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Sommario/riassunto	The immune system detects "danger" through a series of what we call pathogen-associated molecular patterns (PAMPs) or damage-associated molecular pattern molecules (DAMPs), working in concert with both positive and negative signals derived from other tissues. PAMPs are molecules associated with groups of pathogens that are small molecular motifs conserved within a class of microbes. They are recognized by Toll-like receptors (TLRs) and other pattern recognition receptors. A vast array of different types of molecules can serve as PAMPs, including glycans and glycoconjugates. Bacterial lipopolysaccharides (LPSs), endotoxins found on the cell membranes of Gram-negative bacteria, are considered to be the prototypical class of PAMPs. LPSs are specifically recognized by TLR4, a recognition receptor of the innate immune system. Other PAMPs include bacterial flagellin (recognized by TLR5), lipoteichoic acid from Gram-positive bacteria, peptidoglycan, and nucleic acid variants normally associated with viruses, such as double-stranded RNA, recognized by TLR3 or unmethylated CpG motifs, recognized by TLR9. DAMPs, also known as

alarmins, are molecules released by stressed cells undergoing necrosis that act as endogenous danger signals to promote and exacerbate the immune and inflammatory response. DAMPs vary greatly depending on the type of cell (epithelial, mesenchymal, etc.) and injured tissue. Some endogenous danger signals include heat-shock proteins, HMGB1 (high-mobility group box 1), reactive oxygen intermediates, extracellular matrix breakdown products such as hyaluronan fragments, neuromediators, and cytokines like the interferons (IFNs). Non-protein DAMPs include ATP, uric acid, heparin sulfate, and DNA. Furthermore, accumulating evidence supports correlation between alarmins and changes in the microbiome. Increased serum or plasma levels of these DAMPs have been associated with many inflammatory diseases, including gastric and intestinal inflammatory diseases, graft-versus-host disease (GVHD), sepsis and multiple organ failure, allergies particularly in the lungs, atherosclerosis, age-associated insulin resistance, arthritis, lupus, neuro-inflammation/degeneration and more recently in tumors, which is particularly interesting with the emergence of immunotherapies. Therapeutic strategies are being developed to modulate the expression of these DAMPs for the treatment of these diseases. A vast number of reviews have already been published in this area; thus, in an effort to not duplicate what has already been written, we will focus on recent discoveries particularly in disease models that are epidemic in Western society: intestinal chronic inflammatory diseases including GVHD and its relationship with the microbiome, chronic infectious diseases, allergies, autoimmune diseases, neuroinflammation and cancers. We will also focus on the basic cellular roles of macrophages, T cells and B cells. This research topic brings together sixteen articles that provide novel insights into the mechanisms of action of DAMPS/alarmins and their regulation and subsequent immunologically driven responses.