DESCRIPTION FOR THE GENERAL PUBLIC

Brain tumors are among the most frequent causes of death in cancer patients. Each time when we hear the words „brain tumor", we intuitively feel that the diagnosis is not optimistic. Indeed, patients diagnosed with brain tumors usually die during the first year following diagnosis. This is caused mainly by the localization of the tumor. Being confined by the skull bones, the tumor has very little space to grow and quickly starts to exert mechanical pressure on the brain structures, giving a number of symptoms, even when the tumor is only a few millimetres in size. What's more, invasive tumor cells quickly start migrating into the whole brain. In the case of brain tumors, invasion is especially dangerous, since cancer cells not only penetrate into the brain, but lead to its degeneration by damaging its structures and causing neuron death.

Most brain tumors belong to the group of gliomas, because they originate from mutated glial cells. One of the characteristic features of gliomas is their very rapid growth and high tumor cell variability. In each tumor several subtypes of cancer cells can be found, since glioma cells mutate very quickly. These differences become more visible with time. This is one of the reasons why the last, most malignant stage of glioma is called glioblastoma multiforme (GBM). Interestingly, not all cells in such a tumor are invasive. The applied therapy should mainly target the most invasive cells. It is therefore important to study the origins and mechanisms of cancer cell invasiveness. In the last years scientists have been focusing on the analysis of traits responsible for the enhanced invasiveness of certain tumor cells. Such "reconnaissance" helps to fight the enemy more efficiently. Our research group also has some achievements in this field. We found that the increased levels of two proteins – connexin43 (Cx43), responsible for intercellular communication and Snail-1, regulating cell phenotype changes – are responsible for the enhanced invasiveness of prostate cancer cells.

Recently, we observed the same relationship in glioblastoma cells and we would like to analyze them in detail. To achieve this aim, we will select different glioblastoma cell subtypes present in brain tumor cell lines and culture them subpopulations. Such homogenous subpopulations will help us discover why some glioblastoma cells are more invasive than the other and what is the role of Cx43 and Snail-1 in the process of glioma cell invasion. To this end, we will employ microscopy techniques and sophisticated molecular biology tools, such as gene silencing, gene overexpression, mRNA analysis, and proteomics. We will investigate the velocity of movement of different cell types, changes in protein levels, growth rates and the ability of cells to invade rat brain slices maintained in special cultures. We will manipulate the expression levels of Cx43 and Snail-1 proteins to check how they influence the ability of glioblastoma cells to migrate through the brain tissues. We will develop a new method of glioblastoma cell culture, in the form of small spheroids. This will provide a new model of these tumors in laboratory conditions (*in vitro*), much better than previous ones. Finally, we plan to implant selected cells in to the brains of rats to check if our earlier observations will be confirmed in a living organism (*in vivo*). The results of our research will not only provide new information about the regulation of glioblastoma invasiveness, but will also have practical applications. Possibly, the model we develop will become a new, useful tool for brain tumor researchers worldwide.