“Satellite Livers” May Improve Care for End-Stage Liver Failure

Liver cell grafts can restore liver function, according to a new MIT study.

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Liver transplant is considered the only effective treatment for end-stage liver disease, but transplantation comes with risks, including organ rejection and disease recurrence, as well as barriers, such as eligibility and availability. A new study, published in Cell Biomaterials, showed that liver function can be restored when a collection of human liver cells is injected into the fat tissue of mice, offering a potential new treatment option for liver failure.

“We think of these as satellite [or mini] livers,” said Sangeeta Bhatia, MD, PhD, senior author on the paper, in an MIT press release. “If we could deliver these cells into the body, while leaving the sick organ in place, that would provide booster function.”

Over time, chronic hepatitis B, hepatitis C, heavy alcohol consumption and metabolic dysfunction-associated fatty liver disease (MASLD) can lead to serious liver complications, like cirrhosis and hepatocellular carcinoma (HCC), the most common form of liver cancer. End-stage liver disease, or chronic liver failure, is often the result of cirrhosis or HCC.

Getting onto the transplant list involves an extensive evaluation process to determine eligibility and need. According to the United Network for Organ Sharing (UNOS), 8,815 people are currently on the waiting list for a new liver in the United States; however, numerous individuals on that list will not receive a new organ because there are not enough livers to go around.

To learn more about liver transplants, read Hep’s Liver Complications: Liver Transplants Basics. In part, it reads:

> “In some cases, hepatitis causes liver cancer or severe damage to the liver, resulting in end-stage liver disease and ultimately liver failure. At this time, the only effective treatment for end-stage liver disease is a liver transplant.

> The first human liver transplant was attempted in Denver, Colorado, in 1963 by a team headed by Thomas Starzl, MD. Four years later, the procedure was performed successfully. Survival rates have been steadily improving, particularly with the introduction of anti-rejection medications. Liver transplantation is a complicated surgery, requiring lifelong follow-up care. However, liver transplant recipients are usually able to return to normal activities after recovering for several months.
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> Transplant Evaluation
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> You may be referred for a transplant evaluation, although you may not actually need a liver transplant. The evaluation is an extensive process, conducted by a transplant team. Eligibility is determined on a case-by-case basis, but there are general guidelines. Some of these criteria are absolute and some are relative, depending on the practices of specific transplant centers."

For the satellite liver study, the researchers injected human liver cells, or hepatocytes, to precise locations in the fat tissue of mice via guided ultrasound. The human hepatocytes were injected alongside fibroblast cells, which promote blood vessel growth, and hydrogel microspheres, which act as scaffolding for the liver cells.

"If the cells are injected in the absence of these spheres, they would not integrate efficiently with the host, but these microspheres provide the hepatocytes with a niche where they can stay localized and become connected to the host circulation much faster," said Kumar, the paper's lead author, in the MIT press release.

The liver cells survived in the fat tissue of mice for eight weeks, the entire length of the study, suggesting it may be a viable option for long-term treatment of liver disease. Unlike current clinical liver cell infusions, the cells of these tissue grafts do not diffuse throughout the body because of the specific contents (hydrogel microspheres and fibroblasts) of the satellite livers. An injection of liver cells is minimally invasive, and these satellite livers would not be in limited supply, eliminating two major issues regarding liver transplant.

"Unlike organ transplantation, which requires specialized surgical teams, intensive perioperative care, and centralized transplant centers often far from patients, ultrasound-guided, injectable grafts could be implemented in a wider range of clinical settings with reduced infrastructure demands," wrote the study's authors.

The technique still has room for improvement, where incorporating different cells, like epithelial cells, into the scaffolding could allow for tailored treatments. Even varying the degradation of

microspheres in the same graft could change treatment, where initially vessel growth and remodeling is favored and the more stable parts of the microspheres provide long-term mechanical support. Injectable satellite livers need further testing before reaching a clinical setting, but this study shows promise for the future.

“The way we see this technology is it can provide an alternative to surgery, but it can also serve as a bridge to transplantation where these grafts can provide support until a donor organ becomes available,” said Kumar in the MIT press release. “And if we think they might need another therapy or more grafts, the barriers to do that are much less with this injectable technology than undergoing another surgery.”
