The Official Newsletter of the
Keck Medicine of USC
USC Brain Tumor Center
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USC Norris Comprehensive Cancer Center
Keck Medicine of USC

USC BRAIN TUMOR CENTER Report

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WINTER 2024

From the USC BTC Directors

As we step into 2024, we are excited to share with you the latest developments since our Fall 2023 Newsletter. The USC Brain Tumor Center continues to focus on its mission of providing unsurpassed brain tumor care to all patients who face a brain tumor diagnosis, and 2023 was a busier year than ever. We anticipate 2024 to be an even more productive year for the USC BTC!

In this Winter issue, we are thrilled to showcase two important members of our USC Brain Tumor Center, our talented **Neuro-Pathologists Dr. Kyle Hurth** and **Dr. Anna Mathew**, who are responsible for the **surgical neuropathology** services at the USC Brain Tumor Center (USC BTC). Neuropathologists play a critical role in providing the diagnosis after meticulously examining the brain tissue obtained during surgery. Moreover, they actively collaborate with our multidisciplinary team to ensure accurate and comprehensive diagnoses that are becoming more and more precise all the time with advanced in genomic and epigenetic diagnostics.

Turning attention to the events of December of last year, it was a bustling month for the members of our Center. **Dr. Aram Modrek**, who joined our team this year, celebrated the inauguration of his research laboratory at the USC Norris Cancer Center on December 6th, marked by a Ribbon Cutting Ceremony featuring **Dean Carolyn Meltzer** and **Dr. Eric Chang**, Chair of the Department of Radiation Oncology.

Continues on page 2

U.S. News & World Report Best Hospital Ranking - doximity

In early 2024, solicitations to vote for the annual **US News and World Report Best Hospital ranking** will start. Please consider voting for **USC Neurology and Neurosurgery**. Your vote for USC Brain Tumor Center physicians is an endorsement of our work on your patients' behalf. Patients see this ranking as an important credential for an institution. Your support is another way of reassuring your patients that you have referred them to a preeminent institution.

As a valued partner, we are committed to maintaining your trust and look forward to working with you this year.

Neuropathology at the USC Brain Tumor Center

Dr. Mathew and I have been asked to introduce ourselves and describe our role as neuropathologists at the USC Brain Tumor Center. My name is Dr. Kyle Hurth, I am a board-certified neuropathologist who trained at Washington University in Saint Louis. Inspired by the Gateway Arch and the Jefferson National Expansion Memorial, I chose to seek my fortune in the modern West and have been practicing neuropathology at Keck Hospital in Los Angeles since 2013. My colleague Dr. Anna Mathew, also a board-certified neuropathologist trained at USC/LA General Medical Center in Los Angeles and has been practicing at Keck Hospital since 2016. Dr. Mathew and I are responsible for the surgical neuropathology services at the USC Brain Tumor Center (USC BTC).

Kyle Hurth, MD, PhD

Anna Mathew, MD

Neuropathologists are pathologists that have additional training, experience, and expertise in evaluating the pathology of neuropathological processes. Most neuropathologists practicing in the United States have completed separate neuropathology (NP) fellowship training and have passed a separate NP board examination in addition to their anatomic and clinical pathology training and examinations.

In order to describe what we do as neuropathologists at the USC BTC, let us begin where a pathologist will often have their first interaction with a patient, although the patient may not be aware of it. This is when a pathologist is asked to perform an ***intraoperative frozen section***. If you or a loved one has had, or will have, surgery, one of my surgical or clinical colleagues may have described that the biopsy or resection procedure might involve the use of ***frozen section***. A frozen section is performed to help ensure that optimal material is being biopsied and can help guide post-operative tests and therapies. For surgeries involving some organs of the body, frozen sections are also used to assess whether a margin is clear of tumor.

