RESEARCH TOPIC DASMEN8
Investigating 24-hour gene expression rhythms in patients with heart failure

Curriculum DASMEN Standard

Laboratory name and address
Circadian Metabolism Lab
Humanitas University

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Abstract
Mammalian physiology is temporally coordinated by the circadian clock, a cell-autonomous system responsible for daily rhythms in physiology. Growing epidemiological evidences show that circadian disruption is a major risk factor for cardiovascular disease. While studies have suggested an implication of the clock system in the development of heart failure (HF), the underlying mechanisms remain to be elucidated and most findings are limited to animal models due to the lack of human time-series data.
The advent of -omic technologies and the development of appropriate algorithms has enabled the interrogation of rhythmicity of genes from single time-point unordered human samples. In this project we will take advantage of the many available human heart failure transcriptomic datasets and apply state-of-the-art algorithms to identify a signature of 24-hour rhythmicity associated with heart failure patient. To further investigate the significance of data obtained from human datasets we will perform a time resolved single-cell RNA-seq analysis of cells isolated from an animal model of heart failure. This will allow us to identify novel regulatory mechanisms directly linked to the clinical setting.

Main technical approaches
Preferred Basic knowledge in programming language (R and/or Python) is preferred.

Scientific references
Greco CM, Sassone-Corsi P. “Circadian Blueprint of Metabolic Pathways in the Brain” Nat. Rev. Neuroscience 2019 20(2):71-82

S. L. Chellappa, N. Vujovic, J. S. Williams, F. Scheer, Impact of Circadian Disruption on Cardiovascular Function and Disease. Trends Endocrinol Metab 30, 767-779 (2019)

Ruben DR, Hogenesch JB. "A database of tissue-specific rhythmically expressed human genes has potential applications in circadian medicine" Sci Tral Med 2018 10(458):eaat8806

Brief description of the coherence of the project in relation to the PNRR objectives

Studying circadian alterations allows for a more tailored approach that considers timing of drug administration based on the diurnal expression of genes encoding targets, transporters and metabolizing enzymes. By dissecting the circadian signature of patients with heart failure, we will be able to identify a more personalized approach based on the idea of chronotherapy. On one hand, we will be able to maximize the efficacy of therapeutic paradigms, and on the other, we will be able to better time the administration of therapies based on individual chronotypes (circadian phenotypes).

N. of months abroad

6 months, at University of California Irvine (UCI), Department of Computer Science

Type of contract

PhD scholarship of € 18.000 gross per year awarded by Humanitas University on institutional funds and cofounded with PNRR funds under M.D.M. D.D. N. 118/2023.
This sum is exempt from IRPEF income tax according to the provisions of art. 4 of Law no. 476 of 13th August 1984, and is subject to social security contributions according to the provisions of art. 2, section 26 and subsequent sections, of Law no. 335 of 8th August 1995 and subsequent modifications.

Borsa di dottorato pari a € 18.000 annui lordi erogata da Humanitas University su fondi istituzionali e fondi da D.M. 118/2023. Importo non soggetto a tassazione IRPEF a norma dell'art. 4 della L. 13 agosto 1984 n. 476 e soggetto, in materia previdenziale, alle norme di cui all'art. 2, commi 26 e segg., della L. 8 agosto 1995, n. 335 e successive modificazioni.