IL-22 suppresses IFN-γ-mediated lung inflammation in asthmatic patients.

Abstract:

IL-22 controls tissue homeostasis by both proinflammatory and anti-inflammatory effects. However, the anti-inflammatory mechanisms of IL-22 remain poorly investigated. We sought to investigate the anti-inflammatory role for IL-22 in human asthma. T-cell lines derived from lung biopsy specimens of asthmatic patients were characterized by means of flow cytometry. Human bronchial epithelial cells from healthy and asthmatic subjects were stimulated with IL-22, IFN-γ, or the combination of both cytokines. Effects of cytokine stimulation were investigated by using whole-genome analysis, ELISA, and flow cytometry. The functional consequence of cytokine stimulation was evaluated in an in vitro wound repair model and T cell-mediated cytotoxicity experiments. In vivo cytokine expression was measured by using immunohistochemistry and Luminex assays in bronchoalveolar lavage fluid of healthy and asthmatic patients. The current study identifies a tissue-restricted antagonistic interplay of IL-22 and the proinflammatory cytokine IFN-γ. On the one hand, IFN-γ antagonized IL-22-mediated induction of the antimicrobial peptide S100A7 and epithelial cell migration in bronchial epithelial cells. On the other hand, IL-22 decreased epithelial susceptibility to T cell-mediated cytotoxicity by inhibiting the IFN-γ-induced expression of MHC-I,
MHC-II, and CD54/intercellular adhesion molecule 1 molecules. Likewise, IL-22 inhibited IFN-?/-induced secretion of the proinflammatory chemokines CCL5/RANTES and CXCL10/interferon-inducible protein 10 in vitro. Consistently, the IL-22 expression in bronchoalveolar lavage fluid of asthmatic patients inversely correlated with the expression of CCL5/RANTES and CXCL10/interferon-inducible protein 10 in vivo. IL-22 might control the extent of IFN-?/-mediated lung inflammation and therefore play a tissue-restricted regulatory role.