

## Quantikine® human Serpin E1/PAI-1 ELISA

Serpin E1, also known as plasminogen activator inhibitor-1 (PAI-1), is a member of the serpin superfamily of serine protease inhibitors.<sup>1</sup> Serpin E1 is the primary inhibitor of urokinase-type and tissue-type plasminogen activators (uPA and tPA). The PA-plasmin system is involved in multiple physiological and pathological processes such as fibrinolysis, fibrosis, angiogenesis, wound healing, and tumor cell invasion and metastasis.<sup>2</sup> High levels of uPA and serpin E1 correlate with poor prognosis in patients with breast cancer.<sup>3</sup> Serpin E1 has also been linked to such diseases as metabolic syndrome, asthma, major depressive disorder (MDD), and aging-related pathologies.<sup>4-8</sup> Absence of serpin E1 in the plasma causes abnormal bleeding, while high plasma levels are associated with inherited thrombophilia.<sup>9,10</sup>

Synthesized and secreted by many cell types, free serpin E1 is relatively unstable in its active form and readily converts into a latent, inactive form by spontaneous insertion of its reactive center loop (RCL) into the  $\beta$ -sheet core of the protein.<sup>1,9</sup> Binding of vitronectin to serpin E1 stabilizes the active form by preventing the conformation change and also broadens the target specificity of serpin E1 beyond uPA and tPA.<sup>1,11</sup> The current model for the serpin E1- vitronectin complex involves the formation of a 2:1 intermediate and some higher order complexes.<sup>11</sup> The active form of serpin E1 binds tightly with uPA and tPA in a 1:1 ratio. After the formation of an initial docking (Michaelis) complex, the proteases cleave the RCL of serpin E1 to form a stable, covalent complex

resulting in the inactivation of the targeted protease.<sup>1</sup> The deduced amino acid sequence of human serpin E1 is 99.5%, 86.1%, 80.8%, and 78.6% identical to that of chimpanzee, canine, rat, and mouse, respectively.

The Quantikine Serpin E1/PAI-1 Immunoassay is a 4.5-hour solid-phase ELISA designed to measure human serpin E1 in cell culture supernatant, cell lysates, and plasma. The assay has been shown to accurately quantitate active and latent forms and vitronectin complexes, but does not detect recombinant serpin E1 in complex with recombinant uPA or tPA.

### References

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## ELISA & Activity Assay Kits

### Quantikine ELISA Kits

Analyte	Species	Sensitivity	Range	Catalog #	Size
Carbonic Anhydrase IX	Human	4.4 pg/mL	15.6-1000 pg/mL	DCA900	1 Kit
IL-22	Mouse/Rat	8.2 pg/mL	15.6-1000 pg/mL	M2200	1 Kit
Pentraxin 3/TSG-14	Mouse	0.02 ng/mL	0.23-15 ng/mL	MPTX30	1 Kit
Serpin E1/PAI-1	Human	0.14 ng/mL	0.31-20 ng/mL	DSE100	1 Kit
TNF- $\alpha$ /TNFSF1A	Human	0.19 pg/mL	0.5-32 pg/mL	HSTA00D	1 Kit

### Surveyor™ IC (Intracellular) ELISA Kits

HIF-1 $\alpha$	Human/Mouse	NA	125-8000 pg/mL	SUV1935	1 Kit
HSP70	Human/Mouse	NA	156-10,000 pg/mL	SUV1663	1 Kit

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### Highlight: Intracellular Flow Cytometry Products for Phospho-Proteins



Quality | Selection | Performance | Results

## Recombinant & Natural Proteins

Protein	Species	Source	Catalog #	Size
2B4/SLAMF4/Fc Chimera	Human	NS0	1039-2B-050	50 µg
Activin RIIb/Fc Chimera	Mouse	NS0	3725-RB-050	50 µg
AgRP (C-terminal fragment)	Human	<i>E. coli</i>	3726-AG-100	100 µg
Aminopeptidase LRAP/ERAP2	Human	NS0	3830-ZN-010	10 µg
Aminopeptidase N/ANPEP	Human	NS0	3815-ZN-010	10 µg
Angiopoietin-like 3	Mouse	Sf 21	136-AN-050	50 µg
Angiopoietin-like 4	Human	NS0	3485-AN-050	50 µg
βIG-H3	Mouse	NS0	2559-BG-050	50 µg
BMP-4/BMP-7 Heterodimer	Human	<i>E. coli</i>	3727-BP-010	10 µg
BMP-10	Human	CHO	2926-BP-025	25 µg
Cadherin-4/R-Cadherin/Fc Chimera	Human	NS0	2217-CA-050	50 µg
Carboxypeptidase E/CPE	Human	NS0	3587-ZN-010	10 µg
CCL5/RANTES	Feline	<i>E. coli</i>	3819-FR-025	25 µg
Chitotriosidase/CHIT1	Human	NS0	3559-GH-010	10 µg
CMG-2/ANTXR2	Human	NS0	2940-CM-050	50 µg
Cyclophilin A	Human	<i>E. coli</i>	3589-CA-100	100 µg
ECM-1 (Extracellular Matrix Protein 1)	Human	NS0	3937-EC-050	50 µg
Ectodysplasin A (EDA)	Human	NS0	3944-ED-010	10 µg
EGF R/Fc Chimera	Mouse	NS0	1280-ER-050	50 µg
EMMPRIN/Fc Chimera	Human	NS0	972-EMN-050	50 µg
Erythropoietin	Canine	NS0	3816-CE-010	10 µg
Fibroblast Activation Protein α/FAP	Human	Sf 21	3715-SE-010	10 µg
FGF basic (145 aa)	Human	<i>E. coli</i>	3718-FB-01M	1 mg
FGF-22	Human	<i>E. coli</i>	3867-FG-025	25 µg
Fibronectin-1, Fragment 3	Human	NS0	3938-FN-050	50 µg
CX3CL1/Fractalkine (aa 29-102)	Mouse	<i>E. coli</i>	3215-MF-050	50 µg
IGSF4A/SynCAM	Mouse	NS0	1459-S4-050	50 µg
IL-1β/IL-1F2	Canine	<i>E. coli</i>	3747-CL-025	25 µg
IL-12 R β1	Mouse	NS0	1998-B1-050	50 µg
IL-17 R/Fc Chimera	Mouse	NS0	4481-MR-100	100 µg
Integrin αVβ6	Human	CHO	3817-AV-050	50 µg
M-CSF	Human	CHO	216-MCC-010	10 µg
M-CSF R/Fc Chimera	Mouse	NS0	3818-MR-050	50 µg
Matriptase/ST14 Catalytic Domain	Human	<i>E. coli</i>	3946-SE-010	10 µg
Methionine Aminopeptidase 2	Human	Sf 21	3795-ZN-020	20 µg
Neurolysin	Human	<i>E. coli</i>	3814-ZN-010	10 µg
Neuropilin-1	Human	NS0	3870-N1-025	25 µg
Nogo-A/Fc Chimera (aa 1026-1090)	Rat	Sf 21	3728-NG-050	50 µg
Norrin	Mouse	<i>E. coli</i>	3497-NR-025	25 µg
Notch-2/Fc Chimera	Human	CHO	3735-NT-050	50 µg
Pentraxin 2/SAP	Mouse	NS0	2558-SA-050	50 µg
PSP94 (Prostate Secretory Protein 94)	Human	<i>E. coli</i>	3780-PS-050	50 µg
Relaxin-1	Human	<i>E. coli</i>	3257-RN-025	25 µg
Relaxin-2	Human	<i>E. coli</i>	3596-RN-025	25 µg
Relaxin-3	Human	<i>E. coli</i>	3107-RN-025	25 µg
RGM-B (Repulsive Guidance Molecule B)	Human	NS0	3630-RG-050	50 µg
RGM-B (Repulsive Guidance Molecule B)	Mouse	NS0	3597-RG-050	50 µg
RGM-C (Repulsive Guidance Molecule C)	Human	NS0	3720-RG-050	50 µg
RGM-C (Repulsive Guidance Molecule C)	Mouse	NS0	3634-RG-050	50 µg

### BMP-10

BMP-10 is a TGF-β superfamily protein that plays a critical role in heart development. The 60 kDa proprotein is cleaved to yield mature BMP-10, which forms active disulfide-linked non-glycosylated homodimers.<sup>1,2</sup> Mature BMP-10 shares greater than 98% amino acid sequence identity among human, mouse, and rat orthologs, and approximately 50% - 60% with other members of its TGF-β subgroup (BMP-9, GDF-5, -6, and -7).

