

Stem Cell Biology

Focus: Stem Cell Fate & Cancer

Notch Signaling Receptors & Ligands

Notch signaling depends on the differential expression of specific ligands (Jagged or Delta) and receptors (Notch1-4) in adjacent cells. The Notch pathway is involved in embryonic development and control of tissue homeostasis in a variety of adult tissues. Notch regulates cell differentiation, cellular homeostasis and also stem cell maintenance. In adults, Notch signaling is an important regulator of stem cells from a variety of tissues. Since stem cell expansion is a central goal in regenerative medicine and regulated by the Notch pathway, modulation of this pathway will open an avenue for regenerative medicine applications, including hematological and non-hematological diseases, but also for cancer treatment.

REVIEWS: Targeting cancer stem cells by inhibiting Wnt, Notch, and Hedgehog pathways: N. Takebe, et al.; Nat. Rev. Clin. Oncol. 8, 97 (2011) • Cancer stem cells: Z. Yu, et al.; Int. J. Biochem. Cell Biol. 44, 2144 (2012)

Highlight!

NEW Notch1&2 Receptor Products

Antibodies

anti-Notch1 (mouse), mAb (22E5)

AG-20B-0051-C100 100 µg
AG-20B-0051B-C100 Biotin 100 µg

CLONE: 22E5. **ISOTYPE:** Rat IgG2aκ. **SPECIFICITY:** Recognizes endogenous mouse Notch1 receptor. **APPLICATION:** FACS.

anti-Notch2, mAb (16F11)

AG-20B-0052-C100 100 µg
AG-20B-0052B-C100 Biotin 100 µg

CLONE: 16F11. **ISOTYPE:** Rat IgG1κ. **SPECIFICITY:** Recognizes human and mouse endogenous Notch2 receptor. **APPLICATION:** FACS.

Proteins

Notch1 (mouse):Fc (human) (rec.)

AG-40B-0109-C050 50 µg
AG-40B-0109-3050 3 x 50 µg

SPECIFICITY: Binds to mouse DLL4.

Notch2 (mouse):Fc (human) (rec.)

AG-40B-0110-C050 50 µg
AG-40B-0110-3050 3 x 50 µg

SPECIFICITY: Binds to mouse DLL1 and DLL4.

See Pages 6 & 7 for a Full Panel of Biologically Active Notch Ligand Proteins!

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Periostin – Bridge between cancer stem cells (CSCs) and their metastatic niches

Periostin, also termed osteoblast-specific factor 2 (OSF-2), belongs to the family of matricellular proteins. It is composed of a signal sequence, four-coiled fasciclin-like repeats, an N-terminal cysteine-rich region (EMI domain), and heparin-binding domains present in the carboxyl-tail. Periostin contains γ -carboxylglutamate residues that are formed by vitamin K-dependent carboxylation. The N-terminus part of periostin (up to exon 16) is conserved, while the C-terminal region (comprising exon 17-23) gives rise to different splice isoforms upon alternative splicing. The isoforms have a molecular weight range from 83 to 93 kDa. Six different periostin splice isoforms have been reported, but only four of them were sequenced and annotated. Periostin is known to interact with several integrin molecules on cell surfaces and activating the PI3K/Akt and MAPK pathways during tissue development and remodelling. It functions as a cell adhesion molecule for pre-osteoblasts and is thought to be involved in osteoblast recruitment, attachment and spreading. It is involved in processes such as cell motility, adhesion, metastatic growth, angiogenesis and wound healing.

Periostin is overexpressed in various human tumors and accelerates their development by promoting cancer cell survival, epithelial-mesenchymal transition, invasion and metastasis. Recently, periostin was shown to be crucial for cancer stem cell maintenance. Malanchi, et al. (2012) demonstrated that stromal periostin is crucial in metastatic colonization by regulating the interactions between breast cancer stem cells and their metastatic niches.

Periostin is an interesting cancer biomarker, since its upregulation in cancers usually correlates with aggressiveness and/or poor survival. Additionally, periostin was shown to be a relevant biomarker to diagnose idiopathic pulmonary fibrosis (IPF).

LITERATURE REFERENCES: Interactions between cancer stem cells and their niche govern metastatic colonization: I. Malanchi, et al.; *Nature* **481**, 85 (2012) • Periostin, a matricellular protein, plays a role in the induction of chemokines in pulmonary fibrosis: M. Uchida, et al.; *Am. J. Respir. Cell Mol. Biol.* **46**, 677 (2012) • Matricellular proteins: priming the tumour microenvironment for cancer development and metastasis: G.S. Wong & A.K. Rustgi; *Br. J. Cancer* **108**, 755 (2013)

AdipoGen[®]
Connecting Immunology to Metabolism™

NEW



Specific Periostin ELISA Kits for Human or Mouse Periostin Detection

- Optimized for detection in cell culture supernatants, serum or plasma.
- Specific and sensitive for the measurement of natural and recombinant human or mouse periostin.
- Reproducible results with low inter- and intra-assay variation.

Periostin (human) ELISA Kit

AG-45B-0004-KI01 96 wells
SPECIES REACTIVITY: Human
SENSITIVITY: 15 pg/ml
RANGE: 78 to 5000 pg/ml
DETECTION TYPE: Colorimetric
ASSAY TYPE: Sandwich
SAMPLE TYPE: Cell Culture Supernatant, Plasma, Serum

Periostin (mouse) ELISA Kit

AG-45B-0005-KI01 96 wells
SPECIES REACTIVITY: Mouse
SENSITIVITY: 10 pg/ml
RANGE: 31 to 2000 pg/ml
DETECTION TYPE: Colorimetric
ASSAY TYPE: Sandwich
SAMPLE TYPE: Cell Culture Supernatant, Plasma, Serum

Periostin (human) Matched Pair Detection Set

AG-46B-0005-KI01 For 5 x 96 wells
SPECIES REACTIVITY: Human
SENSITIVITY: 30 pg/ml
RANGE: 80 to 5000 pg/ml
DETECTION TYPE: Colorimetric
ASSAY TYPE: Sandwich
SAMPLE TYPE: Cell Culture Supernatant, Plasma, Serum

Periostin (mouse) Matched Pair Detection Set

AG-46B-0002-KI01 For 5 x 96 wells
SPECIES REACTIVITY: Mouse
SENSITIVITY: 20 pg/ml
RANGE: 31 to 2000 pg/ml
DETECTION TYPE: Colorimetric
ASSAY TYPE: Sandwich
SAMPLE TYPE: Cell Culture Supernatant, Plasma, Serum

Detection Sets contain sufficient materials to run ELISAs on 5 x 96-well plates.

Periostin & Specific Periostin Antibodies

Specific Periostin Antibodies

anti-Periostin, mAb (Stiny-1)

AG-20B-0033-C100 100 µg
AG-20B-0033B-C100 Biotin 100 µg

CLONE: Stiny-1. **ISOTYPE:** Mouse IgG1κ. **IMMUNOGEN:** Full-length human periostin. **SPECIFICITY:** Recognizes human and mouse periostin. **APPLICATION:** ELISA, IHC (FS, PS), WB.

