The development of effective methods of treating many diseases, including cancer, is based on the knowledge of molecular mechanisms responsible for their etiology. Research conducted at the cellular level, enabling the recognition of regulation pathways, mechanisms of action and their significance in the process of cancer formation are of great importance in the progress of medicine. An important matter of conducting *in vitro* tests is the best reflection of the conditions inside the tumor. A characteristic feature of the tumor microenvironment is hypoxia – low, non-physiological oxygen tension, that shapes the course of the cancer. The goal of this project is to investigate a potential new pathway regulating *SERPINE1* gene expression in kidney cancer in hypoxia.

SERPINE1 gene encodes the PAI-1 (Plasminogen activator inhibitor 1) protein involved in the fibrinolysis process, but also considered as a marker of poor prognosis in many types of cancer, including kidney cancer. PAI-1 is involved in important processes related to tumor growth, vascularization, tumor cell aggressiveness, and the risk of metastasis. The regulation of Serpine1 expression occurs at several levels in various types of cancers. Growth factors, interleukins, chemokines and small non-coding RNA (microRNA) molecules have been shown to affect the expression of this gene.

GAPDH (3-phosphoglyceroldehyde dehydrogenase) is an enzyme involved in cell metabolic processes (glycolysis), but it can perform other additional functions, including regulation of gene expression by binding to the characteristic sequences of the gene mRNA molecule. Literature data indicate that *SERPINE1* mRNA has these characteristic sequences so it may be a potential target for GAPDH. We obtained preliminary results that show an increased expression of *Serpine1* and *Gapdh* in a murine model of kidney cancer under hypoxia, and bioinformatics analysis showed the interaction between the two genes.

The hypothesis assumes that GAPDH is involved in the regulation of *SERPINE1* expression through binding to mRNA and thereby affects tumor progression.

The aim of the project is to confirm the GAPDH - *SERPINE1* interaction using different models of kidney cancer and to see how the potential new regulation pathway of Serpine1 affects the functioning of cancer cells. To this end, the expression of the *SERPINE1* and *GAPDH* genes will be impaired using genetic engineering methods and functional tests (assessing growth rate, migration capacity, aggressiveness, effect on the formation of blood vessels) will check their effect on cancer cells.

The project is innovative, the GAPDH-*Serpine1* interaction has not been previously studied in any type of cancer. Understanding the new regulation pathway of *SERPINE1* will help to better understand the mechanisms of PAI-1 action in kidney cancer and show new potential therapeutic goals. This proposed program, given the clinically documented importance of PAI-1 in kidney cancer (brands of poor prognosis), may in the future improve the effectiveness of treatment.