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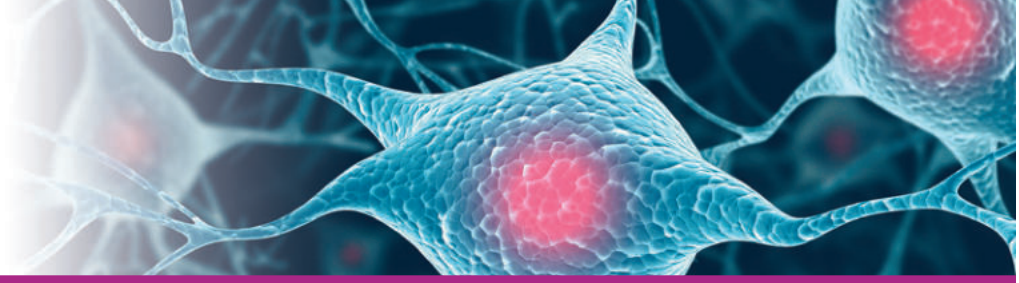
LIFE SCIENCES



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3rd Edition

Neuroscience Research

Focus: Emerging Fields in Neuroinflammation & Neurological Diseases

Interleukin-33

New Function of a Key Cytokine in Brain Development & Neurological Diseases

IL-33, a member of the IL-1 cytokine family, is constitutively expressed in fibroblasts, endothelial and epithelial cells exposed to the environment. IL-33 is a nuclear-associated cytokine that is normally released by damaged or necrotic cells acting as an "alarmin", an immediate indicator of tissue stress.

IL-33 signals through ST2 coupled with the co-receptor IL-1 receptor accessory protein (IL-1RAcP). IL-33 is a potent inducer of type 2 immune responses in the contexts of parasite infections and allergic asthma. New studies have also extended the biology of IL-33 with other functions: i) to induce brown and beige adipocyte thermogenesis and to promote insulin secretion by pancreatic islets; ii) to facilitate Treg proliferation to suppress autoimmunity and potentiate neurological recovery; and iii) to have multiple roles in the brain.

IL-33 is abundantly expressed in specific regions of brain and spinal cord, mediates the interaction between immune, endothelial and CNS (central nervous system) resident cells and plays a key role in the development and homeostasis of the CNS. Astrocytes are the primary source of local IL-33 that stimulates synapse elimination by microglia during early CNS development (see FIGURE 1). Deletion of IL-33 in astrocytes leads to abnormal synaptic connections. IL-33 is involved in the neuroinflammation of many neurological diseases such as Alzheimer's disease (AD) and multiple sclerosis (MS).

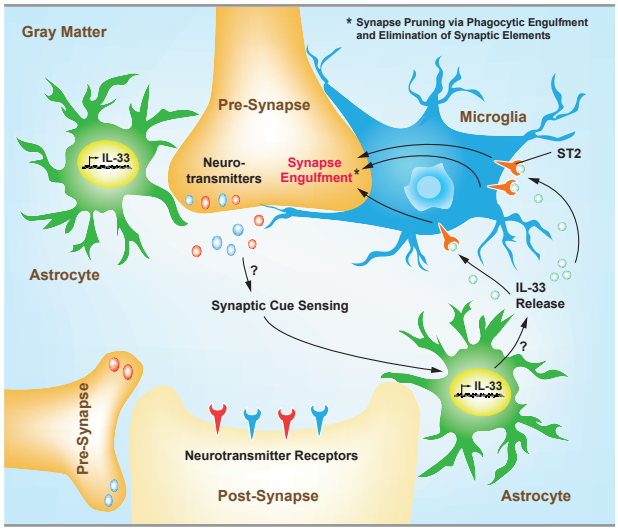


FIGURE 1: Astrocyte-derived IL-33 stimulates synapse elimination by microglia during CNS development.

Different studies suggest that IL-33 is involved in the myelination process during the CNS development and also likely the repair phase in demyelinating diseases such as MS and that IL-33 plays a critical role in the maintenance and repair of aging and stressed neurons during AD.

SELECTED REVIEW ARTICLES

Astrocyte-derived interleukin-33 promotes microglial synapse engulfment and neural circuit development: I.D. Vainchtein, et al.; Science **359,** 1269 (2018) • Expression and Function of IL-33/ST2 Axis in the Central Nervous System Under Normal and Diseased Conditions: K. F Fairlie-Clarke, et al.; Front. Immunol. **9,** 2596 (2018) • IL33: Roles in Allergic Inflammation and Therapeutic Perspectives: B.C.L. Chan, et al.; Front. Immunol. **10,** 364 (2019)

CONTENTS

Interleukin-33	1–2
Post-translational Modifications of Tubulins	3
Inflammasomes & Neurodegeneration	4–5
Progranulin	6–7
PSD-95 – Synaptic Development & Plasticity	7
Notch Signaling & Microtubule Stabilization	8
Mitochondrial Dysfunction	9
Netrin-1 – Neuron Guidance Factor	10
Latest Insight: Irisin in Alzheimer's Disease	10
Dyes & Stains	11
HDAC6 & Alzheimer's Disease	11
Small Molecules for Neuroscience Research	12

UNIQUE

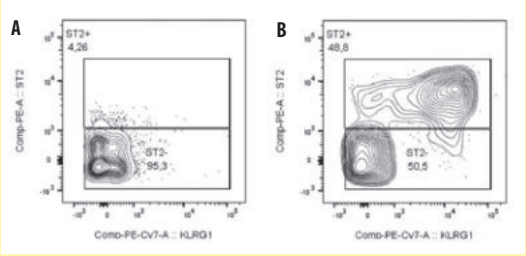
Highly Active Human IL-33 Proteins

IL-33 (oxidation resistant) (human) (rec.)

AG-40B-0160	Untagged	10 µg | 100 µg
AG-40B-0167	His-tagged	10 µg | 100 µg

LIT: Oxidation of the alarmin IL-33 regulates ST2-dependent inflammation: E.S. Cohen, et al.; Nat. Commun. **6,** ID8327 (2015)

FIGURE: Activation *in vivo* of Innate Lymphoid Cells 2 (ILC2) by IL-33 (oxidation resistant) (human) (rec.) (untagged) (AG-40B-0160). Method: C57BL/6 mice were injected daily for 3 days with PBS (Figure A) or IL-33 (oxidation resistant) (human) (rec.) (untagged) (AG-40B-0160) (at 0.4µg per mouse) (Figure B). At day 4, cells from bone marrows were stained and analyzed by flow cytometry. Levels of ST2 and KLRG1 on Innate Lymphoid Cells (gated as lineage negative, CD127 positive cells) are shown. *Picture courtesy of Dr G.Verdeil / Dr S. Trabanelli (Camilla Jandus Group, Department of Fundamental Oncology, University of Lausanne).*



Other Recombinant IL-33 & Related Proteins

PROTEINS	PID
IL-33 (human) (rec.) (untagged)	AG-40B-0038
IL-33 (human) (rec.) (His)	AG-40A-0042
IL-33 (mouse) (rec.) (untagged)	AG-40B-0041
IL-33 (mouse) (rec.) (His)	AG-40A-0053

PROTEINS	PID
ST2 (human):Fc (human) (rec.)	AG-40A-0059
IL-33R [ST2] (human):Fc (human) (rec.)	CHI-HF-21033R
IL-33R [ST2] (mouse):Fc (mouse) (rec.)	CHI-MF-11033R

UNIQUE

IL-33 Blocking Antibody

anti-IL-33 (mouse), mAb (rec.) (blocking) (Bondy-1-1)

AG-27B-0013		100 µg
AG-27B-0013PF	Preservative Free	100 µg | 500 µg | 1mg

Inhibits binding of mouse IL-33 to ST2/IL-1RAcP.

