Microbiology in the Built Environment

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Pediatrics

UC San Diego

SCRIPPS INSTITUTION OF OCEANOGRAPHY

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.
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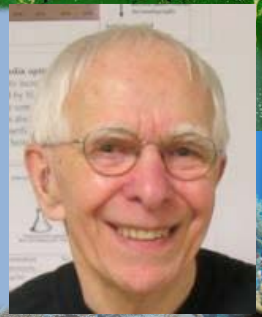
Once the diversity of the microbial world is catalogued, it will make astronomy look like a pitiful science.

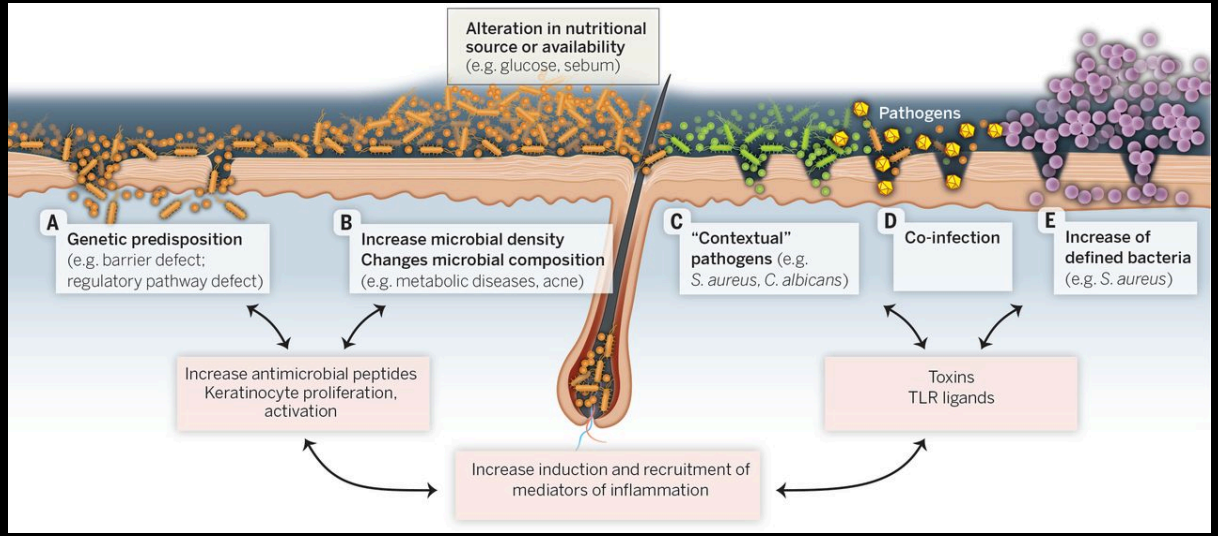
- Julian Davies, Professor Emeritus, Microbiology and Immunology, UBC

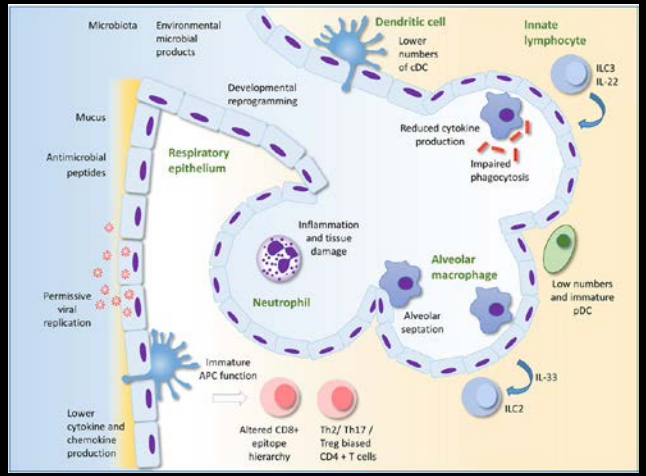




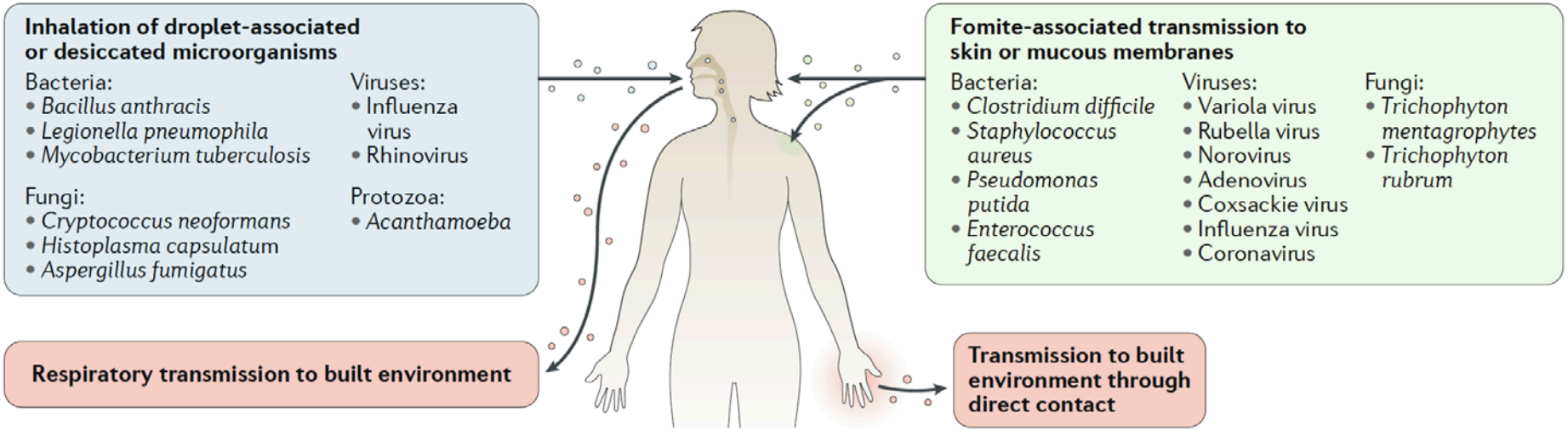



NATIONAL
PARK
SERVICE


Alteration in nutritional source or availability
(e.g. glucose, sebum)
Pathogens
A
Genetic predisposition
(e.g. barrier defect; regulatory pathway defect)
B
Increase microbial density
Changes microbial composition
(e.g. metabolic diseases, acne)
C
"Contextual" pathogens (e.g. S. aureus, C. albicans)
D
Co-infection
E
Increase of defined bacteria
(e.g. S. aureus)
Increase antimicrobial peptides
Keratinocyte proliferation, activation
Toxins
TLR ligands
Increase induction and recruitment of mediators of inflammation

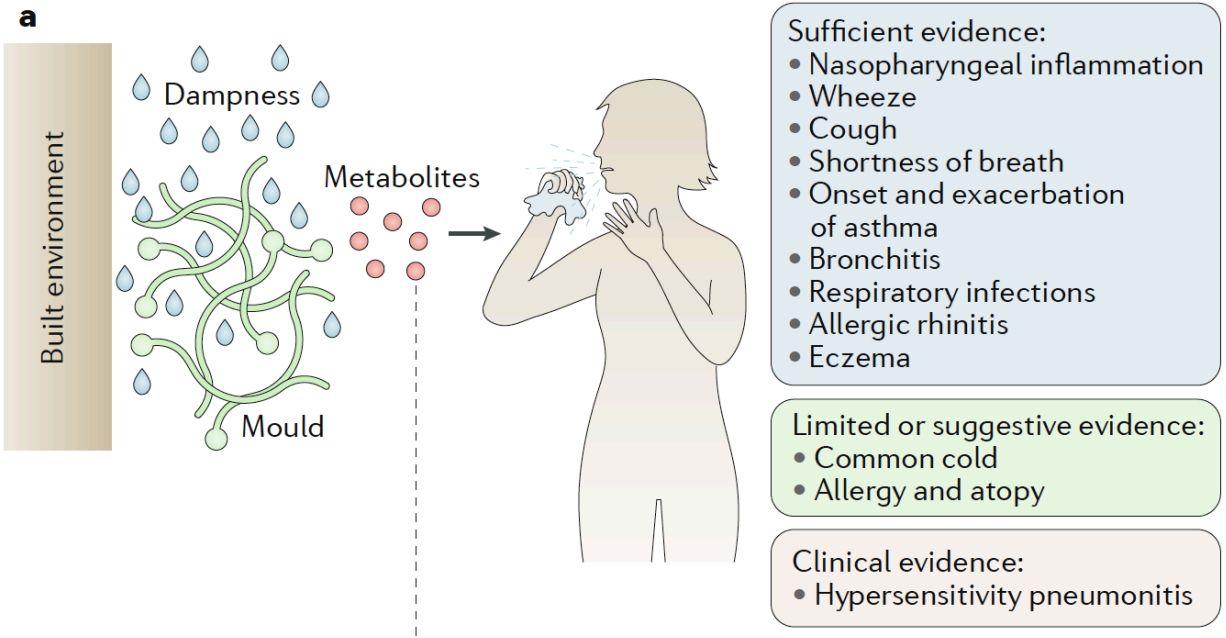

Microbiota
Environmental microbial products
Dendritic cell
Lower numbers of cDC
Innate lymphocyte
ILC3
IL-22
Developmental reprogramming
Mucus
Antimicrobial peptides
Respiratory epithelium
Reduced cytokine production
Impaired phagocytosis
Inflammation and tissue damage
Alveolar macrophage
Neutrophil
Low numbers and immature pDC
Permissive viral replication
Alveolar septation
Immature APC function
IL-33
ILC2
Lower cytokine and chemokine production
Altered CD8+ epitope hierarchy
Th2/ Th17 / Treg biased CD4 + T cells

