This report is dedicated to each and every child diagnosed with a brain tumor.
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CBTN VISION

By *accelerating* the pace of translational research and the *discovery* of new treatments, we are a global community with the shared goal to save children and young adults from brain tumors.

CBTN MISSION

The Children’s Brain Tumor Network is dedicated to driving innovative discovery, pioneering new treatments and accelerating open science to improve health for all children & young adults diagnosed with a brain tumor.

Pictured below: Michelle Monje, MD, PhD, (on right) Principal Investigator at Lucile Packard Children’s Hospital Stanford and member of the CBTN’s Executive Board and Scientific Committee, together with members of the Monje Laboratory team at Stanford. Photo courtesy of Lucile Packard Children’s Hospital Stanford.
Adapting to the COVID-19 Pandemic

CBTN investigators have adapted to challenges from the COVID-19 pandemic while continuing to provide care and keep research efforts moving forward on behalf of children diagnosed with brain tumors.

A NEW RESEARCH CHALLENGE

The global shutdown resulting from the COVID-19 pandemic has significantly impacted our CBTN research network. Laboratory research at numerous member sites was put on hold until new safety protocols could be implemented. Collection, analysis, and sharing of tumor tissue and other biospecimens also paused. Our partner foundations and patient families especially felt the effects of the pandemic on their fundraising and advocacy efforts, but found creative new ways to continue to support the CBTN's research.

As this public health crisis continues to impact communities around the world, the CBTN’s commitment remains undeterred. Thanks to the CBTN’s suite of cloud-based analysis platforms, data is accessible from anywhere on earth, allowing research projects to move forward. As new health and lab safety measures are implemented, biospecimen collection and analysis are steadily returning to their pre-pandemic levels.

CBTN’s patient advocates and research supporters at every level are answering the call to address the unexpected funding challenges. Thanks to these generous financial gifts, the CBTN has continued the development of global collaborations, increased the number of samples in the biorepository, and shared vital data to enable advancements in innovative brain cancer research.

The CBTN is committed to treating childhood brain tumors with the same level of urgency and collaboration as was seen during the development of the COVID-19 vaccines. No single institution can collect enough specimens or data in isolation to make significant advances in brain tumor treatment, so it’s critical to leverage every available resource on behalf of affected children.

The success of the CBTN is thanks to the committed teams of clinicians, researchers, patient families, and many others who won’t stop until every child is cured. The CBTN is extremely grateful for the dedication and partnership of each of these collaborators. Together, we’ve made tremendous strides in our understanding of brain tumor biology and will continue to work to accelerate treatments for each and every patient.

ADAPTING TO A NEW ERA OF RESEARCH

- Globally, the COVID-19 pandemic touched nearly all facets of society, including clinical operations, research, and philanthropy across the CBTN.
- Throughout the pandemic, CTBN and its partners identified additional needs of the childhood brain tumor community.
- Each of the CBTN’s investigators, clinicians, and research coordinators adapted to new research challenges, and by the end of Fiscal Year 20, resumed our tissue collection and analysis efforts across the network.
- The CBTN’s cloud-based analysis platforms enabled the CBTN to increase and expand the amount of research data available to researchers across the globe.

The current pandemic is demonstrating the critical role that global collaboration is playing in the development of treatments for COVID-19. Working together has enabled the medical community to make discoveries faster than ever before. The CBTN was applying these lessons to the treatment of childhood brain tumors, even before the pandemic began. Collaboration and global partnership are woven in the very fabric of the CBTN.
The leadership team of the Children’s Brain Tumor Network (CBTN) could not reflect on this transformative year without first highlighting CBTN’s expanded mission and rebranding from our roots as the Children’s Brain Tumor Tissue Consortium (CBTTC).

This evolution from CBTTC to CBTN ultimately represents our re-commitment to the same values that launched this partnership in 2011 — that innovation and collaboration, combined with a shared vision, will create a future where no child suffers or dies from a brain tumor. The growth we’ve experienced during an unprecedented 2020 has not come without challenges, but the CBTN’s unwavering commitment to think differently and innovate have defined a successful path forward for years to come.

The events of this past year have revealed areas of additional need, including disparities in academic research and clinical care. Investigators from CBTN and the Pacific Pediatric Neuro-Oncology Consortium (PNOC), led by Drs. Cassie Kline and Angela Waanders, are working to address injustice and biases within the brain tumor community, to improve access to care for all patients.

Creative solutions have led to significant triumphs by the CBTN during Fiscal Year (FY) 20. Nineteen research papers utilizing CBTN’s data and specimens were published in 13 scientific journals, including a landmark study published in partnership with the National Cancer Institute’s Clinical Proteomic Tumor Analysis Consortium (CPTAC). This collaborative effort produced a first-in-kind, large-scale analysis of the “proteogenomics” or the proteins of pediatric tumors.

Among several new initiatives has been the establishment of joint CBTN & PNOC disease working groups, each consisting of experts across a number of pediatric brain tumor diagnoses and research emphases. The new working groups each include representation from the clinical, research and patient communities. New working groups are also being considered for many of the especially uncommon types of childhood brain tumors, with the goal to identify and develop new precision clinical trials and therapeutic options for children with brain tumors.

A new face on the leadership team this year is Dr. Brian Rood of Children’s National Hospital, who became Co-Chair of the CBTN Executive Board this summer.

A CBTN investigator since 2015, Dr. Rood brings with him a drive to support collaborative science, transparent data sharing, and the translation of scientific discoveries into new treatments for children and young adults suffering from brain tumors around the world.
The effects of the global pandemic have significantly impacted CBTN’s foundation and philanthropic partnerships. Through the dedication of CBTN’s foundation supporters and families, we’ve been able to sustain and even increase our research activities on behalf of all children with brain tumors. Our network of supporters has responded with new ways to provide the necessary funding for CBTN’s operations and expansion.

Thanks to a generous $1.75 million investment from the Swifty Foundation early in FY 20, 13 new personnel have been added within CBTN’s Research Core and five research initiatives designed for CBTN have been launched to achieve a new level of operational excellence. This increase in experts on staff has thus far enabled the creation of diagnostic workflows critical to the support of clinical trials through our disease working groups.

