

Microbiome & Metabolomics

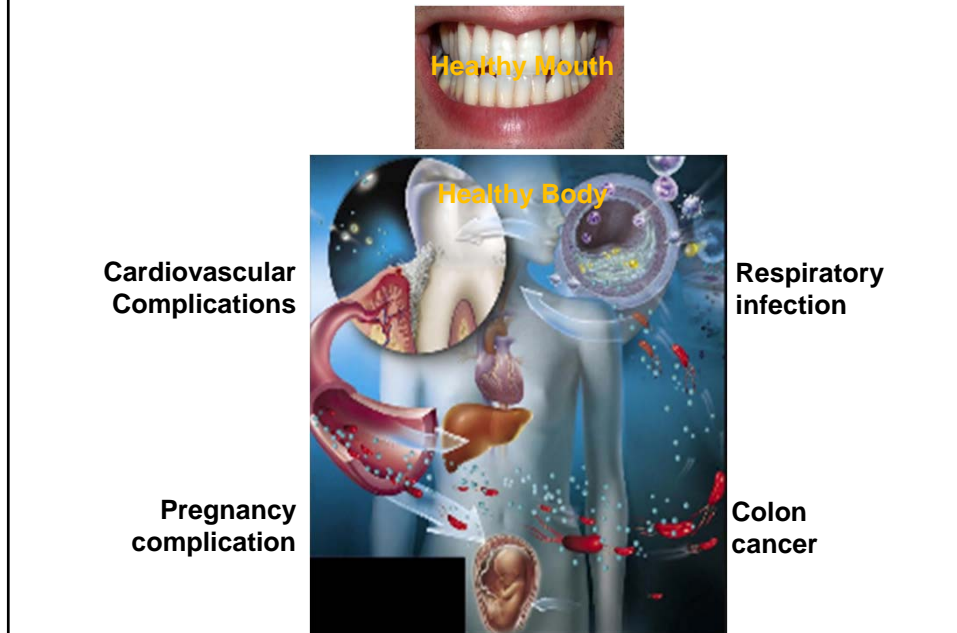
Hui Wu, PHD

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University of Alabama at Birmingham

Outline

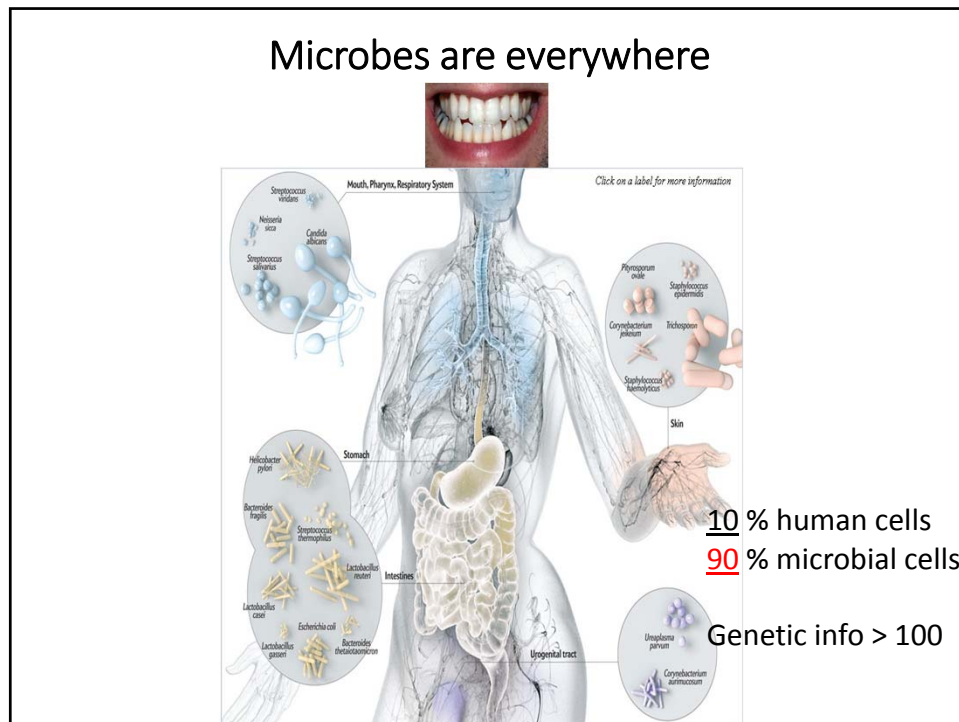
- **Microbe rules the world**
- **Microbial product matters**
- **Examples of microbiome in health and disease**
- **Examples of metabolites in health and disease**
- **Metabolites-mediated bacterial interactions**

Microbial infection and systemic disease



Complex microbial communities-dental plaque





The Human Microbiome Project

- Microbial components of the human genetic and metabolic landscape, and how they contribute to health and disease
- The genomes of microbial symbionts provide traits that humans did not need to evolve on their own
- Humans, a composite of microbial and human cells
- Human genetic landscape dictated by the genes in the human genome and the microbiome
- Human metabolic features, a blend of human and microbial traits

A human 'supraorganism'

Nature **449**, 804-810, 2007

The Human Genome Project

The project funded by the US government in 1990, and declared complete in 2003.

A parallel project by the Celera Genomics in 1998.

