Tittle of Manuscript: **The Role of Pattern Recognition Receptor (PRR) in the Body's Defense System: A Narrative Literature Review**

1.Proofread document received (March 4th, 2022)
-Document from proofreading service
2.Submitted to the journal “Open Access Indonesian Journal of Medical Reviews" (March 9th, 2022)
3.Peer Reviewer results: Revision Required (March 16th, 2022)
4.Revised version received by journal (March 24th, 2022)
5.Paper Accepted for publication (April 2nd, 2023)
6.Galley proof (April 4th, 2023)
7.Paper published (April 5th, 2023)

-Document from proofreading service

March 4th, 2021

HM Publisher
Jl Sirnaraga No 99, 8 Ilir, Ilir Timur 3, Palembang, South Sumatra, Indonesia

CONFIDENTIAL
March 4th, 2021

Certificate Service Confirmation

To whom it may concern,
HM Publisher provided comprehensive editing services for manuscript entitled The Role of Pattern Recognition Receptor (PRR) in the Body's Defense System: A Narrative Literature Review. The edit has achieved Grade A: priority publishing; no language polishing required after editing. Should you require any additional information, please do not hesitate to contact me.

Regards,

Khrishna Murti, PhD
Head of Language Institute-HM Publisher
Email: khrishnamurti@gmail.com

Submitted to the journal "Open Access Indonesian Journal of Medical Reviews" (March 9th, 2022)

The Role of Pattern Recognition Receptor (PRR) in the Body's Defense System: A Narrative Literature Review

Ziske Maritska[1], Rachmat Hidayat[1*]

[1]Department of Biology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

*Email: rachmathidayat@fk.unsri.ac.id

Abstract

Each cell has receptors on the cell surface that specifically bind to solutes (ligands) produced during tissue damage or infection. This review aims to outline the role of PRR on the human body's defense system. The binding of the ligand to its receptor results in activation of intracellular signaling pathways and activation of cells. B and T lymphocytes of the adaptive immune system have developed surface receptors (i.e., T-cell receptors, or TCRs, and B-cell receptors, or BCRs) that bind to a large spectrum of antigens. The cells involved in innate resistance have developed a series of different receptors that recognize a much more limited arrangement of specific molecules. These are referred to as pattern recognition receptors (PRRs), and they recognize molecular patterns in infectious agents or their products (pathogen-associated molecular patterns, or PAMPs), or products of cellular damage (necrosis or apoptosis; molecular-related patterns of damage, or DAMPs). Pattern recognition receptor (PRR) is a receptor complex that interacts with various molecules such as PAMPs and DAMPs. PRR bonds with these molecules play a role in various actions of innate immunity and adaptive immunity.

Keywords: Receptor, Pattern Recognition Receptor, Immunity, TLR, NLRs

1. Introduction

Cells of innate and adaptive immunity must recognize and respond to their environment, whether products of damaged cells or potential pathogenic microorganisms. Each cell has receptors on the cell surface that specifically bind to solutes (ligands) produced during tissue damage or infection. The binding of the ligand to its receptor results in activation of intracellular signaling pathways and activation of cells. L immunocytes B and T of the adaptive immune system have developed surface receptors (i.e., T-cell receptors, or TCRs, and B-cell receptors, or BCRs) that bind to a large spectrum of antigens. The cells involved in innate resistance have developed a

series of different receptors that recognize a much more limited arrangement of specific molecules. These are referred to as pattern recognition receptors (PRRs), and they recognize molecular patterns in infectious agents or their products (pathogen-associated molecular patterns, or PAMPs), or products of cellular damage (necrosis or apoptosis; molecular-related patterns of damage, or DAMPs). PRRs are commonly found in cells at the host interface and the environment (i.e., skin, respiratory tract, gastrointestinal tract, genitourinary tract), where they monitor for cell damage products and potentially infectious microorganisms. Although most PRR is on the surface of cells, some are secreted or intracellular. An example of secreted PRR is the mannose-binding lectin of the complement activation lectin pathway. Cellular PRR includes Toll-like receptors (TLR), complement receptors (CR), scavenger receptors, glucan receptors, and mannose receptors. [1-5] This review aims to outline the role of PRR on the human body's defense system.

Toll-Like Receptor (TLR)

In humans, at least 11 different Toll-like receptors (TLRs) have been described, 10 of which function. They are expressed on the surface of many cells that have direct and initial contact with potential pathogenic microorganisms. These include mucosal epithelial cells, mast cells, neutrophils, macrophages, dendritic cells, and some lymphocyte subpopulations. (Dendritic cells are found in skin, mucosa, and lymphoid tissue, where they have evolved from Langerhans cells and serve as highly specialized initiators of adaptive immune responses.) TLR recognizes a wide variety of PAMPs located on the cell wall or surface of microorganisms (e.g., bacterial lipopolysaccharide [LPS], peptidoglycan, lipoproteins, zymosan yeast, viral coat proteins), other surface structures (e.g., bacterial flagellin), or microbial nucleic acids (e.g., bacterial DNA, viral double-stranded RNA). Some TLRs recognize host factors produced by depressed or damaged cells (e.g., protein breakdown products of the extracellular matrix, chromatin). The interaction between PAMPs and TLRs, with the collaboration of other cellular receptors (e.g., CD14), can result in cell activation and release of solute products (e.g., cytokines) that increase local resistance to pathogenic microorganisms. TLRs are also one of the bridges between innate resistance and adaptive immune response through cytokine induction that enhances lymphocyte response to foreign antigens in pathogens. Genetic polymorphisms in TLRs may explain some of the observed differences between individual resistance and susceptibility to infection. [6-9]

Table 1. Various Toll-Like Receptors (TLRs)

RECEPTORS	CELLULAR EXPRESSION PATTERNS	PAMP INTRODUCTION
TLR1	Cell surface (everywhere): neutrophils, monocytes/macrophages, dendritic cells, T cells, B cells, NK cells	Fungi, bacteria, viruses; forming heterodimer with TLR2 (TLR2 introduction)
TLR2	Cell surface: neutrophils, monocytes/macrophages, dendritic cells	Fungi (zymosan yeast), bacteria (gram-positive peptidoglycan bacteria, lipoproteins), viruses (lipoproteins)
TLR 3	Intracellular: monocytes/macrophages, se dendritic, T cells, NK cells, epithelial cells	Double-chain RNA produced by many viruses
TLR 4	Cell surface: granulocytes, monocytes/macrophages, dendritic cells, T cells, B cells, epithelial cells	Bacteria (especially gram-negative bacteria LPS, lipoteichoic acid), viruses (RSV F protein, hepatitis C)
TLR 5	Cell surface: granulocytes, monocytes/macrophages, dendritic cells, NK cells, epithelial cells	Bacteria (flagellin); forming heterodimer with TLR 4
TLR 6	Cell surface: monocytes/macrophages, dendritic cells, B cells, NK cells	Fungi, bacteria, viruses; forming heterodimer with TLR 2(introduction of TLR 2)
TLR 7	Intracellular: monocytes/macrophages, dendritic cells, B cells	Indeterminate natural ligands; Single-chain viral RNA

TLR 8	Cell surface: monocytes/macrophages, dendritic cells, NK cells	Indeterminate natural ligands; can bind fungal PAMPS or single-chain viral RNA
TLR 9	Intracellular: monocytes/macrophages, dendritic cells, B cells	Bacteria (unmethylated DNA [CpG dinucleotide])
TLR 10	Cell surface: monocytes/macrophages, dendritic cells, B cells	Indeterminate natural ligands; can form heterodimers with TLR 2
TLR 11	The TLR11 gene does not code for a full-length protein in humans	Unknown immune response

Complement receptors

These receptors are found on many innate and adaptive immune response cells (e.g., granulocytes, monocytes/macrophages, lymphocytes, mast cells, erythrocytes, platelets), as well as some epithelial cells. They recognized some of the resulting fragments through activation of the complement system. Under various normal and disease-related conditions, antibody, antigen, and complement immune complexes are formed in the blood and secreted by cells expressing complement-1 receptor (CR1), which binds to C4b, C3b, and C3b decomposition products (e.g., IC3b). CR2 is found in B lymphocytes, as well as dendritic cells and some epithelial cells, and recognizes C3b decomposition products (specifically iC3b). CR2 appears to facilitate B cell function and antibody production. Both CR3 and CR4 are integrins that primarily recognize C3b decomposition products (specifically iC3b). CR3 (integrin Mβ2, also called CD11b/CD18) facilitates phagocytosis by neutrophils and monocytes/macrophages. CR4 (αXββ2, also called CD11c/CD18) is found mainly in platelets. (Integrins are cell surface receptors that have roles in cell adhesion and attachment and mediate intracellular signals in the extracellular matrix) . [10-13]

Receptor scavenger

These receptors are primarily expressed on macrophages and facilitate the recognition and phagocytosis of pathogenic bacteria, as well as damaged cells and soluble lipoprotein changes

associated with blood vessel damage (e.g. high-density lipoprotein [HDL], acetylated low-density lipoprotein [LDL], oxidized LDL). More than eight receptors have been identified. Some scavenger receptors (e.g., SR PSOX) recognize the cell membrane of phospholipid phosphatidylserine (PS). PS is usually sequestered on the cytoplasmic surface of cell membranes, but is externalized under a very limited range of conditions, including erythrocyte aging and cellular apoptosis. Thus, macrophages, through these receptors, can identify and dispose of old red blood cells and cells undergoing apoptosis. Another important scavenger receptor is CD14, which recognizes LPS and LPS-binding protein complexes. LPS-binding proteins are upregulated during inflammation by the cytokines interleukin-6 (IL-6) and IL-1 and help remove LPS bacteria (endotoxins) from circulation. [14-16]

NOD-Like Receptors (NLRs)

NLRs are cytoplasmic receptors that recognize microbial products and damaged cells. At least 22 NLRs have been identified in humans. NOD-1 and NOD-2 are cytoplasmic and recognize peptidoglycan fragments from intracellular bacteria and initiate the production of proinflammatory mediators, such as tumor necrosis factor (TNF) and IL-6. Some NLRs associate with intracellular multiprotein complexes called inflammasomes. Inflammasomes primarily bind to cellular stress-related molecules, a type of DAMP, and through activation of caspases-1 control the activation and secretion of inflammatory cytokines, such as IL-1β. [17-20]

2.Conclusion

Pattern Recognition Receptor (PRR) is a receptor complex that interacts with various molecules such as PAMPs and DAMPs. PRR bonds with these molecules play a role in various actions of innate immunity and adaptive immunity.

