

Pattern recognition receptors in GtoPdb v.2025.3

Clare Bryant¹, Tom P. Monie¹ and Chloe J. Peach²

1. University of Cambridge, UK
2. University of Nottingham, UK

Abstract

Pattern Recognition Receptors (PRRs, [118]) (**nomenclature as agreed by NC-IUPHAR sub-committee on Pattern Recognition Receptors, [21]**) participate in the innate immune response to microbial agents, the stimulation of which leads to activation of intracellular enzymes and regulation of gene transcription. PRRs express multiple leucine-rich regions to bind a range of microbially-derived ligands, termed PAMPs or pathogen-associated molecular patterns or endogenous ligands, termed DAMPS or damage-associated molecular patterns. These include peptides, carbohydrates, peptidoglycans, lipoproteins, lipopolysaccharides, and nucleic acids. PRRs include both cell-surface and intracellular proteins. PRRs may be divided into signalling-associated members, identified here, and endocytic members, the function of which appears to be to recognise particular microbial motifs for subsequent cell attachment, internalisation and destruction. Some are involved in inflammasome formation, and modulation of IL-1 β cleavage and secretion, and others in the initiation of the type I interferon response.

PRRs included in the Guide To PHARMACOLOGY are:

Catalytic PRRs (see links below this overview)

Toll-like receptors (TLRs)

Nucleotide-binding oligomerization domain, leucine-rich repeat containing receptors (NLRs, also known as NOD (Nucleotide oligomerisation domain)-like receptors)

RIG-I-like receptors (RLRs)

[Caspase 4](#) and [caspase 5](#)

Non-catalytic PRRs

[Absent in melanoma \(AIM\)-like receptors](#) (ALRs)

[C-type lectin-like receptors](#) (CLRs)

[Other pattern recognition receptors](#)

[Advanced glycosylation end-product specific receptor](#) (RAGE)

Contents

This is a citation summary for Pattern recognition receptors in the [Guide to Pharmacology](#) database (GtoPdb). It exists purely as an adjunct to the database to facilitate the recognition of citations to and from the database by citation analyzers. Readers will almost certainly want to visit the relevant sections of the database which are given here under database links.

[GtoPdb](#) is an expert-driven guide to pharmacological targets and the substances that act on them. GtoPdb is a reference work which is most usefully represented as an on-line database. As in any publication this work should be appropriately cited, and the papers it cites should also be recognized. This document provides a citation for the relevant parts of the database, and also provides a reference list for the research cited by those parts. For further details see [22].

Please note that the database version for the citations given in GtoPdb are to the most recent preceding version in which the family or its subfamilies and targets were substantially changed. The links below are to the current version. If you need to consult the cited version, rather than the most recent version, please contact the GtoPdb curators.

Database links

Pattern recognition receptors

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=302>

Toll-like receptor family

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=316>

Receptors

TLR1

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1751>

TLR2

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1752>

TLR3

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1753>

TLR4

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1754>

TLR5

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1755>

TLR6

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1756>

TLR7

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1757>

TLR8

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1758>

TLR9

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1759>

TLR10

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1760>

TLR11

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1761>

NOD-like receptor family

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=317>

Receptors

NOD1(nucleotide binding oligomerization domain containing 1)

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1762>

NOD2(nucleotide binding oligomerization domain containing 2)

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1763>

NLRC3

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1764>

NLRC4

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1782>

NLRC5

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1765>

NLRX1

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1766>

CIITA

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1767>

NLRP1

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1768>

NLRP2

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1769>

NLRP3

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1770>

NLRP4

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1771>

NLRP5

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1772>

NLRP6

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1773>

NLRP7

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1774>

NLRP8

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1775>

NLRP9

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1776>

NLRP10

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1777>

NLRP11

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1778>

NLRP12

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1779>
 NLRP13
<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1780>
 NLRP14
<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1781>
 RIG-I-like receptor family
<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=940>
 Introduction to RIG-I-like receptor family
<https://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=940>
 Receptors
 RIG-1 (DEXD/H-box helicase 58)
<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2920>
 MDA5(interferon induced with helicase C domain 1)
<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2921>
 LGP2(DEXH-box helicase 58)
<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2922>

