The Built Environment and it’s Relationship with Childhood Allergic Asthma

Susan V. Lynch, Ph.D.

Associate Professor of Medicine
Director Colitis and Crohn’s Disease Microbiome Research Core
Division of Gastroenterology,
Department of Medicine,
University of California San Francisco.

Childhood Allergic Asthma is Prevalent in Western Nations
Environmental Microbial Exposures are Related to Atopy and Asthma

Ege et al. NEJM 2011
Risk Factors for Childhood Atopy Also Impact the Microbiome

- Factors associated with childhood atopy development:
  - Lack of maternal exposure to livestock or furred pets during pregnancy
  - Formula feeding
  - Caesarian section delivery
  - Maternal antibiotic use during pregnancy
  - Early life antibiotic exposure

Early life fecal enrichment of *Clostridium difficile* or *Escherichia coli* is associated with childhood allergy

Penders et al. Journal of the British Society for Allergy and Clinical Immunology 2006;36:1602-8.

Kaliomaki et al. JACI. 2001;107:129-34.

Rauch et al, unpublished data
What is the Source of Early Life Human Microbial Diversity?

Western Nations

- 86.9% (68.7% in residence)
- 7.6%
- 5.5%

Klepeis et al. 2001 J Expo Anal Env Epid 11:231-52
Hypothesized Causal Pathway of Childhood Allergic Asthma

Hypothesis:
Early life house dust microbial exposures are related to atopy and/or allergic wheeze outcomes in childhood
URECA Study Population

- Prospective cohort study of full-term infants born in low-income, inner-city urban US neighborhoods
- Total of 609 families enrolled 2/05 – 3/07
- Baltimore, Boston, New York City, St. Louis
- House dust collected during the first year of infants life (3 months of age), and atopy defined at age three
Atopic Wheezers Experience Distinct Bacterial Exposures in Early Life

**Protective Taxa**

**Neither vs Atopic:**
*Bifidobacteriaceae, Prevotellaceae, Lachnospiraceae, Ruminococcaceae, Veillonellaceae, Dethiosulfovibrionaceae*

**Neither vs Both:**
*Acidobacteriaceae, Bacteroidaceae, Blattabacteriaceae, Porphyromonadaceae, Prevotellaceae, Rikenellaceae, Catabacteriaceae, Enterococcaceae, Lachnospiraceae, Ruminococcaceae, Veillonellaceae, Gemmatimonadaceae, Planctomycetaceae, Dethiosulfovibrionaceae, Erysipelotrichaceae*

Early-life Dog Exposure is Protective Childhood Against Allergic Disease Development

- Exposure to dogs, and to a lesser extent cats, in early life is protective against childhood allergic disease development


Can Distinct House Dust Exposures Influence Airway Immunity via the Gut Microbiome?

House Dust Exposure Alters Airway Response to Allergen Challenge

Wayne County Health, Environment, Allergy & Asthma Longitudinal Study (WHEALS)

• Birth cohort - sample collection commenced in 2003
• Socio-economic and racially diverse (50% minority)

Do compositionally distinct microbial states exist in the early-life gut microbiota and are they related to allergic sensitization risk?

• **Infants** (median age 201 days; n=168)
• Population-based cohort, cross-sectional study
• Gut microbiome composition examined using 16S V4 and ITS2 rRNA regions on Illumina MiSeq platform
Neonates stratify into three distinct, non-age-related groups.

9.2% of the variation explained (p<0.001)

NGM1 (Bifidobacteriaceae)
NGM2 (Enterobacteriaceae)
NGM3 (Bifido/Entero)

Fujimura, E. et al. In revision
NGMs are Associated with a Significantly Different Relative Risk of PM-Atopy and Asthma

<table>
<thead>
<tr>
<th></th>
<th>IGM2 vs IGM1</th>
<th>p-value</th>
<th>NGM2 vs NGM1</th>
<th>p-value</th>
<th>NGM3 vs NGM1</th>
<th>p-value</th>
<th>NGM3 vs NGM2</th>
<th>p-value</th>
<th>Overall p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atopy (PM)</td>
<td>1.02 (0.59-1.75)</td>
<td>0.94</td>
<td>1.43 (0.73-2.81)</td>
<td>p=0.30</td>
<td>2.94 (1.42-6.09)</td>
<td>p=0.004</td>
<td>2.06 (1.01-4.19)</td>
<td>p=0.048</td>
<td></td>
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<tr>
<td>Parental report of doctor diagnosed asthma$^{1,2}$</td>
<td>0.51 (0.22, 1.17)</td>
<td>0.11</td>
<td>0.87 (0.31-2.50)</td>
<td>p=0.81</td>
<td>2.95 (1.09-7.98)</td>
<td>p=0.033</td>
<td>3.36 (1.10-10.3)</td>
<td>p=0.034</td>
<td>0.13</td>
</tr>
</tbody>
</table>

Fujimura, E. et al. In revision
Inter-Kingdom Dysbiosis Characterizes NGM3

- NGM3 lacks key bacterial species e.g. *Akkermansia muciniphilia*, *Faecalibacterium prausnitzii*, *Lactobacillus ruminus*

Fujimura, E. *et al.* In revision
Hypothesized Causal Pathway of Childhood Allergic Asthma

- N=120 paired house dust/stool samples
- 16S rRNA and ITS2 profiling
- Relationships between built environment microbiota and measured variables, particularly NGM designation
Bacterial House Dust Communities are Related to Occupancy, Ethnicity and Smoking

<table>
<thead>
<tr>
<th></th>
<th>$R^2$</th>
<th>p-value</th>
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<tbody>
<tr>
<td><strong>Environment</strong></td>
<td></td>
<td></td>
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<tr>
<td>Detectible level of can f1 at 1-mo visit</td>
<td>0.013</td>
<td>0.028</td>
</tr>
<tr>
<td>Smoking exposure at 1-mo visit</td>
<td>0.010</td>
<td>0.044</td>
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<tr>
<td>Type of cooking stove (gas or electric)</td>
<td>0.010</td>
<td>0.038</td>
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<tr>
<td><strong>Demographics</strong></td>
<td></td>
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<tr>
<td>Urban</td>
<td>0.012</td>
<td>0.003</td>
</tr>
<tr>
<td>Year home was built</td>
<td>0.018</td>
<td>0.003</td>
</tr>
<tr>
<td>Mom ethnicity</td>
<td>0.012</td>
<td>0.002</td>
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House Dust Fungal Communities Relate to Microbiological and Allergic Features of Occupants

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<tbody>
<tr>
<td><strong>Demographic</strong></td>
<td></td>
<td></td>
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<tr>
<td>Child's Race</td>
<td>0.0222</td>
<td>0.0020</td>
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<tr>
<td><strong>Environmental</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detection of Can f1 at 1 Month Visit</td>
<td>0.0206</td>
<td>0.0100</td>
</tr>
<tr>
<td>Presence of Indoor Dog at 1 Month Visit</td>
<td>0.0172</td>
<td>0.0260</td>
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Moving Forward

• Improved understanding of specific microbial species and encoded functions that transfer from the built environment to the human host and impact health status

• Determine whether the relationships between the microbial built environment and host differs with age, gender, health status, anatomical site etc.
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