Regulation of inflammasomes in autoinflammatory diseases

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The term autoinflammation was coined to describe inflammatory processes that characterize a group of inherited diseases of the innate immune system. Patients with these pathologies display periodic or chronic systemic inflammation, often associated with fevers of unknown origin, and little or no adaptive immunity involvement. The discovery of autoinflammation-causing mutations in several genes uncovered the role of innate immune response pathways such as the inflammasome. These studies have also contributed to the characterization of fundamental inflammation mechanisms that contribute to tissue homeostasis maintenance and whose deregulation can play a significant role in more common diseases. Among those pathways, the NLRP3 inflammasome has been considerably investigated. Gain-of-function mutations in NLRP3 cause Cryopyrin-associated periodic syndrome (CAPS), an autoinflammatory disorder characterized by systemic, cutaneous, musculoskeletal, and central nervous system inflammation. Moreover, NLRP3 importance in regulating innate immune response has been established in a plethora of conditions and diseases. However, the mechanisms leading to the assembly of this inflammasome, and how it is regulated in humans are fundamental questions that are still not fully understood. This projects aims to elucidate the molecular mechanisms and pathways that drive and regulate autoinflammation, define the signaling components that are essential and those that are redundant within those pathways and address the physiological relevance of these components in autoinflammation.