References

- (2006) CpG 7909: PF 3512676, PF-3512676. *Drugs R D* **7**: 312-6 [PMID:16922592]
- Adams JL, Smothers J, Srinivasan R and Hoos A. (2015) Big opportunities for small molecules in immuno-oncology. *Nat Rev Drug Discov* **14**: 603-22 [PMID:26228631]
- Ahlers LR and Goodman AG. (2016) Nucleic acid sensing and innate immunity: signaling pathways controlling viral pathogenesis and autoimmunity. *Curr Clin Microbiol Rep* **3**: 132-141 [PMID:27857881]
- Akira S and Takeda K. (2004) Toll-like receptor signalling. *Nat Rev Immunol* **4**: 499-511 [PMID:15229469]
- Akiyama M, Takeichi T, McGrath JA and Sugiura K. (2017) Autoinflammatory keratinization diseases. *J Allergy Clin Immunol* **140**: 1545-1547 [PMID:28668225]
- Alexopoulou L, Holt AC, Medzhitov R and Flavell RA. (2001) Recognition of double-stranded RNA and activation of NF-kappaB by Toll-like receptor 3. *Nature* **413**: 732-8 [PMID:11607032]
- Babdor J, Descamps D, Adiko AC, Tohmé M, Maschalidi S, Evnouchidou I, Vasconcellos LR, De Luca M, Mauvais FX and Garfa-Traore M *et al.*. (2017) IRAP⁺ endosomes restrict TLR9 activation and signaling. *Nat Immunol* **18**: 509-518 [PMID:28319098]
- Baldwin AG, Brough D and Freeman S. (2016) Inhibiting the Inflammasome: A Chemical Perspective. *J Med Chem* **59**: 1691-710 [PMID:26422006]
- Baldwin AG, Rivers-Auty J, Daniels MJD, White CS, Schwalbe CH, Schilling T, Hammadi H, Jaiyong P, Spencer NG and England H *et al.*. (2017) Boron-Based Inhibitors of the NLRP3 Inflammasome. *Cell Chem Biol* **24**: 1321-1335.e5 [PMID:28943355]
- Barochia A, Solomon S, Cui X, Natanson C and Eichacker PQ. (2011) Eritoran tetrasodium (E5564) treatment for sepsis: review of preclinical and clinical studies. *Expert Opin Drug Metab Toxicol* **7**: 479-94 [PMID:21323610]
- Bassaganya-Riera J, Leber A and Hontecillas R. (2020) 1,3,5-tris(6-methylpyridin-2-yl)oxybenzene derivatives and related compounds as nlrp1 ligands for treating inflammatory diseases Patent number: WO2020010132A1. Assignee: Landos Biopharma, Inc.. Priority date: 02/07/2019. Publication date: 09/01/2020.
- Bazin HG, Murray TJ, Bowen WS, Mozaffarian A, Fling SP, Bess LS, Livesay MT, Arnold JS, Johnson CL and Ryter KT *et al.*. (2008) The 'Ethereal' nature of TLR4 agonism and antagonism in the AGP class of lipid A mimetics. *Bioorg Med Chem Lett* **18**: 5350-4 [PMID:18835160]
- Betschart C, Faller M, Zink F, Hemmig R, Blank J, Vangrevelinghe E, Bourrel M, Glatthar R, Behnke D and Barker K *et al.*. (2022) Structure-Based Optimization of a Fragment-like TLR8 Binding Screening Hit to an *In Vivo* Efficacious TLR7/8 Antagonist. *ACS Med Chem Lett* **13**: 658-664 [PMID:35450354]
- Beutler B, Du X and Poltorak A. (2001) Identification of Toll-like receptor 4 (Tlr4) as the sole conduit for LPS signal transduction: genetic and evolutionary studies. *J Endotoxin Res* **7**: 277-80 [PMID:11717581]
- Biggadike K, Ahmed M, Ball DI, Coe DM, Dalmas Wilk DA, Edwards CD, Gibbon BH, Hardy CJ, Hermitage SA and Hessey JO *et al.*. (2016) Discovery of 6-Amino-2-[[[(1S)-1-methylbutyl]oxy]-9-[5-(1-piperidinyl)pentyl]-7,9-dihydro-8H-purin-8-one (GSK2245035), a Highly Potent and Selective Intranasal Toll-Like Receptor 7 Agonist for the Treatment of Asthma. *J Med Chem* **59**: 1711-26 [PMID:26861551]
- Bleda S and de Haro J. (2018) Identification of a potential inhibitor of NLRP1 inflammasome for the treatment of peripheral arterial disease. *Int J Cardiol* **256**: 30 [PMID:29454411]
- Bleda S, de Haro J, Varela C, Ferruelo A and Acin F. (2016) Elevated levels of triglycerides and vldl-cholesterol provoke activation of nlrp1 inflammasome in endothelial cells. *Int J Cardiol* **220**:

52-5 [PMID:27372042]

