



Invisible Influence: The microbiome in health and disease.

Jack A Gilbert
@gilbertjacka

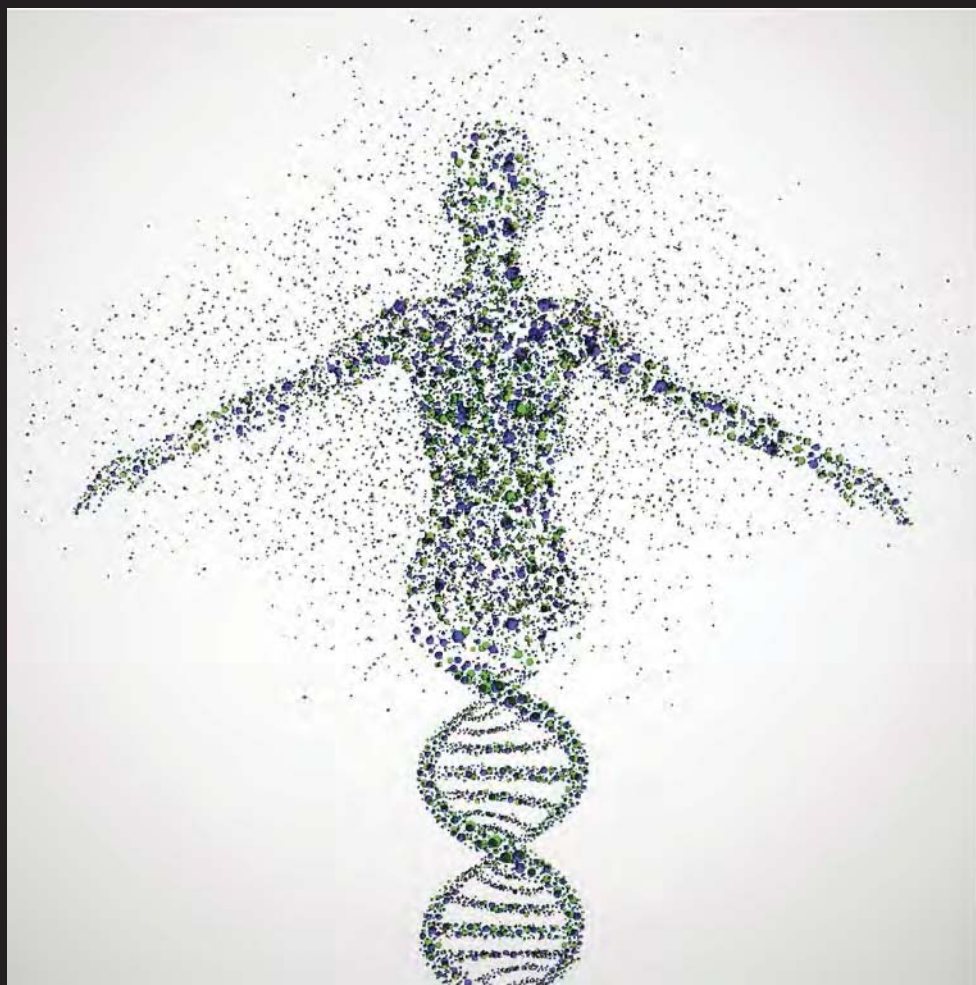


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Biological
Discovery
in Woods Hole

Argonne 
NATIONAL LABORATORY

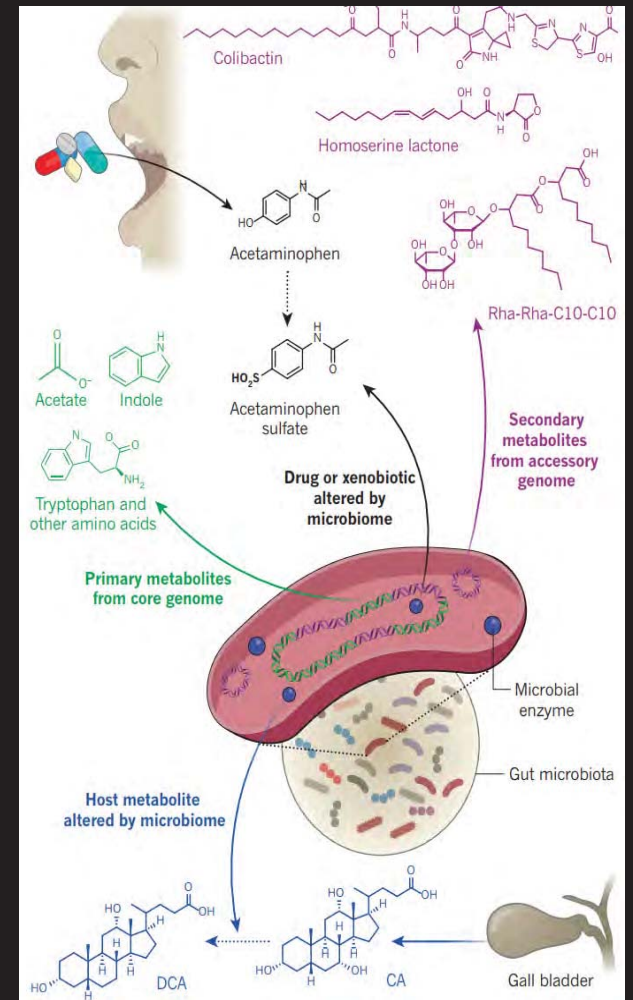


Microbiome Wide Association Studies

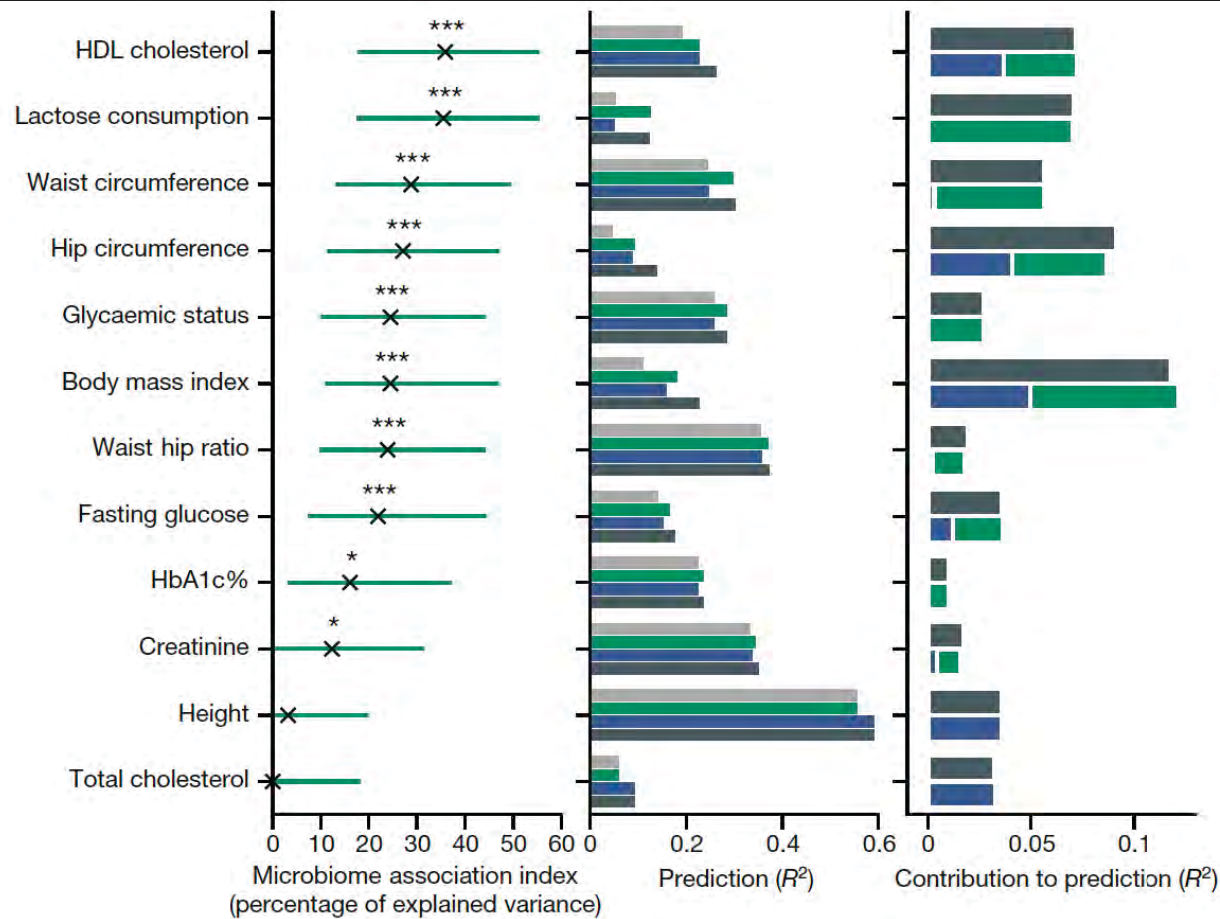
Identifying the association between microbial activity and human health and disease

