This report is dedicated to each and every child diagnosed with a brain tumor.
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Commitment to curing childhood brain tumors

Dedicated to improving treatments and discovering cures for children with brain tumors, the Children’s Brain Tumor Tissue Consortium (CBTTC) is pioneering a new model of innovative medical research through open-science resource sharing; a commitment to global inclusion, transparency, and accountability; and the translation of data into clinical impact.

The leader in childhood brain tumor research

The Children’s Brain Tumor Tissue Consortium (CBTTC) is a collaborative, multi-institutional research program dedicated to the study and treatment of childhood brain tumors. The CBTTC is leading the movement to discover more effective treatments for every diagnosed child by leveraging the power of ‘big data’ and partnering with institutions and researchers across the globe.

Through its state-of-the-art biorepository facility, the development of data and informatics platforms, the implementation of efficient data collection procedures, and the combined expertise of the consortium’s clinicians, researchers and other partners, the CBTTC is uniquely positioned and deeply committed to discover and develop new and more effective treatments for children diagnosed with a brain tumor.
I joined the Children’s Brain Tumor Tissue Consortium (CBTTC) in 2012 out of a growing belief that the only real way to make scientific discoveries at the rate needed to make a significant positive impact on the health outcomes for my patients was through collaboration. I believed (and still do) that my efforts would be well-spent contributing toward growing an infrastructure that removes barriers to large-scale biospecimen and clinical data sharing between scientists at different labs and institutions to accelerate new therapeutics.

It’s been so gratifying to watch the CBTTC grow as more and more investigators from top children’s hospitals and research institutions across the U.S. and around the world have taken that leap of faith to join efforts with CBTTC. And as the scientific advances generated by the CBTTC have steadily accumulated, I too have grown – both personally and professionally.

Once disillusioned by the competitive environment that dictated the pediatric brain tumor research landscape – where labs worked in isolation over months or years; slowly generating enough data and specimens in hopes of being the first to publish research findings – I’ve been proud to take a leading role in what has truly been a revolution in the way the research community embraces cross-institution collaboration and resource sharing. Last year, I took a step further, picking up the mantle of CBTTC Executive Committee Chair, seeking to lead the organization into an exciting new era. And this year, my journey takes me full-circle, away from the Children’s Hospital of Philadelphia, where I spent the first 15 years of my medical career, and back to my Mid-Western roots, joining the Ann & Robert H. Lurie Children’s Hospital of Chicago as the Director of Precision Medicine in Oncology.

There, I will strive to continue expanding the scope and impact of this incredible consortium of scientists, clinicians, patient advocates, and institutions.

Over the past year, the CBTTC has accomplished so much. In September of 2018, we successfully launched the Pediatric Brain Tumor Atlas (PBTA), the largest clinically-annotated collection of pediatric brain tumor clinical and genomic data on earth; un-embargoed and accessible to investigators anywhere on earth. We’ve partnered with other research initiatives and consortia including the Pacific Pediatric Neuro-Oncology Consortium (PNOC), the Clinical Proteomics Tumor Analysis Consortium (CPTAC), and the National Cancer Institute (NCI)-funded Project HOPE. We’ve surpassed 3,300 research study participants, and joined the Swifty Foundation-led Gift From a Child program to empower and assist patient families to take a powerful stand against childhood brain cancer by donating tumor tissue post-mortem. All this and so much more!

We at the CBTTC are thrilled to share further details about our FY-2019 scientific accomplishments with you in this report. I hope you’ll join me in sincerely congratulating and thanking each of our data scientists, platform developers, laboratory investigators, clinicians, and foundation partners for the strides they’ve made this year in bringing us all closer to a future free of brain tumor mortality in children.

With Warm Regards,

Angela J. Waanders, MD, MPH
Executive Chair
CBTTC member institutions have made remarkable progress while achieving numerous achievements during the past year. The launch of the Pediatric Brain Tumor Atlas (PBTA) provided the community with the largest pediatric brain tumor molecular database to date, by allowing researchers and clinicians for the first time to compare pediatric patients to pediatric data, driving the potential for precision medicine for children. The PBTA was the first dataset to be added to the NIH-supported Gabriella Miller Kids First Data Resource Center (Kids First DRC), which is working to understand the developmental biology of pediatric cancers and structural birth defects. As part of the Kids First Data Resource Portal, PBTA data is also helping to empower data sharing, new best practices, and collaboration throughout the pediatric research community.

CBTTC’s efforts to date are built on a model of open-science and collaboration, which allows the CBTTC to rapidly accelerate childhood cancer-specific biobanking, data sharing, and scientific discovery efforts by utilizing resources at its member institutions. This research includes cross-disease and molecular analysis of more than 25,000 human genomes and is enabling researchers to ask important biological questions across unique disease types.

Another hallmark of the CBTTC’s efforts is the successful expansion of molecular data beyond the study of the genome and RNA. CBTTC is closely partnering with the National Cancer Institute (NCI) to generate proteomic data for thousands of brain tumor samples, evidence of the CBTTC’s vision to provide a comprehensive snapshot of each child’s disease. These complete datasets will empower the development of precision therapies for all children diagnosed with a brain tumor.

