

## Basis for Progress in Brain Tumor Therapy

*"The human brain is a most unusual instrument of elegant and as yet unknown capacity." — Stuart Seaton*

The three prior issues of this journal that have been devoted to neuro-oncology (Volume 2, Issue 4, 1995; Volume 5, Issue 2, 1998; Volume 10, Issue 2, 2003) have generally focused on state-of-the-art management techniques and outcomes. Surgical techniques and the evaluation of extent of resection for both primary and metastatic brain tumors have improved immeasurably. Many neurosurgical interventions are now "same-day-surgery" events with little morbidity. Advances such as the stereotactic delivery of radiation are expanding the roles for this treatment modality, and the decreased exposure of the non-involved brain leads to fewer deleterious side effects from treatment. Less progress has occurred, however, with systemic therapies, and overall survival rates of patients with high-grade gliomas remain poor.

This issue begins where the previous one left off. First, the team led by Dr. Vrionis reviews the approaches needed for malignant tumors of the anterior skull base. We emphasize the word *team* here. Nowhere is the need for a team approach to provide optimal care greater than it is for management of these most difficult tumors. The tumors themselves are heterogenous and have different etiologies and histologies. They are localized in an area where surgical access is limited and vital structures are close. When surgery is performed as part of multimodality management, meticulous preoperative planning and operative execution are required to achieve the desired results without incurring excessive morbidity.

The issue then turns to consideration of the exciting preclinical and clinical science that is driving our current clinical trials intended to improve outcomes for patients with brain tumors. Many of us have already experienced the effects of COX-2 inhibitors because we take the newer NSAIDs to ease our aches and pains. Dr. New from MD Anderson Cancer Center in Houston presents, however, the preclinical data that demonstrate significant anti-cancer effects of the COX-2 inhibitors, and then specifically discusses the relevance of these effects to gliomas. Can these well-tolerated agents allow us to treat gliomas better? Perhaps, but more preclinical studies of combinations of agents are needed, followed, of course, by well-designed clinical trials.

Discovering effective strategies to breach the blood-brain barrier to allow ingress of antitumor agents into brain tumors has become almost a holy grail search among

neuro-oncologists. Drs. Black and Ningraj from Cedars-Sinai Medical Center in Los Angeles discuss the blood-brain and blood-tumor barriers and then describe an appealing approach that targets the blood-brain tumor barrier: specific proteins to increase antineoplastic drug delivery selectively and safely to brain tumors.

One of the difficulties in monitoring the extent and activity of malignant gliomas has been the lack of an effective tumor marker. Dr. Sampath and colleagues from Brown Medical School in Rhode Island describe their work that suggests that this particular drawback to effective patient and tumor monitoring might be relieved. They report that VEGF is detectable in CSF much more often in higher-grade than in lower-grade gliomas, and they describe their results evaluating the value of serum levels of recoverin, a protein that binds antibodies expressed in patients with cancer-associated retinopathy — a rare paraneoplastic syndrome.

It is now well-known that active gliomas are associated with systemic energy and that the purported immunologic privilege of the brain is not necessarily an insurmountable obstacle for immunotherapy directed against malignant brain tumors. The last two articles are complementary and amplify these issues: Drs. Fenstermaker and Ciesielski describe some of the studies emanating from Roswell Park, and Dr. Ehtesham and colleagues discuss their work from Cedars-Sinai in Los Angeles.

All of this translational research is exciting and serves a scientific platform to design clinical intervention studies in malignant gliomas. Let us close by quoting from Montaigne: *"It is good to rub and polish our brain against others."*

Steven Brem, MD, FACS

Professor of Interdisciplinary Oncology  
and Neurosurgery  
University of South Florida  
Program Leader, Neuro-Oncology  
Chief, Neurosurgery  
H. Lee Moffitt Cancer Center & Research Institute  
Tampa, Florida

John Horton, MB, ChB, FACP

Interdisciplinary Oncology Program  
H. Lee Moffitt Cancer Center & Research Institute  
University of South Florida  
Tampa, Florida