Research links fatty liver disease to type 2 diabetes

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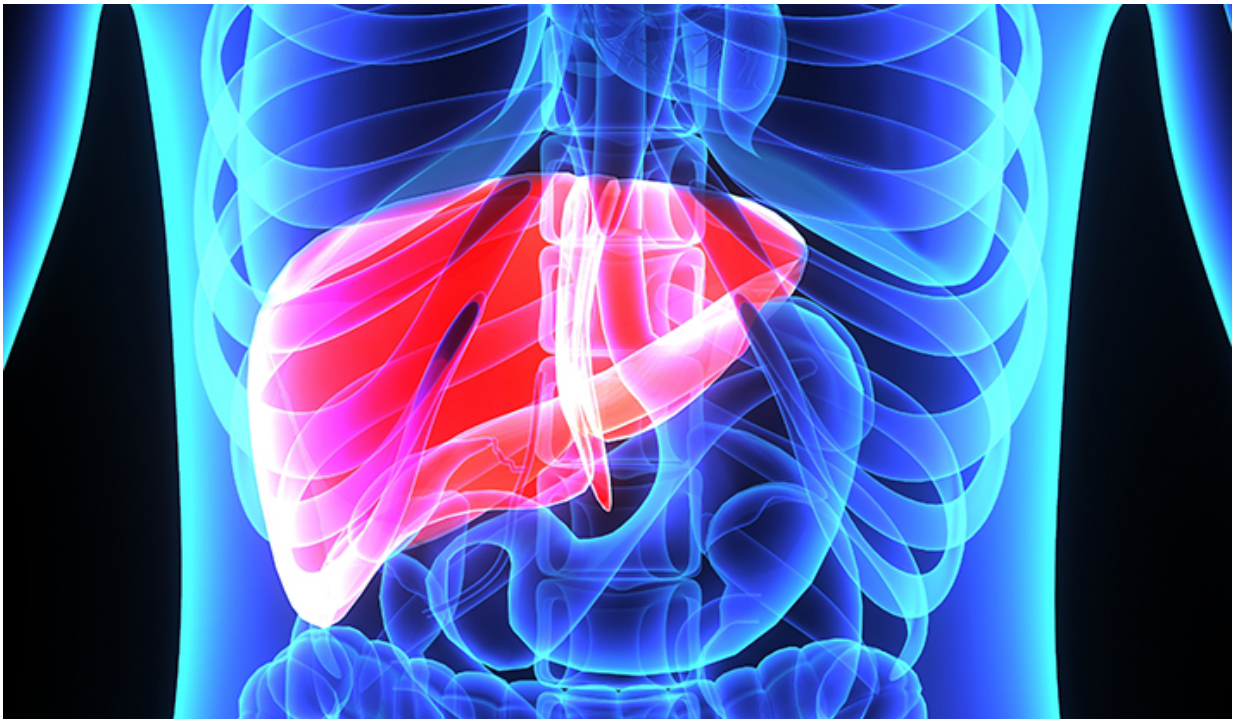

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Insulin resistance in the liver is a major factor in the development of type 2 diabetes, and it is almost always associated with too much fat in the liver—a condition called non-alcoholic fatty liver disease (NAFLD). The question of whether there's a causal link between NAFLD and type 2 diabetes has been unclear. In recent studies, Yale professor of

medicine and investigator of the Howard Hughes Medical Institute, Gerald Shulman has identified factors that cause the normal function of insulin in the liver to go awry in NAFLD.

A new study pinpoints the final link between NAFLD and the changes in insulin and blood sugar that give rise to type 2 diabetes.

In this new study Shulman and his colleagues identified a single amino acid in the insulin receptor that undergoes phosphorylation (a process by which phosphate is added to an amino acid), causing liver insulin resistance in rodent models of NAFLD. "We were able to demonstrate the importance of this amino acid in causing liver insulin resistance associated with NAFLD by mutating this threonine amino acid to an alanine, which cannot undergo phosphorylation, and found that we could prevent hepatic insulin resistance despite the presence of fatty liver disease," Shulman said.

This latest finding gets scientists a step closer to developing new therapies for type 2 diabetes that target the root molecular cause of insulin resistance, as opposed to virtually all current antidiabetic medications which lower blood glucose concentrations without reversing insulin resistance, he noted.

More information: Max C. Petersen et al. Insulin receptor Thr1160 phosphorylation mediates lipid-induced hepatic insulin resistance, *Journal of Clinical Investigation* (2016). DOI: 10.1172/JCI86013

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