

Altering the Microbiome: Can it Impact Health?

September 24, 2015, National Cancer Institute at Frederick MD

Welcome to today's program.

We greatly appreciate the involvement of all of our speakers and committee members, and especially you!

A particular thanks goes to Dr. Howard Young, our host today. And thank you to Kathy Easterday and Chris Graham, who have helped make the process so enjoyable.

In addition, appreciation for their financial support goes to NCI, NIAID, NIAMS and the NIH Office of Research in Women's Health.

If this is the first time you are learning about the BioPharma Research Council, we are a nonprofit association for scientists throughout the many silos of biomedical research- industry, academic, nonprofit, government, and supplier labs and their teams.

We provide educational programs that facilitate interaction in order to stimulate collaborations and partnerships that can spur progress.

Please feel free to be in touch with us to share your thoughts and questions. We are planning programs for 2016, and perhaps we can work together this year!

Best,

Joanne Gere
Executive Director
jgere@biopharmaresearchcouncil.org

Planning Committee:

Howard Young, Ph.D.

Senior Investigator, Cancer and Inflammation Program
Center for Cancer Research, NCI at Frederick, Frederick, MD

Camilia Martin, M.D., M.S.

Assistant Professor of Pediatrics Associate Director, Neonatal Intensive Care Unit
Beth Israel Deaconess Medical Center


Laurel A. Lagenaur, Ph.D.

Director of Research, OSEL, Guest Researcher, NCI

Winston Kuo DMSc, COO, IES Diagnostics

Joanne Gere, Executive Director, BioPharma Research Council






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| 9:00 | <p>Introduction: Joanne Gere, Executive Director, BioPharma Research Council</p> <p>Welcome: Howard Young, Ph.D. Senior Investigator Cancer and Inflammation Program Center for Cancer Research NCI at Frederick, Frederick, MD</p> |
| 9:10 | <p>Keynote: Overview of Progress and Challenges in Probiotic/Prebiotic and Microbiome Research: NIH and Beyond</p> <p>Linda Duffy, Ph.D., MPH</p> <p>Scientific Chair, Trans-NIH DNRC/NCC-PPWG Inter-agency Probiotics and Microbiome SIG Program Director, NP-DER National Center for Complementary and Integrative Health, National Institutes of Health NIH/DHHS</p> |
| 9:40 | <p>Microbiota Dependent Consequences of Infections</p> <p>Denise Morais da Fonseca, Ph.D. Laboratory of Parasitic Diseases National Institutes of Allergy and Infectious Diseases - NIAID/NIH - Bethesda</p> |
| 10:05 | <p>The Gut Microbiota Regulates Murine Cardiac Transplant Outcome</p> <p>Emmanuel F. Mongodin Ph.D. Assistant Professor, Microbiology and Immunology Assistant Professor, Institute for Genome Sciences, University of Maryland School of Medicine</p> |
| 10:30 | Break |
| 11:00 | <p>Studies of the Respiratory Microbiome</p> <p>Barbara Methé Ph.D. Professor, Departments of Human Genome Medicine and Microbial and Environmental Genomics, J. Craig Venter Institute (JCVI)</p> |
| 11:25 | <p>Panel- The Maternal-Fetal Microbiome: Implications for Maternal and Infant Health</p> <p>Moderator: Camilia Martin, M.D., M.S. Assistant Professor of Pediatrics Associate Director, Neonatal Intensive Care Unit Beth Israel Deaconess Medical Center</p> <p>Elizabeth J. Corwin RN, P.D. Associate Dean for Research, Emory University School of Nursing Biobehavioral Determinants of the Microbiome and Preterm Birth in African American Women</p> <p>Juliette C. Madan, MD, MS Associate Professor of Pediatrics, Geisel School of Medicine, Dartmouth The Neonatal Microbiome: Exposures and Outcomes</p> <p>Amanda Prince, Ph.D. Postdoctoral Associate, Baylor College of Medicine We Are What We Eat: True for Babies?</p> |

