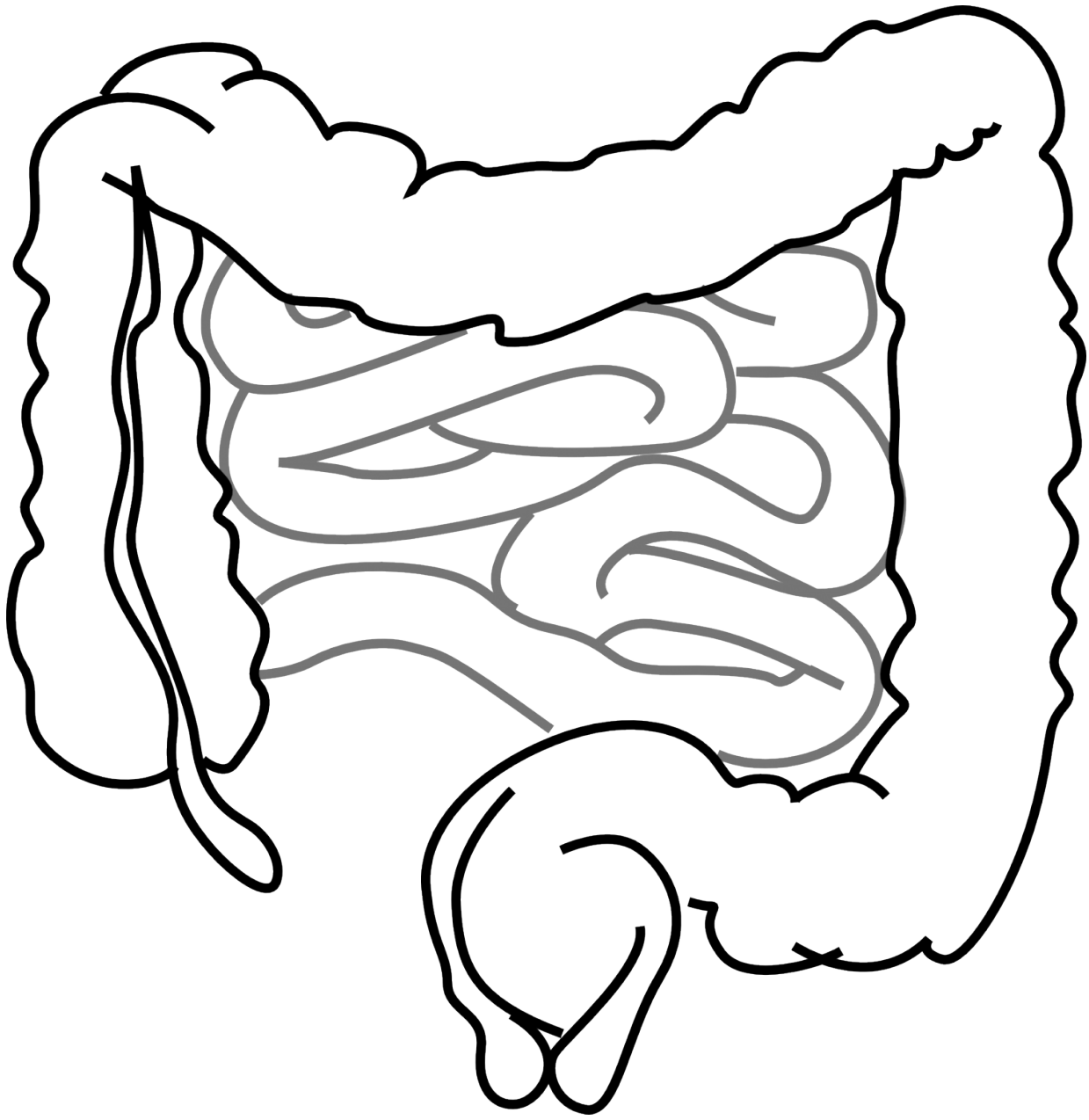
MedicalXpress

Surgery to heal inflamed gut may create new target for disease

February 2 2021



Credit: CC0 Public Domain

A surgical procedure meant to counter ulcerative colitis, an immune disease affecting the colon, may trigger a second immune system attack, a new study shows.

The study results revolve around the immune system, the cells and proteins that destroy invading bacteria and viruses. Activating it brings about inflammation, responses like swelling and pain that result from cells homing in on the site of infection or injury. Autoimmune diseases like ulcerative colitis occur when this system mistakenly damages the body's own tissues.

Colon tissue damaged by the disease is routinely addressed with a "J-pouch" procedure wherein a pouch is surgically constructed from nearby, healthy small intestine tissue to replace the damaged section of the colon. The procedure is designed to restrain the inflammatory attack on the colon, but more than half of these patients, unfortunately, go on to develop inflammation in the J-pouch (pouchitis).

Led by researchers at NYU Grossman School of Medicine, the new investigation showed that some immune cells attacking the colon in ulcerative colitis are the same types attacking the J-pouch. Several varieties of immune cells were found swarming both organs in numbers as high as five times those seen in healthy tissue.

"Our findings suggest that since ulcerative colitis and pouchitis are biologically similar, they may be treated by the same drugs, even though the diseases originate in different parts of the gut," says study co-lead author Jordan Axelrad, MD, MPH. Axelrad is an assistant professor in

the Department of Medicine at NYU Langone Health.

He says starting with the most promising drugs can give medical providers a head start at combating pouchitis and avoiding complications from delayed treatment.

"With our newfound understanding of pouchitis, we can also begin to uncover why some people develop it in the first place and how to prevent it," adds study co-lead author Joseph Devlin, MS, a doctoral candidate at NYU.

Devlin notes that overall, inflammatory bowel diseases, which occur throughout the lining of the digestive tract, progress over time and often resist treatment. By removing a colon damaged by ulcerative colitis, surgeons hope to give the body a chance to start over with fresh tissue unaffected by the disease. As a result, experts were unclear why the new J-pouch would develop an immune reaction.

For their investigation, published in the journal *Gastroenterology* online last month, the research team collected tissue samples from 15 men and women who had undergone J-pouch surgery, of whom 10 developed pouchitis. They compared the gene activity in pouch tissue from these patients with colon tissue samples from 11 patients with ulcerative colitis who did not undergo J-pouch surgery.

Investigators also analyzed the gene activity of 56,000 individual cells using an experimental method called RNA sequencing. They say it is the most detailed analysis of the pouchitis cellular immune response to date, and enabled them to track step-by-step genetic activity in a single cell in any given moment.

"Since using this RNA-sequencing technique has improved our understanding of treatment options for one kind of inflammatory bowel

disease, we can likely use it to assess how effective treatments are for related issues like Crohn's disease," says study co-senior author Ken Cadwell, Ph.D.

Cadwell, an associate professor in the Skirball Institute of Biomolecular Medicine at NYU Langone, cautions that since the investigation focused only on immune cells, it remains unclear how other cells within the J-pouch, such as those that make up the organ's lining, may behave during pouchitis.

He adds that the research team plans to evaluate the same patients before and after J-pouch surgery to see how the immune cell landscape changes over time as inflammation develops. Cadwell is also an associate professor in the Departments of Microbiology and Medicine at NYU Langone.

More information: *Gastroenterology* (2021). DOI: 10.1053/j.gastro.2020.12.030

Provided by NYU Langone Health