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VARIOUS SOURCES OF INFLAMMASOME FORMATION: AN OVERVIEW

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ABSTRACT

Inflammasome are multipotent complexes that play a crucial role in the innate immune response by sensing a wide array of pathogenic and sterile stimuli. Upon activation, these cytosolic sensors initiate caspase-1 activation, leading to the maturation and secretion of pro-inflammatory cytokines such as interleukin-1β (IL-1β) and interleukin-18 (IL-18), and the induction of pyroptosis, an inflammatory form of cell death. Numerous inflammasome types have been identified, including NLRP3, NLRC4, AIM2, NLRP1, and Pyrin, each recognizing distinct triggers. These triggers originate from diverse sources such as pathogen-associated molecular patterns (PAMPs), damage-associated molecular patterns (DAMPs), environmental irritants, metabolic disturbances, and endogenous stress signals. For instance, bacterial toxins, viral nucleic acids, extracellular ATP, uric acid crystals, and mitochondrial dysfunction are well-established activators. Among these, the NLRP3 inflammasome is the most extensively studied due to its sensitivity to a broad spectrum of stimuli and its involvement in numerous inflammatory, autoimmune, and metabolic diseases. Understanding the various sources and mechanisms of inflammasome activation provides critical insights into host defense and disease pathogenesis. Furthermore, it opens new avenues for therapeutic interventions targeting aberrant inflammasome activity. This review provides a comprehensive overview of the known sources of inflammasome formation, highlighting their molecular mechanisms and clinical implications in health and disease.

INTRODUCTION

Inflammasomes are multiprotein complexes of the innate immune system that play a pivotal role in host defense and inflammation. By sensing a wide array of danger signals, they mediate the activation of caspase-1, leading to the maturation of interleukin-1β (IL-1β) and interleukin-18 (IL-18), as well as the induction of pyroptotic cell death. Since their discovery, inflammasomes have been recognized as central hubs linking microbial recognition, cellular stress, and tissue damage to inflammatory responses.[1,2] The sources of Inflammasome activation are diverse and can be broadly categorized into pathogen-associated molecular patterns (PAMPs), damage-associated molecular patterns (DAMPs), and environmental or chemical stimuli. While PAMPs are derived from invading microbes such as bacteria, viruses, fungi, and parasites, DAMPs include host-derived signals such as extracellular ATP, mitochondrial DNA, and crystalline deposits. Environmental particulates and xenobiotics can also act as triggers, highlighting the broad sensitivity of these complexes. Among, the different inflammasomes described to date, NLRP3 has emerged as the most versatile, responding to a wide spectrum of endogenous and exogenous stimuli.[3-5] Others, such as AIM2, NLRC4, NLRP1, and pyrin, exhibit more specific activation profiles.[6] Understanding the sources and mechanisms of inflammasome formation is critical, as dysregulated activation contributes to the pathogenesis of a wide range of inflammatory, metabolic, and neurodegenerative diseases etc.[7]

Overview of Inflammasomes

Inflammasomes are cytosolic multiprotein complexes that function as key components of the innate immune system, linking the detection of harmful stimuli to inflammatory and cell death pathways.[8] First described in 2002, they have been recognized as essential platforms for the activation of caspase-1, which processes the pro-inflammatory cytokines interleukin-1β (IL-1β) and interleukin-18 (IL-18), and mediates pyroptosis, a lytic form of programmed cell death.[9] These responses are critical for controlling infections, but excessive or inappropriate inflammasome activation can drive chronic inflammation and tissue damage.[10] At their core, inflammasomes consist of three main components: A sensor protein, usually a member of the Nod-like receptor (NLR) or AIM2-like receptor (ALR) families, that detects specific triggers. An adaptor protein, most commonly ASC (apoptosis-associated speck-like protein containing a CARD), which bridges the sensor to caspase-1.[11] An effector protease, caspase-1, which executes downstream inflammatory functions. Different types of inflammasomes have been identified based on the sensor involved: NLRP3 inflammasome, the best-characterized, activated by diverse stimuli including ATP, crystalline structures, and pathogens. AIM2 inflammasome, which detects cytosolic double-stranded DNA.[12] NLRC4 inflammasome, activated in response to bacterial flagellin and type III secretion system components. NLRP1 inflammasome, which senses bacterial toxins and proteolytic activity.[13] Pyrin inflammasome, activated by bacterial modifications of host Rho GTPases. Although these inflammasomes vary in their recognition mechanisms, they converge on common downstream pathways, amplifying the inflammatory response.[14] Importantly, their activation is tightly regulated through a two-signal model: a priming step (Signal 1) that induces the expression of inflammasome components, followed by an activation step (Signal 2) triggered by the actual danger signal. This ensures that inflammasomes are activated only under appropriate conditions.[15]

