Disclosures

• Founder and President, BiomeSense Inc.
• Chief Scientific Advisor, 4inno.
• Scientific Advisory Board Biome Makers, Inc.
• Scientific Advisory Board ProDerm IQ
• Scientific Advisory Board DayTwo Inc.
• Scientific Advisory Board Growcentia Inc.
• Scientific Advisory Board Holobiome Inc.
• Scientific Advisory Board for Valent BioSciences.
Once the diversity of the microbial world is catalogued, it will make astronomy look like a pitiful science.

- Julian Davies, Professor Emeritus, Microbiology and Immunology, UBC
Airborne and fomite transmission

Inhalation of droplet-associated or desiccated microorganisms

**Bacteria:**
- Bacillus anthracis
- Legionella pneumophila
- Mycobacterium tuberculosis

**Fungi:**
- Cryptococcus neoformans
- Histoplasma capsulatum
- Aspergillus fumigatus

**Viruses:**
- Influenza virus
- Rhinovirus
- Acanthamoeba

Fomite-associated transmission to skin or mucous membranes

**Bacteria:**
- Clostridium difficile
- Staphylococcus aureus
- Pseudomonas putida
- Enterococcus faecalis

**Viruses:**
- Variola virus
- Rubella virus
- Norovirus
- Adenovirus
- Coxsackie virus
- Influenza virus
- Coronavirus

**Fungi:**
- Trichophyton mentagrophytes
- Trichophyton rubrum

Transmission to built environment through direct contact

Respiratory transmission to built environment

Gilbert and Stephens, Nature Reviews Microbiology, 2019
Airborne and surface microbial metabolic products influence human health

Gilbert and Stephens, Nature Reviews Microbiology, 2019
Genotypes demonstrate increased antibiotic resistance over time

Staphylococcus and Anaerococcus had a consistently greater number of antibiotic resistance genes after 60 days of hospital environmental exposure.

Genomes show a greater non-synonymous to synonymous mutation ratio suggesting extensive selective pressure.

Lax et al., Sci. Trans. Med. 2017
Wetting causes growth – and the abundance of microbes correlates with the abundance of virus like particles.

Lax, Cardona et al Nature Comms. 2019
Bacterial and fungal diversity is well correlated. Bacillus and Pseudomonas growth is anticorrelated. Eurotium grows well without water, and Penicillium does better with water.

Lax, Cardona et al Nature Comms. 2019
Antibacterial alkaloids Nigragillin and Fumigaclavine C correlated with Ascomycota and negatively correlated with the abundance of Bacillus and Pseudomonas. Nigragillin was greatest on MDF and no bacterial growth was detected.
Azoxystrobin (19) was positively correlated with *Bacillus* and negatively correlated with *Pseudomonas*.

Scopoletin (12) was positively correlated with *Pseudomonas* and negatively correlated with *Bacillus*.
Colonization and Succession of Hospital-Associated Microbiota
365 consecutive days: 2 months pre opening, and 10 months post opening

| Patient Skin | | Patient Room | | General |
|--------------|--------------|--------------|--------------|
| Nose         | Nose         | Hand         | Hand         |
| Hand         | Hand         | Axilla       | Shoe         |
| Axilla       | Uniform      | Floor        | Cell Phone   |
| Floor        | Faucet Handle| Bedrail      | Pager        |
| Bedrail      | Glove        | Faucet Handle| Countertop   |
| Faucet Handle| Glove        | Air Filter   | Computer Mouse|
| Glove        | Chair        | Cold Tap Water| Phone       |
| Air Filter   | Chair        | Hot Tap Water|              |

Lax et al., Sci Trans Med 2017
Extremely low biomass prior to occupation – human microbes post colonization

Lax et al., Sci Trans Med 2017
Relative humidity positively correlates with microbial sharing between staff and patients.
Staff were consistently a greater source of bacteria to patients

Lax et al., Sci. Trans. Med. 2017
Mapping microbial highways

Bayesian dynamic maps of microbial species distribution potential between family members and the home surfaces

Lax et al., 2014 Science
Mapping microbial highways

Adding dogs to the home significantly increases microbial transfer between people and surfaces.

