# Thesis Abstract

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Title of Thesis:


The development and application of metabologenomic analysis for the evaluation of intestinal environment

Summary of Thesis:

Intestinal microbiota and their synthetized-metabolites are strongly associated with host physiology. Advances in DNA sequencing and mass spectrometry have enabled accumulation of large amounts of data on the interactions among microbiota, metabolites, and the host. However, there is no well-developed strategy to analyze these datasets. This study aimed to develop an original analytical strategy, metabologenomics, that involves integrated analysis of capillary electrophoresis time-of-flight mass spectrometry (CE-TOFMS)-based metabolome data and high-throughput-sequencing-based microbiome data to evaluate perturbations in environmental factors, such as diet, which influence the intestinal environment. First, the fecal metabolome profiles obtained using eight methods differing in fraction, homogenization solvent, extraction solvent, and the requirement of bacterial cell disruption were compared for comparison using CE-TOFMS-based metabolome analysis. The results suggested that metabolomic profiles could differ based on the extraction method, thereby highlighting the importance of selecting a method suitable for the specific analysis. Second, we conducted a metabologenomic analysis of the metabolome and microbiome data. This analysis revealed that feces of mice fed an American diet, that formulated to match the average daily human nutritional intake in the United State, contained higher levels of butyrate and higher relative abundances of butyrate producers, such as *Oscillospira* and *Ruminococcus*, compared with those of the control diet-fed mice. Additionally, the predicted gene abundance of butyryl CoA:acetate CoA transferase positively correlated with butyrate levels. Finally, human intestinal microbiome and metabolome profiles under three dietary conditions were investigated to evaluate the robustness of the human intestinal environment in response to daily dietary fluctuations. The results suggested that intestinal metabolome and microbiome profiles are different for each individual and are not affected by daily dietary fluctuations in most individuals. Thus, our metabologenomic approach can be utilized to evaluate the intestinal environment and gain insights into complex microbial ecosystems.


Keywords: intestinal microbiota; metabolome; metabologenomics; diet; multi-omics analysis