Thus, inflammasomes represent a critical interface between host defense and pathology, providing protection against infection but also contributing to autoinflammatory and metabolic disorders when dysregulated.

Canonical vs Non-Canonical Inflammasome Pathways

Inflammasome signaling can be broadly divided into canonical and non-canonical pathways, which differ in their initiating sensors, caspase involvement, and mechanisms of cytokine release and cell death. Both contribute to host defense but also play distinct roles in inflammatory pathology.[16]

Canonical Inflammasome Pathway

The canonical pathway is the best-characterized form of inflammasome signaling. It involves activation of caspase-1 following assembly of inflammasomes such as NLRP3, NLRC4, AIM2, NLRP1, or pyrin. Steps of activation: Priming (Signal 1): Recognition of microbial products or cytokines via pattern recognition receptors (PRRs) or Toll-like receptors (TLRs) induces NF-κB–dependent transcription of inflammasome components (e.g., NLRP3, pro-IL-1β, pro-IL-18). Activation (Signal 2): Detection of specific danger signals (e.g., ATP, crystalline particles, cytosolic DNA, bacterial toxins) triggers oligomerization of the sensor, recruitment of ASC, and caspase-1 activation.[17] Downstream effects: Active caspase-1 cleaves pro-IL-1β and pro-IL-18 into their mature forms and processes gasdermin D (GSDMD) to induce pyroptosis. This pathway is central to antimicrobial defense but, when dysregulated, is implicated in autoinflammatory diseases, gout, atherosclerosis, and neurodegenerative disorders.[18]

Non-Canonical Inflammasome Pathway

The non-canonical pathway is distinct in that it does not rely on caspase-1 for initial activation. Instead, it involves caspase-11 in mice (or caspase-4 and caspase-5 in humans) directly sensing bacterial lipopolysaccharide (LPS) within the cytosol.[19] Steps of activation: Direct sensing: Cytosolic LPS binds directly to caspase-4/5/11, causing their oligomerization and activation. Execution: Activated caspases cleave GSDMD, forming membrane pores that induce pyroptosis. Secondary effects: The ensuing potassium efflux and cellular disruption can indirectly activate the NLRP3 inflammasome, leading to caspase-1–dependent cytokine maturation.[20]

Unlike the canonical pathway, the non-canonical route is primarily a cell-intrinsic antibacterial mechanism, especially against Gram-negative bacteria that deliver LPS into the cytoplasm. However, excessive activation contributes to septic shock and systemic inflammation.[21]

Sources and Triggers of Inflammasome Formation

Inflammasome activation can be initiated by a wide range of stimuli, reflecting their role as central hubs of innate immune surveillance. These triggers can be broadly grouped into pathogen-associated molecular patterns (PAMPs), damage-associated molecular patterns (DAMPs), and environmental or chemical stimuli.[22] While different inflammasomes exhibit specificity for particular triggers, many converge on common cellular stress signals such as ionic fluxes, mitochondrial dysfunction, and reactive oxygen species (ROS) production.[23,24]

Pathogen-Associated Triggers (PAMPs)

