



Research Project Proposal
Academic year 2018-2019

Project Nº 23

Title: *Study of target molecules in cardiac fibrosis and development of therapeutic nanoparticles for its treatment*

Department/ Laboratory: *Regenerative Medicine (Lab 1.01, CIMA)*

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Summary

The cardiovascular diseases constitute the greatest health risk in the occidental countries. These pathologies provoke ~30% of the deaths, equivalent to more than 17million annual deaths, from which the ischemia is the principal cause. In the case of myocardial infarction (MI), the main problem is the lack of an effective regeneration of the myocardium after ischemia, which ends up in an irreversible loss of the cardiac tissue and its substitution by a non-functional scar. This remodeling process occurs as consequence of fibroblasts activation which are the principal mediators of collagen deposit and scar formation. Interestingly, different molecular mechanisms are involved in the activation of these cells that are not deeply understood yet. Therefore, as cardiac fibroblasts play a prominent role in heart scarring, it is essential to understand and control their activity in order to develop efficient treatments for heart failure. Based on the analysis of our RNAseq data, we will study the molecular mechanisms involved in fibroblasts activation, using (siRNA) molecules to regulate their action. In vitro studies will be performed in order to determine fibroblasts proliferation (by MTS studies), migration (by imaging analysis) and differentiation by specific-gene and protein expression analysis (by qRT-PCR, Western-blot and ELISA). In vitro results will allow us to perform in vivo studies in a transgenic mouse model where MI will be induced. With that purpose, we will develop an innovative treatment based on the production of Alginate-Nanoparticles (NPs) that will allow localized and specific targets to be modulated, thus achieving an effective treatment. Animals will be treated with the NPs and hearts analysed (by confocal microscopy) to determine their putative benefit and the mechanisms involved. The results obtained from these studies will be of great relevance not only for better understanding the mechanisms of fibrosis in the heart but also to develop future therapeutic strategies. (Possibility of PhD (grant required)).*

yes	X
no	

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