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Title: Involvement of the JAK-STAT3 pathway in a lipopolysaccharide-induced rat model of airway inflammation

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Body: LPS is a component of gram-negative bacteria that induces the transcription of inflammatory cytokines and immunoregulators through TLR4 activation. On the other hand, the JAK family of kinases mediates the cytokine receptor-induced signalling pathways involved in inflammatory processes. The activation of the transcription factors STATs by JAK kinases is a key point in these signals. In this study, the involvement of the JAK-STAT3 pathway in the aerosolized LPS-induced airway inflammation in rats was assessed. Additionally, the effects of LPS on neutrophils in BALF, lung tissue, blood and bone marrow are shown as well as the pattern of cytokines and chemokines induced in BALF and plasma after LPS challenge. Phosphorylation of STAT3 was studied in lung homogenates by ELISA. Localization of phospho-STAT3 (pSTAT3) in lung tissue was also performed by immunohistochemistry. The role of JAK/STAT pathway in airway inflammation was evaluated by assessing the effects of the pan-JAK inhibitor tofacitinib on pSTAT3 expression in lung and on neutrophils and cytokines in BALF. Aerosolized LPS challenge induced an increase in pSTAT3 expression in the lungs. In addition, LPS increased the neutrophils, cytokines and chemokines in BALF. Tofacitinib inhibited the pSTAT3 signal in the lung, significantly reduced lung neutrophilia and inhibited the increase in IL6 in BALF. In summary, this study provides additional characterization of the LPS-induced rat model of airway inflammation and demonstrates the involvement of JAK/STAT3 pathway in this model.