NW Microbiome Network Hosts:

MICROBIOME MIXER

8:30 AM – 9:15 AM	Arrival, check-in, poster set-up; *breakfast available*
9:15 AM – 10:00 AM	Structured Networking; *breakfast available*
10:00 AM – 10:15 AM	Welcome! Introductory Remarks
10:15 AM – 11:45 AM	Individual Presentations Followed by Panel-style Q & A

Can we use microbiomes to predict or diagnose host or environmental health?

Moderator: Chris Gaulke

Brendan Bohannan, PhD

Thomas Sharpton, PhD

Kim Brown, PhD

Ryan McClure, PhD

Justin Merritt, PhD

11:45 AM – 1:00 PM	**Lunch + Poster Session**
1:00 PM – 2:30 PM	Individual Presentations Followed by Panel-style Q & A

Does the future of health care or ecological conservation involve microbiome management?

Moderator: Hannah Tavalire

Natalia Shulzhenko, MD, PhD

Anne Thompson, PhD

Jon M. Jacobs, PhD

Karen Guillemin, PhD

Amy Moran, PhD

2:30 PM – 3:30 PM	Overview: Institutional Resources
3:30 PM – 4:15 PM	Identifying Areas for Future Collaborations
4:15 PM – 4:30 PM	Looking Forward: Closing Remarks

Brendan Bohannan

Brendan Bohannan, Ph.D., is the Alec and Kay Keith Professor of Environmental Studies and Biology at the University of Oregon's Institute of Ecology and Evolution. His research is focused on understanding the causes and consequences of microbial biodiversity. He began his research career studying microbes in non-host environments (such as soil, water, air, and built environments), but over the past 12 years his group has increasingly focused on the microbiomes of humans and other animals (including fish, birds and primates). He is especially interested in how transmission (among hosts, and between hosts and the external environment) interacts with host factors (such as individual genetics and physiology) to determine the composition of host-associated microbiomes. His group is also interested in how host-microbe system-level functions (such as digestion, or stimulation of the immune system) emerge from the complexity of host-microbe interactions. Professor Bohannan is a founding member of the Microbial Ecology and Theory of Animals Center for Systems Biology (an NIH Center of Excellence focused on the application of ecological theory to host-microbe systems) and the Biology and the Built Environment Center (a national center for the study of the microbial ecology of buildings). He is a Fellow of the American Academy of Microbiology, as well as an Aldo Leopold Environmental Leadership Fellow, a Google Science Communication Fellow, and a Wulf Professor of the Humanities. Prof. Bohannan received a Ph.D. in Microbiology from Michigan State University and post-doctoral training in Ecology at the University of Chicago, before joining the Stanford University faculty in 1999. He has been a member of the University of Oregon faculty since 2006

Thomas Sharpton

Thomas Sharpton is an Assistant Professor at Oregon State University. He earned his Ph.D. in Microbiology from the University California at Berkeley in 2009 with a Designated Emphasis in Computational Biology. He subsequently received his postdoctoral training at the Gladstone Institutes in San Francisco, CA, wherein he pioneered computational tools and data resources to characterize the human metagenome. In 2013, he joined OSU as a faculty member in the Departments of Microbiology and Statistics. In addition to teaching students in the classroom, Dr. Sharpton runs an internationally recognized research laboratory that applies molecular, computational, and statistical methods to determine how the gut microbiome influences the health, ecology, and evolution of vertebrates. Dr. Sharpton also serves as the Founding Director of the Oregon State University Microbiome Initiative, which seeks to transform how we study and conceptualize microbiomes, disseminate microbiome-related education and training, and expand the public's involvement and interest in this exciting and rapidly growing research arena.

Kim Brown

I received my Ph.D. from Washington State University in 2004 and completed two post-doctoral training positions. In my first post-doc at the University of Idaho, I worked on the effects of environmental estrogens, specifically the major form of female birth control (17α-ethynylestradiol), and their consequences on male rainbow trout reproductive physiology. From there I moved into cytogenetic research in my second fellowship at Harvard Medical School and Brigham and Women's Hospital in Boston, MA. This work focused on Copy Number Variants (CNVs) in the model organism zebrafish. Future work will combine these interests to look at whether environmental contaminants can alter genome structure.

Ryan McClure

Dr. Ryan McClure's research is focused on using network analyses to understand interactions both within and between microbial species and between microbes and the host. His work mainly focuses on collecting large datasets of transcriptomic and other kinds of -omics data across conditions and environments to determine where there is coordination between species, genes, proteins and metabolites. This data can then be mined to better understanding which species may be particularly important to certain microbiomes and how species within microbiomes may interact. He has applied these approaches to microbiomes of soil and of the human host as well as to individual microbial species such as cyanobacteria and human pathogens. In addition, Dr. McClure has experience in synthetic biology and applies this to better understand and control interactions between microbial species, including those that may be predicted from network analysis.

Justin Merritt

Dr. Merritt's research focuses on the mechanisms used by signal transduction systems to control various virulence properties of several bacterial pathogens associated with oral disease. Research in my laboratory is focused upon the genetic regulatory mechanisms linking the control of various accessory/virulence gene pathways with the sensing of environmental stress. We study members of the human oral flora as our model system for the role of microbial ecology in determining health and disease at mucosal sites in the human body. Our primary organism of interest is Streptococcus mutans, which is one of the principal species responsible for triggering tooth decay (dental caries) as result of dysbiosis among the oral flora. However, our research also often involves studies of a variety of other oral bacterial species, especially for studies of interspecies interactions among the oral flora. In addition, we have recently begun examining the role of Anginosus group streptococci in the formation of oral and systemic abscesses. Treatment of dysbiotic diseases caused by the flora, such as oral diseases, irritable bowel disease, vaginosis, etc. poses a unique challenge because the few species associated with pathology live amongst potentially hundreds of other beneficial species in mixed communities. Thus, the typical antibiotic treatment approaches used for many other types of infections are either ineffective or can result in serious side effects. Ultimately, effective solutions will require new ecological treatment strategies that reestablish symbiosis among the flora.

Natalia Shulzhenko

My main scientific interests are related to understanding how cells of the immune system communicate with other host systems and the resident microorganisms (microbiota) in complex organisms in health and disease. The microbiota exceed 10 times the number of our own body cells and contribute to many physiological processes. This co-existence is beneficial for both sides but has to be tightly regulated in order to prevent disease development. In order to disclose the mechanisms of these physiological and associated pathological processes, I make use of the systems approach and analyze host and microbiota simultaneously. This is done through host transcriptome profiling and global microbiome analysis by microarrays and next generation sequencing to identify the key regulators of the process. These findings are further validated by directed perturbations of host (knockout mice and siRNA) and microbiota (using antibiotics or colonizing germfree mice with specific bacteria or complex microbiota). My recent work on chronic enteropathy in immunodeficient hosts (human and mouse) revealed a crosstalk between the immune system, the microbiota, and the epithelial cells affecting both intestinal and systemic lipid metabolism. I plan to study further the molecular mechanisms of this interaction potentially leading to new therapeutic interventions.

Anne Thompson

Anne Thompson is a Research Assistant Professor in the Biology Department at Portland State University. Thompson's work illuminates the ecology of microorganisms in the Earth's vast open oceans and how they contribute to energy and carbon flow on our planet. Thompson received her PhD from the MIT- Woods Hole Oceanographic Institution Joint Program in Biological Oceanography and has held positions at UC Santa Cruz, BD Biosciences, and the Institute for Systems Biology.

