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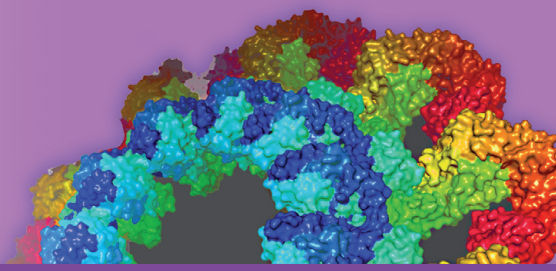
LIFE SCIENCES



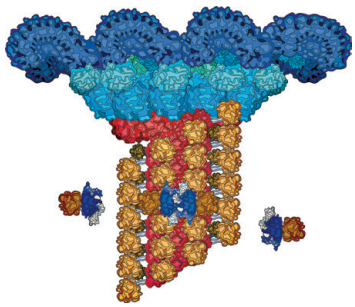
曜鴻生物科技有限公司
Yao-Hong Biotechnology Inc.

THE EXPERT IN

3rd Edition

Inflammasome Research

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 maturation of the cytokines IL-1β and IL-18, and the processing of gasdermin D to mediate cytokine release and pyroptosis 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), **NLRP10** (NALP10), **NLRP12** (NALP12), **Pyrin**, **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)**. For details see our **NLRP3 Inflammasome Wallchart**.

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

The NLRP3 inflammasome: activation and regulation: J. Xu & G. Nunez; Trends Biochem. Sci. **48,** 331 (2023) • How location and cellular signaling combine to activate the NLRP3 inflammasome: A. Akbal, et al.; Cell. Mol. Immunol. **19,** 1201 (2022) • Inflammatory Caspases: Toward a Unified Model for Caspase Activation by Inflammasomes: C. Ross, et al.; Annu. Rev. Immunol. **40,** 249 (2022)

Most Trusted NLRP3 Antibody

THE STANDARD

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.

Over 1000 citations!

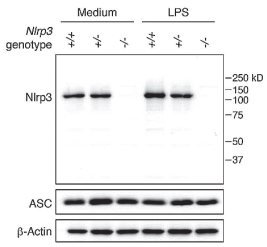


FIGURE: Mouse NLRP3 is detected in mouse macrophages using the monoclonal antibody to NLRP3 (Cryo-2) (Prod. No. AG-20B-0014).

Inflammasome Tools

Specific Caspase-1 Detection with KO-Validated Monoclonal Antibodies

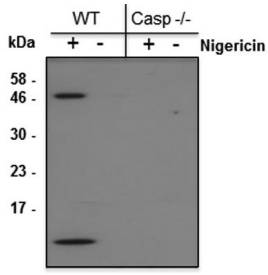
Detection of Activated Mouse p10 & p20 Caspase-1 by Western Blot (WB)

THE STANDARD 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.

FIGURE: Mouse caspase-1 (p10) is detected by immunoblotting using anti-Caspase-1 (p10) (mouse), mAb (Casper-2) (Prod. No AG-20B-0044) in supernatants of differentiated bone marrow-derived dendritic cells (BMDCs) from wild-type and caspase-1-/- mice activated or not by 5 µM nigericin (Prod. No. AG-CN2-0020) for 30 min.

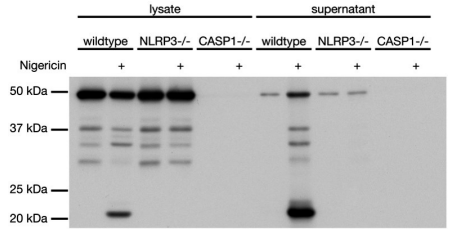


THE STANDARD anti-Caspase-1 (p20) (mouse), mAb (Casper-1)

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 (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.



Detection of Activated Human p20 Caspase-1 by Western Blot (WB)

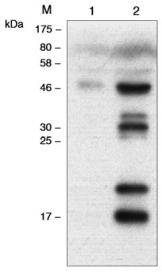
THE STANDARD anti-Caspase-1 (p20) (human), mAb (Bally-1)

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: 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.



Quantitative Measurement of Inflammasome Activation – Caspase-1

A quantitative detection method, alternative to Western blotting, to measure inflammasome activation leading to caspase-1 cleavage and secretion. Learn how to measure inflammasome activation at www.adipogen.com/inflammasomes.

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

AdipoGen® LIFE SCIENCES

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

Key Standard Inflammasome Antibodies

AL177 – Best Tool to measure Asc Specks!

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 cell extracts.

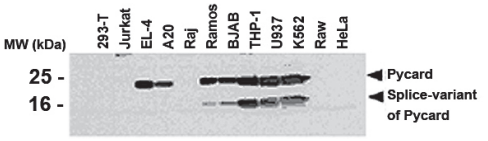


FIGURE: Western blot analysis of human and mouse cell lines using anti-Asc, pAb (AL177) (Prod. No. AG-25B-0006). Total protein extracts from various human (293-T, Jurkat, Raj, Ramos, BJAB, THP-1, U937, K562, Raw, HeLa) and mouse (EL-4, A20) cell lines were run on SDS-PAGE and Pycard detected by anti-Asc,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

Asc Antibody (AL177) Blocking Peptide

AG-37B-0001-C100 100 µg

Asc (AL177) Antibody + Blocking Peptide Set

AG-44B-2000-KI01 1 Set

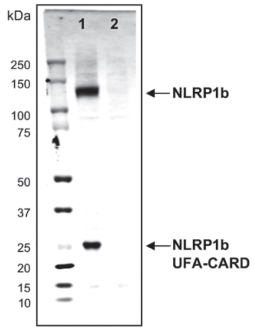
See below for important Asc Protocols & References.

NLRP1 – A New Inflammasome Player

anti-NLRP1b (mouse), mAb (2A12)

AG-20B-0084-C100 100 µg
Application WB

FIGURE: Mouse NLRP1b (mouse) (full-length and UFA-CARD fragment) is detected in cell extracts (about 30 µg) from the mouse cells Raw264.7 (lane 1) or Raw264.7 NLRP1b KO (lane 2) using NLRP1b, mAb (2A12) (Prod. No. AG-20B-0084).



