

Abstract

Background: Vascular endothelial growth factor (VEGF) is known to be associated with the pathogenesis of chronic rhinosinusitis with nasal polyps (CRSwNP). VEGF is produced by a variety of cells including fibroblasts. It was recently reported that prostaglandin (PG) E₂ induces VEGF release by nasal polyp fibroblasts. However, little is known regarding possible regulation of VEGF by other PGs. We have reported that molecules that regulate PGD₂ metabolism play roles in the pathogenesis of CRS including in local eosinophilia and type 2 cytokine production. In the present study, we sought to determine whether PGD₂ regulates VEGF release by nasal polyp fibroblasts.

Methods: Nasal polyp fibroblasts were established from nasal polyps. These fibroblasts were stimulated with serial dilutions of PGD₂ or PGD₂ receptor (DP/CRTH2)-selective agonists in the presence or absence of receptor-selective antagonists. The concentration of VEGF in the culture supernatants was determined using ELISA.

Results: 5 μM of PGD₂ significantly induced VEGF release by nasal polyp fibroblasts. VEGF release was also obtained by stimulation with a DP receptor-selective, but not with a CRTH2 receptor-selective agonist. In addition, PGD₂-induced VEGF release was significantly inhibited by pre-treatment with DP receptor-selective antagonists. In contrast, pre-treatment with a CRTH2 receptor-selective antagonist significantly

enhanced PGD₂-induced VEGF release.

Conclusions: PGD₂ stimulates VEGF production via DP but not CRTH2 receptors in nasal polyp fibroblasts.