

# PREFACE

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Among the new treatments currently being investigated for malignant brain tumors, none is as theoretically appealing as immunotherapy, because it offers the potential for high tumor-specific toxicity. Cancer immunotherapy is currently a rapidly developing field, and new discoveries regarding the immune susceptibility of the central nervous system have made the concept of brain tumor immunotherapy an area of active investigation. Enough information has been gained from basic research and clinical trials to allow the conclusion that immunotherapy for brain tumors is feasible, can evoke relevant biologic responses, and can provide important insights into human biology. Brain tumor immunotherapy still faces great hurdles before it becomes an established clinical therapy. However, the accomplishments in this field to date are impressive, and the intuitive logic of this treatment paradigm offers compelling hope that the immunotherapy of brain tumors may someday succeed.

The aim of *Brain Tumor Immunotherapy* is to organize a thorough critical survey of the field, with contributions from leading researchers and clinicians to help convey the many and significant recent accomplishments within this evolving discipline. We hope our book will provide both clinicians and research scientists with a reasonably comprehensive guide to modern brain tumor immunotherapy and thereby enhance future investigation in the area. The scope of this text will detail some of the laboratory experiments and clinical protocols that are currently being investigated, integrate the available information from previous and ongoing research, and help to define the current status of the field.

The feasibility of immunotherapy for central nervous system cancers is just beginning to be studied through clinical trials. Most of our current understanding of brain tumor immunotherapy has been gleaned through the use of transplantable animal brain tumor models, with the primary hope of predicting therapeutic responses in human tumors. Because of the desperate plight of patients suffering from malignant gliomas and the fact that very few treatment modalities have shown clinical efficacy against this deadly disease, it is difficult to prove that any one animal model is necessarily the most exemplary of human primary brain tumors. Nevertheless, we must caution the reader that some of the most widely used animal models of murine and rat

primary glial neoplasms are not well-suited for evaluating immunologic responses to brain tumors since they have inherent histoincompatibilities that can potentially provide misleading results in immune-competent hosts. For example, the commonly used rat C6 glioma cell line has an uncertain genetic background and therefore may not be syngeneic in the animals in which these cells are transplanted. Because of this, favorable immunotherapeutic responses using animal models must always be interpreted with caution, and extreme prudence should be exercised before basing any clinical trial decisions on information obtained solely from such models. New models developed in syngeneic backgrounds with transgenic methodology may be more useful than older models, which are often chemically induced, highly antigenic, and of questionable genetic background. Yet, these models are still far from duplicating the complexities of clinical brain tumors and the human immune system.

With this caveat in mind, *Brain Tumor Immunotherapy* may be used most effectively as a resource text for neurosurgeons, experimental neuroscientists, clinical neuro-oncologists, tumor immunologists, and others who may wish to explore further research in this field. We have attempted to provide sufficient background information about brain tumor immunotherapy strategies, while hoping to capture a contemporary glimpse of the breadth and depth of this field. This book differs from others currently available, as it is probably one of the only texts dedicated specifically to immunotherapeutic approaches for *central nervous system* malignancies.

Whether it is adoptive cellular immunotherapy, radiolabeled antibodies, cytokine gene therapy, or dendritic cell vaccines, almost every leading neuro-oncology program in the world is investigating some form of brain tumor immunotherapy. The number of clinicians and scientists interested in cancer immunotherapy is increasing. Annual meetings of multiple scientific and clinical disciplines have entire sessions dedicated to the immunobiology of brain tumors. Recent developments in our understanding of molecular microbiology and tumor immunology have resulted in increasingly clever and sophisticated immune-based treatment strategies against cancer. It is our sincere hope that dissemination of such information and further research endeavors in this field will someday translate to true therapeutic benefits for our brain tumor patients.

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