Dear Friends,

Every year, we move ever closer to finding a cure for brain tumors. And every year, we owe much of our progress to your remarkable generosity and goodwill. Thank you.

Your support helps us in many ways – to recruit outstanding young minds, engage in groundbreaking research, run clinical trials and improve therapies. It also helps motivate us even more to succeed in our quest to save lives, for we know you share this vision.

We are working hard toward this goal, and you can read about some of our talented researchers and their breakthroughs in the following pages. I’m also pleased to report on some recent progress of the Brain Tumor Research Center.

In 2008, we were awarded renewed funding for both our Specialized Program in Research Excellence (SPORE) and Program Project Grant for brain tumor research. These designations are reserved for the most promising brain tumor research programs in the nation. They acknowledge our ability to bring together experts in imaging techniques, drug development and drug-delivery strategies to create less invasive ways of diagnosing brain tumors and more effective ways of reaching them with anticancer drugs.

We also have recently received funding to establish a Pediatric Brain Tumor Foundation Institute here at UCSF, which underscores the great strides we are making toward expanding our research on pediatric brain tumors – an area of neuro-oncology where too little progress has been made.

We expect more good work to emerge when we move our laboratories to the new Helen Diller Family Cancer Research Building at the UCSF Mission Bay campus this year. You can read more about our new home in this report.

It is an honor to partner with you in our search for a cure. Our work would not be possible without your contributions, and I am deeply grateful for your belief in our team at the UCSF Brain Tumor Program.

Mitchel S. Berger, MD
Kathleen M. Plant
Distinguished Professor
Director, Brain Tumor Program
Pursuing Uncharted Territory

Tumors consist of a variety of cells, some normal, some cancerous. How the cancer and normal, or host, cells interact has been heavily studied in breast, lung and colon cancers. But little attention has been paid to this microenvironment in brain cancer research.

Now a pioneering scientist at UCSF, Gabriele Bergers, PhD, is mining this arena and discovering new clues that may help fight a virulent, aggressive type of brain tumor.

Bergers and her team are studying the microenvironment of glioblastoma multiforme (GBM), a disease with a median survival of one year. GBM tumors are extremely invasive and smart, says Bergers, who holds the Neill H. and Linda S. Brownstein Endowed Chair in Brain Tumor Research. In order to grow so rapidly, they need to recruit new blood vessels. GBM tumor cells do so by directing the host cells to initiate new blood vessel growth, known as angiogenesis.

Bergers has discovered that a significant percent of the host cells in GBM tumors are bone marrow-derived (immune) cells. Normally, immune cells are beneficial to the body, but the tumor has found a way to change them into tumor-promoting cells. Bone marrow-derived cells have been linked to angiogenesis in breast cancer and now Bergers has shown that these cells operate similarly in GBM.

This finding provides Bergers and others with a target in the battle against this fatal cancer. Existing treatments including anti-angiogenesis therapy, chemotherapy, surgery and radiation can cause hypoxia, a low oxygen condition. Hypoxia can drive the influx of immune cells into the tumor. If scientists can eliminate or block bone marrow-derived cells in GBM, they may be able to improve treatments and extend lives.

Uniting Research to Shed Light on Cancer Stem Cells

For the past four years, scientists at UCSF have combined forces with researchers at leading biotechnology company Genentech to better understand a complex brain cancer. Their teamwork has yielded a wealth of knowledge that may lead to personalized therapies for patients.

The project investigated the biology of deadly glioblastoma multiforme and was led by Michael Prados, MD, FACP, holder of the Charles B. Wilson, MD, Endowed Chair in Neurological Surgery at UCSF. The effort was funded by a prestigious UC Discovery Grant, which fosters public and private sector collaboration on important scientific work.

The cause of this brain cancer is unknown, but neuroscientists have long speculated that glioblastoma tumors arise from a tiny population of cells similar to stem cells. Recent discoveries have identified at least one such cell type, called CD133 positive stem cells.

