AdipoGen®
LIFE SCIENCES

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THE EXPERT IN

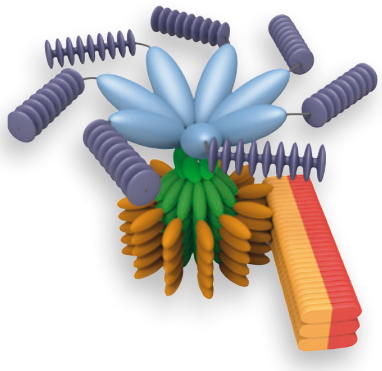
Inflammasome Signaling

From Innate to Adaptive Immunity

Inflammasomes are multi-protein complexes whose activity has been implicated in physiological and pathological inflammation. The hallmarks of inflammasome activation are the secretion of the mature forms of caspase-1 and interleukin-1β (IL-1β) from cells of the innate immune system.

An inflammasome represents a high molecular weight complex that activates inflammatory caspases and cytokines of the IL-1 family (IL-1β, IL-18 and depending on the stimulus also IL-1α). Several inflammasomes have been described which contain different sensor proteins such as **NLRP1** (NALP1), **NLRP3** (NALP3), **IPAF** (NLRC4), **NLRP6** (NALP6), **NLRP12** (NALP12), **RIG-I** and **AIM-2** (absent in melanoma 2). Most of these inflammasomes require the adapter protein **Asc** (apoptosis-associated speck-like protein containing a caspase recruitment domain) to recruit caspase-1 to the inflammasome complex. Upon binding to the inflammasome caspase-1 is cleaved and activated, leading to cleavage of its various targets and causing maturation and secretion of the pro-inflammatory IL-1β. Inflammasomes can be activated through multiple signals including live bacteria, microbial toxins, xeno-compounds, particulates cytoplasmic pathogen-associated molecular patterns **(PAMPs)** and/or endogenous danger signals **(DAMPs)**.

Inflammasome activity has been causally linked to the induction of numerous inflammatory responses, which can be either beneficial or harmful to the organism. Beneficial responses arise by maintaining homeostatic tissue function (detection and repair of tissue damages after trauma or pathogen invasion). Among the harmful inflammatory responses are particle-induced sterile inflammation, caused by host-derived particles such as monosodium urate (MSU) crystals, which are involved in the pathogenesis of gout, as well as environmental and industrial particles such as asbestos, silica and metallic nanoparticles, which induce lung inflammation upon inhalation. Accumulating evidence also implicates inflammasome activity in numerous other diseases, including cancer and the development of metabolic diseases (like type 2 diabetes, atherosclerosis), some neurodegenerative diseases (like Alzheimer, Prion, Parkinson), autoimmune diseases (such as multiple sclerosis) and inflammatory bowel diseases. Beneficial effects for the host include the enhancement of vaccine efficacy.



SELECTED REVIEW ARTICLES

Inflammasomes: mechanism of action, role in disease, and therapeutics: H. Guo, et al.; Nat. Med. **21,** 677 (2015) • Structural mechanisms of inflammasome assembly: A. Lu & H. Wu; FEBS J. **282,** 435 (2015) • Mechanism of NLRP3 inflammasome activation: F.S. Sutterwalam et al.; Ann. N.Y. Acad. Sci. **1319,** 82 (2014) • Activation and regulation of the inflammasomes: E. Latz, et al.; Nat. Rev. Immunol. **13,** 397 (2013) • The inflammasome: an integrated view: O. Gross, et al.; Immunol. Rev. **243,** 136 (2011)

THE STANDARD

NLRP3 Antibody

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

AG-20B-0014-C100 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.

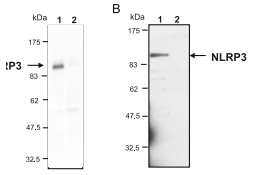


FIGURE: Human and mouse NLRP3/NALP3 are detected in THP1 cells or mouse macrophages, respectively, using anti-NLRP3/NALP3, mAb (Cryo-2) (Prod. No. AG-20B-0014).

Inflammasome Tools

Specific Caspase-1 Detection

Unique mAbs to Detect Activated (p10 & p20) Mouse Caspase-1 by WB

- **Purified mouse monoclonal antibodies (mAbs)**
- **Casper-1 detects the endogenous full-length & activated p20 fragment**
- **Casper-2 detects the endogenous full-length & activated p10 fragment**
- **Outstanding tools to monitor inflammasome activation**
- **Tested by experts in the inflammasome signaling field**
- **No protein precipitation from supernatants is required**

NEW anti-Caspase-1 (p10) (mouse), mAb (Casper-2)

AG-20B-0044-C100		100 µg
AG-20B-0044B-C100	Biotin	100 µg

Clone	Casper-2
Isotype	Mouse IgG2a
Immunogen	Recombinant mouse caspase-1
Application	WB (1µg/ml) (see online protocol)
Specificity	Recognizes endogenous full-length and activated (p10 fragment) mouse caspase-1.