3. References

1.Walsh D, McCarthy J, O'Driscoll C, Melgar S. Pattern recognition receptors–molecular orchestrators of inflammation in inflammatory bowel disease. *Cytokine Growth Factor Rev*. (2013) 24:91–104. doi: 10.1016/j.cytogfr.2012.09.003

CrossRef Full Text | Google Scholar

2. Medzhitov R, Preston-Hurlburt P, Janeway CA Jr. A human homologue of the Drosophila Toll protein signals activation of adaptive immunity. *Nature* (1997) 388:394–7. doi: 10.1038/41131

PubMed Abstract | CrossRef Full Text | Google Scholar

3. Bortoluci KR, Medzhitov R. *Control of infection by pyroptosis and autophagy: role of TLR and NLR. Cell Mol Life Sci.* (2010) 67:1643–51. DOI: 10.1007/S00018-010-0335-5

CrossRef Full Text

4. Matzinger P. Tolerance, danger, and the extended family. *Annu Rev Immunol.* (1994) 12:991–1045. DOI: 10.1146/annurev.iy.12.040194.005015

PubMed Abstract | CrossRef Full Text | Google Scholar

5. Galluzzi L, Vitale I, Aaronson SA, Abrams JM, Adam D, Agostinis P, et al. Molecular mechanisms of cell death: recommendations of the Nomenclature Committee on Cell Death 2018. *Cell Death Differ.* (2018) 25:486–541. DOI: 10.1038/S41418-017-0012-4

PubMed Abstract | CrossRef Full Text | Google Scholar

6. Kerr JF, Wyllie AH, Currie AR. Apoptosis: a basic biological phenomenon with wide-ranging implications in tissue kinetics. *Br J Cancer* (1972) 26:239–57. DOI: 10.1038/bjc.1972.33

PubMed Abstract | CrossRef Full Text | Google Scholar

7. Amarante-Mendes GP, Green DR. The regulation of apoptotic cell death. *Braz J med Biol Res.* (1999) 32:1053–61.

PubMed Abstract | Google Scholar

8. Fadok VA, Bratton DL, Konowal A, Freed PW, Westcott JY, Henson PM. Macrophages that have ingested apoptotic cells *in vitro* inhibit proinflammatory cytokine production through autocrine/paracrine mechanisms involving TGF-beta, PGE2, and PAF. *J Clin Invest.* (1998) 101:890–8. doi: 10.1172/JCI1112

PubMed Abstract | CrossRef Full Text | Google Scholar

9. Medina CB, Ravichandran KS. Do not let death do us part: 'find-me' signals in communication between dying cells and the phagocytes. *Cell Death Differ.* (2016) 23:979–89. DOI: 10.1038/cdd.2016.13

CrossRef Full Text | Google Scholar

10. Hochreiter-Hufford A, Ravichandran KS. Clearing the dead: apoptotic cell sensing, recognition, engulfment, and digestion. *Cold Spring Harb Perspect Biol.* (2013) 5:a008748. doi: 10.1101/cshperspect.a008748

PubMed Abstract | CrossRef Full Text | Google Scholar

11. Cullen SP, Henry CM, Kearney CJ, Logue SE, Feoktistova M, Tynan GA, et al. Fas/CD95-induced chemokines can serve as "find-me" signals for apoptotic cells. *Mol Cell* (2013) 49:1034–48. DOI: 10.1016/J.Molcel.2013.01.025

PubMed Abstract | CrossRef Full Text | Google Scholar

12. Metzstein MM, Stanfield GM, Horvitz HR. Genetics of programmed cell death in *C. elegans: past, present and future. Trends Genet.* (1998) 14:410–6. DOI: 10.1016/S0168-9525(98)01573-X

PubMed Abstract | CrossRef Full Text | Google Scholar

13. Pop C, Salvesen GS. Human caspases: activation, specificity, and regulation. *J Biol Chem.* (2009) 284:21777–81. DOI: 10.1074/JBC. R800084200

PubMed Abstract | CrossRef Full Text | Google Scholar

14. McIlwain DR, Berger T, Mak TW. Caspase functions in cell death and disease. *Cold Spring Harb Perspect Biol.* (2013) 5:a008656. DOI: 10.1101/cshperspect.a008656

PubMed Abstract | CrossRef Full Text | Google Scholar

15. Pereira WO, Amarante-Mendes GP. Apoptosis: a programme of cell death or cell disposal? *Scand J Immunol.* (2011) 73:401–7. DOI: 10.1111/J.1365-3083.2011.02513.x

CrossRef Full Text | Google Scholar

16. Martin SJ, Finucane DM, Amarante-Mendes GP, O'Brien GA, Green DR. Phosphatidylserine externalization during CD95-induced apoptosis of cells and cytoplasts requires ICE/CED-3 protease activity. *J Biol Chem.* (1996) 271:28753 –6. DOI: 10.1074/jbc.271.46.28753

PubMed Abstract | CrossRef Full Text | Google Scholar

17. Amarante-Mendes GP, Finucane DM, Martin SJ, Cotter TG, Salvesen GS, Green DR. Anti-apoptotic oncogenes prevent caspase-dependent and independent commitment for cell death. *Cell Death Differ.* (1998) 5:298–306. DOI: 10.1038/SJ.CDD.4400354

PubMed Abstract | CrossRef Full Text | Google Scholar

18. Tait SW, Green DR. Mitochondrial regulation of cell death. *Cold Spring Harb Perspect Biol.* (2013) 5:a008706. DOI: 10.1101/cshperspect.a008706

PubMed Abstract | CrossRef Full Text | Google Scholar

19. Wertz IE, Dixit VM. Regulation of death receptor signaling by the ubiquitin system. *Cell Death Differ.* (2010) 17:14–24. DOI: 10.1038/cdd.2009.168

PubMed Abstract | CrossRef Full Text | Google Scholar

20. Guicciardi ME, Scratch GJ. Life and death by death receptors. *FASEB* (2009) 23:1625–37. doi: 10.1096/fj.08-111005

PubMed Abstract | CrossRef Full Text | Google Scholar

Submitted to the journal “Open Access Indonesian Journal of Medical Reviews" (March 9th, 2022)

Open Access Indonesian Journal of Medical Reviews

HM Publisher

Submission acknowledgement

Dear author(s),

Ziske Maritska, Rachmat Hidayat* has submitted the manuscript “The Role of Pattern Recognition Receptor (PRR) in the Body's Defense System: A Narrative Literature Review“ to Open Access Indonesian Journal of Medical Reviews. The paper will be screened by editor and reviewed by peer review.

Cordially,

Prof. Paula Magnano, PhD

Editor HM Publisher

(*) Corresponding author

Open Access Indonesian Journal of Medical Reviews

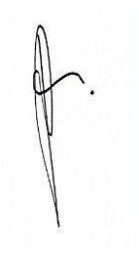
HM Publisher

Peer Review Results

Dear author(s),

Ziske Maritska, Rachmat Hidayat* has submitted the manuscript “The Role of Pattern Recognition Receptor (PRR) in the Body's Defense System: A Narrative Literature Review“ to Open Access Indonesian Journal of Medical Reviews. The decision : Revision Required.

Cordially,



Prof. Paula Magnano, PhD

Editor HM Publisher

(*) Corresponding author

Reviewer 1: Revision required

The Role of Pattern Recognition Receptor (PRR) in the Body's Defense System: A Narrative Literature Review→1

Ziske Maritska[1], Rachmat Hidayat[1*]

[1]Department of Biology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

*Email: rachmathidayat@fk.unsri.ac.id

Abstract→3

Each cell has receptors on the cell surface that specifically bind to solutes (ligands) produced during tissue damage or infection. This review aims to outline the role of PRR on the human body's defense system. The binding of the ligand to its receptor results in activation of intracellular signaling pathways and activation of cells. B and T lymphocytes of the adaptive immune system have developed surface receptors (i.e., T-cell receptors, or TCRs, and B-cell receptors, or BCRs) that bind to a large spectrum of antigens. The cells involved in innate resistance have developed a series of different receptors that recognize a much more limited arrangement of specific molecules. These are referred to as pattern recognition receptors (PRRs), and they recognize molecular patterns in infectious agents or their products (pathogen-associated molecular patterns, or PAMPs), or products of cellular damage (necrosis or apoptosis; molecular-related patterns of damage, or DAMPs). Pattern recognition receptor (PRR) is a receptor complex that interacts with various molecules such as PAMPs and DAMPs. PRR bonds with these molecules play a role in various actions of innate immunity and adaptive immunity.

