intended for use as ancillary materials in GMP manufacturing of investigational or marketed clinical products, such as cell therapy, gene therapy, tissue-engineered products, combination products, or other Advanced Therapy Medicinal Products. They are not therapeutic products or excipient and are not suitable for direct administration to humans.

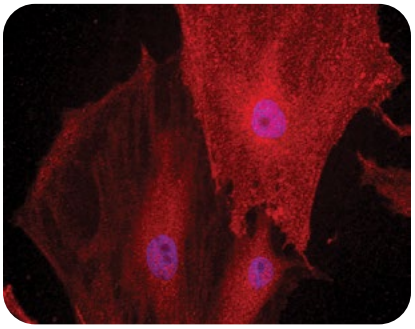
Scan the QR code or visit:
rndsystems.com/gmp

Antibodies Against TGF-β Superfamily Proteins

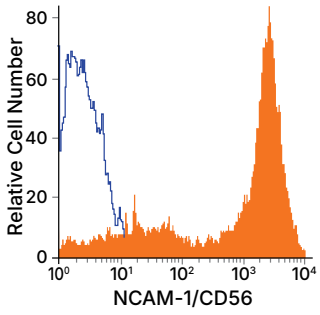
R&D Systems offers a wide selection of antibodies designed for a range of applications including Blocking/Neutralization, Flow Cytometry, ICC and IHC. R&D Systems antibodies are developed, manufactured, and quality tested at our research facility.



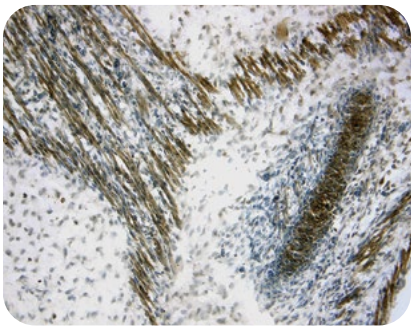
GDF-11/GDF-8 Neutralizing Antibody Blocks GDF-11 Induced Hemoglobin Expression. Recombinant Human/Mouse/Rat GDF-11/BMP-11 (Catalog # 1958-GD) induced hemoglobin expression in the K562 human chronic myelogenous leukemia cell line in a dose-dependent manner (orange line), as measured by the pseudoperoxidase assay. Induction of hemoglobin expression by GDF-11/BMP-11 (25 ng/mL) is neutralized (green line) by increasing concentrations of Mouse Anti-Human GDF-11/GDF-8 Monoclonal Antibody (Catalog # MAB19582). This antibody also neutralizes GDF-8 in a similar bioassay.



Endoglin/CD105 Localized to Plasma Membrane in Rat Mesenchymal Stem Cells. Endoglin/CD105 was detected in immersion fixed undifferentiated rat mesenchymal stem cells using Goat Anti-Rat Endoglin/CD105 Antigen Affinity-purified Polyclonal Antibody (Catalog # AF6440). Cells were stained using the NorthernLights™ 557-conjugated Anti-Goat IgG Secondary Antibody (red; Catalog # NL001) and counterstained with DAPI (blue).



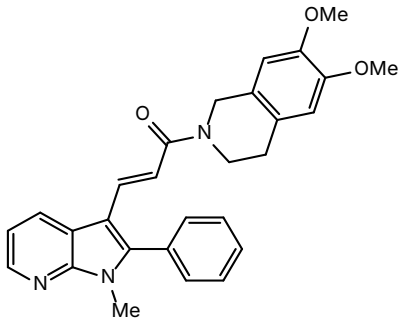
Detection of NCAM-1/CD56 by Flow Cytometry. The Neuro 2A mouse neuroblastoma cell line was stained for NCAM-1/CD56, a receptor for GDNF, with Rat Anti-Mouse NCAM-1/CD56 APC-conjugated Monoclonal Antibody (filled histogram, Catalog # FAB7820A) or isotype control antibody (open histogram, Catalog # IC006A).



