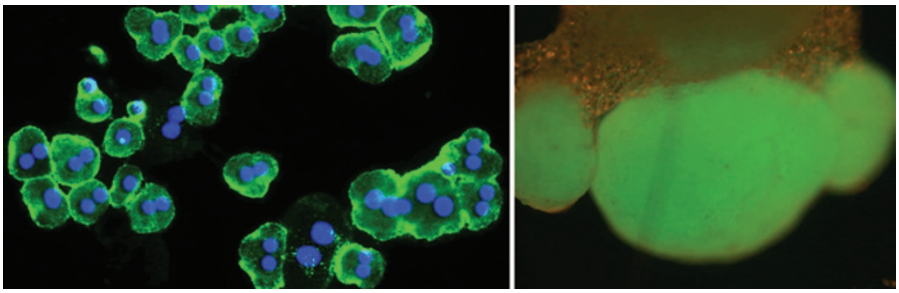
TRANSPLANTATION

Functional ectopic liver tissue in the lymph nodes of mice with lethal liver disease

Owing to a shortage of donor organs, hepatocyte transplantation has the potential to become an important therapeutic alternative for patients with severe liver disease. Furthermore, hepatocyte transplantation could be particularly useful in patients in whom orthotopic liver transplantation is not possible, such as patients of advanced age or those who have comorbidities. However, hepatocyte transplantation has its own set of challenges and drawbacks. One such problem is that many patients with liver disease have cirrhosis and fibrosis, which limits the potential for cell-based therapy.

Previous animal studies have investigated the possibility of hepatocyte transplantation into extrahepatic sites, but with variable results. Eric Lagasse and colleagues decided to investigate whether functional ectopic liver tissue could be developed in the lymph nodes.

Hepatocytes were transplanted by intraperitoneal injection into fumarylacetoacetate hydrolase (*Fah*$^{-/-}$) mice, a model of the human liver disease tyrosinemia type I. 10 weeks after transplantation, these mice demonstrated improvements in their serum levels of aminotransferases, bilirubin and amino acids. Expansion of hepatocytes rescued the mice from lethal hepatic failure.



Hepatocytes (left-hand panel) and functional liver tissue in the lymph nodes of mice (right-hand panel). Courtesy of E. Lagasse.

The authors speculate that the successful engraftment and expansion of hepatocytes in the lymph nodes (compared with other extrahepatic sites) is due to the highly vascularized nature of these organs.

"We are very interested in the possibility of translating this research into patients, and we are in discussion about the potential for a clinical trial in patients with liver diseases," concludes Lagasse.

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Original article Hoppo, T. *et al.* Rescue of lethal hepatic failure by hepatized lymph nodes in mice. *Gastroenterology* **140**, 656–666 (2011)