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Pro-Inflammatory Cytokine and Caspase-1 Responses to Pattern Recognition Receptor Activation of Neutrophils and Dendritic Cells in Behcet's Disease

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Objectives: Activated innate immunity is implicated in the pathogenesis of Behcet's Disease (BD). To clarify the mechanisms of innate immune responses, we investigated inflammasome activation in dendritic cells (DC) and neutrophils, following stimulation with two different pattern recognition receptors (PRR) "RIG-1 like" (RLR) and "NOD-like" (NLR) in patients with BD.

Methods: Sixteen active BD patients with mucocutaneous lesions and 17 healthy controls (HC) were included in this study. Dendritic cells were generated from monocytes. DCs and isolated neutrophils were activated by RLR and NLR ligands. Caspase-1 activation and expressions of p38 and RIP2 were determined by flow cytometry. Levels of IL-1β, IL-6, TNF-α, IFN-α and IL-18 in culture supernatants were measured by ELISA.

Results: Activation of caspase-1 following intracellular PRR stimulation was found to be in similar levels in DCs and neutrophils of BD patients compared to HC. However, activation of DCs from BD patients to NOD2 stimulus measured with the expressions of RIP2, p38 as well as IL-18 levels was found to be slightly defective ($p<0.05$). In neutrophil cultures, IL-6 levels were lower in response to all stimuli in patients with BD compared to HCs ($p<0.01$).

Conclusions: Inflammasome formation following stimulation with NOD1/NOD2 and RIG measured with caspase-1 activation, cytokine levels and expressions of RIP2 and p38 seems to be functionally normal in DCs and neutrophils of BD patients, although slightly defective responses in some pathways and cytokine levels were observed. These results may suggest that caspase-1 independent pathways such as TLRs may be more prominent in BD pathogenesis.

Key words: Behcet's disease, dendritic cells, inflammasome, neutrophils, pattern-recognition receptors