SOST/Sclerostin Expression in Mouse Embryo. SOST/Sclerostin was detected in immersion fixed frozen sections of mouse embryo (15 d.p.c.) using Goat Anti-Mouse SOST/Sclerostin Antigen Affinity-purified Polyclonal Antibody (Catalog # AF1589). Tissue was stained using the Anti-Goat HRP-DAB Cell and Tissue Staining Kit (brown; Catalog # CTS008) and counterstained with hematoxylin (blue).

Tocris™ TGF-β Superfamily-Related Small Molecules

Product Name	Catalog #	Product Description
A 83-01	2939	Selective inhibitor of TGF-β RI, ALK-4 and ALK-7
DMH-1	4126	Selective ALK-2 inhibitor
GW 788388	3264	Potent and selective inhibitor of TGF-β RI
K 02288	4986	Type 1 BMP receptor inhibitor
(5Z)-7-Oxozeaenol	3604	Potent and selective TAK1 MAPKKK inhibitor
N-Acetylpuromycin	5679	Downregulates SnoN and Ski protein expression; promotes TGF-β signaling
R 268712	5288	Potent and selective inhibitor of TGF-βRI
RepSox	3742	Potent and selective inhibitor of TGF-β RI
SB 431542	1614	Potent and selective inhibitor of TGF-β RI, ALK-4 and ALK-7
SB 525334	3211	Selective inhibitor of TGF-β RI
SB 505124	3263	Selective inhibitor of TGF-β RI, ALK-4 and ALK-7
SD 208	3269	Potent ATP-competitive TGF-β RI inhibitor
SIS3	5291	Selective Smad3 inhibitor; inhibits TGF-βR1 signaling



SIS3 (Catalog # 5291)
SIS3 is a selective Smad3 inhibitor, which attenuates TGF-β1-dependent Smad3 phosphorylation and DNA binding. This compound has no effect on Smad2, p38 MAPK, ERK or PI 3-kinase signaling. SIS3 inhibits TGF-β1-induced myofibroblast differentiation of dermal fibroblasts. It also inhibits TGF-β2-induced endothelial cell differentiation in iPSCs.

