USE OF A ROTARY BIOREACTOR FOR THE MATURATION STIMULATION OF PANCREATIC CELLS OBTAINED BY TRANS-DIFFERENTIATION OF HEPATIC CELLS

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Patent application no. A00089/03.03.2021

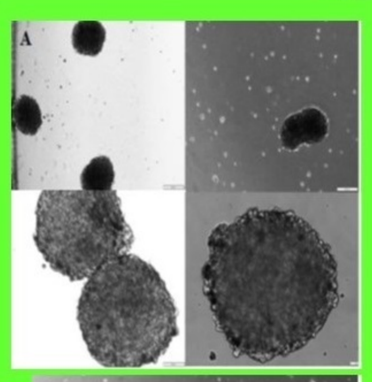
The invention refers to a method and device to obtain and propagate pancreatic cells by the trans-differentiation of human liver cells. The findings in this invention may be applied to other non-tumoral non-proliferating cell types, such as hormone secretory cells, providing a source for auto-transplantation.

Presently, some cellular therapies are in use for patients suffering from diabetes mellitus, starting from beta cells or other cell types obtained from other donors (heterologous transplantation). Efforts are made presently on development and application of other cell sources – like embryonic or induced adult stem cells – as source of proliferation and trans-differentiation into the desired insulin secretory cells.	The transdifferentiated human adult liver cells into pancreatic beta cells, provide an autologous source to replace the original islet population, mainly for type I diabetes mellitus patients. Using autologous liver cell population as source of trans-differentiation overcomes the inconveniences of graft rejection and reduced viability of the graft, and also offers the possibility to store and multiply the trans-differentiated cells when required.	The process involves: - Harvesting a small amount of liver cells form the patient; - Using a vector to trans-differentiate liver cells into pancreatic beta cells - Cultivation and propagation of the trans-differentiated cells to an appropriate population for implantation using a specially designed bioreactor - Preservation of a cell subpopulation for generation of other required batches - Implantation of the cells to the patient/donor - **Construction and use of a rotary bioreactor in pre-established cultivation conditions providing the stimulation of proliferation and maturation of the trans-differentiated cells.**

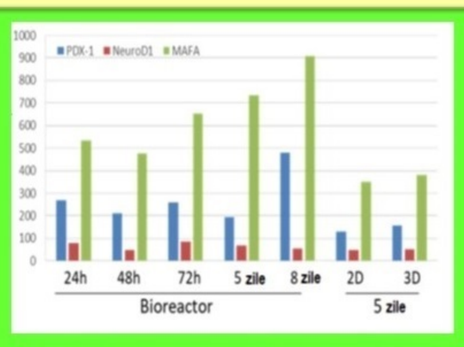
PROBLEM SOLVED: providing a device and methods for propagation and maturation of human transdifferentiated liver cells producing insulin.

ADVANTAGES:
- Providing a device for the efficient cultivation and maturation of human trans-differentiated cells.
- Reproducible performance of the process.
- Achievement of cells for the autologous transplantation.
- Potential application for other cell types used in regenerative medicine.
- Elimination of the need of immunosuppression, mandatory when heterologous transplantation is used

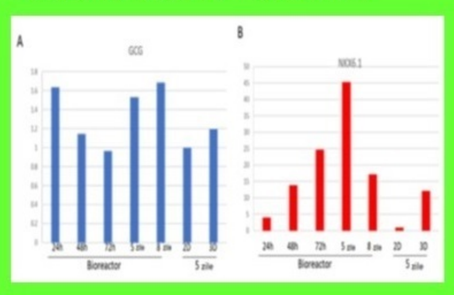
Fig, 1. Diagram of the TD process



Fig, 2. Aspect of TD cells at 72 hrs. (A) and 8 days (B) cultivation in bioreactor

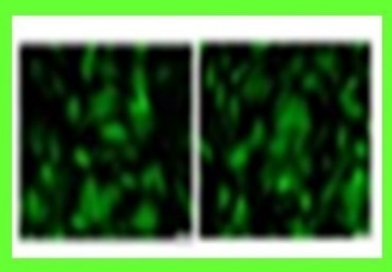


Fig, 3 Gene expression analysis of PDX1, NeuroD1 and MafA



Fig, 4. Gene expression analysis of NKX6.1 and GCG

Fig, 5. C peptide synthesis



Fig, 6. Micrograph of human liver cells transformed with viral vector

Fig, 7. Diabetic mice implanted with human TD pancreatic cells

FUNDED BY PROJECT "DIA-CURE", CONTRACT 148/2016 ID_P_37_794, SMIS 106897

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