SIgN Immunology Seminar



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

Host
Dr Alessandra Mortellaro
Singapore Immunology Network, A*Star

Date
Thursday 1 September 2016

Time
11am – 12pm

Venue
SIgN Seminar Room
Immunos Building
Level 4
Biopolis

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 release of IL-1β via unconventional protein release. In the last years, we have gain substantial insights into the release of IL-1β and other proteins that constitute the secretome of P2X7 receptor activation in macrophages, being some of them dependent on caspase-1 driving pyroptotic cell death. 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 P2X7 receptors with a suitable clinical profile, increase the therapeutic window to treat inflammatory, metabolic and degenerative diseases.