Role of liver sinusoidal endothelial cell (LSEC) progenitors in liver regeneration

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Background: Current thinking is that LSEC play an important role in liver regeneration by providing HGF and restoring the microcirculation. However normal LSEC express little HGF. Our hypothesis is that influx of LSEC progenitor cells (PC) provide the increased HGF and are essential for liver regeneration.

Methods: Bone marrow (BM) and peripheral blood CD133+CD45+CD31+ LSEC PC were isolated by magnetic selection. LSEC PC in the liver were isolated from elutriated LSEC. Bone marrow-derived cells were tracked in rats transplanted with BM from GFP+ transgenic rats. Liver regeneration was examined in the two-thirds partial hepatectomy (PHx) model. BM suppression was induced by long bone irradiation. HGF expression was examined by real-time PCR and western blot.

Results: On day 3 following PHx, there was a 1.5-2-fold increase in LSEC PC proliferation (PCNA stain) in BM and in number of LSEC PC in BM and peripheral blood; 25% of LSEC were of BM origin. HGF mRNA and protein in GFP+ LSEC were 4 to 5-fold higher than in GFP- LSEC. On day 5 following PHx, liver weight of BM suppressed rats was 25% lower than controls; LSEC PC or BM infusion on day 1 increased hepatocyte PCNA+ (5.7 ± 1.0 PCNA+ hepatocytes/HPF vs 14.75 ± 1.5 in LSEC PC infused, p<0.001) and normalized liver regeneration (liver weight p<0.0005: no infusion vs LSEC PC infusion).

Conclusions: Bone marrow LSEC PC are a major contributor to the HGF increase after liver injury. LSEC PC recruitment to the liver is required for normal liver regeneration.

Biography

Assistant professor of Dept. of Hepatic Surgery in Xijing hospital, Xi’an P.R.China. Previously worked in University of Southern California for nearly two years. Mainly worked on liver sinusoidal endothelial cell. Recently found a population of unique progenitor cells for liver sinusoidal endothelial cells. Related findings have been published on Gastroenterology, Hepatology, Plos One etc.