

4th Edition

Neuroscience Research

Focus: Emerging Fields in Neuroinflammation & Neurological Diseases

Irisin/FNDC5 and FNDC4 in Neuroscience

Irisin is a myokine cleaved from fibronectin type III domain-containing protein 5 (FNDC5) and produced mainly by muscle tissues. Irisin increases energy metabolism, regulates glucose homeostasis and is directly related to the browning process, converting white adipose tissue into brown adipose tissue. Irisin acts on bones by improving bone mineral density and has several functions on the brain: i) it improves learning and memory function by regulating the expression of Brain-Derived Neurotrophic Factor (BDNF); ii) it promotes neurogenesis and protects against the neuronal damage caused by oxidative stress, and iii) it enhances brain functions by modulating neurotransmitter secretion. Recent studies showed that FNDC5/Irisin levels are reduced in Alzheimer's disease (AD) cerebrospinal fluid in human and mouse. Irisin, secreted after exercise, plays a beneficial role in brain function and in neurodegenerative diseases such as AD. Addition of AdipoGen Life Sciences' recombinant irisin (Prod. No. AG-40B-0136) in a mice model of AD is neuroprotective, rescues Amyloid- β oligomer-induced memory impairment and increases locomotor activity.

Fibronectin type III domain-containing protein 4 (FNDC4) is an ortholog of FNDC5/Irisin. This hepatokine inhibits lipogenesis *in vitro*, acts as an anti-inflammatory factor on macrophages and promotes fat browning in human visceral adipocytes by acting via its receptor ADGRF5 (also known as GPR116). FNDC4 is a potential biomarker for different inflammatory metabolic diseases as well as some cancers, especially of glioblastoma. FNDC4 promotes tumor proliferation in glioblastoma and glioblastoma patients with elevated FNDC4 expression show poor prognosis.

LIT: Exercise-linked FNDC5/Irisin rescues synaptic plasticity and memory defects in Alzheimer's models: M.V. Lourenco, et al.; Nat. Med. 25, 165 (2019) • Isolation and characterization of Orphan GPR116 mediates the insulin sensitizing effects of the hepatokine FNDC4 in adipose tissue: A. Georgiadi, et al.; Nature Commun. 12, 2999 (2021) • Correlation of the prognostic value of FNDC4 in glioblastoma with macrophage polarization: H. Li, et al.; Cancer Cell Int. 22, 273 (2022)

NEW Potential Biomarker of Glioblastoma

FNDC4 (human) ELISA Kit

AG-45B-0028 96 wells

Sensitivity: 40 pg/ml
Range: 0.078 - 5 ng/ml
Sample: Cell Culture Supernatant, Plasma, Serum

Specificity: Detects human FNDC4 in serum, plasma and cell culture supernatant. It cross-reacts with mouse, rat, monkey and dog FNDC4. It does not cross-react with human, mouse or rat FNDC5/Irisin.



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Other FNDC4, FNDC5 and Irisin Research Reagents

Irisin Reagents	PID
Irisin (rec.) (CHO)	AG-40B-0136
Irisin:Fc (human) (rec.)	AG-40B-0115
Irisin (rec.) (untagged) (E.coli)	AG-40B-0103
anti-Irisin, pAb (IN102)	AG-25B-0027
Irisin Competitive ELISA Kit	AG-45A-0046Y

FNDC4 & FNDC5 Proteins	PID
FNDC4 (rec.) (untagged)	AG-40B-0124
NEW Fc (human):FNDC4 (rec.)	AG-40B-0213
FNDC5 (rec.) (untagged)	AG-40B-0128
FNDC5:Fc (human) (rec.)	AG-40B-0153

Interleukin-33

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/IL-1RAcP. IL-33 is a potent inducer of type 2 immune responses in the contexts of parasite infections and allergic asthma. IL-33 also induces brown and beige adipocyte thermogenesis, promotes insulin secretion by pancreatic islets, facilitates Treg proliferation to suppress autoimmunity and potentiate neurological recovery and has 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 central nervous system (CNS) 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). IL-33 is also an orchestrator of the glioblastoma microenvironment that contributes to tumorigenesis.