Inflammasomes recognize conserved microbial structures, allowing rapid responses to infection. Bacteria: Components such as flagellin (*Salmonella*, *Legionella*), type III secretion system (T3SS) proteins, and pore-forming toxins activate the NLRC4 inflammasome.[25] *Bacillus anthracis* toxins and proteases trigger NLRP1. Viruses: Viral double-stranded DNA activates the AIM2 inflammasome, while RNA viruses such as influenza and SARS-CoV-2 indirectly stimulate NLRP3 via ion channel activity and mitochondrial stress.[25] Fungi: Cell wall components like β-glucans from *Candida albicans* are sensed by NLRP3. Parasites: Protozoans such as *Plasmodium* and *Toxoplasma gondii* activate inflammasomes through host cell damage and release of PAMPs.[26]

Damage-Associated Triggers (DAMPs)

Sterile signals from stressed or dying cells are potent activators of inflammasomes. Metabolic crystals: Monosodium urate (gout), cholesterol (atherosclerosis), and calcium pyrophosphate (pseudogout) crystals activate NLRP3.[27] Extracellular ATP: Released from damaged cells, ATP engages the P2X7 receptor, causing potassium efflux and inflammasome activation. Mitochondrial stress: Damaged mitochondria release ROS, cardiolipin, and mitochondrial DNA, all of which can stimulate NLRP3.[28]

Environmental and Chemical Triggers

Exogenous particles and xenobiotics can also activate inflammasomes. Environmental pollutants: Silica, asbestos, and particulate matter activate NLRP3 through lysosomal destabilization.[29]

Metabolic Dysregulation and Inflammasome Activation

Metabolic homeostasis is tightly linked to innate immune function, and disturbances in cellular or systemic metabolism are potent drivers of inflammasome activation.[30] Among the various inflammasomes, NLRP3 is the most responsive to metabolic cues, integrating signals from nutrient excess, mitochondrial stress, and lipid imbalance.[31] Dysregulated inflammasome activation in metabolic contexts contributes to chronic low-grade inflammation, often termed *metaflammation*, which underlies obesity, type 2 diabetes, atherosclerosis, and related disorders.[32]

Glucose and Energy Metabolism

Hyperglycemia and altered glycolytic flux can enhance inflammasome activation. Elevated glucose levels promote ROS production and mitochondrial dysfunction, both of which act as NLRP3 triggers.[33] In addition, accumulation of advanced glycation end-products (AGEs) in diabetes further stimulates inflammasome assembly. Conversely, certain metabolic intermediates such as succinate and fumarate stabilize HIF-1α, amplifying pro-inflammatory responses.[34]

Lipid Dysregulation

Aberrant lipid metabolism is a strong inducer of inflammasomes. Cholesterol crystals activate NLRP3 in macrophages, driving vascular inflammation and progression of atherosclerosis. Saturated fatty acids (e.g., palmitate) stimulate NLRP3 via mitochondrial ROS, whereas unsaturated fatty acids may have inhibitory effects. Altered ceramide and sphingolipid metabolism also promote inflammasome activation in obesity and insulin resistance.

Mitochondrial Dysfunction

Mitochondria serve as central hubs linking metabolism to immunity. Disturbances in oxidative phosphorylation lead to accumulation of mitochondrial ROS, release of mitochondrial DNA (mtDNA), and exposure of cardiolipin, all of which are potent NLRP3 triggers. Impaired mitophagy, a process that normally removes damaged mitochondria, further exacerbates inflammasome activation in metabolic disease.

Autophagy and Nutrient Sensing Pathways

Autophagy acts as a negative regulator of inflammasomes by clearing damaged organelles and limiting the buildup of DAMPs. Dysregulation of nutrient-sensing pathways, including AMPK and mTOR, alters autophagic flux and can tip the balance toward excessive inflammasome activation. For instance, AMPK activation inhibits NLRP3 by preserving mitochondrial integrity, whereas mTOR over activation promotes inflammasome activity under nutrient-rich conditions.

