

Diabetes debate: Triglycerides form in liver despite insulin resistance

5 January 2015



Credit: Darren Lewis/public domain

Solving one of the great mysteries of type 2 diabetes, a team of Yale researchers found that triglycerides, a type of fat in the blood and liver, are produced in the liver independent of insulin action in the liver.

In type 2 diabetics, insulin fails to suppress [blood sugar](#) production by the liver while paradoxically allowing the production of hepatic triglycerides. This combination results in multiple health risks, including [high blood sugar](#) and fatty liver disease. For years, to gain insight into this phenomenon, researchers focused on the role of altered [insulin action](#) in the liver in the production of triglycerides. However, Yale researchers tested a theory that triglycerides formed in the liver were more dependent on the delivery of fatty acids to the liver than on insulin action.

In their study, the Yale team—led by Gerald I. Shulman, the George R. Cowgill professor of medicine and cellular & molecular physiology—developed a novel method to measure the rate of triglyceride production from [fatty acids](#) in three types of animals: normal rats, insulin-resistant rats fed a high-fat diet, and rats with

genetically modified insulin receptors. They found that in all of the animals tested increased triglyceride production was primarily dependent on fatty acid delivery and not on insulin action in the liver.

The findings also explain the long-standing paradox of why insulin therapy does not exacerbate, but instead reduces, fatty liver disease in patients with [type 2 diabetes](#). "These results provide new insights into the pathogenesis of non-alcoholic liver disease and provides new approaches to treat fatty liver disease, which is now the most common liver disease in the world," said Shulman.

Shulman and his team plan to apply similar methodology to translate their findings to insulin-resistant patients with type 2 diabetes, hyperlipidemia, and [fatty liver disease](#).

The study was published early online in the *Proceedings of the National Academy of Sciences*.

More information: Insulin-independent regulation of hepatic triglyceride synthesis by fatty acids, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1423952112

Provided by Yale University

APA citation: Diabetes debate: Triglycerides form in liver despite insulin resistance (2015, January 5) retrieved 15 November 2022 from <https://medicalxpress.com/news/2015-01-diabetes-debate-triglycerides-liver-insulin.html>

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