BMP-10 is not expressed until after embryonic cardiac patterning and looping are completed.<sup>3-5</sup> Its production appears at the onset of trabeculation and chamber formation.<sup>3-6</sup> Homozygous BMP-10 knockout mice die *in utero* due to arrested cardiac development.<sup>4</sup> BMP-10 is required for maintaining expression of the cardiogenic transcription factors NKX2.5 and MEF2C in developing myocardium and promoting the growth of embryonic cardiomyocytes.<sup>4,7</sup> NKX2.5 itself negatively regulates BMP-10 expression in cardiac myocytes.<sup>7</sup> Multiple human congenital heart defects result from mutations in NKX2.5 and may accompany aberrant BMP-10 expression.<sup>7</sup> In addition, knockout of FKBP12, a putative binding partner and suppressor of both ryanodine Ca<sup>2+</sup> channels and type I receptors of the TGF-β superfamily, induces BMP-10 overexpression and associated myocardial defects.<sup>4</sup> BMP-10 is restricted to the right atrium in the postnatal heart, where it promotes increased cardiomyocyte and heart size.<sup>4,5</sup> BMP-10 has been shown to induce signaling through ALK-1, BMPR-IA, BMPR-IB, and BMPR-II in transfectants and non-cardiac cell lines.<sup>1,2</sup> A functional BMP-10 receptor in the heart has not yet been identified, although deletion of either BMPR-IA or BMP-10 causes similar cardiac morphogenetic abnormalities.<sup>8</sup> In addition to a role in the heart, BMP-10 induces migration, proliferation, and gene expression in dermal endothelial cells, that is typically associated with ALK-1.<sup>2</sup>

R&D Systems now offers recombinant human BMP-10 (Catalog # 2926-BP).

### References

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## Recombinant & Natural Proteins

Protein	Species	Source	Catalog #	Size
Siglec-11/Fc Chimera	Human	CHO	3258-SL-050	50 µg
Slit-3	Mouse	NS0	3629-SL-050	50 µg
SLITRK1	Human	NS0	3009-SK-050	50 µg
SPARC/Osteonectin	Mouse	NS0	942-SP-050	50 µg
TIM-1/KIM-1/HAVCR	Rat	NS0	3689-TM-050	50 µg
Trypsin 1/PRSS1	Human	NS0	3848-SE-010	10 µg
Tryptase β2/TPSB2	Human	NS0	3796-SE-010	10 µg
TSK (Tsukushi)	Human	NS0	3940-TS-050	50 µg
VEGF-B 167	Mouse	<i>E. coli</i>	2595-VE-025	25 µg
WISP-1/CCN4	Mouse	NS0	1680-WS-050	50 µg

## Polyclonal Antibodies

Antibody	Species	Type	Catalog #	Size
Phospho-14-3-3 (S58)	Human/Mouse/Rat/ <i>Xenopus</i>	Rabbit IgG	PPS042	100 µL
14-3-3	Human/Mouse/Rat/ <i>Xenopus</i>	Rabbit IgG	PPS043	100 µL
α1-Acid Glycoprotein	Human	Goat IgG	AF3694	100 µg
Angiotensin-like 3	Human	Sheep IgG	AF3829	100 µg
APP (Amyloid Precursor Protein)	Human/Mouse/Rat/ Canine/Primate	Rabbit IgG	PPS044	100 µL
ASAH2/N-acylsphingosine Amidohydrolase-2	Mouse	Sheep IgG	AF3558	100 µg
ASC (Apoptosis-associated Speck-like Protein Containing a CARD)	Human	Goat IgG	AF3805	100 µg
BAI3 (Brain-specific Angiogenesis Inhibitor 3)	Human	Goat IgG	AF3965	100 µg
BMP-9 Propeptide	Human	Goat IgG	AF3879	100 µg
Bub-1 (Budding Uninhibited by Benzimidazole-1)	Human	Goat IgG	AF3785	100 µg
c-Myc	Human	Goat IgG	AF3696	100 µg
Complement Component C3a	Human	Goat IgG	AF3677	100 µg
N-Cadherin	Human	Sheep IgG	AF1388	100 µg
Carboxypeptidase A1/CPA1	Human	Goat IgG	AF2856	100 µg
Carboxypeptidase A2	Human	Goat IgG	AF2896	100 µg
CCL26-like/Eotaxin-3 Like	Rat	Goat IgG	AF3878	100 µg
CD48/SLAMF2	Human	Goat IgG	AF3644	100 µg
CD177/PRV1	Human	Goat IgG	AF3505	100 µg
Chitotriosidase/CHIT1	Human	Goat IgG	AF3559	100 µg
CMG-2 (Capillary Morphogenesis Gene 2)/ ANTXR2	Mouse	Goat IgG	AF3636	100 µg
Coagulation Factor VII	Mouse	Goat IgG	AF3305	100 µg
COMP/Thrombospondin-5	Human	Goat IgG	AF3134	100 µg
Connexin 43	Human/Mouse/Rat/ Primate	Rabbit IgG	PPS045	100 µL
Phospho-Connexin 43 (S368)	Human/Mouse/Rat/ Primate	Rabbit IgG	PPS046	100 µL
CRY1 (Cryptochrome 1)	Human/Mouse	Goat IgG	AF3764	100 µg
Desmin	Human	Goat IgG	AF3844	100 µg
Dishevelled-3	Human	Sheep IgG	AF3754	100 µg

*Continued on page 4.*

## RGM-B and RGM-C

RGM-B/DRAGON and RGM-C/hemojuvelin join RGM-A as members of the repulsive guidance molecule (RGM) family. These molecules act as bone morphogenetic protein (BMP) co-receptors, although their expression patterns and systemic functions are distinct. The mature forms of human RGM-B and RGM-C share less than 50% identity, but are highly conserved between species.

RGM-B specifically binds BMP-2 and BMP-4 ligands, and associates directly with type I (ALK-2, -3, -6) and type II (Activin RIIA, Activin RII B) BMP receptors.<sup>1</sup> RGM-B is expressed on neuronal cell bodies and proximal axonal segments of the central and peripheral nervous systems in a complementary, non-overlapping pattern relative to RGM-A.<sup>2,3</sup> It interacts homophilically to mediate neuronal adhesion and is potentially cleaved within its VWF domain.<sup>2,3</sup> It is also present throughout the reproductive axis and is important for germ cell formation and maturation.<sup>4</sup>

As a co-receptor, RGM-C enhances BMP-2-mediated upregulation of the hepatic iron regulatory protein, hepcidin.<sup>5</sup> RGM-C is expressed in striated muscle and periportal hepatocytes, and is cleaved intracellularly, with the two fragments remaining associated as a disulfide-linked dimer.<sup>2,6,7,8</sup> Neogenin receptor-mediated shedding of full-length RGM-C may downregulate hepcidin expression.<sup>7,9,10</sup> RGM-C is disrupted in type 2A juvenile hemochromatosis, a hereditary iron homeostasis disorder characterized by excessive iron accumulation.<sup>8,11</sup> In mouse, loss of RGM-C function results in decreased expression of hepcidin and increased iron deposition in liver, pancreas, and heart.<sup>7</sup>

*In addition to RGM-A, R&D Systems now offers recombinant human and mouse forms of RGM-B (Catalog #3630-RG, 3597-RG) and RGM-C (Catalog # 3720-RG, 3634-RG). Also newly available are an anti-mouse RGM-B antibody (Catalog # AF3597) and a biotinylated anti-human RGM-C antibody (Catalog # BAF3720).*

### References

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## Nogo-A

Nogo-A (reticulon-4) is a reticulon family member that has been actively studied because of its growth-inhibitory properties in the central nervous system. Like other reticulons, nogo-A lacks a signal sequence and contains a C-terminal region with two transmembrane domains and an ER-retention motif. Nogo-A shows a punctate intracellular distribution that is localized predominantly to tubular regions within the ER.<sup>1,2</sup> The C-terminus, which is preserved in the shorter nogo-B and nogo-C isoforms, contains the 66 amino acid nogo receptor/p75NTR complex-binding segment that induces growth cone collapse.<sup>2</sup> Two other areas unique to nogo-A block neurite outgrowth and fibroblast spreading.<sup>2</sup>

Nogo-A is increasingly suspected to play a role in the pathophysiology of, or response to, certain neurological disorders. Local increases in nogo-A are found in multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), epilepsy, and schizophrenia.<sup>2-5</sup> Notably, a 20 kDa N-terminal soluble fragment of nogo-A is detected only in the spinal fluid of MS patients. This fragment has the potential to either contribute to the progression of MS or interfere with the regenerative response to demyelination.<sup>3,5</sup> Therapeutic blocking of nogo-A activity has shown promise for enhancing regeneration in models of spinal cord injury and in allowing repair of myelin in MS model systems.<sup>3,6</sup>

Nogo-A is expressed predominantly in oligodendrocytes, but in these cells less than 5% is expressed on the cell surface.<sup>2,3</sup> Due to its prominent expression in the endoplasmic reticulum, a secondary, intracellular function has long been proposed. The membrane topology of nogo-A is unclear and the orientation of N and C termini are variously reported.<sup>2</sup> In addition, the hydrophobic segments, which are longer than typical transmembrane domains, have been proposed to form hairpin structures within membranes. These structures may stabilize the membrane curvature necessary to form tubular regions of the endoplasmic reticulum.<sup>1</sup>

See the *R&D Systems website (www.RnDSystems.com)* for a complete listing of Nogo-related products.