Jon M. Jacobs

Dr. Jon Jacobs is a Senior Research Scientist at Pacific Northwest National Laboratory (PNNL) and Associate Director of the NIH NIGMS Biomedical Technology Research Resource for Proteomic Integrative Biology. Dr. Jacobs background as a biochemist includes over 16 years of experience in the development and application of advanced mass spectrometry based proteomic analysis techniques utilized at PNNL. His expertise lies in the study of complex mammalian and microbial systems, including clinical cohorts and studies focusing on inflammatory responses, infectious diseases, and liver diseases. He has an extensive history of productive collaborations with leading researchers in their fields and helps lead a diverse research team at PNNL for the execution of such applications, but with personal knowledge of the extensive technical analysis and data interpretation through the utilization of the advanced proteomics technologies and related instrumentation.

Karen Guillemin

Karen Guillemin, Philip H. Knight Professor, is a member of the Department of Biology and the Institute of Molecular Biology at the University of Oregon. She is the founding director of the Microbial Ecology and Theory of Animals (META) Center for Host-Microbe Systems Biology, an NIH funded National Center for Systems Biology established in 2012. Guillemin received her bachelor's degree in Biochemical Sciences from Harvard College and her Ph.D. from the Department of Biochemistry at Stanford University School of Medicine, where she worked with Dr. Mark Krasnow studying organ development in the model organism of the fruit fly. She continued her postdoctoral training at Stanford in the Department of Microbiology and Immunology with Dr. Stanley Falkow, investigating the bacterial pathogen and carcinogen, Helicobacter pylori. Since joining the faculty of the University of Oregon in 2001, she has established an independent research program that combines her interests in animal development and bacterial-host interactions. Her research group has been instrumental in pioneering the use of gnotobiotic zebrafish to study how resident microbial communities assemble and modulate host biology.

Amy Moran

I have a long-standing interest in understanding how the T cell microenvironment shapes the immunological response upon T cell activation. I have a broad background in basic immunology with specific training and expertise T cell receptor signal strength and fate decisions, tumor models, and cancer immunotherapy. My current research seeks to understand the mechanism of action of single agent and combination therapies in models of prostate cancer. These studies parlay from work during my postdoctoral training that uncovered novel mechanisms of synergy between OX40 agonists and PD-L1 blockade in models of sarcoma and adenocarcinomas published in The Journal of Immunology and under review in Cancer Cell. Studies in my independent laboratory focus on understanding how hormone ablation therapies reverse immunesenescence in tumor bearing hosts with a particular interest in prostate cancer. These studies explore the metabolic health and plasticity of tumor-antigen specific T cells in aged hosts and the impact of sex steroid ablation and checkpoint blockade on increasing the bioenergetics potential of these cells. In addition, we explore the impact of restoring thymic function together with PD-1 inhibition in tumor-bearing hosts and the impact this has on the immune repertoire, function, and regulatory T cell differentiation.

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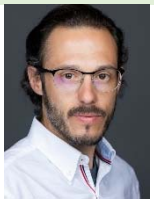	**Manuel**	Garcia-Jaramillo	PhD	Research Associate (Postdoc)

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From the Portland Community

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	**Nelson**	Ting	PhD	Associate Professor
	Doug	Turnbull	PhD	Director, Genomics and Cell Characterization Core Facility

A Metagenomic Meta-Analysis Reveals Functional Signatures of Health and Disease in the Human Gut Microbiome

Oregon State University

Presented at 2018 Lake Arrowhead Microbial Genomics Conference

Courtney Armour

While recent research indicates that human health depends, in part, upon the symbiotic relationship between gut microbes and their host, the specific interactions between a host and its microbiome that define health remain poorly resolved. Metagenomic clinical studies can reveal gut microbial functions that stratify healthy and diseased individuals. However, the typical single-disease focus of microbiome studies limits insight into which microbiome features robustly associate with health, indicate general deviations from health, or predict specific diseases. To improve our understanding of the association between the gut microbiome and health, we conducted the first integrative functional analysis of gut metagenomes by collecting all available clinical metagenomic data, which consists of about 2,000 samples obtained from eight clinical studies. Using a regression modeling approach, we robustly resolve functions in the microbiome that stratify diseased individuals from controls, and when possible control for study-specific effects. Functions that indicate multiple diseases occur at a greater rate than expected by chance, which bolsters the likelihood that these functions contribute to health. We also resolve indicator functions of specific diseases, which point to disease-specific etiologies. Many of these disease indicators also overlap with functions that stratify vertebrate microbiomes relative to free-living microbial communities, further supporting their potential importance to host health. Overall, these results clarify potential microbiome-mediated mechanisms of disease and reveal features of the microbiome that may be useful for the development of microbiome-based diagnostics.

Autoinducer-2 Mediates Growth Mode of Bacterial Communities in the Zebrafish Intestine

University of Oregon

Maria Banuelos

The vertebrate gut is home to a large and diverse microbiota that plays important roles in host health. As we learn more about these microbial communities we are beginning to understand that the spatial organization of these bacterial communities and their growth mode (i.e. planktonic vs aggregated) influence their interactions with one another and the host. However the mechanisms governing spatial organization and growth patterns in vivo are not well understood. Here we investigate the role of bacterial interspecies quorum sensing signal Autoinducer-2 (AI-2) in determining the growth mode and spatial patterning of bacterial communities in vivo. To address this we colonized larval zebrafish with wild type E.coli, AI-2 synthesis mutant âˆ†luxS, or AI-2 signaling mutant âˆ†lsrR. We used light sheet fluorescence microscopy to observe the growth mode and localization of the populations in vivo and measure intestinal abundance of the bacteria. We observe that wild type E.coli are found in large aggregate populations with few planktonic cells while âˆ†luxS consists of many small aggregates and with more planktonic cells. Consistent with previous work from our lab showing that largely aggregated bacterial communities are susceptible to expulsion from the gut, we found the aggregated wild type populations at lower abundance than the more planktonic âˆ†luxS and âˆ†lsrR mutants. We also observe differing spatial localizations between wild type and âˆ†luxS, with the wild type localized more distally along the axis of the intestine, consistent with increased displacement. Lastly, we were able to alter abundance levels of wild type by co-colonizing with strains that change AI-2 concentration in the intestine. This study offers evidence that AI-2 signaling is an important factor in growth mode and spatial organization of bacterial communities in the vertebrate gut that could be used for microbiota engineering.

Molecular composition of field derived microbial necromass

Pacific Northwest National Laboratory

Presented at 2019 Genomic Sciences Program Annual Principal Investigator (PI) Meeting

Sheryl Bell

Crop selection and soil texture influence the physicochemical attributes of the soil, which structures microbial communities and influences soil organic matter formation, cycling and long-term storage. At the molecular scale, microbial metabolites and necromass alter the soil environment, which creates feedbacks that influence ecosystem functions, including soil organic matter accumulation. Yet the generalizable mechanisms regulating the accrual and long term stabilization of soil organic matter are still unclear. By integrating lab to field studies we aim to identify the molecules, organisms and metabolic pathways that control the formation of molecules that contribute to long term organic matter stabilization in bioenergy soils.

Linking Microbial Community Data to Soil Health in Oregon
Chris Burgess
Oregon State University

Soil microbial communities are extremely diverse. Both bacteria and fungi play integral roles in soil function and health; however, many of the current soil health assessments fail to capture a quantification of the microbial diversity in soils. Here we explore the link between microbial community structure and soil health across a regional scale. To capture the heterogeneity present in the landscape, soil samples were collected during late spring and early summer across the state of Oregon. We measured a suite of physical and chemical properties for each soil sample including several metrics in the Cornell assessment of soil health (CASH). Coupled with these measurements there was an onsite evaluation of soil quality. Microbial phylogenetic diversity was determined using amplicon sequencing on an Illumina MiSeqâ€"16S rRNA gene (bacteria) and ribosomal ITS region (fungi). The relationship between community composition and environmental influences was examined using several different multivariate approaches. Large amounts of variation in physical and chemical properties occurred over the sampled areaâ€"pH ranged from 3.5 to 9.5. Bacterial diversity and soil quality were significantly correlated for cropland soils (R2 of 0.20, p-value of 0.015). There was also a link between fungal communities structure and soil quality. Though microbial community composition and diversity are related to several soil health indicators, their relationships to these parameters are noisy, indicating a weak relationship with microbial communities composition to soil health.

