AMMI Canada Medical Student Research Proposal

Project title: *Intermittent Carriage of Antibiotic Resistant Organisms and Enteric Pathogens Among Healthy Fecal Microbiota Transplant Stool Donors*

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Background: Complicated chronic illnesses, such as recurrent *Clostridioides difficile* infection (1) and inflammatory bowel disease (2)(3) have been linked to gastrointestinal dysbiosis in addition to a number of non-gastrointestinal related conditions such as depression, anxiety, cardiovascular disease, asthma, and diabetes. Fecal microbiota transplantation (FMT) has been shown to be effective in patients with *C. difficile* and data suggest potential effectiveness in patients with inflammatory bowel disease and other conditions. While FMT has demonstrated effectiveness or strong promise to improve clinical outcomes and livelihood in patients, the optimal frequency of screening donors to assure safe donor stool is used for FMT has not been well studied.

The Microbiota Therapeutics Outcomes Program (MTOP) is a program that provides FMT for clinical care of patients with recurrent *C. difficile* infection and as part of research for patients with other conditions with associations with gastrointestinal dysbiosis. This program follows and exceeds Health Canada's guidance regarding screening FMT. It accepts healthy stool donors, with no personal or first-degree family history of disease states linked to an abnormal gastrointestinal microbiome. Potential stool donors undergo intake assessment and require negative comprehensive microbiology screening prior to participation. This screening includes culturing stool samples and screening for antimicrobial-resistant organisms (ARO). Prior to release to recipients, the patient is tested again to confirm negative microbiology screening.

On repeat testing, one donor was unexpectedly positive for an ESBL-producing *Klebsiella pneumoniae* and another was positive for sapovirus despite being well with no travel history and no history of antimicrobial treatment. Whether healthy screened donors should have all donations screened to assure no enteric pathogens or ARO is unclear.

Objectives:

1. Determine the prevalence of antibiotic resistant organism (ARO) in a cohort of stool samples collected from donors with no personal or family history of chronic disease.

2. Determine the prevalence of enteric pathogens (EP) in a cohort of stool samples collected from donors with no personal or family history of chronic disease.

Research Design, methods, and analysis:

Donors: This study will include all active MTOP stool donors between March 2017 and May 2019.

ARO Screening: Stool aliquots stored at -80C from each donation will be thawed and tested for ARO [methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), ESBL, and carbapenemase-producing organisms (CPO)] by planting onto Oxoid Denim Blue agar, Oxoid Brilliance VRE agar, and Oxoid MacConkey/cefpodixime agar, respectively following clinical laboratory operating procedures.

Enteric pathogen testing: Stool aliquots stored at -80C from each donation will be thawed and tested using the BioFire FilmArray Gastrointestinal Panel, which tests for pathogens commonly associated with gastroenteritis. This includes *Adenovirus F40/41, Astrovirus, Norovirus GI/II, Rotavirus A, Sapovirus (I, II, IV, and V), Campylobacter, Clostridioides difficle (toxin A/B), Plesiomonas shigelloides, Salmonella, Yersinia enterocolitica, Vibrio (parahaemolyticus, vulnificus,* and *cholerae), Enteroaggregative E. coli, Enteropathogenic E. coli, Enterotoxigenic E. coli, Shiga-like toxin-producing E. Coli stx1/2, Shigella/Enteroinvasive E. coli, Cryptosporidium, Cyclospora cayetanesis, Entamoeba histolytica,* and *Giardia lamblia* (4).

Expected Outcomes: We expect a proportion of donor stool in the MTOP stool donor bank to test positive for a AROs and enteric pathogens given the MTOP anecdotal experience to date. This study will contribute to the understanding of prevalence of ARO and enteric pathogens within a healthy screened stool donor population and will inform FMT donor programs on the optimal frequency of screening donors to assure safe donor stool is used for FMT.

Knowledge translations: Results from this study will be communicated to the infectious

disease, microbiology, and gastrointestinal expert community through an abstract at the AMMI CACMID national meeting and through a published manuscript.

References:

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2. Gupta, S., Vercoe-Allen, E., Petrof E., 2016. Fecal microbiota transplantation: in perspective. Therapeutic Advances in Gastroenterology 9 (2), 229-239.

3. Cui, B., Li, P., Xu, L., Peng, Z., Xiang, J., He, Z., Zhang, T., Ji, G., Nie, Y., Wu, K., Fan, D., Zhang, F., 2016. Step-up fecal microbiota transplantation (FMT) strategy. Gut Microbes 7 (4), 323-328.

4. The BioFire FilmArray Gastrointestinal (GI) Panel. (2019). Retrieved from https://www.biofiredx.com/products/the-filmarray-panels/filmarraygi/