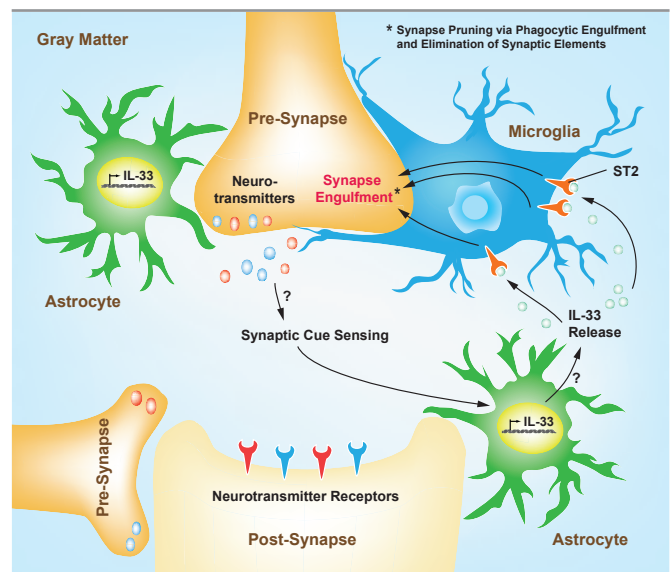


FIGURE 1: Astrocyte-derived IL-33 stimulates synapse elimination by microglia during CNS development.

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) • Therapeutic Opportunities of Interleukin-33 in the Central Nervous System: Y. Sun, et al.; *Front. Immunol.* 12, 654626 (2021) • Dual roles of interleukin-33 in cognitive function by regulating central nervous system inflammation: X. Rao, et al.; *J. Transl. Med.* 20, 369 (2022)

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

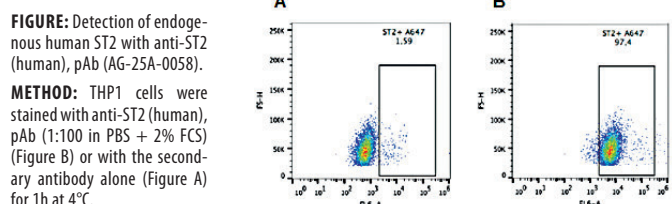


FIGURE: Detection of endogenous human ST2 with anti-ST2 (human), pAb (AG-25A-0058).
METHOD: THP1 cells were stained with anti-ST2 (human), pAb (1:100 in PBS + 2% FCS) (Figure B) or with the secondary antibody alone (Figure A) for 1h at 4°C.

UNIQUE

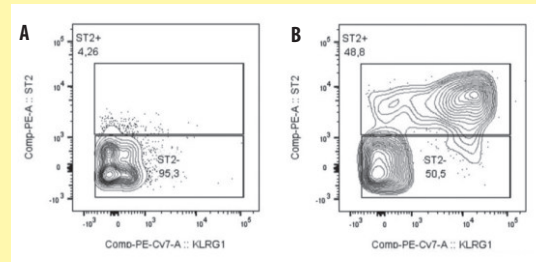
Highly Active Human IL-33 Proteins

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 (human):Fc (human) (rec.)	CHI-HF-21033
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

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 IgG2ak	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

Binds to human and mouse IL-33.

NEW HpARI (CCP1/2) (rec.) (His)

AG-40B-0201 50 µg | 3 x 50 µg

Binds to human and mouse IL-33. Enhances activity of mouse or human IL-33 *in vivo* and *in vitro*.

LIT: HpARI protein secreted by a helminth parasite suppresses interleukin-33: M. Osbourne, et al.; Immunity 47, 739 (2017) • A Truncated Form of HpARI Stabilizes IL-33, Amplifying Responses to the Cytokine: C. Chauche, et al.; Front. Immunol. 11, 1363 (2020)

HpARI is a protein secreted by the mouse parasite *Heligmosomoides polygyrus*. The mature protein HpARI, containing three predicted Complement Control Protein (CCP)-like modules (also known as Short Consensus Repeats (SCRs) or sushi-domains), suppresses type 2 (allergic) immune responses through interference in the interleukin-33 (IL-33) pathway. 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. A non-natural truncation consisting of the first 2 domains of HpARI (CCP1/2) retains IL-33 and DNA binding capacity. HpARI (CCP1/2) is able to stabilize IL-33, increasing its half-life and amplifying its effects. HpARI (CCP1/2) increases IL-33 activity by protecting it from oxidation and proteolytic degradation. HpARI (CCP1/2) (rec.) (His) is a new type of reagent to study IL-33-mediated pathology *in vivo*.

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 extra-synaptic 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 2).

