Researchers use the eye as a window to study liver health

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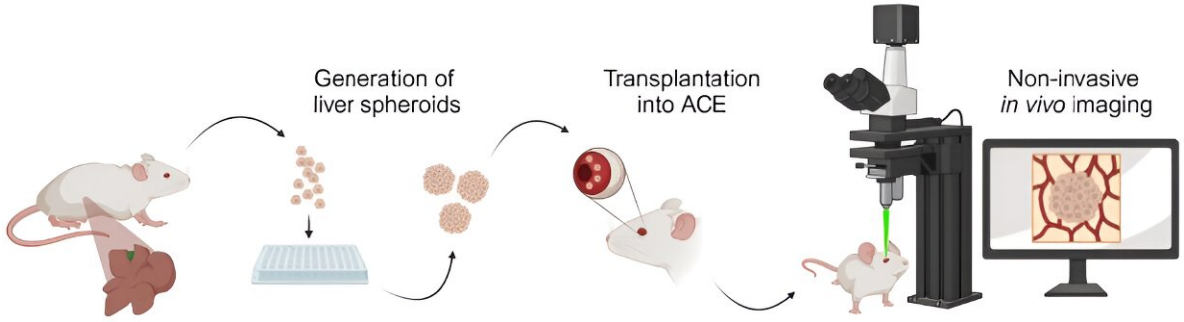

Experimental design of anterior chamber of the eye (ACE) in vivo imaging platform: liver spheroids were generated from primary liver cells (enriched for hepatocytes) and transplanted into the ACE of recipient mice, where they can be longitudinally imaged through the cornea by confocal microscopy. Credit: *Nature Communications* (2024). DOI: 10.1038/s41467-024-45122-4

Researchers at Karolinska Institutet have developed a method to study liver function and disease without requiring invasive procedures. After transplanting liver cells into the eye of mice, the cornea can be used as a window into the body to monitor liver health over time. The study is published in the journal *Nature Communications*.

Imagine if it were possible to study liver cells in a living organism without the need for invasive procedures. Researchers have now shown

that this is possible in mice by transplanting small 3D cell cultures of liver cells, known as spheroids, into the anterior chamber of the eye. The cornea of the eye is then used as a window into the body to get clues about changes in the liver during the mouse's lifetime.

The researchers were able to show that the liver cells attach to the iris of the eye and are supplied with blood vessels and nerves necessary for their function and survival. They also retain their typical liver characteristics and appear to reflect the health of the animal's liver. For example, the spheroids in the eye were found to store fat in a similar way to the liver of the same animal when fed a high-fat diet, meaning that the implant could act as a marker for fatty liver disease.

"This is a unique approach that opens up new opportunities to study the role of the liver in metabolic diseases such as obesity, type 2 diabetes and fatty liver disease," says Noah Moruzzi, assistant professor at the Department of Molecular Medicine and Surgery, Karolinska Institutet and corresponding author of the paper.

"In order to stop or delay disease progression, we need to identify early disease mechanisms, but it has previously been difficult to study the liver without using invasive methods."

Metabolic diseases have increased dramatically in recent years and were previously associated with old age, but today they increasingly develop in younger individuals and obese children. These disorders share similar risk factors and are often presented together in patients with metabolic syndrome. Fatty liver and type 2 diabetes are characterized by dysfunctional lipid metabolism and blood sugar regulation, controlled by the liver and pancreas, respectively.

"Therefore, continuous and detailed monitoring of functional changes in these organs is essential to identify disease mechanisms," says first

author Francesca Lazzeri-Barcelo, Ph.D. student at the same department. "With the new platform, we can now monitor the development of fatty liver at the cellular level and we are excited to start using it to test different drugs and treatment strategies."

Professor Per-Olof Berggren's research group at Karolinska Institutet has been transplanting cells and mini-organs to the anterior chamber of the eye in mice since 2008.

"In recent years, our method has proven to be a powerful research tool for monitoring the insulin-producing pancreatic islets during the development of type 2 diabetes," he says. "Now the platform has been extended to liver research, which shows that there is potential to use the tool also in other medical areas."

More information: Francesca Lazzeri-Barcelo et al, Intraocular liver spheroids for non-invasive high-resolution in vivo monitoring of liver cell function, *Nature Communications* (2024). DOI: 10.1038/s41467-024-45122-4

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