

# Unsaturated fats can help control damaging bouts of inflammation in colitis

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An overly robust immune response to usually harmless germs has been linked to colitis, a potentially severe inflammation of the colon that afflicts millions of people worldwide. A new Yale-led study not only

reveals that the presence of one class of fatty acids is the hidden villain that quietly triggers this inflammation, but also found that another group of fats—unsaturated fats such as those found in olive oil—can alleviate symptoms of colitis in mice.

[The findings](#) were published Feb. 21 in the journal *Nature*.

"How we metabolize fats has a direct connection to [inflammatory response](#) in colitis," said Yale's Richard Flavell, Sterling Professor of Immunobiology and co-corresponding author of the paper.

The cytokine interleukin-10 (IL-10), part of the innate immune system, is essential for suppressing inflammatory responses in the gut. In fact, children born without IL-10 need bone marrow transplants which can produce the cytokine in order to survive. Mice that are genetically altered to lack IL-10 develop severe cases of colitis. Yet despite the importance of IL-10 in maintaining intestinal health, the specific mechanisms through which IL-10 subdues inflammation remain unclear.

In the new study, a team of researchers from Yale and UCLA—led by Autumn York, a former member of Flavell's lab—found that the absence of IL-10 leads to a reorganization of immune cell [fatty acids](#). Specifically, the researchers found that the lack of IL-10 enhanced the production of a particularly damaging type of fatty acid, known as ceramides. High levels of ceramides have been shown to be more predictive of heart disease than cholesterol.

York, now an assistant professor at the University of Washington, wondered what would happen if ceramides were eliminated in [mice](#) with immune systems genetically altered to mimic those of humans. To the surprise of researchers, mice without specific ceramides showed a strong reduction in colitis even in the absence of IL-10. The presence of specific types of fatty acids, they determined, regulated the severity of

the immune response.

"Once we understood what fatty acids were important, we hoped to use our knowledge of metabolic pathways to find a way to counteract these inflammatory fats via dietary correction," York said. Indeed, symptoms of colitis dissipated in mice lacking IL-10 when they were fed a diet of [unsaturated fats](#) such as those found in [olive oil](#).

"Immune cells have evolved to read their environment—and they use this information to dictate the severity of the immune response," York said.

The researchers said that it is possible that diets high in unsaturated fats may be beneficial in treating colitis. They are studying whether similar specific classes of fatty acids might be present in other inflammatory diseases.

**More information:** Autumn G. York et al, IL-10 constrains sphingolipid metabolism to limit inflammation, *Nature* (2024). [DOI: 10.1038/s41586-024-07098-5](https://doi.org/10.1038/s41586-024-07098-5)

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