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

AG-20B-0042-C100		100 µg
AG-20B-0042B-C100	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.

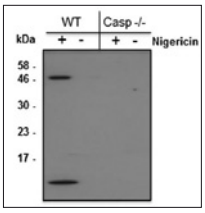


FIGURE: Mouse caspase-1 (p10) is detected by immunoblotting using anti-Caspase-1 (p10) (mouse), mAb (Casper-2) (Prod. No AG-20B-0044).

METHOD: Caspase-1 was analyzed by Western blot in supernatants of differentiated bone marrow-derived dendritic cells (BMDCs) from wild-type and caspase-1-/- mice activated or not by 5µM nigericin (Prod. No. AG-CN2-0020) for 30 min. Supernatants (30µl) were separated by SDS-PAGE under reducing conditions, transferred to nitrocellulose and incubated with anti-Caspase-1 (p10) (mouse), mAb (Casper-2) (1µg/ml). Proteins were visualized by a chemiluminescence detection system.

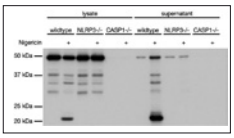


FIGURE: Mouse caspase-1 (p20) is detected by immunoblotting using anti-Caspase-1 (p20) (mouse), mAb (Casper-1) (Prod. No. AG-20B-0042).

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.

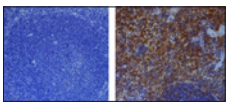


FIGURE: Immunohistochemical staining of endogenous mouse caspase-1 in mouse spleen using anti-Caspase-1 (p20) (mouse), mAb (Casper-1) (Prod. No. AG-20B-0042).

METHOD: Mouse spleen tissues (paraffin sections) from caspase-1 KO (left) or WT (right) mice were stained using anti-Caspase-1 (p20) (mouse), mAb (Casper-1) (Prod. No. AG-20B-0042) (1:500) by standard immunohistochemistry (antigen retrieval performed with sodium citrate).

LITERATURE REFERENCES FOR CASPER1, CASPER2 AND CRYO2: The adaptor ASC has extracellular and 'prionoid' activities that propagate inflammation: B.S. Franklin, et al.; Nat. Immunol. **15,** 727 (2014) • The NLRP3 inflammasome is released as a particulate danger signal that amplifies the inflammatory response: A. Baroja-Mazo, et al.; Nat. Immunol. **15,** 738 (2014)

FROM THE EXPERTS & VALIDATED BY KEY LABORATORIES!

Human Caspase-1 Detection

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

AG-20B-0048-C100		100 µg
AG-20B-0048B-C100	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.

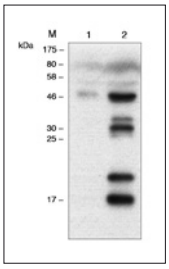


FIGURE: Figure: Human Caspase-1 (p20) is detected by immunoblotting using anti-Caspase-1 (p20) (human), mAb (Bally-1) (Prod. No AG-20B-0048).

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 for 1h (Prod. No. AG-CN2-0020). 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.

LIT: Liver X receptor β activation induces pyroptosis of human and murine colon cancer cells: V. Derangere, et al.; Cell Death Differ. **21,** 1914 (2014)

Caspase-1 Inhibitors

Z-VAD-FMK (Cell permeable)

AG-CP3-0002-M001	1 mg
AG-CP3-0002-M005	5 mg

LIT: Malarial hemozoin is a Nalp3 inflammasome activating danger signal; C. Dostert, et al.; PLoS One **4,** e6510 (2009)

Q-VD-OPh

AG-CP3-0006-M001	1 mg
AG-CP3-0006-3001	3 x 1 mg
AG-CP3-0006-M005	5 mg

For Negative Control see Q-VE-OPh (Prod. No. AG-CP3-0007).

APPLICATIONS: FACS: Flow Cytometry; **FUNC:** Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry **IP:** Immunoprecipitation; **WB:** Western blot

FORMULATION: PF = Preservative free

SPECIES: Hu = Human; **Ms** = Mouse; **Rt** = Rat; **Rb** = Rabbit; **Prm** = Primate

UNIQUE

Asc Antibody AL177

anti-Asc, pAb (AL177)

AG-25B-0006-C100		100 µg
AG-25B-0006PF-C100	Preservative free	100 µg
AG-25B-0006TS-C100	ATTO 647N	100 µg

Source Rabbit

Immunogen Synthetic peptide corresponding to aa at the N-terminal human Asc.

