MedicalXpress

On a quest to improve treatments for inflammatory bowel disease

September 5 2017

Scientist Shomyseh Sanjabi, PhD, joined the Gladstone Institutes seven years ago, and she brought with her a special type of mice that develop inflammatory bowel disease (IBD). Coincidentally, microbiome expert Katherine Pollard, PhD, was looking for a model to study the disease. Particularly because she is an IBD patient herself.

That's how an unlikely collaboration started between an immunology researcher, Sanjabi, and a biostatistician, Pollard. They set out to uncover the role played by bacteria in the gut in IBD.

Your gut contains trillions of bacteria and tiny microbes—collectively called the microbiome—that mainly help with digestion and other bodily functions. But these bacteria have also been linked to IBD. Studies have shown that the microbiome is very different in sick and healthy individuals.

However, scientists don't know if bacteria are responsible for causing IBD, or if IBD causes bacteria in the gut to change. Equipped with Sanjabi's mouse model, she and Pollard realized they now had the tools to answer this "chicken or the egg" question.

Ulcerative colitis and Crohn's disease are the two most common forms of IBD, which is an increasingly prevalent disease in which the immune system attacks tissues in the intestine. Symptoms vary between Improvpatients and can include severe diarrhea, abdominal pain, fatigue, and unintended weight loss.

Pollard has been living with IBD for the past decade.

"Like most patients, I didn't know I had a chronic disease for many years," says Pollard, director of the Convergence Zone at Gladstone. "At first, many people think they may be lactose intolerant or have an allergy to gluten. Then, when the symptoms are serious, they realize they have IBD."

The exact cause of IBD remains unknown. Because is hard to predict who will develop the disease, human studies typically occur after patients are quite sick. At that point, it is hard to determine if gut bacteria triggered IBD.

"These studies are valuable, but they don't reveal much about what causes the disease or how it evolves," explains Gladstone Assistant Investigator Sanjabi. "The mouse model gave us an opportunity to overcome the challenges of a human study and finally conduct a longitudinal study on IBD. We gathered data from birth to adulthood, so we could see the onset and progression of the disease."

The scientists got to work. They monitored the mice's immune system and collected fecal bacteria on a weekly basis. The study's first authors, Thomas Sharpton and Svetlana Lyalina, then analyzed the full DNA sequence of these bacteria.

"We detected changes in the genes of the gut bacteria before any symptom of IBD appeared," says Sanjabi, who is also an assistant professor at the University of California, San Francisco (UCSF). "Most of the changes in bacteria happened at the same time as the immune system started showing signs of an autoimmune disease. This model can help us identify exactly when the disease starts."

The scientists' findings, published today in the open-access journal

mSystems, associate the progression of IBD with parallel changes in what gut bacteria are doing over time. They found that these changes in the microbiome may represent an early indicator of the disease.

Current therapies for IBD are like Band-Aids. They treat the symptoms, but not the root of the problem. If the researchers can pinpoint early signs of IBD and predict who might get sick, they could help develop diagnostic tools and find treatments to address the cause of disease.

"IBD drugs also increase risk for serious infections," says Pollard, also a UCSF professor. "Whenever I travel or visit a hospital, I need to stop my treatment, because it weakens my immune system. We need to discover what contributes to the development and severity of the disease to ensure accurate and effective health care."

Now, Sanjabi and Pollard know more than when they started. But they also have more questions than when they began.

They suspect that IBD is caused by the dynamic interaction between an abnormal immune response and opportunistic bacteria. Their next step will be to test whether they can trigger IBD by manipulating specific gut bacteria.

"This project was so personal because of Katie's own struggles with IBD," says Sanjabi. "She, and so many other patients, deserve better options. My hope is to, one day, develop targeted antibiotic treatments that could get rid of specific bacteria in the gut causing the disease."

Pollard's hope is the same.

"I'm encouraged by our promising results," says Pollard. "We could potentially analyze the microbiome of patient stool to classify and even predict disease. That would be an enormous step in the right direction."

More information: Development of Inflammatory Bowel Disease Is Linked to a Longitudinal Restructuring of the Gut Metagenome in Mice, DOI: 10.1128/mSystems.00036-17 , msystems.asm.org/content/2/5/e00036-17

Provided by Gladstone Institutes