The Official Newsletter of the Keck Medicine of USC

USC Brain Tumor Center Patient referrals, (844) 33-BRAIN (844-332-7246) USC Norris Comprehensive Cancer Center Keck Medicine of USC

USC BRAIN TUMOR CENTER

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From the Director



2022 has been an exceptional year for the USC Brain Tumor Center! Our USC BTC team continues to grow and has been recently enhanced with the addition of several new multidisciplinary team members from a variety of specialties dedicated to the most effective and efficient care for our patients. In this Fall issue of the USC BTC Newsletter, we are very excited to announce the recruitment of **David Tran**, **MD**, **PhD** as the new Co-Director of the USC Brain Tumor Center and Division Chief of Neuro-Oncology. Dr. Tran previously served as Associate Professor of Neurosurgery, Neurology and Medicine at The University of Florida and Associate Director of the Preston A Wells, Jr. Center for Brain Tumor Therapy, McKnight Brain Institute. Dr. Tran is a leading international Neuro-Oncologist, NIH-funded

scientist, clinical trials expert, and computational researcher in brain tumor biology and treatment. He specializes in personalized cancer therapy based on patients' unique health, pathologic, and genomic characteristics. With Dr. Tran's arrival, we are looking forward to advancing both patient care and development of new translational and investigational treatment options at the BTC.

The USC Brain Tumor Center is also looking forward to hosting our **Annual Research Retreat** which will be held at the Health Science Campus on December 9th, 2022. This event will showcase the latest research from major scientists across the USC campuses, as well as our **visiting keynote speaker**, **Dr. Adrianne Boire**, a Neuro-Oncologist from Memorial Sloan Kettering Medical Center.

During the few months since our last newsletter, we had the opportunity to sponsor and participate at the annual **American Brain Tumor Association (ABTA) Brain Tumor 5K run/walk**. Our advancement liaisons for the USC BTC continue to work closely with the USC BTC Advisory Council in promoting the growth of the center. We continue to offer and are always working on expanding our vast **clinical trial portfolio**, with several new trials for glioblastoma, brain metastases and meningiomas opening soon. The **USC BTC Research Advancement Core** continues to make strides on our ongoing BTC Core research projects and we aim to provide true personalized medicine to our patients with brain tumors. The preliminary results of several research projects will be shared at our Annual Brain Tumor Center Retreat in December.

At the USC BTC, our staff understands the difficulties that brain tumor patients and their families often face. To help make these journeys easier, the center offers multiple options that care for the whole patient — not just their diagnosis, including an ever-growing **Monthly Caregiver Support Meeting** led by our BTC social worker Jinsy Rogers.

I want to thank you for your support of the USC BTC and its mission to provide unsurpassed clinical care to patients from all over the world and to cure brain tumors. Heal On!

Gabriel Zada, MD, MS, FAANS, FACS

Professor of Neurological Surgery, Otolaryngology, and Internal Medicine Director, USC Brain Tumor Center gzada@usc.edu



Introducing David D. Tran, MD, PhD The USC Brain Tumor Center welcomes leading international neuro-oncologist.

he Keck School of Medicine of USC (KSOM) Departments of Neurological Surgery and Neurology, the USC Brain Tumor Center (BTC), and the USC Norris Comprehensive Cancer Center (NCCC) are proud to announce the recruitment of Dr. David D. Tran as the Co-Director of the USC Brain Tumor Center and Division Chief of Neuro-Oncology. Dr. Tran will co-direct the USC BTC alongside Dr. Gabriel Zada, Professor of Neurological Surgery (Clinical Scholar), and Josh Neman, PhD, Assistant Professor of Neurological Surgery and Physiology & Neuroscience. Dr. Tran previously served as Associate Professor of Neurosurgery, Neurology, and Medicine at the University of Florida and Associate Director of the Preston A Wells, Jr. Center for Brain Tumor Therapy at the McKnight Brain Institute.

The USC BTC has been a major initiative in Neurosciences and Oncology at KSOM over the past few years and has been supported by the USC NCCC, Keck Medicine of USC, and the Departments of Neurological Surgery, Neurology, and Radiation Oncology. In 2021, Korn Ferry was engaged to lead a national search, co-chaired by Dr. Caryn Lerman, Distinguished Professor and Director of the USC NCCC, and Dr. Gabriel Zada, which culminated in the recruitment of Dr. Tran.