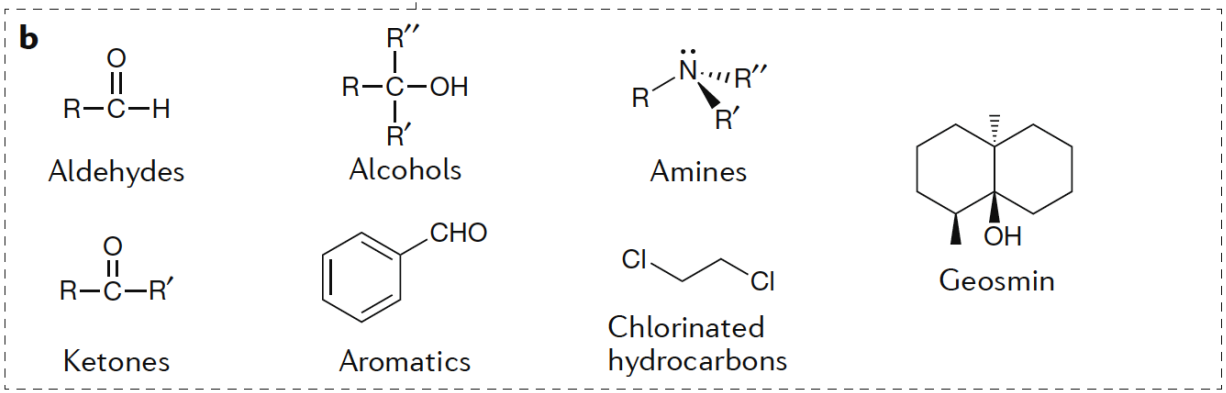
Airborne and fomite transmission



Gilbert and Stephens, Nature Reviews Microbiology, 2019

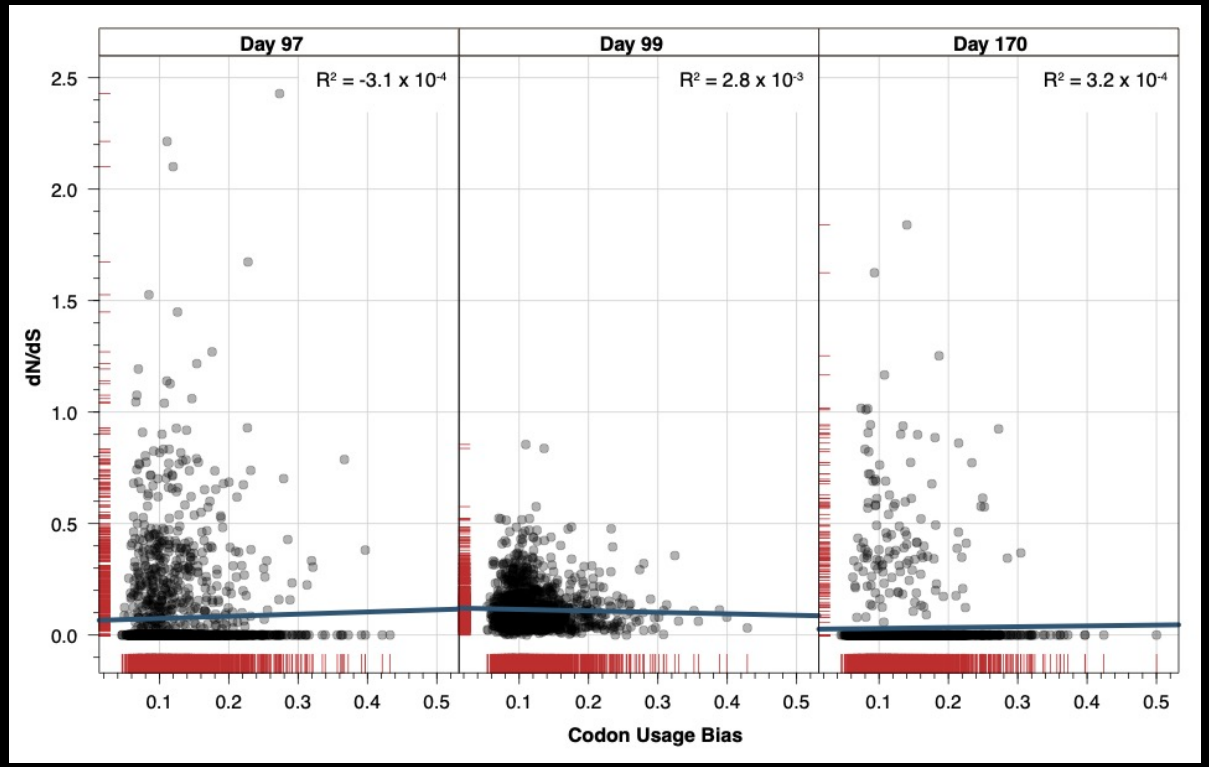
Airborne and surface microbial metabolic products influence human health





Gilbert and Stephens, Nature Reviews Microbiology, 2019

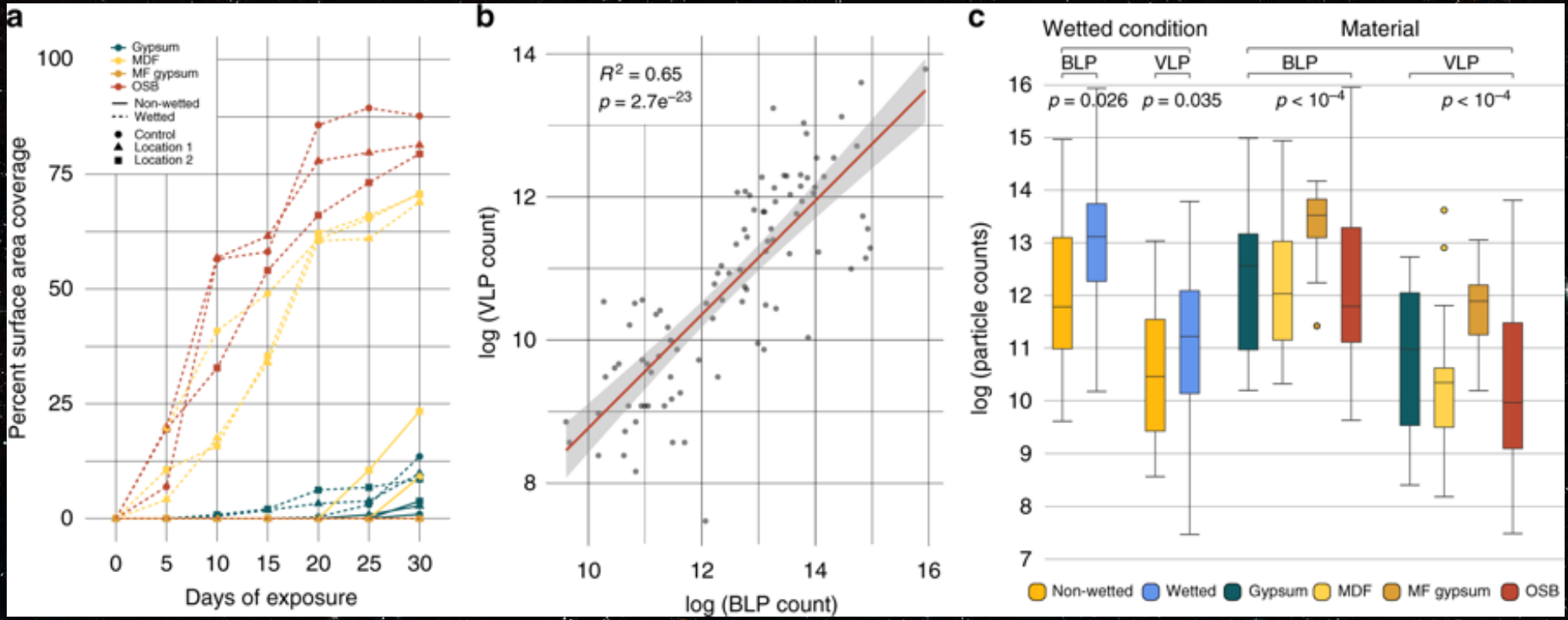
Genotypes demonstrate increased antibiotic resistance over time



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

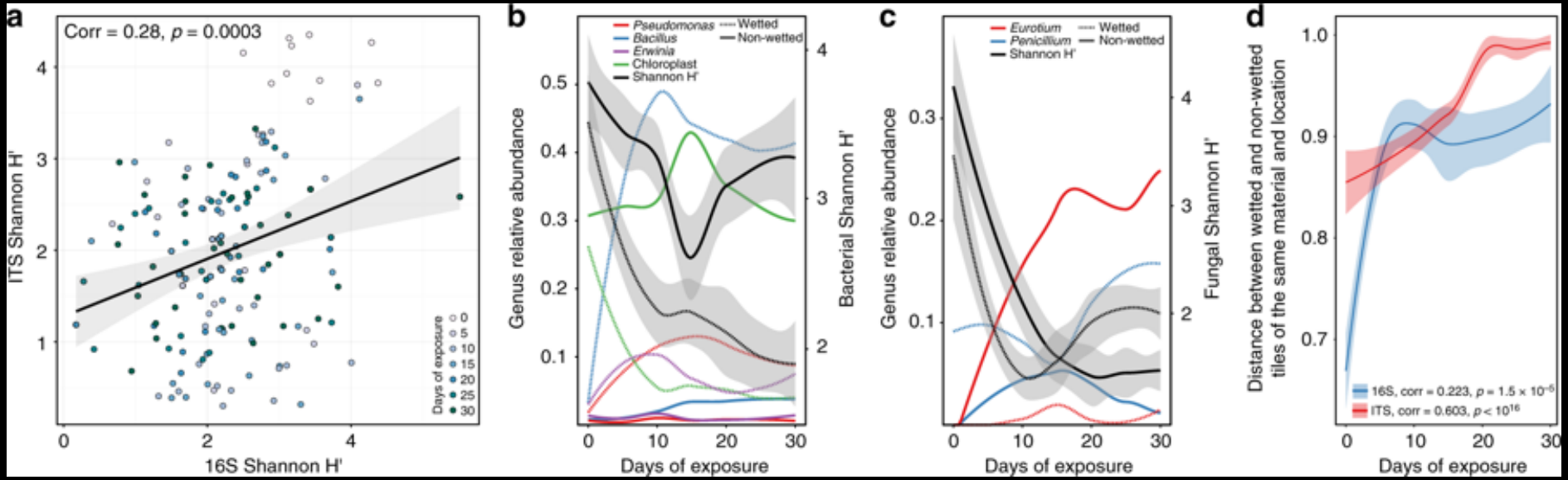
Genomes show a greater non-synonymous to synonymous mutation ratio suggesting extensive selective pressure

