Medical Xpress

Researchers identify a fundamental protein to guarantee liver regeneration

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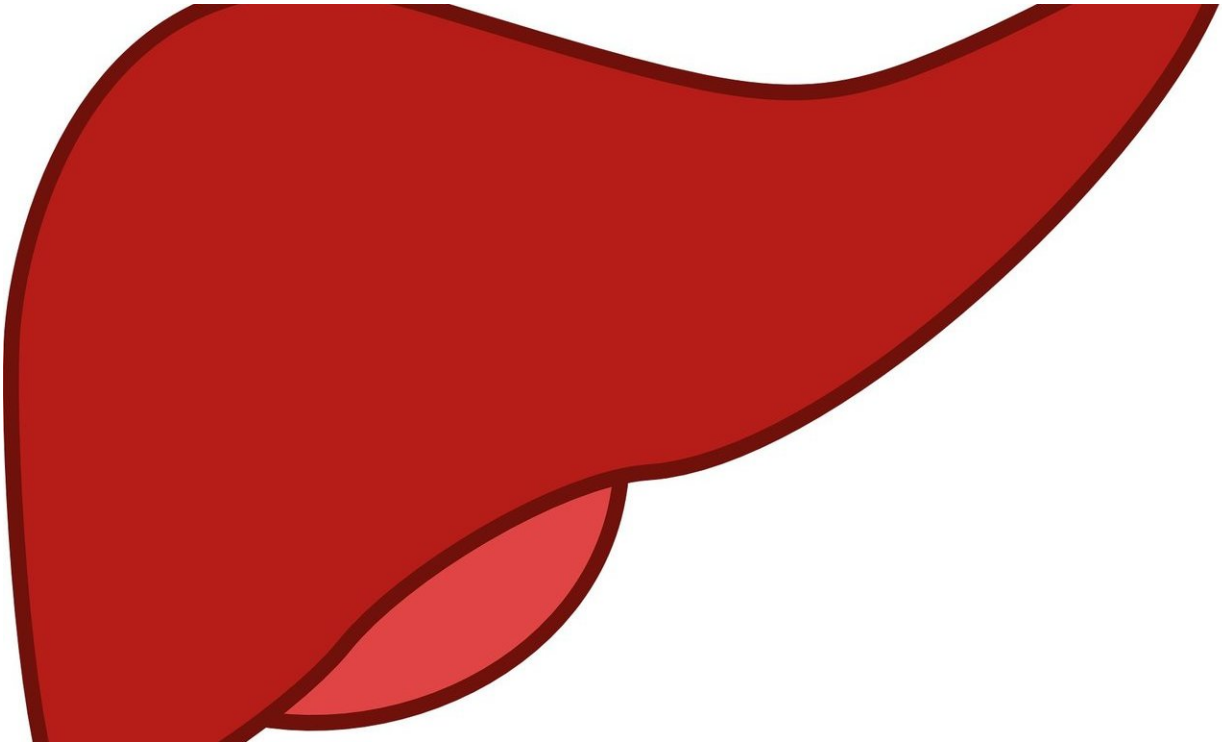

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Researchers from the Faculty of Medicine of the University of Barcelona and the CELLEX Biomedical Research Centre from IDIBAPS, in collaboration with scientists from the University of Sydney, University of London and the Research Institute Sant Joan de Déu, have identified in a study with mice a protein which is fundamental to

guarantee the restoration and regeneration of the liver after a transplant or hepatic surgery.

The study, led by lecturers from the Department of Biomedicine Carles Rentero and Carles Enrich, showed liver regeneration after a resection—an operation which removes a part of the organ—could not happen in mice without the protein Annexin A6 (AnxA6). These results, published in the journal *Hepatology*, could have an impact on the future therapeutic strategy to treat liver damage.

The authors noted that the study is "highly relevant" for the growing number of patients with liver diseases worldwide. For these diseases, the only cure is a liver transplant, generally partial, and then they need the organ to be completely and healthfully restored.

One of the most abundant proteins in the liver

The liver of mammals has the ability to restore after a resection, trauma, or intoxication, as well as in certain physiological situations, such as pregnancy or lactation. This feature of the liver is the basis for success in living donor transplants.

In the study, researchers studied the function of AnxA6, one of the most abundant proteins in the liver, in mice. "This is the first study to identify the function of this protein in the liver in vivo, since its function is quite unknown in physiological processes and disease processes," says Carles Enrich.

The results show how the regeneration of this organ after liver resection did not happen in mice without the mentioned protein, which led to the death of the animals. This was related to an irreversible drop in the levels of glucose in the blood, a fundamental element in hepatic functioning. "To restore a healthy liver after a hepatic resection, the remains of the

organ have to take critical functions, such as maintaining blood glucose levels between meals. For this regeneration to take place, the muscles have to decompose proteins in order to provide its basic constituents, amino acids, so that the cells in the liver can take and use these molecules to create glucose," notes Carles Rentero.

In this sense, researchers saw that mice without AnzA6 did not have basic molecules to start creating glucose. "The study shows that SNAT4 transporters, proteins in the cell membrane that take amino acids, do not appear on the surface of the liver cells in these mice, which makes it impossible to receive fundamental amino acids such as blood alanine, and therefore maintain the production of glucose," notes Carles Enrich.

"Surprisingly," continues the researcher, "the reinsertion of AnxA6 in the liver using gene therapy or putting glucose in a beverage for mice after the surgery restored the survival of these animals."

Potential influence in the research against hepatic damage

According to the researchers, these results shed light on the possibilities regarding whether AnzA6 or blood glucose can play a role when regenerating the liver and lighten liver failure, since it could change medical protocols during the process of liver failure. However, this is very speculative, and it is only a possibility which should be studied," says Carles Rentero.

More information: Anna Alvarez-Guaita et al, Annexin A6 is critical to maintain glucose homeostasis and survival during liver regeneration, *Hepatology* (2020). DOI: 10.1002/hep.31232

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