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Stem cell populations giving rise to liver, biliary tree and pancreas

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Abstract

Multiple populations of determined endodermal stem cells are present in stem cell niches, peribiliary glands (PBGs), found throughout the biliary tree in donors of all ages. PBGs are connected to intrahepatic niches, canals of Hering, and toniches of committed progenitors, pancreatic duct glands (PDGs). The phenotypic traits of the most primitive of these stem cell populations include expression of both liver and pancreatic transcription factors, multiple pluripotency genes, and various other stem cell markers, but not mature cell markers. Their highest numbers are in the hepato-pancreatic common duct and large intrahepatic bile ducts. Their descendants have phenotypic traits implicating maturational lineages along a radial axis within bile duct walls and a proximal-to-distal axis from duodenum to mature cells near or in the liver or pancreas. The stem cells and the maturational lineages constitute a biological framework for hepatic and pancreatic organogenesis throughout life.

The stem cell subpopulations can be isolated by immunoselection and established in culture under wholly defined conditions for self-replication versus for differentiation to various adult fates including hepatocytes, cholangiocytes, or pancreatic islets. Clinical trials are ongoing with hepatic stem cells transplanted via the hepatic artery into the liver of patients with various diseases. Immunosuppression was not required. The transplants have resulted in significant improvements in liver functions and in longer life spans for patients. Our findings suggest great potential for utilizing these stem cell populations in grafts of defined microenvironments for regenerative medicine for liver and pancreas.

Biography

L.M. Reid is a Professor at the UNC School of Medicine, Chapel Hill, NC with a 30+ year career of investigations on mechanisms governing cell differentiation. She pioneered efforts to prove that the liver is organized in maturational lineages of epithelial-mesenchymal partners, with both cell types being derived from stem cells. She and her collaborators were the first to identify rodent and human hepatic stem cells that form liver and now humanbiliary tree stem cells that give rise to both liver and pancreas. She has more than 170 publications and more than 200 patents.