Generation of human iPSC-derived beta cells to study the pathogenesis of type 1 diabetes and screen drugs in vitro

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Organisation

Name of the organisation Université Libre de Bruxelles (ULB)
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SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Basic Research, Translational - Applied Research
Type of method	In vitro - Ex vivo
Specify the type of cells/tissues/organs	Fibroblasts and PBMCs

DESCRIPTION

Method keywords

Pancreatic beta cells
Type 1 diabetes
Monogenic forms of diabetes
Type 2 diabetes
iPSC-derived islet cells
Cytokines
apoptosis
Endoplasmic reticulum stress

Scientific area keywords

Induced pluripotent stem cells
Disease modelling
Diabetes research
Pathogenesis
Diabetes
Pancreatic beta cells

Method description

We used a 7-stage protocol to generate beta cells from human Induced Pluripotent Stem Cells (iPSC) and evaluated whether these cells are responsive to the pro-inflammatory cytokines (IFN?, IL-1?, or IFN?) that play a role in type 1 diabetes (T1D). Our data show that human iPSC-derived beta cells respond to pro-inflammatory cytokines IL-1? + IFN? and IFN?, by activating the same pathogenic processes as adult human primary beta cells. These cells thus provide a useful model to better understand the pathogenesis of T1D and screen for new drugs aiming to protect beta cells in early disease.

Lab equipment

- Incubator;
- Fluorescence microscope;
- Confocal microscope;
- Flow cytometer.

Method status

Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Advantages

These cells present some advantages over primary or clonal human beta cells:
-They can be generated on-demand from iPSCs, contrary to primary human islets that are much less readily available and are often isolated from older donors;
-It is possible to generate iPSC from somatic cells obtained from T1D patients, which will allow the study of molecular mechanisms underlying diabetes-associated SNPs (single nucleotide polymorphisms);
-They represent a valuable tool for the screening for new drugs that may protect beta cells against cytokine-induced cell death in early T1D;
-They express receptors for the pro-inflammatory cytokines IL-1?, IFN?, and IFN? and respond to these cytokines—particularly to IFN? + IL-1? - similarly to adult human islets, the “golden standard” in the field.

Challenges

At the end of the differentiation process, the beta cells are not yet fully mature, and secrete less insulin than adult beta cells.

Modifications

There are major efforts by different groups to improve the differentiation process, and it is highly probable that in the near future it will be possible to achieve iPSC-derived beta cells with a function that is closely similar to adult beta cells.

Future & Other applications

iPSC-derived islet cells may become also a valuable tool for the screening of new drugs to protect beta cells against cytokine-induced cell death in early T1D.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

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