“Everything touches everything”
Jorge Luis Borges

Gilbert et al., 2016 Nature



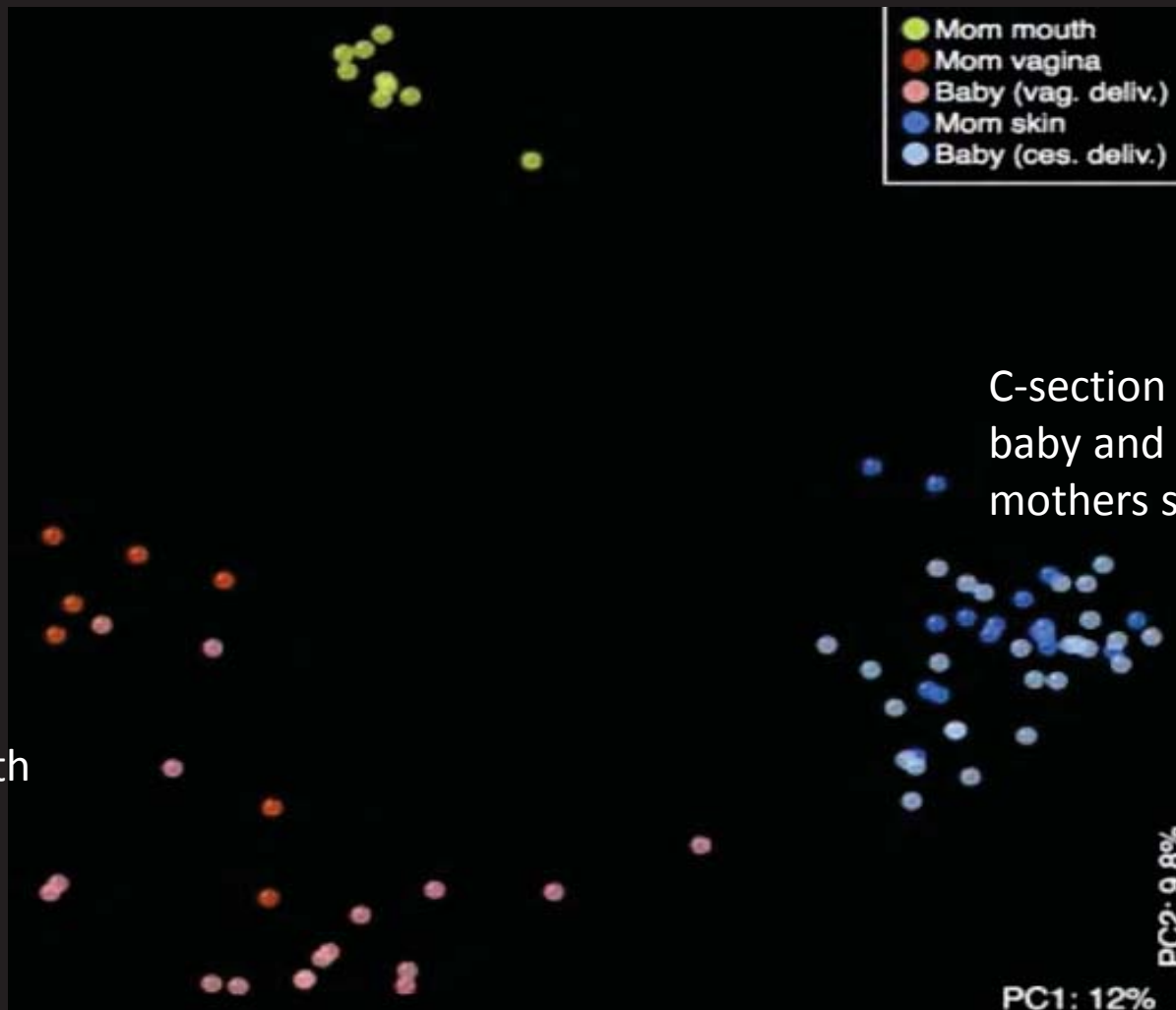
The gut microbiome can explain significant variance in human phenotypes



Rothschild et al., Nature 2018



Vaginal-birth
baby and
vaginal
microbiota



C-section
baby and
mothers skin

PC1: 12%

PC2: 9.8%

Microbially Unique

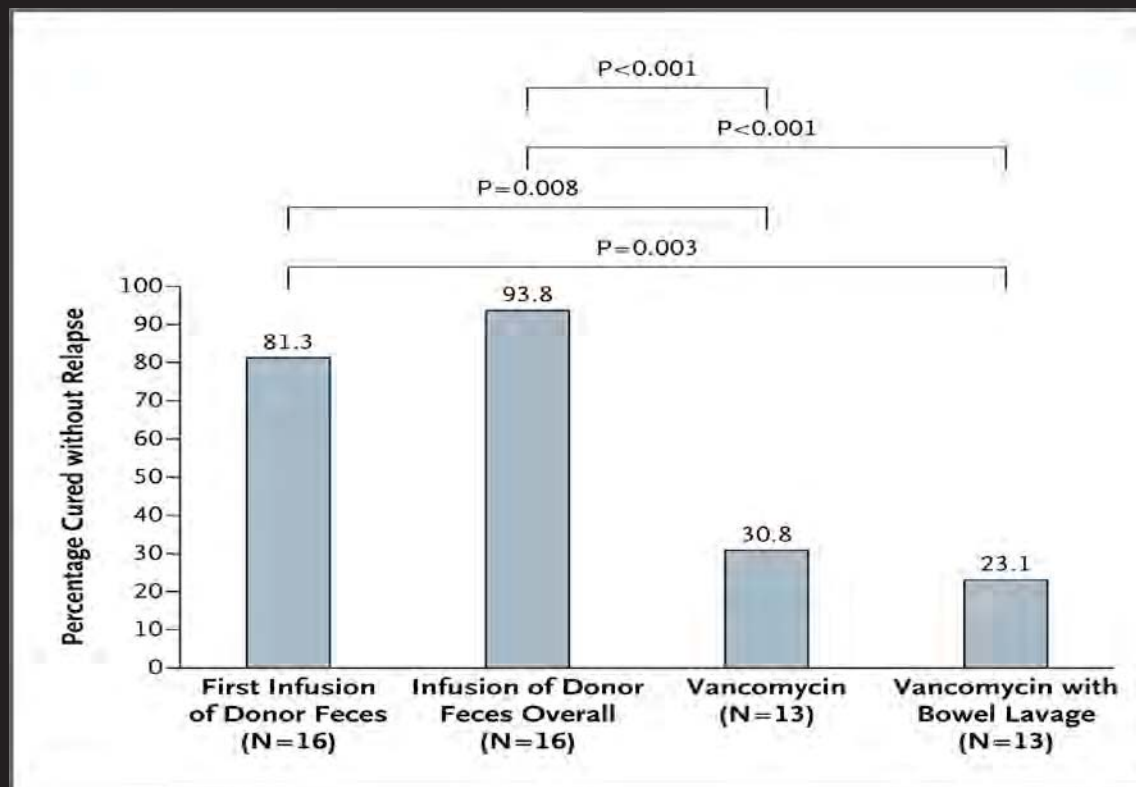


All people have a unique microbiome, because each of us live a unique life; even identical twins!



