Microbiome and Metabolome in Aging:

*Scientific Opportunities in WHI*

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WHI Investigators Meeting
May 4-5, 2017
Columbus, Ohio
Human Microbiome Project

- 300 healthy humans, using Next Gen Seq
- Microbial ecologies of varying diversity
- Majority previously uncultured
- 30 trillion microbiological cells
- 10 trillion mammalian cells

Relman D. Nature 2012;486:194
Microbiota, Metabolome, Health and Aging


Diagram showing the interaction between the host, bacteria, and gut lumen at different stages of development, middle age, and old age. The stages are labeled as Predation, Symbiosis, and Dysbiosis, with changes in immune response and bacterial proliferation over time.
What factors are associated with altered host immune response and development of dysbiosis in aging?

Are there key metabolites and metabolic pathways through which microbial dysbiosis stimulate disease pathogenesis?

Can a key metabolite or metabolic pathway be effectively intervened upon to mitigate disease pathogenesis and clinical manifestations in later life?
Microbiome, Metabolome and Health: *an example*

**Gut Dysbiosis, Choline Metabolism, Atherothrombosis**

- **Environmental perturbation**: dietary choline, carnitine
- **Gut dysbiosis**: shift to *Firmicutes* dominant phylum, increase bacterial production of trimethylamine (TMA)
- **Hepatic upregulation**: Flavin Monooxygenase (FMO) conversion of TMA to trimethylamine-N-oxide (TMAO)
- **Functional effects**:
  - Macrophage activation, foam cell formation
  - Inhibit HDL-C function
  - Stimulate platelet activation
  - Reduce renal function
- **Clinical Manifestations**:
  - Atherothrombotic events (MI, stroke), HFrEF

The Microbiome: definition, measurement and role in epidemiologic research
Betsy Foxman, PhD
Professor of Epidemiology,
Director, Center for Molecular and Clinical Epidemiology of Infectious Diseases
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What is the metabolome & how can it improve understanding disease mechanisms?
Robert Genco, DDS, PhD
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Microbiome & Metabolome Studies in WHI and the Buffalo Clinic Center
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Opportunities for microbiome and metabolome studies in WHI - - Discussion
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