

USC BRAIN TUMOR CENTER

Report

Volume 4 • Issue 3

SUMMER 2024

From the USC BTC Directors



At the USC Brain Tumor Center, we are committed to delivering the best care and support to all of our patients and are excited to share some exciting updates and news in this Summer 2024 Newsletter.

The USC Brain Tumor Center is growing. This summer, we welcome **Dr. Aaron Cohen-Gadol**, Professor of Neurological Surgery, who joined Keck Medicine of USC Department of Neurosurgery. His focus is on the treatment of complex brain and spine tumors. His knowledge and expertise make him a valuable addition to our team and we trust that his contributions will enhance the care of our BTC Patients.

As we continue to make progress in our research and treatment efforts, we are proud to share with you that **Dr. Adam Modrek** and his team received the “**Donald E. And Delia B. Baxter Foundation Fellowship Award**” for \$100k for their grant entitled ‘DNA Damage drives oncogenic epigenetic alterations in glioblastoma’. We congratulate Dr. Modrek and his team and we will share progress on any future work.

We are committed to finding a cure to all brain tumors. We share with you today that **Dr. Thomas Chen** and **Dr. David Tran** will be clinical co-investigators in a trial supported by a California Institute for Regenerative Medicine (CIRM) Grant. This grant supports a clinical trial targeting newly diagnosed high grade glioma (HGG). The USC BTC continues to offer access to expanding clinical trials and are committed to further strengthen and hone our existing portfolio, including opening a new vaccine trial earlier this year for high grade glioma called TVAX.

During the month of May, we focused on raising awareness for brain tumors and sharing the message of

the importance of raising funds for brain cancer research. We are excited to share that thorough the efforts of the USC Brain Tumor Center, the City of Los Angeles and the County of Los Angeles officially declared May 2024 Brain Tumor Awareness Month. Raising funds for brain cancer research is one of our priorities. We want to recognize all our donors for their continued support, and extend our gratitude for all that they make possible. We have amazing partners in our community. Thank you to Smith Brothers Restaurants, STRIDE Pasadena and to Advisory Board Members, Kelly Self and Jeff and Julieta Bennet for your partnership in raising awareness and funds to accelerate research with your philanthropic support.

Our multidisciplinary team continues to assess what more we can do for our patients. In this issue you will find a piece written in collaboration of our clinical care team, that gives advice to brain tumor patients families and caregivers on “**How to Care for Your Loved One with a Brain Tumor**”.

Supporting our brain tumor community is part of our mission. During the spring our USC BTC team participated in brain tumor fundraising events. Our team walked and ran at the **National Brain Tumor Society 5k** in Los Angeles. We are looking forward to an upcoming **ABTA 5k** walk in October 2024.

Education is also essential to our mission. This summer we welcomed three interns in different areas of our Center. We are fortunate to play a part in training the next generation of brain tumor doctors, scientists and administrators. We also had a fantastic turnout at a private club in Los Angeles, where guests listened to members of our team present a talk about Brain Health in 2024. We are looking forward to the fall of 2024 as we prepare for our annual series of regional and national Brain Tumor Conferences.

Thank you for your continued support of our USC Brain Tumor Center. Let’s continue to work together to make a difference in the fight against brain cancer.

Heal on!

David D. Tran, MD, PhD
Co-Director, USC Brain Tumor Center

Gabriel Zada, MD, MS, FAANS, FACS
Co-Director, USC Brain Tumor Center

Josh Neman, PhD
Scientific Director, USC Brain Tumor Center

Introducing Aaron Cohen-Gadol, MD, MSc

Aaron Cohen-Gadol, MD, MSc, is professor and vice chairman of innovation at the Keck School of Medicine of USC Department of Neurological Surgery. Dr. Cohen specializes in the treatment of complex brain and spine tumors, as well as arteriovenous and cavernous malformations, hemifacial spasm and trigeminal neuralgia. Dr. Cohen received his medical degree at the Keck School of Medicine of USC and completed his residency at the Mayo Clinic in Rochester, Minnesota. He also completed fellowship training in two subspecialties, epilepsy surgery (Yale University) and skull base/cerebrovascular surgery (University of Arkansas). Dr. Cohen has a Masters Degree in Clinical Research from Mayo Graduate School and an MBA from the Kelley School of Business. In 2006, Dr. Cohen joined the Department of Neurosurgery at Indiana University School of Medicine, where he has been professor of neurological surgery and Director of Neurosurgical Oncology/Brain Tumor Surgery.