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; Encephalopathy; incontinence; Diarrhea; Rheumatoid arthritis; Cardiovascular Disease; ETC....

Cure Rates of C. Difficile Colitis as a Function of Randomized Treatment Assignment





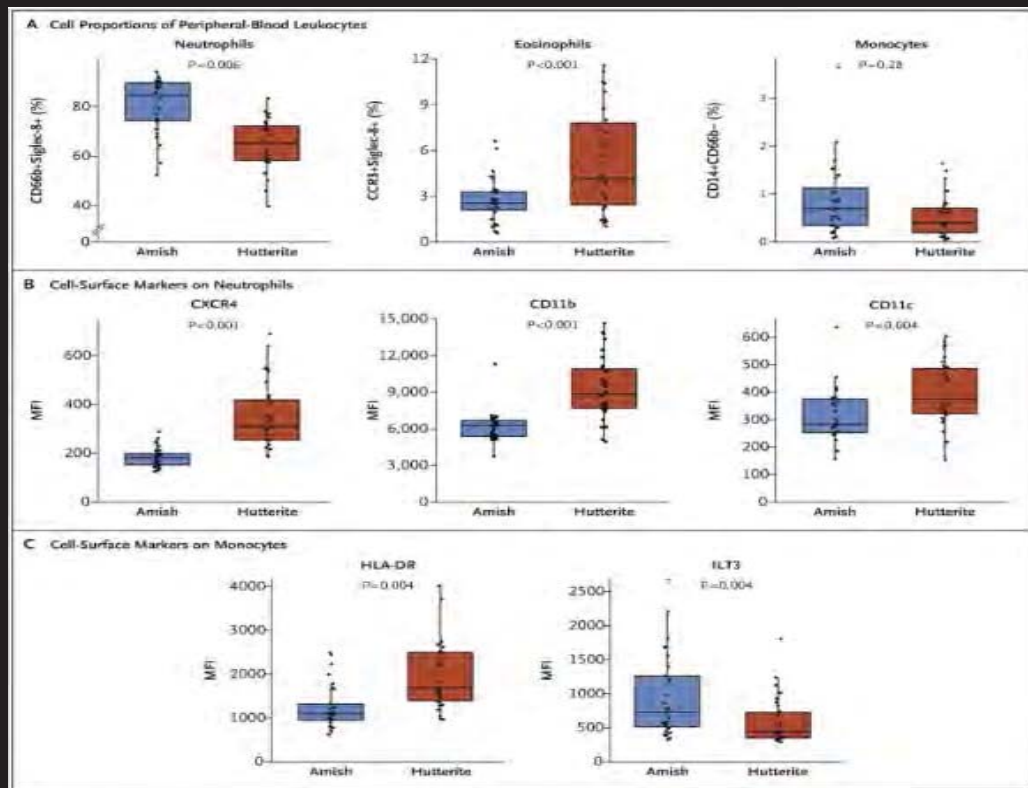
Farm Life

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



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Proportions of Peripheral Blood Leukocytes and cell-surface marker phenotypes in Amish and Hutterite Children

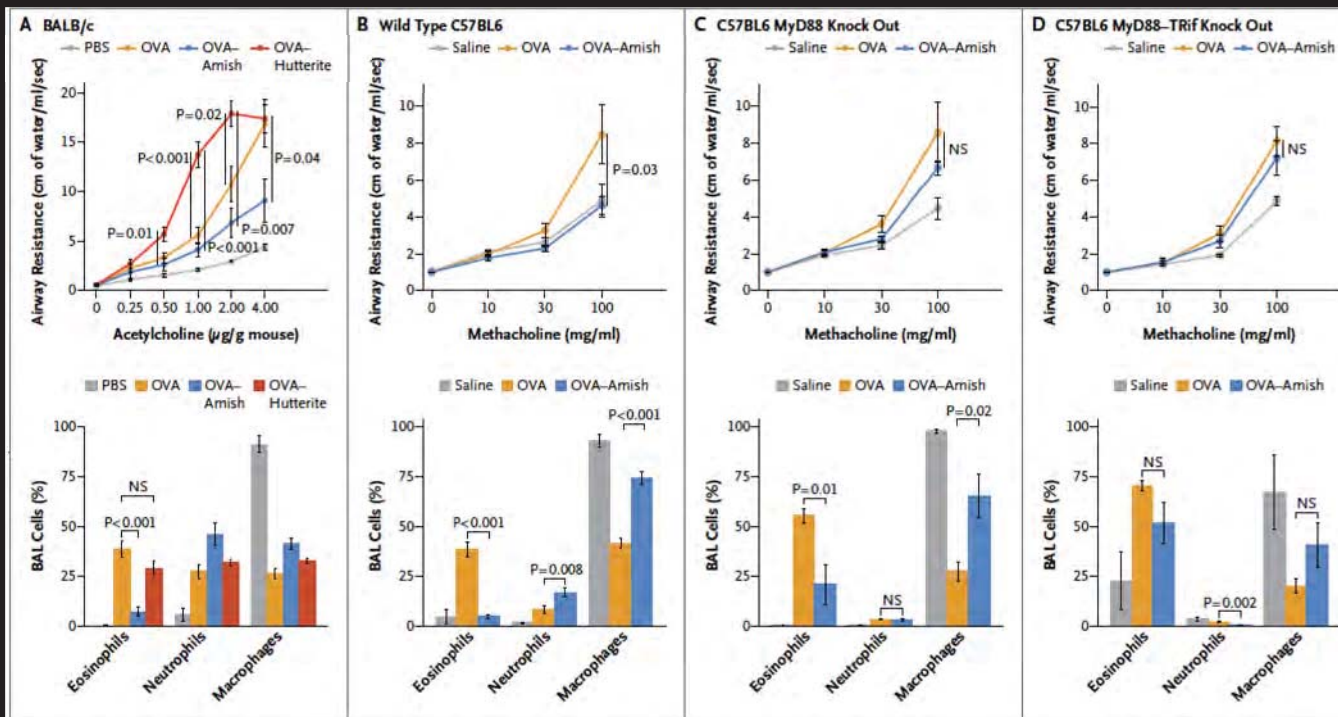


Peripheral-blood leukocytes from Amish children had increased proportions of neutrophils, decreased eosinophils, and similar monocytes compared with Hutterite kids.

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.

Obesity



Morbidly obese man
(385lbs) loses 113lbs by
eating whole grains.