Keywords: Receptor, Pattern Recognition Receptor, Immunity, TLR, NLRs→2

1. Introduction→4

Cells of innate and adaptive immunity must recognize and respond to their environment, whether products of damaged cells or potential pathogenic microorganisms. Each cell has receptors on the cell surface that specifically bind to solutes (ligands) produced during tissue damage or infection. The binding of the ligand to its receptor results in activation of intracellular signaling pathways and activation of cells. L immunocytes B and T of the adaptive immune system have developed surface receptors (i.e., T-cell receptors, or TCRs, and B-cell receptors, or BCRs) that bind to a large spectrum of antigens. The cells involved in innate resistance have developed a

series of different receptors that recognize a much more limited arrangement of specific molecules. These are referred to as pattern recognition receptors (PRRs), and they recognize molecular patterns in infectious agents or their products (pathogen-associated molecular patterns, or PAMPs), or products of cellular damage (necrosis or apoptosis; molecular-related patterns of damage, or DAMPs). PRRs are commonly found in cells at the host interface and the environment (i.e., skin, respiratory tract, gastrointestinal tract, genitourinary tract), where they monitor for cell damage products and potentially infectious microorganisms. Although most PRR is on the surface of cells, some are secreted or intracellular. An example of secreted PRR is the mannose-binding lectin of the complement activation lectin pathway. Cellular PRR includes Toll-like receptors (TLR), complement receptors (CR), scavenger receptors, glucan receptors, and mannose receptors. [1-5] This review aims to outline the role of PRR on the human body's defense system.

Toll-Like Receptor (TLR)

In humans, at least 11 different Toll-like receptors (TLRs) have been described, 10 of which function. They are expressed on the surface of many cells that have direct and initial contact with potential pathogenic microorganisms. These include mucosal epithelial cells, mast cells, neutrophils, macrophages, dendritic cells, and some lymphocyte subpopulations. (Dendritic cells are found in skin, mucosa, and lymphoid tissue, where they have evolved from Langerhans cells and serve as highly specialized initiators of adaptive immune responses.) TLR recognizes a wide variety of PAMPs located on the cell wall or surface of microorganisms (e.g., bacterial lipopolysaccharide [LPS], peptidoglycan, lipoproteins, zymosan yeast, viral coat proteins), other surface structures (e.g., bacterial flagellin), or microbial nucleic acids (e.g., bacterial DNA, viral double-stranded RNA). Some TLRs recognize host factors produced by depressed or damaged cells (e.g., protein breakdown products of the extracellular matrix, chromatin). The interaction between PAMPs and TLRs, with the collaboration of other cellular receptors (e.g., CD14), can result in cell activation and release of solute products (e.g., cytokines) that increase local resistance to pathogenic microorganisms. TLRs are also one of the bridges between innate resistance and adaptive immune response through cytokine induction that enhances lymphocyte response to foreign antigens in pathogens. Genetic polymorphisms in TLRs may explain some of the observed differences between individual resistance and susceptibility to infection. [6-9]

Table 1. Various Toll-Like Receptors (TLRs)

RECEPTORS	CELLULAR EXPRESSION PATTERNS	PAMP INTRODUCTION
TLR1	Cell surface (everywhere): neutrophils, monocytes/macrophages, dendritic cells, T cells, B cells, NK cells	Fungi, bacteria, viruses; forming heterodimer with TLR2 (TLR2 introduction)
TLR2	Cell surface: neutrophils, monocytes/macrophages, dendritic cells	Fungi (zymosan yeast), bacteria (gram-positive peptidoglycan bacteria, lipoproteins), viruses (lipoproteins)
TLR 3	Intracellular: monocytes/macrophages, se dendritic, T cells, NK cells, epithelial cells	Double-chain RNA produced by many viruses
TLR 4	Cell surface: granulocytes, monocytes/macrophages, dendritic cells, T cells, B cells, epithelial cells	Bacteria (especially gram-negative bacteria LPS, lipoteichoic acid), viruses (RSV F protein, hepatitis C)
TLR 5	Cell surface: granulocytes, monocytes/macrophages, dendritic cells, NK cells, epithelial cells	Bacteria (flagellin); forming heterodimer with TLR 4
TLR 6	Cell surface: monocytes/macrophages, dendritic cells, B cells, NK cells	Fungi, bacteria, viruses; forming heterodimer with TLR 2(introduction of TLR 2)
TLR 7	Intracellular: monocytes/macrophages, dendritic cells, B cells	Indeterminate natural ligands; Single-chain viral RNA

TLR 8	Cell surface: monocytes/macrophages, dendritic cells, NK cells	Indeterminate natural ligands; can bind fungal PAMPS or single-chain viral RNA
TLR 9	Intracellular: monocytes/macrophages, dendritic cells, B cells	Bacteria (unmethylated DNA [CpG dinucleotide])
TLR 10	Cell surface: monocytes/macrophages, dendritic cells, B cells	Indeterminate natural ligands; can form heterodimers with TLR 2
TLR 11	The TLR11 gene does not code for a full-length protein in humans	Unknown immune response

Complement receptors

These receptors are found on many innate and adaptive immune response cells (e.g., granulocytes, monocytes/macrophages, lymphocytes, mast cells, erythrocytes, platelets), as well as some epithelial cells. They recognized some of the resulting fragments through activation of the complement system. Under various normal and disease-related conditions, antibody, antigen, and complement immune complexes are formed in the blood and secreted by cells expressing complement-1 receptor (CR1), which binds to C4b, C3b, and C3b decomposition products (e.g., IC3b). CR2 is found in B lymphocytes, as well as dendritic cells and some epithelial cells, and recognizes C3b decomposition products (specifically iC3b). CR2 appears to facilitate B cell function and antibody production. Both CR3 and CR4 are integrins that primarily recognize C3b decomposition products (specifically iC3b). CR3 (integrin Mβ2, also called CD11b/CD18) facilitates phagocytosis by neutrophils and monocytes/macrophages. CR4 (αXββ2, also called CD11c/CD18) is found mainly in platelets. (Integrins are cell surface receptors that have roles in cell adhesion and attachment and mediate intracellular signals in the extracellular matrix) . [10-13]

Receptor scavenger

These receptors are primarily expressed on macrophages and facilitate the recognition and phagocytosis of pathogenic bacteria, as well as damaged cells and soluble lipoprotein changes

associated with blood vessel damage (e.g. high-density lipoprotein [HDL], acetylated low-density lipoprotein [LDL], oxidized LDL). More than eight receptors have been identified. Some scavenger receptors (e.g., SR PSOX) recognize the cell membrane of phospholipid phosphatidylserine (PS). PS is usually sequestered on the cytoplasmic surface of cell membranes, but is externalized under a very limited range of conditions, including erythrocyte aging and cellular apoptosis. Thus, macrophages, through these receptors, can identify and dispose of old red blood cells and cells undergoing apoptosis. Another important scavenger receptor is CD14, which recognizes LPS and LPS-binding protein complexes. LPS-binding proteins are upregulated during inflammation by the cytokines interleukin-6 (IL-6) and IL-1 and help remove LPS bacteria (endotoxins) from circulation. [14-16]

NOD-Like Receptors (NLRs)

NLRs are cytoplasmic receptors that recognize microbial products and damaged cells. At least 22 NLRs have been identified in humans. NOD-1 and NOD-2 are cytoplasmic and recognize peptidoglycan fragments from intracellular bacteria and initiate the production of proinflammatory mediators, such as tumor necrosis factor (TNF) and IL-6. Some NLRs associate with intracellular multiprotein complexes called inflammasomes. Inflammasomes primarily bind to cellular stress-related molecules, a type of DAMP, and through activation of caspases-1 control the activation and secretion of inflammatory cytokines, such as IL-1β. [17-20]

2.Conclusion→5

Pattern Recognition Receptor (PRR) is a receptor complex that interacts with various molecules such as PAMPs and DAMPs. PRR bonds with these molecules play a role in various actions of innate immunity and adaptive immunity.

3. References→6

1.Walsh D, McCarthy J, O'Driscoll C, Melgar S. Pattern recognition receptors–molecular orchestrators of inflammation in inflammatory bowel disease. *Cytokine Growth Factor Rev*. (2013) 24:91–104. doi: 10.1016/j.cytogfr.2012.09.003

CrossRef Full Text | Google Scholar

2. Medzhitov R, Preston-Hurlburt P, Janeway CA Jr. A human homologue of the Drosophila Toll protein signals activation of adaptive immunity. *Nature* (1997) 388:394–7. doi: 10.1038/41131

PubMed Abstract | CrossRef Full Text | Google Scholar

3. Bortoluci KR, Medzhitov R. *Control of infection by pyroptosis and autophagy: role of TLR and NLR. Cell Mol Life Sci.* (2010) 67:1643–51. DOI: 10.1007/S00018-010-0335-5

CrossRef Full Text

4. Matzinger P. Tolerance, danger, and the extended family. *Annu Rev Immunol.* (1994) 12:991–1045. DOI: 10.1146/annurev.iy.12.040194.005015

PubMed Abstract | CrossRef Full Text | Google Scholar

5. Galluzzi L, Vitale I, Aaronson SA, Abrams JM, Adam D, Agostinis P, et al. Molecular mechanisms of cell death: recommendations of the Nomenclature Committee on Cell Death 2018. *Cell Death Differ.* (2018) 25:486–541. DOI: 10.1038/S41418-017-0012-4

PubMed Abstract | CrossRef Full Text | Google Scholar

6. Kerr JF, Wyllie AH, Currie AR. Apoptosis: a basic biological phenomenon with wide-ranging implications in tissue kinetics. *Br J Cancer* (1972) 26:239–57. DOI: 10.1038/bjc.1972.33

