The Microbiome and Human Metabolism

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Outline

- Career Trajectory
- Microbiome
  - Human Metabolism
  - Technological Advances
- The Scientist of Tomorrow
TRI

Translational Research Institute for Metabolism and Diabetes

- Dedicated translational research space @ Florida Hospital, Orlando
- Mission: Innovate, Discover, Cure
- Formula for Success:
  - Facilities
  - Research Niche
  - Built-In Synergy
  - Diversified research portfolio

Definitions: The “Bugs” that Inhabit Us

- **Microbiota**: A microbial community that occupies a given habitat.
- **Microbiome**: The collective genomes of those microorganisms.

*Nutr Rev. 2012; 70:538*
Humans as Superorganisms: We are not Alone

- The human body has 10 times more bacterial than human cells.
- Bacteria make up 1-3% of our body mass.
- The Microbiome: The Second Human Genome?

Tissue Specificity of Human Microbial Communities

Nature, June 14, 2012, Cover Image
NIH Human Microbiome Project

Factors that Influence Microbiome Composition

- **Infancy:**
  - Mode of delivery
  - Genetics
  - Breast milk vs. formula

- **Childhood**
  - Developing immune system
  - Socialization
  - Diet Quality
  - Antibiotics

- **Adolescence/Early Adulthood:**
  - Puberty
  - Sexual Activity
  - Smoking
  - Moving
  - Fitness
  - Diet Experimentation

- **Adulthood**
  - Weight Gain
  - Pregnancy
  - Medication/Illness
  - Travel
  - Aging

The “Aha!” Moment: The Microbiome and Obesity

- Germ-free (GF) mice have smaller fat cells than conventional mice.
- When GF mice are exposed to microbiome from conventionally raised mice:
  - 60% increase in fat cell size
  - Insulin resistance
- Why?
  - Increased harvest of calories from food
  - Increased fat production in liver
  - Suppression of a gene that regulates fat cell size.
Obese adults and adolescents have alterations in the ratio of two bacterial phyla: Firmicutes and Bacteroidetes.
- Proportions shift with weight loss, caloric restriction and bariatric surgery.
  - *Nature*. 2006; 444:1022
- Mice become obese when they receive microbiome from obese, but not lean, twins.
  - *Science*. 2013;341:1241214

Microbial Imbalance (Dysbiosis) & Human Disease

*Acta Diabetol*. 2011. 48:257
How is the Microbiome Linked to Human Metabolism?

- Bile Acids
- Energy Harvest
- Satiety
- Food Intake
- Tissue Metabolism
- Mitochondrial Function

Microbiome to Make Space Food?

https://www.npr.org/sections/thesalt
Tracking Bacteria in the Human Gut

- When bacteria are used therapeutically, how do we know they reached their destination?
  - A study in mice combined genetic engineering and ultrasound to find out.
    - Pilot data indicates this may work in humans.

E. coli bacterium that was genetically engineered to express gas vesicles in order to track its movement through a mouse's body using ultrasound.

The State of Microbiome Therapeutics

- Microbiome transplants used successfully to treat a bacterial infection \( (C. \text{diff}) \) that causes gastrointestinal problems.
- Preliminary data shows the potential microbiome transplants to treat metabolic disease.
- Several companies are actively pursuing microbiome modulating drugs.
The Domains of Microbiome Therapeutics

Healthy Microbiota → Treatment → Diagnosis → Dysbiotic (diseased) microbiota


Filling the Gaps: How Do We Get There?

- Move beyond associations and **define causality**
  - Understand the bugs
  - Impact of host factors
  - Mechanisms
Microbiome Studies at TRI

1. Is the microbiome a *causal* element in human obesity?
2. How is the microbiome *modulated* in type 1 diabetes as body weight increases?
3. Is the microbiome a *biomarker* for liver disease resolution after bariatric surgery?

The Scientist of Tomorrow

- Fearless
- Outside the Box
- Globally Collaborative
- Beyond Self
- Strong Communicator
Advancing Innovation through Impactful Scientific Communication

Ideas + Action = Discoveries

#WeAreSmarterTogether

Questions?

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