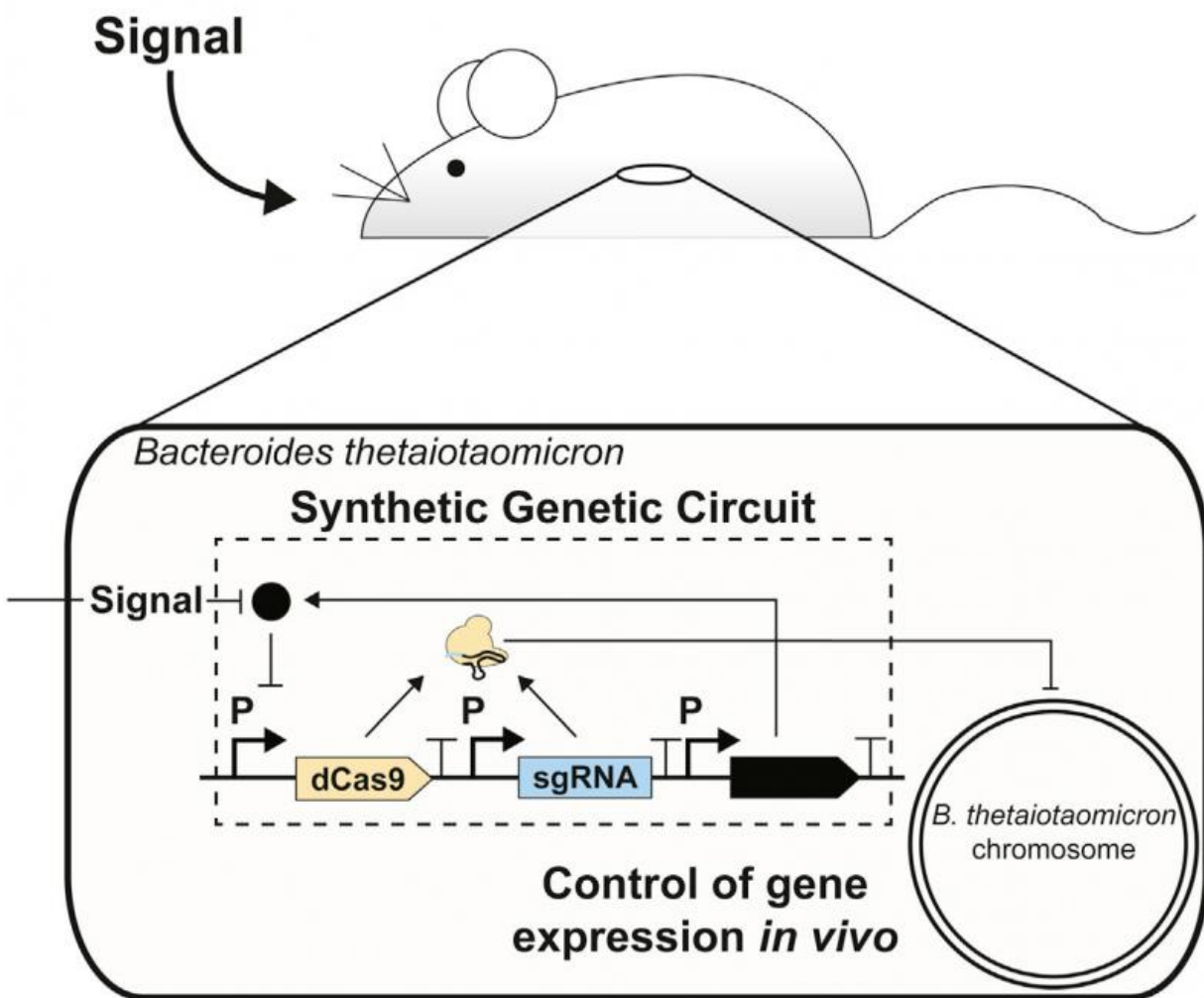


Scientists hack one of the most common bacteria in human intestines

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The development of genetic parts to precisely program the human commensal gut bacterium *Bacteroides thetaiotaomicron* lays the foundation for microbiome engineering. Credit: Mimee and Tucker et al./*Cell Systems* 2015

One of the most common bacteria in the human gut, *Bacteroides thetaiotaomicron*, can now be engineered with new functions and re-introduced into the intestinal tract of a mouse. The work, appearing July 9 in the new journal *Cell Systems*, is a starting point for designing microbes that could eventually deliver drugs or detect long-term changes in the intestines that lead to inflammatory bowel disease or other illnesses.

The idea to bioengineer bacteria for therapeutic purposes isn't new, but not all bacteria are suited for the same tasks. Last year, Harvard scientists created *E. coli* that could be consumed by a mouse to sense conditions in the gut. However, one challenge with *E. coli* is that it is not present in the gut at high levels.

The MIT group, led by synthetic biologists Timothy K. Lu and Christopher Voigt, saw that *Bacteroides* had the potential to express genes on demand. Not to mention, as a [commensal bacteria](#), it has stable, long-term interactions with human cells and other microbes in the intestines. This means a designer bacteria and its offspring would be able to stick around for a while.

"We took a lot of the tools that people are already using in other organisms, (e.g., promoters, ribosome-binding sequences, memory switches, CRISPR interference) and demonstrated that you could port all of these over into *Bacteroides* and get them working," says Lu, study senior author and a biological and electrical engineer at MIT. "We then showed that genetic devices could be implemented in the bacteria and be shown to function in the context of the mouse gut microbiome."

"The culmination of the work is not only do you have an engineered bacterium that's colonized the mouse gut, but you can turn on which

genes in the bacterium are active based on what you feed the mouse," adds Voigt, an MIT biological engineer and study senior author. "That's really something new. It allows you to control what the bacterium is doing at the site of where it's operating."

A few challenges still need to be addressed before moving on to human studies. For instance, colonizing the mouse gut with *Bacteroides* involved giving the animals antibiotics first. Second, the researchers will need to prove that the bacteria can be engineered with more complex behaviors, such as being able to respond to many sensory inputs. The eventual goal would be able to engineer microbes that can alter gene expression based on signals within the intestines. For now, the researchers plan to add their toolbox to Addgene, a nonprofit repository for genetic materials so others can build upon on this work.

"The field has gotten to a point where you can identify an organism of interest and go through a series of steps to really understand how to program that organism," Voigt says. "For us, when we first started thinking about these ideas, even a model organism like *E. coli* just wasn't at a level where we could realize our dreams—that's changed so much in the last decade."

"The big picture is that the bacteria that live in us or on us impact human health in very significant ways and the existing techniques we have to modulate the microbiome—taking antibiotics or changing our diet—are relatively limited," Lu says. "We're hoping that with these tools to precisely engineer the intimate interface between [bacteria](#) and humans we're going to be able to tackle some major health-related problems."

More information: Cell Systems, Mimee and Tucker et al.: "Programming a Human Commensal Bacterium, *Bacteroides thetaiotaomicron*, to Sense and Respond to Stimuli in the Murine Gut Microbiota" [dx.doi.org/10.1016/j.cels.2015.06.001](https://doi.org/10.1016/j.cels.2015.06.001)

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