

Disappearing microbiota and epidemic obesity

Martin J Blaser, MD

Departments of Medicine and Microbiology
New York University School of Medicine
Langone Medical Center
Department of Biology, NYU



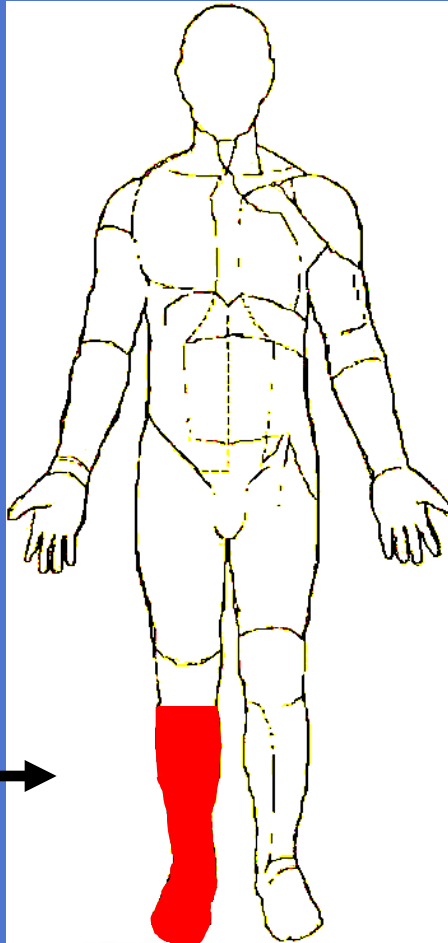


- **Ancient**
- **Niche-specific**
- **Persistent**
- **Conserved**
- **Host-Specific**

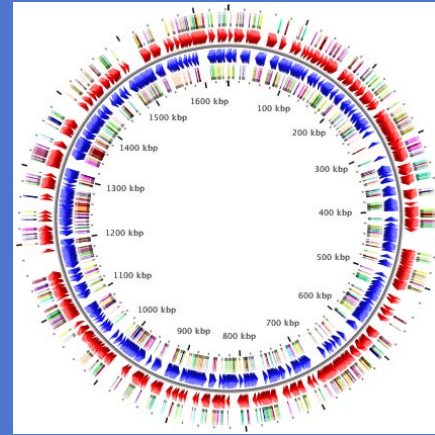
EMBO Rep 2006; 7: 956-960.

Who are we?

10^{14} microbial
← cells



10^{13} human
cells



n

GENOME

⇒ MICROBIOME

Metabolome

EMBO Rep 2006;7:956.

Nature 2007;449:843.

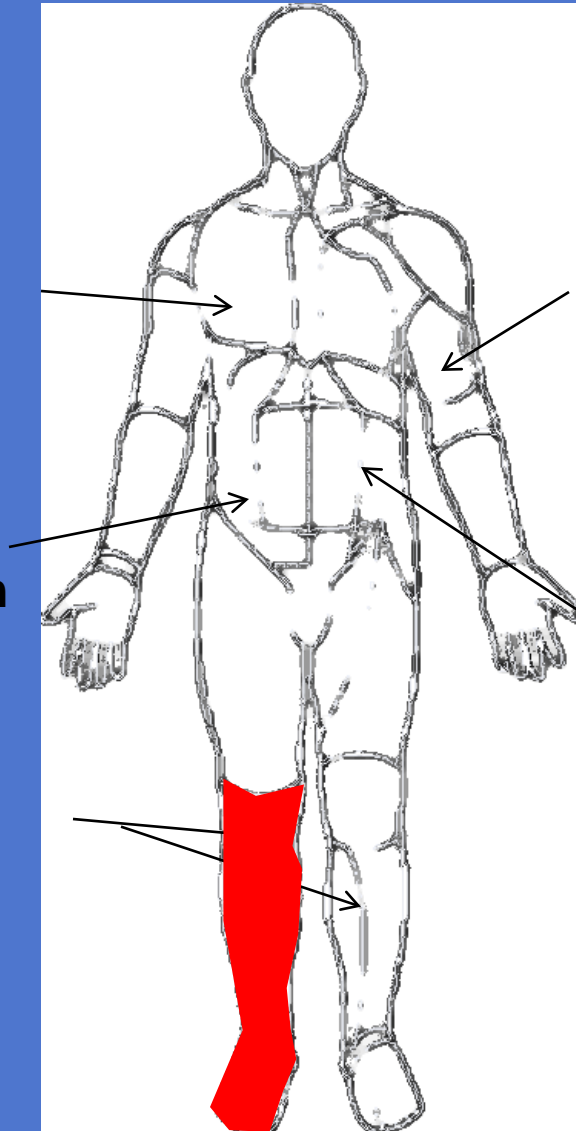
PNAS 2010; 107:6125.

