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The NLRP3 Inflammasome in Age-Related Cerebral Small Vessel Disease Manifestations: Untying the Innate Immune Response Connection

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Abstract

In this narrative review, we present the evidence on nucleotide-binding and oligomerization (NOD) domain-like receptor (NLR) family pyrin domain (PYD)-containing 3 (NLRP3) inflammasome activation for its putative roles in the elusive pathomechanism of aging-related cerebral small vessel disease (CSVD). Although NLRP3 inflammasome-interleukin (IL)-1 β has been implicated in the pathophysiology of coronary artery disease, its roles in cerebral arteriothrombotic micro-circulation disease such as CSVD remains unexplored. Here, we elaborate on the current manifestations of CSVD and its' complex pathogenesis and relate the array of activators and aberrant activation involving NLRP3 inflammasome with this condition. These neuroinflammatory insights would expand on our current understanding of CSVD clinical (and subclinical) heterogenous manifestations whilst highlighting plausible NLRP3-linked therapeutic targets. © 2023 by the authors.

Author Keywords

aging; cerebral ischemia; cerebral small vessel disease; NLRP3 inflammasome; therapeutics

References

- (2018) *Underlying Cause of Death, 1999–2020. CDC WONDER Online Database*, Available online
- Tsao, C.W., Aday, A.W., Almarzooq, Z.I., Alonso, A., Beaton, A.Z., Bittencourt, M.S., Boehme, A.K., Commodore-Mensah, Y.
Heart Disease and Stroke Statistics-2022 Update: A Report from the American Heart Association
(2022) *Circulation*, 145, pp. E153-E639.
- Lampe, L., Kharabian-Masouleh, S., Kynast, J., Arelin, K., Steele, C., Löffler, M., Witte, A.V., Bazin, P.-L.
Lesion location matters: The relationships between white matter hyperintensities on cognition in the healthy elderly
(2017) *J. Cereb. Blood Flow Metab*, 39, pp. 36-43.
29106319
- Pantoni, L.
Cerebral small vessel disease: From pathogenesis and clinical characteristics to therapeutic challenges

- (2010) *Lancet Neurol*, 9, pp. 689-701.
20610345
- Smith, E.E., Markus, H.S.
New Treatment Approaches to Modify the Course of Cerebral Small Vessel Diseases
(2020) *Stroke*, 51, pp. 38-46.
 - Nassir, C.M.N.C.M., Ghazali, M.M., Hashim, S., Idris, N.S., Yuen, L.S., Hui, W.J., Norman, H.H., Na, Y.
Diets and Cellular-Derived Microparticles: Weighing a Plausible Link with Cerebral Small Vessel Disease
(2021) *Front. Cardiovasc. Med*, 8, p. 62.
33718454
 - Mohamed, I.N., Ishrat, T., Fagan, S.C., El-Remessy, A.B.
Role of inflammasome activation in the pathophysiology of vascular diseases of the neurovascular unit
(2015) *Antioxid. Redox Signal*, 22, pp. 1188-1206.
25275222
 - Sandercock, P.A.G., Soane, T.
Corticosteroids for acute ischaemic stroke
(2011) *Cochrane. Database Syst. Rev*, 2011, p. CD000064.
 - Kalra, L., Irshad, S., Hodsoll, J., Simpson, M., Gulliford, M., Smithard, D., Patel, A., Rebollo-Mesa, I.
Prophylactic antibiotics after acute stroke for reducing pneumonia in patients with dysphagia (STROKE-INF): A prospective, cluster-randomised, open-label, masked endpoint, controlled clinical trial
(2015) *Lancet*, 386, pp. 1835-1844.
 - Liu, D., Zeng, X., Li, X., Mehta, J.L., Wang, X.
Role of NLRP3 inflammasome in the pathogenesis of cardiovascular diseases
(2018) *Basic Res. Cardiol*, 113, p. 5.
 - Li, X., Zhang, Y., Xia, M., Gulbins, E., Boini, K.M., Li, P.L.
Activation of Nlrp3 Inflammasomes Enhances Macrophage Lipid-Deposition and Migration: Implication of a Novel Role of Inflammasome in Atherogenesis
(2014) *PLoS ONE*, 9.
 - Varghese, G.P., Folkersen, L., Strawbridge, R.J., Halvorsen, B., Yndestad, A., Ranheim, T., Krohg-Sørensen, K., Aukrust, P.
NLRP3 Inflammasome Expression and Activation in Human Atherosclerosis
(2022) *J. Am. Heart. Assoc*, 5, p. e003031.
27207962
 - Cheng, L., Yin, R., Yang, S., Pan, X., Ma, A.
Rs4612666 polymorphism of the NLRP3 gene is associated with the occurrence of large artery atherosclerotic ischemic strokes and microembolic signals
(2018) *Biomed. Res. Int*, 2018, p. 6345805.
 - Wang, Z., Hu, W., Lu, C., Ma, Z., Jiang, S., Gu, C., Acuña-Castroviejo, D., Yang, Y.
Targeting NLRP3 (nucleotide binding domain, leucine-rich-containing family, pyrin domain-containing-3) inflammasome in cardiovascular disorders
(2018) *Arterioscler. Thromb. Vasc. Biol*, 38, pp. 2765-2779.
 - Shim, D.W., Lee, K.H.
Posttranslational regulation of the NLR family pyrin domain containing 3 inflammasome
(2018) *Front. Immunol*, 9, p. 1054.
29868015

