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The NLRP3 inflammasome: role in metabolic disorders and regulation by metabolic pathways

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Abstract:

Inflammasomes are large multimolecular complexes present in the cytosol of stimulated immune cells; they mediate the activation of caspase-1, leading to cellular pyroptosis. So far, a variety of studies on inflammasomes have emerged, and the best-studied is the NLRP3 inflammasome that is involved in many inflammatory responses. Furthermore, its relationship with metabolism is gaining increasing attention in this field. In this review, we discuss the importance of the NLRP3 inflammasome in metabolic disorders and its close association with metabolic pathways.

Key words: NLRP3 inflammasome, metabolic disorder, metabolic pathway, IL-1β, IL-18.

Innate immune function depends on the recognition of pathogen-associated molecular patterns (PAMPs) and danger-associated molecular patterns (DAMPs). PAMPs are derived from invading pathogens, while DAMPs are induced as a result of endogenous stress. Assembly of the inflammasome is dictated by germline-encoded pattern-recognition receptors in response to PAMPs or DAMPs [1]. The NLRP3 inflammasome (also called NALP3 or cryopyrin) is critical for promoting the caspase-1-dependent maturation of the pro-inflammatory cytokines interleukin (IL)-1β and IL-18. Besides, it has been confirmed to contribute to metabolic disorders, including obesity and type 2 diabetes [2], gout [3], atherosclerosis [4], and neurodegenerative diseases [5]. Furthermore, studies of immunometabolism have revealed distinct crosstalk between metabolic pathways and immune cell functions [6]. Intriguingly, the metabolic pathways (including glycolysis [7], the tricarboxylic acid (TCA) cycle [8], fatty-acids [9], and cholesterol [10] are all associated with activation of the NLRP3