Specific fatty acids may worsen Crohn's disease

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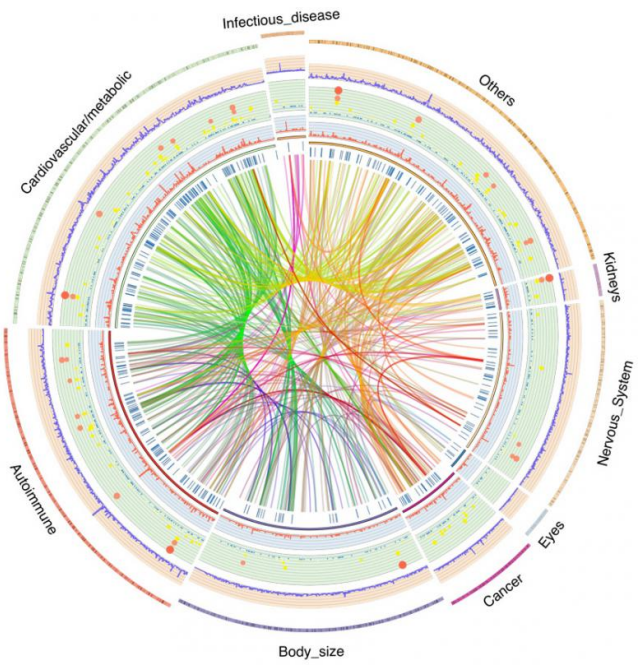

A new software tool allows scientists to link different human diseases and traits through the genetic variations they share. Credit: Liuyang Wang, Dennis Ko lab

Some research has suggested that omega-3 fatty acids, abundant in fish oils, can relieve inflammation in Crohn's disease. But a new study using software developed by Duke scientists hints that we should be paying closer attention to what the other omegas—namely, omega-6 and omega-7—are doing to improve or worsen the disease.

Crohn's disease is an inflammatory disease of the digestive tract that causes abdominal pain, diarrhea, fever and weight loss. Although it is thought to stem from an interplay between environmental and genetic factors, the exact causes are unclear. There is no cure, but people with the disease can avoid flare-ups by taking anti-inflammatory drugs and altering diet.

"Dietary therapies for Crohn's disease should be examined more systematically, and this study provides a good first step," said Dennis Ko, an assistant professor of molecular genetics and microbiology in the Duke School of Medicine.

Published September 15 in *Genome Biology*, the study relied on new software for researchers that identifies connections between seemingly unrelated human diseases and traits through the tiny, risk-conferring genetic variations they have in common.

Research has suggested that high-fat diets may be linked with Crohn's disease, but never have the two been joined through shared genetics. Certain subtle genetic variations—as small as a single-letter change in the DNA—seem to occur more often in people with Crohn's disease. Separate lines of work show that specific genetic variations are linked to higher levels of some fatty acids (molecular building blocks of fat) in the bloodstream.

In the new study, researchers identified genetic overlaps between palmitoleic acid, a type of omega-7 fatty acid, and Crohn's with a software tool they call CPAG ("SEE-PAG"; short for Cross-Phenotype Analysis of GWAS). The software allowed them to compare the results of the more than 1,400 genome-wide association studies (GWAS) that have been published on the topic so far.

"The basis of the approach is simply to ask, 'Is the [genetic] overlap between the two diseases or traits more than you'd expect just by chance?'" said Ko, who is also a member of the Duke Center for Host-Microbial Interactions.

In the past, there hadn't been a way to address that question comprehensively. CPAG will continue to get better with the inclusion of additional data and other researchers can use the software to analyze their own genetic findings in light of all published studies, Ko added.

The software, just like the genome-wide studies it mines, does not predict the relationship between one trait or disease and another, however.

To test whether fatty acid levels in the bloodstream was a cause or a consequence of disease, the researchers turned to a zebrafish model of Crohn's disease that had been developed by Stefan Oehlers, a post-doctoral fellow in David Tobin's group at Duke.

To the researchers' surprise, it wasn't omega-7 (palmitoleic acid) that significantly worsened inflammation but rather its saturated counterpart, palmitic acid, which is found in olive oil, butter, cheese, milk and meat.

Another unexpected finding was that an omega-6 fatty acid (linoleic acid), which is present in vegetable oils, lessened inflammation in the fish. Omega-6 had been shown in a previous study to be lower than normal in the blood of people with Crohn's.

Ko is quick to note that these new findings do not warrant radical dietary changes in people with Crohn's: More studies, including more refined genetic analyses of fatty acids and Crohn's and testing in animal models, are needed.

Study co-author John Rawls of Duke and his group are studying the biological mechanisms underlying the absorption of lipids—fatty acids and related fat molecules—in the guts of zebrafish.

"If we can deepen our understanding of lipid imbalance in Crohn's disease and the consequences of having too much or too little of any one lipid in particular, then we might eventually be able to develop new strategies for managing Crohn's disease and other inflammatory disorders," said Rawls, an associate professor of molecular genetics and microbiology in the Duke School of Medicine.

Until then, Ko and his colleagues will continue to probe the human genome using their new CPAG software and will likely turn up many more leads, Ko said.

More information: "CPAG: software for leveraging pleiotropy in GWAS to reveal similarity between human traits links plasma fatty acids and intestinal inflammation," Liuyang Wang, Stefan H. Oehlers, Scott T. Espenschied, John F. Rawls, David M. Tobin, and Dennis C. Ko. *Genome Biology*, Sept. 15, 2015. DOI: 10.1186/s13059-015-0722-1

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