Application ICC, IHC (PS), IP, WB, FUNC (Inhibition)*

Specificity Recognizes human and mouse Asc.

* Inhibits interaction between Asc and NLRP3, leading to blockade of caspase-1 processing *in vitro*.

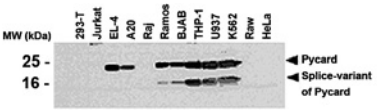
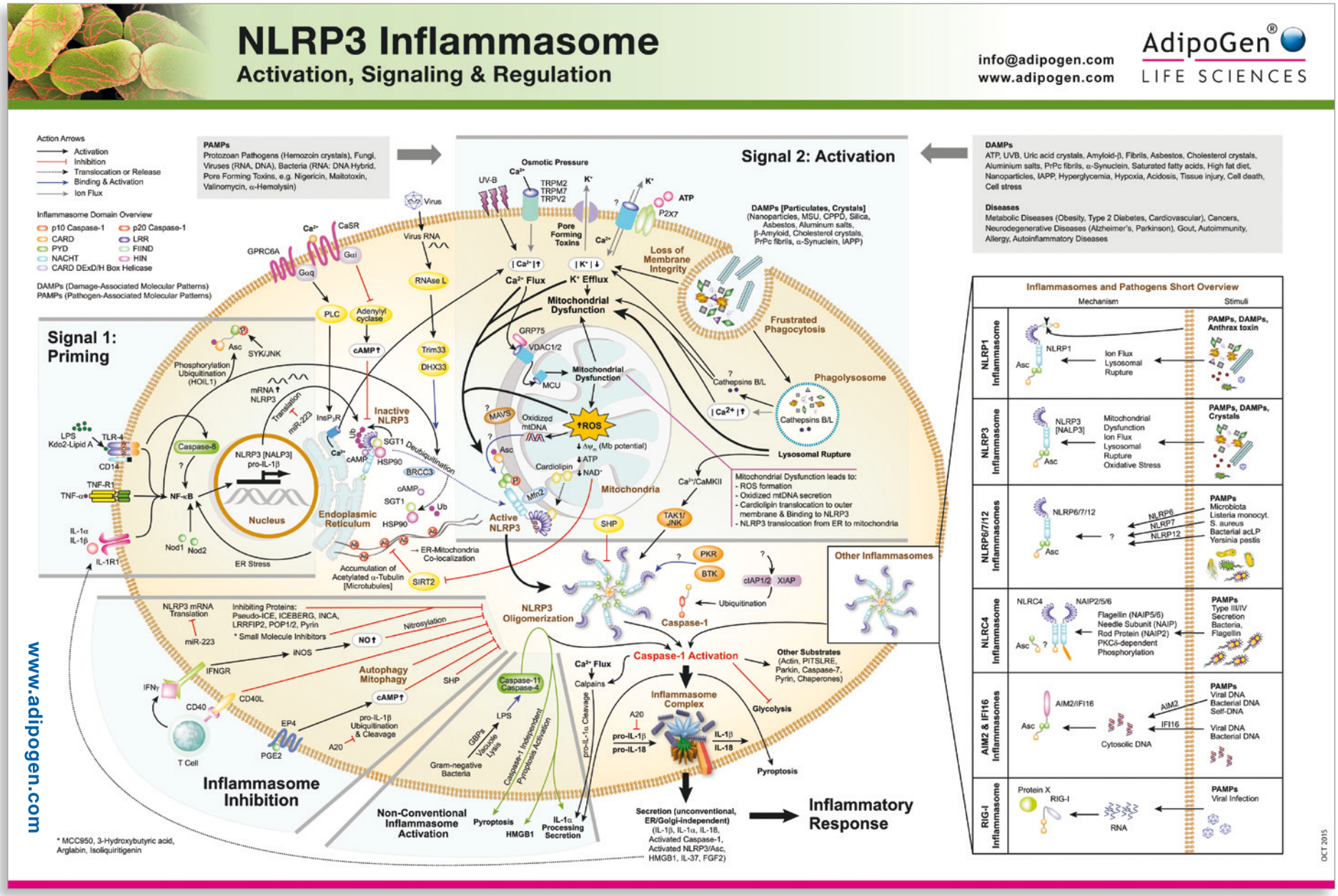


FIGURE: Western blot analysis of human and mouse cell lines using anti-Asc, pAb (AL177) (Prod. No. AG-25B-0006). Total protein extracts from various human (293-T, Jurkat, Raj, Ramos, BJAB, THP-1, U937, K562, Raw, HeLa) and mouse (EL-4, A20) cell lines were run on SDS-PAGE and Pycard detected by anti-Asc, pAb (AL177) at 1:1'000 dilution. Anti-rabbit IgG coupled horse radish peroxidase was used at 1:5'000 dilution for ECL detection.