Clinical Implications

Chronic activation of inflammasomes due to metabolic dysregulation contributes to: Obesity-associated inflammation: adipose tissue macrophages exhibit heightened NLRP3 activity. Type 2 diabetes: NLRP3 activation impairs insulin signaling and β-cell function. Cardiovascular disease: cholesterol-driven inflammasome activity accelerates plaque formation. Non-alcoholic fatty liver disease (NAFLD): lipid-induced NLRP3 activity promotes hepatic inflammation and fibrosis.

Major types of inflammasomes and their sources multiple inflammasome complexes have been described, each defined by the sensor protein that initiates their assembly. These sensors belong primarily to the NOD-like receptor (NLR) family.[35]

Cross-Talk Between Inflammasome Pathways

Although individual inflammasomes have distinct sensors and activation mechanisms, they rarely function in isolation. Instead, extensive cross-talk exists between inflammasome pathways, ensuring integrated immune responses to complex stimuli. This interplay occurs at several levels, including shared signaling intermediates, cooperative activation, and compensatory mechanisms.

Canonical and Non-Canonical Interactions

The non-canonical inflammasome (caspase-4/5 in humans; caspase-11 in mice) directly senses cytosolic LPS and induces pyroptosis via gasdermin D. This event generates potassium efflux, which in turn activates the NLRP3 inflammasome in the canonical pathway. Thus, non-canonical signaling amplifies cytokine maturation (IL-1β, IL-18) through NLRP3, demonstrating a critical point of convergence between pathways.

The inflammasome detects cytosolic DNA, while NLRP3 responds to associated cellular stress, such as mitochondrial ROS or potassium flux. These inflammasomes often act synergistically during infections, where this provides DNA sensing and NLRP3 responds to resulting damage. Together, they ensure robust cytokine release and pyroptotic clearance.

Inflammasomes and Other Cell Death Pathways

Cross-talk extends beyond inflammasomes themselves. Caspase-8, traditionally associated with apoptosis, can substitute for caspase-1 under certain conditions, processing IL-1β and linking inflammasomes to apoptotic machinery. Likewise, necroptotic mediators such as RIPK3 and MLKL can potentiate NLRP3 activation, creating a cell death–inflammation feedback loop.

Regulatory Cross-Talk

Autophagy serves as a negative regulator by degrading inflammasome components and damaged mitochondria. Impaired autophagy permits sustained activation across multiple inflammasomes. Type I interferons (IFN-I) can suppress NLRP3 but promote cytosolic DNA triggering responses, highlighting differential regulation. Metabolic cues such as glycolytic reprogramming influence inflammasome choice, with AMPK and mTOR pathways shaping whether NLRP3 or alternative inflammasomes are favored.

Pathophysiological Implications

The interconnectedness of inflammasome pathways enhances host defense against pathogens with diverse virulence strategies. However, dysregulated cross-talk can amplify pathological inflammation. For example: In sepsis, non-canonical activation drives overwhelming NLRP3 activity, fueling cytokine storms. In autoimmune disease, DNA sensing–NLRP3 synergy promotes aberrant cytokine release. In neurodegeneration, chronic mitochondrial stress sustains NLRP3 activation, which can further recruit additional inflammasomes to amplify injury.[36]

Inflammasomes in Human Disease

While inflammasomes are essential for host defense, their dysregulated or chronic activation contributes to a wide spectrum of human diseases. Excessive production of IL-1β and IL-18, along with pyroptotic cell death, can drive tissue damage and systemic inflammation. Below, major disease contexts linked to aberrant inflammasome activity are outlined.[37]

Autoinflammatory and Autoimmune Diseases

Cryopyrin-Associated Periodic Syndromes (CAPS): Gain-of-function mutations in NLRP3 lead to constitutive inflammasome activation, resulting in recurrent fevers, rash, and systemic inflammation. Familial Mediterranean Fever (FMF): Mutations in the pyrin inflammasome cause inappropriate activation, leading to recurrent inflammatory episodes. Systemic lupus erythematosus (SLE): Aberrant sensing of self-DNA by DNA sensing NLRP3 promotes autoimmune responses. Rheumatoid arthritis: Synovial inflammation is fueled by NLRP3 activation in response to immune complexes and DAMPs.[38]