18. Bou Karroum N, Moarbes G, Guichou JF, Bonnet PA, Patinote C, Bouharoun-Tayoun H, Chamat S, Cuq P, Diab-Assaf M and Kassab I *et al.*. (2019) Novel and Selective TLR7 Antagonists among the Imidazo[1,2-*a*]pyrazines, Imidazo[1,5-*a*]quinoxalines, and Pyrazolo[1,5-*a*]quinoxalines Series. *J Med Chem* **62**: 7015-7031 [PMID:31283223]
19. Brown GJ, Cañete PF, Wang H, Medhavy A, Bones J, Roco JA, He Y, Qin Y, Cappello J and Ellyard JI *et al.*. (2022) TLR7 gain-of-function genetic variation causes human lupus. *Nature* **605**: 349-356 [PMID:35477763]
20. Bruns AM and Horvath CM. (2014) Antiviral RNA recognition and assembly by RLR family innate immune sensors. *Cytokine Growth Factor Rev* **25**: 507-12 [PMID:25081315]
21. Bryant CE, Orr S, Ferguson B, Symmons MF, Boyle JP and Monie TP. (2015) International Union of Basic and Clinical Pharmacology. XCVI. Pattern recognition receptors in health and disease. *Pharmacol Rev* **67**: 462-504 [PMID:25829385]
22. Buneman P, Christie G, Davies JA, Dimitrellou R, Harding SD, Pawson AJ, Sharman JL and Wu Y. (2020) Why data citation isn't working, and what to do about it *Database* **2020** [PMID:32367113]
23. Buschow SI, Biesta PJ, Groothuisink ZMA, Erler NS, Vanwolleghe T, Ho E, Najera I, Ait-Goughoulte M, de Knecht RJ and Boonstra A *et al.*. (2018) TLR7 polymorphism, sex and chronic HBV infection influence plasmacytoid DC maturation by TLR7 ligands. *Antiviral Res* **157**: 27-37 [PMID:29964062]
24. Chamaillard M, Girardin SE, Viala J and Philpott DJ. (2003) Nods, Nalps and Naip: intracellular regulators of bacterial-induced inflammation. *Cell Microbiol* **5**: 581-92 [PMID:12925128]
25. Chan M, Hayashi T, Mathewson RD, Nour A, Hayashi Y, Yao S, Tawatao RI, Crain B, Tsigelny IF and Kouznetsova VL *et al.*. (2013) Identification of substituted pyrimido[5,4-*b*]indoles as selective Toll-like receptor 4 ligands. *J Med Chem* **56**: 4206-23 [PMID:23656327]
26. Chavarría-Smith J and Vance RE. (2015) The NLRP1 inflammasomes. *Immunol Rev* **265**: 22-34 [PMID:25879281]
27. Coll RC, Robertson AA, Chae JJ, Higgins SC, Muñoz-Planillo R, Inserra MC, Vetter I, Dungan LS, Monks BG and Stutz A *et al.*. (2015) A small-molecule inhibitor of the NLRP3 inflammasome for the treatment of inflammatory diseases. *Nat Med* **21**: 248-55 [PMID:25686105]
28. Cooper M, Miller D, Macleod A, Van Wiltenburg J, Thom S, St-Gallay S and Shannon J. (2019) Novel sulfonamide carboxamide compounds Patent number: WO2019008025A1. Assignee: Inflazome Limited. Priority date: 07/07/2017. Publication date: 10/01/2019.
29. Cooper M and O'Neill L. (2021) Treatment or prevention of psychiatric brain disorders using the nlrp3 inhibitor n-((1,2,3,5,6,7-hexahydro-s-indacen-4-yl)carbamoyl)-1 -isopropyl-1 h-pyrazole-3-sulfonamide Patent number: WO2021089781A1. Assignee: Inflazome Limited. Priority date: 07/11/2019. Publication date: 14/05/2021.
30. Cui J, Zhu L, Xia X, Wang HY, Legras X, Hong J, Ji J, Shen P, Zheng S and Chen ZJ *et al.*. (2010) NLRC5 negatively regulates the NF-kappaB and type I interferon signaling pathways. *Cell* **141**: 483-96 [PMID:20434986]
31. Davis BK, Wen H and Ting JP. (2011) The inflammasome NLRs in immunity, inflammation, and associated diseases. *Annu Rev Immunol* **29**: 707-35 [PMID:21219188]
32. Dellacasagrande J. (2011) Humanised antibodies to toll-like receptor 2 and uses thereof Patent number: WO2011003925. Assignee: Opsona Therapeutics Limited. Priority date: 06/07/2009. Publication date: 13/01/2011.
33. Dodé C, Le Dû N, Cuisset L, Letourneur F, Berthelot JM, Vaudour G, Meyrier A, Watts RA, Scott DG and Nicholls A *et al.*. (2002) New mutations of CIAS1 that are responsible for Muckle-Wells syndrome and familial cold urticaria: a novel mutation underlies both syndromes. *Am J Hum Genet* **70**: 1498-506 [PMID:11992256]
34. Farhat K, Riekenberg S, Heine H, Debarry J, Lang R, Mages J, Buwitt-Beckmann U, Röschmann K, Jung G and Wiesmüller KH *et al.*. (2008) Heterodimerization of TLR2 with TLR1 or TLR6 expands the ligand spectrum but does not lead to differential signaling. *J Leukoc Biol* **83**: 692-701 [PMID:18056480]
35. Fitzgerald KA and Kagan JC. (2020) Toll-like Receptors and the Control of Immunity. *Cell* **180**: 1044-1066 [PMID:32164908]
36. Garay RP, Viens P, Bauer J, Normier G, Bardou M, Jeannin JF and Chiavaroli C. (2007) Cancer relapse under chemotherapy: why TLR2/4 receptor agonists can help. *Eur J Pharmacol* **563**: 1-17 [PMID:17383632]
37. Glick G, Ghosh S, Roush WR, Olhava EJ and O'Malley D. (2018) Substituted imidazo-quinolines as nlrp3 modulators Patent number: WO2018152396A1. Assignee: Innate Tumor Immunity Inc.. Priority date: 17/02/2017. Publication date: 23/08/2018.
38. Grandemange S, Sanchez E, Louis-Plence P, Tran Mau-Them F, Bessis D, Coubes C, Frouin E, Seyger M, Girard M and Puechberty J *et al.*. (2017) A new autoinflammatory and autoimmune syndrome associated with NLRP1 mutations: NAIAD (NLRP1-associated autoinflammation with arthritis and dyskeratosis). *Ann Rheum Dis* **76**: 1191-1198 [PMID:27965258]
39. Harrison D, Billinton A, Bock MG, Doedens JR, Gabel CA, Holloway MK, Porter RA, Reader V,