PubMed Abstract | CrossRef Full Text | Google Scholar

7. Amarante-Mendes GP, Green DR. The regulation of apoptotic cell death. *Braz J med Biol Res.* (1999) 32:1053–61.

PubMed Abstract | Google Scholar

8. Fadok VA, Bratton DL, Konowal A, Freed PW, Westcott JY, Henson PM. Macrophages that have ingested apoptotic cells *in vitro* inhibit proinflammatory cytokine production through autocrine/paracrine mechanisms involving TGF-beta, PGE2, and PAF. *J Clin Invest.* (1998) 101:890–8. doi: 10.1172/JCI1112

PubMed Abstract | CrossRef Full Text | Google Scholar

9. Medina CB, Ravichandran KS. Do not let death do us part: 'find-me' signals in communication between dying cells and the phagocytes. *Cell Death Differ.* (2016) 23:979–89. DOI: 10.1038/cdd.2016.13

CrossRef Full Text | Google Scholar

10. Hochreiter-Hufford A, Ravichandran KS. Clearing the dead: apoptotic cell sensing, recognition, engulfment, and digestion. *Cold Spring Harb Perspect Biol.* (2013) 5:a008748. doi: 10.1101/cshperspect.a008748

PubMed Abstract | CrossRef Full Text | Google Scholar

11. Cullen SP, Henry CM, Kearney CJ, Logue SE, Feoktistova M, Tynan GA, et al. Fas/CD95-induced chemokines can serve as "find-me" signals for apoptotic cells. *Mol Cell* (2013) 49:1034–48. DOI: 10.1016/J.Molcel.2013.01.025

PubMed Abstract | CrossRef Full Text | Google Scholar

12. Metzstein MM, Stanfield GM, Horvitz HR. Genetics of programmed cell death in *C. elegans: past, present and future. Trends Genet.* (1998) 14:410–6. DOI: 10.1016/S0168-9525(98)01573-X

PubMed Abstract | CrossRef Full Text | Google Scholar

13. Pop C, Salvesen GS. Human caspases: activation, specificity, and regulation. *J Biol Chem.* (2009) 284:21777–81. DOI: 10.1074/JBC. R800084200

PubMed Abstract | CrossRef Full Text | Google Scholar

14. McIlwain DR, Berger T, Mak TW. Caspase functions in cell death and disease. *Cold Spring Harb Perspect Biol.* (2013) 5:a008656. DOI: 10.1101/cshperspect.a008656

PubMed Abstract | CrossRef Full Text | Google Scholar

15. Pereira WO, Amarante-Mendes GP. Apoptosis: a programme of cell death or cell disposal? *Scand J Immunol.* (2011) 73:401–7. DOI: 10.1111/J.1365-3083.2011.02513.x

CrossRef Full Text | Google Scholar

16. Martin SJ, Finucane DM, Amarante-Mendes GP, O'Brien GA, Green DR. Phosphatidylserine externalization during CD95-induced apoptosis of cells and cytoplasts requires ICE/CED-3 protease activity. *J Biol Chem.* (1996) 271:28753 –6. DOI: 10.1074/jbc.271.46.28753

PubMed Abstract | CrossRef Full Text | Google Scholar

17. Amarante-Mendes GP, Finucane DM, Martin SJ, Cotter TG, Salvesen GS, Green DR. Anti-apoptotic oncogenes prevent caspase-dependent and independent commitment for cell death. *Cell Death Differ.* (1998) 5:298–306. DOI: 10.1038/SJ.CDD.4400354

PubMed Abstract | CrossRef Full Text | Google Scholar

18. Tait SW, Green DR. Mitochondrial regulation of cell death. *Cold Spring Harb Perspect Biol.* (2013) 5:a008706. DOI: 10.1101/cshperspect.a008706

PubMed Abstract | CrossRef Full Text | Google Scholar

19. Wertz IE, Dixit VM. Regulation of death receptor signaling by the ubiquitin system. *Cell Death Differ.* (2010) 17:14–24. DOI: 10.1038/cdd.2009.168

PubMed Abstract | CrossRef Full Text | Google Scholar

20. Guicciardi ME, Scratch GJ. Life and death by death receptors. *FASEB* (2009) 23:1625–37. doi: 10.1096/fj.08-111005

PubMed Abstract | CrossRef Full Text | Google Scholar

Reviewer Comment:

1→ Title of Manuscripts should be explained main review and declared type of literature review: narrative or systematic review.

2→ Keywords should be showed the main words of the study, the authors can use MeSH to develop keywords.

3→ Abstract should be showed the main of background, main of review and conclusion of study.

4→Introduction should be showed the urgency of study (epidemiology data), biological plausibility concept, and lack of knowledge in the study.

5→ Conclusion should more specific and not more showed more review.

6→ Authors must check the references for make update references. References should no more than 10 years.

Reviewer 1: Revision required

The Role of Pattern Recognition Receptor (PRR) in the Body's Defense System: A Narrative Literature Review→1

Ziske Maritska[1], Rachmat Hidayat[1*]

[1]Department of Biology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

*Email: rachmathidayat@fk.unsri.ac.id

Abstract→3

Each cell has receptors on the cell surface that specifically bind to solutes (ligands) produced during tissue damage or infection. This review aims to outline the role of PRR on the human body's defense system. The binding of the ligand to its receptor results in activation of intracellular signaling pathways and activation of cells. B and T lymphocytes of the adaptive immune system have developed surface receptors (i.e., T-cell receptors, or TCRs, and B-cell receptors, or BCRs) that bind to a large spectrum of antigens. The cells involved in innate resistance have developed a series of different receptors that recognize a much more limited arrangement of specific molecules. These are referred to as pattern recognition receptors (PRRs), and they recognize molecular patterns in infectious agents or their products (pathogen-associated molecular patterns, or PAMPs), or products of cellular damage (necrosis or apoptosis; molecular-related patterns of damage, or DAMPs). Pattern recognition receptor (PRR) is a receptor complex that interacts with various molecules such as PAMPs and DAMPs. PRR bonds with these molecules play a role in various actions of innate immunity and adaptive immunity.

Keywords: Receptor, Pattern Recognition Receptor, Immunity, TLR, NLRs→2

1. Introduction→4

Cells of innate and adaptive immunity must recognize and respond to their environment, whether products of damaged cells or potential pathogenic microorganisms. Each cell has receptors on the cell surface that specifically bind to solutes (ligands) produced during tissue damage or infection. The binding of the ligand to its receptor results in activation of intracellular signaling pathways and activation of cells. L immunocytes B and T of the adaptive immune system have developed surface receptors (i.e., T-cell receptors, or TCRs, and B-cell receptors, or BCRs) that bind to a large spectrum of antigens. The cells involved in innate resistance have developed a

series of different receptors that recognize a much more limited arrangement of specific molecules. These are referred to as pattern recognition receptors (PRRs), and they recognize molecular patterns in infectious agents or their products (pathogen-associated molecular patterns, or PAMPs), or products of cellular damage (necrosis or apoptosis; molecular-related patterns of damage, or DAMPs). PRRs are commonly found in cells at the host interface and the environment (i.e., skin, respiratory tract, gastrointestinal tract, genitourinary tract), where they monitor for cell damage products and potentially infectious microorganisms. Although most PRR is on the surface of cells, some are secreted or intracellular. An example of secreted PRR is the mannose-binding lectin of the complement activation lectin pathway. Cellular PRR includes Toll-like receptors (TLR), complement receptors (CR), scavenger receptors, glucan receptors, and mannose receptors. [1-5] This review aims to outline the role of PRR on the human body's defense system.

Toll-Like Receptor (TLR)

In humans, at least 11 different Toll-like receptors (TLRs) have been described, 10 of which function. They are expressed on the surface of many cells that have direct and initial contact with potential pathogenic microorganisms. These include mucosal epithelial cells, mast cells, neutrophils, macrophages, dendritic cells, and some lymphocyte subpopulations. (Dendritic cells are found in skin, mucosa, and lymphoid tissue, where they have evolved from Langerhans cells and serve as highly specialized initiators of adaptive immune responses.) TLR recognizes a wide variety of PAMPs located on the cell wall or surface of microorganisms (e.g., bacterial lipopolysaccharide [LPS], peptidoglycan, lipoproteins, zymosan yeast, viral coat proteins), other surface structures (e.g., bacterial flagellin), or microbial nucleic acids (e.g., bacterial DNA, viral double-stranded RNA). Some TLRs recognize host factors produced by depressed or damaged cells (e.g., protein breakdown products of the extracellular matrix, chromatin). The interaction between PAMPs and TLRs, with the collaboration of other cellular receptors (e.g., CD14), can result in cell activation and release of solute products (e.g., cytokines) that increase local resistance to pathogenic microorganisms. TLRs are also one of the bridges between innate resistance and adaptive immune response through cytokine induction that enhances lymphocyte response to foreign antigens in pathogens. Genetic polymorphisms in TLRs may explain some of the observed differences between individual resistance and susceptibility to infection. [6-9]

Table 1. Various Toll-Like Receptors (TLRs)

