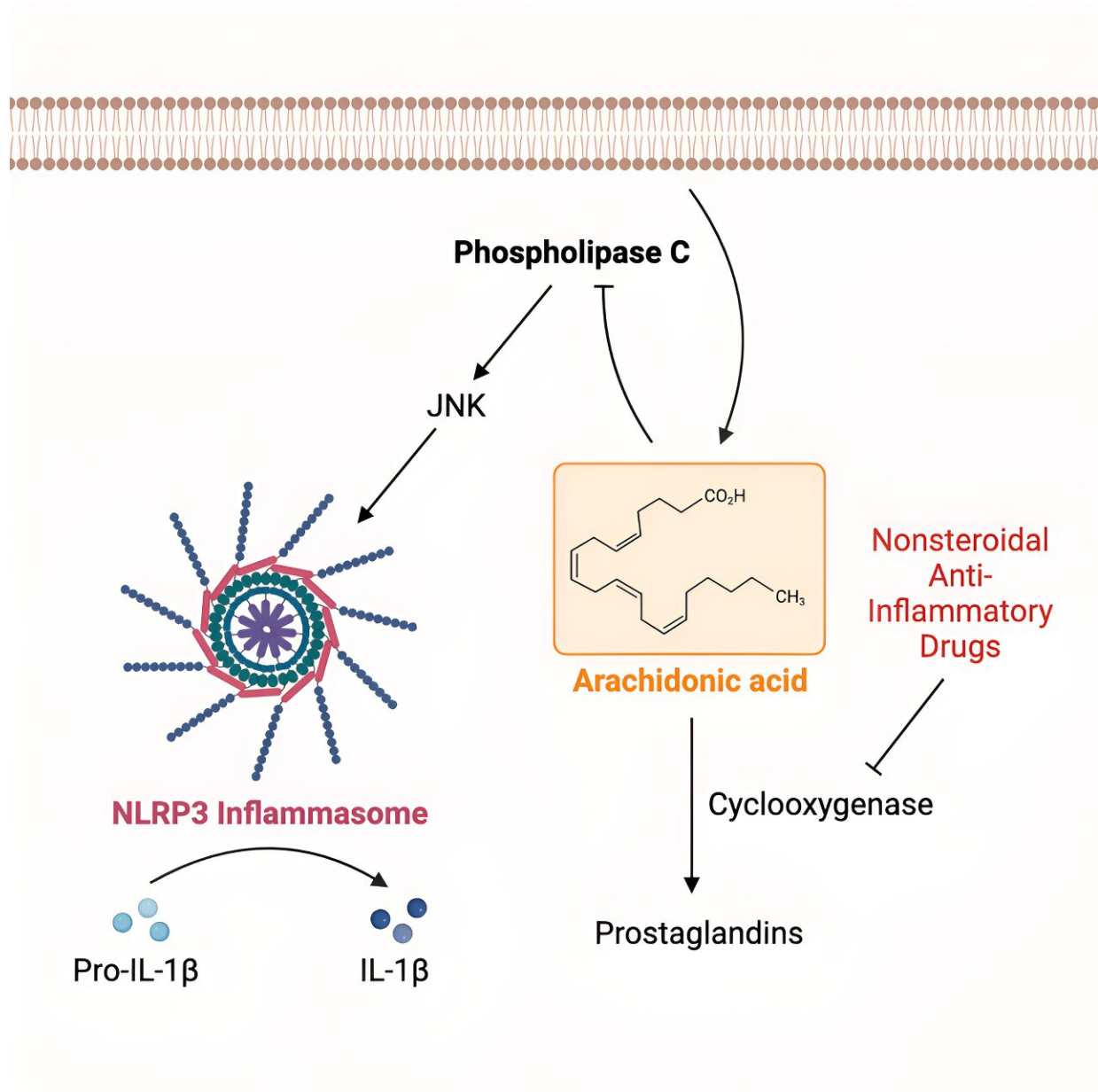


Scientists identify how fasting may protect against inflammation

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Graphical abstract. Credit: *Cell Reports* (2024). DOI: 10.1016/j.celrep.2024.113700

Cambridge scientists may have discovered a new way that fasting helps reduce inflammation, a potentially damaging side-effect of the body's immune system that underlies a number of chronic diseases.