LIT: Functional degradation: a mechanism of NLRP1 inflammasome activation by diverse pathogen enzymes: A. Sandstrom, et al.; Science **364,** eaau1330 (2019)

NLRP3 mAb – See Frontpage.

ZBP1 – Regulator of NLRP3 and Interferon

anti-ZBP1, mAb (Zippy-1)

AG-20B-0010-C100 100 µg
Application ICC, IP, WB

The dsRNA-binding protein ZBP1 is a key factor in interferon biology involved in viral infection and inflammation regulation. It activates the NLRP3 inflammasome, the IFN pathway and different programmed cell deaths regulated by the PANoptosome complexes. Recent studies show that the RNA-editing enzyme ADAR1 prevents ZBP1 activation.

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

Important Protocols for Inflammasome Research:

PROTOCOLS FOR AL177: Measuring inflammasome activation in response to bacterial infection: P. Broz & D.M. Monack; Methods Mol. Biol. **1040,** 65 (2013) • Measuring NLR Oligomerization II: Detection of ASC Speck Formation by Confocal Microscopy and Immunofluorescence: M. Beilharz, et al.; Methods Mol. Biol. **1417,** 145 (2016) • Cell-Free Assay for Inflammasome Activation: Y. Jamilloux & F. Martinon; Methods Mol. Biol. **1417,** 207 (2016) • Instructions for Flow Cytometric Detection of ASC Specks as a Readout of Inflammasome Activation in Human Blood: N. Wittmann, et al.; Cells **10,** 2880 (2021) • ASC Speck Formation after Inflammasome Activation in Primary Human Keratinocytes: N. Smatlik, et al.; Oxid. Med. Cell Longev. **2021,** 7914829 (2021)

PROTOCOLS FOR CASPER-1, CASPER-2, BALLY-1 AND CRYO-2: Measuring the inflammasome: O. Gross; Methods Mol. Biol. **844,** 199 (2012) • Immunoblotting for active caspase-1: C. Jakobs, et al.; Methods Mol. Biol. **1040,** 103 (2013) • Measuring NLR Oligomerization I: Size Exclusion Chromatography, Co-immunoprecipitation, and Cross-Linking: S. Khare, et al.; Methods Mol. Biol. **1417,** 131 (2016) • Assessing Caspase-1 Activation: B. Guey & V. Petrilli; Methods Mol. Biol. **1417,** 197 (2016) • Cell-Free Assay for Inflammasome Activation: Y. Jamilloux & F. Martinon; Methods Mol. Biol. **1417,** 207 (2016)

Other 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
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 (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
Cytosolic Bacteria Sensor					
anti-Pyrin (human), pAb (AL196)	AG-25B-0020	100 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

Quantitative Measurement of Inflammasome Activation – IL-1β

NEW IL-1β (human) ELISA Kit

AG-45B-0021-KI01 96 wells

Isotype Mouse IgG
Specificity Detects human IL-1β.
Species Reactivity Human
Sensitivity 0.7 pg/ml
Range 1.5625 to 100 pg/ml
Assay Type Colorimetric/Sandwich
Sample Type Cell Culture Supernatant, Serum, Plasma

IL-1β is produced in its inactive 35kDa pro-form following priming signals, such as pathogen- or damage-associated molecular patterns (PAMPs or DAMPs) and is subsequently cleaved to its 17kDa active form following inflammasome activation in damaged or diseased states. Active IL-1β has known roles in initiating and propagating sterile inflammation, including macrophage recruitment, activation of the pro-inflammatory cytokine interleukin-6 (IL-6) and modulating chemokine expression.

Our new IL-1β (human) ELISA Kit detects full-length and cleaved human IL-1β in biological fluids with high sensitivity and specificity.

Best Antibody to Detect Cleaved mouse IL-1α (p18) by WB

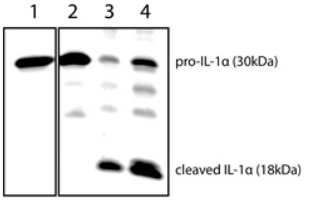
NEW anti-IL-1α (p18) (mouse), mAb (Teo-1)

AG-20B-0064-C100 100 µg

Isotype Mouse IgG
Application WB (1µg/ml)
Specificity Recognizes mouse IL-1α p18 cleaved and full-length fragments.

FIGURE: Mouse IL-1α (full-length p30 and cleaved p18 fragments) are detected by immunoblotting using anti-IL-1α (p18) (mouse), mAb (Teo-1) (Prod. No AG-20B-0064).

METHOD: IL-1α is analyzed by Western blot in cell extracts and supernatants of bone marrow-derived dendritic cells (BMDCs) treated with LPS and several inflammasome activators as indicated. Cell extracts and supernatants were separated by SDS-PAGE under reducing conditions, transferred to nitrocellulose and incubated with anti-IL-1α (p18) (mouse), mAb (Teo-1) (1µg/ml). After addition of an anti-mouse secondary antibody coupled to HRP, proteins were visualized by a chemiluminescence detection system.



1: Lysate of LPS-primed BMDCs
2: Supernatant of LPS + ATP treated BMDCs
3: Supernatant of LPS + Nigericin treated BMDCs
4: Supernatant of LPS + MSU treated BMDCs

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

Priming and Activation of the NLRP3 Inflammasome

NLRP3 is a key component of the inflammasome complex and plays a critical role in the regulation of inflammation. NLRP3 responds to a broad repertoire of stimuli, allowing it to combat a range of viral and bacterial infections such as adenovirus, influenza, Coronavirus, Staphylococcus aureus, Salmonella typhimurium, Listeria monocytogenes and Mycobacterium. These pathogenic stimuli (PAMPs) as well as some other non-pathogenic stimuli (DAMPs) are able to enhance NLRP3 inflammasome activation through a two-step process: priming and activation/triggering.

Signal 1: Priming

Priming serves at least two functions: i) To upregulate the expression of the inflammasome components NLRP3, caspase-1 and pro-IL-1β. This transcriptional upregulation can be induced through the recognition of various pathogen-associated molecular patterns (PAMPs) or damage-associated molecular patterns (DAMPs) that engage pattern-recognition receptors (PRRs) such as Toll-like receptors (TLRs) or nucleotide-binding oligomerization domain-containing protein 2 (NOD2), or through cytokines such as tumor necrosis factor (TNF) and IL-1β that lead to nuclear factor-κB (NF-κB) activation and gene transcription; ii) To induce posttranslational modifications (PTMs) of NLRP3, which stabilize NLRP3 in an auto-suppressed inactive, but signal-competent state. Multiple PTMs have been described for NLRP3, including ubiquitylation, phosphorylation and sumoylation.

Signal 2: Activation/Triggering

Unlike other Pattern Recognition Receptors (PPRs), NLRP3 is activated by a wide variety of unrelated stimuli triggered by bacterial, viral and fungal infections, and in sterile inflammation mediated by endogenous DAMPs and on exposure to environmental irritants. The unifying factor of these activators is that they all induce cellular stress that is sensed by NLRP3. NLRP3 activation involves multiple upstream signals, most of which are not mutually exclusive, including efflux of potassium ions (K^+) or chloride ions (Cl^-), flux of calcium ions (Ca^{2+}), lysosomal disruption, mitochondrial dysfunction, metabolic changes and trans-Golgi disassembly.

The actual activation of the NLRP3 inflammasome is thought to occur through the assembly of the inflammasome complex in response to specific stimuli, such as the presence of pathogen-associated molecular patterns (PAMPs) or the accumulation of danger-associated molecular patterns (DAMPs) signals, such as ATP, uric acid crystals or reactive oxygen species (ROS). Once the inflammasome complex is formed, it activates caspase-1, which cleaves pro-IL-1β and pro-IL-18 into their active forms, leading to the release of these cytokines and the initiation of an immune response. In addition, posttranslational modifications (PTMs) are essential regulators of NLRP3 activation. PTMs influence many aspects of protein function including their activity, degradation, localization, structure, and interactions with other proteins.

SELECTED REVIEW ARTICLES: An update on the regulatory mechanisms of NLRP3 inflammasome activation: S. Paik, et al.; Cell Mol. Immunol. **18,** 1141 (2021) • Mechanisms of NLRP3 priming in inflammaging and age related diseases: A. Gritsenko, et al.; Cytokine Growth Factor Rev. **55,** 15 (2020) • NLRP3 inflammasome priming: A riddle wrapped in a mystery inside an enigma: C.M. McKee & R.C. Coll; J. Leukoc. Biol. **108,** 937 (2020)

Inflammasome "Priming" Activators

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. The synthesis of pro-IL-1β can be induced by many stimuli including TLR ligands and cytokines such as TNF.

LPS, through signaling via TLR4, was and remains the most commonly used ligand to induce pro-IL-1β production due to its potency and ready availability.

In addition, LPS stimulation triggers many of the changes in NLRP3 post-translational modifications (PTMs), such as ubiquitination, a key step of the NLRP3 priming process.

FOR DETAILS SEE: Inflammasome Priming in Sterile Inflammatory Disease: M.N. Patel, et al.; Trends Mol. Med. **23,** 165 (2017) • 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)

Phorbol 12-myristate 13-acetate [PMA]
AG-CN2-0010

TNF-α, Soluble (human) (rec.)
AG-40B-0006

TNF-α (human) (multimeric) (rec.)
AG-40B-0019

TNF-α (mouse) (multimeric) (rec.)
AG-40B-0021

Lipopolysaccharides (LPS)

For a full panel see our Innate Immunity Brochure

Priming Step of Inflammasome Activation – Simple and Convenient!

Discover our Panel of ready-to-use LPS Solutions for Inflammasome Priming Activation. Do not bother anymore to solubilize your LPS, choose and use AdipoGen Life Sciences' homogenous ready-to-use LPS solutions.

Regulation of NLRP3 Inflammasome by PTMs & Protein Binding

NLRP3 is a cytosolic pattern recognition receptor that plays a key role in the regulation of inflammation. The priming and activation of NLRP3 is controlled by a number of post-translational modifications (PTMs) (see below). This is only an overview and not meant to be complete.

1. Phosphorylation:

Phosphorylation regulates NLRP3 activity and is essential to the priming process. NLRP3 is phosphorylated: i) at Ser198 (Ser194 in mouse) by C-Jun N-terminal kinase 1 (JNK1) to facilitate NLRP3 deubiquitination and oligomerization, ii) at four tyrosine residues in the PYD-NACHT polybasic linker, including Tyr132, Tyr136, Tyr145 and Tyr164 by Bruton tyrosine kinase (BTK) to charge neutralization of the polybasic region peptide sequence, to relocalize from intact trans-Golgi network (TGN) to dispersed TGN and to help NLRP3 inflammasome assembly, iii) at Ser5 by AKT or BTK to restrict Asc binding to NLRP3 and inflammasome activation, this step is reversed by the phosphatase PP2A; iv) at Ser295 in human (Ser293 in mouse) by PKD to allow NLRP3 to be released from Golgi to be activated and by PKA to turn off the ATPase activity of NLRP3. Protein tyrosine phosphatase non-receptor type 22 (PTPN22) interacts with and dephosphorylates NLRP3 at Tyr861, a site phosphorylated by a still unknown kinase.

2. Ubiquitination:

The ubiquitination and deubiquitination of NLRP3 has been shown to regulate its stability and activity. Signaling through TLR4 and MyD88 triggers deubiquitination of NLRP3 to induce inflammasome activation. Deubiquitinating enzymes (DUBs) play a vital role in NLRP3 regulation as small molecule inhibitors of DUBs completely block NLRP3 activation. Deubiquitination of the leucine rich repeat (LRR) domain of NLRP3 by BRCC3 is necessary for NLRP3 oligomerization. FBXL2 ubiquitinates the LRR domain of NLRP3 to promote its proteasomal degradation. ARIH2 binds to the NLRP3 NACHT domain to induce K48-linked ubiquitination and subsequent proteasome-mediated degradation of NLRP3. K48-linked ubiquitination of the NLRP3 LRR domain by the E3 ubiquitin ligase MARCH7 induces NLRP3 degradation via autophagy.

3. Sumoylation:

The sumoylation of NLRP3 has been shown to regulate its stability and function. NLRP3 is sumoylated by the small ubiquitin-like modifier (SUMO) E3 ligase MUL1/MAPL and is desumoylated by SENP6 and SENP7 in response to NLRP3 activation signals. Sumoylation can also be activating, as sumoylation by SUMO1 is necessary for NLRP3 activation and desumoylation mediated through SENP3 attenuates activation. Importantly, LPS priming does not appear to affect NLRP3 sumoylation.

Other PTMs also include acetylation (activation, NLRP3 aggregation and association with ASC) or nitrosylation (negative regulator of NLRP3).

Overall, PTMs on NLRP3, Asc or Caspase-1 play a critical role in regulating the activity of NLRP3 and its role in the regulation of inflammation. In addition to transcriptional and posttranslational regulation mechanisms, NLRP3 priming and activation is both, positively and negatively, influenced by several protein binding partners. This includes NIMA-related kinase 7 (NEK7), a serine-threonine kinase, which is a critical component in NLRP3 inflammasome assembly and activation, the PYD-only proteins (POPs), which are small cytoplasmic decoy proteins that regulate inflammasome activation, or CARD-only proteins (COPs), with unclear mechanisms, both in human cells only.

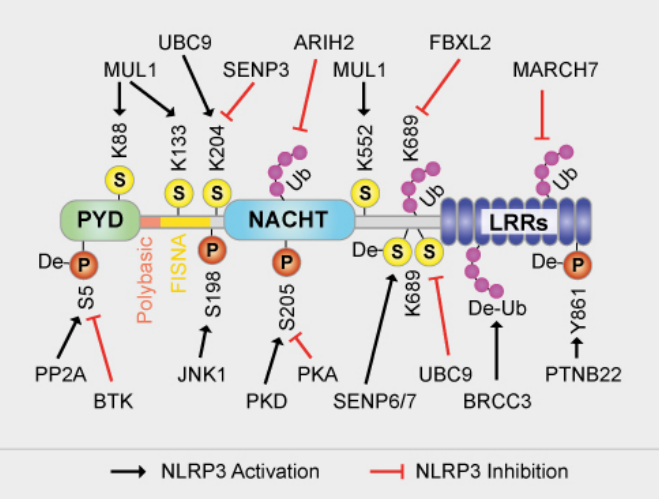


FIGURE: Molecular Structure and Posttranslational Modifications of human NLRP3.

SELECTED REVIEW ARTICLES: The Role of Post-Translational Modifications in Regulation of NLRP3 Inflammasome Activation: J. Xia, et al.; Int. J. Mol. Sci. **24,** 6126 (2023) • Regulation of the NLRP3 Inflammasome by Posttranslational Modifications: S. Zangiabadi & A.A. Abdul-Sater; J. Immunol. **208,** 286 (2022) • PHOrming the inflammasome: phosphorylation is a critical switch in inflammasome signalling: C.M. McKee, et al.; Biochem. Soc. Trans. **49,** 2495 (2021)

Targeting NLRP3 Priming & PTMs

NLRP3 is an attractive target for the development of new anti-inflammatory therapies. Small molecule direct inhibitors of NLRP3 show very promising results. However, there are many other proteins, which are involved in NLRP3 priming (transcriptionally and post-translationally), that could be targeted to prevent NLRP3-driven inflammation.

Selected Small Molecules

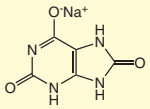
PRODUCT NAME	TARGET	PID
SP 600125	JNK Inhibitor	AG-CR1-3549
CRT0066101 HCl	PDK Inhibitor	AG-CR1-3550
Okadaic acid	PP2A Inhibitor	AG-CN2-0056
WP1130	DUB Inhibitor	AG-CR1-3551
b-AP15	DUB Inhibitor	AG-CR1-3552

Key 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)

N-Acetyl-D-glucosamine
AG-CN2-0489 250 mg | 1 g | 5 g

Acts as a new activator of NLRP3 inflammasome by dissociating the enzyme hexokinase from the mitochondria.

LIT: Hexokinase is an innate immune receptor for the detection of bacterial peptidoglycan: A.J. Wolf, et al.; Cell **166,** 624 (2016)

NLRP3 Inflammasome Inhibitors

Arglabin
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)

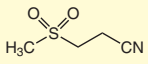
BAY 11-7082
AG-CR1-0013 10 mg | 50 mg

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)

Dapansutrile **BULK AVAILABLE**
AG-CR1-3535 10 mg | 50 mg | 250 mg

Potent, selective and orally active inhibitor of the NLRP3 inflammasome, directly binding to the ATP-binding motif of NLRP3 NACHT domain.



LIT: NLRP3 inflammasome inhibitor OLT1177® suppresses joint inflammation in murine models of acute arthritis: C. Marchetti, et al.; Arthritis Res. Ther. **20,** 169 (2018)

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)

3-Hydroxybutyric acid
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)

Isoliquiritigenin
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)

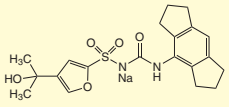
K777 [K11777]
AG-CR1-0158 1 mg | 5 mg

Broad-range cathepsin inhibitor useful for inflammasome inhibition.

LIT: Multiple cathepsins promote inflammasome-independent, particle-induced cell death during NLRP3-dependent IL-1beta activation: G.M. Orlowski, et al.; J. Leukoc. Biol. **102,** 7 (2017)

MCC950 . Na **BULK AVAILABLE**
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)

Prostaglandin E2
AG-CL1-0001 1 mg | 5 mg

Inhibits the NLRP3 ATPase activity, which is required for assembly of the NLRP3-Asc inflammasome complex.

LIT: Prostaglandin E2 Inhibits NLRP3 Inflammasome Activation through EP4 Receptor and Intracellular Cyclic AMP in Human Macrophages: M. Sokolowska, et al.; J. Immunol. **194,** 5472 (2015)

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

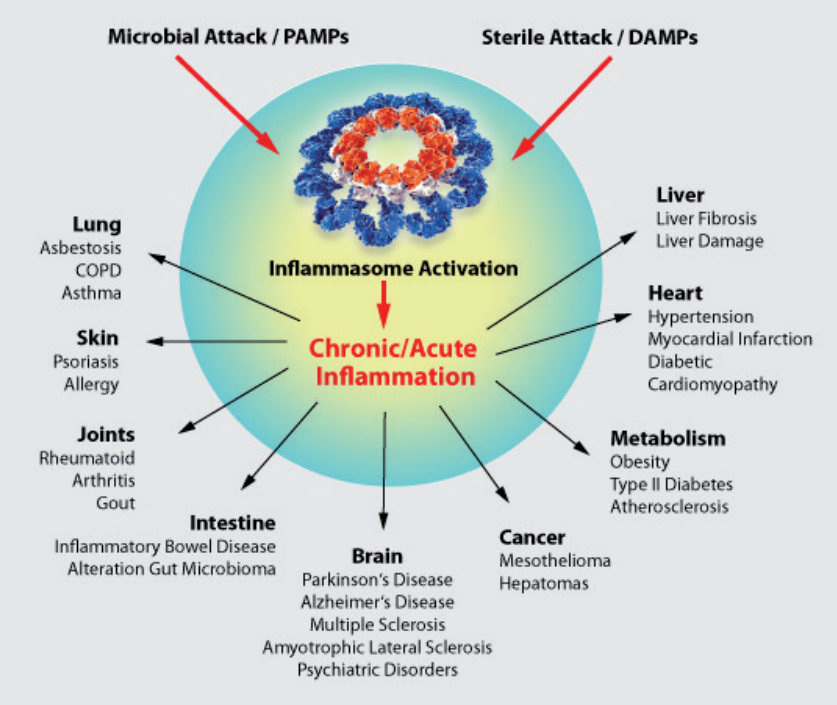
NLRP3 inflammasome inhibitors, reducing ATPase activity of the NLRP3 inflammasome.

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)

Inflammasomes & Their Therapeutic Implications

Aberrant inflammasome activation is implicated in chronic inflammation that leads to the development of many diseases as they play a crucial role in regulating the immune response and the production of pro-inflammatory cytokines. Targeting inflammasomes has become a promising strategy for the treatment of a variety of diseases, including inflammatory diseases (such as arthritis, gout or inflammatory bowel disease), autoimmune diseases (such as lupus or multiple sclerosis), metabolic diseases (such as Type II Diabetes, Obesity or Cardiovascular diseases), cancer, or neurodegenerative diseases. New studies also implicate the NLRP3 inflammasome in other diseases, such as viral infections, sepsis and more.

Inhibiting inflammasome activation or targeting inflammasome components have been shown to be effective in reducing inflammation in animal models of these diseases. Overall, targeting inflammasomes has great therapeutic potential for a variety of diseases and is a promising strategy for the development of new treatments.



SELECTED LATEST REVIEW ARTICLES: Inhibitors of the NLRP3 inflammasome pathway as promising therapeutic candidates for inflammatory diseases: X. Zhang, et al.; Int. J. Mol. Med. **51,** 35 (2023) • Pharmacological Inhibition of the NLRP3 Inflammasome: Structure, Molecular Activation, and Inhibitor-NLRP3 Interaction: Q. Ma; Pharmacol. Rev. **75,** 487 (2023) • Focus on the Role of NLRP3 Inflammasome in Diseases: R. Fusco, et al.; Int. J. Mol. Sci. **21,** 4223 (2020)

Inflammasomes & Metabolic Regulation

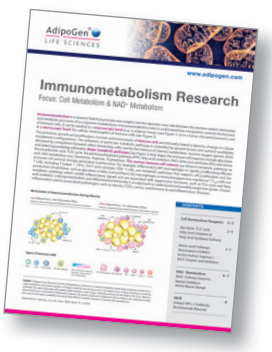
Immunometabolism refers to the study of how metabolic processes and pathways within immune cells influence their function. When immune cells are activated during an inflammatory response, they undergo significant metabolic changes to support their increased energy demands. These changes involve a switch from oxidative phosphorylation to glycolysis, which generates energy more quickly but is less efficient. Inflammasomes are tightly regulated by changes in intracellular metabolic pathways. Recent research has shown that manipulating immunometabolism can modulate the immune response, reduce inflammasome activity and reduce inflammation. Promoting the metabolism of fatty acids or blocking glycolysis in immune cells has been shown to promote an anti-inflammatory response.

SELECTED REVIEW ARTICLES: The NLRP3 inflammasome: regulation by metabolic signals: A. Olona, et al.; Trends Immunol. **43,** 978 (2022) • Targeting immunometabolism as an anti-inflammatory strategy: E.M. Palsson-McDermott & L. O'Neill; Cell Res. **30,** 300 (2020)

Selected Small Molecules

PRODUCT NAME	TARGET	PID
2-Deoxy-D-glucose	Hexokinase Inhibitor	AG-CR1-3681
Dimethyl fumarate	Nrf2 Activator	AG-CR1-3701
Heptelidic acid	GADPH Inhibitor	AG-CN2-0118
Metformin . HCl	ROS Inhibitor	AG-CR1-3689
Rapamycin	mTOR Inhibitor	AG-CN2-0025
TEPP-46	PKM2 Activator	AG-CR1-3687

Ask for our Immunometabolism Research Brochure



Microtubules & Inflammasome Complex Assembly

Microtubules, are cytoskeleton components that are crucial in innate immunity in addition to their general roles in cell division, migration, and morphology. Inflammasomes are assembled from a pattern-recognition receptor, the adapter protein Asc and caspase-1 to process interleukin-1β and IL-18 in response to PAMPs or DAMPs. After priming, NLRP3 is expressed and binds to the intracellular membrane of endoplasmic reticulum and Trans Golgi Network (TGN) and assemble into an oligomeric double-ring cages wrapping the PYD inside, which represents the inactive state. Upon activation, NLRP3 activators induce microtubule polymerization and acetylation. TGN vesicles and NLRP3 are dispersed and further transported to the microtubule-organizing center [MTOC] to engage NEK7 and form the pre-active inflammasome complex (without Asc and pro-Caspase-1) (see our Inflammasome Wallchart). The released oligomeric inactive NLRP3 cage travels from TGNs to MTOCs along microtubules via the HDAC6-Dynein motor machinery that binds to acetylated α-tubulin. The release of TGN vesicles via microtubules allow NLRP3 to be re-localized in the cytosol closer to mitochondria. As a result, Asc and pro-Caspase-1 molecules on the mitochondria come into close proximity and can interact with NLRP3 to form the active NLRP3 inflammasome complex. As indicated above, the acetylation of α-tubulin is crucial during the NLRP3 activation. As a proposed mechanism, NLRP3 activation leads to mitochondrial dysfunction, leading to accumulation of acetylated α-tubulin (see Figure for more detailed steps of the mechanism).

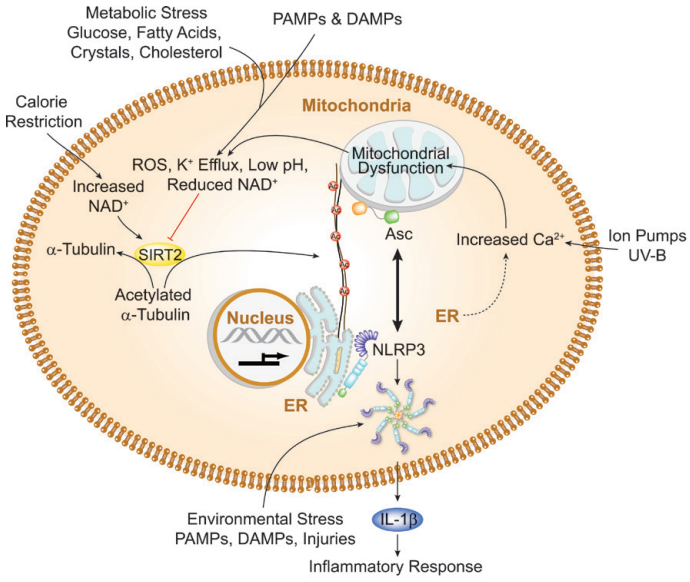


FIGURE: Accumulation of acetylated α-tubulin facilitates the assembly and activation of the inflammasome by opposing Asc on mitochondria to NLRP3 on the endoplasmic reticulum (ER).

LIT: NLRP3 cages revealed by full-length mouse NLRP3 structure control pathway activation: L. Andreeva, et al.; Cell **184,** 6299 (2021) • Caging NLRP3 tames inflammasome activity: K. Schroder & R.C Coll; Cell **184,** 6224 (2021)

UNIQUE

Microtubule Antibodies

PRODUCT NAME	PID	SIZE	SOURCE	APPLICATION
anti-α-Tubulin (acetylated), mAb (TEU318)	AG-20B-0068	100 µg	Mouse IgG1	ICC, WB
NEW **anti-Tubulin (glycylated), pAb (Gly-pep1)**	AG-25B-0034	100 µg	Rabbit	ICC, IP, WB
anti-Tubulin-GTP, mAb (rec.) (MB11)	AG-27B-0009	100 µg	Human IgG2λ	ICC
anti-β-Tubulin (β-monoE), pAb (IN115)	AG-25B-0039	50 µg	Rabbit	ICC, IHC, IP, 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

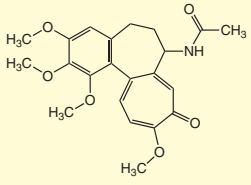
Small Molecule Cytoskeletal Modulators

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.



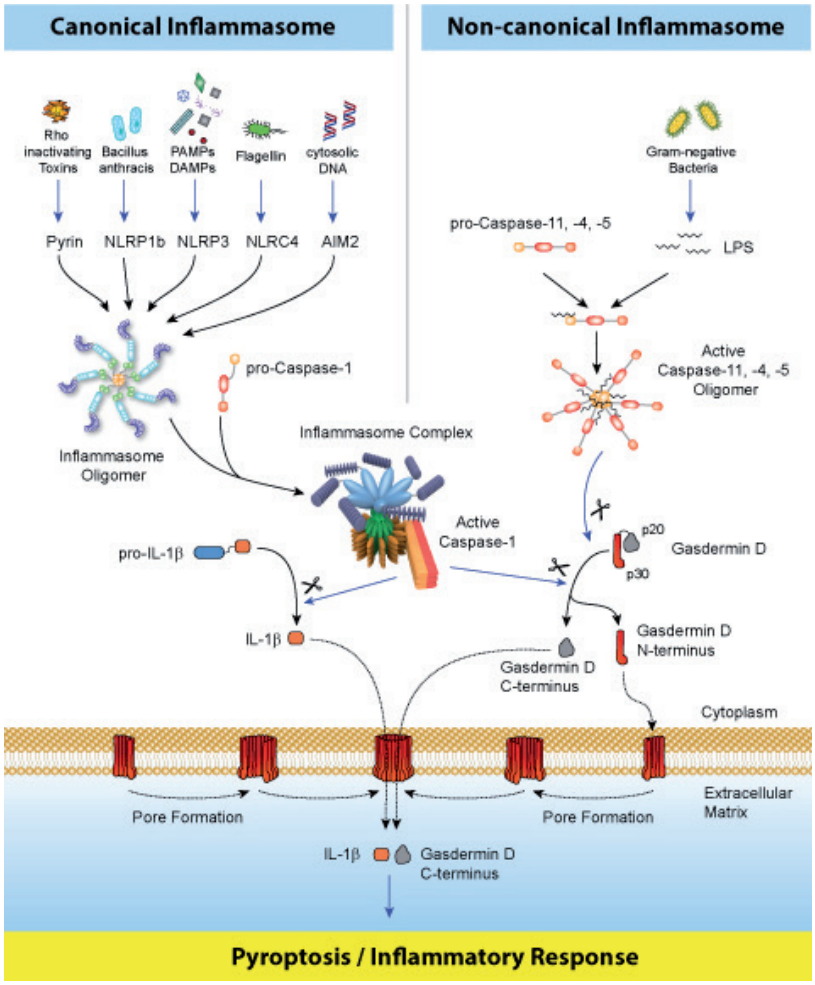
LIT: Microtubule-driven spatial arrangement of mitochondria promotes activation of the NLRP3 inflammasome: T. Misawa, et al.; Nat. Immunol. **14,** 454 (2013)

Dynasore	Dynamin Inhibitor	AG-CR1-0045
Jasplakinolide	F-actin Stabilization	AG-CN2-0037
Latrunculin A	F-actin 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
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

Gasdermin D Signaling – Crossroad between Inflammasome & Pyroptosis Research

Pyroptosis is an inflammatory programmed cell death that is initiated in response to pathogen- or host-derived perturbations of the cytosol. Upon activation of the inflammasome sensors, they activate caspase-1 and other inflammatory caspases that cleave gasdermin D and pro-IL-1β/pro-IL-18, leading to pyroptosis and mature cytokine secretion. Pyroptosis enables intracellular pathogen niche disruption and intracellular content release at the cost of cell death, inducing pro-inflammatory responses in the neighboring cells. IL-1β is a potent pro-inflammatory regulator for neutrophil recruitment, macrophage activation, and T cell expansion. Thus, pyroptosis and cytokine secretion are the two main mechanisms that occur downstream of inflammasome signaling; they maintain homeostasis, drive the innate immune response and shape adaptive immunity.

Gasdermin D (GSDMD) is a central mediator of pyroptotic cell death. It contains a functional N-terminal domain and an inhibitory C-terminal domain. Upon caspase-1/11 cleavage at Asp275 (mouse Asp276) in the interdomain linker located between the two domains of gasdermin D, the cleaved N-terminal fragment of gasdermin D oligomerizes and forms pores on the host cell membrane, leading to cell death called pyroptosis. In addition to inflammatory caspases, caspase-8, which is activated by cell surface death receptor ligation and oligomerization, can trigger GSDMD-dependent pyroptotic cell death.



SELECTED LATEST REVIEW ARTICLES: Uncoupled pyroptosis and IL-1β secretion downstream of inflammasome signaling: Y. Li & Q. Jiang; Front. Immunol. **14,** 1128358 (2023) • Molecular Mechanisms of Pyroptosis; J. Marisa, et al.; Methods Mol. Biol. **2641,** 1 (2023) • Gasdermins gone wild: new roles for GSDMs in regulating cellular homeostasis: C.G. Weindel, et al.; Trends Cell Biol. **(Epub ahead of print)** (2023) • Pyroptosis as a double-edged sword: The pathogenic and therapeutic roles in inflammatory diseases and cancers: Z. Liu, et al.; Life Sci. **318,** 121498 (2023)

UNIQUE

Gasdermin D C-Terminus (mouse-specific) Antibody

NEW **anti-Gasdermin D (mouse), pAb (IN110)**

AG-25B-0036 100 µg

Source	Guinea pig
Immunogen	Recombinant mouse gasdermin D (C-terminus).
Application	ELISA, WB
Specificity	Recognizes full-length and cleaved C-terminus domain of mouse gasdermin D. Does not cross-react with human gasdermin D.

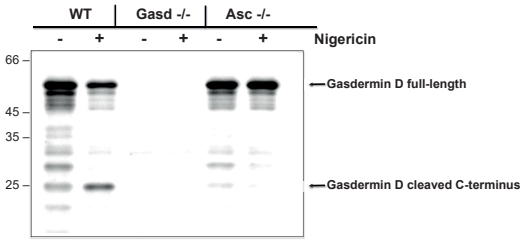


FIGURE: Mouse Gasdermin D (full-length and cleaved p22 fragments) are detected by immunoblotting using anti-Gasdermin D (mouse), pAb (IN110) (Prod. No. AG-25B-0036).

METHOD: Gasdermin D is analyzed by Western blot in cell extracts of bone marrow-derived macrophage cells (BMDMs) (WT, Gasdermin -/- or Asc -/-) treated with LPS (50ng/ml; Prod. No. AG-CU1-0001) for 3h and +/- Nigericin (5µM for 2.5h, Prod. No. AG-CN2-0020). Cell extracts are separated by SDS-PAGE under reducing conditions, transferred to nitrocellulose and incubated with anti-Gasdermin D (mouse), pAb (IN110) (0.5µg/ml). After addition of an anti-guinea pig secondary antibody coupled to HRP (1/5000), proteins are visualized by a chemiluminescence detection system.

Picture courtesy of Prof. Olaf Gross, University Medical Center Freiburg, Germany

AdipoGen® LIFE SCIENCES

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

New Tools to Measure Pyroptosis

UNIQUE

After formation of the pore at the cellular membrane by gasdermin D N-terminal fragment, the role and fate of the **C-terminus fragment** of gasdermin D is still unclear. Using the Gasdermin D (mouse) ELISA Kit (Prod. No. AG-45B-0011), **that detects the C-terminal part of gasdermin D** (as well as the full-length protein), a signal is detected in the **supernatant of cells** dying by pyroptosis, suggesting that the **C-terminal fragment** is released from cells, either by chance due to the presence of a pore or for a specific task not yet clear.

Gasdermin D (mouse) ELISA Kit

AG-45B-0011 — 96 wells

Detects full-length and cleaved C-terminal mouse gasdermin D in cell culture supernatants and cell extracts. Does not cross-react with human gasdermin D.

Sensitivity 14 pg/ml
Range 15.6 to 1000 pg/ml
Sample Cell Culture Supernatant, Cell Lysate

Specificity
Gasdermin D is tested from supernatants of Bone Marrow-Derived Macrophages cells (BMDMs) transfected with LPS from different knockout mice strains (see Figure 1). Only the supernatants from WT and NLRP3$^{-/-}$ strains contain the protein gasdermin D. Gasdermin D is also tested from cell extracts (lysed with a Triton X-100 buffer) of Bone Marrow-Derived Macrophages cells from WT and gasdermin D knockout mice strains (see Figure 2).

FIGURE 1

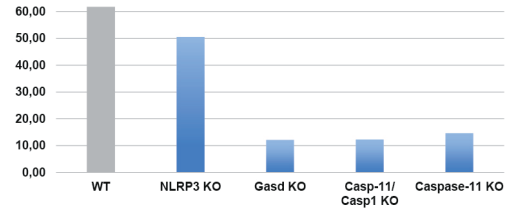
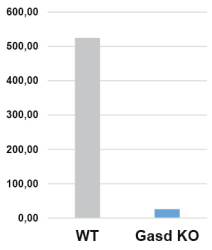


FIGURE 2 Cell extracts



Gasdermin D-induced Pyroptosis Inhibitors

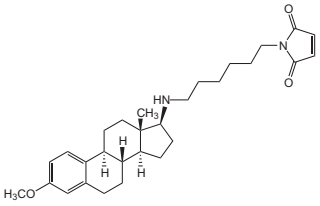
Acting as a gasdermin D N-terminal fragment (GSDMD-N)-induced pyroptosis inhibitor, U-73122 protects against GSDMD-N cytotoxicity in macrophages or against lethal infection in mice.

U-73122

AG-CR1-3698 — 1 mg | 5 mg

Formula $C_{29}H_{40}N_2O_3$
MW 464.6
CAS 112648-68-7

LIT: Lipid peroxidation drives Gasdermin D-mediated pyroptosis in lethal polymicrobial Sepsis: R. Kang, et al.; Cell Host Microbe **24,** 97 (2018)



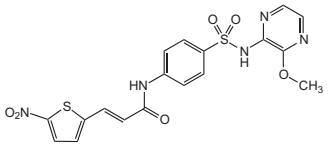
Acting as an inhibitor of gasdermin D that works well for mice studies, Necrosulfonamide binds directly to gasdermin D and inhibits the oligomerization of the N-terminus and therefore the pore formation and pyroptosis.

Necrosulfonamide

AG-CR1-3705 — 5 mg | 25 mg

Formula $C_{18}H_{15}N_5O_6S_2$
MW 461.5
CAS 1360614-48-7

LIT: Chemical disruption of the pyroptotic pore-forming protein gasdermin D inhibits inflammatory cell death and sepsis: J.K. Rathkey, et al.; Sci. Immunol. **3,** eaat2738 (2018)



Gasdermin E – A Pyroptosis Marker

Cleavage of gasdermin E (GSDME) by caspases-3/-7 liberates the N-terminal pyroptosis-inducing domain (GSDME-NT) from its autoinhibitory C-terminal regulatory domain to trigger membrane pores and pyroptosis. Mutations in GSDME in human are associated with development of heritable, nonsyndromal deafness. Abnormalities in pyroptotic cell deaths are associated with a range of human diseases including infections, autoinflammatory disease, neurodegenerative disease and cancer.

NEW **Gasdermin E (human) ELISA Kit**

AG-45B-0024 — 96 wells

Detects the **C-terminal domain** of human gasdermin E as well as the full-length protein. Upon cleavage of gasdermin E and pore formation, the **C-terminus fragment** is released in the extracellular space and is found in serum/plasma. The role of the **C-terminus fragment** of gasdermin protein family is unclear.

Sensitivity 50 pg/ml
Range 0.625 to 4 ng/ml
Sample Cell Culture Supernatant, Plasma, Serum

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.

Activation of the NLRC4 inflammasome and TLR5 by flagellin is an important mechanism for the initiation of the innate immune response to bacterial infections and plays a crucial role in the regulation of inflammation. Dysregulation of the NLRC4 inflammasome has been implicated in the development of a number of diseases, including sepsis, inflammatory bowel disease and certain types of cancer.

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 (native)	AG-40B-0095	100 µg
Flagellin (high purity) (native)	AG-40B-0025	10 µg | 3 x 10 µg
Flagellin (rec.) (His)	AG-40B-0125	10 µg | 3 x 10 µg
NEW **Flagellin (rec.) (untagged) (highly active)**	AG-40B-0243	50 µg
Flagellin (NLRC4 Mutant) (rec.)	AG-40B-0126	10 µg | 3 x 10 µg
Flagellin (TLR5 Mutant) (rec.)	AG-40B-0127	10 µg | 3 x 10 µg

LATEST INSIGHTS

New NLRP10 Activator

m-3M3FBS has been shown *in vitro* to trigger mitochondrial damage and activate NLRP10 (a bona fide inflammasome binding to Asc and Caspase-1) in keratinocytes. NLRP10 acts also as inflammasome in intestine epithelial cells and protects against autoinflammation in the gut.

m-3M3FBS

AG-CR1-3548 — 10 mg | 50 mg

LIT: Mitochondrial damage activates the NLRP10 inflammasome: T. Prochnicki, et al.; Nature Immunol. **24,** 595 (2023) • Epithelial Nlrp10 inflammasome mediates protection against intestinal autoinflammation: D. Zheng, et al.; Nature Immunol. **24,** 585 (2023)

AIM2 Inflammasome Inhibitor

Suramin has been shown to be an effective inhibitor of dsDNA-induced inflammation. Suramin inhibits several dsDNA-binding proteins, including the innate immune pathway cGAS/STING. Most recently mouse and human AIM2 inflammasome has been shown to be reversibly inhibited by Suramin.

Suramin . sodium

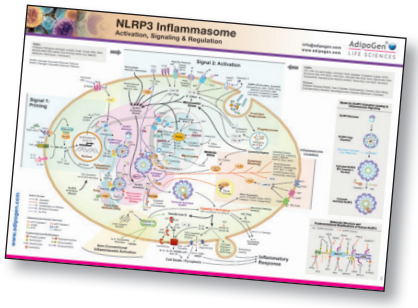
AG-CR1-3575V — 50 mg | 250 mg | 1 g

LIT: Discovery of an inhibitor of DNA-driven inflammation that preferentially targets the AIM2 inflammasome: J.P. Green, et al.; iScience **26,** 106758 (2023)

Wallchart

Ask for our Most Updated NLRP3 Inflammasome Activation, Signaling & Regulation Wallchart

or download at www.adipogen.com



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