LIT: Regulation of de novo adipocyte differentiation through crosstalk between adipocytes and pre-adipocytes: T.D. Challa, et al.; Diabetes **64,** 4075 (2015) • Male-specific IL-33 expression regulates sex-dimorphic EAE susceptibility: A.E. Russi, et al.; PNAS **115,** E1520 (2018)

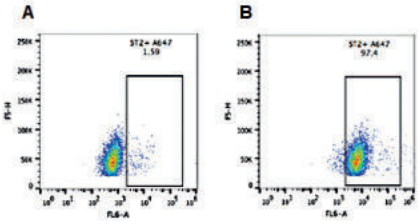
ST2 Antibody for Flow Cytometry

anti-ST2 (human), pAb

AG-25A-0058		100 µg
AG-25A-0058YTD	ATTO 488	100 tests
AG-25A-0058YTS	ATTO 647N	100 tests

FIGURE: Detection of endogenous human ST2 with anti-ST2 (human), pAb (AG-25A-0058).

METHOD: THP1 cells were stained with anti-ST2 (human), pAb (1:100 in PBS + 2% FCS) (Figure B) or with the secondary antibody alone (Figure A) for 1h at 4°C.



Other IL-33 & Related Antibodies

ANTIBODIES	PID	SIZE	ISOTYPE/SOURCE	APPLICATION	SPECIES
anti-IL-33, mAb (IL33026B)	AG-20A-0043	50 µg | 100 µg	Mouse IgG1κ	ELISA, IP, WB	Hu, Ms
anti-IL-33 (human), mAb (IL33305B)	AG-20A-0041	50 µg | 100 µg	Mouse IgG2aκ	FUNC, IHC, IP, WB	Hu
anti-IL-33 (human), pAb	AG-25A-0045	100 µg	Rabbit	ELISA, IHC, WB	Hu
anti-IL-33 (mouse), pAb	AG-25A-0047	100 µg	Rabbit	ELISA, WB	Ms
anti-IL-33 (mouse), mAb (rec.) (Carly-1-4)	AG-27B-0012	100 µg	Human IgG2λ	ELISA, WB	Ms
anti-ST2 (human), mAb (ST33868)	AG-20A-0044	50 µg | 100 µg	Mouse IgG1κ	ELISA, IHC, WB	Hu

UNIQUE

HpARI – Suppressor of Type 2 (Allergic) Immune Response

HpARI (Alarmin Release Inhibitor) (rec.) (His)

AG-40B-0178 — 50 µg \| 3 x 50 µg

Specific for human and mouse.

During cell damage, HpARI gains access to the nucleus of necrotic cells, where it binds directly to IL-33 and nuclear DNA, preventing secretion and binding of IL-33 to its receptor.

LIT: M. Osbourne, et al.; Immunity **47,** 739 (2017)

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APPLICATIONS: FACS: Flow Cytometry; **FUNC:** Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry **IP:** Immunoprecipitation; **WB:** Western blot
SPECIES: Bv = Bovine; **Dg** = Dog; **Dr** = Drosophila; **Hu** = Human; **Mk** = Monkey; **Ms** = Mouse; **Pg** = Pig; **Rt** = Rat; **Rb** = Rabbit; **Prm** = Primate

The Tubulin Code: Post-translational Modifications of Tubulins

In neurons, microtubules, actin filaments and neurofilaments compose the cytoskeleton, maintaining cell polarity, architecture and morphology. Microtubules (MTs) are highly dynamic polymers formed of tubulin α and β heterodimers. Regulation of MTs polymerization is controlled by microtubule associated proteins, post-translational modifications of tubulin α and β, microtubules and signaling molecules. Deregulation of the neuronal cytoskeleton/MT function constitutes a key insult during the pathogenesis of nervous system diseases, including Amyotrophic Lateral Sclerosis, Alzheimer's diseases (AD), Hereditary Spastic Paraplegia, Parkinson's disease (PD) and others. **Post-translational modifications (PTMs)** are highly dynamic and often reversible processes where protein functional properties are altered by addition of a chemical group or another protein to its amino acid residues. Tubulins and microtubules (MTs) are major substrates for PTMs. They include tyrosination/detyrosination, D2-tubulin formation, **acetylation**, phosphorylation, polyamination, ubiquitination, **polyglutamylation** and **glycylation** (see FIGURE 2). PTMs are involved in fine-tuning of interactions between microtubules and different MT-interacting proteins.

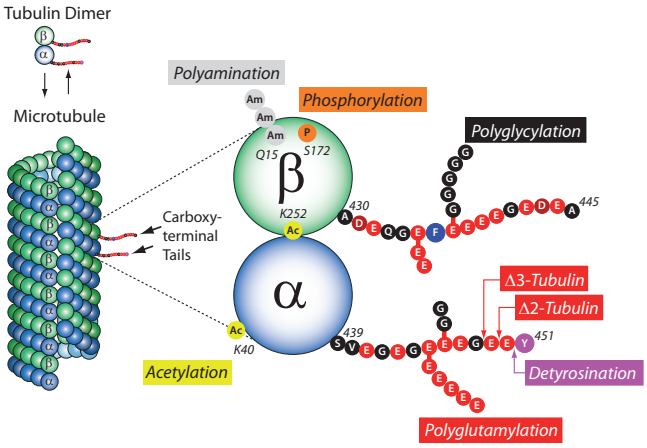


FIGURE 2: Tubulin PTM Overview. *Adapted from C. Janke; J. Cell. Biol.* ***206,*** *461 (2014).*

UNIQUE

Validated Post-translational Modification-specific Antibodies

ANTIBODIES	PID	SIZE	ISOTYPE/SOURCE	APPLICATION
anti-α-Tubulin (acetylated), mAb (TEU318)	AG-20B-0068	100 µg	Mouse IgG1	ICC, WB
anti-Polyglutamylation Modification, mAb (GT335)	AG-20B-0020	100 µg	Mouse IgG1κ	EM, ICC, IHC, IP, WB
anti-Polyglutamylation Modification, mAb (GT335) (Biotin)	AG-20B-0020B	100 µg	Mouse IgG1κ	ICC, IHC, IP, WB
anti-Polyglutamate chain (polyE), pAb (IN105)	AG-25B-0030	50 µg	Rabbit	ICC, IHC, WB
NEW **anti-Tubulin (glycylated), pAb (Gly-pep1)**	AG-25B-0034	100 µg	Rabbit	ICC, IP, WB

Recombinant Microtubule-target Antibodies

ANTIBODIES	PID	SIZE	ISOTYPE/SOURCE	APPLICATION	SPECIES
anti-Tubulin-GTP, mAb (rec.) (MB11) UNIQUE	AG-27B-0009	100 µg	Human IgG2λ	ICC	Hu, Ms, Rt, Dr
anti-α-Tubulin, mAb (rec.) (F2C)	AG-27B-0005	100 µg	Human IgG2λ	ICC, WB	Hu, Ms, Bv
anti-α-Tubulin, mAb (rec.) (F2C) (ATTO 488)	AG-27B-0005TD	100 µg	Human IgG2λ	ICC	Hu, Ms, Bv
anti-β-Tubulin, mAb (rec.) (S11B)	AG-27B-0008	100 µg	Human IgG2λ	ELISA, ICC, WB	Hu, Ms, Rt, Pg, Dr, Mk

Rab1-GTP and Rab6-GTP Specific Antibodies

Rab proteins, members of the small GTPase superfamily, are important regulators of vesicle transport via interactions with effector proteins and motor proteins. Rab1 and 6 are implicated in anterograde and retrograde trafficking in the secretory pathway. Rab1 has been shown to be involved in **autophagy** by helping the formation of the pre-autophagosomal isolation membrane (phagophore). Rab6 also functions as modulator of the unfolded protein response (UPR), helping the recovery from an ER stress insult. Rab6 is upregulated in Alzheimer's disease brain.