Lax et al., 2014 Science
Dogs are Awesome!

My Dog
Captain Beau
Diggely

#dogsinspace
Those that physically interact share more microbial similarity

Lax et al Science 2014
Microbial sharing between college students in a dorm is mediated by the hand-transmission.
Microbial forensics

- Bathroom Door Knob
- Kitchen Counter
- Bedroom Floor
- Kitchen Floor
- Front Door Knob
- Kitchen Light Switch

Legend:
- Red: Person 1
- Orange: Person 2
- Yellow: Person 3
- Light Blue: Dog 1
- Dark Blue: Dog 2
- Blue: Dog 3
- Grey: Unknown
- Person 1 Absent

Time (x-axis) vs. Percentage (y-axis)
Tracking microbial sources in shared spaces:
Air Force Cadets

Sharma et al., Microbiome, 2019
Managing the microbiome indoors

- Increased ventilation
- Controlled exposure to farming environment
- Intentional increase in indoor microbial diversity or abundance of specific taxa
- Using sensors to detect the indoor microbiome
- Change building materials, design and operation to reduce transmission of disease
- Household pets increase microbial exposure
- Reduce surface moisture to prevent unwanted microbial growth

Gilbert and Stephens, Nature Reviews Microbiology, 2019
Amish live on family run farms and have no asthma. Hutterites live on industrial farms and have elevated asthma.
Peripheral-blood leukocytes from Amish children had increased proportions of neutrophils, decreased eosinophils compared with Hutterite kids.

Neutrophils in the Hutterite children were older than in Amish children

Stein et al 2016, NEJM.
Mice which inhaled Amish bedroom dust were not allergic to a dietary antigen

Stein et al 2016, NEJM.
Associating mice with Amish poop protects them against eosinophilia associated with OVA
Two metabolites were significantly elevated in the serum and stool of mice following association with Amish stool. I3AA, indole 3-acetic acid appears to promote an increase in homeostatic eosinophils over more proinflammatory cells.
## Airway microbiota still differentiate asthma phenotypes

### Associations between fungal and bacterial microbiota of airways and asthma endotypes

<table>
<thead>
<tr>
<th>Clinical Variables</th>
<th>Asthmatic subjects (n=39)</th>
<th>Healthy Controls (n=19)</th>
<th>Airway Samples</th>
<th>Microbiome Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Sex, Race, Inhaled &amp; Oral corticosteroid (CS) use, Sinusitis, Atopy status, Serum IgE, FEV1, FeNO, Blood eosinophils, BAL cells</td>
<td><img src="image" alt="Diagram showing T2 status and atopy status" /></td>
<td><img src="image" alt="Diagram showing atopy status" /></td>
<td>Bronchoalveolar lavage (BAL) Endobronchial brushes (EB)</td>
<td>Bacterial (16S) Fungal (ITS)</td>
</tr>
</tbody>
</table>

### Findings

1. **Lower fungal diversity in EB in T2-High asthma**
   - Inverse Simpson Index

2. **Fungal microbiome is different between different asthma endotypes in airways**
   - **BAL**
     - T2-High: *Fusarium*, *Cladosporium*, *Aspergillus*
     - Asthmatics with atopy: *Cladosporium*, *Fusarium*
   - **EB**
     - T2-High: *Trichoderma*
     - T2-Low: *Penicillium*

3. **Generalized Linear Models demonstrate association between fungal microbiome and clinical variables**
   - **FEV1**: *Alternaria*, *Aspergillus*, *Penicillium*
   - **Inhaled CS**: *Alternaria*, *Cladosporium*
   - **Oral CS**: *Cladosporium*
   - **BAL cells**: *Cladosporium*, *Fusarium*, *Trichoderma*

4. **Clear inter-relationships between bacterial and fungal microbiome in airways**

Sharma et al JACI 2019
From two of the world’s top scientists, Dirt Is Good is a Q&A guide to everything you need to know about pregnancy, kids & germs.

At all good bookstores and online retailers now.