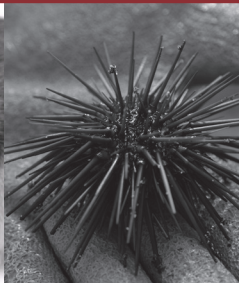# ILAR Roundtable

Animal Models for Microbiome Research: Advancing Basic and Translational Science

A Workshop of the Roundtable on Science and Welfare in Laboratory Animal Use

December 19-20, 2016
500 5th Street NW, Washington DC 20001
National Academies of Sciences, Engineering, and Medicine
Keck Center, Room 100

Our understanding of the contributions of microbial communities that occupy various sites in our bodies to health and disease is advancing rapidly. A large number of international projects have focused on characterizing these communities, which include members of all three domains of life on Earth (i.e. bacteria, archaea and eukarya) and their viruses. These projects have produced experimental and computational resources that enable analysis of community functions. In recent months, the White House launched the National Microbiome Initiative to "foster the integrated study of microbiomes across different ecosystems" (https://www.whitehouse.gov/thepressoffice/2016/05/12/factsheetannouncingnationalmicrobiome-initiative) pulling together federal agencies, academic institutions and private entities.

Most preclinical research has focused on the mouse as a model organism for delineating the mechanisms that shape the assembly and dynamic operations of microbial communities, for performing preclinical proof-of-concept tests of causal relationships between given community configurations/ memberships and host physiologic, metabolic, immune and neurologic phenotypes; and for developing methods to repair or prevent functional abnormalities in these communities that contribute to disease pathogenesis.

This public workshop is designed to examine animal models of microbiome research. Invited speakers will (i) explore how to improve the depth and breadth of analysis of microbial communities using various model organisms; (ii) address the challenges of standardization and biological variability that are inherent in gnotobiotic animal-based research; (iii) examine the predictability and translatability of preclinical studies to humans; and (iv) discuss strategies for expanding the infrastructure and tools for conducting studies in these types of models. They will address gaps, challenges and opportunities in this rapidly expanding field with particular attention to the care, use, and welfare of the gnotobiotic animals.

An individually authored summary of the presentations and discussions at the workshop will be prepared by a designated rapporteur in accordance with institutional guidelines.

Monday, December 19

(Gnotobiotic) Model Organisms and Microbiome Research: Choices, Challenges, and Proposed Solutions

7:30 - 9:00am   **Registration**

9:00   **Animal Models and Microbiome Research: A Trans-Kingdom Perspective**
Herbert "Skip" Virgin, Washington University

9:45   **Coffee Break**

10:00   **Session 1-1. Non-rodent animal models for microbiome research**
Much of current microbiome research has focused on mouse models. As with other branches of preclinical research, exploring the microbiome in other species complements and advances knowledge gleaned from mice. This session will provide perspectives on the benefits and limitations of some of these animal models.

> **C. Elegans -** Buck Samuel, Baylor College of Medicine
> **Drosophila -** Angela Douglas, Cornell University
> **Zebrafish -** Karen Guillemin, University of Oregon
> **Piglets -** Jeff Gordon, Washington University, Planning Committee Member (remotely)

12:00pm   **Lunch** (will not be provided. There is a cafeteria on the third floor of the Keck Center.)

1:00   **Session 1-2. In-Vitro Systems for Characterizing the Properties/Dynamic Operations of Microbial Consortia**
One of the benefits stemming from advances in in vitro systems is the opportunity to reduce the number of animals needed to develop and test hypotheses, and in some cases replace their use entirely. Speakers in this session will present three non-animal systems for microbiome research, including thoughts on their ability to complement animal use now and in the future.

> **Bioreactors -** Robert Britton, Baylor College of Medicine
> **Organoids -** Vincent Young, University of Michigan (Planning Committee Member)
> **Microfluidics: Human organs on chips -**
> Donald Ingber, Wyss Institute at Harvard University (remotely)

2:30   **Coffee Break**

2:45   **Session 1-3. Modeling Human Microbiota in Animal Systems**
Animal models provide opportunities to define the contributions of members of the microbiota to community function and the mechanisms through which they affect various aspects of host biology. This session illustrates current approaches that are being used and how these approaches may be advanced to promote further basic and translational research in this field.

A. Connecting Microbes to Metabolism Using Gnotobiotic Models
- Biologically significant metabolites produced by the gut microbiota: their origins and functions **-** Federico Rey, University of Wisconsin-Madison
- Mechanistic studies of how the gut microbiota influences host metabolism - Patrice Cani, Université Catholique de Louvain, Belgium

B. Revisiting Koch's postulates from a microbial community perspective
- Fusobacterium nucleatum and colorectal carcinogenesis- Wendy Garrett, Harvard T. H. Chan School of Public Health (Planning Committee Member)
- Microbes and atopic disorders - Richard S. Blumberg, Harvard Medical School

C. The interface between microbes and neuroscience
- The effects of the microbiome on the behavior of bees - Nancy Moran, University of Texas at Austin
- Maternal stress and the microbiome: programming of offspring neurodevelopment - Tracy Bale, University of Pennsylvania

5:45   **Adjourn**

Tuesday, December 20

Methodological Challenges in Characterizing Gnotobiotic Animal Models

9:00 **Session 2-1. Reproducibility: Within and Across Experiments**

Creating Stabilized and Defined Microbiomes in Laboratory Animals
Andrew Macpherson, University Hospital, Bern, Switzerland

9:45 **Coffee Break**

10:00 **The role of host genetics -** Aldons J. Lusis, University of California at Los Angeles

The role of immunologic variation - Jeremiah Faith, Icahn School of Medicine

The role of diets: standardization and characterization - Gary Wu, University of Pennsylvania

The role of gender - Alexander Chervonsky, University of Chicago

12:00pm **Lunch** (will not be provided. There is a cafeteria on the third floor of the Keck Center.)

1:00 **Session 2-2. Establishing and Evolving Gnotobiotic Facilities and Their Technologies: Examining the Present and Looking to the Future**
Establishing the necessary infrastructure for microbiome research is challenging. How can a successful gnotobiotic facility be planned? What are some of the attributes that can ensure sustainability, community sharing and support of such a facility (including rederivation and 'archiving' of animals as germfree)? The speakers will share their experiences regarding challenges and solutions encountered. They will also focus on advances in the support systems and facility operations that enable animal care personnel to provide for the improved well being of the specialized animals used in microbiome research.

Establishing a new gnotobiotic facility: Education, missions, and accomodating success - Timothy Hand, University of Pittsburgh

Evolving an established gnotobiotic facility - R. Balfour Sartor, University of North Carolina Chapel Hill

Complex gnotobiology: An emerging paradigm in the era of next generation sequencing - Craig Franklin, University of Missouri

Alternatives to gnotobiotics: Normalizing the environment - Stephen Jameson, University of Minnesota

Veterinary management challenges and future directions, including technical considerations for imaging and surgery in gnotobiotic animals - Betty Theriault, University of Chicago

Unique challenges and future directions related to managing mouse gnotobiotic husbandry facilities - Chriss J. Vowles, University of Michigan

4:30   **Overview of Workshop**
Joseph Newsome and Vincent Young

5:00pm   **Adjourn**