Quantifying Subsurface Biogeochemical Variability in a High Altitude Watershed During Winter Isolation
Jessica Buser
Oregon State University

Subsurface ecosystems in high-altitude watersheds are influenced by hydrologic events that drive the availability of compounds for biotic and abiotic chemistry. Much of this biogeochemistry occurs in the dynamic hyporheic zone (the interface of the river sediment and groundwater) and in groundwater. Hyporheic systems are conspicuously responsive to hydrologic events, and therefore have the ability to alter surface ecosystem geochemistry. High-altitude systems experience isolation during the wintertime due to unsafe or inclement conditions that prevent access to the watershed for research, and consequently many of these systems are not sampled during the winter months. This isolation leads to a distinct gap in biogeochemical knowledge of these systems, which ultimately affects the accuracy and confidence in which these systems are computationally modeled. We deployed and subsequently retrieved OsmoSamplers from the East River (ER), CO watershed to study the aqueous and gaseous chemistry of the waters from the aquifer, river, and hyporheic zone during the winter. Our Shumway well sampler detected ca. 10x higher concentrations in Cl- at the end of winter than during the rest of the year, adding to data previously collected only when the well could be accessed. The sampler also validated sustained low levels of SO4-2 in groundwater through late fall and winter months showing an upward trend as summer started. Methane in the well was near saturating levels through the year. Our 10-month sampler installments in the ER surface water revealed up to 50 ÂµM levels of methane in July through September, an increase compared to ca. 5 ÂµM during most months. In contrast, samples from 20-cm deep in the hyporheic zone showed a spring-to-early summer peak in methane (< 65 ÂµM) before declining. A second set of OsmoSamplers is being used to study the microbiome and metatranscriptome of the ER system.

Mechanisms of Host-Microbiome Response to TCDD Exposure Evaluated Using Mass Spectrometry
Stephen Callister, PhD
Pacific Northwest National Laboratory

2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), a potent environmental toxicant, is present at many dioxin-contaminated sites within the United States and globally. Delineating the health effects and understanding the mechanisms that may be able to protect the host are of significant interest. TCDD mediates most if not all of it biological activity by binding the aryl hydrocarbon receptor (AhR). Previously we have shown that C57BL/6 gnotobiotic mice inoculated with two immune-modulating gut members namely segmented filamentous bacteria (SFB) and Bacteroides fragilis cause transcriptomic changes in the bacterial members when exposed to TCDD. Here we report the global metabolomic and proteomic responses of C57BL/6 gnotobiotic mice exposed to TCDD after colonizing them with SFB, B. fragilis, or both. By analyzing fecal samples, we identified metabolite and protein biomarkers specific to SFB, B. fragilis, and TCDD treatment and demonstrate the impact of TCDD on the host. Even though fecal omics cannot provide a comprehensive view of many molecular interactions within the complex topography and niches in the gut, we show that TCDD exposure to the host also impacts the functional responses associated with the gut microbiota using SFB and B. fragilis as models.

This study expands the current knowledge of host-toxicant interactions and their associations with immune-modulating members of the gut.

History of Breastfeeding but not Mode of Delivery shapes the Gut Microbiome in Childhood
Camille Cioffi, MS
University of Oregon

Background. The naÃ¯ve neonatal gut is sensitive to early life experiences. Events during this critical developmental window may have life-long impacts on the gut microbiota. Two experiences that have been associated with variation in the gut microbiome in infancy are mode of delivery and feeding practices (eg, breastfeeding). It remains unclear whether these early experiences are responsible for microbial differences beyond toddlerhood. Our study examined whether mode of delivery and infant feeding practices are associated with differences in the child and adolescent microbiome. To determine the impacts of these early experiences on the gut microbiome later in childhood, we used an adoption-sibling design to compare genetically related siblings who were reared together or apart. Methods. Gut microbiome samples were collected from 73 children (M = 11 years, SD = 3 years, range = 3-18 years). Parents reported on child breastfeeding history, age, sex, height, and weight. Mode of delivery was collected through medical records and phone interviews. Results. Negative binomial mixture models were conducted to identify whether mode of delivery and feeding practices were related to differences in phylum and genus-level abundance of bacteria found in the gut of child participants. Covariates included age, sex, and body mass index. Genetic relatedness and rearing environment were accounted for as random effects. We observed a significant association between lack of breastfeeding during infancy and a greater number of the genus Bacteroides in stool in childhood and adolescence. Conclusion. Early formula feeding may impart lasting effects on the gut microbiome well into childhood.

Microbiomes and megafauna: exploring the relationships between disease, environment, and the microbiome
Claire Couch
Oregon State University

In the past two decades, multiple studies have demonstrated intimate connections between commensal microbe communities and host health & disease in humans and laboratory animals. However, host-microbiome relationships are poorly understood in most wildlife populations due to the inherent difficulties of wildlife studies, limiting our understanding of long-term patterns and health outcomes of microbial dynamics. For this study, we took advantage of a unique high-resolution, longitudinal dataset collected from a herd of African buffalo in Kruger National Park, South Africa. We examined the relationships of host traits, nutrition & disease with variation in the nasal & gut microbiome. Preliminary results indicate strong associations between the gut microbiome with environmental conditions and nutritional resource ability, and suggestive relationships between nasal microbiome composition and respiratory infections including bovine tuberculosis. and infection by respiratory pathogens including bovine tuberculosis. This study is unprecedented among wildlife microbiome studies in its scope, resolution, and duration, and we expect our results to substantially advance our understanding of how microbiomes function in a natural host population**.**

Children with autism and their typically-developing siblings differ in exact sequence variants and predicted functions of stool-associated microbes.
Presented at ISME
Maude David, PhD
Oregon State University

The existence of a link between the gut microbiome and Autism Spectrum Disorder (ASD) is well established in mice, but in human populations efforts to identify microbial biomarkers have been limited due to a lack of appropriately matched controls, stratification of participants within the autism spectrum, and sample size. To overcome these limitattions we crowdsourced the recruitment of families with age-matched sibling pairs between 2-7 years old (within two years of each other), where one child had a diagnosis of ASD and the other did not. Parents collected stool samples, provided a home video of their ASD children's natural social behavior, and responded online to diet and behavioral questionnaires. V4 16S amplicon sequencing of 117 samples (60 ASD and 57 controls) identified 21 Exact Sequence Variants (ESVs) that differed significantly between the two cohorts: 11 were found to be enriched in neurotypical children (six ESVs belonging to the Lachnospiraceae family), while ten were enriched in children with ASD (including Ruminococcaceae and Bacteroidaceae families). Summarizing the expected KEGG Orthologs of each predicted genome,

the taxonomic biomarkers associated with children with ASD can use amino acids as precursors for butyragenic pathways, potentially alterating the availability of neurotransmitters like glutamate and GABA

Center for Genome Research and Biocomputing at OSU
Ed Davis, PhD
Oregon State University

The Center for Genome Research and Biocomputing at OSU provides services for DNA extraction, 16S and/or ITS amplification, Illumina MiSeq sequencing, and microbiome analysis of samples. We also will work with clients on research design, with particular focus on statistical power and limitations inherent in these types of studies. We recently received a contract from the Soil Health Institute to analyze the microbiomes of, in total, approximately 2000 soil samples from across the U.S., Canada, and Mexico.

