Abstract: **P2573**

**Modelling the duchenne muscular dystrophy-induced dilated cardiomyopathy using patient-specific induced pluripotent stem cells-derived cardiomyocytes.**

**Authors:**
M Souidi¹, Y Sleiman¹, A Moreau¹, P Amedro¹, P Meyer¹, F Rivier¹, A Lacampagne¹, A Meli¹, ¹Laboratory of physiology and experimental medicine of heart and muscles (PhyMedExp) - Montpellier - France,

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Introduction: Duchenne Muscular Dystrophy (DMD) is a X-linked degenerative pathology with a prevalence of 1/3500 boys due to absence of functional dystrophin in muscles. In a late stage of DMD, patients developed a dilated cardiomyopathy (DCM) which can lead to heart failure and premature death.

In the past, we showed that DMD (mdx) mice exhibit a perturbation of the intracellular calcium homeostasis correlated to a pathological remodelling of the calcium ryanodine receptor channel (RyR2) leading to DCM with aging. However, mouse model does not represent a pertinent prototype to study DMD. Human pluripotent stem-cell derived-cardiomyocytes (hiPSC-CMs) are a pertinent tool to model patient-specific inherited cardiac diseases and screen pharmacological drugs in a Petri dish.

Objective: Based on the clinical history of DMD patients in the local Hospital, our main objective is to model DMD-induced DCM using hiPSC-CMs and compare the functional and molecular features with the clinical echocardiography. To that, we hypothesize that hiPSC-CMs are a powerful technology to model in vitro DCM and to better understand the pathophysiological mechanisms underlying DCM.

Methods: 3 blood samples from DMD patients with different DCM degrees of severity and 3 from healthy control (HC) were collected, reprogrammed in hiPSC and differentiated into cardiomyocytes.

Results: Our preliminary data indicate that DMD hiPSC-CMs present an abnormal intracellular calcium homeostasis characterized by the presence of leaky diastolic calcium events compared to HC hiPSC-CMs suggesting a RyR2 dysfunction. In DMD hiPSC-CMs, we also observe alterations in the contractile properties and a perturbation of the mitochondrial respiration.

Conclusion: Our results support the fact that DMD-inducing DCM can be modelled in the dish using patient-specific hiPSC-CMs. Such modelling may provide a better understanding of the pathophysiological mechanisms and the pharmacological treatment of the DMD-induced DCM.