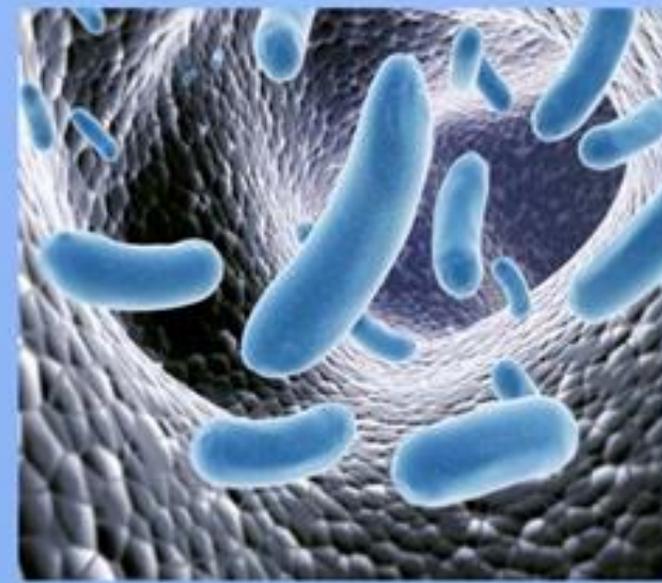# Workshop on Best Practices in Studies of Diet and the Intestinal Microbiome

June 13-14, 2017
Bethesda, MD

National Institute of Diabetes and Digestive and Kidney Diseases

**Sponsors:** USDA-ARS, ILSI NA, and NIH
Organizers: David Klurfeld, Chris Lynch, Robert Karp and Cindy Davis

Disclosures

Workshop Background

1. **Many studies of the intestinal microbiome, whether *in vitro,* in animal models, or in humans report only minimal information on dietary components even though there is substantial evidence that diet modulates the composition of the microbiota.**

2. **Although many aspects of microbiome studies show improved quality control over time, this has not always extended to diet.**

Workshop Objectives
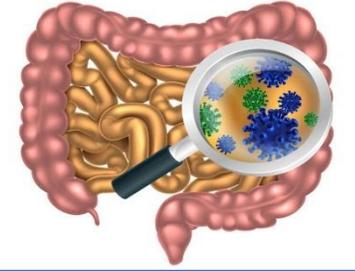
- To improve rigor and reproducibility in research on the colonic microbiome.
- To identify important dietary information that should be reported.
- To identify parameters to consider in the design of studies, particularly for clinical studies, on diet and the intestinal microbiome.
- To publish a summary for the research community in a peer-reviewed journal.

Session 1: Characterization of Dietary Fibers and Other Nutrients that Feed the Microbiome

Speakers: George Fahey, Bruce Hamaker, and Eric Martens

Key points:

1. Fiber is perhaps the most chemically complex food constituent important in human nutrition - explains issues inherent to its definition and analysis
2. Need better information on how foods and food additives lead to shifts in microbial digestion of glycans

Session 2: Animal Models

Speakers: Justin Sonnenburg, Eugene Chang, Andre Marette, Benoit Chassaing, and Kelly Swanson

Key Points:

1. Although the AIN-93 diet is considered the gold standard in nutritional studies that use rodent models, it contains no fermentable dietary fiber
2. Microbiota in mice show circadian rhythm which is shifted by diet
3. Many dietary constituents can modulate the composition and activity of the colonic microbiome- polyphenols, proteins, omega-3 fatty acids
4. Emulsifiers and other GRAS substances may affect microbiota and inflammation
5. Non-rodent models are possibly better models but not validated

Animal Models- Unanswered Questions and Research Gaps

Questions:
1. Are gnotobiotic animals with defined microbiota valid models of animals with natural microbiota?
2. What is the optimal diet for animals studies?
3. What are the causes of variation in both animal and human microbiota?

Gaps:
1. Better tools to study how individual strains colonize the gut
2. Adequate data on organisms other than bacteria such as Archaea, fungi, viruses, parasites and bacteriophage or many of their functional capacities

Session 3: *In Vitro* Models

Speakers: Emma Allen-Vercose and Devin Rose

Key Points:
1. Bioreactors may be excellent model systems for single organisms and complex ecosystems
2. Defined communities allow precise understanding of ecosystem functions
3. *In vitro* systems make it easy to apply treatments, obtain samples and are accessible for 'omics sampling

Gaps:
1. Source of the inoculum- feces
2. Knowledge of the diet of the fecal donor
3. Nature of the nutrient supply
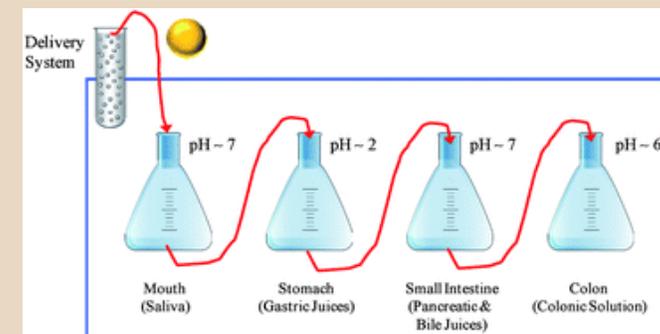
Speakers: Gary Wu, Stephen O'Keefe, Johanna Lampe, Joanne Slavin, Maria Saarella, and Barbara Schneeman

