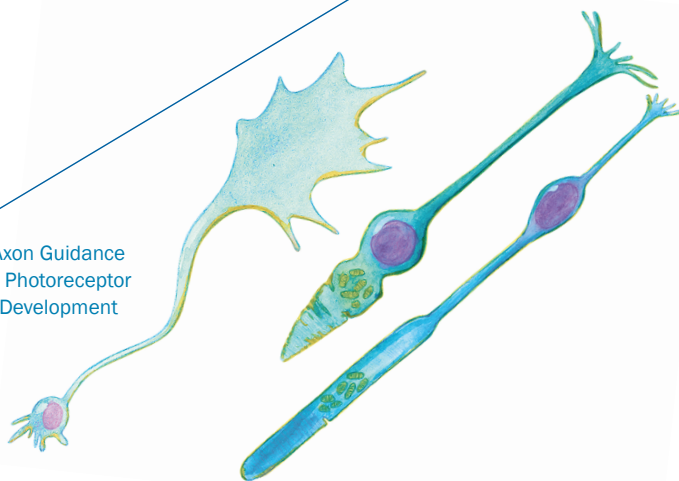
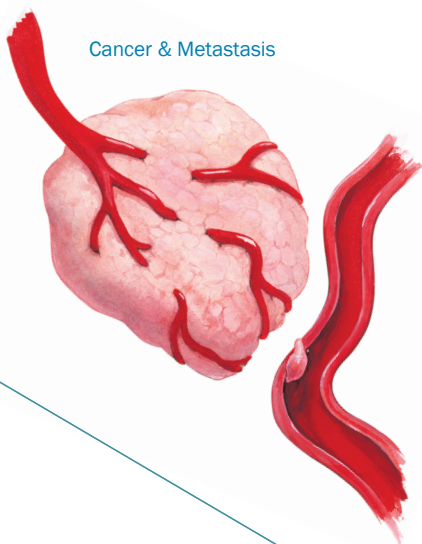


# Products for Semaphorin Research

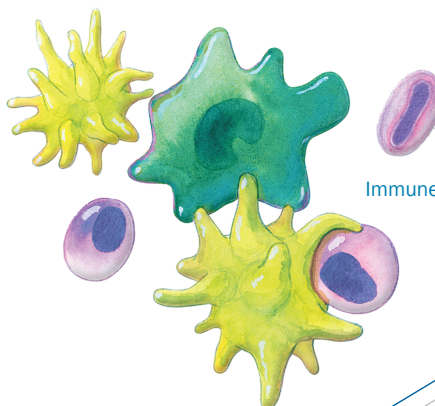
Axon Guidance  
& Photoreceptor  
Development



