Glioblastoma is the most frequent brain tumor, statistically speaking, half of diagnosed patients do not live longer than one and a half year after diagnosis. There is an urgent need to find new method to treat this deadly cancer. Apart from direct changes in the DNA code, there is another layer of alterations/regulations that take place in both physiological and pathophysiological conditions: epigenetic regulation, that does not affect DNA sequence itself, but causes changes in gene expression by for example changing DNA methylation or histone acetylation/methylation. Epigenetics was identified as a driving force of malignant properties of cancer cells. On the other hand transcription factors, proteins activating or repressing gene expression were found to modify epigenetic landscape. Two transcription factors that we and others found to be important in glioblastoma as well as in other cancers are: REST and KAISO. In terms of that project we plan to characterize REST and KAISO role in shaping landscape of DNA methylation, chromatin modifications and interplay between them. We plan to characterize stem-like and plasticity-related properties of glioblastoma cells and how we can interfere these properties by affecting REST and KAISO. Stem-like and plasticity-related properties are believed to be one of the main reasons of our failures in our attempts to treat gliomas. We may understand better how glioma plasticity is maintained by hijacking REST/KAISO transcription factors and knowing this may open cues for targeting this properties by precision therapy.

The Human Genome Sequencing Project ended almost two decades ago and it had taken, the American scientific consortium, 13 years to read the human genome of the size about 3 GB (3 billion bases of DNA in length). Since that moment, technology and our knowledge have advanced and we are now able to complete a similar task in one day. Within two decades from the Human Genome Sequencing project beginning, tumors were found to have very different genomes, containing foreign changes in DNA sequence, comparing to non- tumorigenic genomes. Since then we are learning more an more about how and why tumors are different from normal tissues in terms of their epigenetics. Moreover sequencing technology enabled studying epigenetic changes in high-throughput whole-genome manner. In the project using this technology we will investigate the exact molecular mechanisms related to REST and KAISO gene expression and epigenetics regulation. We plan to turn-off each of transcription factors separately and together to look for synergistic effects of this approach to guide potential therapeutic strategies.

In frames of this project we plan to understand key processes related to glioma cells plasticity and stem-like properties. We hope that investigating REST and KAISO transcription factors affecting these properties we will create impulse for new glioma treatment advancements.