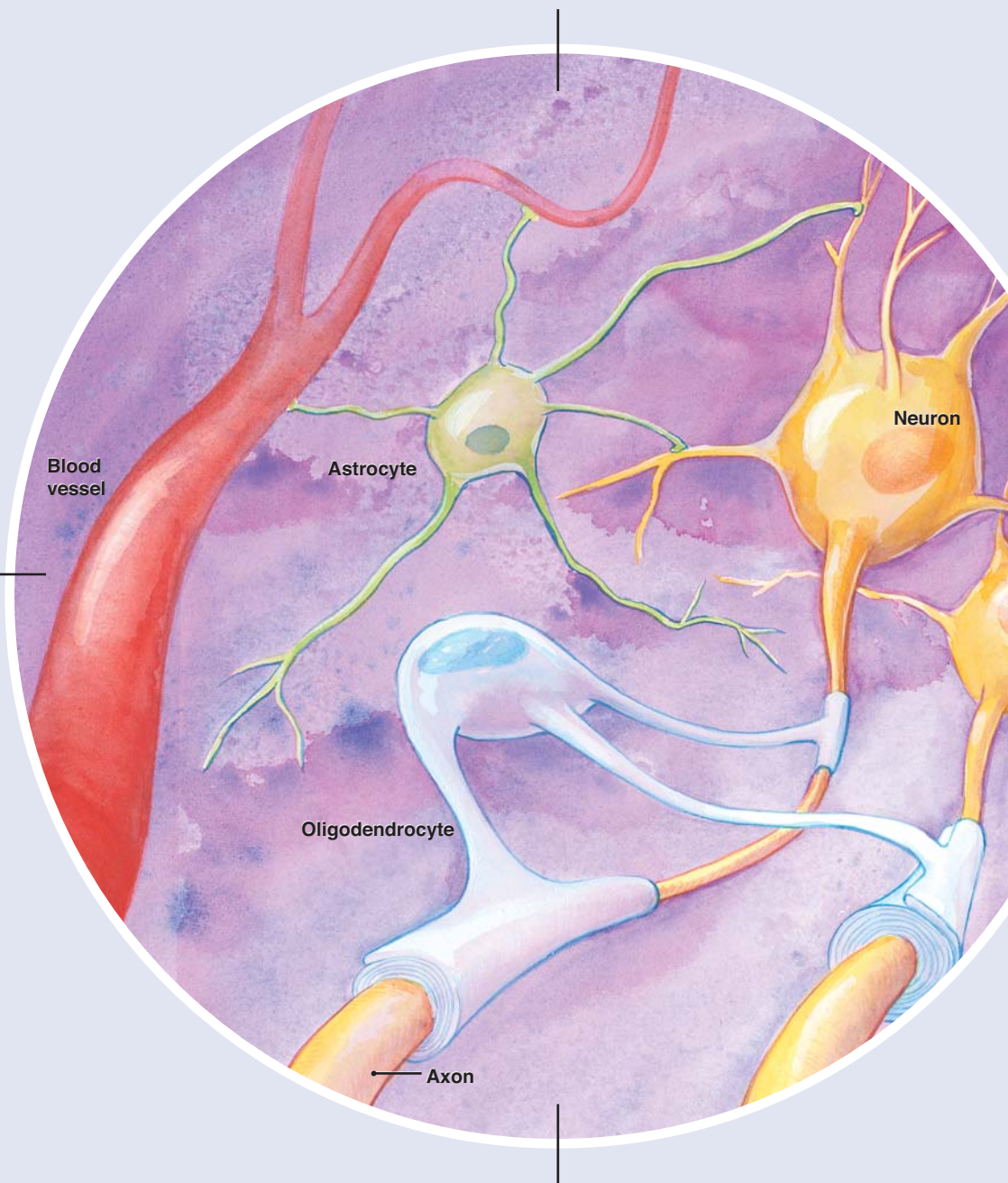


in scope | neuroscience

NEUROSCIENCE RESEARCH REAGENTS | EVERYTHING CYTOKINE & BEYOND



contents:

Tenascin-C & SVZ Stem Cells	2
NGF R/p75 ^{NTR} : Multiple Interactions Underlie Complex Functions	3
R&D Systems' Neuroscience-related Products	4-5
Wnt-5a	6
Wnt Signaling in Commissural Axon Guidance	7
β -Catenin DuoSet [®] IC ELISA Development Kit	8

Proteins | Antibodies | ELISA/Assay Kits | ELISpot Kits | Multiplex Assays
Flow Cytometry Kits | Cell Selection Kits | mRNA Quantitation Kits
Primer Pairs | Assay Services

for

Cytokines | Chemokines | Growth Factors
Cell Adhesion Molecules | Proteases & Inhibitors | Stem Cells
Signal Transduction | Apoptosis | DNA Damage & Repair | Cell Culture

R&D
SYSTEMS

Research Tools for Stem Cell Neurobiology

Research techniques are continually evolving, opening doors for novel approaches in the study of stem cells. Having quality tools to manipulate, expand, and maintain stem/progenitor cells is of critical importance for researchers. R&D Systems offers a wide selection of research tools to facilitate the differentiation, characterization, and isolation of neural stem cells.