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) • Progranulin as a therapeutic target in neurodegenerative diseases: H. Rhinn, et al.; Trends Pharmacol. Sci. 43, 641 (2022) • Lysosomal functions of progranulin and implications for treatment of frontotemporal dementia: M.J. Simon, et al.; Trends Cell Biol. (Epub ahead) (2022)

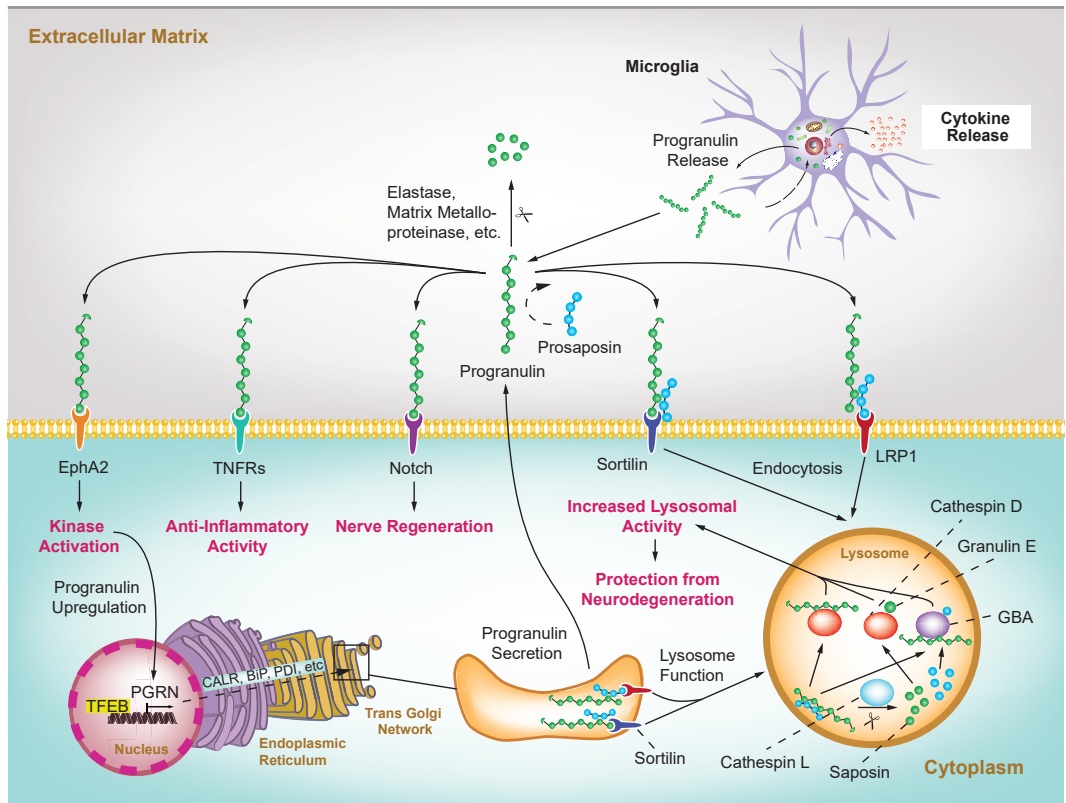


FIGURE 2: The roles and binding partners of progranulin in neuronal cells.

The 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!**



NEW**NEW mAb/mAb-based human Progranulin ELISA Kit****Progranulin (human) ELISA Kit (mAb/mAb)**

AG-45B-0027

96 wells

Sensitivity: 60 pg/ml**Range:** 0.063 ng/ml - 4 ng/ml**Sample:** Cell Culture Supernatant, Plasma, Serum**Specificity:** Detects human Progranulin in serum, plasma and cell culture supernatant.**Ask for our Validation Poster!**

GRN mutations are frequent causes of familial frontotemporal lobar degeneration (FTLD). Progranulin levels in plasma or serum, constitute a reliable, cost-effective biomarker, suitable as a screening tool in patients with familial frontotemporal degeneration. The new mAb/mAb based human Progranulin ELISA Kit has been thoroughly validated and compared to the standard pAb/pAb based ELISA Kit (Prod. No. AG-45A-0018Y) from AdipoGen Life Sciences. With this new ELISA Kit, levels below 50 ng/ml are strongly suggestive of *GRN* mutations. In a validation on 191 patient samples, confirmed by a molecular gene analysis, the new kit provided a sensitivity and specificity of 100% for detecting FTLD mutations.

