Abstract

Background: Hyaluronan is one of the major extracellular matrixes in chronic rhinosinusitis (CRS) associated with tissue remodeling. Prostaglandin D_2 (PGD_2) is also associated with the pathogenesis of CRS. However, little is known about whether PGD_2 regulates hyaluronan production by human airway fibroblasts.

Objective: We sought to determine the effect of PGD_2 on the mRNA expression of three isoforms of membrane-bound hyaluronic acid synthase (HAS1, HAS2 and HAS3) in fibroblasts, the major source of hyaluronan production, derived from CRS patients.

Methods: Nasal polyp-derived fibroblasts (NPDF) and uncinate tissue-derived fibroblasts (UTDF) were established from CRS patients with nasal polyps and those without, respectively. These fibroblasts were stimulated with PGD_2 or PGD_2 receptor (DP/CRTH2)-selective agonists in the presence or absence of receptor-selective antagonists. mRNA levels for HAS1, HAS2 and HAS3 were determined by real-time quantitative PCR.

Results: PGD_2 (1 μM) significantly enhanced HAS1 but not HAS2 or HAS3 mRNA expression by NPDF. Enhanced HAS1 mRNA expression was also obtained by stimulation with a DP receptor-selective agonist, but not with a CRTH2 receptor-selective agonist. In addition, PGD_2-induced HAS1 mRNA expression was significantly inhibited

by pre-treatment with DP receptor-selective antagonists. Similar induction of PGD_2-induced HAS1 mRNA expression was seen in UTDF.

Conclusion: PGD_2 selectively stimulates HAS1 mRNA expression in local fibroblasts in CRS via DP, but not CRTH2, receptors.