Biological questions related to the human microbiome

2. What are these microbes doing?

4. What are the forces that maintain equilibrium among the populations?

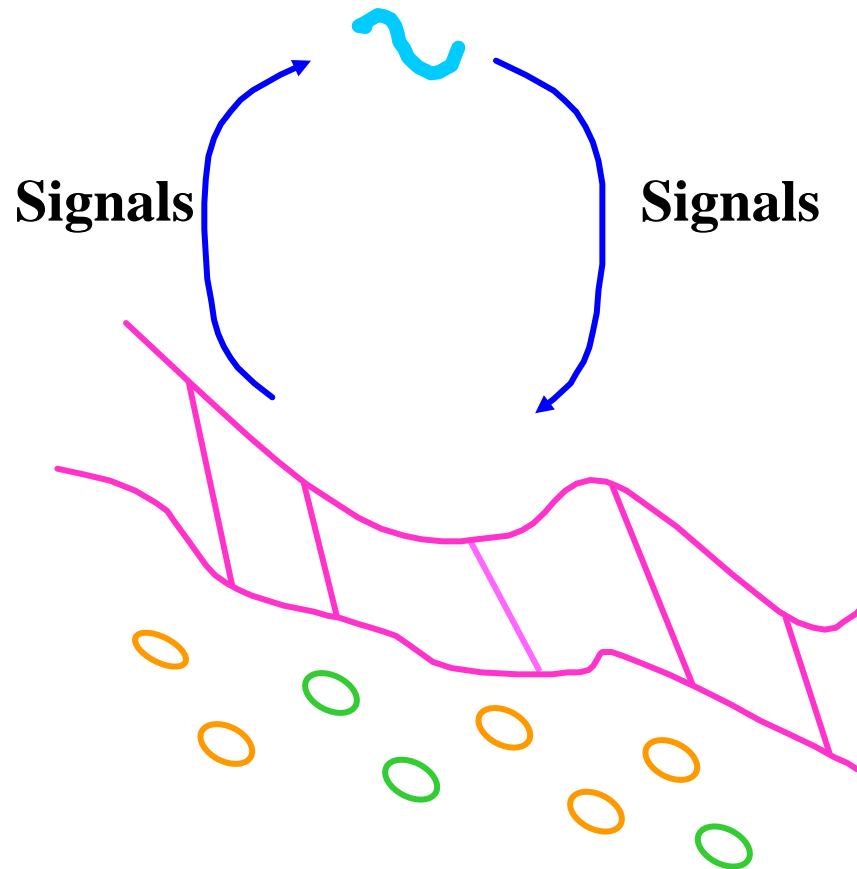
5. What are the unique characteristics of each individual?



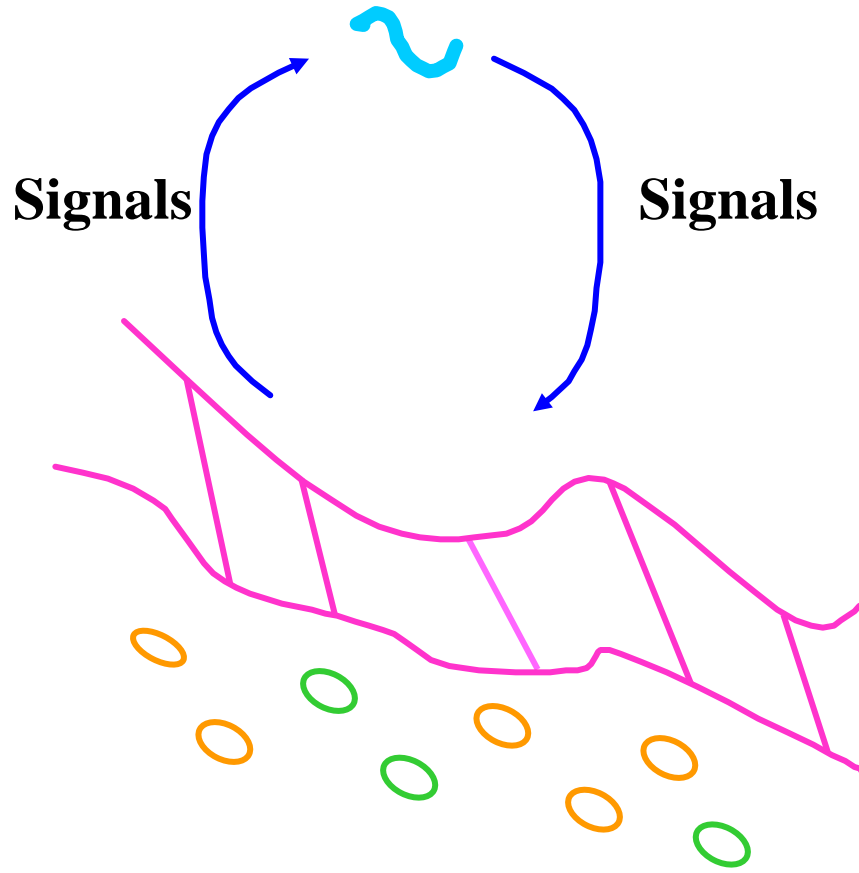
1. What is the identity of the microbes that populate their host?

