

**DEPARTMENT OF MICROBIOLOGY AND IMMUNOLOGY**

1120A MEDICAL SCIENCE RESEARCH BUILDING I

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February 14, 2018

Dear Editor,

We resubmit for your review: “***Spatial variation of the native colon microbiota in healthy adults***” by Kaitlin Flynn and our colleagues. The previous version of this manuscript was submitted on November 15, 2017 and we received a decision on January 16, 2018. That decision encouraged us to submit a revised manuscript once we were able to respond to the reviewers’ comments. We are confident that we have now addressed each of these comments. Although we did not agree with all of their comments regarding our analytical approaches, we feel that the manuscript has been improved because of their helpful input.

As you are aware, there is growing interest in the role of the gut microbiota in a number of diseases including colorectal cancer. This study is unique because it leverages the ability to obtain colonic samples from healthy individuals without subjecting them to a bowel preparation that disturbs the natural microbiota. By obtaining samples from individuals without the bowel preparation, we were able to complete a more representative characterization of the colonic mucosa and lumen than has been possible in the past. In addition, we are using cutting-edge machine learning algorithms to identify the bacterial populations that are signatures of the ascending and descending colon as well as between the luminal contents and mucosa. This is an important analysis to better understand the baseline structure of the human microbiota in the context of understanding the shifts in the microbiota leading to IBD and colorectal cancer.

The data presented in this manuscript are original and the manuscript is not under consideration elsewhere. None of the manuscript contents have been previously published. The manuscript has been deposited on the bioRxiv pre-print server. All authors have read and approved the manuscript for publication. The authors declare no conflicts of interest.

Unfortunately, we must request that **Rob Knight (UCSD)** not be included as an editor or reviewer of this manuscript as previous interactions indicate that he is unable to provide an unbiased review of our work.

Thank you very much for your consideration and we look forward to your response.

Sincerely,

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