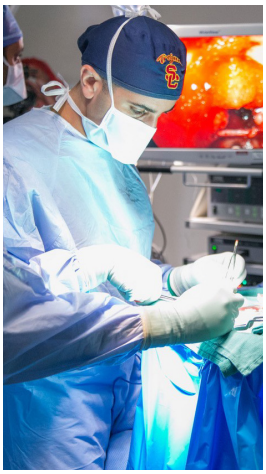
The Official Newsletter of the
Keck Medicine of USC
USC Brain Tumor Center
Patient referrals, (844) 33-**BRAIN** (844-332-7246)

USC Norris Comprehensive Cancer Center
Keck Medicine of USC

USC BRAIN TUMOR CENTER Report

Volume 1 ▪ Issue 3
SUMMER 2021

From the Director



I am quite pleased to share with you our latest quarterly USC Brain Tumor Center (BTC) Newsletter for Summer 2021. Despite the impact of COVID-19 and so many related hurdles in healthcare and science, our BTC team has managed to accomplish amazing things over the course of the past few months and 2021 in general. First and foremost, we are quite pleased to announce that Dr. Vahan Martirosian, Ph.D. in Neuroscience, has joined the BTC team as a research scientist and will be working with Dr. Josh Neman and myself to operationalize our BTC core live tumor collection and cell culture workflow program, which we are very excited about as a major step towards a true practice of personalized medicine for brain tumors.

Secondly, our expert team of care providers and social workers have started a **monthly BTC patient support group**, which we are confident will provide a more comprehensive experience to our BTC patients and their caregivers.

Over the past quarter, our team has been awarded grants for studying acoustic neuromas and other brain tumors using our 7T MRI and has published many high-quality scientific research articles in major journals, some of which are shared in this issue. Over the remainder of 2021, we are looking forward to some major educational conferences in partnership with the **American Brain Tumor Association (ABTA)**, **The Cleveland Clinic**, and our very own **USC Pituitary Center Symposium**. We are also anticipating big news for the BTC which we hope to share in the next USC BTC newsletter!

Please stay tuned, and as always, thank you for your ongoing 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.

Gabriel Zada, MD, MS, FAANS, FACS
Professor of Neurological Surgery, Otolaryngology, and Internal Medicine
Director, USC Brain Tumor Center
gzada@usc.edu

Vahan Martirosian, PhD joins the USC Brain Tumor Center

Dr. Vahan Martirosian, Ph.D. is a new research scientist at the USC Brain Tumor Center. Dr. Martirosian received his B.S. degree in Biological Sciences from the University of California, Irvine. He was awarded the **Excellence in Research** distinction for his work studying the therapeutic benefits of stem cell transplantation in the brain for treatment of chemotherapy-induced chemobrain.

Dr. Martirosian later received his M.S. degree in Molecular Microbiology and Immunology and his Ph.D. in Medical Biology from the University of Southern California under the tutelage of Dr. Josh Neman. His doctoral studies focused on identifying metabolic mechanisms contributing to the metastasis of medulloblastoma, a pediatric brain tumor.

Dr. Martirosian's work at the USC Brain Tumor Center aims to bridge the gap between the clinic and the laboratory to improve outcomes and prognoses of patients with brain tumors. His studies focus on performing translational research on a patient-by-patient basis through the analysis of genomics and drug screening assays to provide more personalized care for patients. Dr. Martirosian believes that strong collaborative effort between scientists and physicians will lead to better treatments for patients, thereby cementing the USC Brain Tumor Center as a leader in brain tumor therapies.

BRAIN TUMOR PATIENT CAREGIVER SUPPORT GROUP

The USC Brain Tumor Center now offers a monthly support group to caregivers of patients living with a brain tumor.