These infrastructure improvements have better positioned CBTN to secure sustainable federal funding from the National Institutes of Health (NIH). In FY20, CBTN submitted its first-ever pediatric brain tumor SPORE (Specialized Programs of Research Excellence) application to the National Institutes of Health, which represented a key opportunity to secure ongoing federal research funding. Results of Pediatric Brain Tumor SPORE submission are expected in FY21.

Global opportunities, unprecedented challenges, and significant achievements have abounded this year, and we, the leadership of the Children’s Brain Tumor Network, have been humbled and gratified to work in service of CBTN’s mission for scientific discoveries that will benefit today’s children.

Gratefully,

BRIAN ROOD, MD
Co-Executive Board Chair
Director, Clinical Neuro-Oncology
Medical Director, Brain Tumor Institute
Children’s National Hospital

MICHAEL PRADOS, MD
Co-Executive Scientific Committee Chair
Co-Project Leader
Pacific Pediatric Neuro-Oncology Consortium
Professor, Neurological Surgery
UCSF Benioff Children’s Hospital

ANGELA WAANDERS, MD, MPH
Co-Executive Board Chair
Director, Precision Medicine Oncology
Ann & Robert H. Lurie Children’s Hospital of Chicago

ADAM RESNICK, PHD
Co-Executive Scientific Committee Chair
Director, Center for Data Driven Discovery in Biomedicine
Children’s Hospital of Philadelphia
**From CBTTC to CBTN**

**A NEW IDENTITY**

The change in our organization’s identity from the Children’s Brain Tumor Tissue Consortium to the Children’s Brain Tumor Network marks a new phase in our efforts on behalf of childhood brain tumor patients everywhere. Now as the CBTN, we will further grow our partnerships and research efforts to cure pediatric brain tumors through innovation, resource sharing, a commitment to global inclusion, and most critically, the translation of data into new clinical trials and increased clinical impact. Through this expanded mission, we are determined to uncover more effective and less toxic therapies to benefit TODAY’s children.

**Measuring Our Growth**

- **25+ MEMBER INSTITUTIONS**
- **3,500+ ENROLLED PARTICIPANTS**
- **45,000+ BIOSPECIMEN SAMPLES**
- **50+ BIOSPECIMEN PROJECTS**
- **100+ DATA PROJECTS**

**AN EXPANDED MISSION**

In order to further accelerate research progress, CBTN is partnering with foundations, public agencies, commercial/pharmaceutical partners, and academic institutions to vastly expand the number of biospecimen and data research projects, as well as supporting increases of precision medicine trials while utilizing CBTN resources to inform trial development and deployment through our partners at PNOC.

Despite the effect of COVID-19 on research across the world, the CBTN continued to expand. A total of 3,546 subjects have been enrolled (an increase of 202 this fiscal year), 45,686 aliquots of precious samples have been added to the biorepository, and highly-valuable, longitudinal clinical data, reports and imaging were collected to enhance the genomic data and samples available.

CBTN not only grew in samples and data, but the network expanded in strategic partnerships with the addition of three new member institutions. Hassenfeld Children’s Hospital at NYU Langone (New York, New York) joined as a primary member site, and both Orlando Health Arnold Palmer Hospital for Children (Orlando, Florida) and Michigan Medicine C.S. Mott Children’s Hospital (Ann Arbor, Michigan) joined as satellite members. At the time of this report, CBTN has approved seven new member sites, all of which are currently onboarding.

In another example of our drive to find cures for our children, CBTN celebrated a significant milestone during Brain Tumor Awareness Month in May. The 100th data project was approved by the CBTN Scientific Committee, exemplifying our commitment to open science and open access to our resources.
A Global Network

CBTN MEMBER INSTITUTIONS

• Ann & Robert H. Lurie Children’s Hospital of Chicago
• Beijing Tiantan Hospital Neurosurgery Center
• Children’s Hospital of Philadelphia (Operations Center)
• Children’s National Hospital
• Dayton Children’s Hospital
• China National Genebank (Beijing Genomics Institute)
• Hudson Institute of Medical Research
• Johns Hopkins Medicine
• Joseph M. Sanzari Children’s Hospital at Hackensack University Medical Center
• Meyer Children’s Hospital
• Seattle Children’s Hospital
• Children’s of Alabama
• Lucile Packard Children’s Hospital Stanford
• UCSF Benioff Children’s Hospital
• UC Santa Cruz Treehouse Childhood Cancer Initiative
• UPMC Children’s Hospital of Pittsburgh
• Wake Forest Baptist Health - Brenner Children's Hospital
• Weill Cornell Medicine Pediatric Brain & Spine Center
• Hassenfeld Children’s Hospital at NYU Langone
• Orlando Health Arnold Palmer Hospital for Children
• Michigan Medicine C.S. Mott Children’s Hospital
• Sydney Children’s Hospital, Randwick
• University Children’s Hospital Zürich
• Doernbecher Children’s Hospital
• St. Louis Children’s Hospital

Interested in joining the CBTN as a member institution?
Email a member of the CBTN Operations Team at research@cbtn.org
Scientific Data Projects (FY20)

Pictured above: The CBTN is using technology and leveraging the power of ‘big data’ to help uncover brain tumor biology. (Photo courtesy of Lucile Packard Children’s Hospital Stanford.)

