Invisible Influence: The microbiome in health and disease.

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Microbiome Wide Association Studies

Identifying the association between microbial activity and human health and disease

“Everything touches everything”

Jorge Luis Borges

Gilbert et al., 2016 Nature
The gut microbiome can explain significant variance in human phenotypes.

Rothschild et al., Nature 2018
Vaginal-birth baby and vaginal microbiota

C-section baby and mothers skin

Vaginal-birth baby and vaginal microbiota
Microbially Unique

All people have a unique microbiome, because each of us live a unique life; even identical twins!
Cancer; Inflammatory bowel disease; Irritable bowel disease; Diverticulosis; Surgical infections; Liver disease; Metabolic syndrome; cardiovascular disease; diabetes; obesity; Acne; Atopic dermatitis; Psoriasis; Auto-immune diseases; Sarcoidosis; Asthma; Seasonal allergies; hormonal imbalance; Dry eyes; Response to vaccines; Food-Pet allergies; Antibiotic recovery; C. difficile colitis; MRSA colitis; Sinusitis; Influenza; HIV/AIDS; Depression; Anorexia; PTSD, Anxiety, Autism, Alzheimer’s, Dental caries; Body odor; Parkinson’s; Dementia; Hyperphagia; Exercise; Smoking; Alcohol; Breast milk vs. Formula; Household Pets; Artificial Sweeteners; Prematurity; Caesarian vs. vaginal birth; polycystic ovaries; Sickle cell disease; Anemia; Renal disease; Chronic pulmonary disease; Type I and Type II Diabetes; Encephalophathy; incontinence; Diarrhea; Rheumatoid arthritis; Cardiovascular Disease; ETC....
Cure Rates of C. Difficile Colitis as a Function of Randomized Treatment Assignment

- First Infusion of Donor Feces (N=16) - 81.3%
- Infusion of Donor Feces Overall (N=16) - 93.8%
- Vancomycin (N=13) - 30.8%
- Vancomycin with Bowel Lavage (N=13) - 23.1%

P-values:
- P<0.001
- P<0.001
- P=0.008
- P=0.003
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, and similar monocytes compared with Hutterite kids.

Neutrophils in the Hutterite children were more aged than in Amish children.

No significant difference in Tregs were observed.

Stein et al 2016, NEJM.
House dust was intranasally administered (over 4-5 weeks) to an ovalbumin mouse model of allergic asthma.

Eosinophilia and airway hyper-responsiveness was exacerbated in mice treated with Hutterite dust extracts.

Inhalation of Amish dust extracts was sufficient to significantly inhibit airway hyper-responsiveness, eosinophilia, and serum ovalbumin-specific IgE levels.

The inhibitory effects of these extracts in wild-type mice probably required innate immunity, because protection was absent in mice deficient in MyD88 and Trif

Stein et al 2016, NEJM.
Morbidly obese man (385lbs) loses 113lbs by eating whole grains.

Liping Zhao – ISME 2012
Some bacteria can make you fat

One bacterium – Enterobacter cloacea B29 made mice obese.

Liping Zhao – ISME 2012
How does a high fat diet induce obesity?

High fat changes the microbiome which affects hepatic hormones, adipose tissue production and appetite

Leone et al., 2015 Cell Host Microbe
Cancer rates in migrants become similar to those in the local population

Nature 411, 390-395 (17 May 2001)
Fusobacterium nucleatum associated with CRC in humans

Recruits infiltrating immune cells and modulates β-catenin signaling

Bifidobacterium can actively enhance the efficacy of immunotherapy

Probiotic dramatically enhances immunotherapy in preclinical tumor models
Manipulating microbes and their metabolites can maximize tumor immunity in mice

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
Microbial forensics
A **strange** new way to solve crimes

The bacteria growing in and on the human body is so unique—and so revealing—that scientists believe germs will soon help catch bad guys.

*By Mandy Oaklander*
Colonization and Succession of Hospital-Associated Microbiota
365 consecutive days: 2 months pre opening, and 10 months post opening

<table>
<thead>
<tr>
<th>Patient Skin</th>
<th>Patient Room</th>
<th>General</th>
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</thead>
<tbody>
<tr>
<td>Nose</td>
<td>Hand</td>
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<tr>
<td>Hand</td>
<td>Axilla</td>
<td>Hand</td>
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<tr>
<td>Axilla</td>
<td>Floor</td>
<td>Shoe</td>
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<td>Countertop</td>
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<tr>
<td>Air Filter</td>
<td>Cold Tap Water</td>
<td>Computer Mouse</td>
</tr>
<tr>
<td>Cold Tap Water</td>
<td>Hot Tap Water</td>
<td>Chair</td>
</tr>
</tbody>
</table>

**Hospital Staff**
- Phone
- Chair
- Phone

**Nurse Station**
- Lax et al., 2017
Genotypes of the same bacteria showed increased ARGs over time. Staphylococcus, Propionibacterium, Anaerococcus and Corynebacterium had a consistently greater number of antibiotic resistance genes after 60 days of hospital environmental exposure.

Lax et al., Sci. Trans. Med. 2017
Staff were consistently a greater source of bacteria to patients

Lax et al., Sci. Trans. Med. 2017
Surgical Infections
Within 24 hours, a lethal *P. aeruginosa* morphotype develops

Microbial phenotype, shaped by the intestinal environment of stress, NOT bacterial species, NOT immune background- caused death in this model.
EXAMPLE:
Potential strategies to alter the gut to reduce the abundance of an organism that can metabolize cycasin to produce the carcinogen methylazoxymethanol (MAM)

Kuntz & Gilbert, Trends in Pharmacological Sciences, 2016
Precision medicine using the microbiome

Gilbert et al., 2016 Nature