Constructing a cardiac cell model from a patient with Fabry Disease

Ana Joana Duarte[1,2,3*], Diogo Ribeiro[1,2,3], Olga Amaral[1,2]

1- Departamento de Genética Humana - Instituto Nacional de Saúde Ricardo Jorge
2- Centro de Estudos de Ciência Animal – Universidade do Porto
3- Instituto de Ciências Biomédicas Abel Salazar – Universidade do Porto

Funding: PTDC/BIM-MEC/4762/2014

* ana.duarte@insa.min-saude.pt

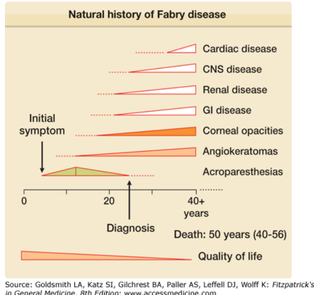
Introduction

Fabry Disease (FD)

- FD is an X-linked disease and one of the commonest Lysosomal Storage Disorders - prevalence of 1:3.000 is suggested due to late-onset variants
- Mutations in the alpha-galactosidase A gene (*GLA*)

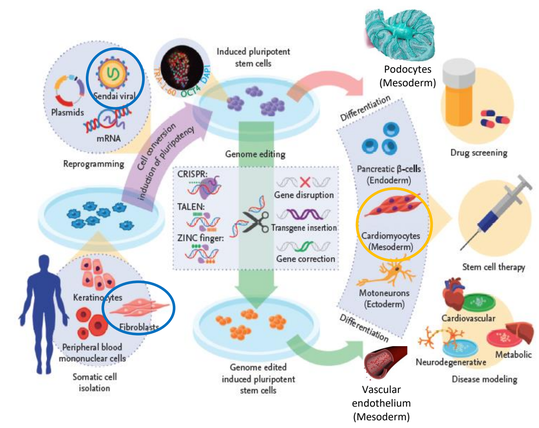
⬇

Accumulation of of globotriaosylceramide (Gb3) and Lyso-Gb3 on lysosomes



Source: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K: *Fitzpatrick's Dermatology in General Medicine, 8th Edition*: www.accessmedicine.com

Induced Pluripotent Stem Cells (iPSCs) and iPSCs-derived Cardiomyocytes



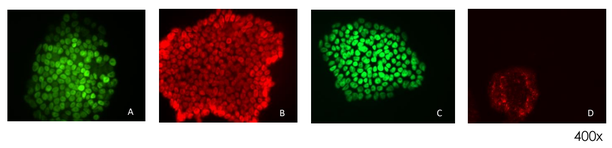
Adapted from Diecke *et al.*, 2014

Methods and Results

Biological Sample: FD fibroblasts from a male patient with the mutation c.860G>A (p.W287X)

Sendai Virus (SeV) Fibroblast Transduction using CytoTune™-iPS 2.0 (Invitrogen™)

FD iPSCs

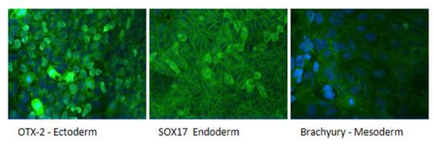


400x

A- Nanog
B- Sox-2
C- Oct-4
D- TRA-1-60

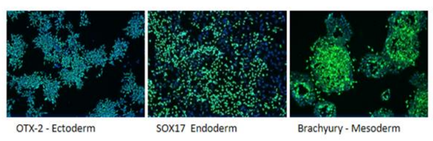
Karyotype: 46,XY

FD iPSCs-differentiation into the 3 Germ layers



Spontaneously embryoid bodies

400x

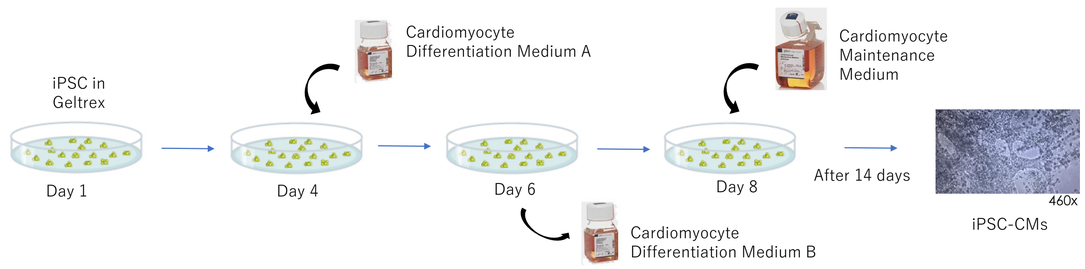


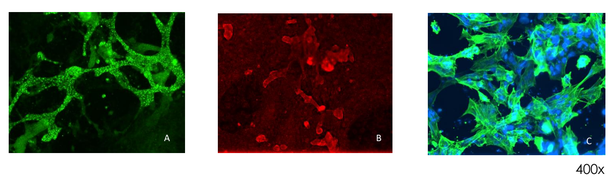
Induced with actives

100x

Methods and Results

iPSCs-derived Cardiomyocytes (iPSC-CMs) using PSC Cardiomyocyte Differentiation Kit (Gibco®)





400x

A - ANP
B - Troponin I
C - Tropomyosin

Conclusions

- We successfully achieve an iPSC line from a patient with Fabry Disease
- Our line has the characteristics of stem cells and has the hability to differentiate into the 3 germ layers
- After induction with specific cardiac effectors we achieved beating iPSC-CMs

Next Steps

- The cardiomyocytes line has to be purified and has to reach a maturation state (usually obtained by electrical and mechanical stimulation)
- Our mature iPSC-CMs have to be analyzed against the initial FD fibroblast to see if the disease features are replicable in the new cell line

References

Diecke S, et al. Korean J Intern Med 2014;29:547-557 | Mehta, AB and Orteu, CH. Chapter 136 - Fabry Disease. Fitzpatrick's Dermatology in General Medicine, 8e, 2012 | Klingelhöfer D. Mol Genet Genomic Med. 2020;8:e1163 | Kuramoto, Y et al. J Mol Cell Cardiol 2018; 121:256-265.