DATA PROJECTS AT A GLANCE

400+ TB OF DATA AVAILABLE
125+ APPROVED DATA PROJECTS
75+ BRAIN / CNS TUMOR TYPES
18 COUNTRIES REPRESENTED
CBTN Scientific Data Projects (FY20)

PROJECT TITLE

Evaluating the Landscape of Compound Heterozygous Variants in Pediatric Diseases
Principal Investigator: Stephen Piccolo, PhD; Brigham Young University

Comparison of CBTTC Patient Data with Molecularly Defined Stem Cell Models of Pediatric Brain Tumors
Principal Investigator: Fredrik Swartling, PhD; Uppsala University, Sweden

Body Mass Index Trajectories in Craniopharyngioma
Principal Investigator: Shana McCormack, MD, MTR; Children's Hospital of Philadelphia

Descriptive “Pharmacogenomics Analysis” of the CBTTC PBTA Cohort
Principal Investigator: Angela Waanders, MD, MPH; Ann & Robert H. Lurie Children’s Hospital of Chicago

Exploring the Possible Role of Mutations in MTOR Pathway Genes in the Pathogenesis of DNET Tumors
Principal Investigator: Anna Maria Buccioniero, MD, PhD; Meyer Children’s Hospital, Italy

PNOC and SJCRH Collaborative DIPG Radiogenomic Investigation
Principal Investigator: John Lucas, Jr., MD, MS; St. Jude Children’s Research Hospital

Landscape of tumor-infiltrating T Cell Repertoire of Pediatric Brain Tumors
Principal Investigator: Gary Kohanbash, PhD; UPMC Children’s Hospital of Pittsburgh

Molecular and Functional Characterization of Childhood Supratentorial Ependymoma
Principal Investigator: Vijay Ramaswamy, MD, PhD, FRCPC; Hospital for Sick Children

Genomic Analysis of Oligodendrogliomas Across Pediatrics, Adolescents, and Adults
Principal Investigator: Adam Resnick, PhD; Children’s Hospital of Philadelphia

Cancer Stemness of Pediatric Tumors
Principal Investigator: Maciej Wiznerowicz, MD, PhD; International Institute for Molecular Oncology, Poland

Targeting Immunosuppressive Macrophage in Pediatric Brain Tumors
Principal Investigator: Erin Crotty, MD; Seattle Children’s Hospital

Detecting Gene Fusions and Subtype Discovery in Pediatric Solid Tumors RNA-Seq Using CICERO
Principal Investigator: Scott Newman, PhD; St. Jude Children’s Research Hospital

Gene Expression Correlates of High-Grade Versus Low-Grade Glioma
Principal Investigator: Chad Creighton, PhD; Baylor College of Medicine

Cross Disease Variant Lookup in CBTTC
Principal Investigator: Yiran Guo, PhD; Children’s Hospital of Philadelphia

Genomics Of Radiation-Induced Cavernomas in Pediatric Tumor Patients
Principal Investigator: YouRong Sophie Su, MD; Hospital of the University of Pennsylvania

NF Hackathon
Principal Investigator: Adam Resnick, PhD; Children’s Hospital of Philadelphia

To learn more about a particular data project, please visit cbtn.org/projects. Viewers can sort by project type, brain tumor type, investigator and other categories. Additional information, including project summaries, project goals, CBTN impact, and links to view the data within CBTN’s affiliate portals are available for review and analysis.
More than 400 terabytes of data are accessible without cost to researchers through CBTN's cloud-based platforms. Much like an application on a smartphone allows users to connect with programs and information, the software platforms utilized by the CBTN allow researchers to view, compute, store and analyze data which is most relevant to their research efforts.
CBTN Data Projects (FY20)

PROJECT TITLE

The Role of Mutational Signatures in the Development of Childhood Cancer
Principal Investigator: Michael Scheurer, PhD, MPH; Baylor College of Medicine

Exploring the Somatic Landscape of Adult and Paediatric Chordoma
Principal Investigator: Adrienne Flanagan, PhD; University College London, England

Mechanistic Modeling of High-Grade Glioma
Principal Investigator: Christoph Wierling, PhD; ALACRiS Theranostics GmbH, Germany

Cross-Species Omics Integration to Identify Oncogenic Events in Pediatric Brain Tumors
Principal Investigator: Junmin Peng, PhD; St. Jude Children's Research Hospital

Brain Match
Principal Investigator: Piyush Joshi, PhD; Hopp-Children's Cancer Center, Heidelberg, Germany

Proteomic Analysis of CBTTC Cell Lines (Procan)
Principal Investigator: Roger Reddel, PhD, MBBS, FRACP, FAAHMS, FAA; Children's Medical Research Institute, Australia

Genetic Variability Across Major Histocompatibility Complex
Principal Investigator: Tristan J. Hayeck, PhD; Children's Hospital of Philadelphia

Investigating Disease Mechanism in Adamantinomatous Craniopharyngioma Using New Cell Line Models
Principal Investigator: Todd Hankinson, MD; Children's Hospital Colorado

Pediatric Pan-Cancer Analysis of Structural Variants
Principal Investigator: Lukas Chavez, PhD; University of California, San Diego

A Study of Outcomes in Patients with CNS Tumors with BCOR Mutations
Principal Investigator: Scott Raskin, DO; Children's National Hospital

Defining the Role of the Histone 3 (H3.3G34R) Mutation in the Pathogenesis of Pediatric High-Grade Astrocytoma
Principal Investigator: Cynthia Hawkins, MD, PhD; Hospital for Sick Children

More than 700 total researchers from all over the world have requested to use CBTN-generated data in their scientific discovery projects. These data projects are exploring the genetic underpinnings of several distinct brain and CNS tumor diagnoses in infants, children, adolescents, and young adults.

High Dimensional Protein Characterization of Tumor Tissues and Relevance to Outcomes in Immunotherapy Clinical Trials
Principal Investigator: Kristina Cole, MD, PhD; Children's Hospital of Philadelphia

Determining Prognostic Factors and Genetic Markers that Impact Survival in Recurrent Pediatric Medulloblastoma
Principal Investigator: Chetan Bettegowda, MD, PhD; Johns Hopkins University

Non-Coding Genetic Events in Medulloblastoma and Ependymoma
Principal Investigator: Marco Gallo, PhD; University of Calgary, Canada

Sex-Specific Gene Expression Signatures in Pediatric Brain Tumors
Principal Investigator: Josh Rubin, MD, PhD; Washington University School of Medicine

Genetic Architecture of Molecular Phenotypes in Pediatric Brain Cancers
Principal Investigator: Sebastian M. Waszak, PhD; Centre for Molecular Medicine, Norway