Lax et al., Sci. Trans. Med. 2017



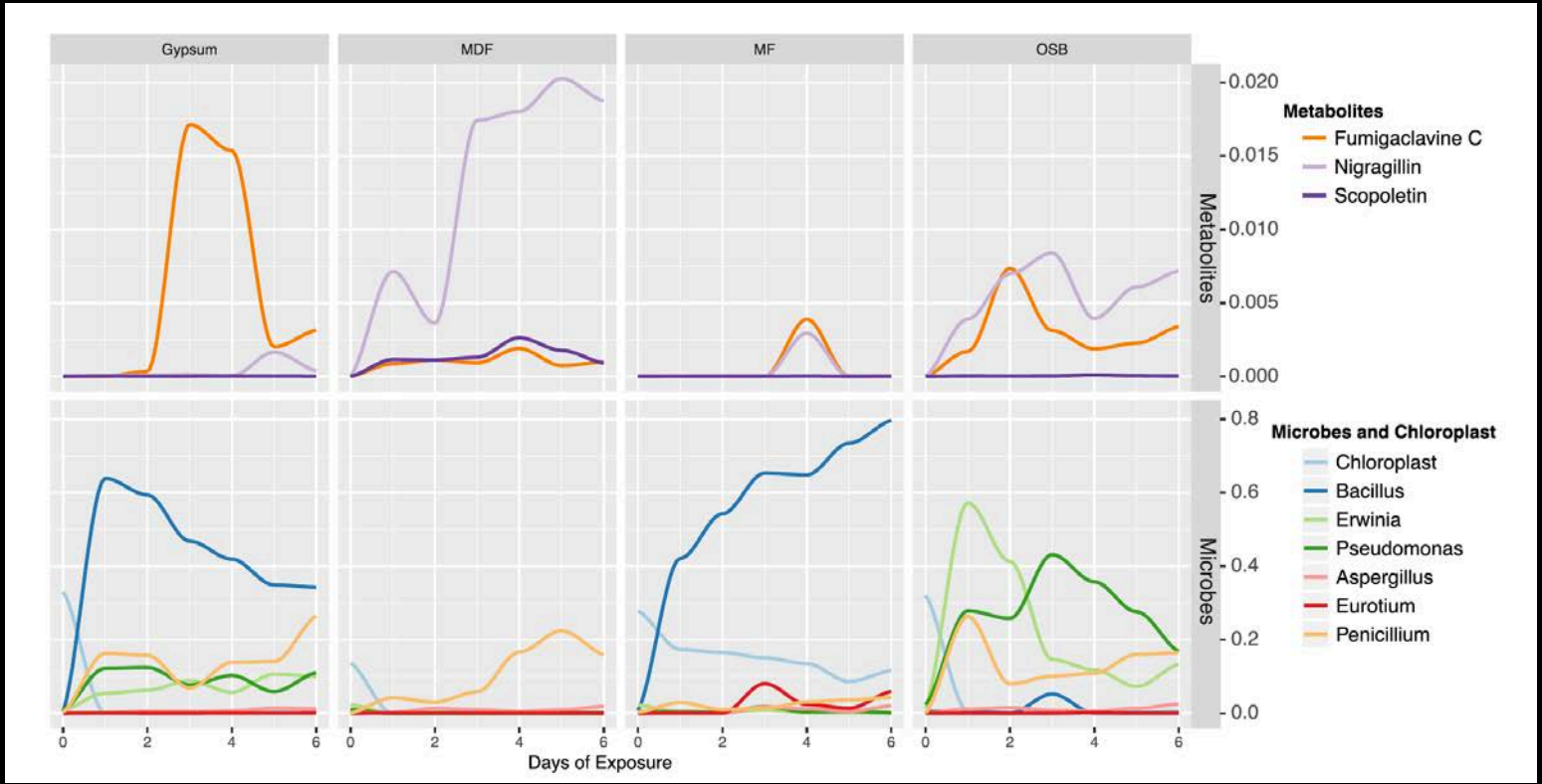
Wetting causes growth – and the abundance of microbes correlates with the abundance of virus like particles.

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.

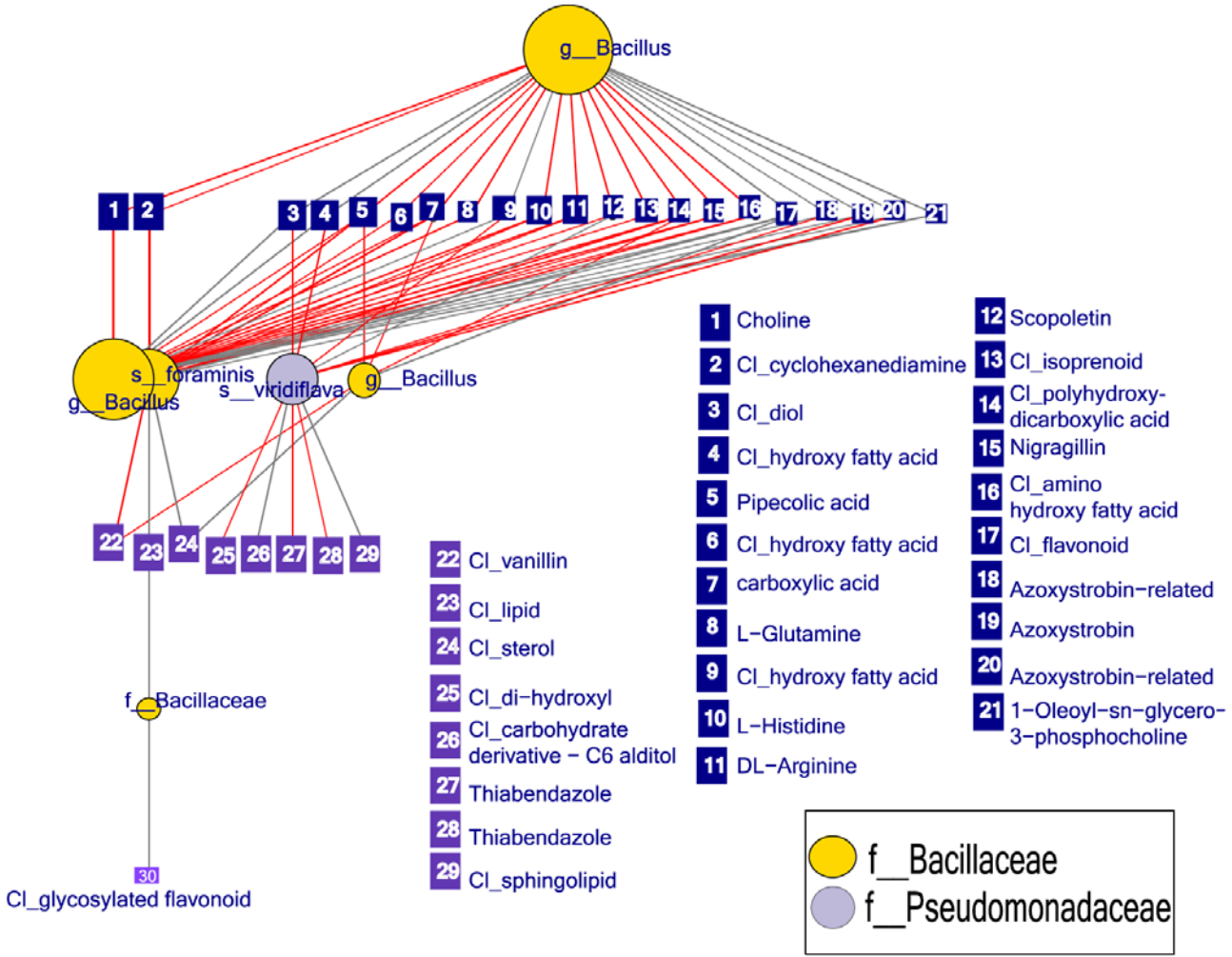
Lax, Cardona et al Nature Comms. 2019



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). wa positively correlated with *Bacillus* and negatively correlated with *Pseudomonas.*

Scopoletin (12) was positively correlated with *Pseudomonas* ar negatively correlated with *Bacillus*



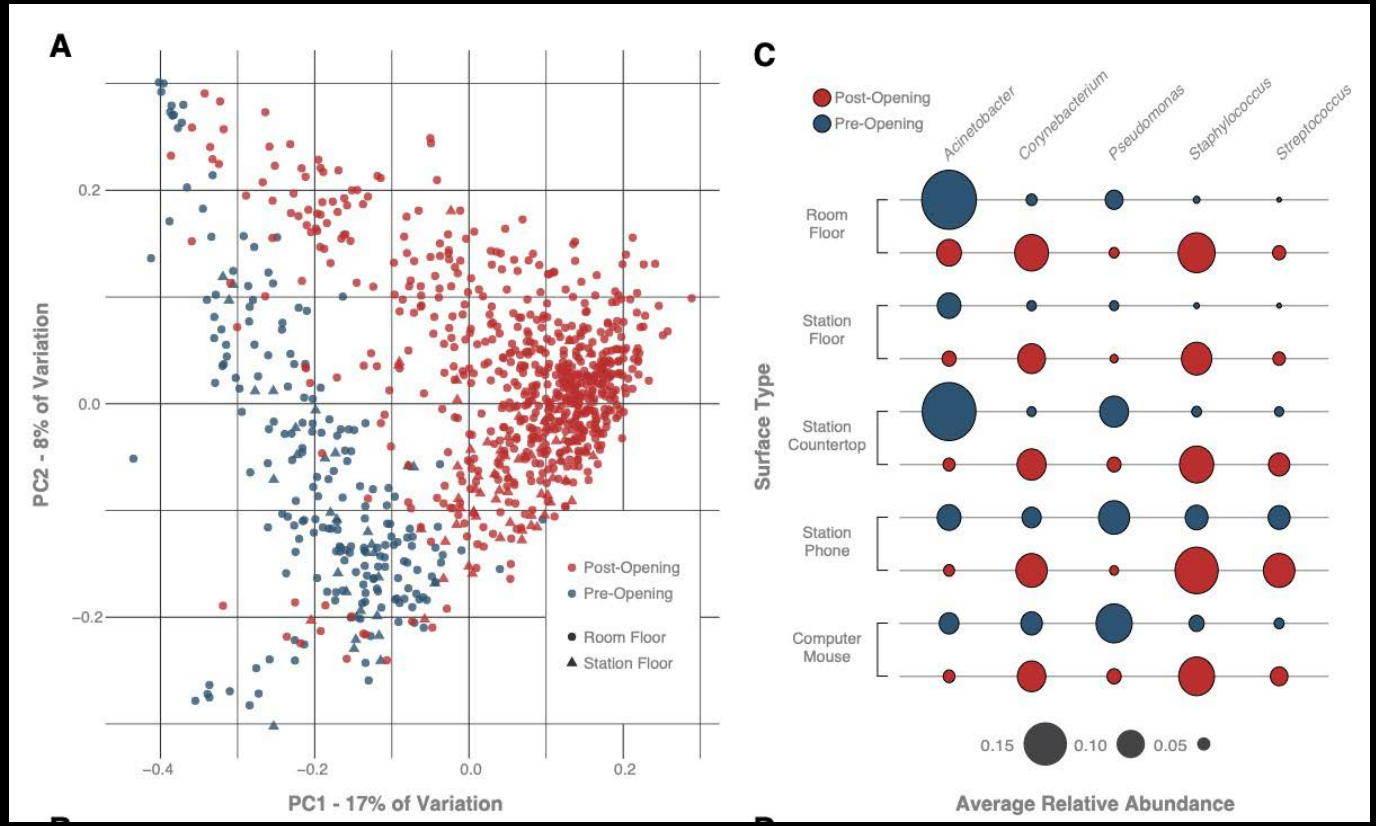
Colonization and Succession of Hospital-Associated Microbiota

