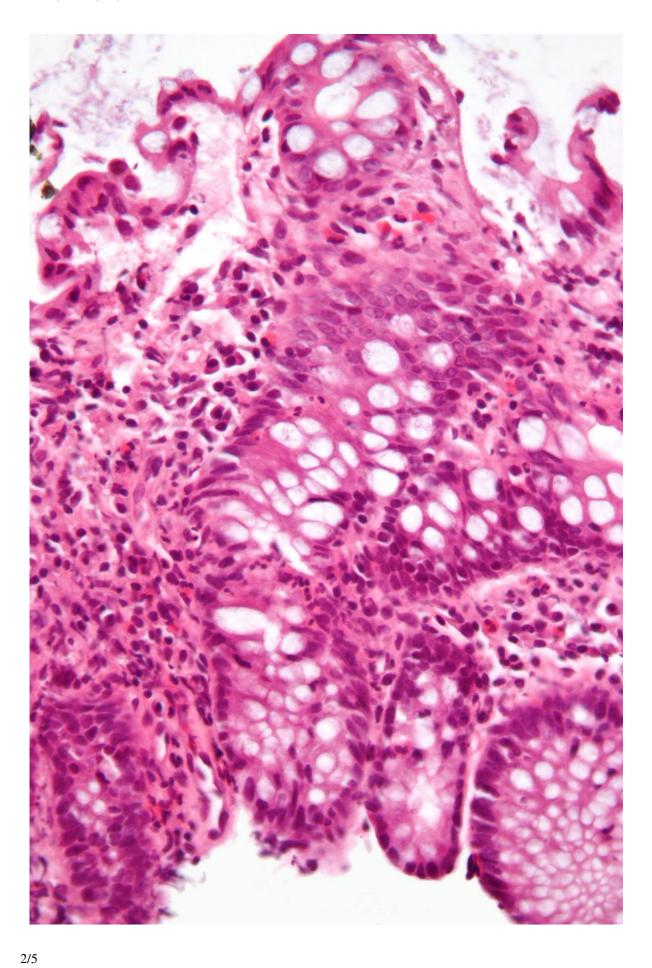


Specialized immune cells could help repair inflammatory bowel disease damage in children

December 10 2019







Micrograph showing inflammation of the large bowel in a case of inflammatory bowel disease. Colonic biopsy. Credit: Wikipedia/CC BY-SA 3.0

A new study suggests that specialized immune cells that dampen inflammation and help repair the gut could be used as a potential therapy for children dealing with the painful symptoms of inflammatory bowel disease (IBD).

The research from BC Children's Hospital and the University of British Columbia shows that a specific type of T cell, called a Tr1 cell, produces a chemical signal that helps repair the barrier formed by cells lining the gut and encourages the production of protective mucus. This study was published in the December issue of *Gastroenterology*.

"This study offers new hope for kids with IBD who urgently need new treatments by showing that Tr1 cells have the potential to reverse the damage caused by IBD," said senior author Dr. Megan Levings, an investigator and head of the Childhood Disease Research Theme at BC Children's and a professor in UBC's department of surgery and school of biomedical engineering. "As a new therapy, Tr1 cells could both suppress the inflammation that is ravaging the lining of the gut and help heal the tissue lining that keeps out harmful bacteria."

Inflammatory bowel <u>disease</u> occurs when the body's immune system mistakenly triggers inflammation in the digestive tract. Inflammation is part of the body's normal response to illness and injury, but in conditions like Crohn's and colitis it can severely damage healthy tissue.

More than 7,000 Canadian children have been diagnosed with IBD and



deal with constant belly pain, cramps, diarrhea and vomiting. These symptoms can lead to malnutrition, weight loss and a lack of energy which can result in missed school days and less time for sports and hobbies. The incidence of two main kinds of IBD—Crohn's disease and ulcerative colitis—is increasing and diagnoses of Crohn's in Canadian kids under 10 have doubled since 1995.

The most common frontline therapy for IBD is the use of antibodies to block inflammation. However, as many as a third of IBD patients do not respond to this treatment—and even if treatment is initially successful, the disease can flare up again later.

"Kids with IBD develop abnormal immune responses to normal gut bacteria," said study co-author Dr. Ted Steiner, an infectious disease specialist, investigator at BC Children's and professor in UBC's department of medicine. "Training our immune system to fight off infections and bad gut bacteria while maintaining normal relationships with the good bacteria is critical for the health of children with these diseases."

"We created self-organized, three-dimensional mini-guts in the lab that we could use to test how Tr1 cells interact with other cells in a more life-like setting," says study co-author Dr. Bruce Vallance, an investigator at BC Children's, the CH.I.L.D. Foundation Chair in Pediatric *Gastroenterology* and professor in UBC's department of pediatrics. "What we found was unexpected, that Tr1 cells can promote the miniguts to release protective mucus and improve the local gut environment. No other types of T cell that we've studied can do this."

Importantly, the researchers found that Tr1 cells isolated from patients with IBD are just as capable of reducing inflammation as those derived from healthy individuals.



"It's not yet clear why people with IBD develop disease if their Tr1 cells are intact, but it could be there are simply too few of these cells to stave off the inflammation," says the study's lead author Dr. Laura Cook, a UBC postdoctoral fellow. "By isolating and boosting the number of these cells in the lab we could one day offer this as a new personalized treatment strategy for children with colitis or Crohn's disease."

Further work is needed to see how these cells can be best nurtured in the lab to ensure that when they are given to children with IBD they will have the best possible chance of relieving the condition. In the future, growing these cells from a patient and then reintroducing them to the gut could be a new cell-based therapy for inflammatory bowel disease.

More information: Laura Cook et al, Suppressive and Gut-Reparative Functions of Human Type 1 T Regulatory Cells, *Gastroenterology* (2019). DOI: 10.1053/j.gastro.2019.09.002

Provided by University of British Columbia

Citation: Specialized immune cells could help repair inflammatory bowel disease damage in children (2019, December 10) retrieved 5 May 2024 from https://medicalxpress.com/news/2019-12-specialized-immune-cells-inflammatory-bowel.html

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