Usually, the creation of a routine microscopic slide for pathological examination can take several hours. This is because for routine microscopy, tissue must first be ***fixed*** in formalin (***fixing*** essentially hardens the structure of the tissue in place, and usually takes several hours). After a tissue is ***fixed*** it is then ***processed*** to remove water and permeate the tissue with paraffin wax (another procedure that can take several hours). ***Processed*** tissue is then ***embedded*** into a small block of paraffin wax to create a ***formalin fixed paraffin embedded (FFPE)*** tissue block. A trained histotechnician then uses a microtome to cut the FFPE block into a ribbon of approximately ten very fine sections of tissue (3-5 microns thick) that are floated in a water bath and carefully picked up onto glass slides. Slides are then routinely stained with hematoxylin and eosin (H&E). This produces H&E stained slides for the pathologist to review. If your physician has ever re-

Continues on page 2

"BTC Directors..." ***continued***

On December 8, The USC Brain Tumor Center hosted the **Inaugural Southern California Brain Tumor Conference** on the USC Health Science Campus. It was a historic event where seven institutions from Southern California participated and attracted over 180 attendees, researchers, clinicians, staff, patients, and caregivers, who all came together to share and discuss diverse perspectives and initiatives to improve patient care in the realm of brain tumor research and treatment.

Our partnership with the USC Norris Comprehensive Cancer Center (USC Norris CCC) is imperative to advancing innovative brain cancer research and the clinical care of brain cancer patients. This year, **Dr. Frances Chow** and **Dr. Josh Neman** were chosen to lead the newly formed **Neuro-Oncology Disease Affinity Group** that brings together clinicians, translational scientists, basic scientists, and population scientists who treat and study primary and metastatic brain malignancies.

One of the primary missions of the USC Brain Tumor Center is to provide high-level support and ease for patients and their caregivers while navigating through a life-changing medical event. In January of this year, the USC BTC in collaboration with USC Norris Comprehensive Cancer Center and **Patient Caregiver Support Group leader, Jinsy Rogers, LCSW** hosted a **"Creativity in the Community"** event. This gathering, led by **artist Krista Machovia** enabled patients and caregivers, tap into their creative side while supporting each other's journeys.

Last but certainly not least, **Dr. Frances Chow**, Neuro-Oncologist for the USC Brain Tumor Center was honored as the recipient of the **"Caregivers Apply Restorative Efforts"** grant. This grant aims to support restorative and wellbeing efforts for healthcare providers.

At the USC Brain Tumor Center, we remain dedicated to expanding our clinical trial portfolio. We are pleased to announce that we have recently opened a **vaccine trial (TVAX)** for **newly diagnosed glioblastoma**. The USC BTC continues to pioneer intranasal drug delivery for a variety of brain tumors under the leadership of **Dr. Thomas Chen**.

We extend our heartfelt gratitude your unwavering support of the USC BTC and its mission to provide unsurpassed clinical care to patients worldwide and to cure brain tumors.

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

"Neuropathology..." ***continued***

quested H&E slides to be reviewed from a previous operation you or a loved one has had, this is what is being asked for.

Even when performed rapidly, FFPE made H&E slides still take several hours to create, a process that is simply too long to wait for a patient under anesthesia during surgery. To speed up this process, pathologists embed tissue, given to them directly by the surgeon in the operating room, into a liquid media that becomes solid when frozen, similar to the solidity of paraffin wax. Tissue can then be cut in a ***cryostat***, a microtome placed into a cooled chamber, to produce slides that can be stained and examined at the time of surgery. The time to produce and interpret a frozen section varies, but is usually performed in approximately 10 to 30 minutes.

Before examining a frozen section slide, Dr. Mathew and I review the patient's history along with any imaging and radiology reports of the tumor the patient has had. Many patients are also presented and discussed at our multi-disciplinary tumor board conference prior to a surgery. Knowing the history and imaging is particularly important in the diagnosis of brain tumors, as imaging replaces the 'gross examination' that is performed for other organ systems, such as large resection specimen with well-defined anatomic landmarks. Reviewing a patient's clinical history and imaging allows us to evaluate the intraoperative frozen sections with respect to the expected possible diagnoses, the ***differential diagnosis***, specific to the patient. This is particularly important in the examination of neuropathology specimens as different diseases and tumors produce different but often overlapping histological patterns.

Permanent H&E-stained sections will usually be available for us to review in a day or two following the surgery. When evaluating both the frozen section and the permanent section slides, a pathologist is looking for and assessing many different histological features unique to the particular lesion and patient's specimen. For example, how cellular is the tissue? Does the process appear gliotic? reactive? infectious? inflammatory? could it be autoimmune? Are vessels involved and how so? Is it demyelinative? neoplastic? If neoplastic, does it appear benign or malignant? low grade or high grade? Does the neoplasm have circumscribed and solid growth or appear to grow infiltratively into adjacent white and grey matter? Is there evidence of necrosis or a destructive process? etc.