CBTTC member institutions have also focused on generating the first molecular map of a developing child at a single-cellular level. In a scientific data project led by Dr. Deanne Taylor of Children’s Hospital of Philadelphia in 2019, investigators provided the roadmap to generate the first human atlas which defines a developing human at the resolution of a single cell.

These data are helping to improve scientific knowledge on the molecular characteristics of healthy and developing organs.

As the CBTTC expands across the globe, new challenges and opportunities will inevitably arise. One of the emerging challenges/opportunities faced by CBTTC has been to ensure the rapid translation of scientific discoveries, along with the wealth of CBTTC-initiated molecular data, into clinical environments. In close collaboration with the Pacific Pediatric Neuro-Oncology Consortium (PNOC), the CBTTC has initiated disease-specific initiatives, comprised of physicians and scientists, which are dedicated to researching specific diseases and disease subtypes.

The CBTTC is uniquely positioned to support and inform clinical interventions through research-based discoveries. With the continued development of the CBTTC’s data analysis platforms, the consortium has the ability to identify mutations or molecular aberrations using research methods, which may have been missed or unknown in a clinical setting. Discussions about the importance of linking molecular and clinical data are also taking place as a result of the CBTTC’s efforts.

The CBTTC looks forward to many additional opportunities to answer research questions during the coming year. Improved collaboration, the development of disease-specific committees, and sharing the CBTTC’s tremendous network of expertise and resources will continue to improve the standard of care for childhood brain tumor patients across the world.

With sincere thanks,

Adam Resnick, PhD
Scientific Co-chair

Javad Nazarian, PhD, MSc
Scientific Co-chair

Children’s Brain Tumor Tissue Consortium
A special thanks

The entire membership and staff of the Children’s Brain Tumor Tissue Consortium would like thank Dr. Javad Nazarian for his dedication and service as Co-chair of the CBTTC Scientific Committee.

Dr. Nazarian will dedicate his efforts to lead a research team to work together across the CBTTC and PNOC to guide biology-informed clinical trials for diffuse midline gliomas (DMGs). This research will potentially serve as a model for other disease-specific committees, who can all harness the power of the CBTTC and advance the development of future clinical trials.

We express our sincere gratitude for his guidance and expertise in the scientific growth of the CBTTC. We wish him all the best in his new role as Head of the DIPG Research Institute of the University Children’s Hospital Zurich.

New Scientific Co-chair

The CBTTC is excited to welcome Michael Prados, MD, of UCSF Benioff Children’s Hospital, as a new Co-chair of the Scientific Committee. Dr. Prados is a leader in the field of neuro-oncology, with more than 25 years of experience in the treatment of both adult and childhood brain tumors. He is currently Project Leader for the Pacific Pediatric Neuro-Oncology Consortium, and will join the CBTTC’s leadership team to help advance the scientific goals of the CBTTC.
At six years old, our son Wyatt’s health declined dramatically over two days and we ended up in the emergency room. We went through the traumatic process of scans, diagnosis, and emergency surgery; followed by radiation treatment. Throughout the process we often questioned both the long-term and short-term effects of the treatments available to Wyatt, likelihood of recurrence, and the potential lifespan of someone with a high-grade anaplastic ependymoma. These are ongoing concerns that will never go away.

The Winning With Wyatt foundation was born out of the experience of a child and family experiencing the diagnosis, treatment, and realization that their lives would never be the same. Success of the foundation has been made possible through the love, concern, commitment and generosity of a community and other families impacted by brain tumors that snapped into action to support pediatric brain tumor research, discover better treatments, and raise awareness of the disease.

We are eternally thankful that Wyatt was treated by Dr. Rishi Lulla and Dr. Stewart Goldman, who provided world-class medical treatment and guidance on navigating some of our more fundamental concerns about the disease, treatment options, and what we could do to make a difference. Through their guidance we became involved and supportive of the Children’s Brain Tumor Tissue Consortium.

We know that discovering impactful, breakthrough treatments improve exponentially with an effective, collaborative model. The CBTTC, through a network of member institutions, philanthropic partners, and brilliant researchers who are actively leveraging the tools and resources available, will accelerate the discovery of new treatments and ultimately discover a cure for pediatric brain tumors.

Children and families impacted by pediatric brain tumors deserve our collective talents and resources at work for them. Through the CBTTC, we are optimistic and confident that together we will win.

Kim and Dan Hare
Winning With Wyatt Foundation
ROBERT CONNOR DAWES FOUNDATION

Inspired by a big heart and brain, the Robert Connor Dawes (RCD) Foundation was created in June 2013 in the memory of 18-year-old American-born Robert Connor Dawes, who lost his 16-month battle with an anaplastic ependymoma brain tumor. The foundation is battling pediatric brain cancer through research, care, and development projects – to fund the science to end pediatric brain cancer and support patients in the meantime.

The foundation operates in Australia and the U.S., where brain cancer kills more children than any other disease. The RCD Foundation funds crucial research projects to improve treatment options, support young patients with at-home rehabilitation like music therapy, and inspire and fund the next generation of brain cancer practitioners and researchers through development initiatives.

The foundation is proud to partner with a well-respected, multi-institutional research program such as the CBTTC. We have recently announced two-year funding for a CRISPR project at the Hudson Institute of Medical Research in Melbourne, Australia.