ANTIBODIES	PID	SIZE	ISOTYPE/SOURCE	APPLICATION	SPECIES
anti-Rab1-GTP, mAb (rec.) (ROF7)	AG-27B-0006	100 µg	Human IgG2λ	ICC, IP	Hu, Ms, Rt, Dg
anti-Rab6-GTP, mAb (rec.) (AA2)	AG-27B-0004	100 µg	Human IgG2λ	ICC	Hu, Ms, Dr
anti-Rab6-GTP, mAb (rec.) (AA2) (ATTO 488)	AG-27B-0004TD	100 µg	Human IgG2λ	ICC	Hu, Ms, Dr

Inflammasomes & Neuroinflammation/Neurodegeneration

Neuroinflammation is an **innate immune response in the CNS** (central nervous system) against harmful and irritable stimuli such as pathogens, metabolic toxic waste or chronic mild stress that occurs in response to trauma, infections and/or neurodegenerative diseases. The main cell types contributing to the innate immune response are microglia, trafficking macrophages and astrocytes. These cells constantly survey the proximal environment through pattern recognition receptors (PRRs) such as Toll-like receptors (TLRs), scavenger receptors (SRs) and **NOD-like receptors (NLRs)** (e.g. inflammasome complexes). These NLRs recognize not only exogenous pathogen-associated molecular patterns (PAMPs) but also endogenous modified molecules called damage-associated molecular peatterns (DAMPs). After activation of the pattern recognition receptors and release of immune molecules (e.g. cytokines), the innate immune system launches inflammatory and regulatory responses in order to counteract infection, injury and maintenance of tissue homeostasis. Although the evolutionary function is neuroprotective, innate immune responses can also promote immunopathology when they are excessive (e.g. chronic neuroinflammation). During chronic activation, the sustained exposure of neurons to pro-inflammatory mediators can cause neuronal dysfunction and contribute to cell death. As chronic neuroinflammation is observed at relatively early stages of neurodegenerative diseases, targeting the mechanisms that drive this process may be useful for diagnostic and therapeutic purposes.

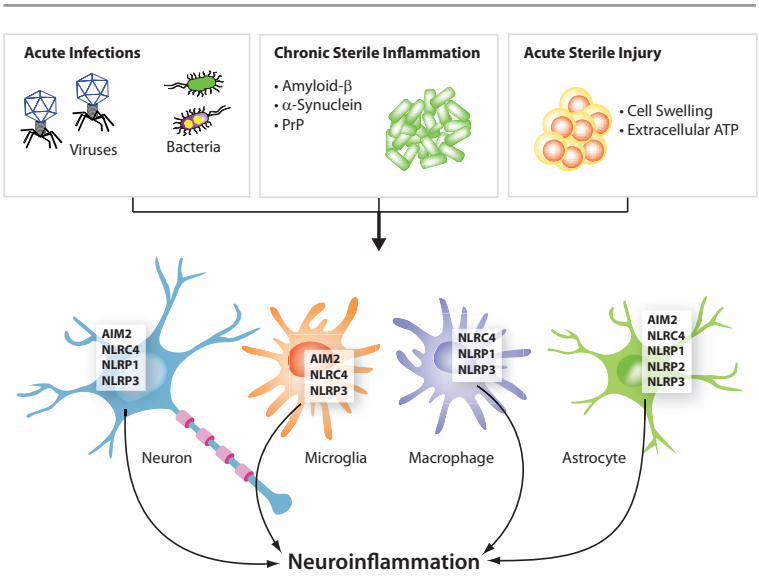


FIGURE 3: Selected activation factors, inflammasome complexes and target cells in the CNS.

Neuroinflammation is mediated in part by protein complexes known as **inflammasomes**. The inflammasomes can be activated in the CNS under diverse conditions that trigger inflammation, including acute infection (e.g. viruses, bacteria), chronic sterile inflammation (e.g. misfolded proteins such as amyloid-β, α-synuclein and prion protein) and acute sterile injury (ATP excess) (see FIGURE 3). Inflammasome activation has been demonstrated in CNS-resident cell types including microglia, astrocytes and neurons. Assembly of inflammasomes (NLRP1/2/3 and NLRC4/IPAF) activates pro-inflammatory caspase-1, which then cleaves the precursor forms of pro-inflammatory cytokines IL-1 and IL-18 into their active forms, as well as the intracellular gasdermin D, which leads to a particular form of inflammatory cell death called pyroptosis. These pro-inflammatory effectors promote a variety of innate immune processes associated with infection, inflammation and autoimmunity, and play an instrumental role in the onset of neuroinflammation and subsequent occurrence of neurodegenerative diseases, cognitive impairment and dementia. NLRP1/2/3 and NLRC4/IPAF inflammasomes may also have a role in the etiologies of depression, Alzheimer's disease (AD) and in metabolic disorders, such as Type II diabetes, obesity and cardiovascular diseases that have been shown to be co-morbid with psychiatric illnesses.

SELECTED REVIEWS: Inflammasomes in the CNS: J.G. Walsh, et al.; Nat. Rev. Neurosci. **15,** 84 (2014) • Innate immune activation in neurodegenerative disease: M.T. Heneka, et al.; Nat. Rev. Immunol. **14,** 463 (2014) • Inflammation in neurodegenerative diseases-an update: S. Amor, et al.; Immunol. **142,** 151 (2014) • Inflammasomes in neuroinflammatory and neurodegenerative diseases. S. Voet, et al.; EMBO Mol. Med. **11,** e10248 (2019)

THE STANDARD

NLRP3 Antibody

anti-NLRP3/NALP3, mAb (Cryo-2)

AG-20B-0014 100 µg

Clone	Cryo-2
Isotype	Mouse IgG2b
Immunogen	Recombinant mouse NLRP3/NALP3 (pyrin domain/aa 1-93)
Application	ICC, IHC, IP, WB (1µg/ml) (see online protocol)
Specificity	Recognizes human and mouse NLRP3/NALP3.

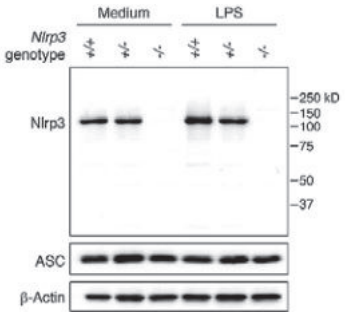


FIGURE: Mouse NLRP3 is detected in mouse macrophages using the monoclonal antibody to NLRP3 (Cryo-2) (Prod. No. AG-20B-0014).

METHOD: Cell extracts from mouse macrophages (BMDMs) WT (+/+) (lane 1), NLRP3 +/- (lane 2) or NLRP3 -/- (lane 3) with or without treatment with LPS (50ng/ml) for 3h, were separated by SDS-PAGE under reducing conditions, transferred to nitrocellulose and incubated with the mAb to NLRP3 (Cryo-2) (1µg/ml). Proteins are visualized by a chemiluminescence detection system.

APPLICATIONS: **FACS:** Flow Cytometry; **FUNC:** Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry **IP:** Immunoprecipitation; **WB:** Western blot
SPECIES: **Bv** = Bovine; **Dg** = Dog; **Dr** = Drosophila; **Hu** = Human; **Mk** = Monkey; **Ms** = Mouse; **Pg** = Pig; **Rt** = Rat; **Rb** = Rabbit; **Prm** = Primate

THE STANDARDS FROM THE EXPERTS & VALIDATED BY KEY LABORATORIES!

