Determined Endodermal Stem Cells from Duodenal Brunner's Glands and Methods of Isolating them.

KEYWORDS

- ❑ STEM CELLS
- ❑ CELL THERAPY
- ❑ AUTOLOGOUS THERAPY
- ❑ LIVER
- ❑ DIABETES

AREA

- ❑ CHEMISTRY & BIOTECHNOLOGY

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Patent Type
Patent for invention.

Co-Ownership
Sapienza 50%, University of North Carolina 50%.

Inventors
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Industrial & Commercial Reference
Biotechnological and Pharmaceutical sectors.

Time to Market
TRL 5 – technology validated in relevant environment.

Availability
Licensing, Research, Development and Experimentation.

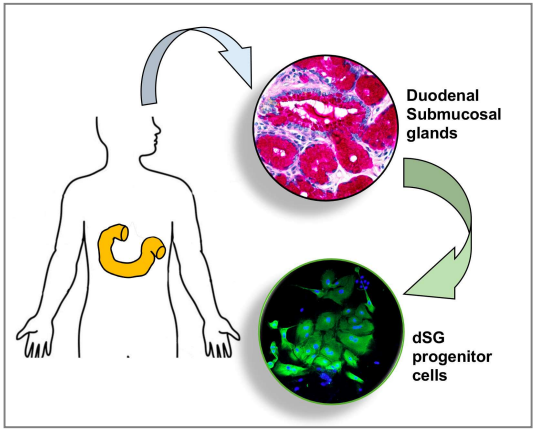

Fig. 1 Stem/progenitor cells are isolated from duodenal submucosal glands.

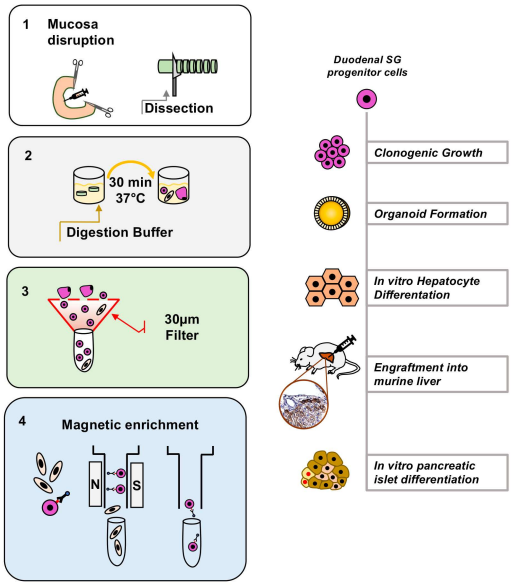

Fig. 2 Procedure for isolation of duodenal submucosal gland cells.

Abstract
The present patent individuates a progenitor cell population within Brunner's Glands in the human duodenum. These cells show phenotypic traits of endodermal stem cells and positivity for pluripotency markers; the present disclosure provides methods of isolating them and provides evidence that these progenitor cells are easily isolated from human duodenum (i.e. organ donors), can be expanded in culture, induced to differentiate towards hepatic and pancreatic lineages, and could repopulate the hepatic parenchyma when injected into the murine liver. Duodenal Brunner's glands could represent a cell source for clinical programs of regenerative medicine, comprising autologous cell therapy.

Pubblicazioni

- ❖ Human duodenal subm ucosal glands contain stem cells with pot enti al for liver and pancreatic regenerative medicine. Cardinale V., Carpino G., Overi D., Safarikia S., Costantini D., Lu W.-Y., Riccioni O., Nevi L., Zhang W., Melandro F., Zizzari I., Moretti M., Chiappetta M.F., Nuti M., Maroder M., Berloco P.B., Forbes S., Reid L., Gaudio E., Alvaro D. Page 466 UEG Journal | Abstract Book 2019 (Poster Presentation).

Fig. 3 Functional properties of isolated duodenal submucosal gland cells.

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Determined Endodermal Stem Cells from Duodenal Brunner's Glands and Methods of Isolating them.

Technical Description

Technical aspects of the present patent relate to a four-step approach that has been developed to isolate stem/progenitor cells from the submucosal glands of the human duodenum. This methodology includes the disruption of the mucosa layer to eliminate intestinal stem cells located into intestinal crypts. Duodenal submucosal gland progenitor cells can grow in vitro as organoids and to maintain their undifferentiated phenotype with null expression of mature cell markers. Duodenal submucosal gland progenitor cells can differentiate into mature towards mature hepatocyte and endocrine pancreatic lineages. Moreover, in vivo experiments individuated their capability to repopulate hepatocyte mass when transplanted into murine liver and to support hepatocyte regeneration in experimentally induced liver disease in mice.

Technologies & Advantages

This disclosure provides a novel source of endoderm progenitor cells with multipotent capability and the procedures to isolate the cells from postnatal duodenum. Human duodenal submucosal gland progenitor cells have the capability to differentiate into hepatocyte and pancreatic β-cells, representing a readily available source obtainable from organ donors. These cells are isolated from organs discarded from transplantation programs and, therefore, the organ procurement for their isolation would be easier compared to obtaining livers for the isolation of mature hepatocytes and hepatic progenitor cells. Remarkably, these cells do not require genetic reprogramming or major manipulation to differentiate into mature fate; therefore, they should be more easily usable in clinical programs compared to reprogrammed cells. Finally, duodenal submucosal gland cells can be retrieved using endoscopy and then used for autologous cell and gene therapies.

Applications

In the field of liver diseases, orthotopic liver transplantation represents the only curative treatment for acute liver failure and end-stage chronic liver disease. Since liver transplantation is limited by a severe shortage of organ donors, cell therapy strategies could represent a feasible alternative option to support liver functions while waiting for organ allocation. However, regenerative medicine approach for liver diseases requires the identification of sustainable and readily available cell sources. Duodenal submucosal glands could represent an autologous and heterologous source of endoderm progenitors. Moreover, their capability to differentiate into pancreatic β-cells opens the possibility of their use in regenerative medicine in diabetic patients.

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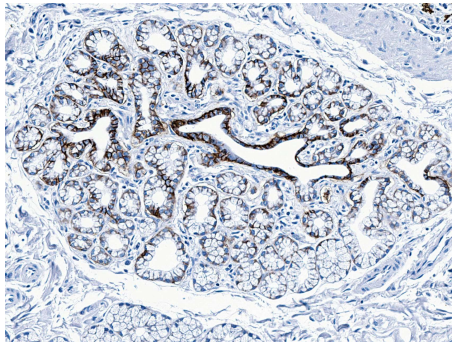
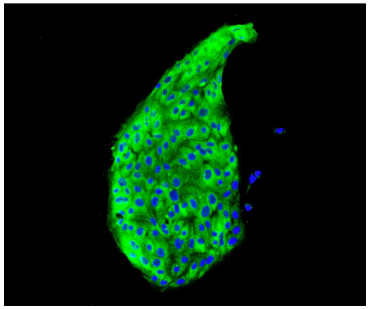


Fig. 4 Pick of EpCAM+ cells within duodenal submucosal glands.

Fig. 5 In vitro Tra-1-60+ stem/progenitor cells after isolation from duodenal submucosal glands.



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