### References

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## Polyclonal Antibodies

Antibody	Species	Type	Catalog #	Size
<i>Continued from page 3.</i>				
DNER (Delta/Notch-like EGF-related Receptor)	Human	Goat IgG	AF3646	100 µg
Dopa Decarboxylase/DDC	Human	Goat IgG	AF3564	100 µg
DPPA4 (Developmental Pluripotency-associated Protein 4)	Human	Sheep IgG	AF3674	100 µg
DPPA4	Mouse	Goat IgG	AF3730	100 µg
DPPA5/ESG1	Mouse	Goat IgG	AF3984	100 µg
DPPII/QPP/DPP7 (Dipeptidyl Peptidase II)	Mouse	Goat IgG	AF3436	100 µg
DPPII/QPP/DPP7	Human	Goat IgG	AF3438	100 µg
DSCAM (Down Syndrome Cell Adhesion Molecule)	Human	Goat IgG	AF3666	100 µg
eEF-2	Human/Mouse/Rat	Goat IgG	AF3806	100 µg
Phospho-Ephrin-B (Y316)	Human/Mouse/Rat/Chicken/Xenopus	Rabbit IgG	PPS047	100 µL
Phospho-Ephrin-B (Y328)	Human/Mouse/Rat/Chicken/Xenopus	Rabbit IgG	PPS048	100 µL
Phospho-Ephrin-B (Y343)	Human/Mouse/Rat/Chicken/Xenopus	Rabbit IgG	PPS049	100 µL
FABP6	Human	Goat IgG	AF3880	100 µg
FAM3A	Human	Goat IgG	AF2865	100 µg
FGF-BP	Human	Goat IgG	AF1593	100 µg
FHR5 (Complement Factor H-related Protein 5)	Human	Goat IgG	AF3845	100 µg
GABA-A-R α1	Mouse/Rat/Chicken	Rabbit Serum	PPS070	50 µL
GABA-A-R α6	Mouse/Rat	Rabbit Serum	PPS071	50 µL
GLI-3	Human	Goat IgG	AF3690	100 µg
GluR2	Human/Mouse/Rat	Rabbit IgG	PPS050	100 µL
GluR2/3	Human/Mouse/Rat	Rabbit IgG	PPS051	100 µL
GRASP (Grip-associated Protein)	Human/Mouse/Rat	Rabbit IgG	PPS052	100 µL
HAND2 (Heart and Neural Crest Derivatives Expressed 2)	Human	Goat IgG	AF3876	100 µg
HES-4 (Hairy and Enhancer of Split 4)	Human	Sheep IgG	AF3600	100 µg
HS6ST2 (Heparan Sulfate 6-O-Sulfotransferase 2)	Human	Goat IgG	AF2710	100 µg
IGFBP-L1	Human	Goat IgG	AF3877	100 µg
IGFBP-rP10	Mouse	Goat IgG	AF3906	100 µg
IL-1β/IL-1F2	Canine	Goat IgG	AF3747	100 µg
IL-4	Bovine	Goat IgG	AF2469	100 µg
IL-33	Mouse	Goat IgG	AF3626	100 µg
Integrin α9	Mouse	Goat IgG	AF3827	100 µg
Integrin αV/CD51	Human	Goat IgG	AF1219	100 µg
Integrin β5	Human	Sheep IgG	AF3824	100 µg
IRAK4	Human	Goat IgG	AF3919	100 µg
JAM-4/IGSF5	Mouse	Goat IgG	AF3836	100 µg
Kallikrein 12	Human	Sheep IgG	AF3095	100 µg
Laminin α4	Mouse	Goat IgG	AF3837	100 µg
Lipin 1	Human	Goat IgG	AF3885	100 µg
Lipocalin-2/NGAL	Rat	Goat IgG	AF3508	100 µg
LIR-8/CD85c	Human	Goat IgG	AF3065	100 µg
LMO4 (LIM Domain Only 4)	Human	Sheep IgG	AF3889	100 µg
MAD2L1	Human/Rat	Goat IgG	AF4005	100 µg
MafF	Human	Goat IgG	AF3917	100 µg

## Polyclonal Antibodies

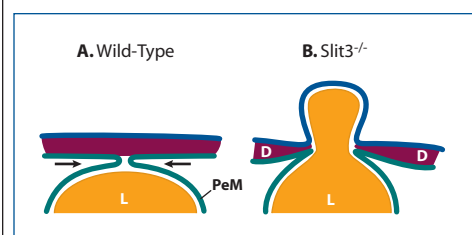
Antibody	Species	Type	Catalog #	Size
MANF (Mesencephalic Astrocyte-derived Neurotrophic Factor)	Human	Goat IgG	AF3748	100 µg
Matrilin-2	Human	Goat IgG	AF3044	100 µg
Matrilin-2	Mouse	Goat IgG	AF3234	100 µg
MGMT	Human	Goat IgG	AF3794	100 µg
β <sub>2</sub> Microglobulin	Rat	Goat IgG	AF3864	100 µg
MKK7	Human	Goat IgG	AF3579	100 µg
MMP-7	Mouse	Goat IgG	AF2967	100 µg
MMP-12	Mouse	Goat IgG	AF3467	100 µg
MUCDHL (Mucin and Cadherin-like Protein)	Human	Goat IgG	AF3826	100 µg
MuSK (Muscle, Skeletal Receptor Tyrosine Kinase)	Human	Goat IgG	AF3904	100 µg
N-WASP	Human	Goat IgG	AF3854	100 µg
NETO2 (Neuropilin and Tolloid-like Protein 2)	Human	Goat IgG	AF3859	100 µg
Phospho-NMDA NR2B (Y1252)	Human/Rat/Primate	Rabbit IgG	PPS056	100 µL
Phospho-NMDA NR2B (Y1336)	Human/Mouse/Rat	Rabbit IgG	PPS057	100 µL
NOMO (Nodal Modulator)	Human	Goat IgG	AF3755	100 µg
NTB-A/SLAMF6	Mouse	Sheep IgG	AF3986	100 µg
OSF-2/Periostin	Human	Goat IgG	AF3548	100 µg
OX40/TNFRSF4	Human	Sheep IgG	AF3388	100 µg
p300	Human	Goat IgG	AF3789	100 µg
p53R2	Human	Goat IgG	AF3788	100 µg
Phospho-PAK-1, 2, 3 (T402)	Human/Mouse/Rat/Primate	Rabbit IgG	PPS058	100 µL
PCPE-1 (Procollagen C-proteinase Enhancer 1)	Mouse	Goat IgG	AF2239	100 µg
Persephin	Mouse	Sheep IgG	AF2479	100 µg
PILR-L (Paired IgG-like Receptor Ligand)	Mouse	Goat IgG	AF3905	100 µg
PKC β1	Human/Rat	Goat IgG	AF3759	100 µg
Plexin C1	Human	Goat IgG	AF3887	100 µg
Profilin-like Protein	<i>T. gondii</i>	Goat IgG	AF3860	100 µg
Proprotein Convertase 9/PCSK9	Human	Sheep IgG	AF3888	100 µg
PSD-95	Human/Mouse/Rat	Rabbit IgG	PPS059	100 µL
PTPN13/PTPL1	Human	Goat IgG	AF3577	100 µg
Phospho-Raf-1 (S301)	Human/Mouse/Rat/ <i>Xenopus</i>	Rabbit IgG	PPS060	100 µL
Phospho-Raf-1 (S642)	Human/Mouse/Rat/ <i>Xenopus</i>	Rabbit IgG	PPS061	100 µL
RBP4 (Retinol-binding Protein 4)	Human	Goat IgG	AF3378	100 µg
Reelin	Mouse	Goat IgG	AF3820	100 µg
Reg IIIa	Mouse	Goat IgG	AF3907	100 µg
RGM-B (Repulsive Guidance Molecule B)	Mouse	Sheep IgG	AF3597	100 µg
Phospho-Ribosomal Protein-S6 (S235/S236)	Human/Mouse/Rat	Rabbit IgG	AF3918	100 µg
RUNX3/CBFA3	Human	Goat IgG	AF3765	100 µg
SCGF (Stem Cell Growth Factor)	Mouse	Goat IgG	AF3729	100 µg
SCP3/SYCP3 (Synaptonemal Complex Protein 3)	Human	Goat IgG	AF3750	100 µg
Serpin E1/PAI-1	Mouse	Goat IgG	AF3828	100 µg
Serum Amyloid A4	Human	Goat IgG	AF3856	100 µg

Continued on page 6.

