Regulatory effect of TLR3 signaling on staphylococcal enterotoxin-induced eosinophilia-associated cytokine production by nasal polyps

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Background: Toll-like receptor 3 (TLR3) is expressed in upper airways, and signals through TLR3 induce the production of pro-inflammatory cytokines including interleukin (IL)-6 and IL-8 by sinonasal tissue cells. However, little is known regarding whether TLR3 signals exert a regulatory effect on the pathogenesis of chronic rhinosinusitis with nasal polyps (CRSwNP), especially on eosinophilic inflammation.

Objective: We sought to investigate the effect of Poly(IC), the ligand for TLR3, on cytokine production by dispersed nasal polyp cells (DNPCs).

Methods: DNPCs were pretreated with or without Poly(IC), and were then cultured in the presence or absence of staphylococcal enterotoxin B (SEB), following which the levels of IL-5, IL-10, IL-13, IL-17A and interferon (IFN)-γ in the supernatant were measured. To determine the involvement of IL-10 and cyclooxygenase in Poly(IC)-mediated signaling, DNPCs were treated with anti-IL-10 monoclonal antibody and diclofenac, respectively. Poly(IC)-induced prostaglandin E\(_2\) (PGE\(_2\)) production was also determined.

Results: Exposure to Poly(IC) induced a significant production of IL-10, but not of IL-5, IL-13, IL-17A or IFN-γ by DNPCs. Pretreatment with Poly(IC) dose-dependently inhibited SEB-induced IL-5, IL-13 and IL-17A, but not IFN-γ production. Neutralization of IL-10 significantly abrogated the inhibitory effect of Poly(IC). Treatment with diclofenac also abrogated the inhibitory effect of Poly(IC) on SEB-induced IL-5 and IL-13 production. However, unlike exposure of diclofenac-treated DNPCs to lipopolysaccharide, the ligand for TLR4, exposure of these cells to Poly(IC) did not enhance IL-5 or IL-13 production. Poly(IC)-induced release of PGE\(_2\) by DNPCs was transient and not significantly higher than controls.

Conclusions & Clinical Relevance: These results suggest that TLR3 signaling regulates eosinophilic inflammation in CRSwNP, at least in part, via IL-10 production. For clinical implications, these observations may provide a basis for novel therapeutic approaches targeting Poly(IC) and other viral components in the management of eosinophilic airway diseases such as CRSwNP, allergic rhinitis and bronchial asthma.