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Celecoxib does not alter intestinal microbiome in a longitudinal diet-controlled study

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## ACCEPTED MANUSCRIPT

Sir,

Rogers and Aronoff in their recent article, "The influence of non-steroidal anti-inflammatory drugs on the gut microbiome" (1), described a study reporting the effects of several different classes of medications on the fecal microbiome. Specifically, they found that NSAIDs reproducibly alter intestinal bacterial composition, depending on which NSAID was used. They describe an ambitious cross-sectional evaluation of 155 community dwellers of all ages from Southeastern Michigan who completed a questionnaire about their medication use in the 30 days prior to a fecal collection using a home stool specimen kit. Aliquots were extracted and analyzed by 16S rRNA pyrosequencing. The authors found enrichment of several different species depending upon the NSAID used, including *Acidaminococcaceae* and *Enterobacteriaceae* species in patients taking celecoxib.

Multiple factors influence the intestinal microbiome, including the subjects' age, gender, and diet, making cross-sectional evaluation of the impact of any single medication difficult. We believe that information about the effects of common medications on the gut microbiome are useful to better clarify the microbiome impact on human disease. Performing such studies longitudinally with both diet and environmental control can reduce the experimental variation.

We performed a longitudinal study of the effects of the celecoxib 200 mg twice daily in a homogeneous group of 10 obese post-menopausal women during analysis of the effects of this drug on adipose tissue inflammation. Recruited subjects were not permitted to consume dietary supplements during the study. Their diets were analyzed using three-day food diaries under the supervision of a research nutritionist and each subject's individual diet was maintained throughout the study period. While subjects were admitted to the metabolic unit of the Rockefeller University Hospital for a two-day run-in period, blood, urine, and stool specimens were obtained. These same samples were obtained again after 10 days receiving celecoxib. Eight subjects also produced a fecal specimen during a visit 7-14 days after leaving the

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