Diet, Microbiome and Health

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Outline

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

- We are a composite of species: human, 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
Human Intestinal Microbiota over the Lifespan

**Newborn**
- Initial gut bacteria (founder species) depends upon delivery mode
  - Vaginal delivery: Lactobacillus, Prevotella spp.
  - Vertical inheritance from mother
  - Cesarean section: Staphylococcus, Corynebacterium, Propionibacterium spp.
  - Higher susceptibility to certain pathogens
  - Higher risk of atopic diseases

**Early childhood**
- New strains (less certain in origin) outcompete old ones
- Rapid increase in diversity
- Early microbiota development = high instability
- Shifts in response to diet, illness

**Adult**
- Highly distinct, differentiated microbiota
- Microbial community may continue to change, but at a slower rate than in childhood

**Elderly**
- Substantially different gut communities than in younger adults


Longevity is associated with enrichment of subdominant taxa that appear to be associated with health—Akkermansia, Bifidobacterium and Christensenellaceae (n=24 for 105-109 years and n=15 for other age groups).

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
Continuous Probiotic Exposure Increases Longevity in Mice

10 month female ICR mice fed a chow diet and gavaged with *Bifidobacterium animalis* subsp. *lactis* LKM512 or vehicle daily for 11 months

The Prebiotic High-Amylose Starch (HAS) Might Increase Longevity

Table 2 Summary of the effects of diet restriction and high-amylose starch

<table>
<thead>
<tr>
<th></th>
<th>Diet restriction</th>
<th>High-amylose starch</th>
<th>HAS references</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammation</td>
<td>↓</td>
<td>↓</td>
<td>Zhou et al. 2008; Shen et al. 2011</td>
</tr>
<tr>
<td>Glucose clearance</td>
<td>Improved</td>
<td>Improved</td>
<td>Robertson et al. 2005; Johnston et al. 2010; Robertson 2012</td>
</tr>
<tr>
<td>Insulin sensitivity</td>
<td>Improved</td>
<td>Improved</td>
<td></td>
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<tr>
<td>Lipogenesis</td>
<td>↓</td>
<td>↓</td>
<td>Higgins et al. 2006; Higgins and Brown 2013</td>
</tr>
<tr>
<td>Body fat</td>
<td>Reduced</td>
<td>Reduced</td>
<td>Keenan et al. 2006, 2013; Charrier et al. 2014</td>
</tr>
<tr>
<td>Cancer risk</td>
<td>↓</td>
<td>↓</td>
<td>Toden et al. 2007; Clarke et al. 2008</td>
</tr>
<tr>
<td>Oxidative Stress</td>
<td>↓</td>
<td>↓</td>
<td>Kwak et al. 2012</td>
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</table>
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 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
Diet and the Microbiome: A Two-Sided Relationship

Microbes (Numbers and Types) ➔ Dietary Components ➔ Microbes (Numbers and Types)
Bacteria Can Generate New **Metabolites** from Dietary Components

<table>
<thead>
<tr>
<th>Food Component</th>
<th>Bacterial Metabolite</th>
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<tbody>
<tr>
<td>Soy</td>
<td>Equol</td>
</tr>
<tr>
<td>Fiber</td>
<td>Butyrate</td>
</tr>
<tr>
<td>Plant Lignans</td>
<td>Enterodiol, Enterolactone</td>
</tr>
<tr>
<td>Ellagic Acid</td>
<td>Urolithins A and B</td>
</tr>
<tr>
<td>Hops</td>
<td>8-Prenylnaringenin</td>
</tr>
<tr>
<td>Linoleic Acid</td>
<td>Conjugated Linoleic Acid</td>
</tr>
</tbody>
</table>
Dietary Fiber and 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.
- Human and animal studies of butyrate production and cancer risk are difficult to perform.
Dietary Fiber and Colon Cancer

Dietary Fiber and Bacterial Diversity

# 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

Diet, Microbial Metabolism and Cardiovascular Disease

Dietary Allicin Reduces Metabolism of L-Carnitine to TMAO

How Diet May Be Contributing to Human Inflammatory Diseases

Strategies for Modulating the Gut Microbiota to Improve Human Health

Sonnenburg and Backhed  Nature 535:56-64, 2016
Can Your Microbiome Tell You What to Eat?

- 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 Metagenomic View of our Dinner Plate

Traditional view
Fruits
Grains
Vegetables
Protein

Metagenomic view

Starch
Polysaccharides
Oligosaccharides
SCFAs (acetate, butyrate, propionate, succinate)

Inulin, fructans
Soy isoﬂavones
Glucosinolates
Xanthohumol
Polyphenols
Porphyrans
Lignans
SCFA

Phosphatidylcholine
Heterocyclic amines
Nitrosamines
Amino acids

Milk oligosaccharides
Fermentation products
Probiotics

I’ll have the Garden Salad, please

We’ll have the Cheeseburger and fries!