immunity is primarily responsible for the elimination, or at least the control, of the invading microbe during the four to seven days required for the establishment of an early adaptive immune response (1–5). Moreover, it is now widely recognized that innate immunity and the resulting inflammatory process play a key role in initiating the adaptive immune response and determining its nature. A distinctive feature of innate immunity is that the response does not increase with successive exposures to the microbes. However, of note, a recent study has described a ''memory'' response by natural killer (NK) cells following infection with mouse cytomegalovirus (6).

Many cells are involved in innate immunity, including phagocytes (e.g., neutrophils, macrophages), dendritic cells (DC), NK cells, and eosinophils. A key characteristic of the cells that form part of the innate immune system is their ability to recognize a wide range of microorganisms through surface receptors (pattern recognition receptors [PRRs]) that recognize invariant molecules present in a wide range of microbes (pathogen-associated molecular patterns [PAMPs]) but not in the host (1). This important area of research has received a remarkable degree of attention over the past few years (1–5,7–10). Examples of PAMPs, which are present in both pathogenic and nonpathogenic microorganisms, include bacterial cell wall peptidoglycans of gram-positive bacteria and lipopolysaccharide (LPS) of gram-negative bacteria.

PRRs can be expressed on the cell membrane, in intracellular compartments or secreted (2–5,7–10). Examples of PRRs expressed on the cell surface include the macrophage scavenger receptor (MSR) that recognizes polyanionic ligands (e.g., dsRNA, LPS), lectin-like binding receptors on NK cells, and macrophage mannose receptors (MMR) that recognize carbohydrate structures present in bacteria and fungal pathogens. Intracellular PRRs include the protein kinase R (PKR) and the 2′-5′-oligoadenylate synthase, which binds dsRNA (present in viruses), as well as the Nucleotide-binding and oligomerization domain containing proteins (NOD), which appear to respond to LPS. Secreted PRRs (e.g., C-reactive protein, mannan-binding lectin, etc.) function by binding to microbes, leading to their elimination by complement-mediated mechanisms or phagocytosis. Toll-like receptors (TLR) are an important family of PRRs that play a pivotal role in innate immune recognition (2–5,7–10). TLR are characterized by extracellular domains that contain leucine-rich repeats and cytoplasmic portions, responsible for intracellular signaling, similar to the intracellular domain of the type 1 interleukin (IL)-1 receptor. Thirteen murine TLR and 10 human TLR, which recognize a variety of different PAMPs, have been

Table 1 Summary of the Properties of Toll-Like Receptors in Humans

TLR	Cell location	Major ligands/agonists	Microbes
TLR1 (+ TLR2)	Surface	Bacterial triacyl lipopeptides	Gram-positive bacteria
TLR2	Surface	Peptidoglycan (PGN) Lipoarabinomannan (mycobacteria) HSP60 Bacterial lipoproteins/lipopeptides GPI anchor (*Trypanosoma cruzi*) Glycolipids Phenol-soluble modulin (*Staphylococcus*) Zymosan (*Saccharomyces cerevisiae*) LPS from *Porphyromonas gingivalis* and *Leptospira interrogans* HA (Hemagglutinin, measles)	Gram-positive and gram-negative bacteria Mycobacteria Mycoplasma Protozoa Fungi Virus
TLR3	Intracellular (endosomal)	dsRNA Poly I:C	Viruses
TLR4	Surface	Enterobacterial LPS Lipoteichoic acid (LTA) HSP60, HSP70 Respiratory syncytial virus F protein Teichuronic acid (*Micrococcus luteous*) Bacterial fimbriae (*Escherichia coli*) Taxol Extra domain A (EDA) of fibronectin Fibrinogen Hyaluronic acid Heparan sulfate	Gram-negative and gram-positive bacteria Chlamydia Viruses
TLR5	Surface	Flagellin	Gram-positive and gram-negative bacteria
TLR6 (+ TLR2)	Surface	Bacterial diacyl lipopeptides	Gram-positive bacteria Mycoplasma
TLR7	Intracellular (endosomal, lysosomal?)	ssRNA (e.g., HIV) Antiviral drugs (imidazoquinoline)	Viral and nonviral ssRNA
TLR8	Intracellular (endosomal, lysosomal?)	ssRNA Antiviral drugs (imidazoquinoline)	Viral and nonviral ssRNA
TLR9	Intracellular (endosomal, lysosomal?)	Unmethylated CpG DNA motifs Viral DNA?	Bacteria Viruses
TLR10	Surface	Unknown	

Note: "?" stands for unknown.

Abbreviations: LPS, lipopolysaccharide; HSP, heat-shock protein.

Source: From Refs. 2–5 and 7–10.