Ischemic heart disease (IHD) and its complications such as heart attack or heart failure, occupy a leading position among the world of cardiovascular disease. The risk of these diseases increases with age, and with demographic projections it is expected to increase the number of patients with an aging population, especially in Western countries, but also in Poland. The current methods for treating ischaemic heart disease include the modification of risk factors, pharmacotherapy and interventional treatment. The technological progress have contributed to the significant reduction of mortality rates in patients with myocardial infraction (MI). On the other hand, however, in the long run the incidence of cardiac insufficiency continues to rise as a consequence of post-infraction remodelling of the cardiac muscle (CM). Modern medicine faces an enormous challenge which requires innovative solutions adapted to new requirements. One strategy to extent the therapeutic panel for the cardiovascular diseases treatment is the use of cell therapy. It is a safe therapy, but not without limitations associated mainly with low efficacy of stem cells nesting in the myocardium. Therefore, in recent years it emphasizes the need to optimize the cell therapy through modification of the stem cells themselves as well as methods of administration and duration of treatment.

The main objective of this project is to develop methods for the safe and efficient transfer of stem cells to pericardium to regenerate damaged heart muscle. For this purpose, we plan to use the best-validated, pre-clinical model of myocardial infarction in pigs, which will be the basis for evaluation of cell therapy.

The project relies on the idea of the pericardium being an easily accessible reservoir which enables prolonged release of drugs and biological agents, which can penetrate into tissues much easily owing to the anatomical proximity to the coronary arteries and myocardium, as well as the biological properties of the visceral pericardium. In turn, controlled release of the chemotactic factor (stromal cell-derived factor, SDF-1α) into the pericardial sac for circulating stem and progenitor cells (SPCs) allows for eliminating the basic technical problem of the stem cell therapy which is a low nesting rate and short retention of the cells injected into heart. Controlled release of SDF-1 from biodegradable microspheres with an adjustable size and degradation rate delivered to the pericardium percutaneously enables the optimization of the method through the selection of such parameters which allow to obtain a gradient of a chemotactic factor sufficient to recruit KMP from peripheral blood. It is to cause the intensification of the repair response occurring naturally after the ischemic damage to the heart.

The method for the delivery of the biological substance is the innovative intrapericardial therapy system developed by the project manager which allows for the delivery of any drug substance to the pericardial sac in a repeatable and controlled manner. Therapy efficacy will be evaluated on the basis of the most precise *in vivo* method for evaluating the heart structure and function: magnetic resonance imaging (cMRI), and histopathological and molecular examinations. The method for documenting the efficacy of the intrapericardial transfer of SDF-1α will be the *in vivo* evaluation of the homing by the SPCs by marking them with the superparamagnetic marker.

We believe that the use of a novel method of treatment based on additional release of chemotactic factor crucial for the regeneration of the heart is a way to eliminate the basic limitations of cell therapy that is short-lived and ineffective nesting stem cells. Validation of this method on a model of large animals will not only allow for the implementation of the intrapericardial therapy in ischemic cardiomyopathy, but also provide a platform for delivering drugs and biological substances to pericardium to enable the treatment of other diseases, ie. bacterial and autoimmune pericarditis or neoplastic diseases.