A prolific contributor to the scientific literature, Dr. Cohen has published more than 560 peer-reviewed papers and is a member of the advisory board of many peer-review journals, including the **Journal of Neurosurgery**, **Neurosurgery**, **Operative Neurosurgery**, and **World Neurosurgery**. In his philanthropic work, he has served on and directed numerous committees in raising funds for medical research, education, and innovation.

Dr. Cohen is the founder of **The Neurosurgical Atlas**, an invaluable compendium of detailed operative videos, 3D models, and interactive neuroanatomy, which is considered an essential resource for neurosurgeons and patients.

“The pursuit of excellence in neurosurgery is a passion and not a job. My philosophy has always been to do the best anyone can, rather than do the best I can. The interest of my patients is the most important consideration in any surgical intervention, and I strive to create a plan of care that I would recommend to my own family.” - **Aaron Cohen-Gadol, MD, MSc**

Caring for Your Loved One with a Brain Tumor

A collaboration between our clinical care team

Facing the complexities of a brain tumor diagnosis can be overwhelming. Patients, their families, friends and caregivers usually feel unprepared once given this diagnosis. Our Clinical Care Team shares with you some valuable insights that might be helpful during this challenging time.

Finding and Utilizing Your Support Team

When your loved one is diagnosed with a brain tumor, it can be scary news. It is important to find your core group, which may be friends or family that can help you and your loved one through the surgery and treatment journey. There may be those that let you know they are available and ask how they can help. Assign specific tasks (such as helping with school drop-offs/pick-ups, transportation getting to and from appointments or helping with feeding pets) to those that are willing to help.

Finding and Utilizing Resources

You may be experiencing a wide range of emotions, and it is important to verbalize how you are coping with a trusted family/friend. There are additional avenues of support, including mentorship programs, support groups and individual therapy. Speak with your organization's social worker to gain a better understanding of the available support options in your area and through your insurance coverage.

Getting Connected to the Right Info

When looking for information on your loved one's diagnosis, it is important to seek advice first from the Neurosurgeon and Neuro Oncologist. When searching online, it is a good idea to seek out trusted sites such as academic hospital systems. Always remember that when hearing about others' stories, keep in mind that everyone's journey is different. Even if your loved one has the same tumor as someone else, they may not have the same experience as that person. Every journey is unique.

Know Your Options

Know your options and ask questions. For some, it can feel daunting to bring up certain concerns and questions to their physician, but it is better to get clarity on what lies ahead than to be in the dark and fear what you don't know. Undergoing chemotherapy and radiation may not be the right decision for every patient, so talk to the doctor about the option of palliative care or hospice. A palliative care team can work alongside your loved one's brain tumor team to make sure that their symptoms are being adequately addressed and the treatments they receive are aligned with their wishes/values. Hospice may be appropriate when they are considering discontinuing tumor treatment and instead focusing on symptom relief at the end of life.

When you select your Care Team

Get to know your care team and how to reach them. Questions big and small can be addressed, in real time or noted for your next appointment, and provide some peace to get those issues off your mind. It

is helpful to have phone numbers and/or emails readily available to you. Find out what form of communication works best for you and your team. Make sure you understand "what's next" before leaving your provider visit—medication schedule and doses, appointments for treatment/imaging/next visit. Take notes if that helps you remember.

Understand your insurance coverage - many plans require prior authorization, or approval, before appointments can be scheduled, especially MRIs, so stay on top of it to avoid delays in scheduling.

At the USC Brain Tumor Center our Multidisciplinary Team is here for you. We understand the journey that lays ahead of you is challenging but we have the confidence that we will guide you and be with you every step of the way.



Pictured left to right: Jinsy Rogers, LCSW, Nancy Hart, RN, MSN, CPON, Frances Chow, MD, Tania Vartanians, MS, PA-C, and Rebekah Ghazaryan, RN, PHN.

The Modrek Lab receives Fellowship Award from the Baxter Foundation

Dr. Aram Modrek and his team have received the "Donald E. and Delia B. Baxter Foundation Fellowship Award" for \$100k from the Baxter Foundation for their grant titled "DNA damage drives oncogenic epigenetic alterations in glioblastoma."