365 consecutive days: 2 months pre opening, and 10 months post opening

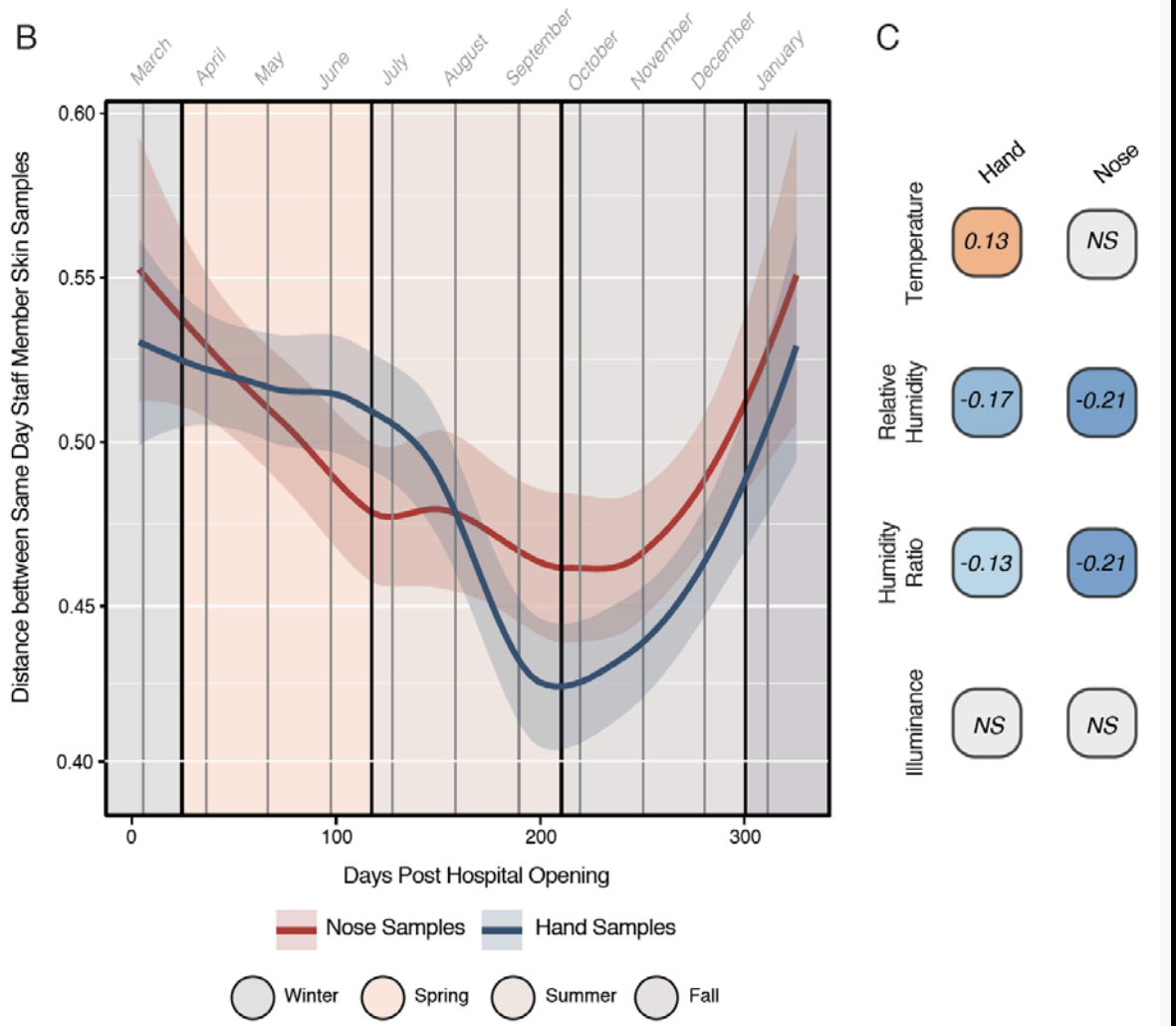
Patient Skin	Nose	Nose	*Hospital Staff*
	Hand	Hand	
	Axilla	Shoe	
Patient Room	Floor	Uniform	
	Bedrail	Cell Phone	
	Faucet Handle	Pager	
	Glove	Countertop	*Nurse Station*
General	Air Filter	Computer Mouse	
	Cold Tap Water	Chair	
	Hot Tap Water	Phone	

Lax et al., Sci Trans Med 2017

Extremely low biomass prior to occupation – human microbes post colonization



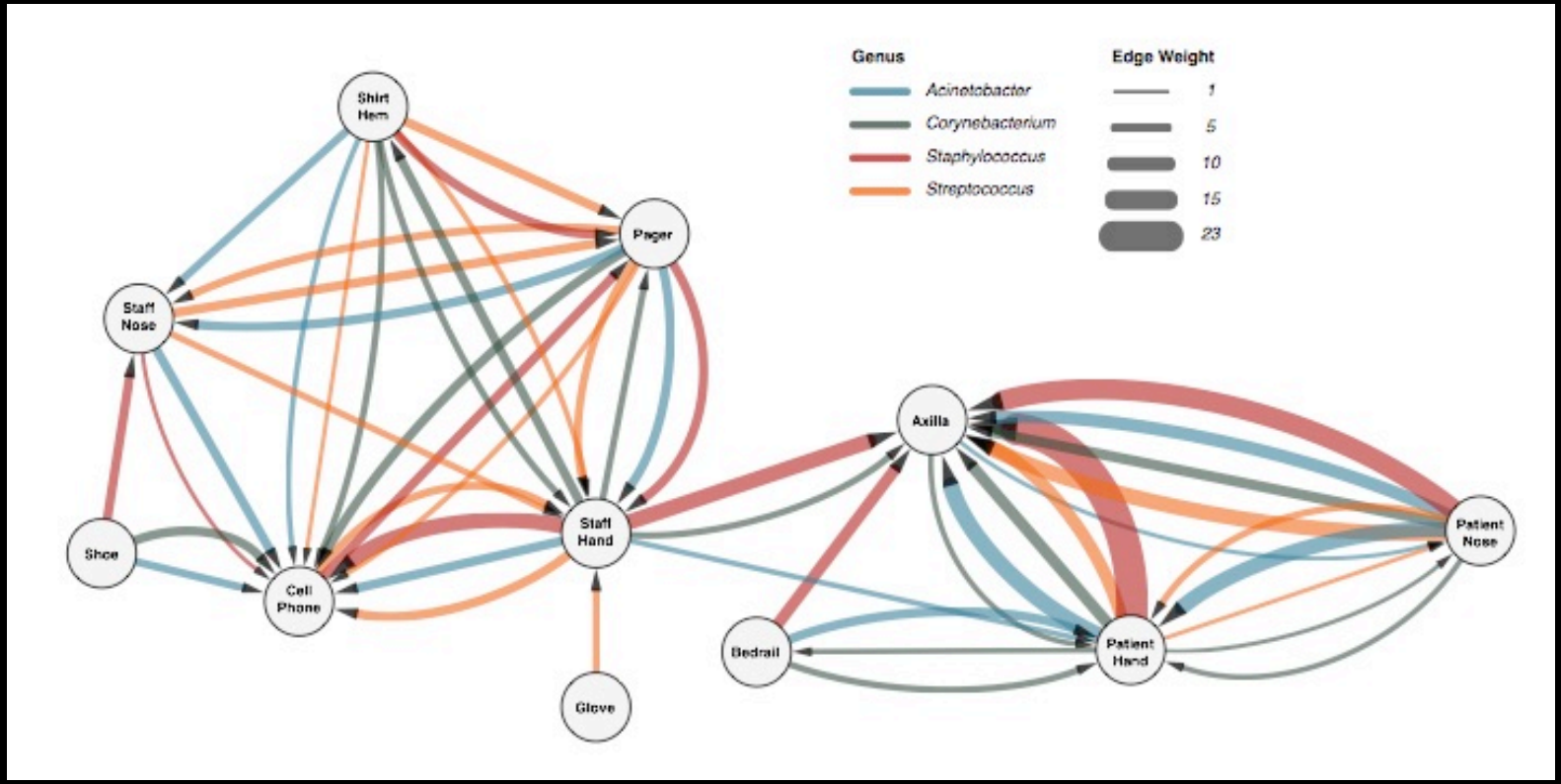
Lax et al., Sci Trans Med 2017



Relative humidity positively correlates with microbial sharing between staff and patients

