

# Multipotent stem cells from the extrahepatic biliary tree and methods of isolating the same.

## KEYWORDS

- REGENERATIVE MEDICINE
- STEM CELLS
- CELL THERAPY
- DIABETES MELLITUS
- LIVER CIRRHOSIS

## AREA

- PHARMACEUTICAL

## CONTACTS

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### Priority Number

Provisional USA 61/256,846 \_ 30.10. 2009.

### Patent Type

Patent for invention.

### Co-Ownership

Sapienza University of Rome 50%,  
University of North Carolina 50%.

### Inventors

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Guido Carpino, Vincenzo Cardinale, Lola M. Reid, Wang Yunfang.

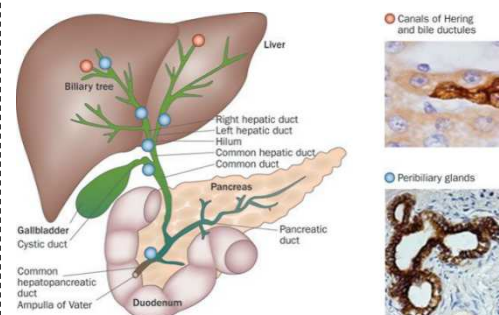
### Industrial & Commercial Reference

Sector pharmaceutical, biotechnological  
and of personalized medicine.

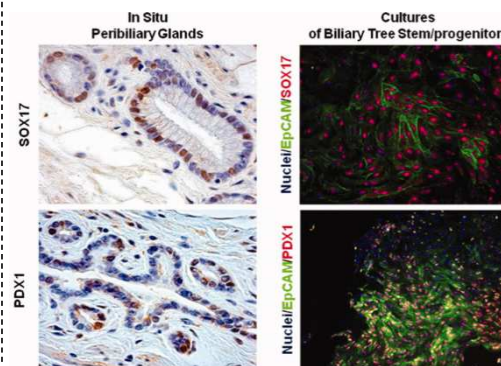
### Time to Market

A phase I / II clinical trial is underway  
demonstrating an advanced state of  
experimentation. The end of phase III  
could be expected in about 10 years.

**LICENSED**



from: Cardinale V et al.  
Nat Rev Gastroenterol Hepatol 2012; 9: 231–240.



from: Cardinale V et al.  
Hepatology 2011; 54(6):2159-72.

### Abstract

The present invention relates to multipotent stem cells of fetal, neonatal, pediatric, and adult biliary tree tissue (including the gallbladder) and capable of maturing into multiple endodermal tissues that include liver, biliary and pancreatic tissues.

The compositions, the methods of identifying and isolating same, their maintaining in culture, expanding same in culture and differentiating or lineage restricting the same in vitro or in vivo to hepatic, biliary or pancreatic fates (e.g. hepatocytes, cholangiocytes, and/or pancreatic islet cells), and finally, methods of using are also provided.

### Publications

- ❖ Cardinale V, Wang Y, Carpino G, Cui CB, Gatto M, Rossi M, Berloco PB, Cantafora A, Wauthier E, Furth ME, Inverardi L, Dominguez-Bendala J, Ricordi C, Gerber D, Gaudio E, Alvaro D, Reid L. Hepatology. Multipotent stem/progenitor cells in human biliary tree give rise to hepatocytes, cholangiocytes, and pancreatic islets. 2011 Dec. 54(6):2159-72.
- ❖ Carpino G, Renzi A, Cardinale V, Franchitto A, Onori P, Overi D, Rossi M, Berloco PB, Alvaro D, Reid LM, Gaudio E. J Anat. Progenitor cell niches in the human pancreatic duct system and associated pancreatic duct glands: an anatomical and immunophenotyping study. 2016 Mar. 228(3):474-86. doi: 10.1111/joa.12418.



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# Multipotent stem cells from the extrahepatic biliary tree and methods of isolating the same.

## Technical Description

An innovative source of multipotent stem cells capable of differentiating into hepatic and biliary cells and pancreatic islets has been discovered.

Localization, phenotypic characteristics, isolation and cultivation techniques are described.

These cells are the only ones currently discovered that can be isolated easily and conspicuously from widely available fetal and adult tissues, such as organ donors, patients undergoing cholecystectomy, or interventions for diseases of the stomach, duodenum or pancreas in which healthy bile ducts are resected, and which have wide differentiation and proliferative capacity and low or absent immunogenicity.

The recipient's gallbladder itself can also be used to isolate autologous cells.

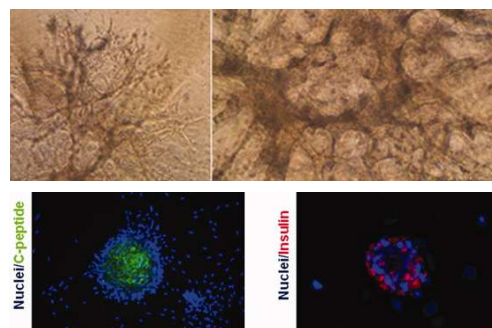
## Technologies & Advantages

Treatment of advanced liver diseases and diabetes, lacks of effective therapies, with the exception of liver or pancreas transplantation, respectively, which are not free of risks, and implicate for the patient the need of an immunosuppressive therapy for the entire lifespan.

Stem/progenitors of the biliary tree are a physiological source of mature cells of the liver and pancreas, and do not require any immunosuppressive therapy to avoid their rejection due to their immunomodulation capacity.

Furthermore, therapy with such cells is potentially autologous.

Therefore, cell therapy based on these cells is immediately applicable as a consolidated therapy without of the need of approval by drug agencies, which instead is necessary and mandatory for embryonic and induced pluripotent stem cells or for mesenchymal stem cells.



from: Cardinale V et al.  
Hepatology 2011; 54(6):2159-72.

This leads to a huge gain in terms of time and resources to achieve the clinical application of biliary stem cells in the treatment of liver disease and diabetes, as demonstrated by an ongoing clinical trial in patients with liver cirrhosis.

## Applications

Regenerative medicine has entered a new phase in which stem cell populations are being transplanted into patients to restore damaged or diseased tissues such as liver and pancreas.

Liver diseases, potentially leading to organ failure due to hepatitis viruses, alcohol consumption, diet and metabolic disorders, and other causes, constitute a major medical burden world-wide.

Similarly, pancreatic diseases, particularly diabetes, are a leading cause of health problems and death world-wide. Stem/progenitor cell therapies represent a possible approach to address these needs for treatment, and clinical programs are expanding worldwide to further explore these novel therapies. Although many types of precursors are being tested for clinical programs treating liver and pancreas, only certain ones are feasible for clinical programs in near future.

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