## Slit3: A Role in Diaphragm Development?

Congenital diaphragmatic hernia (CDH) occurs in 1 of every 2500 live births.<sup>1,2</sup> Anatomically, CDH presents as a discontinuity in the fetal respiratory diaphragm that allows organs in the abdomen to protrude into the thoracic cavity and compromise lung development.<sup>1,2,3</sup> The septum transversum (ST) is a mesodermal shelf that incompletely separates the early pericardial and peritoneal cavities, and ultimately contributes to diaphragm formation.<sup>4</sup> During normal development, the ST is invaded by the developing liver, which will occupy the abdominal side, while the thoracic side becomes tendon. Mesothelium normally invades the ST, separating the liver from the overlying diaphragm and preventing the liver from entering the thoracic cavity (Figure 1A). In CDH, this fails to occur properly.

Although the molecular mechanisms are not clear, Slit3 has been implicated in the development of the diaphragm.<sup>5,6</sup> Slit3 is the most recently discovered member of the Slit family, proteins best known for roles in axon guidance.<sup>7</sup> Slits are often secreted and likely bind to the ROBO family of receptors. Unlike Slit1 and 2, Slit3 principally appears in non-nervous tissue. Notably, Slit3<sup>-/-</sup> mice develop a phenotype reminiscent of CDH (Figure 1B).<sup>5,6</sup> Slit3 is reported to be expressed at the leading edge of the mesothelium as the tissue migrates inward, contributing to the separation of the thoracic and peritoneal cavities.<sup>5</sup> In theory, a failure of the mesothelium to migrate could create a route for liver migration into the thoracic cavity.



**Figure 1.** A: Migrating peritoneal mesothelium (PeM; arrows) separates the liver (L) from the developing diaphragm (D). B: This process fails in Slit3<sup>-/-</sup> mice, allowing protrusion of the liver into the thoracic cavity. Figure adapted from reference 5.

R&D Systems now offers recombinant mouse Slit3 (Catalog # 3629-SL).

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## CHIT1 and CHIA: Chitinases with Different Functions

Chitinases catalyze the hydrolysis of chitin, a linear polymer of  $\beta$ -1,4-linked N-acetylglucosamine (GlcNAc), and a major structural component of the cell wall of fungi and the exoskeleton of insects and crustaceans.<sup>1-3</sup> Although chitin has thus far not been found in mammals, mammalian chitinases may target pathogen-derived chitin. Chitotriosidase (CHIT1) and CHIA are two members of the human chitinase family that structurally are characterized by a chitin-binding type-2 domain at their C-terminus. Both proteins are secreted, exhibit a molecular mass of approximately 50 kDa, and have chitinase and transglycosidase activity. Despite their similarities, the two proteins show distinct expression patterns and have been linked to different pathologies. For example, CHIA is a potential target for asthma therapy, and CHIT1 is the best biomarker for monitoring of Gaucher's disease and is a specific marker of macrophage activation in acute ischemic stroke.<sup>4-7</sup>

R&D Systems newly available recombinant human CHIT1 (Catalog # 3559-GH) is expressed in murine myeloma NS0 cells and purified from conditioned media. It cleaves 4-Methylumbelliferyl- $\beta$ -D-N,N,N'-triacetylchitotriose with a specific activity of >1,500 pmoles/min/ $\mu$ g. When compared to recombinant human CHIA from CHO cells, it exhibits several differences in chitinase activity (see Table 1 for comparison).<sup>2</sup> It is also known that CHIT1 is not stable under acidic pH, as it can be processed into a C-terminally truncated 39 kDa form.<sup>3,8</sup>

R&D Systems now offers an affinity-purified goat anti-human CHIT1 antibody (Catalog # AF3559) that has been validated for Western blot and immunoprecipitation.

**Table 1. CHIT1 and CHIA: Enzyme Properties**

	Mass	pI	pH Optimum	NaCl effect	Stable in acidic pH
<b>CHIA</b>	50 kDa	5.5*	4-5	↑ activity	Yes
<b>CHIT1</b>	50 kDa	7.2	6	↓ activity	No

\* Several alternative splice forms of CHIA exist and the pI was calculated based on protein accession # Q9BZP6.

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## Polyclonal Antibodies

Antibody	Species	Type	Catalog #	Size
<i>Continued from page 5.</i>				
SKI	Human	Goat IgG	AF4025	100 $\mu$ g
SLAP-130	Human	Goat IgG	AF3857	100 $\mu$ g
Snail	Human	Goat IgG	AF3639	100 $\mu$ g
F-Spondin	Human	Goat IgG	AF3135	100 $\mu$ g
Stabilin-1	Human	Sheep IgG	AF3825	100 $\mu$ g
Stabilin-2	Human	Sheep IgG	AF3645	100 $\mu$ g
Phospho-STAT6 (Y641)	Human	Rabbit IgG	AF3717	50 $\mu$ g
Sulfatase Modifying Factor 2/SUMF2	Mouse	Goat IgG	AF3454	100 $\mu$ g
Tenascin R	Human	Goat IgG	AF3865	100 $\mu$ g
Testican 1/SPOCK1	Human	Goat IgG	AF2327	100 $\mu$ g
TFPI (Tissue Factor Pathway Inhibitor)	Mouse	Goat IgG	AF2975	100 $\mu$ g
Thrombomodulin/CD141	Mouse	Goat IgG	AF3894	100 $\mu$ g
TREML2/TLT-2	Human	Goat IgG	AF3259	100 $\mu$ g
Phospho-Tryptophan Hydroxylase (S260)	Human/Mouse/Rat/ <i>Xenopus</i>	Rabbit IgG	PPS063	100 $\mu$ L
URB (Upregulated in BRS-3-deficient Mice)	Human	Goat IgG	AF3410	100 $\mu$ g
Vav-1	Human	Sheep IgG	AF3786	100 $\mu$ g
Versican	Human	Goat IgG	AF3054	100 $\mu$ g

## Monoclonal Antibodies

Antibody	Species	Clone	Catalog #	Size
ADAMTS5	Human	362810	MAB2198	100 $\mu$ g
Aminopeptidase PILS/ARTS1	Mouse	325908	MAB2500	100 $\mu$ g
AMPK $\beta$ 2	Human/Mouse	376938	MAB3808	100 $\mu$ g
ANP (Atrial Natriuretic Peptide)	Human	361101	MAB3366	100 $\mu$ g
APLP-1 (Amyloid Precursor-like Protein 1)	Human	354008	MAB3129	100 $\mu$ g
APLP-1 (Amyloid Precursor-like Protein 1)	Human/Mouse	354020	MAB3908	100 $\mu$ g
ASGR1 (Asialoglycoprotein Receptor 1)	Mouse	352802	MAB2755	100 $\mu$ g
Cannabinoid R1	Human	368302	MAB3834	100 $\mu$ g
Carnosine Dipeptidase 1	Human	352216	MAB2489	100 $\mu$ g
CD4	Feline	372717	MAB2597	100 $\mu$ g
CD27 Ligand/TNFSF7	Human	301731	MAB2738	100 $\mu$ g
CD46	Human	344519	MAB2005	100 $\mu$ g
CD68/SR-D1	Human	298807	MAB20401	100 $\mu$ g
CD160	Mouse	342713	MAB3899	100 $\mu$ g
CD200 R1	Human	380525	MAB3414	100 $\mu$ g
CHL-1/L1CAM-2	Mouse	316316	MAB2147	100 $\mu$ g
CL-P1/COLEC12/SRCL	Human	388306	MAB2690	100 $\mu$ g
CL-P1/COLEC12/SRCL	Human	388305	MAB26901	100 $\mu$ g
CL-P1/COLEC12/SRCL	Mouse	350611	MAB3130	100 $\mu$ g
CL-P1/COLEC12/SRCL	Mouse	350601	MAB31301	100 $\mu$ g
CLEC4F/CLECSF13	Mouse	370901	MAB2784	100 $\mu$ g
Clusterin	Human	350227	MAB2937	100 $\mu$ g
CNP (C-type Natriuretic Peptide)	Human	347608	MAB3127	100 $\mu$ g
CNP Propeptide	Human	347625	MAB3739	100 $\mu$ g
Coagulation Factor III/Tissue Factor	Human	323519	MAB23391	100 $\mu$ g

