RESEARCH TOPIC-MEM15
ROLE OF DNA METHYLATION IN CARDIOVASCULAR DISEASES

Curriculum MEM Standard

Laboratory name: Inflammation and Immunology in Cardiovascular Pathologies, Humanitas University

Pre-clinical Supervisor: Prof. Gianluigi Condorelli

Abstract

Gene expression is needed for the maintenance of cardiovascular diseases under normal conditions and in response to stress. Each cell type of the cardiovascular system has a specific program controlling transcription. Different types of stress induce modifications of these programs, and if prolonged, can lead to altered cardiac phenotype and, eventually, to heart failure. The transcriptional status of a gene is regulated by the epigenome, a complex network of DNA and histone modifications. Until a few years ago, our understanding of the role of the epigenome in cardiovascular disease was limited. But over the last decade, the role of a number of epigenetic modifications, including DNA methylation and hydroxymethylation, histone methylation and acetylation, and changes in chromatin architecture, have emerged as key regulatory mechanisms. Indeed, it is now clear that many levels of regulation contribute in defining the epigenetic landscape required for a correct cardiovascular function, and that their perturbation is responsible for cardiac disease. The aim of our program is to understand the role of DNA methylation and hydroxymethylation in cardiovascular diseases, with a focus on cardiac hypertrophy and atherosclerosis development. Correlations with human diseases will be studied. The project is part of a European partnership and will include research activity in collaboration with two research groups in Spain and France

Main technical approaches
We will use genetically modified mice, in vitro and in vivo cardiovascular physiology assessment, Chromatin immunoprecipitation (ChI, RNA sequencing and bioinformatics to gather insights on the relevance of key epigenetic modifications in our disease models.

Scientific references

1.Greco CM*, Kunderfranco P, Rubino M, Larcher V, Carullo P, Anselmo A, Kurz K, Carell T, Angius A, Latronico MV, Papait P, Condorelli G* (2016). “DNA hydroxymethylation controls cardiomyocyte gene expression in development and hypertrophy” Nature Communications 7:12418

Humanitas University
Via Rita Levi Montalcini 4
20090 Pieve Emanuele (Milano) Italy
Tel +39.02.8224.1 - Fax +39.02.8224.2394
info@hunimed.eu
Website: www.hunimed.eu
C.F. 97692990159

2.Greco CM, Condorelli G. (2015) “Epigenetic modifications and noncoding RNAs in cardiac hypertrophy and failure.” Nature Reviews Cardiology 12(8):488-97

3.Fuster JJ*, Walsh K* et al (2017). Clonal hematopoiesis associated with TET2 deficiency accelerates atherosclerosis development in mice. Science. 355(6327):842-847

Type of contract

Scholarship of € 21.000 gross per year awarded by Istituto Clinico Humanitas. This sum is subject to IRPEF income tax and exempt from social security contributions.

Borsa di studio pari a € 21.000 annui lordi erogata da Istituto Clinico Humanitas. Importo soggetto a tassazione IRPEF ed esente da contribuzione previdenziale.

Humanitas University
Via Rita Levi Montalcini 4
20090 Pieve Emanuele (Milano) Italy
Tel +39.02.8224.1 - Fax +39.02.8224.2394
info@hunimed.eu
Website: www.hunimed.eu
C.F. 97692990159