SPLUNC1 (BIPFA1) Expression in Airway Tissue Compartments and Regulation by IL-13 Exposure of hBEC Obtained from the Severe Asthma Research Protocol (SARPIII)

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Introduction. Asthmatics express less SPLUNC1 (innate defense protein) compared to healthy participants. We hypothesize expression/secretion of SPLUNC1 within airway epithelia will decrease, in an IL-13-dependent mechanism, while SPLUNC1 expression in submucosal glands and tissue will increase in individuals with increased asthma severity when compared to individuals without asthma.

Methods. SARP3 participants (763) underwent sputum induction, bronchoscopy and BAL collection. Airway epithelial cells differentiated at ALI then exposed to IL-13 with basal supernatants collected. SPLUNC1 was quantitated in sputum (N = 4 healthy, N = 20 asthmatic) and hBEC basal supernatants (N = 1 healthy[repeated], N = 3 asthmatic) via ELISA and in endobronchial biopsies (N = 10 healthy, N = 17 asthmatic) via immunofluorescent analysis. Statistics by Student's Test and/or Spearman correlations ($p < 0.05$ significance).

Results. SPLUNC1 secretion in asthmatics wasn't significantly different in sputum (779±590ng/mL to 938±1020ng/mL, $p = 0.56$) yet increased in differentiated hBECs versus healthy (46.5±28.6ng/mL to 17.5±15.3ng/mL, $p < 0.01$). SPLUNC1 overall expression in asthmatics was decreased (29.0±48.70lum/μm^2 to 62.07±99.96lum/μm^2; $p < 0.05$) without difference in submucosal glands versus healthy (977.75±1990.40lum/μm^2 to 572.43±1127.40lum/μm^2; $p = 0.22$). IL-13 (10ng/mL) to asthmatic hBECs decreased SPLUNC1 secretion over time ("No-IL-13": 59.77±50.67ng/mL, Δ-34.44±22.62ng/mL[24hr], $p < 0.05$; Δ-37.78±29.90ng/mL, $p = 0.05$[48hr]; Δ+38.07±1.54ng/mL, $p = 0.1$[72hr]; Δ-8.76+/-41.74ng/mL, $p = 0.7$[96hr]). Healthy SPLUNC1 secretion transiently decreased after IL-13 exposure: at 24hrs, secretion decreased 4.22±0.28ng/mL ($p < 0.01$).

Conclusions. SPLUNC1 expression in airway epithelium, not submucosal glands, nor sputum, was decreased in asthmatics, although N was small in sputum. Asthmatic and healthy hBECs SPLUNC1 secretion was inhibited by IL-13.

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