PacBio sequencing of natural cyanobacterial blooms to study genome sequence and population structure
Theo Dreher, PhD
Oregon State University

We report studies on the consensus genome sequences and the representation of SNPs in the populations of freshwater cyanobacterial blooms, finding a high degree of clonality in these populations that undergo annual boom and bust cycles. Freshwater cyanobacteria are increasingly afflicting lakes and reservoirs with blooms that can be toxic. An Anabaena bloom that occurs annually in Detroit Reservoir in the Cascade foothills is a producer of the toxin cylindrospermopsin. In June 2018, drinking water for the City of Salem, which is derived from Detroit Reservoir, was contaminated with cyanotoxins. We have determined the consensus genome sequence of Anabaena sp. DET69 from that bloom by PacBio sequencing of the uncultured bloom population. Illumina paired-end libraries from the same sample, and from samples of blooms from preceding years, have been used to identify the genetic variation within a single population and between blooms in different years. The results will allow inferences on the diversity, dynamics, and possibly year-to-year evolution of these cyanobacterial populations.

Omics-guided genome remodeling to promote productivity, evolutionary robustness, and biocontainment
Rob Egbert, PhD
Pacific Northwest National Laboratory

As advances in microbial engineering work to meet goals in sustainable bioproduction, cell-based therapeutics, and environmental monitoring, engineered functions often cause poor growth in the microbial host. Growth defects incurred from high expression of heterologous proteins reduce host productivity and leave engineered populations vulnerable to displacement by nonfunctional mutants. Further, culturing microbial cultures in controlled environments such as a bioreactor causes the expression of genes that are unnecessary for host or circuit function, leaving a significant fraction of the proteome dispensable. We are developing proteomics-guided genome remodeling strategies to increase cellular capacity to express synthetic DNA circuits and heterologous biosynthetic pathways. This work includes cellular capacity optimization in a collection of massive genome deletion E. coli variants as well as cross-evaluation of bacteria adapted to human gut, freshwater aquatic and plant rhizosphere environments. We expect this work to inform general genome remodeling strategies to eliminate the dispensable proteome while maintaining physiological robustness, leading to a better understanding of cellular responses to engineered loads and control of the longevity of engineered functions in complex environments.

Characterization of the stool microbiome in Latino, pre-school children by weight status and time
Presented at PAS 2018
Alex Foster, MD, MPH
Oregon Health & Science University

Background: Variations in microbiome composition and relative diversity have been found to be associated with weight status in early childhood. Most studies have been cross-sectional and few clinical studies have examined microbiome changes in children in association with weight and diet change. Methods: Obese, pre-school (2-5-year-old), Latino children provided stool samples at baseline and six-months into a behavioral intervention designed to improve their weight status. Unrelated, normal weight children from also provided stool samples at baseline. Stool community DNA was isolated, and the V1-V3 region of the16S rRNA gene was sequenced. Estimates of within sample diversity (i.e., alpha diversity) were calculated on operational taxonomic unit (OTU) count data, and the Firmicutes:Bacteroidetes (F:B) ratio

was determined on a per-sample basis. Estimates of between sample diversity were generated using the weighted Unifrac metric, differential abundances were evaluated using Wilcoxon rank sum tests, and associations of microbiome features with clinical data were quantified using Spearman rank correlations. Results: For the 30 obese children (mean age 53 months, SD=7) who provided samples at both time points, an overall decrease in BMI z-score from 2.55 to 2.34 (p=0.004, paired sample t-test) was achieved. The 22 children of normal weight had a mean BMI z-score of 0.1 (SD=0.6). There were significant differences between the obese and normal weight children at the OTU level, specifically among Bacteroides-like OTUs. We identified significant correlations between multiple Bacteroides-like OTUs and BMI z-score. There were no significant differences detected at the OTU level between the two time points for obese children when examining the association by weight changes. **Conclusions**: While significant differences exist between obese and normal weight children's gut microbiota composition, we did not detect significant differences over time in the microbiome of obese children who participated in a weight-intervention program, regardless of their change in body weight.

Germ - free Swiss - Webster Mice as a n Animal Model for Obesity and Metabolic Syndrome
Fritz Gombart, PhD
Oregon State University

Dietary compounds from plant sources show promise for treating obesity and metabolic syndrome (MetS), but the mechanism(s) by which they mediate these benefits are poorly understood. Consumption of dietary compounds may alter the composition of the gut microbiota or the gut microbiota may metabolize the compounds, thus altering their bioactivity. To determine if the microbiota mediate the benefits of a particular dietary supplement in treating obesity and MetS, researchers need a commercially available germ-free (GF) mouse model of obesity. Prior studies indicate that GF C57BL/6J mice do not develop obesity and characteristics of MetS, but that C3H mice do. GF C3H are no longer available from commercial vendors, but GF Swiss Webster mice are available and frequently used for GF studies. We hypothesized that when fed a high fat diet (HFD) GF Swiss Webster mice, like their conventional (CV) counterparts, would develop obesity and characteristics of MetS. We fed both CV and GF Swiss Webster mice either a low fat diet (LFD) or a HFD for 10 weeks. Both showed a significant increase in body weight compared to the LFD control. Like their CV counterparts, GF mice became insulin resistant and had elevated LDL-cholesterol and plasma leptin levels compared to the LFD. Furthermore, both GF and CV mice showed a significant increase in relative triglyceride and ceramide levels on a HFD compared to the LFD. In CV mice on a HFD, we observed a significant increase in the top 12 differentiating acyl carnitines, but not in GF mice. We show that both CV and GF Swiss Webster mice become obese and exhibit characteristics of MetS on a HFD. Thus, we propose using GF Swiss Webster mice as an animal model of diet-induced obesity that could assess the role of the microbiota in mediating the benefits of dietary compounds.

Mind the Microbiome: Dietary Intervention and Mental Health Outcomes of Homeless Adults
Britt Gratreak
Oregon Health & Science University

Major dietary changes are known to lead to lasting changes in gut microbiota composition. Alterations in the microbiome have been widely shown to modulate symptoms of psychiatric illnesses such as depression, schizophrenia, and aggressive behaviors through neural, endocrine and immune pathways. Lack of food accessibility is a major concern for people who become homeless. Little data has been collected to examine how the experience of homelessness alters the gut microbiome. Worldwide, the prevalence of mental illness while experiencing homelessness is staggering. Microbiota species of particular interest are from the genera Lactobacillus and Bifidobacterium which have been previously reported to decrease depression and aggressive feelings in adults and in numerous animal models. Butyrate, a short chain fatty acid, is produced by microbes during fermentation of dietary soluble fibers. Butyrate has been shown to have neuroprotective effects against traumatic brain injury and modulate several neuropsychiatric disorders. Multiple mechanisms have been reported for butyrate in the realm of controlling or attenuating inflammation primarily through downregulating NF-κB, an important transcription factor in a cascade of pro-inflammatory cytokines. In this proposed psychobiotics study, in volunteers a daily dietary intervention will be given in the form of yogurt with or without enrichment for butyrate-producing species (*L. rhamnosus* and *L. casei*). A baseline microbiome profile and behavioral assessment will be established prior to dietary intervention. Stool will be collected from participants midway and after the intervention. The stool and salivary microbiomes will be examined by DNA extraction/16S sequencing, and behavioral outcomes of both groups will be assessed after four weeks.

Commensal orthologs of the human autoantigen Ro60 as triggers of autoimmunity in lupus
Presented at Society for Investigative Dermatology meeting, American College of Rheumatology meeting
Teri Greiling, MD, PhD
Oregon Health & Science University

The earliest autoantibodies in lupus are directed against the RNA binding autoantigen Ro60, but the triggers against this evolutionarily conserved antigen remain elusive. We identified Ro60 orthologs in a subset of human skin, oral, and gut commensal bacterial species and confirmed the presence of these orthologs in patients with lupus and healthy controls. Thus, we hypothesized that commensal Ro60 orthologs may trigger autoimmunity via cross-reactivity in genetically susceptible individuals. Sera from human anti-Ro60â€“positive lupus patients immunoprecipitated commensal Ro60 ribonucleoproteins. Human Ro60 autoantigenâ€“specific CD4 memory T cell clones from lupus patients were activated by skin and mucosal Ro60-containing bacteria, supporting T cell cross-reactivity in humans. Further, germ-free mice spontaneously initiated anti-human Ro60 T and B cell responses and developed glomerular immune complex deposits after monocolonization with a Ro60 orthologâ€“containing gut commensal, linking anti-Ro60 commensal responses in vivo with the production of human Ro60 autoantibodies and signs of autoimmunity. Together, these data support that colonization with autoantigen ortholog-producing commensal species may initiate and sustain chronic autoimmunity in genetically predisposed individuals. The concept of commensal ortholog cross-reactivity may apply more broadly to autoimmune diseases and lead to novel treatment approaches aimed at defined commensal species.

