RESEARCH TOPIC MEM3

IPSCs from Duchenne Muscular Dystrophy: perfect genetic correction by chromosome transplantation and generation of 3D cell culture.

Curriculum MEM Standard

Laboratory name
Humanitas stem cell lab, Humanitas Research Hospital

Pre-clinical Supervisor
Marianna Paulis
marianna.paulis@humanitasresearch.it

Stefano Duga
stefano.duga@hunimed.eu

Abstract
In this project we plan to validate a novel approach to gene correction, which could be used for chromosomal abnormalities that cannot be treated with standard gene therapy. The X-linked Duchenne Muscular Dystrophy (DMD), a severe muscle pathology, whose treatment is still unsatisfactory, will be taken as a paradigmatic example of this novel "chromosome therapy".
We will apply to DMD patient-derived induced pluripotent stem cells (iPSCs) a chromosome transplant protocol based on X chromosome transfer via an improved microcell-mediated chromosome transfer set up in our laboratory and will select diploid clones which have replaced the endogenous X chromosome with the exogenous one. Corrected iPSCs will be forced to differentiate toward mature cardiomiocytes by 3D cell culturing.

Main technical approaches

- Experience with iPS cell culture methodology
- Differentiation and basic knowledge of cytogenetic methodologies

Scientific references

1. Paulis M, Susani L, Castelli A, et al. Chromosome Transplantation: A Possible Approach to Treat Human X-linked Disorders. Mol Ther Methods Clin Dev. 2020;17:369-377. doi: 10.1016/j.omtm.2020.01.003.

2. Castelli A, Susani L, Menale C, et al. Chromosome Transplantation: Correction of the Chronic Granulomatous Disease Defect in Mouse Induced Pluripotent Stem Cells. Stem Cells. 2019;37(7):876-887. doi: 10.1002/stem.3006.

3. Paulis M, Castelli A, Susani L, et al. Chromosome transplantation as a novel approach for correcting complex genomic disorders. Oncotarget. 2015;6(34):35218-30. doi: 10.18632/oncotarget.6143.

4. Fortunato F, Rossi R, Falzarano MS, Ferlini A. Innovative Therapeutic Approaches for Duchenne Muscular Dystrophy. J Clin Med. 2021;10(4):820. doi: 10.3390/jcm10040820.

Type of contract

Scholarship of € 21.000 gross per year awarded by Istituto Clinico Humanitas. This sum is subject to IRPEF income tax and exempt from social security contributions.

Borsa di studio pari a € 21.000 annui lordi erogata da Istituto Clinico Humanitas. Importo soggetto a tassazione IRPEF ed esente da contribuzione previdenziale.

Humanitas University
Via Rita Levi Montalcini 4
20090 Pieve Emanuele (Milano) Italy
Tel +39.02.8224.1 - Fax +39.02.8224.2394
info@hunimed.eu
Website: www.hunimed.eu
C.F. 97692990159