RECEPTORS	CELLULAR EXPRESSION PATTERNS	PAMP INTRODUCTION
TLR1	Cell surface (everywhere): neutrophils, monocytes/macrophages, dendritic cells, T cells, B cells, NK cells	Fungi, bacteria, viruses; forming heterodimer with TLR2 (TLR2 introduction)
TLR2	Cell surface: neutrophils, monocytes/macrophages, dendritic cells	Fungi (zymosan yeast), bacteria (gram-positive peptidoglycan bacteria, lipoproteins), viruses (lipoproteins)
TLR 3	Intracellular: monocytes/macrophages, se dendritic, T cells, NK cells, epithelial cells	Double-chain RNA produced by many viruses
TLR 4	Cell surface: granulocytes, monocytes/macrophages, dendritic cells, T cells, B cells, epithelial cells	Bacteria (especially gram-negative bacteria LPS, lipoteichoic acid), viruses (RSV F protein, hepatitis C)
TLR 5	Cell surface: granulocytes, monocytes/macrophages, dendritic cells, NK cells, epithelial cells	Bacteria (flagellin); forming heterodimer with TLR 4
TLR 6	Cell surface: monocytes/macrophages, dendritic cells, B cells, NK cells	Fungi, bacteria, viruses; forming heterodimer with TLR 2(introduction of TLR 2)
TLR 7	Intracellular: monocytes/macrophages, dendritic cells, B cells	Indeterminate natural ligands; Single-chain viral RNA

TLR 8	Cell surface: monocytes/macrophages, dendritic cells, NK cells	Indeterminate natural ligands; can bind fungal PAMPS or single-chain viral RNA
TLR 9	Intracellular: monocytes/macrophages, dendritic cells, B cells	Bacteria (unmethylated DNA [CpG dinucleotide])
TLR 10	Cell surface: monocytes/macrophages, dendritic cells, B cells	Indeterminate natural ligands; can form heterodimers with TLR 2
TLR 11	The TLR11 gene does not code for a full-length protein in humans	Unknown immune response

Complement receptors

These receptors are found on many innate and adaptive immune response cells (e.g., granulocytes, monocytes/macrophages, lymphocytes, mast cells, erythrocytes, platelets), as well as some epithelial cells. They recognized some of the resulting fragments through activation of the complement system. Under various normal and disease-related conditions, antibody, antigen, and complement immune complexes are formed in the blood and secreted by cells expressing complement-1 receptor (CR1), which binds to C4b, C3b, and C3b decomposition products (e.g., IC3b). CR2 is found in B lymphocytes, as well as dendritic cells and some epithelial cells, and recognizes C3b decomposition products (specifically iC3b). CR2 appears to facilitate B cell function and antibody production. Both CR3 and CR4 are integrins that primarily recognize C3b decomposition products (specifically iC3b). CR3 (integrin Mβ2, also called CD11b/CD18) facilitates phagocytosis by neutrophils and monocytes/macrophages. CR4 (αXββ2, also called CD11c/CD18) is found mainly in platelets. (Integrins are cell surface receptors that have roles in cell adhesion and attachment and mediate intracellular signals in the extracellular matrix) . [10-13]

Receptor scavenger

These receptors are primarily expressed on macrophages and facilitate the recognition and phagocytosis of pathogenic bacteria, as well as damaged cells and soluble lipoprotein changes

associated with blood vessel damage (e.g. high-density lipoprotein [HDL], acetylated low-density lipoprotein [LDL], oxidized LDL). More than eight receptors have been identified. Some scavenger receptors (e.g., SR PSOX) recognize the cell membrane of phospholipid phosphatidylserine (PS). PS is usually sequestered on the cytoplasmic surface of cell membranes, but is externalized under a very limited range of conditions, including erythrocyte aging and cellular apoptosis. Thus, macrophages, through these receptors, can identify and dispose of old red blood cells and cells undergoing apoptosis. Another important scavenger receptor is CD14, which recognizes LPS and LPS-binding protein complexes. LPS-binding proteins are upregulated during inflammation by the cytokines interleukin-6 (IL-6) and IL-1 and help remove LPS bacteria (endotoxins) from circulation. [14-16]

NOD-Like Receptors (NLRs)

NLRs are cytoplasmic receptors that recognize microbial products and damaged cells. At least 22 NLRs have been identified in humans. NOD-1 and NOD-2 are cytoplasmic and recognize peptidoglycan fragments from intracellular bacteria and initiate the production of proinflammatory mediators, such as tumor necrosis factor (TNF) and IL-6. Some NLRs associate with intracellular multiprotein complexes called inflammasomes. Inflammasomes primarily bind to cellular stress-related molecules, a type of DAMP, and through activation of caspases-1 control the activation and secretion of inflammatory cytokines, such as IL-1β. [17-20]

2.Conclusion→5

Pattern Recognition Receptor (PRR) is a receptor complex that interacts with various molecules such as PAMPs and DAMPs. PRR bonds with these molecules play a role in various actions of innate immunity and adaptive immunity.

3. References→6

1.Walsh D, McCarthy J, O'Driscoll C, Melgar S. Pattern recognition receptors–molecular orchestrators of inflammation in inflammatory bowel disease. *Cytokine Growth Factor Rev*. (2013) 24:91–104. doi: 10.1016/j.cytogfr.2012.09.003

CrossRef Full Text | Google Scholar

2. Medzhitov R, Preston-Hurlburt P, Janeway CA Jr. A human homologue of the Drosophila Toll protein signals activation of adaptive immunity. *Nature* (1997) 388:394–7. doi: 10.1038/41131

PubMed Abstract | CrossRef Full Text | Google Scholar

3. Bortoluci KR, Medzhitov R. *Control of infection by pyroptosis and autophagy: role of TLR and NLR. Cell Mol Life Sci.* (2010) 67:1643–51. DOI: 10.1007/S00018-010-0335-5

CrossRef Full Text

4. Matzinger P. Tolerance, danger, and the extended family. *Annu Rev Immunol.* (1994) 12:991–1045. DOI: 10.1146/annurev.iy.12.040194.005015

PubMed Abstract | CrossRef Full Text | Google Scholar

5. Galluzzi L, Vitale I, Aaronson SA, Abrams JM, Adam D, Agostinis P, et al. Molecular mechanisms of cell death: recommendations of the Nomenclature Committee on Cell Death 2018. *Cell Death Differ.* (2018) 25:486–541. DOI: 10.1038/S41418-017-0012-4

PubMed Abstract | CrossRef Full Text | Google Scholar

6. Kerr JF, Wyllie AH, Currie AR. Apoptosis: a basic biological phenomenon with wide-ranging implications in tissue kinetics. *Br J Cancer* (1972) 26:239–57. DOI: 10.1038/bjc.1972.33

PubMed Abstract | CrossRef Full Text | Google Scholar

7. Amarante-Mendes GP, Green DR. The regulation of apoptotic cell death. *Braz J med Biol Res.* (1999) 32:1053–61.

PubMed Abstract | Google Scholar

8. Fadok VA, Bratton DL, Konowal A, Freed PW, Westcott JY, Henson PM. Macrophages that have ingested apoptotic cells *in vitro* inhibit proinflammatory cytokine production through autocrine/paracrine mechanisms involving TGF-beta, PGE2, and PAF. *J Clin Invest.* (1998) 101:890–8. doi: 10.1172/JCI1112

PubMed Abstract | CrossRef Full Text | Google Scholar

9. Medina CB, Ravichandran KS. Do not let death do us part: 'find-me' signals in communication between dying cells and the phagocytes. *Cell Death Differ.* (2016) 23:979–89. DOI: 10.1038/cdd.2016.13

CrossRef Full Text | Google Scholar

10. Hochreiter-Hufford A, Ravichandran KS. Clearing the dead: apoptotic cell sensing, recognition, engulfment, and digestion. *Cold Spring Harb Perspect Biol.* (2013) 5:a008748. doi: 10.1101/cshperspect.a008748

PubMed Abstract | CrossRef Full Text | Google Scholar

11. Cullen SP, Henry CM, Kearney CJ, Logue SE, Feoktistova M, Tynan GA, et al. Fas/CD95-induced chemokines can serve as "find-me" signals for apoptotic cells. *Mol Cell* (2013) 49:1034–48. DOI: 10.1016/J.Molcel.2013.01.025

PubMed Abstract | CrossRef Full Text | Google Scholar

12. Metzstein MM, Stanfield GM, Horvitz HR. Genetics of programmed cell death in *C. elegans: past, present and future. Trends Genet.* (1998) 14:410–6. DOI: 10.1016/S0168-9525(98)01573-X

PubMed Abstract | CrossRef Full Text | Google Scholar

13. Pop C, Salvesen GS. Human caspases: activation, specificity, and regulation. *J Biol Chem.* (2009) 284:21777–81. DOI: 10.1074/JBC. R800084200

PubMed Abstract | CrossRef Full Text | Google Scholar

14. McIlwain DR, Berger T, Mak TW. Caspase functions in cell death and disease. *Cold Spring Harb Perspect Biol.* (2013) 5:a008656. DOI: 10.1101/cshperspect.a008656

PubMed Abstract | CrossRef Full Text | Google Scholar

15. Pereira WO, Amarante-Mendes GP. Apoptosis: a programme of cell death or cell disposal? *Scand J Immunol.* (2011) 73:401–7. DOI: 10.1111/J.1365-3083.2011.02513.x

CrossRef Full Text | Google Scholar

16. Martin SJ, Finucane DM, Amarante-Mendes GP, O'Brien GA, Green DR. Phosphatidylserine externalization during CD95-induced apoptosis of cells and cytoplasts requires ICE/CED-3 protease activity. *J Biol Chem.* (1996) 271:28753 –6. DOI: 10.1074/jbc.271.46.28753

PubMed Abstract | CrossRef Full Text | Google Scholar

17. Amarante-Mendes GP, Finucane DM, Martin SJ, Cotter TG, Salvesen GS, Green DR. Anti-apoptotic oncogenes prevent caspase-dependent and independent commitment for cell death. *Cell Death Differ.* (1998) 5:298–306. DOI: 10.1038/SJ.CDD.4400354

PubMed Abstract | CrossRef Full Text | Google Scholar

18. Tait SW, Green DR. Mitochondrial regulation of cell death. *Cold Spring Harb Perspect Biol.* (2013) 5:a008706. DOI: 10.1101/cshperspect.a008706

PubMed Abstract | CrossRef Full Text | Google Scholar

19. Wertz IE, Dixit VM. Regulation of death receptor signaling by the ubiquitin system. *Cell Death Differ.* (2010) 17:14–24. DOI: 10.1038/cdd.2009.168

PubMed Abstract | CrossRef Full Text | Google Scholar

20. Guicciardi ME, Scratch GJ. Life and death by death receptors. *FASEB* (2009) 23:1625–37. doi: 10.1096/fj.08-111005

PubMed Abstract | CrossRef Full Text | Google Scholar

Reviewer Comment:

1→ Title of Manuscripts should be explained main review and declared type of literature review: narrative or systematic review.