In a [paper](#) titled "Arachidonic acid inhibition of the NLRP3 inflammasome is a mechanism to explain the anti-inflammatory effects of fasting," published in *Cell Reports*, the team describes how fasting raises levels of a chemical in the blood known as [arachidonic acid](#), which inhibits inflammation. The researchers say it may also help explain some of the beneficial effects of drugs such as aspirin.

Scientists have known for some time that our diet—particularly a high-calorie Western diet—can increase our risk of diseases including obesity, type 2 diabetes and [heart disease](#), which are linked to [chronic inflammation](#) in the body.

Inflammation is our body's natural response to injury or infection, but this process can be triggered by other mechanisms, including by the so-called "inflammasome," which acts like an alarm within our body's cells, triggering inflammation to help protect our body when it senses damage. But the inflammasome can trigger inflammation in unintentional ways—one of its functions is to destroy unwanted cells, which can result in the release of the cell's contents into the body, where they trigger inflammation.

Professor Clare Bryant from the Department of Medicine at the University of Cambridge said, "We're very interested in trying to understand the causes of chronic inflammation in the context of many

human diseases, and in particular the role of the inflammasome.

"What's become apparent over recent years is that one inflammasome in particular—the NLRP3 inflammasome—is very important in a number of major diseases such as obesity and atherosclerosis, but also in diseases like Alzheimer's and Parkinson's disease, many of the diseases of older age people, particularly in the Western world."

Fasting can help reduce inflammation, but the reason why has not been clear. To help answer this question, a team led by Professor Bryant and colleagues at the University of Cambridge and National Institute for Health in the U.S. studied [blood samples](#) from a group of 21 volunteers, who ate a 500-kcal meal and then fasted for 24 hours before consuming a second 500-kcal meal.

The team found that restricting [calorie intake](#) increased levels of a lipid known as arachidonic acid. Lipids are molecules that play important roles in our bodies, such as storing energy and transmitting information between cells. As soon as individuals ate a meal again, levels of arachidonic acid dropped.

When the researchers studied arachidonic acid's effect in immune cells cultured in the lab, they found that it turns down the activity of the NLRP3 inflammasome. This surprised the team, as arachidonic acid was previously thought to be linked with increased levels of inflammation, not decreased levels.

Professor Bryant, a Fellow of Queens' College, Cambridge, added, "This provides a potential explanation for how changing our diet—in particular by fasting—protects us from inflammation, especially the damaging form that underpins many diseases related to a Western high-calorie diet.

"It's too early to say whether fasting protects against diseases like

Alzheimer's and Parkinson's disease, as the effects of arachidonic acid are only short-lived, but our work adds to a growing amount of scientific literature that points to the health benefits of calorie restriction. It suggests that regular fasting over a long period could help reduce the chronic inflammation we associate with these conditions. It's certainly an attractive idea."

The findings also hint at one mechanism whereby a high-calorie diet might increase the risk of these diseases. Studies have shown that some patients who have a high-fat diet have increased levels of inflammasome activity.

"There could be a yin and yang effect going on here, whereby too much of the wrong thing is increasing your inflammasome activity and too little is decreasing it," said Professor Bryant. "Arachidonic acid could be one way in which this is happening."

The researchers say the discovery may also offer clues to an unexpected way in which so-called non-steroidal anti-inflammatory drugs such as aspirin work. Normally, arachidonic acid is rapidly broken down in the body, but aspirin stops this process, which can lead to an increase in levels of arachidonic acid, which in turn reduce [inflammasome](#) activity and hence inflammation.

Professor Bryant said, "It's important to stress that aspirin should not be taken to reduce risk of long terms diseases without medical guidance, as it can have side effects such as stomach bleeds if taken over a long period."

More information: Milton Pereira et al, Arachidonic acid inhibition of the NLRP3 inflammasome is a mechanism to explain the anti-inflammatory effects of fasting, *Cell Reports* (2024). [DOI: 10.1016/j.celrep.2024.113700](https://doi.org/10.1016/j.celrep.2024.113700)

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