Transkingdom networks as a tool to uncover host-microbiota interactions in metabolic disease
Manoj Gurung, PhD
Oregon State University

During the last decade it became clear that host-associated microbes play critical role in the pathogenesis of different diseases. However, a major challenge is to find which ones of the hundreds of microbial species or their products affect which specific host functions and vice versa. To address this problem, we have developed a new approach named analysis of transkingdom networks, which connects a mammalian host and microbiota genes or taxa. Building a transkingdom network requires establishing microbial and host gene expression networks separately and then integrating those two networks by edges that correspond to potential causal relations. The established predictions are then tested experimentally at the OSU Germfree/Gnotobiotic Mouse Core by colonizing mice with specific members of microbiota. We currently investigate transkingdom networks in a model of diet-induced metabolic syndrome. In this case, we integrated gut microbiome with gene expression network encompassing major metabolic organs, such as liver, fat, muscle and intestine. Some critical inferences from these multi-organ analyses are being validated. Thus, interrogation of transkingdom networks represents an effective method to reveal causal players in host-microbiota interactions.

THE ENTERIC NERVOUS SYSTEM CONTROLS MICROBIAL INDUCED INFLAMMATION BY MODULATING INTESTINAL MOTILITY AND PERMEABILITY
Presented at Federation of Neurogastroenterology and Motility (FNM) 2018
Kristi Hamilton, PhD
University of Oregon

OBJECTIVE: Our goal is to understand mechanisms by which the enteric nervous system (ENS) modulates interactions between intestine-resident microbes and the intestinal tract. Zebrafish is an ideal model to study host-microbe interactions due to the ease of deriving hundreds of genetically related individuals germ-free (GF), the transparency of larval stages enabling live imaging, and the ease of mutagenesis and transgenesis. The ENS innervates the intestinal tract and controls many aspects of intestinal health, including motility and barrier function. Intestinal health can also be significantly affected by the resident microbiota. By studying sox10 mutants that lack an ENS, we showed that the ENS modulates the composition of the intestinal microbiota. This altered microbial community can cause intestinal inflammation as well as decreased barrier function, resulting in hyperpermeability. Probiotics, living microbes that provide benefit to the host and have been a suggested therapeutic for many gastrointestinal disorders, have been used to reduce or prevent intestinal hyperpermeability and alter intestinal motility. In this study, we investigated whether there is correlation between intestinal motility and intestinal inflammation, and whether a human probiotic is able to ameliorate the hyperpermeability that contributes to intestinal inflammation. METHODS: We used a custom-built light

sheet microscope to measure intestinal motility and permeability in living wild type and sox10 mutant zebrafish larvae, and gnotobiogy techniques to investigate whether a beneficial microbe, Escherichia coli HS, could alleviate intestinal hyperpermeability. RESULTS: We discovered that the speed of intestinal contractions is significantly correlated with the level of intestinal inflammation in sox10 mutants. We also found that sox10 mutants have intestinal hyperpermeability that is ameliorated by inoculating them with E. coli HS. CONCLUSION: Our data suggest a mechanism by which host phenotype can influence microbial induced inflammation and a potential new avenue for therapy to improve intestinal barrier function and decrease intestinal inflammation.

The Microbiome of Kombucha SCOBY
Presented at ASBC
Keisha Rose Harrison
Oregon State University

Kombucha is a lightly carbonated tea that continues to disrupt the beverage market. The low-sugar and low-alcohol beverage has only been gaining in popularity in the United States over the last couple of years. What makes kombucha such a challenging beverage to make? The aerobic fermentation process driving kombucha production requires the action of a complex mixture of microorganisms. The flavor attributes and alcohol produced during the process are governed by the starter colony, a symbiotic culture of bacteria and yeast (SCOBY). The composition of the SCOBY is poorly understood which serves to limit the quality control of the commercial production of kombucha. The objective of this research is to profile a diverse array of commercial Kombucha SCOBY by establishing the microbiome. We hypothesize that the SCOBY ecology does not diverge with relative location and common microbial contributors persist. Through a collaboration with Kombucha Brewers International (KBI) we collected 92-commercially provided kombucha biofilms. Prior to this study, the common contributors of the SCOBY ecology had not been well defined. Our results identified Gluconoacetobacter, Lactobacillus, Brettanomyces, and Starmerella as the most abundant taxa across the population independent of geographic origin. Five distinct styles of SCOBY were resolved and representative SCOBY from each group were selected for small batch fermentations. Final microbiome was profiled using high-throughput sequencing to assess ecological community divergence.

Zinc Deficiency and Arsenic Elicit Combined Effects on the Gut Microbiome
Presented at OSU CGRB Conference
Emily Ho, PhD
Oregon State University

My research lab is interested in the impact of nutrients/bioactive food components on chronic disease development. We utilize animal models (rodent and zebrafish) and perform human intervention studies to address these questions. This specific project centers around how nutrient deficiencies may sensitive individuals to toxicological stresses. Chronic arsenic exposure affects 200 million people globally and presents serious health challenges. Dietary micronutrient deficiencies, which are often comorbid with chronic arsenic exposure, can enhance sensitivity to arsenic toxicity. However, the mechanisms that underpin this relationship are incompletely resolved. The gut microbiome interacts with host physiology to promote health, but micronutrient deficiencies can perturb these, which may lead to altered sensitivity to arsenic. We assessed the effect of arsenic exposure on microbial community composition of C57BL/6 mice fed zinc adequate and marginally zinc deficient diets using 16S amplicon sequencing. We correlated taxonomic relative abundances with host DNA damage, adiponectin expression, and plasma zinc concentration to identify taxa that may mediate host physiological responses to arsenic exposure or zinc deficiency. We find that both arsenic exposure and zinc restriction alters microbiome diversity. In combination, arsenic and zinc restriction elicits stronger associations between arsenic concentration and microbial community structure. Arsenic exposure and zinc restriction also results in increased DNA damage and decreased plasma zinc. These physiological changes associate with the abundance of several taxa in the gut microbiome. These data indicate that marginal zinc deficiency sensitizes the microbiome to arsenic exposure and that the microbiome associates with some of the toxicological effects of arsenic.

Zebrafish model for intestinal cancer, nematode infecitons and the gut microbiome
Michael Kent, PhD
Oregon State University

A collaboration between the Kent, Sharpton (Oregon State University) and Guillemin (University of Oregon) is investigating interactions between the intestinal microbiome, the parasitic nematode Pseudocapillaria tomentosa and a novel Mycoplasma sp. similar to Mycoplasma penetrans. To date, we have documented that the nematode causes

profound alterations in the microbiome, including an association with increased Mycoplasma spp. The Kent/Guillemin team has shown that common intestinal cancers in zebrafish are clearly transmissible, and are also associated with a Mycoplasma sp. Last, fish infected with both the nematode and Mycoplasma develop severe inflammation, dysplastic lesions and neoplasms as early as 3 mo post-exposure, whereas neoplasms are only seen after 8-10 mo. in zebrafish infected with just the Mycoplasma sp.

