The main objective of the proposed research project is to understand the role of NADPH oxidase Nox4 in pathomechanism endothelial dysfunction caused by docetaxel as a model of vascular dysfunction induced by chemotherapy. Chemotherapy is the most common kind of therapy for cancer, which significantly increases the survival rate of cancer patients. However, it has been shown that patients treated with chemotherapy suffer from cardiovascular disorders, in particular those linked to hypertension and atherosclerosis. This leads to an increase in mortality of patients who have gone through chemotherapy, due to cardiovascular reasons. The mechanisms of action of neoadjuvant chemotherapy on the biology of endothelial cells are still not fully understood, but most probably the NADPH oxidase and in particular the Nox4 oxidase and the hydrogen peroxide produced by it, plays the key role in this process. To clearly define the role of Nox4 in the examined phenomenon, we propose use of mice with the deleted gene Nox4 ($Nox4^{-/-}$).
We intend to use the Nox4 knock-out mice and wild-type C57BL/6J mice, which will be divided into four groups (n=10 in each group). Depending on the group, they will be injected with docetaxel or placebo. The aortas taken from the mice will be used to examine the vascular function in the organ bath, determine the level of superoxide anion and hydrogen peroxide and to study the level of expression of selected genes, proteins and immunochemistry study.
Our research will allow us to explore the detailed mechanisms of action of docetaxel, which is one of the most popular ingredients of neoadjuvant chemotherapy, on endothelial function. Presented experiment will allow for the determination of the role of Nox4 oxidase in endothelial dysfunction caused by the effect of docetaxel.