In addition to evaluating microscopic findings seen on H&E stained slides, pathologists will often order additional testing to be performed on a specimen to help determine the diagnosis. As stewards of a patient's tissue, pathologists and pathology laboratories will also triage testing ordered by neurooncologists to help guide therapy and better estimate prognosis.

Testing of surgical pathology specimens has evolved greatly over the years. Early on, ***special stains*** using metals like silver or colored dyes were developed to impart differential coloration and staining of tissue structures. They still have some use for specific CNS tumors and are still used for evaluating infectious organisms, it is likely that you may have heard of the Gram stain for bacteria. In the 1980s immunohistochemical (IHC) techniques emerged that could specifically label cell proteins. IHC produces well-known visual patterns for different molecules and tumor types that a pathologist can see under the microscope. IHC is widely available today and is of great value in assisting diagnosis. Most neuropathology surgical specimens have IHC performed on them.

Since approximately the mid-1990s testing for specific chromosomal abnormalities, gene mutations, gene fusions, and other genetic abnormalities emerged and is advancing at a rapid pace. These tests are often lumped together under the term ***molecular pathology***. Molecular pathology plays an important role in the diagnosis of tumors, as tumor types may have unique gene fusions, mutations, and/or chromosomal abnormalities. Molecular testing also helps identify possible targets for therapeutic intervention. The performance of molecular testing is usually performed by laboratories directed by pathologists with subspecialty training in molecular pathology.

As a neuropathologist, molecular testing has led to a large expansion of diagnoses within neuropathology as well as within other branches of pathology. Some refer to this as ***splitting*** as previously diagnoses may have been grouped together into larger categories, that can now be separated and split out by specific molecular findings not apparent by routine microscopic examination.

One of our duties as neuropathologists is to stay current with this knowledge. These developments also give hope for the development of therapies directed at specific molecular changes within tumor cells. It also provides us with many opportunities to play a role in helping our fellow physicians and basic science researchers with assorted clinical studies and research.

Confluence of Minds: Inaugural Southern California Brain Tumor Conference Unites Seven Powerhouses for Neuro-Oncology Advancements

Josh Neman, PhD, Scientific Director, USC Brain Tumor Center

The **Inaugural Southern California Brain Tumor Conference**, held at the USC Health Sciences Campus on December 8, 2023, marked a historic moment in the field of neuro-oncology as seven prominent academic institutions - **USC, CHLA, UCLA, UCI, City of Hope, Cedars Sinai,** and **Pacific Neuroscience Institute (PNI)** - joined forces to discuss the latest advancements and breakthroughs. The USC Brain Tumor Center organized and hosted the conference with the goal of fostering collaboration and sharing expertise, the conference brought together experts in Surgical Neuro-Oncology, Translational Research, Clinical Trials, Brain Tumor Imaging, and Radiation Oncology.

The event, attended by 180 enthusiastic participants, created a platform for researchers, clinicians, patients, and caregivers to share and discuss the latest discoveries, fostering scientific exchange, and promoting the translation of research into clinical practice. The conference was kicked-off by **Dean of the Keck School of Medicine of USC Dr. Carolyn Meltzer** and **Scientific Director of the USC Brain Tumor Center Dr. Josh Neman**. The excitement surrounding the conference was palpable, as it marked the first time that all seven academic centers in Southern California converged to focus on these critical aspects of neuro-oncology.

The conference sessions delved into various facets of brain tumor research and treatment, offering a comprehensive overview of the latest advancements in Surgical Neuro-Oncology, where leading experts, including **Drs. Gabriel Zada (USC), Frank Attenello (USC), Behnam Badie (City of Hope),** and **Garni Barkhodarian (PNI)**, shared their experiences and insights from advances in surgical resection and 3D modeling, genomics, and immunotherapy for primary and metastatic brain tumors.

The Translational Research discussions by **Drs. David Tran (USC), Devon Lawson (UCI), Joshua Breunig (Cedars Sinai),** and **David Nathanson (UCLA)** provided a glimpse into the cutting-edge research bridging the gap between laboratory discoveries and clinical applications focusing on topics such as tumor heterogeneity, immune microenvironment, single-cell genomics, and drug discovery. **Drs. Frances Chow (USC), Katrina O'Halloran (CHLA),** and **Leia Nghiemphu (UCLA)** shared their ongoing clinical trials and collaborative initiatives on CSF liquid biopsies and experimental therapies, aimed at advancing adult and pediatric brain tumor treatments.

