

November 26, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format.

**Title: Restoring the Gut Microbiome for the Treatment of Inflammatory Bowel Diseases**

**Author:** Jessica Ravikoff Allegretti and Matthew J. Hamilton

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 5990

The manuscript has been improved according to the suggestions of reviewers:

1 Thank you very much reviewer 1 for reviewing and your comments.

2 Thank you for your time reviewer 2 and the detailed review and helpful suggestions that have improved this review substantially. Revision has been made according to the suggestions

#### Introduction

(1) More details have been added to introduce the role of the microbiota in the pathogenesis of IBD and reference has been made to another article that will appear in the same issue of *WJG* which reviews in detail the intestinal microbiota.

(2) We completely agree with the statement "it is unclear if these differences are a cause or consequence of the development of IBD" and have added this statement into the introduction.

#### FMT as Therapy for FMT

(1) More details were provided from the study by Borody et al to now include more of the procedure and patient details

(2) Yes, this follow up study of 6 UC patients receiving FMT is discussed and cited.

(3) We agree that the Angelberger et al study from the American J of Gastroenterology 2013 describing the phylotypes of stools after FMT is an important study to include for this review and we have added it in to this section along with a brief description of the study with its conclusions.

#### Limitations

(1) and (2) This section was reorganized per the advisement of reviewer 2 and the new order is: screening, patient preparation, donor selection, stool processing storage and delivery followed by the recent FDA position and then closing remarks

(3) The screening methods were updated and we added that screening may depend on the region of the world where the procedure is being done and there should be input from the infectious disease service. We have added in screening strategies that have been described in the FMT published studies.

(4) The study by Khoruts et al was added from J Clinical Gastroenterology 2010

(5) More information was added and comments about bowel lavage and antibiotics prior to FMT.

- (6) We mentioned that the procedure to deliver the stool may be dependent on what type of IBD a patient has. We did not specifically mention Firmicutes as we could not find mention of this in the literature with respect to FMT.
- (7) Information on transplanting frozen stool and anaerobes in the stool was added along with the relevant citations.
- (8) We agree with the statement and have emphasized the potential long term risks of FMT that are not known at this time.
- (9) We added in a sentence about how disease severity and timing of FMT in the IBD disease course will be important aspects to study in the future.
- (10) We added in the Schwartz et al study from the American J of Gastroenterology 2013 regarding the potential for the transmission of infections during FMT.
- (11) We like this sentence and use it as our concluding sentence!

Minor comments- these misspellings have been fixed. Thank you.

3 Thank you reviewer 3 for your comments. We were invited by the editors of the *WJG* to write a Topic Highlight with a focus on Inflammatory Bowel Disease. With the recent attention on the gut microbiota and fecal transplant, we thought it would be appropriate and interesting to the readers to review any literature in this area (not too much) as well as provide some commentary regarding the potential successes and limitations of FMT in IBD. The "Topic Highlight" allows us to do both.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

Matthew J. Hamilton M.D.  
Division of Gastroenterology  
Brigham and Women's Hospital  
Harvard Medical School  
Boston, MA 02115 U.S.A  
Fax: +  
E-mail: [mjhamilton@partners.org](mailto:mjhamilton@partners.org)