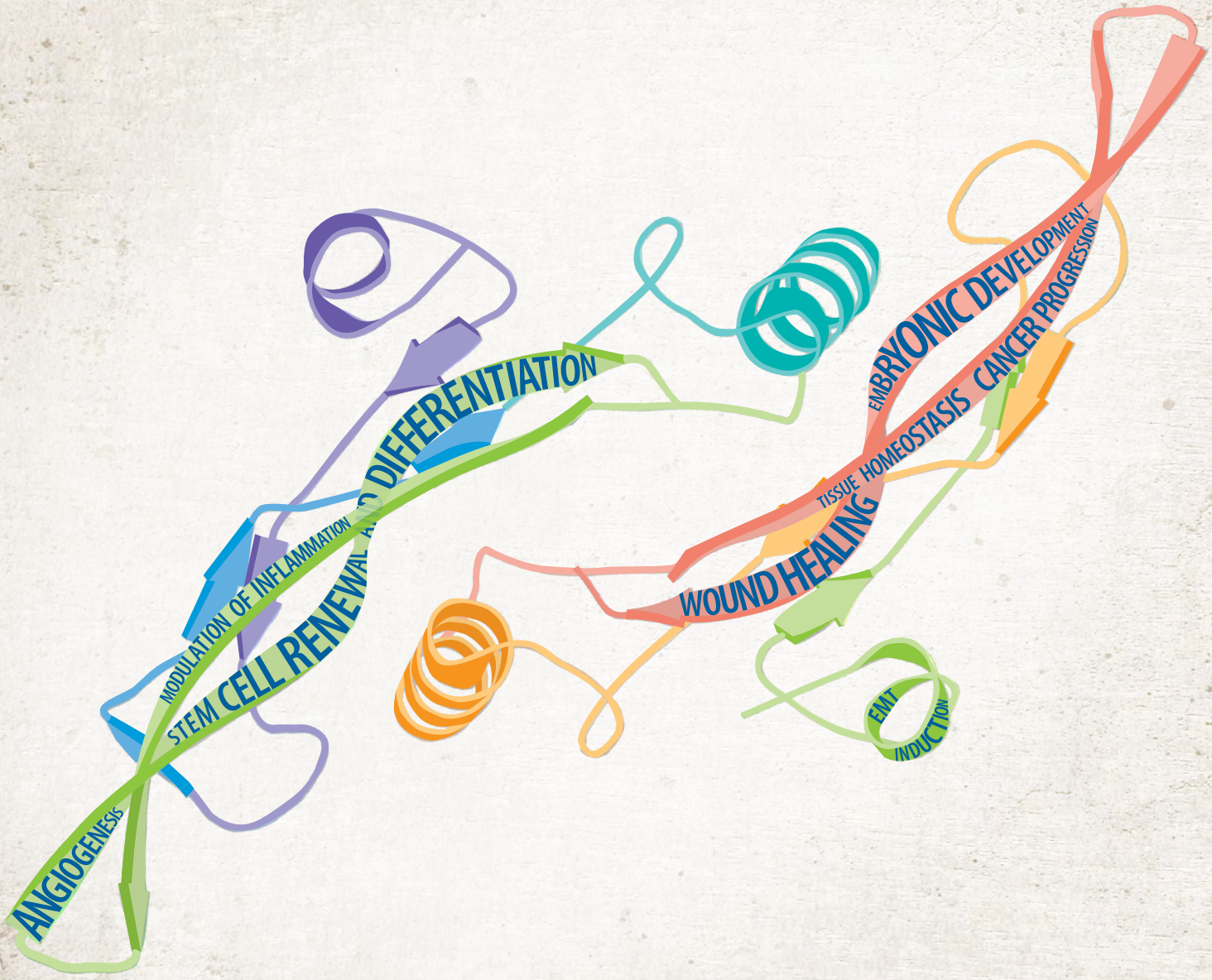
R&D SYSTEMS™
a bio-techne brand

TGF-β Superfamily



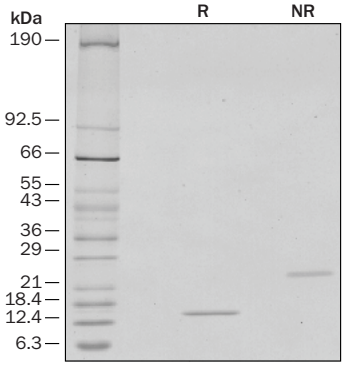
CELEBRATING
TGF-β1
30 YEARS
1985–2015

Proteins for TGF-β Superfamily Research

The R&D Systems selection of TGF-β superfamily proteins has several distinguishing features that make them the most reputable in the industry.

Ligands are Dimerized for Maximum Bioactivity

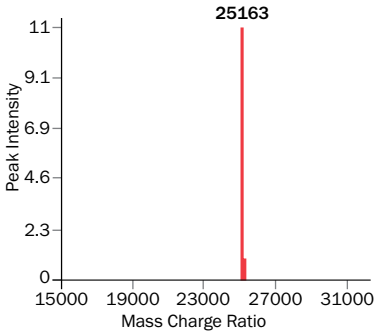
All of our ligands are produced and tested with rigorous quality standards to guarantee that they form bioactive homo- or heterodimers.



Activin A Dimerization Verified by SDS-PAGE. 1 µg/lane of Recombinant Human/Mouse/Rat Activin A (Catalog # 338-AC) was resolved with SDS-PAGE. Under reducing (**R**) conditions the Activin A monomer is shown as a 14 kDa band. Under non-reducing (**NR**) conditions the Activin A homodimer resolves as a 24 kDa band.

World Class Purity for Worry-Free Experimentation

Our proteins are highly pure and, at minimum, must meet our industry-leading endotoxin specification (< 0.1 EU/µg).



