

College of Liberal Arts and Sciences
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Inflammasome assembly – an example of balance control in the immune system

Abstract:

Inflammasomes are mega-Dalton protein complexes that initiate inflammation responses and play important roles in the innate immune system. Upon activation, inflammasomes recruit and activate the effector protein caspase-1. Caspase-1 in turn cleaves the Gasdermin D (GSDMD) protein to release its Nterminal domain, which inserts into the cell membrane to punch holes on the cell surface. As a result, the host cell will undergo pyroptotic cell death (pyroptosis) and release the cell contents into the extracellular environment. Pro-inflammatory cytokines IL-1 β and IL-18, both activated by caspase-1, will also be released to activate the downstream inflammation reactions. Here we combine electron cryo-microscopy (cryoEM) with biochemical and functional studies to elucidate the structural mechanisms underlying the regulation and assembly of inflammasome complex.