Liping Zhao – ISME 2012

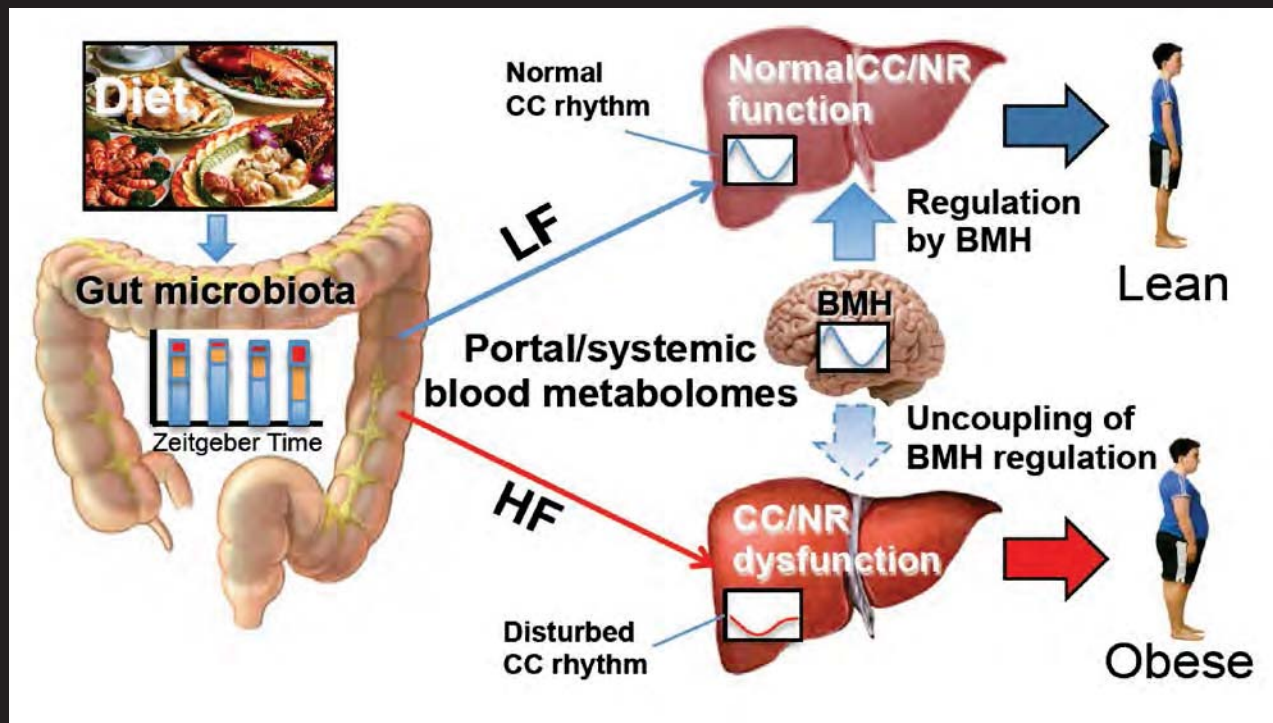
Some bacteria can make you fat



One bacterium –
Enterobacter cloacae B29
made mice obese.

Liping Zhao – ISME 2012

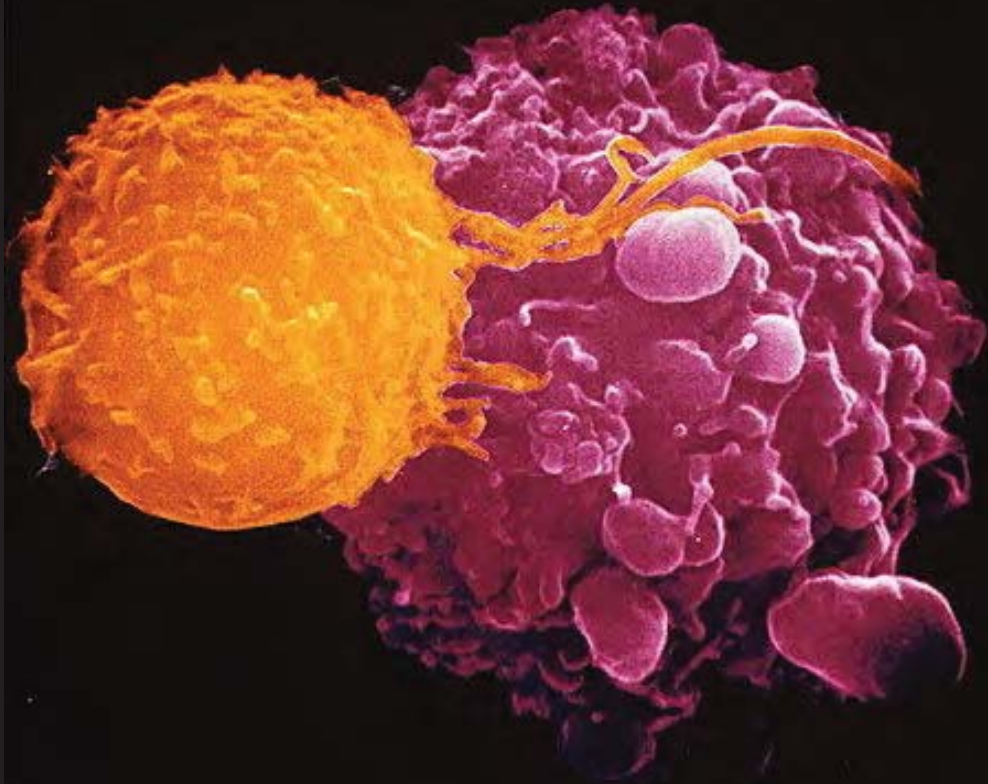
How does a high fat diet induce obesity?



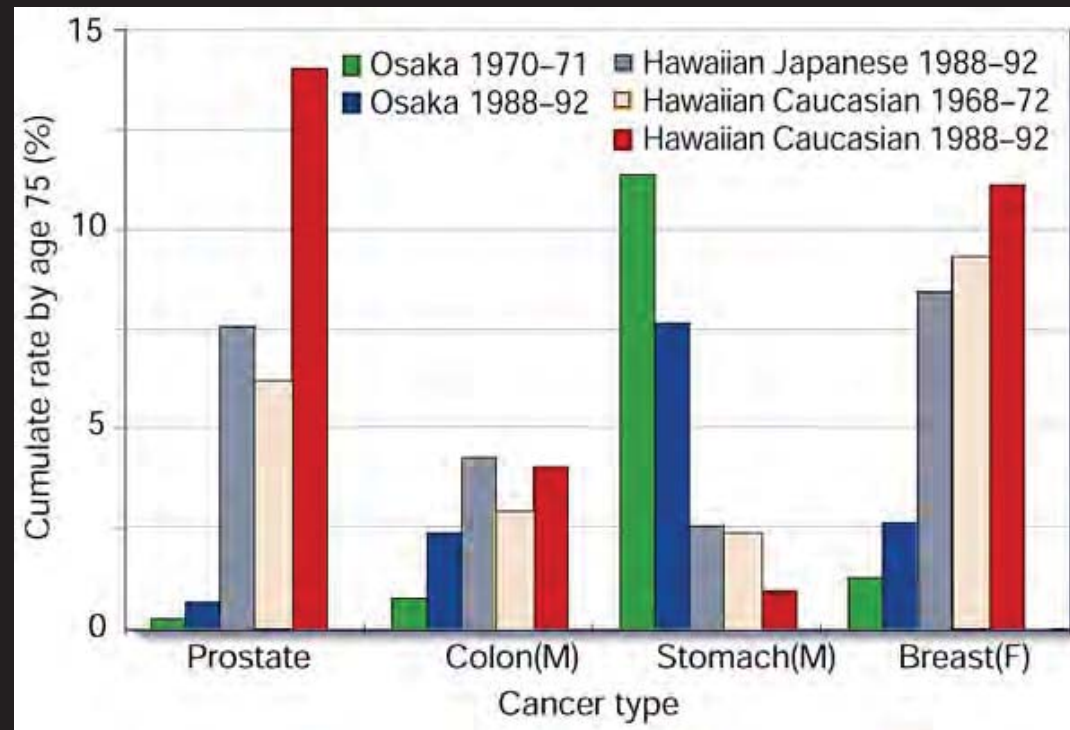
High fat changes the microbiome which affects hepatic hormones, adipose tissue production and appetite