Metabolic Disorders

Gout and Pseudogout: Deposition of monosodium urate and calcium pyrophosphate crystals activates NLRP3, causing intense joint inflammation. Type 2 Diabetes Mellitus (T2DM): Chronic NLRP3 activation in adipose tissue and pancreatic β-cells impairs insulin sensitivity and secretion. Atherosclerosis: Cholesterol crystals and oxidized LDL activate NLRP3 in macrophages, driving plaque formation. Non-alcoholic fatty liver disease (NAFLD): Lipid accumulation and mitochondrial dysfunction stimulate NLRP3, contributing to hepatic inflammation and fibrosis.[39,40]

Neurodegenerative Diseases

Alzheimer's disease: Amyloid-β aggregates activate NLRP3, leading to IL-1β release and microglial-driven neuroinflammation. Parkinson's disease: Misfolded α-synuclein triggers NLRP3, amplifying neuronal injury. Multiple sclerosis (MS): Inflammasome-mediated IL-1β promotes demyelination and immune cell infiltration into the CNS. Traumatic brain injury (TBI): DAMPs released from injured neurons stimulate inflammasomes, worsening secondary injury.[41]

Infectious Diseases

Bacterial infections

Salmonella, *Shigella*, and *Legionella* activate NLRC4 via flagellin and secretion systems. *Francisella tularensis* is recognized by cytosolic DNA. Viral infections: Influenza virus, HIV, and SARS-CoV-2 stimulate NLRP3 through ion flux and mitochondrial stress. Cytosolic viral DNA activates. Parasitic infections: *Plasmodium* species trigger NLRP3 during malaria, contributing to cerebral pathology.[42]

Clinical Implications

The discovery of inflammasomes has profoundly shaped our understanding of inflammation in human health and disease. Their ability to integrate microbial, metabolic, and environmental signals places them at the center of many chronic inflammatory and degenerative conditions. Consequently, inflammasomes and their downstream mediators have become attractive diagnostic biomarkers and therapeutic targets.[43]

Diagnostic and Prognostic Value

Biomarkers of activity: Elevated levels of IL-1β, IL-18, and pyroptosis-associated proteins (e.g., gasdermin D fragments) in serum or tissues can reflect inflammasome activation[44]. Disease monitoring: In gout, rheumatoid arthritis, or CAPS, inflammasome-related cytokines serve as indicators of disease activity and therapeutic response. Precision medicine: Genetic screening for inflammasome mutations (e.g., *NLRP3*) enables early diagnosis of autoinflammatory syndromes.[45]

Therapeutic Targeting

Direct inhibitors: Small-molecule NLRP3 inhibitors (e.g., MCC950) have shown promise in preclinical models of autoinflammatory, metabolic, and neurodegenerative diseases. Cytokine blockade: Clinically approved drugs such as anakinra (IL-1 receptor antagonist), canakinumab (anti–IL-1β antibody), and rilonacept (IL-1 trap) are effective in conditions like CAPS, gout, and systemic juvenile idiopathic arthritis.[46]

Repurposed agents: Colchicine, widely used for gout, reduces NLRP3 activity via microtubule disruption. Certain statins and metformin may exert secondary inflammasome-inhibiting effects through metabolic regulation.[47,48]

Risks of Inflammasome Modulation

While inhibition offers therapeutic potential, suppression of inflammasome activity carries risks: Infection susceptibility: Diminished IL-1β responses can impair host defense against bacteria, fungi, and viruses. Tumor dynamics: As inflammasomes exert context-dependent effects in cancer, their blockade may inadvertently alter tumor surveillance.[49,50]

FUTURE DIRECTIONS

Selective targeting: Developing therapies that inhibit pathogenic inflammasome activity without compromising host defense remains a major challenge. Combination therapies: Pairing inflammasome inhibitors with metabolic or immune-modulating drugs may enhance efficacy in complex diseases.[51] Biologics vs. small molecules: Monoclonal antibodies target cytokines downstream, while next-generation small molecules aim at inflammasome sensors directly, offering more precise control.[52]

