Universidad de Navarra
Facultad de Ciencias

MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2022-2023

Project Nº 17 ASIGNADO

Title: *In vitro and in vivo assessment of the myocardial antifibrotic effect of a novel epigenetic regulation inhibitor*

Department/ Laboratory
Lab. of Heart Failure. Program of Cardiovascular Disease, CIMA.

Director 1 *Arantxa González Miqueo*
Contact: *amiqueo@unav.es*
Codirector: *Mª Ujué Moreno Zulategui*
Contact: *mumoreno@unav.es*

Summary

Heart failure (HF) is one of the leading causes of mortality and hospitalization. Even with the optimal treatments available the prognosis is appalling, suggesting that current therapies are not effective enough. Diffuse myocardial fibrosis is a key pathophysiological mechanism underlying HF, having a detrimental impact on cardiac function and patient's prognosis. Currently, there are no specific treatments for myocardial fibrosis in HF.
Myocardial fibrosis is characterized by an excessive deposition collagen fibers and other extracellular matrix proteins. Cardiac fibroblasts are activated to myofibroblast and enhance their pro-synthetic phenotype. Epigenetic regulation through methylation has been proposed as a potential relevant mechanism in this process. In this context, CIMA has developed a dual G9a histone-methyltransferase and DNA-methyltransferase-1 inhibitor (CM-272) with proven hepatic anti-fibrotic effects.
Our aim is to verify the myocardial anti-fibrotic potential of CM-272. The direct effect of CM-272 on fibroblast proliferation, differentiation, methylation profile and function will be tested in human adult cardiac fibroblasts exposed to the pro-fibrotic triggers present in HF, such as proinflammatory cytokines (TGF-β, interleukins), hypoxia, or endothelium-derived extracellular vesicles (by RT-PCR and western blot). In vivo, the anti-fibrotic effects of CM-272 administration will be assessed in a model of HF due to pressure overload (transverse aortic constriction). The impact on cardiac function parameters (by echocardiography) and fibrosis (by histological molecular analyses) will be assessed.
This study will be a proof of concept to establish whether CM272 might be a novel therapy for the specific treatment myocardial fibrosis in HF.

yes	X
no	

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