ATS 2022 Highlights

Respiratory Structure and Function Early Career Professionals

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Get to know members of the RSF Assembly

Is your research clinical, basic science or translational?

Basic Science

Tell us about your research?

One of the hallmark features of asthma is alteration of the lung tissue due to changes in the extracellular matrix (ECM). Collagen 4 Alpha 3 (COL4A3) is one of the principal components of the lung basement membrane. My research particularly focuses on investigating possible avenues by which COL4A3 expression is being reduced in asthmatic airways.

Where do you see yourself in 5 years?

One of the roles I see myself in is a scientific advisor either in the academia or industry

What do you find is the major benefit of RSF Assembly Membership?

As an early career researcher, it is important to network and engage with fellow professionals and the RSF assembly sets the stage perfectly to do that. The assembly is a very engaging and supportive community to foster network or scientific collaborations.

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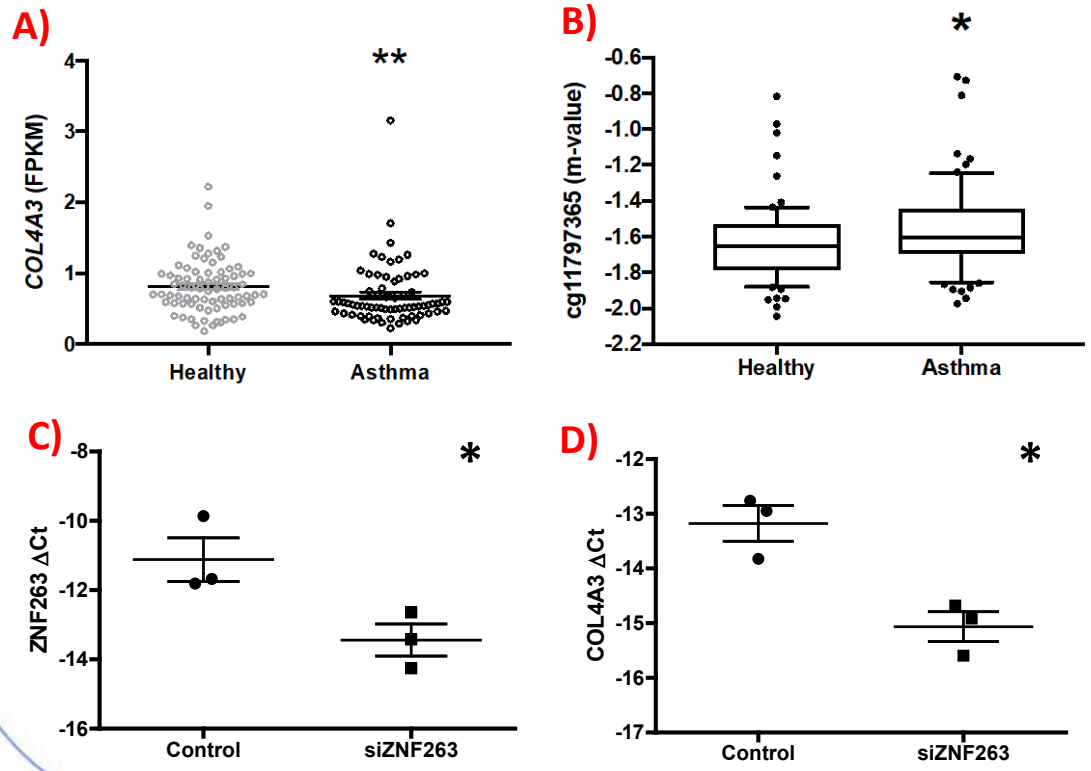

Abstract Title: Analysing the enhancing effect of ZNF263 on COL4A3 expression

Objective: Reduction of COL4A3, one of the six isoforms of collagen 4, in asthmatic airways results in increased inflammation and angiogenesis, implicating it as a central part of asthma pathogenesis. However, to date, the path underlying these diminished COL4A3 levels has been elusive. A possible epigenetic mechanism underlying the reduction of COL4A3 expression has been investigated. The hypothesis of my project is that decreased expression levels of COL4A3 are due to the result of a specific methylation which in turn disrupts the binding of the enhancer ZNF263.

Methods: Bronchial biopsies of 76 patients with asthma and 83 controls were subjected to RNA sequencing and DNA methylation bead arrays to identify expression and methylation changes. Effects of ZNF263 silencing, using small interfering RNA, on the COL4A3 expression were studied using qPCR.

Results: COL4A3 expression was decreased in asthmatic bronchial epithelial cells (FPKM): 0.68±0.05, n=76, p<0.01) vs controls (FPKM: 0.81±0.04, n=83) (A). DNA methylation of cg11797365 is significantly increased in asthmatic bronchial epithelial cells (m-value±SE:-1.56±0.03, p<0.05) as compared to control subjects (m-value±SE: -1.63 ± 0.02) (B). HeLA cells transfected with ZNF263 siRNA post 24 hours show a significant silencing (mean ΔCt ± SEM: -13.14 ± 0,4664 N=3, p<0.05 (C) and COL4A3 expression is reduced in cells treated with ZNF263 siRNA post 24 hours of transfection (mean ΔC_t ± SEM: -15.06 ± 0.2741 N=3, p<0.05) (D).

Conclusion: These findings indicate an epigenetic modification as a contributing factor for the loss of COL4A3 expression in asthmatic airway epithelium.