3. How is the host responding to them?

Schematic of interaction between co-evolved colonizing microbe and host



Schematic of interaction between co-evolved colonizing microbe and host

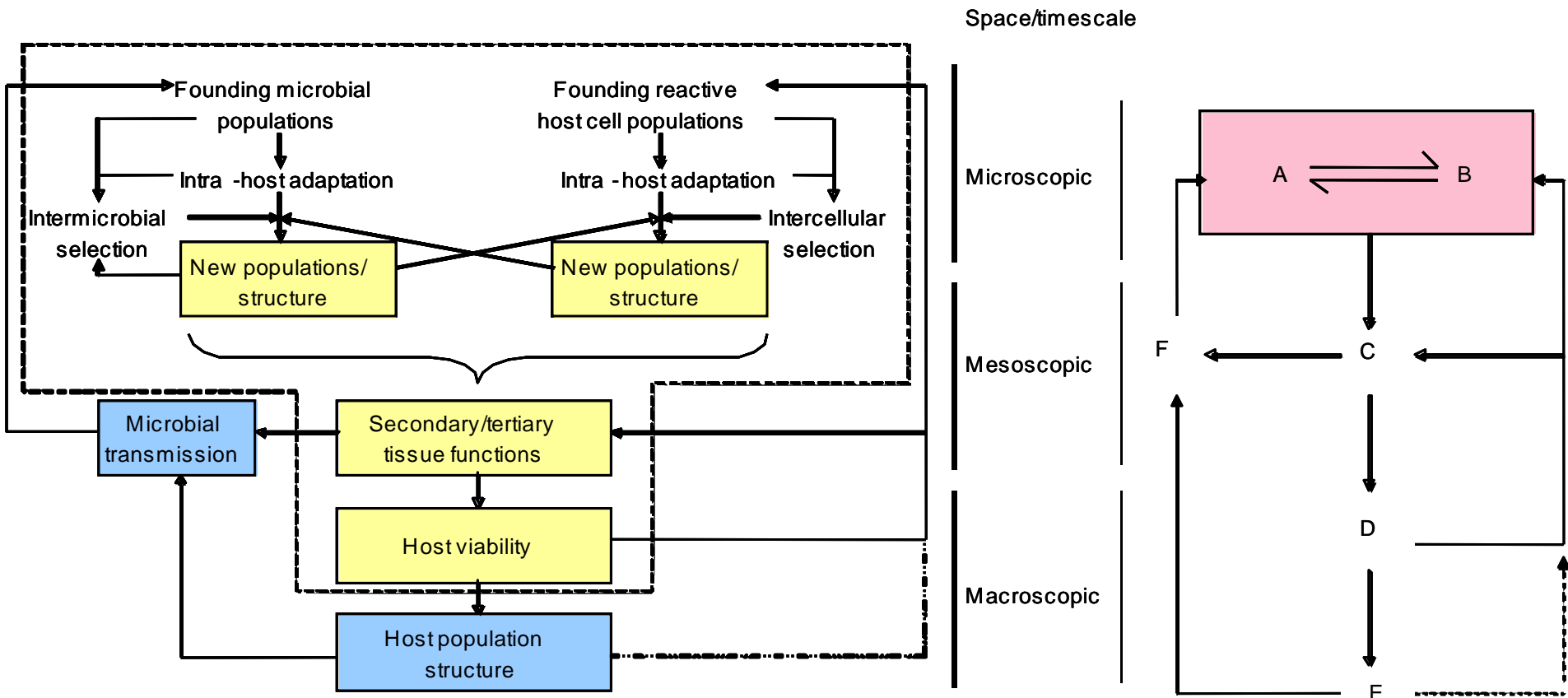


•Robust
•Resilient



Perturbation?

Relationships between co-evolved hosts and persistent microbes in a Nash equilibrium



The “Disappearing Microbiota” Hypothesis

- With changing human ecology beginning in the late 19th century, there have been dramatic changes affecting the transmission and maintenance of the indigenous microbiota.
- These changed circumstances have affected the composition of our indigenous microbiota.
- The changed composition affects human physiology, and thus disease risk.

EMBO Rep 2006; 7:956-60.

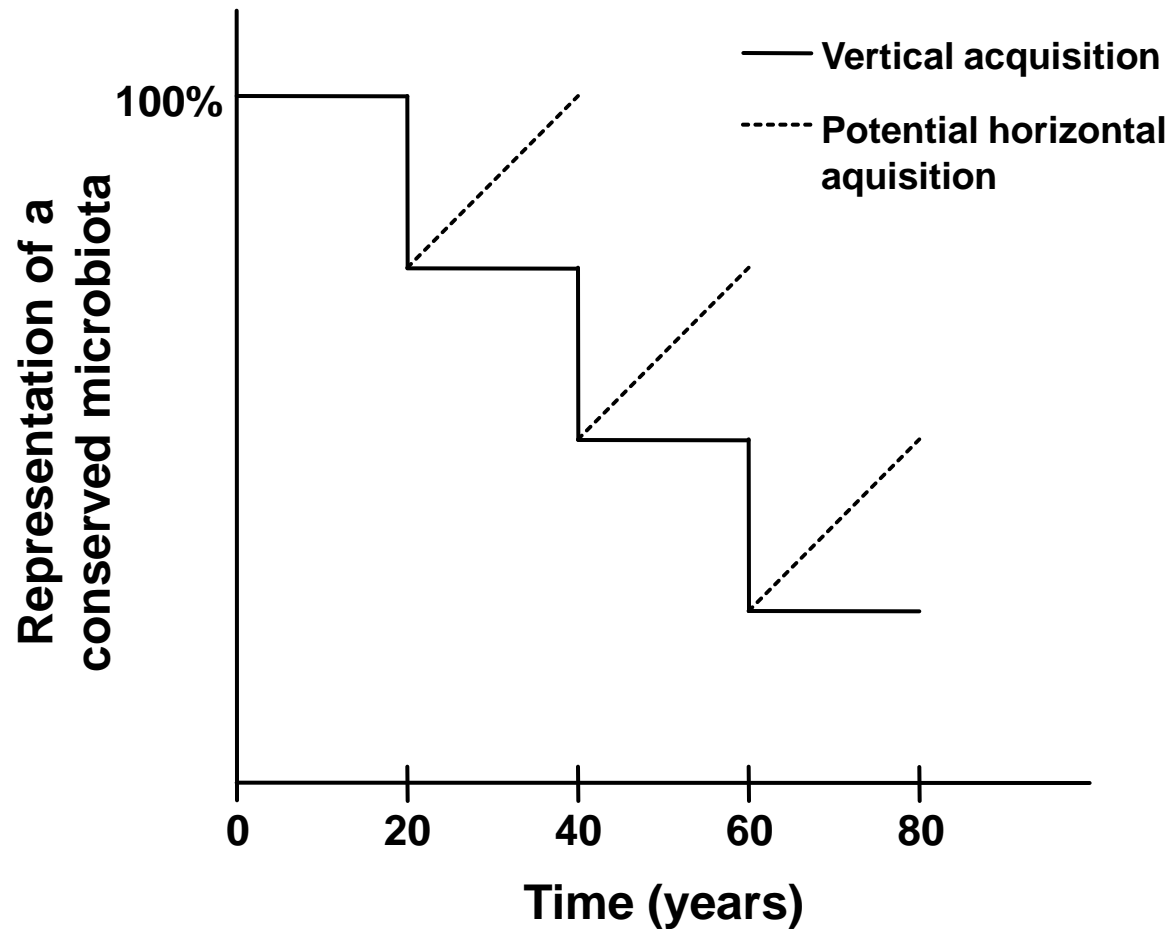
Can Prev Res 2008; 1:308-311.

