Overview of the Microbiome in Health and Disease

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1. What is the microbiome?
2. What is the evidence that diet can influence the microbiome?
3. How can the microbiome influence the response to dietary components?
4. What is the relationship between diet, the microbiome and disease risk?
The Human Microbiome

- We are a composite of species: eukaryotic, bacterial, viral-up to 10x more microbial cells than human.
- Gut Microbiota = microbes in our GI tract, ~100 trillion organisms.
- Microbiome = their collective genome, >100 times as many genes as human genome.
What Do Microbes Do For Us?

- Provide ability to harvest nutrients
- Produce additional energy otherwise inaccessible to the host
- Produce vitamins
- Metabolize carcinogens
- Prevent colonization by pathogens
- Assist in the development of a mature immune system
NIH Human Microbiome Project (2008-2012)

Phase 1: Survey of the microbiome in humans
“Who’s there?”

Is there a “core” microbiome?

Clinically healthy
- 300 male/female
- 18-40 y.o.
- 5 major body regions (18 body sites)
- Up to 3 visits in 2 yrs
- No antibiotics, probiotics, immunomodulators

Microbiome-associated conditions
- Skin: eczema, psoriasis, acne
- GI/oral: esophageal adenocarcinoma, necrotizing enterocolitis, pediatric IBS, ulcerative colitis, Crohn’s Disease
- Urogenital: bacterial vaginosis, circumcision, sexual histories

Healthy cohort study

Demonstration Projects
In healthy American adults, the microbial community composition in each part of the body is unique.

- For each person, est. 1,000 bacterial species and 2,000,000 bacterial genes.
- Total pool, est. 10,000 species and 8,000,000 genes.
- However, genetic potential of each microbiome is less variable.

References:

Phase 2: Integrative HMP “iHMP” what are they doing?

Biological properties of both the microbiome and the host
- microbial composition & multi ‘omics (i.e., transcripts, proteins & metabolites) from microbiome and host
- longitudinal cohort studies
- integrated datasets as a community resource

Exemplar microbiome-associated human conditions:

**Dynamics of Pregnancy and Preterm Birth:**
Vaginal & gut microbiomes and host (mother, infant) properties

**Dynamics of Inflammatory Bowel Disease Onset:**
GI microbiome and host properties

**Dynamics of Type 2 Diabetes Onset:**
GI & nasal microbiomes and host properties
Diet Shapes Diversity in Gut Microbiome
Diet Shapes Gut Microbial Profiles in Humans

Evidence From:
Observational studies
- Globally distinct populations
- Long-term food pattern consumption- Enterotypes

Short-term dietary interventions
- Low- versus high-fiber diets
- Animal versus plant food sources
- Macronutrient ratios

Global Population Differences: Children in Rural Africa (BF) versus Urban Europe (EU)

Different dietary intake results in differences in gut bacteria:

A: Burkina Faso, Africa
- Dietary intake, ages 1-6
  - 672.2-996.1 kcal/day
  - Protein: 30.9-40.2 g
  - Fat: 18.9-31.2 g
  - Carbohydrate: 102.6-148.6 g

B: European Union, Italy
- Dietary intake, ages 1-6
  - 1068.7-1512.7 kcal/day
  - Protein: 41.9-66.7 g
  - Fat: 56.1-73.9 g
  - Carbohydrate: 190.0-290.0 g

Diet Alters Microbial Activity and Gene Expression

Short-term consumption of diets composed entirely of animal or plant products:

- Alters microbial community structure
- Overwhelms inter-individual differences in gene expression
- Modifies metabolic pathways

Diet Dominates Host Genotype in Shaping the Mouse Gut Microbiota

5 Inbred and >200 outbred mouse strains were fed a low fat, high-plant polysaccharide diet (LFPP: 22.2% KCAL protein, 16% fat, 61% CHO) and a high fat, high-sugar diet (HFHS: 14.8% KCAL protein, 40.6% CHO, 44.6% fat).