Lax et al., Sci. Trans. Med. 2017

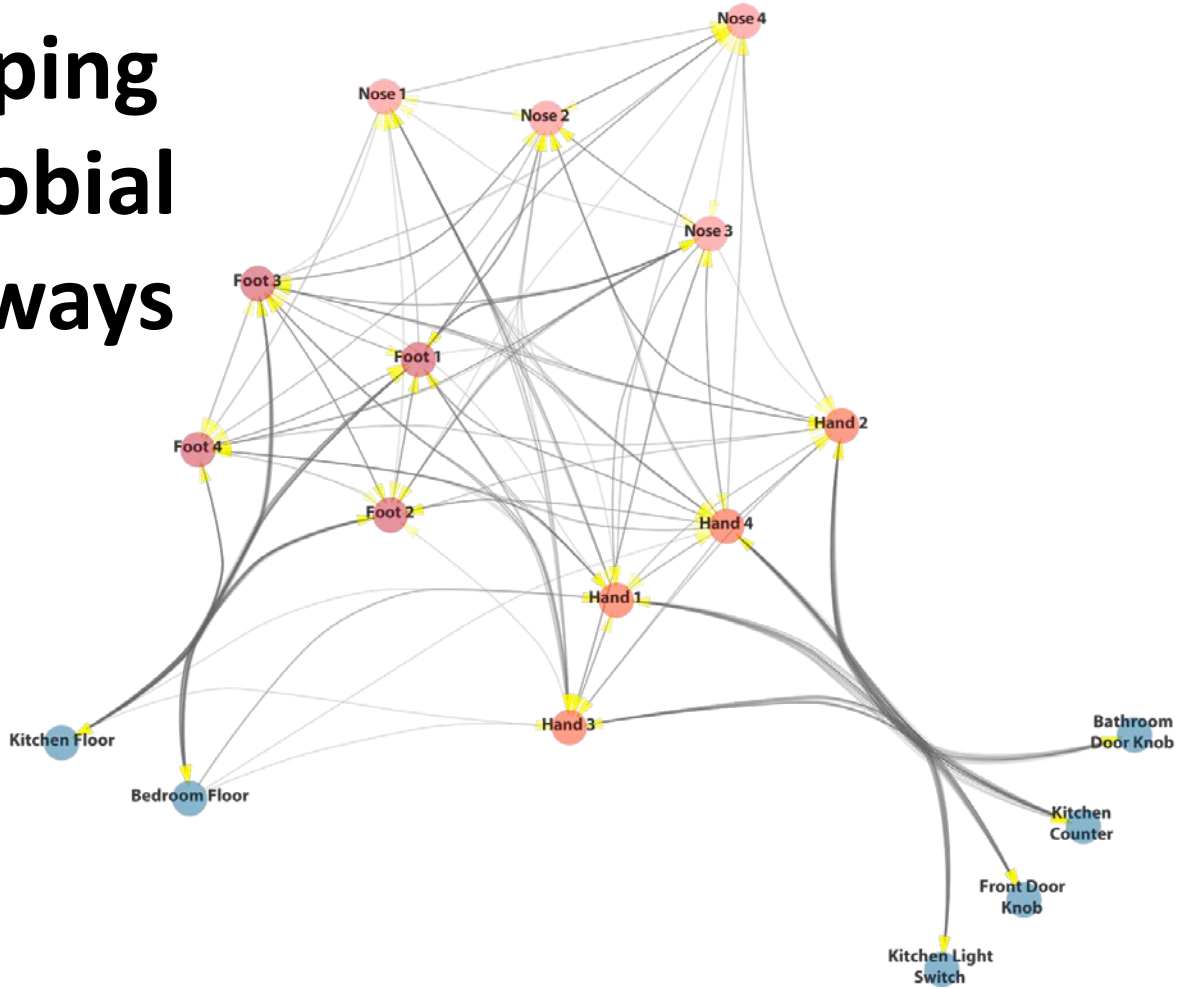
Staff were consistently a greater source of bacteria to patients



Lax et al., Sci. Trans. Med. 2017

Mapping microbial highways

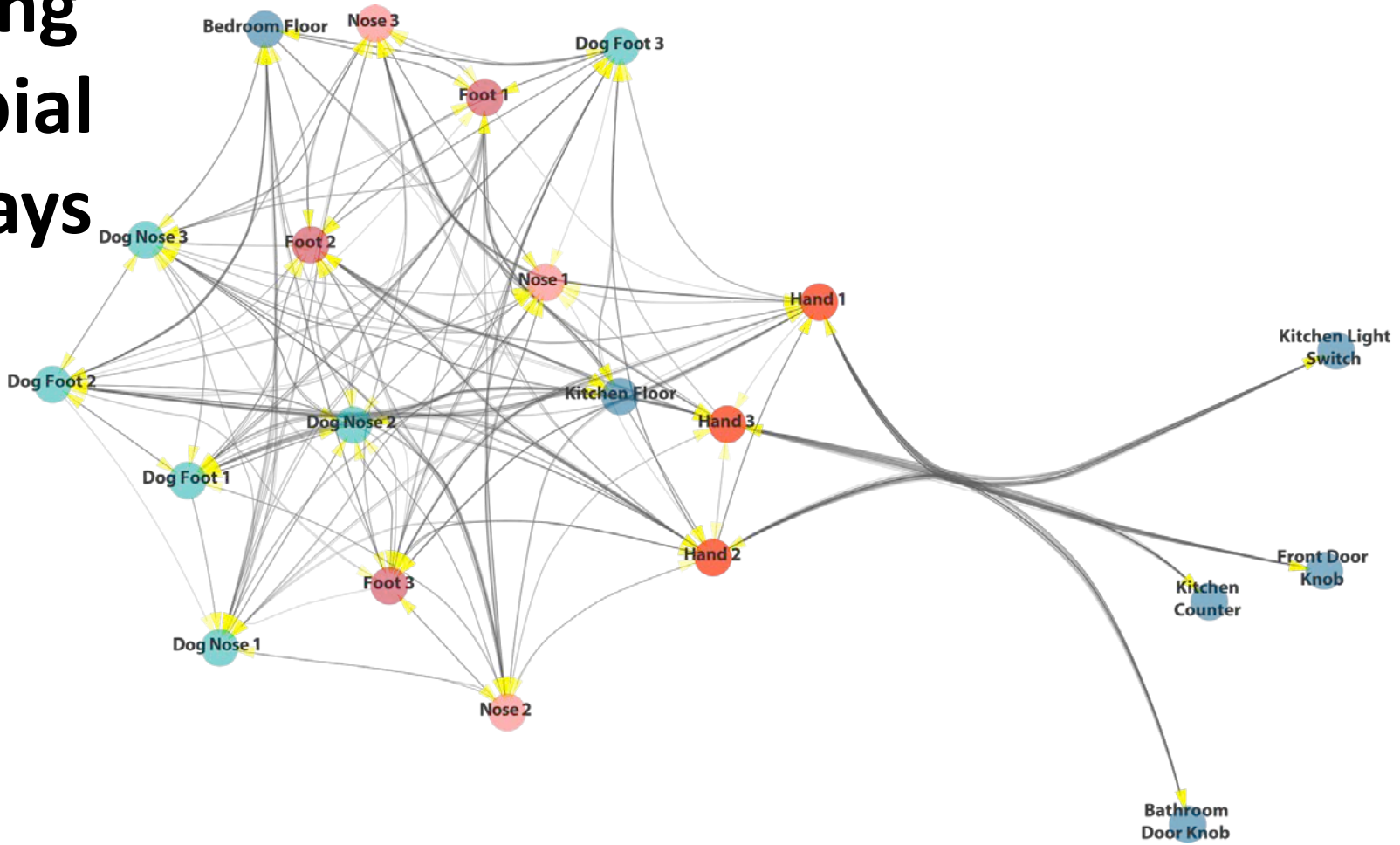
Lax et al., 2014 Science



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

Mapping microbial highways

Lax et al., 2014 Science

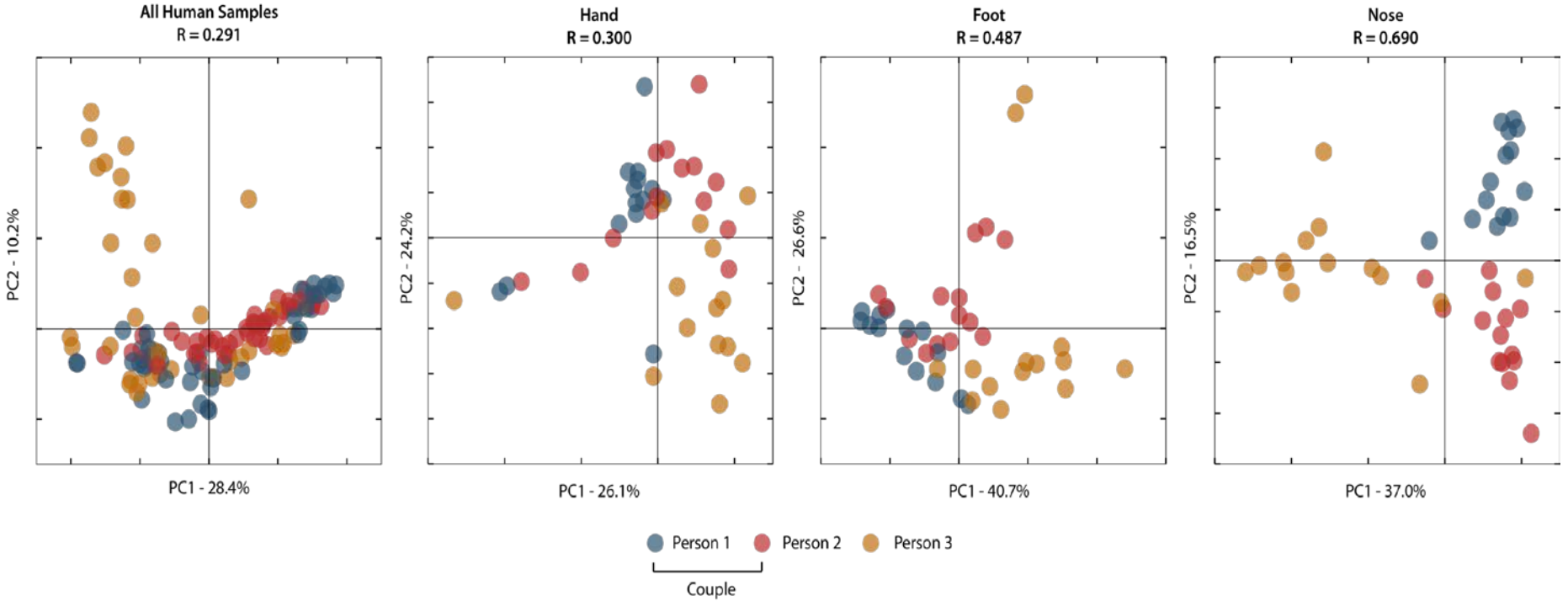


Dogs are Awesome!