Key points:
1. Large differences in hunter-gatherer or agrarian versus western diets in microbiota and metabolome
2. Controlled feeding studies are useful for investigating the effect on gut microbiota and host response but they have limitations (access to tissues of interest, mostly short-term outcomes, challenges establishing causality)
3. Studies with fiber mixtures suggest interventions can support GI microbiota during antibiotic treatment
4. Fiber recommendations should be based on colonic microbiota requirements not cardiovascular health

Human Studies: Unanswered Questions and Research Gaps

Questions:

1. Does diet affect recovery of gut microbiota after disruption- antibiotics, infections?
2. Why does diet explain about 60% of the variation in the gut microbiome of mice but only about 10% in humans?

Gaps:

1. Better methods to determine dietary exposure
2. There is no biomarker that reflects dietary fiber intake or status
3. Many issues ignored in studies of the human intestinal microbiota- feces collected; baseline microbiota
4. Lack of basic information on how transit time affects composition of the colonic microbiota
5. Prebiotics- no prospective cohort studies linking changes in the fecal microbiota with health endpoints

Conclusions

➢ **In the absence of clearly superior dietary approaches for specific research questions, the main recommendation is to provide as much detail as possible about feeding and housing conditions of test subjects, so that other researchers can reproduce the work.**

➢ **Characterization of a core, healthy microbiota (and more usefully, their metabolic functions) remains elusive.**

➢ **This emerging field needs to move from associations to causality which will be catalyzed by knowing in as much detail as possible about what is ingested, how it is metabolized, and the health consequences derived from these processes.**

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http://ods.od.nih.gov

bacteria are my friends
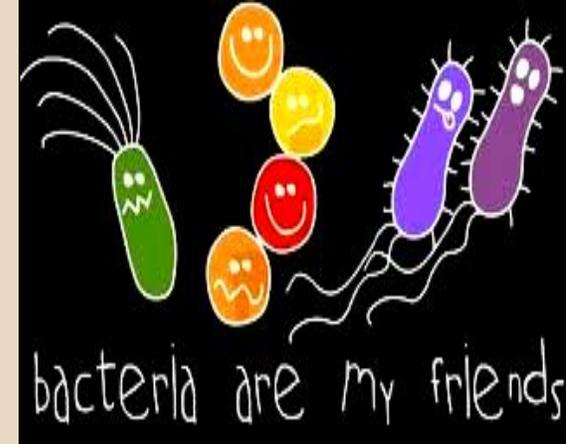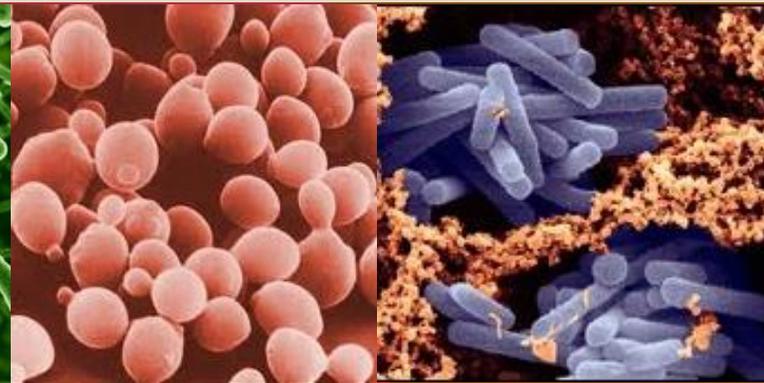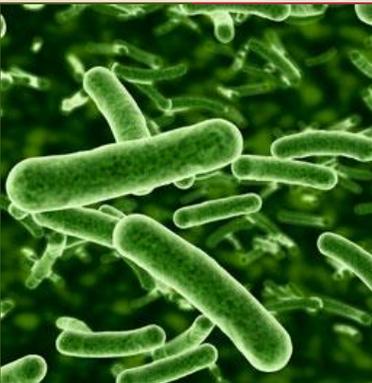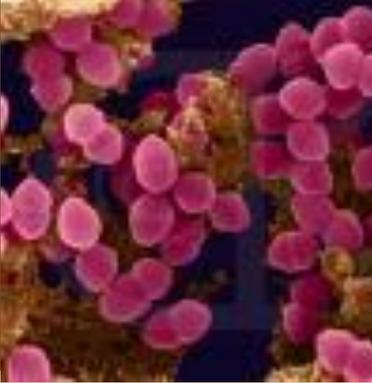
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