Smoking, Nicotine, ACE2, and SARS-CoV-2

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SARS-CoV
(SARS from 2003)
&
SARS-CoV-2
(COVID-19)

Spike Glycoprotein (S)

Attachment

Activation

ACE2

TMPRSS2

Airway Cell

Infection

Leung JM, Eur Resp J 2020
ACE/Ang II and ACE2/Ang (1-7) axes are balanced in younger, healthier, normotensive individuals (South and Brady, 2020).
Entry of SARS-CoV-2 causes shedding and downregulation of host ACE2 receptors (Verdecchia et al., 2020 and Samavati et al., 2020)

Vasoconstriction
Inflammation
Pro-fibrotic

Vasodilation
Anti-inflammation
Anti-oxidative stress
Anti-fibrotic
<table>
<thead>
<tr>
<th><strong>St. Paul’s Hospital Bronchoscopy Biobank</strong></th>
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</thead>
<tbody>
<tr>
<td>Over 700 bronchoscopies are performed each year at SPH</td>
</tr>
<tr>
<td>~200 patients have allowed us to collect additional research samples during their clinical procedure</td>
</tr>
<tr>
<td>~100 patients have undergone research bronchoscopies</td>
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<td>Airway epithelial cells, bronchoalveolar lavage, oral washes, and blood have been collected</td>
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</tbody>
</table>
ACE-2 Elevation in Smokers

Zhang H, AJRCCM 2020

Cai G, AJRCCM 2020

Jacobs M, Eur Resp J 2020
ACE2: Dose Response Relationship
Role of Secretory Cells

Human Trachea

ACE2+: Coronavirus Receptor

- Basal cells
- Basal-proliferating
- Ciliated cells
- Goblet/Club cells
- Ionocytes
- KRT8+ intermediate
- Neuroendocrine cells
- SMG-basal
- SMG-secretory
Non-smokers vs. smokers: ACE2 co-expression

![Bar chart showing the percentage of cells expressing ACE2 in non-smokers and smokers across different cell types.](chart.png)

- ACE2⁺
- MUC5AC⁺/ACE2⁺
- MUC5AC⁻/ACE2⁺
- Goblet/Club cluster/ACE2⁺
- Other clusters/ACE2⁺

Legend:
- Non-smokers
- Smokers

Smith JC, Dev Cell 2020
Summary

• Upregulation of ACE2 in the airways and lungs of smokers

• This upregulation may be mediated by nicotinic receptors and the expansion of secretory cells in the airway

• The clinical implications of these findings – whether protective or harmful – as they relate to SARS-CoV-2 infection, however, have yet to be determined
Thank You

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