McGowan Institute for Regenerative Medicine
A program of the University of Pittsburgh and UPMC

Metabolic Disorder Treatment Through Liver Cell Transplant

Management of patients with hepatic failure and liver-based metabolic disorders is complex and expensive. Hepatic failure results in impaired coagulation, altered consciousness and cerebral function, a heightened risk of multiple organ system failure, and sepsis. Liver transplantation is often the only available treatment option for severe, even if transient, hepatic failure. Patients with life-threatening liver-based metabolic disorders similarly require organ transplantation even though their metabolic diseases are typically the result of a single enzyme deficiency, and the liver otherwise functions normally.

More than 17,000 patients currently await liver transplantation in the United States, a number that seriously underestimates the number of patients that need treatment, as it has been estimated that more than a million patients in the United States could benefit from transplantation. Unfortunately, use of whole liver transplantation to treat these disorders is limited by a severe shortage of donors and by the risks associated with major surgery. Hepatocyte transplantation holds great promise as an alternative to organ transplantation for the treatment of liver diseases, and numerous pre-clinical studies indicate that transplants consisting of isolated liver cells can correct various metabolic deficiencies of the liver and can reverse hepatic failure.

The study transplant procedure headed by Ira Fox, MD (director of the Center for Innovative Regenerative Therapies, a collaborative effort between the Children's Hospital of Pittsburgh of UPMC and the McGowan Institute for Regenerative Medicine, and a professor of surgery at the University of Pittsburgh School of Medicine), which involves injection of isolated hepatocytes into the liver through the portal vein, is far less intrusive than transplantation of the whole liver and could be performed on severely ill patients with relatively low risk. In the presence of normal host liver architecture, the transplanted cells integrate into the host liver, providing considerable restorative potential. Because the native liver is not removed, the transplanted hepatocytes need only improve some of the functions of the failing liver and need not replace all hepatic functions.

Although clinical trials of hepatocyte transplantation have demonstrated the long-term safety of the procedure, only partial correction of metabolic disorders has been achieved, and the degree to which donor hepatocytes have restored failing livers has not been adequate to circumvent the need for organ replacement.

As reported by Jessica Wapner, *Scientific American*, hepatocyte transplantation could treat an estimated half of the metabolic disorders currently indicated for liver transplants, replacing "perhaps up to 10 percent of pediatric transplant candidates," Dr. Fox says, along with many

adult patients. Anyone living with phenylketonuria (PKU)—the disorder occurs in about 1 of every 15,000 newborns in the U.S.—could also benefit. The most common indications for adult liver transplant, cirrhosis-induced liver failure and hepatitis C, cannot be treated by cell-only transplantation because the abnormal structure of the diseased organ will not allow new cells to survive.

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Scientific American

Children's Hospital of Pittsburgh of UPMC Transplant Study

ClinicalTrials.gov: Hepatocyte Transplantation for Liver Based Metabolic Disorders

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