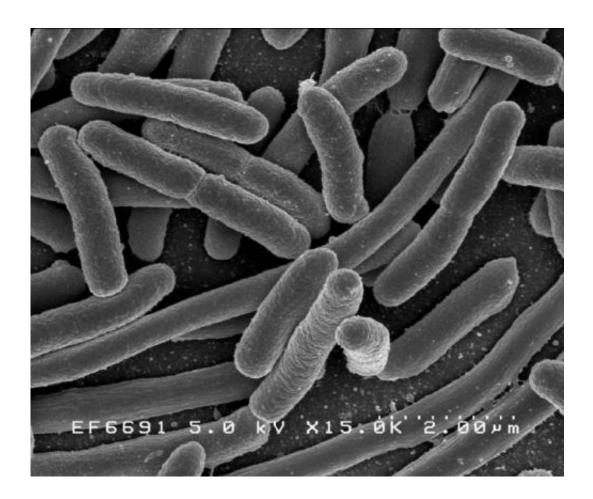


E. coli bacteria found to exploit Crohn's disease inflammation

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Escherichia coli. Credit: Rocky Mountain Laboratories, NIAID, NIH

A multi-year study of the role of E. coli gut bacteria in Crohn's disease finds that intestinal inflammation liberates chemicals that nourish the bacteria's growth and promotes its ability to cause inflammation.



The results identify new avenues for treatments that selectively disrupt the compounds that feed E. coli.

The study was published April 12 in the journal *JCI Insight*, and focuses on ileal Crohn's disease, an inflammatory bowel disease that affects the last part of the small intestine.

A particular type of E. coli, called adherent and invasive E.coli (AIEC), which stick to and invade cultured <u>epithelial cells</u> from the intestine (the gut lining) and replicate in defensive white blood cells (macrophages), has been isolated in 21 to 63% of patients with ileal Crohn's disease, leading researchers to suspect AIEC plays a key role in the disease process.

The researchers adopted a patient-based multidisciplinary approach to identify factors found in patients associated with ileal AIEC, and the impact of these factors on growth and virulence of AIEC. Dr. Shiying Zhang, a senior research associate in the College of Veterinary Medicine, spearheaded the experiments related to AIEC, guided by the multi-pronged analyses of Dr. Xochitl Morgan at the University of Otago.

"This study gives us a whole new patient-based roadmap of things we might want to target to stop Crohn's associated E.coli from growing and inciting inflammation," said senior author Kenneth Simpson, professor in the Department of Clinical Sciences in the College of Veterinary Medicine and at Weill Cornell Medicine in New York City.

Genetic defects, diet and gut <u>bacteria</u> are all suspected to play roles in Crohn's disease. Studies have shown that inflammation and the composition of the microbiome (gut bacteria populations) are interlinked, such that when the gut is inflamed, the microbiome switches from more beneficial bacteria to more unfriendly bacteria, such as E.



coli.

In this study, the research team characterized the ileal microbiome, chemical environment and cultivable bacteria along with the genetic predisposition of patients with and without Crohn's disease. They wanted to answer why intestinal inflammation drives a shift towards E.coli across people, dogs, cats and mice.

"Our thought was that this type of E.coli may use substances generated by intestinal inflammation to grow and outcompete other bacteria," Simpson said. "Essentially we found that the ileal mucosa provides an extensive menu of chemicals that AIEC can mix and match for growth and virulence."

The researchers determined that inflammation creates a chemical environment that is enriched in a number of compounds (called metabolites), notably phospholipids and <u>amino acids</u>, that Crohn's associated E.coli can selectively use for growth, energy, stress resistance and movement towards the gut lining.

They next determined that phospholipid associated ethanolamine, and glutamine, accentuated the aggressive behavior of AIEC in cultured cells, and they linked use of ethanolamine to intestinal inflammation in a model of <u>inflammatory bowel disease</u>.

Previous studies have identified that people with ileal Crohn's disease have defects in genes that impair the ability of macrophages to kill AIEC. This study links E.coli survival in the gut to their ability to replicate in macrophages. "Adherent Invasive E. coli is really hardy and its ability to survive in the inflamed gut, where other bacteria perish, may also enable it to thrive within the macrophages of a Crohn's susceptible individual, "Simpson said.



The team found that E. coli in many people with Crohn's are resistant to multiple classes of antibiotics. They believe that indiscriminate use of antibiotics may promote gut E. coli and related bacteria that can then exploit a susceptible individual.

More information: Shiying Zhang et al, Mucosal metabolites fuel the growth and virulence of E. coli linked to Crohn's disease, *JCI Insight* (2022). DOI: 10.1172/jci.insight.157013

Provided by Cornell University

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