Leone et al., 2015 Cell Host Microbe

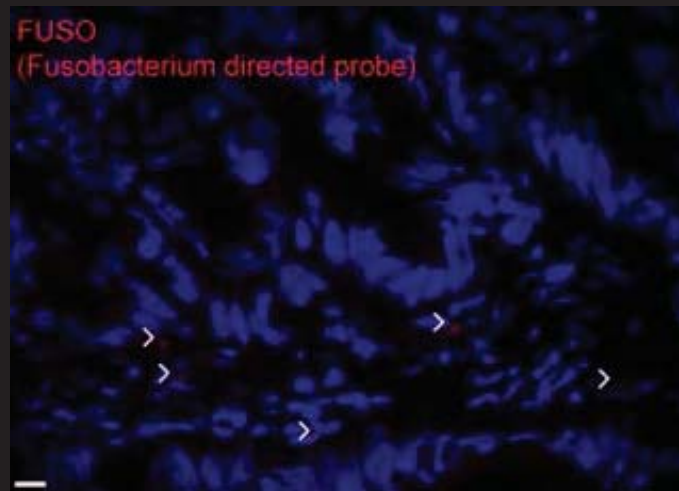
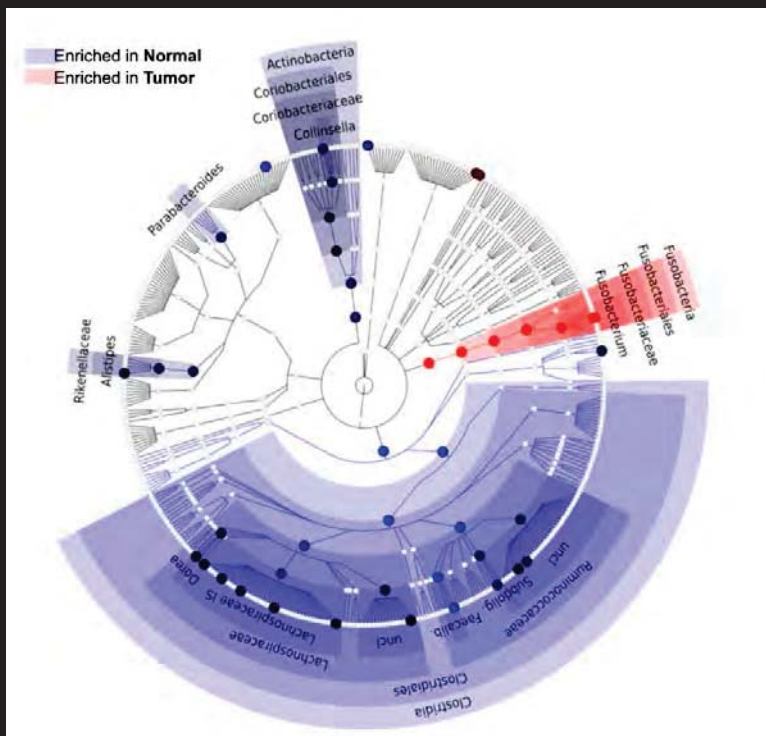
CANCER



Cancer rates in migrants become similar to those in the local population



Fusobacterium nucleatum associated with CRC in humans

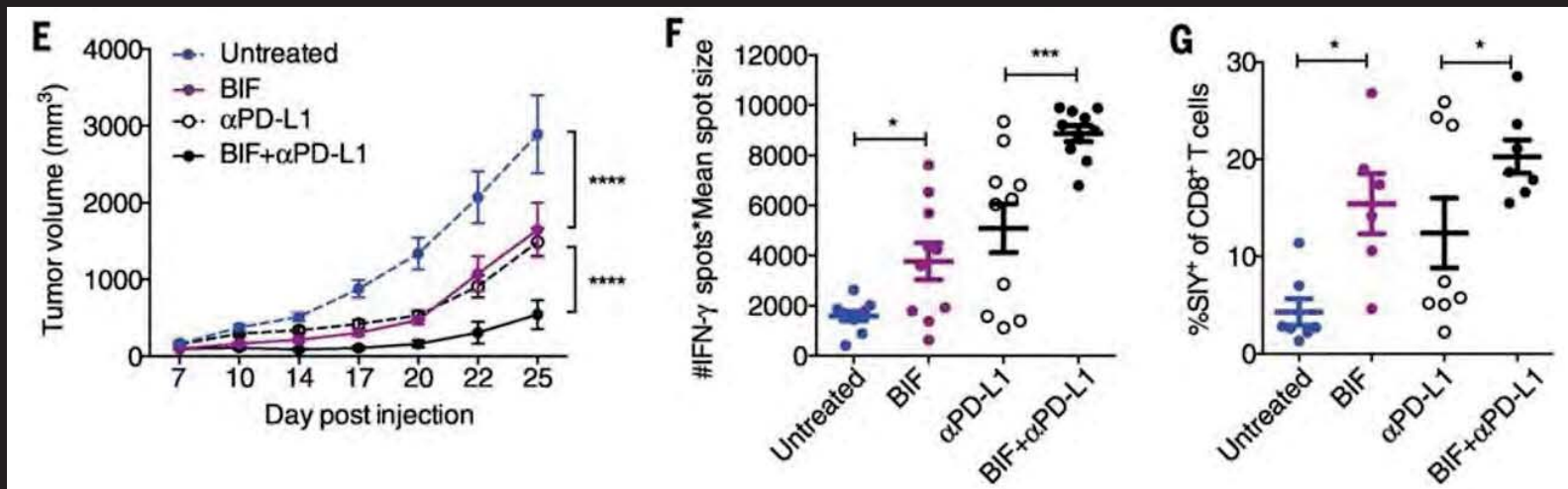


Recruits infiltrating immune cells and modulates β -catenin signaling

Castellari et al. *Fusobacterium nucleatum* infection is prevalent in human colorectal carcinoma. *Genome Res* 2012;22:299–306. Kostic et al. Genomic analysis identifies association of *Fusobacterium* with colorectal carcinoma. *Genome Res* 2012;22:292–8.

Bifidobacterium can actively enhance the efficacy of immunotherapy

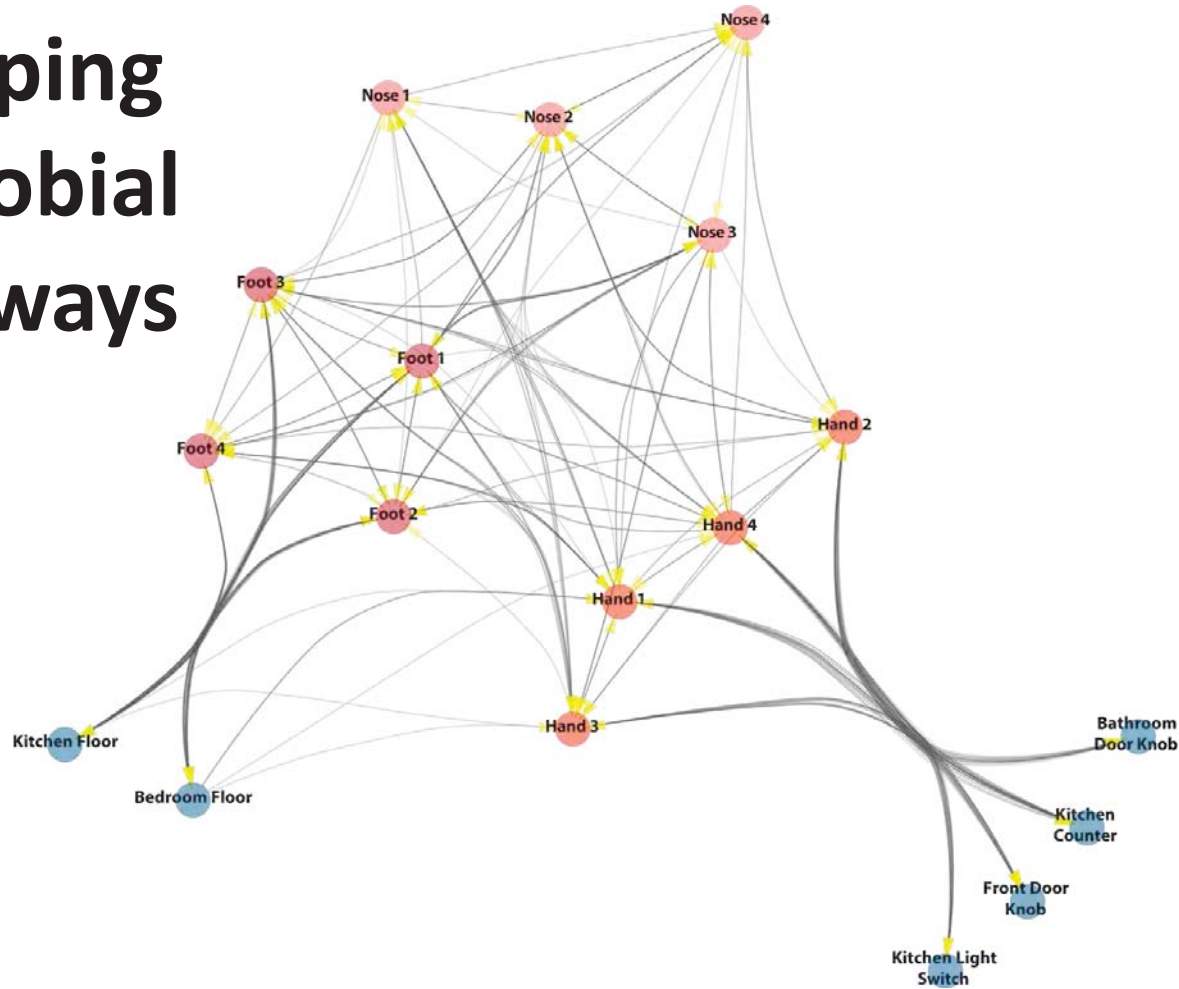
Probiotic dramatically enhances immunotherapy in preclinical tumor models
Manipulating microbes and their metabolites can maximize tumor immunity in mice



