CHRD 2021: Abstract & Poster Submission Form

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Research Category:

- ◉ Basic Science
- ○ Clinical
- ○ Community Health / Policy

What was your role in the project?

- ☐ Design
- ☑ Perform Experiments
- ☑ Analyze Data
- ☑ Write Abstract
- ☐

Presenter Status:

- ◉ Undergraduate Students
- ○ Masters Student
- ○ PhD Student
- ○ Post-Doctoral Fellows
- ○ Residents
- ○ Non-Trainee

Title

Prenatal Environment and Respiratory Disease: The Impact of Chronic Nicotine Exposure on Elastin and TGF-β Signaling

Background

Asthma is the most common chronic disease amongst children and chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide. Prenatal exposure to cigarette smoke increases the risk of childhood asthma and may predispose individuals to developing COPD. Pilot data demonstrates that fibroblasts chronically exposed to nicotine produce less elastin. Elastin is an extracellular matrix protein important in pathology of chronic lung disease. The transforming growth factor beta (TGF-β) signalling pathway, which may be altered by chronic nicotine exposure, regulates elastin production. In COPD, decreased elastin leads to increased lung compliance. In severe asthma, increased elastin contributes to airway remodelling.

Objective

We hypothesize that chronic nicotine exposure reduces TGF-β signalling by increasing negative regulators of TGF-β.

Methods

Human lung fibroblasts (HLF) from three female non-smokers were cultured in normal growth media with or without 10μM nicotine for five days. Cells were growth arrested for 24 hours, RNA was isolated, and cDNA made. Changes in abundance of 40 genes involved in TGF-β signalling were measured using qPCR. Relative abundance in the nicotine condition was calculated and normalized to three housekeeping genes. Genes with the greatest change in abundance are presented as mean fold change (Log2) ± SD, with significance defined as $p<0.05$ (n=3).

Results

Nicotine significantly decreased TGFB1 abundance (-0.492 ± 0.229, p=0.04). MAP2K2 (-0.363 ± 0.059, p=0.05), SERPINE1 (-0.521 ± 0.378, p=0.14), and TGFBR1 (-0.391 ± 0.234, p=0.08) were also downregulated, although not significantly. Nicotine slightly increased MAP2K6 abundance (0.433 ± 0.095, p=0.1). Negative regulators of TGF-β signalling, such as Smad7 (-0.055 ± 0.220), were not altered.

Conclusion

A decrease in autocrine TGF-β signaling following nicotine exposure may mediate the loss of elastin in HLF. Additionally, increased MAP2K6 abundance, which stabilizes elastin mRNA, may increase elastin mRNA in response to inflammatory stimuli. This could align with airway remodelling seen in asthma.

Authors

- For each author, please click "**[+] Add Item**" and provide the author's information

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