These cells comprise less than 5 percent of the tumor, yet they appear to multiply and “nourish” the tumor, allowing it to grow. CD133 positive stem cells remain remarkably resistant to standard therapies. Advances in targeting and removing these stem cells could lead to more effective treatments and possibly halt the disease.

Scientists collaborated to better understand how these cells function. In one of the more promising experiments, UCSF isolated and grew tumors from CD133 positive stem cells and studied them in mouse models. In a co-ordinated effort, Genentech used state-of-the-art technology to extensively analyze the stem cell and primary tumor DNA and RNA. By correlating all their findings, the investigators at UCSF and Genentech gathered a remarkable amount of data with great potential for new research into tailored therapies for glioblastoma patients. Prados and his team are now pursuing another UC Discovery Grant to continue this productive collaboration.
Gliomas are the most common type of malignant brain tumor and the most deadly. Their causes, however, remain a mystery. Unlike the association between cigarettes and lung cancer, there is no “smoking gun” for glioma and other brain tumors. Many potential causes exist, ranging from inherited genetic factors to developmental factors, such as immunity, to external ones, such as high-dose radiation.

Scientists at UCSF are pursuing multiple avenues to understand these malignancies. One such route is epidemiology, the study of diseases in populations. Margaret Wrensch, PhD, who holds the Stanley D. Lewis and Virginia S. Lewis Endowed Chair in Brain Tumor Research, is examining the epidemiology of glioma and recently has made significant progress. Wrensch has led the San Francisco Bay Area Adult Glioma Study for 18 years. The study has recruited 2,000 patients and 1,000 controls, giving scientists enough blood samples to conduct large-scale genotyping panels.

She and colleagues have just completed the first genome-wide association study for glioblastoma, the most common and aggressive type of glioma. The findings are promising. Using both their own data and data from The Cancer Genome Atlas, they have discovered a number of inherited genetic variations that are more common in the glioma patients than among people without the disease.

Key to her success is collaboration. Wrensch serves as U.S. vice president of the Brain Tumor Epidemiology Consortium, which brings together researchers from around the world. The data and shared experiences gained from this and other large-scale collaborations are indispensible, she says. Collaborators at the Mayo Clinic have confirmed some of the Wrensch group findings and a joint paper is under review. Studying these inherited variations may eventually shed light on what causes this devastating disease.

Brain tumor treatments can be hard on anyone – surgery is risky and chemotherapy can cause many side effects. But these procedures, which also take an emotional toll on families, are especially taxing for children.

Nalin Gupta, MD, PhD, who holds the Dennis Bruce Dettmer Endowed Chair in Pediatric Neurosurgery, is an expert on the difficulties confronting kids with brain tumors. He and Mitch Berger, MD, director of the Brain Tumor Program, are heading a multi-investigator research program at UCSF that is defining the basic biology of several types of childhood brain tumors and ways to improve therapies. The project is funded by the Pediatric Brain Tumor Foundation of the United States.

Along with Graeme Hodgson, PhD, Gupta is developing a new class of drugs called small interfering RNAs (siRNAs). In laboratory tests, these agents have been effective in turning off specific biochemical pathways that allow tumors to grow. They also aim to find new ways to administer these drugs that are more effective and less harmful to a child’s body and brain. One method, convection-enhanced delivery, entails injecting siRNAs directly into the tumor, which avoids complications in other parts of the body. Directing high concentrations of drugs into the brain may also lead to a better response.

Another approach is delivering siRNAs through the nasal cavity. Pathways (possibly nerves or blood vessels) appear to carry agents from the nasal area into parts of the brain. Intranasal treatment is advantageous because it doesn’t require brain injections and can be given repeatedly. Gupta and his team are testing both methods on rodent brainstems with the hope that their findings may eventually provide a brighter outlook for even the youngest patients.
We are pleased to recognize donors who made gifts of $100 or more to the Brain Tumor Program from January 1, 2008, to December 31, 2008.

