ADVERTISEMENT FEATURE

A sharper diagnosis for ulcerative colitis

Researchers have zeroed in on the cause of ulcerative colitis. Their findings could lead to MORE ACCURATE DIAGNOSTIC TOOLS.

A simple blood test could be an alternative to colonoscopies for the diagnosis of ulcerative colitis.

Andrew Brookes/Image Source/Getty

Masahiro Shiokawa (left) and Takeshi Kuwada (right) in a laboratory at Kyoto University.

The MBL manufacturing facility in Ina-shi, Nagano, Japan.

Ulcerative colitis is a type of chronic inflammatory bowel disease that causes painful ulcers and irritation in the large intestine. In North America alone, it is estimated to affect more than 750,000 people.

While the condition is relatively common, researchers have struggled to pin down a specific cause. Diagnosis is sometimes difficult, with clinicians relying on invasive colonoscopies or endoscopies that are costly and time-consuming. Distinguishing between ulcerative colitis and other types of inflammatory bowel disease, such as Crohn's disease and Behçet's disease, is also a challenge as, superficially, they have similar features.

Although researchers have long suspected that an overactive immune system is the main cause of ulcerative colitis, revealing the specific autoantibodies – components of the immune system that mistakenly attack the body – and the proteins they target has remained a challenge.

"If we had a biomarker, we would be able to diagnose ulcerative colitis with more confidence," says Masahiro Shiokawa, a gastroenterologist at the Kyoto University Graduate School of Medicine.

In 2021, Shiokawa and his colleague, Takeshi Kuwada, also at Kyoto University, made a leap forward. They discovered that patients with ulcerative colitis carry autoantibodies that target integrin alpha-v/beta-6, a protein that connects epithelial cells in the intestine to other types of tissue.

As these autoantibodies are most often seen in patients with ulcerative colitis, rather than other bowel diseases, they have the potential to be used as reliable markers for diagnosis and could help clinicians track disease severity, says Shiokawa.

In partnership with Medical & Biological Laboratories (MBL), the researchers are using their findings to develop a fast, cost-effective, and accurate diagnostic test kit for ulcerative colitis. The discovery could also one day lead to the development of more targeted treatments for the condition, which currently has no cure.

TRACKING DOWN KILLER ANTIBODIES

Shiokawa and Kuwada's revelations on the key players behind ulcerative colitis came off the back of their previous investigations into the immune drivers of another disease: autoimmune pancreatitis.

In 2018, the team discovered that patients with autoimmune pancreatitis had autoantibodies that targeted fragments of laminin 511, a protein interacting with integrins to help cells stick together. These autoantibodies were not present in healthy controls.

As autoimmune pancreatitis is sometimes associated with ulcerative colitis, the researchers wondered whether similar autoimmune features underpin the two conditions.

"We knew that it was important to focus on the integrin family of proteins," says Shiokawa. "Our hypothesis was that the autoantigen of autoimmune pancreatitis is related to the autoantigen of ulcerative colitis."

To find out if this was the case, the researchers and their team took blood samples from 112 patients with ulcerative colitis and 155 patients with other intestinal diseases. The team screened the blood samples for 23 integrin proteins, which help connect cells to surrounding tissue.

They found that 92% of the patients with ulcerative colitis carried autoantibodies that home in on the integrin alpha-v/beta-6 autoantigen. By contrast, only roughly 5% of the control patients had these autoantibodies, suggesting that they are distinct markers of ulcerative colitis. The level of autoantibodies present in the patients' blood was also linked to the severity of the disease, hinting they could be used to monitor the condition's progression.

When the researchers analysed the ulcerative colitis patients' sera, they discovered that the autoantibodies prevented the integrin alpha-v/beta-6 protein from binding with fibronectin, another type of protein that is involved in cell adhesion and tissue repair. This disruption may cause the cells that line the large intestine to peel off and form ulcers, a key feature of the disease.

TEAMING UP FOR BETTER DIAGNOSTICS

In addition to pinpointing a possible cause of ulcerative colitis, Shiokawa and Kuwada knew they had hit upon a biomarker that could be used to diagnose the disease with greater accuracy and precision.

Their discovery prompted the researchers to partner with MBL to develop a diagnostic test kit that can detect the presence of integrin alpha-v/beta-6 autoantibodies with a simple blood test that costs a fraction of conventional diagnostic procedures.

"Colonoscopies take at least one day to complete and can cost up to $200. But if the new testing kit is available, it will take roughly only 15 minutes to draw a blood sample and provide an appropriate result at a reasonable cost," says Shiokawa.

Unlike colonoscopies, the blood test doesn't require patients to fast or take laxatives in the days before the procedure. It also doesn't carry some of the risks that come with these invasive procedures, such as tearing the large intestine, or abdominal pain.

In January 2022, the researchers are planning to conduct a nationwide study on the kit in hospitals across Japan to test out its potential as a diagnostic tool that can be used in the clinic.

"We hope that it will be used in hospitals and clinical practice in Japan within the next two years," says Shiokawa. "The next step would be to take the kit to hospitals worldwide."

The team have also started developing a drug that wipes out the cells that produce anti-integrin alpha-v/beta-6 antibodies. They hope that the drug will be a step towards finding a cure for the disease.

"The only current treatments for ulcerative colitis are immunosuppressant drugs," says Shiokawa. "This autoantibody destroys epithelial cells, so we want to develop a drug that targets it." ■

MBL MEDICAL & BIOLOGICAL LABORATORIES CO., LTD.
A JSR Life Sciences Company

Advertiser retains sole responsibility for content