This is a genetic screening project using a more focused targeted library that the Hudson Institute has developed and is working collaboratively with CBTTC. The goal is to advance new targets for pediatric brain cancers across the globe.

Collaboration is instrumental in every aspect. Brain cancer is a tremendously complicated disease. There are now 140 known subtypes of brain cancer, so it won’t be cured by one person, one lab, or one country.

The RCD Foundation is committed to funding research that is collaborative between researchers, institutions, countries, and funding bodies around the world.

Robert Connor Dawes Foundation

CBTTC: By the numbers

- MORE THAN 3,300 SUBJECTS ENROLLED
- OVER 150 SCIENTIFIC PROJECTS COMPLETED OR IN PROGRESS
- 16 MEMBER INSTITUTIONS LOCATED ACROSS THE GLOBE
The success of the CBTTC is due in large part to the global collaboration between many of the leading childhood brain tumor research and treatment centers located throughout the United States, Europe, Asia, and Australia. The 16 CBTTC member institutions contribute disease and scientific expertise; develop precision-based clinical trials; enroll research subjects; and collect biospecimens, clinical data, and other information needed for research. Together, these data and specimens provide researchers with a comprehensive view of childhood brain tumor biology and development and allow the discovery of more effective therapies for children.
The CBTTC provides an integrated, trans-national platform of biospecimens and analytical tools for many of the most highly skilled researchers in pediatric neuro-oncology to address fundamental questions in the biology of treatment-resistant brain tumors, thus opening the way for new paradigm-changing insights and eventually cures.
CBTTCC: A new research model

The CBTTC’s collaborative network of experts and member institutions has transformed the traditional research model and is working to accelerate discoveries for all children diagnosed with a brain tumor.

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<th>TRADITIONAL RESEARCH MODEL</th>
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<th>CBTTC RESEARCH MODEL</th>
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<tr>
<td>LIMITED TO LOCAL SUBJECTS ENROLLED AT A SINGLE INSTITUTION</td>
<td>MORE THAN 3,300 STUDY PARTICIPANTS ENROLLED ACROSS MULTIPLE INSTITUTIONS</td>
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<tr>
<td>ONE PROJECT AT ONE INSTITUTION</td>
<td>OVER 150 SCIENTIFIC PROJECTS AT 16 MEMBER INSTITUTIONS LOCATED AROUND THE WORLD</td>
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<td>DATA ARE SILOED OR UNAVAILABLE UNTIL PUBLISHED IN ACADEMIC JOURNALS</td>
<td>NEARLY 400 TB OF DATA ARE ACCESSIBLE IN REAL-TIME THROUGH CLOUD-BASED PLATFORMS</td>
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<td>ANALYSIS IS LIMITED TO PROJECT SCOPE, BUDGET AND AVAILABILITY</td>
<td>COMPREHENSIVE ANALYSIS OF BRAIN TUMOR DATA USING MULTIPLE ANALYSIS METHODS SIMULTANEOUSLY</td>
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Scientific biospecimen projects

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<th>Proposals approved from FY19</th>
<th>Proposals converted into data access projects</th>
<th>Projects awaiting input from requestor</th>
<th>Projects approved/under revision for 2020</th>
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During FY 19, five new scientific biospecimen projects were approved by the CBTTC. Note: The CBTTC Scientific Committee was able to identify four requests for specimens where genomic data was already available. Projects are listed by date of approval by the Scientific Committee.

CBTTC_0025 Development of Preclinical Models of Pediatric Ependymoma  
Principal Investigator: Ching Lau, MD, PhD - Connecticut Children’s Hospital

CBTTC_0030 Interactions Between Astrocytes and Tumor Cells are Critical for Medulloblastoma Growth  
Principal Investigator: Zeng-Jie Yang, MD, PhD - Fox Chase Cancer Center at Temple Health

CBTTC_0029: Molecular Analysis of the Cellular Ecosystem of Childhood Ependymoma (Phase 2 Samples)  
Principal Investigator: Pablo Gonzalez Camera, PhD - University of Pennsylvania

CBTTC_0033: Center for Pediatric Tumor Cell Atlas  
Principal Investigator: Kristina Cole, MD, PhD - Children’s Hospital of Philadelphia

CBTTC_0034: Pediatric Brain Tumor miRNA profiling for the Cohort of Children’s Brain Tumor Tissue Consortium Specimens  
Principal Investigator: Mateusz Koptyra, PhD - Children’s Hospital of Philadelphia

CBTTC_0035: Elucidating the Somatic Epigenetic Landscape of Pediatric Meningioma and Schwannoma  
Principal Investigator: Sameer Agnihotri, PhD - UPMC Children’s Hospital of Pittsburgh

CBTTC_0037: Project HOPE  
Principal Investigator: Adam Resnick, PhD - Children’s Hospital of Philadelphia
The CBTTC Scientific Committee is committed to accelerating and increasing the best pediatric brain tumor research. In addition to providing biospecimens to researchers during FY19, the Scientific Committee was able to identify four requests for specimens where genomic data was already available. Utilizing data in place of biospecimens enabled select researchers to move forward with their discovery projects in an accelerated timeline while preserving the specimens for additional requests. The use of this available data is highlighted within the 31 data requests approved during FY19. The Scientific Committee is dedicated to supporting each proposal that is submitted through the CBTTC. In addition to the review process, the CBTTC Scientific Committee consulted and provided additional recommendations on one project that will move forward in 2020. Projects below are listed by date of approval by the Scientific Committee.

