Detection of Microbial Pathogens by Pattern Recognition Receptors

Pattern recognition receptors (PRRs) play a critical role in the detection of invading pathogens and subsequent activation of the innate immune response. This response provides the first line of defense against infectious disease and is primarily mediated by phagocytic, antigen-presenting cells such as macrophages and dendritic cells. PRRs expressed by these cells, including membrane-associated Toll-like receptors (TLRs), and cytoplasmic Nod-like receptors (NLRs) and retinoic acid inducible gene I-like helicase receptors (RLRs), recognize specific, conserved pathogenassociated molecular patterns (PAMPs) that are present in microbial proteins, nucleic acids, lipids, and carbohydrates. These PAMP-containing molecules act as ligands to trigger PRR-dependent intracellular signaling pathways that ultimately induce the expression of pro-inflammatory and antiviral cytokines. Secretion of these cytokines at the site of an infection promotes the recruitment of neutrophils and natural killer (NK) cells, which eliminate pathogenic microbes and infected cells. Ten TLRs, 23 NLRs, and 3 RLRs have been identified in humans to date, with only a subset of well-characterized NLR (NOD1, NOD2, NALP1, NALP3, IPAF) and RLR (RIG-1, MDA5) family members shown here. These PRRs are characterized by a variable number of ligandsensing leucine-rich repeats (LRR) at their Nterminal (TLRs), or C-terminal (NLRs) ends, and one or more protein-protein interaction (TIR, CARD, PYR), or oligomerization (NACHT) domain(s). Genetic variations that alter the functions of PRRs are associated with increased susceptibility to infectious diseases (TLRs), as well as autoinflammatory (NLRs) and autoimmune (TLRs and NLRs) disorders.



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