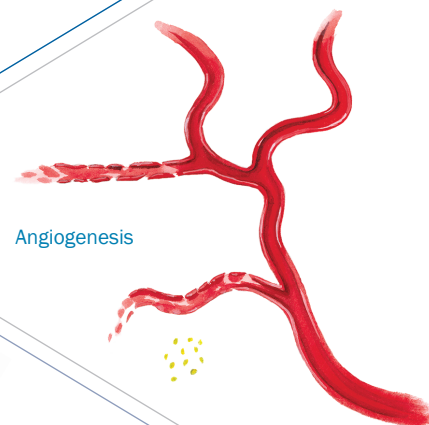
Cancer & Metastasis



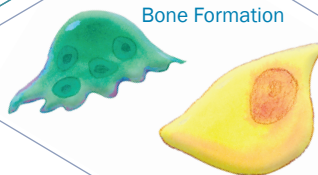
Immune Function



Angiogenesis



Bone Formation

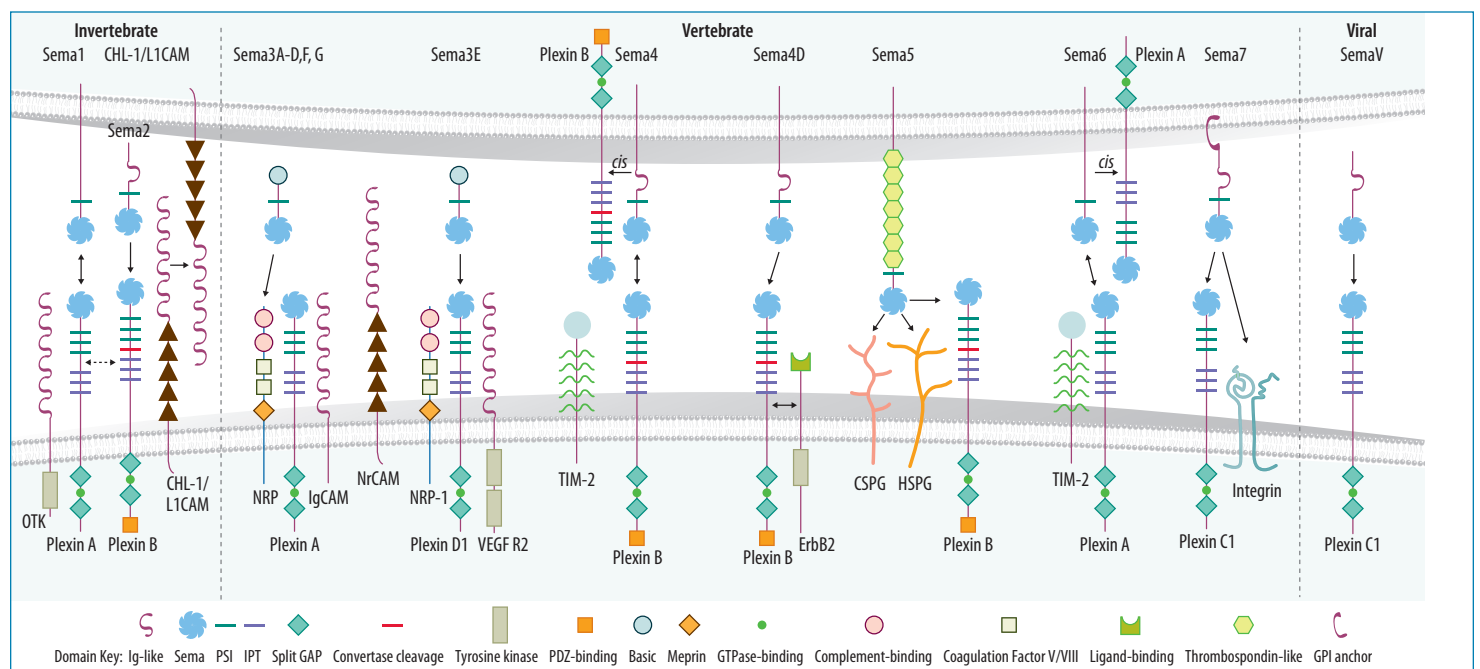


# Semaphorins, Plexins, Neuropilins, and Related Molecules

Initially characterized as axon guidance cues, Semaphorins have since been shown to mediate a wide range of biological activities including lymphocyte activation, photoreceptor development and survival, angiogenesis, bone remodeling, cell migration, oncogenesis, and phototransduction. Given the broad scope of biological activities, it is not surprising that defects in Semaphorin activity have been implicated in a number of pathological conditions including retinal degeneration, oncogenesis, and neurodegenerative disorders.

Semaphorins are an evolutionarily conserved family of secreted and membrane-associated proteins that have been divided into eight subclasses based on sequence and structural similarity. Class 1 and 2 Semaphorins are expressed in invertebrates, Class 3 are expressed in vertebrates, and the eighth class, referred to as Class V, includes Semaphorins that are expressed in viruses. Although most Semaphorins share less than 50% amino acid identity, all contain a conserved extracellular domain of approximately 500 amino acids known as the Semaphorin (sema) domain. The sema domain contains several highly conserved cysteine residues and a beta propeller structural motif that is found in other multi-functional proteins such as Integrins.

The diverse biological activities mediated by Semaphorins can be attributed to differences in their expression patterns, receptor binding and mechanisms of signal transduction. Secreted Semaphorins (Classes 2, 3, and V) serve as ligands to elicit biological responses, while membrane-associated Semaphorins (Classes 1, 4, 6, and 7) not only serve as ligands, but also as receptors capable of mediating reverse signaling. Several receptors, co-receptors, and receptor binding partners have been identified, but Plexins and Neuropilins act as the primary Semaphorin receptors. Plexins are divided into four subclasses and enable Semaphorins to exert pleiotropic effects by associating with a variety of co-receptors. While most membrane-bound Semaphorins directly bind to Plexins, Class 3 Semaphorins, with the exception of Sema3E, require Neuropilins as obligate co-receptors. Neuropilins act as the ligand binding domain of the holoreceptor and may facilitate signal transduction by stimulating a conformational change in Plexin. Given their wide range of activities, it is likely that more receptors and co-receptors that mediate Semaphorin activity will be identified.



**Semaphorin Classification, Domain Structure, and Receptor Interactions.** Semaphorins signal via specific receptors and are dependent on a variety of co-receptor molecules.