**CBTTC_D0024: Cancer Predisposition in Pediatric Brain Tumors**  
*Principal Investigator:* Suzanne McFarland, MD - Children’s Hospital of Philadelphia

**CBTTC_D0025: Genomic Landscape of Mixed Glial Neuronal Tumors**  
*Principal Investigator:* Lea Surrey, MD - Children’s Hospital of Philadelphia

**CBTTC_D0026: Cracking the Histone Code: Characterizing Pediatric Brain Tumor Epigenetics using Cerebrospinal Fluid**  
*Principal Investigator:* Daphne Li, MD - Ann & Robert H. Lurie Children's Hospital of Chicago

**CBTTC_D0031: Identifying New Cell Surface Targets for Immunotherapy Treatment of Poor Prognosis Pediatric Brain Tumors**  
*Principal Investigator:* Misty Jenkins, PhD - Walter and Eliza Hall Institute of Medical Research

**CBTTC_D0027: Identify Novel Therapeutic Targets and Biomarkers in Non-coding Genome of Pediatric Cancers**  
*Principal Investigator:* Lihua Zou, PhD - Northwestern University

**CBTTC_D0030: Immunogenomic Landscape of Pediatric Cancers**  
*Principal Investigator:* Trevor Pugh, PhD - University Health Network

**CBTTC_D0028: Testing/Evaluation of Cell Lines**  
*Principal Investigator:* Mateusz Koptyra, PhD - Children’s Hospital of Philadelphia

**CBTTC_D0033: Characterizing the Prevalence of ETMR by Molecular Signature**  
*Principal Investigator:* Derek Hanson, MD - Hackensack University Medical Center

**CBTTC_D0034: Deciphering the Molecular Characteristics of Pediatric Meningiomas**  
*Principal Investigator:* Nadia Dahmane, PhD - Weill Cornell Brain and Spine Center

**CBTTC_D0035: Germline Variants in Pediatric Glioblastoma**  
*Principal Investigator:* Adam Resnick, PhD - Children’s Hospital of Philadelphia

**CBTTC_D0036: Integrative Functional Genomics of Recurrent Childhood Medulloblastoma**  
*Principal Investigator:* Javad Nazarian, PhD - Children’s National Health System
SCIENTIFIC DATA PROJECTS (CONT.)

CBTTC_D0037: Comprehensive Genomic and Immune Signature Profiling of Ependymoma and Diffuse Intrinsic Pontine Glioma  
Principal Investigator: Kathleen Schieffer, PhD - Nationwide Children’s Hospital

CBTTC_D0032: Detection of Cooperative and Mutually Exclusive Genetic Alterations in Pediatric Cancer  
Principal Investigator: Patrick Kemmeren, PhD - Princess Máxima Center for Pediatric Oncology

CBTTC_D0039: Genomic Correlates with Radiation Injury  
Principal Investigator: Oren Becher, MD - Ann & Robert H. Lurie Children’s Hospital of Chicago

CBTTC_D0038: Predictive Models for Transcriptome Variations  
Principal Investigator: Yoseph Barash, PhD - University of Pennsylvania

CBTTC_D0041: The Study of ATRX, ALT and Replicative Stress in Pediatric Brain Tumors/Center for Pediatric Tumor Cell Access  
Principal Investigator: Kristina Cole, MD, PhD - Children’s Hospital of Philadelphia

CBTTC_D0042: Hudson Monash Paediatric Precision Medicine Program  
Principal Investigator: Ron Firestein, MD, PhD - Hudson Institute of Medical Research
SCIENTIFIC DATA PROJECTS (CONT.)

CBTTC_D0045: Heath Disparities of Pediatric Brain Tumors
Principal Investigator: Xiao-Nan Li, MD, PhD - Ann & Robert H. Lurie Children's Hospital of Chicago

CBTTC_D0044: Long Non-coding RNA Signature of Medulloblastoma and AT/RT subtypes
Principal Investigator: Ranjan Perera, PhD - Johns Hopkins All Children’s Hospital

CBTTC_D0046: Access to CBTTC Data for Use in Kids First/CAVATICA
Principal Investigator: Amanda Saratsis, MD - Ann & Robert H. Lurie Children's Hospital of Chicago

CBTTC_D0040: Germline mtDNA Variants and Somatic mtDNA Mutations in Pediatric Brain Tumors
Principal Investigator: Xiaowu Gai, PhD - Children's Hospital Los Angeles

CBTTC_D0047: Pediatric Brain Tumor Classification and Segmentation using Transfer Learning from Adult Datasets
Principal Investigator: Roy Campbell, PhD - University of Chicago at Urbana-Champaign

CBTTC_D0051: Alternative Splicing in CBTTC Data
Principal Investigator: Shihao Shen, PhD - Children's Hospital of Philadelphia

CBTTC_D0048: Comprehensive Analysis of Structural Variants in Pediatric Brain Tumors
Principal Investigator: Lixing Yang, PhD - University of Chicago

