Glioblastoma multiforme (GBM) is a very aggressive, inevitably lethal brain tumor, with a median overall survival of only 15 months from the moment of diagnosis. Standard treatment consists of surgical resection of the tumor, combined with chemo- and radiotherapy, however it still remains palliative. The main reason for poor clinical outcome of GBM patients is flawed immune response occurring in tumor microenvironment. Paradoxically, immune cells which should protect us from cancer, are the ones which contribute to supporting its growth.

Microglia, immune cells of the brain, and macrophages, which infiltrate the glioma microenvironment from the periphery, undergo re-programming during tumor progression. Thereby, instead of fighting the cancer, they act as its allies. These pro-tumorigenic cells are collectively called glioma-associated microglia and macrophages (GAMs) and constitute up to 30% of the tumor mass. Therefore, finding and targeting the mechanism responsible for driving GAMs tumor-supportive functions could lead to unlocking anti-glioma response and to prolonging survival of patients.

Our recent study indicated that the protein SorLA is of high relevance for shaping pro-tumorigenic functions of microglia exposed to glioma, as its depletion evokes inflammatory activation of the cells and inhibits tumor progression in a murine model of glioma. Due to the fact that SorLA regulates secretion of biologically active proteins, we propose that its depletion stimulates release of anti-tumorigenic, pro-inflammatory factors by GAMs, which results in limited tumor growth.

**The aim of the project is therefore to reveal how SorLA influences the overall character of murine glioma microenvironment.** For this purpose, **we are going to uncover differences between proteins secreted into glioma interstitial fluid of wild type (WT) and SorLA-depleted (SorLA-KO) mice** by using mass spectrometry as well as standard techniques of molecular biology. Thereby, we will be able to uncover pro-tumorigenic processes which are dependent on SorLA. Next, **we aim to check whether exacerbated inflammatory state in SorLA-KO glioma microenvironment influences infiltration of effector immune cells**, ready to fight with the tumor. To verify this hypothesis, we will perform cytometric analysis of WT and SorLA-KO glioma microenvironments and identify the number of various immune cells infiltrating them.

In summary, we will use the combination of proteomic and cytometric studies which will let us understand the consequences of SorLA-dependent, pro-tumorigenic functions of GAMs. We believe that this new knowledge will bring us closer to the step, when we will be able to overcome immunosuppressive character of GBM microenvironment, thereby increasing effectiveness of therapies and prolonging patients' lifetime.