

Discovery points to new approach for diabetes therapy

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Nutrition experts at Oregon State University have essentially "cured" laboratory mice of mild, diet-induced diabetes by stimulating the production of a particular enzyme.

The findings could offer a new approach to diabetes therapy, experts say, especially if a drug could be identified that would do the same thing, which in this case was accomplished with [genetic manipulation](#).

Increased levels of this enzyme, called fatty acid elongase-5, restored normal function to diseased livers in mice, restored normal levels of [blood glucose](#) and insulin, and effectively corrected the risk factors incurred with diet-induced diabetes.

"This effect was fairly remarkable and not anticipated," said Donald Jump, a professor of nutrition and exercise sciences at Oregon State, where he is an expert on [lipid metabolism](#) and principal investigator with OSU's Linus Pauling Institute.

"It doesn't provide a therapy yet, but could be fairly important if we can find a drug to raise levels of this enzyme," Jump said. "There are already some drugs on the market that do this to a point, and further research in the field would be merited."

The studies were done on a family of enzymes called "fatty acid elongases," which have been known of for decades. Humans get essential [fatty acids](#) that they cannot naturally make from certain foods in their

diet. These essential fatty acids are converted to longer and more unsaturated fatty acids. The fatty acid end products of these reactions are important for managing metabolism, inflammation, cognitive function, [cardiovascular health](#), reproduction, vision and other metabolic roles.

The enzymes that do this are called fatty acid elongases, and much has been learned in recent years about them. In research on diet-induced obesity and diabetes, OSU studied enzyme conversion pathways, and found that elongase-5 was often impaired in mice with elevated insulin levels and diet-induced obesity.

The scientists used an established system, based on a recombinant adenovirus, to import the gene responsible for production of elongase-5 into the livers of obese, diabetic mice. When this "delivery system" began to function and the mice produced higher levels of the enzyme, their diet-induced liver defects and elevated blood sugar disappeared.

"The use of a genetic delivery system such as this was functional, but it may not be a permanent solution," Jump said. "For human therapy, it would be better to find a drug that could accomplish the same thing, and that may be possible. There are already drugs on the market, such as some fibrate drugs, that induce higher levels of elongase-5 to some extent."

There are also drugs used with diabetic patients that can lower blood sugar levels, Jump said, but some have side effects and undesired complications. The potential for raising levels of elongase-5 would be a new, specific and targeted approach to diabetes therapy, he said. While lowering blood sugar, the elevated levels of elongase-5 also reduced triglycerides in the liver, another desirable goal. Elevated triglycerides are associated with "fatty liver," also known as non-alcoholic fatty liver disease. This can progress to more severe liver diseases such as fibrosis, cirrhosis and cancer.

Further research is needed to define the exact biological mechanisms at work in this process, and determine what the fatty acids do that affects carbohydrate and triglyceride metabolism, he said. It appears that high fat diets suppress elongase-5 activity.

"These studies establish a link between fatty acid elongation and hepatic glucose and triglyceride metabolism," the researchers wrote in their report, "and suggest a role for regulators of elongase-5 activity in the treatment of diet-induced hyperglycemia and fatty liver."

More information: The study was published in the Journal of Lipid Research.

Provided by Oregon State University

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