We are excited to announce the launch of our brain tumor caregiver support group. This group will provide 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

Acoustic Neuroma Association Awards Research Grant to Study Facial Nerve Anatomy Using Novel 7T Magnetic Resonance Imaging

The **Acoustic Neuroma Association Research Committee** reviewed research proposals and awarded a research grant of $25,000 to Ben Strickland, MD. In an effort to more readily identify the course of the facial nerve in large **vestibular schwannoma (VS)** surgeries, Dr. Strickland's research proposes applying the novel 7T magnetic resonance imaging (MRI). The program, ***"Ultra-high Field 7T Magnetic Resonance Imaging for Predictive Localization of the Facial Nerve in the Presence of Large Vestibular Schwannoma"***, will compare facial nerve recognition in preoperative large vestibular schwannoma (Koos grade 3-4) patients on the 7T MRI compared to the traditional 3T.

Improved facial nerve visualization preceding attempted surgical resections can guide the surgeon's expectations on where the facial nerve is located with respect to the tumor and thus prevent delayed recognition of the facial nerve and prevent facial nerve injury.

Vestibular schwannoma are benign tumors originating from Schwann cells of the vestibulocochlear nerve accounting for approximately 10% of intracranial neoplasms. While treatment strategies must be tailored to a case-by-case basis, the modalities most often utilized include a combination of surgical resection or radiosurgery.

Regardless of the employed treatment, the approach to the VS is always a risk / benefit analysis weighing the risk intervention poses to eloquent neurovascular structures against the benefit of obtaining tumor control and symptom relief. Paramount to this conversation is the **preservation of facial nerve function**. While early identification of the facial nerve is a surgical priority during tumor exposure, it is not always possible if the tumor is large and distorts normal anatomy. This leads to surgeons relying on distorted anatomic relationships and constant probing with a facial nerve stimulator in an attempt to identify the facial nerve prior to performing any radical tumor resection.

Gabriel Zada, MD, MS, and Ben Strickland, MD

The **Acoustic Neuroma Association's mission** is to be the premier resource for the acoustic neuroma community by informing, educating, and supporting those affected by acoustic neuroma brain tumors.

The American Brain Tumor Association Announces the 2020 Lucien Rubinstein Award Recipient, Edith Yuan, MS

Edith Yuan, MS

The **American Brain Tumor Association** has chosen Edith Yuan, M.S. for the **2020 Lucien Rubinstein Award**. As a member of Dr. Frank Attenello's laboratory, Edith's project, **"Effects of Silencing Long Non-Coding RNA on the Malignancy of Glioblastomas"**, studied a type of molecule in cells called long **non-coding RNA (lncRNA)** and their impact on **glioblastoma (GBM)**. Edith is a **2020 ABTA Jack & Fay Netchin Medical Student Summer Fellowship Recipient** and a third-year medical student at the University of Southern California Keck School of Medicine. The Lucien Rubinstein Award is given to an ABTA Medical Student Summer Fellow who scored the highest marks from a panel of expert reviewers on the student's final research report. The award is named in honor of the late Lucien J. Rubinstein, MD, who was a pioneer in neuropathology at the University of Virginia and a world-renowned brain tumor researcher.

Edith's project helped identify how a novel lncRNA affects resistance to the **chemotherapy drug temozolomide (TMZ)**, a standard therapy to treat GBM. She found that by decreasing the lncRNA level, the cancer cells respond better to TMZ. This cancer cell response indicated that the lncRNAs may be a promising target for overcoming resistance to TMZ in patients with GBM.

"It is a tremendous honor to receive the Rubinstein Award. Being recognized for my research in neuro-oncology is an unbelievably great achievement, and I am deeply grateful for the opportunity and support of the ABTA, my school, and my mentor," said Edith. "The Rubinstein Award serves as an inspiration and encouragement to continue neuro-oncology research as a medical student and as a future physician-scientist."

Although, the Covid-19 pandemic presented several challenges to Edith's work, Dr. Attenello commended Edith's motivation in completing the project. "When faced with obstacles, Edith is motivated to understand the challenge by referring to literature or trying alternative methods, constantly improving her problem-solving skills. The ABTA fellowship has provided her with unparalleled experiences in learning how to become a scientist. These experiences and skills will translate into better patient care as well."

This year the **USC Brain Tumor Center** will sponsor the **American Brain Tumor Association National Conference**, September 11-12, 2021.

