Let’s make liver

Detoxification is what livers do best, and regenerating after toxic insults is what livers do second best. All that proliferative capacity suggests that liver stem cells might be a very different and more prevalent beast than stem cells from other organs. But, on page 173, Suzuki et al. report that the fetal mouse liver, just like the adult bone marrow, has as its founder a relatively rare and undifferentiated cell type.

Suzuki et al. have attempted to isolate liver stem cells before, but their isolation strategy fell short of allowing clonal analysis. Now they add one additional selection marker (cMet, the receptor for hepatocyte growth factor) and use cell sorting to achieve a 560-fold enrichment for hepatic colony-forming units in culture (H-CFU-Cs). These single cells do not express markers for either hepatocytes or cholangiocytes (the cells that form bile ducts), and are capable of self-renewal both in vitro (single cells can be replated to yield more undifferentiated cells) and in vivo (recently divided cells have the undifferentiated phenotype). Signs of differentiation arise, however, with longer times in culture.

Even more extensive differentiation can be seen in vivo, with transplanted H-CFU-Cs growing to form functional parts of liver, bile duct, pancreas and intestine. Thus, Suzuki et al. may have discovered an endodermal stem cell, or at least a liver stem cell with impressive abilities to transdifferentiate if placed in the right environment. This flexibility may be paired with the superior proliferative capabilities of differentiated hepatocytes during the process of liver regeneration.