## Proof in the poop: Genetically modified bacteria may be used to treat digestive ailments

Ever get the urge to be like a unicorn and poop rainbows? It may sound crazy, but someday, soon, patients suspected of having potentially devastating gastrointestinal conditions, such as Crohn disease or ulcerative colitis may able to do just that.

Using special genes conferring luminescence by manufacturing proteins that light up with fluorescent colors, the diagnosis could be made a lot easier. The system can be arranged so that the genes are turned on by markers such as inflammation.

## Turning on a genetic switch

Genetic engineering has progressed to the point that pretty much any gene can be inserted into the genome of a given organism. Additionally, the genes can be engineered to turn on, turn off, or modify production of the gene products based on environmental factors, such as temperature or pH, or the presence of particular chemical agents.

For years, researchers have been using modified bacterial strains such as *Listeria* and *E. coli* to carry medications for conditions, obesity in particular. Even more ambitiously, a team at the Massachusetts Institute of Technology (MIT) has been working with *Bacteroides thetaiotaomicron* a common gut bacterial strain. Unlike Listeria and E. coli, *B. thetaiotaomicron* is cleared very slowly from the body, so potentially it can be utilized to deliver gene products that will be produced in the gut over longer periods compared with gene products produced by the other bacterial strains.

Currently the <u>research</u> focusses on mice models of human gastrointestinal disease, but enormous clinical potential may lie around the corner. By using *B. thetaiotaomicron* to carry genes coding for proteins that light up in various colors, the team is pioneering a potential game changing method for quick diagnosis that potentially could be applied to any condition manifesting with changes within the human gut.

"You can turn on genes in the bacterium based on what you feed the mouse," explained Christopher Voigt, the MIT biologist who is one of two senior authors on a new <u>study</u> describing the technique.in the prestigious journal Cell Systems.

To insert additional segments, and pretty much edit the transferred genes in as much detail as needed, Voigt and his colleagues have been taking full advantage of CRISPR interference technology, known commonly as DNA scissors.

The other senior author, Timothy Lu, added more about the potential of the MIT research direction. "You could engineer a *Bacteroides* to live in the gut and detect when inflammation is just starting, and then flipa switch to turn your poop a certain color, so that you can seek treatment right away," Lu explained. "Or, scientists could insert DNA segments into Bacteroides that create therapeutic molecules like aspirin, Lu said.

## Inflammatory gut diseases

Being able to color code poop based on the presence, and even degree, of inflammation has major implications when it comes to inflammatory bowel disease (IBD). The most well-known IBD conditions are Crohn disease and ulcerative colitis, and together IBD conditions affect roughly 1.6 million Americans. Each year, some 70,000 new cases are diagnosed in the US, and the gold standard for diagnosis is colonoscopy.

Because it is rather invasive and uncomfortable, people tend to avoid colonoscopy, and while it is recommended for early detection of cancer for those in their 50s and beyond, younger people do not need to have it unless they're at particular risk for gastrointestinal malignancy, or if they need it for a workup on other conditions, such as IBD. While any patient would still needed colonoscopy for a definitive diagnosis of IBD, a fluorescent poop test for inflammation would be an easy way of identifying people who are likely to have IBD, while elimination others who might have less serious conditions not requiring colonoscopy.

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