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Press release
For immediate release

New mechanism discovered in liver metabolism
A specific protein supports energy production in individuals who are overweight

Graz, 11 September 2025: Excess weight is frequently accompanied by profound changes in the metabolism. The liver, which plays a key role in supplying energy to the body, is particularly affected. In individuals with obesity, liver cells are often limited in their ability to convert fats and other nutrients into energy. These disorders can favor the development of other diseases such as fatty liver disease or diabetes. A Med Uni Graz study on this subject was recently published in the journal *Science Translational Medicine*.

Important findings in obesity research at the Medical University of Graz

In the study, a Medical University of Graz research team led by Martin Wagner of the Division of Gastroenterology and Hepatology and Katrin Panzitt of the Diagnostic and Research Institute of Pathology found out that the farnesoid X receptor (FXR) plays a key role in how liver cells produce energy in individuals with obesity. The FXR is a receptor that reacts to signals from bile components and controls the activity of many genes in the liver.

The study examined liver samples from patients who had received either a placebo or the drug obeticholic acid (OCA). OCA is a selective activator of the FXR receptor. It appeared that FXR in individuals with obesity binds more strongly to DNA, taking over the control of metabolic processes.

FXR activation led to an improvement in main functions of the cell powerhouses, the mitochondria. Above all, fat metabolism (ß oxidation) and energy production through oxidative phosphorylation were increased. At the same time, there was a reduction in the formation of harmful oxygen radicals, which can otherwise cause cellular stress.

Mechanisms that protect the liver

Another important finding: In subjects with obesity who had received OCA, the levels of the antioxidant glutathione returned to normal. Glutathione works like a shield against oxidative stress and is critical to the stability and health of liver cells.

"The results indicate that selective activation of the FXR receptor may be able to help treat metabolic disorders associated with obesity and protect the liver cells from harm. As a result, the liver can burn fatty acids better, use energy more efficiently and reduce the amount of damaging byproducts such as free radicals. A promising approach is opening up for future

therapies that not only improve energy production but also increase the resistance of the liver to threats," says co-author Katrin Panzitt.

"The findings are based on extensive analysis of the (epi)genome, which has only become possible through specially developed bioinformatic analysis procedures. Co-first author Emilian Jungwirth, who did a doctorate in our group, developed these methods in cooperation with TU Graz," adds project leader Martin Wagner.

Link to the study:
https://www.science.org/doi/10.1126/scitranslmed.adn4558

Further information and contact

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Profile of Martin Wagner
After receiving his doctorate, Martin Wagner worked in positions as a third-party funded assistant, postdoctoral research associate, intern and resident physician as well as an assistant professor. In 2014 he finished his habilitation in the field of internal medicine and became a medical specialist. Since 2016 he has worked as an associate professor. Wagner is head of the Translational Nuclear Receptor Research in Liver Metabolism research unit at the Division of Gastroenterology and Hepatology. His main research areas are molecular biology, gastroenterology and hepatology, in particular cholestase, nuclear receptors, autophagy, bile acid metabolism and metabolic-associated fatty liver disease.

Profile of Katrin Panzitt
After receiving her doctorate at the Med Uni Graz Institute of Pathology, Katrin Panzitt was a postdoc in Graz and then at Baylor College of Medicine in Houston before returning to Graz in 2013. In 2021 she finished her habilitation and was granted the right to teach at the university level (*venia legendi*). Her main research areas are pathophysiology, medicinal molecular biology and gastroenterology with a special emphasis on noncoding RNA, nuclear receptors and ChIP analysis.