Precursor to ulcerative colitis in healthy individuals years before onset of disease

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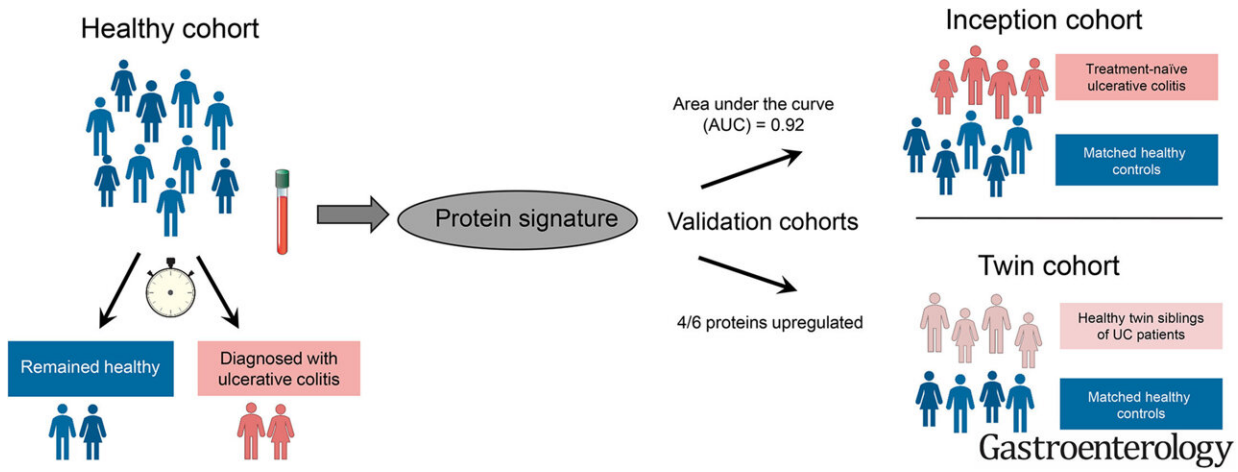

Graphical abstract. Credit: DOI: 10.1053/j.gastro.2021.07.026

After the first symptoms, the diagnosis of the bowel disease ulcerative colitis may take a few months. As shown in a study at Örebro University, there is, however, a precursor to the disease already several years before its onset.

"This is the first time that research has been able to identify, in detail, the type of inflammation that exists in healthy individuals who later in life develop ulcerative colitis," says Daniel Bergemalm, physician and researcher on gastrointestinal diseases.

Ulcerative colitis is an inflammatory bowel disease (IBD), with symptoms normally setting in between late adolescence and the age of 30. What causes it is not yet known, but there is lots to suggest that the disease is a result of an interplay between genetic and environmental factors and that gut flora definitely plays a part.

"One problem for research is that once the disease has flared up, the immune system is under such stress that any factors that do have an impact, risk drowning in the noise of the severe inflammation," says Daniel Bergemalm, specialist and lead author of the study published in the scientific journal *Gastroenterology*.

Instead of looking for clues in the hyperactive immune system of those affected by the disease, in this study, researchers chose to go back in time to find out what happens before the onset of the symptoms of ulcerative colitis.

This opportunity is offered via the "Northern Sweden Health and Disease Study", where blood samples from a large group of individuals have been collected on a regular basis since the 1980s.

"The blood samples provided us with a unique opportunity to do a first major study of the causes of ulcerative colitis. We could access blood samples from individuals who were healthy at the time of sampling, but who developed the disease later in life," says Daniel Bergemalm who is affiliated with the research group Inflammatory bowel disease (IBD) and translational gastroenterology.

The time between the blood samples and the onset of the disease varied between 1 and 15years. Researchers were able to see patters in some 90 selected inflammation molecules and of these proteins identify six specific ones.

"We already knew that the level of some of these proteins increased in individuals with ulcerative colitis. For the first time, we were able to see that they were also present in healthy individuals long before they developed any symptoms," says Daniel Bergemalm.

The research team proceeded to test the six proteins against a European collaboration that lists patients with established ulcerative colitis—and had their findings confirmed.

In addition, the researchers in the study have compared blood samples from sets of twins where one has ulcerative colitis and the other does not. The twins both share genetic profile and have grown up in the same environment.

"It turns out that four of the six proteins we'd identified were also found in the healthy twins, which indicates that a combination of genetic and environmental factors contributes to these four proteins being activated," says Daniel Bergemalm.

Finding these six proteins brings the researchers one step closer to understanding the causes of ulcerative colitis.

"We don't know if this kind of protein change can also be found in other inflammatory diseases. But it can become a part of the treatment once we know what triggers the disease," says Daniel Bergemalm.

The research is now to be extended to include further biobanks. The number of proteins examined are also to be extended—from the some 90 original ones in the study to several hundred—to enable researchers to paint a better picture of how the immune system as a whole is linked to the bowel disease.

Today, there are no definite ways of preventing ulcerative colitis.

"Unfortunately, as physicians, we have no lifestyle advice to offer. There really aren't enough studies for us to draw any conclusions and give advice on diet, even if the gut flora probably does play a part," says Daniel Bergemalm.

He views dietary advice and probiotics as having potential for preventing the disease in the future.

"The liquid diet some children with ulcerative colitis are on is very effective. But there are few adults in the world who would tolerate getting their nutrition via a tube," he says.

Today, ulcerative colitis is treated with different drugs.

"It is possible that we in the future could use blood samples from individual patients to see what has caused the disease in that particular person—and on that basis tailor the drug treatment," says Daniel Bergemalm.

More information: Daniel Bergemalm et al, Systemic inflammation in pre-clinical ulcerative colitis, *Gastroenterology* (2021). DOI: 10.1053/j.gastro.2021.07.026

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