GDF-11/BMP-11 Purity Confirmed by Mass Spectrometry. ESI analysis of Recombinant Human/Mouse/Rat GDF-11/BMP-11 (Catalog # 1958-GD) shows a peak at 25163 Da, corresponding to the calculated molecular mass of the disulfide linked homodimer, 25163 kDa.

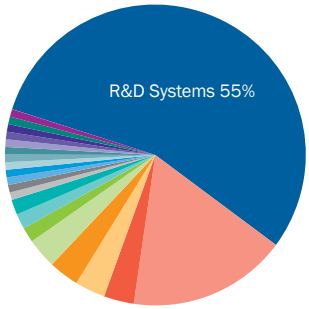
Bulk Availability

All of our proteins are available for bulk purchase. Stock up and...

- Get high quality proteins for a low price
- Maintain a reliable supply of industry standard reagents
- Have confidence in experimental consistency

Most Referenced

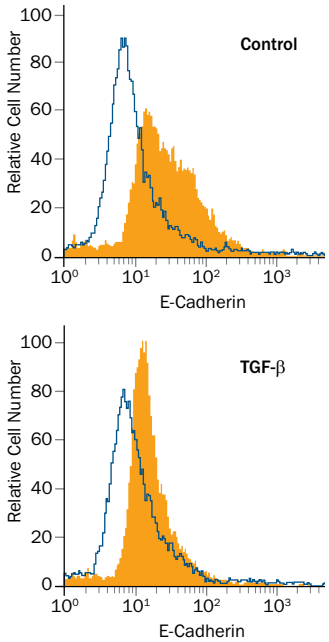
R&D Systems recombinant TGF-β superfamily proteins are the most cited in scientific literature.



A literature survey of 1,125 manuscripts containing 15,180 product citations from 16 different journals related to cancer, immunology, neuroscience, and stem cells was conducted. Within this data, 1,586 total protein citations were identified with 123 related to the TGF-β superfamily. Of those, R&D Systems was the most referenced source (55% of the total cited proteins). The remaining 45% of TGF-β protein citations were distributed across 20 other companies, with contributions ranging between 1% and 17% of the total TGF-β protein citations found during this survey.

