

# Microbiome and Metabolome in Aging:

## *Scientific Opportunities in WHI*

Michael J. LaMonte, PhD, MPH, University at Buffalo

Betsy Foxman, PhD, University of Michigan

Robert J. Genco, DDS, PhD, University at Buffalo

Jean Wactawski-Wende, PhD, University at Buffalo

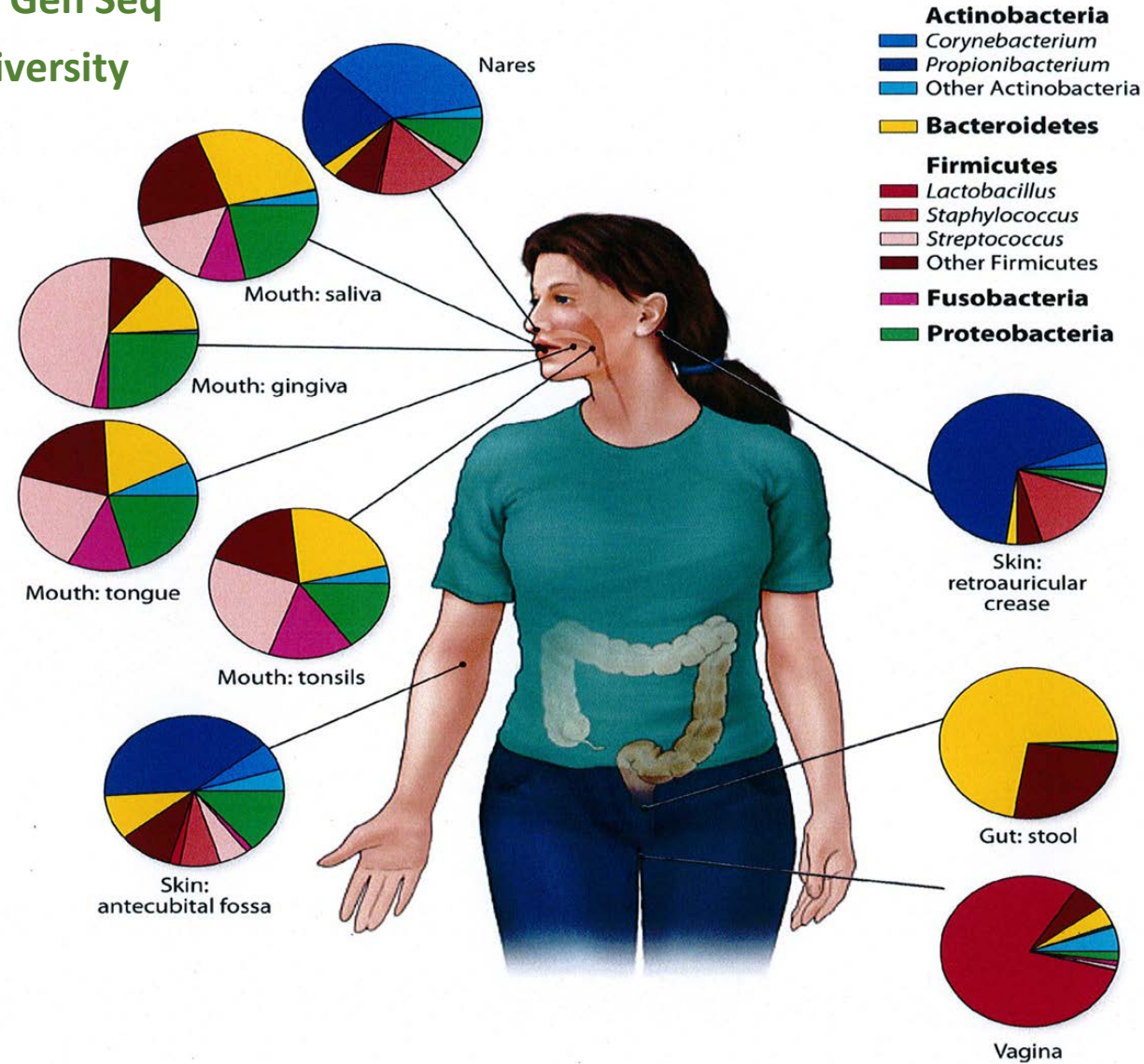
WHI Investigators Meeting

May 4-5, 2017

Columbus, Ohio

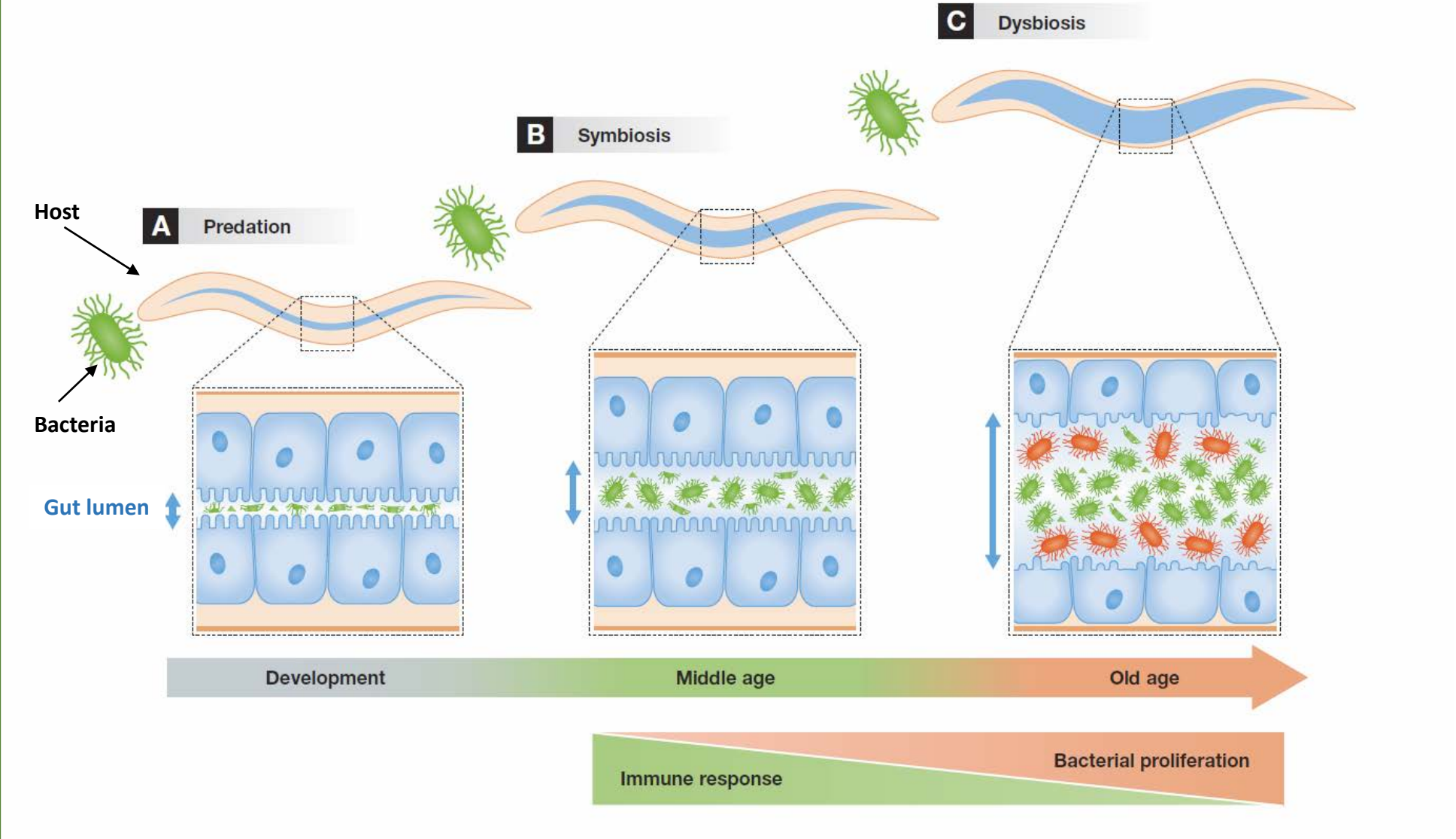
# Human Microbiome Project

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

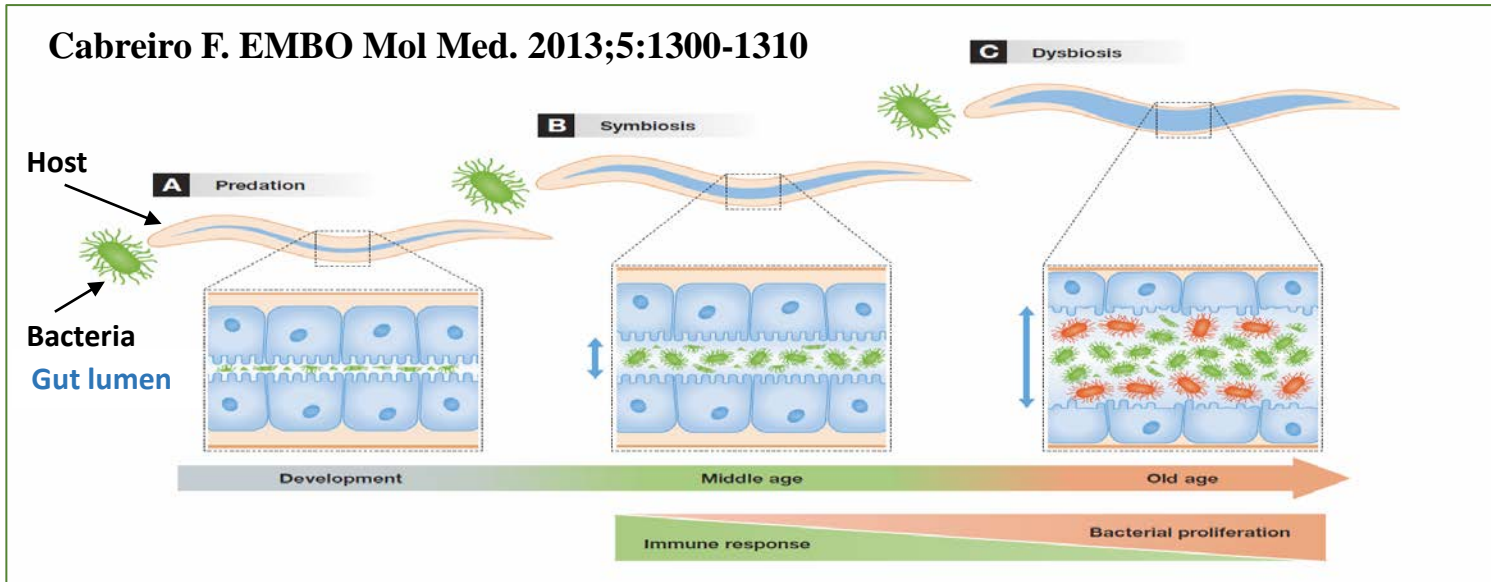


# Microbiota, Metabolome, Health and Aging

Cabreiro F. EMBO Mol Med. 2013;5:1300-1310