Capacity-3 billion bps

Major advance in DNA sequencing

versus **the Human Microbiome Project**

Microbiome Analysis-microbial profiling/genomics



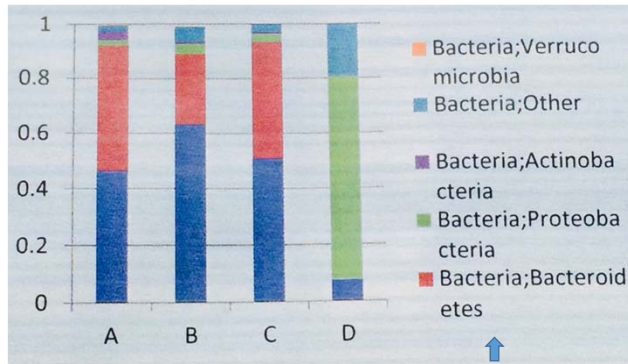
Plaque or saliva



PCR with bar coded primers specific for 16S rDNA region for amplification

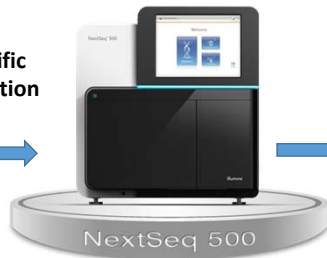


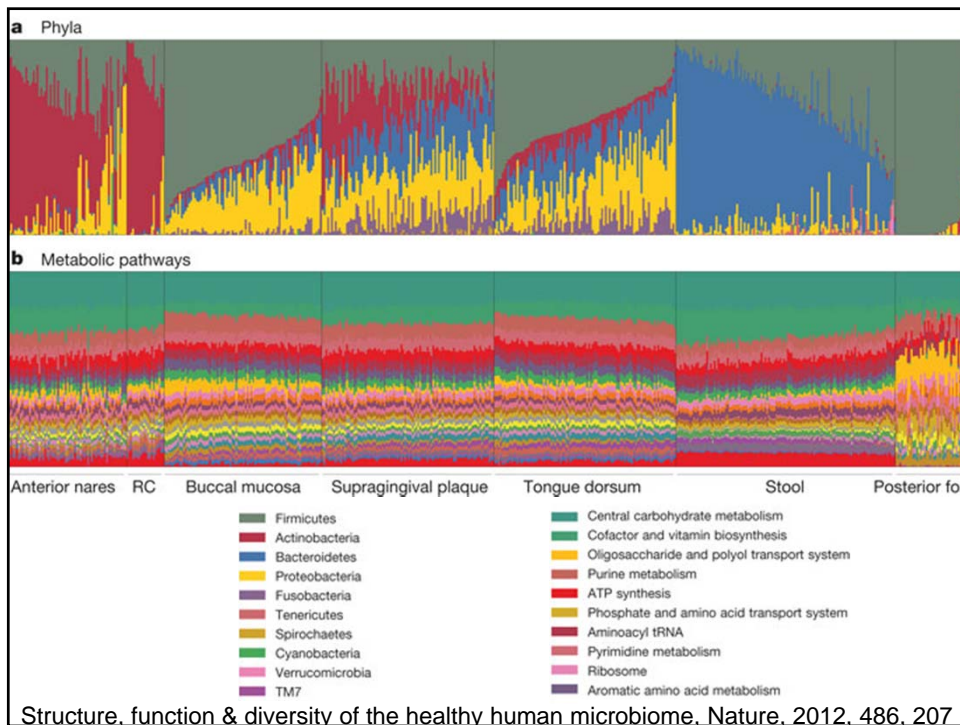
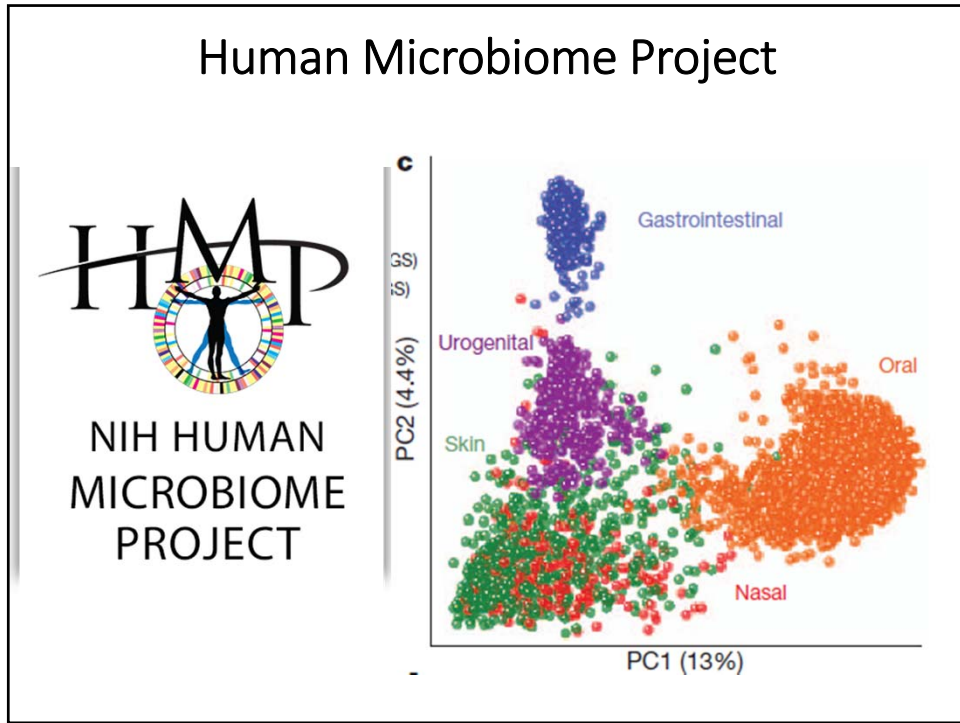
Metagenomics

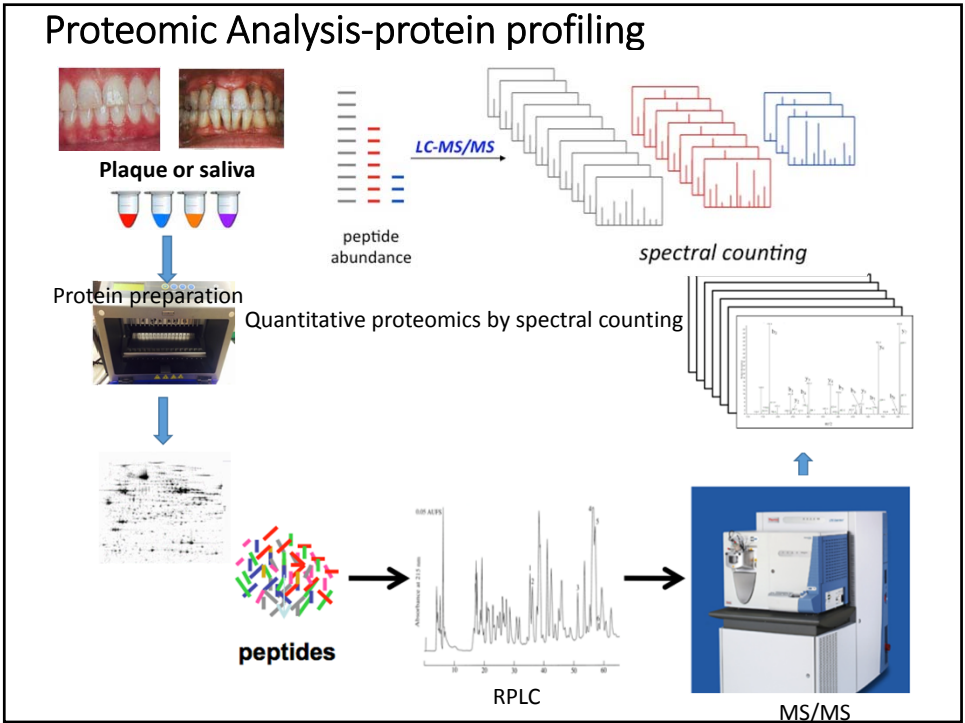
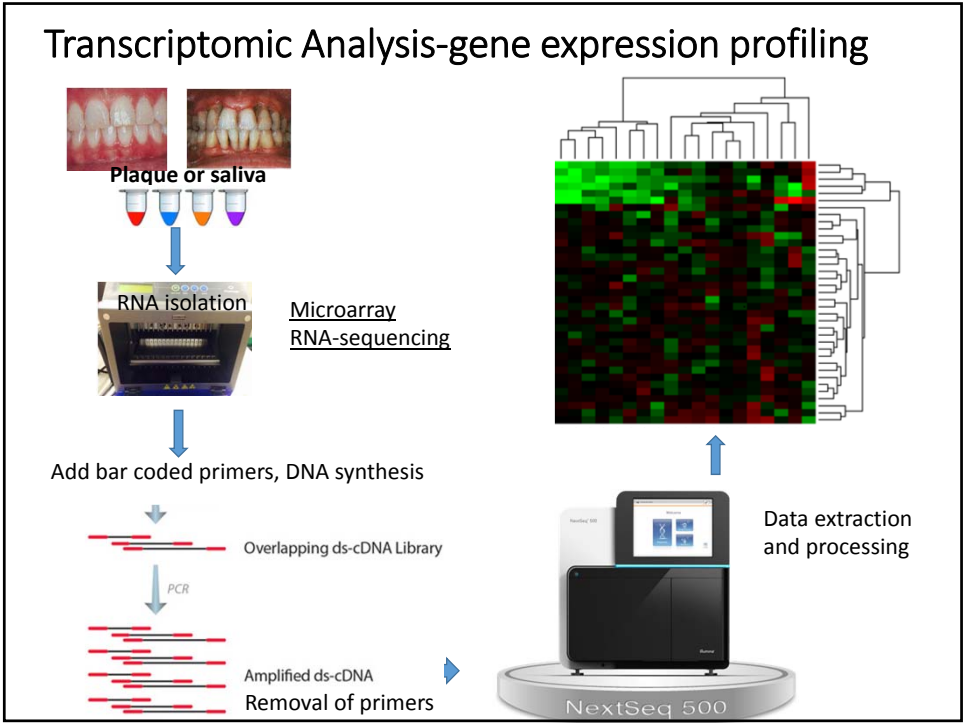