Immunoblotting for Activated/Cleaved Caspase-1

anti-Caspase-1 (p20) (mouse), mAb (Casper-1)

AG-20B-0042		100 µg
AG-20B-0042B	Biotin	100 µg

Clone Casper-1
Isotype Mouse IgG1
Immunogen Recombinant mouse caspase-1
Application WB (1µg/ml) (see online protocol), IHC (PS), IP
Specificity Recognizes endogenous full-length and activated (p20 fragment) mouse caspase-1.

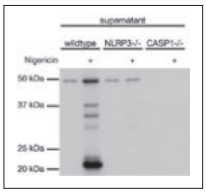


FIGURE: Mouse caspase-1 (p20) is detected by immunoblotting using anti-Caspase-1 (p20) (mouse), mAb (Casper-1) (Prod. No. AG-20B-0042).

METHOD: Caspase-1 was analyzed by Western blot in cell extracts and supernatants of differentiated bone marrow-derived dendritic cells (BMDCs) from wild-type, NLRP3-/- and caspase-1-/- mice activated or not by 5µM Nigericin (Prod. No. AG-CN2-0020) for 30 min. Cell extracts and supernatants were separated by SDS-PAGE under reducing conditions, transferred to nitrocellulose and incubated with anti-Caspase-1 (p20) (mouse), mAb (Casper-1) (1µg/ml). Proteins were visualized by a chemiluminescence detection system.

anti-Caspase-1 (p20) (human), mAb (Bally-1)

AG-20B-0048		100 µg
AG-20B-0048B	Biotin	100 µg

Clone Bally-1
Isotype Mouse IgG1
Immunogen Recombinant human caspase-1
Application WB (1µg/ml) (see online protocol)
Specificity Recognizes endogenous full-length and activated (p20 fragment) human caspase-1.

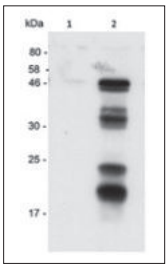


FIGURE: Human Caspase-1 (p20) is detected by immunoblotting using anti-Caspase-1 (p20) (human), mAb (Bally-1) (Prod. No AG-20B-0048).

METHOD: Caspase-1 was analyzed by Western blot in supernatants of THP1 cells differentiated for 3h with 0.5 µM PMA (Prod. No. AG-CN2-0010) and activated (lane 2) or not (lane 1) by 5 µM Nigericin (Prod. No. AG-CN2-0020) for 1h. Supernatants (30µl) were separated by SDS-PAGE under reducing conditions, transferred to nitrocellulose and incubated with anti-Caspase-1 (p20) (human), mAb (Bally-1) (1µg/ml). Proteins were visualized by a chemiluminescence detection system.

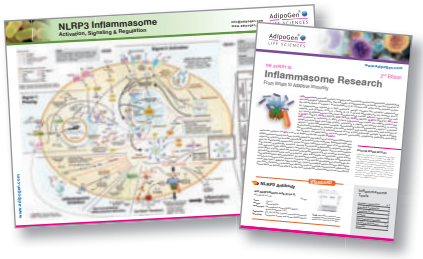
Standard Inflammasomes Signaling Antibodies

ANTIBODIES	PID	SIZE	SPECIFICITY
anti-Asc, pAb (AL177)	AG-25B-0006	100 µg	Recognizes human and mouse Asc.
anti-Caspase-1 (p10) (mouse), mAb (Casper-2)	AG-20B-0044	100 µg	Recognizes endogenous full-length and activated (p10 fragment) of mouse caspase-1.
anti-Caspase-4 /11 (p20), mAb (Flamy-1)	AG-20B-0060	100 µg	Recognizes endogenous full-length and activated (p20) fragment of mouse and human caspase-4/11.
anti-IL-1α (p18) (mouse), mAb (Teo-1)	AG-20B-0064	100 µg	Recognizes full-length and cleaved (p18) fragment of mouse IL-1α.
anti-Caspase-8 (mouse), mAb (1G12)	AG-20T-0137	100 µg	Recognizes full-length and cleaved (p18) fragment of mouse caspase-8.
anti-Caspase-8 (human), mAb (C15)	AG-20B-0057	50 µg | 100 µg	Recognizes the p18 subunit of human caspase-8.
anti-Gasdermin D (mouse), pAb (IN110)	AG-25B-0036	100 µg	Recognizes full-length and cleaved C-terminus domain of mouse gasdermin D.

Key NLRP3 Inflammasome Activators and Inhibitors

BULK

PRODUCT NAME	PID	SIZE	DESCRIPTION
Monosodium urate (crystals)	AG-CR1-3950	2 mg | 2 x 2 mg	Potent NLRP3 inflammasome activator.
Monosodium urate (ready-to-use)	AG-CR1-3951	10 mg	Potent NLRP3 inflammasome activator.
Nigericin . Na	AG-CN2-0020	5 mg | 25 mg	Potent NLRP3 inflammasome activator.
MCC950 . Na (water soluble)	AG-CR1-3615	1 mg | 5 mg | 10 mg	Potent and selective NLRP3 inflammasome inhibitor.



For a comprehensive Overview on Unique Inflammasome Reagents ask for AdipoGen Life Sciences' Inflammasome Signaling Brochure & Wallchart!

Progranulin – Marker of Neuroinflammation

Progranulin (PGRN) is a cysteine-rich protein, composed of seven ~6kDa granulin (GRN) proteins, that shows multifunctional biological activities, including major roles in cancer, inflammation, metabolic disease and neurodegeneration, especially as a valuable biomarker for Frontotemporal Lobar Degeneration (FTLD). PGRN is an abundant, non-conventional, stress-induced, extracellular matrix-bound secreted growth factor-like molecule and cytoplasmic chaperone, that functions in a cellular and disease specific pattern. PGRN binds to several functionally different receptor families in a cell/tissue specific and condition/disease-dependent manner. For example, PGRN binding with TNFR and DR3 has an important anti-inflammatory role in immune cells, particularly Tregs and macrophages. PGRN/Ephrin type-A receptor 2 (EphA2) interaction is involved in the proliferative influence of PGRN. PGRN binds and activates Notch receptors, enhancing the regenerative capacity of injured neurons. PGRN is also a lysosomal resident protein and sortilin and lipoprotein receptor-related protein 1 (LRP1) have been demonstrated to be the lysosomal trafficking receptors for PGRN with the help of Prosaposin. In the brain, PGRN is primarily expressed in mature neurons and microglia. Absence of progranulin in microglia causes increased production and release of multiple cytokines, suggesting that PGRN regulates microglia activation. PGRN seems to affect microglial proliferation, recruitment, differentiation, activation and phagocytosis, suggesting that PGRN plays a central role in the regulation of neuroinflammatory responses. In neurons, PGRN i) co-localizes in late endosomes and early lysosomes with the transmembrane protein TMEM106B, ii) co-localizes with markers such as BDNF along axons, iii) influences synaptic structure and function at synaptic and extrasynaptic sites, where it is secreted in an activity-dependent manner, and iv) extracellular PGRN is endocytosed and delivered to lysosomes. The lysosomal function of PGRN is not well characterized, but probably involves regulation of proteins such as cathepsins, glucocerebrosidase (GBA) or TMEM106B and likely contributes to neurodegeneration (see FIGURE 4).