CONCLUSION

Inflammasomes are central regulators of innate immunity, bridging the detection of microbial threats, sterile damage, and metabolic disturbances to inflammatory and cell death pathways. Over the past two decades, significant advances have unraveled their molecular mechanisms, sources of activation, and cross-talk with other immune pathways. While this knowledge has illuminated their essential role in host defense, it has also revealed their pathogenic potential when activation becomes excessive or uncontrolled. Clinically, aberrant inflammasome activity contributes to a wide spectrum of diseases, ranging from autoinflammatory syndromes and metabolic disorders to neurodegeneration, infection, and cancer. Their dual role as protectors in acute infection and drivers of chronic inflammation underscores the delicate balance they maintain within the immune system.[53]

Ongoing research has propelled inflammasomes from basic immunology into the therapeutic spotlight, with IL-1–blocking agents already in clinical use and novel direct inflammasome inhibitors under active development. Future strategies must refine the ability to selectively target pathogenic inflammasome activity while preserving protective immune functions.[54

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CONFLICT OF INTEREST

There is no conflict of interest to publish this article in this journal.

REFERENCES

1. Zheng, D., Liwinski, T. & Elinav, E. Inflammasome activation and regulation: toward a better understanding of complex mechanisms. *Cell discovery,* 2020; **6**: 36.
2. Lamkanfi, M. & Dixit, V. M. Inflammasomes: guardians of cytosolic sanctity. *Immunological reviews,* 2009; **227:** 95–105.
3. Patel, S. Danger-associated molecular patterns (DAMPs): the derivatives and triggers of inflammation. *Current allergy and asthma reports,* 2018; **18:** 63.
4. Tanaka, K. & Heil, M. Damage-associated molecular patterns (DAMPs) in plant innate immunity: applying the danger model and evolutionary perspectives. *Annual review of phytopathology,* 2021; **59:** 53–75.
5. Liston, A. & Masters, S. L. Homeostasis-altering molecular processes as mechanisms of inflammasome activation. *Nature Reviews Immunology,* 2017; **17:** 208–214.
6. Singh, G. B. *et al.* Nicotine instigates podocyte injury via NLRP3 inflammasomes activation. *Aging (Albany NY),* 2019; **11:** 12810.
7. Oh, S. *et al.* Integrated NLRP3, AIM2, NLRC4, Pyrin inflammasome activation and assembly drive PANoptosis. *Cellular & Molecular Immunology* **20**, 1513–1526 (2023).
8. Gross, O., Thomas, C. J., Guarda, G. & Tschopp, J. The inflammasome: an integrated view. *Immunological reviews,* 2011; **243:** 136–151.
9. Molla, M. D. *et al.* Role of caspase-1 in the pathogenesis of inflammatory-associated chronic noncommunicable diseases. *Journal of inflammation research,* 2020; 749–764.
10. McIntire, C. R., Yeretssian, G. & Saleh, M. Inflammasomes in infection and inflammation. *Apoptosis* , 2009; **14:** 522–535.
11. Lugrin, J. & Martinon, F. The AIM 2 inflammasome: sensor of pathogens and cellular perturbations. *Immunological reviews,* 2018; **281:** 99–114.
12. Próchnicki, T., Mangan, M. S. & Latz, E. Recent insights into the molecular mechanisms of the NLRP3 inflammasome activation. *F1000Research* **5**, F1000 Faculty Rev–2016; 1469.
13. Zhao, Y. *et al.* The NLRC4 inflammasome receptors for bacterial flagellin and type III secretion apparatus. *Nature,* 2011; **477:** 596–600.
14. Dufies, O. & Boyer, L. RhoGTPases and inflammasomes: Guardians of effector-triggered immunity. *PLoS Pathogens,* 2021; **17:** e1009504.

