

7. Innate Immunity II

LEARNING OBJECTIVES:

1. Appreciate the ancient origins of the innate immune recognition systems.
2. Understand the concept of the pathogen-associated molecular pattern (PAMP) and be able to name five examples of PAMPS.
3. Become acquainted with the variety of cellular and soluble receptors involved in PAMP recognition.
4. Be able to describe the intracellular signaling events that follow activation of Toll-like receptors.
5. Become familiar with the inflammasome, its components, and its significance in human disease.
6. Be able to describe the transition of immune recognition from innate to adaptive in the course of the immune response.

SUMMARY

1. Innate immunity is conserved throughout evolution and is triggered by recognition of “pathogen-associated molecular patterns” (e.g., LPS) by “pattern recognition receptors.”
2. Collectins (e.g., SP-A, C1q, MBP) recognize carbohydrates on pathogen surfaces and perform multiple anti-microbial functions (e.g., opsonization). Collectins are essential for innate immunity, but also help clear apoptotic debris.
3. Members of the Scavenger Receptor superfamily recognize bacteria as well as glucose-modified proteins and oxidized lipoproteins. They are implicated in the response to infection as well as atherosclerosis and other degenerative diseases.
4. TLR4 is the major LPS receptor in mammalian cells. TLR4 triggers activation of NF- κ B (leading to production of TNF- α , for example). Other TLRs recognize additional microbial products. NOD-like receptors (NLRs) are intracellular sensors of bacterial products that activate the “inflammasome,” triggering caspase-dependent maturation of IL-1.
5. Dendritic cells undergo a maturation program: immature DCs, which traffic to the periphery, capture antigen, and mature DCs, which traffic to the lymph node, present antigen. Innate immune stimuli trigger DC maturation, which upregulates co-stimulatory molecules and facilitates antigen presentation. Thus, the innate immune response ushers in the acquired immune response.
6. NK cells, a component of innate immunity, especially to viruses, represent an early source of IFN- γ and serve to stimulate macrophages and DCs in inflammatory sites. Additional components of the antiviral response include intracellular dsRNA sensors (RIG-like proteins) that activate the IRF pathway to signal antiviral gene expression.