'Genetic scalpel' can manipulate the microbiome, study shows

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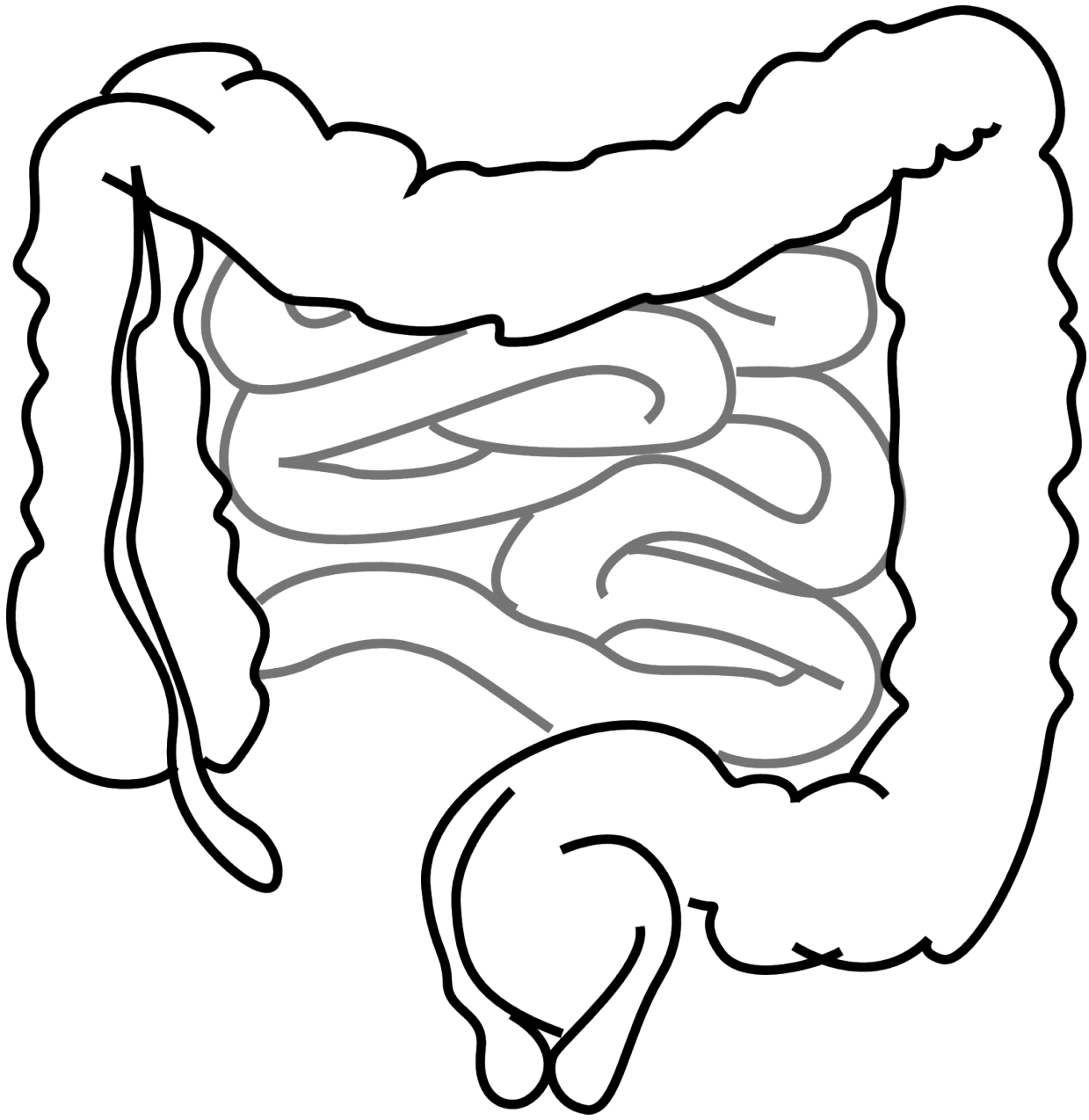

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The gut microbiome is crucial to health, encompassing bacterial communities that possess a hundred times more genes than the human genome. Its complexity has hampered investigation of possible roles of the microbiome in a host of maladies, including infectious and autoimmune diseases, obesity, and even behavioral disorders.

Yale University researchers have developed new methods for regulating gene activity in a widespread group of microbiome bacteria in the gut of living mice—a crucial step in understanding microbiome's impact on health and disease, they report in the April 20 issue of the journal *Cell*.

"We and others have been frustrated with the clumsy tools available for studying the microbiome—it felt like trying to perform surgery with boxing gloves," said Andrew Goodman, associate professor of microbial pathogenesis at the Microbial Sciences Institute at West Campus and senior author of the paper. "We hope these new methods replace the boxing gloves with a scalpel."

First author Bentley Lim, along with Michael Zimmermann and Natasha Barry in the Goodman lab, engineered a "dimmer switch" for controlling gene expression in Bacteroides, the most common family of bacteria found in the human gut. This switch can turn gene expression up, down, or off in response to an artificial chemical not found in mice or their diets. By simply adding or withdrawing this chemical from the mouse's drinking water, the researchers were able to precisely track in real time the effects of altering gene activity in the microbiome inside the gut of living mice.

The team used these tools to understand how pathogens dine off sugars that microbiome bacteria strip from the gut wall in their search for food. By controlling the timing and extent of this activity, the researchers were able to measure how long these leftovers remain available for pathogens. The findings help explain how antibiotics counterintuitively increase the levels of these delicacies for pathogens and may one day help create more effective infectious disease therapies, the authors say.

"We can now study bacterial communities in various states and pinpoint specific genes and pathways involved in a variety of functions," Lim said. "If we are to find ways to intervene in these processes, we must first understand them at this level."

Provided by Yale University