What would it take to make FMT mainstream? Two publications consider the opportunities

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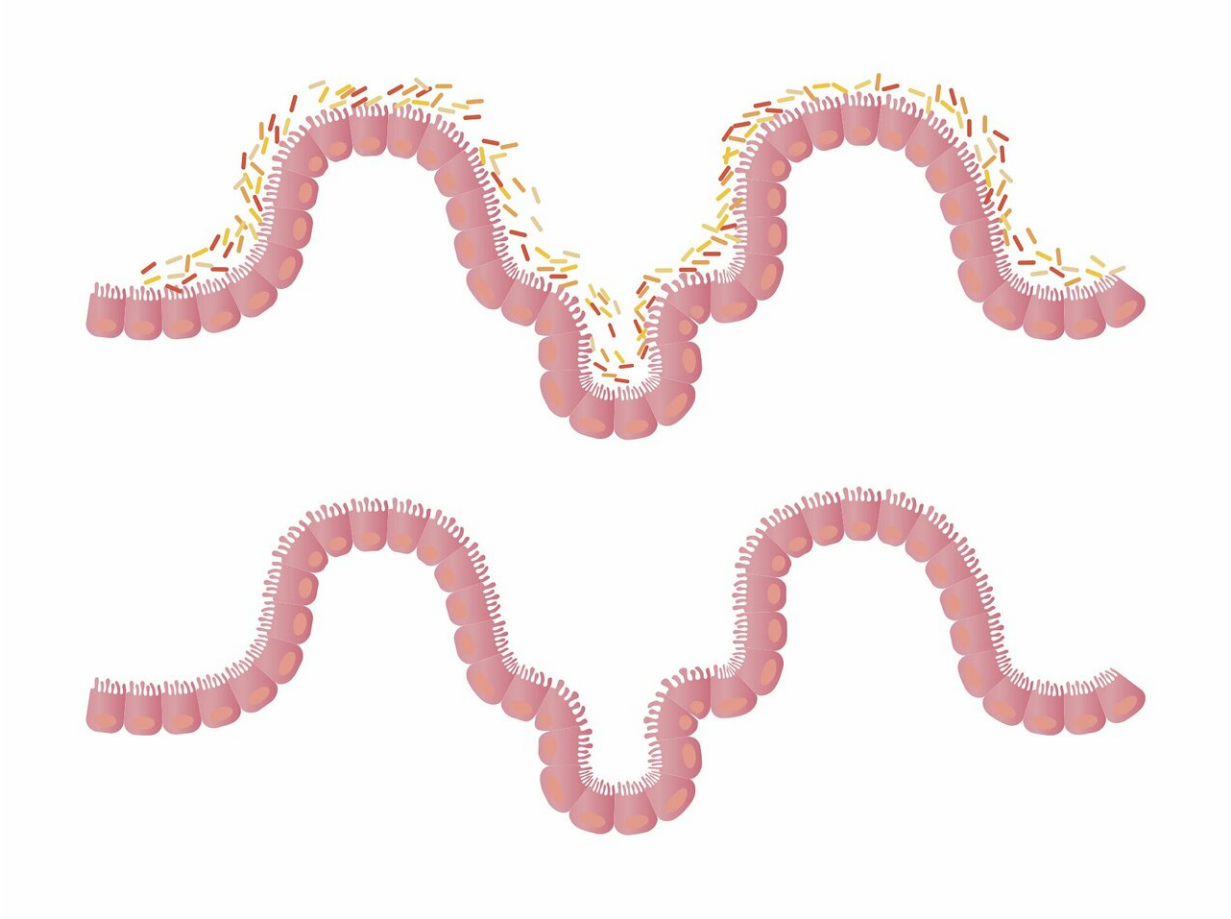

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Many of the microbes that live in your gut are also found in your stool, and fecal microbiota transplants (FMTs) are being studied to determine whether they can improve health outcomes in patients with various diseases such as ulcerative colitis and Crohn's disease. However, it is important to recognize that FMT does carry some risk such as bloodstream infections and the transmission of drug-resistant bacteria. Furthermore, FMT treatment for most microbiome-associated diseases has not been rigorously studied in humans—and any such studies would be subject to regulation by the Food and Drug Administration. In a pair of forums publishing February 12 in the journal *Cell Host & Microbe*, clinicians and an FDA scientist detail some areas of FMT research that could facilitate the development of safe and effective FMT therapies for patients.

Currently, the FDA has stated that it intends to exercise enforcement discretion regarding the investigational new drug (IND) requirements for the use of FMT to treat Clostridioides difficile infections not responsive to standard therapies, provided that the treating physician obtains adequate informed consent. This means that, while the treatment is not yet approved, it is sometimes used in this particular situation without submitting an IND to the FDA. Investigators or practitioners who are using FMT to treat other diseases or conditions still need to submit an IND to the FDA. In addition, researchers are evaluating different preparations of FMT including autologous FMT and material provided by stool banks. Also, several manufacturers are developing FMT with the goal of licensure. "We are excited about the opportunity to move the fecal microbiota transplant field forward, particularly where FMT may represent an opportunity to improve outcomes for patients," says Kate Markey, a hematology physician at the Memorial Sloan Kettering Cancer Center and corresponding author of one of the forums.

At this time, the methods to collect and prepare the donated material are not sophisticated, and the optimal FMT product characteristics, such as

the best bacterial composition for a specific outcome, are not known. The FDA is working to provide stakeholders information about donor screening and testing and manufacturing considerations for FMT. "While this information is routinely communicated by the FDA during public scientific meetings, we hope this forum provides a mechanism to provide this information to a broader audience," says Paul Carlson, an FDA principal investigator in the Laboratory of Mucosal Pathogens and Cellular Immunology and corresponding author of the other forum. "We want to give an overview of FDA regulation of fecal microbiota for transplantation and lay out some considerations for investigators to help ensure the safety of patients and the viability of the bacteria in the transplanted material."

These considerations include a reference list of potential pathogens for donor screening to exclude donors with a high risk of pathogen exposure. Further, Dr. Carlson provides considerations for manufacturing processes and controls, such as the use of anaerobic chambers during FMT manufacturing to preserve potentially useful bacteria that may be highly sensitive to oxygen. At this time, given the lack of knowledge about the optimal bacterial composition of FMT used to treat a particular disease, loss of these anerobic organisms may negatively impact effectiveness.

The authors say that placebo controlled clinical trials of FMT to treat a particular disease are important to demonstrate safety and effectiveness and advance the scientific understanding of FMT. "The next steps are further clinical trials with the array of products either now available or in development. As current trials reach completion, the true potential of this therapy will become clear," says Markey.

While there is still much work to be done before we see mainstream usage of FMT, Dr. Carlson says that the "FDA is engaged and continues to work with people conducting clinical trials using FMT."

More information: Kate A. Markey et al. Therapeutics Targeting the Gut Microbiome: Rigorous Pipelines for Drug Development, *Cell Host & Microbe* (2020). DOI: 10.1016/j.chom.2020.01.022

Paul E. Carlson. Regulatory Considerations for Fecal Microbiota Transplantation Products, *Cell Host & Microbe* (2020). DOI: 10.1016/j.chom.2020.01.018

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