Dr. Tran is a leading international neuro-oncologist, NIH-funded investigator, clinical trials expert, and computational researcher in brain tumor biology, treatment and immunotherapy. Dr. Tran's research aligns directly with recent efforts by the USC NCCC to launch the CAR-T cell immunotherapy program and numerous computational biology efforts underway at KSOM, USC NCCC, and USC Viterbi School of Engineering. Dr. Tran will play prominent roles in the USC BTC and the USC NCCC, as well as be at the forefront of several initiatives recently prioritized by the KSOM, Keck Medicine of **USC Neurosciences Strategic** Plan, and the Moonshots of Cancer and Neurosciences set forth by President Folt in her 2022 State of the University address. This recruitment will also significantly bolster education in Neuro-Oncology, research mentoring, and help to establish a clinical fellowship in Neuro-Oncology.

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The USC Brain Tumor Center to host their Annual Research Retreat

The USC Brain Tumor Center is looking forward to hosting our Annual Research Retreat which will be held at the Health Science Campus on December 9th, 2022. This event will showcase the latest research, technologies, clinical trials, and treatments for all types of brain tumors, from leading scientists and clinicians from Keck Medicine, Norris Comprehensive Cancer Center, Children's Hospital Los Angeles and USC Keck School of Medicine, as well as our visiting keynote speaker, Dr. Adrianne Boire, a Neuro-Oncologist from Memorial Sloan Kettering Medical Center. The retreat will be followed by a poster session while enjoying appetizers and beverages.

Keck Medicine of USC **USC Brain Tumor Center** nual Research Retreat FRIDAY, DECEMBER 9, 2022 1:00 - 6:00pm HOSTED BY Gabriel Zada, MD, MS, David Tran, MD, PhD, AND Josh Neman, PhD equote Freaker ADRIENNE BOIRE, MD, PHD resentations by GABRIEL ZADA, MD, MS JOSH NEMAN, PHD ANAT ERDREICH-EPSTEIN, MD, PHD FRANCES CHOW, MD PAUL NEWTON, PHD FRANK ATTENELLO, MD, MS BODOUR SALHIA, PHD eric L. Chang, MD, PhD BEN ELLINGSON, PHD MARK S. SHIROSHI, MD LOCATION: USC Health Sciences Conference Center Hyatt House USC, 1616 San Pablo Street (North of Alcazar Street) (HYBRID) Poster Session to follow. Passed hors d'oeuvres and beverages

Cardinal Supporter **Gamma**Tile



The USC BTC team Runs Big at the ABTA BT5K

n Saturday November 5th the USC Brain Tumor Center was a Gold Sponsor for the American Brain Tumor Association Annual Breakthrough for Brain Tumors BT5K- Los Angeles. The funds raised by this event support the ABTA's mission of providing critical funding for brain tumor research and patient support services.

Our BTC Team and our families came together in person to run/walk the BT5K and we were one of the top teams raising funds for this wonderful event that took place in Pasadena this year. We look forward to sponsoring the ABTA again next year and we hope that you can join us in supporting this wonderful organization.

USC Brain Tumor Center Advancement Liaison Update

n this season of thanks, the USC Brain Tumor Center extends its gratitude for the continued support from our donors, who have helped us raise nearly \$100,000 so far this year. Philanthropic support serves as a catalyst ensuring that our physicians, researchers and staff continue to excel in the mission to provide innovative and compassionate treatment to our patients, while also pursuing novel clinical and scientific research that will lead to better outcomes in the future. We also want to give special thanks to the members of our USC Brain Tumor Center Clinical Advisory Council, who lend their time, treasure and talent to ensure that the USC Brain Tumor Center is the best center for brain tumor care. Thank you to Dr. David Aroesty, Alexandra Clark, Karen Landry, Thomas Palffy, Kelly & Joe Self, Julieta Bennett, and Anna Zaich! Wishing you all a very joyous holiday season ahead.

If you would like more information on how to support the USC Brain Tumor Center, please contact **Nicole Measles**, or **Brian Loew**. If you wish to make a gift online, you can do so by **clicking here**.



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Brian Loew Senior Director of Development, Neurosciences Email: brian.loew@med.usc.edu Cell: (213) 308-4764

SELECTED PUBLICATIONS

IOURNAL OF NEUROSURGERY

Use of predictive spatial modeling to reveal that primary cancers have distinct central nervous system topography patterns of brain metastasis. Neman J, Franklin M,

Madaj Z, Deshpande K, Triche TJ, Sadlik G, Carmichael JD, Chang E, Yu C, Strickland BA, Zada G.