Stem Cell Marker Antibodies

- ABCG2
- A2B5
- β III-Tubulin (Tuj1)
- Islet-1
- Nestin
- Notch 1, 2
- Nucleostemin
- Oligodendrocyte Marker O1, O4
- Otx2
- Pax 6, 7
- SSEA-1
- Sox2
- Tenascin C
- Tenascin R

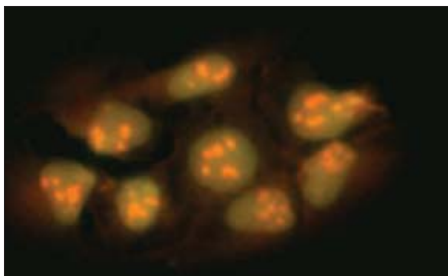


FIGURE 1. Detection of Nucleostemin in the nuclei of human U2OS cells using R&D Systems' goat anti-Nucleostemin affinity-purified polyclonal antibody (Catalog # AF1638). Cells were stained using Rhodamine Red-conjugated donkey anti-goat IgG secondary antibody and counterstained with Fluoro Nissl (green).

Please visit www.RnDSystems.com/StemCell for a complete listing of stem cell products.

Representatives from R&D Systems will be available at the annual Society for Neuroscience meeting in San Diego, CA. Please visit our booth (#4902) and attend our workshop entitled *Ex Vivo Culture of Neural Stem Cells*. The workshop will focus on how neural stem cells can be expanded *in vitro*, and how culture conditions may affect proliferation and lineage selection.

Tenascin-C & SVZ Stem Cells

The extracellular matrix (ECM) is a general term for noncellular materials that provide cohesion and support to the general organism. While the most common fibrous components of the ECM are the Collagens (20 different varieties), some of the more unique and intriguing molecules are the Tenascins.¹ Tenascins make up a small family of matrix molecules that contain repeating EGF-like and fibronectin type III modules.^{2,5} Tenascin is an amalgam of two Latin words, *tenere*: "to hold," and *nasci*: "to be born." The molecule was independently described as present in both tendons (to hold) and embryonic connective tissue (to be born).⁵ Tenascin-C (TN-C) is synthesized as a 2019 amino acid precursor with an N-terminal "Tenascin assembly domain," 13 full EGF-like modules, and 14 type III fibronectin-like domains. The assembly domain directs the formation of a disulfide-linked homohexamer (or hexabrachion) with six "arms." The molecule has 64 potential alternate splice forms, all based on the presence or absence of fibronectin domains 6 to 11 (otherwise called A1, A2, A4, B, C, and D).⁴ In mouse brain, there are 27 known isoforms.^{2,4}

Tenascins are of interest because of their unusual effects on cells. While matrix molecules often provide a framework for cell spreading, adhesion, and/or growth factor storage, TN-C would seem to inhibit cell adhesion, while promoting mitosis (and cell migration under certain circumstances).^{6,7} In the nervous system, interest in TN-C has focused on its regulation of stem cell development in the subventricular zone (SVZ) of the brain. In the neonatal mouse, the SVZ is one of at least two areas known to contain neural stem cells.⁸ In this region, there are four functionally different cell types: Ependyma, type A cells/neuroblasts, type B cells/SVZ astrocytes, and type C cells/immature precursors. The type B cells/SVZ astrocytes are believed to be neuronal stem cells. These cells divide and give rise to type C cells/immature precursors, which then "mature" into type A cells/neuroblasts.⁹ Various soluble mediators in this stem cell niche drive the production of the different cell types. Normally, early stem cells first respond to FGF basic by proliferating and upregulating the expression of the EGF receptor (EGF R). These cells often become glia. These processes are blocked by BMP-4.¹⁰ In the absence of TN-C, BMP-4 would seem to predominate and promote neuronal development. Type B cells/SVZ astrocytes, however, are believed to make TN-C. When TN-C is secreted, it apparently interferes with BMP activity, again promoting an EGF R phenotype (Figure 1).^{7,11} Thus, an extracellular matrix molecule may well play a central and autocrine role in growth factor-induced neuro- and gliogenesis.¹¹

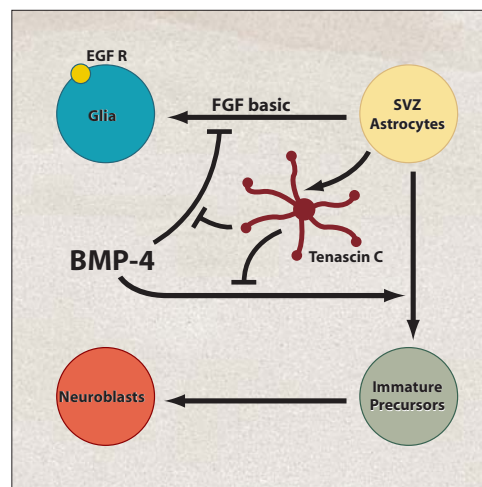


FIGURE 1. In a process inhibited by BMP-4, SVZ astrocytes respond to FGF basic with an upregulation of EGF R and a shift toward glial fate. TN-C may enhance FGF basic sensitivity and decrease sensitivity to BMP-4, thus promoting this developmental progression.

