Induced pluripotent stem cells (iPS), first created by the group of Professor S. Yamanaka in 2006 as a result of genetic reprogramming of differentiated skin cells, became not only scientific field of interest, but were also shown to be powerful tool for disease modeling and drug testing. In addition, one of their key applications is an attempt to use these cells in the regenerative medicine. Thanks to their pluripotency, iPS can be successfully propagated and differentiated into various types of tissues, becoming an excellent source of cells for transplantation and repair of damaged organs. Recently, rapid development of iPS technology, particularly including human iPS (hiPS), also accelerates the development of personalized medicine, allowing to obtain an autologous cells for any patient. In addition, similarly to other cells, hiPS can secrete **extracellular vesicles (EVs)** - small (50 nm to 1µm) circular membrane structures released from the cell surface. As EVs can contain bioactive cargo in the form of cytoplasmic and surface proteins, transcription factors, as well as nucleic acids, they occurred to be considered as an important mediators of cell-to-cell communication, but also as paracrine factors involved in the regeneration of damaged cells.

However, despite the advanced research, still many aspects of hiPS biology and their response to external factors remain unknown. Moreover, effective differentiation protocols of these cells remain insufficient, which carries the risk of tumor formation after hiPS transplantation. Hence, further studies are required to fully understand the molecular aspects and the biological potential of hiPS-EVs One of the interesting approaches is the use of reduced oxygen level (hypoxia), comparing to its atmospheric concentrations (21% O_2; normoxia). Recent studies indicate that hypoxia, as better suited to the physiological conditions present in cell niches, may positively influence cell behavior, promoting the proliferation and differentiation of various types of cells, including stem cells. In addition, oxygen deficiency is often found in damaged tissues, including cardiovascular ischemia, which may affect the fate of residual cells. **However, to our knowledge, the effect of hypoxia on molecular status and functional properties of hiPS-EVs has never been investigated, making it reasonable to address this issue in the proposed Project.**

Therefore, the aim of the Project will be the multiparameter molecular characterization of the effect of hypoxic conditions (3% and 5% O_2) on hiPS-EVs compared to normoxia (21% O_2). By utilization of modern molecular biology methods, we plan to perform detailed genetic and functional analyzes of hiPS-EVs obtained from hiPSCs culture at different oxygen concentrations, including their impact on human heart cells in vitro, as well as evaluation of regenerative potential in mouse model of acute myocardial infarction. Obtained results will expand our knowledge about the potential use of hiPS-EVs for the treatment of cardiovascular dysfunctions, considered as one of the leading cause of death in developed countries.