PANCREAS' GENERATION AND REGENERATION BY STEM CELLS

Possible treatment for diabetes and other pancreatic diseases

Author: Leire Pedrosa Eguílaz
Degree: Biochemistry
Faculty: Science and Bioscience, Universitat Autònoma de Barcelona, Catalonia (Spain)

Abstract

There are a lot of diseases caused by tissue degeneration or errors in the organs. Current treatment are organ transplants or using mechanical systems such as dialyzer. However, all of them have defect. Thus, researchers are interested in tissue engineering.
Tissue engineering develops biological structures to generate tissues that allow restore, maintain or improve tissue or organ functionality. For instance, is been investigated the differentiation of Stem Cells (SC) to pancreatic cells that can secrete insulin and the others molecules that have to be secreted by pancreas to be functional. Nevertheless, the whole organ has not been constructed yet. Thus, the main objective of this area is found a good protocol that allow construct whole pancreas or, at least, functional islets .

Tissue engineering

Tissue engineering's objectives

- Combine materials and cells
- Evaluate the viability of cells used and the capacity of them to associated to other biomaterials.
- Evaluate the functionality in the host.

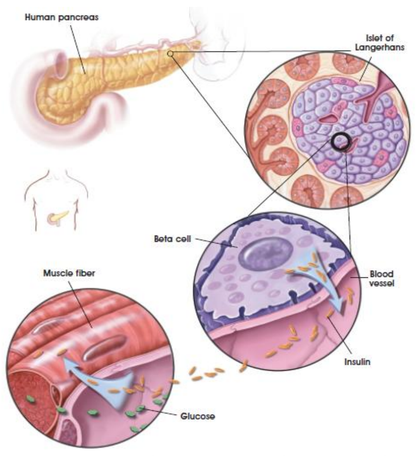
Tissue engineering methodology's

- Transfer cells
- Cells induction
- Make a construct
  - Things that we will need
    - Cells
    - Support materials
    - Signal molecules

Pancreas as an example to tissue engineering

Human pancreas

Structure

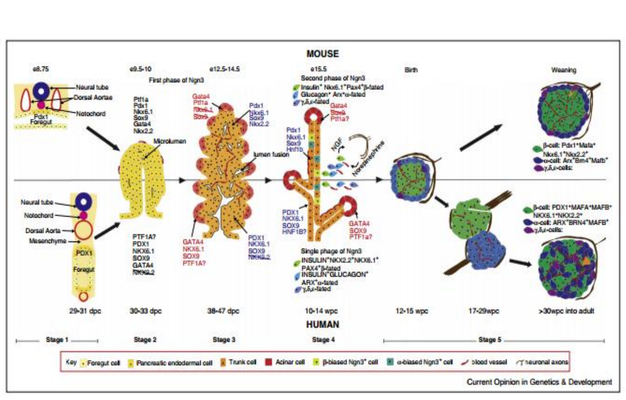


National Institutes of Health. Stem Cell Information (2001)

Exocrine pancreas → enzymes to digestion
- Acinars cells
- Lobules

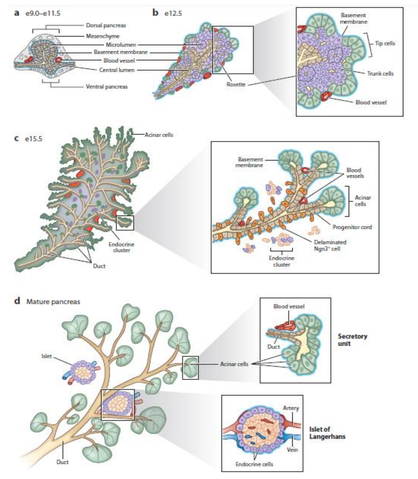
Endocrine pancreas = Langerhans islets → hormones
- β-cells → insulin
- α-cells → glucagon
- δ-cells → somatostatin
- γ-cells → polypeptides

Development *in vivo*



Comparison of development of mouse pancreas and human pancreas. *(Current Opinion in Genetics & Development (2015)) 32:171–180*

It is important to know the differences and similarities, to get a correct protocols to obtain differentiation in vitro.

