The Lung Microbiome in Asthma and COPD

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What do we know about the lung microbiome?

• Very little
• Could be exceedingly important
• Vast majority of bacteria are non-cultured
• PCR to identify species is limited to detect anticipated bacteria
• 165 ribosomal RNA chips better (validation needed)
  ~8,500 taxa


What do we know about the lung microbiome?

• Structural complexity of microbial communities, rather than simply the presence of individual species, can be important in determining states of health vs. disease.
• Difference in the structure or composition of a microbial community affects function exerted by the community.

Our microbiome

- Our immunologic fate is intertwined with the microorganisms we evolved with
- Outnumbered 100 trillion bacterial cells in our bodies to 10 trillion of our own cells
- Commensal organisms promote absorption of nutrients, aid in vitamin metabolism, and protect mucosal surface from pathogenic organisms
  - Modulate immune function and maintenance of mucosal homeostasis


Germ free mice

- Allergen challenge produces more AHR, TH2 cytokine expression, and airway inflammation than mice under pathogen free conditions
  - Alterations in dendritic cells (antigen presenting cells) and macrophages occur
  - Dendritic cells extend outside epithelium into lumen to sample bacteria without disruption of the integrity of epithelial barrier


Upper respiratory tract (URT) vs. lower (LRT) in normal healthy individuals

- Bacterial families similar

Asthma

Is Asthma an infectious Disease?

Bacterial burden – endobroncial brush

16S rRNA PCR Product (ng µL⁻¹)

Healthy Asthma

Variability and community diversity relates to BHR

NMDS demonstrates similarity in community composition. No inherent units.

Location Distribution

Asthma, COPD, Normal


Asthma control and disordered microbial communities in the lower airways of patients with chronic asthma

Leung, D. Preliminary data

A = asthma. Similar = expansion > 10% of nl. Dissimilar = expansion of other bacteria

PCR +: Asthma (n=55) and Controls (n=20)

Mycoplasma

Chlamydia

Change in FEV\(_1\) after tx. depends on PCR status

![Chart showing change in FEV\(_1\) after tx. depending on PCR status.](chart.png)


Airway AA1 (Mast Cell) in PCR (+) and (-) subjects

![Chart showing airway AA1 (Mast Cell) in PCR (+) and (-) subjects.](chart.png)


COPD

**Taxonomic Classification in BAL Phylum**

<table>
<thead>
<tr>
<th>Phylum</th>
<th>Healthy Smokers</th>
<th>Smokers with COPD</th>
<th>Non-Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteria</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Actinobacteria</td>
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<td></td>
<td></td>
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<tr>
<td>Proteobacteria</td>
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</table>


**Taxonomic Classification in BAL Genus**

<table>
<thead>
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<th>Genus</th>
<th>Healthy Smokers</th>
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<th>Non-Smokers</th>
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<tbody>
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</table>


**BAL Abundance Table. Top 10 of 51**

<table>
<thead>
<tr>
<th>Rank</th>
<th>Name</th>
<th>Total # Sequences</th>
<th># Subjects Occurred/Total</th>
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<tr>
<td>1</td>
<td>Pseudomonas</td>
<td>78319</td>
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<tr>
<td>2</td>
<td>Streptococcus</td>
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<tr>
<td>3</td>
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<td>19916</td>
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<tr>
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<td>Fusobacterium</td>
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<tr>
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<td>Veillonella</td>
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<td>Porphyromonas</td>
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<tr>
<td>7</td>
<td>Leptotrichia</td>
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<tr>
<td>10</td>
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</tbody>
</table>

Bacterial Community Membership


Bacterial Community in Lung Airways


COPD: Azithromycin for prevention of exacerbations

Albert R et al. NEJM 2011;365:689-698
**Conclusion**

- A totally new area of important research to determine the lung microbiome and how alterations affect, propagate, and/or induce asthma and COPD
- New therapies to return microbiome to normal so as to improve and/or eliminate disease