Socioeconomic Status Factors Associated with Increased Incidence of Community-Associated Clostridium difficile Infection

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Background. Recurrent *Clostridium difficile* infection (rCDI) poses major challenges to healthcare providers and patients. Fecal Microbiota Transplantation (FMT) is an effective therapy for rCDI, but the exact mechanism of its efficacy is unknown. Current metagenomics literature indicates that abundance of Bacteroidetes and Firmicutes may protect against CD proliferation and recurrence. However, this is too broad to be useful for developing refined and targeted microbial-specific therapy for rCDI, because the long-term safety of FMT remains unknown. We examined the phylogeny of bacteria pre- and post-FMT to determine the key organisms associated with successful FMT to the genera level.

Methods. A subset of patient stool samples ($n = 35$) from a phase 2 study comparing fresh vs. frozen FMT for rCDI was sequenced at four time points: pre-FMT; at day 10; at week 5; and at week 13, following the last FMT. The matching donor stool was sequenced simultaneously with the corresponding patients’ pre- and post-FMT samples.

Using the binary outcome to a single FMT as the response, we have developed an in-house machine learning algorithm, Φ-LASSO, to isolate key genera using the bacterial phylogenetic structure.

Engraftment was defined as: newly detected operational taxonomic unit (OTUs) in the patient post-FMT, which were present in the donor but undetected in the patient pre-FMT. Augmentation was defined as: non-donor OTUs whose levels substantially increased post-FMT. Figure 1 (below) displays the distribution of engrafted and augmented OTUs at varying thresholds. We observed increases over time points within each threshold level.

Results. *Akkermansia*, Blautia and Roseburia appear to be key genera for successful FMT. The Φ-LASSO fits with consistently positive coefficients, see Figure 2.

Conclusion. In this preliminary study, using Φ-LASSO, we have shown that specific microbes to the genera level are uniformly present in successful FMT. This information may lead to developing refined and targeted microbial-therapy based on the genera level.

Figure 1: Observed (a) engraftment of distinct donor OTUs on patients and (b) augmentation of distinct OTUs in patients for day 10 (D10), week 5 (W5), and week 13 (W13) post-treatment.

Figure 2: Fitted coefficients for donor OTUs selected by Φ-LASSO.

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