



MASTER'S DEGREE IN BIOMEDICAL RESEARCH

Research Project Proposal

Academic year 2024-2025

Project Nº 22					
Title: Investigating transthyretin amyloid cardiomyopathy through advanced disease modeling					
Department/ Laboratory <i>Biomedical Engineering Program/ Cardiac Tissue Engineering Group, Laboratory 1.01, CIMA</i>					
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Summary <i>Short summary of the project with a maximum extension of 250 words, including the goals and the methodology that will be used</i>					
<p>Transthyretin (TTR) amyloid cardiomyopathy (ATTR-CM) is a disease caused by the abnormal production of misfolded transthyretin protein by liver cells, which is then released systemically and its amyloid deposition in other organs has important disease implications. Specifically, aggregates of these misfolded or misassembled cross-beta-sheet amyloid fibrils in the heart is linked to cardiac toxicity and progression towards heart failure. Presenting itself in 2 forms, aggregates of wild-type (TTR) are found in approximately 25% of the over-80s, whilst the familial form is associated to a more aggressive cardiomyopathic phenotype. Our lack of deep understanding of the mechanisms driving disease render a poor prognosis for patients, with survival after diagnosis currently set around 5-15 years. Intensive research, which includes the development of new and relevant models for disease investigation and therapeutic discovery, are needed. In the present project, we aim to develop an integrated tissue engineered-based model of ATTR-CM. This will include the derivation of hiPSC cell lines from diseased patients and their differentiation towards the main cellular players of the disease including hepatocytes as the source of TTR amyloid, and cardiac cells as the developers of the cardiomyopathic phenotype. Model generation will be based on state-of-the art differentiation methods, frontline biofabrication and biomaterials (3D printing) and the application of modern transcriptome analysis. All in all, we will develop a relevant human 3D model of ATTR-CM, uniting all the relevant pieces of the complex puzzle that is the disease.</p>					
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yes	X				
no					
Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?					