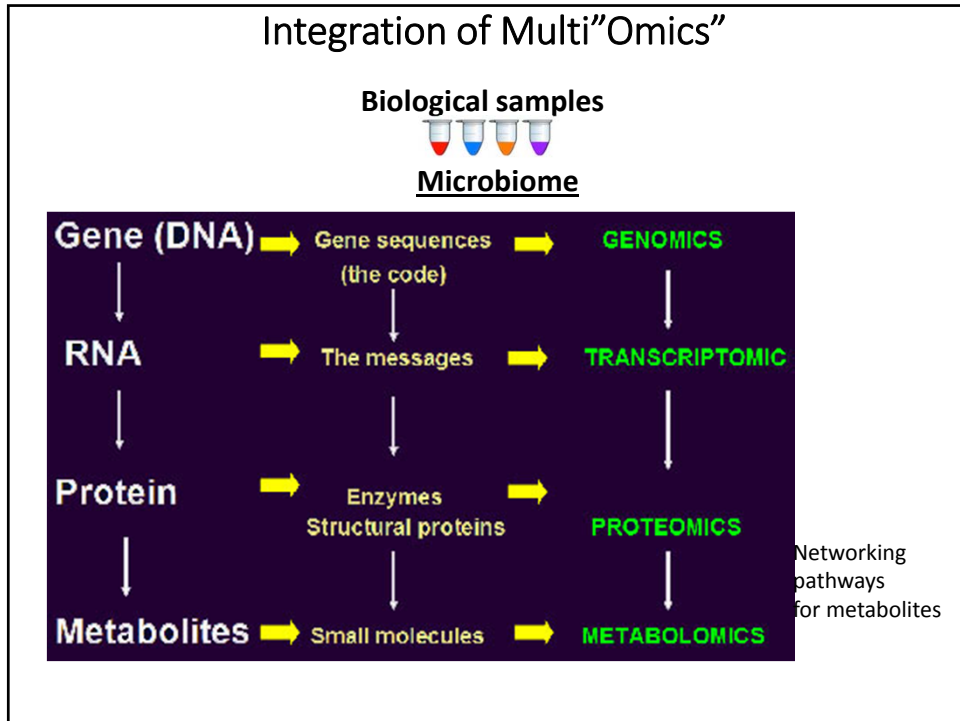
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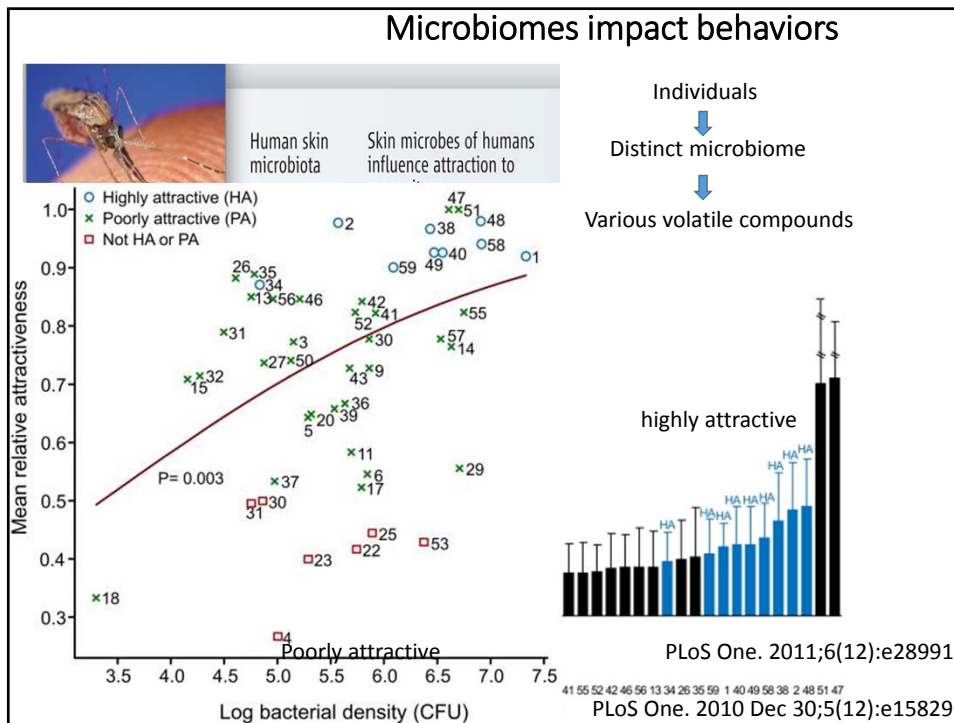
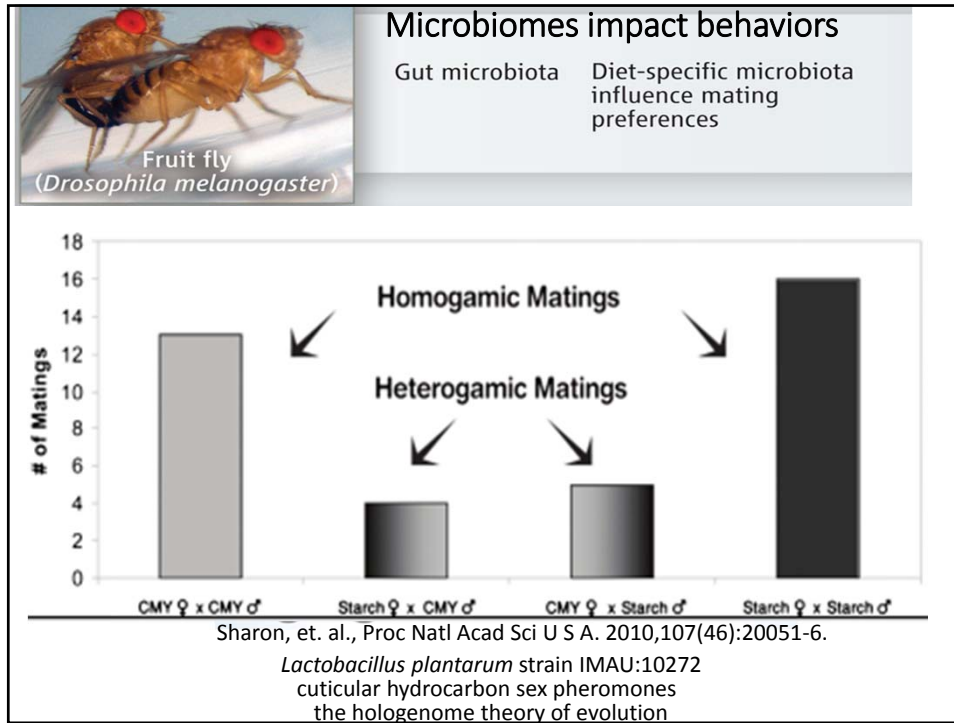


