Beyond liver transplants: Acutely damaged livers may be repaired via transplanted hepatocytes

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A research team from the National Taiwan University Hospital has evaluated the efficiency of transplanted hepatocyte (liver) cells in animal models severely damaged by two kinds of chemical toxicity to see whether and how transplanted hepatocytes were able to efficiently repopulate the toxin-induced, severely damaged livers.

The results of this study are published in the current double issue of *Cell Transplantation* (18:10/11) and are freely available on-line at http://www.ingentaconnect.com/content/cog/ct/.

The study was carried out in the on-going effort to evaluate hepatocyte transplantation as an alternative to liver transplantation, not only because of the current shortage of liver donors for transplantation, but also because successful cell transplantation is simpler, less invasive and less expensive than organ (i.e., liver) transplantation.

The researchers found that animal model of livers with damage induced from combined retrosine-plus-D-galactosamine (as opposed to animals infused with single toxins) were subject to "massive repopulation of the liver by transplanted hepatocyte cells and hepatocyte growth factor genes."

"We observed rapid infiltration of transplanted hepatocytes into the necrotic and inflammatory hepatic parenchyma within 24 hours of the

R+D-gal treated liver, but not the D-gal alone or R-alone treated livers," reported corresponding author Dr. Mei-Hwei Chang. "This result suggests that the higher proliferative activity of transplanted hepatocytes (as compared to host hepatocytes) take over regeneration signals and proliferate. This finding is clinically important because hepatocyte growth factor (HGF) and levels of transforming growth factor-a (TGF-a) - which are known to stimulate cell proliferation - are strongly elevated in patients with acute liver failure." Post-hepatocyte transplantation, the researchers also analyzed hepatic stellate cell (HSC) activation and matrix metalloproteinase expression (MMP2). They found that HCS activation, which is crucial in liver repair after hepatic damage and plays a role in hepatocyte engraftment, was prolonged, but declined after four weeks.

"This suggests that prolonged activation of HSC in acute hepatic injury is beneficial to the proliferation of transplanted cells," commented Dr. Chang.

The researchers also noted that the expression and activity of MMP2 genes were "consistent with the kinetics of HSC activation."

"This is an interesting model where massive liver cell death is imposed over a background where the native liver fails to regenerate," said section editor Dr. Stephen Strom, professor in the Division of Cellular and Molecular Pathology at the University of Pittsburgh. "These are important pre-clinical studies because of the similarities of this model to Acute Liver Failure (ALF) in human patients. The enhanced proliferation of donor cells following transplantation helps to explain why the transplantation of even relatively small numbers of hepatocytes can reverse liver failure."

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