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# The inflammasome of activated human B-lymphocytes regulates IL-1β and IgM: A crosstalk between the innate and the adaptive immune response

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The NLRP3 inflammasome is activated in response to different bacterial, viral and fungal pathogens and serves as modulator of different pattern recognition receptor signalling pathways. Herein, we have investigated the role of NLRP3 in human circulating B-lymphocytes and identify that it is essential for two independent processes, pro-inflammatory cytokine and antibody regulation. Our results show that β-glucan stimulated B lymphocytes secrete IL-1β, which is important in the host defence against Pneumocystis and other fungal infections. IL-1β maturation and secretion by circulating B-lymphocytes is regulated by the NLRP3 inflammasome, which was dependent on ATP and potassium (K+) efflux. The inhibition of NLRP3 and CASP1 by specific inhibitors abolished the secretion of IL-1β. β-glucan mediated IL-1β secretion was partially mediated by Dectin-1 activation via SYK and the transcription factors NF-κB and AP-1. Furthermore, we demonstrated that B-lymphocytes activated by unmethylated CpG motifs, found in bacterial DNA, induced the production and secretion of IgM antibodies. Interestingly, this process also requires the activation of the NLRP3 inflammasome. Similar to IL-1β, B-lymphocyte stimulation by CpG resulted in NLRP3 and CASP1 activation. IgM production was inhibited by specific CASP1 and NLRP3 inhibitors and was dependent on ATP and potassium (K+) efflux. Furthermore, we identified that CPG-stimulated IgM secretion unlike IL-1β was mTOR-mediated. In conclusion, this study identifies the NLRP3 inflammasome as modulator of the innate and adaptive immune systems in response to fungal and bacterial stimuli in human circulating B-lymphocytes.

## Biography

Eva M Carmona is a Physician-Scientist, whose research is focused on understanding the role of infection and chronic inflammation in the development of interstitial lung diseases (ILD). Her research to date has focused on understanding the immunomodulatory effects of fungal beta-glucans (BG) in innate immune cells. Particularly, she has characterized the role of BG on dendritic cells and their participation in T-cell polarization (Th1 and Th17). Currently, her group is interested in determining the mechanisms by which BG modulate B-lymphocyte activation and how BG-activated B-lymphocytes may drive the development of inflammation and fibrosis in a subset of patients with ILD. Her group has recently shown that BG activated B-lymphocytes release a pro-inflammatory cytokine profile that participates in neutrophil recruitment potentially contributing to lung epithelial damage. Herein, they have identified the NLRP3 inflammasome of circulating human B-lymphocytes as a key component in innate and adaptive immune response in response to fungal and bacterial antigens

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