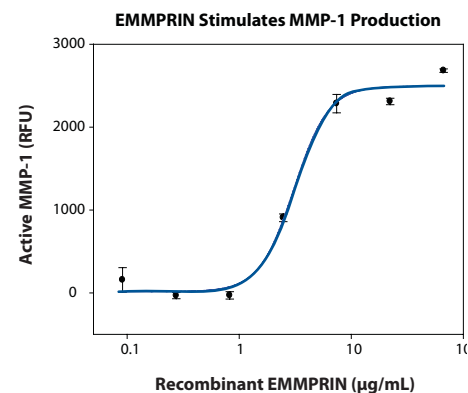
# Monoclonal Antibodies

Antibody	Species	Clone	Catalog #	Size
Coagulation Factor III/Tissue Factor	Mouse	355220	MAB3178	100 µg
COMP/Thrombospondin-5	Human	360215	MAB3134	100 µg
Complement Component C1qA	Human	394107	MAB4035	100 µg
CRHBP (Corticotropin-releasing Hormone Binding Protein)	Mouse	356803	MAB3087	100 µg
CRISP-2	Human	350814	MAB2575	100 µg
Crossveinless-2	Mouse	349920	MAB2299	100 µg
Cyr61/CCN1	Human	365108	MAB4055	100 µg
DNER (Delta/Notch-like EGF-related Receptor)	Human	348112	MAB3646	100 µg
DNER	Human	348117	MAB36461	100 µg
EDG-8 (Endothelial Differentiation, Sphingolipid G-protein-coupled Receptor)	Human	282503	MAB3964	100 µg
Epimorphin/Syntaxin 2	Human	338824	MAB2936	100 µg
ESAM (Endothelial Cell-selective Adhesion Molecule)	Mouse	340212	MAB2827	100 µg
FABP1	Human	328605	MAB29641	100 µg
FAM3B (Family with Sequence Similarity 3B)	Human	365505	MAB2866	100 µg
FAM3C	Mouse	372018	MAB2868	100 µg
FATP5 (Fatty Acid Transport Protein 5)	Human	390917	MAB3897	100 µg
FLRT1 (Fibronectin Leucine-rich Transmembrane Protein 1)	Human	357721	MAB2794	100 µg
FLRT2	Human	367205	MAB2877	100 µg
FPRL2 (Formyl Peptide Receptor-like 2)	Human	374822	MAB3896	100 µg
HIN-1/Secretoglobulin 3A1	Mouse	368203	MAB2954	100 µg
Iduronate 2-Sulfatase/IDS	Human	331320	MAB2449	100 µg
IL-4	Porcine	99605	MAB6543	100 µg
IL-6	Porcine	90613	MAB6861	100 µg
IL-17C	Mouse	311523	MAB2306	100 µg
IL-19	Human/Mouse	350114	MAB2915	100 µg
IL-19	Mouse	350105	MAB29151	100 µg
IL-23	Mouse	320229	MAB1619	500 µg
IL-27 EBI3	Mouse	355022	MAB18341	100 µg
IL-32α	Human	373812	MAB3040	100 µg
INSRR (Insulin Receptor-related Protein)	Human	326903	MAB30551	100 µg
Insulysin/IDE	Human	334501	MAB2496	100 µg
IRS-1	Human/Mouse	52906	MAB3978	100 µg
Kallikrein 11	Human	371604	MAB15951	100 µg
Kallikrein 12	Human	364926	MAB4034	100 µg
Kallikrein 12	Human	364932	MAB40341	100 µg
Kallikrein 13	Human	341419	MAB2625	500 µg
Kallikrein 14	Human	337903	MAB2626	100 µg
KOR (Kappa Opioid Receptor)	Human	387301	MAB3895	100 µg
LMIR3/CD300LF	Mouse	305835	MAB27881	100 µg
Lumican	Human/Mouse	358022	MAB2846	100 µg
MafK	Human/Mouse	381923	MAB3809	100 µg
Meprin α Subunit	Human	364312	MAB3220	100 µg
MFG-E8 (Milk Fat Globule EGF Factor 8)	Mouse	340614	MAB2805	100 µg
Mimecan	Human	329816	MAB2660	100 µg
MKK7	Human	324302	MAB3579	100 µg
MMP-7	Mouse	377314	MAB2967	100 µg

continued on page 8.

## EMMPRIN & Tumor Progression

Extracellular matrix metalloproteinase (MMP) inducer (EMMPRIN), also known as basigin and CD147, is a multifunctional transmembrane immunoglobulin superfamily protein with significant roles in tissue remodeling and energy metabolism.<sup>1,2</sup> As such, it is often overexpressed in tumors and its expression has been correlated with tumor progression.<sup>1,2</sup> EMMPRIN was named due to its ability to induce MMP expression, especially MMP-1 (Figure 1), -2 and -3, and membrane-type MMP (MT-MMP), by stromal fibroblasts in the vicinity of EMMPRIN-expressing tumors.<sup>1,2</sup> Subsequently, urokinase-type plasminogen activator (uPA), hyaluronan, and VEGF have also been identified as EMMPRIN-inducible proteins, further strengthening its connection with tissue remodeling, angiogenesis, and cancer.<sup>3,5</sup> EMMPRIN expression is tightly regulated with its intramembrane binding partner, the amino acid transporter CD98hc.<sup>6</sup> Since EMMPRIN is also complexed with monocarboxylate transporters, including the MCT1 lactate transporter, levels of the EMMPRIN/CD98 complex are strongly correlated with cellular metabolic rate. In addition to its cell-surface expression, tumor cells are able to release an active 22 kDa fragment or active full-length EMMPRIN in microvesicles.<sup>7,8</sup>



**Figure 1.** Normal human lung fibroblast cells were cultured on microplates coated with R&D Systems recombinant human EMMPRIN/Fc chimera (Catalog # 972-EMN) for 3 days. EMMPRIN stimulated a dose-dependent increase in levels of active MMP-1 in the culture supernatant as measured using R&D Systems Fluorokine® E Human MMP-1 Kit (Catalog # F1M00).

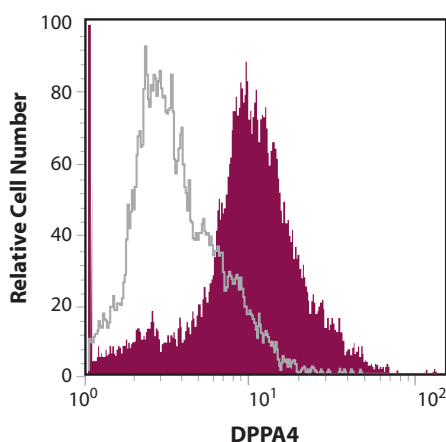
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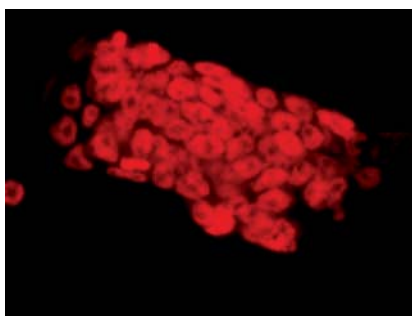
## DPPA4 as a Marker of Pluripotency

DPPA4 (developmental pluripotency-associated 4) was first identified as a gene with an expression pattern similar to Oct-4. It is expressed in pluripotent cells such as mouse and human embryonic stem (ES) and embryonal carcinoma cells, and mouse embryonic germ cells. *In vivo*, DPPA4 is restricted to the pluripotent cells of the mouse blastocyst and the developing germ line.<sup>1-3</sup> DPPA4 expression rapidly decreases during differentiation of germ cells *in vivo* and ES cells *in vitro*, making it valuable as a marker of the undifferentiated state.<sup>2</sup>

R&D Systems now offers an anti-mouse DPPA4 polyclonal antibody (Catalog # AF3730), and anti-human unconjugated and biotin-conjugated polyclonal antibodies (Catalog # AF3674, BAF3674).



