thank you
Dear friends,

The past year has been a productive and exciting one for us here in the Brain Tumor Program at UCSF. In the following pages, you will read about a variety of groundbreaking and innovative research that is aiding in the fight against brain tumors, ultimately improving outcomes for our patients. We would be unable to carry out this critical work without your support; thank you for advancing our efforts.

In these times of financial uncertainty, philanthropy is more important than ever. To secure external funding from sources such as the National Institutes of Health, our researchers must first conduct nascent investigations that yield the pilot data necessary for the grant application process. We therefore rely on private contributions to underwrite vital, early-stage research endeavors.

I want you to know that two exciting later-stage opportunities were awarded to our program in 2009. The California Institute for Regenerative Medicine (CIRM) awarded us a grant to use genetically modified neural stem cells that carry a tumor-killing drug to treat brain tumors. We also leveraged private support to obtain funding from the National Cancer Institute for the UCSF Brain Tumor Specialized Program of Research Excellence (SPORE), through which we are translating laboratory findings into new therapeutic treatments for brain tumors. This report provides more details about these five innovative SPORE projects.

As we continue to make strides in our goal to eradicate brain tumors, we remain immensely grateful for your partnership. On behalf of everyone in the UCSF Brain Tumor Program, I thank you again for fostering the pioneering investigations that move us ever closer toward a cure.

Sincerely,

Mitchel S. Berger, MD
Chair, Department of Neurological Surgery
Kathleen M. Plant Distinguished Professor
Director, Brain Tumor Program
UCSF Brain Tumor Program:  
A Specialized Program of Research Excellence (SPORE)

Approximately 20,000 people in the United States are diagnosed with malignant brain tumors each year. Although considerable improvements have been made, the survival rate for individuals with brain tumors remains unacceptably low. Brain tumors are a significant health problem in the U.S. and serious efforts must be made to improve patient survival.

In the UCSF Brain Tumor Program, a number of talented scientists are working on this very problem. The UCSF Brain Tumor SPORE — one of only four brain SPORE centers in the U.S. — currently includes five projects focused on improving the diagnosis and treatment of brain tumors by applying laboratory advances to the clinical setting. Projects range from longitudinal studies of glioma survival in adults to the development of novel targeted delivery mechanisms for drug therapies. The National Cancer Institute's (NCI) choice of UCSF as a brain SPORE center is a testament to the breadth and depth of talented investigators and clinicians in the Brain Tumor Program. Only the most promising brain tumor research programs are awarded this important designation.

The UCSF SPORE is a multidisciplinary and collaborative group. It comprises basic researchers, physicians, and population scientists, concentrated in the areas of epidemiology, cancer genetics, cancer biology, and molecular therapeutics. The program encompasses the UCSF Department of Neurological Surgery; the UCSF Neuro-Oncology service; the basic scientists in the UCSF Brain Tumor Research Center; and other UCSF investigators.

While the NCI provides funding for the Brain Tumor SPORE projects, there are still many other needs in the Brain Tumor Program. Private philanthropy enables us to support groundbreaking investigations in new areas of interest. In turn, these findings inform the development of improved therapies for brain tumors, which provide the promise of healthier outcomes for our patients.

SPORE PROJECT #1  
Providing More Accurate Prognoses

Principal Investigator:  
Margaret R. Wrensch, MPH, PhD  
Stanley D. Lewis and Virginia S. Lewis  
Endowed Chair in Brain Tumor Research

Clinical Co-Principal Investigator:  
Michael D. Prados, MD, FACP  
Charles B. Wilson, MD, Endowed Chair

Currently, physicians assess a tumor’s shape and form to aid in diagnosis and determine prognosis – a subjective method that is an imprecise predictor of tumor behavior. In an effort to provide glioma patients with a clearer picture of probable outcomes, Drs. Wrensch and Prados are using SPORE funding to conduct the San Francisco Bay Area Adult Glioma Survival Study.

This critical investigation is aimed at identifying characteristics of tumors and patients that better define glioma subtype and prognosis. Specifically, Drs. Wrensch and Prados are evaluating factors associated with survival including age, personal and family medical histories, diet, smoking and alcohol consumption prior to diagnosis, and other demographic factors like education. They are also examining the correlation between tumor markers found in specific types of gliomas and survival rates.

