

Microenvironment dependent disruption of tumor capillaries using diamond nanoparticles in treatment of highly vascularized tumors

Development of new blood vessels is essential for growth and metastasis of tumours, in which tumor microenvironment and related with it pro-angiogenic and pro-inflammation factors plays crucial roles. Tumor microenvironment also leads to the formation of tumor endothelial cells, which, because of physiological and molecular changes, contributes to tumor development, malignancy and metastasis.

The development of blood vessels is a necessary process for the growth and metastasis of tumors. The key role in this process is played by the tumor microenvironment and associated pro-angiogenic and pro-inflammatory factors produced by cancer cells. The tumor microenvironment leads to a change in phenotype of endothelial cells to cancerous endothelial cells, which, as a result of changes at the physiological and molecular level, stimulate tumor development, malignancy and metastasis. Grade IV glioma, hepatocellular carcinoma and breast cancer are characterized by intense vascularization, high malignancy, and invasive phenotype. One of the strategies to fight highly vascularized tumors is to lead to a strong degradation of the tumor blood vessels network, which, when used appropriately, can lead to tumor size decrease and reduction of metastasis.

The presented project will use a strategy to reduce tumor blood vessels through specific interaction of diamond nanoparticles with membranes of endothelial cells. The project's innovation lies in the specific degradation of only blood vessels that are in the tumor microenvironment. At the same time, diamond nanoparticles do not show toxicity to cells other than endothelial cells. The research will use *in vitro* models - cell cultures, spheroids and *in vivo* models - bio-print models, tumor tumors grown on the chorioallantoic membrane of a chicken embryo and a mouse model.

The proposed research may contribute to the development of new anti-vesicular strategies by better understanding the physiology of tumor endothelial cells and the tumor microenvironment. Research on endothelial cells will provide new information about their involvement in pathological conditions and especially in cancer.