Providing comprehensive treatment and specialized care for every child

The Pediatric Brain Tumor Center at UCSF

UCSF Children's Hospital will move to a new facility in 2014 located at the campus at Mission Bay.

University of California
San Francisco
UCSF
Neurological Surgery

UCSF Children's Hospital

The Pediatric Brain Tumor Center at UCSF is dedicated exclusively to providing comprehensive, compassionate care for children suffering from brain tumors. Our unique program combines the advanced treatments and technologies of a world-class university hospital with personalized care from a group of highly skilled specialists. The team at UCSF is made up of board-certified and fellowship-trained pediatric neurosurgeons, neuroradiologists, neuro-oncologists, and radiation oncologists, as well as physicians, nurses, and hospital staff from a variety of pediatric subspecialties. This team approach, from initial diagnosis through treatment and recovery, sets us apart from other centers and is one reason why US News & World Report has ranked the Children's Neurosurgery and Neurology services at UCSF among in the best in the nation.

As treatments continue to improve and children survive to become young adults, they will often face ongoing challenges to their health and emotional and social well-being. To meet those challenges, our Survivors of Childhood Cancer program helps patients understand and cope with the late effects of therapy and to find support for life after cancer.

Even at hospitals like UCSF, however, the best that modern medicine has to offer is not enough to heal every patient. Which is why until there is a cure for pediatric brain cancer, the most important tool driving the future of care is biomedical research. Our team's vast experience with performing translational research and clinical trials has culminated in the recent establishment of a Pediatric Brain Tumor Foundation Institute at UCSF. Located at the new, state-of-the-art Helen Diller Family Cancer Research Building on UCSF's Mission Bay campus, the Institute is poised to become a world leader in pediatric brain tumor research. We are proud to be able to partner with the Pediatric Brain Tumor Foundation in working toward the eradication of this disease and making the future for children with brain tumors more hopeful.

Clinical Care

Pediatric Neuro-oncology

At UCSF, a team of specialists with a variety of expertise and pediatric fellowship training collaborate to develop comprehensive treatment plans for children with brain and spinal cord tumors. Pediatric neuro-oncologists provide care based on the specific needs of each patient and family.

Left: Pediatric neurosurgeons, neuro-oncologists, and radiation oncologists meet during weekly tumor board to discuss difficult or unusual cases. From left to right: Anuradha Banerjee MD, Mitchel Berger MD, Michael Prados MD, Daphne Haas-Kogan MD, Kurtis Auguste MD, and Nalin Gupta MD, PhD.

Below: Neuro-oncologist Anuradha Banerjee MD gives a physical exam to a pediatric brain tumor patient.

Some of the most common types of pediatric brain tumors treated include:

- Medulloblastoma
- Ependymoma
- Brainstem glioma
- Astrocytoma
- Craniopharyngioma

For tumors that are difficult to treat with standard therapy, patients have the opportunity to enroll in clinical trials. The Pediatric Brain Tumor Center at UCSF participates in national cooperative clinical trials, ensuring that our patients consistently have access to the most promising treatments for pediatric tumors of the brain and spinal cord.

Pediatric Brain Tumor Consortium

UCSF is one of nine institutions in the United States selected to participate in the Pediatric Brain Tumor Consortium (PBTC) for clinical trials, sponsored by the National Institutes of Health. Through the PBTC we are able to conduct phase I and II trials of promising therapeutic drugs, new biological therapies, treatment delivery technologies, and radiation treatment strategies for all types of CNS tumors.

Children's Oncology Group

The Children's Oncology Group combines the efforts of the major pediatric clinical trials groups based in North America – the Children's Cancer Group, the Pediatric Oncology Group, the Intergroup Rhabdomyosarcoma Study Group, and the National Wilms' Tumor Study Group (NWTSG) – to accelerate the search for a cure and prevention of cancer in children and adolescents.

Industry Partnerships

In addition to participating in major clinical trials consortia, UCSF performs trials of industry-sponsored investigational agents. Leading biotechnology companies Genentech, AstraZeneca, and Wyeth Pharmaceuticals are among those partnering with UCSF to better understand complex brain cancers.

In the Pipeline: MEK Inhibitors

As a key component of a signaling pathway that is dysregulated in many cancers, mitogen-activated ERK kinase (MEK) is a possible target for new therapies. Inhibitors of MEK are being developed to stop the unchecked signaling of growth factors that leads to tumor proliferation. Currently, UCSF investigators are planning a phase I study of a MEK inhibitor to treat pediatric patients with low-grade glioma.