Standard Inflammasomes Signaling Antibodies

PRODUCT NAME	PID	SIZE	SOURCE/ISOTYPE	SPECIES	APPLICATION
Nod-like Receptors (NLRs)					
anti-NAIP1/2/5 (mouse), mAb (Naipa-1)	AG-20B-0045	100 µg	Mouse IgG2bκ	Ms	WB
anti-NLRP1/NALP1 (human), pAb (AL176)	AG-25B-0005	100 µg	Rabbit	Hu	WB
anti-NLRP3/NALP3, mAb (Cryo-2)	AG-20B-0014	100 µg	Mouse IgG2b	Hu, Ms	ICC, IHC, IP, WB
anti-NLRP3/NALP3 (mouse), mAb (Cryo-1)	AG-20B-0006	100 µg	Mouse IgG2b	Ms	WB
anti-NLRP6/NALP6 (human), mAb (Clint-1)	AG-20B-0046	100 µg	Mouse IgG1κ	Hu	WB
anti-NLRP12/NALP12 (human), pAb (AL236)	AG-25B-0021	100 µg	Rabbit	Hu	IP, WB
anti-Nod1 (human), pAb (AL184)	AG-25B-0013	50 µg	Rabbit	Hu	WB
RIG-like Helicases (RLHs) – Antiviral Signaling					
anti-RIG-I, mAb (Alme-1)	AG-20B-0009	100 µg	Mouse IgG1	Hu, Ms	IHC, IP, WB
anti-RIG-I, mAb (Alme-1) (Biotin)	AG-20B-0009B	100 µg	Mouse IgG1	Hu, Ms	IHC, IP, WB
anti-Cardif (human), mAb (Adri-1)	AG-20B-0004	100 µg	Mouse IgG2b	Hu	ICC, IHC, IP, WB
anti-MDA5 (mouse), pAb (AL180)	AG-25B-0001	100 µl	Rabbit	Ms	IHC, WB
anti-MDA5 (human), mAb (Hely-1)	AG-20B-0013	100 µg	Mouse IgG1	Hu	ELISA, IP, WB
anti-NS3 (HCV), mAb (1B6)	AG-20B-0001	100 µg	Mouse IgG1	HCV	ICC, WB
anti-NS5B (HCV), mAb (5B-3B1)	AG-20B-0002	100 µg	Mouse IgG2b	HCV	WB
anti-NS5B (HCV), mAb (blocking) (5B-12B7)	AG-20B-0003	100 µg	Mouse IgG2a	HCV	ICC, IP, FUNC (Blocking)
Cytosolic DNA Sensor					
anti-AIM2 (human), mAb (3B10)	AG-20B-0040	100 µg	Mouse IgG1	Hu	ICC, WB
Signaling Antibodies					
anti-Asc [Pycard], pAb (AL177)	AG-25B-0006	100 µg	Rabbit	Hu, Ms	ICC, IHC (PS), IP, WB, FUNC (Blocking)
anti-Asc [Pycard], pAb (AL177) (preservative free)	AG-25B-0006PF	100 µg	Rabbit	Hu, Ms	ICC, IHC (PS), IP, WB, FUNC (Blocking)
anti-Asc, pAb (AL177) (ATTO 647N)	AG-25B-0006TS	100 µg	Rabbit	Hu, Ms	ICC, IHC (PS), IP, WB, FUNC (Blocking)
anti-Pyrin (human), pAb (AL196)	AG-25B-0020	100 µg	Rabbit	Hu	IP, WB
anti-TRAM (human), pAb (AL239)	AG-25B-0011	50 µl	Rabbit	Hu	WB
anti-TRIF (human), pAb (AL227)	AG-25B-0008	50 µg	Rabbit	Hu	IP, WB
Cytosolic PAMPs Sensors					
anti-Caspase-4/11 (p20), mAb (Flamy-1)	AG-20B-0060	100 µg	Mouse IgG2bκ	Hu, Ms	IP, WB
anti-Caspase-4/11 (p20), mAb (Flamy-1) (Biotin)	AG-20B-0060B	100 µg	Mouse IgG2bκ	Hu, Ms	IP, WB
anti-Caspase-11 (p20) (mouse), mAb (Flamy-2)	AG-20B-0061	100 µg	Mouse IgG2bκ	Ms	ELISA, WB



Caspase-1 — Quantitative Measurement of Inflammasome Activation

A quantitative detection method, alternative to Western blotting, to measure inflammasome activation leading to caspase-1 cleavage and secretion. How to measure inflammasome activation? See our manual on www.adipogen.com.