REFERENCES

1. Bosman, F.T. & I. Stamenkovic (2003) *J. Pathol.* **200**:423.
2. Weller, A. *et al.* (1988) *J. Cell Biol.* **107**:2341.
3. Matsumoto, K. *et al.* (2002) *Exp. Mol. Pathol.* **72**:186.
4. Joester, A. & A. Faissner (1999) *J. Biol. Chem.* **274**:17144.
5. Chiquet-Ehrismann, R. *et al.* (1986) *Cell* **47**:131.
6. Chiquet-Ehrismann, R. & R.P. Tucker (2004) *Int. J. Biochem. Cell Biol.* **36**:1085.
7. Garcion, E. *et al.* (2001) *Development* **128**:2485.
8. Doetsch, F. (2003) *Curr. Opin. Genet. Dev.* **13**:543.
9. Lim, D.A. *et al.* (2000) *Neuron* **28**:713.
10. Lillien, L. & H. Raphael (2000) *Development* **127**:4993.
11. Garcion, E. *et al.* (2004) *Development* **131**:3423.

NGF R/p75^{NTR}: Multiple interactions underlie complex functions

The neurotrophins (NGF, BDNF, NT3, and NT4) are a family of proteins that mediate their effects by binding to the Trk receptors A through C, and NGF R/p75^{NTR}. The Trks are well-described tyrosine kinases known for their roles in cell survival, synapse formation, synaptic plasticity, and axon guidance.^{1,2} NGF R is a biochemical, structural, and physiological outlier among the neurotrophin receptors. Unlike the Trks, NGF R exhibits little selectivity for individual neurotrophins. It also has no intrinsic tyrosine kinase activity. In fact, it is a member of the tumor necrosis (TNF) superfamily (TNFRSF16). The cytoplasmic portion of the receptor contains a death domain and the extracellular region exhibits a tandem array of cysteine-rich domains characteristic of the TNF receptor family. The crystal structure of NGF bound to NGF R has recently been determined and suggests that the complex exists in a 2:1 stoichiometry, unlike the dimeric form of NGF bound to TrkA.^{3,4}

NGF R has remarkable functional diversity due to its array of putative ligands and co-receptors (Figure 1). Whether NGF R is an inducer of apoptosis or survival is highly context-dependent. For instance, co-expression of Trks with NGF R can change the effect of a neurotrophin from pro-apoptotic to pro-survival.⁵ Interaction between NGF R and Trks may also enhance receptor selectivity for a particular neurotrophin.⁶ Neurotrophins are synthesized in a pro form and are cleaved to produce the mature protein. Although capable of binding the mature protein, recent evidence suggests that some NGF R effects may be mediated by the pro-neurotrophin. Pro-NGF is an effective inducer of NGF R-mediated apoptosis *in vitro*, and similar activities have been described in *in vivo* systems as well.⁷⁻¹⁰ Recently, Sortilin, a vesicular sorting protein and Neurotensin receptor, has been implicated as an NGF R co-receptor necessary for pro-NGF-mediated apoptosis.¹¹

Interestingly, NGF R appears to act as a receptor or co-receptor for several ligands that are unrelated to the neurotrophin family. For instance, NGF R binds several pathology-associated proteins/peptides including amyloid β (A β), rabies virus glycoprotein (RVG), and prion peptide (PrP).¹² A β and PrP appear to affect cell survival although the physiological importance of this activity continues to be elucidated.¹³⁻¹⁵ Myelin proteins

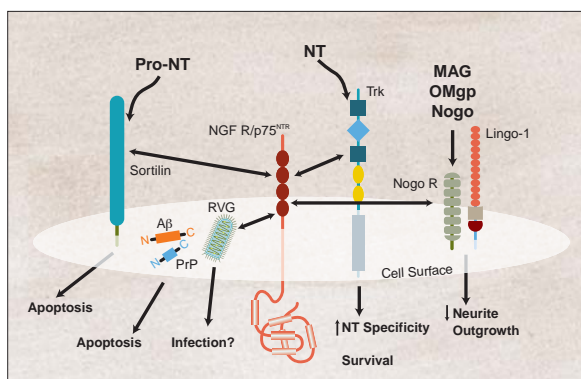


FIGURE 1. The many functions of the NGF R/p75^{NTR} are regulated by novel interactions with several different ligands and co-receptors.

including MAG, OMgp, and Nogo inhibit neurite outgrowth and may play a role in preventing regeneration following injury.¹⁶ Their receptor, Nogo R, has no known signaling capability. It has been demonstrated that NGF R acts as a Nogo R co-receptor, mediating inhibitory effects on neurite outgrowth.¹⁷ Recently, Lingo-1, a novel brain-specific transmembrane protein, has been identified as an additional component of the NGF R/Nogo R receptor complex, and is necessary for myelin inhibition of neurite growth.¹⁸