Surgery for Pediatric Brain Tumors

Advances in neurosurgical equipment and techniques have dramatically lowered the morbidity and mortality that can result from surgery for pediatric brain tumors. UCSF's Pediatric Brain Tumor Center is equipped with the most up-to-date imaging and surgical navigation systems available, allowing removal of the tumor without injuring structures critical to normal brain function. The pediatric neurosurgery program is based at both UCSF Children's Hospital and Children's Hospital & Research Center Oakland.

Left: Chief of Pediatric Neurological Surgery, Nalin Gupta MD, PhD and Matthew Potts MD insert electrodes into the brain to localize the source of intractable seizures caused by an insular brain tumor.

Below: Pediatric neurologist Joseph Sullivan MD watches the progress on a neuronavigation system showing real-time updates of a tumor resection.

Neuronavigation

High-resolution magnetic resonance imaging (MRI) and functional imaging techniques identify the exact location of the tumor, the blood supply, and the metabolic activity of different tissues within the tumor. This information is used to plan and simulate the shortest and safest route through brain tissue well in advance of surgery, improving assessment of risk and preventing postoperative neurological deficits.

Functional Imaging

Functional maps of the brain and specific MR sequences reveal information that cannot be seen on conventional MR images. These maps are combined with standard preoperative MR images to guide surgery.

- Functional MRI (fMRI): Localization of language and motor centers in the brain can be visualized using noninvasive fMRI techniques. Although patient cooperation is required, these techniques have been tailored for pediatric patients and are commonly used at UCSF. fMRI was approved for clinical use in 2007.
- Diffusion tensor imaging (DTI): The location and direction of white matter pathways can be determined by examining the diffusion of water molecules in the brain. This tool is particularly useful to identify motor pathways that extend from the brain cortex to the spinal cord.
- MR spectroscopy (MRS): MRS provides information on metabolic activity within the tumor and can help distinguish areas of tumor from necrosis or normal brain. This technique is also helpful to identify areas of brain tissue that appear normal on routine MRI but actually contain infiltrating tumor cells.

Magnetoencephalography (MEG)

UCSF is one of a few institutions with MEG capabilities. Using very sensitive magnetic sensors, areas of seizure activity associated with brain tumors can be identified and targeted for removal.

Intraoperative Imaging

Computed tomography (CT) and MRI scans performed during surgery allows continual updating of preoperative image sets so the surgical team can actively evaluate the extent and position of the tumor as it is being removed. Integrating these scans with information from functional imaging techniques can further enhance safety by identifying regions amenable to surgery or regions of eloquent cortex.

Cortical Mapping

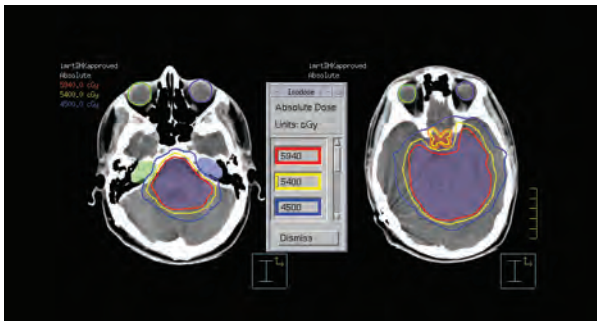
Brain mapping techniques are essential to identifying and avoiding injury to vital sites of language, motor, and sensory function. Many of these techniques were pioneered at UCSF and are performed either during awake craniotomy or by placing subdural grids in young patients unable to tolerate awake craniotomy. In general, awake craniotomy is performed on patients older than 12 to 14 years of age.

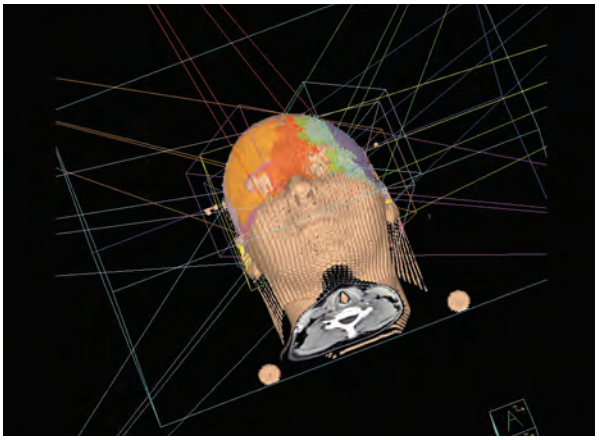
Cranial Nerve Monitoring

The surgical team at the Pediatric Brain Tumor Center includes electrodiagnostic specialists who have expertise in monitoring cranial nerves during surgery, greatly facilitating safe excision of the tumor.

