DESCRIPTION FOR THE GENERAL PUBLIC

Cancer is second, after cardiovascular diseases, cause of death in developed countries. Main reason of deaths caused by cancer are metastasis - secondary outbreak of disease, resulting in a transfer of cells detached from the tumor to others places in organism. One of mechanisms determining cancer metastasis is the epithelial - mesenchymal transition (EMT) - morphological and physiological changes associated with weakness of cell junctions. In this process the cancer tissue becomes less solid, which leads to the separation of individual cells and increases probability of metastasis.

Nanotechnology - technology of objects smaller than 100 nanometers in at least one dimension, is intensively developing branch of science, which gains we encounter more and more often in everyday life. The properties of nanomaterials are significantly different from those in the macro scale. High expectations are layed in use of nanotechnology in modern oncology. Nanomaterials as often used as contrast medium, cytostatic drugs carriers or therapeutical substances in photodynamic and phototermic therapy. However, there are increasing concerns about the safety of nanomaterials. Currently, we are not able to clearly determine how nanomaterials impact on the human body. In recent years, there are further indications of their broader toxicity, as well as information on potential carcinogens.

The purpose of this project is to determine the impact of selected nanomaterials - silver nanoparticles and multi-wall carbon nanotubes on the modulation of EMT. Research hypothesis assumes that the selected nanomaterials can regulate EMT, both inducing and inhibiting specific elements of the process. It has been shown that in mice exposed to multiwall carbon nanotubes, come to induce EMT, leading to lung fibrosis. On the other hand, gold nanoparticles have demonstrated the ability to inhibit EMT in various cellular models of ovarian cancer. The role of nanoparticles in EMT is not clear, but given the fact that this is an important mechanism of cancer metastasis, it seems important to conduct studies in this field.

The study will be conducted *in vitro* using cell cultures. The selected MDA-MB-436 cells derived from human breast cancer is a common model for studies of cancer metastasis. After optimizing the culture conditions, preliminary tests will be carried using colorimetric assays to determine the toxicity of nanomaterials. In EMT, epithelial cells lose their character, decreasing the level of proteins characteristic for that epithelial morphology (epithelial factors) and increasing the level of proteins characteristic for mesenchymal phenotype. The expression of these proteins will be determined by expression of the genes encoding them, and the level of protein visualised by immunohistochemical staining. Changes the expression of EMT markers is conditioned by the action of specific transcription factors that control gene replication. Thus, the next step of the proposed research project is to check the level of transcription factors. Moreover, activation of selected signaling pathways, governining the most important functions of cells (proliferation, apoptosis, etc.) will be assessed by immunofluorescence staing to answer the question, which of the signaling pathways in MDA-MB-436 is activated when cells are exposed to nanomaterials. During EMT cell morphology is changed. Process results in reorganization of the cytoskeleton, which is network of fibrous proteins that make organelles not flow freely in the cytoplasm. The most important protein in the cell cytoskeleton is actin, which fluorescence staining and confocal microscopy observation will determine potential changes of cytoskeleton through incubation of the cells with selected nanomaterials.

Number of human deaths from cancer continues to grow. Therefore, it seems important to searching for new forms of therapy, but also to identify potential factors that promote cancer development. Although nanotechnology has enormous potential to improve human life, we can not ignore reports about the potential toxicity of nanomaterials, including their participation in the process of carcinogenesis. Described in the project set of experiments, which can we classified as a fundamental research, would significantly enrich the knowledge in pharmacology, toxicology and public health. The proposed project will allow determine the contribution of selected nanomaterials on the process of metastasis of malignant tumors. Depending on obtained results, it may open up new therapeutic possibilities, but also may lead to the introduction of appropriate regulations at the international level, which are missing in the current legislation.