J Neurosurg. 2021 Jul 16;136(1):88-96. doi: 10.3171/2021.1.JNS203536. PMID: 34271545; PMCID: PMC8824486.

Brain metastasis is the most common intracranial neoplasm. Although anatomical spatial distributions of brain metastasis may vary according to primary cancer subtype, these patterns are not understood and may have major implications for treatment. The results of this study support the hypothesis that there is a nonuniform spatial distribution of brain metastasis to preferential brain regions that varies according to cancer subtype in patients treated with Gamma Knife radiosurgery. These topographic patterns may be indicative of the abilities of various cancers to adapt to regional neural microenvironments, facilitate colonization, and establish metastasis. For the first time, the authors have presented two predictive models to show that brain metastasis, depending on its origin, in fact demonstrates distinct geographic spread within the central nervous system. These findings could be used as a predictive diagnostic tool and could also potentially result in future translational and therapeutic work to disrupt growth of brain metastasis on the basis of anatomical region.



selectivity of a circadian clock modulator with antiglioblastoma efficacy. Miller S, Kesherwani M, Chan P, Nagai Y, Yagi M, Cope J, Tama F, Kay SA, Hirota T.

CRY2 isoform

Proc Natl Acad Sci U S A. 2022 Oct 4;119(40):e2203936119. doi: 10.1073/pnas.2203936119. Epub 2022 Sep 26. PMID: 36161947; PMCID: PMC9546630.

The mammalian cryptochrome isoforms, CRY1 and CRY2, are core circadian clock regulators that work redundantly. Recent studies revealed distinct roles of these closely related homologs in clock output pathways. Isoform-selective control of CRY1 and CRY2 is critical for further understanding their redundant and distinct roles. KLOO1 was the first identified small-molecule CRY modulator that activates both CRY1 and CRY2. SHP656 is an orally available KLOO1 derivative and has shown efficacy in blood glucose control and inhibition of glioblastoma stem cell (GSC) growth in animal models. However, CRY isoform selectivity of SHP656 was uncharacterized, limiting understanding of the roles of CRY1 and CRY2. Here, we report the elucidation of CRY2 selectivity of SHP656. We also identified the R form of SHP656 (called SHP1703) as the active isomer. Treatment with SHP1703 effectively reduced GSC viability. Our results suggest a direct role of CRY2 in glioblastoma antitumorigenesis and provide a rationale for the selective modulation of CRY isoforms in the therapeutic treatment of glioblastoma and other circadian clock-related diseases.

Magnetic Resonance in Medicine MR multitasking-based dynamic imaging for cerebrovascular evaluation (MT-DICE): Simultaneous quantification of permeability and leakage-in-

sensitive perfusion by dynamic T1/T2* mapping.

Hu Z, Christodoulou AG, Wang N, Xie Y, Shiroishi MS, Yang W, Zada G, Chow FE, Margol AS, Tamrazi B, Chang EL, Li D, Fan Z.

Magn Reson Med. 2023 Jan;89(1):161-176. doi: 10.1002/ mrm.29431. Epub 2022 Sep 21. PMID: 36128892.

This study developed an MR multitasking-based dynamic imaging for cerebrovascular evaluation (MT-DICE) technique for simultaneous quantification of permeability and leakage-insensitive perfusion with a single-dose contrast injection. MR multitasking is used to model the data into six dimensions, including three spatial dimensions for whole-brain coverage, a saturation-recovery time dimension, and a TE dimension for dynamic T1 and T2* quantification, respectively, and a contrast dynamics dimension for capturing contrast kinetics. Both permeability and perfusion parameters demonstrated good to excellent intersession agreement with the lowest intraclass correlation coefficients at 0.694. Contrast kinetic parameters in all healthy subjects and patients were within the literature range. Based on dynamic T1/ T2* mapping, MT-DICE allows for simultaneous quantification of permeability and leakage-insensitive perfusion metrics with a single-dose contrast injection.

BRAIN TUMOR PATIENT CAREGIVER SUPPORT GROUP The USC Brain Tumor Center offers a monthly support group to caregivers of patients living with a brain tumor

Our Brain Tumor Caregiver Support Group provides the opportunity for family and friends of patients with brain tumors to come together and find common ground to help each other. We hope that each participant will come away feeling more supported in caring for their loved ones and have a safe space to discuss the challenges and victories in being a caregiver.