Aram Modrek, MD, PhD

The research team is investigating non-genetic chemical scars left on the blueprints on cells from our therapy, and that the cancer cells use these scars to behave in a more aggressive manner. Dr. Modrek and team have found that DNA damage leaves behind non-genetic changes in the blueprints of cancer cells.

These non-genetic changes include chemical modifications such as DNA methylation, changes in the organization and orientation of DNA, expression of genes, and many other changes. Cancer cells may use these non-genetic changes to alter how they interpret and express the DNA, or blueprints, and behave in a more aggressive and treatment-resistant manner. By understanding the process that leads to these alterations, the team hopes to find therapeutic strategies that block this process and disable the ability of cancer cells to adapt to our widely used therapies.

The Modrek Laboratory is in the Department of Radiation Oncology at the Keck School of Medicine of USC. They are a member of the USC

Norris Comprehensive Cancer Center, Epigenetic Regulation in Cancer Program and the USC Brain Tumor Center.

The laboratory's mission is to determine how the genome is altered by DNA damage and investigate the impact of these changes on gene regulation and treatment resistance in brain tumors using cutting edge techniques and approaches.

By understanding how our genomes adapt to therapy, the laboratory aims to find ways to stop this process and render cancer cells more effective therapy.

To learn more about the Modrek Lab visit www.modreklab.com.



Pictured left to right: Rebekah Ghazaryan, RN, PHN, Jinsy Rogers, LCSW, Nancy Hart, RN, MSN, CPON, David Tran, MD, PhD, Paul Krekorian, Steven Giannotta, MD, Gabriel Zada, MD, MS, Paola Mork, MHA, and Josh Neman, PhD.

City of Los Angeles and the County of Los Angeles officially declare May 2024 Brain Tumor Awareness Month

The City of Los Angeles and the County of Los Angeles officially declare May of 2024 **Brain Tumor Awareness Month**, through the efforts of the USC Brain Tumor Center.

Los Angeles City Council President Paul Krekorian presented the resolution to the USC Brain Tumor Center at Keck Medicine of USC. During his remarks he stated that “increased public awareness of brain tumors through advocacy and support for vital research, as well as education about the impact brain tumors

have on the lives of patients and their families are critical to finding a cure”.

Simultaneously **Los Angeles County Supervisor Lindsey Horvath**, passed the resolution that recognizes the USC Brain Tumor Center at Keck Medicine of USC for “their heroic contributions” to addressing the needs of the brain tumor community in the County of Los Angeles, for making extraordinary efforts in raising awareness about brain tumors and the importance of educating the communities and being an advocate for the development of a cure.

By declaring May as Brain Tumor Awareness month, the city and county of Los Angeles took a tremendous leap to raise public awareness about the causes, symptoms and treatment options available for those affected by brain tumors.

We are extremely grateful to the City and County of Los Angeles who also recognized the hard work our team (medical professionals, researchers, staff and advocates) at the USC Brain Tumor Center is doing to conquer and cure brain tumors.

Gene Therapy Trial Tests Cancer-killing Virus in Brain Tumors

The \$11.8 million was awarded by the California Institute for Regenerative Medicine (CIRM)

Dr. Thomas Chen and Dr. David Tran will be clinical co-investigators in a trial supported by \$11.8 million CIRM award to Noriyuki Kasahara, MD, PhD of UCSF. This grant will support a clinical trial targeting newly diagnosed high-grade gliomas. High-grade gliomas are fast-growing cancers that form



Thomas Chen, MD, PhD

in the brain or spinal cord that are difficult to treat and have a dismal prognosis.

This first-in-human clinical trial will evaluate the safety and efficacy of this novel gene therapy technology, originally developed in Dr. Kasahara's lab, in newly diagnosed high-grade gli-



David D. Tran, MD, PhD

oma patients. This trial will be conducted at three institutions in California, USC being one of them. The clinical trial will be for 70 patients.

“This first-in-human clinical trial in newly diagnosed high-grade gliomas represents a novel treatment approach that aims to advance management of this devastating disease,” said Dr. Abla Creasey, PhD, Vice President of Therapeutics Development at CIRM.