Nature Rev Microbiol 2009; 7:887-94.

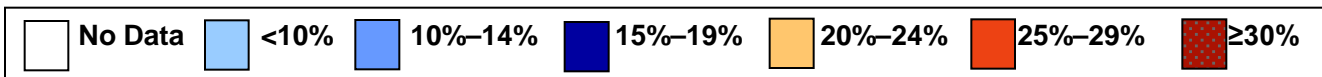
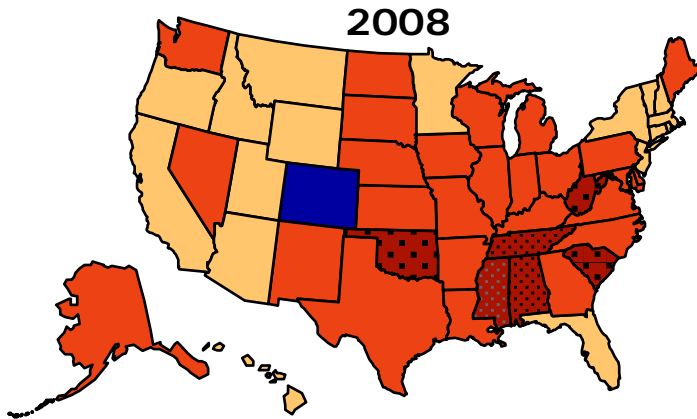
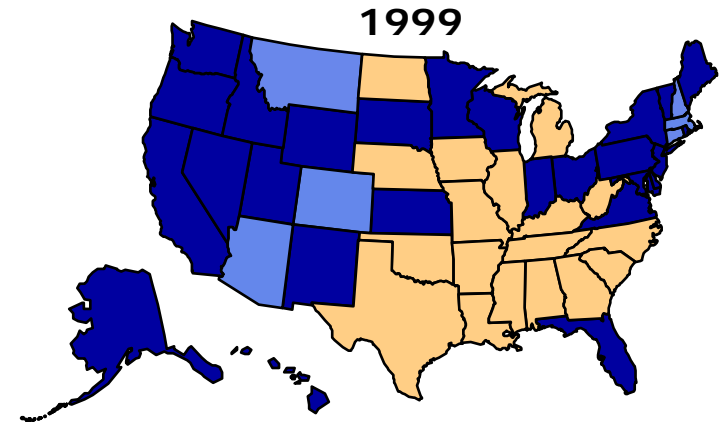
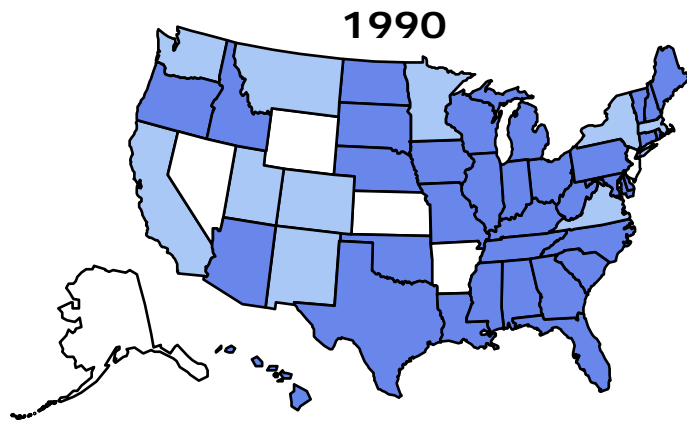
Examples of changes in human ecology that may affect microbial transmission

- Clean water
- Smaller families
- Caesarian section
- Formula feeding of infants
- Amalgam dental fillings
- Antibiotic use

