MODELLO SCHEDA RELAZIONE DOTTORANDI

Al collegio docenti del Dottorato in Medicina Molecolare

Dr.ssa/Dott. Giammarino Lucrezia

Ciclo XXXVI Tutor Prof.ssa Elisabetta Cerbai

Attività scientifica svolta nel 2° anno di Dottorato, Anno Accademico 2021/2022

INTRODUCTION

Duchenne muscular dystrophy (DMD) is a disorder characterized by progressive degeneration of skeletal, smooth and cardiac muscles associated with an important cardiac dysfunction. Considering the low representativeness of animal models and the scarce availability of human samples, induced pluripotent stem cells (iPSCs) represent a good model to study the mechanisms underlying this disease, allowing to maintain the patient's genetic heritage and can be differentiated into several cell types, including cardiomyocytes.

MATERIALS AND METHODS

IPSCs are obtained by reprogramming of isolated monocytes from healthy donors and DMD patients and differentiated into cardiomyocytes by using of a long-term culture on monolayer. Around day 15, to start from this monolayer, to increase cell maturation we formed engineered heart tissues (EHTs). During EHT-hiPSC-CMs maturation, were carried out spontaneous measurements of auxotonic contractions by optical tracking; around day 50 we performed mechanical investigations in isometric conditions and electrophysiological measurements of action potential and calcium transients by using two specific fluorescent dyes (Cal590 and Fluovolt) for calcium and membrane voltage, respectively. In addition, we are tested a compound that act as a membrane stabilizer (p188) to evaluate the role of membrane damage, one of the main features of DMD-cardiomyocytes, caused of dystrophin deficiency.

RESULTS

Evaluation of auxotonic contractions show that tension increases during maturation in CTRL-line and in DMD-line as well as spontaneous frequencies decreases in both lines tested. Moreover, in isometric conditions active tension increase significantly in DMD-EHTs compared to control but we don't observe significant differences in duration of twitch and in action potential and calcium transient kinetics. As for comparison between DMD-EHTs with p188, preliminary results show that APD50 of treated EHTs is shorter compated to non-treated cells.

ABSTRACTS AND WEBINARS

- Synaptic stimulation protects against pathological tau by enhancing lysosomal degradation. Dott. Davide Tampellini, Inserm –Neuroscience, Université Paris Sud-Saclay, 27.10.21;
- Selective autophagy of the Endoplasmic Reticulum: mechanisms, regulations, and functions. Prof. Carmine Settembre, Telethon Institute of Genetics and Medicine (TIGEM) e Dipartimento di Medicina clinica e Chirurgia, Università di Napoli Federico II, 17.11.21;
- An electron microscopy view into 2 killers: SARS-CoV-2 and Mycobacterium tuberculosis infections induce lipid accumulations in lung. Dr. Nicole Van Der Wel, Amsterdam University Medical Center, Department of Medical Biology, 01.12.21;
- 7.02.22: IPAM 3Days for 3Rs: REPLACEMENT, Istituto Superiore di Sanità – ISS, Dipartimento di Sicurezza Alimentare, Nutrizione e Sanità Pubblica Veterinaria – SANV;
- 14.02.22: IPAM 3Days for 3Rs: REDUCTION, Istituto Superiore di Sanità – ISS, Dipartimento di Sicurezza Alimentare, Nutrizione e Sanità Pubblica Veterinaria – SANV;
- 18.02.22: Functional dynamics of chromatin topology in human cardiogenesis and disease. Alessandro Bertero, Armenise-Harvard Lab of Heart Engineering and Developmental Genomics Molecular Biotechnology Center, University of Turin, Department of Molecular Biotechnology and Health Sciences;
- Writing scientific papers in English, University of Pisa, 24.05.22, 10.00-19.30;
- Active lesson soft skill, 26.05.22, 10.00-13.00;
- Soft Skill: il diritto dei brevetti, 27.05.22, 09.00-13.00;
- Soft Skill: Spin off e Start up della ricerca: il modello di business e i regolamenti, 31.05.22, 08.30-18.30;
- Soft Skill: Spin off e Start up della ricerca: l'ecosistema di innovazione a supporto delle Start up, 07.06.22, 10.00-13.00;
- Soft Skill: comunicare in ricerca, 20.06.22, 09.00-18.00;
- Soft Skill: Fare ricerca per l'inclusione sociale 10.00-13.00, 27.06.22;
- Soft skill: "*Lavoro editoriale per l'editoria scolastica e universitaria 01.07.22, 09.00- 18.00;*
- Taking iPSC-derived muscle cells to the clinic (20.09.22);
- Third transnational project meeting – EASY GOV- Laboratory Management Platform (23.09.22, 09.00-14.00);

- “Economia circolare: buone pratiche dalla ricerca all’innovazione” - Venerdì 30 settembre 2022 *Aula Franco Romani, Presidio San Francesco dell'Università di Siena (Piazza San Francesco 7), ore 10-13*;
- Genetics of hemophilia A and B, Jill Johnsen, University of Washington, 03.10.22;
- Mechanisms of Autonomic Dysfunction, Dr. Oscar Vivas, University of Washington, 06.10.22.

CONGRESSES

- Frontiers in Cardiovascular Biomedicine FCVB; Moderated poster session: Extracellular stiffness as a determinant of cardiac dysfunction in Duchenne’s Muscular Dystrophy: a study on human iPSC-derived cardiomyocytes 28.04.22-01.05.22, Budapest;
- YRP 2022, Oral presentation, Electro-mechanical Investigation of Duchenne Muscular Dystrophy Using Human Engineered Heart Tissues, 13.06.22-15.06.22 Bertinoro;
- Heart’s Florence day, Villa la Quiete, Florence, Moderated Poster Session.

STAYS IN FOREIGN LABORATORIES

- HAMM Lab, Dept. Of Bioengineering, University of Washington, Seattle (WA)