Mechanisms of Medulloblastoma Formation
Principal Investigator: Erwin G. Van Meir, PhD; University of Alabama at Birmingham

Identifying the Cells of Origins of Brain Tumors Using Somatic Mutations
Principal Investigator: Gilad Evrony, MD, PhD; NYU School of Medicine
Scientific Specimen Projects (FY20)

Pictured above: Investigators at Hudson Institute of Medical Research examining a sample collection tube. Biospecimens donated to the CBTN are essential to learn more about brain tumor biology to design precision treatments for children and young adults. (Photo courtesy of Hudson Institute of Medical Research)

SPECIMEN PROJECTS AT A GLANCE

- 43,500+ AVAILABLE BIOSPECIMENS
- 70+ APPROVED SPECIMEN PROJECTS
- 40+ BRAIN / CNS TUMOR TYPES
- 13 COUNTRIES REPRESENTED
CBTN Specimen Projects (FY20)

PROJECT TITLE

Released Tumor DNA in the CSF for the Diagnosis and Monitoring of Pediatric Brain Tumors
Principal Investigator: Chetan Betagowda, MD, PhD; Johns Hopkins University

Germline and Somatic Determinants of Paediatric Brain Tumor Evolution
Principal Investigators: Sorana Morrissy, PhD; Marco Gallo, PhD; University of Calgary, Canada

Oncolytic Virus to Potentiate Immune-Checkpoint Blockade in Immunologically Cold Pediatric Brain Tumors
Principal Investigator: Aaron Diaz, PhD; University of California, San Francisco

Exploring the Possible Role of Mutations in MTOR Pathway Genes in the Pathogenesis of DNET Tumors
Principal Investigator: Anna Maria Buccoliero, MD, PhD; Meyer Children’s Hospital, Italy

Molecular and Functional Characterization of Childhood Supratentorial Ependymoma
Principal Investigator: Vijay Ramaswamy, MD, PhD, FRCPC; Hospital for Sick Children

Genomic Analysis of Oligodendrogilomas Across Pediatrics, Adolescents, and Adults
Principal Investigator: Adam Resnick, PhD; Children’s Hospital of Philadelphia

Elucidating the Role of Driver Mutations in Pediatric High-Grade Glioma
Principal Investigator: Thomas De Raedt, PhD; Children’s Hospital of Philadelphia

Disclosing Chromatin Accessibility in Brain Tumor Cells After Treatment by Cracking a ‘Nucleosomal Code’
Principal Investigator: Jakub Mieczkowski, PhD; Nencki Institute of Experimental Biology, Poland

CBTTC Cell Lines High Throughput Drug Screening Study
Principal Investigator: Adam Resnick, PhD; Children’s Hospital of Philadelphia

Elucidate Potential Therapeutic Targets in H3.3G34 Mutant Phgg Cells
Principal Investigator: Zhiguo Zhang, PhD; Columbia University

Microglial Mosaic in BRAFV600E Glioma
Principal Investigator: Estibaliz Lopez-Rodrigo, MD; Memorial Sloan Kettering Cancer Center

Circular RNAs in Medulloblastoma
Principal Investigator: Peter George Zaphiropoulos, PhD; Karolinska Institutet, Sweden

Genetic Susceptibility to Medulloblastoma
Principal Investigator: Maral Adel Fahmideh, PhD; Baylor College of Medicine

Using Whole Genome Bisulfite Sequencing to Identify Novel Therapeutic Targets in DIPG and ATRT
Principal Investigator: Eric Raabe, MD, PhD; Johns Hopkins University

Defining the Role of the Histone 3 (H3.3G34R) Mutation in the Pathogenesis of Pediatric High Astrocytoma
Principal Investigator: Cynthia Hawkins, MD, PhD; The Hospital for Sick Children

The resources available to researchers through the CBTN include biospecimens, cell lines, preclinical models, and longitudinal clinical and multi-omic data representing many distinct brain and CNS tumor diagnoses in infants, children, adolescents, and young adults.
CBTN Specimen Projects (FY20)

The CBTN’s specimen resources, brought together by scientists on four continents, are available by request and without cost to those interested in studying childhood brain tumors. On average, sample requests are processed in six months, and data access requests in two weeks. Interested researchers can request specimens at cbtn.org/histologies

**PROJECT TITLE**

**The Role of Genetic Factors in Ependymoma Susceptibility**
Principal Investigator: Maral Adel Fahmideh, PhD; Baylor College of Medicine

**Genomic Analysis of Chordomas Across Pediatrics, Adolescents, and Adults**
Principal Investigator: Adam Resnick, PhD; Children’s Hospital of Philadelphia

**Identification of Circulating Noncoding RNAs and Metabolites in Cerebrospinal Fluid in Medulloblastoma Patients**
Principal Investigator: Ranjan J. Perera, PhD; Johns Hopkins University

**Identification of Circulating Noncoding RNAs and Metabolites in Cerebrospinal Fluid in Medulloblastoma Patients**
Principal Investigator: Ranjan J. Perera, PhD; Johns Hopkins University

**Therapeutic Targeting of the Blood-Brain Barrier in Pediatric Malignant Brain Tumors**
Principal Investigator: Sadhana Jackson, MD; National Institutes of Health

**Targeting Medulloblastoma by Regulating RNA Binding Proteins**
Principal Investigator: Robert Schnep, MD, PhD; Emory University

**Regional Response to ONC201 in Pediatric High-Grade Glioma**
Principal Investigator: Carl Koschmann, MD; University of Michigan

**CRISPR Screen in G34R/V High-Grade Glioma**
Principal Investigator: Mariella Filbin, MD, PhD; Dana Farber Cancer Institute

**Impeding LIN28 Function in ATRT**
Principal Investigator: Giselle Saulnier Sholler, MD; Helen DeVos Children’s Hospital

**Proteomic Analysis of CBTTC Cell Lines (Procan)**
Principal Investigator: Roger Reddel, PhD, MBBS, FRACP, FAAHMS, FAA; Children’s Medical Research Institute, Australia

**Personalized Therapy for High-Risk Ependymoma of Childhood**
Principal Investigator: Vijay Ramaswamy, MD, PhD, FRCPC; Hospital for SICK Children

**Investigating Disease Mechanism in Adamantinomatous Craniopharyngioma Using New Cell Line Models**
Principal Investigator: Todd Hankinson, MD; Children’s Hospital Colorado

**Targeting Regions of Converging Synteny in Pediatric and Canine Glioma**
Principal Investigator: Roel Verhaak, PhD; The Jackson Laboratory
Publications
Over the course of FY20, there has been a significant increase in publications resulting from CBTN’s collaborations with more than 100 investigators. CBTN placed 15 publications in more than 10 scientific journals, and at the time of this report, submitted five publications which are awaiting approval, five under review for submission, and three abstract (listed below). Highlighting the translational work of the CBTN, the research topics span basic research, bioinformatics, and clinical research.