The Brain Tumor Imaging and Radiation Oncology sessions explored innovative approaches to delivering precise and effective radiation therapies and imaging for brain tumors. The cross-institutional presentations by **Drs. Lindsay Hwang (USC), Tania Kaprealian (UCLA),** and **Aram Modrek (USC)** facilitated a rich exchange of ideas, methodologies, and best practices, fostering a sense of unity among professionals dedicated to enhancing patie nt outcomes. The conference concluded with the scientific poster sessions from all the participating institutions, where attendees had the opportunity to present their research and findings. The poster sessions proved to be a vibrant forum for networking, collaboration, and discussions, further enhancing the sense of community among the participants.

One of the truly inspirational moments at the Southern California Brain Tumor Conference was **"The Hayden M. Gidan Compassionate Care Fund Presentation"** given by **Jinsy Rogers**, the USC Brain Tumor Center Social Worker. Ms. Rogers' presentation resonated profoundly with both medical professionals, community, and family members, emphasizing the significance of a mindful journey through cancer treatment. Jinsy Rogers brought a unique perspective to the conference, drawing from her experience as a Social Worker, supporting individuals and families navigating the complexities of brain tumor diagnoses and treatments. Her talk was a poignant reminder of the human side of medicine, transcending clinical discussions to focus on the emotional and psychological aspects of the cancer journey.

Overall, the Southern California Brain Tumor Conference not only marked a significant milestone in the regional neuro-oncology community but also laid the foundation for ongoing collaboration and advancements in the field. The success of this inaugural event sets a promising precedent for future conferences, reinforcing the importance of bringing together diverse perspectives to drive innovation and improve patient care in the realm of brain tumor research and treatment.

Modrek Laboratory Ribbon-Cutting Ceremony

Aram Modrek, MD, PhD

The Modrek Lab held a ribbon cutting ceremony to celebrate the opening of their new laboratory as a part of the growing USC Brain Tumor Center. The Modrek Lab is in the Department of Radiation Oncology and was able to open its doors with support from the Keck School of Medicine and Norris Comprehensive Cancer Center. The laboratory team will be led by Dr. Aram Modrek, MD, PhD, a radiation oncologist who splits his time between seeing patients and brain tumor research.

The focus of the Modrek lab is to understand how brain tumors adapt and evade our most effective therapies. Radio- and chemotherapy work by creating damage in the blueprints (DNA) of cancer cells, yet malignant brain tumors regrow after treatment. Paradoxically, treated tumors don't always have new oncogene mutations in their DNA, but the cancer that grows back is more resistant to additional rounds of therapy. This raises an open question in cancer biology that the Modrek lab studies: How did our treatment change the tumor? And, how can we make tumors more sensitive to therapy?

Neuro-Oncology Disease Affinity Group

Frances Chow, MD

Josh Neman, PhD

Dr. Frances Chow and **Dr. Josh Neman** are pleased to announce the newly-formed **Neuro-Oncology Disease Affinity Group** at Norris Comprehensive Cancer Center. The group brings together clinicians, translational scientists, basic scientists, and population scientists who treat and study primary and metastatic CNS malignancies. The aims are to (1) develop collaborations between scientists, (2) identify tools to expand research capabilities, (3) foster the translation of basic and preclinical research to clinical trials, (4) maximize grant funding, and (5) strategically guide scientific initiatives at Norris and CHLA. Meetings are held on the 1st Friday of each month, from 1-2pm. To join, please contact Dr. Chow: chow@med.usc.edu.

Featured collaborators include:

- **Aram Modrek MD, PhD** on Massively Parallel Multi-Target Guide RNAs for CRISPR-Cas9 Mediated Screens and Therapeutics in Brain Tumors
- **Joseph Wiemels, PhD** on Pediatric/Young Adult Research & the USC Brain Tumor Bank
- **Rituparna Ganguly, PhD** and **Kelsey Poorman, PhD** on Caris Next Generation Sequencing Tools & Databases to Expand Research
- **Bodour Sahlia, PhD** on Preclinical Models Shared Resource
- **Dan Weisenberger, PhD** on Developing Methylation-Based Signatures in Brain Cancer

Care for the Caregiver

Dr. Frances Chow is a recipient of the Keck Medicine **"Caregivers Apply Restorative Efforts"** grant to support restorative and wellbeing efforts for healthcare providers. Brain tumor specialists are at a particularly high risk of burnout from the burden of care, rapid turnover of patients, and limited therapeutic options for brain tumors.

