Scientists develop new compound that reverses fatty liver disease

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(Phys.org)—Scientists from the Florida campus of The Scripps Research Institute (TSRI) have developed the first synthetic compound that can reverse the effects of a serious metabolic condition known as fatty liver disease. True to its name, the disease involves an abnormal buildup of fat in the liver.

The compound—known as SR9238—is the first to effectively suppress lipid or fat production in the liver, eliminating inflammation and reversing fat accumulation in animal models of fatty liver disease. The new compound also significantly lowered total cholesterol levels, although precisely how that occurred remains something of a mystery.

"We've been working on a pair of natural proteins called LXRα and LXRβ that stimulate fat production in the liver, and we thought our compound might be able to successfully suppress this process," said Thomas Burris, a professor at TSRI who led the study, which was recent published in an online edition of the journal *ACS* Chemical Biology. "Once the animals were put on the drug, we were able to reverse the disease after a single month with no adverse side effects—while they ate a high-fat diet."

Fatty liver, which often accompanies obesity and type 2 diabetes, frequently leads to more serious conditions including cirrhosis and liver cancer. The condition affects some 10 to 24 percent of the general population, according to a 2003 study in GUT, an international journal of gastroenterology and hepatology.

Burris and his colleagues designed SR9238 so that it would be quickly metabolized in the liver to minimize migration of the drug into the bloodstream, which could lead to side effects.

In the study, mice were fed a high-fat diet for 14 weeks prior to treatment with SR9238. After one month of treatment, the scientists found that the liver's fat-producing genes were repressed and fat expression in the liver was reduced up to 90 percent.

In addition, the scientists observed an 80 percent reduction of the enzyme responsible for producing cholesterol (3-Hydroxy-3-methylglutaryl coenzyme A Reductase)—the same enzyme targeted by statins.

Markers for liver damage were down as well, which suggests the compound may also have the potential to treat alcohol-related fatty liver damage.

More information: "A Liver Selective LXR Inverse Agonist that Suppresses Hepatic Steatosis" pubs.acs.org/doi/abs/10.1021/cb300541g

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