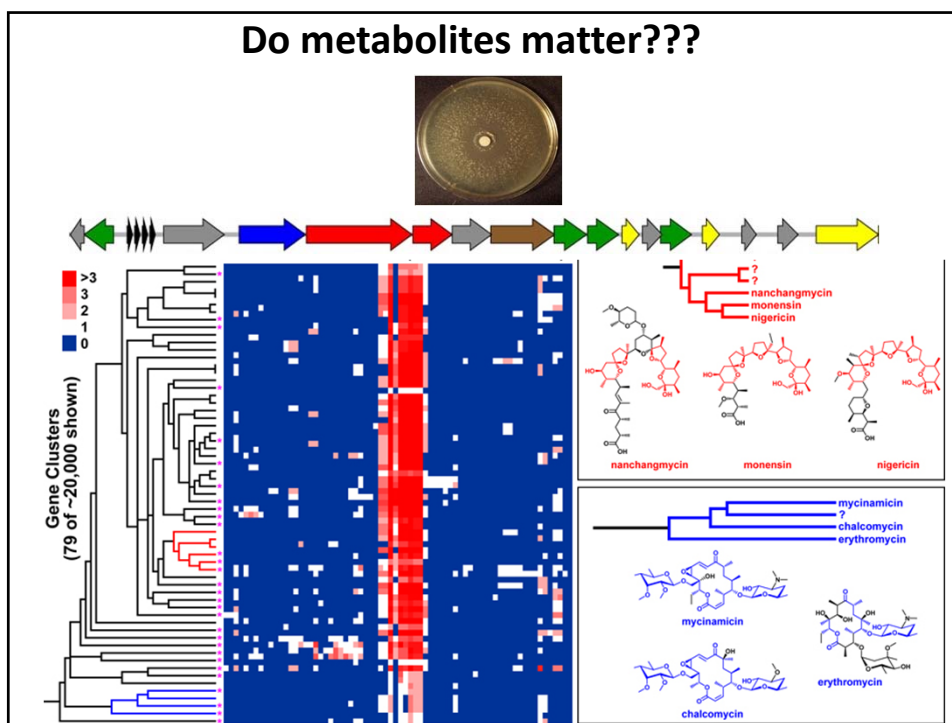






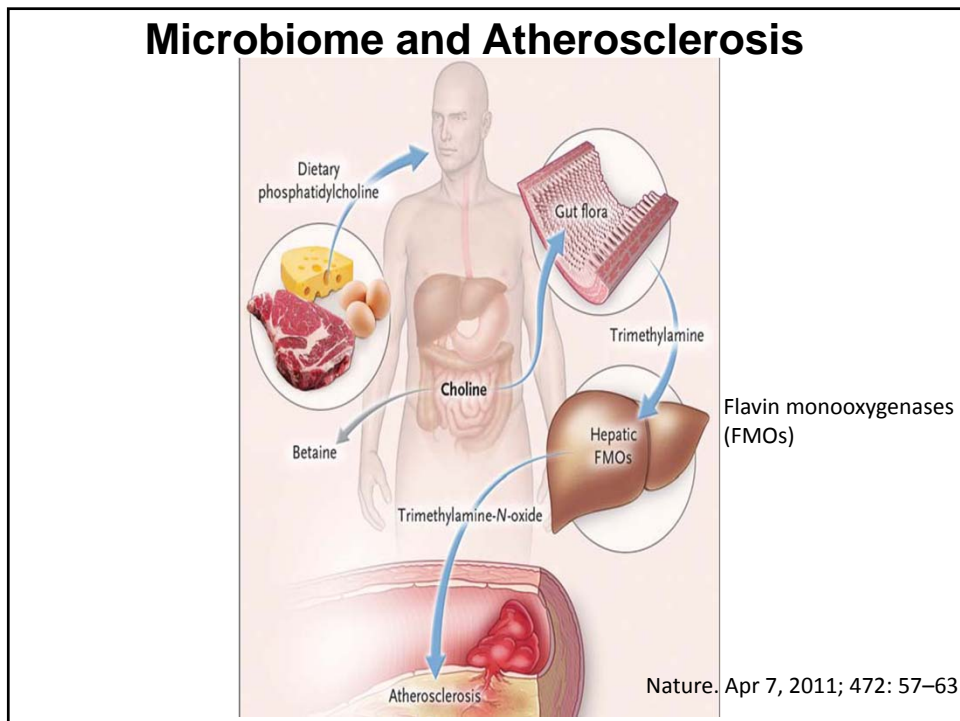
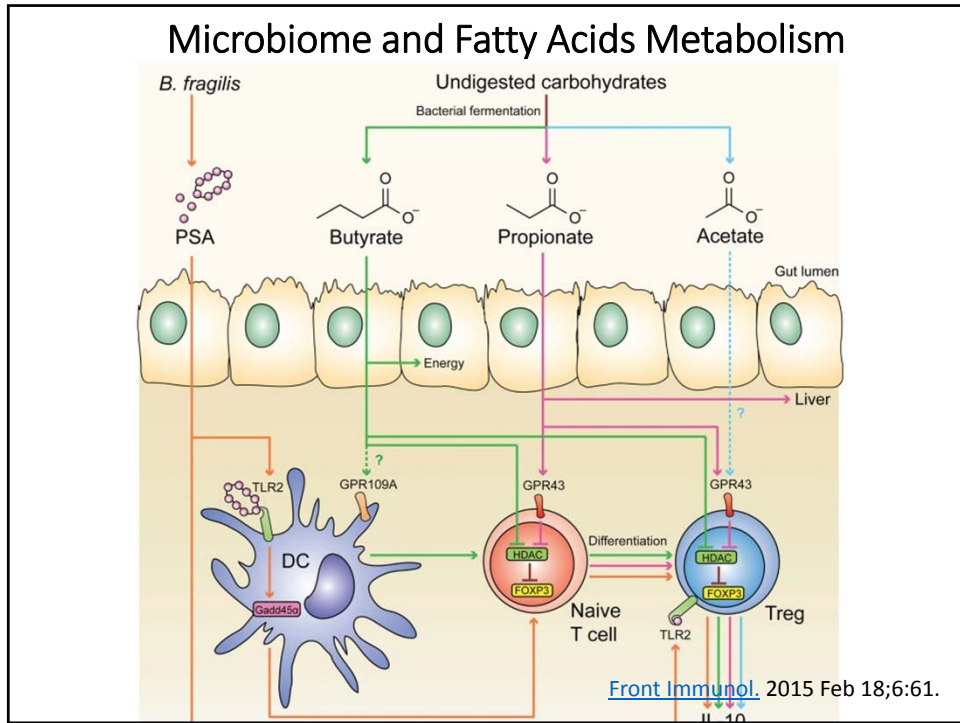
Microbiomes impact behaviors	
 Fruit fly <i>(Drosophila melanogaster)</i>	Gut microbiota Diet-specific microbiota influence mating preferences
 Mosquito <i>(Anopheles gambiae)</i>	Human skin microbiota Skin microbes of humans influence attraction to mosquitoes
 Mouse	<i>Lactobacillus rhamnosus</i> The probiotic <i>L. rhamnosus</i> decreases anxiety in mice <u>Fighting microbes or Farming microbes?</u>

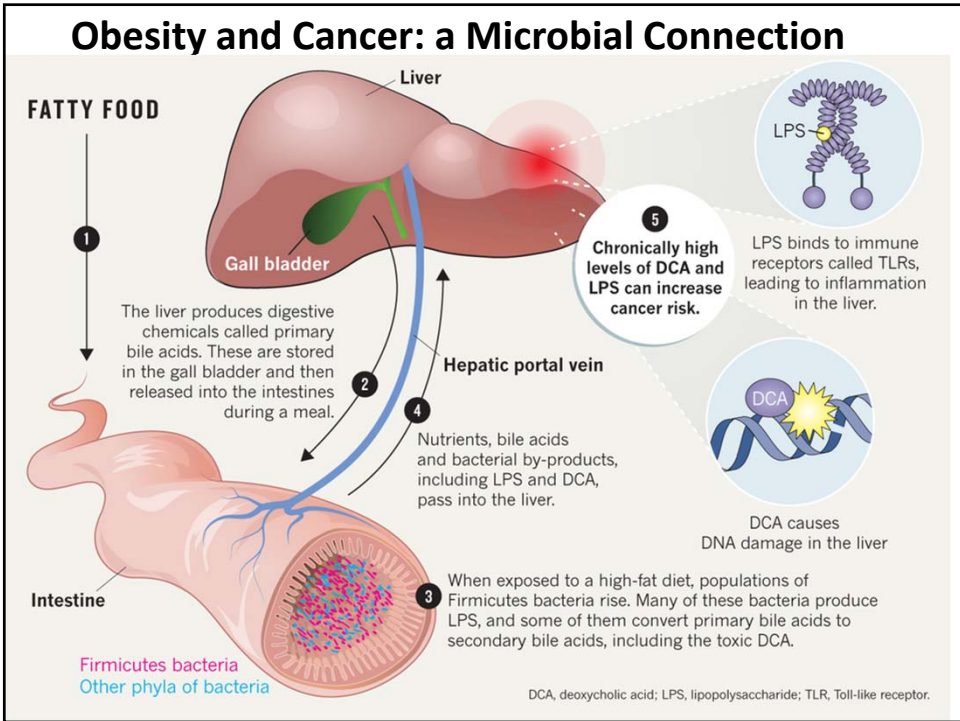
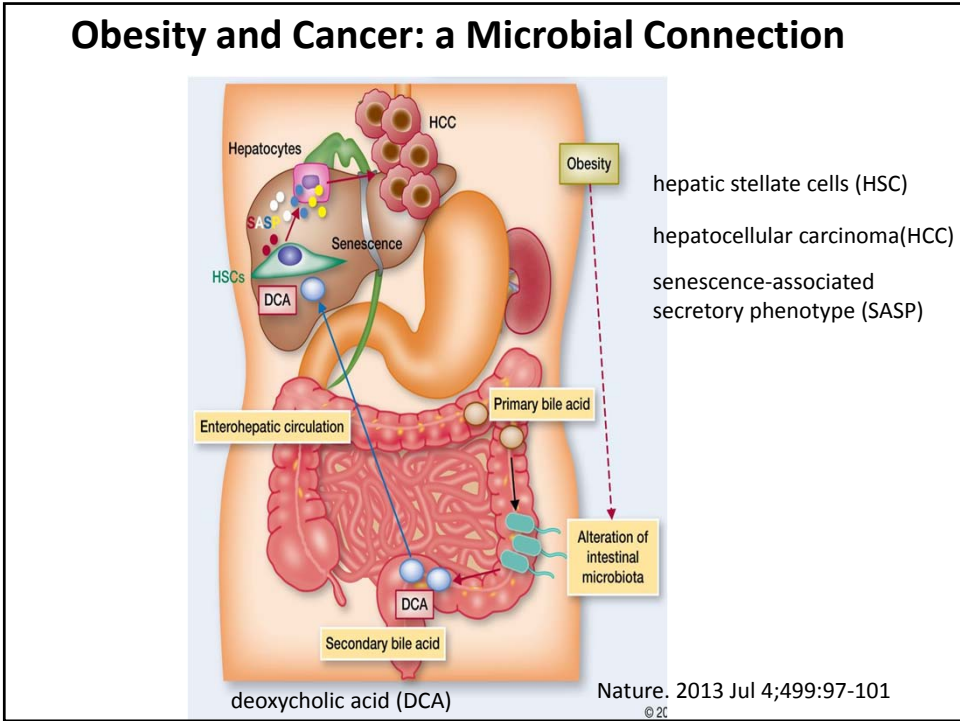


