



Research Project Proposal
Academic year 2018-2019

Project Nº 26

Title: Collagen cross-linking in heart failure, a new central player in cardiac dysfunction

Department/ Laboratory Laboratory of Heart Failure and Myocardial Remodeling. Program of Cardiovascular Diseases. CIMA

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Summary

Heart failure (HF) is one of leading causes of death and hospitalization in Western countries. Myocardial fibrosis, commonly found in HF patients, is determined not only by an increase in the quantity of collagen but also by alterations in its quality. In particular, an increase in the degree of collagen cross-linking (CCL), that renders fibres stiffer and more resistant to degradation, is associated with increased stiffness of the left ventricle, increased filling pressures and a worse prognosis in HF patients. Beyond passively increasing the stiffness of the left ventricle, alterations in CCL may affect the behavior of neighboring cells. The aim of this study is to analyze the mechanisms involved in cardiac CCL in response to several stimuli involved in HF development and to evaluate the impact of increased CCL on the morphology and function of cardiac cells (fibroblasts and cardiomyocytes).

1) Mechanism regulating CCL in response to mechanical, neurohumoral and chemical factors will be studied in freshly isolated human cardiac fibroblasts. The effect of the stimuli on non coding RNAs regulating CCL (e.g. miR-19b and WISPER) and on the enzymes directly involved in this process will be evaluated.

2) The impact of increased stiffness of the extracellular matrix (15kPa-80kPa) will be assessed in human cardiac fibroblasts and in isolated adult rat cardiomyocytes. In fibroblasts their activation, proliferation and secretory phenotype will be assessed. In cardiomyocytes, hypertrophy, stiffness, death and mitochondrial function (as an index of the energetic metabolism) will be measured.

Table with 2 columns and 2 rows: yes, no, X

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