USC Brain Tumor Center hosts luncheon at the California Club

On May 15th, 2024 the Brain Tumor Center had the honor of hosting an informational luncheon at the prestigious California Club in the heart of downtown Los Angeles.

Dr. Steven Giannotta, Chair of USC's Neurosurgery department, presented speakers, **Dr. William Mack**, **Dr. Helena Chui**, and **Dr. Gabriel Zada**. It was a resounding success and a significant event for USC's Neurosurgery and Neurology departments.

Dr. William Mack, who specializes in **endovascular neurosurgery** presented on cutting-edge science in stroke prevention. Dr. Mack highlighted advanced treatments like clot retrievals and stent placements at Keck Medicine.

Dr. Helena Chui, Chair of the Neurology department and internationally recognized expert in **Alzheimer disease** and **vascular cognitive impairment**, delivered a compelling talk on Alzheimer's disease and discussed ongoing research aimed at preserving memory and developing new treatments to slow disease progression.

Dr. Gabriel Zada, Co-director of the Brain Tumor Center, showcased USC's leadership in **brain tumor treatment** and care. In addition, Dr. Zada highlighted expertise in **minimally invasive endoscopic surgeries** for skull base tumors and pituitary tumors. Dr. Zada's presentation also featured USC's **advanced 7 Tesla imaging** capabilities.

The event concluded with an engaging Q&A session, where attendees had the

opportunity to interact directly with the speakers and delve deeper into the topics discussed. The positive feedback heard during the post-event discussions reflected the high level of interest and satisfaction among the attendees. The luncheon not only served as a platform to share state-of-the-art treatments and research but also strengthened the connection between USC's medical advancements and the community. The event was both informative and well-received, setting the stage for future engagements aimed at further educating and engaging the public.

For updates on future events hosted by the USC Brain Tumor Center and USC's Neuroscience department, interested individuals are encouraged to follow them on Instagram.

The USC Brain Tumor Center participates in the National Brain Tumor Society Los Angeles 5K Walk/Run

The USC Brain Tumor Center is a proud sponsor of the **National Brain Tumor Society (NBTS)**. This past spring on a beautiful and crisp Saturday morning, members of our team raised funds and participated in the **NBTS Los Angeles 5K Walk/Run**.

The event was created to raise awareness and funding that is used to support brain tumor patients and their families. The 5K walk or race is a family-friendly event for all ages.

Dr. Steven Giannotta, Chair of the Keck Medicine of USC Department of Neurological Surgery and a member of the USC Brain Tumor Center spoke to the participants that morning about the importance of events like these and the crucial role they play in raising awareness and funds for brain cancer research.

We enjoyed sharing stories and congregating with brain tumor patients, their families and caregivers and even showed big spirit and competition during the race.



USC Brain Tumor Center Fundraising Events



STRIDE Fundraiser

On May 11, BTC Advisory Council member, **Kelly Self**, partnered with **STRIDE Pasadena** to host a fundraiser class in support of the USC Brain Tumor Center. It was a full-house with 24 attendees joining in the treadmill-based workout class. As a brain tumor survivor herself, Kelly shared how fortunate she felt to find her way to Dr. Zada and the BTC, and she thanked everyone for their participation and donations.

All fees for the fundraiser class were donated directly to the USC BTC with many additional donations coming from the amazing STRIDE community throughout the day. The BTC sends huge thanks to Kelly for spearheading the effort, and to **Misa Dugally** and **Katie Ownbey**, the wonderful co-founders of STRIDE, who donated their time and space.



Bennett Salon Dinner

On the evening of June 20, **Julieta** and **Jeffrey Bennett** hosted a dinner for the USC Brain Tumor Center at a private club in Pasadena. Guests heard from

the Center directors: Neurosurgeon **Dr. Gabriel Zada, MD**, Neuro Oncologist **Dr. David Tran, MD, PhD**, and Neuroscientist **Dr. Josh Neman, PhD** and Keck School of Medicine of USC leader, **Dean Carolyn Meltzer, MD**.

Dean Meltzer began the program with an introduction of her role and overview of how the USC Brain Tumor Center fits within the medical school's mission and priorities.

The directors shared highlights of the groundbreaking work being led by the center team and guests engaged the doctors with many thoughtful questions around the advancement of research in treating brain tumors.