Caspase-1 (mouse) Matched Pair Detection Set

AG-46B-0003-KI01 — For 5 x 96 well plates

Specificity	Detects mouse caspase-1 (p10 and p20 domain).
Species Reactivity	Mouse
Sensitivity	100 pg/ml
Range	0.15 ng/ml to 10 ng/ml
Assay Type	Colorimetric/Sandwich
Sample Type	Cell Culture Supernatant

Caspase-1 (mouse) ELISA Kit

AG-45B-0002-KI01 — 96 wells

Specificity	Detects mouse caspase-1 (p10 and p20 domain).
Species Reactivity	Mouse
Sensitivity	33 pg/ml
Range	15 to 1000 pg/ml
Assay Type	Colorimetric/Sandwich
Sample Type	Cell Culture Supernatant, Serum, Plasma

Inflammasome Signaling-related Proteins & Antibodies

PRODUCT NAME	PID	SIZE
IL-1β (human) (rec.) (untagged)	AG-40B-0023	10 µg | 3 x 10 µg
IL-1β (mouse) (rec.) (untagged)	AG-40B-0086	10 µg | 3 x 10 µg
IL-1R1 (human):Fc (human) (rec.)	AG-40B-0024	50 µg | 3 x 50 µg
anti-IL-1α (mouse), mAb (Bamboo-1)	AG-20B-0050	100 µg
anti-IL-1α (mouse), mAb (Bamboo-2)	AG-20B-0058	100 µg
IL-1α (mouse) ELISA Kit	AG-45B-0003	96 wells
NEW **IL-1α (mouse) Matched Pair Detection Set**	AG-46B-0004	1 Set
NEW **anti-IL-1α (p18) (mouse), mAb (Teo-1)**	AG-20B-0064	100 µg
anti-IL-1R2 (mouse), mAb (rec.) (Praxy-1-1)	AG-27B-0011	100 µg

Inflammasome "Priming" Activators

Priming of the NLRP3 Inflammasome

The most prominent function of the **NLRP3 inflammasome** is the processing and activation of pro-interleukin-1β (pro-IL-1β). Yet most cells do not express pro-IL-1β and thus prior expression of pro-IL-1β is required. This can be achieved by stimulating receptors such as TLRs (e.g. through LPS), NODs, TNF-Rs (e.g. through TNF-α) or IL-1R1 (through IL-1α and IL-1β) that activate NF-κB and initiate pro-IL-1β transcription. This process of pro-IL-1β induction is called **priming** (**Signal 1**). Priming also induces NF-κB-dependent transcription of NLRP3.

An additional stimulus (**Signal 2**) results in the activation of the NLRP3 inflammasome and subsequent initiation of downstream signaling. In the absence of priming, NLRP3 inflammasome-dependent caspase-1 activation can also be observed, but IL-1β secretion is absent.

FOR DETAILS SEE: Critical functions of priming and lysosomal damage for NLRP3 activation: V. Hornung & E. Latz; Eur. J. Immunol. **40,** 620 (2010) • The inflammasomes: K. Schröder & J. Tschopp; Cell **140,** 821 (2010)

TNF-α, Soluble (human) (rec.)

AG-40B-0006 — 10 µg | 50 µg | 3 x 50 µg

TNF-α (human) (multimeric) (rec.)

AG-40B-0019 — 10 µg | 3 x 10 µg

TNF-α (mouse) (multimeric) (rec.)

AG-40B-0021 — 10 µg | 3 x 10 µg

Lipopolysaccharides (LPS)

For a full panel see our Innate Immunity Brochure

Microtubules & Inflammasome Complex Assembly

Inflammasomes are assembled from a pattern-recognition receptor, the adapter protein Asc and caspase-1 to process interleukin-1β (IL-1β) and IL-18 in response to microbial components or damage-associated signals. Recently, it was shown that **microtubules** might have a central role in the assembly of the NOD, LRR and PYD domain-containing protein 3 (NLRP3) inflammasome. Inhibitors of microtubule polymerization (such as colchicine and nocodazole) significantly decrease the levels of IL-1β that is produced in response to NLRP3 inflammasome activators. However, microtubules did not contribute to the activation of the NLRP3 inflammasome in a phagocytosis-dependent manner. Instead, they are required in a dynein-dependent manner for the relocalization of the mitochondria close to the endoplasmic reticulum following stimulation by inducers of the NLRP3 inflammasome. As a result of this microtubule-dependent process, Asc molecules on the mitochondria came into close proximity and could interact with NLRP3 on the endoplasmic reticulum (ER). NLRP3 activators induce microtubule polymerization and acetylation, with concomitant binding of dynein to acetylated α-tubulin.