- Moossavi, M., Parsamanesh, N., Bahrami, A., Atkin, S.L., Sahebkar, A.
Role of the NLRP3 inflammasome in cancer
(2018) *Mol. Cancer*, 17, p. 158.
30447690
- Latz, E., Xiao, T.S., Stutz, A.
Activation and regulation of the inflammasomes
(2013) *Nat. Rev. Immunol*, 13, pp. 397-411.
- Kelley, N., Jeltema, D., Duan, Y., He, Y.
The NLRP3 inflammasome: An overview of mechanisms of activation and regulation
(2019) *Int. J. Mol. Sci*, 20.
- Menu, P., Vince, J.E.
The NLRP3 inflammasome in health and disease: The good, the bad and the ugly
(2011) *Clin. Exp. Immunol*, 166, pp. 1-15.
- Ting, J.P.Y., Davis, B.K.
CATERPILLER: A novel gene family important in immunity, cell death, and diseases
(2005) *Annu. Rev. Immunol*, 23, p. 387.
- Sharif, H., Wang, L., Wang, W.L., Magupalli, V.G., Andreeva, L., Qiao, Q., Hauenstein, A.V., Mao, Y.
Structural mechanism for NEK7-licensed activation of NLRP3 inflammasome
(2019) *Nature*, 570, pp. 338-343.
- Lammerding, L., Slowik, A., Johann, S., Beyer, C., Zendedel, A.
Poststroke inflammasome expression and regulation in the peri-infarct area by gonadal steroids after transient focal ischemia in the rat brain
(2016) *Neuroendocrinology*, 103, pp. 460-475.
- Jo, E.K., Kim, J.K., Shin, D.M., Sasakawa, C.
Molecular mechanisms regulating NLRP3 inflammasome activation
(2016) *Cell Mol. Immunol*, 13, pp. 148-159.
26549800
- Toma, C., Higa, N., Koizumi, Y., Nakasone, N., Ogura, Y., McCoy, A.J., Franchi, L., Taniguchi, S.I.
Pathogenic *Vibrio* activate NLRP3 inflammasome via cytotoxins and TLR/nucleotide-binding oligomerization domain-mediated NF- κ B signaling
(2010) *J. Immunol*, 184, pp. 5287-5297.
20348425
- Saha, S., Buttari, B., Panieri, E., Profumo, E., Saso, L.
An overview of Nrf2 signaling pathway and its role in inflammation
(2020) *Molecules*, 25.
- Bauernfeind, F.G., Horvath, G., Stutz, A., Alnemri, E.S., MacDonald, K., Speert, D., Fernandes-Alnemri, T., Fitzgerald, K.A.
Cutting Edge: NF- κ B Activating Pattern Recognition and Cytokine Receptors License NLRP3 Inflammasome Activation by Regulating NLRP3 Expression
(2009) *J. Immunol*, 183, pp. 787-791.
- Herman, F.J., Pasinetti, G.M.
Principles of inflammasome priming and inhibition: Implications for psychiatric disorders
(2018) *Brain Behav. Immun*, 73, pp. 66-84.
- Gaidt, M.M., Hornung, V.
Alternative inflammasome activation enables IL-1 β release from living cells