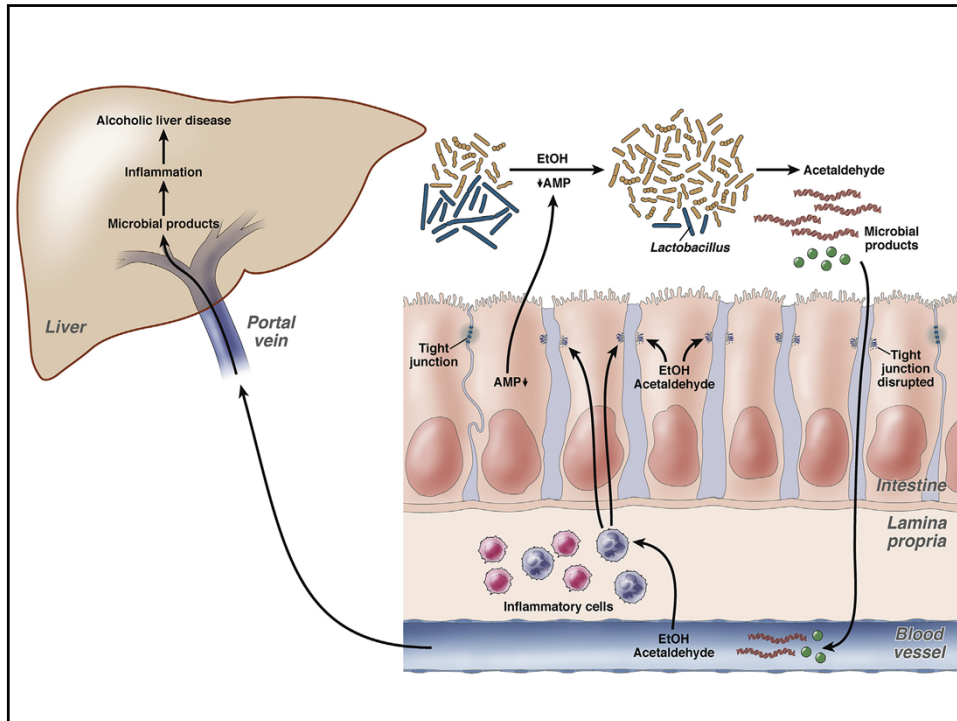


Microbiome and Carb Metabolism

- **Carbohydrates:** humans and bacterial nutrients
- **Human and mammals:** disaccharides and starches
- **Microbes:** complex polysaccharides by Carohydrate-active enzymes: glycoside hydrolases, carb esterases, glycosyltransferases and polysaccharide lyases
- **Biogeographical distribution of microbiome/ genes/pathways** such as simple Carb transport PTS small intestine>colon
- **Probing** microbe altered pathways in the development of metabolic disorders in humans







Gut Bacteria and the Workings of Our Minds

Of Humans
MRI scans to look at the brains
the types of bacteria in their guts

Of Mice
Changes gut microbiota alter mouse behavior
Bold to timid, brain-derived neurotrophic factor

Probiotics alters brain activity
Gastroenterology, 144, 1394–1401. June 2013
Cell, 155,1451–63, 19 December 2013

Gut Bacteria & Healthful Chocolate



Cocoa powder (polyphenols and Fibers)

Smaller molecules
short fatty chain acids

2014 American Chemical Society meeting



Gut Microbes and Your Weight

Slimming gut microbes?

Microbe transplants from obese humans



Science, 6 September 2013: **341(6150)**

Oral bacteria in systemic conditions

Fusobacterium nucleatum

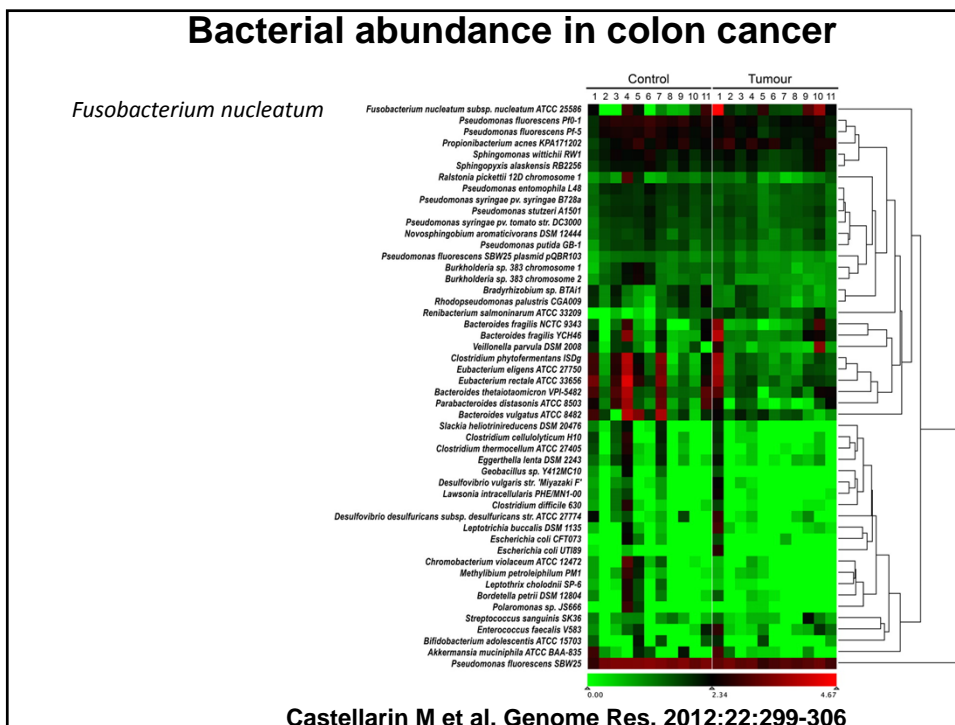
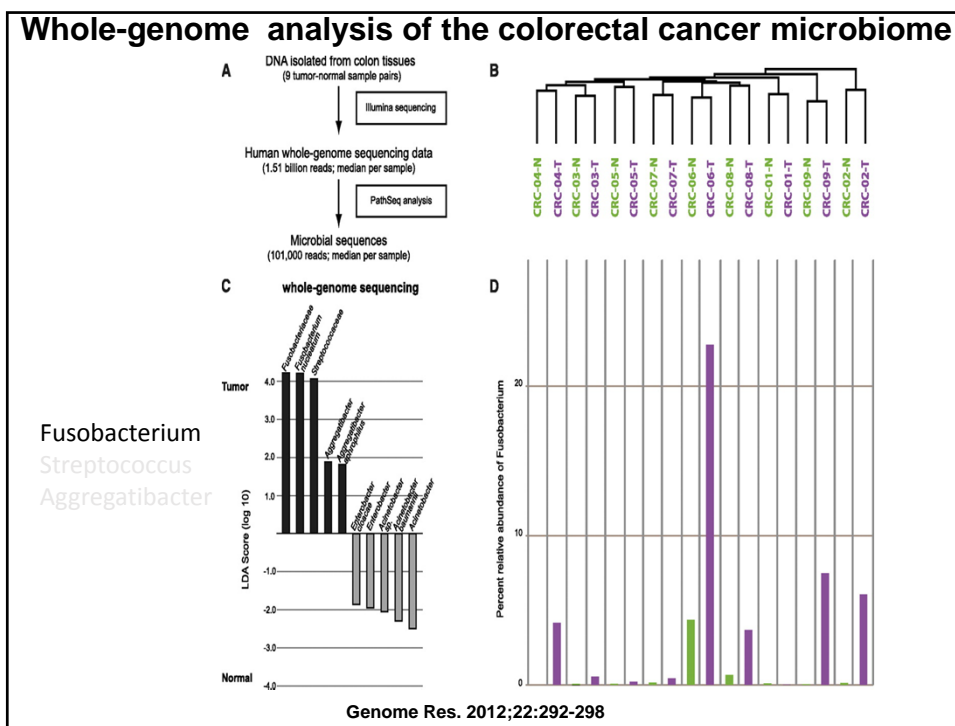
Fusobacterium & Colon Cancer