2→ Keywords should be showed the main words of the study, the authors can use MeSH to develop keywords.

3→ Abstract should be showed the main of background, main of review and conclusion of study.

4→Introduction should be showed the urgency of study (epidemiology data), biological plausibility concept, and lack of knowledge in the study.

5→ Conclusion should more specific and not more showed more review.

6→ Authors must check the references for make update references. References should no more than 10 years.

Revised version received by journal (March 24th, 2022)
Open Access Indonesian Journal of Medical Reviews Vol 3 Issue 2 2023

Open Access Indonesian Journal of Medical Reviews
Journal Homepage: https://hmpublisher.com/index.php/OAIJMR

The Role of Pattern Recognition Receptor (PRR) in the Body's Defense System: A Narrative Literature Review

Ziske Maritska[1], Rachmat Hidayat[1*]

[1]Department of Biology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

ARTICLE INFO

Keywords:
Immunity
NLRs
Pattern recognition receptor
Receptor
TLR

***Corresponding author:**
Rachmat Hidayat

E-mail address:
rachmathidayat@fk.unsri.ac.id

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/oaijmr.v3i2.300

A B S T R A C T

Each cell has receptors on the cell surface that specifically bind to solutes (ligands) produced during tissue damage or infection. This review aimed to describe the role of PRR in the human body's defense system. The binding of the ligand to its receptor results in the activation of intracellular signaling pathways and cell activation. The B and T lymphocytes of the adaptive immune system have developed surface receptors (that is, the T-cell receptor, or TCR, and the B-cell receptor, or BCR) that bind a broad spectrum of antigens. The cells involved in innate resistance have developed a distinct set of receptors that recognize a much more limited array of specific molecules. These are called pattern recognition receptor (PRR), and they recognize the molecular patterns in infectious agents or their products (pathogen-associated molecular patterns, or PAMP) or products of cellular damage (necrosis or apoptosis; molecular pattern-associated damage, or DAMPs). In conclusion, the pattern recognition receptor (PRR) is a receptor complex that interacts with various molecules, such as PAMP and DAMPs. PRR bonds with these various molecules and play a role in various actions of innate immunity and adaptive immunity.

1. Introduction

Cells of innate and adaptive immunity must recognize and respond to their environment, whether the product of damaged cells or potential pathogenic microorganisms. Each cell has receptors on the cell surface that specifically bind to solutes (ligands) produced during tissue damage or infection. The binding of the ligand to its receptor results in the activation of intracellular signaling pathways and cell activation. The B and T lymphocytes of the adaptive immune system have developed surface receptors (that is, the T-cell receptor, or TCR, and the B-cell receptor, or BCR) that bind a broad spectrum of antigens. The cells involved in innate resistance have developed a distinct set of receptors that recognize a much more limited array of specific molecules. These are called pattern recognition receptor (PRR), and they recognize the molecular patterns in infectious agents or their products (pathogen-associated molecular patterns, or PAMP) or products of cellular damage (necrosis or apoptosis; molecular pattern-associated damage, or DAMPs). PRRs are commonly found on cells at the host-environmental interface (i.e., skin, respiratory tract, gastrointestinal tract, genitourinary tract), where they monitor the breakdown products of cells and potentially infectious microorganisms. Although most of the PRR is on the cell surface, some are secreted or intracellular. An example of a secreted PRR is the mannose-binding lectin of the complement-activating lectin pathway. Cellular PRR include toll-

like receptors (TLR), complement receptors (CR), scavenger receptors, glucan receptors, and mannose receptors.[1-5] This review aimed to describe the role of PRR in the human body's defense system.

Toll-like receptor (TLR)

In humans, at least 11 distinct toll-like receptor (TLR) have already been described 10 among their works. They are expressed on the surface of many cells that have direct and initial contact with potential pathogenic microorganisms. These include mucosal epithelial cells, mast cells, neutrophils, macrophages, dendritic cells, and some lymphocyte subpopulations. (Dendritic cells are found in skin, mucosa, and lymphoid tissue, where they have developed from Langerhans cells and function as highly specialized initiators of adaptive immune responses.) TLR recognizes a wide variety of PAMP located on the cell wall or surface of microorganisms (e.g., lipopolysaccharides bacterial [LPS], peptidoglycan, lipoprotein, yeast zymosan, viral coat protein), other surface structures (e.g., bacterial flagellin), or microbial nucleic acids (e.g., bacterial DNA, viral double-stranded RNA). Some TLRs recognize host factors produced by stressed or damaged cells (e.g., breakdown products of extracellular matrix proteins, chromatin). Interactions between PAMPs and TLRs, in collaboration with other cellular receptors (e.g., CD14), can result in cell activation and release of soluble products (e.g., cytokines) that enhance local resistance to pathogenic microorganisms. TLRs are also one of the bridges between innate resistance and adaptive immune response through the induction of cytokines that increase lymphocyte response to foreign antigens in pathogens. Genetic polymorphisms in TLRs may explain some of the differences observed between individual resistance and susceptibility to infection.[6-9]

Table 1. Various toll-like receptors (TLR).

Receptors	Cellular expression patterns	PAMP recognition
TLR1	Surface cells (everywhere): neutrophils, monocytes/macrophages, dendritic cells, T cells, B cells, NK cells	Fungi, bacteria, viruses; forms a heterodimer with TLR2 (TLR2 recognition)
TLR2	Surface cells: neutrophils, monocytes/macrophages, dendritic cells	Fungi (zymosan yeast), bacteria (gram-positive bacterial peptidoglycan, lipoprotein), viruses (lipoprotein)
TLR 3	Intracellular: monocytes/macrophages, dendritic cells, T cells, NK cells, epithelial cells	Double-stranded RNA produced by many viruses
TLR 4	Surface cells: granulocytes, monocytes/macrophages, dendritic cells, T cells, B cells, epithelial cells	Bacteria (especially gram-negative bacteria LPS, lipoteichoic acid), viruses (RSV F protein, hepatitis C)
TLR 5	Surface cells: granulocytes, monocytes/macrophages, dendritic cells, NK cells, epithelial cells	Bacteria (flagellin); form a heterodimer with TLR 4
TLR 6	Surface cells: monocytes/macrophages, dendritic cells, B cells, NK cells	Fungi, bacteria, viruses; forms a heterodimer with TLR 2(TLR 2 recognition)
TLR 7	Intracellular: monocytes/macrophages, dendritic cells, B cells	Indeterminate natural ligand; single-stranded viral RNA
TLR 8	Surface cells: monocytes/macrophages, dendritic cells, NK cells	Indeterminate natural ligand; can bind to fungal PAMPS or single-stranded viral RNA
TLR 9	Intracellular: monocytes/macrophages, dendritic cells, B cells	Bacteria (Unmethylated DNA [CpG dinucleotide])
TLR 10	Surface cells: monocytes/macrophages, dendritic cells, B cells	Indeterminate natural ligands; can form heterodimers with TLR 2
TLR 11	The TLR11 gene does not encode the full-length protein in humans	The immune response is unknown

Complement receptors

These receptors are found on many cells of innate and adaptive immune response (e.g., granulocytes, monocytes/macrophages, lymphocytes, mast cells, erythrocytes, platelets), as well as some epithelial cells. They recognize some of the resulting fragments through activation of the complement system. Under a variety of normal and disease-related conditions, antibody, antigen, and complement immune complexes are formed in the blood and secreted by cells expressing complement surface receptor-1 (CR1), which binds to the breakdown products C4b, C3b, and C3b. (e.g., IC3b). CR2 is found on B lymphocytes, as well as dendritic cells and some epithelial cells, and recognizes the breakdown products of C3b (especially iC3b). CR2 appears to facilitate B cell function and antibody production. Both CR3 and CR4 are integrins that primarily recognize the breakdown products of C3b (specifically iC3b). CR3 (integrin Mβ2, also called CD11b/CD18) facilitates phagocytosis by neutrophils and monocytes/macrophages. CR4 (αXββ2, also called CD11c/CD18) is found mainly in platelets. (Integrins are cell surface receptors that have a role in cell adhesion and attachment and mediate intracellular signals in the extracellular matrix).[10-13]

Scavenger receptors

These receptors are primarily expressed on macrophages and facilitate recognition and phagocytosis of pathogenic bacteria, as well as damaged cells and soluble lipoprotein changes associated with vascular damage (eg, high-density lipoprotein [HDL], acetylated low-density lipoprotein [LDL], oxidized LDL). More than eight receptors have been identified. Some scavenger receptors (e.g., SR PSOX) recognize the cell membrane phospholipid phosphatidylserine (PS). PS is normally sequestered on the cytoplasmic surface of the cell membrane. However, it externalized under a very limited range of conditions, including senescence of erythrocytes and cellular apoptosis. Thus, macrophages, through these receptors, can identify and remove senescent red blood cells and cells undergoing apoptosis. Another important scavenger receptor is CD14, which recognizes the LPS and LPS-binding protein complexes. LPS-binding protein is upregulated during inflammation by the cytokines interleukin-6 (IL-6) and IL-1 and helps remove bacterial LPS (endotoxin) from circulation.[14-16]

NOD-like receptors (NLRs)

NLRs are cytoplasmic receptors that recognize microbial products and damaged cells. At least 22 NLRs have been identified in humans. NOD-1 and NOD-2 are cytoplasmic and recognize peptidoglycan fragments from intracellular bacteria and initiate the production of proinflammatory mediators, such as tumor necrosis factor (TNF) and IL-6. Some NLRs are associated with a complex multi-protein called the intracellular inflammasome. Inflammasome It primarily binds to cellular stress-related molecules, a type of DAMP, and through activation of caspases-1, controls the activation and secretion of inflammatory cytokines, such as IL-1β.[17-20]

2. Conclusion

Pattern recognition receptor (PRR) is a receptor complex that interacts with various molecules, such as PAMP and DAMPs. PRR bonds with these various molecules and play a role in various actions of innate immunity and adaptive immunity.