- (2017) *Curr. Opin. Immunol*, 44, pp. 7-13.
27842238
- Song, N., Li, T.
Regulation of NLRP3 inflammasome by phosphorylation
(2018) *Front. Immunol*, 9, p. 2305.
 - Shao, B.Z., Xu, Z.Q., Han, B.Z., Su, D.F., Liu, C.
NLRP3 inflammasome and its inhibitors: A review
(2015) *Front. Pharmacol*, 6, p. 262.
 - Parvathenani, L.K., Tertyshnikova, S., Greco, C.R., Roberts, S.B., Robertson, B., Posmantur, R.
P2X7 mediates superoxide production in primary microglia and is up-regulated in a transgenic mouse model of Alzheimer's disease
(2003) *J. Biol. Chem*, 278, pp. 13309-13317.
 - Pelegrin, P., Surprenant, A.
Pannexin-1 mediates large pore formation and interleukin-1 β release by the ATP-gated P2X7 receptor
(2006) *EMBO J*, 25, pp. 5071-5082.
17036048
 - Savio, L.E.B., de Andrade Mello, P., Da Silva, C.G., Coutinho-Silva, R.
The P2X7 receptor in inflammatory diseases: Angel or demon?
(2018) *Front. Pharmacol*, 9, p. 52.
29467654
 - Yamasaki, Y., Matsuura, N., Shozuhara, H., Onodera, H., Itoyama, Y., Kogure, K.
Interleukin-1 as a pathogenetic mediator of ischemic brain damage in rats
(1995) *Stroke*, 26, pp. 676-681.
7709417
 - Wang, H., Chen, H., Jin, J., Liu, Q., Zhong, D., Li, G.
Inhibition of the NLRP3 inflammasome reduces brain edema and regulates the distribution of aquaporin-4 after cerebral ischaemia-reperfusion
(2020) *Life Sci*, 251, p. 117638.
 - Li, J., Liu, Z., Wang, L., Xu, H., Wang, Y.
Thousand and one kinase 1 protects MCAO503 induced cerebral ischemic stroke in rats by decreasing apoptosis and pro-inflammatory factors
(2019) *Biosci. Rep*, 39.
BSR20190749
 - Friedlander, R.M., Gagliardini, V., Hara, H., Fink, K.B., Li, W., MacDonald, G., Fishman, M.C., Yuan, J.
Expression of a Dominant Negative Mutant of Interleukin-1 β Converting Enzyme in Transgenic Mice Prevents Neuronal Cell Death Induced by Trophic Factor Withdrawal and Ischemic Brain Injury
(1997) *J. Exp. Med*, 185, pp. 933-940.
 - Caso, J.R., Moro, M.A., Lorenzo, P., Lizasoain, I., Leza, J.C.
Involvement of IL-1 β in acute stress-induced worsening of cerebral ischaemia in rats
(2007) *Eur. Neuropsychopharmacol*, 17, pp. 600-607.
 - Liang, H., Sun, Y., Gao, A., Zhang, N., Jia, Y., Yang, S., Na, M., Fang, X.
Ac-YVAD-cmk improves neurological function by inhibiting caspase-1-mediated inflammatory response in the intracerebral hemorrhage of rats
(2019) *Int. Immunopharmacol*, 75, p. 105771.
Available online

- Moriwaki, T., Takagi, Y., Sadamasa, N., Aoki, T., Nozaki, K., Hashimoto, N.
(2006) *Impaired Progression of Cerebral Aneurysms in Interleukin-1-Deficient Mice*, Available online
- Li, F., Chen, Y., Li, Y., Huang, M., Zhao, W.
Geniposide alleviates diabetic nephropathy of mice through AMPK/SIRT1/NF- κ B pathway
(2020) *Eur. J. Pharmacol*, 886, p. 173449.
- Che Mohd Nassir, C.M.N., Zolkefley, M.K.I., Ramli, M.D., Norman, H.H., Abdul Hamid, H., Mustapha, M.
Neuroinflammation and COVID-19 Ischemic Stroke Recovery—Evolving Evidence for the Mediating Roles of the ACE2/Angiotensin-(1–7)/Mas Receptor Axis and NLRP3 Inflammasome
(2022) *Int. J. Mol. Sci*, 23.
- Taoka, T., Naganawa, S.
Imaging for central nervous system (CNS) interstitial fluidopathy: Disorders with impaired interstitial fluid dynamics
(2021) *Jpn. J. Radiol*, 39, pp. 1-14.
- Gaberel, T., Gakuba, C., Goulay, R., De Lizarrondo, S.M., Hanouz, J.-L., Emery, E., Touze, E., Gauberti, M.
Impaired Glymphatic Perfusion After Strokes Revealed by Contrast-Enhanced MRI
(2014) *Stroke*, 45, pp. 3092-3096.
25190438
- Franceschi, C., Garagnani, P., Parini, P., Giuliani, C., Santoro, A.
Inflammaging: A new immune–metabolic viewpoint for age-related diseases
(2018) *Nat. Rev. Endocrinol*, 14, pp. 576-590.
- Ismael, S., Zhao, L., Nasoohi, S., Ishrat, T.
Inhibition of the NLRP3-inflammasome as a potential approach for neuroprotection after stroke
(2018) *Sci. Rep*, 8, p. 5971.
29654318
- Song, H.L., Zhang, S.B.
Therapeutic effect of dexmedetomidine on intracerebral hemorrhage via regulating NLRP3
(2019) *Eur. Rev. Med. Pharmacol. Sci*, 23, pp. 23-2612.
- Xu, W., Li, T., Gao, L., Zheng, J., Yan, J., Zhang, J., Shao, A.
Apelin-13/APJ system attenuates early brain injury via suppression of endoplasmic reticulum stress-associated TXNIP/NLRP3 inflammasome activation and oxidative stress in a AMPK-dependent manner after subarachnoid hemorrhage in rats
(2019) *J. Neuroinflammation*, 16, p. 247.
31791369
- Rubio-Perez, J.M., Morillas-Ruiz, J.M.
A review: Inflammatory process in Alzheimer’s disease, role of cytokines
(2012) *Sci. World J*, 2012, p. 756357.
- Saresella, M., La Rosa, F., Piancone, F., Zoppis, M., Marventano, I., Calabrese, E., Rainone, V., Clerici, M.
The NLRP3 and NLRP1 inflammasomes are activated in Alzheimer’s disease
(2016) *Mol. Neurodegener*, 11, p. 23.
- Italiani, P., Puxeddu, I., Napoletano, S., Scala, E., Melillo, D., Manocchio, S., Angiolillo, A., Vitale, E.