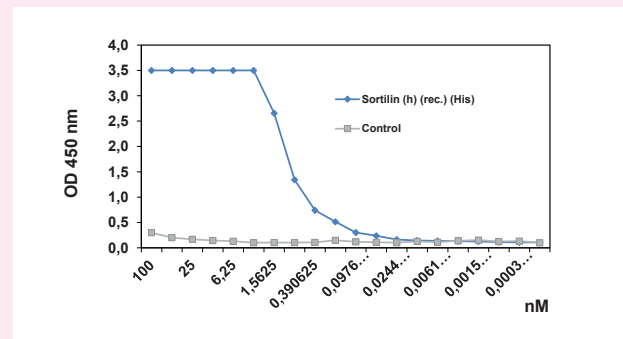
NEW Progranulin Receptor Sortilin**Sortilin (human) (rec.) (His)**

AG-40B-0229

50 µg

Binds to human Progranulin (untagged) (Prod. No. AG-40A-0188Y).

FIGURE: Progranulin (human) (rec.) (untagged) (Prod. No. AG-40A-0188Y) is coated on an ELISA plate at 1 µg/ml overnight at 4°C. Sortilin (human) (rec.) (His) (Prod. No. AG-40B-0229) or a control His tagged protein (Prod. No. AG-40B-0177) is added (starting at a concentration of 100nM with a twofold serial dilution) during one hour at RT and the interaction is then detected using an anti-His antibody coupled to HRP.

**Tag-free Progranulins****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 (binding to Sortilin)
- 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)

BULK**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

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 patterns (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.

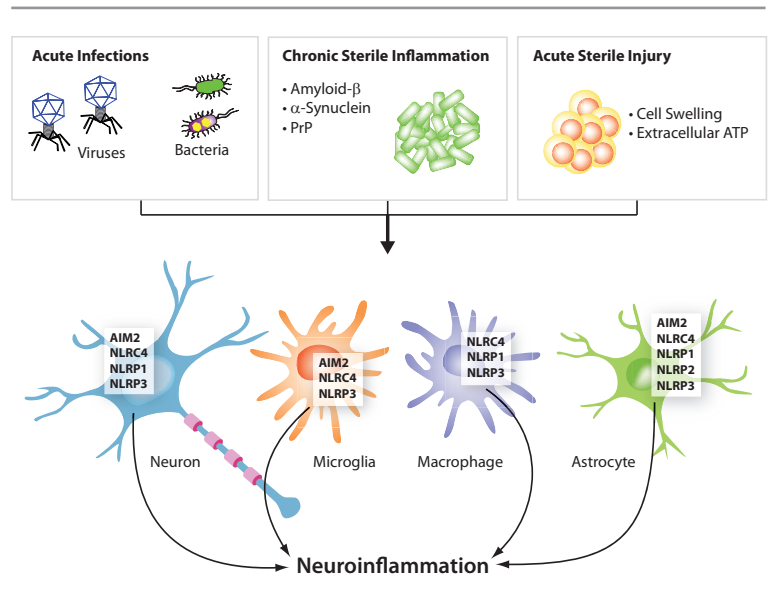


FIGURE 3: Selected activation factors, inflammasome complexes and target cells in the CNS.

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), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS) 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) • Inflammasomes in neuroinflammatory and neurodegenerative diseases: S. Voet, et al.; EMBO Mol. Med. **11**, e10248 (2019) • The Role of the Inflammasome in Neurodegenerative Diseases: F. Piancone, et al.; Molecules **26**, 953 (2021) • NLRP3 and Infections: β -Amyloid in Inflammasome beyond Neurodegeneration: G. Sita, et al.; Int. J. Mol. Sci. **22**, 6984 (2021) • Targeting Inflammasomes to Treat Neurological Diseases: J.D. Lunemann, et al.; Ann. Neurol. **90**, 177 (2021) • Parkinson's disease: connecting mitochondria to inflammasomes: G.M.E.P. Lawrence, et al.; Trends Immunol. (Epub ahead) (2022)

NEW

NLRP3 Inflammasome Starter Sets *Key Antibodies for Western Blotting*

NLRP3 Inflammasome Human Antibodies Starter Set	AG-44B-0008
NLRP3 Inflammasome Mouse Antibodies Starter Set	AG-44B-0009
NLRP3 Inflammasome Human Reagents Starter Set	AG-44B-0010
NLRP3 Inflammasome Mouse Reagents Starter Set	AG-44B-0011

THE STANDARDS FROM THE EXPERTS & VALIDATED BY KEY LABORATORIES!

