Indian Institute of Science
Centre for BioSystems Science and Engineering
MRDG-BSSE Seminar

26th November 2019 (Tuesday), 04:00 PM, CES Seminar Hall, 3rd floor, Biological Sciences Building

A Novel Quantitative Approach For Understanding Strain Level Microbiota Dynamics After Fecal Transplantation For Several Diseases

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ABOUT THE SPEAKER

Dr. Varun Aggarwala graduated from IIT Guwahati with a B.Tech degree in Computer Science and Engineering. He then received his M.S.E. degree in Computer Science (School of Engineering and Applied Science) and Ph.D. in Genomics and Computational Biology (Perelman School of Medicine), respectively, from the University of Pennsylvania. Currently, he is working as a postdoctoral fellow, under Prof. Jeremiah Faith, in Genetics and Genomics Institute at Mount Sinai. He is interested in the transmission of genetic material (both human and microbes) between individuals in both health and disease. He was awarded the best poster prize at the Penn Department of Genetics retreat for the year 2015. He was also selected as a semi-finalist for ASHG/ Charles J Epstein Trainee Award for excellence in human genetic research for the year 2015. He served as a reviewer for Nature Genetics, Nature Communications, BMC Gastroenterology and ad-hoc reviewer for journals, Genome Biology and PLoS Pathogens.

ABSTRACT

Background: Human gut microbiota has an active role in both health and disease. Several placebo controlled clinical trials that manipulate gut microbiome through fecal microbiota transplantation (FMT from healthy donors to patients), have reported success for recurrent *C. diff* infection (~90% remission) and Ulcerative colitis (~30% remission). However, FMT in its current form is a black box with no clarity on its design, dosage, predictors for response and mechanism of action. Previous analysis of FMT have shown microbial changes in patients post FMT, but used profiling methods that were limited to analyzing broad community changes (at the genus or species level) in the microbiome. The functional impact of the gut microbiota is at the level of strains, but no suitable approach exists to detect and track strains across samples.

Hypothesis: A selection of microbial strains is associated with remission post FMT and quantifying the engraftment of donor strains in patients after FMT can improve study design and find effective strains for precision therapy.

Approach: We first perform high-throughput anaerobic bacterial culture from donor fecal samples, and isolate and sequence microbial strains. Next, I detect and track them in recipient samples (post FMT) with a novel sequence based algorithm, *Strainer*. My algorithm finds informative kmers for each reference strain, and can detect them in complex metagenomic communities with high precision and recall (AUC > 0.85) at shallow sequencing depth.

Dataset used: We work with several ($n = 14$) clinical FMT interventions in patients with recurrent *C diff* infection, and have samples at different timepoints post FMT (upto 1 year apart). We also have access to multiple timepoints from the largest FMT clinical trial (FOCUS, with $n = 55$) on Ulcerative Colitis patients, which received the FMT from a mixture of donors.

Results: Will discuss in the seminar! (Some teasers: (1) Higher engraftment is associated with clinical endpoints. (2) We detect (and validate by culturing) long term stable engraftment (even at 1 year) of donor strains in patients post FMT.)