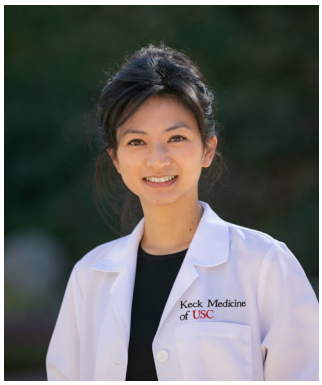
The USC Brain Tumor Center was launched in 2020 during the height of the COVID pandemic. Since our inauguration, we have provided top-quality care for hundreds of patients and families challenged by devastating diagnoses. Dr. Chow's initiative will fund measures to improve teamwork, recognize and appreciate team members, honor patients to provide emotional self-care, and serve as a think tank for initiatives to drive the Brain Tumor Center forward. This project is critical to rejuvenate the work culture, teamwork, and emotional strength of the members of the Brain Tumor Center who continuously strive to serve and improve the lives of patients with brain tumors.

Dr. Frances Chow has served as the Wellness & Burnout Committee Chair for the USC Department of Neurology since 2022. She is a strong advocate for physician well-being, leadership development, and performance improvement.

Creativity in the Community

Jinsy Rogers, LCSW

Recently, I have been struck by the ways in which the arts can be therapeutic and meaningful for people in general and wondered how we can translate this into caring for our patients and caregivers that we serve at the USC Brain Tumor Center. I became connected with Krista Machovina, who is a cancer survivor and volunteer artist with a non profit organization called the **Art of Elysium** which creates art programs to support individuals through difficult emotional life challenges. The event was held for caregivers of any brain tumor patient across Southern California to help them tap into their creative side, engaging in an activity that was cathartic while also having space to connect with others. During the activity, we were able to talk about experiences in being a caregiver, which was a wonderful parallel to our monthly caregiver support group. We hope to make this a regular event for both patients and caregivers!



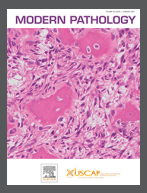
Norris Community Outreach & Engagement Liaison

Dr. Frances Chow has been appointed a **Scientific Liaison** for the **Norris Community Outreach & Engagement (COE) Office**. Her role is to develop bidirectional relationships between Keck/Norris scientists and the local Angeleno community by connecting researchers with community organizations and providing opportunities in the community for scientific collaboration, dissemination, and education. As a Scientific Liaison, Dr. Chow serves as a representative of the **Translational and Clinical Sciences Program (TACS)**, which is led by **Dr. Fumito Ito, MD, PhD**, and includes 61 members with expertise to discover and develop innovative treatments and biomarkers to improve clinical outcomes for cancer patients. TACS members' research encompasses adult and pediatric cancers, and solid and hematological malignancies, with a sharp focus on tumor types that represent significant cancer burdens and disparities in our catchment area.

SELECTED PUBLICATIONS

Prevalence of Frontotemporal Dementia in Females of 5 Hispanic Families With R159H VCP Multisystem Proteinopathy. *Shmara A, Gibbs L, Mahoney RP, Hurth K, Goodwill VS, Cuber A, Im R, Pizzo DP, Brown J, Laukaitis C, Mahajan S, Kimonis V.* *Neurol Genet. 2023 Jan 11;9(1):e200037. doi: 10.1212/NXG.0000000000200037. PMID: 36644447; PMCID: PMC9833818..*

Missense variants of the valosin-containing protein (VCP) gene cause a progressive, autosomal dominant disease termed VCP multisystem proteinopathy (MSP1). The disease is a constellation of clinical features including inclusion body myopathy (IBM), Paget disease of bone (PDB), frontotemporal dementia (FTD), and amyotrophic lateral sclerosis (ALS), typically reported at a frequency of 90%, 42%, 30%, and 9%, respectively. The Hispanic population is currently underrepresented in previous reports of VCP myopathy. We expand our genotype-phenotype studies in 5 Hispanic families with the c.476G>A, p.R159H VCP variant. Studying each VCP variant in the context of ethnic backgrounds is pivotal in increasing awareness of the variability of VCP-related diseases across different ethnicities, enabling early diagnosis, and understanding the mechanism for these genotype-phenotype variations.