- Circulating levels of IL-1 family cytokines and receptors in Alzheimer's disease: New markers of disease progression?**
(2018) *J. Neuroinflammation*, 15, pp. 1-12.
- Antony, P.M.A., Diederich, N.J., Krüger, R., Balling, R.
The hallmarks of Parkinson's disease
(2013) *FEBS J*, 280, pp. 5981-5993.
Available online
 - Tan, E.K., Chao, Y.X., West, A., Chan, L.L., Poewe, W., Jankovic, J.
Parkinson disease and the immune system—Associations, mechanisms and therapeutics
(2020) *Nat. Rev. Neurol*, 16, pp. 303-318.
32332985
 - Trudler, D., Nazor, K.L., Eisele, Y.S., Grabauskas, T., Dolatabadi, N., Parker, J., Sultan, A., Levites, Y.
Soluble α -synuclein-antibody complexes activate the NLRP3 inflammasome in hiPSC-derived microglia
(2021) *Proc. Natl. Acad. Sci. USA*, 118.
e2025847118, 33833060
 - Gritsenko, A., Green, J.P., Brough, D., Lopez-Castejon, G.
Mechanisms of NLRP3 priming in inflammaging and age related diseases
(2020) *Cytokine Growth Factor Rev*, 55, pp. 15-25.
32883606
 - Youm, Y.-H., Grant, R.W., McCabe, L.R., Albarado, D.C., Nguyen, K.Y., Ravussin, A., Pistell, P., Laque, A.
Canonical Nlrp3 inflammasome links systemic low-grade inflammation to functional decline in aging
(2013) *Cell Metab*, 18, pp. 519-532.
24093676
 - Cordero, M.D., Williams, M.R., Ryffel, B.
AMP-activated protein kinase regulation of the NLRP3 inflammasome during aging
(2018) *Trends Endocrinol. Metab*, 29, pp. 8-17.
29150317
 - Marín-Aguilar, F., Lechuga-Vieco, A.V., Alcocer-Gómez, E., Castejón-Vega, B., Lucas, J., Garrido, C., Peralta-Garcia, A., Quiles, J.L.
NLRP3 inflammasome suppression improves longevity and prevents cardiac aging in male mice
(2020) *Aging Cell*, 19, p. e13050.
 - Navarro-Pando, J.M., Alcocer-Gómez, E., Castejón-Vega, B., Navarro-Villarán, E., Condés-Hervás, M., Mundi-Roldan, M., Muntané, J., Wang, C.
Inhibition of the NLRP3 inflammasome prevents ovarian aging
(2021) *Sci. Adv*, 7, p. eabc7409.
 - Osorio, F.G., Bárcena, C., Soria-Valles, C., Ramsay, A.J., de Carlos, F., Cobo, J., Fueyo, A., López-Otín, C.
Nuclear lamina defects cause ATM-dependent NF- κ B activation and link accelerated aging to a systemic inflammatory response
(2012) *Genes Dev*, 26, pp. 2311-2324.
 - Wu, J.J., Liu, J., Chen, E.B., Wang, J.J., Cao, L., Narayan, N., Fergusson, M.M., Springer, D.A.
Increased mammalian lifespan and a segmental and tissue-specific slowing of aging after genetic reduction of mTOR expression
(2013) *Cell Rep*, 4, pp. 913-920.