ACCEPTED PUBLICATIONS (15)


Publications (Cont.)

**SUBMITTED: 5**


Submitted an abstract titled ‘Reconstructing the Gene Regulatory Landscape of Pediatric Brain Tumors’ to the 2020 ISMB meeting (Regulatory and Systems Genomics track)

‘The Immunogenomic Landscape of Primary Pediatric Solid Tumours’ (Submitted to Cancer Cell)

**PENDING SUBMISSION: 5**

‘High-grade glioma cell line models for pediatric cancer’. Mateusz Koptyra, Komal S. Rathi, Valerie Baubet, Jo Lynne Rokita

‘OPEN PBTA Manuscript’

‘CBTN Resource Paper’ being reviewed submission to J Neuro-Oncology and Neurosurgery

‘A Transcriptome-based Classifier to Determine Molecular Subtypes in Medulloblastoma’.

Ammar S. Naqvi, Brian Ennis, Krutika S. Gaonkar, Michael Koldobskiy, Yuankun Zhu, Miguel A. Brown, Bo Zhang, Phillip B. Storm, Adam C. Resnick, Jo Lynne Rokita (2020). ‘Molecular mechanisms and functional impact of aberrant splicing in diffuse intrinsic pontine gliomas’.

**SCIENTIFIC CONFERENCE ABSTRACTS: 5**


Payal Jain presented to the AACR virtual meeting (June 22-24). Her abstract was #6746: ‘Novel BRAF gene fusions in pediatric histiocytic neoplasms respond differently to RAF targeted therapies based on dimerization pr’.


Submitting an abstract to the AACR conference ‘Tumor heterogeneity: from single cells to clinical impact’, to be held in Philadelphia on September 10-13. Preparing a manuscript entitled “Cell Ecosystem and Signaling Pathways of Posterior Fossa Childhood Ependymoma Revealed by Single-Cell Transcriptomic Profiling”; - plan to submit for publication this fall.
Patient Partnerships

Pictured above: Investigators at Hudson Institute of Medical Research examining a sample collection tube. Biospecimens donated to the CBTN are essential to learn more about brain tumor biology to design precision treatments for children and young adults. (Photo courtesy of Hudson Institute of Medical Research)
ADVOCACY IN ACTION: DIPG AWARENESS DAY

On Thursday, February 13, 2020, at the Rayburn House Office Building in Washington, DC, diffuse intrinsic pontine glioma (DIPG) patient and family advocates joined national experts in childhood brain tumor research, as well as representatives from government and industry, at a Congressional Briefing titled DIPG, Pediatric Brain Cancer and the Importance of H. Res. 114. Presented by the DIPG Advocacy Group in collaboration with Congresswoman Jackie Speier (D-CA), the event was held to urge the 116th Congress to pass U.S. House Resolution 114 (H. Res. 114).

H. Res. 114 calls for the designation of the 17th of May each year as “DIPG Awareness Day” to raise awareness and encourage research into cures for diffuse midline gliomas (including DIPG), and for childhood cancers in general; as well as to open opportunities for data-sharing, and to push for increased private and public funding for research and new clinical trials for treatment. Additionally, the resolution would help to provide patient families and doctors with more information about available experimental research, clinical trials, and/or treatment strategies. beginning at the time of diagnosis.

CBTN and PNOC investigators Dr. Adam Resnick and Dr. Sabine Mueller joined a panel of experts to deliver remarks on the state of research for these conditions. Jace Ward, a 21-year-old college student who was diagnosed with DIPG brain cancer in May of 2019, also shared remarks about his brain tumor journey. Since his diagnosis, Jace has become a leading patient voice, speaking to researchers, funders, public policymakers, and the community at-large to instill a sense of urgency in the discovery of new treatment strategies.

FOUNDATION PARTNERSHIPS

A NEW FOUNDATION COUNCIL

During FY20, CBTN worked to better understand and support the needs of the patient community by hosting listening tours with each of CBTN’s Advisory Council member foundations. The Advisory Council, launched in 2017, was created with the goal of supporting CBTN’s vision and mission through advocacy, philanthropic and community-focused efforts.

Thanks to feedback and insights collected during the foundation listening tours, CBTN restructured its foundation and donor partnerships into a new Executive Council.

The new Executive Council will be charged with informing and partnering with CBTN leadership, acting as community stakeholder representatives, and driving the national and global impact of CBTN.

Executive Council members provide a minimum annual gift of $25,000 and participate in quarterly meetings over a two-year membership commitment. Executive Council members also support CBTN through their service in one of two subcommittees, the Finance & Funding Subcommittee or the Advocacy & Awareness Subcommittee.

If you are interested in learning more about the CBTN Executive Council, contact Gerri Trooskin, Director of Partnerships at troosking@chop.edu.
A CALL TO ACTION

Jace Ward is a junior at Kansas State University studying business and pre-law. On May 17, 2019, following multiple rounds of tests and uncertainty, Jace was diagnosed with a diffuse intrinsic pontine glioma, or DIPG.

Jace has become a strong advocate for the brain tumor patient community by bringing attention to these under-represented conditions. His mantra throughout his treatment has been, “I can’t die, I’m busy.”