3. References

1. Walsh D, McCarthy J, O'Driscoll C, Melgar S. Pattern recognition receptors–molecular orchestrators of inflammation in inflammatory bowel disease. Cytokine Growth Factor Rev. 2013; 24: 91–104.
2. Medzhitov R, Preston-Hurlburt P, Janeway CA Jr. A human homologue of the Drosophila Toll protein signals activation of adaptive immunity. Nature. 1997; 388: 394–7.
3. Bortoluci KR, Medzhitov R. Control of infection by pyroptosis and autophagy: role of TLR and NLR. Cell Mol Life Sci. 2010; 67: 1643–51

4. Matzinger P. Tolerance, danger, and the extended family. Annu Rev Immunol. 1994; 12: 991–1045.
5. Galluzzi L, Vitale I, Aaronson SA, Abrams JM, Adam D, Agostinis P, et al. Molecular mechanisms of cell death: recommendations of the Nomenclature Committee on Cell Death 2018. Cell Death Differ. 2018; 25: 486–541.
6. Kerr JF, Wyllie AH, Currie AR. Apoptosis: a basic biological phenomenon with wide-ranging implications in tissue kinetics. Br J Cancer. 1972; 26: 239–57.
7. Amarante-Mendes GP, Green DR. The regulation of apoptotic cell death. Braz J Med Biol Res. 1999; 32: 1053–61.
8. Fadok VA, Bratton DL, Konowal A, Freed PW, Westcott JY, Henson PM. Macrophages that have ingested apoptotic cells in vitro inhibit proinflammatory cytokine production through autocrine/paracrine mechanisms involving TGF-beta, PGE2, and PAF. J Clin Invest. 1998; 101: 890–8.
9. Medina CB, Ravichandran KS. Do not let death do us part: 'find-me' signals in communication between dying cells and the phagocytes. Cell Death Differ. 2016; 23: 979–89.
10. Hochreiter-Hufford A, Ravichandran KS. Clearing the dead: apoptotic cell sensing, recognition, engulfment, and digestion. Cold Spring Harb Perspect Biol. 2013; 5: a008748.
11. Cullen SP, Henry CM, Kearney CJ, Logue SE, Feoktistova M, Tynan GA, et al. Fas/CD95-induced chemokines can serve as "find-me" signals for apoptotic cells. Mol Cell. 2013; 49: 1034–48.
12. Metzstein MM, Stanfield GM, Horvitz HR. Genetics of programmed cell death in C. elegans: past, present and future. Trends Genet. 1998; 14: 410–6.
13. Pop C, Salvesen GS. Human caspases: activation, specificity, and regulation. J Biol Chem. 2009; 284: 21777–81.
14. McIlwain DR, Berger T, Mak TW. Caspase functions in cell death and disease. Cold Spring Harb Perspect Biol. 2013; 5: a008656.
15. Pereira WO, Amarante-Mendes GP. Apoptosis: a programme of cell death or cell disposal? Scand J Immunol. 2011; 73: 401–7.
16. Martin SJ, Finucane DM, Amarante-Mendes GP, O'Brien GA, Green DR. Phosphatidylserine externalization during CD95-induced apoptosis of cells and cytoplasts requires ICE/CED-3 protease activity. J Biol Chem. 1996; 271: 28753–6.
17. Amarante-Mendes GP, Finucane DM, Martin SJ, Cotter TG, Salvesen GS, Green DR. Anti-apoptotic oncogenes prevent caspase-dependent and independent commitment for cell death. Cell Death Differ. 1998; 5: 298–306.
18. Tait SW, Green DR. Mitochondrial regulation of cell death. Cold Spring Harb Perspect Biol. 2013; 5: a008706.
19. Wertz IE, Dixit VM. Regulation of death receptor signaling by the ubiquitin system. Cell Death Differ. 2010; 17: 14–24.
20. Guicciardi ME, Gores GJ. Life and death by death receptors. FASEB. 2009; 23: 1625–37.

Paper Accepted for publication (April 2nd, 2023)

Open Access Indonesian Journal of Medical Reviews

HM Publisher

Letter of Acceptance

Manuscript “The Role of Pattern Recognition Receptor (PRR) in the Body's Defense System: A Narrative Literature Review“ by Ziske Maritska, Rachmat Hidayat*, has been accepted to publish in Open Access Indonesian Journal of Medical Reviews Vol 3 issue 2 in April 2023.

Cordially,

Prof. Paula Magnano, PhD

Editor HM Publisher

(*) Corresponding author

The Coresponding Author can access the acount in website :

https://hmpublisher.com/index.php/OAIJMR/login

User: dr_rachmat_hidayat

Password: 210587

Open Access Indonesian Journal of Medical Reviews

Journal Homepage: https://hmpublisher.com/index.php/OAIJMR

The Role of Pattern Recognition Receptor (PRR) in the Body's Defense System: A Narrative Literature Review

Ziske Maritska[1], Rachmat Hidayat[1*]

[1]Department of Biology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

ARTICLE INFO

Keywords:
Immunity
NLRs
Pattern recognition receptor
Receptor
TLR

***Corresponding author:**
Rachmat Hidayat

E-mail address:
rachmathidayat@fk.unsri.ac.id

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/oaijmr.v3i2.300

A B S T R A C T

Each cell has receptors on the cell surface that specifically bind to solutes (ligands) produced during tissue damage or infection. This review aimed to describe the role of PRR in the human body's defense system. The binding of the ligand to its receptor results in the activation of intracellular signaling pathways and cell activation. The B and T lymphocytes of the adaptive immune system have developed surface receptors (that is, the T-cell receptor, or TCR, and the B-cell receptor, or BCR) that bind a broad spectrum of antigens. The cells involved in innate resistance have developed a distinct set of receptors that recognize a much more limited array of specific molecules. These are called pattern recognition receptor (PRR), and they recognize the molecular patterns in infectious agents or their products (pathogen-associated molecular patterns, or PAMP) or products of cellular damage (necrosis or apoptosis; molecular pattern-associated damage, or DAMPs). In conclusion, the pattern recognition receptor (PRR) is a receptor complex that interacts with various molecules, such as PAMP and DAMPs. PRR bonds with these various molecules and play a role in various actions of innate immunity and adaptive immunity.

1. Introduction

Cells of innate and adaptive immunity must recognize and respond to their environment, whether the product of damaged cells or potential pathogenic microorganisms. Each cell has receptors on the cell surface that specifically bind to solutes (ligands) produced during tissue damage or infection. The binding of the ligand to its receptor results in the activation of intracellular signaling pathways and cell activation. The B and T lymphocytes of the adaptive immune system have developed surface receptors (that is, the T-cell receptor, or TCR, and the B-cell receptor, or BCR) that bind a broad spectrum of antigens. The cells involved in innate resistance have developed a distinct set of receptors that recognize a much more limited array of specific molecules. These are called pattern recognition receptor (PRR), and they recognize the molecular patterns in infectious agents or their products (pathogen-associated molecular patterns, or PAMP) or products of cellular damage (necrosis or apoptosis; molecular pattern-associated damage, or DAMPs). PRRs are commonly found on cells at the host-environmental interface (i.e., skin, respiratory tract, gastrointestinal tract, genitourinary tract), where they monitor the breakdown products of cells and potentially infectious microorganisms. Although

most of the PRR is on the cell surface, some are secreted or intracellular. An example of a secreted PRR is the mannose-binding lectin of the complement-activating lectin pathway. Cellular PRR include toll-like receptors (TLR), complement receptors (CR), scavenger receptors, glucan receptors, and mannose receptors.[1-5] This review aimed to describe the role of PRR in the human body's defense system.

Toll-like receptor (TLR)

In humans, at least 11 distinct toll-like receptor (TLR) have already been described 10 among their works. They are expressed on the surface of many cells that have direct and initial contact with potential pathogenic microorganisms. These include mucosal epithelial cells, mast cells, neutrophils, macrophages, dendritic cells, and some lymphocyte subpopulations. (Dendritic cells are found in skin, mucosa, and lymphoid tissue, where they have developed from Langerhans cells and function as highly specialized initiators of adaptive immune responses.) TLR recognizes a wide variety of PAMP located on the cell wall or surface of microorganisms (e.g., lipopolysaccharides bacterial [LPS], peptidoglycan, lipoprotein, yeast zymosan, viral coat protein), other surface structures (e.g., bacterial flagellin), or microbial nucleic acids (e.g., bacterial DNA, viral double-stranded RNA). Some TLRs recognize host factors produced by stressed or damaged cells (e.g., breakdown products of extracellular matrix proteins, chromatin). Interactions between PAMPs and TLRs, in collaboration with other cellular receptors (e.g., CD14), can result in cell activation and release of soluble products (e.g., cytokines) that enhance local resistance to pathogenic microorganisms. TLRs are also one of the bridges between innate resistance and adaptive immune response through the induction of cytokines that increase lymphocyte response to foreign antigens in pathogens. Genetic polymorphisms in TLRs may explain some of the differences observed between individual resistance and susceptibility to infection.[6-9]

Table 1. Various toll-like receptors (TLR).

