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Editorial Note

Purinergic signaling in infection and autoimmune disease

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ABSTRACT

Purinergic signaling plays a key role in inflammatory processes and modulates immune responses against a variety of bacterial and eukaryotic parasites. Here we highlight the role of purinergic receptor activation in infection and autoimmune diseases. Purinergic signaling and inflammasomes modulate the host immune response against chlamydial infections. In addition, increasing evidence suggests that purinergic signaling contributes to Schistosomiasis morbidity, a neglected tropical disease caused by parasitic worms called schistosomes. Finally, the P2X7 receptor and NLRP3 inflammasome have been described to be involved in the pathogenesis of systemic lupus erythematosus, suggesting that these signaling pathways as suitable therapeutic targets for management and treatment of different immune diseases.

The initial reports on Purinergic Signaling date from the 1920s, when Drury and Szent-Gyorgyi [1] described the effects of adenine compounds on the circulatory system of mammals. In the 1950s, adenosine triphosphate (ATP) was described as a possible neurotransmitter based on studies that showed its release from sensory nerves [2,3]. However, the effects of purines on intercellular signaling responses were only recognized in the 1970s, after the studies published by Burnstock et al. [4], which culminated in the development of the purinergic hypothesis [5].

Since then, especially in the last three decades, purinergic signaling has been widely studied in various physiological and pathological conditions of different tissues [6]. Today, we know that extracellular adenine nucleotides and the nucleoside adenosine modulate neuronal and non-neuronal mechanisms, such as immune responses and inflammation, through purinergic receptors [7].

The first report on the involvement of extracellular ATP in inflammatory responses also dates from the 1970s, when Dahlquist and Diamant [8] showed that extracellular ATP induced histamine release in mast cells. Further, also studying mast cells, Cockcroft and Gomperts [9] reported the expression of a specific receptor for extracellular ATP, later identified as the P2X7 subtype.

Currently, nucleotides are described as extracellular signaling molecules, which are essential for the initiation and

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progression of inflammatory responses [10]. They are involved in activation and recruitment of leukocytes to the sites of infection, as well as the production of inflammatory mediators, such as IL-1β release following inflammasome activation [10,11]. Extracellular ATP is now accepted as a proinflammatory molecule that acts as a "danger signal" in the extracellular medium and modulates immune responses against a variety of bacterial and protozoan parasites [10,12–14].

In this forum, we have selected three elegant reviews that highlight the role of purinergic receptor activation in infection and autoimmune disease. Pettengill and co-authors [15] review how purinergic signaling and inflammasome activation affects the host immune response against chlamydial infection. Bacterial species belonging to the family Chlamydiaceae are obligate intracellular pathogens, which induce prolonged localized inflammation and tissue damage. Chlamydiae are sensitive to changes in the normal cellular function of their hosts. Therefore, the activation of purinergic signaling responses, as well as the assembly of the inflammasome and subsequent caspase activation that in turn processes pro-IL-1β into its mature form, significantly influence the efficiency of chlamydial infection. In another important review, Silva [16] highlights the role of purinergic signaling in schistosomiasis. This neglected tropical chronic inflammatory disease is caused by a protozoan parasite belonging to the genus *Schistosoma*. As discussed by Silva, increasing evidence suggests that changes in extracellular nucleotide metabolism and, consequently, in the activation and function of both P1 and P2 purinergic receptors (e.g. the P2X7 receptor) contribute to disease morbidity. Finally, Di Virgilio and Giuliani [17] discuss the crucial role of the P2X7 receptor and NLRP3 inflammasome in the development of autoimmunity and tissue damage in systemic lupus erythematosus.

In summary, the aim of this forum is to provide a representative overview of the contribution of purinergic signaling and inflammasome activation to inflammatory and immune responses during infection by extracellular and intracellular parasites and autoimmune disease. In addition, such reviews have clinical relevance to the biomedical area since they point to purinergic signaling and inflammasomes as suitable therapeutic targets for management and treatment of different immune diseases.

Conflicts of interest

The authors declare that they have no conflict of interest.

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