Dr. Zada closed the evening by sharing the opportunity to accelerate research with philanthropic support.

SMITH BROTHERS RESTAURANTS

Dinner with Purpose

In support of...
Keck Medicine of USC
USC Brain Tumor Center

Smith Brothers Restaurant Corporation and Keck Medicine of USC Brain Tumor Center invite you to join us in the fight against brain cancer.

Dine with us at all three of the Smith Brothers Restaurants: Smitty's Grill, Parkway Grill, and Arroyo Chop House on every Thursday in May, and a percentage of the proceeds will be donated to support the invaluable research being done at Keck Medicine of USC Brain Tumor Center.

Thursday, May 2
Thursday, May 9
Thursday, May 16
Thursday, May 23
Thursday, May 30

ARROYO CHOP HOUSE
626.277.7483
arroyochop@smibros.com
530 S. Arroyo Parkway, Pasadena

Smitty's GRILL
626.792.8999
smittysgrill.com
110 S. Lake Ave., Pasadena

Parkway Grill
626.796.1801
parkwaygrill.com
510 S. Arroyo Parkway, Pasadena

The Smith Brothers Restaurants partner to raise funds for the USC Brain Tumor Center

In honor of Brain Tumor Awareness Month, the **Smith Brothers Restaurants (Parkway Grill, Arroyo Chop House, Smitty's Grill)** generously committed a portion of their May proceeds to the USC Brain Tumor Center.

For the second year in a row, Pasadena diners were able to contribute to our center by enjoying a lovely evening out with friends and family.

We are so grateful for Gregg and Robert Smith for their continued support!

Save the Date 25th Annual Brain Tumor Update and 14th Annual Symposium on Brain Metastases and Spine Tumors

November 2-3, 2024
Moxy+AC Hotel
Downtown Los Angeles
Live Conference



Presented by:



Register:

<https://keckusc.cloud-cme.com/brainmets2024>

Giving to the USC Brain Tumor Center Fund Provides Across-the-Center Support

Our **USC Brain Tumor Center Fund** provides flexible financial support to be utilized at the discretion of center leadership, making these funds crucial for unexpected equipment needs or to pursue new, early-stage research projects not covered via the Center's NIH or NCI research funding awards.

The fund is wholly comprised of gifts big and small from the gracious generosity of our donors. This recent fiscal year, we received over 130 gifts to the Brain Tumor Center Fund, totaling over \$200,000 that helps the Center grow and thrive.

We want to recognize all our donors for their continued support and to extend our gratitude for all that you make possible.

Thank you for your continued support of the USC Brain Tumor Center and for your partnership in advancing our brain tumor research and innovations in patient care.

Training the Next Generation - USC Brain Tumor Center High School Summer Internship Program

The overall goal of the **USC Brain Tumor Center High School Summer Internship Program** is to educate and inspire the next generation of brain tumor doctors, scientists, and administrators.

This year our Interns had the opportunity to be mentored by members of our USC BTC Team in different areas, gained hands-on experience, and contributed to our ongoing research and patient care efforts.

They now join us in spreading awareness about the important work that is being done at the USC BTC to find a cure for brain cancer.

We are grateful to the members of our team who spent time with our interns this summer and we thank them for sharing their passion and commitment to the Brain Tumor Center and its mission



The USC BTC Tissue Core

"Ben, our summer intern, joined our lab at the beginning of June. His smile, joy, and passion for neuroscience transformed the atmosphere of our lab. Our goal was to teach him the process of transforming tissue from the body into cell lines. He learned various techniques such as cell culture, tumor processing, ICC, IHC, and qPCR and drug screening.

Having Ben and training him reminded us of the cyclical nature of science and the importance of passing on our knowledge. We trained Ben in the hope that he will continue the path that USC BTC has begun, whether as a young neuroscientist,

scientist, or physician. We envision him contributing to ongoing research, precision medicine for patients, and discovering new treatments and procedures for brain tumors.

At BTC Tissue Core, our primary goal is to advance precision medicine for patients. We focus on tailoring medical treatment to the individual characteristics of each patient, especially those with brain tumors. By analyzing the genetics of each patient, we aim to develop targeted therapies that are more effective and have fewer side effects.