Tested in Biologically-Relevant Systems

Each TGF-β superfamily protein is tested in an appropriate biological system to accurately determine its functional efficacy.



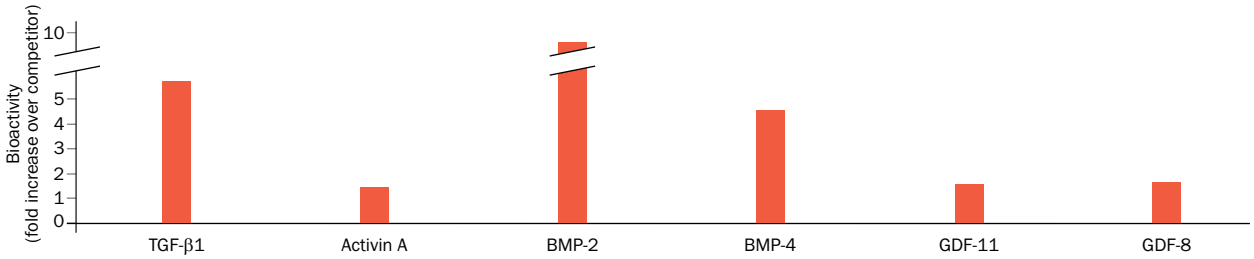
TGF-β1 Induces Epithelial to Mesenchymal Transition. Epithelial to Mesenchymal Transition (EMT) was induced in the A549 human lung carcinoma cell line with cell culture media supplemented with Recombinant Human (rh)TGF-β1 (Catalog # 240-B). Control cells were cultured without rhTGF-β1. EMT induction was confirmed at 48 h by flow cytometric staining for E-Cadherin (filled; Catalog # FAB18381P), an epithelial cell marker, or an isotype control (open; Catalog # IC0041P). TGF-β1 decreased the expression of E-Cadherin.

Cover image depicts the secondary structure of homodimeric human TGF-β1. Graphic was generated using PyMOL molecular graphics (www.pymol.org) from RCSB Protein Data Bank file 3KFD. Referenced from Radaev *et al.* (2010) J. Biol. Chem. **285**:14806. The biological processes listed are placed for artistic purposes only and do not reflect the specific function of the associated TGF-β structure.

Superior Bioactivity

Recombinant TGF-β Superfamily Ligands

Molecule	TGF-β1	Activin A	BMP-2	BMP-4	GDF-11/BMP-11	GDF-8
Species	Human*, Mouse	Human, Mouse, Rat	Human, Mouse, Rat	Human*, Mouse	Human, Mouse, Rat	Human, Mouse, Rat
ED_{50}	0.04–0.2 ng/mL	0.2–1.2 ng/mL	40–200 ng/mL	2.5–15 ng/mL	1–4 ng/mL	2–10 ng/mL
Catalog #	240-B, 7666-MB	338-AC	355-BM	314-BP, 5020-BP	1958-GD	788-G8
Available as GMP-grade	Yes	Yes	Yes	Yes	Coming Soon	Yes



R&D Systems Recombinant TGF-β1, Activin A, BMP-2, BMP-4, GDF-11, and GDF-8 Exhibit 1.5-fold or 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. *Data for Recombinant Human TGF-β1 and BMP-4 bioactivity are shown in this graph.

ProDots™ Proteins: Simplifying Cell Culture

ProDots Proteins are R&D Systems industry-leading quality, highly bioactive proteins packaged into easy-to-use lyophilized "dots."

