Nicotine Promotes Fibroblast Senescence

The Role of Early Life Exposures on Chronic Lung Disease Development

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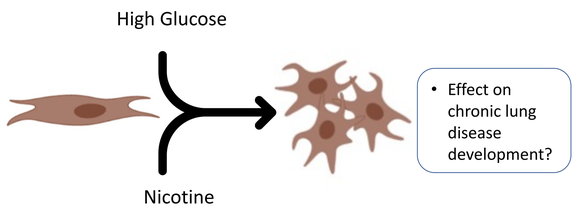
INTRODUCTION

- Asthma and chronic obstructive pulmonary disorder (COPD) are prevalent chronic lung diseases that are important for child health
- Asthmatic airways can become **inflamed** and remodelled, leading of fibrosis and inflammation in the airway
- Small airway **fibrosis** and elastin degradation are characteristic of COPD
- Maternal Diabetes and Smoking increases the risk for asthma later in life. Moreover, Asthma increases the risk of COPD later in life. Does hyperglycaemia and nicotine exposure in early life also increase COPD risk?
- Cellular senescence is the state of **irreversible growth arrest** characterized by **the proinflammatory** Senescence Associated Secretory Phenotype (SASP)
- SASP may play a role in the development of chronic lung disease
- **We hypothesize that exposure to hyperglycaemia and/ or nicotine will accelerate the transition to senescence in human lung fibroblast.**

AIM

To investigate the effects of hyperglycaemia and/or nicotine on human lung fibroblast phenotype



- Senescence cells may contribute to the development of chronic lung disease
- Understanding this relationship may help alleviate the burden of Chronic lung disease on child and adult health

ACKNOWLEDGEMENTS

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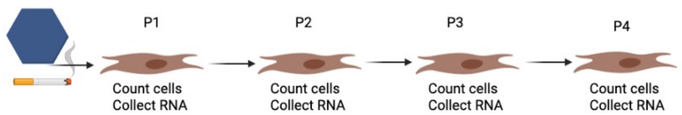
METHODS

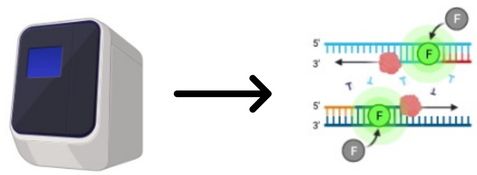
Cell Culture

- Cells were continuously cultured in Low Glucose (LG) (5.5mM), High Glucose (HG) (33mM), Low Glucose+ Nicotine (N) (10uM) and High Glucose + Nicotine (10uM)
- Cells were counted, doubling times calculated and RNA was collected at each passage while a portion of the culture was allowed to continue



Real Time-PCR

- RNA that was collected was converted to cDNA and qPCR analysis was performed
- Markers measured
  - Lamin B1-Senesence Marker. **Decreases with senescence**
  - P21-Senesence Marker. **Increases with senescence**
  - IL8-SASP Marker. **Increases with SASP**



RESULTS (N=1)

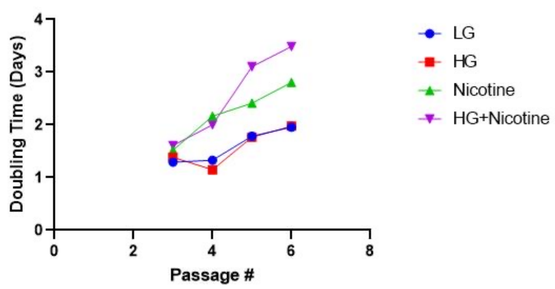


Figure 1. Fibroblast doubling times as a function of passage number

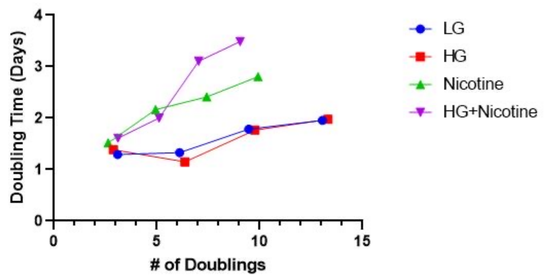


Figure 2. Fibroblast doubling times as a function of doublings

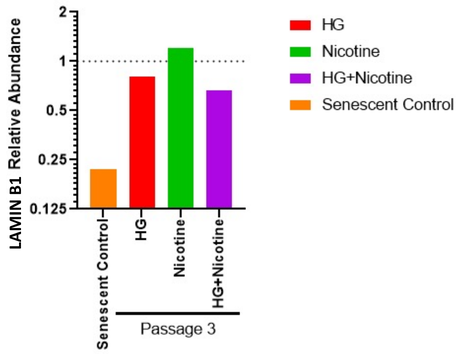


Figure 3. Relative abundance of LAMINB1 at passage 3 in each exposure. LG cells serve as senescent control

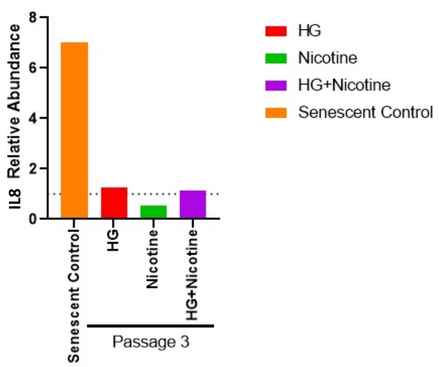


Figure 4. Relative Abundance of IL8 at passage 3 in each exposure. LG cells serve as senescent control

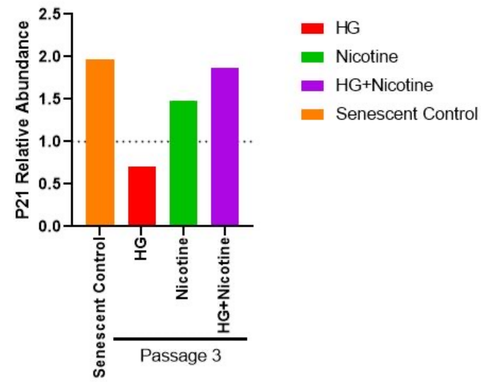


Figure 5. Relative abundance of P21 at passage 3 in each exposure. LG cells serve as senescent control

CONCLUSION

Co-exposure to hyperglycaemia and nicotine

- Largest P21 increase observed in co exposure
- Largest decrease in Lamin B1 observed in co exposure
- Decrease in IL8 observed
- Substantially decreased proliferation rate

FUTURE DIRECTION

- Increase sample size to further understand relationship
- Explore more markers of SASP
- Protein quantification