LIT: Interactions between cancer stem cells and their niche govern metastatic colonization: I. Malanchi, et al.; Nature **481**, 85 (2012)

anti-Periostin, mAb (Stiny-3)

AG-20B-0055-C100 100 µg
AG-20B-0055B-C100 Biotin 100 µg

CLONE: Stiny-3. **ISOTYPE:** Mouse IgG2bκ. **IMMUNOGEN:** Full-length mouse periostin (isoform 5). **SPECIFICITY:** Recognizes human and mouse periostin. **APPLICATION:** ELISA.

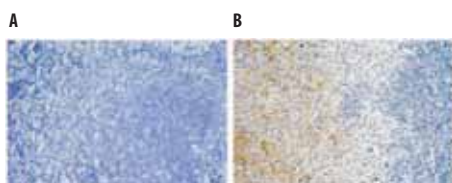


FIGURE: Immunohistochemical staining of endogenous human Periostin in normal breast (A) and human breast cancer (B) tissues (paraffin sections) by using Periostin, mAb (Stiny-1) (Prod. No. AG-20B-0033).

Periostin Protein

Periostin (mouse) (rec.)

AG-40B-0081-C010 10 µg
AG-40B-0081-3010 MultiPack 3 x 10 µg

SOURCE: CHO cells. **SEQUENCE:** Mouse periostin (aa 24-783) (isoform 5) is fused at the C-terminus to a FLAG®-tag. **MW:** ~85kDa. **PURITY:** ≥95% (SDS-PAGE). **ENDOTOXIN CONTENT:** <0.01EU/µg.



ANGPTL Proteins in Cancer Metastasis & Stem Cells

The multifunctional matricellular protein angiopoietin-like 4 (**ANGPTL4**) promotes the dissociation of endothelial cell-cell junctions and is a metastasis progression gene. By mediating endothelial disruption and trans-endothelial tumor cell passage, ANGPTL4 is an important protein to study tumor microenvironments and its metastatic niche. Recently, it was also shown to maintain hematopoietic stem cells (HSCs) *ex vivo*.

LILRB2 and its mouse ortholog PIRB were discovered as receptors for angiopoietin-like proteins 2 and 3 (ANGPTL2 and ANGPTL3). Binding of ANGPTL2&3 to the receptors supported *ex vivo* expansion of HSCs and demonstrated the functional significance of these classical immune-inhibitory receptors in maintenance of stemness of normal adult stem cells and in support of cancer development.

LIT: Inhibitory receptors bind ANGPTLs and support blood stem cells and leukaemia development: J. Zheng, et al.; Nature **485**, 656 (2012) • Angiopoietin-like-2 and -3 act through their coiled-coil domains to enhance survival and replating capacity of human cord blood hematopoietic progenitors: H.E. Broxmeyer, et al.; Blood Cells Mol. Dis. **48**, 25 (2012) • Angptl4 maintains in vivo repopulation capacity of CD34+ human cord blood cells: U. Blank, et al.; Eur. J. Haematol. **89**, 198 (2012)

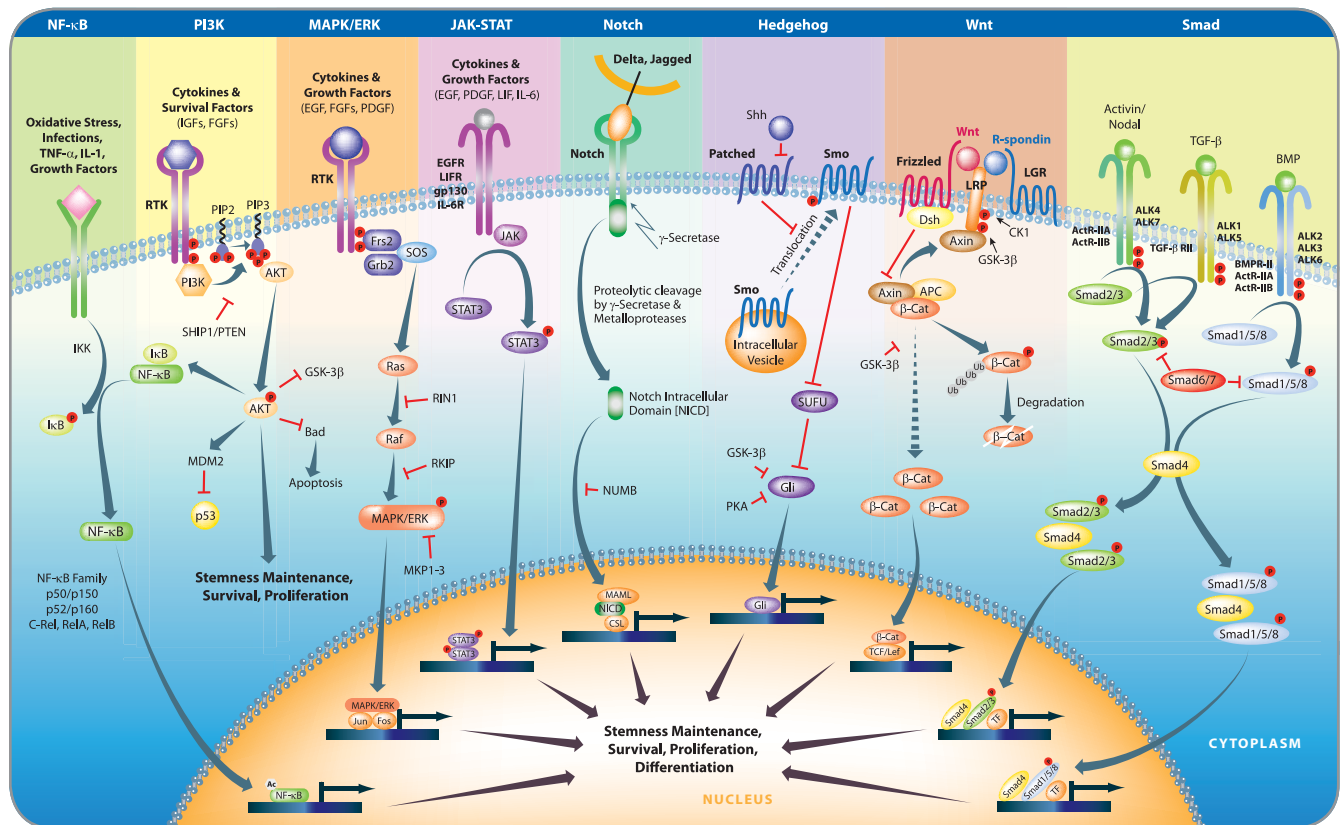
PRODUCT NAME	PID	SIZE
ANGPTL2 (CCD) (human) (rec.)	AG-40A-0087	10 µg
ANGPTL2 (FLD) (human) (rec.)	AG-40A-0083	10 µg
ANGPTL3 (human) (rec.)	AG-40A-0051	10 µg
ANGPTL3 (CCD) (human) (rec.)	AG-40A-0069	10 µg
ANGPTL3 (FLD) (human) (rec.)	AG-40A-0071	10 µg
ANGPTL3 (mouse) (rec.)	AG-40A-0082	10 µg
ANGPTL3 (CCD) (mouse) (rec.) (His)	AG-40A-0103	10 µg
ANGPTL3 (FLD) (mouse) (rec.)	AG-40A-0096	10 µg

PRODUCT NAME	PID	SIZE
ANGPTL4 (human) (rec.)	AG-40A-0033	10 µg
ANGPTL4 (CCD) (human) (rec.)	AG-40A-0065	10 µg
ANGPTL4 (FLD) (human) (rec.)	AG-40A-0070	10 µg
ANGPTL4 (mouse) (rec.)	AG-40A-0075	10 µg
ANGPTL4 (CCD) (mouse) (rec.) (His)	AG-40A-0104	10 µg
ANGPTL4 (FLD) (mouse) (rec.)	AG-40A-0115	10 µg
ANGPTL4 (FLD) (rat) (rec.)	AG-40A-0175	10 µg

All proteins are also available as 50 µg sizes!

AdipoGen® offers a wide range of ANGPTL proteins, antibodies and ELISA kits!

Signaling Pathways – Controlling Stem Cell Fate



Since the discovery that embryonic stem cells are maintained in a pluripotent state through the interplay of a number of key signal transduction pathways, it is becoming increasingly clear that stemness and pluripotency are defined by the complex molecular convergence of these pathways and regulated by the core stem cell transcription factors. The integration of extrinsic and intrinsic signals is required to preserve the self-renewal and tissue regenerative capacity of stem cells, while protecting them from malignant conversion or loss of proliferative potential by death, differentiation or senescence. Numerous intrinsic signals as well as microenvironmental cues from their niche allow stem cells to maintain epigenetic marks enabling their self-renewal. Furthermore, a constant communication with their niche enables adult stem cells to perceive and respond to environmental changes, balancing their growth and regenerative potential or initiating terminal differentiation programs. Several developmentally conserved signaling pathways have emerged as important control devices of stem cell fate, including Notch, Wingless-type (Wnt), Sonic hedgehog (Shh), Jak-STAT, MAPK/ERK, PI3K, NF-κB and Smad pathways, being hallmarks of stem cell and cancer signaling. These multiple pathways have been shown to be implicated in the maintenance of tissue homeostasis, proliferation or differentiation in embryonic stem cells (ESCs), induced pluripotent stem cells (iPS cells), adipose-derived stromal/stem cells (ASCs) and also in tumorigenesis. Interruption of these stem cell signaling pathways has been shown to be implicated in carcinogenesis and the generation of “cancer stem cells.”

The origins of cancer stem cells (CSCs) and the methods to identify them is of very high interest since the “cancer stem cell hypothesis”. The existence of subpopulations of tumor cells with stem-like characteristics has significant therapeutic implications. The stem-like phenotype includes indefinite self-replication, pluripotency and importantly, resistance to chemotherapeutics. Thus, it is plausible that CSCs, regardless of their origin, may escape standard therapies and cause disease recurrences and/or metastasis after apparently complete remissions. Consequently, the idea of selectively targeting CSCs with novel therapeutics is gaining considerable interest. The stem cell fate signaling pathways are intensively studied putative therapeutic targets in CSCs, and several investigational inhibitors are being developed.

SELECTED REVIEW ARTICLES

Signaling pathways in cancer and embryonic stem cells: O. Dreesen & A.H. Brivanlou; *Stem Cell Rev.* **3**, 7 (2007) • Signaling pathways governing stem-cell fate: U. Blank, et al.; *Blood* **111**, 492 (2008) • Cancer stem cells: markers or biomarkers? W.A. Woodward & E.P. Sulman; *Canc. Metast. Rev.* **27**, 459 (2008) • Turning cancer stem cells inside out: an exploration of glioma stem cell signaling pathways: Z. Li, et al.; *J. Biol. Chem.* **284**, 16705 (2009) • Signaling circuitries controlling stem cell fate: to be or not to be: R. Iglesias-Bartolome & J.S. Gutkind; *Curr. Opin. Cell Biol.* **23**, 716 (2011) • Cancer stem cells: the development of new cancer therapeutics: R. Scatenena, et al.; *Expert Opin. Biol. Ther.* **11**, 875 (2011) • Controlling the stem cell compartment and regeneration in vivo: the role of pluripotency pathways: K. Greenow & A.R. Clarke; *Physiol. Rev.* **92**, 75 (2012) • Cancer stem cells: distinct entities of dynamically regulated phenotypes? Y. Li & J. Latorra; *Canc. Res.* **72**, 576 (2012)

BULK available!

Leukemia Inhibitory Factor (LIF)

LIF has the capacity to induce terminal differentiation in leukemic cells. Its activities also include the induction of hematopoietic differentiation in normal and myeloid leukemia cells, the induction of neuronal cell differentiation and the stimulation of acute-phase protein synthesis in hepatocytes. LIF maintains the pluripotency of mouse embryonic stem cells (mESCs). hESCs require FGF-2 (Prod. No. AG-40T-0040) as a factor.

PRODUCT NAME	PID	SIZE
LIF (human) (rec.)	AG-40B-0093-C010	10 µg
MultiPack	AG-40B-0093-3010	3 x 10 µg
BULK	AG-40B-0093-C100	100 µg

Stem Cell Modulators

PRODUCT NAME	PID	SIZE
Apicidin Promotes either self-renewal or differentiation of ES cells	AG-CN2-0087	1 mg 5 mg
6BIO Wnt pathway antagonist • Promotes self-renewal of mouse and human ES cells	AG-CR1-0056	1 mg 5 mg 25 mg
BIX 01294 (free base) Stem cell inducer	AG-CR1-0051	1 mg 5 mg 25 mg
BIX 01294 . trihydrochloride Stem cell inducer	AG-CR1-0150	1 mg 5 mg 25 mg
IWR-1-endo Potent and reversible cell permeable Wnt pathway signaling inhibitor	AG-CR1-3581	5 mg 25 mg
LY-294,002 Diminishes the ability of leukemia inhibitory factor (LIF) to maintain self-renewal with cells concomitantly adopting a differentiated morphology	AG-CR1-0108	1 mg 5 mg 25 mg
MS-275 Promotes either self-renewal or differentiation of ES cells	AG-CR1-0032	1 mg 5 mg 25 mg
PD 98,059 MEK inhibitor • Enhances the self-renewal of mouse ES cells in the presence of leukemia inhibitory factor (LIF)	AG-CR1-0118	1 mg 5 mg 10 mg 50 mg
PD 184,352 MEK inhibitor • In combination with the GSK-3β inhibitor CHIR99021 and FGFR inhibitor SU-5402 helps to sustain selfrenewal in human ESCs	AG-CR1-0029	1 mg 5 mg
Pifithrin-α . HBr An inhibitor of p53-dependent apoptosis • Increases the survival of hemopoietic clonogenic cells	AG-CR1-0004	5 mg 10 mg 25 mg
Shz-1 Enhancer of regenerative repair	AG-CR1-3502	1 mg 5 mg
Trichostatin A Promotes either self-renewal or differentiation of ES cells	AG-CN2-0108	1 mg 5 mg

Notch Processing Inhibitors

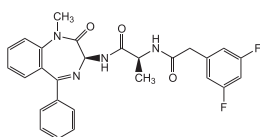
Compound E

AG-CR1-0081-C250
AG-CR1-0081-M001
AG-CR1-0081-M005

250 µg
1 mg
5 mg

Formula: C₂₇H₂₄F₂N₄O₃
MW: 490.5
CAS: 209986-17-4

Non-competitive γ-secretase inhibitor •
Notch processing inhibitor.



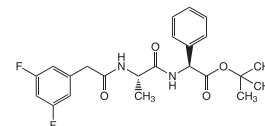
DAPT

AG-CR1-0016-M005
AG-CR1-0016-M025

5 mg
25 mg

Formula: C₂₃H₂₆F₂N₂O₄
MW: 432.5
CAS: 208255-80-5

Cell permeable γ-secretase inhibitor •
Notch processing inhibitor.

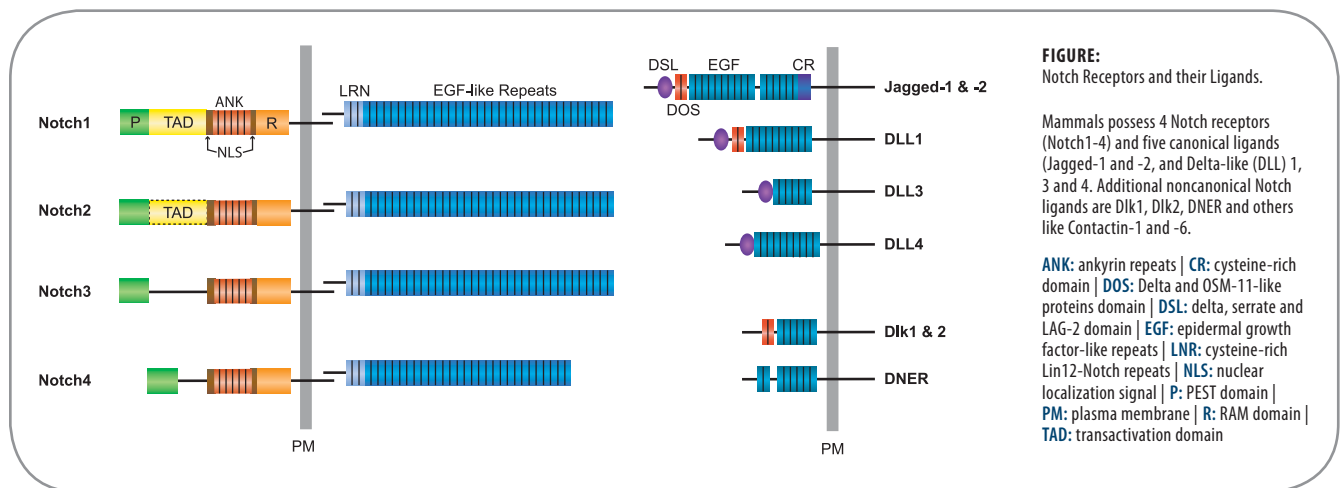


Notch Signaling

The highly conserved Notch signaling pathway regulates many different cell fate decisions. It is important for pattern formation during development such as neurogenesis, angiogenesis or myogenesis and regulates T cell development and stem cell maintenance. Furthermore, it is also involved in cellular processes throughout adulthood. Signaling via Notch occurs between neighbouring cells and both the receptor and its ligands. Notch ligands are transmembrane proteins with a Delta/Serrate/Lag-2 (DSL)-domain and varying numbers of EGF-like repeats. The canonical Notch ligands include Jagged-1, Jagged-2, DLL1, DLL3 and DLL4. The non-canonical Notch ligands Dlk1, Dlk2 and DNER lack the DSL domain. Other non-canonical ligands (e.g. contactin-1, contactin-6, periostin) are thought to act as co-ligands to enhance or inhibit Notch

activation and might be important modulators of the Notch pathway.

The Notch pathway plays an important role in many different processes in a wide range of tissues, this is why dysregulated Notch signaling has been associated with various human diseases such as cancer, immune disorders, developmental syndromes, stroke and cognitive symptoms. Several approaches including γ -secretase inhibitors, antibodies that inhibit specific Notch receptors, ligands, or other pathway components or expression of Jagged-1 or DLL-1 Fc fusion proteins to modulate Notch signaling are explored to treat Notch-associated cancers and other diseases associated with Notch pathway malfunction.



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Notch Ligand ELISA Kits



DLK1, Soluble (human) ELISA Kit

AG-45A-0032EK-KI01	96 wells
AG-45A-0032TP-KI01	2 x 96 wells
AG-45A-0032PP-KI01	5 x 96 wells

SPECIES REACTIVITY:	Human
SENSITIVITY:	336 pg/ml
RANGE:	0.47 to 30 ng/ml
DETECTION TYPE:	Colorimetric
ASSAY TYPE:	Sandwich
SAMPLE TYPE:	Cell Culture Supernatant, Serum

DLL1, Soluble (human) ELISA Kit

AG-45A-0027EK-KI01	96 wells
AG-45A-0027TP-KI01	2 x 96 wells
AG-45A-0027PP-KI01	5 x 96 wells

SPECIES REACTIVITY:	Human
SENSITIVITY:	120 pg/ml
RANGE:	0.125 to 8 ng/ml
DETECTION TYPE:	Colorimetric
ASSAY TYPE:	Sandwich
SAMPLE TYPE:	Cell Culture Supernatant, Plasma, Serum

DNER, Soluble (human) ELISA Kit

AG-45A-0045EK-KI01	96 wells
AG-45A-0045TP-KI01	2 x 96 wells
AG-45A-0045PP-KI01	5 x 96 wells

SPECIES REACTIVITY:	Human
SENSITIVITY:	358 pg/ml
RANGE:	0.5 to 32 ng/ml
DETECTION TYPE:	Colorimetric
ASSAY TYPE:	Sandwich
SAMPLE TYPE:	Cell Culture Supernatant, Plasma, Serum

Biologically Active Notch Ligand Proteins

Contactin-1 (human):Fc (human) (rec.)

AG-40A-0168 10 µg | 50 µg

Contactin-6 (human):Fc (human) (rec.)

AG-40A-0156 10 µg | 50 µg

DLK1 (human) (rec.)

AG-40A-0133 10 µg | 50 µg

DLK1 (human):Fc (human) (rec.)

AG-40A-0118 10 µg | 50 µg

DLK1 (mouse):Fc (human) (rec.)

AG-40A-0107 10 µg | 50 µg

DLK2 (human):Fc (human) (rec.)

AG-40A-0158 10 µg | 50 µg

DLL1 (human) (rec.)

AG-40A-0073 10 µg | 50 µg

DLL1 (human):Fc (human) (rec.)

AG-40A-0116Y 10 µg | 50 µg

DLL1 (mouse):Fc (human) (rec.)

AG-40A-0148 10 µg | 50 µg

DLL3 (human):Fc (human) (rec.)

AG-40A-0113 10 µg | 50 µg

DLL3 (ED) (mouse):Fc (human) (rec.)

AG-40A-0178 10 µg

DLL4 (human):Fc (human) (rec.)

AG-40A-0077Y 10 µg | 50 µg

DLL4 (mouse):Fc (human) (rec.)

AG-40A-0145 10 µg | 50 µg

DNER (ED) (human) (rec.)

AG-40A-0137Y 10 µg | 50 µg

DNER (ED) (human):Fc (human) (rec.)

AG-40A-0119 10 µg | 50 µg

DNER (ED) (mouse):Fc (human) (rec.)

AG-40A-0177 10 µg

Jagged-1 (human):Fc (human) (rec.)

AG-40A-0081 10 µg | 50 µg

Jagged-1 (mouse):Fc (human) (rec.)

AG-40A-0157 10 µg | 50 µg

Jagged-2 (human):Fc (human) (rec.)

AG-40A-0155 10 µg

Jagged-2 (mouse):Fc (human) (rec.)

AG-40A-0183 10 µg | 50 µg

Notch Target

HES1 (human) (rec.) (His)

AG-40A-0180 10 µg | 50 µg

Now available from AdipoGen® – BULK QUANTITIES at affordable costs!

Specific Notch Ligand Antibodies

HUMAN SPECIFIC ANTIBODIES	PID	SIZE	APPLICATIONS	SOURCE/ISOTYPE
DLK1 (human), mAb (PF299-1)	AG-20A-0070	50 µg 100 µg	ELISA, FACS, IHC, WB	Mouse IgG1κ
DLK1 (human), mAb (PF13-3)	AG-20A-0069	50 µg 100 µg	ELISA, FACS, IHC, WB	Mouse IgG1κ
DLK1 (human), pAb	AG-25A-0092	100 µg	ELISA, WB	Rabbit
DLK1 (human), pAb	AG-25A-0091	100 µg	ELISA, FACS, WB	Rat
DLL1 (human), mAb (D1L165-6)	AG-20A-0074	50 µg 100 µg	ELISA, WB	Mouse IgG1κ
DLL1 (human), pAb	AG-25A-0079	100 µg	ELISA, WB	Rat
DLL1 (human), pAb	AG-25A-0062	100 µg	ELISA, IHC, WB	Rabbit
DLL4 (human), mAb (DL86-3AG)	AG-20A-0080	50 µg 100 µg	ELISA, WB	Mouse IgG1κ
DLL4 (human), pAb	AG-25A-0080	100 µg	ELISA, WB	Rat
DNER (human), mAb (DR324-4)	AG-20A-0078	50 µg 100 µg	ELISA, WB	Mouse IgG2ακ
DNER (human), pAb	AG-25A-0102	100 µg	ELISA, WB	Rabbit
Jagged-1 (human), mAb (J1G53-3)	AG-20A-0049	100 µg	ELISA, FACS, IHC, WB	Mouse IgG1κ
Jagged-1 (human), mAb (J1G53-3) (FITC)	AG-20A-0049F	50 µg	FACS	Mouse IgG1κ
Jagged-1 (human), mAb (J1G53-3) (PerCP)	AG-20A-0049PC	50 µg	FACS	Mouse IgG1κ
Jagged-1 (human), mAb (J1G74-7)	AG-20A-0050	100 µg	ELISA, FACS, WB	Mouse IgG1κ
Jagged-1 (human), pAb	AG-25A-0081	100 µg	ELISA, WB	Rat
MOUSE SPECIFIC ANTIBODIES	PID	SIZE	APPLICATIONS	SOURCE/ISOTYPE
DLK1 (mouse), mAb (PF105B)	AG-20A-0057	50 µg 100 µg	ELISA, WB	Rat IgG2ακ
DLK1 (mouse), mAb (PF183E)	AG-20A-0058	50 µg 100 µg	ELISA, WB	Rat IgG2ακ
DLL1 (mouse), mAb (D1L357-1-4)	AG-20A-0085	50 µg 100 µg	ELISA, WB	Rat IgG2κ
DLL1 (mouse), mAb (30B11.1)	AG-20B-0053	100 µg	FACS, ICC	Rat IgG2ακ
DLL4 (mouse), mAb (9A1.5)	AG-20B-0054	100 µg	FACS, ICC	Rat IgG1κ

Sonic Hedgehog Signaling (Shh)

The Sonic Hedgehog (Shh) signaling pathway plays key roles in embryonic development, formation and maintenance of cancer stem cells (CSCs) and acquisition of epithelial-to-mesenchymal transition (EMT). Since CSCs and EMT are important for cancer cell invasion, metastasis, drug resistance and tumor recurrence, inhibition of the Hh signaling pathway is believed to be an important target for cancer therapy. Recently, several small-molecule inhibitors of Shh signaling were developed and synthesized for cancer treatment.

REVIEW: Targeting the Hedgehog signaling pathway for cancer therapy: Y. Li, et al.; Expert Opin. Ther. Targets **16**, 49 (2012)



Standard Sonic Hedgehog Signaling Modulators

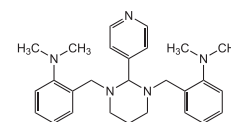
GANT61 [NSC 136476]

AG-CR1-3561-M001 1 mg
AG-CR1-3561-M005 5 mg

Formula: C₂₇H₃₅N₅ **MW:** 429.6 **CAS:** 500579-04-4

Sonic hedgehog (Shh) pathway inhibitor • Cell permeable GLI antagonist

LIT: Inhibition of GLI-mediated transcription and tumor cell growth by small-molecule antagonists: M. Lauth, et al.; PNAS **104**, 8455 (2007)



SAG

AG-CR1-3506-M001 1 mg
AG-CR1-3506-M005 5 mg

Formula: C₂₈H₂₈ClN₃OS **MW:** 490.1 **CAS:** 912545-86-9

Sonic hedgehog (Shh) pathway agonists • Cell permeable and water soluble (Prod. No. AG-CR1-3585) smoothend (Smo) agonists

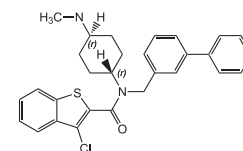
LIT: Small-molecule modulators of Hedgehog signaling: identification and characterization of Smoothened agonists and antagonists: M. Frank-Kamenetsky, et al.; J. Biol. **1**, 10 (2002)

SAG . dihydrochloride (water soluble)

AG-CR1-3585-M001 1 mg
AG-CR1-3585-M005 5 mg

Formula: C₂₈H₂₈ClN₃OS . 2HCl . H₂O **MW:** 490.1 . 72.9 . 18.0
CAS: 364590-63-6

AG-CR1-3506



NEW SAG Analog (highly active)

AG-CR1-3518-M001 1 mg

Formula: C₂₈H₂₇Cl₂N₃OS (*cis*-isomer) **MW:** 524.5

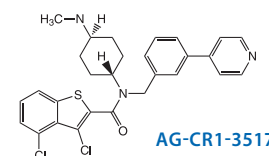
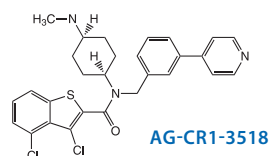
Sonic hedgehog (Shh) pathway agonists • Cell permeable smoothend (Smo) agonists

LIT: Potent small molecule Hedgehog agonists induce VEGF expression in vitro: K. Seifert, et al.; Bioorg. Med. Chem. **20**, 6465 (2012)

NEW SAG Analog (LowTox)

AG-CR1-3517-M001 1 mg

Formula: C₂₈H₂₇Cl₂N₃OS (*trans*-isomer) **MW:** 524.5



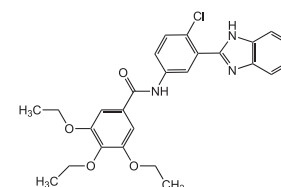
SANT-2

AG-CR1-3514-M001 1 mg
AG-CR1-3514-M005 5 mg

Formula: C₂₆H₂₆ClN₃O₄ **MW:** 480.0 **CAS:** 329196-48-7

Sonic hedgehog (Shh) pathway inhibitor • Cell permeable potent smoothened (Smo) antagonist

LIT: Small molecule modulation of Smoothened activity: J.K. Chen, et al.; PNAS **99**, 14071 (2002)



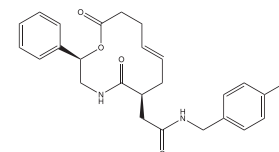
Robotnikinin

AG-CR1-0069-M001 1 mg

Formula: C₂₅H₂₇ClN₂O₄ **MW:** 454.9

Synthetic. Sonic hedgehog (Shh) pathway inhibitor/modulator

LIT: A small molecule that binds Hedgehog and blocks its signaling in human cells: B.Z. Stanton, et al.; Nat. Chem. Biol. **5**, 154 (2009)



Sonic Hedgehog Modulators – Designed by Nature

Cyclopamine

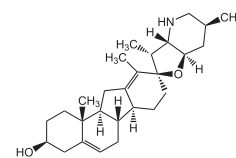
AG-CN2-0028-M001 1 mg

AG-CN2-0028-M005 5 mg

Formula: C₂₇H₄₁NO₂ **MW:** 411.6 **CAS:** 4449-51-8

Sonic hedgehog (Shh) pathway inhibitor • Directly inhibits smoothened (Smo)

LIT: The teratogenic Veratrum alkaloid cyclopamine inhibits sonic hedgehog signal transduction: J.P. Incardona, et al.; Development 125, 3553 (1998)



Forskolin

AG-CN2-0089-M001 1 mg

AG-CN2-0089-M005 5 mg

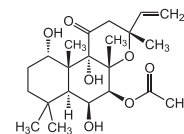
AG-CN2-0089-M025 25 mg

AG-CN2-0089-M050 50 mg

Formula: C₂₂H₃₄O₇ **MW:** 410.5 **CAS:** 66428-89-5 and 66575-29-9

Sonic hedgehog (Shh) pathway inhibitor

LIT: Forskolin, a Hedgehog signal inhibitor, inhibits cell proliferation and induces apoptosis in pediatric tumor cell lines: H. Yamanaka, et al.; Mol. Med. Rep. 3, 133 (2010)



(-)-Epigallocatechin gallate [EGCG]

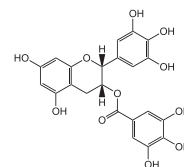
AG-CN2-0063-M025 25 mg

AG-CN2-0063-M100 100 mg

Formula: C₂₂H₁₈O₁₁ **MW:** 458.4 **CAS:** 989-51-5

Sonic hedgehog (Shh) pathway modulator • PTCH and Gli1 inhibitor

LIT: The role of nutraceuticals in the regulation of Wnt and Hedgehog signaling in cancer: F.H. Sarkar, et al.; Cancer Metastasis Rev. 29, 383 (2010) (Review)



Resveratrol

AG-CN2-0033-M050 50 mg

AG-CN2-0033-M100 100 mg

AG-CN2-0033-M500 500 mg

AG-CN2-0036-M050 50 mg

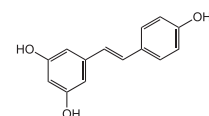
AG-CN2-0036-M100 100 mg

AG-CN2-0036-M500 500 mg

Formula: C₁₄H₁₂O₃ **MW:** 228.2 **CAS:** 501-36-0

Sonic hedgehog (Shh) pathway modulator • Gli1 mRNA expression inhibitor

LIT: Common botanical compounds inhibit the hedgehog signaling pathway in prostate cancer: A. Slusarz, et al.; Cancer Res. 70, 3382 (2010)



Curcumin (high purity)

AG-CN2-0059-M010 10 mg

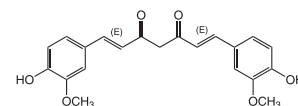
AG-CN2-0059-M050 50 mg

AG-CN2-0059-M250 250 mg

Formula: C₂₁H₂₀O₆ **MW:** 368.4 **CAS:** 458-37-7

Sonic hedgehog (Shh) pathway modulator • Downregulates Shh and Gli1

LIT: The role of nutraceuticals in the regulation of Wnt and Hedgehog signaling in cancer: F.H. Sarkar, et al.; Cancer Metastasis Rev. 29, 383 (2010) (Review)



Highlight!

FGFs & Stem Cells

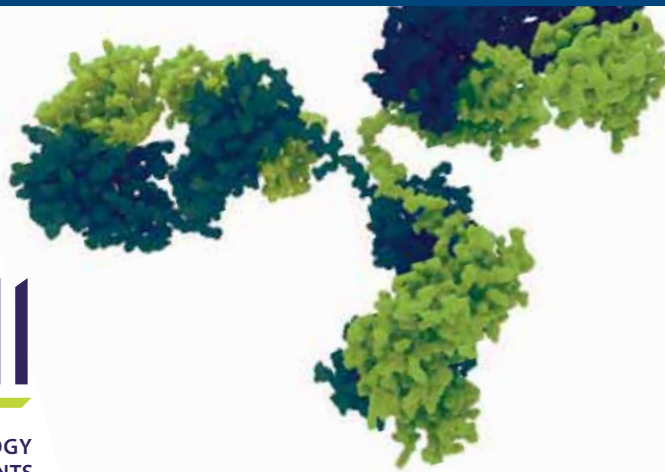
Fibroblast growth factors (FGFs) play an important role in the regulation of proliferation and differentiation in stem cells. FGFs are amongst the most common growth factors used to expand stem cells, including human embryonic stem cells (hESCs), trophoblast stem cells (TSCs) and neural stem cells (NSCs). Moreover, it has been recently recognized that FGFs are useful for culturing cancer stem cells. FGF-2 is required for maintaining pluripotency of human ESCs. FGF-21 acts as a critical regulator of glucose and lipid metabolism and of bone marrow mesenchymal stem cells (BMMSCs) differentiation.

LIT: Control of Stemness by Fibroblast Growth Factor Signaling in Stem Cells and Cancer Stem Cells: N. Gotoh; Curr. Stem Cell Res. Ther. 4, 9 (2009) (Review)

PRODUCT NAME	PID	SIZE	SOURCE	ENDOTOXIN
FGF-2 (human) (rec.)	AG-40T-0040	10 µg 50 µg	E. coli	<0.1EU/µg
FGF-21 (human):Fc (human) (rec.)	AG-40A-0095	10 µg 50 µg	HEK 293 cells	<0.1EU/µg
FGF-21 (mouse):Fc (human) (rec.)	AG-40A-0097	10 µg 50 µg	HEK 293 cells	<0.1EU/µg



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Human CD Monoclonal Antibodies for Stem Cell Research!

PID (*)	PRODUCT NAME	LABELS & DYES										FAB		APPLICATIONS						
		Preservatives	Preservative Free	Biotin	FITC	R-PE	APC	PE-Cy7	DyLight350	F(ab)2	Fab	FUNC	ELISA	FACS	ICC	IHC	IP	WB		
ANC-152	CD7 (human), mAb (3A1E)	x	x	x	x	x								x		x				
ANC-156	CD9 (human), mAb (5N4)	x	x	x	x	x										x				
ANC-157	CD10 (human), mAb (5N5c)	x	x	x	x	x										x			x	
ANC-163	CD14 (human), mAb (UCHM1)	x	x	x	x	x										x				
ANC-164	CD15 (human), mAb (AHN1.1)	x	x	x	x									x		x				
ANC-173	CD24 (human), mAb (BA-1)	x	x	x	x											x				
ANC-178	CD29 (human), mAb (4B7R)	x	x	x	x	x										x			x	
ANC-179	CD30 (human), mAb (AC10)	x	x	x		x	x									x				
ANC-180	CD31 (human), mAb (158-2B3)	x	x	x	x	x										x				
ANC-182	CD33 (human), mAb (WM-53)	x	x	x	x	x										x				
ANC-183	CD34 (human), mAb (43A1)	x	x	x	x	x	x									x			x	
ANC-187	CD38 (human), mAb (AT1)	x	x	x	x	x										x				
ANC-190	CD41a (human), mAb (96.2C1)	x	x	x	x	x										x				
ANC-193	CD44 (human), mAb (BU52)	x	x	x	x	x			x							x				
ANC-352	CD44 (human), mAb (BU75)	x	x	x	x	x										x			x	
ANC-196	CD45 (human), mAb (C11)	x	x	x	x	x	x									x				
ANC-199	CD48 (human), mAb (5-4.8)	x	x	x	x	x										x				
ANC-200	CD49d (human), mAb (BU49)	x	x	x	x	x										x				
ANC-356	CD49f (human), mAb (BQ16)	x	x	x	x	x										x		x	x	
ANC-202	CD51 (human), mAb (P2W7)	x	x	x	x	x										x				
ANC-205	CD54 (D1) (human), mAb (15.2)	x	x	x	x	x										x	x	x	x	
ANC-206	CD54 (D2) (human), mAb (8.4A6)	x	x	x	x	x										x	x	x		
ANC-308	CD56 (human), mAb (ANC7C7)	x	x	x	x	x	x									x	x			
ANC-208	CD56 (human), mAb (ERIC-1)	x	x	x												x	x	x	x	
ANC-209	CD57 (human), mAb (NK-1)	x	x	x	x											x				
ANC-261	CD62L (human), mAb (LAM1-116)	x	x	x	x	x	x									x				
ANC-252	CD62P (human), mAb (G1)	x	x	x	x	x			x							x				
ANC-223	CD71 (human), mAb (DF1513)	x	x	x	x	x										x	x			
ANC-302	CD81 (human), mAb (1.3.3.22)	x	x	x	x	x										x			x	
ANC-326	CD105 (human), mAb (5N6)	x	x	x	x	x										x		x		
ANC-327	CD106 (human), mAb (1.G11B1)	x	x	x	x	x										x	x	x	x	
ANC-338	CD117 (human), mAb (57A5)	x	x	x		x	x									x				
ANC-348	CD127 (human), mAb (ANC8F2)	x	x	x	x	x										x				
ANC-393	CD166 (human), mAb (3A6)	x	x	x	x	x										x				
ANC-271	CD271 [NGFR] (human), mAb (ANC271/3D7)	x	x													x	x			

(*) The AnceLL Product # is build by the prefix (ANC-), main PID (3 digits) and a suffix (3 digits). The last 3 digits define the labels:
 -020 = Preservatives | -820 = Preservative Free | -030 = Biotin | -040 = FITC | -050 = R-PE | -060 = APC | -520 = F(ab)2 |
 -580 = Fab | -070 = PE-Cy7 | -350 = DyLight350
FAB: Fragment Antigen Binding; **FACS:** Flow Cytometry; **FUNC:** Functional Application; **ICC:** Immunocytochemistry;
IHC: Immunohistochemistry; **IP:** Immunoprecipitation; **WB:** Western Blot

Highlights

anti-CD28 (human), mAb (ANC28.1/5D10)

ANC-177-020 100 µg
 ANC-177-820 Preservative free 100 µg
 ANC-177-030 Biotin 100 µg
 ANC-177-040 FITC 120 tests
 ANC-177-050 R-PE 120 tests
 ANC-177-520 F(ab')2 100 µg

CLONE: ANC28.1/5D10. **ISOTYPE:** Mouse IgG1κ. **SPECIES:** Human. **APPLICATION:** ELISA, FACS, FUNC (Stimulates expression of IL-2 from CD28+ cells).

anti-CD105 (human), mAb (SN6)

ANC-326-020 100 µg
 ANC-326-820 Preservative free 100 µg
 ANC-326-030 Biotin 100 µg
 ANC-326-040 FITC 120 tests
 ANC-326-050 R-PE 120 tests

CLONE: SN6. **ISOTYPE:** Mouse IgG1κ. **SPECIES:** Human. **APPLICATION:** FACS, IHC, FUNC (Augments binding of TGF-β1 to CD105 expressing leukemia cells).

anti-CD117 (human), mAb (57A5)

ANC-338-020 100 µg
 ANC-338-820 Preservative free 100 µg
 ANC-338-030 Biotin 100 µg
 ANC-338-060 APC 120 tests
 ANC-338-050 RP-E 120 tests

CLONE: 57A5. **ISOTYPE:** Mouse IgG1. **SPECIES:** Human. **APPLICATION:** FACS.

anti-CD152 [CTLA-4] (human), mAb (ANC152.2/8H5)

ANC-359-020 100 µg
 ANC-359-820 Preservative free 100 µg
 ANC-359-030 Biotin 100 µg
 ANC-359-040 FITC 120 tests
 ANC-359-050 R-PE 120 tests
 ANC-359-520 F(ab')2 100 µg
 ANC-359-580 Fab 100 µg

CLONE: ANC152.2/8H5. **ISOTYPE:** Mouse IgG1κ. **SPECIES:** Cat, Cow, Dog, Human, Pig. **APPLICATION:** ELISA, FACS, FUNC (Blocking).



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Essential Synergistic Growth Factors for Stem Cell Mobilization

Stem Cell Factor (SCF)

Stem Cell Factor (SCF or kit-ligand) regulates hematopoietic stem cells (HSCs) in the stem cell niche in the bone marrow. It has been shown to increase the survival of HSCs *in vitro* and contributes to the self renewal and maintenance of HSCs *in vivo*.

PRODUCT NAME	PID	SIZE	SOURCE
SCF (human) (rec.) (His)	CHI-HR-200SCF	10 µg 50 µg	E. coli
SCF (human):Fc (human) (rec.)	CHI-HF-210SCF	10 µg 50 µg	CHO cells
SCF (human):Fc (human) (rec.) (non-lytic)	CHI-HF-220SCF	50 µg	CHO cells
SCF (human):Fc (mouse) (rec.)	CHI-HF-211SCF	50 µg	CHO cells
SCF (mouse):Fc (mouse) (rec.)	CHI-MF-110SCF	50 µg	CHO cells
SCF (mouse):Fc (mouse) (rec.) (non-lytic)	CHI-MF-120SCF	50 µg	CHO cells
SCF (rat):Fc (mouse) (rec.)	CHI-RF-311SCF	10 µg 50 µg	CHO cells

CSF3 [G-CSF]

Colony-stimulating factor 3 (CSF3, also known as granulocyte colony-stimulating factor (G-CSF)), is widely used as a mobilizer of bone marrow stem cells. CSF3 activates multiple signaling pathways, including the JAK/STAT, Ras/MAPK and PI3K/Akt pathways, thereby promoting survival, proliferation, differentiation and mobilization of haematopoietic stem and progenitor cells.

PRODUCT NAME	PID	SIZE	SOURCE
CSF3 (mouse):Fc (mouse) (rec.)	CHI-MF-110CSF3	10 µg 50 µg	CHO cells

SELECTED REVIEW ARTICLES

The synergy between stem cell factor (SCF) and granulocyte colony-stimulating factor (G-CSF): molecular basis and clinical relevance: R.F. Duarte & D.A. Franf; *Leuk. Lymphoma* **43**, 1179 (2002) • The role of ancestim (recombinant human stem-cell factor, rhSCF) in hematopoietic stem cell mobilization and hematopoietic reconstitution: K.E. Herbert, et al.; *Expert Opin. Biol. Ther.* **10**, 113 (2010) • The colony-stimulating factors and cancer: D. Metcalf; *Nat. Rev. Cancer* **10**, 425 (2010) (Review)

IL-6

Maintains bone marrow-derived mesenchymal stem cell stemness

IL-6 (human) (rec.) (His)

CHI-HR-20006-C010	10 µg
CHI-HR-20006-C050	50 µg

IL-6 (human):Fc (human) (rec.)

CHI-HF-21006-C050	50 µg
CHI-HF-21006-3050	3 x 50 µg

IL-6 (human):Fc (human) (rec.) (non-lytic)

CHI-HF-22006-C050	50 µg
CHI-HF-22006-3050	3 x 50 µg

IL-6 (mouse):Fc (mouse) (rec.) (non-lytic)

CHI-MF-12006-C050	50 µg
CHI-MF-12006-3050	3 x 50 µg

IL-6 (mouse):Fc (human) (rec.)

AG-40B-0108-C010	10 µg
AG-40B-0108-3010	3 x 10 µg

IL-6R (human):Fc (human) (rec.)

CHI-HF-21006R-C050	50 µg
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PEDF & Stem Cells

Pigment epithelium-derived factor (PEDF) has been recently reported to be sufficient to maintain the self-renewal of pluripotent human embryonic stem cells (hESCs).

LIT: The emerging role of PEDF in stem cell biology: M. Elahy, et al.; J. Biomed. Biotechnol. **2012**, 239091 (2012) • Pedf & stem cells: niche vs. nurture: P. Fitchev, et al.; Curr. Drug Deliv. (Epub ahead of print) (2013)

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN
PEDF (human) (rec.)	AG-40B-0077	10 µg 3 x 10 µg	CHO cells	<0.02EU/µg
new PEDF (mouse) (rec.)	AG-40B-0118	10 µg 3 x 10 µg	CHO cells	<0.01EU/µg
ANTIBODIES	PID	SIZE	SOURCE/ISOTYPE	APPLICATIONS
new PEDF (human), mAb (rec.) (Serpy-1-4)	AG-27B-0014	100 µg	Human IgG2λ	ELISA, WB
new PEDF, pAb (IN104)	AG-25B-0029	100 µg	Rabbit	ELISA, WB

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Rock Inhibitors

Human embryonic stem cells (hESCs) and human induced pluripotent stem cells (hiPSCs) promise new avenues for medical innovation. These human cells share many similarities with mouse counterparts, including pluripotency and they exhibit several unique properties. A technical problem for various cellular manipulations is the phenomenon of dissociation-induced apoptosis, which is unique to human pluripotent stem cells. This type of apoptosis is suppressed by ROCK inhibitors and brought a revolutionary change to this troublesome situation.

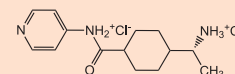
REVIEW: Lonely death dance of human pluripotent stem cells: ROCKing between metastable cell states: M. Ohgushi & Y. Sasai; Trends Cell Biol. **21**, 274 (2011)

Y-27632 . 2HCl

AG-CR1-3564-M001 1 mg
AG-CR1-3564-M005 5 mg
AG-CR1-3564-M025 25 mg

Formula: C₁₄H₂₁N₃O . 2HCl **MW:** 247.3 . 73.0 **CAS:** 146986-50-7

Potent, cell permeable, selective and ATP-competitive Rho-associated protein kinases inhibitor, including p160ROCK, ROCKII and PRK2 inhibitor

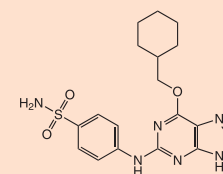


NU6102

AG-CR1-0020-M001 1 mg
AG-CR1-0020-M005 5 mg

Formula: C₁₈H₂₂N₆O₃S **MW:** 402.5 **CAS:** 444722-95-6

Potent CDK1/cyclin B (IC₅₀ = 9.5 nM) and CDK2/cyclin A3 (IC₅₀ = 5.4 nM) inhibitor • 1'000-fold more potent than NU2058 • Selective for CDK1 and CDK2 compared to CDK4/D1 (IC₅₀ = 1.6 µM), DYRK1A (IC₅₀ = 0.9 µM), PDK1 (IC₅₀ = 0.8 µM) and ROCKII (IC₅₀ = 0.6 µM) • Inhibits cell growth



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