

# Cell transplantation procedure may one day replace liver transplants

August 26 2015

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Liver transplantation is currently the only established treatment for patients with end stage liver failure. However, this treatment is limited by the shortage of donors and the conditional integrity and suitability of the available organs. Transplanting donor hepatocytes (liver cells) into the liver as an alternative to liver transplantation also has drawbacks as the rate of survival of primary hepatocytes is limited and often severe complications can result from the transplantation procedure.

In an effort to find potential therapeutic alternatives to whole [liver transplantation](#) and improve the outcomes of hepatocyte transplantation, this study tested the therapeutic efficacy and feasibility of transplanting multi-layered sheets of hepatocytes and fibroblasts ([connective tissue cells](#)) into the subcutaneous cavity of laboratory rats modeled with end stage [liver failure](#). The results of the study demonstrated that the cells in the multi-layered hepatocyte sheets survived better than cells transplanted by traditional methods and that the cells proliferated, maintaining liver function in the test animals for at least two months.

Their study will be published in a future issue of *Cell Transplantation* and is currently freely available on-line as an unedited [early e-pub](#).

"Until now, no studies have successfully investigated the use of hepatocyte sheet engineering therapy for treating liver disease," said Dr. Susumu Eguchi of the Nagasaki University Graduate School of Biomedical Sciences in Nagasaki, Japan. "Our study demonstrated that multi-layered hepatocyte sheets generated from primary hepatocytes and

primary skin fibroblasts were able to proliferate after transplantation and support the host liver function while improving the serum albumin level up to the normal range within two months."

The researchers called the fibroblasts "feeder cells" that helped preserve the "high viability and functionality" of the hepatocytes in both in vitro and in vivo studies. The researchers also noted that in other methods of hepatocyte transplantation such as intrasplenic (through the spleen) or intraportal, only a small number of hepatocytes can be transplanted at one time, and many die. By contrast, the transplanted cell sheets showed "dramatically higher albumin expression levels" in vivo one month after transplantation into the subcutaneous cavity.

"Hypoxia is a major cause of poor hepatocyte survival" wrote the researchers. "Therefore, immediately after transplantation, all transplanted cells are supplied with oxygen only from surface diffusion because of the lack of capillary vessels when other methods of transplantation are used."

However, in the current study it was observed that merely one week after transplantation, the hepatocyte sheets were permeated with multiple capillary vessels, reported the researchers. That the hepatocytes were close to blood vessels confirmed that vascularization is crucial for their survival and function, they said.

"Tissue engineering has become an attractive target for regenerative medicine, and we believe that hepatocyte sheet transplantation technology offers a great therapeutic opportunity both for the treatment of metabolic liver diseases and providing support for [liver function](#) in patients with end stage [liver](#) failure," concluded the researchers.

"Stratifying hepatocytes on non-parenchymal cells has been shown to contribute to hepatocyte survival and functional integrity" said Dr.

Stephen Strom, Professor at the Department of Laboratory Medicine, Division of Pathology at Karolinska Institutet in Sweden. "The observed benefits may likely be attributed to the non-parenchymal cells, fibroblasts in this case, conferring essential cytokines and extracellular matrix (ECM) components to the hepatocytes. The present study contributes to the current dialogue about this technique by elucidating some of the physiological mechanisms underpinning its effectiveness. Future studies should be aimed at further assessing the clinical potential of this method."

**More information:** Baimakhanov, Z.; Yamanouchi, K.; Sakai, Y.; Koike, M.; Soyama, A.; Hidaka, M.; Takatsuki, M.; Fujita, F.; Kanetaka, K.; Kuroki, T.; Eguchi, S. Efficacy of multi-layered hepatocyte sheet transplantation for radiation-induced liver damage and partial hepatectomy in a rat model. *Cell Transplant*. Appeared or available online: July 28, 2015. [ingentaconnect.com/content/cog...](http://ingentaconnect.com/content/cog...)  
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Provided by Cell Transplantation Center of Excellence for Aging and Brain Repair

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