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Positions:

Professor, Departments of Medicine, of Cell Biology and of Pathology
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Research interests:

A number of years ago, we developed a cell transplantation system to follow the proliferation, lineage fate and repopulation capacity of liver stem/progenitor cells, using a marker gene, dipeptidyl peptidase IV (DPPIV). This cell transplantation system has also been used to identify stem cells in the fetal liver that are bipotent, proliferate extensively for up to one year after their transplantation, differentiate into both hepatocyte and bile duct cells, form completely new liver lobules and replace 25-30% of hepatic mass in normal adult rats. With fetal liver stem/progenitor cells, liver replacement occurs by cell competition, a mechanism originally described in *Drosophila* during embryonic wing development more than 30 years ago. Current studies are focused on four major projects: 1) isolation and characterization of liver stem cells, 2) repopulation of the liver by transplantation of fetal liver stem cells and identifying genes that regulate this process by a mechanism of cell competition; 3) identifying genes that increase liver gene replacement in aging rats by augmenting cell competition, and 4) treatment of chronic liver diseases by *ex vivo* gene therapy, using stem cells and reengineered hepatocytes exhibiting augmented proliferative activity to more effectively repopulate the liver. In other studies, we have transplanted human cord blood stem cells into NOD/Scid mice with conversion of some of these cells into hepatocytes. We are also studying the ability of human and mouse embryonic stem (ES) cells to differentiate into hepatocytes and repopulate the liver and are planning to study liver repopulation by transplanted iPS cells. The long-range goal of these and other above studies is to identify methods to effectively repopulate the human liver with engineered hepatic-derived cells.

Current grant funding:

RO1 DK17609-34A1 (Shafritz) NIH/NIDDK	07/01/2008–06/30/2013 (no-cost extension) Protein synthesis in normal and regenerating liver
P30 DK41296-21 (Shafritz) NIH/NIDDK	06/01/2009–05/31/2014 Liver Pathobiology and Gene Therapy Research Core Center

Five recent publications:

1. Oertel M, Menthena A, Dabeva MD, Shafritz DA. Cell competition leads to a high level of normal liver reconstitution by transplanted fetal liver stem/progenitor cells. ***Gastroenterology,*** 2006, 130:507–20.
2. Nierhoff D, Levoci L, Schulte S, Goeser T, Rogler LE, Shafritz DA. New cell surface markers for murine fetal hepatic stem cells identified through high density cDNA microarrays. ***Hepatology***, 2007, 46:535–47.
3. Oertel M, Menthena A, Chen YQ, Teisner B, Harken-Jensen C, Shafritz DA. Purification of fetal liver stem/progenitor cells containing all the repopulation potential for normal adult rat liver. ***Gastroenterology*** 2008, 134:823–32.
4. Shafritz DA, Oertel M. Model systems and experimental conditions that lead to effective repopulation of the liver by transplanted cells. ***Int. J. Biochem. Cell. Biol.*** 2011, 43:198–213.
5. Menthena A, Koehler CI, Sandhu JS, Yovchev MI, Hurston E, Shafritz DA, Oertel M. Activin A, $p^{15INK4b}$ signaling, and cell competition promote stem/progenitor cell repopulation of livers in aging rats. ***Gastroenterology***. 2011, 140:1009–20.