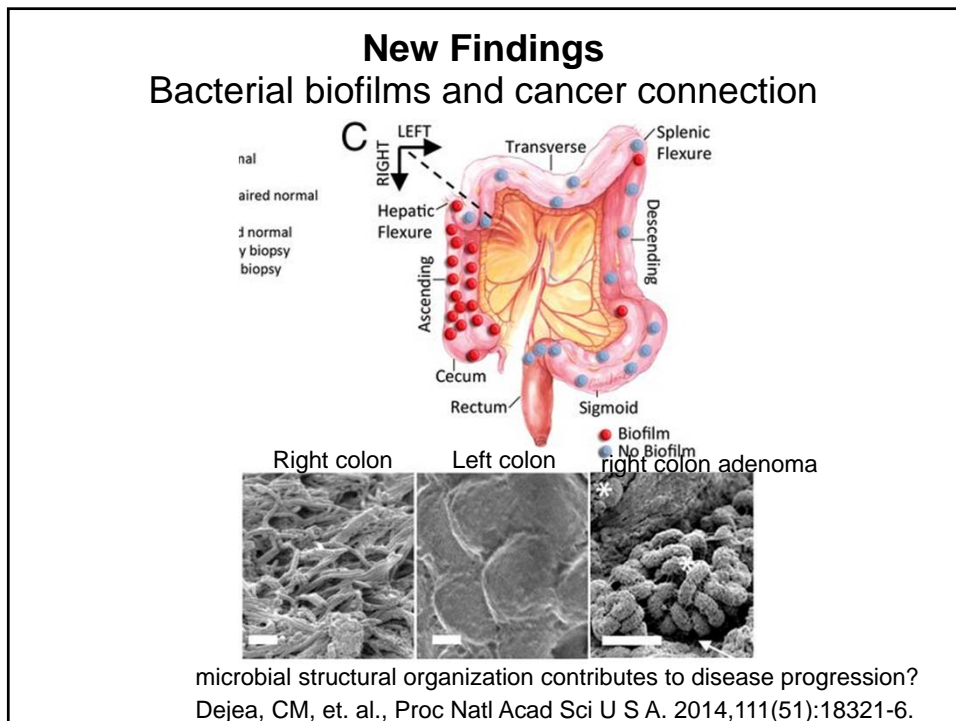
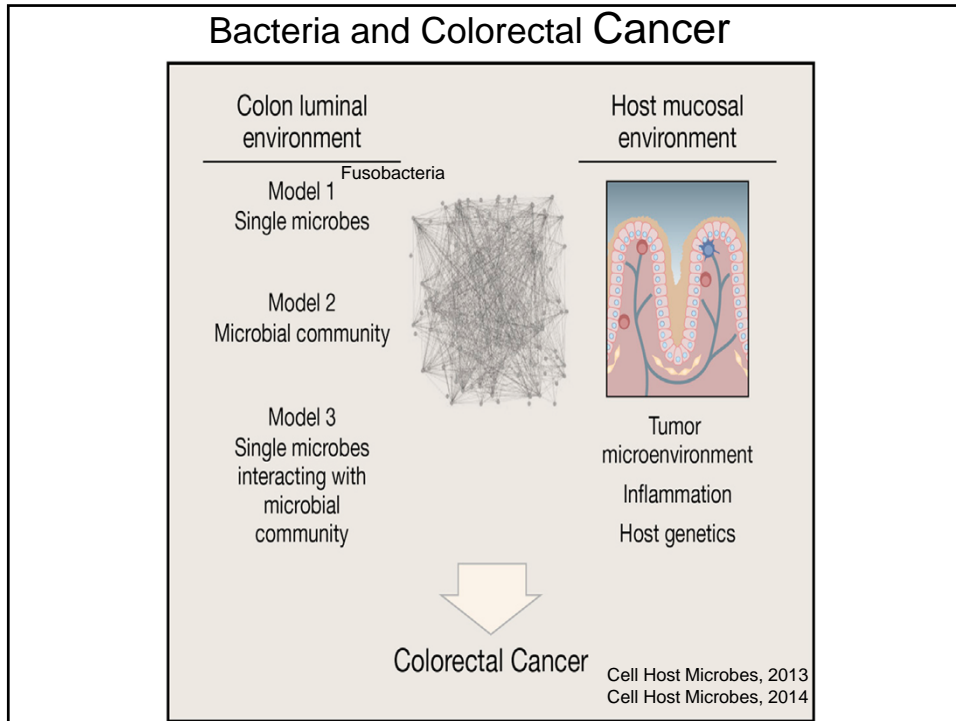


