

Affiliation: Masaryk University, Faculty of Medicine

Study program: PhD program Biomedical Sciences **Specialization:** Biochemistry and Molecular Biology

Workplace: International Clinical Research Center of St. Anne's University Hospital

Mode: Full-time

Supervisor: Giancarlo Forte

Lab's website: www.fnusa-ctm.org

Title: Pathological mechanosensing in cardiac cell nucleus

Brief annotation:

Despite the advances in therapies and prevention, heart failure (HF) remains the leading cause of mortality worldwide (over 1.8 million deaths / year, equal to 37% of all deaths). Data produced in my laboratory indicate that ECM maladaptive remodelling might impact on cardiomyocyte function by affecting the integrity of the nucleus through LINC complex. Additionally, my research group found that YAP hyperactivation in patient-derived cardiac fibroblasts promotes ECM pathological remodeling (Perestrelo et al, Circ Res 2021), thus promoting the fibrotic process and heart failure. In a different experimental setting, we also showed YAP sustained activity in fibroblasts affects neighboring cell response by acting on their linker of nucleoskeleton and cytoskeleton (LINC) complex and possibly on chromatin accessibility (in preparation).

The PhD student will engage in a project intended to investigate the interaction between ECM remodeling and nucleoskeleton integrity in cardiomyocytes, with a specific attention to the regulation of chromatin accessibility. The methods adopted will be super-resolution microscopy, FLIM-FRET and, possibly, ATAC-seq. The use of induced pluripotent stem cells (iPSC), iPSC-derived organoids and engineered heart tissues (EHTs) is envisaged.

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Requirements: Master degree in biological sciences or similar. Experience with cell culture.

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