Vetizou et al. *Science* 2015 & Sivan et al. *Science* 2015



Mapping microbial highways

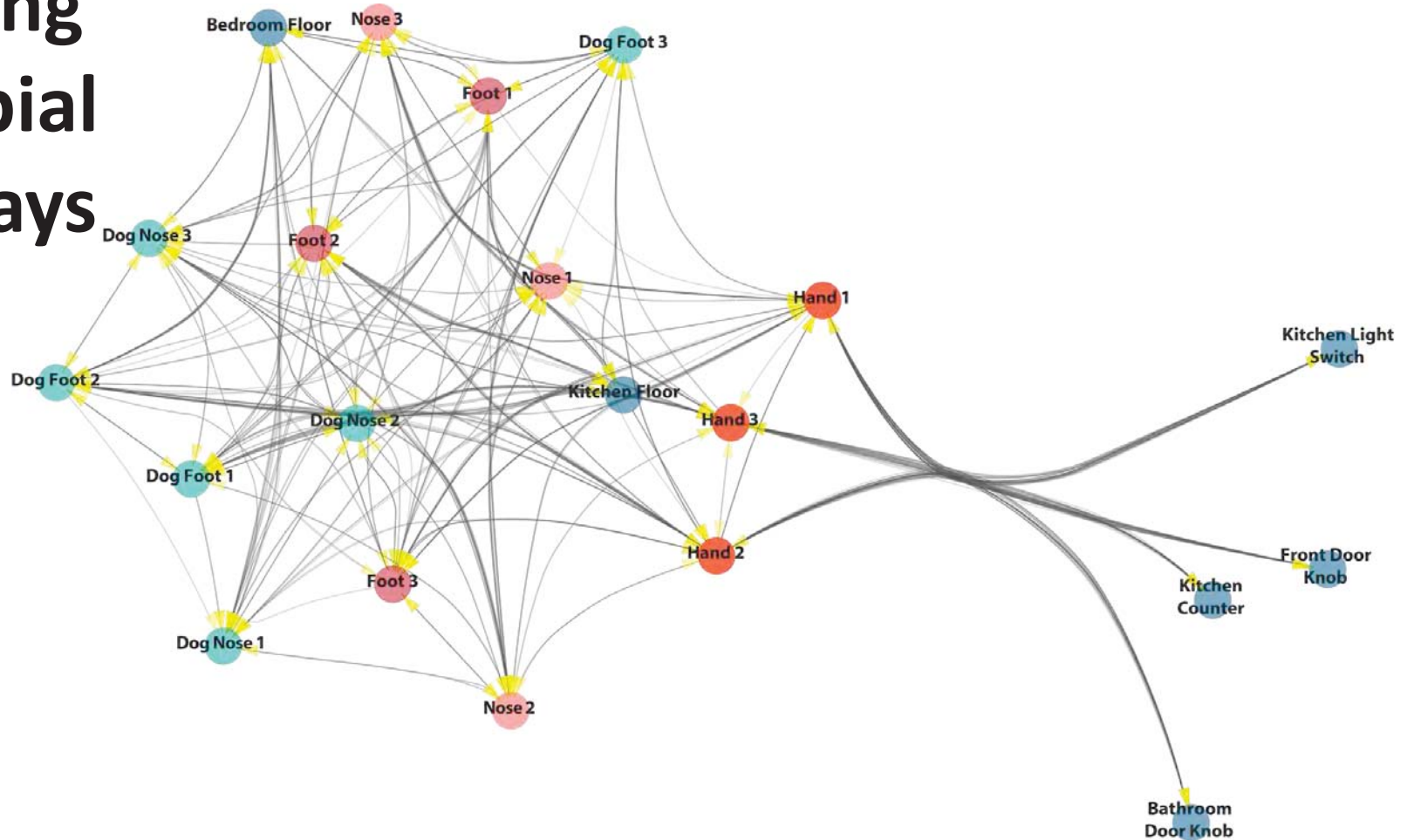


Lax et al., 2014 Science

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

Mapping microbial highways

Lax et al., 2014 Science

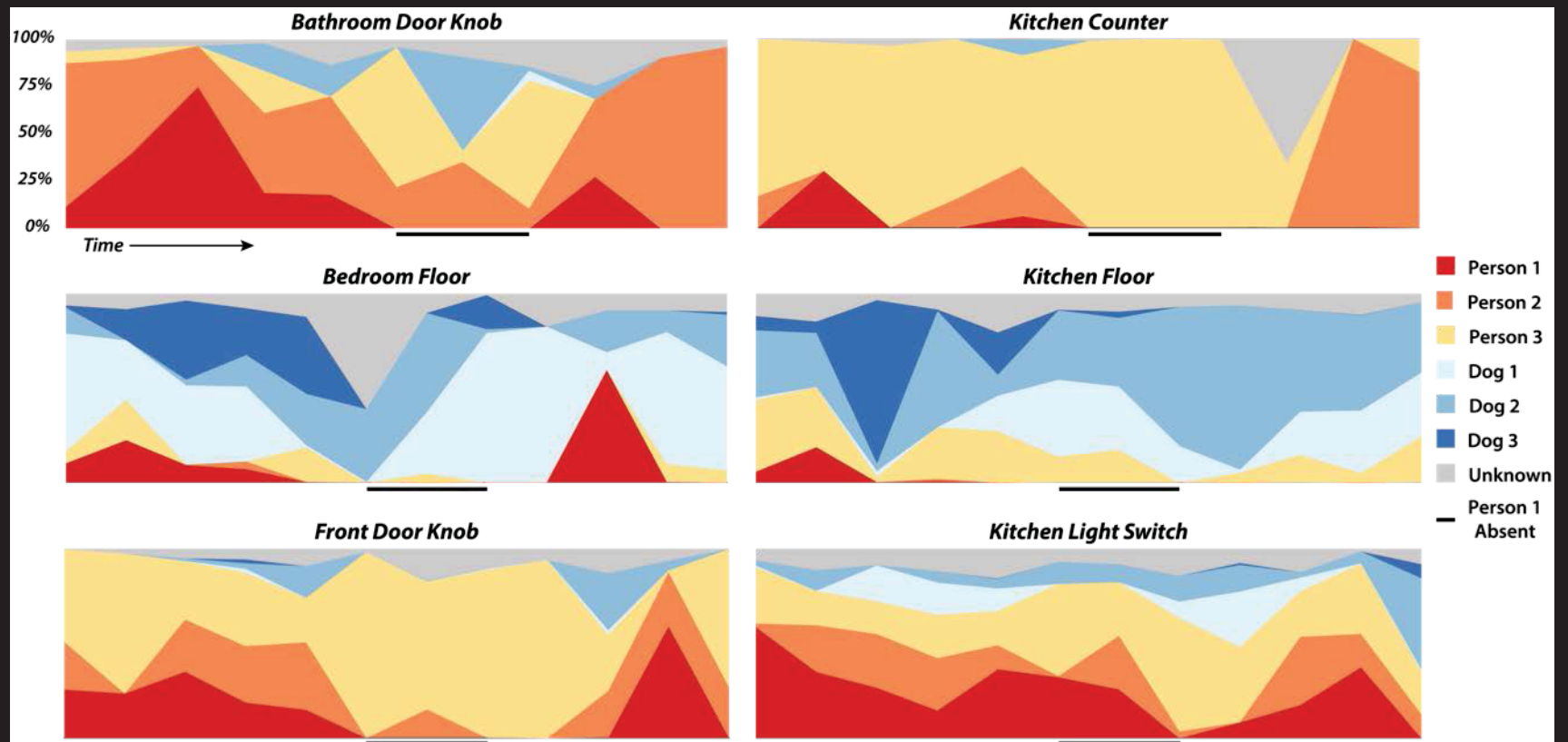


Dogs are Awesome!