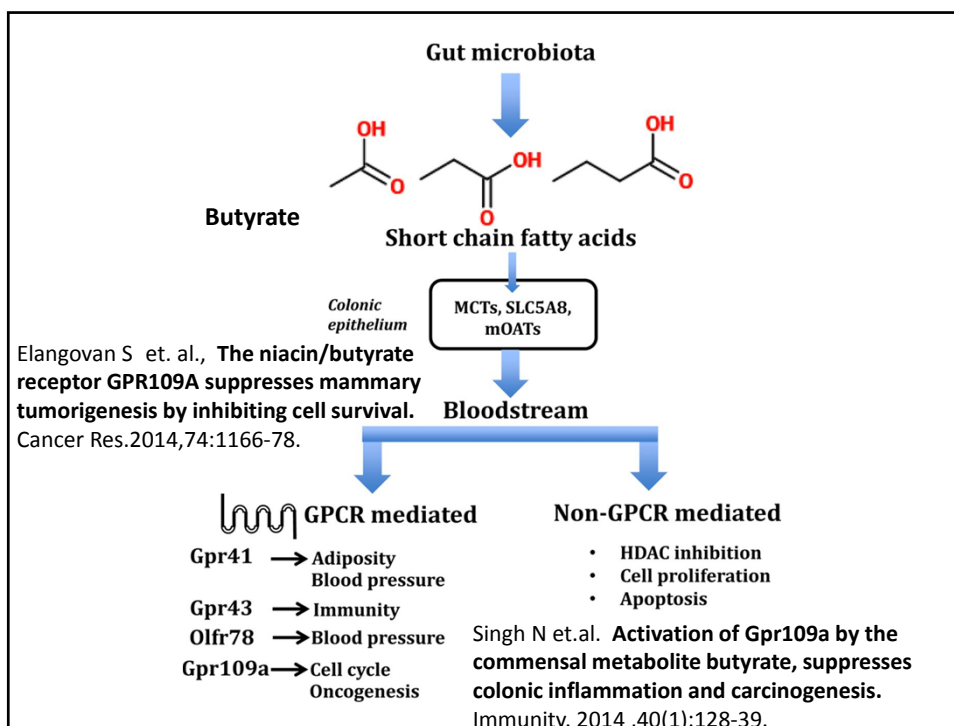
Fusobacterium nucleatum



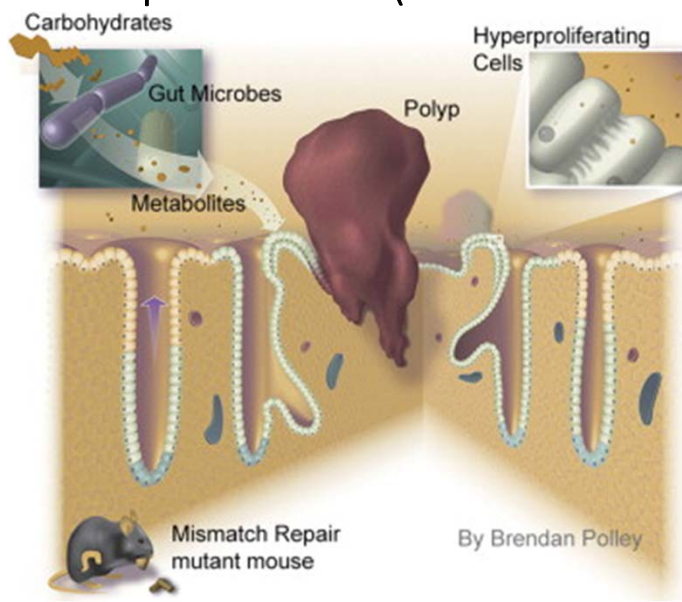
- [Kostic AD et. al., Cell Host Microbe](#) 2013, 14:207-15.
[Rubinstein MR et. al., Cell Host Microbe](#), 2013, 14:195-206.
[Castellari M et. al., Genome Res.](#) 2012, 22:299-306.
[Kostic AD et. al., Genome Res.](#) 2012, 2:292-8.

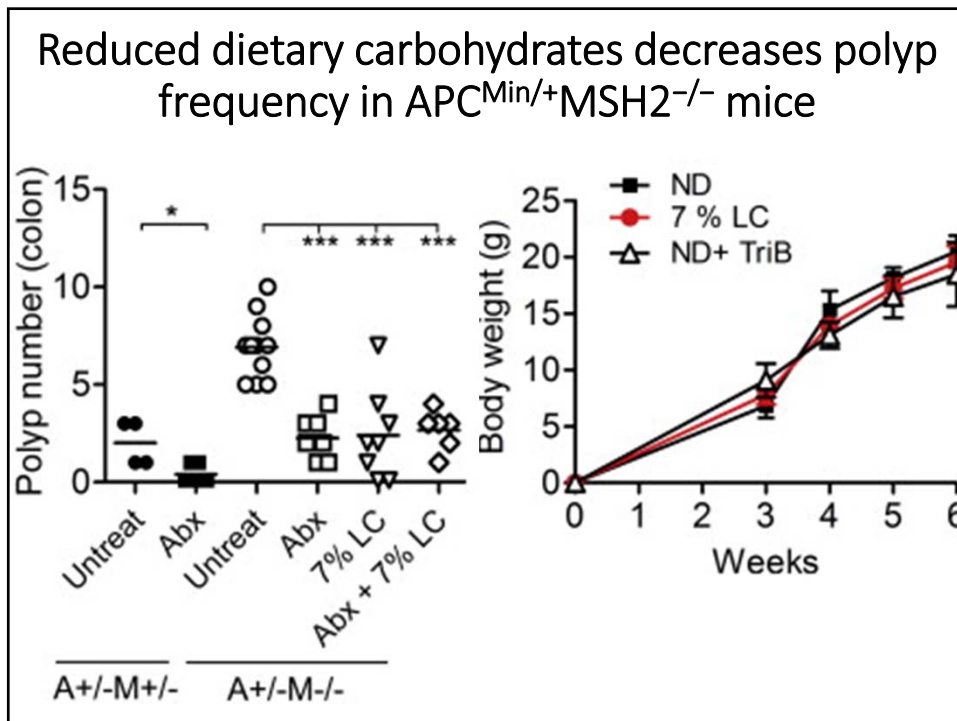
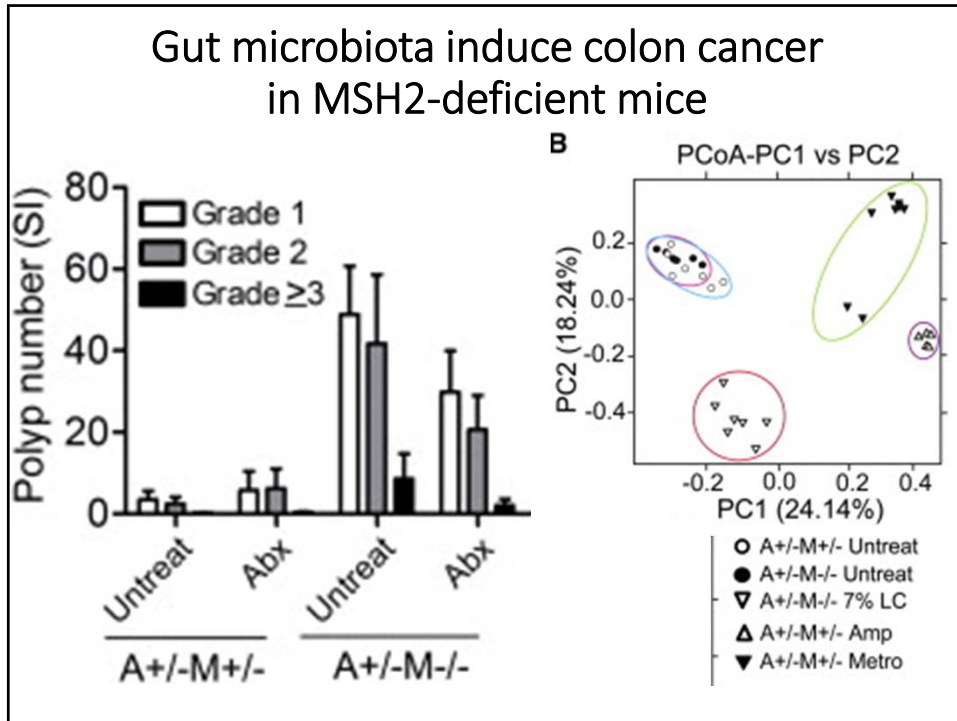