**Figure 1.** Detection of DPPA4 by flow cytometry. Ntera2 human teratocarcinoma stem cells were stained with R&D Systems biotinylated anti-human DPPA4 (Catalog # BAF3674, red histogram) or control antibody (open histogram), followed by PE-conjugated streptavidin (Catalog # F0040).



**Figure 2.** Detection of DPPA4 in the nuclei of Ntera2 cells using R&D Systems anti-mouse DPPA4 polyclonal antibody (Catalog # AF3730) and R&D Systems NorthernLights-557-conjugated secondary antibody (Catalog # NL001).

## References

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## Monoclonal Antibodies

Antibody	Species	Clone	Catalog #	Size
<i>continued from page 7.</i>				
Pro-MMP-7	Mouse	377313	MAB29671	100 µg
MMR (Macrophage Mannose Receptor)	Mouse	310301	MAB2535	100 µg
Nectin-3	Human	337407	MAB3064	100 µg
Nephrilysin-2/MMEL1/MMEL2	Human	353207	MAB2340	100 µg
Netrin-G2a	Mouse	349719	MAB2744	100 µg
Neuropilin-2	Human	257103	MAB22151	100 µg
β-NGF	Human	347112	MAB2562	100 µg
NRAGE	Human	353124	MAB3835	100 µg
Osteoactivin/GPNMB	Human	303822	MAB25501	100 µg
Osteoadherin	Mouse	348423	MAB3308	100 µg
p38 β	Human	280071	MAB3274	100 µg
PBEF/Visfatin	Human/Mouse	362616	MAB4044	100 µg
PRDC (Protein Related to Dan and Cerberus)	Mouse	377407	MAB2069	100 µg
Protein S/PROS1	Human	391609	MAB4036	100 µg
Relaxin-1	Human	351713	MAB3257	100 µg
Relaxin-1	Human	361505	MAB32571	100 µg
Relaxin-2	Human	349102	MAB2804	100 µg
Relaxin-3	Human	332112	MAB3107	100 µg
S100A10	Mouse	344015	MAB2377	100 µg
S100P	Human	357517	MAB2957	100 µg
SCF (Stem Cell Factor)	Canine/Feline	371907	MAB2268	100 µg
Semaphorin 3A	Human	215803	MAB1250	100 µg
Semaphorin 7A	Human	310829	MAB20681	100 µg
SLITRK1	Human	327808	MAB3009	100 µg
Smad2	Human	376520	MAB4037	100 µg
Smad3	Human	378611	MAB4038	100 µg
SorCS3	Mouse	339615	MAB30671	100 µg
Sortilin	Human/Mouse	334708	MAB3154	100 µg
SR-AI/MSR1	Human	351620	MAB27081	100 µg
Syndecan-3	Human	374420	MAB3539	100 µg
TAPP1 (Tandem PH Domain-containing Protein 1)	Human	376409	MAB4039	100 µg
TCCR/WSX-1 (T Cell Cytokine Receptor)	Mouse	263503	MAB21091	100 µg
TFPI-2 (Tissue Factor Pathway Inhibitor 2)	Mouse	375717	MAB4045	100 µg
Latent TGF-β bp2	Human	327318	MAB3850	100 µg
TNF-α/TNFSF1A	Porcine	103302	MAB6903	100 µg
Tryptase β-2/TPSB2	Human	349406	MAB3796	100 µg
Tryptase β-2/TPSB2	Human	349414	MAB37961	100 µg
UGRP1 (Uteroglobulin-related Protein 1)	Mouse	381707	MAB3465	100 µg
Vasostatin	Human	326203	MAB3898	100 µg
Vitronectin	Mouse	347312	MAB3875	100 µg
Wnt-5b	Mouse	325004	MAB3006	100 µg
West Nile Virus NS3 Protease	Viral	345713	MAB2907	100 µg
West Nile Virus NS3 Protease	Viral	345712	MAB29071	100 µg

## Labeled Antibodies

### Biotinylated Antibodies

Antibody	Species	Type	Catalog #	Size
Artemin	Human	Goat IgG	BAF2589	50 µg
BMP-9	Human	Goat IgG	BAF3209	50 µg
Carboxypeptidase A2	Human	Goat IgG	BAF2896	50 µg
Claspin	Human	Goat IgG	BAF3310	50 µg
Coagulation Factor XIV/Protein C	Human	Goat IgG	BAF3349	50 µg
Cubilin	Human	Sheep IgG	BAF3700	50 µg
DPPA4 (Developmental Pluripotency-associated Protein 4)	Human	Sheep IgG	BAF3674	50 µg
DPP11/QPP/DPP7 (Dipeptidyl Peptidase 2)	Human	Goat IgG	BAF3438	50 µg
Endoglycan	Mouse	Goat IgG	BAF3534	50 µg
FABP9	Mouse	Goat IgG	BAF2750	50 µg
GDF-9 Propeptide	Mouse	Goat IgG	BAF3536	50 µg
Granzyme B	Human	Goat IgG	BAF2906	50 µg
RGM-C (Repulsive Guidance Molecule C)	Human	Goat IgG	BAF3720	50 µg
SCP3/SYCP3 (Synaptonemal Protein 3)	Human	Goat IgG	BAF3750	50 µg
Serpin E2/PN1	Human	Goat IgG	BAF2980	50 µg
Sleeping Beauty Transposase	Multi-species	Goat IgG	BAF2798	50 µg
SOX21	Human	Goat IgG	BAF3538	50 µg
Syndecan-3	Human	Goat IgG	BAF3539	50 µg
TCAM-1	Mouse	Goat IgG	BAF3546	50 µg
UGRP1 (Uteroglobulin-related Protein 1)	Mouse	Goat IgG	BAF3465	50 µg
Wnt-9b	Mouse	Goat IgG	BAF3669	50 µg

## Labeled Antibodies

### Fluorochrome-labeled Antibodies

Antibody	Species	Label	Catalog #	Size
ADAM15	Human	APC	IC935A	100 Tests
Akt (pan)	Human/Mouse/Rat	APC	IC2055A	100 Tests
Akt (pan)	Human/Mouse/Rat	Fluorescein	IC2055F	100 Tests
Akt (pan)	Human/Mouse/Rat	PE	IC2055P	100 Tests
Akt1	Human	APC	IC17751A	100 Tests
Akt1	Human	Fluorescein	IC17751F	100 Tests
Akt1	Human	PE	IC17751P	100 Tests
Akt2	Human	APC	IC23152A	100 Tests
Akt2	Human	PE	IC23152P	100 Tests
CD44	Human	Fluorescein	FAB3660F	100 Tests
CD44	Human	PE	FAB3660P	100 Tests
CD68	Human	PE	IC20401P	100 Tests
CRHR-1 (Corticotropin-releasing Hormone Receptor 1)	Human	APC	FAB3930A	100 Tests
CRHR-1	Human	PE	FAB3930P	100 Tests
CXCL1/GRO $\alpha$	Human	Fluorescein	IC275F	100 Tests
CXCL4/PF4	Human	APC	IC7952A	100 Tests
CXCL4/PF4	Human	Fluorescein	IC7952F	100 Tests
CXCL4/PF4	Human	PE	IC7952P	100 Tests

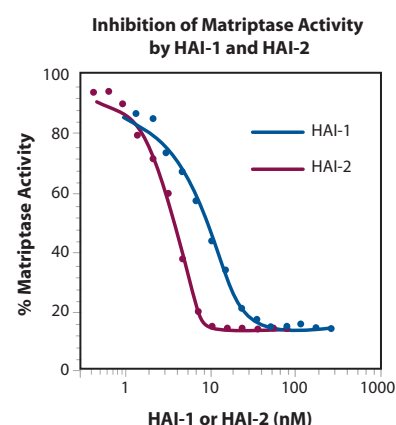
continued on page 10.

