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Drug dramatically reduces diabetes symptoms in mice

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Can diabetes be prevented and even reversed? Yes, it can—at least in genetically obese mice, according to a newly published study by led by researchers Bruce Hammock at the University of California, Davis, and Joan Clària at the University of Barcelona. The research involves a potent enzyme inhibitor discovered by Hammock's laboratory that dramatically reduces inflammation, inflammatory pain and neuropathic pain.

In the study, published in the *Proceedings of the National Academy of Sciences*, an enzyme called soluble epoxide hydrolase, or sEH, inhibitor both prevented the onset of diabetes and reversed the effects of diabetes in obese mice.

"Our previous studies show the drug we are working on will reduce the symptoms of diabetes in mice by itself," Hammock said, "but the excitement about Joan Clària's work is that if the mice have a genetically increased level of omega-3 fatty acids—the drug offers prevention or cure in mice."

The Centers for Disease Control and Prevention estimates that 29.1 million Americans, or 9.3 percent of the population, have diabetes, which is characterized by abnormal blood glucose levels. This includes 8.1 million undiagnosed cases.

The new drug apparently works by stabilizing metabolites of an omega-3 fatty acid called DHA. These metabolites are thought to contribute to the

beneficial effects of a diet high in omega-3 fatty acids, Hammock said. Previous UC Davis research in the laboratories of Hammock, Nipavan Chiamvimonvat, Robert Weiss, Anne Knowlton and Fawaz Haj showed that the enzyme reduces or reverses such diabetes-linked medical issues as renal failure, hypertension, diabetic pain, hardening of the arteries and heart failure.

"This exciting research brings mechanistic detail to understanding how omega-3 fatty acids in the diet exert important health effects," said J. Bruce German, director of the UC Davis Foods for Health Institute, Department of Food Science and Technology, who was not involved in the diabetes-based research.

Clària is an associate professor at the Barcelona University School of Medicine and a senior consultant at the Biochemistry and Molecular Genetics Service of the Hospital Clínic of Barcelona.

In the paper, titled "Inhibition of Soluble Epoxide Hydrolase Modulates Inflammation and Autophagy in Obese Adipose Tissue and Liver: Role for Omega-3 Epoxides," Clària described the administration of the sEH inhibitor as "a promising strategy to prevent obesity-related co-morbidities."

Clària said the study also sheds more light on the role of sEH and omega-3 epoxides in insulin-sensitive tissues, especially the liver.

More information: "Inhibition of soluble epoxide hydrolase modulates inflammation and autophagy in obese adipose tissue and liver: Role for omega-3 epoxides." *PNAS* 2014 ; published ahead of print December 30, 2014, DOI: 10.1073/pnas.1422590112

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