SELECTED PUBLICATIONS

Advanced ADC Histogram, Perfusion, and Permeability Metrics Show an Association with Survival and Pseudoprogression in Newly Diagnosed Diffuse Intrinsic Pontine Glioma: A Report from the Pediatric Brain Tumor Consortium.
S Vajapeyam, D Brown, C Billups, Z Patay, G Vezina, MS Shiroishi, M Law, P Baxter, A Onar-Thomas, JR Fangusaro, IJ Dunkel, TY Poussaint
AJNR Am J Neuroradiol. 2020 Apr;41(4):718-724. doi: 10.3174/ajnr.A6499. Epub 2020 Apr 2.

Diffuse intrinsic pontine glioma is a lethal childhood brain cancer with dismal prognosis and MR imaging is the primary methodology used for diagnosis and monitoring. Our aim was to determine whether advanced diffusion, perfusion, and permeability MR imaging metrics predict survival and pseudoprogression in children with newly diagnosed diffuse intrinsic pontine glioma. Baseline values, post-radiation therapy changes, and longitudinal trends for all metrics were evaluated for associations with survival and pseudoprogression.

Improved Glioma Grading Using Deep Convolutional Neural Networks. ***S Gutta, J Acharya, MS Shiroishi, D Hwang, KS Nayak***
AJNR Am J Neuroradiol. 2021 Jan;42(2):233-239. doi: 10.3174/ajnr.A6882. Epub 2020 Dec 10.

Accurate determination of glioma grade leads to improved treatment planning. The criterion standard for glioma grading is invasive tissue sampling. Recently, radiomic features have shown excellent potential in glioma-grade prediction. These features may not fully exploit the underlying information in MR images. The objective of this study was to investigate the performance of features learned by a convolutional neural network compared with standard radiomic features for grade prediction.

Medulloblastoma Uses GABA Transaminase to Survive in the Cerebrospinal fluid Microenvironment and Promote leptomeningeal Dissemination. ***Vahan Martirosian, Krutika Deshpande, Hao Zhou, Keyue Shen, Kyle Smith, Paul Northcott, Michelle Lin, Vazgen Stepanosyan, Diganta Das, Jan Remsik, Danielle Isakov, Adrienne Boire, Henk De Feyter, Kyle Hurth, Shaobo Li, Joseph Wiemels, Brooke Nakamura, Ling Shao, Camelia Danilov, Thomas Chen, Josh Neman***
Cell Rep. 2021 Jun 29;35(13):109302. doi: 10.1016/j.celrep.2021.109302.

Medulloblastoma (MB) is a malignant pediatric brain tumor arising in the cerebellum. Although abnormal GABAergic receptor activation has been described in MB, studies have not yet elucidated the contribution of receptor-independent GABA metabolism to MB pathogenesis. We find primary MB tumors globally display decreased expression of GABA transaminase (ABAT), the protein responsible for GABA metabolism, compared with normal cerebellum. Our studies suggest ABAT expression fluctuates depending on metabolite changes in the tumor microenvironment, with nutrient-poor conditions upregulating ABAT expression.

Comorbid Depression in Surgical Cancer Patients Associated with Non-routine Discharge and Readmission.
Casey Jarvis, Phillip A Bonney, Edith Yuan, Li Ding, Frances Chow, Anthony W Kim, William Mack, Gabriel Zada, Frank Attenello
Surg Oncol. 2021 Jun;37:101533. doi: 10.1016/j.suronc.2021.101533. Epub 2021 Feb 12.

To characterize the rates of depression across primary cancer sites, and determine the effects of comorbid depression among surgical cancer patients on established quality of care indicators, non-routine discharge and readmission. Patients undergoing surgical resection for cancer were selected from the Nationwide Readmissions Database (2010-2014). Multivariable analysis adjusted for patient and hospital level characteristics to ascertain the effect of depression on post-operative outcomes and 30-day readmission rates. Non-routine discharge encompasses discharge to skilled nursing, inpatient rehabilitation, and intermediate care facilities, as well as discharge home with home health services. Rates of depression vary amongst surgically treated cancer patients by primary tumor site. Comorbid depression in these patients is associated with increased likelihood of non-routine discharge and readmission.

