

Global Prebiotic Association Young Researcher Awards - Entry #347

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PhD

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Please indicate which category you're applying for:

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<https://microbiomejournal.biomedcentral.com/articles/10.1186/s40168-023-01724-6>

Please provide a summary of your research(limit 250 words)

The observation that the intestinal microbiota is central in the development of IBD suggests that dietary fiber, microbiota's primary source of nourishment, could play a pivotal role in these chronic diseases. Accordingly, in mice models, enriching diets with specific soluble fibers remodels microbiota composition and function in a way that impact colitis sensitivity. In humans, a recent study suggested that, in select IBD patients, the intestinal microbiota might influence the impacts of fiber exposure. Hence, we sought here to define the extent to which individual microbiotas varied in their responsiveness to purified soluble fiber supplementation. Moreover, we investigated the extent to which such variance might impact proneness to colitis. Using an innovative in vitro microbiota modelling system, we importantly observed a high level of inter-individual variation in microbiota responsiveness to inulin and psyllium: while microbiotas from select donors exhibited stark fiber-induced

modulation in their composition, pro-inflammatory potential, and metabolomic profile (thus termed fiber-sensitive), others were only minimally impacted (and termed fiber-resistant). Furthermore, germfree mice transplanted with fiber-sensitive microbiota identified above exhibited colitis highly modulated by soluble fiber consumption, while mice receiving fiber-resistant microbiotas displayed colitis severity irrespective of fiber exposure. Hence, we report here that the extent to which select soluble fibers alter proneness to colitis is highly influenced by an individual's microbiota signature. Further investigation of individual microbiota responsiveness toward specific dietary fiber consumption will pave the way to personalized fiber-based intervention, both in IBD patients and healthy individuals.

Please provide a summary of methods (limit 250 words)

To define individual's microbiota responsiveness, the MiniBloReactor Arrays (MBRAs) in vitro fermentation continuous model was used, allowing parallel anaerobic culture of 6 healthy human microbiotas. After 3-days stabilization, the MBRA microbiota were administered soluble fiber inulin or psyllium, or the insoluble fiber cellulose, as control (0.02% w/v) for 7 days, with each conditions being studied in triplicate. MBRA microbiota were analyzed for bacterial load (using qPCR with universal 16S primers), microbiota composition (through 16S rRNA gene sequencing with the Illumina technique), microbiota pro-inflammatory potential (using TLR4 and TLR5 reporter cells allowing quantification of bioactive levels of lipopolysaccharides (LPS) and flagellin, respectively). In order to identify sensitive and resistant microbiota toward fiber exposure, a Principal Coordinates Analysis (PCoA) of the Bray Curtis distance was then computed on these parameters, 48h upon fibers exposure.

To investigate the extent to which microbiota responsiveness toward a specific dietary fiber intervention could influence proneness to colitis, we colonized germ-free C57BL/6 mice with fecal transplants from one donor identified as fiber-sensitive and one identified as fiber-resistant. Following 1-week of microbiota stabilization, recipient mice were administered compositionally-defined diets containing either cellulose, inulin or psyllium. 19 days later, mice were subjected to a one-week course of DSS exposure, enabling investigation of both donor-dependent and fiber-dependent modulation of intestinal inflammation. Fecal samples were collected throughout the experiment and analyzed for microbiota composition and pro-inflammatory potential. Colitis severity was assessed by well-established macroscopical, histological and molecular markers.

Please provide a summary of your results (limit 250 words)

In depth microbiota phenotyping revealed stark differences between donors' microbiota in response to fiber exposure. Donors 2, 4, and 6 displayed changes in composition upon exposure to inulin or psyllium, relative to cellulose-treated MBRA microbiota. We next investigated the impact of inulin and psyllium supplementation on microbiota pro-inflammatory potential, quantifying bioactive levels of LPS and flagellin. We observed that the extent to which MBRA microbiota expression of LPS and flagellin is modulated by fiber exposure was highly individualized: microbiota from donors 2 and 4 harboured levels that were highly modulated by soluble fiber inulin and/or psyllium, while microbiota from donors 1 and 5 had stable and fiber-independent LPS and flagellin bioactive levels. Through computational approach, we identified fiber-resistant microbiota (donor 1, 5 and 6), which didn't exhibit any treatment-based modulation upon inulin or psyllium exposure. In stark contrast, microbiota from donor 2 and 3 were identified as fiber-sensitive, harbouring strong fiber-based clustering. In order to identify features in baseline microbiota that might predict fibers responsiveness, metagenomic analysis comparing the fiber-resistant and the fiber-sensitive donors revealed two important differences: the presence of *Faecalibacterium prausnitzii* only in fiber-resistant microbiotas; and an increased abundance of CAZymes in sensitive microbiotas. Finally, by using germfree mice with a humanized microbiota, we importantly revealed a fibre-induced modulation of colitis severity only in mice transplanted with fibre-sensitive microbiota, while mice transplanted with fibre-resistant micorbiota developed colitis irrespective of the fiber being consumed.

Please provide a statement about what, in your opinion, makes this paper outstanding and why it fits into the grant category you selected. (limit 250 words)

Our study importantly highlights that the impact of soluble fibers on intestinal health is highly context dependant. with a central role being played by the intestinal microbiota. Indeed, while epidemiological studies suggest th the consumption of fiber-rich diets correlates with a reduced incidence of IBD (Kuang, R. & Binion, D. G. (202. numerous clinical studies suggest that once the disease is established, some IBD patients experience intolerance to fermentable fiber-rich foods with diseases flare (Valcheva R. et al. (2022); Armstrong, H. K. et al. (2023)). Here, we revealed that the extent to which soluble fiber promotes or demotes intestinal health is fully dependant on an individual's pre-existing intestinal microbiota. Hence, these results importantly pave the way for the development of personalized fiber- and microbiota-based intervention, both in IBD patients and in healthy individuals. Moreover, our findings were key to initiate an important new collaborative line between the laboratory of Dr. Benoit Chassaing (INSERM, Paris, France) and Dr. Heather Armstrong (University of Manitoba, Canada) in order to further investigate the role played by individual's gut microbiota in promoting or demoting intestinal inflammation through fiber sensitivity in IBD patients. Of note, the importance of our study was highlighted by Dr. Andreu Prados nd Dr. Natasha Haskey in a commentary in the "Nutritional therapy for IBD" magazine online, where they highlighted our important findings that one fiber does not fit all (<https://www.nutritionaltherapyforibd.org/news/individual-gut-microbiome-influences-the-impact-of-inulin-and-psyllium-on-colitis>).

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