- Pavillard, L.E., Cañadas-Lozano, D., Alcocer-Gómez, E., Marín-Aguilar, F., Pereira, S., Robertson, A.A.B., Muntané, J., Quiles, J.L.
NLRP3-inflammasome inhibition prevents high fat and high sugar diets-induced heart damage through autophagy induction
(2017) *Oncotarget*, 8, p. 99740.
- Smith, E.E.
Clinical presentations and epidemiology of vascular dementia
(2017) *Clin. Sci*, 131, pp. 1059-1068.
28515342
- Prabhakaran, S., Naidech, A.M.
Ischemic brain injury after intracerebral hemorrhage: A critical review
(2012) *Stroke*, 43, pp. 2258-2263.
22821611
- Chojdak-Lukasiewicz, J., Dziadkowiak, E., Zimny, A., Paradowski, B.
Cerebral small vessel disease: A review
(2021) *Adv. Clin. Exp. Med*, 30, pp. 349-356.
- Nassir, C., Ghazali, M., Safri, A., Jaffer, U., Abdullah, W., Idris, N., Muzaimi, M.
Elevated Circulating Microparticle Subpopulations in Incidental Cerebral White Matter Hyperintensities: A Multimodal Study
(2021) *Brain Sci*, 11.
- Li, X., Yan, X., Wang, Y., Wang, J., Zhou, F., Wang, H., Xie, W., Kong, H.
NLRP3 inflammasome inhibition attenuates silica-induced epithelial to mesenchymal transition (EMT) in human bronchial epithelial cells
(2018) *Exp. Cell Res*, 362, pp. 489-497.
29258746
- Lee, N., Ong, L., Gyawali, P., Nassir, C., Mustapha, M., Nandurkar, H., Sashindranath, M.
Role of Purinergic Signalling in Endothelial Dysfunction and Thrombo-Inflammation in Ischaemic Stroke and Cerebral Small Vessel Disease
(2021) *Biomolecules*, 11.
34356618
- Pérez-Mato, M., Iglesias-Rey, R., Vieites-Prado, A., Dopico-López, A., Argibay, B., Fernández-Susavila, H., da Silva-Candal, A., Günther, A.
Blood glutamate EAAT2-cell grabbing therapy in cerebral ischemia
(2019) *EBioMedicine*, 39, pp. 118-131.
- Yang, Q., Zhou, J.
Neuroinflammation in the central nervous system: Symphony of glial cells
(2019) *Glia*, 67, pp. 1017-1035.
- Hung, W., Ho, C., Pan, M.
Targeting the NLRP3 inflammasome in neuroinflammation: Health promoting effects of dietary phytochemicals in neurological disorders
(2020) *Mol. Nutr. Food Res*, 64, p. 1900550.
- Théry, C., Witwer, K.W., Aikawa, E., Alcaraz, M.J., Anderson, J.D., Andriantsitohaina, R., Antoniou, A., Atkin-Smith, G.K.
Minimal information for studies of extracellular vesicles 2018 (MISEV2018): A position statement of the International Society for Extracellular Vesicles and update of the MISEV2014 guidelines
(2018) *J. Extracell Vesicles*, 7, p. 1535750.
- DiSabato, D.J., Quan, N., Godbout, J.P.
Neuroinflammation: The devil is in the details