I have great hope and also frustration as I survey the landscape of data, research, and clinical trials. I feel the momentum rising in pockets like CBTN and yet I face the reality that my tumor won’t wait until we all agree on the most perfect ways to structure collaboration and trials.

Since my diagnosis 18 months ago, I have watched a child die nearly every single day from DIPG alone; with parents sharing their heartbreaking progression. In the last decade, 1.3 million years of life have been lost to pediatric cancer - each one stolen away from children with unique talents and purpose in the world.

What is to blame for the lack of progress in childhood brain tumor research? Is it lack of funding? Extreme caution in trials? Inability to effectively share and analyze data and biospecimens?

Whatever the reason, I can guarantee every patient family knows, without a doubt, how much more important it is to efficiently share their child’s data, tumor tissue, and biospecimens than to keep those valuable resources locked away. Each one would opt for broadly sharing these resources for one main reason: No family who has experienced the pain of childhood cancer would wish it on any other.

I have great hope because I have had some success in treatment when I have used my data through CBTN for analysis by trial investigators, pharmaceutical companies and doctors.

“DIPG won’t wait. We know it is possible to use urgency to chart a new course; we have seen this during the COVID-19 crisis. Urgency requires a united commitment to somewhat rebellious collaboration. It requires deciding a patient deserves the right to life and the pursuit of life-extending treatments. It will require bravery to change institutional thinking.”

Still, far too few discoveries have been made in past decades and now we must play catch up. No one can better teach us bravery in action than a child with brain cancer. Let’s start right now by really seeing the child, each child, as if he or she is our own. Let’s work urgently to save them.

In the words of the late Congressman John Lewis, “If not us, then who? If not now, then when?”

Friends, we each get one life to make an impact. My case is not any different than yours. None of us know how many days we have on earth to do our best work. Use every single one.

- Jace
Scientific Community Partnerships

Members of the Centre for Cancer Research at the Hudson Institute of Medical Research, including Ron Firestein, MD, PhD and Jason Cain, PhD of the CBTN Scientific Committee (Photo courtesy of Hudson Institute of Medical Research).
PNOC 008

CBTN continued its collaborative efforts with the Pacific Pediatric Neuro-Oncology Consortium (PNOC) through the PNOC008 trial titled, ‘A Pilot Trial Testing the Clinical Benefit of Using Molecular Profiling to Determine an Individualized Treatment Plan in Children and Young Adults with High-grade Glioma’.

The first subject was enrolled in April of 2019. With a target of 1-2 subjects per month across any PNOC site that is IRB approved for the study, tumor samples are collected for clinical genomics, which are generated in the CLIA-certified lab at UCSF followed by the production of a clinical report. If additional tissue is available, the sample is sent for research sequencing first via the Division of Genomic Diagnostics at CHOP for extractions and then to a third-party vendor to generate the data.

Once the data is received, analysis is run against the Pediatric Brain Tumor Atlas (PBTA) with another clinical report being produced. Both reports are provided to the PNOC Tumor Board for review and to aid in treatment decisions for the subject. The data then is incorporated back into the PBTA to inform on treatment decisions for future subjects. In 2020, 19 patients were enrolled, nine of which had sequencing completed through the Division of Genomic Diagnostics at CHOP.

CBTN/PNOC WORKING GROUPS

This year, CBTB launched a new collaborative effort with our partners at the Pacific Pediatric Neuro-Oncology Consortium (PNOC), supporting our increased focus on clinical trial and clinical decision support. Seven CBTN/PNOC Disease Working Groups have been formed to focus research efforts for a number of histologies and research areas.

Working groups have been established for: medulloblastoma, diffuse midline glioma, AT/RT, low-grade glioma, ependymoma, craniopharyngioma, and imaging. Each working group has their own goals, convene once every month, and collaborate on preclinical and clinical research. The groups are facilitated with CBTN by allowing for sharing of resources, clinical data, biospecimens, preclinical models and genomic and proteomic data that can be used to develop new data-driven clinical trials.

If you would like to participate or learn more about the CBTN/PNOC working groups, please email Ryan Velasco, Research Program Coordinator, (velascor@chop.edu).

CBTN/PNOC WORKING GROUP LEADS

MEDULLOBLASTOMA LEADS
- Robert Wechsler-Reya, PhD; Sanford Burnham Prebys
- Tabitha Cooney, MD; UCSF Benioff Children’s Hospital

CRANIOPHARYNGIOMA LEADS
- Cassie Kline, MD; Children’s Hospital of Philadelphia
- Fatema Malbari, MD; Texas Children’s Hospital

LOW GRADE GLIOMA LEADS
- Angela Waanders, MD, MPH; Ann & Robert H. Lurie Children’s Hospital of Chicago
- Daphne Adele Haas-Kogan, MD; Dana-Farber Cancer Institute
- Pratiti Bandopadhayay, MBBS, PhD; Dana-Farber Cancer Institute
- Joanna Phillips, MD, PhD; UCSF Helen Diller Family Comprehensive Cancer Center

AT/RT LEADS
- Ashley Margol, MD, MS; Children’s Hospital Los Angeles
- Annie Huang, MD, PhD, FRCP(C); SickKids
- Eric Raabe, MD, PhD; Johns Hopkins School of Medicine

EPENDYOMA LEADS
- Eugene Hwang, MD; Children’s National Hospital
- Mariella Filbin, MD, PhD; Dana-Farber Cancer Institute
- Steven Mack, PhD; Texas Children’s Hospital
- Derek Hanson, MD; Hackensack Meridian Health

DIFFUSE MIDLINE GliOMA LEADS
- Sabine Mueller, MD, PhD; Children’s Hospital Zurich
- Javad Nazarian, PhD; Children’s Hospital Zurich

IMAGING WORKING GROUP LEADS
- Josh Rubin, MD, PhD; Washington University School of Medicine, St. Louis
- Javier Villaneuva-Meyer, MD; University of California San Francisco
- S. Ali Nabavizadeh, MD; University of Pennsylvania
OPEN PBTA

Developed by the CBTN in collaboration with the Pacific Pediatric Neuro-Oncology Consortium (PNOC), the Pediatric Brain Tumor Atlas (PBTA) is a 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. This foundational dataset was released on the NIH Common Fund-supported Gabriella Miller Kids First Data Resource Portal and CAVATICA workspace.