- Easily rolls out of vial and into cell culture media
- Dissolves instantly
- Maximum protein recovery
- Guaranteed stability at 2–8 °C for 6 months

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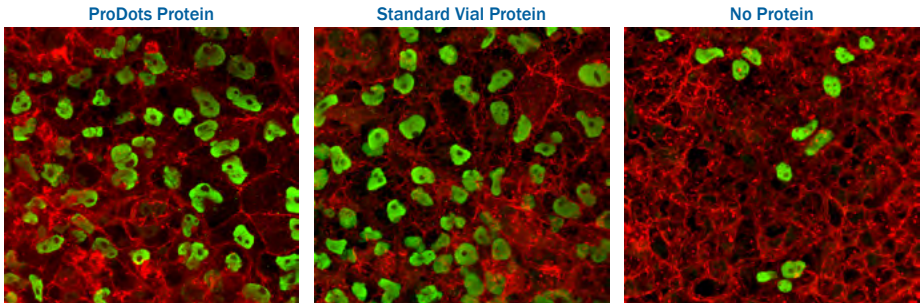
rndsystems.com/ProDots

TGF-β Superfamily ProDots Proteins

Molecule	Catalog #
TGF-β1	PRD240
Activin A	PRD338

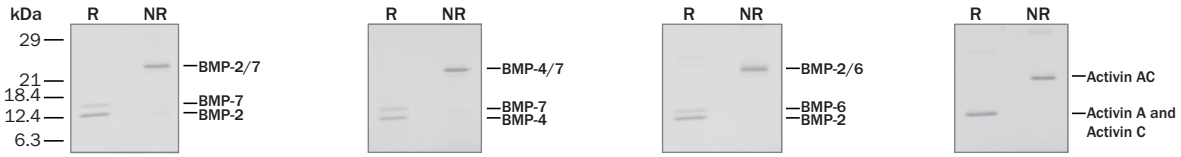


ProDots Recombinant Human/Mouse/Rat Activin A Promotes the Differentiation of Pluripotent Stem Cells into Endoderm. BG01V human embryonic stem cells were differentiated into endoderm using media supplemented with ProDots Recombinant Human/Mouse/Rat Activin A (Catalog # PRD338) or with R&D Systems standard retail Recombinant Human/Mouse/Rat Activin A (Catalog # 338-AC). Control cells were cultured in medium without recombinant Activin A. Differentiation into endoderm was confirmed by positive-staining for Claudin-6 (red) and Sox17 (green) using the Mouse Anti-Human Claudin-6 Monoclonal Antibody (Catalog # MAB3656) and the Goat Anti-Human Sox17 Polyclonal Antibody (Catalog # AF1924), respectively. BG01V human embryonic stem cells are licensed from ViaCyte, Inc.

Proteins for TGF-β Superfamily Research, continued

TGF-β Superfamily Heterodimers: Exclusive Availability

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



BMP and Activin Heterodimer Formation Confirmed with SDS-PAGE. Recombinant Human (rh)BMP-2/BMP-7, rhBMP-4/7, rhBMP-2/6, and rhActivin AC protein are manufactured and shipped as bioactive, disulfide-linked heterodimers. SDS-PAGE of each protein under non-reducing (**NR**) conditions shows the molecular weight (**kDa**) of the intact heterodimer. Under reducing (**R**) conditions the heterodimers separate into monomers as indicated on each respective SDS-PAGE. Under reducing conditions, the intensities of the silver stain for the heterodimer subunits reflect the differential staining affinity of the individual protein subunits.

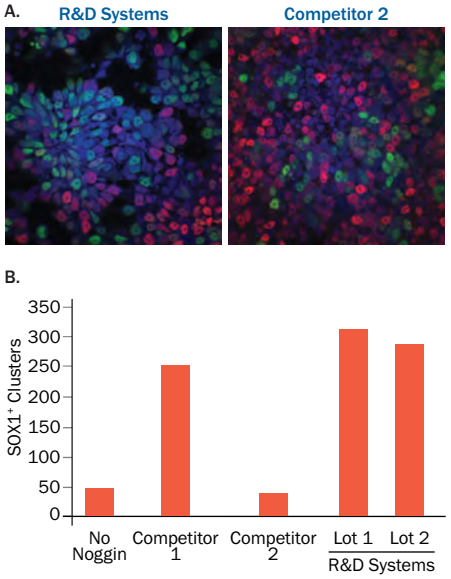
Additional Select TGF-β Superfamily Ligands, Receptors, and Regulators