## Human Matriptase/ST14

Human matriptase, encoded by the ST14 gene, is also known as TADG-15, epithin, and MT-SP1.<sup>1</sup> It is thought to have a significant role in tumor biology and may be a novel target for cancer therapy.<sup>2</sup> It is also expressed in most human epithelia and is important in several normal physiological processes.<sup>1</sup> For example, it activates prostaticin to initiate a protease cascade that is essential for epidermal differentiation, and it converts single-chain IGFBP-rp1 into the two-chain form.<sup>3,4</sup>

Matriptase is a type II transmembrane serine protease with a complex modular structure.<sup>1</sup> The 855 amino acid (aa) sequence of human matriptase consists of a cytoplasmic tail (aa 1-55), a transmembrane domain (aa 56-76), and an extracellular portion (aa 77-855). The latter contains the following domains: an SEA (aa 86-201), two CUB (aa 214-334 and 340-447), four LDLRA (aa 452-486, 487-523, 524-560, and 566-603), and a serine protease domain (aa 615-855). The physiological activation of the single-chain zymogen requires multiple steps including cleavage at the SEA domain, transport to the cell-surface in association with HAI-1, and auto-cleavage at QAR-V<sup>615</sup>VGG.<sup>1</sup> Activated matriptase is inhibited by HAI-1, and the resulting HAI-1 complex can be shed from the cell surface.<sup>1</sup>

R&D Systems now offers recombinant human matriptase (Catalog # 3946-SE). The R&D Systems enzyme corresponds to the catalytic domain, and is inhibited effectively by the serine protease inhibitors HAI-1 and HAI-2 (Figure 1).



**Figure 1.** The ability of R&D Systems human recombinant matriptase (Catalog # 3946-SE; 13.5 nM) to cleave the fluorogenic substrate Boc-QAR-AMC is inhibited in a dose-dependent manner by either R&D Systems human recombinant HAI-1 (Catalog # 1048-PI) or HAI-2 (Catalog # 1106-PI).

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## Relaxin Family

Primarily known as a polypeptide hormone of pregnancy, relaxin promotes growth and softening of the cervix, and development of the mammary gland in rodents.<sup>1,2</sup> In addition, this member of the structurally-related insulin/relaxin superfamily promotes angiogenesis, influences cardiovascular regulation, and mediates tissue remodeling events that prepare target tissues for pregnancy-related organ adaptation.<sup>3</sup> In males, prostatic relaxins are anti-apoptotic and contribute to development and maintenance of male fertility.<sup>1</sup> Although the physiological role of relaxin in reproduction varies across species, the presence of circulating relaxin during non-pregnancy and the synthesis of relaxin by non-reproductive organs (brain, kidney, heart, lung) suggest a more global contribution of this hormone's actions.

Human relaxin-1, -2, and -3 confer activity by binding to leucine-rich G protein-coupled receptors LGR7 and LGR8, leading to an increase in cAMP.<sup>1,4</sup> In support of previously described anti-fibrotic and cardio-protective functions in transgenic mice, administration of human relaxin-2 has an anti-hypertrophic and anti-apoptotic effect in rodent cardiomyocytes.<sup>1,5,6</sup> Furthermore, relaxin-1 and LGR7 mRNA and protein have been found in mammalian arteries *in vivo*, suggesting that endogenous relaxin production may regulate local vascular function.<sup>7</sup> Relaxin acting through LGR7 has also been implicated as pro-oncogenic in human prostate and thyroid cancer.<sup>8,9</sup> In contrast to relaxin-1 and -2, relaxin-3 is preferentially expressed in the brain, acting as a neuropeptide involved in stress responses and food intake.<sup>10,11</sup>

### R&D Systems Human Relaxin Research Tools

	Protein Catalog #	Antibody Catalog #
<b>Relaxin-1</b>	3257-RN	MAB3257, MAB32571
<b>Relaxin-2</b>	3596-RN	MAB2804
<b>Relaxin-3</b>	3107-RN	MAB3107

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## Labeled Antibodies

### Fluorochrome-labeled Antibodies

Antibody	Species	Label	Catalog #	Size
<i>continued from page 9.</i>				
CXCR4	Mouse	PE	FAB21651P	100 Tests
Phospho-EGF R (Y1173)	Human	Fluorescein	IC1095F	100 Tests
Phospho-EGF R (Y1173)	Human	PE	IC1095P	100 Tests
Phospho-EGF R (Y845)	Human	Fluorescein	IC3394F	100 Tests
Phospho-EGF R (Y845)	Human	PE	IC3394P	100 Tests
Fcγ RI/CD64	Human	APC	FAB12571A	100 Tests
Fcγ RI/CD64	Human	Fluorescein	FAB12571F	100 Tests
Fcγ RI/CD64	Human	PE	FAB12571P	100 Tests
Fcγ RIII/CD16	Mouse	APC	FAB19601A	100 Tests
IFN-γ	Bovine	APC	IC2300A	100 Tests
IFN-γ	Bovine	PE	IC2300P	100 Tests
IL-2	Porcine	Fluorescein	IC6521F	100 Tests
IL-2	Porcine	PE	IC6521P	100 Tests
IL-12 Rβ2	Human	APC	IC1959A	100 Tests
IL-12 Rβ2	Human	PE	IC1959P	100 Tests
IL-17 R	Human	APC	FAB177A	100 Tests
IL-17 R	Human	Fluorescein	FAB177F	100 Tests
IL-17 R	Human	PE	FAB177P	100 Tests
ILT2/CD85j	Human	APC	FAB20171A	100 Tests
ILT2/CD85j	Human	Fluorescein	FAB20171F	100 Tests
ILT2/CD85j	Human	PE	FAB20171P	100 Tests
ILT3/CD85k	Human	APC	FAB24251A	100 Tests
ILT3/CD85k	Human	Fluorescein	FAB24251F	100 Tests
ILT3/CD85k	Human	PE	FAB24251P	100 Tests
ILT4/CD85d	Human	APC	FAB2078A	100 Tests
ILT4/CD85d	Human	Fluorescein	FAB2078F	100 Tests
Jagged 1	Human	Fluorescein	FAB1277F	100 Tests
Nectin-4	Human	APC	FAB2659A	100 Tests
Nectin-4	Human	PE	FAB2659P	100 Tests
Phospho-p53 (S15)	Human	PE	IC18392P	100 Tests
PAR2	Human	PE	FAB3949P	100 Tests
TIM-3	Human	PE	FAB2365P	100 Tests
TLR2	Mouse	Fluorescein	FAB1530F	100 Tests
TLR4	Mouse	PE	IC2759P	100 Tests
TrkC	Human	PE	FAB373P	100 Tests

## ELISA & Activity Assay Development Kits

### DuoSet™ ELISA Development Systems

Product	Species	Catalog #	Reagents For*
Decorin	Mouse	DY1060	15 Plates
DPPIV/CD26	Human	DY1180	15 Plates
EGF	Mouse	DY2028	15 Plates
Furin	Human	DY1503	15 Plates
Hyaluronan	Multi-species	DY3614	5 Plates <sup>†</sup>
IL-2 R $\alpha$	Mouse	DY2438	15 Plates
IL-17B R	Human	DY1207	15 Plates
Prolactin	Human	DY682	15 Plates
VEGF	Canine	DY1603	15 Plates

\*Also available in 45 plate Economy Packs.

<sup>†</sup>Hyaluronan Development Kits are also available in 15 plate Economy Packs.

### DuoSet IC Intracellular ELISAs & Activity Assays

Product	Species	Catalog #	Reagents For*
Phospho-MEK1 (S218/S222)/MEK2 (S222/S226)	Human	DYC2506-2	2 Plates
Total Insulin R/CD220	Human	DYC1544-2	2 Plates
Phospho-M-CSF R	Human	DYC3268-2	2 Plates
Total SCF R/c-kit	Human	DYC332-2	2 Plates
Phospho-SCF R/c-kit	Human	DYC3527-2	2 Plates

\*Also available in 5 plate packs and 15 plate Economy Packs.