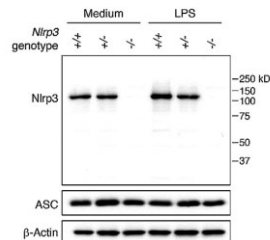
Most Trusted NLRP3 & Activated Caspase-1 KO-Validated Antibodies

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

AG-20B-0014 100 µg
AG-20B-0014B Biotin 100 µg

Clone Cryo-2
Isotype Mouse IgG2b
Immunogen Recombinant mouse caspase-1
Applications ICC, IHC, IP, WB
Specificity Recognizes human and mouse NLRP3/NALP3.

FIGURE: Mouse NLRP3 is detected in mouse macrophages (BMDMs) WT +/+ (lane 1), NLRP3 +/- (lane 2) or NLRP3 -/- (lane 3), with or without treatment with LPS (50 ng/ml) for 3 h, using the monoclonal antibody to NLRP3 (Cryo-2) (Prod. No. AG-20B-0014).



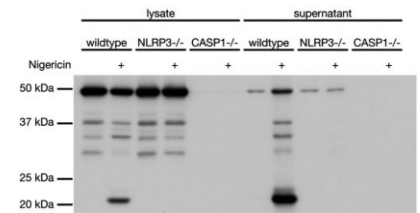
Over 1000 citations!

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
Applications WB (1 µg/ml) (see online protocol), IHC, 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) in cell extracts and supernatants of differentiated bone marrow-derived dendritic cells (BMDCs) from wildtype, NLRP3 -/- and caspase-1 -/- mice.



The 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-1 (p20) (human), mAb (Bally-1)	AG-20B-0048	100 µg	Recognizes endogenous full-length and activated (p20 fragment) human 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-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.
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-NLRP1/NALP1 (human), pAb (AL176)	AG-25B-0005	100 µg	Recognizes human NLRP1/NALP1.
NEW anti-NLRP1b (mouse), mAb (2A12)	AG-20B-0084	100 µg	Recognizes mouse and rat NLRP1b.
anti-ZBP1, mAb (Zippy-1)	AG-20B-0010	100 µg	Recognizes human and mouse ZBP1.

Key NLRP3 Inflammasome Activators and Inhibitors

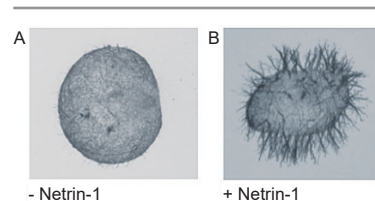
BULK

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.
NEW Dapansutril	AG-CR1-3535	10 mg 50 mg 250 mg	Potent and selective NLRP3 Inflammasome inhibitor.
MCC950 . Na (water soluble)	AG-CR1-3615	1 mg 5 mg 10 mg	Potent and selective NLRP3 inflammasome inhibitor.

For a complete Overview: www.adipogen.com/inflammasomes

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. 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).



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 commissural 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 (250 ng/ml). Axons were then stained with an anti- β -tubulin antibody.

SELECTED REVIEW ARTICLES

Netrin-1 regulates somatic cell reprogramming and pluripotency maintenance: D. Ozmadenci, et al; Nat. Commun. **6**, 7398 (2015) • Revisiting Netrin-1: One Who Guides (Axons): N.P. Boyer & S.L. Gupton; Front. Cell Neurosci. **12**, 221 (2018) • Netrin-1 in Glioblastoma Neovascularization: The New Partner in Crime? X. Vasquez, et al; Int. J. Mol. Sci. **22**, 8248 (2021)

UNIQUE Biologically Active Human Netrin-1

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

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 μ g 500 μ g	Human IgG2	ELISA, FUNC	Hu, Ms

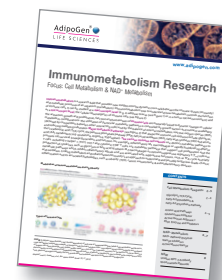
LIT: Epidermal Growth Factor Receptor-Dependent Mutual Amplification between Netrin-1 and the Hepatitis C Virus: M.L. Plissonnier, et al; PLoS Biol. **14**, e1002421 (2016) • Targeting netrin-1/DCC interaction in diffuse large B-cell and mantle cell lymphomas: T. Broutier, et al; EMBO Mol. Med. **8**,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

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. Thus damaged mitochondria may lead to neuronal death. Many **neurodegenerative diseases** such as Alzheimer's disease (AD), Parkinson's disease (PD), and Multiple Sclerosis (MS) are **associated with dysfunction of mitochondrial dynamics or metabolism**.