Ben's enthusiasm for learning and his curiosity about science rekindled our own motivation. It reminded us of the importance of our work and strengthened our resolve to advance the BTC Tissue Core's research. His time with us has reinforced our commitment to precision medicine, inspiring us to strive for breakthroughs that will improve patient outcomes and revolutionize treatment options. Thank you Ben!"
- Saman Sedighi, MD, Research Associate USC Brain Tumor Center



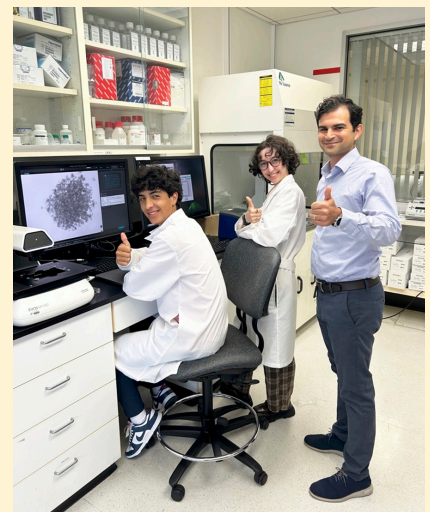
Social Media Administrative Internship

"Lauren met with me weekly to learn about the USC BTC's social media platform content creation, strategies, analytics and measurement. She diligently studied content from multiple organizations and sources, applying this knowledge to create two-three days of content for the USC BTC

Social Media Handles during the duration of her internship.

Lauren's self-motivation and enthusiasm for research and content creation were evident as she focused on producing effective and engaging posts. She demonstrated understanding our audience and successfully interpreted analytics.

Lauren shared her enthusiasm for learning Marketing and PR through social media channels in a health-care program. Thank you Lauren!"
- Paola Mork, MHA, Manager, USC Brain Tumor Center



Brain Tumor Cell Responses to Radiation and Drug Therapies

"The Modrek Lab hosted high school student Connor Mork through the USC Brain Tumor Center internship program. Connor's project focused on understanding how primary brain tumors respond to radiation-drug combinations.

He acquired skills in microscopy, tumor cell culture, and coding to develop methods for quantifying tumor cell responses during radiation and drug treatments.

Through Connor's determination and problem-solving skills, he made contributions to our research and demonstrated the ability to grasp complex scientific concepts, which will undoubtedly serve him well in his future academic and professional endeavors. Thank you Connor!"
- Aram Modrek, M.D., Ph.D., Assistant Professor of Radiation Oncology



Save the Date!

2ND ANNUAL

Southern California

BRAIN TUMOR CONFERENCE

Friday, December 6, 2024

HSC Conference Center, USC Health Sciences Campus

SELECTED PUBLICATIONS



Metabolic Insight into Glioma Heterogeneity: Mapping Whole Exome Sequencing to In Vivo Imaging with Stereotactic Localization and Deep Learning.

Servati M, Vaccaro CN, Diller EE, Pellegrino Da Silva R, Mafra F, Cao S, Stanley KB, Cohen-Gadol AA, Parker JG.

Metabolites. 2024 Jun 16;14(6):337. doi: 10.3390/metabolites14060337.

Intratumoral heterogeneity (ITH) complicates the diagnosis and treatment of glioma, partly due to the diverse metabolic profiles driven by underlying genomic alterations. While multiparametric imaging enhances the characterization of ITH by capturing both spatial and functional variations, it falls short in directly assessing the metabolic activities that underpin these phenotypic differences. This gap stems from the challenge of integrating easily accessible, collocated pathology and detailed genomic data with metabolic insights. This study presents a multifaceted approach combining stereotactic biopsy with standard clinical open-craniotomy for sample collection, voxel-wise analysis of MR images, regression-based GAM, and whole-exome sequencing. This work aims to demonstrate the potential of machine learning algorithms to predict variations in cellular and molecular tumor characteristics.



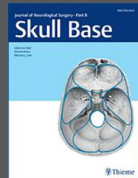
Image-based assessment of natural killer cell activity against glioblastoma stem cells.

Du Y, Metcalfe S, Akunapuram S, Ghosh S, Spruck C, Richardson AM, Cohen-Gadol AA, Shen J.

FEBS Open Bio. 2024 Jun;14(6):1028-1034. doi: 10.1002/2211-5463.13818.