SELECTED REVIEWS: The lysosomal function of progranulin, a guardian against neurodegeneration: D.H. Paushter, et al.; Acta Neuropathol. **136,** 1 (2018) • Progranulin: A conductor of receptors orchestra, a chaperone of lysosomal enzymes and a therapeutic target for multiple diseases: Y. Cui, et al.; Cytokine Growth Factor Rev. **45,** 53 (2019)

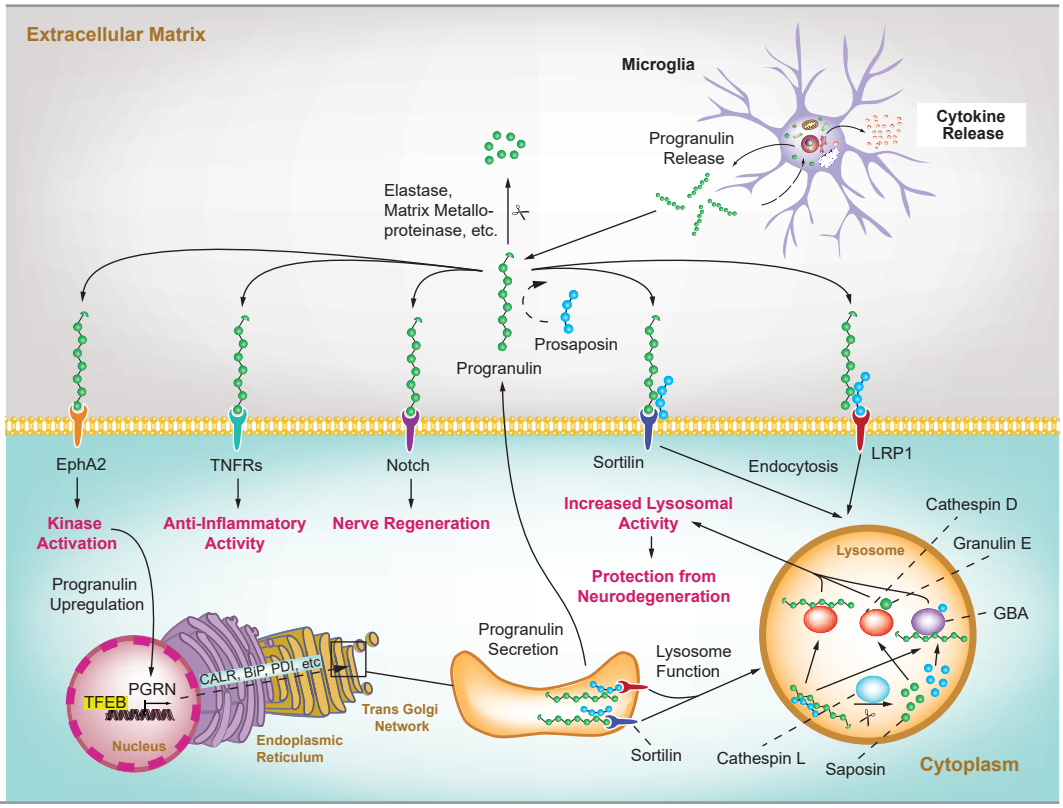


FIGURE 4: The roles and binding partners of progranulin in neuronal cells.

Standard Progranulin ELISA Kits

Progranulin (human) ELISA Kit	AG-45A-0018Y
Progranulin (mouse) ELISA Kit	AG-45A-0019Y
Progranulin (rat) ELISA Kit	AG-45A-0043Y

- ***Trusted Reproducible Results!***
- ***Used to Determine Cut-Off values for FTLD!***
- ***Cited in Hundreds of Scientific Publications!***

AdipoGen® LIFE SCIENCES

APPLICATIONS: FACS: Flow Cytometry; **FUNC:** Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry **IP:** Immunoprecipitation; **WB:** Western blot
SPECIES: Bv = Bovine; **Dg** = Dog; **Dr** = Drosophila; **Hu** = Human; **Mk** = Monkey; **Ms** = Mouse; **Pg** = Pig; **Rt** = Rat; **Rb** = Rabbit; **Prm** = Primate

Tag-free Progranulins

BULK

Progranulin (human) (rec.) (untagged)
AG-40A-0188Y 10 µg | 50 µg

Progranulin (mouse) (rec.) (untagged)
AG-40A-0189Y 10 µg | 50 µg

Progranulin (rat) (rec.) (untagged)
AG-40A-0196Y 10 µg | 50 µg

- *Higher activity compared to tagged Progranulins*
- *Suitable for in vitro and in vivo studies*
- *Reflects the native sequence with no additional amino acids*
- *Affinity purified*
- *Low endotoxin levels (<0.01EU/µg)*

Progranulin Antibodies & Tagged Proteins

ANTIBODIES	PID	SIZE	ISOTYPE/SOURCE	APPLICATION	SPECIES
anti-Progranulin (human), pAb	AG-25A-0112	100 µg	Guinea pig	ELISA, IHC, WB	Hu
anti-Progranulin (mouse), pAb	AG-25A-0093	100 µg	Rat	ELISA, WB	Ms

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
Progranulin (human) (rec.)	AG-40A-0068Y	10 µg | 50 µg	HEK293 Cells	<0.01EU/µg	Hu
Progranulin (rat) (rec.)	AG-40A-0194	10 µg | 50 µg	HEK293 Cells	<0.1EU/µg	Rt

Related Products

ANTIBODIES	PID	SIZE	ISOTYPE/SOURCE	APPLICATION	SPECIES
anti-Granulin C (human), pAb	AG-25A-0090	100 µg	Rabbit	ELISA, WB	Hu

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
Granulin C (human) (rec.) (His)	AG-40A-0129	10 µg | 50 µg	E. coli	<1EU/µg	Hu

PSD-95 – Key Protein in Synaptic Development & Plasticity

PSD-95 is a member of proteins located at a specialized postsynaptic membrane region, called the postsynaptic density (PSD). PSD-95 is the most abundant scaffold protein specifically enriched in the PSD. Through its PDZ domains, PSD-95 assembles various synaptic components at the PSD including intracellular signaling molecules (e.g. SynGAP and kalirin-7), ion channels (e.g. stargazin/AMPA receptors [AMPARs] and NMDA receptors) and cell adhesion molecules (e.g. neuroligin). PSD-95 plays a primary role in synaptic development and maturation and is regulated by palmitoylation at its N-terminal cysteine residues leading to its postsynaptic targeting. Palmitoylated PSD-95 is almost exclusively localized at excitatory synapses in neurons.

SELECTED REVIEWS: Posttranslational Modifications Regulate the Postsynaptic Localization of PSD-95: D. Vallejo, et al.; Mol. Neurobiol. **54,** 1759 (2017) • Role of Palmitoylation of Postsynaptic Proteins in Promoting Synaptic Plasticity: L. Matt, et al.; Front. Mol. Neurosci. **12,** 8 (2019)

UNIQUE

anti-PSD-95 (palmitoylated), mAb (rec.) (PF11)

AG-27B-0021 100 µg

Clone PF11
Isotype Human IgG2
Immunogen Palmitoylated PSD-95
Application ICC, IHC
Specificity Recognizes human, mouse and rat palmitoylated PSD-95.

LIT: Local palmitoylation cycles define activity-regulated postsynaptic subdomains: Y. Fukata, et al.; J. Cell Biol. **202,** 145 (2013)

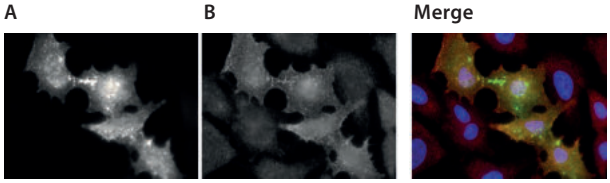


FIGURE: Palmitoylated PSD-95 is detected by immunocytochemistry using anti-PSD-95 (palmitoylated), mAb (rec.) (PF11) (Prod. No AG-27B-0021).

