

IPSCs generation, characterization and differentiation for LGMDR4 patients



WWW.LGMD2E.ORG

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Background

LGMDR3-2D, LGMDR4-2E, LGMDR5-2C are recessive autosomal diseases, there are no specific treatments, except for some physical therapies that prevent worsening of muscle contractures and therapies associated with cardiac and respiratory problems. There are currently no in vitro models for LGMDR4-2E, there is only one iPSC line (JUCTCi017-A) from a patient with limb-girdle muscular dystrophy (LGMD) due to a homozygous p.Lue287Ser fs14* mutation in the SGCB gene. N. A. Ababneh et Al. 2021. In 2023, GFB promoted and funded the IPSCs GENERATION, CHARACTERIZATION AND DIFFERENTIATION FOR LGMDR4 PATIENTS Project, intending to create a new tool to study this disease and to evaluate the impact of new therapies on these cells.

Objectives

This project aims to create in vitro human models of the disease to test drugs, validate treatments, and study mechanisms.

Methods

The project consists of 3 phases:

1 Step

April 2023
sampling (concluded)

Prof. Yvan Torrente collected and processed blood samples from 3 patients. (PBMCs)

PATIENTS STUDIED

patients 1 and 2: c.377_384 dup mutation in homozygosity on exon 3.

Phenotype: symptoms before the age of 10, loss of ambulation before the age of 18 (group 1). High-grade restrictive dysventilatory syndrome.

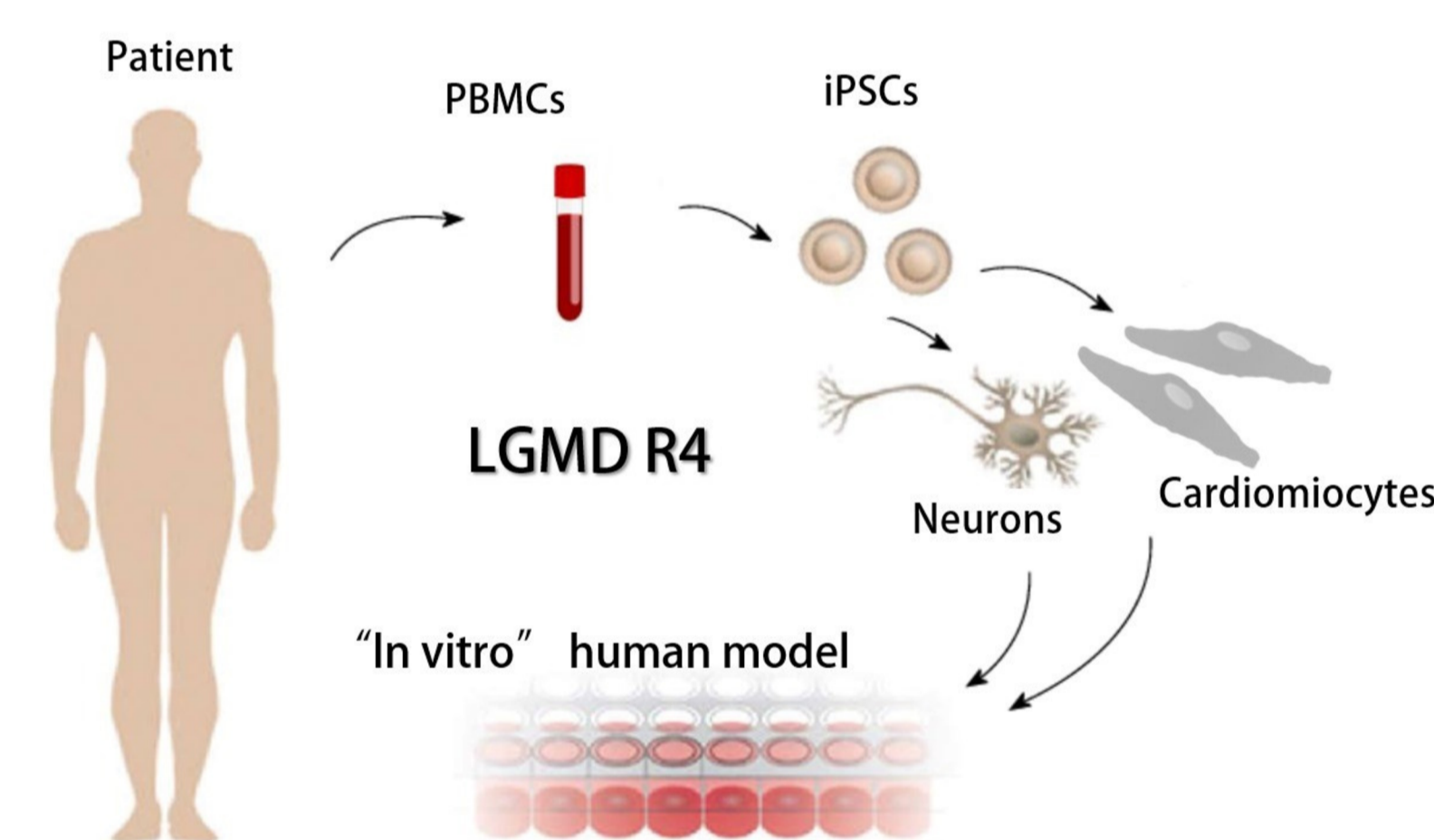
patient 3: c. 341>t and c. 906insATGTTTGG mutations in heterozygosity on exons 3 and 6.

Phenotype: symptoms after the age of 10, loss of ambulation after the age of 18 (group 2). High-grade restrictive dysventilatory syndrome.

2 Step

April 2023 - December 2023
IPSCs generation (concluded)

3 IPSCs cell lines were produced by Dr. F. Gros-Louis in Quebec - Canada by reprogramming human cells using Sendai virus and complete characterization.



3 Step

From January 2024
IPSCs Differentiation (ongoing)

IPSCs lines will be differentiated into cardiomyocytes by Prof. G. Pompilio at Centro Cardiologico Monzino, Milan Italy. They will study:

- the effect of mutation at the transcriptional
- the vitality of cardiomyocytes.
- electrical and contractile component
- and other.

Next Steps

Subsequently, IPSCs cells will be used by other laboratories in further differentiation projects, in the following clinical centers:

- Prof. Massimiliano Cerletti, University College London UK
- Prof. Yvan Torrente, Policlinico and Milan University, Italy
- Dr. Sanchez Carles Riera, La Sapienza University, Rome, Italy
- and other.



Conclusions

The IPSC Cell lines generated are functional and ready to be differentiated, by all who will have research projects aimed at curing LGMD2E/R4.

Those interested in participating in the project can send a proposal to the GFB Foundation: presidenza@beta-sarcoglicanopatie.it

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