My Dog
Captain Beau
Diggely

Microbial forensics



unusual activity

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



Staging a burglary in the name of science, detectives break into a house through a front window

hind
by the "burglars"

Colonization and Succession of Hospital-Associated Microbiota

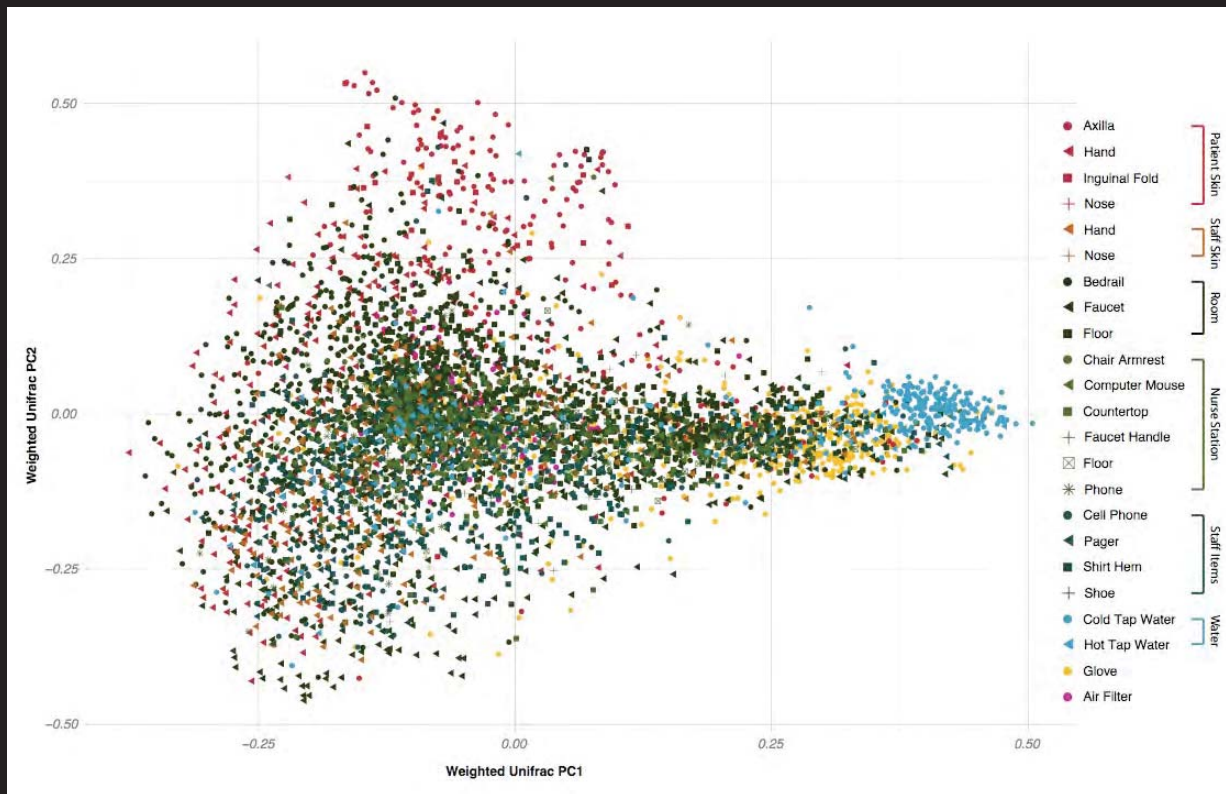


365 consecutive days: 2 months pre opening, and 10 months post opening

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

Lax et al., 2017

Genotypes of the same bacteria showed increased ARGs over time



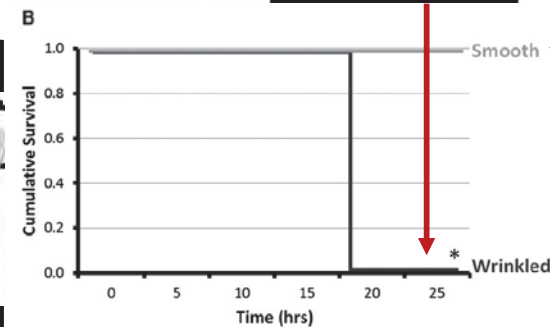
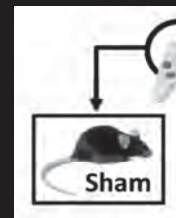
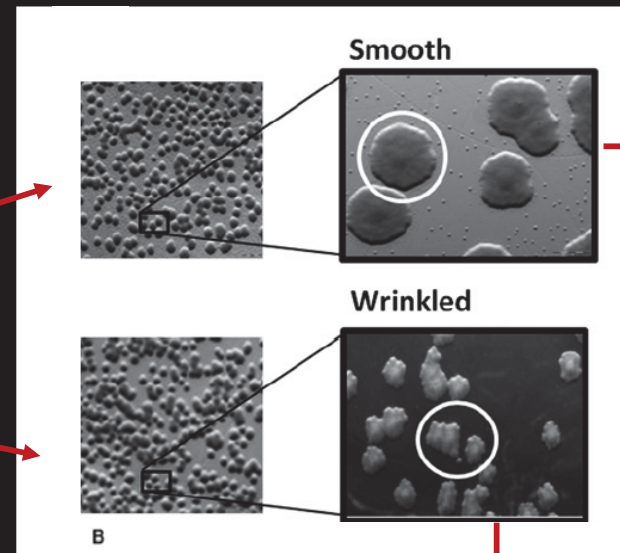
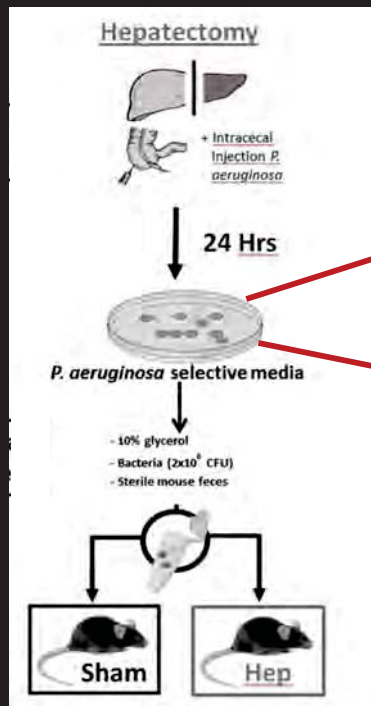
Staphylococcus, Propionibacterium, Anaerococcus and Corynebacterium had a consistently greater number of antibiotic resistance genes after 60 days of hospital environmental exposure

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



Surgical Infections

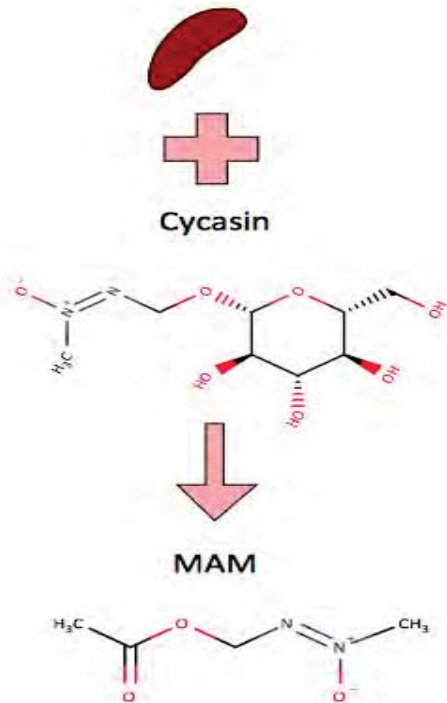
Within 24 hours, a lethal *P. aeruginosa* morphotype develops



