

Anti-inflammatory mechanism of dieting and fasting revealed

16 February 2015

Researchers at Yale School of Medicine have found that a compound produced by the body when dieting or fasting can block a part of the immune system involved in several inflammatory disorders such as type 2 diabetes, atherosclerosis, and Alzheimer's disease.

In their study, published in the Feb. 16 online issue of *Nature Medicine*, the researchers described how the compound β -hydroxybutyrate (BHB) directly inhibits NLRP3, which is part of a complex set of proteins called the inflammasome. The inflammasome drives the [inflammatory response](#) in several disorders including autoimmune diseases, type 2 diabetes, Alzheimer's disease, atherosclerosis, and autoinflammatory disorders.

"These findings are important because endogenous metabolites like BHB that block the NLRP3 inflammasome could be relevant against many [inflammatory diseases](#), including those where there are mutations in the NLRP3 genes," said Vishwa Deep Dixit, professor in the Section of Comparative Medicine at Yale School of Medicine.

BHB is a metabolite produced by the body in response to fasting, high-intensity exercise, [caloric restriction](#), or consumption of the low-carbohydrate ketogenic diet. Dixit said it is well known that fasting and calorie restriction reduces inflammation in the body, but it was unclear how immune cells adapt to reduced availability of glucose and if they can respond to metabolites produced from fat oxidation.

Working with mice and [human immune cells](#), Dixit and colleagues focused on how macrophages—specialized immune cells that produce inflammation—respond when exposed to ketone bodies and whether that impacts the inflammasome complex.

The team introduced BHB to mouse models of inflammatory diseases caused by NLRP3. They

found that this reduced inflammation, and that inflammation was also reduced when the mice were given a [ketogenic diet](#), which elevates the levels of BHB in the bloodstream.

"Our results suggest that the endogenous metabolites like BHB that are produced during low-carb dieting, fasting, or high-intensity exercise can lower the NLRP3 inflammasome," said Dixit.

More information: The ketone metabolite β -hydroxybutyrate blocks NLRP3 inflammasome-mediated inflammatory disease, *Nature Medicine*, [dx.doi.org/10.1038/nm.3804](https://doi.org/10.1038/nm.3804)

Related paper: A small - molecule inhibitor of the NLRP3 inflammasome for the treatment of inflammatory diseases, *Nature Medicine*, [dx.doi.org/10.1038/nm.3806](https://doi.org/10.1038/nm.3806)

See: [Team uncovers marvel molecule that could lead to treatments for inflammatory diseases](#)

Provided by Yale University

APA citation: Anti-inflammatory mechanism of dieting and fasting revealed (2015, February 16) retrieved 29 October 2022 from

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