RBX Abstract for ASM Microbe 2017

Abstract may have up to 2200 characters, which does not include title, authors, affiliations, and funding acknowledgement. Tables and graphics (maximum of 500 characters) are included in the character count. Spaces are not counted.

Track: Antimicrobial Agents and Infectious Diseases
Subtrack: Experimental therapeutics
Keywords: *Clostridium difficile, microbiota-based therapy, human microbiome project*
Current Character Count: 1965 of allowed 2200 characters including figure legend

Changing the Microbiome: Patients with a Successful Outcome Following Microbiota-Based RBX2660 Treatment Trend Toward Human Microbiome Project Healthy Subjects' Profile

K. Blount[1], C. Jones[1], B. Shannon[2], S. Carter[2]

[1]Rebiotix Inc, Roseville, MN, [2] BioRankings LLC, St. Louis, MO

Background: Recurrent *Clostridium difficile* infections (rCDI) are associated with decreased taxonomic diversity in patients' intestinal microbiome compared to healthy microbiomes. RBX2660 is a standardized microbiota-based drug designed to rehabilitate a patient's microbiota. The effect of RBX2660 on rCDI patient microbiomes was evaluated by comparing pre- and post-treatment samples collected from PUNCH CD2—a randomized, double-blind, placebo-controlled study—to the healthy intestinal microbiome defined by the Human Microbiome Project (HMP).

Methods: Subjects with rCDI were randomized to receive blinded treatment by enema of 2 doses of RBX2660 (Group A), 2 doses of placebo (Group B), or 1 dose of RBX2660 and 1 dose of placebo (Group C), with doses 7 days apart. Voluntary stool samples were collected from all subjects at baseline and at 7, 30, and 60 days after treatment. For this analysis, samples were selected from subjects determined to be responders per protocol (i.e. success), defined as the absence of rCDI-associated diarrhea for 8 weeks after treatment.

Relative taxonomic abundances at the class level were determined using 16s rRNA sequencing analysis for 94 stool samples collected from 45 patients in Groups A and C. Relative abundance data were grouped longitudinally and compared to HMP data using a Bray-Curtis dissimilarity calculation. Additional analyses were performed based on the Dirichlet-Multinomial distribution to compare group mean relative taxonomic abundances, pi.

Results: Pretreatment patient microbiomes were less diverse and more divergent from the "healthy" HMP microbiome, with specific taxonomic distributions that are consistent with previous microbiomic analyses of CDI patients. After treatment, patient microbiomes became more closely related to the HMP over time, with the largest shift observed after 7 days.

Conclusion: Results show RBX2660 treatment shifts patient intestinal microbiomes closer to a healthy microbiome.

This analysis was funded by Rebiotix Inc., Roseville, MN.

Figure 1. ML estimates (MLE) of pi for microbiomes from HMP and subjects treated with RBX2660. The

category 'no match' represents taxa that were not present in both HMP and RBX2660 datasets.