- (2016) *J. Neurochem*, 139, pp. 136-153.
26990767
- Shen, H., Guan, Q., Zhang, X., Yuan, C., Tan, Z., Zhai, L., Hao, Y., Han, C.
New mechanism of neuroinflammation in Alzheimer's disease: The activation of NLRP3 inflammasome mediated by gut microbiota
(2020) *Prog. Neuro Psychopharmacol. Biol. Psychiatry*, 100, p. 109884.
32032696
 - Rui, W., Li, S., Xiao, H., Xiao, M., Shi, J.
Baicalein attenuates neuroinflammation by inhibiting NLRP3/caspase-1/GSDMD pathway in MPTP-induced mice model of Parkinson's disease
(2020) *Int. J. Neuropsychopharmacol*, 23, pp. 762-773.
32761175
 - Tong, Y., Ding, Z.-H., Zhan, F.-X., Cai, L., Yin, X., Ling, J.-L., Ye, J.-J., Wang, Z.-H.
The NLRP3 inflammasome and stroke
(2015) *Int. J. Clin. Exp. Med*, 8, p. 4787.
26131053
 - Wei, P., Yang, F., Zheng, Q., Tang, W., Li, J.
The potential role of the NLRP3 inflammasome activation as a link between 609 mitochondria ROS generation and neuroinflammation in postoperative cognitive dysfunction
(2019) *Front Cell Neurosci*, 13, p. 73.
 - Zhang, Y., Liu, L., Liu, Y.-Z., Shen, X.-L., Wu, T.-Y., Zhang, T., Wang, W., Jiang, C.-L.
NLRP3 inflammasome mediates chronic mild stress-induced depression in mice via neuroinflammation
(2015) *Int. J. Neuropsychopharmacol*, 18, p. pyv006.
25603858
 - Freeman, L., Guo, H., David, C.N., Brickey, W.J., Jha, S., Ting, J.P.Y.
NLR members NLRC4 and NLRP3 mediate sterile inflammasome activation in microglia and astrocytes
(2017) *J. Exp. Med*, 214, pp. 1351-1370.
 - Gong, Z., Pan, J., Shen, Q., Li, M., Peng, Y.
Mitochondrial dysfunction induces NLRP3 inflammasome activation during cerebral ischemia/reperfusion injury
(2018) *J. Neuroinflammation*, 15, p. 242.
 - Yang, F., Wang, Z., Wei, X., Han, H., Meng, X., Zhang, Y., Shi, W., Pang, Q.
NLRP3 deficiency ameliorates neurovascular damage in experimental ischemic stroke
(2014) *J. Cereb Blood Flow Metab*, 34, pp. 660-667.
 - Xiao-Yu, Q.U., Zhang, Y.M., Li-Na, T.A.O., Huan, G.A.O., Jing-Hui, Z.H.A.I., Jing-Meng, S.U.N., Yan-Qing, S.O.N.G., Zhang, S.X.
XingNaoJing injections protect against cerebral ischemia/reperfusion injury and alleviate blood-brain barrier disruption in rats, through an underlying mechanism of NLRP3 inflammasomes suppression
(2019) *Chin. J. Nat. Med*, 17, pp. 498-505.
 - Zhang, Y., Li, X., Qiao, S., Yang, D., Li, Z., Xu, J., Li, W., Liu, W.
Occludin degradation makes brain microvascular endothelial cells more vulnerable to reperfusion injury in vitro
(2021) *J. Neurochem*, 156, pp. 352-366.
32531803

- Wang, S., Yao, Q., Wan, Y., Wang, J., Huang, C., Li, D., Yang, B.
Adiponectin reduces brain injury after intracerebral hemorrhage by reducing NLRP3 inflammasome expression
(2020) *Int. J. Neurosci*, 130, pp. 301-308.
- Ward, R., Li, W., Abdul, Y., Jackson, L., Dong, G., Jamil, S., Filosa, J., Ergul, A.
NLRP3 inflammasome inhibition with MCC950 improves diabetes-mediated cognitive impairment and vasoneuronal remodeling after ischemia
(2019) *Pharmacol. Res*, 142, pp. 237-250.
30818045
- An, P., Xie, J., Qiu, S., Liu, Y., Wang, J., Xiu, X., Li, L., Tang, M.
Hispidulin exhibits neuroprotective activities against cerebral ischemia reperfusion injury through suppressing NLRP3-mediated pyroptosis
(2019) *Life Sci*, 232, p. 116599.
31247210
- Guo, Z., Yu, S., Chen, X., Zheng, P., Hu, T., Duan, Z., Liu, X., Zhu, W.
Suppression of NLRP3 attenuates hemorrhagic transformation after delayed rtPA treatment in thromboembolic stroke rats: Involvement of neutrophil recruitment
(2018) *Brain Res. Bull*, 137, pp. 229-240.
- Xiao, L., Zheng, H., Li, J., Wang, Q., Sun, H.
Neuroinflammation mediated by NLRP3 inflammasome after intracerebral hemorrhage and potential therapeutic targets
(2020) *Mol. Neurobiol*, 57, pp. 5130-5149.
32856203
- Banerjee, G., Kim, H.J., Fox, Z., Jäger, H.R., Wilson, D., Charidimou, A., Na, H.K., Werring, D.J.
MRI-visible perivascular space location is associated with Alzheimer's disease independently of amyloid burden
(2017) *Brain*, 140, pp. 1107-1116.
- Wharton, S.B., Simpson, J.E., Brayne, C., Ince, P.G.
Age-Associated White Matter Lesions: The MRC Cognitive Function and Ageing Study
(2015) *Brain Pathol*, 25, pp. 35-43.
- Charidimou, A., Boulouis, G., Haley, K., Auriel, E., van Etten, E.S., Fotiadis, P., Reijmer, Y., Dipucchio, Z.Y.
White matter hyperintensity patterns in cerebral amyloid angiopathy and hypertensive arteriopathy
(2016) *Neurology*, 86, pp. 505-511.
- Charidimou, A., Boulouis, G., Pasi, M., Auriel, E., van Etten, E.S., Haley, K., Ayres, A., Goldstein, J.N.
MRI visible perivascular spaces in cerebral amyloid angiopathy and hypertensive arteriopathy
(2017) *Neurology*, 88, pp. 1157-1164.
- Wardlaw, J.M., Smith, C., Dichgans, M.
659 Mechanisms of sporadic cerebral small vessel disease: Insights from neuroimaging
(2013) *Lancet Neurol*, 12, pp. 483-497.
- Wu, X., Zhang, H., Qi, W., Zhang, Y., Li, J., Li, Z., Lin, Y., Chen, X.
Nicotine promotes atherosclerosis via ROS-NLRP3-mediated endothelial cell pyroptosis
(2018) *Cell Death Dis*, 9, p. 171.
29416034