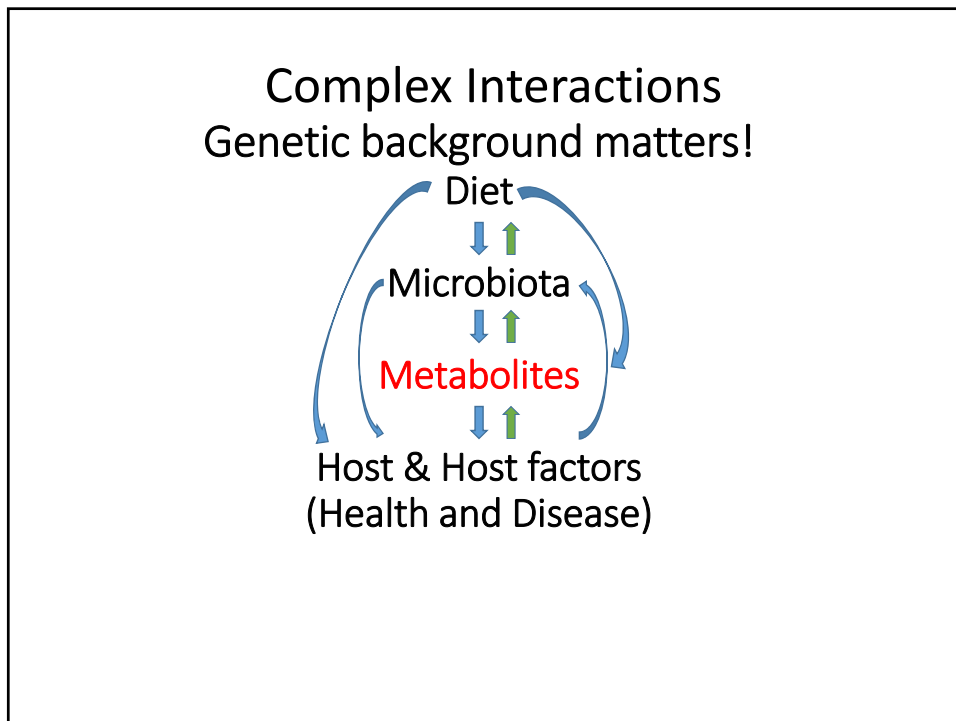
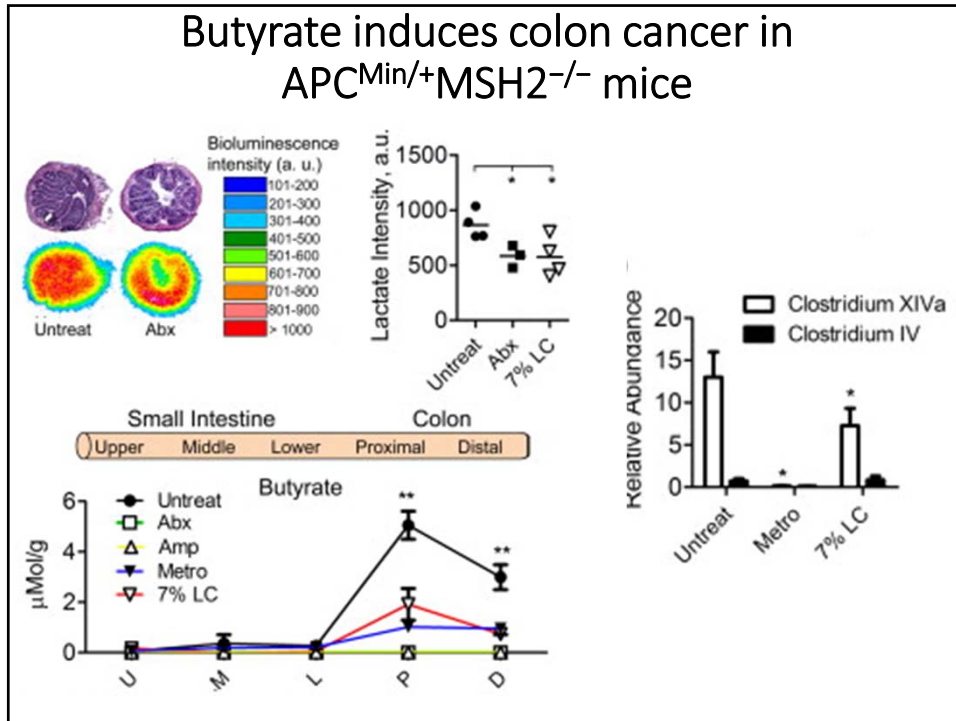




Microbial Metabolism Drives Transformation of Colon Epithelial Cells(Msh2-deficient)



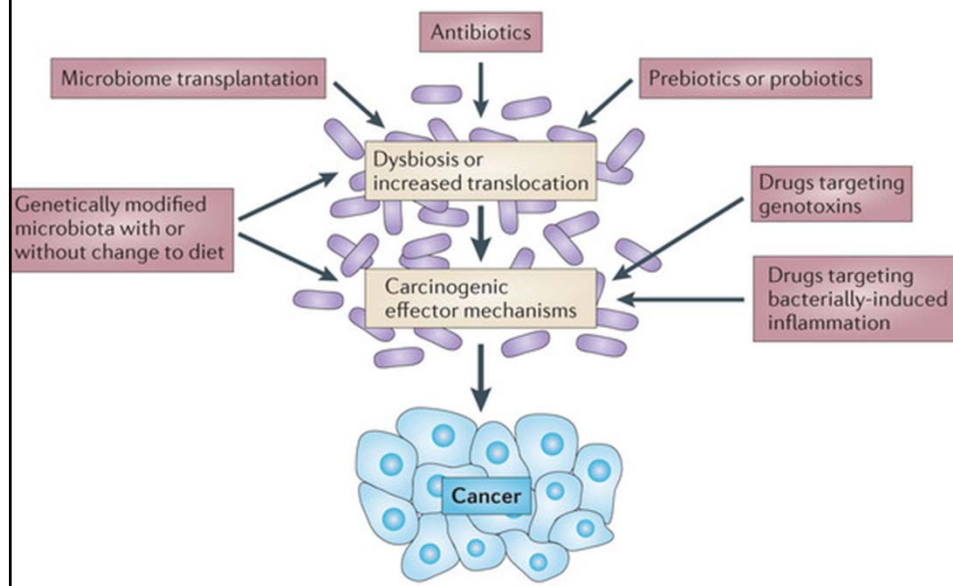


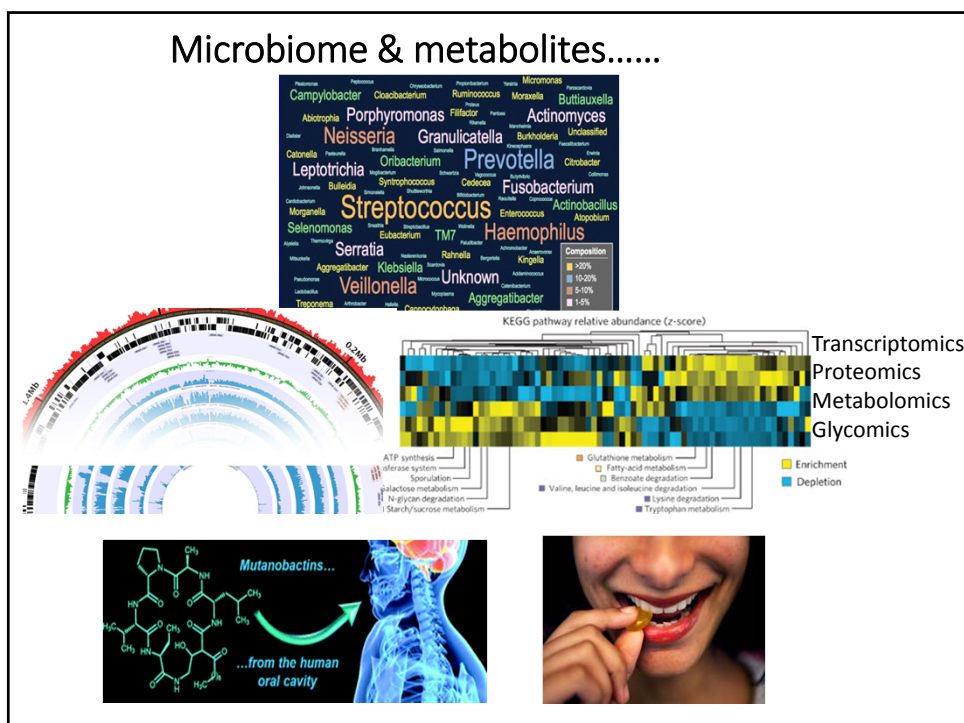


What's next?

- Presence in the tumor environment
- Progression of tumor and bacterial infection
- Role in tumorigenesis via inflammation mechanisms
- Tumor diagnostics
 - Fusobacterium biomarkers
- Bacterial cancer therapy

Microbiome- and metabolites-targeted Therapies





Program in Microbiome & Overall Health

Mission

- **Microbiota-based biomarker discovery**
- **Microbiota-targeted therapies**
- **Integration of Dentistry and Medicine**
- **Engaging practicing dentists and physicians via Dentistry Practice based Research Network**

National Dental Practice-Based Research Network



- A 7-year support of \$70 million by NIDCR
- Practicing dentists & academic scientists
- Address day-to-day issues in oral healthcare
- Extend practitioner participation from all areas across the country
- Dr. Greg Gilbert, Director, UAB School of Dentistry
- Headquarter in Birmingham, Alabama

Microbes rule the world



Cocoa powder (polyphenols and Fibers)

Smaller molecules
short fatty chain acids

2014 American Chemical Society meeting



Thank you!