Ultrasound

Intraoperative ultrasound is a safe method used to determine depth, tissue consistency, and proximity to anatomic and vascular structures. When used in the operating room, ultrasound provides real-time updates regarding extent of resection.





Above: Intensity modulated radiation therapy (IMRT) allows treatment of the tumor while sparing important normal structures such as the ears (shown in the right axial slice) and the optic chiasm (shown in the left axial slice). This technology limits both short- and long-term toxicities for patients.

Right: Three-dimensional rendition of the beam arrangement for conformal radiation therapy for the treatment of a brain tumor.

Radiation Oncology

The goal of radiation therapy is to treat the tumor and areas at risk for tumor spread, while minimizing doses to normal structures. The developing brains of young children are especially vulnerable to damage from radiation, making it critical to target the tumor as accurately as possible. At UCSF, we have the technology to design treatment plans that are extremely accurate and chosen for the tumor type, the child's developmental stage, and the patient's individual anatomy.

Intensity Modulated Radiation Therapy (IMRT)

Physicians at UCSF have used IMRT to treat cancer patients for over 10 years, giving us more experience with this treatment modality than most other places in the U.S. Using computer optimization, multiple small fields are designed to give a complex and conformal radiation dose distribution. At UCSF, there are six treatment machines capable of delivering IMRT plans. It is routinely used to treat tumors in challenging locations.

Gamma Knife® Radiosurgery

A finely focused, high dose of radiation is delivered directly to the tumor from 200 sources that converge precisely on the target area. By having lower doses of radiation from multiple sources converge on a single location, normal tissue in the path receives a minimal dose, reducing the chance of radiation injury. A team with expertise in the Gamma Knife discusses eligible patients during a weekly conference, and it can be an excellent option for treating a variety of primary and metastatic pediatric brain tumors.

CyberKnife® Radiosurgery

The CyberKnife uses image guidance and robotics to maintain a high degree of precision and is particularly useful for tumors that are close to critical structures. A robotic arm fitted with a linear accelerator aims many small radiation beams at the tumor from multiple angles. This allows us to give a high radiation dose to the tumor and a low radiation dose to the surrounding normal tissues. The robotic arm automatically compensates for any movement to ensure accurate delivery of each radiation beam.

Hyperthermia

Hyperthermia refers to the use of heat treatments to kill cancer cells. Hyperthermia enhances the effects of other cancer treatments, so it is almost always given in combination with radiation therapy, chemotherapy, or both. It is particularly useful for treatment of recurrent cancer in an area of the body that has already received radiation therapy. UCSF is home to the largest and most versatile hyperthermia program on the West Coast.

Brachytherapy

Brachytherapy is a method of delivering radiation to tumors by placing radioactive sources either within or immediately adjacent to tumor tissue. Because the radiation source is very close to the tumor, radiation can go directly to the tumor without traveling through normal tissue.

Intraoperative Radiation Therapy (IORT)

During the surgical procedure, while the wound is open, the surgeon discusses with the radiation oncologist the areas of the tumor bed where tiny fragments of tumor may remain. The sensitive normal tissues are moved out of the radiation field, and then the radiation oncologist directs a single high dose of radiation to the area most at risk for residual disease.

Three Dimensional Conformal Radiation Therapy (3DCRT)

This technique involves imaging, accurate radiation dose calculation, computer-optimized treatment planning, and computer-controlled treatment delivery. Treatment-planning CT scans are merged with diagnostic quality images, such as MRI and positron emission tomography scans, to maximize our ability to target tumors. All of our linear accelerators are equipped with computer-controlled, beam-shaping devices called multileaf collimators. These permit fast and efficient delivery of 3DCRT and IMRT plans.