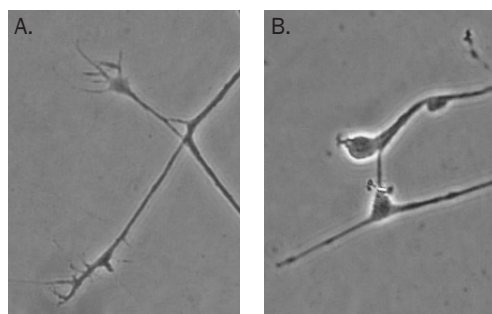
# Select Products for Semaphorins, Plexins, Neuropilins, and Related Molecules

Molecule	Recombinant and Natural Proteins	Antibodies	ELISAs
<b>Semaphorins</b>			
Semaphorin 3A	H M	H (FC, WB) M (FC)	
Semaphorin 3B	M	M (ICC, WB)	
Semaphorin 3C	H M	H (ICC, IHC, WB) M (ICC, IHC, WB)	
Semaphorin 3E	H M	H (FC, ICC, IHC, WB) M (ICC, IHC, WB)	H
Semaphorin 3F	M	H (WB) M (IHC, WB)	
Semaphorin 4A	H	H (FC, IHC, WB) M (B/N, FC)	
Semaphorin 4B		H (FC, WB) M (FC, WB)	
Semaphorin 4C	H M	H (IHC, SW, WB) M (FC, ICC, IHC, SW, WB) R (ICC, IHC, SW, WB)	
Semaphorin 4D/CD100	H M	H (FC, ICC, WB) M (FC, IHC, WB)	
Semaphorin 4F	M	M (FC, IHC, WB)	
Semaphorin 4G	H M	H (IHC, WB) M (IHC, WB)	
Semaphorin 5A	H M	H (ICC, IHC, WB) M (ICC, IHC, WB) R (ICC, IHC, WB)	
Semaphorin 5B	H M		
Semaphorin 6A	H M	H (FC, IHC, WB) M (IHC, WB)	
Semaphorin 6B	H M	H (IHC, WB) M (IHC, WB)	
Semaphorin 6C	H M	H (WB) M (IHC, WB)	
Semaphorin 6D	H M	H (WB)	
Semaphorin 7A	H M	H (FC, WB) M (SW, WB)	
<b>Plexins</b>			
Plexin A1	M	H (FC, ICC, WB) M (FC, ICC, IHC, WB)	
Plexin A2	M	H (FC, ICC, SW, WB) M (FC, ICC, SW, WB) R (FC, ICC, SW, WB)	
Plexin A3		M (IHC, WB) R (IHC, WB)	
Plexin A4	H	H (FC, WB) M (WB) R (WB)	
Plexin B1		H (FC, IHC, WB)	
Plexin B2	H M	H (FC, IHC, WB) M (FC, IHC, WB)	
Plexin B3	H	H (FC, WB) M (FC, IHC, WB) R (FC, IHC, WB)	
Plexin C1	H M	H (FC, IHC, WB) M (FC, IHC, WB)	
Plexin D1	H	H (B/N, FC, IHC, WB)	
TEM7/PLXDC1		H (WB)	

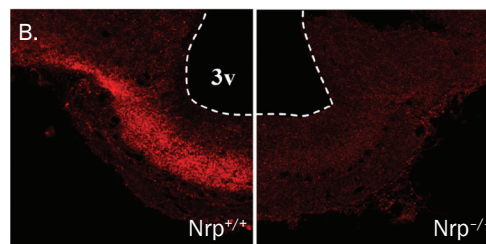
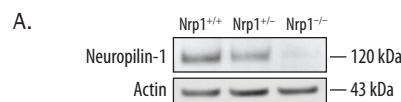
Molecule	Recombinant and Natural Proteins	Antibodies	ELISAs
<b>Neuropilins</b>			
Neuropilin-1	H M R	H (B/N, FC, IHC, WB) M (B/N, FC, IHC, WB) R (B/N, FC, IHC, WB)	H
Neuropilin-2	H M R	H (B/N, FC, IHC, SW, WB) M (B/N, IHC, SW, WB) R (B/N, FC, IHC, SW, WB)	
<b>Other Semaphorin-Related Molecules</b>			
CD45	H M	H (FC, ICC) M (FA, FC, ICC, IHC, IP, WB)	
CD72	H	M (ICC, WB)	
DCBLD2/ESDN	H	H (FC, WB) M (FC, WB)	
ErbB2/Her2	H	H (B/N, ELISA, FC, ICC, IHC, SW, WB) M (FC, IHC, WB)	H
HGF	H M Ca	H (B/N, ELISA, IHC, WB) M (ELISA, IHC, WB) Ca (WB)	H M R
Integrin $\alpha 1\beta 1$	H M		
L1CAM	H M	H (IHC, WB) M (FC)	
NrCAM	H M	H (ELISA, IHC, WB) M (WB) R (WB)	H
TIM-2	M	M (IHC, WB)	
TREM-2	H M	H (FC, ICC, WB) M (FC, ICC, WB)	
VEGF R2/KDR/Fik-1	H M	H (B/N, ELISA, FC, ICC, IHC, WB) M (B/N, ELISA, FC, ICC, IHC, WB)	H M

