

Ghrelin mitigates liver fibrosis in animal models; regulates human fibrosis

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Spanish researchers determined that rats treated with recombinant ghrelin displayed a reduction in liver fibrosis. Ghrelin, a stomach hormone, reduced the amount of fibrogenic cells by 25% in the treated rodents. Research further showed ghrelin prevented acute liver damage and reduced oxidative stress and inflammation in the animal models. Details of this study are published in the March issue of *Hepatology*, a journal of the American Association for the Study of Liver Diseases.

Liver diseases, such as hepatitis viruses, [cirrhosis](#), and hepatocellular [carcinoma](#) (HCC, liver cancer), affect more than 5 million Americans with over 85,000 new cases of hepatitis reported annually, according to estimates from the [Centers for Disease Control and Prevention](#) (CDC). The World Health Organization reports over 2 billion people worldwide have some type of viral hepatitis. Those living with chronic liver disease are subject to further damage caused by fibrosis, a scarring of the liver that can lead to liver failure and the ultimate need of transplantation.

"Currently, there are no effective anti-fibrotic therapies for patients with liver disease," said Ramón Bataller, M.D., from the Hospital Clínic in Barcelona, Spain and lead author of the study. "Our aim was to determine if recombinant [ghrelin](#) could regulate the formation of fibrous tissue associated with chronic [liver damage](#)." Ghrelin is a growth hormone that plays a major role in the regulation of appetite and is primarily produced in the stomach. Prior studies have shown that ghrelin also has protective effects in other areas of the body including the pancreas, heart and gastrointestinal tract.

To assess chronic liver disease, the research team induced liver injury and fibrosis in male rats by prolonged bile duct ligation. The animals were separated into groups of 12 animals: group 1 received a saline solution, group 2 the rat recombinant ghrelin, and group 3 the ghrelin receptor agonist. Results showed that liver collagen increased 7-fold compared to control rats. Analysis revealed those animals treated with ghrelin displayed only mild collagen deposits with a decrease in fibrosis of roughly 40%.

Acute liver disease was studied in male rats by forming 3 experimental groups of 8 animals. The control group received saline and olive oil, group 2 was administered saline and carbon tetrachloride (CCl₄ - to induce [liver failure](#)), and group 3 was given CCl₄ along with ghrelin. In the group treated with ghrelin, researchers documented a marked reduction in liver cell damage and a decrease infiltration of inflammatory cells. Further examination found that ghrelin weakened the effects of on CCl₄ on the pathways involved in hepatocyte survival and proliferation.

"In our study, we demonstrate that recombinant ghrelin regulates the fibrogenic response of the liver to acute and chronic disease. Ghrelin naturally produced in the body also inhibits the development of fibrosis in animal models and humans," said Dr. Bataller.

Researchers also analyzed ghrelin serum levels in blood samples from human patients who were asked to fast overnight. The samples collected included 67 patients with chronic hepatitis C, 24 with alcoholic hepatitis, and 24 healthy controls. In both patient groups with liver disease the ghrelin serum levels were significantly lower compared with the healthy control. Lower ghrelin serum levels were found in patients with advanced fibrosis than in those with mild fibrosis.

"Our results indicate that ghrelin may be useful in treating patients with

liver disease and fibrosis by preventing scar tissue formation," suggested Dr. Bataller. In studies that tested ghrelin in patients with anorexia, gastroparesis (slow digestion caused by nerve or muscle damage), cachexia (physical wasting), and chronic heart failure the hormone was well tolerated, causing only a mild decrease in blood pressure. "Further studies should evaluate the safety and efficacy of ghrelin in patients with [chronic liver disease](#)," the authors concluded.

More information: "Ghrelin attenuates hepatocellular injury and liver fibrogenesis in rodents and influences fibrosis progression in humans." Montserrat Moreno, Javier Chaves, Pau Sancho-Bru, Fernando Ramalho, Leandra Ramalho, Maria L Mansego, Carmen Ivorra, Marlene Dominguez, Laura Conde, Cristina Millán, Montserrat Marí, Jordi Colmenero, Juan Lozano, Pedro Jares, Josep Vidal, Xavier Forns, Vicente Arroyo, Juan Caballería, Pere Ginès and Ramón Bataller. *Hepatology*; Published Online: March 1, 2010 ([DOI: 10.1002/hep.23421](#)); Print Issue Date: March 2010.

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