

## On PAMPs and DAMPs

A major focus in this issue of *Journal of Innate Immunity* is the role of pattern recognition receptors and molecules (PRRs and PRMs), pathogen-associated molecular patterns (PAMPs), and danger-associated molecular patterns (DAMPs) in inflammatory diseases. The clinical importance of these molecules is shown in a study by Marco B. Hansen and coworkers, who report that the reduced levels of PRMs of the lectin pathway of complement seen in patients with a necrotizing soft tissue infection are associated with an increased 28-day and also long-term mortality rate [1].

Retinoic acid-inducible gene 1 (RIG-I) is another important PRR, and Sailen Barik [2] has written an excellent review on RIG-I and its function for this issue. Notably, RIG-I-like receptors execute their antiviral activity by recognizing RNA from certain viral species, resulting in the release of interferon- $\beta$  and other proinflammatory cytokines [3]. This mechanism also involves the translocation of RIG-I to mitochondria, a mechanism critical for the induction of interferon expression [4]. Considering the importance of PRRs with regard to sensing invading pathogens, it is still an open question whether these receptors are able to distinguish between pathogenic bacteria and the normal flora. Is there a need for an additional danger signal similar for the adaptive immune system and, as proposed by Polly Matzinger [5], could DAMPs fulfill this function? These questions are still unanswered and hopefully new and exciting explanations will emerge in the future.

Apart from DAMPs, danger signals can be triggered by stress stimuli. Vedrana Mijošek and colleagues describe how endoplasmic reticulum (ER) stress considerably contributes to inflammatory reactions in bronchial epithelial cells [6]. In a series of elegant experiments the au-

thors show that this effect relies on the PERK-dependent activation of p38 and ERK, and ATF6-mediated basal expression of p38. ER stress is also part of the pathology of chronic obstructive pulmonary disease (COPD) [7] and thus their findings may help to explain why antimicrobial agents such as collagen IV can be upregulated in lung tissue, as observed in biopsies and fibroblasts from COPD patients [8].

The respiratory tract is also a common site for viral infections. Spyridon Makris and colleagues provide convincing evidence that alveolar macrophages can combat infections caused by respiratory syncytial virus (RSV) also in the absence of type I interferons [9]. As type I interferons play important roles in many viral infections [10–13], these findings make alveolar macrophages the ideal sensors of RSV infections and important initiators of immune responses in the lung [9].

Inflammasome formation can be triggered by the activation of PRRs such as NLRP3 [14]. Marlene Ballbach and her collaborators studied how inflammable products can induce the generation of myeloid-derived suppressor cells (MDSCs) [15]. Though MDSCs were first described more than 20 years ago, these cells have only recently attracted considerable interest [16]. In their article, the authors speculate that increased MDSC levels can be used as therapeutic targets in autoinflammatory diseases.

CRISPR-Cas9 genome-editing technology is a wonderful new tool with which to study intracellular downstream mechanisms. Christoph Paone and his coworkers employed this technology to show an involvement of the tyrosine kinase Pyk2 in complement-mediated phagocytosis [17]. They found that this mechanism is completely dependent on CR3-mediated phagocytosis, but not Fc $\gamma$ R-mediated phagocytosis. It will be interesting to see wheth-

er this finding has clinical implications. For instance, Annalucia Serafino and colleagues recently reported that thymosin  $\alpha_1$  can boost complement receptor-mediated phagocytosis by activating a TRAF6-atypical protein kinase C- $\text{I}\kappa\text{B}$  kinase signaling pathway [18]. Notably, many of these signaling events involve an activation of Pyk kinases.

The content of this issue elegantly illustrates the ever evolving field of innate immunity and we hope that the readership will find the articles interesting and thought provoking.

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