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| 12:15 | Lunch |
| 1:15 | <p>Next-Generation Microbial Therapeutics for Prevention and Treatment of Disease</p> <p>Robert Britton Ph.D. Professor, Therapeutic Microbiology Laboratory Department of Molecular Virology and Microbiology Alkek Center for Metagenomics and Microbiome Research Baylor College of Medicine</p> |
| 1:50 | <p>Modifying the Vaginal Microbiome to Protect Against HIV</p> <p>Laurel A. Lagenaur, Ph.D. Director of Research, OSEL, Guest Researcher, NCI</p> |
| 2:15 | Break |
| 2:35 | <p>Fecal Microbiota Transplantation: Promises and Pitfalls</p> <p>Suchi Hourigan, MD Pediatric Gastroenterologist, Pediatric Specialists of Virginia Director of Microbiome Research, Inova Translational Medicine Institute Director of Pediatric Research, INOVA Assistant Professor, Adjunct, Johns Hopkins School of Medicine</p> |
| 3:00 | <p>Fecal Microbiota Transplantation as a Therapeutic for HIV Associated Gut Dysbiosis</p> <p>Stanley Langevin, Ph.D. Senior Research Scientist Department of Microbiology, University of Washington</p> |
| 3:25 | <p>Panel: Addressing Microbiome Data Generation and Analysis</p> <p>Winston Kuo DMSc, COO, IES Diagnostics (Moderator)</p> <p>Amiran Dzutsev MD, Ph.D. Staff Scientist, Laboratory of Experimental Immunology Cancer and Inflammation Program, NCI</p> <p>Rashmi Sinha, Ph.D. Deputy Branch Chief and Senior Investigator Division of Cancer Epidemiology & Genetics, NCI</p> <p>Jason T. Ladner, Ph.D. Center for Genome Sciences United States Army Medical Research Institute of Infectious Diseases</p> |
| 4:15 | Closing Remarks- Dr. Kuo |
| | <p>Manipulating the Microbiome: Can it impact Health? Subject to Change www.biopharmaresearchcouncil.org</p> <p>Contact: Joanne Gere, Executive Director, BioPharma Research Council jgere@biopharmaresearchcouncil.org</p> |





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Speaker Bios and Abstracts:

Robert Britton, Ph.D.

Professor, Therapeutic Microbiology Laboratory
Department of Molecular Virology and Microbiology, Baylor College of Medicine
Member of the Alkek Center for Metagenomics and Microbiome Research

Dr. Britton earned his B.S. in Biology at the University of Nebraska-Lincoln in 1989. From 1990-1996 he completed his PhD work with Dr. James R. Lupski in the area of cell cycle regulation of *Escherichia coli* at Baylor College of Medicine. From 1996-2002 he performed postdoctoral research with Dr. Alan Grossman at MIT in the areas of Gram-positive cell cycle research and applying newly developed microarray technology to *Bacillus subtilis*.

His first faculty position (2003-2014) was in the Department of Microbiology and Molecular Genetics at Michigan State University, where he rose to the rank of Professor. During this time he interacted closely with members of the National Center for Microbial Ecology and developed a research program focused on probiotic bacteria and their interactions with animals and humans. In 2010, he became interested in how the microbiome impacts the ability of pathogens to invade the host and has led a team that developed *in vitro* and *in vivo* models to study the function of human microbial communities. In 2014 he moved the Therapeutic Microbiology Laboratory to Baylor College of Medicine where the main focus of his group is to identify next-generation microbial therapeutics for the prevention and treatment of human disease.

Elizabeth Corwin, Ph.D., RN, FAAN

Associate Dean for Research and Professor, Nell Hodgson Woodruff School of Nursing, Emory University

Elizabeth Corwin, PhD, RN, FAAN, is the Associate Dean for Research and Professor at the Nell Hodgson Woodruff School of Nursing at Emory University. Dr. Corwin is a Physiologist and a family nurse practitioner. Dr. Corwin's research is aimed at uncovering the biological mechanisms responsible for adverse outcomes in pregnant and postpartum women, especially low-income and minority women as well as their infants, with a focus on the effect of chronic stress on the microbiome. She is Principle Investigator on two NIH-funded studies focused on maternal and infant health: "Biobehavioral Determinants of the Microbiome and Preterm Birth in Black Women" (R01NR014800) and "Maternal Stress and the Gut-Brain Axis in African American Infants" (R01MD009746).