Radiation Therapy for Brain Metastases: A Systematic Review. ***Adam Garsa, Julie Jang, Sangita Baxi, Christine Chen, Olamigoke Akinniranye, Owen Hall, Jody Larkin, Aneesa Motala, Susanne Hempel***
Pract Radiat Oncol. Sep-Oct 2021;11(5):354-365. doi: 10.1016/j.prro.2021.04.002. Epub 2021 Jun 9.

This evidence report synthesizes the available evidence on radiation therapy for brain metastases. Despite the substantial research literature on radiation therapy, comparative effectiveness information is limited. There is a need for more data on patient-relevant outcomes such as quality of life, functional status, and cognitive effects.

In vivo CRISPR Screening for Novel Noncoding RNA Functional Targets in Glioblastoma Models. ***Frank Attenello, Kathleen Tsung, Isaac Bishara, Yong-Hwee Eddie Loh, Thomas Chen***
J Neurosci Res. 2021 Sep;99(9):2029-2045. doi: 10.1002/jnr.24850. Epub 2021 May 10.

CRISPR screens have been utilized heavily in vitro to identify functional coding and noncoding genes in a large number of cell types, including glioblastoma (GB), though no prior study has described the evaluation of CRISPR screening in GB in vivo. Here, we describe a protocol for targeting and transcriptionally repressing GB-specific long noncoding RNAs (lncRNAs) by CRISPR interference (CRISPRi) system in vivo, with tumor growth in the mouse cerebral cortex. Given the target-specific parameters of each individual screen, we list general steps involved in transducing guide RNA libraries into GB tumor lines, maintaining sufficient coverage, as well as cortically injecting and subsequently isolating transduced screen tumor cell populations for analysis.

CLINICAL TRIALS: Now Enrolling at the USC Brain Tumor Center

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

Olaparib in Treating Patients with Advanced Glioma, Cholangiocarcinoma, or Solid Tumors with IDH1 or IDH2 Mutations

This phase 2 trial studies how well Olaparib works in treating patients with recurrent glioma, cholangiocarcinoma, or solid tumors with IDH1 or IDH2 mutations. Olaparib may stop the growth of tumor cells by blocking some of the enzymes needed for cell growth. ClinicalTrials.gov Identifier: NCT03212274

Study to Evaluate Eflornithine + Lomustine vs Lomustine in Recurrent Anaplastic Astrocytoma (AA) Patients (STELLAR)

The purpose of this study is to compare the efficacy and safety of eflornithine in combination with Lomustine, compared to Lomustine taken alone, in treating patients whose Anaplastic Astrocytoma has recurred/progressed after radiation and temozolomide chemotherapy. ClinicalTrials.gov Identifier: NCT02796261

An Open-Label, Phase 1/2A Dose Escalation Study of Safety and Efficacy of NEO100 in Recurrent Grade IV Glioma

NEO100-01 is a Phase 1/2A open-label study of perillyl alcohol (NEO100) in patients with recurrent glioma. NEO100 is delivered four times a day by intranasal administration using a nebulizer and nasal mask for up to 6 months. There is no placebo arm. This is the first nasal administration in the US. ClinicalTrials.gov Identifier: NCT02704858

Standard Chemotherapy vs Chemotherapy Guided by Cancer Stem Cell Test in Recurrent Glioblastoma (CSCRGBM)

This study will confirm the utility of chemosensitivity tumor testing on cancer stem cells (ChemoID) as a predictor of clinical response in malignant brain tumors such as recurrent glioblastoma and anaplastic astrocytoma. Patients with an unlimited number of recurrences and multifocal disease are candidates for this study. ClinicalTrials.gov Identifier: NCT03632135

Observation or Radiation Therapy in Treating Patients with Newly Diagnosed Grade II Meningioma That Has Been Completely Removed by Surgery (NRG-BN003)

