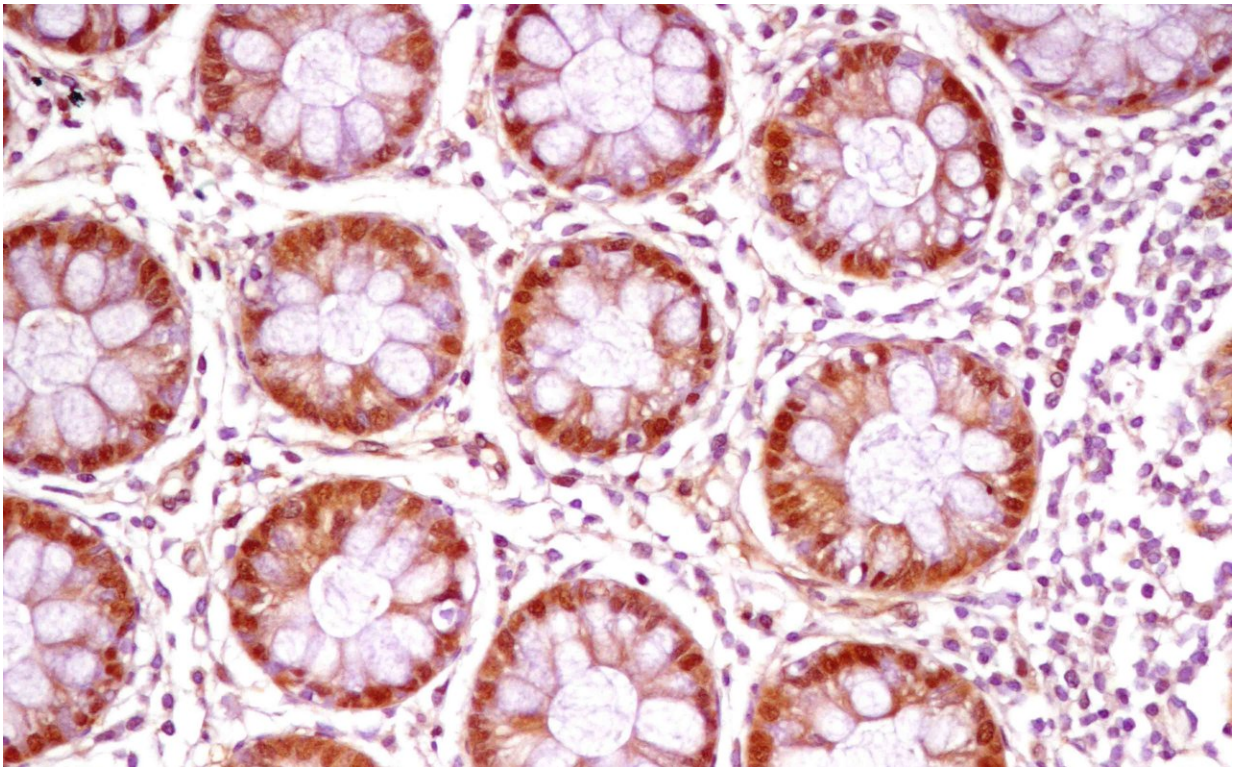


# Body knows best: A natural healing mechanism for inflammatory bowel disease

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The cross-section of the inner lining of a human gut adjacent to a cancerous tumor. The enzyme ASL (red-brown), which helps manufacture nitric oxide, has accumulated in unusually high amounts in cells of the lining, probably in an attempt to alleviate the inflammation that commonly occurs in the gut of colon cancer patients. Credit: Weizmann Institute of Science

Treating inflammatory diseases of the bowel is extremely challenging:

Genes, gut microbes and disrupted immune function all contribute. Weizmann Institute of Science researchers are proposing a way around this complexity. In a study in mice, published in *Cell Reports*, they have found a way to trigger a natural defense mechanism that prompts the body itself to alleviate intestinal inflammation.

The study, led by veterinarian Dr. Noa Stettner, who is also a Ph.D. student in the lab of Dr. Ayelet Erez in the Biological Regulation Department, focused on nitric oxide (NO), a signaling molecule involved in a variety of biological processes. Scientists have long tried to determine what role NO plays in such inflammatory conditions as Crohn's [disease](#) and ulcerative colitis, but NO alleviated [intestinal inflammation](#) in some circumstances and promoted it in others.

The Weizmann researchers hypothesized that the paradoxical findings might arise because NO has different effects in different types of cell in the gut. They genetically engineered mice to block NO production exclusively in certain types of [cells](#): either in the cells making up the inner lining of the gut or in immune cells. They found that the symptoms of a colitis-like disease got worse when NO synthesis was blocked in the gut cells; but they improved when NO was blocked in [immune cells](#), particularly in large cells called macrophages.

The scientists concluded if inflammatory bowel diseases are treated by raising NO levels, it may cause side effects in cells outside the gut lining. Stettner, with the help of collaborators at the Weizmann Institute and elsewhere, set out to develop a method for boosting NO production only in the gut lining cells.

They relied on Erez's earlier finding that an enzyme called ASL that is responsible for the making of the amino acid arginine, the raw material from which the body manufactures NO. The researchers turned to two natural substances: fisetin, which is present in apples, persimmons and

strawberries elevated ASL levels, and citrulline, found in watermelon, beets, and spinach increased ASL activity.

The two supplements, when given together, promoted the manufacture of NO exclusively in cells of the inner lining of the gut. Most important, in mice, the symptoms of an inflammatory disease in the gut improved significantly.

The treatment also had a beneficial effect on colon cancer, which is known to be aggravated by [gut inflammation](#). In mice with tumors of the colon, intestinal inflammation subsided and their tumors decreased in number and size after receiving the supplements.

If this approach is shown to raise NO levels in the inner lining cells in humans, it may help treat inflammatory bowel diseases ? and potentially even colon cancer. The fact that it makes use of over-the-counter nutritional supplements should facilitate its implementation.

**More information:** Noa Stettner et al. Induction of Nitric-Oxide Metabolism in Enterocytes Alleviates Colitis and Inflammation-Associated Colon Cancer, *Cell Reports* (2018). [DOI: 10.1016/j.celrep.2018.04.053](#)

Provided by Weizmann Institute of Science

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