

Gallbladder is a highly available source of multipotent progenitor/stem cells with hepatocyte, cholangiocyte and pancreatic potentialities

Guido Carpino^{1,2}, Vincenzo Cardinale¹, Raffaele Gentile¹, Paolo Onori³, Rossella Semeraro¹, Antonio Franchitto¹, Daniela Bosco¹, Angelo Iossa¹, Chiara Napoletano¹, Giuseppe D'Argenio⁴, Marianna Nuti¹, Nicola Caporaso⁴, Pasquale Berloco¹, Lola Reid⁵, Domenico Alvaro¹ and Eugenio Gaudio¹

¹"Sapienza" University of Rome, Rome, Italy

²University of Rome "Foro Italic", Rome, Italy

³University of L'Aquila, L'Aquila, Italy

⁴University of Naples "Federico II", Naples, Italy,

⁵University of North Carolina at Chapel Hill, NC, USA

Biliary tree stem/progenitor cells (BTSCs) have been identified in glands of normal human extrahepatic bile ducts (Mancino M et al., 2007; Gaudio et al., 2009) and are able to generate in vitro and in vivo mature cells of the hepato-biliary and pancreatic endocrine lineages (Carpino et al., 2012). The aims of the present study have been to investigate in normal and pathological gallbladders: i) the presence and location of BTSCs and ii) the possibility to isolate, culture and differentiate BTSCs. Our results showed that, in normal and pathological gallbladders, the surface epithelium contained cells with the phenotype of BTSCs. Tissue digestion resulted in the isolation of 15 ± 3.7 and 13.3 ± 3.6 million viable cells from normal and pathological gallbladder, respectively. In vitro, single EpCAM sorted cells showed a clonogenic capacity maintaining an endodermal-like phenotype for more than a month. When transferred into differentiation conditions, cells differentiated to a distinct fate resulting in cords of albumin-secreting hepatocytes, branching ducts of secretin receptor+ cholangiocytes or functional pancreatic islets. In vivo, EpCAM+ cells injected into fibrotic livers of SCID mice resulted in repopulation of mice livers by albumin-producing human hepatocytes. In conclusion, normal and pathological gallbladders contain easily isolable cells with the phenotype and the biological properties of BTSCs.

Reference

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Gaudio et al. (2009) New Insights into Liver Stem Cells. *Dig Liver Dis* 41:455-62

Carpino et al. (2012) Biliary Tree Stem/Progenitor Cells in Glands of Extrahepatic and Intrahepatic Bile Ducts: an Anatomical in Situ Study Yielding Evidence of Maturational Lineages. *J Anat* 220:186-99.

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