



MASTER'S DEGREE IN BIOMEDICAL RESEARCH

Research Project Proposal

Academic year 2024-2025

Project Nº 02

Title: Targeting inflammation in heart failure with preserved ejection fraction

Department/ Laboratory *Laboratory of Heart Failure, Division of Cardiovascular Disease, CIMA*

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Summary *Short summary of the project with a **maximum extension of 250 words**, including the goals and the methodology that will be used*

Heart failure with preserved ejection fraction (HFpEF) is a complex and heterogenous syndrome associated with multiple comorbidities like hypertension, diabetes or chronic kidney disease and with other cardiac complications like atrial fibrillation (AF). HFpEF is a leading cause of mortality and hospitalization, and specific treatments improving clinical outcomes and quality of life are lacking. Low-grade inflammation, triggered by metabolic stress and other comorbidities, may drive HFpEF development as well as atrial myopathy and dysfunction in AF. However, the potential functional benefit of treatments targeting inflammatory pathways has not yet been demonstrated in HFpEF. In this project we will investigate the role of pro-inflammatory pathways during ventricular and atrial remodelling in HFpEF.

Our aims are to: 1) Characterize pro-inflammatory phenotypes in AF and HFpEF progression to improve patient diagnosis and risk stratification; 2) Identify the role of pro-inflammatory cells and pathways in the development of HFpEF in rodent models; 3) Evaluate the cardioprotective effects of anti-inflammatory therapies including monoclonal antibodies against IL-6.

In order to do so, in serum from HFpEF and AF patients we will assess pro-inflammatory pathways to define specific molecular signatures. We will also study inflammation and activation of the inflammasome in ventricular and atrial tissue from patients with HFpEF and/or AF. On the other hand, in a model combining hypertension with chronic kidney disease we will determine the role of IL6, IL1 β and the inflammasome in driving ventricular and atrial remodelling. The impact on cardiac function parameters (by echocardiography) and cardiac remodelling (i.e. hypertrophy, fibrosis, vascular dysfunction) (by histological molecular analyses) will be analyzed.

yes	X
no	

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