SELECTED REVIEW ARTICLES:

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) • Targeting mitochondria in the regulation of neurodegenerative diseases: A comprehensive review: S.K. Maurya, et al; J. Neurosci. Res. **100**, 1845 (2022) • Mitochondria research and neurodegenerative diseases: On the track to understanding the biological world of high complexity: D. Mendes, et al; Mitochondrion **65**, 67 (2022)



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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 disease (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, **polyglutamylolation** and **glycylation** (see Figure 4). PTMs are involved in fine-tuning of interactions between microtubules and different MT-interacting proteins.

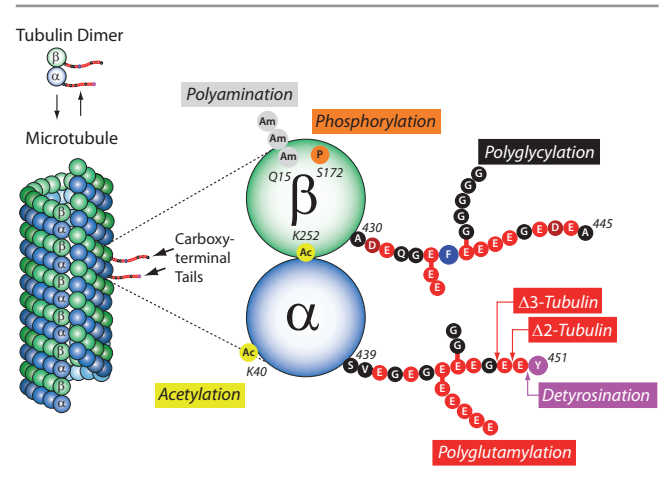


FIGURE 4: Tubulin PTM Overview. Adapted from C. Janke; J. Cell. Biol. 206, 461 (2014).

UNIQUE

Validated Post-translational Modification-specific Antibodies

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

Standard Validated Microtubule-target Antibodies

ANTIBODIES	PID	SIZE	ISOTYPE/SOURCE	APPLICATION	SPECIES
anti-Tubulin-GTP, mAb (rec.) (MB11) UNIQUE	AG-27B-0009	100 μ g	Human IgG2 λ	ICC	Hu, Ms, Rt, Dr
anti-α-Tubulin, mAb (rec.) (F2C)	AG-27B-0005	100 μ g	Human IgG2 λ	ICC, WB	Hu, Ms, Bv
NEW anti-β-Tubulin, mAb (AXO45)	AG-20B-0085	100 μ g	Mouse IgG1	ICC, IHC, IP, WB	Hu, Ms, Ciliates
NEW anti-β-Tubulin (β-monoE), pAb (IN115)	AG-25B-0039	100 μ g	Rabbit	ICC, IHC, IP, WB	Hu, Ms
anti-β-Tubulin, mAb (rec.) (S11B)	AG-27B-0008	100 μ g	Human IgG2 λ	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. In the secretory pathway Rab1 and 6 are implicated in anterograde and retrograde trafficking. Rab1 has been shown to be involved in **autophagy** by helping the formation of the pre-autophagosomal isolation membrane (phagophore). Rab6 functions as modulator of the unfolded protein response (UPR), helping the recovery from an ER stress insult. Rab6 is upregulated in Alzheimer's disease brains.

ANTIBODIES	PID	SIZE	ISOTYPE/SOURCE	APPLICATION	SPECIES
anti-Rab1-GTP, mAb (rec.) (ROF7)	AG-27B-0006	100 μ g	Human IgG2 λ	ICC, IP	Hu, Ms, Rt, Dg
anti-Rab6-GTP, mAb (rec.) (AA2)	AG-27B-0004	100 μ g	Human IgG2 λ	ICC	Hu, Ms, Dr
anti-Rab6-GTP, mAb (rec.) (AA2) (ATTO 488)	AG-27B-0004TD	100 μ g	Human IgG2 λ	ICC	Hu, Ms, Dr