Left: Kate Rauen MD examines a young patient at the NF/Ras Pathway Clinic

Below: At UCSF, a family-centered approach is important to creating successful treatment and follow-up plans

Germline mutation in the NF1 or NF2 gene may be the first hit in the two-hit cancer theory. Another genetic mutation, such as in the p53 tumor suppressor gene, may result in malignant transformation.

NF/Ras Pathway Clinic

Pediatric patients with neurofibromatosis (types 1 and 2) are predisposed to a number of cancers, including CNS tumors involving the brain, cranial nerves, or spinal cord. The biological behavior of CNS tumors occurring in patients with neurofibromatosis is often different than the behavior of the same tumor type occurring sporadically in patients without neurofibromatosis. The type of mutation in the NF1 or NF2 gene often influences the severity of the disease and the phenotype.

Providing care for individuals with rare syndromes like neurofibromatosis is challenging, particularly since even specialty care providers may not be well versed in rare disorders.

The UCSF NF/Ras Pathway Clinic provides unique care for patients with syndromes causing germline mutations in genes encoding components of the Ras/mitogen-activated protein kinase (MAPK) pathway. Although individually rare, this group of genetic syndromes has a common underlying pathology, resulting in an overlap in clinical features. This commonality inspired the concept for this pathway-based (instead of disease-based) clinic. Unlike other clinics, the UCSF NF/Ras Pathway Clinic provides a smooth transition from pediatric to adult care for these individuals with multi-specialty needs.

Pediatric Neuroendocrinology

Approximately 60 to 70% of children with brain tumors suffer from hormonal dysfunction – especially those patients with tumors in the posterior fossa or those who undergo radiation or chemotherapy.

The brain is involved in regulating six hormonal systems:

- Autonomic function
- Puberty and gonadal secretion
- Water balance and antidiuretic hormone secretion
- Growth and growth hormone secretion
- Metabolism and thyroid hormone secretion
- Stress and adrenal hormone secretion

One or all of these systems may be affected by the tumor or treatment. Every patient at UCSF is evaluated by a pediatric endocrinologist with the goal of improving quality of life and survival. Endocrine abnormalities may persist for 10 years following radiation therapy, and patients at UCSF are followed for 10 years to assess possible delayed effects of radiation.

Above and right: With help from her mother Nikki Farris, and UCSF occupational therapist Christina Carter, 6-year-old Grace Farris recovers from surgery for a dysembryoplastic neuroepithelial tumor, or DNET, and works on her motor skills during a rehabilitation session. “Our experience has been wonderful,” says Mrs. Farris. “It’s so hard to find all the doctors and experts you need in one place, but that’s what UCSF offers.”

Palliative Care

Palliative care for children embraces physical, emotional, social, and spiritual elements and should begin early as a standard component of the treatment plan. At UCSF Children’s Hospital, our COMPASS CARE program focuses on enhancing quality of life and support for family by managing pain and symptoms and ensuring a child’s comfort through treatment, death, and bereavement. Additional services include a family support program and resource library; sibling services; special rooms in the pediatric unit to provide a private atmosphere and extra measures of comfort during end-of-life care; and assistance in identifying community home care or hospice resources. At UCSF, palliative care is not separate from curative care and is integrated into the overall care plan from the point of initial diagnosis.

Inpatient & Outpatient Pediatric Rehabilitation

Our comprehensive inpatient rehabilitative services include three hours of therapy per day, six days per week and a coordinated team approach with:

- Evaluation and planning meetings upon admission
- Weekly team meetings
- Family meetings
- Discharge planning
- Psychosocial support
- 24-hour medical coverage from in-hospital physicians
- School program with special education teachers
- Community re-entry
- Integrative health services
- Spiritual services

The inpatient rehabilitation team includes:

- Pediatric rehabilitation physicians
- Nurse manager
- Nurse practitioner
- Physical therapists
- Occupational therapists
- Speech language pathologists
- Child life specialists
- Dietitians
- Special education teachers
- Social workers
- Pediatric subspecialists
- Pediatric hospitalists

Rehabilitation for children following brain-tumor treatment may also be managed through the Pediatric Rehabilitation Clinic where care is coordinated with a wide range of available medical, therapeutic, and support services. If needed, short-term physical, occupational, and speech therapy can be provided by our expert pediatric therapists in the Outpatient Pediatric Therapy Center.