- Scanlon J and Schooley K *et al.*. (2023) Discovery of Clinical Candidate NT-0796, a Brain-Penetrant and Highly Potent NLRP3 Inflammasome Inhibitor for Neuroinflammatory Disorders. *J Med Chem* **66**: 14897-14911 [PMID:37874905]
40. Harton JA and Ting JP. (2000) Class II transactivator: mastering the art of major histocompatibility complex expression. *Mol Cell Biol* **20**: 6185-94 [PMID:10938095]
 41. Hayashi F, Smith KD, Ozinsky A, Hawn TR, Yi EC, Goodlett DR, Eng JK, Akira S, Underhill DM and Aderem A. (2001) The innate immune response to bacterial flagellin is mediated by Toll-like receptor 5. *Nature* **410**: 1099-103 [PMID:11323673]
 42. He C, Liu J, Li J, Wu H, Jiao C, Ze X, Xu S, Zhu Z, Guo W and Xu J *et al.*. (2024) Hit-to-Lead Optimization of the Natural Product Oridonin as Novel NLRP3 Inflammasome Inhibitors with Potent Anti-Inflammation Activity. *J Med Chem* **67**: 9406-9430 [PMID:38751194]
 43. He H, Jiang H, Chen Y, Ye J, Wang A, Wang C, Liu Q, Liang G, Deng X and Jiang W *et al.*. (2018) Oridonin is a covalent NLRP3 inhibitor with strong anti-inflammasome activity. *Nat Commun* **9**: 2550 [PMID:29959312]
 44. Heil F, Ahmad-Nejad P, Hemmi H, Hochrein H, Ampenberger F, Gellert T, Dietrich H, Lipford G, Takeda K and Akira S *et al.*. (2003) The Toll-like receptor 7 (TLR7)-specific stimulus loxoribine uncovers a strong relationship within the TLR7, 8 and 9 subfamily. *Eur J Immunol* **33**: 2987-97 [PMID:14579267]
 45. Hemmi H, Kaisho T, Takeuchi O, Sato S, Sanjo H, Hoshino K, Horiuchi T, Tomizawa H, Takeda K and Akira S. (2002) Small anti-viral compounds activate immune cells via the TLR7 MyD88-dependent signaling pathway. *Nat Immunol* **3**: 196-200 [PMID:11812998]
 46. Hemmi H, Takeuchi O, Kawai T, Kaisho T, Sato S, Sanjo H, Matsumoto M, Hoshino K, Wagner H and Takeda K *et al.*. (2000) A Toll-like receptor recognizes bacterial DNA. *Nature* **408**: 740-5 [PMID:11130078]
 47. Henao-Mejia J, Elinav E, Jin C, Hao L, Mehal WZ, Strowig T, Thaïss CA, Kau AL, Eisenbarth SC and Jurczak MJ *et al.*. (2012) Inflammasome-mediated dysbiosis regulates progression of NAFLD and obesity. *Nature* **482**: 179-85 [PMID:22297845]
 48. Henmyr V, Carlberg D, Manderstedt E, Lind-Halldén C, Säll T, Cardell LO and Halldén C. (2017) Genetic variation of the Toll-like receptors in a Swedish allergic rhinitis case population. *BMC Med Genet* **18**: 18 [PMID:28228119]
 49. Hoffman HM, Mueller JL, Broide DH, Wanderer AA and Kolodner RD. (2001) Mutation of a new gene encoding a putative pyrin-like protein causes familial cold autoinflammatory syndrome and Muckle-Wells syndrome. *Nat Genet* **29**: 301-5 [PMID:11687797]
 50. Hozumi H, Fujisawa T, Nakashima R, Johkoh T, Sumikawa H, Murakami A, Enomoto N, Inui N, Nakamura Y and Hosono Y *et al.*. (2016) Comprehensive assessment of myositis-specific autoantibodies in polymyositis/dermatomyositis-associated interstitial lung disease. *Respir Med* **121**: 91-99 [PMID:27888997]
 51. Huynh AS, Chung WJ, Cho HI, Moberg VE, Celis E, Morse DL and Vagner J. (2012) Novel toll-like receptor 2 ligands for targeted pancreatic cancer imaging and immunotherapy. *J Med Chem* **55**: 9751-62 [PMID:23098072]
 52. Ii M, Matsunaga N, Hazeki K, Nakamura K, Takashima K, Seya T, Hazeki O, Kitazaki T and Iizawa Y. (2006) A novel cyclohexene derivative, ethyl (6R)-6-[N-(2-Chloro-4-fluorophenyl)sulfamoyl]cyclohex-1-ene-1-carboxylate (TAK-242), selectively inhibits toll-like receptor 4-mediated cytokine production through suppression of intracellular signaling. *Mol Pharmacol* **69**: 1288-95 [PMID:16373689]
 53. Imamura R, Wang Y, Kinoshita T, Suzuki M, Noda T, Sagara J, Taniguchi S, Okamoto H and Suda T. (2010) Anti-inflammatory activity of PYNOD and its mechanism in humans and mice. *J Immunol* **184**: 5874-84 [PMID:20393137]
 54. Ingalls RR, Monks BG, Savedra R, Christ WJ, Delude RL, Medvedev AE, Espevik T and Golenbock DT. (1998) CD11/CD18 and CD14 share a common lipid A signaling pathway. *J Immunol* **161**: 5413-20 [PMID:9820516]
 55. Ising C, Venegas C, Zhang S, Scheiblich H, Schmidt SV, Vieira-Saecker A, Schwartz S, Albasset S, McManus RM and Tejera D *et al.*. (2019) NLRP3 inflammasome activation drives tau pathology. *Nature* **575**: 669-673 [PMID:31748742]
 56. Jayabalan N, Oronsky B, Cabrales P, Reid T, Caroen S, Johnson AM, Birch NA, O'Sullivan JD and Gordon R. (2023) A Review of RRx-001: A Late-Stage Multi-Indication Inhibitor of NLRP3 Activation and Chronic Inflammation. *Drugs* **83**: 389-402 [PMID:36920652]
 57. Jeong E and Lee JY. (2011) Intrinsic and extrinsic regulation of innate immune receptors. *Yonsei Med J* **52**: 379-92 [PMID:21488180]
 58. Jerala R. (2007) Structural biology of the LPS recognition. *Int J Med Microbiol* **297**: 353-63 [PMID:17481951]
 59. Jiang H, He H, Chen Y, Huang W, Cheng J, Ye J, Wang A, Tao J, Wang C and Liu Q *et al.*. (2017) Identification of a selective and direct NLRP3 inhibitor to treat inflammatory disorders. *J Exp Med* **214**: 3219-3238 [PMID:29021150]
 60. Jurk M, Heil F, Vollmer J, Schetter C, Krieg AM, Wagner H, Lipford G and Bauer S. (2002)

Human TLR7 or TLR8 independently confer responsiveness to the antiviral compound R-848. *Nat Immunol* **3**: 499 [PMID:12032557]

