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New insights into inflammasome activation, interleukin-1β release and inflammatory cell death

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Date: **08/11/19- 12:30 h**
Place: Salón de Actos CIPF

Abstract: Inflammatory diseases affect over 80 million people worldwide and accompany many diseases of industrialized countries, being the majority of them infection-free conditions. We now know that innate immunity is the main coordinator and driver of inflammation through the secretion of cytokines and other signaling proteins upon innate immune cell activation by pathogen associated molecular patterns. The activation of purinergic P2X7 receptors in immune cells by extracellular ATP is a novel and increasingly validated “sterile” pathway to initiate inflammation. P2X7 receptor induces the activation of the NLRP3 inflammasome and caspase-1, leading to the unconventional release of IL-1β via plasma membrane permeabilization. In the last years, we have gain substantial insights into the release of IL-1β and other cytosolic proteins through the formation of gasdermin D pores on the plasma membrane and the execution of a specific type of inflammatory cell death called pyroptosis. Extracellular ATP, the physiological P2X7 receptor agonist, is a crucial danger signal released by stressed or injured cells, and one of the most important mediators of infection-free inflammation. We have recently translated this knowledge to human clinical pathology, where the development of selective NLRP3 antagonists with a suitable clinical profile, increase the therapeutic window to treat inflammatory, metabolic and degenerative diseases.

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Hafner-Bratkovič, et al. NLRP3 lacking the leucine-rich repeat domain can be fully activated via the canonical inflammasome pathway. *Nat Commun*. 2018;9:5182

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