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Glands of bile and pancreatic ducts as a niche of biliary stem cells and pancreatic committed progenitors

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Peribiliary glands (PBGs) in bile duct walls (Carpino et al., 2012), and pancreatic duct glands (PDGs) associated with pancreatic ducts contain a continuous, ramifying network of cells in overlapping maturational lineages (Wang et al., 2013). Our aims have been to investigate the presence of stem/progenitor cells within glands associated with bile and pancreatic ducts. Our results showed that proximal (PBGs)-to-distal (PDGs) maturational lineages start near the duodenum with cells expressing markers of pluripotency (NANOG, OCT4, and SOX2) and proliferation (PCNA), and early hepato-pancreatic commitment (SOX9, SOX17, PDX1, and LGR5), transitioning to PDG cells with no expression of pluripotency or self-replication markers, maintenance of pancreatic genes (PDX1), and expression of markers of pancreatic endocrine maturation (NGN3, MUC6, and insulin). Biliary tree-derived cells behaved as stem cells in culture under expansion conditions, proliferating for months as undifferentiated cells; on the other hand, pancreas-derived cells underwent only approximately 8-10 divisions, then partially differentiated towards an islet fate. Both could be driven for an islet fate (HDM-P), to form spheroids with ultrastructural, electrophysiological and functional characteristics of neo-islets, including glucose regulatability. Implantation of these neo-islets into epididymal fat pads of immunocompromised diabetic mice was able to alleviate hyperglycemia by the secretion of glucose-regulated human C-peptide.

References

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Keywords

Peribiliary glands, stem cell, multipotent, bile duct.