REFERENCES

- Chao, M.V. (2003) *Nat. Rev. Neurosci.* **4**:299.
- Teng, K.K. & B.L. Hempstead (2004) *Cell. Mol. Life. Sci.* **61**:35.
- He, X.L. & K.C. Garcia (2004) *Science* **304**:870.
- Wiesmann, C. *et al.* (1999) *Nature* **401**:184.
- Yoon, S.O. *et al.* (1998) *J. Neurosci.* **18**:3273.
- Bibel, M. *et al.* (1999) *EMBO J.* **18**:616.
- Lee, R. *et al.* (2001) *Science* **294**:1945.
- Beattie, M.S. *et al.* (2002) *Neuron* **26**:375.
- Harrington, A.W. *et al.* (2004) *Proc. Natl. Acad. Sci. USA* **101**:6226.
- Srinivasan, B. *et al.* (2004) *J. Biol. Chem.* July: Epub ahead of print.
- Nykjaer, A. *et al.* (2004) *Nature* **427**:823.
- Butowt, R. & C.S. von Bartheld (2003) *Eur. J. Neurosci.* **17**:673.
- Della-Bianca, V. *et al.* (2001) *J. Biol. Chem.* **276**:38929.
- Yaar, M. *et al.* (1997) *J. Clin. Invest.* **100**:2333.
- Zhang, Y. *et al.* (2003) *J. Neurosci.* **23**:7385.
- McGee, A.W. & S.M. Strittmatter (2003) *Trends Neurosci.* **26**:193.
- Wang, K.C. *et al.* (2002) *Nature* **420**:74.
- Mi, S. *et al.* (2004) *Nat. Neurosci.* **7**:221.

Neurotrophic/Growth Factors & their Receptors

R&D Systems offers a broad array of products for the study of neurotrophic and growth factors and their receptors in various animal models.

LIGANDS	BINDING PROTEINS	RECEPTORS
Artemin GDNF Neurturin		GFR α -1 GFR α -2 GFR α -3 GFR α -4 Ret
BDNF β -NGF NT-3 NT-4		NGF R TrkA TrkB TrkC
CNTF		CNTF R α gp130 LIF R
EGF Neuregulins		EGF R ErbB2 ErbB3 ErbB4
FGFs	FGF-BP	FGF R1 FGF R2 FGF R3 FGF R4 FGF R5
IGF-I	ALS IGFBPs	IGF-1 R
PDGF-AA PDGF-AB PDGF-BB PDGF-CC PDGF-DD		PDGF R α PDGF R β
VEGF VEGF-B VEGF-C VEGF-D		Neuropilin-1 Neuropilin-2 VEGF R1 VEGF R2 VEGF R3

Please visit our website at www.RnDSystems.com for more information.

Neuroscience Research Reagents

ANALYTE	PROTEIN	ANTIBODY	ELISA/ASSAY	PRIMER PAIR
A2B5		H M R Ch		
Activin A	H M R	H M R	H	
Activin AB	H			
Activin B	H			
Activin C		H M		
Activin RIA	H	H		
Activin RIB	H	H M		
Activin RIIA	H	H		
Activin RIIB	H	H		
Adiponectin	H M	H M	H M	
Agrin	R	R		
AgRP	H	H M	H	
ALK-1	H M	H M		
ALK-7	R	R		
Artemin	M	M		
BACE-1	H	H		H M
BACE-2				H M R
BDNF	H	H	H	
BMP-1	H			
BMP-2	H Z	H Z	H M R	
BMP-3	H	H		
BMP-3b	H	H		
BMP-4	H Z	H Z	H	
BMP-5	H	H	H	
BMP-6	H	H	H	
BMP-7	H	H	H	
BMP-8		H		
BMPR-IA	H M	H		
BMPR-IB	H M	H M		
BMPR-II	H	H		
β-Catenin		H M R	H	
CHL-1/L1CAM-2	H M			
Chordin	M	M		
Chordin-Like 1	H			
CNTF	H R	H R	H R	
CNTF Rα	H R	H R		
Collagen I	R B			
Collagen IV	M			
Contactin-1	H	H		
Contactin-2	H			
Contactin-4	H			
Cripto	M	M		
Cripto-1	H	H		
Cryptic	H	H M		
DAN	H M	H M	H	
DCC*	M	M		
Desert Hedgehog		M		
Dkk-1	H M	H		
Dkk-3		H M		
Dkk-4	H	H		

ANALYTE	PROTEIN	ANTIBODY	ELISA/ASSAY	PRIMER PAIR
DLL4	H M	M		
EGF	H M	H	H	
EGF R	H	H M	H	
Endocan	H	H M		
EphA1	H	H		
EphA2	M	M		
EphA3	M	M		
EphA4	M	M		
EphA5	R	R		
EphA6	M	M		
EphA7	M	M		
EphA8	M	M		
EphB1	R	R		
EphB2	M	M		
EphB3	M	M		
EphB4	M	M		
EphB6	M	M		
<i>Please visit www.RnDSystems.com for Ephrins.</i>				
ErbB2	H	H	H	
ErbB3	H	H	H	
ErbB4	H	H	H	
FGF acidic	H B	H B	H	
FGF basic	H B	H B	H	H
FGF R1	H	H		
FGF R2	H M	H M		
FGF R3	H M	H M	H	
FGF R4	H	H		
FGF R5 β		M		
FGF-3	H	H		
FGF-4	H	H	H	
FGF-5	H	H		
FGF-6	H	H	H	
FGF-8	M	H M		
FGF-9	H	H	H	
FGF-10	H	H		
FGF-11		H		
FGF-13		H		
FGF-16	H	H		
FGF-17	H	H		
FGF-19	H	H		
FGF-BP	R	H R		
Fibronectin	H B			
Frizzled-1		H M		
Frizzled-2	M	M		
Frizzled-3		H M		
Frizzled-4	M	H M		
Frizzled-5	H	H		
Frizzled-6		M		
Frizzled-7		H M		
Frizzled-8	M	M		

