RESEARCH TOPIC MECM_23

Circadian Regulation of Immune Responses in Cardiac Fibrosis and Heart Failure

Curriculum

MECM Standard

Research Area

Cardio

Laboratory name

Circadian Metabolism Lab, Via Rita Levi Montalcini 4

Research Supervisor

Prof. Carolina Magdalen Greco carolina.greco@hunimed.eu

Abstract

Heart failure remains a leading cause of morbidity and mortality worldwide. Despite major advances in cardiovascular research, patient outcomes remain poor, with persistently high mortality rates. Cardiac fibrosis—a common co-morbidity of heart failure—drives disease progression by exacerbating cardiac dysfunction and increasing mortality risk. Notably, there are currently no approved therapies that directly target cardiac fibrosis, underscoring a critical unmet clinical need.

Circadian rhythms regulate nearly all aspects of physiology. These endogenous, cell-intrinsic clocks are synchronized by environmental cues, enabling organisms to anticipate and adapt to daily changes. Disruption of circadian rhythms is increasingly recognized as a contributor to cardiovascular disease, although the underlying mechanisms remain poorly understood.

Emerging evidence suggests that circadian clocks regulate myofibroblast differentiation, while circadian control of immune responses can either promote or suppress fibroblast activation. However, whether and how these mechanisms operate in the heart remains unknown.

This PhD project will systematically investigate how circadian regulation of immune responses influences cardiac fibroblast function and the progression of fibrosis in heart failure. We hypothesize that inflammatory signals act as extrinsic amplifiers of stress-induced, circadian-dependent fibroblast activation. To test this, the project will examine circadian variation in immune cell populations and inflammatory mediators, and their association with fibroblast activation, using both preclinical models and a cohort of heart failure patients.

By integrating molecular biology, immunophenotyping, multi-omics approaches, and in vivo models, the project will help define a circadian–immune–fibrotic signature of heart failure. This work will lay the foundation for the development of personalized, circadian-based therapeutic strategies for heart failure.

Main technical approaches

Previous experience in cell culture, flow cytometry, and/or molecular biology is desirable.

Scientific references

1. Caputo R, Greco CM. “Circadian rhythms and cardiac physiology: An essential interplay.” International Review of Cell and Molecular Biology 2025

2. Panico C, et al. “Single-Cell RNA Sequencing Reveals Metabolic Stress-Dependent Activation of Cardiac Macrophages in a Model of Dyslipidemia-Induced Diastolic Dysfunction.” Circulation. 2024

3. Greco CM, et al. “S-Adenosyl-L-Homocysteine Hydrolase Links Methionine Metabolism to the Circadian Clock and Chromatin Remodeling” Science Advances 2020 6(51):eabc5629

4. Greco CM, Sassone-Corsi P. “Personalized medicine and circadian rhythms: Opportunities for modern society” J Exp Med. 2020 217(6):e20200702

5. El Jamal N, et al. "The Circadian Biology of Heart Failure" Circ Res 2023 Jan 20;132(2):223-237. doi: 10.1161/CIRCRESAHA.122.321369

Type of contract

Scholarship of € 24.500 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 € 24.500 annui lordi erogata da Istituto Clinico Humanitas. Importo soggetto a tassazione IRPEF ed esente da contribuzione previdenziale.

Humanitas University – Via Rita Levi Montalcini, 4 – 20072 Pieve Emanuele (MI) Italy
CF 97692990159 – Tel. 02.8224.3777 – info@hunimed.eu – hunimed.eu