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Introduction – Brain Tumor Immunotherapy

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The poor prognosis of glioblastoma (GBM) mandates new therapies. With FDA approval of several immunotherapy agents over the past few years, much attention and resources have been directed towards new immune based approaches and therapies in all cancer types. Immunotherapy for gliomas has been an area of immense interest. In this special issue of *Journal of Neuro-Oncology*, we have gathered renowned experts in the various disciplines of immunotherapy to discuss the current state, obstacles thus far encountered, and newly emerging issues of immune-based therapies in neuro-oncology.

Immunotherapy is an approach that is well suited to take on the global nature of malignant gliomas. Initial bias for GBM therapy arose from the notion that the central nervous system (CNS) is immune privileged. However, we have come to appreciate that this concept is a gross oversimplification and that parts of the CNS are able to induce robust immune responses.

Current strategies for immunotherapy include cytokine therapies, passive therapies, and active therapies. We have seen exciting new therapeutic approaches emerge over the last decade, such as dendritic cell vaccines, peptide vaccines, heat shock proteins, and checkpoint inhibitors. While we have already observed antitumor immune responses, effective immunotherapy for GBM is a particularly daunting challenge. Challenges include the tumor-induced immunosuppressive environment and the paucity of identified tumor-specific antigens. Tumors have usurped our normal mechanisms to prevent autoimmunity to evade the immune system. We have also come to appreciate that tumor induced immunosuppression is local and systemic, as well as tumor specific. In addition, tumor heterogeneity highlights the fact that we have yet to identify the appropriate candidate and requisite number and repertoire of tumor-specific antigens.

Immunotherapy has mandated a new paradigm for clinical trial design. As a result, we have encountered new challenges in defining response, identifying appropriate candidates, and in integrating immune-based therapies into the current standard of care. Furthermore, the criteria for defining response by imaging need to be redefined.

Defining the role of immunotherapy as a stand-alone therapy or in combination is actively being investigated. It is unclear if chemotherapy and radiation facilitate or inhibit antitumor immune responses. In addition, identification and characterization of relevant immune response biomarkers has been under intense investigation.

In this special issue of the *Journal of Neuro-Oncology*, we will discuss the current state of immunotherapy approaches for brain tumors, obstacles to generating effective immunotherapeutic approaches, challenges of immunotherapy in clinical trial design, redefining imaging responses, and the future of immunotherapy in neuro-oncology. We hope that the articles presented here will further the enthusiasm for this field and generate new ideas and approaches that may realize the promise of immunotherapy for brain tumors.

Sincerely yours,

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Biographies