Ligands	
Activin B	Human, Mouse New!
Activin AB	Human
Activin C	Human, Mouse
BMP-3	Human
BMP-5	Human, Mouse
BMP-6	Human, Mouse
BMP-7	Human, New! Mouse
BMP-9	Human, Mouse
BMP-10	Human, Mouse
BMP-15	Human
GDF-1	Human
GDF-3	Human, Mouse
GDF-5	Human, New! Mouse
GDF-6	Mouse
GDF-7	Human, Mouse
GDF-9	Human, Mouse
GDF-15	Human New!
GDNF	Human, Rat
LAP (TGF-β1)	Human
Inhibin A	Human, New! Mouse New!
Nodal	Human, Mouse
TGF-β2	Human, New! Mouse
TGF-β3	Human* New!

*A new version expressed in mammalian cells (Catalog # 8420-B3)

Receptors	
Activin RIA	Human, Mouse
Activin RIB	Human, Mouse
Activin RIIA	Human, Mouse
Activin RIIB	Human, Mouse
ALK-1	Human, Mouse
BMPR-IA/ALK-3	Human, Mouse
BMPR-IB/ALK-6	Human, Mouse
BMPR-II	Human, Mouse
Endoglin	Human, Mouse, Rat
TGF-β RI/ALK-5	Human, Mouse
TGF-β RII	Human, New! Mouse New!
TGF-β RIII	Human, Mouse

Regulators	
BAMBI/NMA	Human, Mouse New!
Chordin	Mouse
Chordin-like 1	Human
Chordin-like 2	Mouse
COCO	Human, Mouse
Cripto	Human, Mouse
Decorin	Human, Mouse
Follistatin	Human, Mouse
GASP-1, 2	Human
Gremlin	Human, Mouse
Noggin	Human, Mouse
PRDC/GREM2	Human, New! Mouse New!
SOST/Sclerostin	Human, Mouse
TSG	Human, Mouse

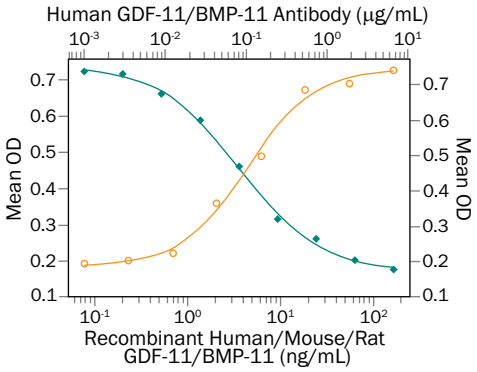


Superior and Consistent Pluripotent Stem Cell Differentiation with R&D Systems Recombinant Human Noggin. BG01V human embryonic stem cells were cultured in Mouse Embryonic Fibroblast Conditioned Media supplemented with FGF basic (5 ng/mL). Stem cells were driven into early cells of the neuroectoderm using 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 from R&D Systems or Noggin from Competitor 2. (**B**) $SOX1^+$ clusters were quantified under each of the indicated culture conditions. 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. BG01V human embryonic stem cells are licensed from ViaCyte, Inc.

Modulation of TGF-β Superfamily Signaling Pathways

Blocking and Neutralizing Antibodies: Trusted Bioactivity

Molecule	Species	Catalog #
Activin A	Human, Mouse, Rat	MAB3381
BMP-2/BMP-4	Human	MAB3552
BMP-4	Human	MAB757
BMP-6	Human	MAB507
BMP-7	Human	MAB3541
BMP-9	Human, Mouse	MAB3209
GDF-11/GDF-8	Human	MAB19582
GDF-8/Myostatin	Human, Mouse, Rat	AF788
GDNF	Human, Rat	AF-212-NA
TGF-β 1/1.2	Multi-species	AF-101-NA

