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

Kaylene Normand1,2, Shana Kahnamoui1,2,3, Christopher D. Pascoe1,2,3
1Children’s Hospital Research Institute of Manitoba, 2University of Manitoba 3Department of Physiology and Pathophysiology

Background
Prenatal exposure to cigarette smoke increases risk of respiratory disease
- Risk of asthma(2)
- Possible predisposition to COPD (Chronic obstructive pulmonary disease) development(2)

Elastin abundance is altered in chronic respiratory disease
- Elastin levels ↑ in severe asthma = disorganization(9)
- Elastin levels ↓ in COPD = increased lung compliance(3)

Chronic nicotine exposure decreases baseline elastin expression in lung fibroblasts

TGF-β signalling may be altered by chronic nicotine exposure
TGF-β (Transforming Growth Factor Beta) is a profibrotic cytokine secreted during inflammation and cell death. TGF-β promotes elastin mRNA stabilization in lung fibroblasts(5).

Aim
To determine if chronic nicotine exposure causes alterations to the TGF-β signalling pathway which modulate changes in elastin expression

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

Methods

Cell Culture
- Human lung fibroblasts cultured with 10μM nicotine

RNA Isolation
- cDNA Synthesis
- qPCR

Statistical Analysis
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
Two main genes were altered in expression in the nicotine-treated cells. TGFβ1 (Transforming growth factor beta 1) was significantly downregulated (-0.492 ± 0.229, p=0.04*), while MAP2K6 (Mitogen activated protein kinase kinase 6) was upregulated (0.433 ± 0.095, p=0.1).

TGFβ1 is the ligand that initiates signalling along the pathway
- ↓TGFβ1 = ↓Elastin
MAP2K6 propagates the signal initiated by TGFβ1
- ↑MAP2K6 = ↑Elastin

Decreased baseline TGF-β signalling in cells chronically exposed to nicotine

Conclusion
A decrease in autocrine TGF-β signalling following nicotine exposure may mediate the loss of elastin in human lung fibroblasts. 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.

References

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