

**MEDICAL BIOLOGY – FOUR YEAR, FULL-TIME DOCTORAL STUDIES**  
**in the Center for Translational medicine, International Clinical Research Center**  
**(FNUSA-ICRC)**

Research area: Cell mechanobiology

Dissertation topic: **Study of the mechanoresponsive network in heart biology and disease**

Summary: Cardiomyopathies are forms of cardiovascular diseases causing alterations in the structure and function of heart muscle, compromising the ability of the myocardium to contract, and, therefore leading to death or progressive heart failure in most of the cases. Although the pathophysiological mechanisms associated with each type of disease might be diverse, all of them concur finally in the failure of the contractile muscle to efficiently and timely develop the force necessary for contraction. Given the mechanical origin of these alterations, mechanosensing pathways are emerging as a key component in the reorganization of tissue in such diseases, and consequently, they are interesting as a potential therapeutic target in view of the setup of new treatments.

Several molecules have been described as mechanoresponsive at a cellular level, such as the calcium channel TRPV4, focal adhesion proteins such as Vinculin, or nuclear envelope components, such as Lamins.

Similarly, signals transduction systems, such as the Hippo pathway, can transform the mechanic cues arising from cell environment into a transcriptional response. However, although all of them have been shown to respond to similar mechanical inputs, the interplay among their elements remains poorly understood.

Therefore, the goal of this project will be to explore the possible interplay among the different mechanosensing pathways in heart biology and disease. The experimental models to be used will be human induced pluripotent stem cell (hiPSC) derived cardiomyocytes and human tissue samples obtained from healthy donors and heart failure patients.

Aims to be reached in the dissertation:

- Characterization of active mechanoresponsive pathways in cardiac cells in vitro
- Characterization of active mechanoresponsive pathways in adult human cardiac tissue
- Identification of alterations of mechanosensors in cardiac pathologies

Number of accepted applicants: 1

Funding: Beyond standard MU scholarship student usually gets a contract at supervisor's grants or institutional projects.

Prerequisites and requirements for applicants and students

- Complete Master's degree in molecular biology, biochemistry or similar field
- Essential training in a range of molecular biology techniques relevant to basic research
- Well-organised, motivated and passionate
- Fluent in English on a daily basis

- Teaching around 100 - 250 hours within standard 4-year studies
- Fellowship abroad (min. 1 month) on a foreign institution during the studies

Other obligations and recommendations: <http://www.med.muni.cz/index.php?id=795>

Supervisor's name: **Giancarlo Forte, Ph.D.**

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Supervisor's 5 best articles: Nat Commun. 2017;8:15321  
ACS Nano 2014;8: 2033-2047  
Adv Mater 2011;23: 514-518  
Front Physiol 2014;5:210  
Stem Cells 2008;26: 2093-2103

Success in grant competitions – recently finished or currently ongoing grants:

- H2020-MSCA-RISE-2015. Tracking nano-bioproceses using Super-Resolution Microscopy Techniques” (NANOSUPREMI) (project number 690901). €150.000 (2016-2018)
- INTERREG V-A ATCZ133 “Competence Center for Mechanobiology in Regenerative Medicine”. € 235.000 (2017-2020)
- Czech Ministry of Education (OP VVV). “Unveiling the molecular determinants of aging to design new therapeutics” (MAGNET). € 7.276.106 (2017-2022)
- Czech Ministry of Education. National Sustainability Project (NPU II), “Translational Medicine”. € 37.000.000 (2016-2020)

International cooperation:

Technical University of Vienna (Austria), University of Melbourne (Australia), University Campus Bio-Medico in Rome (Italy), University of Porto (Portugal), Tokyo Women's Medical University (Japan).

Successful PhD graduates and their further fulfilment: Mrs. Sara Romanazzo, Waseda University (Japan)