When: Second Thursday of each month 4-5:00p.m. Location: Remote, via Zoom Contact for Zoom link: Jinsy Rogers, LCSW, (323) 865-6057, Jinsy.Rogers@med.usc.edu For more information, please contact Jinsy Rogers or Nancy Hart, Nurse Navigator, RN, (844) 332-7246, Nancy.Hart@med.usc.edu

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. As a trusted leader in the field of Neurosurgery, USC strives to serve patients with the highest quality of care and the latest innovative technologies. USC is the first in Southern California to offer the latest FDA-cleared GammaTile Therapy for the treatment of brain tumors.

GammaTile is a bioresorbable collagen carrier implanted during the last 5 minutes of brain tumor resection surgery that immediately delivers radiation therapy to eliminate residual tumor cells. Each tile contains 4 embedded Cesium-131 (Cs-131) radiation sources that provide a therapeutic dose of radiation while protecting healthy brain tissue.

In a clinical study, GammaTile Surgically Targeted Radiation Therapy significantly delayed the time to tumor recurrence for patients with brain tumors. Additionally, patients receive their GammaTile radiation



treatment while going about their routine daily life thus shortening the total number of visits needed for fractionated radiation to just 4 weeks. It is hoped that a shortened course of radiation will help preserve their quality of life.

We are featuring two clinical trials with GammaTile in metastatic

brain tumors (STaRT, NCT04365374) and newly diagnosed glioblastoma (GESTALT, NCT05342883).

Have you or someone you know recently been diagnosed with a brain tumor? Choosing the right treatment can be challenging. USC now offers GammaTile Therapy, a new targeted-radiation therapy designed to delay brain tumor recurrence while limiting the impact on healthy brain tissue. To find out more about this and other breakthrough treatments, speak to our specialized brain tumor team at 844-33-Brain or contact Frances Chow, MD at fchow@usc.edu.

	Trial	Interventions	Phase
	Brain Metastasis		
1	Stereotactic Radiosurgery (SRS) Compared with Collagen Tile Brachytherapy	• GammaTile • Stereotactic radiosurgery	Phase 1
2	Single Fraction Stereotactic Radiosurgery Compared with Fractionated Stereotactic Radiosurgery in Treating Patients with Resected Metastatic Brain Disease (CTSU-A071801)	 Single fraction SRS Fractionated SRS 	Phase 3
	Glioblastoma		
3	A Phase 1/2 Study of Selinexor and Temozolomide in Recurrent Glioblastoma	• Selinexor + Temozolomide • Temozolomide	Phase 1/2
4	An Open-Label, Phase 1/2A Dose Escalation Study of Safety and Efficacy of NE0100 in Recurrent Grade IV Glioma	• Perillyl alcohol (inhaled)	Phase 1/2A
5	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
6	Prospective Randomized Placebo-Controlled Trial of SurVaxM Plus Adjuvant Temozolomide for Newly Diagnosed Glioblastoma (SURVIVE)	 SurVaxM + Standard therapy Placebo + Standard therapy 	Phase 2
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	A Phase 1/2 Study of Nivolumab Plus or Minus Ipilimumab in Combination with Multi-Fraction SRS for Recurrent High-Grade Radiation-Relapsed Meningioma	• SRS+Nivolumab+lpilimumab • SRS+Nivolumab	Phase 1/2
11	An Open-Label, Phase 2 Study of NEO100 in Participants with Residual, Progressive or Recurrent High-grade Meningioma	• Perillyl alcohol (inhaled)	Phase 2
12	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

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REVOND EXCEPTIONAL MEDICINE **USC Brain Tumor Center** 1441 Eastlake Avenue Los Angeles, CA 90033 Patient referrals, (844) 33-BRAIN (844-332-7246) NONPROFIT ORG U.S. POSTAGE PAID **UNIVERSITY OF** Southern CALIFORNIA

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

Me Are the USC Brain Tumor Center

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To refer a patient, please call (844) 33-BRAIN (844-332-7246)

Make a Gift. Because of your support, we can provide Exceptional Medicine. Please contact Brian Loew, Senior Director of Development, Neurosciences, at Brian.Loew@med.usc.edu or visit www.keckmedicine.org/btc-donations

For more information about brain tumor clinical trials, please contact Aida Lozada, Clinical Trials Manager, at Aida.Lozada@med.usc.edu

Please email us with your questions at BTC@med.usc.edu

Learn more at: BTC.keckmedicine.org

