

Cancer is a disease which occurs as a result of changes in cells leading to their uncontrolled growth and division. Development of cancer may be due to genetic factors. Some genes that are over-stimulated may produce an increased amount of proteins, which in the next stage may be misused by the cell e.g. to induce increased proliferation and division, inducing the progression of cancer. Cancer is the second leading cause of death worldwide just after cardiovascular disease. According to the World Health Organization (WHO), the incidence of cancer and the associated mortality are increasing every year. There are over one hundred different types of human cancers. Cancer therapy is often based on surgical intervention, chemotherapy, radiation therapy or targeted therapy. The chances of recovery depend not only on the early recognition of the symptoms of the disease, but also on the selectivity and effectiveness of the treatment. Unfortunately, currently used therapies are burdened with many side effects and complications such as nausea, vomiting, skin changes, anemia or hair loss.

In the presented project, we propose to develop a basis for the design of new, effective molecular tools that have the chance to selectively reduce the proliferation of cancer cells. It has been known for some time that many oncogenes have specific structures, called G-quadruplexes, that act as triggers in the formation of RNA and proteins. Blocking these triggers leads to inactivation of the oncogene and, as a result, also blocks the proliferation of cancer cells. To achieve high selectivity of deactivating the oncogene trigger, it is necessary to use appropriate tools. We believe that properly developed short, artificial DNA fragments introduced into the cancer cell can provide high selectivity and strong interactions with the oncogene trigger by changing its structure from G-quadruplex to another, called triplex. Such triplex should effectively block the proliferation of cancer cells. Therefore, as part of the project, we plan to: (i) synthesize a pool of artificial DNA fragments to optimize their composition, length and resistance to cellular environment, (ii) test the strength of their interaction with the oncogene trigger, (iii) analyze inhibitory properties of novel tools in proliferation, invasion and migration assays using cancer cells, (iv) study their stability under cellular conditions.

We plan to conduct our research *in vitro* and to verify our results in studies on cancer cell lines (cervical cancer, breast cancer) to check the universality of antitumor activity. The results of our research will certainly broaden the general knowledge on interactions and equilibrium between nucleic acids forming higher-order structures. The detailed research proposed in the project as basic research may contribute in the future to facilitate the design of oligonucleotide drugs with anti-cancer properties and provide the basis for the development of a new targeted therapy, which is currently considered the most promising method of cancer treatment.