Exploring the linkage between behavior changes and the gut microbiome and metabolome in C57BL/6 mice
Presented at American Society for Mass Spectrometry 2018
Young-Mo Kim, PhD
Pacific Northwest National Laboratory

While the interactions between the microbiome and host are essential for determining health and disease states, detailed understanding of the inter-connected metabolisms of individual microbes and the host is limited due to the chemical complexity and inhomogeneity of food sources, the biological variability of hosts, and variations in environmental exposures. To begin to address this, we utilized conventional, germ-free (GF), and GF mice inoculated with specific bacteria to understand the complex link between the microbiome, metabolome and behavior changes, and using metabolomics analyses to measure changes in the fecal, blood, and brain metabolomes. This is among the first efforts to explore the linkage between behavior changes and the gut microbiome/metabolome.

Phylogenetic, genomic, and biogeographic characterization of a novel and ubiquitous marine invertebrate-associated Rickettsiales parasite
Presented at American Society of Microbiology 2018 Meeting
Grace Klinges
Oregon State University

Bacterial symbionts are integral to the health and homeostasis of invertebrate hosts. Notably, members of the Rickettsiales genus Wolbachia influence several aspects of the fitness and evolution of their terrestrial hosts, but few analogous partnerships have been found in marine systems. We report here the genome, phylogenetics, and biogeography of a ubiquitous and novel Rickettsiales species that associates with marine invertebrates. We previously showed that this bacterium was found in scleractinian corals, responds to nutrient exposure, and associated with reduced host growth and increased mortality. Genome annotation demonstrates that this bacterium, like other Rickettsiales, has a reduced genome indicative of a parasitic lifestyle. Phylogenetic analysis places this Rickettsiales within a new genus we define as â€œCandidatus Marinoinvertebrata.â€ Using the Earth Microbiome Project, we also demonstrate that members of â€œCandidatus Marinoinvertebrataâ€ are found globally in dozens of invertebrate lineages. The coral-associated â€œCandidatus M. rohweriiâ€ is the first complete genome in this new clade. â€œCa. M. rohweriiâ€ lacks genes to synthesize most sugars and amino acids, but possesses several genes linked to pathogenicity including Tlc, an antiporter that exchanges host ATP for ADP, and a complete Type IV secretion system. Despite its inability to metabolize nitrogen, â€œCa. M. rohweriiâ€ possesses the NtrY-NtrX two-component system involved in sensing and responding to extracellular nitrogen. Given these data, we hypothesize that â€œCa. M. rohweriiâ€ reduces coral health by consuming host nutrients and energy, thus weakening and eventually killing host cells. Lastly, we hypothesize that nutrient enrichment, which is increasingly common on coral reefs, encourages unrestricted growth of â€œCa. M. rohweriiâ€ in its host by providing abundant N-rich metabolites to be scavenged.

Molecular Commensalism of the Oral Microbiome
Jens Kreth, PhD
Oregon Health & Science University

The commensal oral microbiome has evolved with the human host to support colonization of the various intraoral sites without triggering a significant immune response or pathology. In exchange, the commensal microbes provide critical protection against invading pathogens and might aid in the development of a functional immune system. The underlying microbial ecology that sustains symbiosis with the host can be disturbed, selecting for the overgrowth of a dysbiotic community that can trigger dental diseases, such as caries and periodontitis. Although the mechanisms of molecular pathogenesis in oral diseases are well characterized, much less is known about the molecular mechanisms used by the commensal flora to maintain oral health.

Development and Analysis of Reduced Complexity Microbial Consortia Emerging from Native Grassland Soil Systems
Presented at Genomic Sciences Program Meeting, 2019
Ryan McClure, PhD
Pacific Northwest National Laboratory

Soil microbial communities are critical to the overall carbon cycle and to the decomposition of complex biopolymers such as chitin and cellulose. Despite the critical nature of these microbiomes, a detailed understanding of how the interactions between members lead to emergence of community functions is lacking. In order to gain a more detailed view of the soil environment, we took an approach based on developing and analyzing reduced complexity microbial consortia that contain fewer species than the native soil but are still representative of this site and are more experimentally tractable. We hypothesize that predictable reaction modules exist and that analysis of these model consortia can identify these reaction modules, and other fundamental aspects of soil microbiome interactions. These interactions and aspects can then be tested in a specific, robust manner in the native soil sites. We collected native soil that was then diluted to various levels, ranging from 10-1 to 10-4 and cultured in irradiated sterile native soil. We found that culturing these dilutions in soil for 15 weeks lead to stable microbial consortia containing both bacteria and fungi. We also found that emerging communities were highly representative of the native soil site. In addition to cultivation in soil, we also developed consortia on plates using chitin as a major source of carbon and nitrogen. These plate communities represented microbiomes that were even further reduced in complexity while again containing a diverse community of several different phyla. Constructed reduced complexity consortia provide a means to more powerfully leverage high-throughput, multi-omic techniques to better characterize these interactions and the major constituent players that are a part of them. Further knowledge of these interactions will help us better understand the overall metaphenome of soil systems, especially as they respond to critical perturbations including drought

Understanding Microbiomes as Ecological Systems
Beth Miller, PhD
University of Oregon

Microbiomes are, like any other assemblage of species, complex systems that must play by the rules of ecology. Interactions between species, dispersal between hosts, and selection by the host can all lead microbial communities to assemble and function in complicated ways. Questions such as how microbiomes recover from antibiotic disturbance or how diversity is maintained in a microbiome are fundamentally ecological questions that can be addressed with ecological theory. However, because much of ecological theory was developed with lakes and prairies in mind, there are aspects of host-microbiome biology that require re-thinking traditional assumptions. We are pushing ecological theory to incorporate more of the biological realities of host-microbiomes (for example, environmental reservoirs for microbes dispersing between hosts) to achieve greater synthesis between ecology and microbiome research.

Using Proteomics-SIP to define Resource Partitioning of Diatom- and Cyanobacteria-derived Carbon in the Marine Microbial Loop
Ryan Mueller, PhD
Oregon State University

Defining ecological roles of the individual heterotrophic populations that compose complex microbial communities refines our understanding of how energy and matter are recycled in the biosphere. This endeavor has become feasible with technological advances that allow for targeted identification of cells that respond when molecules of interest are amended to a functioning ecosystem. Here we employ stable isotope probing combined with protein mass spectrometry to track the assimilation of 13C-labeled algal biomass by microbial populations in coastal seawater. Isotope-enriched exudate and lysate fractions from axenic Thalassiosira pseudonana and Synechococcus sp. cultures were amended to seawater microcosms. We found distinct community-level labeling patterns across the four substrate treatments and population-level specialization on each substrate that was phylogenetically-conserved in broad taxonomic groups. Alpha-proteobacteria, particularly Roseobacter clade and Rhodobacteraceae populations (e.g., Planktomarina and Lentibacter), were superior competitors for cyanobacteria exudates, and assimilated this substrate with higher efficiency than other taxa. Bacteroidetes populations dominated uptake of the diatom lysate, with nearly half of total proteins produced de novo by this lineage incorporating added substrate during the 15-hour incubation period. The relative DNA GC content and amino acid C:N ratio of highly-labeled proteins in Alpha-proteobacteria (high, low) and Bacteroidetes (low, high) were associated with substrate specialization patterns based on stoichiometric differences between cyanobacteria exudate and diatom lysate. Taken together, we find significant phylogenetically-

conserved specialization on complex autochthonous resources by coastal heterotrophic microbes, which, when combined with known environmental constraints and biological interactions, helps refine our understanding of organic matter turnover in the coastal ocean.Â

Intra-annual variation of soil microbial communities
Presented at Ecology of Soil Microorganisms; Helsinki, Finland
Dave Myrold, PhD
Oregon State University

There have been many studies of the biogeography of soil microorganisms, which have provided meaningful insights into the determinants of soil microbial community structure. Relatively little research has been done on the temporal dynamics, or stability, of microbial communities. We sampled five soils representing three climatic regions in Oregon, USA, on a monthly basis. Bacterial (16S rRNA gene) and fungal (ribosomal ITS region) community composition was assessed by amplicon sequencing. For three of the five soils we found that within site variability of microbial communities was greater than within year variability. At two of the sites, however, we observed seasonal dynamics of microbial community structure despite the spatial variability of microbial communities. These results have potential implications for sampling soil microbial communities.

Analyzing the microbiome of both the core and rind of different types of cheeses produced at Oregon State University
Si Hong Park, PhD
Oregon State University

Understanding the microbiome community of cheese is important in the industry, since the microbiota contributes the physicochemical and sensory properties of cheese. Development of a NGS (next generation sequencing) technology helps researchers produce huge amount of genomic information, with fast and low cost, which can improve the understanding of microbial properties of target foods. This study aimed to understand the microbiome community differences between different locations (core, rind, and mixed) and types (cheddar, provolone, and Swiss) of cheeses. At the taxonomic level, different types of cheese exhibit different microbial compositions (Swiss and provolone cheese are dominated by Streptococcus, while Lactococcus is the most prevalent bacterium on cheddar cheese). In comparing the microbial richness among different types of cheese, porter-soaked cheddar cheese exhibited the highest microbial richness, while smoked provolone had the lowest. On the same cheese sample, the rind region exhibited higher microbial richness than the inner region. Lastly, microbial communities were found to be clustered in the same types of cheese, indicating similar microbial diversity.

LONGITUDINAL CHANGES DURING PREGNANCY IN GUT MICROBIOTA AND METHYLMERCURY BIOMARKERS, AND REVERSAL OF MICROBE-EXPOSURE CORRELATIONS
Sarah Rothenberg, MS, D.Env.
Oregon State University

Objective: Gut microorganisms contribute to the metabolism of environmental toxicants, including methylmercury (MeHg). Our main objective was to investigate whether associations between biomarkers for prenatal MeHg exposure and maternal gut microbiota differed between early and late gestation. Methods: Maternal blood and stool samples were collected during early (8.3â€“17 weeks, n=28) and late (27â€“36 weeks, n=24) gestation. Total mercury and MeHg concentrations were quantified in biomarkers, and inorganic mercury was estimated by subtraction. The diversity and structure of the gut microbiota were investigated using 16S rRNA gene profiling (n=52). Biomarkers were dichotomized, and diversity patterns were compared between high/low mercury concentrations. Spearman's correlation was used to assess bivariate associations between MeHg biomarkers (stool, blood, and meconium), and 23 gut microbial taxa (genus or family level, >1% average relative abundance). Results: Within-person and between-person diversity patterns in gut microbiota differed between early/late gestation. The overall composition of the microbiome differed between high/low blood and stool MeHg concentrations during early gestation, but not late gestation. Ten (of 23) taxa were significantly correlated with MeHg biomarkers (increasing or decreasing); however, associations differed, depending on whether the sample was collected during early or late gestation. A total of 43% of associations (69/161) reversed the direction of correlation between early/late gestation. Conclusions: The time point at which a maternal fecal sample is collected may yield different associations between gut microorganisms and MeHg biomarkers, which may be due in part to remodeling of maternal microbiota during pregnancy. Our results suggest the effectiveness of dietary interventions to reduce prenatal MeHg exposure may differ between early and late gestation.

A Novel Nutritional Formulation Containing the Prebiotic Human Milk Oligosaccharide 2'-Fucosyllactose May Improve Gastrointestinal Quality of Life and Beneficially Alter the Gut Microbiome in Adults with Gastrointestinal Dysfunction

National University of Natural Medicine

Presented at Diet and Optimum Health (Linus Pauling Institute), International Congress on Integrative Medicine and Health

Jenn Ryan, ND, MS

Purpose: Gut dysbiosis, disruption in the homeostasis of the intestinal microbiota, contributes to the pathogenesis of many gastrointestinal disorders. Human milk oligosaccharides (HMOs), which are naturally occurring in human milk, are considered bifidogenic and butyrogenic. In breast-fed infants, they serve as primary substrates for select Bifidobacterium spp. and are metabolized into butyrate by butyrate-producing gut microbiota. UGIR is a formulation that provides nutritional support for adults with gastrointestinal dysfunction; it contains a combination of essential macro and micronutrients and prebiotics, including 2'-fucosyllactose (2'FL). This study reports novel data on the effect of 2'FL, in the context of a comprehensive nutritional formulation, in adults with gastrointestinal dysfunction. Methods: Adults with IBS, ulcerative colitis, Crohn's disease or celiac disease were recruited from four U.S. medical practices. Participants received one serving of UGIR twice daily for six weeks. Outcome measures included the Gastrointestinal Quality of Life Index (GIQLI) and a stool analysis panel. Results: Twelve participants completed the study. GIQLI total score, gastrointestinal symptoms domain, and social function domain scores improved ($P<0.05$). Butyrate, acetate, and total SCFAs increased ($P<0.05$). Several commensal bacteria increased including Bifidobacterium spp., Bifidobacterium longum, Faecalibacterium prausnitzii, Aneurotruncus colihominis, and Pseudoflavonifractor spp. ($P<0.05$). Conclusions: UGIR consumption was associated with reduced gastrointestinal symptoms, increased fecal SCFAs, increases in several beneficial gut microbes (including species that have been shown to consume 2'FL as a substrate in vitro), increases in butyrate-producing species, and increases in species that have been previously shown to be low in patients with IBS, IBD, and celiac disease. It is plausible that the improvements in commensal gut microbiota and butyrate levels contributed to the clinical benefits demonstrated on the questionnaire. These results suggest that UGIR may be a promising novel nutritional formulation that could be used in the management of gastrointestinal dysfunction associated with gut dysbiosis.

Ogg1 deficiency induces changes in intestinal microbiome correlated with increased intestinal inflammation

Oregon Health & Science University

Holly Simon, PhD

OGG1-deficient animals have increased propensity to age-induced and diet-induced metabolic diseases, including insulin resistance and fatty liver. Since the intestinal microbiome is increasingly understood to play a role in modulating host metabolic responses, we examined changes in gut microbial populations in Ogg1-/- mice subjected to different nutritional challenges. Relative abundance of several members of the Clostridia and Bacteroidia classes were significantly correlated with host body weight and body fat, with an increased prevalence of species associated with chronic intestinal inflammation observed in Ogg1-/- mice. To determine if these changes correlated with increased inflammation, we induced an acute inflammatory state in the colon using dextran sulfate sodium (DSS)-induced colitis. In contrast to wild-type controls, the Ogg1 knockout mice exposed to this challenge experienced considerably greater weight loss, lethargy, and severe diarrhea with evidence of blood in the fecal matter. Colonic tissues were harvested for ultrastructural examination, and epithelial cells were harvested for DNA damage assessment. Histopathologic analyses for induction of acute ulcerative colitis were based on goblet cell depletion, mucosal thickening, and inflammatory infiltrate. These data revealed that the colons of Ogg1-deficient mice showed mild symptoms of pre-existing disease, even prior to DSS challenge, consistent with the increased presence of pro-inflammatory pathogens in their feces. Tissues derived from Ogg1 knockout mice were twice as severely affected by DSS challenge relative to WT controls, confirming a much more severe inflammatory response in the Ogg1-deficient mice. Analyses of the levels of oxidative DNA base damage revealed trends for increased damage in the repair-deficient mice. These data suggest that in contrast to the suppression of airway and gastric inflammation previously observed for Ogg1-deficient mice, deficiency in Ogg1 renders mice extremely susceptible to colonic inflammation. Further, these data point to alterations in the intestinal microbiome as potential mediators of the intestinal inflammatory response.