In FY20, CBTN researchers 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 expertise 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 patents.

The OpenPBTA Project is organized on GitHub, which allows data scientists to work together. Bioinformaticians and data scientists anywhere on earth are invited to join the project at the OpenPBTA GitHub Analysis Repository. This crowd-sourced, open-analysis effort is contributing to a manuscript that will provide a detailed, molecular picture of the more than 30 pediatric brain tumor types represented within the PBTA. The completed manuscript will help laboratory scientists and clinicians to more clearly identify, describe, and chart how cancerous brain cells mutate and propagate separate from normal tissue cells. The OpenPBTA manuscript will continue to evolve and expand, with updates available in real-time and on an on-going basis. This will allow for continuous team science efforts and provide an expanding resource to empower additional scientific discoveries.

To learn more about the Open PBTA initiative, visit cbtn.org or ccdatalab.org/openpbta.

GIFT FROM A CHILD

Gift from a Child (GFAC), supported by the Swifty Foundation, ensures patients and families can donate samples of brain tumor tissue at the end of life. The gift of post-mortem tissue donation benefits other children diagnosed with a pediatric brain tumor and can provide families with hope and consolation during a time of loss.

GFAC Centers of Excellence, including the newest site at Weill Cornell Medicine, work to collect, process and track donations to the CBTN. This initiative allows each donated sample to provide the greatest possible impact on children’s brain tumor research.

The collection of these samples is key to further understand the biological and molecular changes that occur within brain tumors, especially in tumors that were not surgically possible to biopsy or resect due to location. In addition to tumor tissue, this effort allows the collection of normal brain tissue samples to use for comparison.

To learn more about Gift from the Child initiative, visit cbtn.org or giftfromachild.org.
CAVATICA AUSTRALIA

Beginning in February of 2020, The Children’s Brain Tumor Network joined an international alliance including the Australian Research Data Commons (ARDC), Bioplatforms Australia, the Australian BioCommons, Children’s Cancer Institute in Australia, The Gabriella Miller Kids First Data Resource Center (Kids First DRC), and Seven Bridges Genomics to expand use of the CAVATICA data analysis platform into Australia, utilizing Amazon Web Services in Sydney and piloting new capabilities to support Australian initiatives such as Zero Childhood Cancer (Zero).

These CBTN partners aim to build a computational infrastructure that will harmonize data from Zero, with the genomic datasets of CBTN and the Kids First DRC. The effort will help to improve researchers’ understanding of rare pediatric brain cancer subtypes.

“\textit{The expansion of CAVATICA has already enhanced international collaboration by providing easier and faster approaches to sharing data and analyzing rare childhood cancer data.}

Since we know so little about many pediatric cancer subtypes, it is essential that we share data globally. We may be able to better understand how to treat an Australian patient’s tumour by comparing it to larger numbers of American patients.

The innovative technology of CAVATICA enables researchers from Australia and the United States to seamlessly share data and novel analysis methods with ease, driving improved outcomes and novel research."

Mark Cowley, PhD
Associate Professor & Computational Group Leader
Children’s Cancer Institute

OLIGONATION

Oligodendroglioma is rare, occurring in less than one percent of pediatric brain tumor patients under 14 years of age, although slightly more often in teens and young adults. These and other factors present challenges to identify clinical trials or promising research advancements for young people who develop an Oligodendroglioma. And because Oligodendroglioma tends to be a slow growing cancer, the lack of short term ‘endpoints’ for Oligo trials makes it more difficult to recruit support from researchers, drug companies, and government agencies such as the Federal Drug Administration (FDA).

Without sufficient data to develop hypotheses or the preclinical tools to test them, progress is difficult. To address these needs, OligoNation was founded in 2014 and has since raised over $1.3 million for research. With an initial emphasis on translational research, OligoNation is now focusing efforts on biobanking and facilitating preclinical research (cell-line and PDX model development) that will lead to more clinical trials for Oligodendroglioma.

As CBTN and OligoNation align on many of the same goals, a new partnership was formed during FY20 to establish a pipeline for gathering Oligodendroglioma tissue samples and providing data to the research community. A collated sample listing from across CBTN, the University of Pennsylvania and OligoNation have undergone whole-genome and RNA sequencing. Once analysis of the 122 DNA and 62 RNA Oligo cohorts is completed, the findings will be made available to benefit the research and patient community.

NF2 BIOSOLUTIONS

To support expanded cross-disease research, CBTN partnered with NF2 Biosolutions, a nonprofit organization dedicated to finding an effective treatment or cure for Neurofibromatosis 2 (NF2). NF2 is a disease characterized by tumors on the spinal and cranial nerves, with over fifty percent of the cases inherited. The afflicted often suffer hearing and vision loss.

By leveraging the CBTN’s infrastructure and resources, NF2 Biosolutions will refer patients to CBTN Clinical Research Coordinators, who will consent and coordinate the collection of samples and data from previous and upcoming surgeries. Any data generated will be available for research and also allow cross-disease analysis to expand potential findings.

To learn more, visit nf2biosolutions.org
Scientific Community Resources

USER SUPPORT OFFICE HOURS

To provide technical support and resources for the CBTN research community, ‘user support office hours’ were instituted during FY20. These open information sessions allow researchers to ask questions or view tutorials from experts on the CBTN Operations Team. Topics range from how to navigate CBTN’s analysis platforms, to querying data, to discovering or creating pipelines and workflows.

Researchers and clinicians seeking to learn more about the CBTN’s available pediatric brain tumor data are invited to join each monthly session. During these sessions, tutorials and support topics for using platforms including CAVATICA, PedcBioPortal and the Gabriella Miller Kids First Data Research Portal are available upon request.

INTERESTED IN JOINING OFFICE HOURS?

Contact a member of the CBTN operations team for meeting information, to submit questions, or suggest discussion topics.