CBTTC_D0054: Discover New Therapeutics for DIPG Using a Systems-based Approach
Principal Investigator: Bin Chen, PhD - Michigan State University

CBTTC_D0055: Relationships Between Genomic, Imaging, and Histopathologic Characteristics in Pediatric Brain Tumors
Principal Investigator: Benjamin Hartley, MD - Weill-Cornell Brain and Spine Center

CBTTC_D0053: Germline Determinants of Pediatric Brain Tumors
Principal Investigator: Sorana Morrissy, PhD - University of Calgary

CBTTC_D0049: Epigenetic Drivers in Medulloblastoma
Principal Investigator: Alexandros Tzatsos, MD, PhD - George Washington University

CBTTC_D0050: Epigenetic Drivers in Diffuse Intrinsic Pontine Gliomas (DIPG)
Principal Investigator: Alexandros Tzatsos, MD, PhD - George Washington University

CBTTC_D0052: Molecular Characterization of Choroid Plexus Tumors
Principal Investigator: Christian Thomas, MD - Institute of Neuropathology Münster

CBTTC_D0058: Germline and Somatic Microsatellite Genotypes in Pediatric Brain Tumors
Principal Investigator: Brian Rood, MD - Children’s National Health System
Funded by the National Cancer Institute (NCI) through Federal Fiscal Year 2020, Project HOPE (High Grade Glioma Omics in PEdiatrics) is a consortium-based project to conduct brain tumor research in both adult and pediatric glioma patients with an initial focus on single-cell sequencing. This is part of the NCI Eliminate Cancer Initiative, National Brain Tumor Society (NTBS), and Pediatric Brain Tumor Foundation (PBTF)’s U.S. Brain Cancer Mission, and articulates the needs and challenges for improving therapeutics in both children and adults. The HOPE/CARE initiative received $4 million in supplemental funding.

Utilizing biospecimens, data and analysis platforms through the CBTTC, PNOC, and the Gabriella Miller Kids First Data Resource Center, the project’s primary initial aims are:

- Single cell sequencing of cancer cells in pediatric and AYA high-grade gliomas
- Single cell sequencing of tumor-infiltrating immune cells in pediatric and AYA high-grade gliomas
- Single nucleus sequencing of the non-immune microenvironment of pediatric and AYA high-grade gliomas
- Epigenetic profiling of matched samples by EPIC (850K) arrays or whole genome bisulfite sequencing

The Project HOPE Pediatric Working Group includes Mariella G. Filbin, MD, PhD of Dana-Farber/Boston Children’s Cancer and Blood Disorders Center; Michele Monje, MD, PhD of Stanford University Medicine; Adam Resnick, PhD of Children’s Hospital of Philadelphia; and Michael D. Prados, MD of the Helen Diller Family Comprehensive Cancer Center at the University of California, San Francisco.

Project HOPE presents a wealth of opportunities for researchers and clinicians across the country. The project represents a rich, multi-omic platform in the setting of rare disease in children that provides rich datasets to advance research. Effective utility of these data will enhance ‘precision medicine’ towards improved stratifications and therapeutics; helping to improve clinical trial design and outcomes for patients.
Led by the Children’s Brain Tumor Tissue Consortium (CBTTC) and the Pacific Pediatric Neuro-Oncology Consortium (PNOC), the Pediatric Brain Tumor Atlas (PBTA) is a collaborative global effort to accelerate discoveries for therapeutic intervention for children diagnosed with brain tumors through the non-embargoed, pre-publication release of one of the largest genomic datasets for pediatric brain tumors to date. The first dataset release of the PBTA occurred September 10th, 2018 on the NIH Common Fund-supported Gabriella Miller Kids First Data Resource Portal and CAVATICA workspace.

PBTA data include matched tumor/normal tissue, whole genomes (WGS), exomes (WES), transcriptomes (RNA-Seq), proteomics, miRNA, longitudinal clinical data, pathology reports, and imaging data including MRIs, radiology reports, and histology slides. Additionally, processed data files for somatic mutations, somatic copy number and structural alterations, gene and transcript-level expression data, gene fusions, and harmonized clinical data are included.

Together, with our patient and foundation partners, CBTTC and PNOC have amassed more than 381TB of clinical and multi-omic data – open to researchers anywhere on earth without embargo – to empower breakthroughs that will save children’s lives.

The PBTA has grown to encompass more than 40 different types of pediatric brain and central nervous system (CNS) tumors, representing roughly 1,000 study participants.

Recently, researchers from the Center for Data-Driven Discovery in Biomedicine (D³b) at Children’s Hospital of Philadelphia (CHOP) and the Childhood Cancer Data Lab (CCDL) at Alex’s Lemonade Stand Foundation set out to launch the OpenPBTA Project, a first-in-kind collaborative, crowd-sourcing analytic global initiative.

This new open science project seeks to harness the collective will and brain power of the biomedical research and data informatics community to comprehensively describe the PBTA and accelerate scientific discoveries that will lead to clinical impact for childhood cancer patients.

Learn more about the Pediatric Brain Tumor Atlas and Project Open PBTA at: https://cbttc.org/pediatric-brain-tumor-atlas/
The 5th Annual CBTTC Investigator Meeting was a great success, and CBTTC would like to thank all attendees and supporters for making this year’s meeting a productive, interactive event.

