Research Project Proposal
Academic year 2019-2020

Project Nº 29

Title: *Dechipering the role of specific transcriptional regulators in cardiovascular progenitors derived from human iPSCs.*

Department/ Laboratory: Department of Regenerative Medicine, Laboratory 1.01, CIMA.

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Summary

Induced pluripotent stem cells (iPSCs) have emerged as a powerful source of cells for stem cell therapy, disease modeling, drug screening and developmental biology. The human heart has very little reparative and regenerative ability after injury; actually, myocardial infarction is followed by a remodeling process of the myocardial tissue that includes hypertrophy and fibrotic scar. Stem cell therapy has brought modest benefits in cardiac regenerative medicine. In this arena, iPSC-derived cardiovascular progenitors (CVPs) have emerged as promising candidates that would enable the recovery of both cardiac and vascular components of the heart. However, mechanisms and conditions to maintain multipotent CVPs in self-renewal and create clinically relevant numbers of CVPs remain elusive.

In our laboratory we have generated several lineage tracing mouse models for CVPs and established iPSCs from these mice (Linares *et al.*, *Stem Cell Res.* 2016; Linares *et al.*, *Stem Cell Res.* 2018). These iPSCs upon differentiation express a green fluorescent protein that allows the identification of CVPs and their cell progeny (cardiomyocytes, smooth muscle and endothelial cells). We identified four regulators of transcription to be specifically increased in CVPs in a genome-wide study, and found that these regulators were also upregulated in CVPs derived from human iPSC. Recently, we have created an inducible system (lentiviral construct) to tightly control the expression of these genes. The candidate during his/her Master project will analyze how the different levels of these regulators might influence CVP fate, and ultimately, unveil their mechanism of action at single-cell resolution.

yes	**X**
no	

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?