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. The activation of the **Notch signaling pathway** results in stabilization of microtubules leading to the regulation of axonal morphology, with thicker neurites, fewer branches and loss of synaptic varicosity. This Notch-dependent stabilization of microtubules is likely due to the 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	Dynamain 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
Vincristine . sulfate	Microtubule Depolymerization	AG-CN2-0446

p75NTR – New Recombinant Mouse-specific Antibodies

Neurotrophins have been known as the critical factors in development and functioning of the nervous system. It has been demonstrated that neurotrophins exert their effects such as proliferation, differentiation, survival and apoptosis by binding to two types of surface receptors, the tyrosine kinase receptor (Trk) family and the p75 neurotrophin receptor (p75NTR). p75NTR is expressed by many cell types including neurons, Schwann cells, mesenchymal stem/stromal cells, follicular dendritic cells and melanocytes. Presence of this receptor supports uptake of intracellular calcium, but not mobilization.

ANTIBODIES	PID	SIZE	ISOTYPE/SOURCE	APPLICATION	SPECIES
NEW anti-p75NTR (mouse), mAb (rec.) (SH325-G7)	AG-27B-6326	50 μ g	Human IgG1	ELISA, FACS, WB	Ms
NEW anti-p75NTR (mouse), mAb (rec.) (SH325-B6)	AG-27B-6327	50 μ g	Human IgG1	ELISA, FACS	Ms
NEW anti-p75NTR (mouse), mAb (rec.) (SH325-A11)	AG-27B-6328	50 μ g	Human IgG1	ELISA, FACS	Ms

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 region (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 [AMPA] 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 μ g

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)

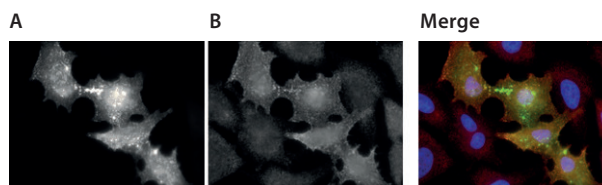


FIGURE: Palmitoylated PSD-95 is detected by ICC using anti-PSD-95 (palmitoylated), mAb (rec.) (PF11) (AG-27B-0021). HeLa cells are co-transfected with DHHC2 (palmitoylating enzyme) and PSD-95-GFP (A) or DHHC2 alone (B).

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.
Biocytine	CDX-B0412	100 mg 250 mg	Anterograde, retrograde, or intracellular neuroanatomical tracer.
BAPTA-AM	CDX-B0285	25 mg 100 mg	Fluorescent membrane-permeable Ca ²⁺ chelator. Blocks neuronal Ca ²⁺ -activated K ⁺ channel currents.
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'-Diocetadecyl-3,3',3'-tetramethylindocarbocyanine 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 <i>in vivo</i> and <i>in vitro</i> .
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.
FURA 2-AM	CDX-F0014	1 mg	Fluorescent membrane-permeable Ca ²⁺ chelator. Measuring intracellular calcium mobilization after activation of GPCRs and neuronal ion channels.
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.

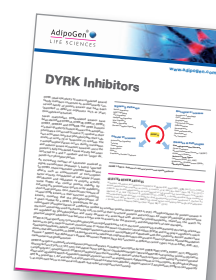
HDAC6 Inhibitors & Alzheimer's Disease

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 = 15 nM	Other HDACs (IC ₅₀ = >15 μM), HDAC8 (IC ₅₀ = 0.9 μM)
Nexturastat A	AG-CR1-3901	1 mg 5 mg	IC ₅₀ = 5.02 nM	Other HDACs (IC ₅₀ = 3-10 μM)
Nexturastat B	AG-CR1-3902	1 mg 5 mg	IC ₅₀ = 3 nM	HDAC1 (IC ₅₀ = 0.9 μM)
ACY-775	AG-CR1-3903	1 mg 5 mg	IC ₅₀ = 7.5 nM	HDAC1-9 (IC ₅₀ = 1-10 μM)
DMAPB	AG-CR1-3904	1 mg 5 mg	IC ₅₀ = 114 nM	Other HDACs (IC ₅₀ = 1-8 μM)
PMPH	AG-CR1-3905	1 mg 5 mg	IC ₅₀ = 11 nM	HDAC1 (IC ₅₀ = 1.5 μM)
DABPH	AG-CR1-3906	1 mg 5 mg	IC ₅₀ = 12 nM	HDAC1 (IC ₅₀ = 6.8 μM)
MBIMPH	AG-CR1-3907	1 mg 5 mg	IC ₅₀ = 9 nM	Other HDACs (IC ₅₀ = 0.1-12 μM)
MBIMPH F-Analog 1 . HCl	AG-CR1-3908	1 mg 5 mg	IC ₅₀ = 3 nM	Other HDACs (IC ₅₀ = 0.03-20 μM)
MBIMPH F-Analog 2	AG-CR1-3909	1 mg 5 mg	IC ₅₀ = 5 nM	Other HDACs (IC ₅₀ = 0.2-11 μM)
MPI_5a	SYN-3040	1 mg 5 mg 10 mg	IC ₅₀ = 36 nM	Other HDACs (IC ₅₀ = 2-50 μM)

