Aim of this study is to understand process of division of heart cells (cardiomyocytes) obtained from human induced pluripotent stem cells (hiPSC-CMs). In defined conditions hiPSCs can give rise to virtually all cell types found in adult body. Therefore they might serve as tool for testing toxicity of new drugs to various cell types and for investigating of various cell mechanisms. Biological material needed for generation of hiPSC might be obtained painlessly and non-invasively. Thus hiPSC might be generated in relatively short time. These cells might be the future of personalized and regenerative medicine.

Current knowledge suggests that human adult heart possess modest regenerative properties. However regenerative potential of heart is not enough to overcome deleterious effect of myocardial infarction. Nevertheless it is very important information which suggests that upon proper stimulation human cardiomyocytes can start dividing again.

At early stage of pregnancy, development of heart mainly relies on division of cardiomyocytes. During pregnancy there are hypoxic conditions in uterus and only source of energy are glucose and lactate.

It was shown that hypoxia promotes division of cardiomyocytes in adult organism and switch from glucose, which is present in placenta, to fatty acids, which are found in mothers' milk, as main energy source induces maturation of cardiomyocytes which in turn results in cell-cycle withdrawal. Another interesting factor influencing division of cardiomyocytes are microRNA (miRNA). miRNA are short, non-coding RNAs which can inhibit other genes. miRNAs which belongs to miRNA-15 family were shown to downregulate genes involved in cell cycle. miR-15 family was shown to increase shortly after birth, which correlates with inhibition of cardiomyocyte divisions.

It might be speculated that during first stages of pregnancy hypoxic conditions, availability of glucose only and lack of miR-15 family are responsible of cardiac divisions.

To date, there are many studies addressing the issue of cardiomyocyte divisions. However in majority they are focused on one, particular factor which might not be enough to fully understand mechanisms governing divisions of cardiomyocytes. Therefore we would like to perform complex studies involving investigation of hypoxia; availability of glucose only and lack of miR-15 family in model of human cardiomyocytes.

Aims of the study:

1. Assessment of impact of switch from glucose to fatty acid as main source of energy cardiomyocyte divisions.
2. Check if silencing of antiproliferative miR-15 family will positively affect cardiomyocyte divisions.
3. Check if hypoxic conditions will have an impact on divisions of human cardiomyocytes.
4. Determine if combination of all discussed factors: hypoxia, glucose and lack of antiproliferative miR-15 will have additive or synergistic effect on cardiomyocyte divisions.

In case of severe myocardial infarction the only solution for patient is heart transplantation which is remarkably reduced due to chronic shortage of donors. Therefore there is need to develop new pharmacotherapy which will aim to reconstitute lost heart tissue. Pharmacotherapy which is used nowadays is basing on methods developed 30 years ago and they aims only to increase functionality of remaining cardiac tissue. Obtained results will help us to better understand the mechanisms of divisions of human cardiomyocytes and might contribute to development of new pharmacotherapy strategies and boost progress in personalized and regenerative medicine.