On March 11, the scientific session began by outlining how to access data generated by the Pediatric Brain Tumor Atlas (PBTA). Dr. Adam Resnick, the CBTTC Scientific Co-chair, reviewed the types of data generated to date, and Dr. Allison Heath performed a live demo of how to access the research platforms to review and analyze the different types of data available. The second session - CBTTC Scientific Project Updates - began with an overview of current approved biospecimen and data projects by Dr. Javad Nazarian, CBTTC Scientific Co-chair. Four investigators presented on their projects to highlight the potential translational impact to the clinic, including Dr. Brian Rood from Children’s National Health System, Dr. Sameer Agnihotri from UPMC Children’s Hospital of Pittsburgh, Dr. Kristina Cole from Children’s Hospital of Philadelphia, and Dr. Michael Prados from UCSF Benioff Children’s Hospital.

The afternoon session included remarks from Dr. Marilyn Li of Children’s Hospital of Philadelphia on how CBTTC is directly contributing to the American Association of Cancer Research – Project GENIE.

Dr. Jie Ma, an invited speaker from Xinhua Hospital (affiliated to Shanghai Jiao Tong University School of Medicine) in Shanghai, China, described the newly-formed Chinese Children’s Neuro-Oncology group which includes 35 institutions across mainland China.

Dr. Michael Prados, PNOC Project Leader, ended the afternoon session with highlights from the Pacific Pediatric Neuro-Oncology Consortium (PNOC). The meeting ended with a panel forum with CBTTC Leadership (Executive Board Chair, Scientific Co-Chairs) fielding questions from the audience and partner foundations.
During FY-2019, the CBTTC partnered with the Clinical Proteomic Tumor Analysis Consortium (CPTAC), a program within the National Cancer Institute (NCI) and part of the National Institutes of Health (NIH), to comprehensively characterize both the genomes and proteomes of many cancer types. This process of characterization is also known as cancer proteogenomics. CPTAC’s mission is to accelerate precision oncology through state-of-the-art proteogenomics and create open-source community resources.

Henry Rodriguez, PhD, Director of the Office of Cancer Clinical Proteomics Research (NCI) which administers the CPTAC program, and Adam Resnick, PhD, Scientific Co-chair of the CBTTC and principal investigator at Children’s Hospital of Philadelphia along with Dr. Brian Rood MD, principal investigator from Children’s National Health System, together seized the opportunity to work in partnership on this first-of-its-kind pilot study, making the first steps toward finding targeted therapeutic solutions for pediatric brain tumors using proteogenomics, and making that research openly and rapidly available to the public.

Joining forces, CPTAC investigators proteomically profiled more than 200 pediatric tumors across seven different subtypes from samples collected by the CBTTC. Genomic characterization was conducted by CBTTC-based initiatives, with proteomic characterization performed at the Fred Hutchinson Cancer Research Center (CPTAC Proteogenomic Translational Research Center) and Harvard Medical School, followed by data analysis involving CPTAC Proteogenomic Data Analysis Center sites at University of Michigan, Washington University, New York University and Mount Sinai – Icahn School of Medicine. The coming months will be dedicated to analyzing the data using CPTAC-developed tools to gain insight into the biology of each tumor subtype, including their immune cell characteristics and their kinase/substrate regulations.

As CPTAC is a community resource project, the rich multi-omic datasets produced global proteomics, phosphoproteomics, genomics, RNA-sequencing, pathology, and operative reports, and MRI scans which are all now available on NCI’s CPTAC data portal and NIH’s recently launched Gabriella Miller Kids First Data Resource Center.

The driver of this joint study is the commitment to data-sharing and open science. Coming together has given both CPTAC and CBTTC cancer researchers an opportunity to expand their available resources for answering important biological questions. It also promotes the development of new technologies by experts in the field to generate innovative ways to make important steps toward discovery. The pediatric and proteomic communities have used their collective expertise to better understand the mechanisms of pediatric tumors, improve the process of target protein identification, and potentially improve cancer treatments. Drs. Rodriguez, Resnick, and Rood are hopeful that upon analysis of these unique samples, new clues can be uncovered that better define the next steps for expanding this pilot effort and advancing the required knowledge for the underlying biology in pediatric brain tumors; bringing new hope to patients.

This ground-breaking research is now available to the public to allow cancer researchers, clinicians, and bioinformaticists from all over the world to be involved in finding targeted cancer therapies. Along with this current dataset, the CPTAC program has generated and published proteomic data on a number of cancers that are freely available to the public.
It is known that brain tumors can evolve overtime from the moment of diagnosis – making their treatment sometimes very difficult. Heartbreakingly, one out of every five children diagnosed with a brain tumor will succumb to their illness; possibly losing their battle to a tumor that has become significantly different to the one that was first detected. In addition, due to tumor type or location, some brain tumors are extremely dangerous (if not entirely impossible) to resect from the living brain. These significant facts underlie the critical importance and priceless value of blood, CSF, and tissue samples obtained from childhood brain tumor patients post-mortem. Having access to such samples enables an increased molecular understanding of fatal childhood brain tumors for current and future investigators.

As more parents and families recognize the importance of autopsy donations, the call for a structured national donation program is more apparent.

