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

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SCOPE OF THE METHOD

<table>
<thead>
<tr>
<th>The Method relates to</th>
<th>Human health</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Method is situated in</td>
<td>Basic Research, Translational - Applied Research</td>
</tr>
<tr>
<td>Type of method</td>
<td>In vitro - Ex vivo</td>
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<tr>
<td>This method makes use of</td>
<td>Human derived cells / tissues / organs</td>
</tr>
<tr>
<td>Specify the type of cells/tissues/organs</td>
<td>Fibroblasts and PBMCs</td>
</tr>
</tbody>
</table>

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 (IFNγ, IL-1β, or IFNα) that play a role in type 1 diabetes (T1D). Our data show that human iPSC-derived beta cells respond to pro-inflammatory cytokines IL-1β + IFNγ and IFNα, 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 aimed 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-1β, IFNγ, and IFNα and respond to these cytokines—particularly to IFNγ + IL-1β—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**


**Associated documents**

**Links**
ULB Center for Diabetes Research
Indiana Biosciences Research Institute

PARTNERS AND COLLABORATIONS

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