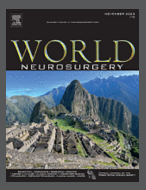


Highly Multiplexed Spatially Resolved Proteomic and Transcriptional Profiling of the Glioblastoma Microenvironment Using Archived Formalin-Fixed Paraffin-Embedded Specimens. *Kim Y, Danaher P, Cimino PJ, Hurth K, Warren S, Glod J, Beechem JM, Zada G, McEachron TA.* *Mod Pathol. 2023 Jan;36(1):100034. doi: 10.1016/j.modpat.2022.100034. PMID: 36788070; PMCID: PMC9937641.*

Glioblastoma is a heterogeneous tumor for which effective treatment options are limited and often insufficient. Few studies have examined the intratumoral transcriptional and proteomic heterogeneity of the glioblastoma microenvironment to characterize the spatial distribution of potential molecular and cellular therapeutic immunooncology targets. We applied an integrated multimodal approach comprised of NanoString GeoMx Digital Spatial Profiling, single-cell RNA-seq (scRNA-seq), and expert neuropathologic assessment to characterize archival formalin-fixed paraffin-embedded glioblastoma specimens. Clustering analysis and spatial cluster maps highlighted the intratumoral heterogeneity of each specimen. Mixed cell deconvolution analysis revealed that neoplastic and vascular cells were the prominent cell types throughout each specimen, with macrophages, oligodendrocyte precursors, neurons, astrocytes, and oligodendrocytes present in lower abundance and illustrated the regional distribution of the respective cellular enrichment scores. The spatial resolution of the actionable immunotherapeutic landscape showed that robust B7H3 gene and protein expression was broadly distributed throughout each specimen and identified STING and VISTA as potential targets. Lastly, we uncovered remarkable variability in VEGFA expression and discovered unanticipated associations between VEGFA, endothelial cell markers, hypoxia, and the expression of immunoregulatory genes, indicative of regionally distinct immunosuppressive microdomains. This work provides an early demonstration of the ability of an integrated panel-based spatial biology approach to characterize and quantify the intrinsic molecular heterogeneity of the glioblastoma microenvironment.

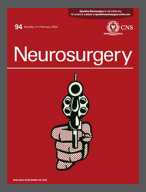
A repository of grade 1 and 2 meningioma MRIs in a public dataset for radiomics reproducibility tests. *Vassantachart A, Cao Y, Shen Z, Cheng K, Gribble M, Ye JC, Zada G, Hurth K, Mathew A, Guzman S, Yang W.* *Med Phys. 2023 Oct 10. doi: 10.1002/mp.16763. Epub ahead of print. PMID: 37815256.*

Meningiomas are the most common primary brain tumors in adults with management varying widely based on World Health Organization (WHO) grade. However, there are limited datasets available for researchers to develop and validate radiomic models. The purpose of our manuscript is to report on the first dataset of meningiomas in The Cancer Imaging Archive (TCIA). Potential applications: Grade 1 and 2 meningiomas have different treatment paradigms and are often treated based on radiologic diagnosis alone. Therefore, predicting grade prior to treatment is essential in clinical decision-making. This dataset will allow researchers to create models to auto-differentiate grade 1 and 2 meningiomas as well as evaluate for other pathologic features including mitotic index, brain invasion, and atypical features. Limitations of this study are the small sample size and inclusion of only two MRI sequences. However, there are no meningioma datasets on TCIA and limited datasets elsewhere although meningiomas are the most common intracranial tumor in adults.



Clinical Implications of Pituitary Adenomas Exhibiting Dual Transcription Factor Staining: A Case Series of 27 Patients. *Bove I, Cheok SK, Feng JJ, Briggs RG, Ruzevick J, Cote DJ, Shah I, Little A, Laws E, Castro AV, Carmichael J, Shiroishi M, Hurth K, Zada G.* *World Neurosurg. 2023 Nov 14:S1878-8750(23)01599-1. doi: 10.1016/j.wneu.2023.11.036. Epub ahead of print. PMID: 37967742.*

According to the 2017 World Health Organization classification of neuro-endocrine tumors, pituitary adenomas (PAs) are classified according to immunoexpression of the pituitary-specific transcription factors (TFs). A small subset of PAs exhibit multiple TF staining on immunohistochemistry and we present a series of 27 pathologically-confirmed cases of dual TF staining PAs (dsTF-PAs), and report clinically relevant implications. PAs exhibiting dsTF-PAs represent a small but clinically relevant diagnostic subset of PAs according to the 2021 World Health Organization criteria, as a majority are GH-producing. Precise classification using TF staining plays a key role in understanding the biology of these tumors. Favorable outcomes can be achieved in this subset of PAs with evolving TF classification.