Survivors of Childhood Cancer Program

Innovations in cancer treatment have allowed more children with brain tumors to become young adults. However, many new therapies are known to cause long-term side effects that can arise years and even decades after treatment ends. Therefore, it is critical that cancer survivors receive long-term follow-up care by heath care providers knowledgeable about their medical history.

Pediatric cancer survivors may face a host of issues including:

- Secondary cancers
- Fertility problems
- Obesity
- Psychological and emotional problems
- Learning difficulties
- Therapy-related organ dysfunction
- Access to healthcare and problems obtaining insurance

Survivors Clinic

The Survivors Clinic is offered monthly for survivors of pediatric cancer who are at least two years from treatment completion. The clinic visit includes a consultation with a pediatric cancer specialist, nurse, social worker, and school liaison. The entire visit takes one or more hours and includes:

- Physical exam with a cancer specialist and nurse to review the patient's original diagnosis, treatments received, and the effects of therapy on the patient's present and future health. The latest research regarding the patient's treatments, potential side effects, and diagnosis are also discussed.
- Consultation with a social worker to discuss school, work, emotional, and family issues. If needed, referrals to support programs are provided.
- Consultation with a school liaison about educational benefits available to cancer survivors and potential learning obstacles associated with certain cancer treatments.

The Survivor Health Passport

After visiting the Survivors Clinic, patients receive a Survivor Health Passport, a wallet-sized card that includes information on a patient's disease and treatment history, risk factors, and follow-up recommendations. The Survivor Health Passport should be carried by patients and shared with other health care providers to ensure the best possible follow-up care.

Koret Family House

The Koret Family House is a not-for-profit organization providing temporary housing to families of seriously ill children receiving treatment at the UCSF Children's Hospital. Qualifying families live more than 50 miles from UCSF, and many live at or below the low-income status.

Since the average length of treatment for children with brain tumors is six weeks, being close to the hospital is critical. The Family House's two locations are in close proximity to UCSF Children's Hospital and feature private rooms along with common areas that include dining and kitchen facilities, family rooms, libraries, playrooms, and laundry rooms.

Research

Since the Brain Tumor Research Center was established at UCSF in 1972, it has become a world leader in translational brain tumor medicine. An extraordinary team of scientists and physicians collaborate to analyze real obstacles to therapy seen in the clinic and apply that to the goals of our research laboratories. The vast experience of our neuro-oncology group with developing new therapies and leading clinical trials has earned us an international reputation in this field, culminating with the establishment of a Pediatric Brain Tumor Foundation Institute at UCSF (see next page). With every study and clinical trial we are increasing our understanding of what causes pediatric brain tumors and how to create effective treatments.

Pediatric Clinical Research Center

UCSF's Pediatric Clinical Research Center (PCRC) is a specialized research unit where experimental therapies can be given in an effort to improve outcomes for severely ill children. The PCRC is one of the Clinical & Translational Science (CTSI) Clinical Research Centers supported by the National Institutes of Health and designed to facilitate translational research in a number of medical disciplines. By providing infrastructure and expertise, a large body of experimental research for rare diseases like pediatric brain tumors can be performed, which would not otherwise be possible.

A corps of highly skilled pediatric nurses, as well as neonatal and critical care nurses, screen patients for studies and work with their families. All are well versed in the unique requirements of working with children and in providing the warmth and empathy needed by critically ill children and their families.

The Helen Diller Family Cancer Research Building was designed by renowned architect Rafael Vinoly and houses all the laboratories of the UCSF Brain Tumor Research Center, including those investigating pediatric brain tumors.

Helen Diller Family Comprehensive Cancer Center and Cancer Research Building

On June 2, 2009, UCSF opened the doors of the new Helen Diller Family Cancer Research Building at Mission Bay. At over 160,000 square feet, it has more than doubled the laboratory space exclusively dedicated to cancer research and is the first UCSF building specifically focused on translational research for one particular disease. By housing all cancer specialists at UCSF under one roof, we are creating vast opportunities for new partnerships among investigators researching different cancers, as well as among bench scientists and clinicians.

The Research Building is a component of the UCSF Helen Diller Family Comprehensive Cancer Center, which combines basic science, clinical research, epidemiology/cancer control, and patient care throughout UCSF. It is designated a comprehensive cancer center by the National Cancer Institute – established by a rigorous evaluation process to exhibit scientific excellence and the capability to integrate a diversity of research approaches to focus on the problem of cancer. In 2014, UCSF will open a new children's, women's specialty, and cancer hospital complex at the Mission Bay campus (see cover). This new hospital will set a world-class standard for the care of pediatric cancer patients and further the Center's mission to conquer cancer worldwide through innovation and education.

