Secreted aspartic proteases of *Candida albicans* activate the NLRP3 inflammasome.

Pietrella D, Pandey N, Gabrielli E, Pericolini E, Perito S, Kasper L, Bistoni F, Cassone A, Hube B, Vecchiarelli A (2013) Secreted aspartic proteases of *Candida albicans* activate the NLRP3 inflammasome. *Eur J Immunol* 43(3), 679-692.

Abstract

In a recent report, we demonstrated that distinct members of the secreted aspartic protease (Sap) family of Candida albicans are able to induce secretion of proinflammatory cytokines by human monocytes, independently of their proteolytic activity and specific pH optima. In particular, C. albicans Sap2 and Sap6 potently induced IL-1β, TNF-α, and IL-6 production. Here, we demonstrate that Sap2 and Sap6 proteins trigger IL-1β and IL-18 production through inflammasome activation. This occurs via NLRP3 and caspase-1 activation, which cleaves pro-IL-1β into secreted bioactive IL-1β, a cytokine that was induced by Saps in monocytes, in monocyte-derived macrophages and in dendritic cells. Downregulation of NLRP3 by RNA interference strongly reduced the secretion of bioactive IL-1β. Inflammasome activation required Sap internalization via a clathrin-dependent mechanism, intracellular induction of K(+) efflux, and ROS production. Inflammasome activation of monocytes induced by Sap2 and Sap6 differed from that induced by LPS-ATP in several aspects. Our data reveal novel immunoregulatory mechanisms of C. albicans and suggest that Saps contribute to the pathogenesis of candidiasis by

fostering rather than evading host immunity.

Involved units

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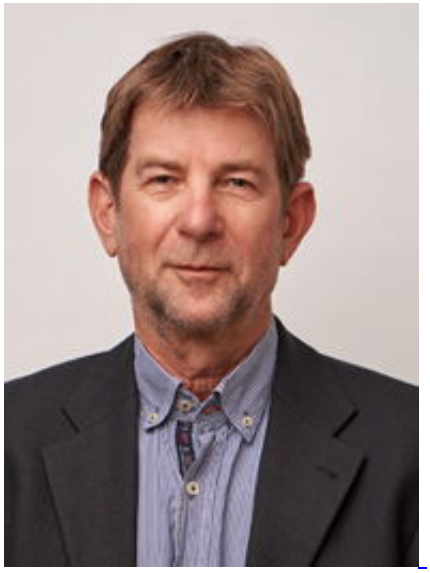

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Topics

Interactions with immune cells (MPM)

Identifier

doi: 10.1002/eji.201242691

PMID: 23280543