KEY |

H Human **R** Rat **A** Amphibian **Ca** Canine **Ns** Species Non-specific
M Mouse **P** Porcine **B** Bovine **Ch** Chicken **Z** Zebrafish

ANALYTE	PROTEIN	ANTIBODY	ELISA/ASSAY	PRIMER PAIR
GDF-1		M		
GDF-3		M		
GDF-5	M	M		
GDF-6	M			
GDF-7	M	M		
GDF-8	M	M		
GDF-9		M		
GDF-11	H			
GDF-15	H	H		
GDNF	H R	H	H	
GFAP				H M R
GFR α -1	H R	H R		
GFR α -2	H M	H M		
GFR α -3	H	H		
GFR α -4		H M		
gp130	H M	H M	H	
Gremlin	M	M		
Growth Hormone	H	H R		
Growth Hormone R	H M R	H M R		
Hip	M	M		
IGFBP-1	H M	H M	H	
IGFBP-2	H M	H M	H M	
IGFBP-3	H M	H M	H M	
IGFBP-4	H	H	H	
IGFBP-5	H M	H M	M	
IGFBP-6	H M	H M	H M	
IGFBP-rp1	H	H		
IGF-I	H M	H M	H M	
IGF-I R	H	H	H	
IGF-II	H M	H M	M	
Indian Hedgehog	M	M		
Insulin		H M B		
Insulin R	H	H		
Integrin α 2		H M		
Integrin α 3		H		
Integrin α 4		H		
Integrin α 5		H M		
Integrin α 6		H M B		
Integrin α E		M		
Integrin α M		H M		
Integrin α V		H		
Integrin α X		H		
Integrin β 1		H		
Integrin β 2		H		
Jagged 1	R	H R		
Jagged 2		H		
Kallikrein 8	H	H		
KGF/FGF-7	H Ca	H	H	
Kremen-1	M	M		
Kremen-2	H M			

ANALYTE	PROTEIN	ANTIBODY	ELISA/ASSAY	PRIMER PAIR
Laminin I	M			
LAP (TGF- β 1)	H	H		
Latent TGF- β 1	H		H	
Latent TGF- β bp1		H		
MAG	R	R		
NCAM				H M R
NCAM-L1	H	H		
Neogenin*	M	M		
Nestin		H		H M R
Netrin-1*	M Ch	M Ch		
Netrin-2*	Ch	Ch		
Netrin-4*	H M	H		
Netrin-G1a*	M	M		
Neuropilin-1*	R	R		
Neuropilin-2*	R	H R		H M R
Neurotrimin		H		
Neurturin	H M	H M		
β -NGF	H M R	H R	H R	H M R
NGF R/TNFRSF16	H M	H M		H M R
Nodal	M	M		
Noggin	M	M		
Nogo R	H M	H M		
Nope	M	M		
Notch-1	R			
Notch-2	R	R		
Notch-3	H M	H M		
NrCAM	H			
NRG-1- α	H	H		
NRG-1- β 1	H	H	H	
NRG-3		M		
NT-3	H	H	H	
NT-4	H	H	H	
OCAM		M		
Oligodendrocyte Marker O1		H M R Ch		
Oligodendrocyte Marker O4		H M R Ch		
Otx2		H		
Parkin		H		
PDGF	H P	H		
PDGF R α	H M	H M		H
PDGF R β	H M	H M	H	H M R
PDGF-A				H M
PDGF-AA	H R	H R	H	
PDGF-AB	H R		H M R	
PDGF-B		H		H
PDGF-BB	H R	H	H	
PDGF-C	M	H M		
PDGF-CC	H			
PDGF-D		H		

KEY |

H Human
M MouseR Rat
P PorcineA Amphibian
B BovineCa Canine
Ch ChickenNs Species Non-specific
Z Zebrafish

Wnt-5a

The Wnts are a family of glycoproteins with several putative functions in the nervous system including regulating pattern formation, cell growth, neural crest development, synapse formation, axon guidance, and neurodegenerative disease.¹⁻³ Wnt signaling cascades include the canonical Wnt/ β -Catenin pathway leading to β -Catenin accumulation, and the non-canonical Wnt/ Ca^{2+} pathway accompanied by intracellular Ca^{2+} release.⁴ Wnt-5a, specifically, acts via the Wnt/ Ca^{2+} pathway, and in several contexts may suppress canonical signaling.⁵ Functionally, it may regulate gastrulation, limb development, AP axis extension, hematopoiesis, and tumor invasiveness.⁶⁻⁹ In the nervous system, it has putative roles in dopaminergic differentiation and pituitary organogenesis, and is expressed by several brain tumor types.¹⁰⁻¹²

REFERENCES

1. Patapoutian, A & L.F. Reichardt (2000) *Curr. Opin. Neurobiol.* **10**:392.
2. Zou, Y. *et al.* (2004) *Trends Neurosci.* **27**:528.
3. Caricasole, A. *et al.* (2003) *Trends Pharm. Sci.* **24**:233.
4. Miller, J.R. (2001) *Genome Biol.* **3**:REVIEWS3001.
5. Kuhl, M. (2004) *Front. Biosci.* **9**:967.
6. Yamanaka, H. *et al.* (2002) *EMBO Rep.* **3**:69.
7. Terry, P. *et al.* (1999) *Development* **126**:1211.
8. Austin, T.W. *et al.* (1997) *Blood* **89**:3624.
9. Weeraratna, A.T. *et al.* (2002) *Cancer Cell* **1**:279.
10. Castelo-Branco, G. *et al.* (2003) *Proc. Natl. Acad. Sci. USA* **100**:12747.
11. Cha, K.B. *et al.* (2004) *Mech. Dev.* **121**:183.
12. Howng, S.L. *et al.* (2002) *Cancer Lett.* **183**:95.