61. Karki R, Man SM and Kanneganti TD. (2017) Inflammasomes and Cancer. *Cancer Immunol Res* **5**: 94-99 [PMID:28093447]
62. Kawai T and Akira S. (2007) Antiviral signaling through pattern recognition receptors. *J Biochem* **141**: 137-45 [PMID:17190786]
63. Kawasaki K, Akashi S, Shimazu R, Yoshida T, Miyake K and Nishijima M. (2000) Mouse toll-like receptor 4.MD-2 complex mediates lipopolysaccharide-mimetic signal transduction by Taxol. *J Biol Chem* **275**: 2251-4 [PMID:10644670]
64. Khan PM, Correa RG, Divlianska DB, Peddibhotla S, Sessions EH, Magnuson G, Brown B, Suyama E, Yuan H and Mangravita-Novo A *et al.*. (2011) Identification of Inhibitors of NOD1-Induced Nuclear Factor- κ B Activation. *ACS Med Chem Lett* **2**: 780-785 [PMID:22003428]
65. Kuenzel S, Till A, Winkler M, Häsler R, Lipinski S, Jung S, Grötzinger J, Fickenscher H, Schreiber S and Rosenstiel P. (2010) The nucleotide-binding oligomerization domain-like receptor NLRC5 is involved in IFN-dependent antiviral immune responses. *J Immunol* **184**: 1990-2000 [PMID:20061403]
66. Lamphier M, Zheng W, Latz E, Spyvee M, Hansen H, Rose J, Genest M, Yang H, Shaffer C and Zhao Y *et al.*. (2014) Novel small molecule inhibitors of TLR7 and TLR9: mechanism of action and efficacy in vivo. *Mol Pharmacol* **85**: 429-40 [PMID:24342772]
67. Larson P, Kucaba TA, Xiong Z, Olin M, Griffith TS and Ferguson DM. (2017) Design and Synthesis of N1-Modified Imidazoquinoline Agonists for Selective Activation of Toll-like Receptors 7 and 8. *ACS Med Chem Lett* **8**: 1148-1152 [PMID:29152046]
68. LeibundGut-Landmann S, Waldburger JM, Krawczyk M, Otten LA, Suter T, Fontana A, Acha-Orbea H and Reith W. (2004) Mini-review: Specificity and expression of CIITA, the master regulator of MHC class II genes. *Eur J Immunol* **34**: 1513-25 [PMID:15162420]
69. Li L, Liu X, Sanders KL, Edwards JL, Ye J, Si F, Gao A, Huang L, Hsueh EC and Ford DA *et al.*. (2019) TLR8-Mediated Metabolic Control of Human Treg Function: A Mechanistic Target for Cancer Immunotherapy. *Cell Metab* **29**: 103-123.e5 [PMID:30344014]
70. Li L, Yu H, Jiang Y, Deng B, Bai L, Kijlstra A and Yang P. (2016) Genetic Variations of NLR family genes in Behcet's Disease. *Sci Rep* **6**: 20098 [PMID:26833430]
71. Liu Y, Olagnier D and Lin R. (2016) Host and Viral Modulation of RIG-I-Mediated Antiviral Immunity. *Front Immunol* **7**: 662 [PMID:28096803]
72. Liu YR, Yan X, Yu HX, Yao Y, Wang JQ, Li XF, Chen RN, Xu QQ, Ma TT and Huang C *et al.*. (2017) NLRC5 promotes cell proliferation via regulating the NF- κ B signaling pathway in Rheumatoid arthritis. *Mol Immunol* **91**: 24-34 [PMID:28865311]
73. Lu H, Dietsch GN, Matthews MA, Yang Y, Ghanekar S, Inokuma M, Suni M, Maino VC, Henderson KE and Howbert JJ *et al.*. (2012) VTX-2337 is a novel TLR8 agonist that activates NK cells and augments ADCC. *Clin Cancer Res* **18**: 499-509 [PMID:22128302]
74. Lucas K and Maes M. (2013) Role of the Toll Like receptor (TLR) radical cycle in chronic inflammation: possible treatments targeting the TLR4 pathway. *Mol Neurobiol* **48**: 190-204 [PMID:23436141]
75. Mach B, Steimle V and Reith W. (1994) MHC class II-deficient combined immunodeficiency: a disease of gene regulation. *Immunol Rev* **138**: 207-21 [PMID:8070816]
76. Mackay A, Velcicky J, Gommermann N, Mattes H, Janser P, Wright M, Dubois C, Brenneisen S, Ilic S and Vangrevelinghe E *et al.*. (2024) Discovery of NP3-253, a Potent Brain Penetrant Inhibitor of the NLRP3 Inflammasome. *J Med Chem* **67**: 20780-20798 [PMID:39574318]
77. Mackman RL, Mish M, Chin G, Perry JK, Appleby T, Aktoudianakis V, Metobo S, Pyun P, Niu C and Daffis S *et al.*. (2020) Discovery of GS-9688 (Selgantolimod) as a Potent and Selective Oral Toll-Like Receptor 8 Agonist for the Treatment of Chronic Hepatitis B. *J Med Chem* **63**: 10188-10203 [PMID:32407112]
78. Mangan MS and Latz E. (2014) NLRC3 puts the brakes on STING. *Immunity* **40**: 305-6 [PMID:24656040]
79. Mangan MSJ, Olhava EJ, Roush WR, Seidel HM, Glick GD and Latz E. (2018) Targeting the NLRP3 inflammasome in inflammatory diseases. *Nat Rev Drug Discov* **17**: 688 [PMID:30116046]
80. Mangan MSJ, Olhava EJ, Roush WR, Seidel HM, Glick GD and Latz E. (2018) Targeting the NLRP3 inflammasome in inflammatory diseases. *Nat Rev Drug Discov* **17**: 588-606 [PMID:30026524]
81. Mao T, Israelow B, Lucas C, Vogels CBF, Gomez-Calvo ML, Fedorova O, Breban MI, Menasche BL, Dong H and Linehan M *et al.*. (2022) A stem-loop RNA RIG-I agonist protects against acute and chronic SARS-CoV-2 infection in mice. *J Exp Med* **219** [PMID:34757384]
82. Marchetti C, Swartzwelter B, Gamboni F, Neff CP, Richter K, Azam T, Carta S, Tengesdal I, Nemkov T and D'Alessandro A *et al.*. (2018) OLT1177, a β -sulfonyl nitrile compound, safe in humans, inhibits the NLRP3 inflammasome and reverses the metabolic cost of inflammation. *Proc Natl Acad Sci USA* **115**: E1530-E1539 [PMID:29378952]
83. Martinon F, Pétrilli V, Mayor A, Tardivel A and Tschopp J. (2006) Gout-associated uric acid

