The Association Between Antibiotics, the Intestinal Microbiome, and risk for Type-2 Diabetes

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Introduction: The human microbiome consists of thousands of microbial species colonizing all mucosal surfaces. Perturbations of the microbiome may place people at increased risk of diverse diseases. This study sought to develop models to predict how antimicrobial treatment alters both the composition and overall diversity of the intestinal ecological microbiome. The impact of antibiotics on the microbiome are incompletely understood. This study investigated the effects on the microbiome of Zosyn (piperacillin/tazobactam) and cefepime, two drugs with similar clinical indications among hospitalized patients.

Hypothesis: We hypothesized that Zosyn would more profoundly decrease beneficial organisms while increasing the abundance of microorganisms believed to cause inflammation and contribute to metabolic disease. We also hypothesized that detailed investigation of species-specific interactions would reveal which species were critical for maintaining microbial diversity and preventing metabolic dysfunction with lasting effects.

Methods: Stool samples obtained from 135 high risk hospitalized patients having at least two samples within 90 days were subjected to shotgun sequence analysis. Microbial community structure was determined using bioinformatics tools. Serial samples from the same patient were compared, and differences in microbial abundance expressed in relation to the time between samples and days of antibiotic exposure. Species-species and species-drug interaction networks were determined using correlation analysis.

Results: Results to date show that Zosyn produced a statistically significant effect on multiple *Klebsiella spp.* over a 2-week time frame. Both Zosyn and cefepime demonstrated negative Pearson's correlations in *E. coli*. Pearson's correlations in various *Klebsiella spp.* demonstrated varying degrees of both positive and negative associations for both Zosyn and cefepime. Next steps for the study are to begin designing mechanistic models that illustrate the overall microbial diversity changes and interspecies networking interactions.

Conclusions: Moving forward we plan to continue our investigation not only to understand the qualitative changes in the intestinal microbiome but also to understand and create interactive predictive models that will allow us to understand better how changes on the individual species level of a specific organism affect other organisms to better understand the diversity shifts following antibiotic treatment.

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