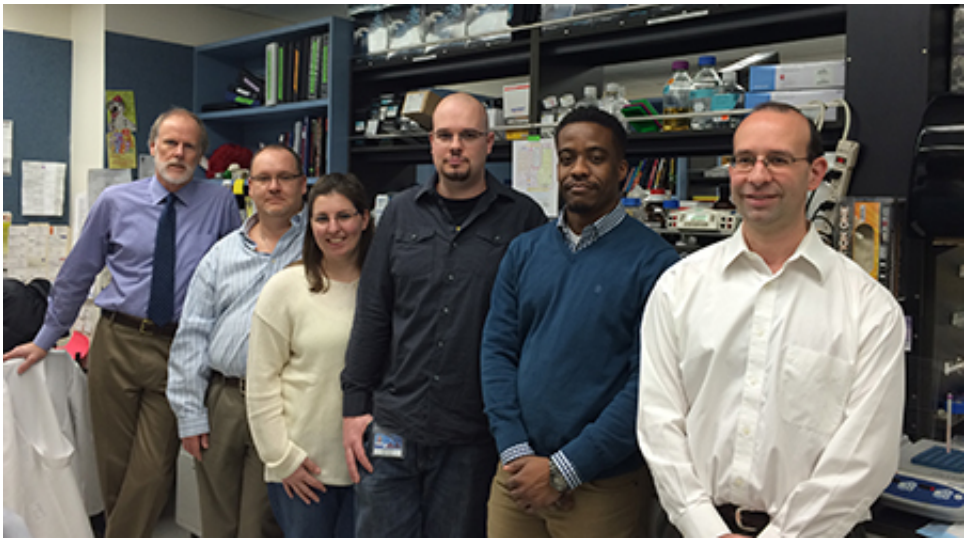
Drug stops fatty liver disease from causing inflammation, scarring

February 18 2015



SLU scientists are searching for fatty liver disease therapies. Pictured in the lab are Brent A. Neuschwander-Tetri, M.D., Thomas Burris, Ph.D., Kristine Griffett, Ph.D., Ryan D. Welch, Colin A. Flaveny, Ph.D.,and Grant R. Kolar, Ph.D.

Doctors believe that up to 30 percent of the U.S. population may have fat accumulation in the liver, known as non-alcoholic fatty liver disease (NAFLD), that can lead to a range of damaging health consequences.

In a study published in *Molecular Metabolism*, Saint Louis University researchers have tested in an animal model a promising drug candidate that stopped fatty liver disease from progressing to the stage that causes

severe liver damage.

In some people, fat in the liver is simply a warning sign. In others, however, fatty liver disease will develop with inflammation and cirrhosis (scarring). This form of fatty liver disease is called NASH (nonalcoholic steatohepatitis), and can lead to liver cancer or liver failure, requiring a transplant. Currently, there are no approved treatments for NASH, though some early stage clinical trials have shown promise.

Thomas Burris, Ph.D., chair of pharmacological and physiological science at Saint Louis University, led a team of researchers in developing and testing a drug that suppresses lipogenesis, a key characteristic of NASH, in hopes of stopping its progression.

"We focused on a receptor that regulates fat synthesis and transport," said Burris. "The drug is liver specific, so it gets to the liver, stays there and reduces the liver's ability to produce fat."

The research team used a special high trans-fat, high fructose diet designed by Brent A. Neuschwander-Tetri, M.D, director of gastroenterology and hepatology at SLU, to mimic in an animal model the liver disease people develop.

Then, the mice were treated with the drug that Burris developed: SR9238, a liver-specific LXR inverse agonist.

"We weren't sure if this would slow down the whole process of NASH," Burris said. "But, it really does shut it down. It stops the scarring and damage."

Since NASH in people is caused by many factors in addition to the types of food that people eat, the researchers were encouraged by these results.

Burris hopes the findings may lead to more treatment options for this increasingly prevalent illness. As with all laboratory research, this drug will need to be tested in clinical trials to determine its safety and effectiveness in people before it can be considered as a therapy for NASH.

More information: *Molecular Metabolism*, www.molmetab.com/article/S2212 … (15)00022-8/abstract

Provided by Saint Louis University