Drs. Wrensch and Prados are confident that insights gleaned from this study will help clinicians both to refine treatments based on individual characteristics, and to provide patients with more accurate prognoses at the time of diagnoses.
Using Innovative Technology to Manage Brain Tumors

Principal Investigator: 
Sarah J. Nelson, PhD
Margaret Hart Surbeck Distinguished Professor in Advanced Imaging

Clinical Co-Principal Investigator: 
Susan M. Chang, MD
Lai Wan Kan Endowed Chair

Determining whether a tumor responds to treatment is an essential component of managing brain cancer, yet the process can be difficult. The magnetic resonance imaging (MRI) techniques that are often used can provide ambiguous results and do not always accurately capture a tumor’s response to treatment since gliomas vary in shape and size and have poorly defined margins.

To remedy the shortfalls inherent in conventional imaging techniques, Drs. Nelson and Chang are exploring the value of magnetic resonance spectroscopy imaging (MRSI), a technique that is used along with MRIs to determine cellular activity, in predicting the biological behavior of gliomas after surgical resection and treatment.

Although a tumor’s histological grade is an important predictor of outcome, tumors of the same grade respond to treatments and progress differently. Drs. Nelson and Chang are examining whether MRSI can serve as a useful tool in highlighting differences among tumors of the same grade and measuring a patient’s therapeutic response.

Technological advances such as the MRSI have the potential to augment the way physicians care for patients with brain tumors. Drs. Nelson and Chang believe that these imaging techniques will enable them to design individualized treatment plans, more effectively measure a patient’s response to therapies, and improve the ability to manage brain tumors in safe and non-invasive ways.

Developing Novel Targeted Therapeutics

Principal Investigator: 
John W. Park, MD
Associate Clinical Professor

Clinical Co-Principal Investigator: 
Mitchel S. Berger, MD
Kathleen M. Plant Distinguished Professor

High-grade gliomas remain a surgically challenging disease, largely because these tumors infiltrate the surrounding normal brain tissue. The usefulness of chemotherapy and radiation therapy is limited by a number of factors, including the difficulty of targeting just the tumor tissue and the inability to achieve effective exposure within the brain without causing excessive toxicity in the rest of the body. One of the objectives in the field of brain tumor research is to create drug-delivery systems that can selectively and efficiently target the tumor cells themselves.

A UCSF breast cancer research project has resulted in the development of an immunoliposome technology. Liposomes are tiny bubbles constructed of the same material as cell membranes. Filled with drugs, liposomes attach to cell membranes and deliver their contents directly to the cell. Drs. Park and Berger are now applying this technology to brain tumor treatment: they are designing immunoliposomes that target only glioma cells and contain a variety of toxic small molecules and nucleic acids.

Following evaluation in the laboratory, Dr. Berger will test the most promising of these immunoliposomes in clinical trials. If successful, this approach will allow clinicians to increase drug delivery to brain tumors selectively, resulting in improved outcomes with fewer negative effects than currently available therapies. It will also have a significant impact on the prognosis of some of the most challenging tumors.
SPORE PROJECT #4

Matching Tumors and Therapies to Improve Outcomes

Principal Investigator:  
William A. Weiss, MD, PhD  
Professor

Clinical Co-Principal Investigator:  
Daphne A. Haas-Kogan, MD  
Professor

Basic science research shows that irregularities in the biochemical signaling pathway called PI(3)K play a key role in the development and maintenance of gliomas. Numerous clinical trials are underway in which novel agents that affect this pathway are tested on brain tumor patients. However, clinicians currently have no way to predict which tumors will respond to particular agents.

Drs. Weiss and Haas-Kogan are engaged in a SPORE investigation to discover markers in tumors that will help to “match” the tumors with effective pathway-inhibiting drugs. By doing so, they hope to increase the efficacy of the therapy and, ultimately, promote survival among glioma patients.

To achieve this, Dr. Weiss is working to identify the components of the pathway that are the most promising targets for inhibition. Using brain tumor samples, his team is creating molecular profiles and correlating them with patient outcomes. Based on these findings, Dr. Haas-Kogan is identifying a subset of current glioma patients who are likely to benefit from this type of therapy.

Additionally, they are analyzing tumors from patients who are enrolled in clinical trials of PI(3)K-inhibiting drugs. By retroactively correlating each tumor's molecular profile with its response to the tested therapeutic agent, they hope to verify that tumors possess molecular markers that clinicians can use to guide their choice of inhibitor agents.