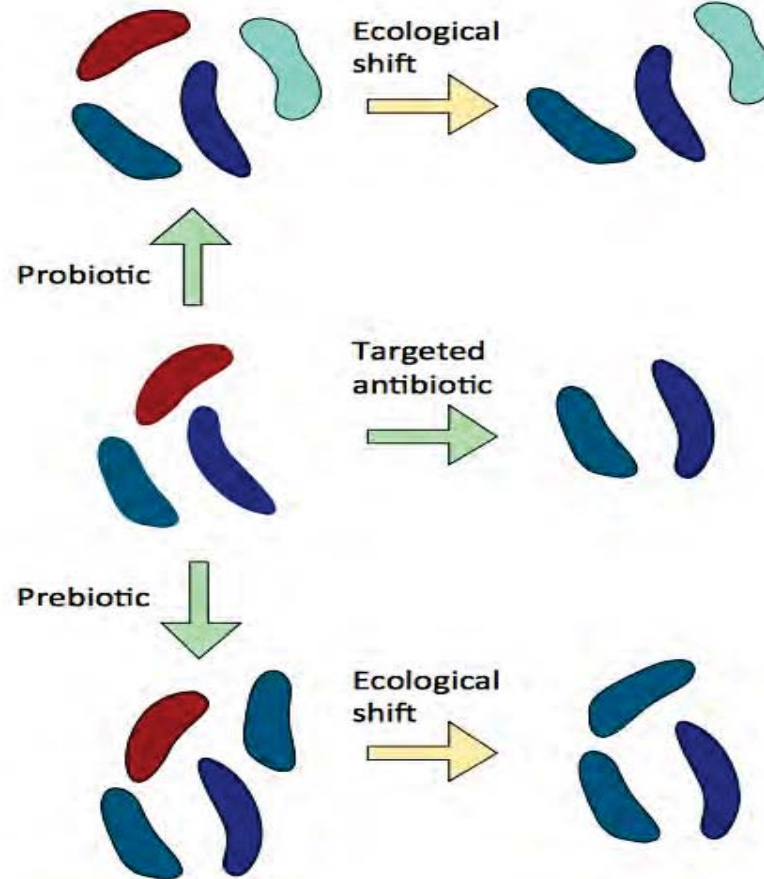
Microbial phenotype, shaped by the intestinal environment of stress, NOT bacterial species, NOT immune background- caused death in this model.



(A) *Metagenomic insight*



(B) *16S assay and diagnosis*



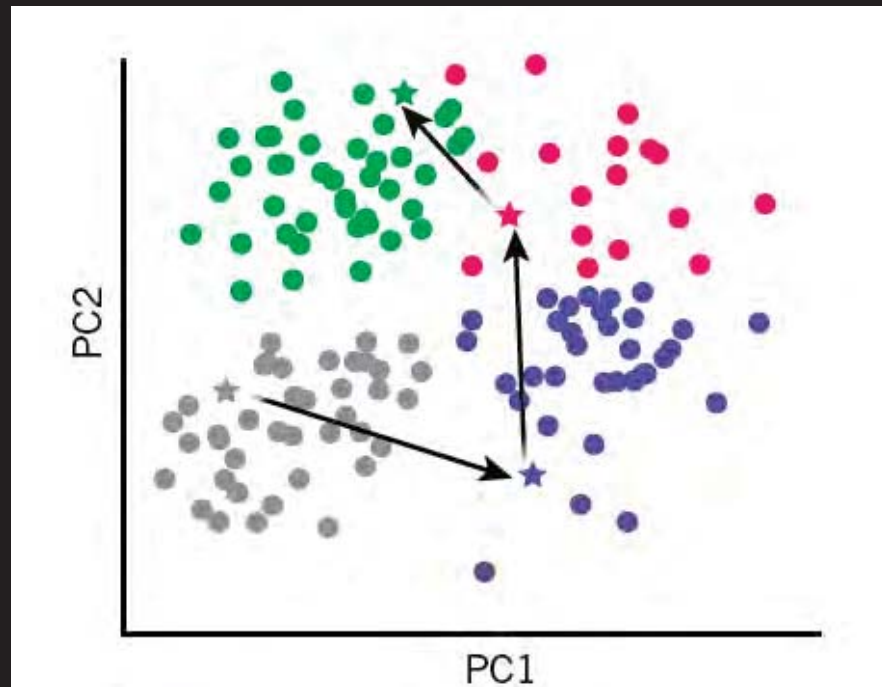
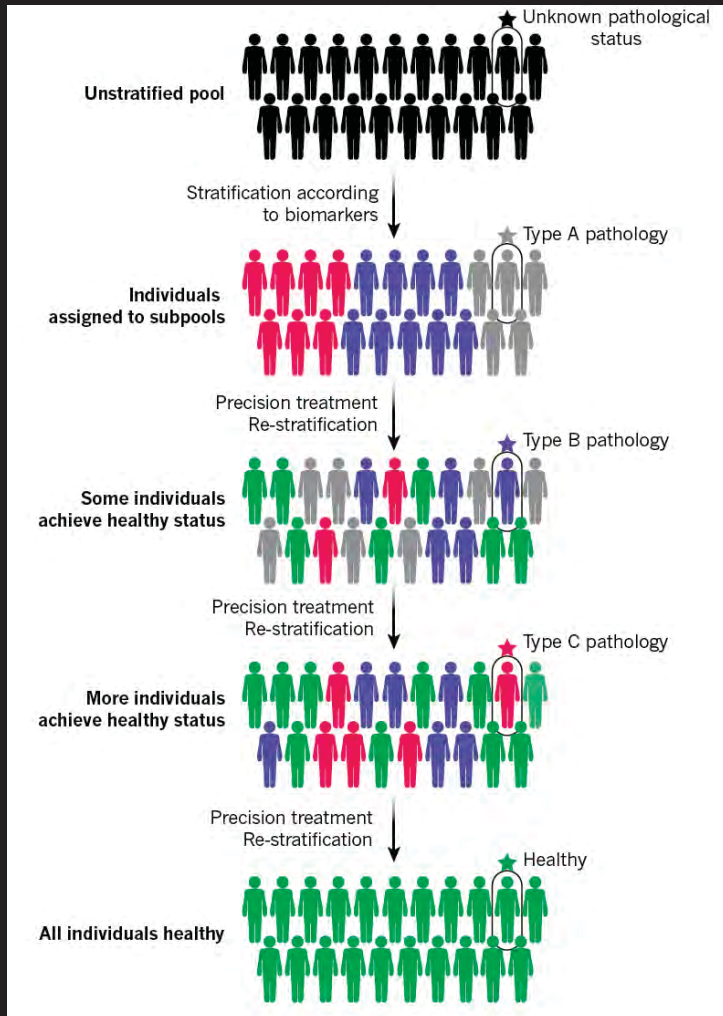
Microbiome and Precision Medicine

EXAMPLE:
Potential strategies to alter the gut to reduce the abundance of an organism that can metabolize cycasin to produce the carcinogen methylazoxymethanol (MAM)

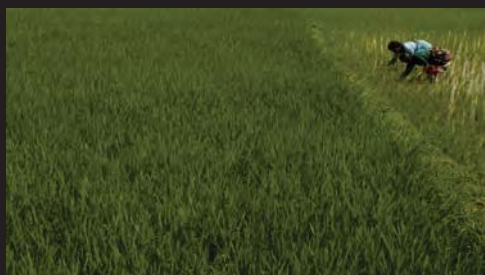
Kuntz & Gilbert, Trends in Pharmacological Sciences, 2016

Spatz et al, Proc. Soc. Exp. Biol. Med. 1967

Precision medicine using the microbiome



Gilbert et al., 2016 Nature



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