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SIgN Immunology Seminar



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New mechanisms of inflammasome activation and autoinflammation

Host
Dr Alessandra Mortellaro
Singapore Immunology Network,

Date
Friday
24 March 2017

Time
2pm – 3pm

Venue
SIgN Seminar Room
Immunos Building
Level 4
Biopolis

The innate immune system is the first line of defence against infection. Our genome encodes cell surface innate immune sensors that directly detect pathogens, but also a series of cytoplasmic sensors that can form inflammasome complexes. As we recently discussed in Nature Reviews Immunology, most inflammasome sensors do not directly detect pathogens, but instead monitor homeostasis-associated molecular patterns in the cell, and alert the host to danger indirectly. This enables a single sensor to detect a wide variety of invading pathogens, however leaves the host open to inadvertent activation of the pathway causing sterile autoinflammatory disease.

We have now identified actin polymerisation as a key homeostatic process monitored by the inflammasome sensor Pyrin. Specifically, mutations in the actin-depolymerizing cofactor Wdr1, lead to increased actin polymerisation, and trigger Pyrin in mice and humans. We have also identified mutations in Pyrin itself which determine how this inflammasome is activated mechanistically, and results in a novel autoinflammatory skin disease. We show that these patients can be treated by targeting the downstream cytokine produced by the inflammasome, IL-1b.