Receptors	Cellular expression patterns	PAMP recognition
TLR1	Surface cells (everywhere): neutrophils, monocytes/macrophages, dendritic cells, T cells, B cells, NK cells	Fungi, bacteria, viruses; forms a heterodimer with TLR2 (TLR2 recognition)
TLR2	Surface cells: neutrophils, monocytes/macrophages, dendritic cells	Fungi (zymosan yeast), bacteria (gram-positive bacterial peptidoglycan, lipoprotein), viruses (lipoprotein)
TLR 3	Intracellular: monocytes/macrophages, dendritic cells, T cells, NK cells, epithelial cells	Double-stranded RNA produced by many viruses
TLR 4	Surface cells: granulocytes, monocytes/macrophages, dendritic cells, T cells, B cells, epithelial cells	Bacteria (especially gram-negative bacteria LPS, lipoteichoic acid), viruses (RSV F protein, hepatitis C)
TLR 5	Surface cells: granulocytes, monocytes/macrophages, dendritic cells, NK cells, epithelial cells	Bacteria (flagellin); form a heterodimer with TLR 4
TLR 6	Surface cells: monocytes/macrophages, dendritic cells, B cells, NK cells	Fungi, bacteria, viruses; forms a heterodimer with TLR 2(TLR 2 recognition)
TLR 7	Intracellular: monocytes/macrophages, dendritic cells, B cells	Indeterminate natural ligand; single-stranded viral RNA
TLR 8	Surface cells: monocytes/macrophages, dendritic cells, NK cells	Indeterminate natural ligand; can bind to fungal PAMPS or single-stranded viral RNA
TLR 9	Intracellular: monocytes/macrophages, dendritic cells, B cells	Bacteria (Unmethylated DNA [CpG dinucleotide])
TLR 10	Surface cells: monocytes/macrophages, dendritic cells, B cells	Indeterminate natural ligands; can form heterodimers with TLR 2
TLR 11	The TLR11 gene does not encode the full-length protein in humans	The immune response is unknown

Complement receptors

These receptors are found on many cells of innate and adaptive immune response (e.g., granulocytes, monocytes/macrophages, lymphocytes, mast cells, erythrocytes, platelets), as well as some epithelial cells. They recognize some of the resulting fragments through activation of the complement system. Under a variety of normal and disease-related conditions, antibody, antigen, and complement immune complexes are formed in the blood and secreted by cells expressing complement surface receptor-1 (CR1), which binds to the breakdown products C4b, C3b, and C3b. (e.g., IC3b). CR2 is found on B lymphocytes, as well as dendritic cells and some epithelial cells, and recognizes the breakdown products of C3b (especially iC3b). CR2 appears to facilitate B cell function and antibody production. Both CR3 and CR4 are integrins that primarily recognize the breakdown products of C3b (specifically iC3b). CR3 (integrin Mβ2, also called CD11b/CD18) facilitates phagocytosis by neutrophils and monocytes/macrophages. CR4 (αXββ2, also called CD11c/CD18) is found mainly in platelets. (Integrins are cell surface receptors that have a role in cell adhesion and attachment and mediate intracellular signals in the extracellular matrix).[10-13]

Scavenger receptors

These receptors are primarily expressed on macrophages and facilitate recognition and phagocytosis of pathogenic bacteria, as well as damaged cells and soluble lipoprotein changes associated with vascular damage (eg, high-density lipoprotein [HDL], acetylated low-density lipoprotein [LDL], oxidized LDL). More than eight receptors have been identified. Some scavenger receptors (e.g., SR PSOX) recognize the cell membrane phospholipid phosphatidylserine (PS). PS is normally sequestered on the cytoplasmic surface of the cell membrane. However, it externalized under a very limited range of conditions, including senescence of erythrocytes and cellular apoptosis. Thus, macrophages, through these receptors, can identify and remove senescent red blood cells and cells undergoing apoptosis. Another important scavenger receptor is CD14, which recognizes the LPS and LPS-binding protein complexes. LPS-binding protein is upregulated during inflammation by the cytokines interleukin-6 (IL-6) and IL-1 and helps remove bacterial LPS (endotoxin) from circulation.[14-16]

NOD-like receptors (NLRs)

NLRs are cytoplasmic receptors that recognize microbial products and damaged cells. At least 22 NLRs have been identified in humans. NOD-1 and NOD-2 are cytoplasmic and recognize peptidoglycan fragments from intracellular bacteria and initiate the production of proinflammatory mediators, such as tumor necrosis factor (TNF) and IL-6. Some NLRs are associated with a complex multi-protein called the intracellular inflammasome. Inflammasome It primarily binds to cellular stress-related molecules, a type of DAMP, and through activation of caspases-1, controls the activation and secretion of inflammatory cytokines, such as IL-1β.[17-20]

2. Conclusion

Pattern recognition receptor (PRR) is a receptor complex that interacts with various molecules, such as PAMP and DAMPs. PRR bonds with these various molecules and play a role in various actions of innate immunity and adaptive immunity.

3. References

1. Walsh D, McCarthy J, O'Driscoll C, Melgar S. Pattern recognition receptors–molecular orchestrators of inflammation in inflammatory bowel disease. Cytokine Growth Factor Rev. 2013; 24: 91–104.
2. Medzhitov R, Preston-Hurlburt P, Janeway CA Jr. A human homologue of the Drosophila Toll protein signals activation of adaptive immunity. Nature. 1997; 388: 394–7.

3. Bortoluci KR, Medzhitov R. Control of infection by pyroptosis and autophagy: role of TLR and NLR. Cell Mol Life Sci. 2010; 67: 1643–51
4. Matzinger P. Tolerance, danger, and the extended family. Annu Rev Immunol. 1994; 12: 991–1045.
5. Galluzzi L, Vitale I, Aaronson SA, Abrams JM, Adam D, Agostinis P, et al. Molecular mechanisms of cell death: recommendations of the Nomenclature Committee on Cell Death 2018. Cell Death Differ. 2018; 25: 486–541.
6. Kerr JF, Wyllie AH, Currie AR. Apoptosis: a basic biological phenomenon with wide-ranging implications in tissue kinetics. Br J Cancer. 1972; 26: 239–57.
7. Amarante-Mendes GP, Green DR. The regulation of apoptotic cell death. Braz J Med Biol Res. 1999; 32: 1053–61.
8. Fadok VA, Bratton DL, Konowal A, Freed PW, Westcott JY, Henson PM. Macrophages that have ingested apoptotic cells in vitro inhibit proinflammatory cytokine production through autocrine/paracrine mechanisms involving TGF-beta, PGE2, and PAF. J Clin Invest. 1998; 101: 890–8.
9. Medina CB, Ravichandran KS. Do not let death do us part: 'find-me' signals in communication between dying cells and the phagocytes. Cell Death Differ. 2016; 23: 979–89.
10. Hochreiter-Hufford A, Ravichandran KS. Clearing the dead: apoptotic cell sensing, recognition, engulfment, and digestion. Cold Spring Harb Perspect Biol. 2013; 5: a008748.
11. Cullen SP, Henry CM, Kearney CJ, Logue SE, Feoktistova M, Tynan GA, et al. Fas/CD95-induced chemokines can serve as "find-me" signals for apoptotic cells. Mol Cell. 2013; 49: 1034–48.
12. Metzstein MM, Stanfield GM, Horvitz HR. Genetics of programmed cell death in C. elegans: past, present and future. Trends Genet. 1998; 14: 410–6.
13. Pop C, Salvesen GS. Human caspases: activation, specificity, and regulation. J Biol Chem. 2009; 284: 21777–81.
14. McIlwain DR, Berger T, Mak TW. Caspase functions in cell death and disease. Cold Spring Harb Perspect Biol. 2013; 5: a008656.
15. Pereira WO, Amarante-Mendes GP. Apoptosis: a programme of cell death or cell disposal? Scand J Immunol. 2011; 73: 401–7.
16. Martin SJ, Finucane DM, Amarante-Mendes GP, O'Brien GA, Green DR. Phosphatidylserine externalization during CD95-induced apoptosis of cells and cytoplasts requires ICE/CED-3 protease activity. J Biol Chem. 1996; 271: 28753–6.
17. Amarante-Mendes GP, Finucane DM, Martin SJ, Cotter TG, Salvesen GS, Green DR. Anti-apoptotic oncogenes prevent caspase-dependent and independent commitment for cell death. Cell Death Differ. 1998; 5: 298–306.
18. Tait SW, Green DR. Mitochondrial regulation of cell death. Cold Spring Harb Perspect Biol. 2013; 5: a008706.
19. Wertz IE, Dixit VM. Regulation of death receptor signaling by the ubiquitin system. Cell Death Differ. 2010; 17: 14–24.
20. Guicciardi ME, Gores GJ. Life and death by death receptors. FASEB. 2009; 23: 1625–37.

CERTIFICATE

OF PUBLICATION

For the article titled:

The Role of Pattern Recognition Receptor (PRR) in the Body's Defense System: A Narrative Literature Review

Authored by;

Ziske Maritska, Rachmat Hidayat

Published in

Open Access Indonesian Journal of Medical Reviews Volume 3 Issue 2 2023

Indexed in: