Microbiomes in Transition
Seminar Series

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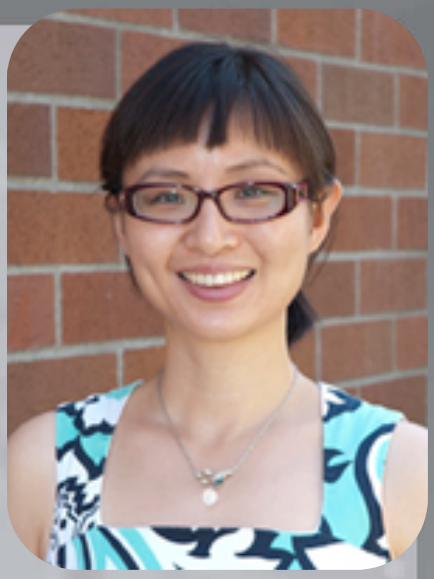

Gut Microbiome: A Novel Frontier for Xenobiotic Metabolism in the Host Liver

Presented by:

Dr. Julia Yue Cui

University of Washington

Abstract: Accumulating data in the literature have demonstrated the critical roles of intestinal bacteria on the host intermediary metabolism including obesity and type II diabetes. Relatively less is known regarding the impact of intestinal bacteria on the hepatic expression of various drug-metabolizing enzymes and transporters (together called "drug-processing genes") as well as the hepatic metabolism of xenobiotics. The goal of this study was to utilize germ-free mice and second- generation sequencing technology to determine the impact of alterations in gut microbiome on the hepatic drug-processing gene expression and xenobiotic metabolism. RNA-Sequencing demonstrated that in livers of germ-free mice, there was a marked decrease in the hepatic expression and enzyme activity of cytochrome P450 (Cyp) 3a, which is a major class of phase-I enzyme involved in the biotransformation of over two-thirds of the drugs prescribed in the market; in contrast, there was a marked increase in the hepatic expression and enzyme activity of Cyp4a, which is important for lipid metabolism. Chromatin immunoprecipitation and qPCR results suggested that this was likely due to attenuated pregnane X receptor signaling but enhanced peroxisome proliferator-activated receptor signaling. During liver development, the presence of intestinal microbiota markedly impacted the normal ontogeny of many hepatic drug-processing genes in a gender-specific manner. Introducing exogenous bacteria by probiotics or conventionalization also influenced the hepatic drug-processing capacities. Finally, the environmental chemical polybrominated diphenyl ethers (PBDEs) mediated alterations in many hepatic drug-processing genes depended on the presence of a normal configuration of the gut microbiome, and the germ-free conditions altered the amount of certain phenolic metabolites of PBDE-47. In conclusion, gut microbiome critically impacts the expression of drug-processing genes and the metabolism xenobiotics of the host liver.

Date:
Wednesday,
Feb. 18th, 2016

Location:
BSF Darwin (1007)

Time: 11:00 AM

U.S. DEPARTMENT OF ENERGY

Host: Aaron Wright & Brain Thrall, 5-5920 & 1-7307

Christina Stevenson, 1-6558