

Doctoral study program: Biomedical Sciences (at Department of Biology)

Form: *doctoral* (*present*)

Department: Mechanobiology of Disease, FNUSA-ICRC

Supervisor: Vladimir Vinarsky, PhD

Ph.D. position: Dissection of YAP1 activity on sarcomere maturation and force generation in human

cardiomyocytes.

Annotation

Reactivation of developmental pathways is an emerging avenue in efforts to regenerate adult failing heart. Hippo pathway effector YAP1, key player during development, which is deactivated in an adult heart, is one of such targets. While the Hippo mediated (pro-proliferative) effects of YAP1 activity have been thoroughly explored, the effects of Hippo independent activation of YAP1 on sarcomere structure, maturation, and force development are just starting to be explored.

The student will work with *in vitro* model of pluripotent stem cell derived cardiomyocytes. Initially the student will prepare inducible human pluripotent stem cell lines to 1. silence endogenous YAP1 2. induce expression of mutated variants of YAP1. Next, impact of temporally restricted expression of YAP1 variants on cardiomyocyte mechanosensing, maturation, and force production using super-resolution microscopy, traction force microscopy in single cell cultivation model will be assessed. Finally, mechanistic understanding of the process will be facilitated by identification of interactors and transcription factors mediating differential outcomes of different mutant forms of YAP1.

Funding of the research

The research will be funded by sources from MUQUABIS (Grant agreement ID: 101070546), institutional support, and further grants which will be obtained in the future

Information on funding PGS positions

The program requires that all PhD students have some means of financial support of min. 25 000 CZK per month. This is often a combination of various sources (grants, scholarship etc.)

Requirements for the student according to the Board for the PhD studies

The student's minimum publication activity within the course of study is one first-author publication with an IF value above the median in the field or 2 first-author publications in journals with an IF value in the 3rd quartile in the field (Q3). A condition for successful completion of the studies is also a foreign internship of at least 1 month, which is an inseparable part of the studies. As part of their studies, students will also participate in the teaching.

Supervisor

Mgr. Vladimir Vinarsky, PhD