

Glioblastoma multiforme (GBM) is a malignant brain tumor with a very poor prognosis for the patients. The etiology and pathogenesis of this disease are still not understood, which hinders development of successful therapies. High percentage of glioblastomas were found to be positive for human cytomegalovirus (HCMV), which was shown to be associated with worse prognosis for the patients. Anti-HCMV treatments have shown increase in survival rates for GBM patients, confirming influence of HCMV infection on the outcome of the disease. This strongly suggests that HCMV infection contributes to development and pathogenesis of glioblastoma. Consequently, HCMV is believed to have oncomodulatory properties in case of glioblastoma.

One of the HCMV proteins found in high percentage of glioblastomas is immediate early protein 1 (IE1). In glioblastoma cells we detected a novel localization pattern of IE1 protein on mitotic chromosomes, which seems to be specific to these type of cancer cells.

The goal of this project is to study association of HCMV IE1 protein with chromosomes in glioblastoma cells. We plan to map the domain that determines the specific localization pattern of the IE1 protein and use this information to create a mutant that does not form this pattern. Comparing the proteins interacting with the normal and mutant IE1 protein we aim to identify those interactors responsible for the specific localization pattern. We plan to study the functional significance of the novel IE1 localization pattern by testing its involvement in attachment of the viral genome to chromosomes, disruption of centromeres and regulation of viral life cycle. We believe that unravelling the function of IE1 specific localization will not only further our understanding of the role that HCMV plays in glioblastoma, but may aid in future development of new therapeutic approaches targeting viral persistence.