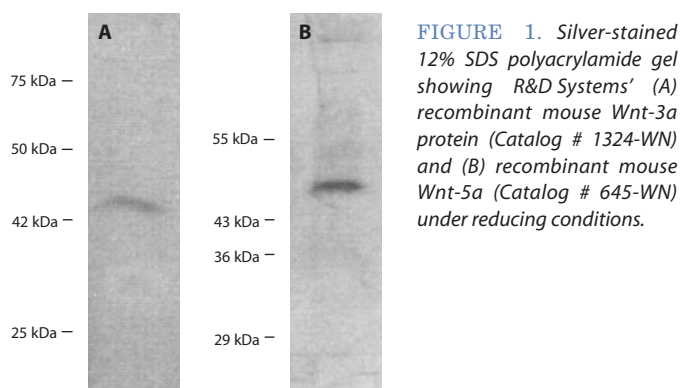


FIGURE 1. Silver-stained 12% SDS polyacrylamide gel showing R&D Systems' (A) recombinant mouse Wnt-3a protein (Catalog # 1324-WN) and (B) recombinant mouse Wnt-5a (Catalog # 645-WN) under reducing conditions.

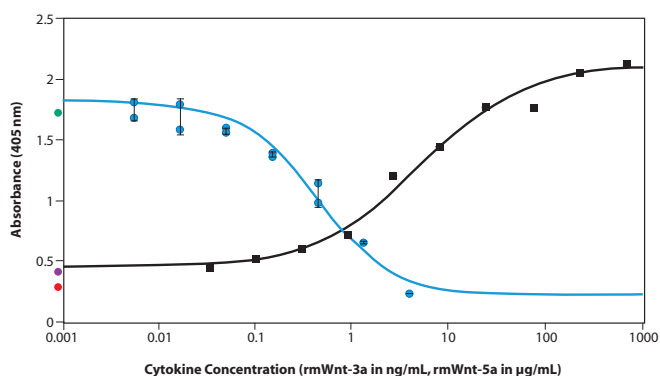


FIGURE 2. Wnt-3a and Wnt-5a have opposing effects on alkaline phosphatase (AP) expression in MC3T3E1 pre-osteoblasts. Wnt-3a enhances BMP-2 (5 ng/mL) induced differentiation in a dose dependent fashion (black). BMP-2 is added at 5 ng/mL and causes a minimal increase in AP on its own at this concentration (purple) as compared to untreated (red) cells. Wnt-5a diminishes the ability of Wnt-3a to induce AP expression in a dose dependent manner (blue). Wnt-3a added at 20 ng/mL and BMP-2 at 5 ng/mL (green) results in significant AP expression that is reduced with increasing amounts of Wnt-5a.

ANALYTE	PROTEIN	ANTIBODY	ELISA/ASSAY	PRIMER PAIR
Presenilin-1		H	H	
Presenilin-2		H		
Prolactin	H M	H M		
Prolactin R	H M R	H R		
RAGE	H M R	H M R	H	
Resistin	M	H M	H M	
Ret	H M	H M		
ROBO1		R		
S100B		H		
SAP	H R			
Semaphorin 3A	H	H		
Semaphorin 3C		M		
Semaphorin 6A	H	H M		
Semaphorin 6B		H		
Semaphorin 6D		H		
Semaphorin 7A		M		
sFRP-1	H	H		
sFRP-2	M			
sFRP-3	H M	H M		
sFRP-4	H	H		
Sonic Hedgehog	H M	H M	M	
SOST	H M	H M		
Synuclein- α		H		
TGF- β 1	H P	Ns	H M R P	H M
TGF- β 1.2	H	Ns		
TGF- β 2	H P	Ns	H	H
TGF- β 3	H	Ns	H	H M R
TGF- β 5	A	Ns		
TGF- β RI	M	M		H M R
TGF- β RII	H M	H M		
TGF- β RIIb	H	H		
TGF- β RIII	H	H		
TrkA	H R	H		
TrkB	H M	H M		
TrkC	H M	H M		
TSG	M	M		
UNC5H1*	R			
UNC5H2*	R	R		
UNC5H3*	H	H		
UNC5H4*	H	H		
VEGF	H M R Ca Z	H M R Z	H M R	H M
VEGF R1	H M	H M	H M	H M
VEGF R2	H M	H M	H M	H M
Wnt-1		M		
Wnt-3a	M	M		
Wnt-4		M		
Wnt-5a	M	M		
Wnt-10b		M		

* These products are covered under one or more patents held by the Regents of the University of California.