- She, Y., Shao, L., Zhang, Y., Hao, Y., Cai, Y., Cheng, Z., Deng, C., Liu, X.
Neuroprotective effect of glycosides in Buyang Huanwu Decoction on pyroptosis following cerebral ischemia reperfusion injury in rats
(2019) *J. Ethnopharmacol*, 242, p. 112051.
31279072
- Zhu, S., Zhang, Z., Jia, L.Q., Zhan, K.X., Wang, L.J., Song, N., Liu, Y., Guan, L.
Valproic acid attenuates global cerebral ischemia/reperfusion injury in gerbils via anti-pyroptosis pathways
(2019) *Neurochem. Int*, 124, pp. 141-151.
30611759
- Downs, K.P., Nguyen, H., Dorfleutner, A., Stehlik, C.
An overview of the non-canonical inflammasome
(2020) *Mol. Aspects Med*, 76, p. 100924.
- El-Sharkawy, L.Y., Brough, D., Freeman, S.
Inhibiting the NLRP3 inflammasome
(2020) *Molecules*, 25.
- Varon, D., Shai, E.
Platelets and their microparticles as key players in pathophysiological responses
(2015) *J. Thromb. Haemost*, 13, pp. S40-S46.
- Badimon, L., Suades, R., Fuentes, E., Palomo, I., Padró, T.
Role of platelet-derived microvesicles as crosstalk mediators in atherothrombosis and future pharmacology targets: A link between inflammation, atherosclerosis, and thrombosis
(2016) *Front. Pharmacol*, 7, p. 293.
- Jiang, H., He, H., Chen, Y., Huang, W., Cheng, J., Ye, J., Wang, A., Liu, Q.
Identification of a selective and direct NLRP3 inhibitor to treat inflammatory disorders
(2017) *J. Exp. Med*, 214, pp. 3219-3238.
- Dai, Z., Chen, X.Y., An, L.Y., Li, C.C., Zhao, N., Yang, F., You, S.T., Jiang, C.
Development of novel tetrahydroquinoline inhibitors of NLRP3 inflammasome for potential treatment of DSS-induced mouse colitis
(2020) *J. Med. Chem*, 64, pp. 871-889.
- Mahmoud, T.N., El-Maadawy, W.H., Kandil, Z.A., Khalil, H., El-Fiky, N.M., El Alfy, T.S.M.A.
Canna x generalis LH Bailey rhizome extract ameliorates dextran sulfate sodium induced colitis via modulating intestinal mucosal dysfunction, oxidative stress, inflammation, and TLR4/NF- κ B and NLRP3 inflammasome pathways
(2021) *J. Ethnopharmacol*, 269, p. 113670.
33301917
- Tomani, J.C.D., Kagisha, V., Tchinda, A.T., Jansen, O., Ledoux, A., Vanhamme, L., Frederich, M., Souopgui, J.
The inhibition of NLRP3 inflammasome and IL-6 production by hibiscus noldeae baker f. Derived constituents provides a link to its anti-inflammatory therapeutic potentials
(2020) *Molecules*, 25.
33066442
- Ahn, J.-H., Park, Y.-L., Song, A.-Y., Kim, W.-G., Je, C.-Y., Jung, D.-H., Kim, Y.-J., Kim, D.-J.
Water extract of Artemisia scoparia Waldst. & Kitam suppresses LPS-induced cytokine production and NLRP3 inflammasome activation in macrophages and alleviates carrageenan-induced acute inflammation in mice
(2021) *J. Ethnopharmacol*, 268, p. 113606.