Glioblastoma (GBM) poses a significant challenge in oncology and stands as the most aggressive form of brain cancer. A primary contributor to its relentless nature is the stem-like cancer cells, called glioblastoma stem cells (GSCs). GSCs have the capacity for self-renewal and tumorigenesis, leading to frequent GBM recurrences and complicating treatment modalities. While natural killer (NK) cells exhibit potential in targeting and eliminating stem-like cancer cells, their efficacy within the GBM microenvironment is limited due to constrained infiltration and function. To address this limitation, novel investigations focusing on boosting NK cell activity against GSCs are imperative. This study presents two streamlined image-based assays assessing NK cell migration and cytotoxicity towards GSCs. It details protocols

and explores the strengths and limitations of these methods. These assays could aid in identifying novel targets to enhance NK cell activity towards GSCs, facilitating the development of NK cell-based immunotherapy for improved GBM treatment.



Endoscopic Endonasal Approach to the Ventral Petroclival Fissure: Anatomical Findings and Surgical Techniques.

Xu Y, Mohyeldin A, Lee CK, Nunez MA, Mao Y, Cohen-

Gadol AA, Fernandez-Miranda JC.

J Neurol Surg B Skull Base. 2023 Jun 12;85(4):420-430. doi: 10.1055/a-2088-3086.

The endoscopic endonasal approach has emerged as an excellent option for the treatment of lesions involving the petroclival fissure (PCF). Here, we investigate the surgical anatomy of the ventral PCF and its application in endoscopic endonasal surgery. This study provides a detailed investigation of the microsurgical anatomy of the ventral part of PCF, relevant surgical approaches, and technical nuances that may facilitate its safe exposure intraoperatively.



Efficient Prodrug Activator Gene Therapy by Retroviral Replicating Vectors Prolongs Survival in an Immune-Competent Intracerebral Glioma Model.

Chen SH, Sun JM, Chen BM,

Lin SC, Chang HF, Collins S, Chang D, Wu SF, Lu YC, Wang W, Chen TC, Kasahara N, Wang HE, Tai CK. *Int J Mol Sci*. 2020 Feb 20;21(4):1433. doi: 10.3390/ijms21041433.

Prodrug activator gene therapy mediated by murine leukemia virus (MLV)-based retroviral replicating vectors (RRV) was previously shown to be highly effective in killing glioma cells both in culture and in vivo. To avoid receptor interference and enable dual vector co-infection with MLV-RRV, we have developed another RRV based on gibbon ape leukemia virus (GALV) that also shows robust replicative spread in a wide variety of tumor cells. We evaluated the potential of GALV-based RRV as a cancer therapeutic agent by incorporating yeast cytosine deaminase (CD) and *E. coli* nitroreductase (NTR) prodrug activator genes into the vector. The expression of CD and NTR genes from GALV-RRV achieved highly efficient delivery of these prodrug activator genes to RG-2 glioma cells, resulting in enhanced cytotoxicity after administering their respective prodrugs 5-fluorocytosine and CB1954 in vitro. In an immune-competent

intracerebral RG-2 glioma model, GALV-mediated CD and NTR gene therapy both significantly suppressed tumor growth with CB1954 administration after a single injection of vector supernatant. However, NTR showed greater potency than CD, with control animals receiving GALV-NTR vector alone (i.e., without CB1954 prodrug) showing extensive tumor growth with a median survival time of 17.5 days, while animals receiving GALV-NTR and CB1954 showed significantly prolonged survival with a median survival time of 30 days. In conclusion, GALV-RRV enabled high-efficiency gene transfer and persistent expression of NTR, resulting in efficient cell killing, suppression of tumor growth, and prolonged survival upon CB1954 administration. This validates the use of therapeutic strategies employing this prodrug activator gene to arm GALV-RRV, and opens the door to the possibility of future combination gene therapy with CD-armed MLV-RRV, as the latter vector is currently being evaluated in clinical trials.



Highly efficient and tumor-restricted gene transfer to malignant gliomas by replication-competent retroviral vectors.

Wang WJ, Tai CK, Kasahara N, Chen

TC. *Hum Gene Ther*. 2003 Jan

20;14(2):117-27. doi: 10.1089/104303403321070810.