My Dog
Captain Beau
Diggely

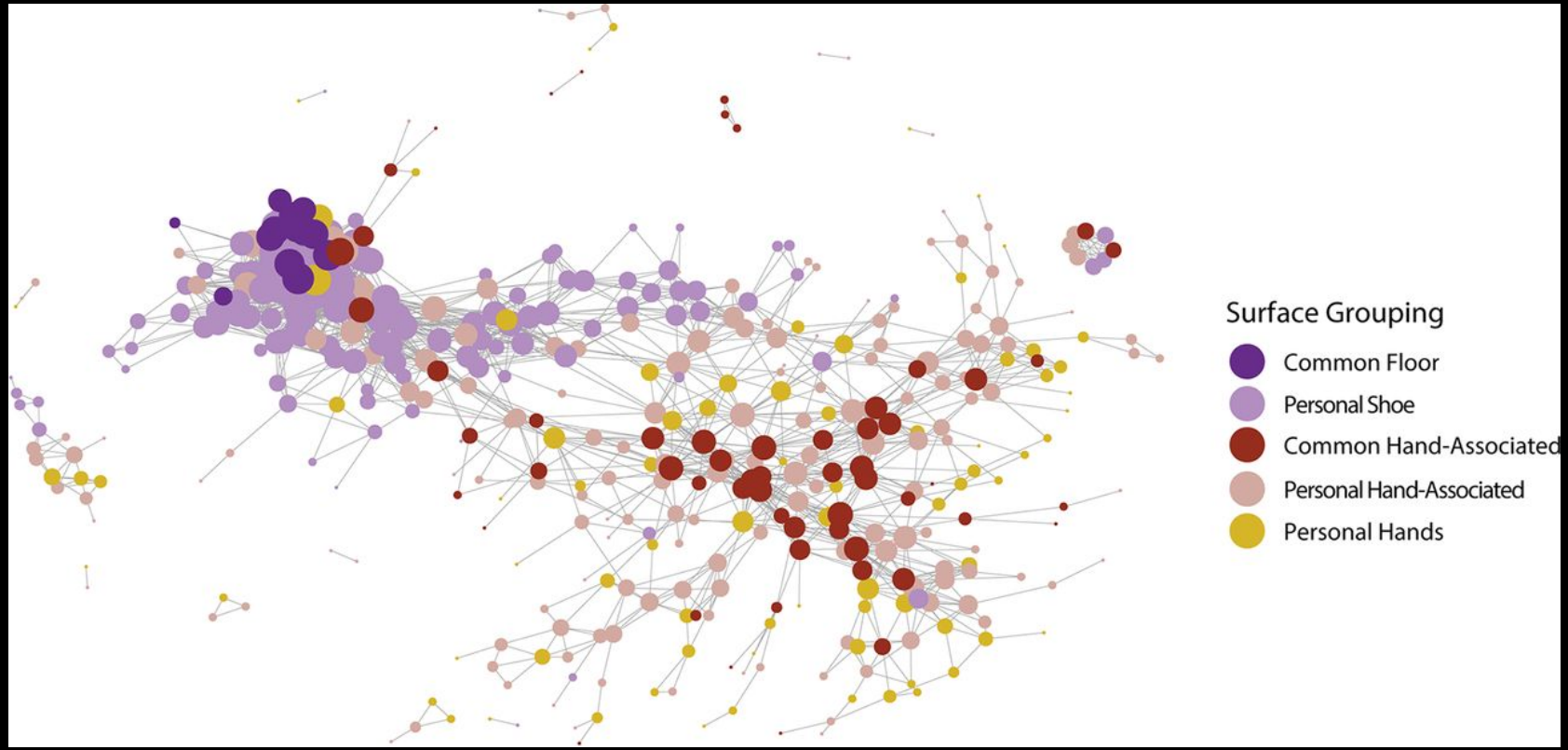
#dogsinspace

Those that physically interact share more microbial similarity



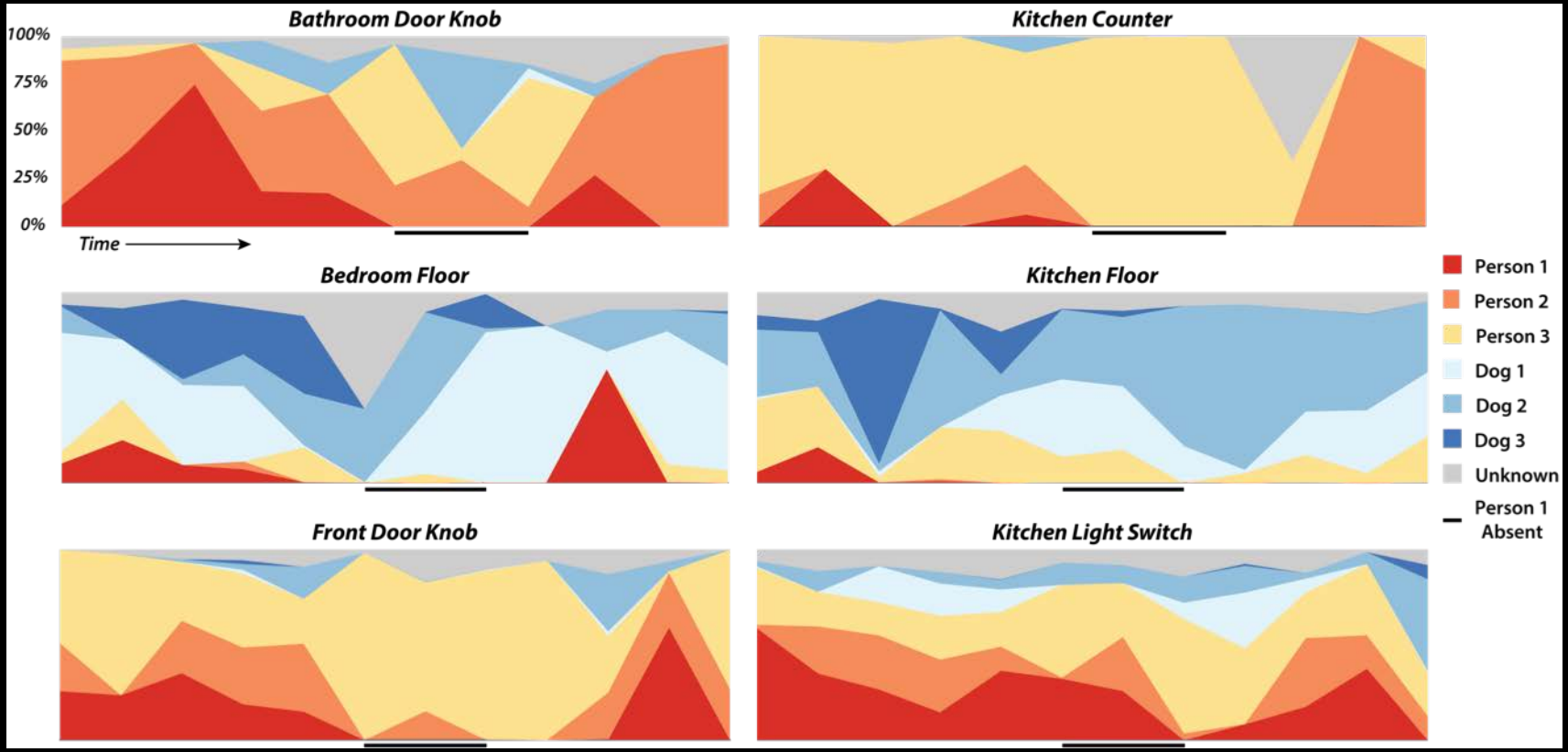
Lax et al Science 2014

Microbial sharing between college students in a dorm is mediated by the hand-transmission

