New insights into inflammasome signalling and inhibition

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Inflammasomes are signalling hubs that assemble in response to cell stress or microbial infection, and provide an activation platform for the zymogen protease, caspase-1. Upon activation, caspase-1 triggers the maturation and secretion of potent pro-inflammatory mediators (interleukins (IL)-1β and -18) and induces cell lysis, culminating in the activation of the immune system and antimicrobial defence. Inflammasome signalling can, however, also drive pathology in a range of human auto-inflammatory, inflammatory, metabolic and neurodegenerative diseases. Here we reveal natural mechanisms by which cells shut down inflammasome signalling to restore homeostasis following host-protective immune responses, and how a small molecule inflammasome inhibitor can silence pathological inflammasome signalling for therapeutic management of disease.