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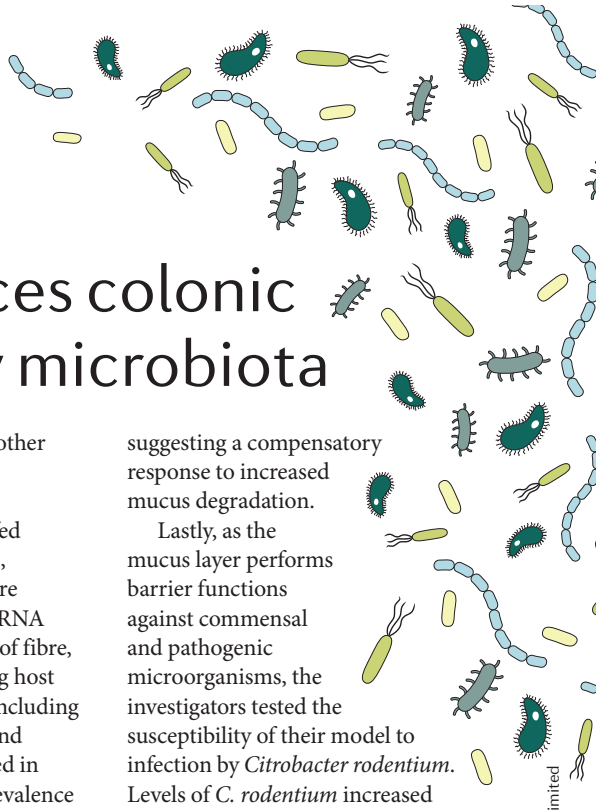

GUT MICROBIOTA

Low dietary fibre induces colonic mucus layer erosion by microbiota

Diets low in fibre markedly alter gut microbiota composition in mice and can increase susceptibility to infection via erosion of the intestinal mucus layer, according to new research.

Dietary fibre is important as a nutritional substrate for gut microbiota. Whereas the human genome encodes only a small number of polysaccharide-digesting enzymes, the gut microbiome encodes thousands of such proteins, catalysing the depolymerization and fermentation of diverse dietary polysaccharides. The effect of low-fibre diets — common in developed countries — on gut microbiota and subsequent host health was unknown, leading Eric Martens and colleagues to test the hypothesis that fibre-deprived microbiota would instead metabolize the protective colonic mucus layer.

First, the authors developed a simplified model of the human gut microbiota in gnotobiotic mice. "By working with germ-free mice, in which we can implant a simpler but still representative community (here 14 species), we were able to reduce the system to a manageable level of complexity," explains Martens. "All 14 bacterial species were fully sequenced and some have been deeply studied, making it much easier to connect responses by particular gut bacteria to dietary and other nutrient cues."

Mice colonized with the synthetic microbiota were fed fibre-rich or fibre-free diets, and daily faecal samples were analysed by 16S ribosomal RNA sequencing. In the absence of fibre, species capable of degrading host mucosal polysaccharides (including *Akkermansia muciniphila* and *Bacteroides caccae*) increased in abundance, whereas the prevalence of species specialized in degrading fibre (notably *Eubacterium rectale* and *Bacteroides ovatus*) decreased. RNA sequencing of caecal samples revealed that bacterial transcripts encoding enzymes for the metabolism of dietary fibre were less abundant in mice on fibre-free diets; by contrast, levels of transcripts encoding enzymes catalysing the metabolism of host polysaccharides, such as mucosal *O*-glycans, were increased in these animals.

Next, the researchers assessed whether colonic mucus layer thickness was altered by these diets. Mice fed a fibre-rich diet had the thickest mucus layer, fivefold thicker than the fibre-free diet group. Caecal tissue transcripts revealed a small increase in expression of *Muc2* (the major colonic mucin gene) in mice fed a fibre-free diet compared with those fed a fibre-rich diet, suggesting a compensatory response to increased mucus degradation.

Lastly, as the mucus layer performs barrier functions against commensal and pathogenic microorganisms, the investigators tested the susceptibility of their model to infection by *Citrobacter rodentium*. Levels of *C. rodentium* increased tenfold and colonized the colonic epithelium in greater density in mice fed a fibre-free diet, leading to markedly increased morbidity in this group — at day 10 after infection, 60% of the fibre-free group were euthanized due to excessive weight loss, compared with none of the fibre-rich group.

Martens now plans to address whether these changes are applicable to other diseases. "We hypothesize that dietary fibre deprivation results in mucus layer erosion in hosts that have defects making them more susceptible to IBD and colorectal cancer, which are more chronic, long-term disease progressions," he comments.

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