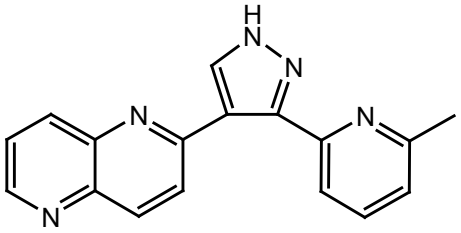


GDF-11/GDF-8 Neutralizing Antibody Blocks GDF-11 Induced Hemoglobin Expression. Recombinant Human/Mouse/Rat GDF-11/BMP-11 (Catalog # 1958-GD) induces hemoglobin expression in the K562 human chronic myelogenous leukemia cell line in a dose-dependent manner (orange line), as measured by the pseudoperoxidase 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). The ND_{50} is typically 0.04–0.2 µg/mL. This antibody also neutralizes GDF-8 in a similar bioassay.

TOCRIS™
a bio-techne brand

TGF-β Superfamily-Related Small Molecules
from Tocris Bioscience

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
ITD1	5068	Selective inhibitor of TGF-β signaling
K 02288	4986	Type 1 BMP receptor inhibitor
LY 364947	2718	Selective inhibitor of TGF-β RI
(5Z)-7-Oxozeaenol	3604	Potent and selective TAK1 MAPKKK inhibitor
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



***RepSox* - Catalog # 3742**
RepSox is a selective inhibitor of TGF-β RI/ALK-5 (IC_{50} values are 4 and 23 nM for TGF-β RI autophosphorylation and TGF-β RI binding respectively). This compound is selective for TGF-β RI over a range of kinases, including p38 MAPK, JNK1 and GSK3 (IC_{50} > 16 µM). RepSox enhances the efficiency of cellular reprogramming and replaces SOX2 by inducing Nanog expression.

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

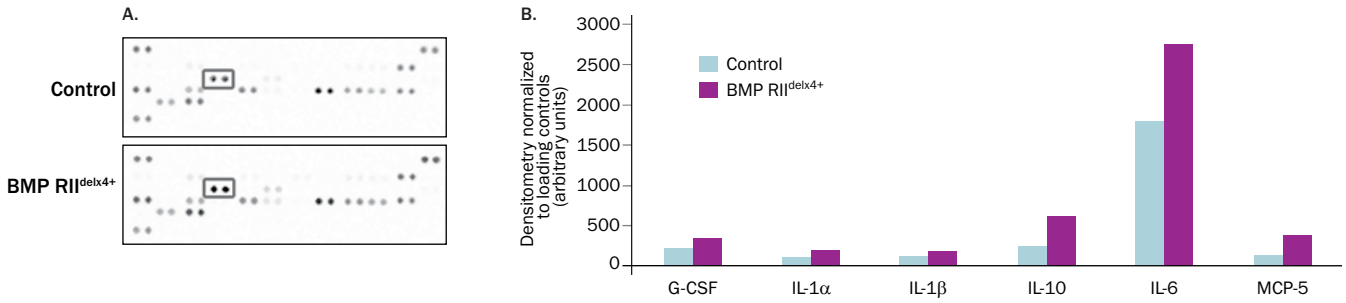
Luminex® Performance Assays

Flexible - up to 100 biomarkers can be simultaneously profiled

Economical - assays require a small sample volume (<50 µL)

Time-saving - all assays can be performed in 3-3.5 hrs

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

	Catalog #		
Kit	Human	Mouse	Rat
Cytokine Array, Panel A	ARY005	ARY006	ARY008
XL Cytokine Array	ARY022	ARY028	–
Angiogenesis Array	ARY007	ARY015	–

Investigate non-canonical TGF-β signaling

Array	Catalog #
Human Phospho-Mitogen-activated Protein Kinase (MAPK) Antibody Array	ARY002B
Human Phospho-Kinase Array	ARY003B

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rndsystems.com/proteomeprofiler

Luminex Performance Assays

R&D Systems Luminex 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 Performance Assay Panels

Human High Sensitivity Cytokine Panel A
Human High Sensitivity Cytokine Panel B
Human Angiogenesis Panel
Human TGF-β Panel