- crystals activate the NALP3 inflammasome. *Nature* **440**: 237-41 [PMID:16407889]
84. Matsumiya T and Stafforini DM. (2010) Function and regulation of retinoic acid-inducible gene-1. *Crit Rev Immunol* **30**: 489-513 [PMID:21175414]
 85. Maver A, Lavtar P, Ristić S, Stopinšek S, Simčič S, Hočevár K, Sepčić J, Drulović J, Pekmezović T and Novaković I *et al.*. (2017) Identification of rare genetic variation of NLRP1 gene in familial multiple sclerosis. *Sci Rep* **7**: 3715 [PMID:28623311]
 86. McBride C, Trzoss L, Povero D, Lazic M, Ambrus-Aikelin G, Santini A, Pranadinata R, Bain G, Stansfield R and Stafford JA *et al.*. (2022) Overcoming Preclinical Safety Obstacles to Discover (S)-N-((1,2,3,5,6,7-Hexahydro-s-indacen-4-yl)carbamoyl)-6-(methylamino)-6,7-dihydro-5H-pyrazolo[5,1-b][1,3]oxazine-3-sulfonamide (GDC-2394): A Potent and Selective NLRP3 Inhibitor. *J Med Chem* **65**: 14721-14739 [PMID:36279149]
 87. Meier A, Chang JJ, Chan ES, Pollard RB, Sidhu HK, Kulkarni S, Wen TF, Lindsay RJ, Orellana L and Mildvan D *et al.*. (2009) Sex differences in the Toll-like receptor-mediated response of plasmacytoid dendritic cells to HIV-1. *Nat Med* **15**: 955-9 [PMID:19597505]
 88. Miao EA, Andersen-Nissen E, Warren SE and Aderem A. (2007) TLR5 and Ipaf: dual sensors of bacterial flagellin in the innate immune system. *Semin Immunopathol* **29**: 275-88 [PMID:17690885]
 89. Milam EC, Futran J and Franks Jr AG. (2016) Anti-MDA5 Antibody Dermatomyositis Overlap with Systemic Lupus Erythematosus: A Case Report and Review of the Literature. *Open Rheumatol J* **10**: 122-128 [PMID:28077979]
 90. Monnet E, Lapeyre G, Poelgeest EV, Jacqmin P, Graaf K, Reijers J, Moerland M, Burggraaf J and Min C. (2017) Evidence of NI-0101 pharmacological activity, an anti-TLR4 antibody, in a randomized phase I dose escalation study in healthy volunteers receiving LPS. *Clin Pharmacol Ther* **101**: 200-208 [PMID:27706798]
 91. Morin MD, Wang Y, Jones BT, Mifune Y, Su L, Shi H, Moresco EMY, Zhang H, Beutler B and Boger DL. (2018) Diprovocims: A New and Exceptionally Potent Class of Toll-like Receptor Agonists. *J Am Chem Soc* **140**: 14440-14454 [PMID:30272974]
 92. Nakamura T, Wada H, Kurebayashi H, McInally T, Bonnert R and Isobe Y. (2013) Synthesis and evaluation of 8-oxoadenine derivatives as potent Toll-like receptor 7 agonists with high water solubility. *Bioorg Med Chem Lett* **23**: 669-72 [PMID:23265901]
 93. Nakao Y, Funami K, Kikkawa S, Taniguchi M, Nishiguchi M, Fukumori Y, Seya T and Matsumoto M. (2005) Surface-expressed TLR6 participates in the recognition of diacylated lipopeptide and peptidoglycan in human cells. *J Immunol* **174**: 1566-73 [PMID:15661917]
 94. Neerincx A, Lautz K, Menning M, Kremmer E, Zigrino P, Hösel M, Büning H, Schwarzenbacher R and Kufer TA. (2010) A role for the human nucleotide-binding domain, leucine-rich repeat-containing family member NLRC5 in antiviral responses. *J Biol Chem* **285**: 26223-32 [PMID:20538593]
 95. Oh DY, Baumann K, Hamouda O, Eckert JK, Neumann K, Kücherer C, Bartmeyer B, Poggensee G, Oh N and Pruss A *et al.*. (2009) A frequent functional toll-like receptor 7 polymorphism is associated with accelerated HIV-1 disease progression. *AIDS* **23**: 297-307 [PMID:19114863]
 96. Ohashi K, Burkart V, Flohé S and Kolb H. (2000) Cutting edge: heat shock protein 60 is a putative endogenous ligand of the toll-like receptor-4 complex. *J Immunol* **164**: 558-61 [PMID:10623794]
 97. Oosting M, Cheng SC, Bolscher JM, Vestering-Stenger R, Plantinga TS, Verschuere IC, Arts P, Garritsen A, van Eenennaam H and Sturm P *et al.*. (2014) Human TLR10 is an anti-inflammatory pattern-recognition receptor. *Proc Natl Acad Sci USA* **111**: E4478-84 [PMID:25288745]
 98. Pan Y, Wang Y, Xu J, Wu J, Chen Q, Zeng G and Zhao G. (2017) TG and VLDL cholesterol activate NLRP1 inflammasome by Nuclear Factor-κB in endothelial cells. *Int J Cardiol* **234**: 103 [PMID:28062143]
 99. Park BS, Song DH, Kim HM, Choi BS, Lee H and Lee JO. (2009) The structural basis of lipopolysaccharide recognition by the TLR4-MD-2 complex. *Nature* **458**: 1191-5 [PMID:19252480]
 100. Peri F and Calabrese V. (2014) Toll-like receptor 4 (TLR4) modulation by synthetic and natural compounds: an update. *J Med Chem* **57**: 3612-22 [PMID:24188011]
 101. Place DE and Kanneganti TD. (2018) Recent advances in inflammasome biology. *Curr Opin Immunol* **50**: 32-38 [PMID:29128729]
 102. Plantinga TS, Johnson MD, Scott WK, van de Vosse E, Velez Edwards DR, Smith PB, Alexander BD, Yang JC, Kremer D and Laird GM *et al.*. (2012) Toll-like receptor 1 polymorphisms increase susceptibility to candidemia. *J Infect Dis* **205**: 934-43 [PMID:22301633]
 103. Poltorak A, He X, Smirnova I, Liu MY, Van Huffel C, Du X, Birdwell D, Alejos E, Silva M and Galanos C *et al.*. (1998) Defective LPS signaling in C3H/HeJ and C57BL/10ScCr mice: mutations in Tlr4 gene. *Science* **282**: 2085-8 [PMID:9851930]
 104. Sabbah A, Chang TH, Harnack R, Frohlich V, Tominaga K, Dube PH, Xiang Y and Bose S. (2009) Activation of innate immune antiviral responses by Nod2. *Nat Immunol* **10**: 1073-80 [PMID:19701189]

