increased-microbial-diversity-recipients-fmt-recurrent-clostridium-difficile-infectionINCREASED MICROBIAL DIVERSITY FOUND IN SUCCESSFUL RECIPIENTS OF NEXT-GENERATION FMT FOR RECURRENT *CLOSTRIDIUM DIFFICILE* INFECTION

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Background: Studies have reported that patients with recurrent *Clostridium difficile* infection (CDI) have low fecal microbiota diversity and that diversity increases after successful fecal microbiota transplant (FMT). We evaluated the gut microbiota of patients with recurrent CDI after successful and unsuccessful treatment with a next-generation FMT.

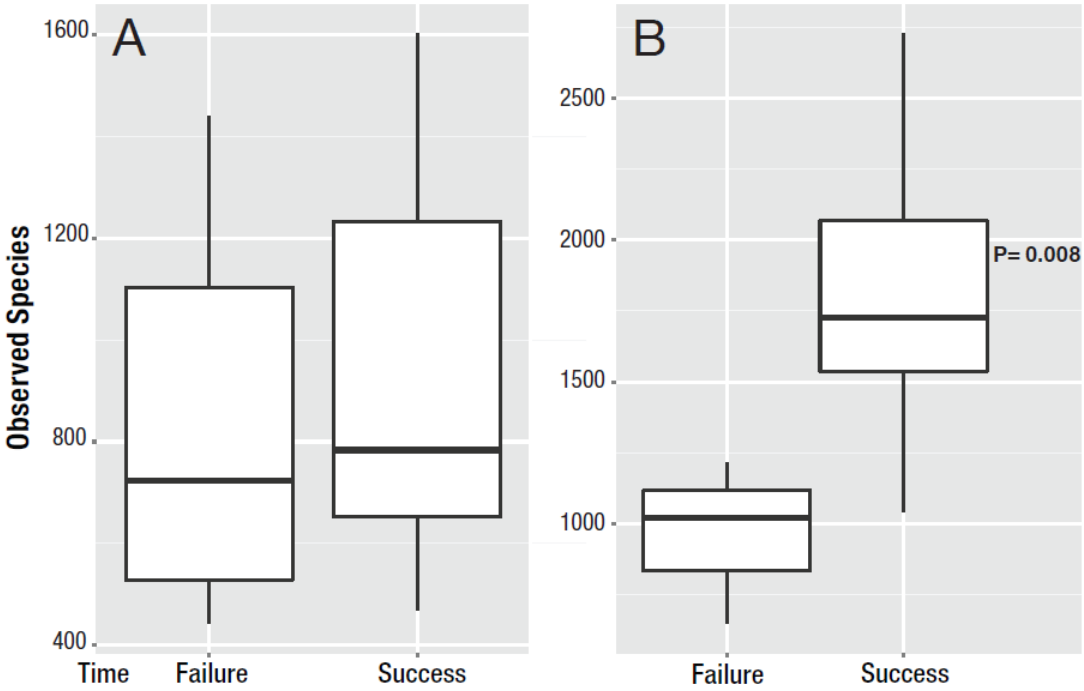
Methods: The fecal microbiota of a subset of 17 patients who participated in the PUNCH CD study assessing RBX2660, a microbiota-based drug, for recurrent CDI were characterized at 7 and 60 days post treatment using 16S rRNA gene sequencing in a post-hoc analysis. The patients (median 69.2 years; 65% female; 94% white) included 8 successes with 1 dose of RBX2660; 6 with 2 doses and 3 failures with 2 doses. All patients received a standardized 7-day course of vancomycin prior to dose 1 of RBX2660 via enema. A second dose was permitted within 10 days of recurrence; administered without antibiotic pretreatment. DNA sequencing was performed on an Illumina MiSeq platform. The 16S sequences were clustered into operational taxonomic units and used to determine within-sample diversity and taxonomic composition at each time point. Weighted Unifrac analysis was used to determine differences between sample diversity.

Results: At 7 days post FMT there was no significant difference in diversity between successes and failures with RBX2660; there was a trend toward higher diversity in successes. However, at day 60, there was a significantly higher microbial richness in patients with treatment success compared with failure, P =0.008. Successfully treated patients had increased microbial diversity, regardless of whether they had 1 or 2 doses of RBX2660, Figure1. Although underpowered, Unifrac analysis suggested that the microbial diversity of successfully treated patients was similar to each other and dissimilar to failures, P=0.05, Figure 2.

Conclusion: Patients with recurrent CDI who responded to treatment with RBX2660 had a more diverse gut microflora at day 60 compared with patients who failed treatment but not at day 7. The results suggest a time dependence for re-establishing a diverse microbiome and confirm that high microbial diversity is associated with successful treatment of recurrent CDI.

Key words: Fecal microbiota transplant, FMT, *Clostridium difficile* infection

Figure 1. Rarefied to 20,000 Operational Taxonomic Unit Observations Per Sample



Treatment Outcome at Day 7 – Dose 1 Only

Treatment Outcome at Day 60

Figure 2. Weighted Unifrac Principal Coordinates Analysis at Day 60