Carmody et al., Cell Host & Microbe 17:72-84, 2015
Dietary Modulation of Gut Microbiota

- **Probiotics**: foods or dietary supplements that contain live bacteria
- **Prebiotics**: nondigestible food ingredient, which selectively stimulates the growth of gut bacteria
- **Synbiotics**: combination of a probiotic with a prebiotic
- **Other factors**: tea, cocoa, wine polyphenols, spices
Change in Bacterial Abundance After Consumption of Cocoa-Derived Flavanols

*Bifidobacterium spp* (Feces)  
*Lactobacillus (casei group)* (Distal colon contents)

Cocoa powder consumption decreased TNF-α and TLR-2, -4 and -9 gene expression in intestinal tissues

Jang, S. et al., J. Nutr., 2016
Diet and the Microbiome: A Two-Sided Relationship

Microbes (Numbers and Types) ↔ Dietary Components
### Bacteria Can Produce New Compounds from Food Components

<table>
<thead>
<tr>
<th>Food Component</th>
<th>Bacterial Metabolite</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary fiber</td>
<td>Butyrate and other SCFAs</td>
</tr>
<tr>
<td>Choline, carnitine</td>
<td>Trimethylamine</td>
</tr>
<tr>
<td>Soy isoflavones</td>
<td>Equol, O-desmethylangolensin</td>
</tr>
<tr>
<td>Plant lignans</td>
<td>Enterodiol, enterolactone</td>
</tr>
<tr>
<td>Ellagitannins</td>
<td>Urolithins A and B</td>
</tr>
<tr>
<td>Anthocyanins</td>
<td>Hippuric acid &amp; small phenolics</td>
</tr>
<tr>
<td>Glucosinolates</td>
<td>Isothiocyanates</td>
</tr>
</tbody>
</table>
Dietary Fiber and Cancer

- Dietary fiber is associated with decreased risk of colon cancer
- Dietary fibers are fermented by colonic bacteria to form short chain fatty acids
- Butyrate is the most widely studied and the preferred energy source of colonocytes
- Butyrate has differential effects in normal versus cancer cells
Dietary Fiber and Colon Cancer

Dietary Fiber and Bacterial Diversity

Mice fed a high fiber diet have more fiber-degrading bacteria, a thick mucus lining and are protected from *Citrobacter rodentium* infection.

A fiber-deprived gut microbiota promotes expansion and activity of colonic mucosa-degrading bacteria and are susceptible to *C. rodentium* infection and colitis.

Purified prebiotic fibers do not alleviate degradation of the mucus layer.

Germ free mice on either diet have a thin mucus layer but are protected from pathogen infection.

Metabolism of Ellagitannins

## Urolithin Excretion After Intake of Different Ellagic Acid Containing Foods

<table>
<thead>
<tr>
<th>Food</th>
<th>Excretion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strawberry (250 g)</td>
<td>0.06-6.3</td>
</tr>
<tr>
<td>Raspberry (225 g)</td>
<td>0.21-7.6</td>
</tr>
<tr>
<td>Red wine (300 ml)</td>
<td>1.8-7.4</td>
</tr>
<tr>
<td>Walnut (35 g)</td>
<td>1.2-81.0</td>
</tr>
</tbody>
</table>

N=10 volunteers

Dietary Allicin Reduces Metabolism of L-Carnitine to TMAO

1. Organisms living on and within food have the potential to be either friends or foes to the consumer.
2. The human microbiome may decrease in diversity due to exposure to antibiotics, the consumption of a high-fat and high-sugar diet and decreased consumption of dietary fiber.
3. Decreased diversity can increase susceptibility to invasive food-borne pathogens such as *Clostridium*, *Staphylococcus aureus*, *Escherichia coli* and *Listeria monocytogenes*.
4. These organisms have greater potential to colonize and outcompete the host-associated community during dysbiosis.
5. Some bacteria that are normal constituents of the microbiome and are sold as probiotics have the ability to become pathogenic such as *Escherichia coli*.

High interpersonal variability in post-meal glucose observed in an 800-person cohort

Using personal and microbiome features enables accurate glucose response prediction

Prediction is accurate and superior to common practice in an independent cohort

Short-term personalized dietary interventions successfully lower post-meal glucose

A Metagenonomic View of our Dinner Plate

Take Home Messages

1. Microbiome research is an emerging area of science and there are many research opportunities available.

2. The microbiome is integral to human physiology, maintenance of health and development of disease.

3. There is a two-sided relationship between diet and the microbiome.

4. The food industry needs to actively stay informed about advances in this field.
I’ll have the Garden Salad, please

We’ll have the Cheeseburger and fries!