The effect of maternal status on the resident microbiota of the next generation

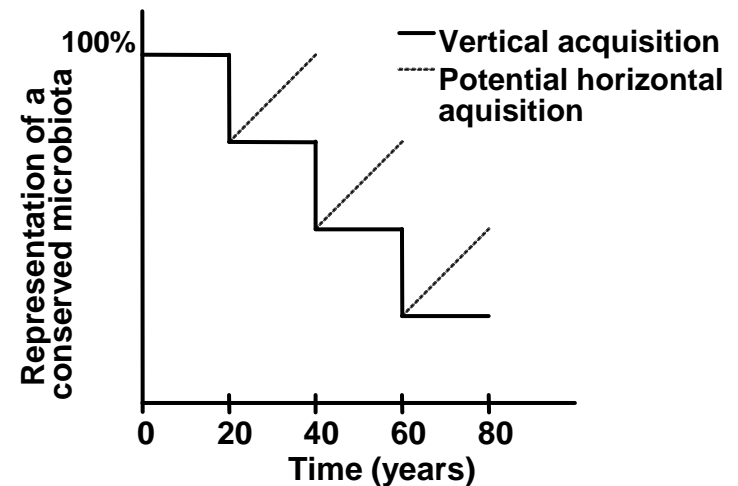
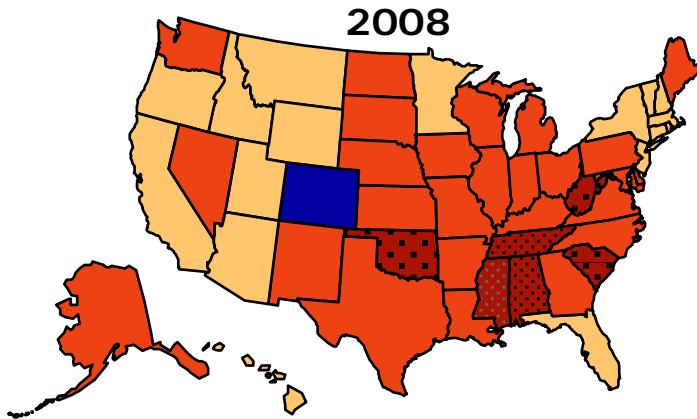
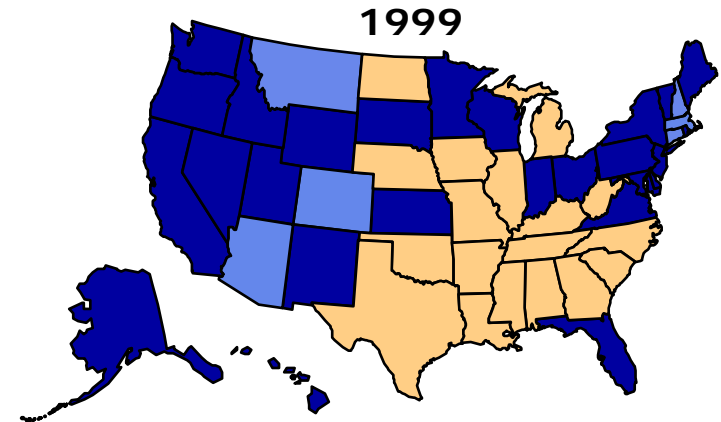
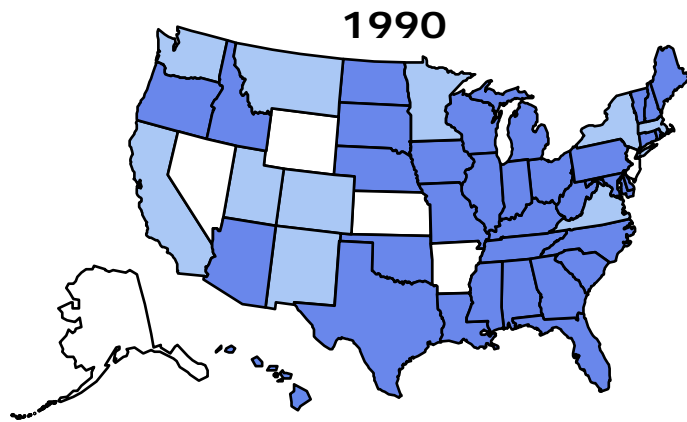


Obesity trends among US adults



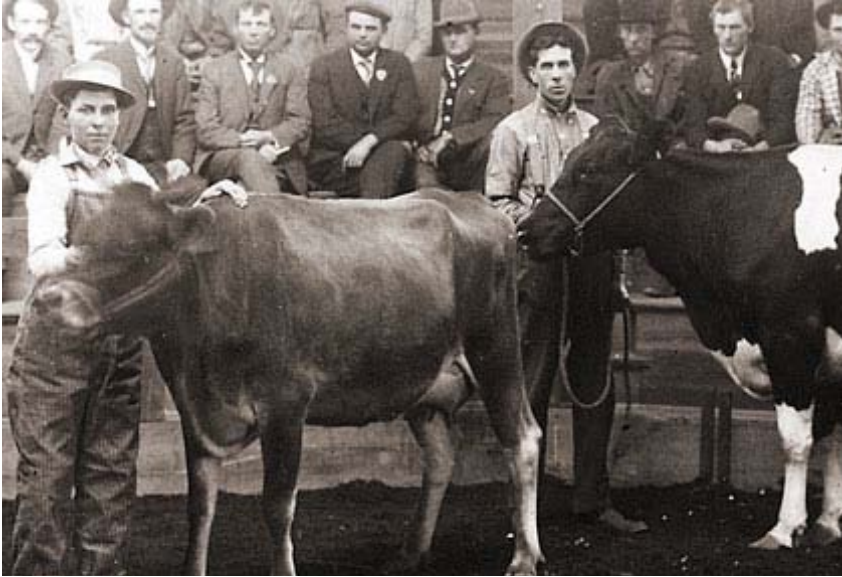
Source: CDC Behavioral Risk Factor Surveillance System

Is epidemic obesity related to a disappearing microbiota?

