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IBD

Parasites promote protective microbiota

The high incidence of IBD in the developed world might be explained by the hygiene hypothesis, which suggests that reduced environmental exposure to microbes and parasites has made some people susceptible to autoimmune diseases. Now, new research on the effects of helminth infection in a model of IBD supports this hypothesis, showing that these parasites can promote colonization of protective bacterial taxa that replace pro-inflammatory species.

The authors of the latest study previously found that in mice lacking *Nod2*, a Crohn's disease susceptibility gene, intestinal inflammation was dependent on a particular microbe — *Bacteroides vulgatus*. "Helminth infections and the incidence of Crohn's disease have a striking inverse relationship," explains author Ken Cadwell. "We wondered if our *Nod2* mutant mouse model might be a great system to examine this [correlation] because the main defect seemed to be goblet cell mucus production, and the immune response to parasite infections leads to production of mucus by goblet cells."

First, using histopathological analyses, the infection of *Nod2*-knockout mice using two species of helminths was shown to ameliorate intestinal defects, mediated by an immune response to the helminths that increased mucus production. By analysing bacteria from stool samples, helminth infection was shown to expand intestinal colonization by strains of Clostridiales that directly suppressed inflammation-causing *B. vulgatus* and other Bacteroidales.

As mucin, a component of mucus, promoted *in vitro* growth of Clostridiales, these results indicate that the intestinal response to helminth infection might favour Clostridiales expansion, which then inhibit colonization by inflammatory bacteria. Furthermore, the researchers characterized the gut microbiota of helminth-infected indigenous people in Malaysia, showing that the taxa associated with helminth-infected humans were similar to the protective microbiota in the *Nod2* mutant mice.

Laura Marshall/NPG

This work links the protective effects of helminths to immune-mediated restructuring of the gut microbiota. Helminth-based therapy has been considered for IBD, but the latest findings suggest that it might only be effective in individuals with certain genetic variants or gut microbiota.

"Our findings raise the possibility that we can target the immune response or go directly to the microbiota as a way to avoid using live helminths for therapy," reports Cadwell. Regarding future work, he adds, "we are very interested in understanding the mechanism by which Clostridiales is protective, and whether there are specific Clostridiales strains associated with helminth infections that are more anti-inflammatory than others."

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ORIGINAL ARTICLE Ramanan, D. *et al.* Helminth infection promotes colonization resistance via type 2 immunity. *Science* http://dx.doi.org/10.1126/science.aaf3229 (2016)