# Microbiota, Metabolome, Health and Aging



## Important Knowledge Gaps:

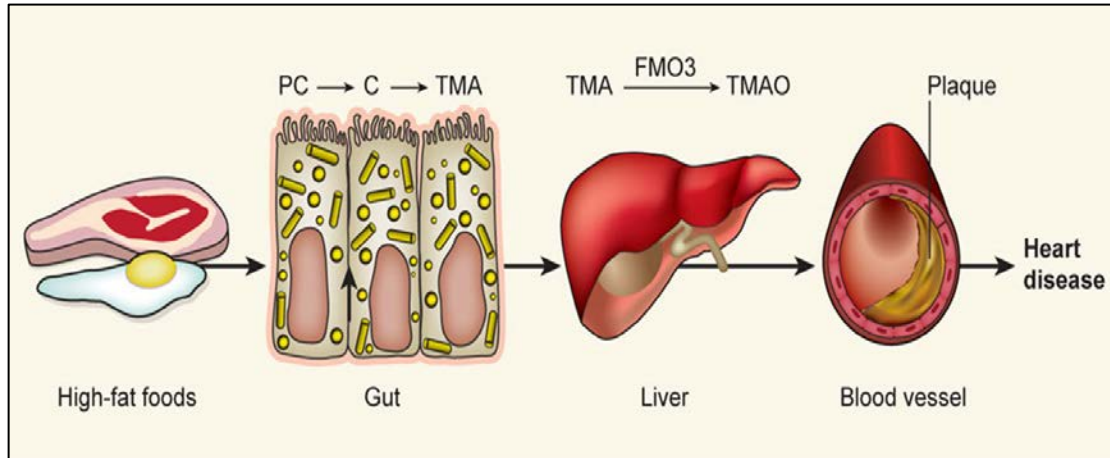
What **factors** are associated with altered host immune response and development of **dysbiosis in aging**?

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



# Microbiome and Metabolome in Aging: *Scientific Opportunities in WHI*



## ***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

University of Michigan



## ***What is the metabolome & how can it improve understanding disease mechanisms?***

Robert Genco, DDS, PhD

SUNY Distinguished Professor of Oral Biology and Microbiology,

Director, Microbiome Research Center

University at Buffalo, The State University of New York



## ***Microbiome & Metabolome Studies in WHI and the Buffalo Clinic Center***

Michael LaMonte, PhD, MPH

Research Associate Professor of Epidemiology,

University at Buffalo, The State University of New York



## ***Opportunities for microbiome and metabolome studies in WHI - - Discussion***

Jean Wactawski-Wende, PhD

SUNY Distinguished Professor of Epidemiology,

Dean, School of Public Health and Health Professions

University at Buffalo, The State University of New York