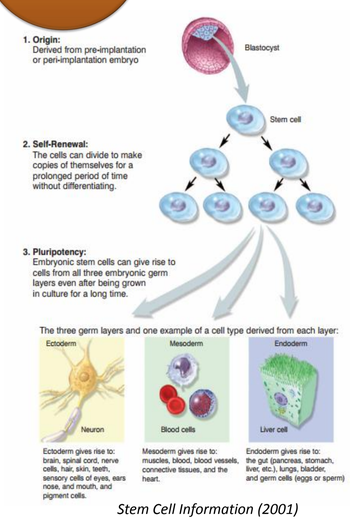


Development of pancreas of mouse (*Annu. Rev. Cell Dev. Biol. (2013) 29:81-105)*

Results *in vitro*

Stem cells that can be isolated and converted into pancreatic cells

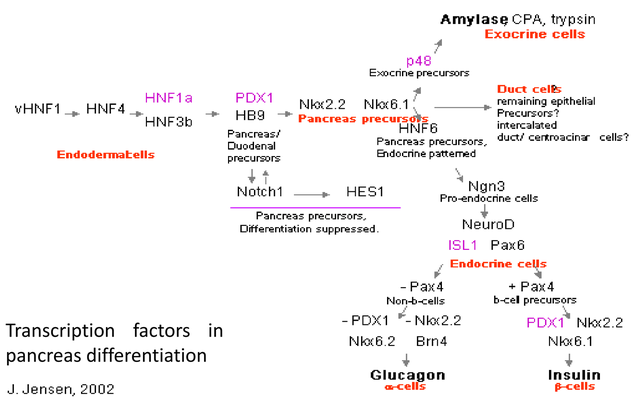
Embryonic Stem Cells (ESC)



Stem Cell Information (2001)

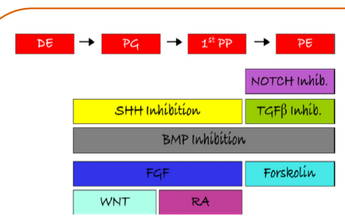
Reserve's SC
- Bonner-Weir et al. pancreatic cells by isolated duct's cells
- Habener et al. pancreatic cells by Nestin+ cells
- Nostro et al. Tansdifferentiation of α cells to beta cells by over-express Pax4

Stem cells' differentiation



Transcription factors in pancreas differentiation

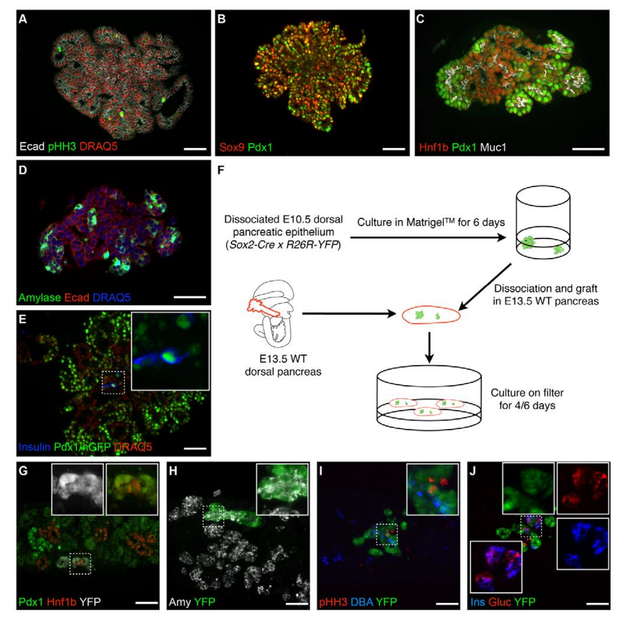
J. Jensen, 2002



Schematic representation of the signaling pathway that regulate the development of first transition endocrine cells from hPSCs, *in vitro*. *Seminars in Cell & Developmental Biology (2012) 23:701-710*

Markers to confirm differentiation

- Endoderm
  - Foxa2
  - Sox17
  - CER1
  - CXCR4
- Endocrine
  - CD142
  - IGF



Results of differentiation of mESC to pancreatic cells
(A-E) immunohistochemistry of organoids
(A) Epitelial (E-catherin) and proliferative cells (pHH3)
(B,C) Pancreatic cells
(D) Exocrine cells in periphery
(E) Endocrine cells in center
(G-J) Grown in vitro in host epithelium
(*Development* (2013) 140: 4452–4462)

Conclusions

Tissue engineering is a good future option to treat diseases related to tissue damage, but have yet to perfect the protocols to get the whole organ.
The cell induction is not a good option because induce a specific area of the body is complicated; maybe if we add growth factors, other cells will active their proliferation and turn on a tumor. Therefore, an alternative option is transplant differentiated cells. The main inconvenient is that if add Langerhans islets, the most of patients loss the cells functionality. Thus, as the isolation of SC and their differentiation to pancreatic cells, in vitro, is possible, we have to improve the protocols to achieve whole functional organ.