This randomized trial studies how well radiation therapy works compared with observation in treatment patients with newly diagnosed grade II meningioma that has been completely removed by surgery. Radiation therapy uses high energy x-rays to kill the tumor cells and shrink tumors. ClinicalTrials.gov Identifier: NCT03180268

Stereotactic Radiosurgery (SRS) Compared with Collagen Tile Brachytherapy

This trial will be a randomized controlled study comparing the efficacy and safety of intraoperative radiation therapy using GammaTile versus SRS 3-4 weeks following metastatic tumor resection. GammaTile is a biocompatible permanently implanted system. Each GammaTile unit is composed of a collagen "tile" that contains 4 Cesium-131 (Cs-131) titanium-encased sources. ClinicalTrials.gov Identifier: NCT04365374

A Study of Selinexor in Combination with Standard of Care Therapy for Newly Diagnosed or Recurrent Glioblastoma

This is a global multicenter, open-label, randomized study to evaluate a combination regimen with or without Selinexor. The study will independently evaluate 3 different combination regimens in 3 treatment arms in participants with new glioblastoma, MGMT promotor unmethylated disease in Arm A, MGMT methylated in Arm B, and participants with recurrent glioblastoma regardless of MGMT status in Arm C. ClinicalTrials.gov Identifier: NCT04421378

Trial of Enzastaurin Plus Temozolomide During and Following Radiation Therapy in Patients with Newly Diagnosed Glioblastoma with or Without the Novel Genomic Biomarker, DGM1

This study will be conducted as a randomized, double-blind, placebo-controlled, multi-center trial. Enzastaurin will be added to the standard treatment of radiation and chemotherapy in patients with glioblastoma. Patients will be evaluated for the biomarker DGM1, which in other cancer types was shown to correlate with improved survival upon treatment with Enzastaurin. ClinicalTrials.gov Identifier: NCT03776071

Single Fraction Stereotactic Radiosurgery Compared with Fractionated Stereotactic Radiosurgery in Treating Patients with Resected Metastatic Brain Disease (CTSU- A071801)

This phase 3 trial studies how well single fraction stereotactic radiosurgery works compared with fractionated stereotactic radiosurgery in treating patients with cancer that has spread to the brain from other parts of the body and has been removed by surgery. Single fraction stereotactic radiosurgery is a specialized radiation therapy that delivers a single, high dose of radiation directly to the tumor and may cause less damage to normal tissue. Fractionated stereotactic radiosurgery delivers multiple, smaller doses of radiation therapy over time. ClinicalTrials.gov Identifier: NCT04114981

Pivotal, Randomized, Open-label Study of Optune® Concomitant with RT & TMZ for the Treatment of Newly Diagnosed GBM (EF-32)

This study will test the effectiveness and safety of Optune® given concomitantly with radiation therapy (RT) and temozolomide (TMZ) in newly diagnosed GBM patients, compared to radiation therapy and temozolomide alone. In both arms, Optune® and maintenance temozolomide are continued following radiation therapy. Optune® is a medical device that has been approved for the treatment of recurrent and newly diagnosed glioblastoma (GBM) by the Food and Drug Administration (FDA) in the United States, and Optune® has obtained a CE mark in Europe for recurrent and newly diagnosed GBM. ClinicalTrials.gov Identifier: NCT04471844

A Phase I/II Study of Nivolumab plus or minus Ipilimumab in Combination with Multi-Fraction Stereotactic Radiosurgery for Recurrent High-Grade Radiation-Relapsed Meningioma

This trial studies the side effects and best dose of nivolumab when given together with multi-fraction stereotactic radiosurgery with or without ipilimumab in patients with recurrent grade II-III meningioma. Immunotherapy with the checkpoint inhibitors nivolumab and ipilimumab - may help the immune system attack cancer, and interfere with tumor growth and spread. Stereotactic radiosurgery is a specialized radiation therapy that delivers a single, high dose of radiation directly to the tumor and may cause less damage to normal tissue. ClinicalTrials.gov Identifier: NCT3604978

Keck Medicine of USC

BEYOND EXCEPTIONAL MEDICINE™

USC Brain Tumor Center
1441 Eastlake Avenue
Los Angeles, CA 90033
Patient referrals, (844) 33-**BRAIN** (844-332-7246)

USC has the highest volume of neurosurgical brain tumor cases of any academic center in SoCal.