Keynote: Linda Duffy, Ph.D., MPH

Scientific Chair, Trans-NIH DNRC/NCC-PPWG
Inter-agency Probiotics and Microbiome SIG
Program Director, NP-DER
National Center for Complementary and Integrative Health, National Institutes of Health NIH/DHHS

The overview provides insights into the molecular basis of therapeutic applications of selective probiotic microorganisms and metabolites, and the interaction between microbial-host metabolites and molecular signatures gaining attention as potential therapeutic strategies for cancers, metabolic syndrome, diabetes, obesity, and neurocognitive disorders. Understanding the pharmacologic effect of the gut microbiota on response to drugs is an essential step towards tailored vaccines and other therapies that would be more efficient, cost-effective, and with lower adverse drug events.

Specific strains of probiotics has been shown to have modulatory effects on intestinal and systemic immune responses in animal models and forms the rationale basis for human studies with vaccines. Bioactive microencapsulation and nanoparticulate systems are being used for different drug delivery systems and increasingly applied to probiotic food products. Through rigorous characterization of nutraceutical interactions between the diet and the microbiota, metabolomics is providing new ventures for validating biomarkers needed to advance probiotic/prebiotic strategies in modulating the microbiota toward the improvement of human health.

Dr. Linda Duffy is a Health Scientist Administrator at the National Institutes of Health/National Center for Complementary and Integrative Health. Dr. Duffy also serves as the Trans-NIH and Inter-agency Scientific Chair of the Probiotics/Prebiotics and Microbiome Working Group under the NIH Office of the Director on partnering initiatives with federal government agencies and the White House Office of Science and Technology Policy. Her position focuses on building Programs as Centers of Excellence in natural products research, with special emphasis on probiotic/prebiotic foods and pharmacologic safety studies on gut microecology and microbiome.

Her research includes health impacts on immunologic inflammatory responses, maternal-child health, brain-gut interactions, obesity, and aging. Before returning to federal government in 2004, Dr. Duffy served as Professor in joint appointments in the School of Medicine, at the University of Buffalo for over 15 years. She has published over 100 articles, and has been an Invited Speaker at many National and International Conferences over her 30 year career. She recently co-authored an article addressing *progress and challenges in developing metabolic footprints from diet in human gut microbial cometabolism* and has contributed to white papers and Evidence Reports informing science policy on the topic.

Suchitra Hourigan, MD

Pediatric Gastroenterologist, Pediatric Specialists of Virginia
Director of Microbiome Research, Inova Translational Medicine Institute Director of Pediatric Research, INOVA
Assistant Professor, Adjunct, Johns Hopkins School of Medicine

Suchitra Hourigan, MD, is a Pediatric Gastroenterologist at Pediatric Specialists of Virginia, and an Assistant Professor at the Johns Hopkins School of Medicine. Her research is in the role of *Clostridium difficile* colonization and infection in inflammatory bowel disease, fecal microbiota transplantation in children and the developing intestinal microbiome of full term and preterm infants and associated health outcomes. She leads current microbiome studies at the Inova Translational Medicine Institute.

Winston Kuo DMSc

COO, IES Diagnostics

Winston Kuo is the founder of Harvard Medical School's Laboratory for Innovative Translational Technologies, which was an integral part of the Clinical and Translational Science Award program, Dr. Kuo has founded and supported many programs that spur biomedical research.

He initiated and participated with the FDA in a large-scale comprehensive study evaluating the clinical utility of gene expression technologies, published in *Nature Biotechnology* (July 2006). He sits on the NIH/SBIR grant review study section and is a peer reviewer for the Qatar National Research Fund.

Dr. Kuo's clinical and translational initiatives have expanded globally in developing countries such as Brazil, China, Mongolia, Nigeria, Saudi Arabia and South Africa, focusing upon accelerating understanding of mechanisms that affect human disease; catalyzing the identification and development of useful biomarkers; and speeding the development of therapeutics in patients. Dr. Kuo has also instructed in the Innovation for Economic Development program at the Harvard Kennedy School of Government.