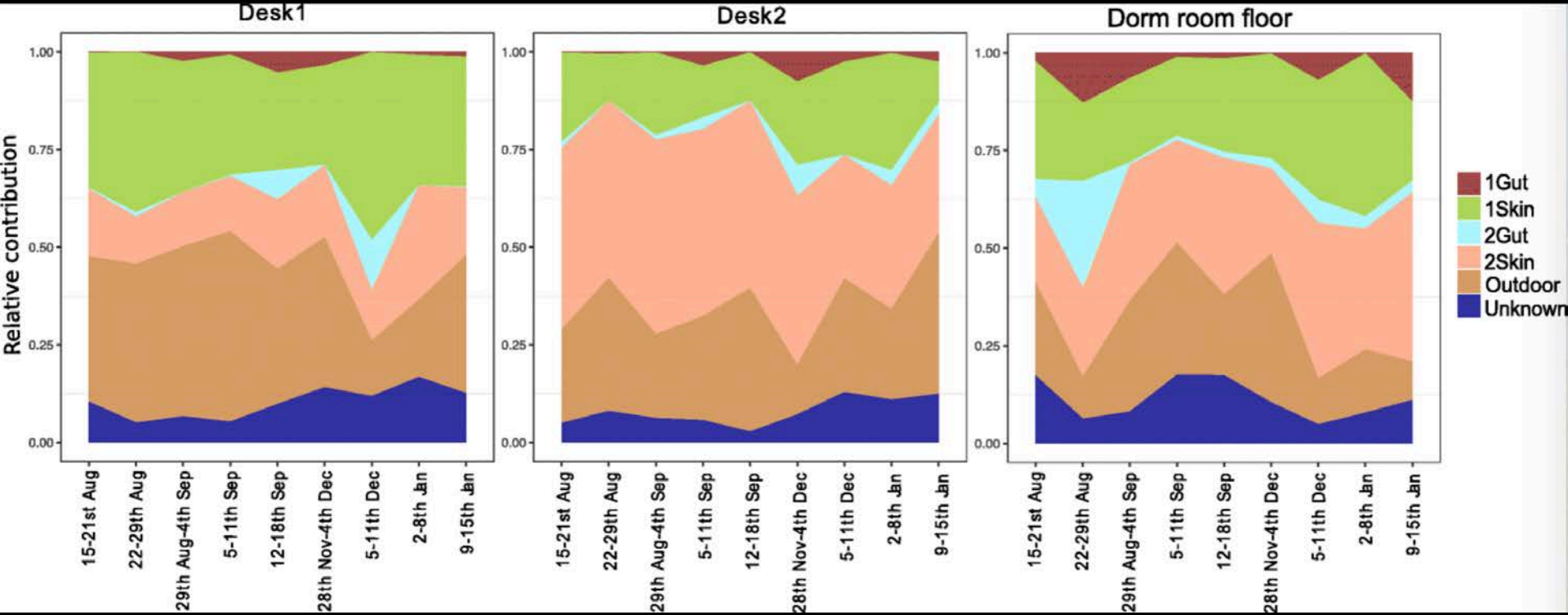


Richardson et al mBio 2019

Microbial forensics

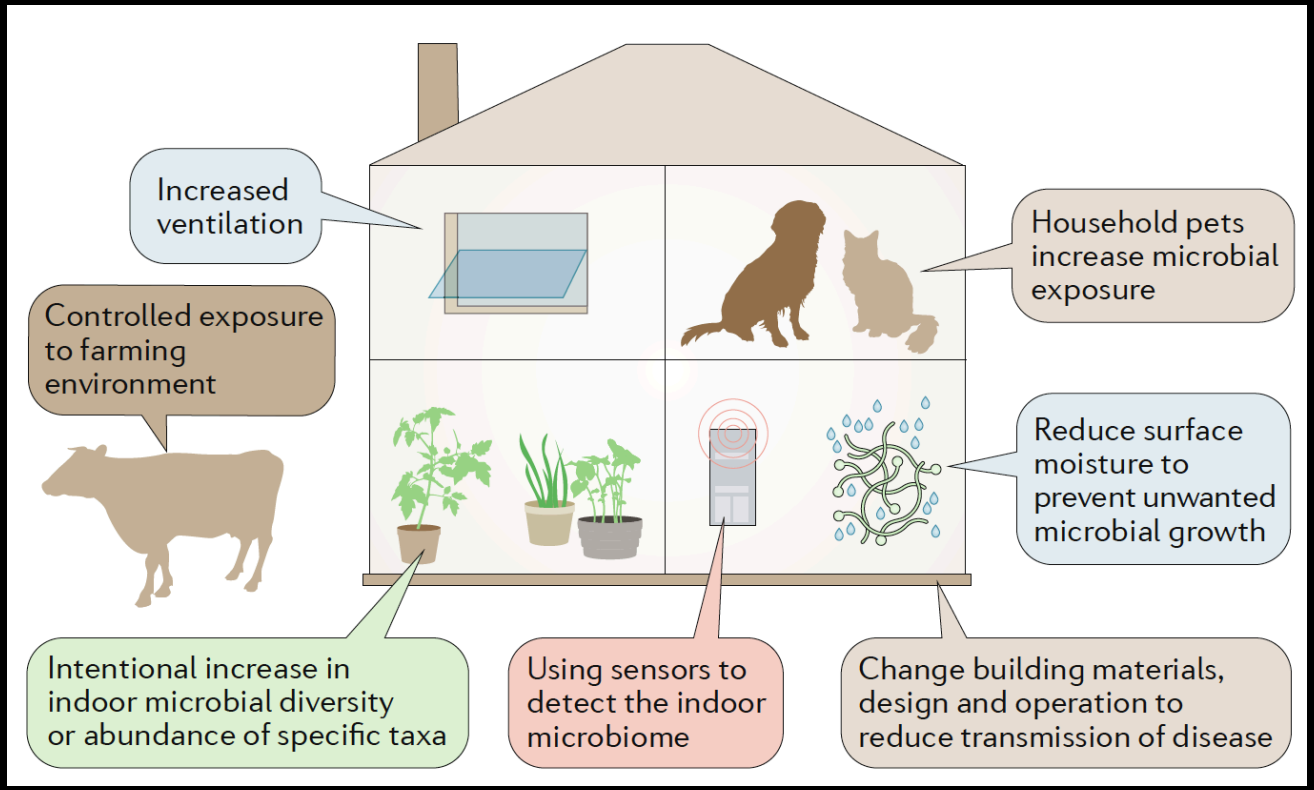


Tracking microbial sources in shared spaces: Air Force Cadets



Sharma et al., Microbiome, 2019

Managing the microbiome indoors

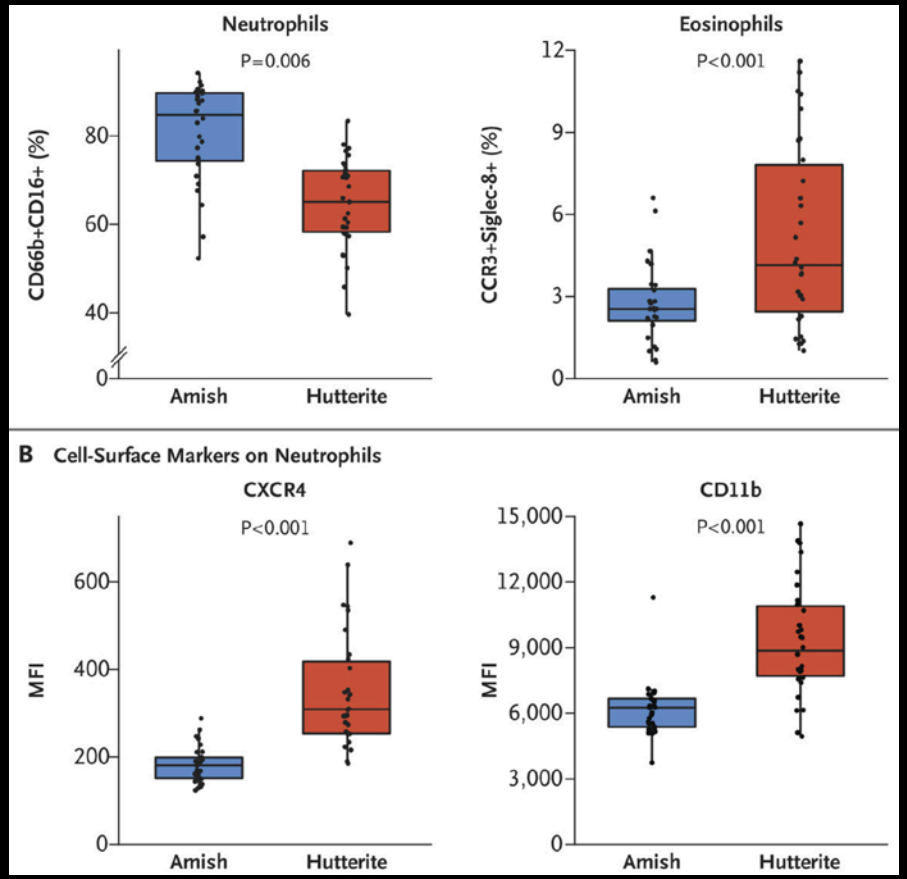


Gilbert and Stephens, Nature Reviews Microbiology, 2019

Farm Life

Amish live on family run farms and have no asthma. Hutterites live on industrial farms and have elevated asthma

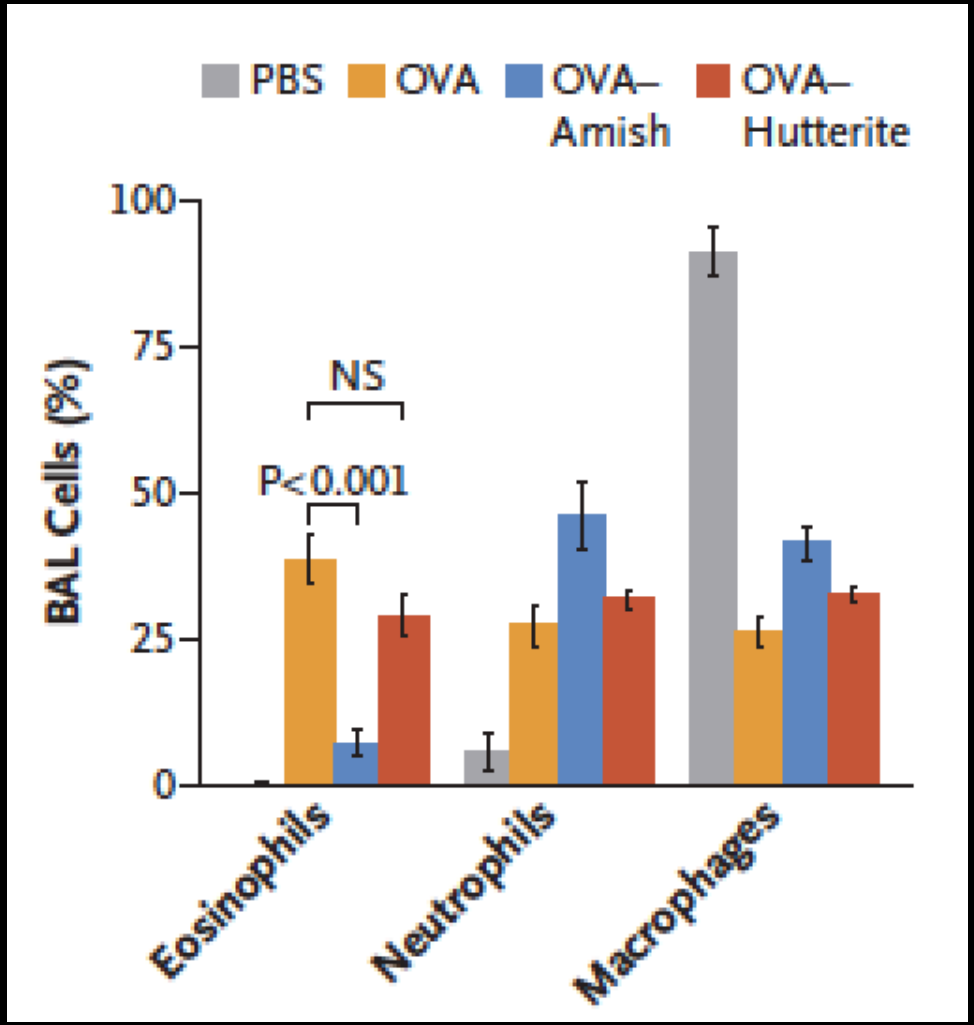
The children's immune systems tell the story



Peripheral-blood leukocytes from Amish children had increased proportions of neutrophils, decreased eosinophils compared with Hutterite kids.

