發炎體與痛風發炎的免疫機轉

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Acute gouty arthritis is an inflammatory disease resulting from the precipitation of monosodium urate (MSU) crystals in joints. MSU crystals can activate a variety of innate immune cells (e.g., monocytes, macrophages, neutrophils, mast cells, and dendritic cells) to produce proinflammatory cytokines such as IL-1β and TNF. In vivo studies have shown that MSU-induced neutrophilic inflammation is strongly attenuated in IL-1 receptor-deficient mice, indicating that IL-1β plays an essential role in mediating gouty inflammation. The production of IL-1β by immune cells requires two signals: first various danger signals activate IL-1β gene expression, and the processing of pro-IL-1β into mature IL-1β by caspase-1 requires a second signal that activates the inflammasome. The inflammasome is a multiprotein complex that consists of a NOD-like receptor (NLR), ASC, and caspase-1. MSU crystals has been shown to specifically activate the NLRP3 inflammasome. Colchicine, a potent drug for treating gouty arthritis, can inhibit MSU crystal activation of the NLRP3 inflammasome and block the release of IL-1β. Proof of concept has been established in clinical trials of several IL-1 inhibitors, both for treatment and prophylaxis of gout flares. These agents include anakinra, an IL-1R antagonist, rilonacept, an IL-1 decoy receptor, and canakinumab, an anti-IL-1β monoclonal antibody. I will review the mechanism of MSU crystal-induced inflammasome activation and the clinical trial results of using IL-1 blockers for treatment and prophylaxis of gouty arthritis.