## ELISpot Kits & Reagents

### ELISpot Kits

Product	Species	Catalog #	Size
Granzyme B	Human	EL2906	1 Kit

### ELISpot Development Modules

Product	Species	Catalog #	Size
Granzyme B	Human	SEL2906	1 Kit

## Antibody Controls

Antibody	Species	Catalog #	Size
Normal Rabbit IgG Allophycocyanin Control	Rabbit	IC105A	50 $\mu$ g
Normal Rabbit IgG Fluorescein Control	Rabbit	IC105F	50 $\mu$ g
Normal Rabbit IgG Phycoerythrin Control	Rabbit	IC105P	50 $\mu$ g

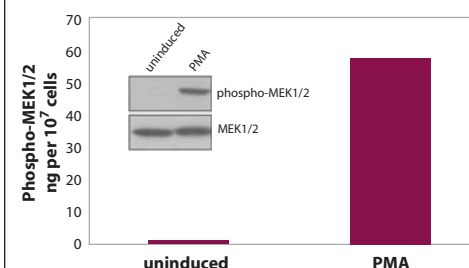
## Fluorogenic Peptide Substrate

Product	Catalog #	Size
pERTKR-AMC	ES013	10 mg

## Phospho-MEK1/MEK2 DuoSet IC ELISA

Mitogen-activated protein kinase kinase 1 (MAP2K1) and MAP2K2, also known as MEK1 and MEK2, are members of the *Ste7* grouping of kinases.<sup>1</sup> As part of the Raf/MEK/ERK signal transduction module, MEK1 and MEK2 regulate cellular proliferation, differentiation, and survival. Dual-specificity protein kinases, MEK1 and MEK2 phosphorylate and activate the mitogen-activated protein kinases ERK1 and ERK2 at threonine and tyrosine positions within the phospho-acceptor sequence T-E-Y.<sup>2</sup>

MEK1 and MEK2 activation occurs through phosphorylation by Raf family members at two neighboring serine residues: S218 and S222 of human MEK1, and S222 and S226 of human MEK2.<sup>3</sup> Specific Raf isoforms activate MEK1 and MEK2 differentially. A-Raf is a weak activator, while B-Raf activates MEK1 preferentially, and Raf-1 efficiently activates both MEKs.<sup>4</sup> Phosphorylation of MEK1 by p21-activated kinase-1 (PAK1) at S298 helps prime MEK for activation by Raf, while phosphorylation by an unknown kinase at S212 sharply decreases MEK1 activity.<sup>5,6</sup>



**Figure 1.** Lysates prepared from human HeLa cells either uninduced or induced with 200 nM PMA (20 min) were assessed for phospho-MEK1/2 using R&D Systems Phospho-MEK1 (S218/S222)/MEK2 (S222/S226) DuoSet IC ELISA (Catalog # DYC2506). The same lysates were also immunoblotted (inset) with either R&D Systems anti-phospho-MEK1 (S218/S222)/MEK2 (S222/S226) polyclonal antibody (Catalog # AF2506) or R&D Systems anti-MEK1/MEK2 monoclonal antibody (Catalog # MAB2678). The DuoSet IC ELISA results correlate well with the Western blot results.

### References

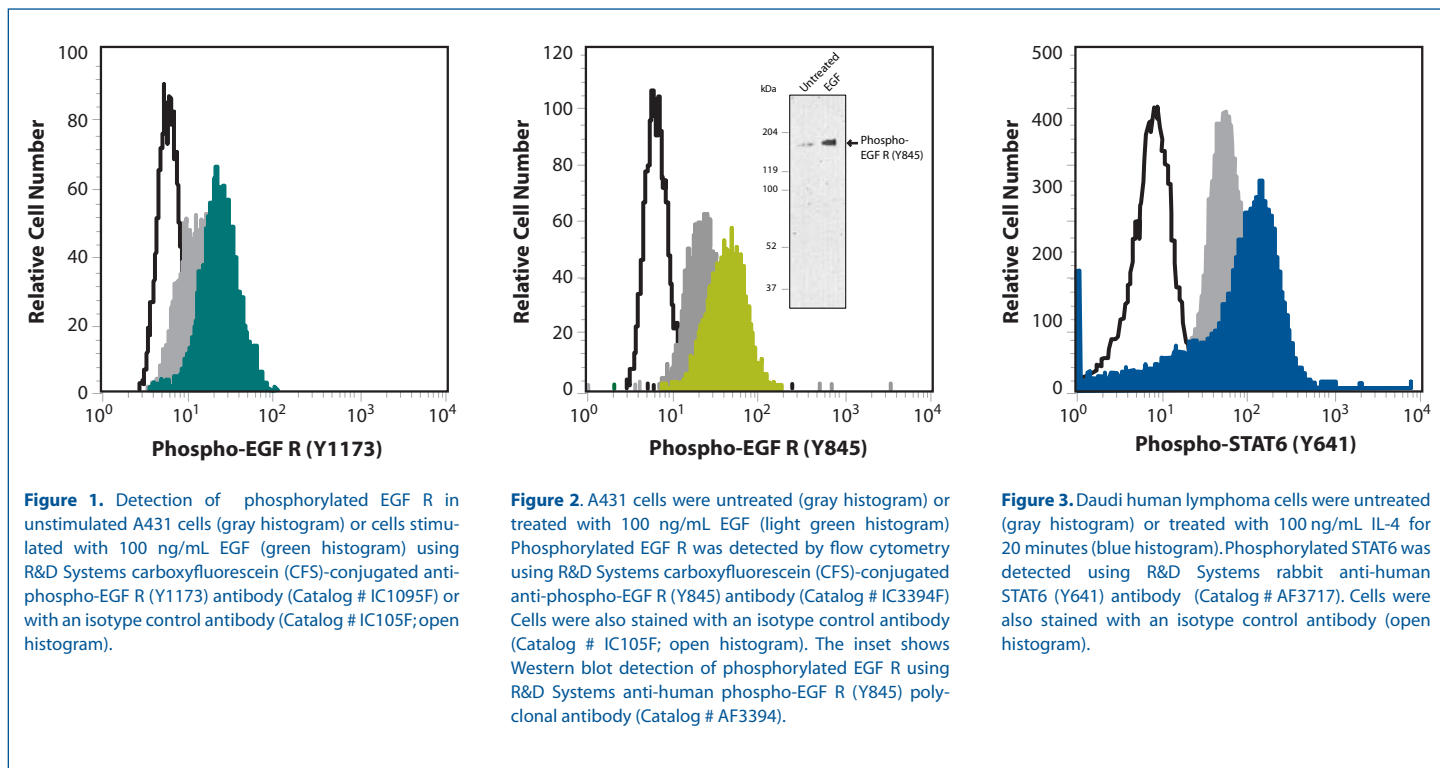
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# Intracellular Flow Cytometry Products for Phospho-Proteins

R&D Systems has developed several phospho-specific antibodies that allow researchers to perform quantitative and multiparameter analysis of protein phosphorylation by flow cytometry. Binding of ligand to EGF R induces autophosphorylation on multiple tyrosine residues. Phosphorylation of Y1173 (Figure 1) creates a binding site for the protein tyrosine phosphatase SHP-1, while phosphorylation of Y845 (Figure 2) is associated with the regulation of receptor function and tumor progression. Phosphorylation of Y641 on STAT6 is crucial for dimerization and nuclear translocation (Figure 3).

Measuring protein phosphorylation by flow cytometry has distinct advantages over traditional Western blot. For instance, Western blot measures overall phosphorylation in cell lysates, while flow cytometry assesses each cell individually and offers the potential to monitor phosphorylation in a subpopulation of cells.

See pages 9 and 10 of this newsletter for all newly available fluorochrome-conjugated antibodies.



**Figure 1.** Detection of phosphorylated EGF R in unstimulated A431 cells (gray histogram) or cells stimulated with 100 ng/mL EGF (green histogram) using R&D Systems carboxyfluorescein (CFS)-conjugated anti-phospho-EGF R (Y1173) antibody (Catalog # IC1095F) or with an isotype control antibody (Catalog # IC105F; open histogram).

**Figure 2.** A431 cells were untreated (gray histogram) or treated with 100 ng/mL EGF (light green histogram). Phosphorylated EGF R was detected by flow cytometry using R&D Systems carboxyfluorescein (CFS)-conjugated anti-phospho-EGF R (Y845) antibody (Catalog # IC3394F). Cells were also stained with an isotype control antibody (Catalog # IC105F; open histogram). The inset shows Western blot detection of phosphorylated EGF R using R&D Systems anti-human phospho-EGF R (Y845) polyclonal antibody (Catalog # AF3394).

**Figure 3.** Daudi human lymphoma cells were untreated (gray histogram) or treated with 100 ng/mL IL-4 for 20 minutes (blue histogram). Phosphorylated STAT6 was detected using R&D Systems rabbit anti-human STAT6 (Y641) antibody (Catalog # AF3717). Cells were also stained with an isotype control antibody (open histogram).



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