The first large randomized phase III trial in gene therapy demonstrated no improvement in the survival of patients injected with packaging cells that produced conventional replication-defective retroviral vectors carrying the herpes simplex virus thymidine kinase gene, a disappointing result that was attributed to extremely poor levels of transduction efficiency. To circumvent this problem, we have developed a modified replication-competent retrovirus (RCR) that is capable of transducing human glioma cell lines A-172, U-87, T-98G, U-373, and U-138 and rat glioma cell lines C6 and 9L, over multiple infection cycles in vitro, resulting in a tremendous enhancement in transduction efficiency over conventional replication-defective retroviral vectors at the same dose. Treatment of U-87 intracranial gliomas with RCR vectors carrying the yeast cytosine deaminase suicide gene followed by 5-fluorocytosine prodrug administration resulted in 100% survival over a 60-day follow-up period, compared with 0% survival of control groups receiving vector alone or prodrug alone. Our results demonstrate that RCR vectors can achieve therapeutically significant levels of transduction in malignant human gliomas, and that RCR vector spread after intratumoral injection is restricted to the tumor itself.

CLINICAL TRIALS:
Now Enrolling at the
USC Brain Tumor Center

Have you or someone you know recently been diagnosed with a brain tumor? Choosing the right treatment can be challenging. To find out more about our breakthrough treatments, contact our specialized brain tumor team at (844) 33-BRAIN (844-332-7246) or email frances.chow@med.usc.edu.



Newly Open: USC partners with TVax Biomedical to open the TVI-Brain-1 cancer vaccine

The USC Brain Tumor Center is now recruiting patients to a phase 2b personalized vaccine-based immunotherapy trial for newly diagnosed glioblastoma. TVI-Brain-1 (TVax Biomedical) is a treatment that uses each patient's own cancer cells collected during surgery to create a cancer-targeting vaccine. When the body is exposed to the vaccine, it stimulates T cells, which are harvested from the blood and are subsequently stimulated, expanded, and infused back to the patient. ClinicalTrials.gov identifier NCT05685004.

Trial	Interventions	Phase	
Brain Metastasis			
1	Stereotactic Radiosurgery (SRS) Compared with Collagen Tile Brachytherapy	<ul style="list-style-type: none"> • GammaTile • Stereotactic radiosurgery 	Phase 1
Glioblastoma			
2	An Open-Label, Phase 1/2A Dose Escalation Study of Safety and Efficacy of NEO100 in Recurrent Grade IV Glioma	<ul style="list-style-type: none"> • Perillyl alcohol (inhaled) 	Phase 1/2A
3	A Phase 1/2 Study of Selinexor and Temozolomide in Recurrent Glioblastoma	<ul style="list-style-type: none"> • Selinexor + Temozolomide • Temozolomide 	Phase 1/2
4	Testing the Addition of the Immune Therapy Drugs, Tocilizumab and Atezolizumab, to Radiation Therapy for Recurrent Glioblastoma (BN010)	<ul style="list-style-type: none"> • Radiation + Tocilizumab + Atezolizumab • Radiation + Tocilizumab 	Phase 2
5	Multi-Center Randomized Controlled Phase 2b Clinical Trial to Evaluate the Safety and Efficacy of TVI-Brain-1 Combined with Conformal Radiotherapy and Temozolomide Compared to Standard Therapy as a Treatment for Newly Diagnosed O6-Methylguanine Methyltransferase Negative (MGMT Unmethylated) Grade 4 Astrocytoma (GBM)	<ul style="list-style-type: none"> • TVI-Brain-1 + Radiation + Temozolomide • Standard therapy 	Phase 2b
6	GammaTile and Stupp in Newly Diagnosed GBM (GESTALT)	<ul style="list-style-type: none"> • GammaTile + Standard therapy • Standard therapy 	Phase 4
Meningioma			
7	An Open-Label, Phase 2 Study of NEO100 in Participants with Residual, Progressive or Recurrent High-grade Meningioma	<ul style="list-style-type: none"> • Perillyl alcohol (inhaled) 	Phase 2
8	Observation or Radiation Therapy in Patients with Newly Diagnosed Grade II Meningioma That Has Been Completely Removed by Surgery (NRG-BN003)	<ul style="list-style-type: none"> • Radiation • Standard therapy 	Phase 3

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