Host genetics, gut microbiome and environmental exposures are all important determinants of our health. Understanding their interactions and impacts on the host requires integrating big data approaches with cutting-edge analytical platforms to enable both comprehensive measurement and systems-level data interpretation. In this seminar, I will discuss the current big data challenges and computational approaches within the context of gene-environment-microbiome (GEM) interactions. I will introduce several bioinformatics tools developed recently in my group for metabolomics, microbiome and toxicogenomics. Finally, I will proposal a systems metabolomics platform to help dissect GEM interactions using a C. elegans model.