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Fecal transplants restore healthy bacteria and gut functions

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Fecal microbiota transplantation—the process of delivering stool bacteria from a healthy donor to a patient suffering from intestinal infection with the bacterium *Clostridium difficile*—works by restoring healthy bacteria and functioning to the recipient's gut, according to a study published this week in *mBio*, the online open-access journal of the American Society for Microbiology.

The study provides insight into the structural and potential metabolic changes that occur following fecal transplant, says senior author Vincent B. Young, MD, PhD, an associate professor in the Department of Internal Medicine/Infectious Diseases and the Department of Microbiology & Immunology at the University of Michigan in Ann Arbor. The transplants, which have been successful at curing more than 90 percent of recipients, have been used successfully since the 1950s, he says, though it hasn't been clear how they work to recover gut function.

"The bottom line is fecal transplants work, and not by just supplying a missing bug but a missing function being carried out by multiple organisms in the transplanted feces," Young says. "By restoring this function, *C. difficile* isn't allowed to grow unchecked, and the whole ecosystem is able to recover."

Young and colleagues used DNA sequencing to study the composition and structure of fecal microbiota (bacteria) in stool samples from 14 patients before and two to four weeks after fecal transplant. In 10 of the patients, researchers also compared stool samples before and after

transplant to samples from their donors. All transplant patients, treated at the Essentia Health Duluth Clinic in Minnesota, had a history of at least two recurrent *C. difficile* infections following an initial infection and failed antibiotic therapy.

Studying families of bacteria in the samples, investigators found marked differences among donor, pre-transplant and post-transplant samples. However, those from the donors and post-transplant patients were most similar to each other, indicating that the transplants at least partially returned a diverse community of healthy gut bacteria to the recipients. While not as robust as their donors, the bacterial communities in patients after transplant showed a reduced amount of Proteobacteria, which include a variety of infectious agents, and an increased amount of *Firmicutes* and *Bacteroidetes* bacteria typically found in healthy individuals, compared to their pre-transplant status.

Then, using a predictive software tool, researchers analyzed the relationship between the community structure of the micoorganisms and their function, presumably involved in maintaining resistance against CDI.

They identified 75 metabolic/functional pathways prevalent in the samples. The samples taken from patients before transplant had decreased levels of several modules related to basic metabolism and production of chemicals like amino acids and carbohydrates, but were enriched in pathways associated with stress response, compared to donor samples or post-transplant samples.

CDI has significantly increased during the past decade, Young says, with previous studies estimating there are more than 500,000 cases of CDI in the United States annually, with health care costs ranging from $1.3 billion to $3.4 billion. Up to 40 percent of patients suffer from recurrence of disease following standard antibiotic treatment. In a

healthy person, gut microorganisms limit infections but antibiotics are believed to disrupt the normal structure of these microoganisms, rendering the gut less able to prevent infection with *C. difficile*.

Further identification of the specific microorganisms and functions that promote resistance of bacterial colonization, or growth, may aid in the development of improved CDI treatments, Young says: "If we can understand the functions that are missing, we can identify supplemental bacteria or chemicals that could be given therapeutically to help restore proper gut function."

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