HIV COPD: could differential host recognition of the lung microbiome be contributing to pulmonary disease?

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No Differences Exist in the Lung Microbiome between Healthy HIV+ and HIV- Individuals

Cribbs et al. Microbiome 2016
Adaptive Immunity is Altered in Advanced COPD and HIV Infection

Hogg et al. NEJM 2004
B-Cell Depleted Mice (μMT) Do Not Develop COPD

Opsonization of IgG-bound Bacteria Leads to Inflammatory Response

Could immunoglobulin binding of the lung bacterial community be contributing to lung disease in HIV?
Magnetic-Activated Cell Sorting

Immunoglobulin-bound Bacterium
Magnetic-Activated Cell Sorting

Immunoglobulin-bound Bacterium

Syto BC

IgG PE
Magnetic-Activated Cell Sorting

Immunoglobulin-bound Bacterium

Anti-PE Micro Bead
Magnetic-Activated Cell Sorting

Sample that passes through columns is IgG-negative.

Bacteria remaining in columns is IgG-positive and plunged into separate conicals.
Magnetic-Activated Cell Sorting Previously Used to Study Immunoglobulin Binding in Gut Microbiome

Can MACS be used to separate IgG-bound bacteria in the lungs?
MACS can sort immunoglobulin-bound bacteria from unbound in BAL fluid.
<table>
<thead>
<tr>
<th></th>
<th>HIV+</th>
<th>HIV-</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of Participants, n</strong></td>
<td>43</td>
<td>22</td>
</tr>
<tr>
<td><strong>Age, mean (Range)</strong></td>
<td>51.9 (29-67)</td>
<td>50.7 (37-64)</td>
</tr>
<tr>
<td><strong>Male, n (%)</strong></td>
<td>32 (73)</td>
<td>15 (68)</td>
</tr>
<tr>
<td><strong>Race, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>13 (30)</td>
<td>12 (54)</td>
</tr>
<tr>
<td>Black</td>
<td>28 (65)</td>
<td>3 (32)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (5)</td>
<td>3 (14)</td>
</tr>
<tr>
<td><strong>COPD, n (%)</strong></td>
<td>32 (74)</td>
<td>8 (36)</td>
</tr>
<tr>
<td><strong>Ever Smoker, Yes (%)</strong></td>
<td>31 (72)</td>
<td>12 (55)</td>
</tr>
<tr>
<td><strong>Pack-years, median (Range)</strong></td>
<td>14 (0-48)</td>
<td>6.2 (0-54)</td>
</tr>
<tr>
<td><strong>CD4 Count, median (Range)</strong></td>
<td>731 (43-1505)</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Receiving ART, n (%)</strong></td>
<td>30 (70)</td>
<td>N/A</td>
</tr>
</tbody>
</table>
IgG-bound bacteria are more abundant in the lungs of HIV-infected individuals

Taxonomic Differences Seen Between HIV+ and HIV- Individuals Only in IgG+ Fraction


HIV Status

Negative
Positive

p<0.002

p=0.25
In HIV+ individuals, *Pseudomonas* is the most abundant IgG-bound bacteria.
Among HIV+ Individuals, Pulmonary Dysfunction is not Associated with Increased IgG-bound Bacteria in the Lungs

Among HIV+ Individuals, the IgG-bound Bacterial Community Stratifies by DLCO

Diminished

Normal

p=0.01

Conclusions

• MACS is a novel method for sorting IgG-bound from unbound bacteria in the lungs.

• HIV+ individuals have more IgG-bound bacteria in the lungs, and these bound bacterial communities are distinct from those in HIV- individuals.

• Among HIV+ individuals, changes in the IgG-bound bacterial community stratify by host DLCO.

• Adaptive immunity in HIV COPD may be a therapeutic target and further study is warranted.
Thank You!

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- Georgios Kitsios, MD

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