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New strategy to lower blood sugar may help in diabetes treatment

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Some treatments for type 2 diabetes make the body more sensitive to insulin, the hormone that lowers blood sugar. But new research at Washington University School of Medicine in St. Louis suggests a different strategy: slowing the production of glucose in the liver.

Working in mice, the researchers showed they could reduce glucose production in the liver and lower blood sugar levels. They did so by shutting down a liver protein involved in making glucose, an approach that may work in patients with type 2 diabetes.

The research is published online Sept. 3 in *Cell Metabolism*.

"We think this strategy could lead to more effective drugs for type 2 diabetes," said principal investigator Brian N. Finck, PhD, associate professor of medicine in the Division of Geriatrics and Nutritional Science. "A drug that shuts down glucose production has the potential to help millions of people affected by the most common form of diabetes."

Finck worked with researchers at the University of Texas Southwestern Medical Center and the biopharmaceutical company Metabolic Solutions Development Co.

The company is involved in clinical trials that are evaluating the drug compound MSDC-0602 as a treatment for diabetes. The new study demonstrates that the compound works, at least in part, by inhibiting a protein that's key to glucose production in the liver.

The research team, led by first author Kyle S. McCommis, PhD, a postdoctoral research scholar, cut sugar production in liver cells by inhibiting a key protein involved in transporting pyruvate, a building block of glucose, from the bloodstream into the energy factories of liver cells, called mitochondria.

Previous research had suggested interfering with pyruvate may limit glucose production in the liver, but this study is the first to demonstrate the critical role played by the pyruvate transport protein.

In addition to diabetes, the researchers also think that interfering with pyruvate transport may help patients with nonalcoholic fatty liver disease, a condition common in people with obesity.

More information: McCommis KS, Chen Z, Fu X, McDonald WG, Colca JR, Kletzien RF, Burgess SC, Finck BN. Loss of mitochondrial pyruvate carrier 2 in liver leads to defects in gluconeogenesis and compensation via pyruvate-alanine cycling. *Cell Metabolism*, published online Sept. 3, 2015. DOI: dx.doi.org/10.1016/j.cmet.2015.07.028

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