Scan the QR code or visit:
tocris.com

Multiplex Assays for TGF-β Superfamily Signaling

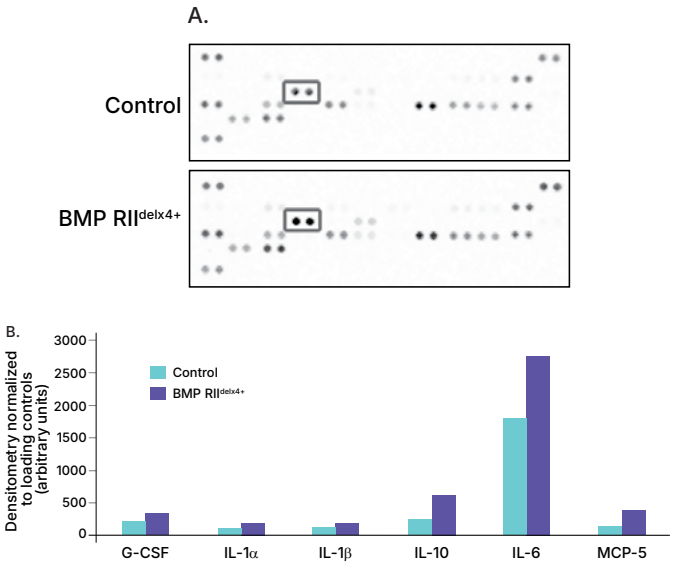
Proteome Profiler™ Antibody Arrays

Rapid—analyze the expression level of dozens of proteins simultaneously

Economical—contains 4 membranes—each antibody is spotted in duplicate

Versatile—over 25 arrays for both intra- and extracellular factors

Proteome Profiler: Increase Your Potential for Discovery



Proteome Profiler Mouse Cytokine Array Detects Aberrant Cytokine Production in Macrophages from BMP RII^{delx4+} Transgenic Mice. Macrophages isolated from control and BMP RII^{delx4+} mice were activated in culture using lipopolysaccharide. Supernatants were collected after 24 h and assayed using the Proteome Profiler Mouse Cytokine Antibody Array (Catalog # ARY006). (A) Representative arrays of activated Control and BMP RII^{delx4+} macrophage supernatants. The set representing Interleukin (IL)-6 is boxed in gray. (B) Densitometry histograms of selected analytes from activated Control (blue) and BMP RII^{delx4+} (purple) macrophage supernatants. IL-1α, IL-1β, IL-6, IL-10, G-CSF, and MCP-5 are increased in BMP RII^{delx4+} mice compared to control. All changes are significant at $p<0.01$ by ANOVA. **Adapted from Talati M.**, *et al.* (2014) PLoS ONE **9**: e94119.

Investigate the Functional Effects of TGF-β Signaling Pathways

Kit	Catalog #		
	Human	Mouse	Rat
Cytokine Array, Panel A	ARY005B	ARY006	ARY008
XL Cytokine Array	ARY022B	ARY028	-
Angiogenesis Array	ARY007	ARY015	-

Investigate Non-Canonical TGF-β Signaling

Array	Catalog #
Human Phospho-Kinase Array	ARY003C

Luminex® High Performance Assays

R&D Systems Luminex® High Performance Assays are designed to maximize assay accuracy and precision while preserving the benefits of multiplexing. Choose analytes from established panels and select “premixed” or “end-user mixed” options.

TGF-β Superfamily-Related Luminex High Performance Assay Panels

	Polystyrene Beads	Magnetic Beads
Human High Sensitivity Cytokine Panel A	✓	✓
Human High Sensitivity Cytokine Panel B	-	✓
Human Angiogenesis Panel	✓	✓
Human TGF-β Panel	✓	✓

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rndsystems.com/luminex

Products for TGF-β Superfamily Research

Molecules	Molecule	Antibodies	Proteins & Enzymes	ELISAs	Luminex Assays
Activin Family					
Ligands	Activin A	H M R	H M R	H M R	
	Latent Activin A		H		
	Activin AB		H		
	Activin AC Heterodimer		H		
	Activin B	H	H M		
	Activin C	H M	H M		
	Inhibin				H
	Inhibin α	H	H M		
Receptors	Activin RIA/ ALK-2	H	H M		
	Activin RIB/ ALK-4	H M	H M		
	Activin RIIA	H	H M		
	Activin RIIA/B	H			
	Activin RIIB	H	H M		
BMP Family					
Ligands	BMP-1/PCP	H H	H H		
	BMP-2	H Z	H M R Z	H M R	H
	BMP-2/ BMP-4 Heterodimer	H Z			
	BMP-2/ BMP-6 Heterodimer		H		
	BMP-2/BMP-7 Heterodimer	H	H		
	BMP-2a		Z		
	BMP-3	H	H		
	BMP-3b/ GDF-10	H	H		
	BMP-4	H M Pr Z	H M Z	H	H
	BMP-4/BMP-7 Heterodimer		H		
	BMP-5	HM	HM	H	
	BMP-6	HM	HM	H	
	BMP-7	HM	HM	H	
	BMP-8	H			
	BMP-8a		HM		
	BMP-8b	HM			
	BMP-9	H M Pr	HM	HM	H
	BMP-10	HM	HM	HM	
	BMP-15/ GDF-9B	HMR	H		
	Decapenta-plegic DPP	D	D		
GDF Family					
Ligands	GDF-1	H M	H		
	GDF-3	H M	H M		
	GDF-5/ BMP-14	M	H M	M	
	GDF-6/ BMP-13	M	M		
	GDF-7/ BMP-12	M	H M		
	GDF-8/ Myostatin	H M R	H M R	H Ms	
	GDF-9	H M Ha	H M		