Dr. Kuo is a founder and Trustee of the Otto Heinrich Warburg Cancer Research Foundation. He sits on the editorial boards of multiple peer reviewed journals, and is Editor-in Chief of the *Journal of Circulating Biomarkers* and *NanoBioMedicine* (both of which he founded). He has consulted with the NIH on interdisciplinary outreach, and sits on a number business and nonprofit Scientific Advisory Boards, including the BioPharma Research Council. He received is Doctor of Medical Sciences (DMSc), Oral and Computational Biology from Harvard Medical School.

Laurel Lagenaur, Ph. D.

Director of Research, OSEL, Guest Researcher, NCI

Dr. Lagenaur received her doctorate in Microbiology and Immunology from Stanford University, and completed post-doctoral training at the University of California, San Francisco studying HIV-associated viral infections. She joined Osel in 1998 and was the principal investigator on Osel's first research grant to develop MucoCept-HIV as a novel live biotherapeutic to prevent HIV transmission in women. She moved to Bethesda with her husband (who is an investigator in the NIH intramural program) and became a guest researcher at NIH.

Dr. Lagenaur is a molecular biologist with extensive experience in virology and bacteriology. Her research interests are in modulating the vaginal microbiome to improve Women's Health and to prevent HIV.

Juliette C. Madan, MD, MS

Associate Professor Pediatrics, Division of Neonatology, Dartmouth Hitchcock Medical Center

Dr. Juliette Madan is an Associate Professor of Pediatrics at the Geisel School of Medicine and a physician-scientist in the division of neonatology. She is a translational researcher in the Children's Environmental Health and Disease Prevention Research Center at Dartmouth, where she leads one section of the large epidemiological study of 1,500 mother-baby dyads with a focus on environmental exposures, the neonatal microbiome, and their relationship to health and disease. Dr. Madan's research on the neonatal microbiome continues in high-risk populations including premature infants, infants and young children with CF, with work on identifying nutritional or probiotic regimens that might alter disease progression and promote health.

Camilia R. Martin, M.D., M.S.

Assistant Professor of Pediatrics, Harvard Medical School

Though once thought to be a sterile environment, the in-utero environment is exposed to the maternal microbiome which may subsequently determine the timing of labor and early fetal colonization.

After birth the diet, environment, and medication exposures further direct the microbiome defining patterns that influence the balance between health and disease. In the preterm infant, this includes necrotizing enterocolitis, lung disease and sepsis. In later infancy and childhood the microbiome has been linked to asthma, celiac disease, diabetes, and obesity.

Early strategies in manipulating the microbiome have the potential to optimize immune ontogeny in the preterm infant residing in a high-risk environment and reduce the likelihood of acute and long-term morbidities.

Dr. Martin will address these concepts, as well as the role of the microbiome/organisms in labor and risk of premature delivery, formula vs breast milk, h2 blockers and antibiotics, infant colonization patterns, and the linkage of the microbiome to asthma, celiac disease, diabetes, and obesity.

Barbara Methé Ph.D.

Professor, Human Genome Medicine and Microbial and Environmental Genomics, J. Craig Venter Institute (JCVI)

A variety of microbial communities and their genes (the microbiome) exist throughout the human body that play fundamental roles in human health and disease. Studies of the respiratory microbiome are challenging prior assumptions while generating novel insights into airway health and disease. For example, this presentation will present results from a pilot study in which associations between the host immune response to the intranasal live attenuated vaccine (LAIV) and changes in bacterial composition were examined. Findings include that activation of a type I IFN-mediated antiviral response may foster the disproportionate emergence of potentially pathogenic species such as *Staphylococcus aureus*.

Dr. Methé is a Professor in the Departments of Human Genome Medicine and Microbial and Environmental Genomics at the J. Craig Venter Institute (JCVI) and she is Science Coordinator of the JCVI Metagenomics Group. Among recent projects, she was a leader of JCVI's participation in the National Institutes of Health (NIH) funded Human Microbiome Project including efforts in metagenomics and single cell genomics. She is currently leading a variety of metagenomic-based projects funded by the Department of Energy, National Science Foundation and NIH.

Emmanuel Mongodin, Ph.D.

