Cancer incidence and mortality numbers are alarming and continue to grow worldwide. Cancer is the second most frequent cause of death globally, right after cardiovascular diseases. Gliomas are the most common malignant brain tumors in adults, including ependymomas, oligodendrogliomas, and astrocytomas. The highest grade glioma, glioblastoma multiforme (GBM), is a highly aggressive tumor that arises from glial cells and accounts for about 15% of brain tumors. GBM has a poor prognosis with a median survival time of 12-15 months and a 5-year survival rate of less than 5%. The current standard treatment for GBM involves aggressive tumor resection followed by temozolomide chemotherapy and radiotherapy. However, these treatments have limitations and can cause side effects in normal tissues, underlining the urgent need for new therapeutic strategies.

Immunotherapy offers an unique approach by utilizing the immune system to specifically target and eliminate cancer cells while preserving healthy tissues. It can also target metastasized lesions and improve the quality of life for patients. The most promising immunotherapeutic approaches in oncology currently are presented by monoclonal antibodies and adoptive cell transfer (ACT) therapies. Monoclonal antibodies have been successfully used in clinical settings, but their large size limits tumor penetration. Smaller antibody fragments and derivatives have been developed to overcome this limitation. ACT involves transferring tumor-reactive immune cells, such as CAR T cells, which have shown effectiveness in treating hematological malignancies. CARs are engineered fusion proteins expressed on T cells' surface, and their specificity is determined by the monoclonal antibody used to build them.

The crucial factor in designing optimal immunotherapeutic strategies for oncologic application is the choice of target. The ideal cancer therapy eliminates only malignant cells, preserving the healthy ones. The most prominent tumor-associated antigens utilized in clinical trials in GBM immunotherapy are EGFR, EGFRvIII, HER2, B7-H3, EphA2, and GD2. However discovery of new TAA is still dramatically needed to provide efficient immunotherapeutic approaches. One of the recently discovered immunotherapeutic target, which can have significant potential in GBM treatment is IL13Rα2. IL13Rα2 is expressed almost exclusively on cancer cells and is a clinically validated target for biologic therapeutics. Malignant diseases with known IL13Rα2 upregulation include but are not limited to high grade gliomas, malignant peripheral nerve sheath tumors, colon, pancreatic and ovarian cancers, as well as melanoma. Recent studies suggest that overexpression of IL13Rα2 is detected in up to 83% of malignant pediatric brain tumors, including DMG, and up to 78% of adult GBM. Furthermore, IL13Rα2 significantly correlates with poor prognosis in high grade gliomas. Hence targeting IL13Rα2 seems to be promising immunotherapeutic target in high grade gliomas, in particular in glioblastoma multiforme.

The urge for therapeutic application of Abs and CAR T cells allied to advances and innovation in molecular biology throughout the years allowed the development of several methods for mAb production.
Several methods have been developed for antibody production, including hybridoma technology and antibody phage display technology. Antibody phage display allows the generation of fully human antibodies without animal immunization. Phage display antibodies libraries containing millions of antibody variants are used for this purpose.

With the dynamic development of immunotherapy field in oncology we propose to address this issue by development novel antibody fragments in the format of single chain variable fragments (scFv) against not prototypical therapeutic target in GBM, IL13Rα2. The molecules will be obtained by innovative phage display technology with in-house built antibody-DNA library and tested for their specific binding to GBM cell lines expressing IL13Rα2.