DEPARTMENT OF BIOLOGICAL SCIENCES
PH.D. VIVA VOCE

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Development of computational models and algorithms for designing of novel microbiome-based therapeutics

Our understanding of the human microbiome has enhanced significantly with rapid advancements in sequencing technologies and availability of new computational tools. The population-specific differences in human microbiome due to diet, geographical location, age etc. play a key role in determining human health and metabolism and the gut microbiome dysbiosis is often found to be associated with various metabolic diseases. Microbiome studies also suggest that differences in gut microbiome can drastically alter the therapeutic outcomes of ingested drugs, which is one of the reasons for their differential responses in different individuals. Thus, a precise knowledge of the complete microbial potential is required such as identification of taxonomic, functional and metabolic biomarkers in a given microbiome, and prediction of the gut microbes, which can directly and/or indirectly affect the efficacy and toxicity of drug molecules. Therefore, development of highly accurate and robust computational approaches will be very helpful in determining the microbial insights from large-scale omics data.

To explore the microbial potential in an environment, an efficient and accurate taxonomic classifier named '16S Classifier' and an orthology-based functional classifier named 'Woods' were developed. To study the association of microbes with critical diseases, 16SrRNA and metabolomic analyses were performed using fecal samples from patients of autism spectrum disorder and colorectal cancer. Furthermore, novel methods such as 'HyPe' for the identification of novel peptidoglycan hydrolases, and 'BioFin' for the prediction of novel anti-microbial and anti-biofilm peptides/proteins, were developed for the identification and designing of novel alternatives to antibiotics. To understand the functional role of gut microbes and to predict the microbial enzymes responsible for the metabolism of xenobiotic/drug molecules, a novel approach 'DrugBug' was developed by integrating machine learning and chemoinformatics approaches. The metabolism of FDA-approved drugs was predicted using DrugBug, and the results were compiled as a comprehensive database. DrugBug predicted metabolism of amphetamine was validated using structural and experimental methods. Further, 'ToxiM' tool was developed to predict the toxicity of the metabolites. The above work provides novel machine learning-based tools for metagenomic analysis and provides new insights on the microbiome-mediated xenobiotic metabolism. Taken together, the developed methods and approaches would be very useful in designing novel and efficient microbiome-based therapeutics.

References:

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