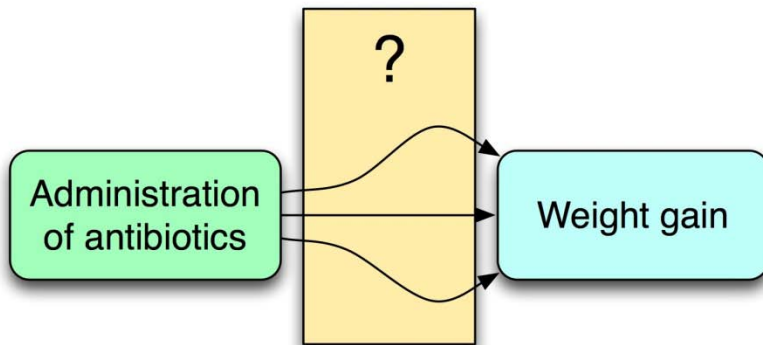




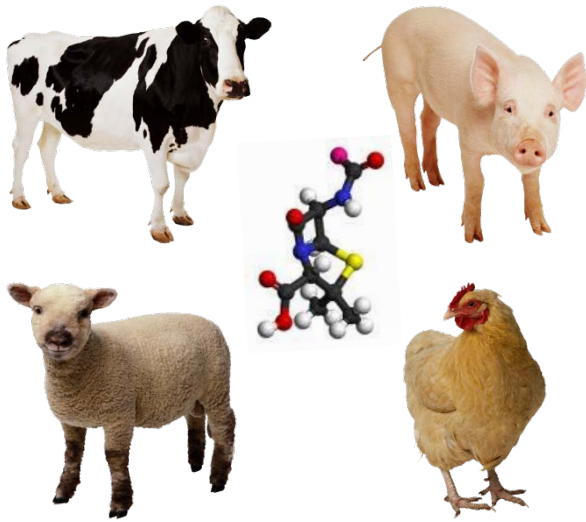
Use of antibiotics on the farm



- >50 years of antibiotic use for growth promotion
- Economically beneficial
- Low level exposure (subtherapeutic) is sufficient for effect
- Mechanism of action: unknown

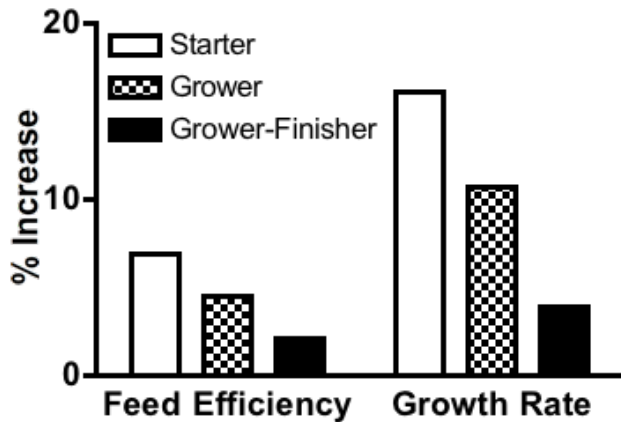


Sub-therapeutic antibiotic treatment (STAT) used in agriculture for growth promotion of livestock

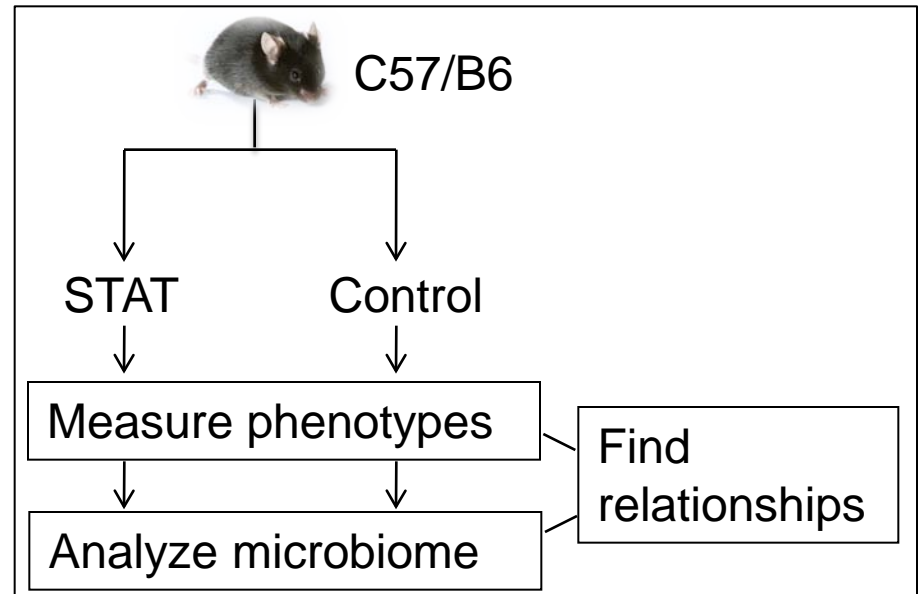


Antibiotic	Class	Target
Bambermycin	Glycolipid	Cell wall
Virginiamycin*	Streptogramin	Protein synthesis
Avilamycin	Orthosomycin	Protein synthesis
Bacitracin*	Cyclic peptide	Cell wall synthesis
Monensin	Ionophore	Cell membrane
Carbadox*	Quinoxaline	DNA Synthesis

Effect of STAT in Swine



(Adapted from Zimmerman, J Animal Sci, 1986)



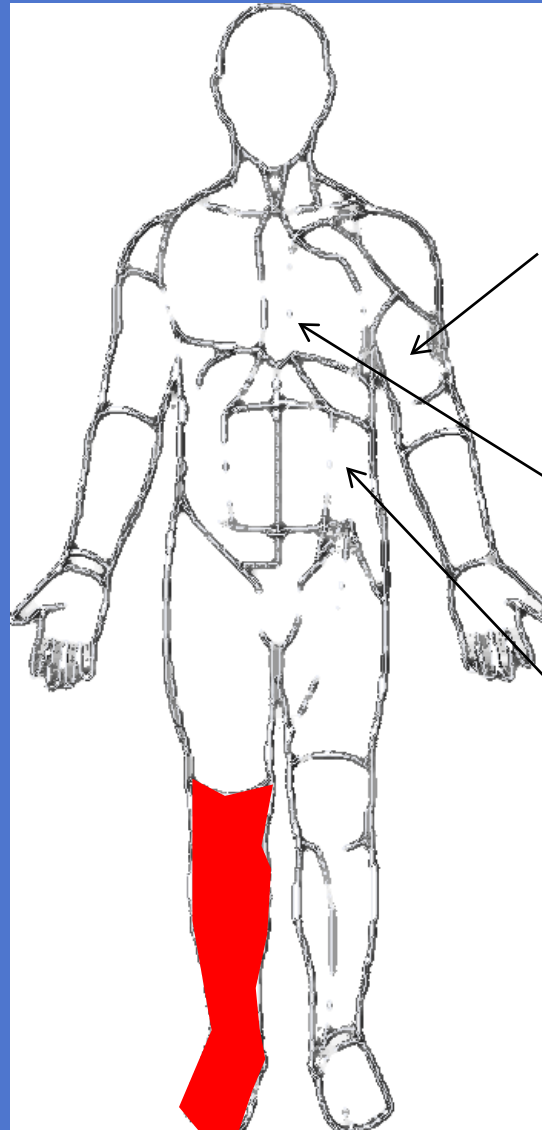
Biological questions related to the human microbiome