In December of 2018, the CBTTC and Swifty Foundation worked together to develop such a program. On Sunday, Dec. 9, the two organizations brought together families from all over the country to the Children’s Hospital of Philadelphia to discuss the formation and expectations of this national initiative. Families that were able to donate autopsy specimens as well as families who were not given the option to donate provided valuable insight from their various experiences. The Swifty and CBTTC team listened to what these families shared, and worked on developing a program that would be impactful to both families and researchers.

Following the meeting, in January 2019, the Swifty Foundation officially launched the Gift from a Child initiative in partnership with the CBTTC, which focuses on the establishment of a national autopsy donation organization. In order to support the growing need for donated autopsy specimens, the Swifty Foundation identified four Centers of Excellence dedicated to this program: Children’s Hospital of Philadelphia (CBTTC Operations Center), Children’s National Health System, Ann & Robert H. Lurie Children’s Hospital of Chicago, and Stanford University Medical Center. Each institution has a designated Tissue Navigator responsible for discussing and coordinating autopsy donations for families who choose to participate. Specimens donated through the Gift from a Child program are entered into the CBTTC pipeline to reach as many researchers as possible.

The mission of this initiative is to provide families from any location in the United States with the option to donate. The program works in concert with local hospitals, pathology groups, funeral homes, and various medical team members to ensure that a donation can be made possible. All individuals involved in the donation handle all elements of the process with the utmost care and respect. Many families voice how the decision to donate provides them with comfort by allowing them to take action when all other options have been exhausted. The Gift from a Child program is committed to carrying on the legacy of these precious children by supporting families and research with each and every donation.
In February of 2019, the CBTTC was thrilled to share that Wake Forest Baptist Health – Brenner Children's Hospital joined our network of Member Institutions as a satellite site of Children’s National Health System. David E. Kram, MD is the CBTTC Principal Investigator at Brenner Children’s.

Dr. Kram is primarily focused on developing innovative models of pediatric brain tumors for in vivo and in vitro investigation. Additionally, he is interested in outcomes research, including radiation effects on the developing brain.

Wake Forest Baptist Health is a preeminent academic medical center with two main components as an integrated clinical system – anchored by Wake Forest Baptist Medical Center, an 885-bed tertiary-care hospital in Winston-Salem – that includes Brenner Children’s, five community hospitals, more than 300 primary and specialty care locations, and more than 2,000 physicians; and Wake Forest School of Medicine, a recognized leader in experiential medical education and groundbreaking research that includes Wake Forest Innovations, a commercialization enterprise focused on advancing health care. Wake Forest Baptist Health’s clinical, research, and educational programs are consistently rated among the best in the country by U.S. News & World Report.

Brenner Children’s Hospital is honored to join the Children’s Brain Tumor Tissue Consortium. We look forward to a multidisciplinary and collaborative relationship with the other institutions involved in the research dedicated to the study and treatment of childhood brain tumors. We hope that our discoveries will forever change the treatment.
Advisory Council

The CBTTC Advisory Council was organized in 2017 and is comprised of 14 patient and family foundations which are each invested in advancing the research activities of the CBTTC. These foundations partner together to advise and advocate for CBTTC initiatives, in addition to providing financial support toward CBTTC operations. All members of the Advisory Council are encouraged to collaborate together and play an active role in supporting childhood brain tumor research.

During FY19, the Advisory Council members partnered together to execute a strategic social media campaign, which included participation from astronauts in the NASA space program. These efforts, along with other partnered CBTTC initiatives, are helping the CBTTC more effectively represent and meet the needs of brain tumor patients and their families across the globe.

SPECIAL THANKS TO AL GUSTAFSON

In recognition of his outstanding contributions, the entire CBTTC membership extends sincere thanks to Al Gustafson of the Swifty Foundation upon completing his term as Liaison to the Executive Board. Al’s insights and leadership helped to unify the members of the Advisory Council and improved coordination between CBTTC leadership and members of the Advisory Council. The CBTTC is sincerely grateful for Al’s service in this role and looks forward to his continued partnership and support of CBTTC.

To learn more about how to join/support the CBTTC Advisory Council, email communications@cbttc.org or visit cbttc.org/getinvolved

CBTTC ADVISORY COUNCIL MEMBERS
A look ahead: Strategic objectives

CBTTC Executive Board FY20 Objectives (to be reassessed each quarter):

Objective 1: Establish CBTTC as the premier childhood brain tumor research consortium driving accelerated clinical translation on behalf of both family and research communities

Objective 2: Increase CBTTC institutional impact, site engagement on leadership, scientific engagement on leadership, scientific collaborations, and operations activities

Objective 3: Develop a sustainable CBTTC financial strategy that supports growth and scaling of impact

ADDITIONALLY FUNDED OBJECTIVES

- Increase use of biospecimens
- Drive targeted data generation efforts in FY20 to increase overall completion of PBTA as aligned with clinical trials in PNOC
- Prepare available tissue and cell lines (~70) for research including validating and performing genomic and RNA sequencing on all lines
- Establish a molecular clinical trial team to develop clinical trials and clinical decision support
Financial report

The CBTTC is primarily supported through the generous philanthropic efforts of all its donors as well as additional infrastructure support provided by the Children’s Hospital of Philadelphia, including the Division of Neurosurgery and the Center for Data Driven Discovery in Biomedicine (D³b).