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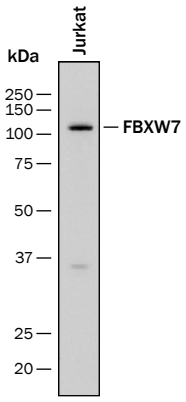
Antibodies to Visualize TGF-β Superfamily Signaling

Molecule	Species	Application	Catalog #
Endoglin/CD105	Human	FC	FAB10971 - various conjugates available
	Rat	ICC, IHC, IP, WB	AF6440
FBXW7/Cdc4	Human	WB	MAB7776
Follistatin	Human	IHC, WB	MAB669
GDF-11/BMP-11	Human	IHC, WB	MAB19581
NCAM-1/CD56	Mouse	FC	FAB7820 - various conjugates available
Ret	Mouse	IHC, WB	AF482
Smad7	Human, Mouse, Rat	IHC, WB	MAB2029
SOST/Sclerostin	Mouse	IHC, WB	AF1589
STAT3	Human, Mouse, Rat	ICC, IP, FC, WB	MAB1799

Application Key: **FC** Flow Cytometry **ICC** Immunocytochemistry **IHC** Immunohistochemistry **IP** Immunoprecipitation **WB** Western blot

Emerging TGF-β Signaling Molecule

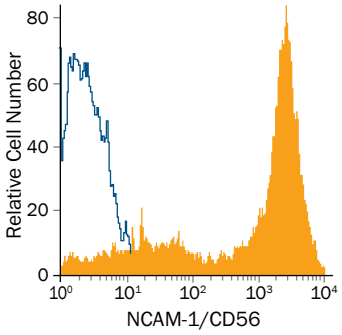
FBXW7/Cdc4



Detection of Human FBXW7/Cdc4 by Western Blot. FBXW7/Cdc4 Regulates TGF-β-dependent Cell Growth and Migration. This western blot uses the Mouse Anti-Human FBXW7/Cdc4 Monoclonal Antibody (Catalog # MAB7776) and HRP-conjugated Anti-Mouse IgG Secondary Antibody (Catalog #HAF018) to detect FBXW7/Cdc4 in Jurkat human acute T cell leukemia cell line lysates.

Reliable Antibody for Flow Cytometry

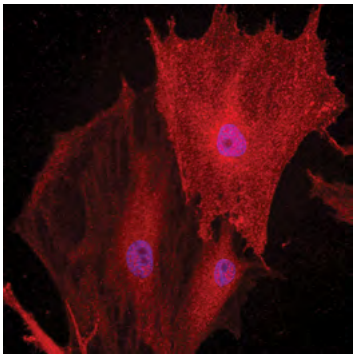
NCAM-1/CD56



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).

New Release!

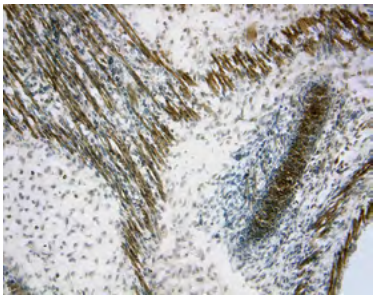
Rat Endoglin/CD105



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).

Highly Published

SOST/Sclerostin



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). *Relevant citations for SOST/Sclerostin can be viewed on rndsystems.com.

TGF-β Superfamily Signaling

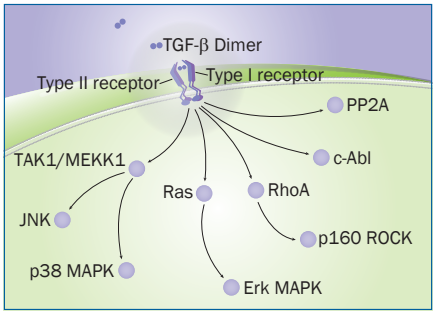
TGF-β ligands activate SMAD-dependent pathways to regulate tissue development and homeostasis, including cell proliferation, differentiation, inflammation, angiogenesis, and epithelial to mesenchymal transition. The diverse actions of the TGF-β superfamily are also due, in part, to the recruitment of SMAD-independent signaling pathways.