Ilseung Cho



Laurie Cox



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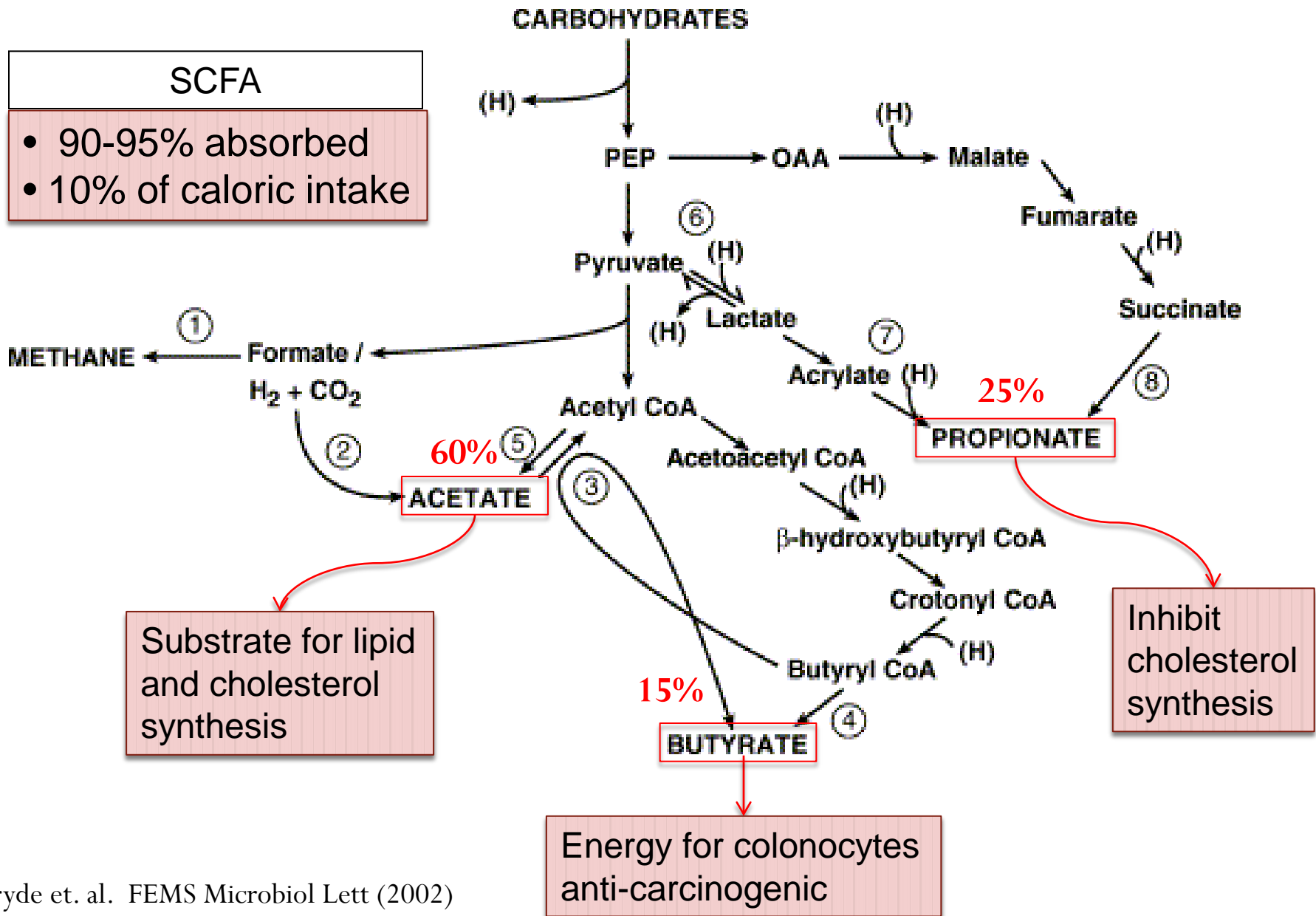
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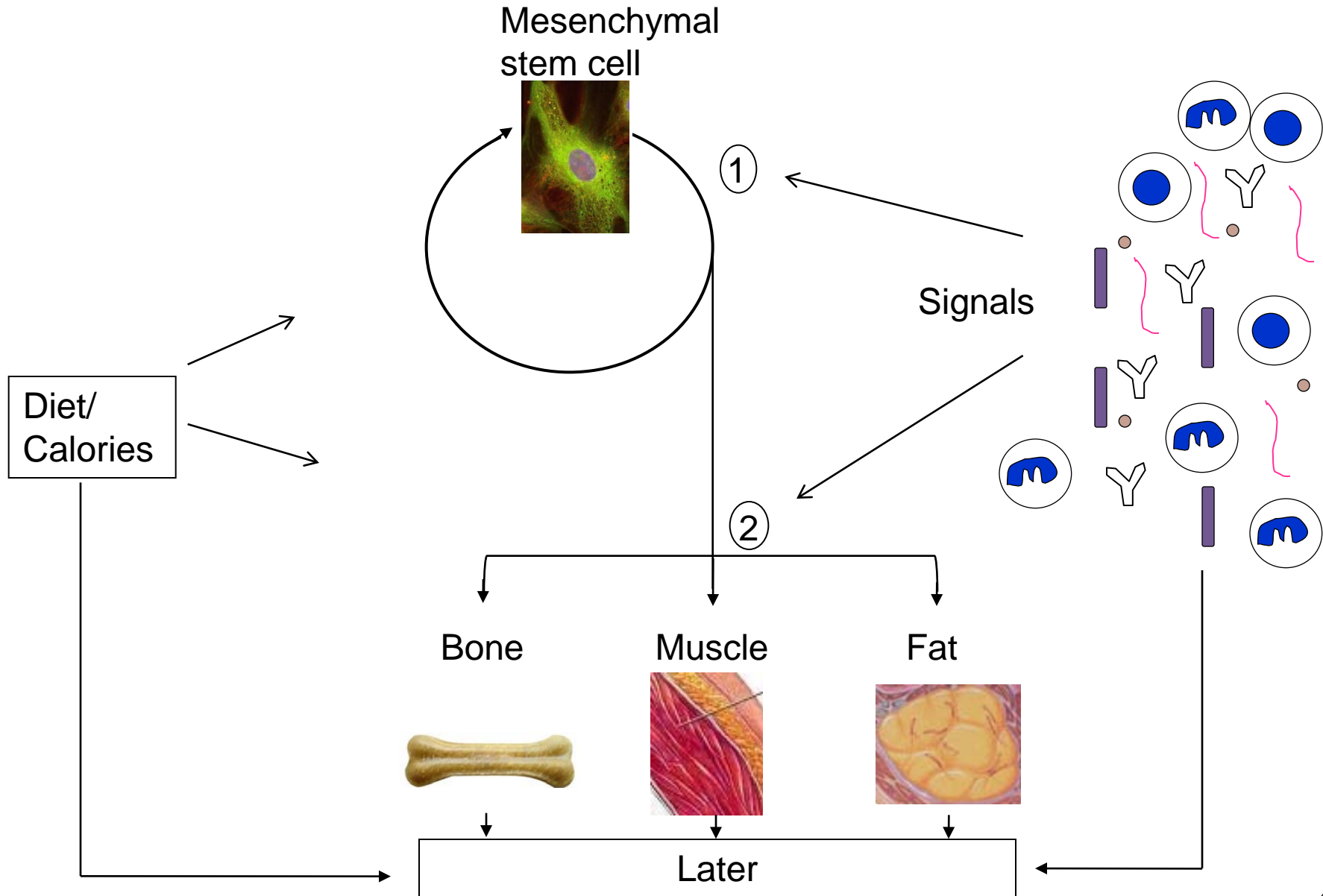
Antibiotics as:

