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

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ABSTRACT

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 M β 2, also called CD11b/CD18) facilitates phagocytosis by neutrophils and monocytes/macrophages. CR4 (α X β 2, 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-1 β .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.

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