Notch Signaling & Neurogenesis

Notch signaling plays critical roles in neural stem cell maintenance and neurogenesis. Notch functions depend on regulation and cross-talk with other regulatory mechanisms. Deregulation of Notch signaling is involved in many neurodegenerative diseases and brain disorders. ADAM17/TACE, an ectodomain shedding protease, is responsible for the processing of a diverse variety of membrane-anchored cytokines, including the extracellular Notch Receptor 1. It has roles in neurodegenerative diseases and in several physiological processes including proteolysis, adhesion, intracellular signaling, migration and proliferation. **ADAM17/TACE** plays a key role in **impairing neurogenesis in brain injuries**, thus becoming a new therapeutic target to promote endogenous neurogenesis to regenerate brain injuries.

SELECTED REVIEWS: Role of Notch Signaling Pathway in Glioblastoma Pathogenesis: R: Bazzoni, et al.; Cancers **11,** E292 (2019) • ADAM17/TACE: a key molecule in brain injury regeneration: S. Dominguez-Garcia, et al.; Neural Regen. Res. **14,** 1378 (2019)

Potent ADAM17 Blocking Antibodies

anti-ADAM17 (human), mAb (rec.) (blocking) (D1(A12)) (preservative free)

AG-27B-6000PF 100 µg

anti-ADAM17 (human), mAb (rec.) (blocking) (D1(A12)) (Fab Fragment) (His) (preservative free)

AG-27B-6003PF 100 µg

Recognizes the catalytic and non-catalytic domain of human ADAM17 (TACE) through its variable light (VL) domain and variable heavy (VH) domain, respectively. Does not bind recombinant mouse ADAM17 ectodomain.

Functional Application (Blocking): Inhibits ADAM17 activity at 15µg/ml (200nM).

LIT: Cross-domain inhibition of TACE ectodomain: C.J. Tape, et al.; PNAS **108,** 5578 (2011)

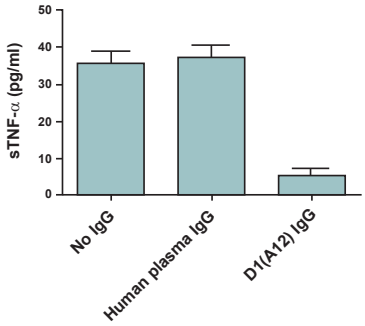


FIGURE: D1(A12) IgG inhibits constitutive shedding of TNF-α from IGROV1 (human ovarian cancer cell line) into culture medium. Medium was collected after 48 hours of incubation with or without IgGs at 200nM.

Visit www.adipogen.com for a Comprehensive Panel of Validated Notch Pathway Reagents!

Microtubule Stabilization & Axonal Morphology

Several studies show that the morphology of the neuron can be influenced by **microtubule** and **actin filament cytoskeleton** dynamics, and that neurite outgrowth can be modulated with stabilizing and destabilizing agents. Activation of the **Notch signaling pathway** results in stabilization of microtubules leading to regulation of axonal morphology, with thicker neurites, fewer branches and loss of synaptic varicosity. This Notch-dependent stabilization of microtubules is likely due to increase in acetylation and polyglutamylation of α-tubulins, both of which are markers of stable microtubules.

LIT: Notch signalling in adult neurons: a potential target for microtubule stabilization: S.A. Bonini, et al.; Ther. Adv. Neurol. Disord. **6,** 375 (2013) • Microtubule-stabilizing agents as potential therapeutics for neurodegenerative disease: K.R. Brunden, et al.; Bioorg. Med. Chem. **22,** 5040 (2014)

Small Molecule Cytoskeletal Modulators

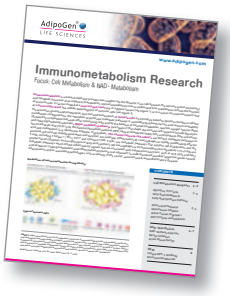
Dynasore	Dynamin Inhibitor	AG-CR1-0045
Jasplakinolide	F-actin Stabilization	AG-CN2-0037
Latrunculin A	F-actin Depolymerization	AG-CN2-0027
Latrunculin B	F-actin Depolymerization	AG-CN2-0031
Swinholide A	F-actin Inhibitor	AG-CN2-0035
Cytochalasin B	Actin Depolymerization	AG-CN2-0504
Cucurbitacin E	Actin Depolymerization	AG-CN2-0474
Colchicine	Microtubule Inhibitor	AG-CN2-0048
Colcemid	Microtubule Inhibitor	AG-CR1-3567
Ilimaquinone	Microtubule Inhibitor	AG-CN2-0038
Nocodazole	Microtubule Inhibitor	AG-CR1-0019
Paclitaxel	Microtubule Stabilizer	AG-CN2-0045
Phomopsin A	Microtubule Inhibitor	AG-CN2-0515
Podophyllotoxin	Microtubule Inhibitor	AG-CN2-0049
Pseudolaric acid B	Microtubule Inhibitor	AG-CN2-0083

APPLICATIONS: FACS: Flow Cytometry; **FUNC:** Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry **IP:** Immunoprecipitation; **WB:** Western blot
SPECIES: Bv = Bovine; **Dg** = Dog; **Dr** = Drosophila; **Hu** = Human; **Mk** = Monkey; **Ms** = Mouse; **Pg** = Pig; **Rt** = Rat; **Rb** = Rabbit; **Prm** = Primate

Mitochondria and Neurodegenerative Diseases

Mitochondria are organelles responsible for orchestrating cellular energy production pathways, including the metabolic tricarboxylic acid (TCA) cycle to generate metabolites and ATP. They are highly dynamic organelles and constantly undergo fission and fusion to regulate their morphology, size and number. Mitochondrial dynamics are dependent on the metabolism regulation. Dysfunction of mitochondria fission/fusion can lead to the accumulation of abnormal mitochondria and contribute to cellular damage. Neurons consume the most energy, have a highly complex morphology, and are particularly dependent on mitochondrial function and thus damaged mitochondria may lead to neuronal death. Many **neurodegenerative diseases** such as Alzheimer's disease (AD), Parkinsons's disease (PD), and multiple sclerosis (MS) are **associated with dysfunction of mitochondrial dynamics or metabolism**.

SELECTED REVIEWS: Mitochondrial Dynamics and Metabolic Regulation: T. Wai & T. Langer; Trends Endocrinol. Metab. **27,** 105 (2016) • Metabolic regulation of mitochondrial dynamics: M. Prashant & D.C. Chan; J. Cell Biol. **212,** 379 (2016)



Ask for AdipoGen Life Sciences' Immunometabolism Brochure!

IDH1 – Biomarker and Target for Glioma and Glioblastoma

Isocitrate Dehydrogenase 1 (IDH1) is a soluble, cytosolic enzyme involved in the TCA metabolic cycle. The most notable mutation in this enzyme, R132H, is clinically indicated in the majority of astrocytomas and oligodendroglial tumors, with the mutation being associated with more favorable prognosis and increased survival in those patients. IDH1 R132H is also useful in the differential diagnosis between anaplastic glioma and glioblastoma.

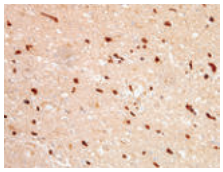
IHC GRADE IHC-Competent Antibody

NEW anti-IDH1 (R132H Mutant) (human), mAb

AG-20B-6024 — 100 µl | 1 ml

Clone	AG-IHC132
Isotype	Mouse IgG1
Immunogen	Synthetic IDH1 peptide
Application	IHC
Specificity	Recognizes human IDH1 mutated at R132H.

FIGURE: Immunohistochemical staining of mutated IDH1 (R132H) in formalin-fixed and paraffin-embedded (FFPE) human astrocytoma tissue.



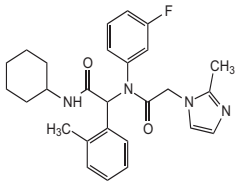
POTENT IDH1 (R132H) Inhibitor

AGI-5198

AG-CR1-3528 — 5 mg | 25 mg

Formula	$C_{27}H_{31}FN_4O_2$
MW	462.6
CAS	1355326-35-0

Potent and selective inhibitor of IDH1 (isocitrate dehydrogenase 1) R132H and R132C mutants *in vitro* with IC_{50} values of 0.07 and 0.16 µM, respectively. Does not inhibit wild-type IDH1 or any of the examined IDH2 isoforms (IC_{50}>100µM).



UNIQUE

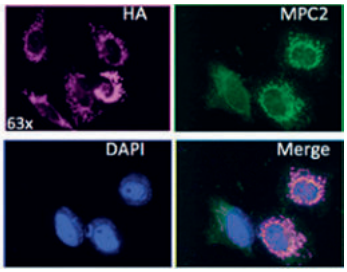
Mitochondrial Pyruvate Carrier 2 (MPC-2) Monoclonal Antibody

NEW anti-MPC-2, mAb (JCM-1)

AG-20B-0071 — 100 µg

Clone	JCM-1
Isotype	Mouse IgG2bκ
Application	WB (1µg/ml), IP (1:200), ICC (1:400)
Specificity	Recognizes endogenous human and mouse MPC-2.

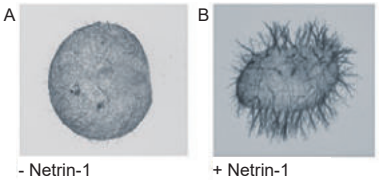
FIGURE: Immunofluorescence analysis of HeLa cells overexpressing hMPC2-HA.
Picture Courtesy of Sylvie Montessuit, Jean-Claude Martinou Lab, University of Geneva



Netrin-1 – Neuron Guidance Factor Involved in iPS Regulation

Netrin-1 is a guidance molecule that triggers either attraction or repulsion effects on migrating axons of neurons, interacting with the receptors **DCC** or **UNC5** (A to D). It has been proposed that DCC and UNC5 are dependence receptors that, in the absence of netrin-1, promote apoptosis. This pro-apoptotic activity requires initial caspase cleavage of the receptor's intracellular domain. Netrin-1 is therefore a pro-survival factor acting by blocking cell death induced by its unbound receptors. Netrin-1 protects neurons from death during development and favors tumor epithelial cells survival in some types of cancers. It interacts with the orphan amyloid precursor protein (APP), a protein component of the amyloid plaques that are associated with Alzheimer's disease (AD). Netrin-1 also inhibits remyelination of neurons in Multiple Sclerosis (MS) (and other progressive demyelinating diseases) by inhibiting oligodendrocyte precursor migration. Recently, Netrin-1 has been described to be the **5th Element of classical iPS cell factors**. Netrin-1 functions in protecting embryonic stem cells from apoptosis and addition of recombinant Netrin-1 improves the generation of mouse and human iPS cells (induced Pluripotent Stem Cells).

REVIEWS: Netrin-1 in the developing enteric nervous system and colorectal cancer: S.Y. Ko, et al.; Trends Mol. Med. **18,** 544 (2012) • Netrin-1 regulates somatic cell reprogramming and pluripotency maintenance: D. Ozmadenci, et al.; Nat. Commun. **6,** ID7398 (2015)



Picture courtesy of Dr. Véronique Corset, Prof. Patrick Mehlen Lab, Centre Léon Bérard, Lyon

FIGURE: Netrin-1 (human):Fc (human) (rec.) (Prod. No. AG-40B-0075) induces outgrowth of the commisural axon.

METHOD: Dorsal spinal cords were dissected out from E13 rat embryos and cultured in collagen matrix in the presence or absence of netrin-1 (250ng/ml). Axons were then stained with an anti-β-tubulin antibody.

UNIQUE Biologically Active Human Netrin-1

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
Netrin-1 (human) (rec.)	AG-40B-0040	10 µg | 3 x 10 µg | 100 µg	HEK293 Cells	<0.01EU/µg	Hu, Ms, Rt
Netrin-1 (human):Fc (human) (rec.)	AG-40B-0075	10 µg | 3 x 10 µg | 100 µg	HEK293 Cells	<0.1EU/µg	Hu, Ms, Rt
UNC5B (human):Fc (human) (rec.)	AG-40B-0037	50 µg | 3 x 50 µg	HEK293 Cells	<0.1EU/µg	Hu, Ms

NEW Potent Netrin-1 Blocking Antibody

ANTIBODY	PID	SIZE	ISOTYPE/SOURCE	APPLICATION	SPECIES
anti-Netrin-1 (human), mAb (rec.) (blocking) (2F5) (preservative free)	AG-27B-0018PF	100 µg | 500 µg	Human IgG2	ELISA, FUNC	Hu, Ms

LIT: Epidermal Growth Factor Receptor-Dependent Mutual Amplification between Netrin-1 and the Hepatitis C Virus: M.L. Plissonnier, et al.; PLoS Biol. **14,** e1002421 (2016) • Targeting netrin-1/DCC interaction in diffuse large B-cell and mantle cell lymphomas: T. Broutier, et al.; EMBO Mol. Med. **8,** 96 (2016)

LATEST INSIGHT

Protective Role of Irisin in Alzheimer's Disease

Irisin is a protein cleaved from fibronectin type III domain-containing protein 5 (FNDC5) and has a beneficial role in adipose tissues, bone and brain. A recent study published in Nature Medicine by the labs of O. Arancio, S.Ferreira & F.G. de Felice (Rio de Janeiro, Brazil, New York, US and Kingston, Canada, respectively) showed that FNDC5/Irisin levels are reduced in Alzheimer's disease (AD) cerebrospinal fluid in human and mouse and that beneficial effects of exercise on synaptic plasticity and memory in AD models are mediated by FNDC5/Irisin. Addition of AdipoGen Life Sciences' recombinant Irisin (Prod. No. AG-40B-0136) in a mice model of AD was neuroprotective and rescued Amyloid-β oligomer-induced memory impairment. AdipoGen Life Sciences provides the best recombinant Irisin/FNDC5 proteins, antibody and ELISA kit to study Irisin and FNDC5 *in vitro* and *in vivo*.

LIT: Exercise-linked FNDC5/irisin rescues synaptic plasticity and memory defects in Alzheimer's models: M.V. Lourenko, et al.; Nat. Med. **25,** 165 (2019)

PROTEINS	PID
Irisin (rec.) (CHO)	AG-40B-0136
Irisin:Fc (human) (rec.)	AG-40B-0115
Irisin (rec.) (untagged) (E.coli)	AG-40B-0103
FNDC5 (rec.) (untagged)	AG-40B-0128
FNDC5:Fc (human) (rec.)	AG-40B-0153

PROTEINS	PID
anti-Irisin, pAb (IN102)	AG-25B-0027
Irisin Competitive ELISA Kit	AG-45A-0046Y

AdipoGen® LIFE SCIENCES

APPLICATIONS: FACS: Flow Cytometry; **FUNC:** Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry **IP:** Immunoprecipitation; **WB:** Western blot
SPECIES: Bv = Bovine; **Dg** = Dog; **Dr** = Drosophila; **Hu** = Human; **Mk** = Monkey; **Ms** = Mouse; **Pg** = Pig; **Rt** = Rat; **Rb** = Rabbit; **Prm** = Primate

