Gut microbiomes may hold clues to IBD treatment's likelihood of success

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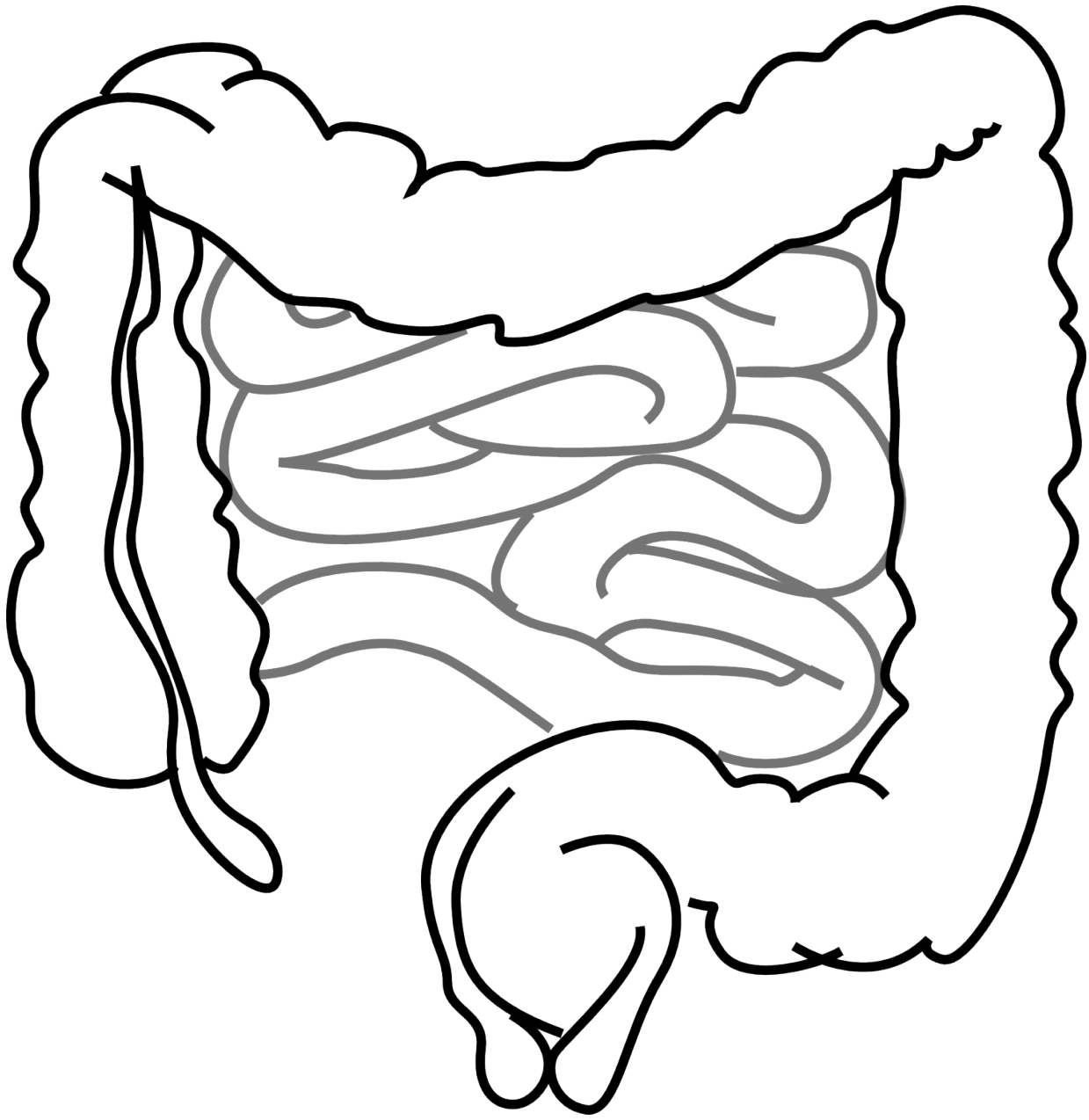

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The constitution of an IBD patient's microbiome may help predict whether treatment with a therapeutic antibody will prove fruitful, according to an early-stage study.

Treatment for inflammatory bowel diseases (IBD), like ulcerative colitis (UC) and Crohn's disease (CD), is currently a process of trial and error. Try one treatment, look for a response. If the patient does not improve, try the next treatment. And then the next. While researchers have tried to develop predictive tools that use patients' clinical features or genetics to help physicians home in on the most beneficial therapy more quickly, none have yet proven robust or accurate enough for widespread use.

In a study reported today in *Cell Host and Microbe*, Ashwin Ananthakrishnan (a gastroenterologist at Massachusetts General Hospital), Chengwei Luo, Ramnik Xavier, and colleagues set out to explore whether patients' microbiomes might hold markers that could provide the predictive power they have sought.

The team studied the gut microbiome profiles of 85 IBD patients receiving vedolizumab (an antibody that dampens inflammation in the gut), measuring the species composition and microbial activities in samples collected before and at multiple timepoints after starting treatment. They then compared those profiles with patients' responses.

Some surprising patterns arose from the data. Those patients whose IBD symptoms resolved after 14 weeks on the treatment were more likely to carry specific kinds of bacteria in their gut at the start of therapy. In particular, CD patients who responded to treatment carried higher levels

of Roseburia inulinivorans and Burkholderiales species—and had more diverse bacterial communities overall—in their guts before treatment than patients who did not respond.

More interesting, however, was that what the microbes were doing was a stronger predictor of treatment success than just the microbes' identity. The team identified 13 metabolic pathways that were more active in the gut bacteria of CD patients who went into remission, including pathways that produce molecules thought to reduce inflammation.

To assess the profiles' predictive value, the team fed their data into a neural network-based machine learning tool called vedoNET and compared its results with the patients' experiences. The tool produced its most accurate predictions when using patients' clinical information, species level, and pathway data.

While the team notes that the study needs to be repeated with larger groups of patients and in the context of other treatments, their findings suggest that as clinical sequencing becomes more ubiquitous, it should be feasible to screen IBD patients' gut flora and use those data to guide treatment decisions.

More information: Ashwin N. Ananthakrishnan et al. Gut Microbiome Function Predicts Response to Anti-integrin Biologic Therapy in Inflammatory Bowel Diseases, *Cell Host & Microbe* (2017). DOI: 10.1016/j.chom.2017.04.010

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