Email us at research@cbtn.org

EXPANDED RESOURCE REQUESTS

After receiving feedback from researchers about the CBTN’s specimen request process, CBTN has phased out its quarterly request periods, allowing researchers to submit specimen requests at any time. This update was made possible through the formation of two review groups within the CBTN Scientific Committee. Members of the CBTN Scientific Committee review and provide feedback and/or approval for all submitted project requests. The CBTN also accepts requests for cell lines and data projects year-round, which are available to researchers anywhere on earth.

NEED TO REQUEST SPECIMENS OR DATA?

For information and instructions on submitting a request to CBTN biosamples, cell lines and data, visit cbtn.org/research-resources

(Photo courtesy of Meyer Children’s Hospital in Florence, Italy)
Advancing Our Mission

Pictured above: Chanel Keoni, BS, a Neurosurgery Lab Coordinator at Dayton Children’s Hospital. (Photo courtesy of Dayton Children’s Hospital)
CBTN Executive Board FY21 Objectives

DRIVING INNOVATIVE, PIONEERING, OPEN SCIENCE

Objective 1
Strategically growing the number of CBTN members in the U.S. and internationally will drive the availability, utilization and increased volume of pediatric brain tumor resources, research, and increase the network of collaborative innovative experts overcoming the inter-related barriers to advancing pediatric brain tumor research.

Objective 2
Increase the number of U.S. and international research projects, and discoveries supported by CBTN aligned to the open science model for release without embargo of data, biospecimens and preclinical models throughout the research community.

Objective 3
Increase the number of U.S. and international precision medicine clinical trials and therapeutic treatment decision mechanisms supported by CBTN’s pediatric and AYA data to allow clinical trials to be designed and supported by pediatric and AYA brain tumor data.

Objective 4
Improve equity of global access to healthcare and to clinical trials by developing CBTN led research looking at health disparities in pediatric brain tumor patients.

Objective 5
Increase and drive patient and foundation collaborations to develop partnered research projects, clinical trials, collaborative opportunities aligned with CBTN’s vision and mission to improve treatments, outcomes and quality of life.

DEVELOPING AND SUSTAINING ESSENTIAL STRATEGIC PARTNERSHIPS

Objective 1
Increase and drive governmental pediatric brain tumor research in the U.S. and internationally for increased resources, collaboration and expertise in pediatric brain and AYA brain tumor.

Objective 2
Increase and drive commercial partnerships to drive the utilization of first class innovative solutions and technology for pediatric brain tumor research.

Objective 3
Establish pharmaceutical partnerships for the development of pediatric brain tumor clinical trials and therapies supported by CBTN.

DRIVING EDUCATION AND TRAINING

Objective 1
Develop strategic higher-education partnerships and programs to support the study of pediatric brain tumors.
NEW CBTN WEBSITE

Growth from CBTTC to CBTN has continued into FY21 with the launch of our redesigned website (cbtn.org) in October 2020. With a greater focus on the CBTN’s scientific discovery projects, the new CBTN website provides opportunities for visitors to explore, learn, and connect with CBTN investigators, foundations, and research partners.

CBTN website visitors can explore the biospecimen and data project pages while learning more about the research teams, institutions, and foundations involved with each project. Users can also view project goals, funding needs and each project’s impact to the CBTN. The redesigned member institution pages allow visitors to learn more about the investigators, clinicians, research coordinators, and other CBTN research team members at each CBTN member institution. Each section of the website is linked to other relevant informational cards including publications, presentations and news items.

Additional website features highlight CBTN’s research findings, including a ‘Publications’ section, an ‘About Us’ section which shares how CBTN empowers discovery through data-driven research, foundation partner pages which highlight the critical role of the patient communities in the CBTN mission, a newly-designed donation platform, and much more.

CBTN/CPTAC PROTEOMICS PAPER

CBTN and the Clinical Proteomic Tumor Analysis Consortium (CPTAC) collected and analyzed genetic, genomic, and proteomic data from multiple types of brain tumors in children. The research team consists of collaborators from the Icahn School of Medicine at Mount Sinai, the National Cancer Institute, Fred Hutchinson Cancer Research Center, Children’s National Hospital and Children’s Hospital of Philadelphia.

This paper is the first large-scale multicenter study focused on pediatric brain tumors, available online in Cell on Nov. 25, 2020. A comprehensive “proteogenomic” analysis of the proteins, genes, and RNA transcription involved in pediatric brain tumors has yielded a more complete understanding of these tumors, which are the leading cause of cancer-related death in children. The results could help physicians more accurately identify different types of tumors and methods for treating them.

This study is the first comprehensive survey of genomics (aims to characterize DNA sequence alterations in samples), transcriptomics (aims to quantify copies of RNAs), global proteomics (aims to identify and quantify proteins), and phosphoproteomics (quantifies active proteins) across a large cohort of 218 tumor samples representing seven distinct types of brain tumors.

By characterizing biological themes that are shared among these different types of tumors, the study revealed new insights which suggest that current treatments being used for specific tumor types could be applied to others that share the same proteomic features. Through leveraging the rich clinical outcome data of this cohort, the research team also identified new prognostic biomarkers for a type of tumor known as high-grade glioma (HGG). When HGG tumors have a genetic mutation known as a H3K27M mutation, they tend to be very aggressive and the patients have relatively short survival time. However, in those without the mutation, this study suggests that the abundance of proteins named IDH1 and IDH2 in the tumor tissues could help to identify which tumors with the non-mutated H3K27M gene may be less aggressive.

The data analysis also showed key biological differences in samples from primary and recurrent tumors from the same patients, indicating the need for independent assessment and therapeutic decisions for these tumors.
Financial Summary

The CBTN is truly grateful to have been supported by Children’s Hospital of Philadelphia, including the Division of Neurosurgery and the Center for Data Driven Discovery in Biomedicine (D³b), as well as the generosity of individuals, families and foundations since its inception. These philanthropic efforts highlight the network of partners who are dedicated to the CBTN’s mission and vision.

**FY19-20 CBTN FINANCIAL SUMMARY**

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*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 the D³b Center, and gift processing and donor relations support from CHOP Foundation.*
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