

# 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

<b>The Method relates to</b>	Human health
<b>The Method is situated in</b>	Basic Research, Translational - Applied Research
<b>Type of method</b>	In vitro - Ex vivo
<b>This method makes use of</b>	Human derived cells / tissues / organs
<b>Specify the type of cells/tissues/organs</b>	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 $\gamma$ , IL-1 $\alpha$ , or IFN $\beta$ ) 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 $\alpha$  + IFN $\beta$  and IFN $\beta$ , 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 $\alpha$ , IFN $\gamma$ , and IFN $\alpha$  and respond to these cytokines—particularly to IFN $\gamma$  + IL-1 $\alpha$  - 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**

Demine, S., Schiavo, A.A., Marín-Cañas, S. et al. Pro-inflammatory cytokines induce cell death, inflammatory responses, and endoplasmic reticulum stress in human iPSC-derived beta cells. *Stem Cell Res Ther* 11, 7 (2020). <https://doi.org/10.1186/s13287-019-1523-3>

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### **Associated documents**

### **Links**

ULB Center for Diabetes Research  
Indiana Biosciences Research Institute

## PARTNERS AND COLLABORATIONS

### Organisation

**Name of the organisation** Université libre de Bruxelles

**Department** Center for Diabetes Research

**Country** Belgium

**Geographical Area** Brussels Region

**Name of the organisation** Indiana Biosciences Research Institute

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