Microbiome genomics and bionformatics at the OSU Center for Genome Research and Biocomputing — Oregon State University

Brett Tyler, PhD

The Center for Genome Research and Biocomputing (CGRB) provides high throughput DNA extractions for microbiome analysis and DNA sequencing on the HiSeq3000, MiSeq and PacBio Sequel platforms. The CGRB has several staff bioinformaticists who can assist with data analysis. The CGRB also maintains a high performance computing platform with 4.5 PB storage, 5272 processor cluster, and 16 machines with 1 TB RAM. Also includes GPUs (14 Tesla P100's; 18 Tesla V100's) for deep learning approaches.

Treatment of Diet-Induced Obese Mice with Xanthohumol and its Non-Estrogenic Derivatives DXN and TXN Modulates Composition of the Fecal Microbiota, Bile Acids and is Associated with Improvement of Metabolic Syndrome Biomarkers — Oregon State University

Presented at LPI International Conference

Yang Zhang, MS

Xanthohumol (XN), a prenylated flavonoid found in hops, reduces weight gain and improves dysfunctional glucose and lipid metabolism in preclinical animal models of diet-induced obesity (DIO) and metabolic syndrome (MetS). Gut microbes can metabolize XN into a potent phytoestrogen, 8-prenylnaringenin (8-PN). To address concerns with phytoestrogen exposure, in a previous study we tested two hydrogenated XN derivatives, Î±, Î² -dihydro-XN (DXN) and tetrahydro-XN (TXN), that cannot be metabolically converted into 8-PN. We fed C57BL/6J mice a high-fat diet (HFD) or HFD containing XN, DXN or TXN for 13 weeks with a submaximal dose (for XN) of 30 mg/kg/day to compare differences in pharmacological response among the three compounds. All three compounds improved impaired glucose tolerance in mice compared to the HFD control; however, only the derivatives significantly decreased HOMA-IR and leptin. We hypothesized that XN and its hydrogenated derivatives mediate their beneficial effects by improving barrier function of the gut, thus reducing inflammation, and modulating composition of the gut microbiota. We observed a significant association in the structure and membership of the microbiota with treatment. The compounds significantly decreased the percentages of Bacteroidetes and Tenericutes. Specifically, TXN treatment significantly changed bile acid composition and decreased inflammation induced by the HFD in white adipose tissue and the colon. Moreover, transkingdom network analysis revealed potential bacteria modulators Marvinbryantia, Romboutsia and other undefined genera from the Lachnospiraceae family in the interaction with host energy and bile acid metabolism. We postulate that TXN treatment ameliorates DIO and the concomitant symptoms of MetS by changing the composition of the gut microbiota, bile acid metabolism and host energy metabolism. This research was supported by NIH grant 5R01AT009168 from the NCCIH to AFG, JFS and CSM, and NIH grant 1R01AT009168, Hopsteiner Inc., NY, and the Buehler-Wang Research Fund.

Notes

Poster Titles

A Metagenomic Meta-Analysis Reveals Functional Signatures of Health and Disease in the Human Gut Microbiome
Presented at 2018 Lake Arrowhead Microbial Genomics Conference
Courtney Armour

Autoinducer-2 Mediates Growth Mode of Bacterial Communities in the Zebrafish Intestine
Maria Banuelos

Molecular composition of field derived microbial necromass
Presented at 2019 Genomic Sciences Program Annual Principal Investigator (PI) Meeting
Sheryl Bell

Linking Microbial Community Data to Soil Health in Oregon
Chris Burgess

Quantifying Subsurface Biogeochemical Variability in a High Altitude Watershed During Winter Isolation
Jessica Buser

Mechanisms of Host-Microbiome Response to TCDD Exposure Evaluated Using Mass Spectrometry
Stephen Callister, PhD

History of Breastfeeding but not Mode of Delivery shapes the Gut Microbiome in Childhood
Camille Cioffi, MS

Microbiomes and megafauna: exploring the relationships between disease, environment, and the microbiome
Claire Couch

Children with autism and their typically-developing siblings differ in exact sequence variants and predicted functions of stool-associated microbes.
Presented at ISME
Maude David, PhD

Center for Genome Research and Biocomputing at OSU
Ed Davis, PhD

PacBio sequencing of natural cyanobacterial blooms to study genome sequence and population structure
Theo Dreher, PhD

Omics-guided genome remodeling to promote productivity, evolutionary robustness, and biocontainment
Rob Egbert, PhD

Characterization of the stool microbiome in Latino, pre-school children by weight status and time
Presented at PAS 2018
Alex Foster, MD, MPH

Germ - free Swiss - Webster Mice as a n Animal Model for Obesity and Metabolic Syndrome
Fritz Gombart, PhD

Mind the Microbiome: Dietary Intervention and Mental Health Outcomes of Homeless Adults
Britt Gratreak

Commensal orthologs of the human autoantigen Ro60 as triggers of autoimmunity in lupus
Presented at Society for Investigative Dermatology meeting, American College of Rheumatology meeting
Teri Greiling, MD, PhD

Transkingdom networks as a tool to uncover host-microbiota interactions in metabolic disease
Manoj Gurung, PhD

THE ENTERIC NERVOUS SYSTEM CONTROLS MICROBIAL INDUCED INFLAMMATION BY MODULATING INTESTINAL MOTILITY AND PERMEABILITY
Presented at Federation of Neurogastroenterology and Motility (FNM) 2018
Kristi Hamilton, PhD

The Microbiome of Kombucha SCOBY
Presented at ASBC
Keisha Rose Harrison

Zinc Deficiency and Arsenic Elicit Combined Effects on the Gut Microbiome
Presented at OSU CGRB Conference
Emily Ho, PhD

Zebrafish model for intestinal cancer, nematode infecitons and the gut microbiome
Michael Kent, PhD

Exploring the linkage between behavior changes and the gut microbiome and metabolome in C57BL/6 mice
Presented at American Society for Mass Spectrometry 2018
Young-Mo Kim, PhD

Phylogenetic, genomic, and biogeographic characterization of a novel and ubiquitous marine invertebrate-associated Rickettsiales parasite
Presented at American Society of Microbiology 2018 Meeting
Grace Klinges

Molecular Commensalism of the Oral Microbiome
Jens Kreth, PhD

Development and Analysis of Reduced Complexity Microbial Consortia Emerging from Native Grassland Soil Systems
Presented at Genomic Sciences Program Meeting, 2019
Ryan McClure, PhD

Understanding Microbiomes as Ecological Systems
Beth Miller, PhD

Using Proteomics-SIP to define Resource Partitioning of Diatom- and Cyanobacteria-derived Carbon in the Marine Microbial Loop
Ryan Mueller, PhD

Intra-annual variation of soil microbial communities
Presented at Ecology of Soil Microorganisms; Helsinki, Finland
Dave Myrold, PhD

Analyzing the microbiome of both the core and rind of different types of cheeses produced at Oregon State University
Si Hong Park, PhD

LONGITUDINAL CHANGES DURING PREGNANCY IN GUT MICROBIOTA AND METHYLMERCURY BIOMARKERS, AND REVERSAL OF MICROBE-EXPOSURE CORRELATIONS
Sarah Rothenberg, MS, D.Env.

A Novel Nutritional Formulation Containing the Prebiotic Human Milk Oligosaccharide 2'-Fucosyllactose May Improve Gastrointestinal Quality of Life and Beneficially Alter the Gut Microbiome in Adults with Gastrointestinal Dysfunction
Presented at Diet and Optimum Health (Linus Pauling Institute), International Congress on Integrative Medicine and Health
Jenn Ryan, ND, MS

Ogg1 deficiency induces changes in intestinal microbiome correlated with increased intestinal inflammation
Holly Simon, PhD

Microbiome genomics and bionformatics at the OSU Center for Genome Research and Biocomputing
Brett Tyler, PhD

Treatment of Diet-Induced Obese Mice with Xanthohumol and its Non-Estrogenic Derivatives DXN and TXN Modulates Composition of the Fecal Microbiota, Bile Acids and is Associated with Improvement of Metabolic Syndrome Biomarkers
Presented at LPI International Conference
Yang Zhang, MS