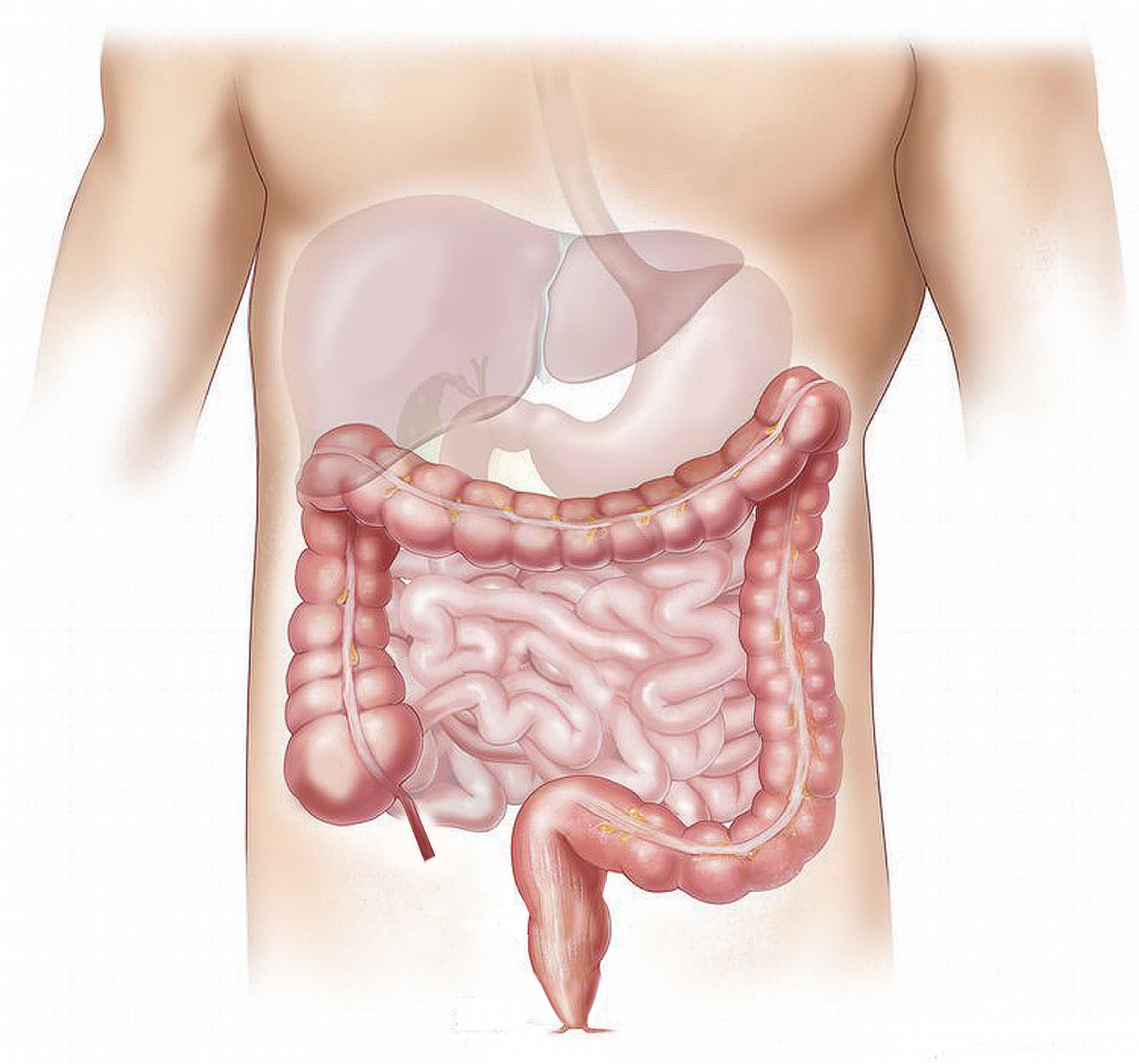
Scientists have found a new mechanism for the liver cell regeneration

August 25 2017



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An international research collaborative has demonstrated for the first time the role of cholangiocytes (epithelial bile duct cells) in liver regeneration. The results of the study are highly promising for regenerative medicine and the fight against liver disease. The team's findings have been published in *Nature*.

The liver is one of the few organs in the human body that is capable of regenerating. In the event of liver damage as a result of trauma or chronic disease, the main liver cells—hepatocytes, which are responsible for all basic liver functions—are able to regenerate by dividing into new hepatocytes. Stimulation of liver regeneration is an acute problem for medical practitioners and researchers, but the details of this mechanism and whether other types of hepatic cells are involved in the process of the formation of new hepatocytes remains unclear.

An international group of scientists used transgenic mice as test subjects; in doing so, they managed to simulate liver damage common to humans. The experiment was carried out on two independent transgenic mouse models, within which the ability of hepatocytes to divide was intentionally reduced in order to evaluate the contribution of other liver cells to regeneration. As a result, it was shown that bile duct epithelial cells—cholangiocytes—are involved in the regeneration of hepatocytes. Also, the scientists suggest that the potential for regeneration in hepatocytes derived from cholangiocytes may be higher than in normal hepatocytes.

Yuri Kotelevtsev, Skoltech Professor and deputy director of the Skoltech Center for Translation Medcine, said, "A little over a year ago, I met with my colleagues from the University of Edinburgh to create joint scientific projects. I told them about how in our research center at Skoltech, under the guidance of Professor Victor Koteliansky, we

managed to adjust the technology of liver gene knockdown. This technology has been well known for about seven years, but its application, in vivo, requires a high experimental level and is still only available in a few academic laboratories. It turned out that the laboratory of Professor Stuart Forbes was working on a problem in the solution of which knockdown could quickly confirm the hypotheses of the key role of cholangiocytes in liver regeneration. The contribution of Skoltech and MIT is that we created and provided lipid nanoparticles with siRNA to beta 1 integrin that blocked the expression of this gene in the hepatocytes in mice, and subsequent observations over the phenotype of the model obtained allowed for the identification of cholangiocytes, which are involved in the regeneration of the liver. Currently, the Scottish Center for Regenerative Medicine, under the leadership of Professor Forbes, is beginning work aimed at isolating and transplanting autologous cholangiocytes to patients with cirrhosis of the liver. We are now continuing the collaboration with Professor Forbes' lab. We are engaged in testing new target genes, the blocking of which could prevent or stabilize the processes associated with fibrosis and subsequent cirrhosis of the liver."

More information: Raven, Alexander, Wei-Yu Lu, Tak Yung Man, Sofia Ferreira-Gonzalez, Eoghan O'Duibhir, Benjamin J. Dwyer, John P. Thomson, et al. "Cholangiocytes Act as Facultative Liver Stem Cells during Impaired Hepatocyte Regeneration." *Nature* 547, no. 7663 (July 20, 2017): 350–54. DOI: 10.1038/nature23015

Provided by Skolkovo Institute of Science and Technology