Asst Professor, Microbiology and Immunology & Institute for Genome Sciences, Univ of Maryland School of Medicine

The microbiota has a profound systemic effect on immunity with consequences for graft survival, rejection, and inflammation. Additionally, pro- and anti-inflammatory fecal microbiota and specific components of the microbiota can be defined and manipulated.

Denise Morais da Fonseca, Ph.D.

Laboratory of Parasitic Diseases, National Institutes of Allergy and Infectious Diseases, National Institutes of Health

Dr. Morais da Fonseca obtained her Ph.D. in 2010 from the University of São Paulo - Brazil on the regulation of the immune response following immunotherapy in airway allergic inflammation. Following a postdoctoral fellowship at the University of São Paulo on immune regulation during intestinal parasitic infections, she joined the Laboratory of Parasitic Diseases - National Institutes of Allergy and Infectious Diseases in 2012 as post-doctoral fellow. Since then, she has been working on understanding how acute infections at mucosal barrier sites, such as the gut, have long-term impacts on tissue function and homeostasis.

Amanda Prince, Ph. D.

Postdoctoral Associate, Aagaard Lab, Dept. of Obstetrics and Gynecology, Baylor University

Dr. Amanda Prince is a Postdoctoral Fellow at Baylor College of Medicine under the mentorship of Dr. Kjersti Aagaard since 2013. She recently received a Ruth L. Kirschstein National Research Service Award with a focus on the role of maternal diet on the offspring microbiome and is a member of the Center for Reproductive Medicine at Baylor. She graduated from Cornell College with a BA in Biochemistry and Molecular Biology and received her PhD in Biomedical Sciences from the University of Massachusetts Medical School with an emphasis on immunology and virology.

Rashmi Sinha, Ph.D.

Deputy Branch Chief of the Nutritional Epidemiology Branch and
Principal Investigator, NIH-AARP Diet and Health Study Division, Cancer Epidemiology & Genetics, NCI

Dr. Sinha's research goal is to explain the complex role of diet in cancer etiology, using an interdisciplinary approach that integrates biological mechanisms with epidemiologic studies. Dr. Sinha is a well-respected researcher and has made substantial impact in the field of diet and cancer. She is now actively working on the involvement of the microbiome in the gastrointestinal system.

She has undertaken an ambitious plan to apply this exciting new technology to population-based studies. Few epidemiologic studies have evaluated the role of the human microbiota in health with the degree of standardization necessary for translational applications. She has brought together an interdisciplinary team from over 20 microbiome research institutions to work together to develop best practices and to identify sources of potential measurement error through rigorous studies in the Microbiome Quality Control Study. This effort will improve the state-of-the-art in several key topics ranging from sample collection to meta-analysis and reproducibility and promote open sharing of standard operating procedures and best practices throughout the field.

Howard Young, Ph.D.

Senior Investigator, Cancer and Inflammation Program, Center for Cancer Research, NCI at Frederick

Howard Young received his PhD from the Department of Microbiology and Immunology at the University of Washington and did postdoctoral research under Drs. Edward Scolnick and Wade Parks at the National Cancer Institute. He joined the National Cancer Institute in 1983 and became Deputy Chief of the NCI Laboratory of Experimental Immunology in 2006. His research has focused on the analysis of cytokine gene expression and signaling with a special emphasis on the molecular characterization of the transcriptional and posttranscriptional regulation of Interferon-gamma in NK cells. Most recently, his laboratory has developed novel mouse models of lupus and aplastic anemia based on chronic expression of low levels of this important immunoregulatory molecule in the murine C57BL/6 genetic background and the Balb/c genetic background, respectively. He is also collaborating with a laboratory in Malaysia on the development of probiotic microorganisms as carriers for vaccine delivery systems.

Dr. Young is a former President of the International Society for Interferon and Cytokine Research and is a co-recipient (with Dr. Sidney Pestka) of the first Distinguished Service Award from the ISICR, is a two time recipient of the National Cancer Institute Director's Award for Mentoring and is a recipient of the National Public Service Award from the American Society for Public Administration and the National Academy of Public Administration. He has also served as Chair of the Immunology Division of the American Society for Microbiology, Chair of the NIH Immunology Interest Group and Cytokine Interest Group and is a member of the American Academy of Microbiology.