15. Fontana, M. F. & Vance, R. E. Two signal models in innate immunity. *Immunological reviews*, 2011; **243:** 26–39.
16. KSHIRASAGAR, N., PUCHCHAKAYALA, G. & Balamurugan, K. Formulation and Characterization of Diclofenac Diethylamine Loaded Microsponge Based Gel for Sustained Drug Delivery. *International Journal of Pharmaceutical Research (09752366),* 2020; **12**.
17. Storek, K. M. & Monack, D. M. Bacterial recognition pathways that lead to inflammasome activation. *Immunological reviews*, 2015; **265**: 112–129.
18. Leal, V. N. C. & Pontillo, A. in *NLR Proteins: Methods and Protocols*, Springer, 2023; 1–27.
19. Yi, Y. S. Caspase-11 non-canonical inflammasome: a critical sensor of intracellular lipopolysaccharide in macrophage-mediated inflammatory responses. *Immunology*, 2017; **152**: 207–217.
20. Gebai, A. *Structural characterization of the lipopolysaccharide-induced non-canonical inflammatory response*. (McGill University (Canada), 2016).
21. Finethy, R. *et al.* Dynamin-related Irgm proteins modulate LPS-induced caspase-11 activation and septic shock. *EMBO reports*, 2020; **21:** e50830.
22. Lin, H., Xiong, W., Fu, L., Yi, J. & Yang, J. Damage-associated molecular patterns (DAMPs) in diseases: implications for therapy. *Molecular Biomedicine*, 2025; **6**: 60.
23. Kanneganti, T.-D. The inflammasome: firing up innate immunity. *Immunological reviews*, 2015**; 265:** 1.
24. Li, C., Chen, M., He, X. & Ouyang, D. A mini-review on ion fluxes that regulate NLRP3 inflammasome activation. *Acta biochimica et biophysica Sinica*, 2021; **53:** 131–139.
25. Ratner, D., Orning, M. P. A. & Lien, E. Bacterial secretion systems and regulation of inflammasome activation. *Journal of Leucocyte Biology*, 2017; **101**: 165–181.
26. Briard, B., Malireddi, R. S. & Kanneganti, T.-D. Role of inflammasomes/pyroptosis and PANoptosis during fungal infection. *PloS pathogens*, 2021; **17:** e1009358.
27. Galozzi, P. *et al.* Regulation of crystal induced inflammation: current understandings and clinical implications. *Expert Review of Clinical Immunology*, 2021; **17:** 773–787.
28. Dosch, M., Gerber, J., Jebbawi, F. & Beldi, G. Mechanisms of ATP release by inflammatory cells. *International journal of molecular sciences*, 2018; **19:** 1222.
29. Kanno, S. NLRP3 Inflammasome-Mediated Toxicity of Fibrous Particles. *Biological Effects of Fibrous and Particulate Substances*, 2016; 27–50.

