Editorial

Oval cells in the liver: A putative stem cell compartment

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In animal models of liver regeneration and carcinogenesis a distinct cell population has been identified. They were named by Farber (1956) as oval cells due to their oval nucleus and a high nuclear to cytoplasmic ratio. There is evidence that they represent a heterogeneous population the majority of which have a dual phenotype as they express hepatocyte and bile duct antigens. They also express markers characteristic of stem cells such as "stem cell factor" and its receptor c-kit, bcl2, and cytokeratin 14. In rodents they are considered as facultative and bipotent progenitors either of hepatocytes or cholangiolar cells as they can transform to mature hepatocytes or bile duct epithelial cells.[1-5]

The putative stem cell in human liver has long been sought by numerous investigators and currently there is strong evidence that rodent's oval cell counterpart exist in normal liver. These cells are the progeny of biliary located stem cells, scattered most probably in any part of the intrahepatic biliary system. Recent research indicates that the canals of Hering consist of or harbot facultative hepatic stem cells with features of oval cells. The stimulus for oval cell proliferation occurs during liver injury regardless of aetiology and is a feature of liver cell regeneration and inflammatory diseases of hepatitic or cholestatic type. Published data indicate that the extent of oval cell proliferation relates to the severity of inflammatory liver diseases and as they function as stem cells they may represent a vulnerable compartment to carcinogenic influences with subsequent development of hepatocellular or cholangiolar carcinoma. Oval cells are not detectable by light microscopy unless they have undergone marked proliferation but even then they must be visualised by immunohistochemical or molecular biology methods in order to reveal their dual differentiation and stem as cell phenotype. They express a-fetoprotein, albumin and as they lack the BDI antigen which characterises mature bile duct epithelium the hepatocytic differentiation become evident. They also express cytokeratins characteristic of biliary epithelial cells such as keratin 19 and enzymes specific to bile ducts as well as other antigens such as OV-6 and the glutathione-S-transferases (GST).

In the current issue of this journal the paper of Tsamantas et al[6] refers to the role of oval cells in chronic hepatitis B and C. They claim that by using abs to CK19 and GST-π they can detect true oval cells but until now for definite identification of oval cells it is essential to demonstrate the dual epithelial phenotype of this type of cell as well as markers of its stem cell state. Nevertheless their work is in line with recent studies that indicate oval cell proliferation in viral hepatitis, an observation that requires further evaluation as to its significance in the evolution of chronic hepatitis and liver carcinogenesis.

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