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The role of JAK-STAT signaling in neutrophilic lung inflammation

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Background/aims Neutrophilic lung inflammation is a common feature of chronic inflammatory lung diseases like COPD and corticosteroid-resistant asthma resulting in exacerbation. The IL23-Th17 axis is a major contributor to neutrophilic inflammation. Exposure of the airway epithelium to triggering agents enables the release of IL23 from the antigen-presenting cells. IL23 binds to its receptors, associated with TYK2 and JAK2 on T naïve cells. This eventually leads to the phosphorylation of STAT4 and STAT3 and subsequently Th17 polarization. A major Th17 cytokine, IL17 binds to its receptor on structural and immune cells and results in the release of IL8 and GMCSF leading to neutrophil recruitment and activation. Thus, we aim to investigate the potential role of TYK2-JAK2 kinases and associated cytokines in the IL-23-Th17 axis of neutrophilic lung inflammation. Results Functional assays on neutrophils to study ROS production and migration were performed. IL17 and IL23 pretreatments significantly increased ROS production compared to control in neutrophils. IL17 significantly increased the migration of neutrophils and enhanced IL8-stimulated chemotaxis. The expression of TYK2 and JAK2 was studied in the various immune cell populations in whole blood of allergic and non-allergic donors using flow cytometry. Non-allergic donors showed significantly higher expression of TYK2 and JAK2 compared to allergic donors. Conclusions Our results indicate that IL17 and IL23 might be potential players in neutrophilic lung inflammation, affecting neutrophil migration and ROS production. TYK2 and JAK2 are differentially expressed in immune cell populations from allergic donors compared to healthy controls. From our preliminary data, we conclude that IL17 and IL23 directly affect neutrophil functions. In further experiments, we plan to evaluate neutrophil function and JAK-STAT expressions in samples from patients with COPD and non-allergic asthma.