Molecules	Molecule	Antibodies	Proteins & Enzymes	ELISAs	Luminex Assays
GDF Family					
Ligands	GDF-11/ BMP-11	H M R	H M R	H	
	GDF-11/ GDF-8	H M R			
	GDF-15	H M Pr	H M	H M R	H M
GDNF Family					
Ligands	Artemin	H M	H M	H M	
	GDNF	H R	H R	H	H
	Neurturin	H M	H M		
	Persephin	H M	H M	H	
Receptors	Gas1	H M	H M	H M	
	GFRα-1/ GDNF Rα-1	H R	H R		
	GFRα-2/ GDNF Rα-2	H M	H M		
	GFRα-3/ GDNF Rα-3	H M	H M		
	GFRα-4/ GDNF Rα-4	H M			
	GFRα-like	M			
	NCAM-1/ CD56	H M R Pr	H M	H	H
	Ret	H M	H M	H	
	Syn-decan-3	H M	H M	H	
RGM Family					
Ligands	RGM-A	H M Ch	H M	H M R	
	RGM-B	H M	H M	H	
	RGM-C/ Hemojvelin	H M	H M	H M R	
TGF-β Family					
Ligands	LAP (TGF-β1)	H M	H	H	
	TGF-β	Ms			
	TGF-β1	H M Ms	H M P E	H M R P Ca	Ms
	TGF-β1, 2, 3	Ms			Ms
	TGF-β1.2	Ms	H		
	TGF-β1/1.2	Ms			
	TGF-β2	M Ms	H M P	H M R P Ca	Ms
	TGF-β2/1.2	Ms			
	TGF-β3	Ms	H	H	Ms
	TGF-β5	Ms	A		
TGF-β Superfamily					
Modulators	Amnion-less	H M	H		
	BAMBI/ NMA	H M	H M		
	Caronte	Ch	Ch		
	Cerberus 1	H M	M		
	Chordin	M	M	M	
	Chor-din-like 1/ CHRDL1	H	H		
	Chor-din-like 2/ CHRDL2	H M	H M		

Molecules	Molecule	Antibodies	Proteins & Enzymes	ELISAs	Luminex Assays
TGF-β Superfamily					
Modulators	COCO	H M	H M	H	
	CRIM1	H	H M		
	Cripto	H M Pr	H M	H	H
	Crossvein-less-2/ CV-2	H M	H M		
	Cryptic	H M	H		
	DAN	H M	H M	H M	
	Decorin	H M	H M	H M	
	Dermato-pontin	H	H M		
	FBXW7/ Cdc4	H			
	Follistatin	H M	H M	H	H
	Follista-tin-like 4/ FSTL4	H M R	H		
	Follista-tin-like 5/ FSTL5		H M		
	Follista-tin-related Gene Protein/ FLRG	H M	H M	H	H
	GASP-1/ WFIKKNRP	H	H	H	
	GASP-2/ WFIKKN	H	H	H	
	GFRα-like	M			
	Gremlin	M	H M	M	
	IGSF1				
	Nicalin	H M R			
	Noggin	M	H M		
	NOMO	H			
	PRDC/ GREM2	M	H M	M	
	SCUBE3		H		
	SOST/ Sclerostin	H M	H M	H M R	H
	TAZ/ WWTR1	H			
	Latent TGF-β bp1	H			
	Latent TGF-β bp2/ LTBP-2	H			
	Latent TGF-β bp4	M	H		
	TGIF1	H			
	TMEFF1/ Tomoreg-ulin-1	H M			
	TSG	M	H M		
	Tsukushi/ TSK	H M	H		
	USAG1	H	H M		
	USP9x		H		

Molecules	Molecule	Antibodies	Proteins & Enzymes	ELISAs	Luminex Assays
Smad Family					
Intra-cellular Singalling	HIC5/TG-FB1I1	H			
	MAGI2	H M			
	Smad1	H			
	Smad2	H M D			
	Smad2/3	H M			
	Smad3	H M			
	Smad4	H			
	Smad5	H			
	Smad7	H M R			
	Smad8	H			
	Smad9	H M			
	TGIF1	H			
Others					
Ligands	Vasorin/ SLIT-like 2	H	M		
	Lefty	H M			
	Lefty-1	M	M		
	Lefty-2	M			
	Lefty-A	H	H		
	MIS/AMH	H M R	H	H	
	Nodal	H M	H M		

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