Dyes & Stains for Neuron Labeling

PRODUCT NAME	PID	SIZE	DESCRIPTION
N-(2-Aminoethyl)biotinamide . HCl	CDX-A0191	50 mg | 1 g	Used for neuronal tracing studies by visualizing neural architecture and for the identification of gap junction coupling.
3,3'-Dipropylthiacarbocyanine iodide	CDX-D0007	250 mg | 500 mg	Carbocyanine dye used for detection of calcium channels and other ion transport systems, mitochondrial activity, and neurons and brain tissue.
4-Di-2-ASP	CDX-D0012	1 g | 5 g	Cationic mitochondrial dye staining presynaptic nerve terminals independent of neuronal activity. Used to image neuronal cells in live animals.
1,1'-Dioctadecyl-3,3,3',3'-tetramethylindo-carbocyanine perchlorate	CDX-D0230	100 mg | 1 g	Endoplasmic reticulum membrane stain. Used as retrograde stain for neurons; provides intense, long-lasting staining of live neurons *in vivo* and *in vitro*.
5,7-Dihydroxytryptamine . HBr	CDX-H0026	10 mg | 25 mg | 250 mg	Autofluorescent serotonin derivative. Can be used for the identification of living serotonergic neurons even in the presence of dopaminergic neurons.
Hydroxystilbamidine bis(methanesulfonate)	CDX-H0100	10 mg	Hydroxystilbamidine (also called Fluoro Gold) is a cationic dye used for staining DNA and RNA and also frequently used as a retrograde neuronal tracer.
Sulforhodamine 101	CDX-S0025	100 mg | 500 mg	Sulforhodamine 101 is a non-fixable red fluorescent dye used as a specific marker for astrocytes and an activity-dependent probe for monitoring regulated exocytosis. In addition to labeling astrocytes, it also labels myelinating oligodendrocytes.

HDAC6 Inhibitors & Alzheimer's Disease

HDAC6 is one isoform of a family of HDAC enzymes that catalyze the removal of functional acetyl groups from proteins. It almost exclusively deacetylates cytoplasmic proteins. HDAC6 plays a pivotal role in the removal of misfolded proteins and is being investigated as target for lymphoid malignancies. Numerous recent studies have linked altered HDAC6 activity to the pathogenesis of neurodegenerative diseases that are characterized by misfolded protein accumulation.

SELECTED REVIEWS: The role of HDAC6 in Alzheimer's disease: L. Zhang, et al.; J. Alzheimers Dis. **33,** 283 (2013) • The therapeutic hope for HDAC6 inhibitors in malignancy and chronic disease: S.N. Batchu, et al.; Clin. Sci. **130,** 987 (2016) • HDAC6 as a potential therapeutic target for peripheral nerve disorders: R. Prior, et al.; Expert Opin. Ther. Targets **22,** 993 (2018)

PRODUCT NAME	PID	SIZE	HDAC6 INHIBITION	SELECTIVITY TOWARDS OTHER HDACS
Tubastatin A [TubA]	AG-CR1-3900	10 mg	IC_{50}=15nM	Other HDACs (IC_{50}= >15μM), HDAC8 (IC_{50}=0.9μM)
Nexturastat A	AG-CR1-3901	1 mg | 5 mg	IC_{50}=5.02nM	Other HDACs (IC_{50}=3-10μM)
Nexturastat B	AG-CR1-3902	1 mg | 5 mg	IC_{50}=3nM	HDAC1 (IC_{50}=0.9μM)
ACY-775	AG-CR1-3903	1 mg | 5 mg	IC_{50}=7.5nM	HDAC1-9 (IC_{50}=1-10μM)
DMAPB	AG-CR1-3904	1 mg | 5 mg	IC_{50}=114nM	Other HDACs (IC_{50}=1-8μM)
PMPH	AG-CR1-3905	1 mg | 5 mg	IC_{50}=11nM	HDAC1 (IC_{50}=1.5μM)
DABPH	AG-CR1-3906	1 mg | 5 mg	IC_{50}=12nM	HDAC1 (IC_{50}=6.8μM)
MBIMPH	AG-CR1-3907	1 mg | 5 mg	IC_{50}=9nM	Other HDACs (IC_{50}=0.1-12μM)
MBIMPH F-Analog 1 . HCl	AG-CR1-3908	1 mg | 5 mg	IC_{50}=3nM	Other HDACs (IC_{50}=0.03-20μM)
MBIMPH F-Analog 2	AG-CR1-3909	1 mg | 5 mg	IC_{50}=5nM	Other HDACs (IC_{50}=0.2-11μM)
MPI_5a	SYN-3040	1 mg | 5 mg | 10 mg | 50 mg | 100 mg	IC_{50}=36nM	Other HDACs (IC_{50}=2-50μM)

DYRK, Down Syndrome and MDR7

Please ask for our "DYRK Inhibitors" Product Flyer!

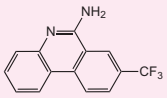
Lead Compounds for Neurodegenerative Diseases

Anti-Prion Agents – Protein Aggregation Inhibitors

6-Amino-8-trifluoromethylphenanthridine

AG-MR-C0031 — 1 mg | 5 mg | 25 mg

Formula: $C_{14}H_9F_3N_2$
MW: 262.2
CAS: 651055-83-3



6-Aminophenanthridine

AG-MR-C0029 — 1 mg | 5 mg | 25 mg

Chloroguanabenz . acetate

AG-MR-C0036 — 1 mg | 5 mg

Selective N- & P/Q-type Ca^{2+}-Channel Agonist

GV-58

AG-MR-C0035 — 1 mg | 5 mg

Anti-Alzheimer's Disease (AD) Agent

Leucettine L41

AG-MR-C0023 — 1 mg | 5 mg | 25 mg

Alzheimer's Disease (AD) Accelerator

Aftin-4

AG-MR-C0014 — 1 mg | 5 mg | 25 mg

Aftin-5

AG-MR-C0015 — 1 mg | 5 mg | 25 mg

Fipronil

AG-CR1-3648 — 100 mg | 1 g

Potent and Selective γ-Secretase Inhibitor

Compound E

AG-CR1-0081 — 250 µg | 1 mg | 5 mg

Selected Agonists and Antagonists

PRODUCT NAME	ACTIVITY	PID	SIZE
epi-Aszonalenin A	Substance P inhibitor	AG-CN2-0163	1 mg | 5 mg
Bilobalide	GABA(A) receptor antagonist	AG-CN2-0026	10 mg | 50 mg
Cyclopenin	AChE inhibitor	AG-CN2-0134	1 mg | 5 mg
Debromohymenialdisine	Potential anti-Alzheimer's agent	AG-CN2-0068	100 µg
EM574 [Motilide]	Motilin receptor agonist	AG-CN2-0102	250 µg | 1 mg
Flibanserin	5-HT1A receptor agonist and 5-HT2A antagonist	CDX-F0337	5 mg | 25 mg
Fulvic acid	Tau and Aβ aggregation inhibitor	AG-CN2-0135	1 mg | 5 mg
Carbamoylcholine chloride	Non-selective agonist nAChR and mAChR	AG-CR1-3649	100 mg | 1 g
Hyperforin . DCHA	TRPC6 channel activator	AG-CN2-0008	500 µg | 1 mg
20-Hydroxyecdysone	GABA(A) receptor modulator	AG-CN2-0072	5 mg | 10 mg | 50 mg
MTEP	Potent mGluR5 antagonist	AG-CR1-0022	5 mg | 25 mg
NG 012	NGF potentiator	AG-CN2-0155	1 mg | 5 mg
Pseurotin D	Neuroleptic agent	BVT-0426	1 mg | 5 mg
Rotenone	OXPHOS inhibitor used to induce Parkinson's diseases-like syndrome in experimental animal model	AG-CN2-0516	1 g | 5 g
Territrem B	AChE inhibitor	AG-CN2-0142	500 µg | 1 mg
Serratol	TRPV3 activator	AG-CN2-0483	5 mg
SNC80	δ-Opioid receptor agonist	AG-CR1-0017	5 mg | 25 mg
Umbellulone	Selective TRPA1 activator	AG-CN2-0085	10 mg
URMC-099	MLK-3 inhibitor for treatment of Parkinson's disease	SYN-1211	1 mg | 5 mg | 10 mg | 50 mg | 100 mg

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