Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2017-2018

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Project Nº 23
Title: Study of the epigenetic mechanisms involved in fibroblasts activation in Myocardial Infarction
Department/ Laboratory: Stem Cell Laboratory (1.01) /Center for Applied Medical Research (CIMA).
Director: Dra. Beatriz Pelacho **Contact: bpelacho@unav.es**
Summary The cardiovascular diseases constitute the greatest health risk in the occidental countries. According with the last inform of the World Health Organization (http://www.who.int/cardiovascular_diseases/en) these pathologies provoke at the global level, around 30% of the deaths, equivalent to more than 17 million annual deaths, from which the ischemia is the principal cause (1). In the case of myocardial infarction, 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 (2). Interestingly, different epigenetic mechanisms are involved in the activation of these cells that are not deeply understood yet (3,4). 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. In this project, we will study the epigenetic mechanisms involved in fibroblasts activation by using small molecules to regulate their activity. In vitro studies will be performed in order to determine the activity and mechanisms of action of the molecules by analysing fibroblasts proliferation (by MTS studies) and differentiation by specific-gene and protein expression analysis (qRT-PCR, Western blot and ELISA techniques will be performed). Also molecular mechanisms will be determined by analysing DNA and histones methylation/acetylation (by Western-blot). In vitro results will allow us to perform in vivo studies in a mouse model of myocardial infarction. Animals will be treated with the selected molecules and hearts analysed (by immunofluorescence techniques) 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.

References

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2. Travers JG, Kamal FA, Robbins J et al. Cardiac Fibrosis: The Fibroblast Awakens. **Circulation Research (**2016) 118(6):1021-40.

3. Boon RA, Dimmeler S. MicroRNAs in myocardial infarction. **Nature Reviews Cardiology** (2015) 12(3):135-42.

4. Neary R, Watson CJ Baugh JA. Epigenetics and the overhealing wound: the role of DNA methylation in fibrosis. **Fibrogenesis & Tissue Repair** (2015) 8:18