Note: Other resources provided by Children’s Hospital of Philadelphia, not reflected in these numbers, include use of the Hospital’s state-of-the-art biorepository, bioinformatics platforms developed through other grants and mechanisms, additional staff support from the more than 60 members of D³b, and gift processing and donor relations support from the CHOP Foundation.

### FY 18-19 CBTTC FINANCIAL SUMMARY

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FY 18-19 CBTTC FINANCIAL SUMMARY

$600,000
$500,000
$400,000
$300,000
$200,000
$100,000
$0

Personnel | Member Sites | Supplies & Shipping | Other | Cores | Travel | Investigator Meeting | Budgeted Amount | Actual Total
Executive Board members

**Ann & Robert H. Lurie Children’s Hospital of Chicago**
Oren Becher, MD
Stewart Goldman, MD
Amanda Saratsis, MD
**Angela Waanders, MD, MPH - Executive Chair**

**Children’s Hospital of Philadelphia**
Michael Fisher, MD
Jena Lilly, MS
Jane Minturn, MD, PhD
Adam Resnick, PhD
Jay Storm, MD

**Children’s National Health System**
Javad Nazarian, PhD, MSc
Brian Rood, MD

**Johns Hopkins All Children’s Hospital**
Eric Jackson, MD
Eric Raabe, MD, PhD
Stacie Stapleton, MD

**Lucile Packard Children’s Hospital Stanford**
Gerald Grant, MD, FACS
Michelle Monje, MD, PhD
Sonia Partap, MD

**Seattle Children’s Hospital**
Russ Geyer, MD
Sarah Leary, MD

**UCSF Benioff Children’s Hospital**
Nalin Gupta, MD, PhD
Sabine Mueller, MD, PhD, MAS
Joanna Phillips, MD, PhD

**UPMC Children’s Hospital of Pittsburgh**
Ian Pollack, MD

**Weill Cornell Medicine Pediatric Brain & Spine Center**
Nadia Dahmane, PhD
Jeff Greenfield, MD, PhD

**Children’s Brain Tumor Foundation**
Anita Nirenberg - Community Representative

**Swifty Foundation**
Al Gustafson - Advisory Council Liaison
Scientific Committee members

**Ann & Robert H. Lurie Children's Hospital of Chicago**
Oren Becher, MD  
Amanda Saratsis, MD  
Angela Waanders, MD, MPH  
Nitin Wadhwani, MD

**Beijing Tiantan Hospital Neurosurgery Center**
Shida Zhu

**Children's Hospital of Philadelphia**
Kristina Cole, MD, PhD  
Mateusz Koptyra, PhD  
Adam Resnick, PhD; Co-chair  
Mariarita Santi-Vicini, MD, PhD  
Jay Storm, MD

**Children's National Health System**
Miriam Bornhorst, MD  
Eugene Hwang, MD  
Robert Keating, MD  
Suresh Magge, MD  
Javad Nazarian, PhD, MSc; Co-chair  
Brian Rood, MD

**Dayton Children's Hospital**
Ayman El-Sheikh, MD  
Robert Lober, MD, PhD

**Hackensack Meridian Health Network**
Derek Hanson, MD

**Hudson Institute of Medical Research**
Jason Cain, PhD

**Johns Hopkins All Children's Hospital**
Mari Groves, MD  
Eric Jackson, MD  
Michael Koldobskiy, MD, MS, PhD  
Eric Raabe, MD, PhD  
Fausto Rodriguez, MD  
Jeffrey Rubens, MD  
Stacie Stapleton, MD

**Lucile Packard Children's Hospital Stanford**
Gerald Grant, MD, FACS  
Michelle Monje, MD, PhD  
Sonia Partap, MD

**Meyer Children's Hospital**
Anna Maria Buccoliero, MD  
Chiara Caporalini, MD  
Mirko Scagni, MD

**Seattle Children's Hospital**
Bonnie Cole, MD  
Courtney Crane, PhD  
Sarah Leary, MD  
Jim Olsen, MD, PhD  
Nicholas Vitanza, MD

**UCSC Treehouse Childhood Cancer Initiative**
Holly Beale, PhD  
Olena Morozova, PhD  
Sofie Salama, PhD

**UCSF Benioff Children's Hospital**
Nalin Gupta, MD, PhD  
Sabine Mueller, MD, PhD, MAS  
Joanna Phillips, MD, PhD  
Michael Prados, MD

**UPMC Children's Hospital of Pittsburgh**
Sameer Agnihotri, PhD  
Kimberly Diamond  
Bao Li Hu, PhD  
Gary Kohanbash, PhD  
Ian Pollack, MD  
Clayton Wiley, MD, PhD

**Weill Cornell Medicine Pediatric Brain & Spine Center**
Nadia Dahmane, PhD  
Oliver Elemento, PhD  
Jeff Greenfield, MD, PhD  
Christopher Mason, PhD  
David Pisapia, MD  
Praveen Raju, MD, PhD

**Wake Forest Baptist Health**
David Kram, MD  
Aleksander Skardal, PhD

**Children's Brain Tumor Foundation**
Anita Nirenberg, PhD - Community Representative

**Dragon Master Foundation**
Amanda Haddock - Advisory Council Liaison