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NEW Potential anti-Alzheimer Agent

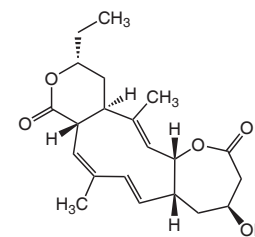
UNIQUE
NEW Collinolactone

BVT-0480

250 µg | 1 mg

Formula C₂₁H₂₈O₅
MW 360.45

CAS 2733581-46-7

Source Isolated from *Streptomyces* sp.


Collinolactone is a potential anti-Alzheimer agent with Aβ-disaggregating activity. It also has neuroprotective and anti-neurodegenerative effects by reducing intracellular oxidative stress.

LIT: Rhizolutin, a novel 7/10/6-tricyclic dilactone, dissociates misfolded protein aggregates and reduces apoptosis/inflammation associated with Alzheimer's Disease: Y. Kwon, et al.; *Angew. Chem. Int. Ed.* **59**, 22994 (2020) • Structure of cyclodecatriene collinolactone, its biosynthesis, and semisynthetic analogues: effects of monoastal phenotype and protection from intracellular oxidative stress: J.C. Schmid, et al.; *Angew. Chem. Int. Ed.* **60**, 23212 (2021)

Selected Agonists and Antagonists

PRODUCT NAME	ACTIVITY	PID	SIZE
Aftin-5	Alzheimer's Disease (AD) accelerator	AG-MR-C0015	1 mg 5 mg 25 mg
6-Aminophenanthridine	Anti-prion agent, inhibiting protein aggregation	AG-MR-C0029	1 mg 5 mg 25 mg
(+)-Bicuculline	GABA(A) receptor antagonist	CDX-B0239	25 mg 500 mg
Bilobalide	GABA(A) receptor antagonist	AG-CN2-0026	10 mg 50 mg
Capsaicin from <i>Capsicum annuum</i>	Potent TRPV1 agonist	CDX-C0941	50 mg 250 mg 1 g
Compound E	Potent and selective γ-Secretase inhibitor	AG-CR1-0081	250 µg 1 mg 5 mg
DAPT	Cell-permeable γ-Secretase inhibitor	AG-CR1-0016	5 mg 25 mg
Debromohymenialdisine	Potential anti-Alzheimer's agent	AG-CN2-0068	100 µg
Entacapone	Potent COMT inhibitor used for Parkinson's disease treatment	AG-CR1-3708	5 mg 25 mg
Fipronil	Alzheimer inducing agent (Alzheimerogen)	AG-CR1-3648	100 mg 1 g
Fulvic acid	Tau and Aβ aggregation inhibitor	AG-CN2-0135	1 mg 5 mg
GABA [γ-Aminobutyric acid]	GABA(A) and GABA(B) receptor agonist	AG-CR1-3664	1 g
GV-58	Selective N- & P/Q-type Ca ²⁺ -channel agonist	AG-MR-C0035	1 mg 5 mg
Hyperforin . DCHA	TRPC6 channel activator	AG-CN2-0008	500 µg 1 mg
Leucettine L41	Potent DYRK inhibitor	AG-MR-C0023	1 mg 5 mg 25 mg
MTEP	Potent mGluR5 antagonist	AG-CR1-0022	5 mg 25 mg
Pellitorine	Tingling-inducing agent / TRPV1 antagonist	AG-CN2-0009	1 mg 5 mg 25 mg
Pseurotin D	Neuroleptic agent	BVT-0426	1 mg 5 mg
Resiniferatoxin	Highly potent TRPV1 agonist	AG-CN2-0534	0.1 mg 0.5 mg
SB366791	Potent and selective TRPV1 antagonist	AG-CR1-0034	5 mg 25 mg
Serratal	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 100 mg
URMC-099	MLK-3 inhibitor for treatment of Parkinson's disease	SYN-1211	1 mg 5 mg 10 mg

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