Wnt Signaling in Commissural Axon Guidance

During development, neurons respond to attractive and repulsive guidance cues in the extracellular environment. Commissural axons of the dorsolateral spinal cord take a trajectory toward the floor plate, traverse the ventral midline, and then turn sharply along the longitudinal axis toward the brain (Figure 1).^{1,2} Attractive guidance cues, such as Netrin-1 and Shh, and repulsive cues such as BMP-7 and GDF-7, are responsible for their initial ventral growth.³⁻⁵ As the axons cross the midline, they no longer respond to chemoattractants and instead become responsive to several chemorepellents. These chemorepellents, including Slits, Semaphorins, and Ephrins, stop axons from re-crossing the midline and guide them into the anterior-posterior axis.³

What are the factors that influence this sharp turn in the anterior direction? In a test of candidate molecules such as HGF, FGFs, BMPs, Wnts, and Shh, Lyuksytova *et al.* demonstrate that only the Wnts (-1, -4, -5a, -6, and -7b) stimulate the extension of axons that have crossed the midline.⁶ However, none were capable of influencing the outgrowth of "pre-crossing" commissural axons. Wnt expression patterns, as detected by *in situ* hybridization in mouse embryos, indicate that Wnt-4 exhibits a decreasing anterior-posterior gradient along the floor plate at developmental stages necessary to influence the turning of commissural axons (Figure 1).⁶ Wnt-5a and -7b also show expression in the spinal cord in regions where

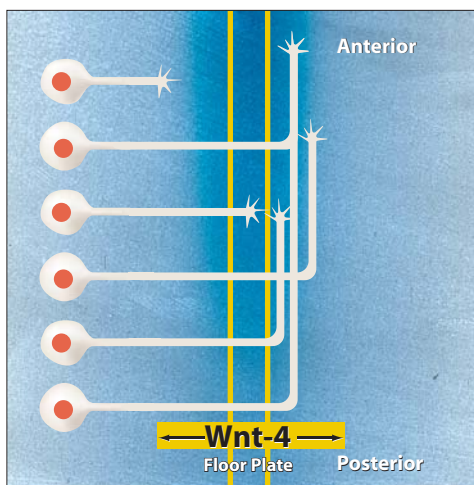


FIGURE 1. An "open book" schematic illustrates that an anterior to posterior gradient of Wnt-4 guides post-crossing commissural axons on their turn along the longitudinal axis of the spinal cord.

commissural axon turning occurs, but without a perceivable gradient. In addition, Wnt inhibitor molecules such as sFRP-1, -2, and -3, block the growth effect of Wnt-4 on "post-crossing" commissural axons, and severely impair anterior turning after midline crossing.⁶ A role for Wnts in the anterior-posterior guidance of commissural axons is further supported by experiments involving the Wnt receptors: the Frizzled family and the LRP6 co-receptor. Frizzled-3, -8, and -9 are expressed in the spinal cord during the time when commissural axons are making their anterior turn.⁶ In mouse embryos with a null mutation of Frizzled-3, pathways of "pre-crossing" commissural axons are normal, while the "post-crossing" axons project randomly along the anterior-posterior axis.⁶ All other markers of spinal cord development and patterning appear normal, suggesting that the effect is due to faulty Wnt signaling in the guidance of axons and not to a more general patterning defect during spinal cord development.^{6,7} Rather surprisingly, and despite other axial patterning defects, LRP6 knock-out mice do not demonstrate any abnormal phenotype in either the ability of commissural axons to migrate toward and cross the midline, or in making their anterior turn.^{6,8} This suggests that the attractive mechanism for Wnt/Frizzled does not occur through the canonical Wnt pathway, but likely involves a Wnt-4/Frizzled-3 signaling pathway that does not require an LRP co-receptor.

REFERENCES

1. Bovolenta, P. & J. Dodd (1990) *Development* **109**:435.
2. Imondi, R. & J.B. Thomas (2003) *Science* **302**:1903.
3. Dickson, B.J. (2002) *Science* **298**:1959.
4. Charron, F. *et al.* (2003) *Cell* **113**:11.
5. Butler, S.J. & J. Dodd (2003) *Neuron* **38**:389.
6. Lyuksytova, A.I. *et al.* (2003) *Science* **302**:1984.
7. Wang, Y. *et al.* (2002) *J. Neurosci.* **22**:8563.
8. Pinson, K.I. *et al.* (2000) *Nature* **407**:535.

BMP Family Antibodies for Neuroscience Research

R&D Systems offers a variety of application-validated antibodies for the study of bone morphogenetic proteins (BMPs) and growth differentiation factors (GDFs), key factors in neurodevelopment, neurodegenerative disorders, and protection against neuronal damage.

