Despite very significant progress in cancer research, this disease remains a major cause of death worldwide. According to the World Health Organization, every year more than 8 million people die of cancer. Therefore there is an urgent need for research into molecular mechanisms of development and progression of cancer, with the ultimate goal of developing new methods of prevention and treatment of this disease.

Skin cancers are the most common human cancers, and more and more people become ill and die of these cancers. Annually worldwide there are between 2 and 3 million new cases of non-melanoma skin cancers, and about 132,000 new cases of melanoma. Surgical removal of the tumor is still the primary method to treat these diseases, but this method is not always effective; moreover, it is painful and often disfiguring for the patient, especially when the removed section of the skin is large. This is why we need new methods of prevention and early detection and treatment of this type of cancer.

According to the American Cancer Society, kidney cancer is one of the 10 most common types of cancer. In its treatment currently used chemotherapy and radiotherapy prove ineffective, and approved medicines often have serious side effects. If after surgical removal of the tumor there is a relapse of disease, prognoses for patients are poor. It should be emphasized that kidney cancer in the early stages of development may not cause any symptoms, and therefore early diagnosis of kidney cancer is very difficult. In later stages the symptoms are similar to symptoms of other diseases such as kidney stones or urinary infections. Therefore there is an urgent need for new methods of combating this type of cancer.

The risk of cancer depends on many factors, which also include genetic characteristics of the patient; this also applies to skin cancer and kidney cancer. Our laboratory investigates a specific family of genes called GRHL. These genes play a special role: they regulate the functioning of other genes. Analyses carried out by us and other research teams have demonstrated that all the genes from the GRHL family are important in cancer. Experiments on animals have established that mice with impaired GRHL genes display an increased incidence of cancer. Furthermore, the analyses of tumors surgically removed from human patients have shown that the development of many types of cancer is often accompanied by changes in the functioning of genes from the GRHL family. These include cancers of the breast, skin, liver, stomach and colon. Moreover, these genes are not merely passive indicators of progression of tumor growth, but they also have a direct influence on the process of carcinogenesis. Further tests were carried out using human cells grown in laboratory dishes. They have proven that switching off GRHL genes in non-tumor cells often leads to them acquiring the characteristics of tumor cells, while restoring the proper functioning of GRHL genes in cancer cells causes them to lose the characteristics of cancer cells. On the basis of these observations, we put forward a hypothesis that the correct functioning of GRHL genes is essential for their anti-oncogenic function, therefore mutations which affect the functioning of these genes impair their antitumor roles and thereby increase the risk of cancer in affected people.

Our preliminary results suggest that some mutations in the genes from the GRHL family occur with statistically significantly altered frequencies in patients with skin cancer or kidney cancer. In our project we are going to explain the impact of these mutations on the functioning of GRHL genes. If our investigations confirm the significance of these mutations in cancer, it will be possible to use this information to identify people with increased risk of cancer. Such people could then take appropriate steps to protect themselves from the disease; for example, in the case of skin cancer they could avoid excessive sunbathing. Such people could also have regular check-ups, as early diagnosis greatly increases the chances of successful treatment of cancer.

The ultimate goal of the proposed research is to characterize the mechanisms regulating functioning of genes from the GRHL family. If these mechanisms could be enhanced or inhibited by specific drugs or other chemical compounds, it would be possible to predict which compounds may affect the processes leading to changes in activity of GRHL genes. The above-mentioned examples demonstrate that a change in GRHL gene activity in tumor cells often results in loss of tumor characteristics by these cells, which is why such compounds could be used to treat these types of tumors. Therefore our studies, although not aimed at immediate practical applications or use, may prove practically useful in the future, contributing to the development of new therapies against cancer. Thus the economic and social impact of our work can be very far-reaching.