Peroxiredoxins as potential therapeutic targets in glioblastoma - description for the general public:

Glioblastoma (GBM) is the most common and aggressive brain tumor. Its causes appear extremely complex and have so far escaped clear definition. In spite of the progress made in understanding of GBM biology made during the past decade, the median survival time of patients with this tumor is still less than one year. Standard treatment of GBM consisting of maximal safe surgical resection, radio- and chemotherapy is largely inefficient mainly due to infiltrative growth pattern. Moreover, side effects of each treatment cause significant decrease in quality of life. Therefore, continuous efforts should be made to find new molecular targets and effective therapies of GBM. The key premise is that a potential drug should display antiproliferative activity in tumor cells without affecting adjacent non-transformed tissues.

Overproduction of reactive oxygen species (ROS) is a consequence of an intense metabolism of GBM cells, and is additionally promoted by treatment with several drugs .In non-tumor cells, increased ROS levels produce oxidative stress which triggers cell death. In order to survive the stress, GBM cells adapt to the oxidative conditions by upregulation of the antioxidant enzymes. Growing evidence suggests that increased levels of these enzymes contribute to resistance of GBM cells to treatment.

Peroxiredoxins (PRDX) are one of the families of antioxidant enzymes. These proteins are upregulated in several types of tumors and promote their malignant phenotype. So far, increased level of two of PRDX enzymes has been documented ion GBM tissues compared to non-neoplastic brain tissues and recent data suggest that they promote proliferation and resistance to treatment of GBM cells. The role of the remaining PRDX enzymes in GBM has not been studied so far. Our preliminary data imply that they may contribute to proliferation and survival of GBM cells. The aim of this project is to elucidate the role of PRDX proteins in the phenotype of GBM and to verify the hypothesis that they may be potential therapeutic targets in these tumors. Towards this end, we will compare the levels of the particular PRDX enzymes in GBM and non-neoplastic brain tissues. Moreover, we will examine the effect of inhibition of these enzymes on the proliferation and survival of GBM cells.

The current state of knowledge on the role of PRDX proteins in GBM enforces the use of *in vitro* models which are a prerequisite of further experimenting *in vivo*. To this end, in the present study we will use GBM tissue obtained from patients cells isolated therefrom. In a more distant perspective, results from this project might constitute a basis for studies in *in vivo* models and subsequently, allow to design of new treatment modalities of GBM.