BMP/GDF Family Antibodies

ANALYTE	SPECIES	POLYCLONAL ANTIBODY	MONOCLONAL ANTIBODY
BMP-2	Human		W E
BMP-2a	Zebrafish		B W F
BMP-2/4	Human	W E I	B W E
BMP-3	Human	W E I	
BMP-3b/GDF-10	Human	W E I	
BMP-4	Zebrafish		W E
BMP-4	Human	B W E	B W E
BMP-5	Human	B W E I	B W E
BMP-6	Human	B W E I	B W E
BMP-7	Human	W E	B W E I
BMP-8	Human	W E	W E
BMPR-1A/ALK-3	Human	W E F	
BMPR-1B/ALK-6	Human	W E F	W E
BMPR-1B/ALK-6	Human/Mouse		W E F
BMPR-II	Human	B W E I F	W E
GDF-5/BMP-14	Mouse	W I	W I
GDF-7/BMP-12	Mouse	W E	

*Bioassay: Neutralization and/or Adhesion Blockade

B = Bioassay W = Western Blot E = ELISA
I = IHC F = Flow Cytometry

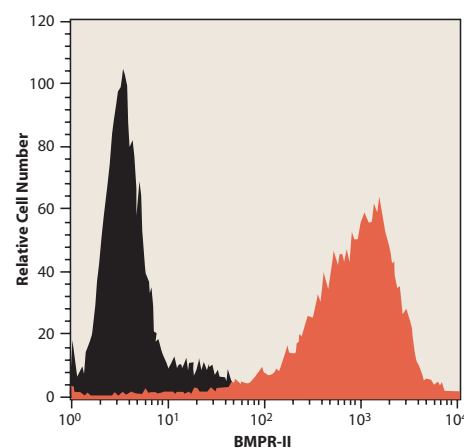


FIGURE 1. Reactivity of BMPR-II on human prostate adenocarcinoma (PC3) cells using R&D Systems' goat anti-human BMPR-II affinity purified polyclonal antibody (Catalog # AF811). Cells were stained using a PE-conjugated anti-goat IgG secondary antibody (red). Control staining is shown in black.

Please visit www.RnDSystems.com/BMPFamily for a complete listing of BMP products.

β -Catenin DuoSet[®] IC ELISA Development Kit

β -Catenin is a multifunctional intracellular protein with diverse roles such as transcriptional developmental target gene and structural protein in cell adhesion. It is also an oncoprotein, and when unregulated, is associated with several cancers.

There are thought to be multiple "pools" of β -Catenin in the cytosol. The largest is believed to be structural, and is associated with actin and membrane-bound Cadherins. β -Catenin serves as a bridge between the Cadherin C-terminus and actin-associated α -Catenin.^{1,2} β -Catenin is also well known for its involvement in canonical Wnt signaling pathways. It exists in a complex that includes Axin, CK-I, APC, and GSK-3 β . It is repressed via CK-I and GSK-3 β phosphorylation, qualifying it for ubiquitination and degradation. Wnt signaling interrupts this process, resulting in unphosphorylated β -Catenin accumulation, nuclear translocation, and gene activation.^{3,5} β -Catenin may also serve as a mediator for steroid hormone signaling. It associates with the androgen receptor following androgen

binding, and this complex is known to translocate to the nucleus and activate genes.⁶ In another putative pool, β -Catenin is in a complex with Presenilin-1, PKA, and GSK-3 β . PKA and GSK-3 β can phosphorylate and repress β -Catenin activity in a manner parallel to, but independent of the Wnt-regulated Axin complex.⁷

R&D Systems offers a Human DuoSet IC ELISA Kit for accurately quantifying intracellular β -Catenin levels (Figure 1). DuoSet IC ELISA Kits contain the basic components necessary for sandwich ELISA development.

For details see our website at www.RnDSystems.com.

REFERENCES

1. van Noort, M. *et al.* (2002) *J. Biol. Chem.* **277**:17901.
2. Gooding, J.M. *et al.* (2004) *BioEssays* **26**:497.
3. Polakis, P. (2002) *Curr. Biol.* **12**:R499.
4. Hagen, T. *et al.* (2002) *J. Biol. Chem.* **277**:23330.
5. Ban, K.C. *et al.* (2003) *Cancer Lett.* **199**:201.
6. Mulholland, D.J. *et al.* (2002) *J. Biol. Chem.* **277**:17933.
7. Kang, D.E. *et al.* (2002) *Cell* **110**:751.

Quantification of β -Catenin in Human Cell Lines

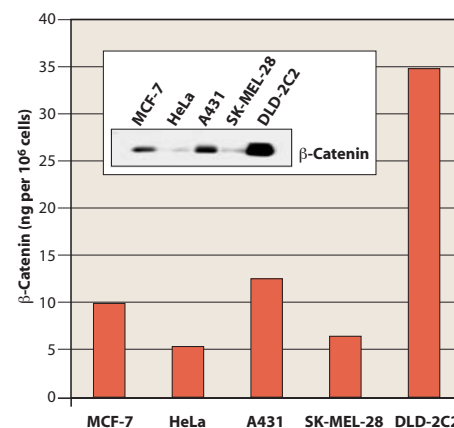


FIGURE 1. Lysates from human MCF-7, HeLa, A431, SK-MEL-28, and DLD-2C2 cell lines were assessed for β -Catenin levels using R&D Systems' β -Catenin DuoSet IC ELISA (Catalog # DYC1329). The same lysates were also electrophoresed and immunoblotted (inset) with R&D Systems' mouse anti-human β -Catenin monoclonal antibody (Catalog # MAB1329). The DuoSet IC ELISA results correlate well with β -Catenin levels as detected by Western blot.



R&D Systems, Inc.
614 McKinley Place NE
Minneapolis, MN 55413
Tel: (612) 379-2956
(800) 343-7475
Fax: (612) 656-4400
www.RnDSystems.com



PRSR STD
U.S. POSTAGE
PAID
R&D SYSTEMS

Change Service Requested