High-grade gliomas are the most frequent and most aggressive tumors of the central nervous system. Despite a multimodal treatment which consists of maximal save neurosurgical resection followed by radio- and chemotherapy, these patients display a serious loss of function and face a median survival of only 15 months. Hence, these patients are in high need of new treatment modalities. During the last decennium, researchers have investigated the potential of immunotherapy to induce tumor regression in these patients. The aim of this treatment strategy is to induce or to improve a specific immune response against the tumor to eradicate residual tumor cells that resisted conventional treatment strategies. Despite the observation of promising antitumor effects in a subgroup of patients, the therapeutic benefits that are observed with immunotherapy are still limited. A major hurdle is the presence of a tumor microenvironment that is capable of suppressing an immune attack thereby preventing tumor cell death. Insights into the different mechanisms that are important for the induction and maintenance of such a local tumor immunosuppressive environment are crucial for the development of more potent immunotherapeutic strategies for high-grade glioma patients.

A part of my research consists of unraveling the potential role of galectin-1, a sugar-binding protein, in the development of an immune suppressive environment in high-grade gliomas. Recent data have demonstrated that the expression level of galectin-1 is significantly higher in high-grade gliomas as compared to low-grade gliomas and healthy brain and that high expression levels of galectin-1 are positively correlated with the grade of malignancy and with a worse prognosis. By using a mouse model for high-grade gliomas we were able to demonstrate a role for galectin-1 in the regulation of myeloid cells towards the tumor microenvironment. Depletion of galectin-1 in the tumor resulted in a significant decrease in the percentage of myeloid cells within the tumor microenvironment and in a significant longer median survival of these mice. In addition, mice that were treated with immunotherapy and that were inoculated with galectin-1-depleted tumor cells displayed the best overall survival. Furthermore, we demonstrated that depletion of galectin-1 in high-grade glioma cells significantly decreased the number of blood vessels within the tumor, thereby preventing tumor growth. All together, these data stimulate the clinical evaluation of galectin-1 inhibitors as an adjuvant new treatment strategy in patients with high-grade glioma.

Thus far it is unknown whether galectin-1 is predominantly present in the tumor of high-grade glioma patients, or whether this lectin can also be detected in the blood of these patients. As most of the patients diagnosed with high-grade glioma have a damaged blood-brain barrier it is likely that galectin-1 could also been detected in the blood of these patients. To investigate this, another part of my doctoral research focused on the comparison of galectin-1 serum levels between healthy controls and patients with a high-grade glioma. Both patients with a first diagnosis of a high-grade glioma and patients with a recurrent high-grade glioma were included in this prospective study. The results of this explorative study demonstrated that galectin-1 serum levels are significantly higher in both patient subgroups. Hence, galectin-1 serum levels could potentially be a good parameter to identify patient subgroups that are likely to benefit from galectin-1 targeted therapy. This type of therapy is currently under development by our research group and others. Further longitudinal research is, however, required and ongoing to evaluate whether galectin-1 serum levels in patients with high-grade gliomas have a potential value as an additional diagnostic marker or as a marker of treatment response and/or prognosis.