- agents of change?
- probes of physiology?

Short chain fatty acid production in the large intestine

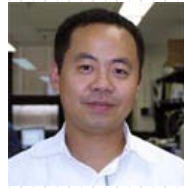


A model of early life development



STAT Research Team

Ilseung Cho



Laurie Cox



Shingo Yamanishi



Zhan Gao

Alex Alekseyenko

Barbara Methe

Jiri Zavadil

Yael Nobel

Mouse Care

Minso Kim, John Hwang
Mahak Jain, Doug Mahana,

MRI

Sungheon Kim

*Supported in part by 1UL1RR029893 from the
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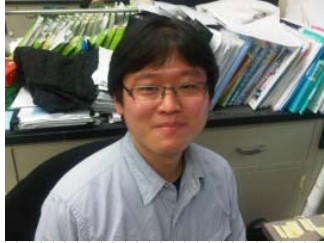


Langone Medical Center

Differences in the theoretical constructs of the hygiene and disappearing microbiota hypotheses

Criterion	Hygiene	Disappearing microbiota
Relevance of environmental exposures		
Farm animals	High	Nil
Pets	High	Nil
Soil and dirt	High	Nil
Other children	Moderate	High
Mother	Nil	High
Father	Nil	Moderate
Relevance of antibiotic use	No	High
Ability to define critical players	Difficult	Definable
Evolutionary basis	?	High

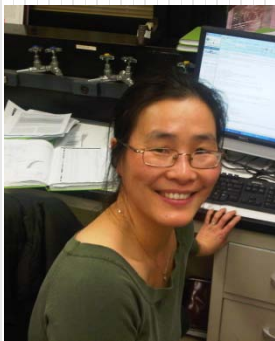
Posters at IHMC, Vancouver



Shingo Yamanishi-Regulation of hepatic metabolism in mice exposed to sub-therapeutic antibiotic treatment (STAT).

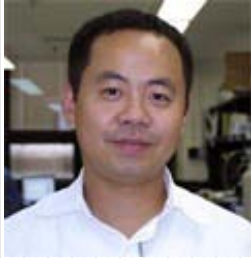


Laurie Cox-Cholesterol-lowering dietary fiber perturbs murine intestinal microbiota.



Zhan Gao-*E. coli* strains from South American hunter-gatherers living in isolated villages.

Posters at IHMC, Vancouver



Ilseung Cho-Variable recovery of the major phyla of the gut microbiome after colonoscopy bowel preparation.

Proton pump inhibitors significantly alter the taxonomic composition and butyrate metabolic capacity of the colonic microbiome.



Alex Alekseyenko-Analysis of high-throughput 16S community sequencing data in R.