How the Human Microbiome Impacts Our Health

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Facts

- $10^{30}$ microbes in/on the ocean, terrestrial ecosystems, plants, and animals
- Microbes = Bacteria or Eukaryotes
- Human body $\rightarrow$ skin, mouth, airways, GI, vagina
Definitions

- Microbes = microscopic living organisms
- Microbial communities = microbiota
- Mutualists = both host + microbe benefit
- Commensal = one partner benefits + other partner unharmed/unaffected
- Pathogenic = one partner benefit + one partner harmed
December 2007 announced the Human Microbiome Project

Part of Roadmap for Medical Research
  - Identifying and sequencing the biome may be more important than the human genome

$100 million in grants over the next five years

Requires new technologies

The HMP plans to sequence, or collect from associated efforts, a total of 3000 reference genomes isolated from human body sites.
The gut microbiota in development and disease

Therapeutic modulation of the gut microbiota: from the cradle to the grave.

Holmes E et al. Sci Transl Med 2012;4:137rv6-137rv6
The Impact of the Gut Microbiota on Human Health: An Integrative View
You are what you eat
Immune system control of the microbiota

L V Hooper et al. Science 2012;336:1268-1273
How microbiota shape host immunity.

L V Hooper et al. Science 2012;336:1268-1273
Asthma

• More courses of antibiotics, more asthma
• Infants who got even one course of antibiotics during their first year may have double the risk of getting asthma later in childhood
• 65% of children prescribed at least one course of antimicrobials during first year of life
• Average child in U.S. and other developed countries receives 10–20 courses of antibiotics by the time he or she is 18 years old
Allergies

- Kids who tested positive for C. difficile as babies were twice as likely to have asthma at age 6 or 7
- 7% had asthma, 22% had a food sensitization, 12% recently had eczema
- Having a skewed mix of gut bacteria species early on, especially lacking a diverse range of bacteria, reduces the early stimulation of the immune system, which could lead to more allergies later
Guts to brains – how the microbiome shapes our minds
GF mice display increased spontaneous motor activity.
GF mice display reduced anxiety-like behavior
Gareau MG, et al. 2010

• **Objective**
  – Investigate effects of acute enteric infection OR absence of gut microbiota on behavior, anxiety and non-spatial memory formation

• **Methods**
  – Non-invasive enteric pathogen *Citrobacter rodentium*
  – C57BL/6 mice & Swiss-Webster *mice* (germ-free & controls)
Exposure to water avoidance stress (WAS) alters non-spatial memory in C. rodentium-infected mice at 10 days after infection, which is prevented by pretreatment with probiotics.

Germ-free (GF) mice display normal anxiety levels, but lack memory.
The Intestinal Microbiota Affect Central Levels of Brain-Derived Neurotropic Factor and Behavior in Mice

A

Before treatment

During treatment

Cage
ATM

1 2 3 4 5 6 1 2 3 4 5 6

B

Control

ATM

Relative intensity

0.0 0.2 0.4 0.6 0.8 1.0

Relative front

C

Control

ATM

Relative intensity

0.0 0.2 0.4 0.6 0.8 1.0

Relative front

D

Control

ATM

Actinobacteria
Firmicutes
Verrumicrobia
γ- proteobacteria
Bacteroides
Other

E

$10^{12}$

$10^{10}$

$10^{8}$

$10^{6}$

$10^{4}$

$10^{2}$

$10^{0}$

Aerobic

Anaerobic

Control

ATM

Gastroenterology Volume 141, Issue 2 2011 599 - 609.e3
Oral ATM treatment alters mouse behavior promoting exploration. Results of step-down and light/dark preference tests in orally ATM-treated mice (n = 39), mice 2 weeks after ATM treatment (n = 19), and control mice (n = 47). BDNF protein ...
Bacteria with guts
Gastrointestinal Microbiome Signatures of Pediatric Patients With Irritable Bowel Syndrome

Figure 2  The pediatric gut microbiomes of children with IBS are characterized by greater abundance of ?-proteobacteria. (italic)A (italic) Percentage of all bacterial classes represented. (italic)B (italic) Percentage of bacte...
Host responses to the human microbiome
The bacteria that make you fat
Reduced diversity of the gut microbiota in obese individuals

Obesity

- Each of us has a unique population of bacteria in our digestive tract
- Fall into one of two bacterial divisions
  - Bacteroidetes
  - Firmicutes
- Which group is dominant may have an impact on weight
- Firmicutes activate enzymes that promote the storage of fat in fat cells
Human gut microbes associated with obesity

Nature 444, 1022-1023, 2006
Effects of the gut microbiota on obesity and glucose homeostasis

Figure 1  Gut microbiota regulation of host metabolism. The gut microbiota suppresses enterocyte expression of Angptl4; this alleviates LPL inhibition and promotes LPL-mediated triglyceride storage in adipose tissue. In addition, reduced Angptl4 l...
Preference (A), raw intake (B), and calorie intake from intralipid emulsions (C) in GF and NORM C57B6/J mice

http://www.plosone.org/article/info:doi/10.1371/journal.pone.0039748
Intestinal epithelial protein expression of satiety peptide in GF & NORM mice.

http://www.plosone.org/article/info:doi/10.1371/journal.pone.0039748
Plasma levels of leptin, ghrelin, and PYY in GF and NORM mice

http://www.plosone.org/article/info:doi/10.1371/journal.pone.0039748
Effect of Antimicrobials

- Killing friendly flora might be linked to non-infectious diseases
- Type I diabetes doubled
- Inflammatory bowel disease
- Asthma
- Obesity
- Cancer

Effects of Fish Oil on Microbiome

• Increase some beneficial microbes

• Decrease essential (SFB, *Clostrium cocoides*), invasive microbes (*Enterococcus fecalis*).
Host responses to the human microbiome
Summary

• Microbiome play a major role in health
• There are tremendous market possibility
  – Probiotics
  – Prebiotics
  – Compound have impact on microbiome
• Many compounds may act through microbiome