The Pediatric Brain Tumor Foundation Institute at UCSF

The Pediatric Brain Tumor Foundation (PBTF) has established a world-class research institute at UCSF to define the poorly understood basic biology of several types of childhood brain tumors and improve therapies. As the largest non-governmental source of funding for childhood brain tumor research, the PBTF is dedicated to eradicating childhood brain tumors through supporting medical research, increasing public awareness, and providing educational and emotional support to children and families affected by this disease. The PBTF, based in Asheville, North Carolina, also supports Research Institutes at Duke University and The Hospital for Sick Children in Toronto.

The research program of the PBTF Institute at UCSF focuses on medulloblastoma and brainstem glioma – alternately the most common and least treatable types of pediatric brain tumors.

Central Nervous System Development and Brainstem Glioma Tumorigenesis

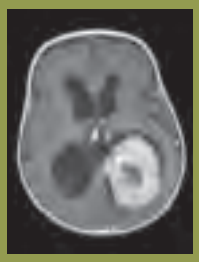
Principle Investigators: Arturo Alvarez-Buylla PhD and David H. Rowitch MD, PhD

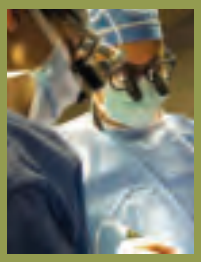
Because of its invasive nature, surgically inaccessible location within the brainstem, and resistance to conventional treatment, brainstem glioma remains incurable. In children, there is a well-defined area of dividing cells within the pons that resemble neural stem cells and may give rise to brainstem glioma. By exploring this recent discovery, Drs. Rowitch and Alvarez-Buylla hope to identify the source of this tumor type, providing a new target for therapy.

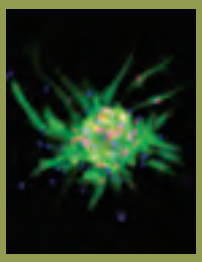
MYCN and Medulloblastoma Tumorigenesis

Principle Investigator: William A. Weiss MD, PhD

Medulloblastoma is the most common type of brain tumor in children. Laboratory experiments in animal models have shown that abnormalities in expression of the Mycn oncogene likely contribute to development of this disease – aberrant expression occurs in greater than 95% of medulloblastoma tumors. By developing therapies to specifically target Mycn, Dr. Weiss and his colleagues hope to slow or halt progression of medulloblastoma.







Above, left: Magnetic resonance imaging provides detailed information on location and extent of pediatric brain tumors.

Above, middle: Pediatric neurosurgeons at UCSF use state-of-the-art surgical techniques to achieve maximal safe resections

Above, right: Neural stem cells may be the origin of pediatric brainstem glioma

Left: PBTF Institute investigator C. David James PhD is developing new models of pediatric brain tumors to test novel therapeutic agents in the laboratory

Novel Therapeutic Strategies for Pediatric Brain Tumors

Principle Investigators: Nalin Gupta MD, PhD and C. David James PhD

Drs. Gupta and James are focusing on the emerging role of small interfering RNA (siRNA) molecules as therapeutic tools. In laboratory tests, these agents have been effective in turning off specific biochemical pathways that allow tumors to grow. This research is being coupled with new drug-delivery strategies such as intranasal delivery, which carries agents from the nasal area into parts of the brain through pathways that possibly involve nerves or blood vessels. Systemically administered drugs have a limited capability to enter the brain, resulting in high systemic toxicity and minimal concentrations in the central nervous system. Intranasal delivery is a noninvasive method that could be given repeatedly without the need for surgery or systemic injections.

Tissue Bank & Animal Core

Principal Investigator: C. David James PhD

The Tissue Bank at UCSF has several thousand brain tumor specimens and several hundred pediatric brain tumor specimens. Detailed analysis of these specimens identifies genetic clues that may explain their origin. When new targets have been identified and therapies developed, reliable animal models are critical for testing response to therapy prior to clinical trials in humans. The UCSF Animal Core, lead by Dr. James, uses transplantable xenograft, allograft, and isograft tumor models in support of pediatric brain tumor translational research.

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