Research on the mechanisms of tumor formation was started in the 19th century. One of the first researchers, who was investigated the formation of tumor secondary foci was Stephen Paget, who in 1889 published his “seed and soil hypothesis ". He stated that certain, but not all, cancer cells ("the seed") have a specific affinity for localized tissue ("soil"). Only when the "seed" and "soil" fit together, the metastasis can occur.

Cancer is a heterogeneous cluster of cells with different properties that may result from random genetic and / or epigenetic changes. Tumors located within the tumor may vary in their proliferative potential, ability to undergo apoptosis, or resistance to chemical substances. Similarly to the ability of tumor cells to create metastases - not all primary tumor cells are capable of producing secondary tumors. In recent years, the role of tumor stem cells in the development and progression of cancer has been emphasized. Metastasis is one of the stages of tumor progression, and the acquisition of this ability is associated with a number of tumor changes, both at DNA level (somatic mutations, epigenetic changes), and RNA or proteins (impaired expression of genes encoding proteins responsible for proper function of the cells).

As a result of these changes, in a process called the epithelial-mesenchymal transition occurring in the primary tumor, tumor cells acquire the ability to be released from the original locus, to survive under non-adhesion conditions, and thus to move within blood and lymphoid vessels to distant locations and to settle their.

Glioblastoma multiforme (GBM) is not only the most common but also the most malignant tumor of the Central Nervous System (CNS). The median survival for GBM patients is between 12 and 14 months from diagnosis, and the five-year survival is observed in only 5% of cases. CNS tumors, account for only 2% of all diagnosed primary tumors. However, despite in such a low frequency, they are responsible for nearly 10% of deaths in patients suffering from cancer. Due to the very aggressive and invasive nature of gliomas, a contemporary treatment regimen involving resection of the tumor, radiotherapy and chemotherapy, does not give satisfactory results.

Aggressive growth of GBM tumors and the difficulty of developing an effective treatment regimen moved to the intensive research in order to know and understand the changes occurring at the molecular level, which could become the basis for new therapies. Several studies of gene expression profile showed significant differences between tumors and allowed to divide glioma subtypes, which in traditional histopathological methods are indistinguishable. **Since extracranial metastases are extremely rare in GBM, invasion and migration are still the main features of GBM spreading.** Creating GBM secondary foci in the brain dramatically shortens the lifespan of the patient and makes the disease incurable at this stage.

One of the main features that distinguish GBM from other cancers is its extraordinary diversity in terms of its constituent cells- so called heterogeneity of the tumor. It is assumed now that one of the most important cells for the development of GBM are glioma stem cells (GSC). The GSC’s characteristic is extremely important, because they determine processes such as: unlimited cell proliferation, the ability to form secondary cancers, and finally resistance to the conventional chemotherapeutic agents.

The main goal of this project is the characteristics of the new class of RNA – circular RNAs, especially their potential in the tumor secondary foci formation at distinct sites of the brain. These regulatory RNA might have the potential diagnostic and prognostic value for patients suffering from brain tumors.

In order to know the function and regulatory mechanisms of circRNAs we will apply RNAi approach with a set of different short RNA-siRNAs. The function of the ncRNAs of interest will be evaluated in cell line culture, but with special attention to the patient-derived cell lines with reservoir of GSC, to bring this approach more to the reality. The physiological importance of circRNAs in GBM will be evaluated in the animal model, where the potential for EMT will be established. The understanding of the processes leading to EMT occurring in the primary tumor site, its association with cancer stem cells may lead to the knowledge of important elements that could serve in the future as new targets for new cancer therapies.