**Species Key:** H Human M Mouse R Rat Ca Canine

**Application Key:** B/N Blocking/Neutralization ChIP Chromatin Immunoprecipitation ELISA ELISA Capture and/or Detection FC Flow Cytometry ICC Immunocytochemistry IHC Immunohistochemistry IP Immunoprecipitation SW Simple Western™ WB Western blot

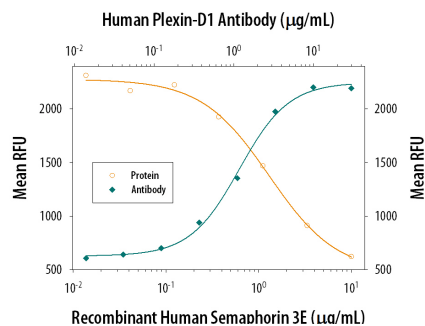


**Semaphorin 3A-Induced Growth Cone Collapse.** A fully extended chick dorsal root ganglion growth cone in the presence of Recombinant Human  $\beta$ -NGF (Catalog # 256-GF) was untreated (A) or treated with Recombinant Human Semaphorin 3A (Catalog # 1250-S3; B). Treatment with Recombinant Human Semaphorin 3A induced growth cone collapse.

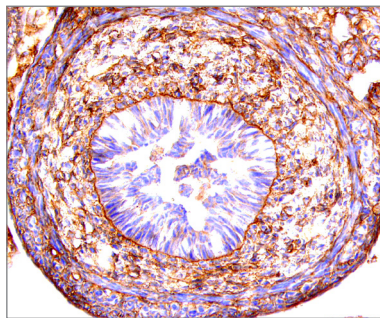


**Detection of Neuropilin-1 by Western Blot and Immunohistochemistry.** A. Western blot shows lysates of mouse hypothalamus. The membrane was probed with a Goat Anti-Mouse/Rat Neuropilin-1 Antigen Affinity-Purified Polyclonal Antibody (Catalog # AF566) followed by a HRP-conjugated anti-goat secondary antibody. Neuropilin-1 was detected in lysates from mice homozygous for wild-type Nrp1 ( $Nrp1^{+/+}$ ) as well as heterozygous mice expressing one functional copy of Nrp1 ( $Nrp1^{+/-}$ ). Neuropilin-1 was not detected in mice that are homozygous for non-functional Nrp1 ( $Nrp1^{-/-}$ ). Actin is shown as a loading control. B. Neuropilin-1 was detected in immersion-fixed frozen sections of mouse brain using a Goat Anti-Mouse/Rat Neuropilin-1 Antigen Affinity-Purified Polyclonal Antibody (Catalog # AF566). The tissue was stained with an Alexa Fluor® 568-conjugated anti-goat secondary developing reagent (red). Neuropilin-1 immunoreactivity was detected in the median eminence of Nrp1 ( $Nrp1^{+/+}$ ) mice. Adapted from: Hanchate, N.K. (2012) PLoS Genet. 8:e1002896.

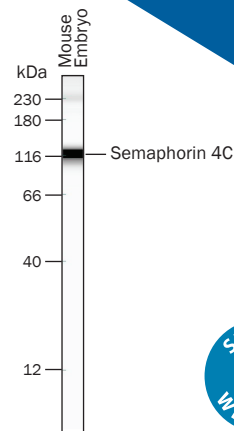
## Expect Publication Quality Data from R&D Systems® Premium Quality Products



**Proliferation Inhibited by Semaphorin 3E and Neutralization by Human Plexin D1 Antibody.** Recombinant Human Semaphorin 3E (Catalog # 3239-S3) inhibits proliferation in the HUVEC human umbilical vein endothelial cell line in a dose-dependent manner (orange line). Activity elicited by 5 µg/mL Recombinant Human Semaphorin 3E is neutralized (green line) by increasing concentrations of a Goat Anti-Human Plexin D1 Antigen Affinity-Purified Polyclonal Antibody (Catalog # AF4160).



**Plexin C1 in Mouse Embryo.** Plexin C1 was detected in immersion-fixed frozen sections of mouse embryonic gut (12 d.p.c.) using a Mouse Anti-Human Plexin C1 Monoclonal Antibody (Catalog # MAB3887). The tissue was stained using the Anti-Mouse HRP-DAB Cell & Tissue Staining Kit (Catalog # CTS002; brown) and counterstained with hematoxylin (blue). Specific staining was localized to plasma membranes.



**Detection of Mouse and Rat Semaphorin 4C by Simple Western™** Simple Western™ lane view shows lysates of mouse embryo tissue (15 d.p.c.). A specific band was detected for Semaphorin 4C at approximately 117 kDa (as indicated) using a Sheep Anti-Mouse/Rat Semaphorin 4C Antigen Affinity-Purified Polyclonal Antibody (Catalog # AF6120) followed by a HRP-Conjugated Donkey Anti-Sheep IgG Secondary Antibody (Catalog # HAF016).

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