

Hepato-Gastroenterology/Lipids

Effect of host liver cell proliferation on homing and phenotype of transplanted hepatic stellate cells after partial hepatectomy in rats

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Partial hepatectomy (PH) is a classical model of acute liver damage. Restoration of parenchymal and nonparenchymal liver cell populations after PH has its own dynamic of proliferation and differentiation. One of the proliferating cells markers is Ki-67, chosen in our study to determine regenerating cell population. Differentiation of liver cells is under control of hepatic stellate cells (HSC) that create microenvironment for progenitor cells during liver development and regeneration. At the same time HSC are regional stem cells of the liver. The aim of the study was to determine the influence of host liver cell proliferation on homing and phenotype of transplanted HSC after PH in rats.

Rat HSC were isolated by collagenase-pronase perfusion of the liver with further gradient centrifugation in histodenz. We had 2 experimental groups: 1) PH without transplantation; 2) PH with intraportal transplantation of HSC, transduced with adenoviral vector containing red fluorescent protein (RFP) to visualize transplanted cells. Liver paraffin slices (1,5,7,14,21,28 days after transplantation) were stained with antibodies against Ki-67, RFP, desmin (HSC marker), CK19 (cholangiocytes marker).

In both groups during the first 7 days actively proliferated only hepatocytes, during 7-14 days number of Ki-67+hepatocytes decreased, after 14 days appeared proliferating Ki-67+ HSC; Ki-67+cholangiocytes were only detected after 21 days. Thus, after PH first proliferate hepatocytes, then start nonparenchymal HSC and the last react cholangiocytes. Transplanted RFP+cells during the first week retained morphology and phenotype of hepatocytes, after 14 days they were RFP+/Desmin+ HSC, after 21 days

found as RFP+/CK19+ cholangiocytes. Localization and phenotype of transplanted cells is strongly related with dynamic of host hepatic cell population proliferation. Work supported by Program of Competitive Growth of KFU.