The poor prognosis for patients with malignant or metastatic glioma and the toxic side effects of currently available multimodality treatment including surgery, radiation therapy and chemotherapy necessitate the development of more effective tumor selective therapies. To this end, targeted therapies have emerged as an attractive option. Accumulating evidence suggests that certain molecular pathways are selectively upregulated in tumor vs. normal cells. Some of these pathways have been shown to be instrumental in proliferation, migration, invasion, angiogenesis and/or survival in preclinical models. These would appear to represent ideal therapeutic targets, as their antagonism may lead to an improvement in the therapeutic ratio.

In this special issue of glioma therapy, four distinguished scientists will focus on the current mechanisms of glioma progression and invasion as well as the development, promise and challenge of a novel therapy in malignant glioma. Malignant gliomas are among the most angiogenic of cancers, and the vascular endothelial growth factor is the dominant angiogenic mediator in these tumors. Therefore, a major current focus in neuro-oncology is to further develop anti-angiogenic strategies for malignant glioma. This issue begins with a novel aspect of angiogenesis with NG2-mediated pericyte-endothelial interactions communicated by Dr. Stallcup. Alterations in cell to cell and cell to ECM interactions are associated with glioma progression. Changes in the expression or function of adhesion molecules and cell surface proteoglycans (PGs) have all been documented in the progression of primary melanomas. NG2, a large chondroitin PGs, interacts with a variety of ECM components to alter cellular morphology and proliferation. Dr. Stallcup describes a role for NG2 as signal-transducing molecules that initiate or modify intracellular signal cascades important for cell adhesion, motility, invasion and the angiogenesis of glioma cells. In the second article in this issue, Park et al. describes hyaluronic acid (HA), the principal glycosaminoglycan in the ECM component of the brain, and considered to be one of the critical factors for glioma invasion. The authors introduce us to HA-induced signaling cascades in malignant glioma and suggest that effectively blocked HA-induced signaling might be clinically valuable as a novel anti invasive agent for glioma.

The current state of the art of available molecular approaches for glioma, with a particular focus on gene therapy is reviewed by Drs. Natsume and Yoshida and encompasses suicide gene therapy, immune gene therapy and oncolytic viral therapy, which have been studied in previous and ongoing clinical trials. Dr. Todo will discuss on the potential applications of “Armed” oncolytic herpes simplex viruses as novel antitumor agents in the treatment of glioma, especially the concept of antitumor efficacy augmentation using oncolytic HSV 1 armed with an immunostimulatory gene.
The ultimate goal of a cancer therapist is to tailor therapy that takes into account and exploits an individual tumor’s unique biological features. Malignant glioma is characterized by invasion of the surrounding normal brain tissues and the interactions between cell surface molecules and ECM secreted by glioma cells. Furthermore, the present evidence indicates that the resistance of these tumors to current therapies is attributable to a small subpopulation of cancer initiating cells or stem cells. As we learn more about the biology of stem cells and the molecular mechanisms that mediate their tumor-tropism and we identify ECM component of stem cell niche for specific tumor types, the clinical utility of cell based delivery strategies as described in this issue becomes increasingly evident.

Sincerely,

Takahiro Ochiya Ph.D.
Guest Editor