- Zhao, J., Wang, Z., Yuan, Z., Lv, S., Su, Q.
Baicalin ameliorates atherosclerosis by inhibiting NLRP3 inflammasome in apolipoprotein E-deficient mice
(2020) *Diabetes Vasc. Dis. Res.*, 17.
1479164120977441, 33269624
- Ho, S.C., Chang, Y.H.
Comparison of inhibitory capacities of 6-, 8- and 10-Gingerols/shogaols on the canonical NLRP3 inflammasome-mediated IL-1beta secretion
(2018) *Molecules*, 23.
29466287
- Tapia-Abellán, A., Angosto-Bazarra, D., Martínez-Banaclocha, H., de Torre-Minguela, C., Cerón-Carrasco, J.P., Pé-rez-Sánchez, H., Arostegui, J.I., Pelegrin, P.
MCC950 closes the active conformation of NLRP3 to an inactive state
(2019) *Nat. Chem. Biol.*, 15, pp. 560-564.
- Krishnan, S.M., Ling, Y.H., Huuskes, B.M., Ferens, D.M., Saini, N., Chan, C.T., Diep, H., Kemp-Harper, B.K.
Pharmacological inhibition of the NLRP3 inflammasome reduces blood pressure, renal damage, and dysfunction in salt-sensitive hypertension
(2019) *Cardiovasc. Res.*, 115, pp. 776-787.
30357309
- Yin, D., Zhou, S., Xu, X., Gao, W., Li, F., Ma, Y., Sun, D., Liu, H.
Dexmedetomidine attenuated early brain injury in rats with subarachnoid haemorrhage by suppressing the inflammatory response: The TLR4/NF- κ B pathway and the NLRP3 inflammasome may be involved in the mechanism
(2018) *Brain Res*, 1698, pp. 1-10.
- Shi, Y., Wang, H., Zheng, M., Xu, W., Yang, Y., Shi, F.
Ginsenoside Rg3 suppresses the NLRP3 inflammasome activation through inhibition of its assembly
(2020) *FASEB J*, 34, pp. 208-221.
- He, H., Jiang, H., Chen, Y., Ye, J., Wang, A., Wang, C., Liu, Q., Jiang, W.
Oridonin is a covalent NLRP3 inhibitor with strong antiinflammasome activity
(2018) *Nat. Commun*, 9, p. 2550.
- Zhao, G., Zhang, T., Ma, X., Jiang, K., Wu, H., Qiu, C., Guo, M., Deng, G.
Oridonin attenuates the release of pro-inflammatory cytokines in lipopolysaccharide-induced RAW264. 7 cells and acute lung injury
(2017) *Oncotarget*, 8, p. 68153.
28978105
- Sun, R., Peng, M., Xu, P., Huang, F., Xie, Y., Li, J., Hong, Y., Zhu, W.
Low-density lipoprotein receptor (LDLR) regulates NLRP3-mediated neuronal pyroptosis following cerebral ischemia/reperfusion injury
(2020) *J. Neuroinflammation*, 17, p. 330.
33153475
- Marchetti, C., Swartzwelter, B., Gamboni, F., Neff, C.P., Richter, K., Azam, T., Carta, S., D'Alessandro, A.
OLT1177, a β -sulfonyl nitrile compound, safe in humans, inhibits the NLRP3 inflammasome and reverses the metabolic cost of inflammation
(2018) *Proc. Natl. Acad. Sci. USA*, 115, pp. E1530-E1539.
29378952
- Lonnemann, N., Hosseini, S., Marchetti, C., Skouras, D.B., Stefanoni, D., D'Alessandro, A., Dinarello, C.A., Korte, M.

The NLRP3 Inflammasome Inhibitor OLT1177 Rescues Cognitive Impairment in a Mouse Model of Alzheimer's Disease,
Available online

- Huang, Y., Jiang, H., Chen, Y., Wang, X., Yang, Y., Tao, J., Deng, X., Jiang, W.
Tranilast directly targets NLRP3 to treat inflammasome-driven diseases
(2018) *EMBO Mol. Med*, 10, p. e8689.
- Chen, Y., Li, R., Wang, Z., Hou, X., Wang, C., Ai, Y., Shi, W., Xiao, X.
Dehydrocostus lactone inhibits NLRP3 inflammasome activation by blocking ASC oligomerization and prevents LPS744 mediated inflammation in vivo
(2020) *Cell Immunol*, 349, p. 104046.
- Inoue, M., Shinohara, M.L.
Nlrp3 inflammasome and MS/EAE
(2013) *Autoimmune Dis*, 2013, p. 859145.
- Kuo, P.C., Weng, W.T., Scofield, B.A., Furnas, D., Paraiso, H.C., Intriago, A.J., Bosi, K.D., Yen, J.H.
Interferon- β alleviates delayed tPA-induced adverse effects via modulation of MMP3/9 production in ischemic stroke
(2020) *Blood Adv*, 4, pp. 4366-4381.
- Guarda, G., Braun, M., Staehli, F., Tardivel, A., Mattmann, C., Förster, I., Farlik, M., Romero, P.
Type I interferon inhibits interleukin-1 production and inflammasome activation
(2011) *Immunity*, 34, pp. 213-223.

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