Research Project Proposal
Academic year 2020-2021

Máster en Investigación Biomédica

Project Nº 19

Title: *Unfolded protein response and myocardial fibrosis in heart failure.*

Department/ Laboratory *Laboratory of Heart Failure and Myocardial Remodelling. Program of Cardiovascular Diseases (CIMA).*

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Summary

Heart failure (HF) is a complex syndrome representing one of the leading causes of mortality and hospitalizations in Western countries including Spain. Importantly, even with the optimal pharmacological treatment, the prognosis is very bad, with a survival rate below 40% five years after diagnosis, suggesting that the therapies currently available are not effective enough. Therefore it is essential to identify new targets involved in the onset and progression of this disease.

One of the main histopathological alterations underlying the development of HF is myocardial fibrosis, which increases left ventricular stiffness contributing to the impairment of cardiac function. A key step in this process is the activation of myofibroblasts which acquire a highly active secretory phenotype. Recent data suggest that the unfolded protein response (UPR) may play a role in HF progression and in myocardial fibrosis.

In this conceptual framework this project has 2 objectives:

1) To study in available cardiac samples of animal models of HF UPR-related pathways and their association with myocardial remodeling.

2) To study in freshly isolated human cardiac fibroblasts the effect of different pro-fibrotic factors (transforming growth factor-β, hypoxia, matrix stiffness) on the UPR and the potential impact of modulating that pathway.

The methodology of the project will include cell culture techniques, histological immunodetection and analysis, and molecular biology studies (RNA isolation, real time PCR and RNA silencing).

yes	
no	**X**

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