105. Salunke DB, Yoo E, Shukla NM, Balakrishna R, Malladi SS, Serafin KJ, Day VW, Wang X and David SA. (2012) Structure-activity relationships in human Toll-like receptor 8-active 2,3-diamino-furo[2,3-c]pyridines. *J Med Chem* **55**: 8137-51 [PMID:22924757]
106. Saresella M, La Rosa F, Piancone F, Zoppis M, Marventano I, Calabrese E, Rainone V, Nemni R, Mancuso R and Clerici M. (2016) The NLRP3 and NLRP1 inflammasomes are activated in Alzheimer's disease. *Mol Neurodegener* **11**: 23 [PMID:26939933]
107. Scholl T, Mahanta SK and Strominger JL. (1997) Specific complex formation between the type II bare lymphocyte syndrome-associated transactivators CIITA and RFX5. *Proc Natl Acad Sci USA* **94**: 6330-4 [PMID:9177217]
108. Schroder K and Tschopp J. (2010) The inflammasomes. *Cell* **140**: 821-32 [PMID:20303873]
109. Schwandner R, Dziarski R, Wesche H, Rothe M and Kirschning CJ. (1999) Peptidoglycan- and lipoteichoic acid-induced cell activation is mediated by toll-like receptor 2. *J Biol Chem* **274**: 17406-9 [PMID:10364168]
110. Sharma N and Jha S. (2016) NLR-regulated pathways in cancer: opportunities and obstacles for therapeutic interventions. *Cell Mol Life Sci* **73**: 1741-64 [PMID:26708292]
111. Sherer BA and Brugger N. (2017) Polycyclic tlr7/8 antagonists and use thereof in the treatment of immune disorders Patent number: WO2017106607A1. Assignee: Merck Patent Gmbh. Priority date: 17/12/2015. Publication date: 22/06/2017.
112. Shimazu R, Akashi S, Ogata H, Nagai Y, Fukudome K, Miyake K and Kimoto M. (1999) MD-2, a molecule that confers lipopolysaccharide responsiveness on Toll-like receptor 4. *J Exp Med* **189**: 1777-82 [PMID:10359581]
113. Souyris M, Cenac C, Azar P, Daviaud D, Canivet A, Grunenwald S, Pienkowski C, Chaumeil J, Mejia JE and Guéry JC. (2018) TLR7 escapes X chromosome inactivation in immune cells. *Sci Immunol* **3** [PMID:29374079]
114. Souyris M, Mejia JE, Chaumeil J and Guéry JC. (2019) Female predisposition to TLR7-driven autoimmunity: gene dosage and the escape from X chromosome inactivation. *Semin Immunopathol* **41**: 153-164 [PMID:30276444]
115. Stöver AG, Da Silva Correia J, Evans JT, Cluff CW, Elliott MW, Jeffery EW, Johnson DA, Lacy MJ, Baldrige JR and Probst P *et al.* (2004) Structure-activity relationship of synthetic toll-like receptor 4 agonists. *J Biol Chem* **279**: 4440-9 [PMID:14570885]
116. Sun S, Li Z, Huang C, Liu J, Yu Q, Jiang X, Yue K, Zhao J, Xu T and Liu Y *et al.* (2023) Discovery of Novel 2,3-Dihydro-1*H*-indene-5-sulfonamide NLRP3 Inflammasome Inhibitors Targeting Colon as a Potential Therapy for Colitis. *J Med Chem* **66**: 16141-16167 [PMID:38029358]
117. Sönmez HE and Özen S. (2017) A clinical update on inflammasomopathies. *Int Immunol* **29**: 393-400 [PMID:28387826]
118. Takeuchi O and Akira S. (2010) Pattern recognition receptors and inflammation. *Cell* **140**: 805-20 [PMID:20303872]
119. Takeuchi O, Kawai T, Mühlradt PF, Morr M, Radolf JD, Zychlinsky A, Takeda K and Akira S. (2001) Discrimination of bacterial lipoproteins by Toll-like receptor 6. *Int Immunol* **13**: 933-40 [PMID:11431423]
120. Takeuchi O, Sato S, Horiuchi T, Hoshino K, Takeda K, Dong Z, Modlin RL and Akira S. (2002) Cutting edge: role of Toll-like receptor 1 in mediating immune response to microbial lipoproteins. *J Immunol* **169**: 10-4 [PMID:12077222]
121. Tarafdar A, Hopcroft LE, Gallipoli P, Pellicano F, Cassels J, Hair A, Korfi K, Jørgensen HG, Vetrie D and Holyoake TL *et al.* (2017) CML cells actively evade host immune surveillance through cytokine-mediated downregulation of MHC-II expression. *Blood* **129**: 199-208 [PMID:27793879]
122. Thornton P, Reader V, Digby Z, Smolak P, Lindsay N, Harrison D, Clarke N and Watt AP. (2024) Reversal of High Fat Diet-Induced Obesity, Systemic Inflammation, and Astroglialosis by the NLRP3 Inflammasome Inhibitors NT-0249 and NT-0796. *J Pharmacol Exp Ther* **388**: 813-826 [PMID:38336379]
123. Ting JP, Lovering RC, Alnemri ES, Bertin J, Boss JM, Davis BK, Flavell RA, Girardin SE, Godzik A and Harton JA *et al.* (2008) The NLR gene family: a standard nomenclature. *Immunity* **28**: 285-7 [PMID:18341998]
124. Tschopp J, Martinon F and Burns K. (2003) NALPs: a novel protein family involved in inflammation. *Nat Rev Mol Cell Biol* **4**: 95-104 [PMID:12563287]
125. Uematsu S and Akira S. (2008) Toll-Like receptors (TLRs) and their ligands. *Handb Exp Pharmacol*: 1-20 [PMID:18071652]
126. van der Made CI, Simons A, Schuurs-Hoeijmakers J, van den Heuvel G, Mantere T, Kersten S, van Deuren RC, Steehouwer M, van Reijmersdal SV and Jaeger M *et al.* (2020) Presence of Genetic Variants Among Young Men With Severe COVID-19. *JAMA* **324**: 663-673 [PMID:32706371]
127. Wang W, Wang C, Gong Y and Zhang X. (2018) Inhibition of NLRP1 inflammasome might be a novel therapeutic target in the treatment of peripheral arterial disease. *Int J Cardiol* **256**: 29 [PMID:29454409]
128. Wang Y, Su L, Morin MD, Jones BT, Whitby LR, Surakattula MM, Huang H, Shi H, Choi JH and