SMAD-Dependent Signaling

Receptor and SMAD Preference

Ligand	Type II Receptor	Type I Receptor	R-Smad	Co-Receptor	**Regulating Molecules** (Sharing interaction with ligand)
TGF-β	TGF-β RII	ALK-5	Smad2/3	Betaglycan (TGF-β2✦) Endoglin (ALK-1 specific) CD109	α_2-Macroglobulin, BAMBI/NMA*, Biglycan, BMP-1, Cripto*, Decorin, Dermatopontin, KCP/Crim2, LAP, LTBPs, Soluble Betaglycan, Soluble TGF-β RII, Tolloid, Vasorin
		ALK-2	Smad1/5/8		
		ALK-1			
Activin	Act RII/IIB	ALK-4	Smad2/3		Activin AB/BC/AE/CE, BAMBI/NMA*, Coco, Cripto, DAN, Endoglin, FLRG, Follistatin, Inhibin-Betaglycan*, KCP/Crim2
		ALK-2	Smad1/5/8		
Inhibin	Act RII/IIB			Betaglycan✦	
	BMP RII/IIB				
BMP	BMP RII	ALK-1	Smad1/5/8	RGM-A/-B/-C	BAMBI/NMA*, BMP-1, Caronte, Cerebrus, Chordin-Tsg, Chordin-like 1, Chordin-like 2, Coco, CRIM1, Endoglin, FLRG, Follistatin, FSTL4, Gremlin, Inhibin-Betaglycan*, KCP/Crim2, Nodal-BMP-7, Noggin, Noggin-SOST, PRDC, Soluble ALK-3, SOST, USAG-1
		ALK-2			
		ALK-3			
		ALK-6			
	Act RII/IIB	ALK-4	Smad2/3		
		ALK-5			
		ALK-7			
		ALK-2	Smad1/5/8		
GDF	BMP RII	ALK-5	Smad2/3	Cripto (GDF-1/3)✦	Cryptic, DAN, Follistatin, GASP-1, GASP-2, Pro-peptide (GDF-8,-11)
		ALK-6	Smad1/5/8		
	Act RIIB	ALK-4	Smad2/3		
		ALK-5			
		ALK-6	Smad1/5/8		
Nodal	Act RI/IIB	ALK-4	Smad2/3	Cripto✦	BMP7-Nodal, Cerebrus, DAN, Lefty, TMEFF1
		ALK-7			
Lefty	Act RI/IIB			Cripto (+Nodal)✦	
MIS	MIS RII	ALK-2	Smad1/5/8	**Abbreviations:** ALK - Activin-like kinase, BAMBI - BMP and activin membrane-bound inhibitor, CV-2 - Crossveinless-2, FLRG - Follistatin-related gene, FSTL4 - Follistatin-like 4, GASP - Growth and differentiation factor-associated serum protein, IGSF1 - Immunoglobulin superfamily member 1, KCP - Kielin/chordin-like protein, LTBPs - Latent TGF-β binding proteins, MIS - Müllerian inhibiting substance, Tsg - Twisted gastrulation, PRDC - Protein related to DAN and cerberus, SOST - Sclerostin, TMEFF1 - Tomoregulin-1, TSK - Tsukushi, USAG-1 - Uterine sensitization-associated gene-1. **Note:** The GDNF family utilizes a Receptor Tyorosine Kinase (RET) for signal transduction and is not included in the chart above.	
		ALK-3			
		ALK-6			
Key: ✦ Required ✶ Membrane-based					

SMAD-Independent Signaling



TGF-β superfamily ligands can activate a number of Smad-independent signaling pathways, including Ras/MAPK, PI 3-K/Akt, p38, JNK, and RhoA/ROCK in a cell type-specific and context-dependent manner. Activation of these pathways contributes to the variety of cellular responses induced by TGF-β superfamily members.

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