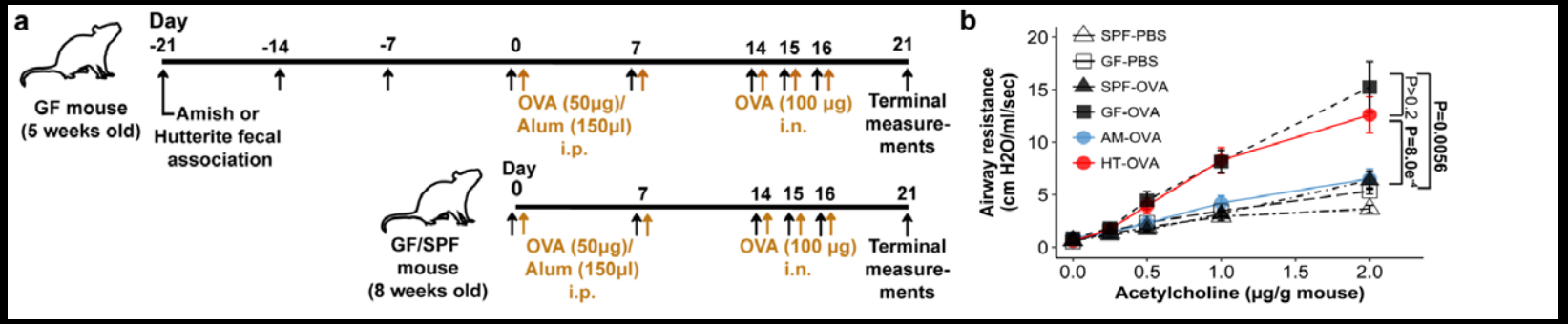
Neutrophils in the Hutterite children were older than in Amish children

Stein et al 2016, NEJM.

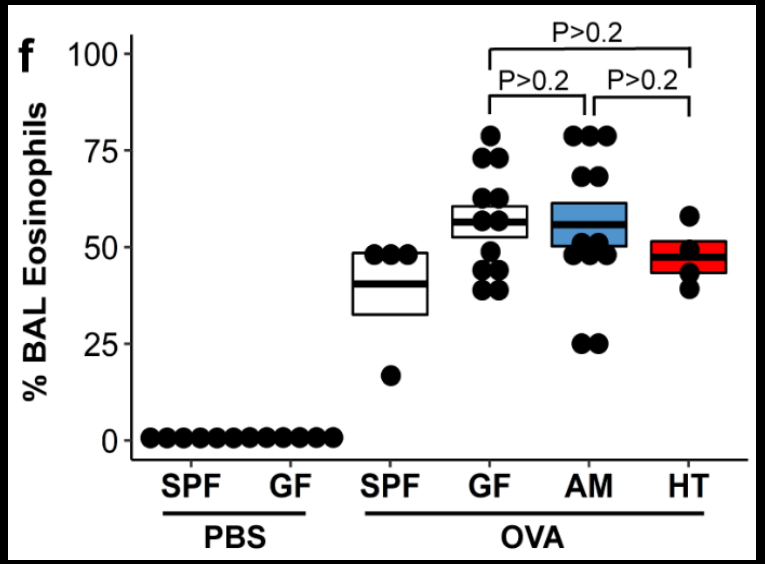


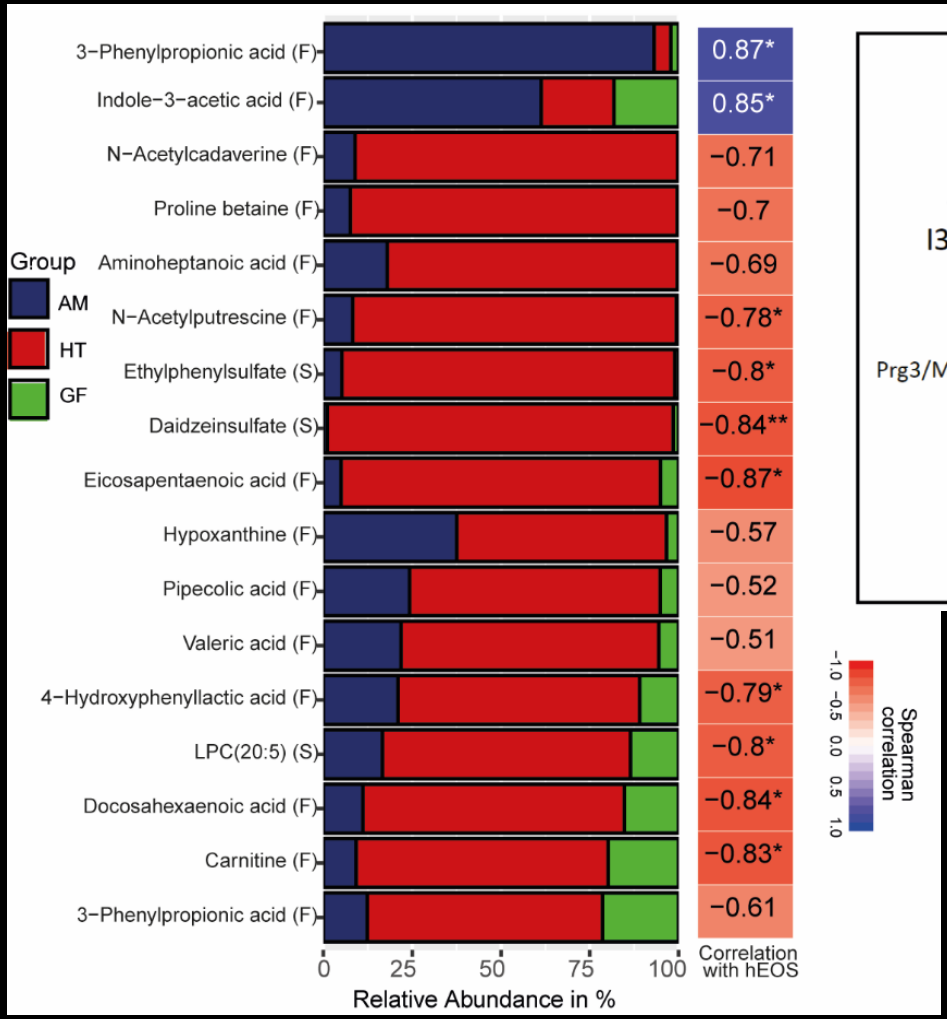
Mice which inhaled Amish bedroom dust were not allergic to a dietary antigen

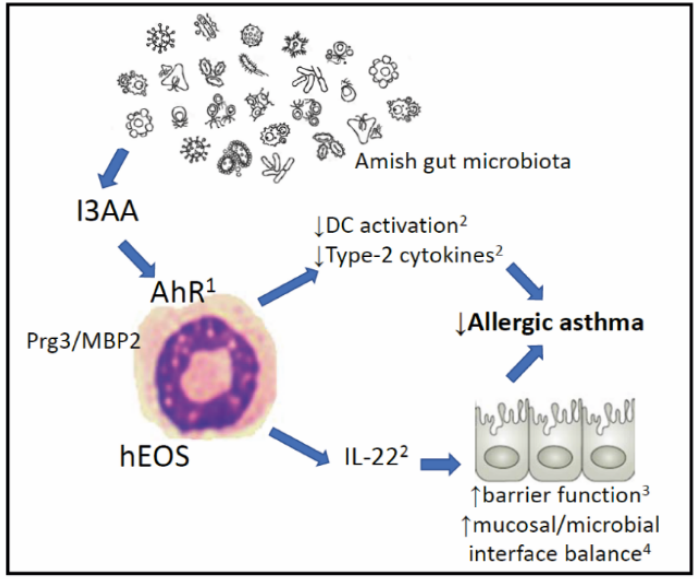
Stein et al 2016, NEJM.



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 Iindole 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

Clinical Variables

Age, Sex, Race, Inhaled & Oral corticosteroid (CS) use, Sinusitis, Atopy status, Serum IgE, FEV1, FeNO, Blood eosinophils, BAL cells

Asthmatic subjects (n=39) | **Healthy Controls (n=19)**

T2 status | Atopy status

T2-High (n=10) | T2-Low (n=29) | – atopy (ANA, n=18) | + atopy (AA, n=21) | – atopy (CNA, n=12) | + atopy (CA, n=7)

Airway Samples

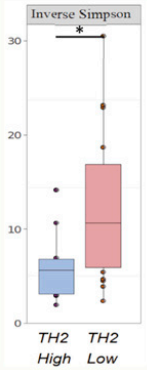
Bronchoalveolar lavage (BAL)
Endobronchial brushes (EB)

Microbiome Analysis

Bacterial (16S)
Fungal (ITS)

Findings

(1) Lower fungal diversity in EB in T2-High asthma



(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

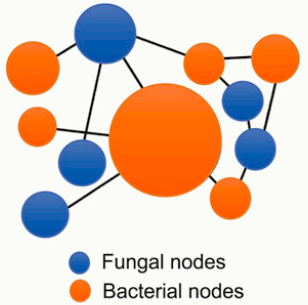
FEV1: *Alternaria, Aspergillus, Penicillium*

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

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