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INTRODUCTION

During the first year of PhD, I focused my work on two different projects: 1) generation of skeletal muscle fibres from human induce pluripotent stem cells (iPSCs) obtained from healthy donor and Duchenne muscular dystrophy (DMD) patients, to obtain an in vitro representative model of the disease. 2) isolation of single viable cardiomyocytes (CMS) from human surgical biopsies of patients affected by Hypertrophic Cardiomyopathy (HCM), to test the safety and investigate the mechanisms of action of Cibenzoline (CB) and Mavacamten (MYK).

MATERIALS AND METHODS

The iPSCs were obtained by reprogramming monocytes from a healthy donor and a DMD patient and were induced to differentiate into skeletal myofibres through a protocol consisting in the addition of three culture media in a predetermined sequence, to induce their differentiation into skeletal progenitors, myoblasts and myotubes. The cells obtained were analyzed by immunofluorescence to assess the presence of specific myogenic markers (PAX7, MHC) of each stage of differentiation. Human adult CMS were enzymatically and mechanically isolated from surgical HCM samples and then used for patch clamp and Ca^{2+} imaging experiments, in absence and presence of CB or MYK (1-4-1 OHM).

RESULTS AND CONCLUSIONS

The control line was successfully differentiated into skeletal myoblasts. Indeed, our results show, at early stages, the expression of the myogenic precursor Pax7, while at later stages of maturation also myosin (MHC) is expressed. In the future, I will apply the same protocol also to the DMD line. Regarding drug tests on human HCM CMS, CB shows the ability to block the cardiac sodium current with a higher selectivity for the late component, acting as a negative inotropic drug with potential additional antiarrhythmic effects. MYK inhibited the contraction machinery, without altering Ca^{2+} handling, thus acting as a strong negative inotropic agent, without altering the electrophysiological profile of treated cells.

Courses

- Soft skills: ricerche bibliografiche e open access & science, Silvia Aurigi, Cristina Mencarelli, 07/05/2021;
- Soft skills: diritto dei brevetti, Vittorio Santoro, 10/05/2021; ● Soft skills: diritto dei brevetti, Alessandro Palmieri, 11/05/2021 ;
- Soft skills: diritto dei brevetti, Alessandro Palmieri, 12/05/2021;
- Soft skills: diritto dei brevetti, Vittorio Santoro, 13/05/2021;
- Soft skills: i rapporti tra scienza e società: tra persistenze e cambiamenti, Agnes Allansdottir, 31/05/2021;
- Soft skills: analisi della risposta immunitaria alla vaccinazione e all'infezione: dalla fase di sperimentazione a quella di analisi dati tramite un approccio di systems biology, Annalisa Ciabattini, Elena Pettini, 08/06/2021;
- Soft skills: spin offe start up della ricerca: l'ecosistema di innovazione e supporto delle start up, Francesco Maria Senatore, 15/06/2021.

Webinar

- Control of Ca²⁺ in the heart free and beyond. David Eisner. 14/01/21 ;
- Connexin43 hemichannels and intracellular calcium: an axis of dysfunction in sudden cardiac death. Mario Delmar. 19/01/21;
- EuroCVP 2021. 10/06/2021-12/06/2021•,
- Minisimposio sulla sperimentazione animale in medicina: un percorso di scienza, storia, diritto, etica e medicina. "Il cervello tra homo sapiens e primati non umani: sviluppo, evoluzione e potenzialità". 21/06/2021 ;
- Le implicazioni etiche e legali della terapia genica e dell'editing genomico. 01/07/2021 ;
- Workshop gruppo cardio-genetica: le cardiomiopatie pediatriche. 20/09/2021;
- Minisimposio sulla sperimentazione animale: aspetti storici, etici, giuridici. Coordinato dall 'Università di Ferrara e Università di Camerino. ProffMichele Simonato, Luciano Fadiga, Paolo Pinton, Roberto Ciccocioppo. 23/09/2021 ;
- Open science and Covid-19: collaborare per contrastare la pandemia. Disponibilità e uso dei dati epidemiologici in pandemia: difficoltà e opportunità. In collaborazione con l'Istituto Superiore di Sanità (ISS). 28/09/2021.

● Conferences

- 40^o Congresso nazionale della società italiana di farmacologia (SIF), 09/03/2021-13/03/2021; • Congresso: Advances in Cardiomyopathies, Centro Congressi, Firenze, 9/09/21-10/09/2021.
- Congresso Telethon sulla Cardiomiopatia dilatativa associata a Distrofia Muscolare di Duchenne, Villa La Quiete, Firenze 06/10/2021.

Abstract

- Extracellular stiffness as a determinant of cardiac dysfunction in Duchenne's Muscular Dystrophy: a study on human iPSC-derived cardiomyocytes. Società italiana di Farmacologia (SIRC). Imola 2021.