UNIVERSITÀ DEGLI STUDI DI PADOVA

PROJECT

Tutor's Name	Prof. Nicola Ferri
Cotutor's Name	Dr. Maria Giovanna Lupo

1) Project title

Reparative mechanisms in coronary microenvironment during acute myocardial infarction

2)Abstract (max 500 words)

Thrombosis is a major complication of cardiovascular disease, leading to myocardial infarction, acute ischemic stroke, or venous thromboembolism. Developments in thrombectomy have provided new opportunities to study thrombus composition which may help to understand mechanisms of disease and underpin improvements in treatments. The present project aimed to characterize the cellular composition of thrombus derived from patients with myocardial infarction (MI). We will search for multipotent cells including the mesenchymal stem cells (MSCs), with tissue reparative function. MSCs exhibit antiapoptotic, anti-inflammatory and immunomodulatory properties regulating the behavior of immune cells, including macrophages, which play an important role in atherosclerosis. This analysis may identify a particular stem cell subtype with important reparative activities after the MI. In addition, stem cells secrete various immunomodulator factors and extracellular vesicles (EVs) which act as paracrine mediators. By collecting both arterial and venous blood samples, we plan to characterize, by Luminex-xMAP® technology the chemokines release into the circulation after MI that may be implicated in MSCs recruitment and homing. In addition, we will perform a proteomic analysis of EVs derived from blood samples collected during thromboaspiration. Mesenchymal stem cells will be isolated from the blood of patients and cultured in vitro to study their regenerative potential towards the endothelial cells and immunomodulation activities on macrophages. The thrombus composition and circulating protein patterns will be then utilized as predictors of clinical outcomes of patients after MI. This statistical analysis as well as the analysis of proteome data and single cell RNAseq will require a dedicated bioinformatician. Considering the normal clinical intervention observed at Department of Cardiology - Hospital of Venezia-Mestre (Italy) we plan to collect approximately 60-80 thrombus and blood samples during the first 33 months of the study with a 1 month follow up for cardiological evaluation of patents and a second single cell RNAseq analysis from blood samples. By bioinformatic and statistical analysis we will associate the amount and the phenotypic characteristics of MSCs with clinical outcome of patients evaluated by doppler echocardiography