

The leading cause of death in Poland and in Europe is cardiovascular disease, including myocardial infarction (MI). Myocardial infarction is mainly caused by a blockage that prevents blood from flowing to the heart (ischemia). The cardiac muscle does not get enough blood, is subjected to ischemia, hypoxia, and dies. The standard procedure for the treatment of MI is coronary reperfusion - the restoration of the blood flow through blocked coronary artery as soon as possible. Unfortunately, that restoration of blood flow to ischemic myocardium inflicts additional damage - the ischemia/reperfusion injury (I/R). An important factor contributing to I/R injury is an excessive formation of reactive oxygen species, oxidative stress and degradation of contractile proteins by proteolytic enzymes. Searching for new agents that could protect the heart against I/R injury is a challenge for cardiology. Klotho protein was identified in 1997 in mice. Klotho-deficient mice had a short lifespan, infertility and several age-related disorders, such as atherosclerosis and osteoporosis. Importantly, recent research proved that Klotho protein deficiency is associated with cardiovascular disease. The antioxidative and protective role of Klotho protein has been also established. Thus, the aim of our study is to evaluate Klotho protein as a potential cardioprotective agent and to document the alterations of Klotho expression in cardiac cells under I/R injury. To document protective role of Klotho on cardiac cells, recombinant Klotho protein will be administered and the molecular mechanism of Klotho cardioprotection will be studied. The following models of I/R injury will be used: Human Cardiac Myocytes (HCM) line, isolated rat hearts perfused with the Langendorff method and isolated rat cardiomyocytes. Cardiomyocytes will be subjected to chemical I/R injury. Isolated rat hearts will be subjected to global, no-flow ischemia by cessation of perfusion. The research includes biochemical and genetic analyses, qualitative and quantitative analyses of protein production, assessment of cell contractility, determination of heart hemodynamic functions. The results of our research can be particularly important in the field of cardiology, giving a chance for a new strategy for the prevention and treatment of ischemic heart damage. This study may answer the question whether Klotho could be a new therapeutic agent in myocardial infarction.