



Research Project Proposal

Academic year 2019-2020

Project Nº 48

Title: Study of the molecular mechanisms involved in fibroblasts activation and differentiation in Myocardial Infarction

Department/ Laboratory

Medicina Regenerativa - 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 and differentiation of these cells that are not deeply understood yet.

Therefore, since 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 previous RNAseq studies where several pro-fibrotic genes have been identified, we will study the molecular mechanisms involved in fibroblasts activation, using a CrisprCas9 system to regulate the action of specific genes. In vitro studies will be performed in order to determine fibroblasts proliferation (by MTS studies), migration (by imaging analysis) and differentiation capacity (by qRT-PCR, Western-blot and ELISA), after gene deletion. In vitro results will allow us to perform in vivo studies in a transgenic Cas9-expressing mouse model where MI will be induced. With that purpose, we will design and develop Lentiviral vectors coding for guide RNAs (sgRNAs) that will be delivered to CRISPRize specific genes, thus achieving an effective treatment. Animals will be treated with the viral vectors 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	<input checked="" type="checkbox"/>	Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?
no	<input type="checkbox"/>	



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