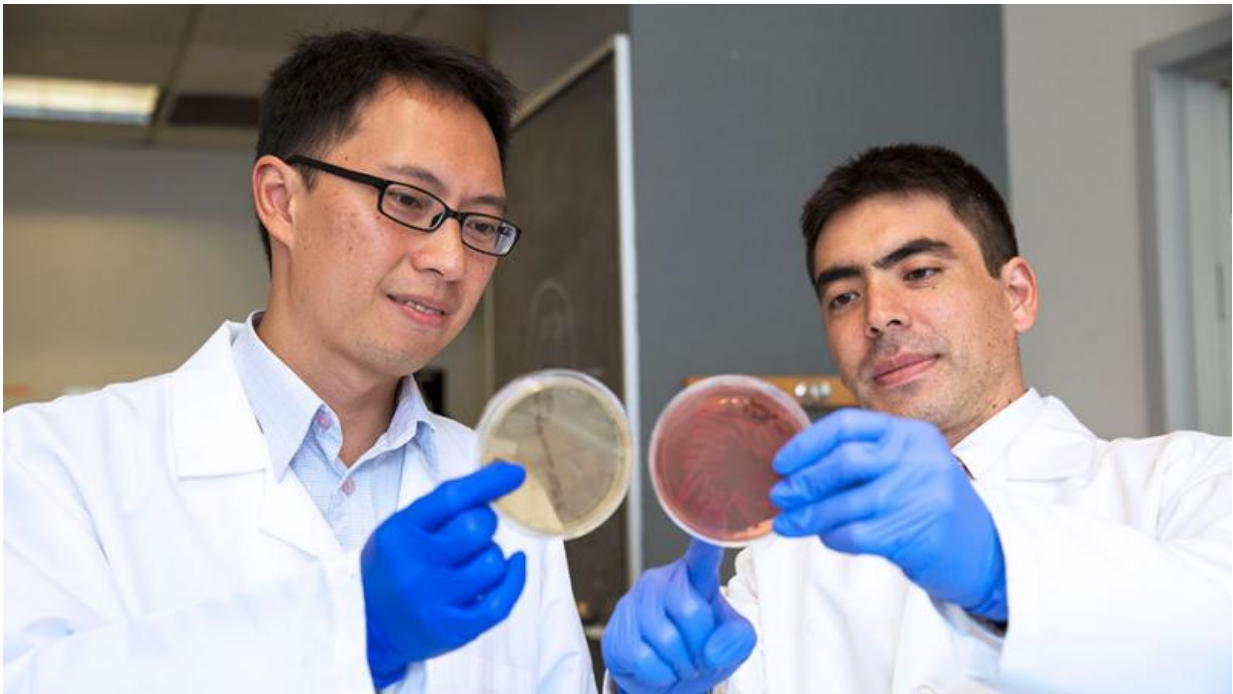


Parasitic infection enables helpful bacteria to displace harmful ones in mice and humans

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P'ng Loke, PhD, and Ken Cadwell, PhD, examine bacterial plates in the Cadwell lab at NYU Langone's Skirball Institute of Biomolecular Medicine

Infection with worms may counter inflammatory bowel diseases (IBD) by triggering immune responses that change the mix of bacteria, or microbiome, in the gut. This is according to a study led by researchers from NYU Langone Medical Center and published online April 14 in the journal *Science*.

The study results support the hygiene hypothesis, which in the case of IBD, argues that the absence of exposure to worms in too-clean modern living spaces has left some with oversensitive, gut-based [immune](#) systems vulnerable to inflammatory diseases. Gut worms have helped to train and balance immune systems throughout human evolution but are now missing in developed nations, which are known to have the highest rates of Crohn's disease and ulcerative colitis.

In the newly published study, the researchers found that mice infected with intestinal worms experienced as much as a thousand-fold decrease in *Bacteroides*—a group of bacterial species linked by past studies to higher risk for IBD. At the same time, the number of *Clostridia*, a bacterial species known to counter inflammation, increased tenfold. The investigators argue that the immune response to the worms triggers the growth in *Clostridia*, which then either outcompete *Bacteroides* for nutrients or release toxins that can harm them.

"Our findings are among the first to link parasites and bacteria to the origin of IBD, supporting the hygiene hypothesis," says study co-senior investigator and parasitologist P'ng Loke, Ph.D. Loke, an associate professor at NYU Langone, says this model may also be applicable to other autoimmune diseases, including multiple sclerosis, rheumatoid arthritis, and type 1 diabetes, in which processes meant to attack foreign invaders instead become oversensitive and react to the body's own cells.

Also among the study's key findings was that people in rural parts of Malaysia, a region known to have low rates of IBD but a high incidence of worm infections, had significantly more *Clostridia* and fewer *Bacteriodes* in their microbiomes than people comprising a nearby urban population. In addition, the researchers found that people who were treated and dewormed had less *Clostridia* and more *Bacteriodes*.

"Our study could change how scientists and physicians think about

treating IBD," says study co-senior investigator and microbiologist Ken Cadwell, PhD, an assistant professor at NYU Langone's Skirball Institute of Biomolecular Medicine. "Patient testimonials and anecdotes lead many to think that worms directly cure IBD, while in reality, they act on the [gut bacteria](#) thought to cause the disease."

Loke also led a study, published in the journal *PLOS Pathogens* in 2012, which found that giving worm eggs to monkeys protected them from the simian version of IBD. Worm eggs may be able to trick the immune system into thinking it has a worm infection, and to trigger a specific kind of worm-related response that counters gut inflammation.

Along the same lines, future treatments might include giving patients some form of the immune chemicals produced by immune cells in the presence of worm infection, like interleukin 13, Cadwell says. Such treatments may be acceptable to patients as long as they know they cannot possibly get worms in the process.

As part of the new study, the NYU Langone team fed between 10 and 15 parasitic whipworm eggs to mice lacking a gene called NOD2, which is tied to several immune disorders, including IBD. After the [worms](#) matured, the investigators measured the amount of Bacteroides and Clostridia in the mice's intestines and stool and noted the presence or absence of IBD. They found that many of the symptoms of IBD, such as intestinal bleeding and ulceration, went away along with almost all Bacteroides, while the Clostridia levels increased.

For another part of the study, the researchers compared the bacteria found in 75 members of the Orang Asli indigenous people in rural Malaysia to those of 20 people living in urban Kuala Lumpur. Researchers found that rural people had much fewer Bacteroides than city dwellers.

Cadwell says he and Loke plan to investigate how *Clostridia* outcompete *Bacteroides*, and search for harmless *Clostridia* species that can still induce this effect. In addition, they intend to explore the way worm infections alter gut bacteria as the foundation of treatments for several inflammatory diseases.

More information: D. Ramanan et al. Helminth infection promotes colonization resistance via type 2 immunity, *Science* (2016). [DOI: 10.1126/science.aaf3229](https://doi.org/10.1126/science.aaf3229)

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