Role of stem cell- derived extracellular vesicles in regulation of autophagy and mitochondrial homeostasis in cardiac cells after ischemic injury (MiRegEV)

Extracellular vesicles (EVs) represent vesicular biological nanoparticles, released by several various cell types, including mesenchymal stem/ stromal cell (MSCs), and carrying bioactive molecules such as e.g. proteins and small regulatory RNA transferring several bioactive molecules (including regulatory miRNAs) which may be transferred to other cells impacting on their functions and biological properties.

Growing evidence including our results, indicate that MSC-EVs may transfer their cargo to mature cardiac cells, modulating their functions both *in vitro* and *in vivo* and enhancing pro-regenerative processes ongoing in heart tissue after ischemia/ reperfusion (I/R) injury such as acute myocardial infarction (AMI).
Our recently published studies indicated pro-regenerative role od especially bioactive miRNAs, regulating expression of various genes, depending on their activity and pathways or processes they may regulate in a cell, including cardiac cells.

Autophagy, and their unique type – mitophagy regulating mitochondrial homeostasis, which undergo complex regulation by several signaling pathways, which may lead to adaptive or excessive activation of this process resulting in cardiac tissue repair or adverse remodeling, eventually leading to functional impairment of entire organ.
Our current studies indicates a presence of several miRNAs potentially regulating processes of autophagy and mitophagy in cardiac cells, and play a role as either activators or inhibitors of these processes.

Thus, the major aim of this Project will be to investigate a role of such selected microRNAs, transferred to cardiac cells by MSC-EVs, in regulating process of autophagy, mitophagy in cardiac tissue, which will be addressed in several advanced in vitro studies (including use of 3D cardiac microtissues) and in myocardium in vivo (following MSC-EV injection into ischemic heart after AMI).

The expected outcomes of the Project will not only provide new knowledge on mechanisms underlying pro-regenerative activity of MSC-EVs in cardiac, but may also may provide some new perspectives for future strategies enhancing hart repair in patients after myocardial infarction.