Regulation of inflammatory response by extracellular ATP and P2X7 receptor signalling: through and beyond the inflammasome

Desde 2014-09-01 hasta 2019-08-31, proyecto en curso

Coste total: EUR 1 794 948
Aportación de la UE: EUR 1 794 948
Coordinado en: Spain

Objetivo

Inflammatory diseases affect over 80 million people worldwide and accompany many diseases of industrialized countries, being the majority of them infection-free conditions. There are few efficient anti-inflammatory drugs to treat chronic inflammation and thus, there is an urgent need to validate novel targets. We now know that innate immunity is the main coordinator and driver of inflammation. Recently, we and others have shown that the activation of purinergic P2X7 receptors (P2X7R) in immune cells is a novel and increasingly validated pathway to initiate inflammation through the activation of the NLRP3 inflammasome and the release of IL-1β and IL-18 cytokines. However, how NLRP3 sense P2X7R activation is not fully understood. Furthermore, extracellular ATP, the physiological P2X7R agonist, is a crucial danger signal released by injured cells, and one of the most important mediators of infection-free inflammation. We have also identified novel signalling roles for P2X7R independent on the NLRP3 inflammasome, including the release of proteases or inflammatory lipids. Therefore, P2X7R has generated increasing interest as a therapeutic target in inflammatory diseases, being drug like P2X7R antagonist in clinical trials to treat inflammatory diseases. However, it is often questioned the functionality of P2X7R in vivo, where it is thought that extracellular ATP levels are below the threshold to activate P2X7R. The overall significance of this proposal relays to elucidate how extracellular ATP controls host-defence in vivo, ultimately depicting P2X7R signalling through and beyond inflammasome activation. We foresee that our results will generate a leading innovative knowledge about in vivo extracellular ATP signalling during the host response to infection and sterile danger.

Información relacionada

Informes resumidos
Periodic Report Summary 2 - DANGER ATP (Regulation of inflammatory response by extracellular ATP and P2X7 receptor signalling: through and beyond the inflammasome.)
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Beneficiarios

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