30. Próchnicki, T. & Latz, E. Inflammasomes on the crossroads of innate immune recognition and metabolic control. *Cell metabolism*, 2017; **26**: 71–93.
31. Traba, J. & Sack, M. N. The role of caloric load and mitochondrial homeostasis in the regulation of the NLRP3 inflammasome. *Cellular and Molecular Life Sciences*, 2017; **74:** 1777–1791.
32. Mastrocola, R. *et al.* Metaflammation: tissue-specific alterations of the NLRP3 inflammasome platform in metabolic syndrome. *Current Medicinal Chemistry*, 2018; **25**: 1294–1310.
33. Chen, Y. *et al.* Contribution of redox-dependent activation of endothelial Nlrp3 inflammasomes to hyperglycemia-induced endothelial dysfunction. *Journal of molecular medicine*, 2016; **94:** 1335–1347.
34. Muthyalaiah, Y. S., Jonnalagadda, B., John, C. M. & Arockiasamy, S. Impact of Advanced Glycation End products (AGEs) and its receptor (RAGE) on cancer metabolic signaling pathways and its progression. *Glycoconjugate journal*, 2021; **38:** 717–734.
35. Kshirasagar, N., Puchchakayala, G. & Balamurugan, K. Comparative Pharmacokinetic Studies of Marketed and Microsponges Gel Loaded with Diclofenac Diethylamine in Rabbits. *Research Journal of Pharmacy and Technology*, 2021; **14:** 6385–6391.
36. Kshirasagar, N., Malvey, S., Harika, G. & Kumar, M. Formulation and Evaluation of Flurbiprofen Loaded Microsponges in Capsule for Sustained Drug Delivery. *Mathews J Pharma Sci.*, 2023; **7**: 16.
37. Kshirasagar, N. *et al.* Design and In Vitro Evaluation of Gastro Retentive Sustained Release Tablets of Ketorolac Tromethamine. *Journal of Pharma Science* **2**, 01 (2017).
38. Hoffman, H. M., Kuemmerle-Deschner, J. B. & Goldbach-Mansky, R. in *Textbook of Autoinflammation*, Springer, 2019; 347–365.
39. Horvath, G. L., Schrum, J. E., De Nardo, C. M. & Latz, E. Intracellular sensing of microbes and danger signals by the inflammasomes. *Immunological reviews*, 2011; **243**: 119–135.
40. Lukens, J. R., Gross, J. M. & Kanneganti, T.-D. IL-1 family cytokines trigger sterile inflammatory disease. *Frontiers in immunology*, 2012; **3:** 315.
41. Alemán-Villa, K. M. *et al.* Neuroinflammation across the spectrum of neurodegenerative diseases: mechanisms and therapeutic frontiers. *Neuroimmunomodulation*, 2025; **32:** 278–305.
42. Bryant, C. E. in *Inflammasome Biology*, Elsevier, 2023; 383–397.

43. Kim, M. E. & Lee, J. S. Molecular foundations of inflammatory diseases: insights into inflammation and inflammasomes. *Current Issues in Molecular Biology,* 2024; **46:** 469–484.
44. Elias, E. E., Lyons, B. & Muruve, D. A. Gasdermins and pyroptosis in the kidney. *Nature Reviews Nephrology,* 2023; **19:** 337–350.
45. Spel, L. & Martinon, F. Inflammasomes contributing to inflammation in arthritis. *Immunological reviews,* 2020; **294:** 48–62.
46. Zheng, Y. *et al.* MCC950 as a promising candidate for blocking NLRP3 inflammasome activation: A review of preclinical research and future directions. *Archiv der Pharmazie,* 2024; **357:** e2400459.
47. Dalbeth, N., Lauterio, T. J. & Wolfe, H. R. Mechanism of action of colchicine in the treatment of gout. *Clinical therapeutics,* 2014; **36**: 1465–1479.
48. Demidowich, A. P., Davis, A. I., Dedhia, N. & Yanovski, J. A. Colchicine to decrease NLRP3-activated inflammation and improve obesity-related metabolic dysregulation. *Medical hypotheses*, 2016; **92:** 67–73.
49. Deets, K. A. & Vance, R. E. Inflammasomes and adaptive immune responses. *Nature immunology,* 2021; **22:** 412–422.
50. Tapia, M. A. *et al.* Relapse-like behavior and nAChR sensitization following intermittent access nicotine self-administration. *Neuropharmacology,* 2022; **212:** 109066.
51. Cao, X., Cordova, A. F. & Li, L. Therapeutic interventions targeting innate immune receptors: a balancing act. *Chemical Reviews*, 2021; **122:** 3414–3458.
52. Yadav, L. S., Samruddhi, H., Raju, A. B. & Mallamma, T. Cytokines, Kinases, and Beyond: Advancing Next-generation Immunomodulatory Strategies and Precision Small-molecule Therapies in Autoimmune Disease. *Asian Journal of Pharmaceutical Research and Health Care,* 2025; **17:** 209–219.
53. Kshirasagar, N., Puchchakayala, G. & Balamurugan, K. INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES, (2019).
54. Malvey, S. & Kshirasagar, N. Development and Evaluation of floating pulsatile drug delivery system of meloxicam. *Chronicles of Pharmaceutical Science*, 2018; **2:** 474–492.