SPORE PROJECT #5

Improving Vaccine Therapy for Gliomas

Principal Investigator:  
Andrew T. Parsa, MD, PhD  
Reza and Georgianna Khatib Endowed Chair in Skull Base Tumor Surgery

Clinical Co-Principal Investigator:  
Russell O. Pieper, PhD  
Suzanne Marie and Robert Vincent Haderle Endowed Chair in Molecular Neuro-Oncology

The standard course of treatment for most gliomas includes surgery, chemotherapy, radiation therapy, or a combination. A new approach to treating brain tumors is currently under investigation: the use of vaccines to solicit an immunotherapy response in the patient. Although several clinical trials have shown the feasibility, safety, and anecdotal efficacy of glioma vaccines, a functional vaccine therapy has yet to be developed.

Current glioma vaccines are designed to provoke an immune response by activating two types of cells in the human body: natural killer (NK) cells and T-cells. Drs. Parsa and Pieper have found that glioma cells interfere with the activation of NK and T-cells, muting the efficacy of the vaccine. They have also found that a single biochemical pathway in the body is responsible both for the growth and maintenance of gliomas and the over-production of these inhibitor proteins, effectively providing a double layer of protection for the tumor.

Drs. Parsa and Pieper are working to confirm the role of the biochemical pathway in glioma vaccine resistance. They hope to improve the efficacy of the vaccines by manipulating this pathway in patients in an ongoing clinical trial of a newly developed vaccine. If successful, this work may lead to the implementation of the first functional vaccine therapy for the treatment of human brain tumors.
### Brain Tumor Program Faculty

<table>
<thead>
<tr>
<th>Name</th>
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<td>Margaret R. Wrench, MPH, PhD</td>
<td>Stanley D. Lewis and Virginia S. Lewis Endowed Chair in Brain Tumor Research Professor in Residence</td>
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Annual Brain Tumor Symposium

Each year, the UCSF Brain Tumor Program hosts a Brain Tumor Symposium where clinical and research leaders discuss their recent findings in brain tumor science and demonstrate how their investigations are bringing us closer to finding a cure for brain cancer. The 2009 speakers and their topics included:

Sarah J. Nelson, PhD:
Better Ways to See Brain Tumors

Gabriele Bergers, PhD:
Blood Vessels and Brain Tumors

William A. Weiss MD, PhD:
Finding New Therapies

C. David James, PhD:
Preclinical Models for Therapeutic Testing

Michael D. Prados, MD, FACP:
Translational Research Program in Neuro-Oncology

In addition to hearing from these members of the UCSF brain tumor faculty, attendees received guided tours of the state-of-the-art UCSF Helen Diller Family Cancer Research Building, which houses the Brain Tumor Research Center; the Cancer Research Institute, a consortium of laboratories where researchers study the basic biological mechanisms of cancer; and laboratories devoted to research in pediatric oncology, population sciences, prostate cancer, and other urologic cancers.

The Brain Tumor Symposium is an excellent opportunity for patients, families, and community members to learn about the latest development in brain tumor research. This year, the 2010 Brain Tumor Symposium will be held following the annual Helen Diller Family Comprehensive Cancer Center’s Scientific Symposium, a two-day conference where leaders in brain tumor research from across the country discuss their work. During the Brain Tumor Symposium, UCSF faculty will summarize and review, in lay terms, the research and treatment developments described during the Scientific Symposium.

Please mark your calendar for October 22 for the 2010 Brain Tumor Symposium. Invitations and RSVP information will be mailed in September.

Contact Us

For more information on supporting the Brain Tumor Program at the UCSF Helen Diller Family Comprehensive Cancer Center, please contact:

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UCSF Foundation website:
ucsf.edu/support

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Join us!

Brains on Bikes
April 9, 2010 – The Plaza, Mission Bay – Noon

Help send off Anne Feeley, a glioblastoma multiforme survivor, on a nationwide bike ride to increase public awareness about cancer and raise research funds along the way. To follow Anne on her remarkable journey, visit brainsonbikes.org.

Helen Diller Family Comprehensive Cancer Center Showcase
May 12, 2010 – Mission Bay – 2:30 to 7:00 p.m.

The UCSF Brain Tumor Program will be one of 10 cancer programs highlighted at this event designed to provide the latest information about UCSF’s advancements in cancer research. Please visit http://cancer.ucsf.edu/2010showcase for event information and registration.

Brain Tumor Program Annual Symposium
October 22, 2010 – Mission Bay – 3:00 to 6:00 p.m.

Learn about the latest brain tumor research being conducted by UCSF faculty. RSVP information and additional details will be mailed in September.