MOTHER’S MILK AND THE MICROBIOME

Tiffany Weir, PhD
Assistant Professor
Food Science and Human Nutrition
Colorado State University
WHAT IS THE MICROBIOME AND WHAT DOES IT DO?
The Gut Microbiome

- **Stomach**: $0-10^2$
  - Lactobacillus
  - Candida
  - Streptococcus
  - *Helicobacter pylori*
  - Peptostreptococcus

- **Duodenum**: $10^2$
  - Streptococcus
  - Lactobacillus

- **Distal ileum**: $10^7-10^8$
  - Clostridium
  - Streptococcus
  - Bacteroides
  - Actinomycinae
  - Corynebacteria

- **Jejunum**: $10^2$
  - Streptococcus
  - Lactobacillus

- **Colon**: $10^{11}-10^{12}$
  - Bacteroides
  - Clostridium groups IV and XIV
  - Bifidobacterium
  - Enterobacteriaceae

- **Proximal ileum**: $10^3$
  - Streptococcus
  - Lactobacillus
Getting to know your gut microbiota

A huge quantity (hundreds of trillions) of bacteria and other microorganisms inhabit your intestines fulfilling key functions for your health and wellbeing.

- **Gut microbiota’s weight** can reach up to 1 to 2 Kg.
- **95%** of our bacteria are located in the gastrointestinal (GI) tract.

- Bacteria are **10 to 50 times** smaller than human cells.
- In our body, microbes outnumber human cells by **10:1**.
- Laid end to end, our body’s bacteria would circle the Earth **2.5 times**.

The GI tract surface is as big as 2 tennis courts: **400 m²**.
Protective functions

I. Direct inhibition

II. Nutrient/receptor competition

III. Stimulation of immune defenses

- plasma cell
- T-cell
- cytokines/chemokines
- nutrients/receptors
- defensins
- commensal
- pathogen
- PAMP-receptor
- bacteriocin
- slgA
- mucin

Curr Opin Microbiol 14:82-91, 2011
Video Link

http://link.brightcove.com/services/player/bc pid1966016696001?bckey=AQ~~,AAAByWTdmvk~,YEX2I6TuT0mdQPquhJg1bWcq9Ufv7FQ~&bclid=0&bctid=2144234478001
• **Indigestible carbohydrates**
  - Bacteria encode enzymes we lack
  - Polysaccharides ---> SCFAs that “feed” colonic epithelial cells.

• **Fat**
  - New study (in zebrafish) demonstrates that Firmicutes assist in dietary fat absorption

• **Protein**
  - Proteolytic processes degrade proteins into amino acids

• **Synthesis of essential amino acids**
  - Microbially synthesized amino acids (leucine) can contribute 19-22% of daily requirements.

• **Synthesis of vitamins**
  - Intestinal microbes synthesize vitamin K and B vitamins, which are frequently absorbed directly through the intestinal epithelia.
  - B12: site of synthesis vs absorption

• **Absorption of ions (Calcium, Magnesium, iron)**
Microbial products interact with cells to regulate:
- Glucose use
- Fat storage
- Food transit
- Feelings of satiety
• Germ-free mice required 30% more calories to maintain same weight as normal littermates
• Germ-free mice transplanted with normal microflora gained weight.
• Increased energy harvest associated with higher levels of the phylum Firmicutes

* Turnbaugh and Bäckhed studies from Gordon lab (2006)
Ley et al. 2006. Nature
When co-housed the “lean” mice transferred their microbes and their phenotype to the “obese” animals!

Balance in the Gut

Microbial Metabolites

Dietary fiber
Resistant starch

Healthy microbiota

- Trophic effect
- Epithelial barrier establishment
- Treg development
- Anti-inflammation

- Carcinoma
- Atherosclerosis
- Adipogenesis
- Autism spectrum disorder

Cholesterol
Choline
L-Carnitine

Altered microbiota

HOW DO WE GET THESE MICROBES?

Why birth influences and early feeding patterns are CRITICAL for a healthy microbiome.
Colonization Influences

Factors influencing mother gut microbiota
- Pregnant weight gain
- Antibiotic exposure
- Hygiene and social condition

Mother–child symbiosis
- High-fat mother’s milk
- Intensive care at birth
- Delivery and feeding modality

Factors influencing child gut microbiota
- Bacteria in amniotic fluid
- Smoking in pregnancy
- Gestational metabolic abnormalities
- Antibiotic exposure
- Weight at birth
- Gestational age

Microbial Dynamics in Infancy

- Bacteroidaceae
- Lachnospiraceae
- Ruminococcaceae
- Prevotellaceae
- Enterobacteriaceae
- Veillonellaceae
- Bifidobacteriaceae
- Clostridiaceae
- Lactobacillaceae

Birth 1 month 6 months 12 months 2 - 3 years

Bacterial diversity

Interindividual variability
Pregnancy leads to alterations in a woman’s microbiota that increase metabolic challenges.