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Saving Lives in Memory of a Daughter Lost

Sami Disharoon loved to climb tall trees and big rocks. She went parasailing and snorkeling. The 8-year-old was fearless, even when diagnosed with a brain stem tumor.

“She wasn’t scared. She didn’t ask ‘why me?’” says her mother, Janet Disharoon. “Sami was a trooper.”

After her diagnosis in May 1998, Sami underwent six weeks of radiation at a Sacramento hospital.

She started third grade in September. By October the tumor had spread and doctors began chemotherapy. In November the family traveled to Disneyland, Sami’s final wish. When their plane landed back in California, they went straight to the hospital where Sami died the next day. “We wanted to bring her home,” says Janet, “but we couldn’t.”

During those six traumatic months, friends and neighbors in the Disharoon’s small town rallied to their aid. They brought food and held spaghetti dinners to raise money. “Everyone wanted to help us,” Janet says. “That was just so wonderful.”

After her daughter died, Janet carried that goodwill forward and started the Sami Disharoon Brain Tumor Research Foundation. It is staffed by all volunteers, many of whom have lost children to brain tumors. The foundation raises money and for the past 10 years has donated those funds to the UCSF Pediatric Brain Tumor Program. It has contributed almost $500,000 to date. “We wanted to support a place that was going to make a difference and find a cure as soon as possible,” Janet says.

“We could not be more grateful to Janet, her family and everyone involved with the Disharoon Foundation,” says Mitch Berger, MD, the program’s director. “Their dedication is helping advance our research to give children with brain tumors a fighting chance – and one day, to be able to beat tumors altogether.”

Donating in Gratitude for Health and Motherhood

Nearly a decade ago, Liz Holzemer was diagnosed with a meningioma brain tumor. The second most common primary brain tumor, it develops from the arachnoid layer of the meninges, the membranes that surround the brain and spinal cord. The majority of meningioma tumors (90 percent) are benign. However, when benign tumors grow, constricting and affecting the brain, they can cause headaches, seizures, neurologic deficits, disability and can even be life-threatening.

Holzemer’s tumor was discovered after her attempts to start a family with her husband, Mark, a former pitcher for the Oakland A’s. She underwent a successful surgery to remove the tumor, and is today the mother of two children. Following her recovery, Holzemer founded Meningioma Mommas, a nonprofit organization committed to finding a cure for meningioma brain tumors. The Meningioma Mommas have become significant donors to the UCSF Meningioma Research Laboratory led by surgeon Michael McDermott, MD, who holds the Robert M. and Ruth L. Halperin Endowed Chair in Meningioma Research, and basic scientist Anita Lal, PhD, the lab’s director. They work to discover the genetic changes and abnormalities that cause the development of meningiomas. Recently McDermott and Lal successfully engineered a mouse model that closely mirrors malignant meningioma in humans. This representation will serve as the preclinical model for studying the progression of the disease and testing new therapeutic agents. They have also completed a molecular classification of the disease, which will aid in identifying and diagnosing specific tumor grades (benign, atypical and malignant).

“We could not be more grateful to Janet, her family and everyone involved with the Disharoon Foundation,” says Mitch Berger, MD, the program’s director. “Their dedication is helping advance our research to give children with brain tumors a fighting chance – and one day, to be able to beat tumors altogether.”

Liz Holzemer (center) and Mike McDermott (right) enjoy a moment with visiting lecturer and neurosurgeon Peter Black
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New Helen Diller Family Cancer Research Building Enhances Collaboration

UCSF celebrates the opening of the Helen Diller Family Cancer Research Building at the Mission Bay campus. Designed by noted architect Rafael Viñoly, the state-of-the-art facility houses laboratories focused on prostate and other urologic cancers, the Brain Tumor Research Center, Population Sciences and the Cancer Research Institute, a consortium of laboratories that investigates the basic biological mechanisms of cancer. The close proximity of scientists attacking cancer from all angles fosters a rich cross-pollination of ideas, which will lead to new techniques to prevent, diagnose and treat this disease.
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