- Wang KW *et al.*. (2016) TLR4/MD-2 activation by a synthetic agonist with no similarity to LPS. *Proc Natl Acad Sci USA* **113**: E884-93 [PMID:26831104]
129. Webber SE and Appleman JR. (2019) Tlr7 agonists Patent number: [WO2019226977A1](#). Assignee: Primmune Therapeutics, Inc.. Priority date: 25/05/2018. Publication date: 28/11/2019.
 130. Westerveld GH, Korver CM, van Pelt AM, Leschot NJ, van der Veen F, Repping S and Lombardi MP. (2006) Mutations in the testis-specific NALP14 gene in men suffering from spermatogenic failure. *Hum Reprod* **21**: 3178-84 [PMID:16931801]
 131. Wu J, Qin L, Ding X and Li C. (2024) NLRP3 inflammasome inhibitors and uses thereof Patent number: [WO2024240153A1](#). Assignee: Insilico Medicine Ip Limited. Priority date: 21/05/2024. Publication date: 28/11/2024.
 132. Yau AC, Piehl F, Olsson T and Holmdahl R. (2017) Effects of C2ta genetic polymorphisms on MHC class II expression and autoimmune diseases. *Immunology* **150**: 408-417 [PMID:27861821]
 133. Yoshimura A, Lien E, Ingalls RR, Tuomanen E, Dziarski R and Golenbock D. (1999) Cutting edge: recognition of Gram-positive bacterial cell wall components by the innate immune system occurs via Toll-like receptor 2. *J Immunol* **163**: 1-5 [PMID:10384090]
 134. Youm YH, Nguyen KY, Grant RW, Goldberg EL, Bodogai M, Kim D, D'Agostino D, Planavsky N, Lupfer C and Kanneganti TD *et al.*. (2015) The ketone metabolite β -hydroxybutyrate blocks NLRP3 inflammasome-mediated inflammatory disease. *Nat Med* **21**: 263-9 [PMID:25686106]
 135. Yu CH, Moecking J, Geyer M and Masters SL. (2018) Mechanisms of NLRP1-Mediated Autoinflammatory Disease in Humans and Mice. *J Mol Biol* **430**: 142-152 [PMID:28733143]
 136. Zhai Z, Liu W, Kaur M, Luo Y, Domenico J, Samson JM, Shellman YG, Norris DA, Dinarello CA and Spritz RA *et al.*. (2017) NLRP1 promotes tumor growth by enhancing inflammasome activation and suppressing apoptosis in metastatic melanoma. *Oncogene* **36**: 3820-3830 [PMID:28263976]
 137. Zhang L, Mo J, Swanson KV, Wen H, Petrucelli A, Gregory SM, Zhang Z, Schneider M, Jiang Y and Fitzgerald KA *et al.*. (2014) NLRC3, a member of the NLR family of proteins, is a negative regulator of innate immune signaling induced by the DNA sensor STING. *Immunity* **40**: 329-41 [PMID:24560620]
 138. Zhang S, Hu Z, Tanji H, Jiang S, Das N, Li J, Sakaniwa K, Jin J, Bian Y and Ohto U *et al.*. (2018) Small-molecule inhibition of TLR8 through stabilization of its resting state. *Nat Chem Biol* **14**: 58-64 [PMID:29155428]
 139. Zhong FL, Mamaï O, Sborgi L, Boussofara L, Hopkins R, Robinson K, Szeverényi I, Takeichi T, Balaji R and Lau A *et al.*. (2016) Germline NLRP1 Mutations Cause Skin Inflammatory and Cancer Susceptibility Syndromes via Inflammasome Activation. *Cell* **167**: 187-202.e17 [PMID:27662089]