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INFECTION

Microbiota reconstitution for resistance to *Clostridium difficile* infection—fight fire with fire?

Targeted and precise reconstitution of the gut microbiota, down to a single bacterial species, confers resistance to *Clostridium difficile* infection, according to a new study published in *Nature*. The research identifies another *Clostridium* spp. in particular as a promising probiotic that could be used in the treatment and prevention of *C. difficile* infection.

> “...*C. scindens* ... markedly increased resistance to *C. difficile* after antibiotic exposure...”

“*C. difficile* infection has become a major problem in hospitalized patients and generally occurs in patients following antibiotic treatment,” explains author Eric Pamer. “Studies have demonstrated that loss of microbiota diversity and potentially the loss of specific bacterial species renders patients susceptible to *C. difficile* infection,” he adds. As such, the new study’s main aim was to identify those bacterial species in the normal, healthy gut microbiota that could help combat this pathogen.

First, the researchers found that different antibiotics had differing effects on the gut microbiota and susceptibility to *C. difficile* infection in mice. For instance, clindamycin resulted in long-lasting susceptibility to infection; by contrast, ampicillin induced transient susceptibility. The different antibiotic regimens did not alter bacterial diversity substantially, but did cause distinct changes to the composition of the gut microbiota in these mice.

Using a combination of mouse studies, examination of human samples and mathematical modelling, the investigators identified specific bacterial taxa (common to both mice and humans) that correlated with resistance to *C. difficile* infection. In particular, *C. scindens* was pinpointed as a key microbe associated with this resistance. Experiments in mice showed that, compared with controls, administration of *C. scindens* alone or in a consortium of other resistance-associated bacteria markedly increased resistance to *C. difficile* after antibiotic exposure in a manner that was dependent on secondary bile acid metabolism. Notably, *C. scindens* expresses enzymes crucial for secondary bile acid synthesis that are not common among other intestinal bacteria.

This new study reveals approaches in the rational design of targeted antimicrobial therapies. “Future studies will use this computational and experimental platform to identify the optimal combination of bacterial species for resistance to *C. difficile* infection and to determine the best approach for administration,” says Pamer.

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