Maternal obesity is a strong predictive factor of childhood obesity and may be due to microbiota effects.
Mode of Delivery

Table 1

<table>
<thead>
<tr>
<th>Cesarean Delivery Associated Childhood Diseases</th>
<th>1,2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Allergic Rhinitis</strong></td>
<td></td>
</tr>
<tr>
<td>All Cesareans</td>
<td>1.37 (1.14-1.63)</td>
</tr>
<tr>
<td>Repeat Cesareans Only</td>
<td>1.78 (1.34-2.37)</td>
</tr>
<tr>
<td><strong>Asthma</strong></td>
<td></td>
</tr>
<tr>
<td>All Cesareans</td>
<td>1.24 (1.01-1.53)</td>
</tr>
<tr>
<td>Female</td>
<td>1.53 (1.10-2.10)</td>
</tr>
<tr>
<td>Female &amp; Repeat Cesarean</td>
<td>1.83 (1.13-2.97)</td>
</tr>
<tr>
<td><strong>Celiac Disease</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.80 (1.13-2.88)</td>
</tr>
<tr>
<td><strong>Diabetes Mellitus (Type 1)</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.19 (1.04-1.36)</td>
</tr>
<tr>
<td><strong>Gastroenteritis</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.31 (1.24-1.38)</td>
</tr>
<tr>
<td><strong>Gastroenteritis AND Asthma</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.74 (1.36-2.23)</td>
</tr>
</tbody>
</table>

1 Data from references 46, 47, 50
2 Odds Ratio (OR) with 95% CI versus vaginal delivery

Restoring Microbiota

1. [Illustration of a person lying down with a bandage, possibly representing a patient undergoing antibiotic treatment (ABX) and a book.] 1 h

2. [Diagram showing the transfer of a sterile container from one hand to another, indicating the handling of a sterile object.

3. [Sequence of illustrations showing the application of microbiota from the mouth, face, and rest of the body. Text: Mouth, Face, Rest of the body.]

Image: M.J. Schoen

Breast vs. Formula

Mother’s Milk Microbiome

[Graph showing the microbiome distribution across different body sites and samples.]
Oligosaccharides

Human

- Oligosaccharides: 8%
- Proteins: 6%
- Fats: 32%
- Lactose: 54%

Cow

- Oligosaccharides: 27%
- Proteins: 32%
- Fats: 41%

* An estimate. Oligosaccharide content varies over time and between individuals.
How they work...

A. Pathogen
B. Bacterial lectin
C. Glycocalyx

HMO

Altered glycan-related gene expression
Care and Feeding of the Microbiota
Fat or Fiber?

Animal-based diet: increased fat and protein, reduced fiber

Plant-based diet: increased fiber intake and decreased fat/protein

Change in community structure from baseline was significant with animal-based diet, but returned when normal diet resumed.

David et al., Nature 2014
Prebiotics are non-living indigestible polysaccharides (food components) that stimulate the growth of beneficial bacteria.
Prebiotic Sources

- **Diet**
  - Major dietary sources are consumed in limited amounts in a typical American diet
  - Studies may reveal “new” dietary prebiotics
- **Supplements**
- **Fortification in foods**
  - Yogurt
  - Infant formula
  - Artificial sweeteners

<table>
<thead>
<tr>
<th>Foods with Prebiotics</th>
<th>Prebiotic fiber by weight</th>
<th>Amount needed for 6g serving</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chicory Root</td>
<td>64.6%</td>
<td>9.3 g</td>
</tr>
<tr>
<td>Jerusalem Artichoke</td>
<td>31.5%</td>
<td>19 g</td>
</tr>
<tr>
<td>Dandelion greens</td>
<td>24.3%</td>
<td>24.7 g</td>
</tr>
<tr>
<td>Raw garlic</td>
<td>17.5%</td>
<td>34.3 g</td>
</tr>
<tr>
<td>Raw leek</td>
<td>11.7%</td>
<td>51.3 g</td>
</tr>
<tr>
<td>Raw onion</td>
<td>8.6%</td>
<td>69.8 g</td>
</tr>
<tr>
<td>Cooked onion</td>
<td>5%</td>
<td>120 g</td>
</tr>
<tr>
<td>Raw asparagus</td>
<td>5%</td>
<td>120 g</td>
</tr>
<tr>
<td>Raw wheat bran</td>
<td>5%</td>
<td>120 g</td>
</tr>
<tr>
<td>Whole wheat flour, cooked</td>
<td>4.8%</td>
<td>125 g</td>
</tr>
<tr>
<td>Raw banana</td>
<td>1%</td>
<td>600 g</td>
</tr>
</tbody>
</table>
Probiotics are live bacteria or yeast that when eaten in sufficient amounts can be beneficial for intestinal health.
Probiotic sources

- Food sources:
  - Fermented dairy foods like yogurt, kefir products, and aged cheeses
  - Some fermented non-dairy foods including kimchi, sauerkraut, and kombucha
  - Supplemented non-fermented foods: Good Belly

Slide from Katie McGirr, CSU Extension
VSL3: High Dose Probiotic

- Currently approved in the US as a medical food to be used for the treatment of IBS
- Synergistic combination of common probiotic species
- Claims to deliver the highest number of live, active cells of any probiotic available.
  - Formulations range from 112.5-900 BILLION cells
Summary

• Both pre-pregnancy weight and weight gain during pregnancy may influence long-term metabolic function in the infants via microbiota influences.

• Consuming high fiber and fermented foods during pregnancy and limiting high fat foods may help with infant microbiota optimization.

• Unnecessary antibiotics (both during pregnancy and in infants) can compromise development of the microbiota.

• Breastfeeding provides the infant with pre- and probiotics necessary for early immune development.