

# iPSCs-derived model to study Klinefelter syndrome

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## Organisation

**Name of the organisation** Université Catholique de Louvain (UCL)

**Department** Institut de recherche expérimentale et Clinique

**Country** Belgium

**Geographical Area** Brussels Region

## Partners and collaborations

Geneva University Hospitals

## 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>Specify the type of cells/tissues/organs</b>	Skin fibroblasts from KS patient

## DESCRIPTION

### Method keywords

Primordial germ cells

Germ cell differentiation

Post-meiotic cells

Klinefelter syndrome iPSCs

### **Scientific area keywords**

Klinefelter syndrome

Male infertility

Induced pluripotent stem cells

Disease modelling

### **Method description**

We developed an innovative model to study the effect of the supernumerary X chromosome on KS features. The model was generated using induced pluripotent stem cells (iPSCs) from patients with Klinefelter syndrome (KS) i.e. with a 47, XXY karyotype. In order to compare the potentials of both 47XXY-iPSCs and 46XY-iPSCs to differentiate into the germ cell lineage, we developed a directed differentiation protocol by testing different combinations of factors including bone morphogenetic protein 4 (BMP4), glial-derived neurotrophic factor (GDNF), retinoic acid (RA) and stem cell factor (SCF) for 42 days. Importantly, we found a reduced ability of 47XXY-iPSCs to differentiate into germ cells when compared to 46XY-iPSCs. In particular, upon germ cell differentiation of 47XXY-iPSCs, we found a reduced proportion of cells positive for BOLL, a protein required for germ cell development and spermatogenesis, as well as a reduced proportion of cells positive for MAGEA4, a spermatogonia marker. This reduced ability to generate germ cells was not associated with a decrease of proliferation of 47XXY-iPSC-derived cells but rather with an increase of cell death upon germ cell differentiation as revealed by an increase of LDH release and of caspase-3 expression in 47XXY-iPSC-derived cells.

### **Lab equipment**

- Cell irradiation for mitotic inactivation ;
- Culture facility.

### **Method status**

Published in peer reviewed journal

## PROS, CONS & FUTURE POTENTIAL

### Advantages

Applicable to different cell lines for comparative studies.

### Challenges

Define culture conditions to obtain sufficient amount of cells.

### Modifications

- Not for the generation of iPSCs ;
- Ongoing studies to define optimized culture conditions.

### Future & Other applications

Provides an excellent in vitro model to unravel the pathophysiology and to design potential treatments for KS patients.

## REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

### References

Botman O, Hibaoui Y, Giudice MG, Ambroise J, Creppe C, Feki A and Wyns C (2020) Modeling Klinefelter Syndrome Using Induced Pluripotent Stem Cells Reveals Impaired Germ Cell Differentiation. Front. Cell Dev. Biol. 8:567454. doi: 10.3389/fcell.2020.567454

Wyns C, Botman O. Induced pluripotent stem cell potential in medicine, specifically focused on reproductive medicine. Front Surg. 2014; 1: 5. Published online 2014 March 24

### Links

[Gynaecology research group](#)

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