As a proposed mechanism, NLRP3 activation leads to mitochondrial dysfunction followed by a decrease of the mitochondrial coenzyme NAD^+ concentration, which in turn inactivates the NAD^+-dependent α-tubulin deacetylase sirtuin 2. This results in the accumulation of acetylated α-tubulin and the subsequent organelle translocation process.

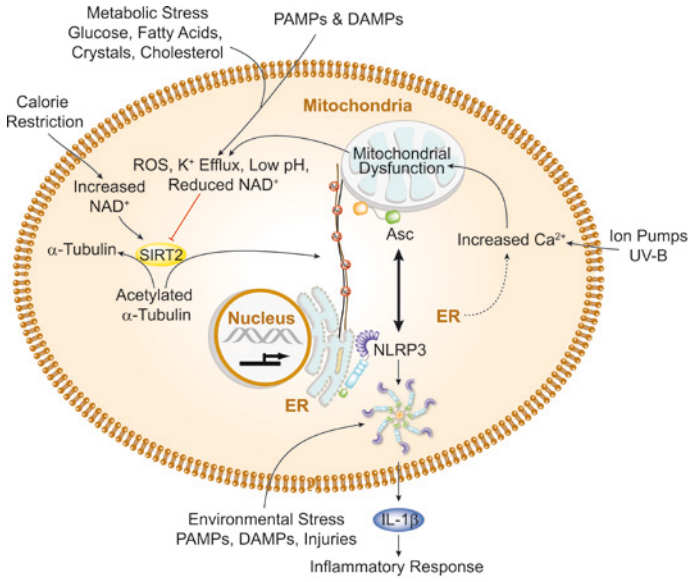


FIGURE: Accumulation of acetylated α-tubulin facilitates the assembly and activation of the inflammasome by opposing Asc on mitochondria to NLRP3 on the endoplasmic reticulum (ER).

LIT: Microtubule-driven spatial arrangement of mitochondria promotes activation of the NLRP3 inflammasome: T. Misawa, et al.; Nat. Immunol. **14,** 454 (2013)

UNIQUE

Microtubule Antibodies

PRODUCT NAME	PID	SIZE	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 IgG1k	EM, ICC, IP, WB
anti-Polyglutamylation Modification, mAb (GT335) (Biotin)	AG-20B-0020B	100 µg	Mouse IgG1k	ICC, IP, WB
anti-Polyglutamate chain (polyE), pAb (IN105)	AG-25B-0030	50 µg	Rabbit	ICC, WB

Small Molecule Cytoskeletal Modulators

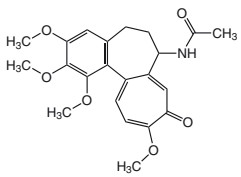
THE SOURCE

Colchicine

AG-CN2-0048 500 mg | 1 g

Microtubule inhibitor. Inhibits acetylated α-tubulin mediated transport of mitochondria and subsequent apposition of Asc on mitochondria to NLRP3 on the endoplasmic reticulum.

LIT: Microtubule-driven spatial arrangement of mitochondria promotes activation of the NLRP3 inflammasome: T. Misawa, et al.; Nat. Immunol. **14,** 454 (2013)



Dynasore	Dynamin Inhibitor	AG-CR1-0045
Jasplakinolide	F-actin Stabilization	AG-CN2-0037
Latrunculin A	F-actin Depolimerization	AG-CN2-0027
Latrunculin B	F-actin Depolimerization	AG-CN2-0031
Swinholide A	F-actin Inhibitor	AG-CN2-0035
Cytochalasin H	Actin Depolimerization	BVT-0447
Sceptrin . 2HCl	Actin Depolimerization	AG-CN2-0440
Colcemid	Microtubule Inhibitor	AG-CR1-3567
Ilimaquinone	Microtubule Inhibitor	AG-CN2-0038
Nocodazole	Microtubule Inhibitor	AG-CR1-0019
Paclitaxel	Microtubule Stabilizer	AG-CN2-0045
Podophyllotoxin	Microtubule Inhibitor	AG-CN2-0049
Pseudolaric acid B	Microtubule Inhibitor	AG-CN2-0083
Thiocolchicine	Microtubule Inhibitor	AG-CN2-0074

AdipoGen® LIFE SCIENCES

APPLICATIONS: FACS: Flow Cytometry; **FUNC:** Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry **IP:** Immunoprecipitation; **WB:** Western blot **EM:** Electron Microscopy

FORMULATION: PF = Preservative free

SPECIES: Hu = Human; **Ms** = Mouse; **Rt** = Rat; **Rb** = Rabbit; **Prm** = Primate

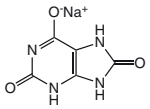
NLRP3 Inflammasome Activators

Monosodium urate

AG-CR1-3950 (crystals) 2 mg | 2x 2 mg
AG-CR1-3951 (ready-to-use solution) 10 mg

Biological Activity Tested!

Potent NLRP3 inflammasome activator.



LIT: Gout-associated uric acid crystals activate the NALP3 inflammasome: F. Martinon, et al.; Nature **440,** 237 (2006)

Nigericin . Na

AG-CN2-0020 5 mg | 25 mg

Potent NLRP3 inflammasome activator.

LIT: Cryopyrin activates the inflammasome in response to toxins and ATP: S. Mariathasan, et al.; Nature **440,** 228 (2006)

7BIO

MR-C0020 10 mg | 50 mg

Induces necrosis and consequently NLRP3 inflammasome activation.

LIT: Cutting edge: Necrosis activates the NLRP3 inflammasome: H. Li, et al.; J. Immunol. **183,** 1528 (2009)

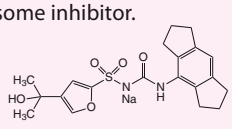
NLRP3 Inflammasome Inhibitors

NEW MCC950 . Na

AG-CR1-3615 1 mg | 5 mg | 10 mg

Potent and selective NLRP3 inflammasome inhibitor.

LIT: A small-molecule inhibitor of the NLRP3 inflammasome for the treatment of inflammatory diseases: R.C. Coll, et al.; Nat. Med. **21,** 248 (2015)

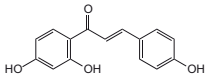


Isoliquiritigenin LATEST INSIGHT

AG-CN2-0459 10 mg | 50 mg

Inhibits NLRP3-activated Asc oligomerization. Blocks priming and activation step.

LIT: Isoliquiritigenin is a potent inhibitor of NLRP3 inflammasome activation and diet-induced adipose tissue inflammation: H. Honda, et al.; J. Leukoc. Biol. **96,** 1087 (2014)

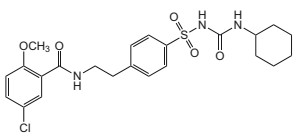


Glyburide (USP)

AG-CR1-3613 1 g | 5 g | 10 g

NLRP3 inflammasome inhibitor.

LIT: A small-molecule inhibitor of the NLRP3 inflammasome for the treatment of inflammatory diseases: R.C. Coll, et al.; Nat. Med. **21,** 248 (2015)

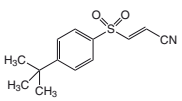


BAY 11-7082

AG-CR1-0013 10 mg | 50 mg

NLRP3 inflammasome inhibitors, reducing ATPase activity of the NLRP3 inflammasome.

LIT: Anti-inflammatory compounds parthenolide and Bay 11-7082 are direct inhibitors of the inflammasome: C. Juliana, et al.; J. Biol. Chem. **285,** 9792 (2010)



Parthenolide

AG-CN2-0455 10 mg | 50 mg | 250 mg

NLRP3 inflammasome inhibitors, reducing ATPase activity of the NLRP3 inflammasome.

LIT: Anti-inflammatory compounds parthenolide and Bay 11-7082 are direct inhibitors of the inflammasome: C. Juliana, et al.; J. Biol. Chem. **285,** 9792 (2010)

Arglabin LATEST INSIGHT

AG-CN2-0458 1 mg | 5 mg

NLRP3 inflammasome inhibitor.

LIT: Anti-Inflammatory and antiatherogenic effects of the NLRP3 Inflammasome inhibitor Arglabin in ApoE2.Ki mice fed a high-fat diet: A. Abderrazak, et al.; Circulation **131,** 1061 (2015)

Vinpocetine

AG-CN2-0454 20 mg | 100 mg

NLRP3 inflammasome inhibitor.

LIT: Vinpocetine inhibits amyloid-beta induced activation of NF-κB, NLRP3 inflammasome and cytokine production in retinal pigment epithelial cells: R.T. Liu, et al.; Exp. Eye Res. **127,** 49 (2014)

3-Hydroxybutyric acid LATEST INSIGHT

AG-CR1-3616 (R)-3-Hydroxybutyric acid 25 mg | 100 mg
AG-CR1-3617 (S)-3-Hydroxybutyric acid 25 mg | 100 mg

NLRP3 inflammasome inhibitors. Prevent K^+-efflux and consequently reduce Asc oligomerization and speck formation.

LIT: The ketone metabolite β-hydroxybutyrate blocks NLRP3 inflammasome-mediated inflammatory disease: Y.H. Youm, et al.; Nat. Med. **21,** 263 (2015)

Resveratrol

AG-CN2-0033 50 mg | 100 mg | 500 mg

NLRP3 inflammasome inhibitor.

LIT: Resveratrol inhibits NLRP3 inflammasome activation by preserving mitochondrial integrity and augmenting autophagy: Y.P. Chang, et al.; J. Cell Physiol. **230,** 1567 (2015)

Flagellin – NLRC4/NAIP5 Inflammasome Activators

THE SOURCE

Toll-like receptor 5 (TLR5) recognizes **flagellin** from both Gram-positive and Gram-negative bacteria. Activation of the receptor stimulates the production of proinflammatory cytokines, such as TNF-α, through signaling via the adapter proteins MyD88, TIRAP and TRIF. Flagellin is the subunit protein which polymerizes to form the filaments of bacterial flagella. It activates the innate immune system not only through the TLR5, but also through the intracellular NAIP5/NLRC4 (IPAF) inflammasome protein.

AdipoGen Life Sciences offers different types of **low endotoxin** and **high purity flagellins,** including pathway specific mutants. The Flagellin (NLRC4 Mutant) (rec.) (Prod. No. AG-40B-0126) is only detected by TLR5 not by NLRC4, whereas the Flagellin (TLR5 Mutant) (rec.) (Prod. No. AG-40B-0127) is only detectd by NLRC4.

PRODUCT NAME	PID	SIZE
Flagellin	AG-40B-0095	100 µg
Flagellin (high purity)	AG-40B-0025	10 µg | 3 x 10 µg
Flagellin (rec.)	AG-40B-0125	10 µg | 3 x 10 µg
NEW **Flagellin (NLRC4 Mutant) (rec.)**	AG-40B-0126	10 µg | 3 x 10 µg
NEW **Flagellin (TLR5 Mutant) (rec.)**	AG-40B-0127	10 µg | 3 x 10 µg

Inflammasomes – Therapeutic Implications

IL-1β is a key player in the inflammatory response, moving inflammatory caspases and inflammasomes in an important role in several diseases (see FIGURE). Several human hereditary or acquired diseases have been linked to elevated IL-1β, some of which can be treated by antagonists against IL-1β or its receptor. A number of diseases, known as cryopyrin-associated periodic syndromes (CAPS), have been directly linked to NLRP3 mutations.

Gout, an autoinflammatory disease characterized by severe joint inflammation, as well as the development of type 2 diabetes mellitus (T2DM) and insulin resistance are associated to elevated IL-1β levels. Thus by functioning as a sensor for metabolic stress, like in the form of monosodium urate (MSU) or hyperglycemia, the NLRP3 inflammasome likely contributes to the pathogenesis of gout or T2DM, respectively. In addition, several cancers have been associated to inflammasome-dependent inflammatory processes. Several inflammasome regulators (e.g. pyrin) were shown to have a significant relevance in diseases and may allow novel entry points for disease treatment.

SELECTED LATEST REVIEW ARTICLES: Inflammasomes: mechanism of action, role in disease, and therapeutics: H. Guo, et al.; Nat. Med. **21,** 677 (2015) • Targeting the NLRP3 inflammasome in chronic inflammatory diseases: current perspectives: E. Ozaki, et al.; J. Inflamm. Res. **8,** 15 (2015) • NOD-Like Receptors: Master Regulators of Inflammation and Cancer: M. Saxena & G. Yeretssian; Front. Immunol. **5,** 327 (2014)

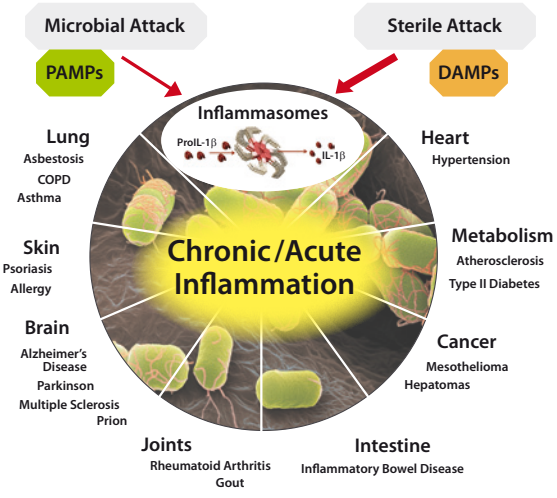


FIGURE: Overview on inflammasome-associated diseases.

LATEST INSIGHT

NLRP3 goes beyond the inflammasome

M. Bruchard, et al. (2015) recently demonstrated inflammasome-independent transcriptional functions for NLRP3, in which NLRP3 was able to interact with IRF4 and with DNA in $CD4^+$ T cells to control TH2 polarization. NLRP3 expression in $CD4^+$ T cells was shown to have physiological relevance in asthma and cancer by favoring TH2 polarization, asthma development and TH2 cell-dependent tumor growth.

LIT: The receptor NLRP3 is a transcriptional regulator of TH2 differentiation: M. Buchard, et al.; Nature Immunol. **16,** 859-870 (2015)

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