



Research Project Proposal
Academic year 2021-2022
Máster en Investigación Biomédica

Project Nº 42

Title: Mechanobiology for cardiac regeneration

Department/ Laboratory Laboratory where the project will be carried out indicating Department, Area, Faculty, CUN, CIMA etc.
Cima Lab 1.01

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Summary:

Mechanical signals transmitted through the extracellular matrix (ECM) and neighbouring cells have emerged as key elements regulating stem cell differentiation, tissue homeostasis and regeneration. Infarcted and hypertrophied hearts are generally stiffer than normal tissue, and it is nowadays well established that this increase in stiffness negatively affects cardiac cell behaviour. In light of this evidence, understanding how mechanics drive cardiac tissue regeneration is of utmost importance.

Recent studies in other organs and systems have shown that mechanical forces are transmitted from the cell microenvironment all the way to the cell nucleus, where they play a fundamental role. For instance, forces applied to the nucleus can stretch chromatin and enable access of the transcription machinery. Recently, we demonstrated that forces to the cell nucleus alter the conformation of nuclear pore complexes (NPCs), increasing the import of the major transcriptional regulator YAP and driving transcription. This direct role of nuclear force is highly relevant for the following main reason: the nucleus is the organelle in charge of transcription, the master process that drives cell phenotype and thereby regeneration.

This project consists on understanding the molecular mechanisms that govern force induced cardiac cell reprogramming and regeneration. For that the student will be using molecular tools in combination with human iPSC cardiomyocytes that are available in the lab. Specifically, the tutee will use nesprin FRET sensors available in addgene and will also design plasmids that will be needed for the study. The student will also learn and extensively use the advanced microscopy facilities of CIMA.

yes	<input type="checkbox"/>
no	<input checked="" type="checkbox"/>

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