Neurotropism of SARS-CoV-2: A Pathological Examination of Neurosurgical Specimens. *Fujii T, Rennert RC, Hurth KM, Ward PM, Campan M, Mathew AJ, Dubeau L, Wallace WD, Liu CY, Russin JJ.* *Neurosurgery. 2024 Feb 1;94(2):379-388. doi: 10.1227/neu.0000000000002684. Epub 2023 Sep 20. PMID: 37728367.*

Neurological manifestations may occur in more than 80% of patients hospitalized with COVID-19 infection, including severe disruptions of the central nervous system (CNS), such as strokes, encephalitis, or seizures. Although the primary pathophysiological mechanism for the effects of COVID-19 in CNS remains unknown, evidence exists for both direct injury from neuroinvasion and indirect effects from disruptions in systemic inflammatory and coagulation pathways. In this study, we analyzed CNS tissue from living patients to better understand these processes.The CNS is likely not a significant viral reservoir during mild-to-moderate COVID-19 infection, although direct neuroinvasion is not definitively excluded. Additional testing to help elucidate the relative contributions of direct and indirect pathways for CNS injury from COVID is warranted.

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	• GammaTile • Stereotactic radiosurgery	Phase 1
	Glioblastoma		
2	A Phase 1/2 Study of Selinexor and Temozolomide in Recurrent Glioblastoma	• Selinexor + Temozolomide • Temozolomide	Phase 1/2
3	An Open-Label, Phase 1/2A Dose Escalation Study of Safety and Efficacy of NEO100 in Recurrent Grade IV Glioma	• Perillyl alcohol (inhaled)	Phase 1/2A
4	A Phase 2, Open-Label, Single-Arm, Multicenter Study to Evaluate the Efficacy and Safety of Pemigatinib in Participants With Previously Treated Glioblastoma or Other Primary Central Nervous System Tumors Harboring Activating FGFR 1-3 Alterations (FIGHT-209).	• Pemigatinib	Phase 2
5	Testing the Addition of the Immune Therapy Drugs, Tocilizumab and Atezolizumab, to Radiation Therapy for Recurrent Glioblastoma (BN010)	• Radiation + Tocilizumab + Atezolizumab • Radiation + Tocilizumab	Phase 2
6	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)	• TVI-Brain-1 + Radiation + Temozolomide • Standard therapy	Phase 2b
7	Enzastaurin Plus Temozolomide During and Following Radiation Therapy in Patients with Newly Diagnosed Glioblastoma with or Without the Novel Genomic Biomarker, DGM1	• Enzastaurin + Standard therapy • Standard therapy	Phase 3
8	GammaTile and Stupp in Newly Diagnosed GBM (GESTALT)	• GammaTile + Standard therapy • Standard therapy	Phase 4
9	Pivotal, Randomized, Open-label Study of Optune® Concomitant with RT & TMZ for the Treatment of Newly Diagnosed GBM (EF-32)	• Optune + Standard therapy • Standard therapy	N/A
	Meningioma		
10	An Open-Label, Phase 2 Study of NEO100 in Participants with Residual, Progressive or Recurrent High-grade Meningioma	• Perillyl alcohol (inhaled)	Phase 2
11	Observation or Radiation Therapy in Patients with Newly Diagnosed Grade II Meningioma That Has Been Completely Removed by Surgery (NRG-BN003)	• Radiation • Standard therapy	Phase 3

Keck Medicine of USC
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At the USC Brain Tumor Center, our mission is to provide exceptional, comprehensive and innovative concierge-style treatment plans for adults and children with all types of brain tumors and related conditions. Giveto.USC.edu

We Are the USC Brain Tumor Center

NEUROSURGERY
Gabriel Zada, MD, MS
Thomas Chen, MD, PhD
Josh Neman, PhD
Frank Attenello, MD, MS
Steven Giannotta, MD
Cheng Yu, PhD
Oscar Aurelio, PhD
Camelia Danilov, PhD
Reza Ghodsi, PhD
Radu Minea, MD
Steve Swenson, PhD
Weijun Wang, MD

NEUROLOGY
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