- California's Office of Statewide Health Planning and Development (OSHPD), Calendar Year 2019, most recent data available.

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
Hee-Yeon Cho, PhD
Camelia Danilov, PhD
Reza Ghodsi, PhD
Vahan Martirosian, PhD
Radu Minea, MD
Steve Swenson, PhD
Wei Jun Wang, MD

NEUROLOGY
Helena Chui, MD

NEURO-ONCOLOGY
Frances Chow, MD
James Hu, MD
Tania Vartanians, MS, PA-C

RADIATION ONCOLOGY
Shelly Bian, MD
Eric Chang, MD, FASTRO
Adam Garsa, MD
Richard Jennelle, MD
Jason Ye, MD

NEURO-RADIOLOGY
Jay Acharya, MD
John Go, MD
Paul Kim, MD
Mark Shiroishi, MD

NEURO-PATHOLOGY
Samuel Guzman, MD
Kyle Hurth, MD, PhD
Anna Mathew, MD
Michael Selsted, MD, PhD

NORRIS CANCER CENTER
Dennis Deapen, DPH
Caryn Lerman, PhD

NEURO-OPHTHALMOLOGY
Kimberly Gokoffski, MD, PhD

ADVANCED IMAGING (USC Laboratory of Neuro Imaging)
Vishal Patel, MD
Arthur Toga, PhD
Paul Thompson, PhD
Danny Wang, PhD

BIOINFORMATICS AND TRANSLATIONAL GENOMICS
John Carpten, PhD
David Craig, PhD
Bodour Salhia, PhD
Daniel Weisenberger, PhD

CLINICAL TRIALS
Trey Garrett
Sandy Leong, BSN, RN, CCRP
Aida Lozada, MA

MOLECULAR BIOLOGY AND TRANSLATIONAL RESEARCH
Peggy Farnham, PhD
Suhn Rhie, PhD
Axel Schoenthal, PhD
Jean Chen Shih, PhD
Anna Wu, PhD
Min Yu, PhD
Berislav Zlokovic, PhD

BIOSTATISTICS AND NEURO-EPIDEMIOLOGY
Steven Yong Cen, PhD
Roberta Mckean-Cowdin, PhD
Kimberly Siegmund, PhD
Joseph Wiemels, PhD

CHLA
Shahab Asgharzadeh, MD
Jaclyn Beigel, PhD
Peter Chiarelli, MD, PhD
Jason Chu, MD, MSc
Tom Davidson, MD
Susan Durham, MD, MS
Anat Epstein-Erdrich, MD, PhD
Debra Hawes, MD
Mark Krieger, MD
C. Jason Liu, MD, PhD
Ashley Margol, MD, MS
Rex Moats, PhD
Nathan Robison, MD

VITERBI SCHOOL OF ENGINEERING
Mark E. Davis, PhD
Ellis Meng, PhD
Krishna Nayak, PhD
Paul K. Newton, PhD

CALTECH
Shuki Bruck, PhD
Wei Gao, PhD
Viviana Gradinaru, PhD
James Heath, PhD
Yu-Chong Tai, PhD

NURSING
Brenda Avalos, RN
Nancy Hart, RN, MSN, CPON
Rebekah Ghazaryan, RN
Erika Gonzales, RN

SOCIAL WORK
Jinsy Rogers, LCSW

DEVELOPMENT
Brian Loew
Sonali Perera

ADMINISTRATIVE
Nikos Carli
Richard Hagy, PhD
Paola Mork, MHA
Jerry Moses
Jacqueline Sandoval, MD

Keck Medicine of USC

USC Brain Tumor Center

Find us · Follow us · See us · Watch us

Stay in Touch

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**