The children's brain tumor network (CBTN) - Accelerating research in pediatric central nervous system tumors through collaboration and open science

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Abstract

Pediatric brain tumors are the leading cause of cancer-related death in children in the United States and contribute a disproportionate number of potential years of life lost compared to adults. Moreover, survivors frequently suffer long-term side effects, including secondary cancers. The Children's Brain Tumor Network (CBTN) is a multi-institutional international clinical research consortium created to advance therapeutic development through the collection and rapid distribution of biospecimens and data via open-science research platforms for real-time access and use by the global research community. The CBTN's 32 member institutions utilize a shared regulatory governance architecture at the Children's Hospital of Philadelphia to accelerate and maximize the use of biospecimens and data. As of August 2022, CBTN has enrolled over 4700 subjects, over 1500 parents, and collected over 65,000 biospecimen aliquots for research. Additionally, over 80 preclinical models have been developed from collected tumors. Multi-omic data for over 1000 tumors and germline material are currently available with data generation for > 5000 samples underway. To our knowledge, CBTN provides the largest open-access pediatric brain tumor multi-omic dataset annotated with longitudinal clinical and outcome data, imaging, associated biospecimens, child-parent genomic pedigrees, and in vivo and in vitro preclinical models. Empowered by NIH-supported platforms such as the Kids First Data Resource and the Childhood Cancer Data Initiative, the CBTN continues to expand the resources needed for scientists to accelerate translational impact for improved outcomes and quality of life for children with brain and spinal cord tumors.

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Introduction

Brain and other central nervous system (CNS) tumors are the leading cause of cancer-related death in children and frequently result in substantial long-term morbidity and disability [1]. Despite scientific advances in brain tumor biology across a large number of tumor types and histologies, improvements in long-term survival and quality of life for CNS tumors have remained elusive compared to other childhood cancers. Barriers to therapeutic advancement include lack of clinically-annotated biospecimens, insufficient preclinical models, and siloed, disconnected datasets [2].

The mission of the Children's Brain Tumor Network (CBTN, https://cbtn.org/), launched in 2011 as the Children's Brain Tumor Tissue Consortium (CBTTC), is to serve as a collaborative multi-institutional research consortium with a publicly-accessible biosample and data repository dedicated to the study and treatment of childhood brain tumors. CBTN seeks to address critical unmet needs for integrated, large-scale biospecimen, multi-omic, and longitudinally clinically-annotated resources. As of 2022, the CBTN comprises 32 member institutions within the United States, Italy, Switzerland, and Australia. To overcome the challenges of global, collaborative research and siloed resources, CBTN spearheaded the development of cloud-based informatics and data applications that allow researchers to access and collaboratively analyze datasets. As such, CBTN's foundation of “Innovation through Collaboration” is being realized through its creation of a state-of-the-art biorepository, innovative analytics platforms, and real-time sharing of data and specimens. By design, CBTN initiatives build upon the success of The Cancer Genome Atlas (TCGA) and Therapeutically Applicable Research To Generate Effective Treatments (TARGET) consortia by further developing standards for the collection of specimens and comprehensive longitudinal clinical data while addressing gaps in pediatric brain tumor representation in such resources. Recently, CBTN resources have contributed to the development of cross-disease resources such as the Gabriella Miller Kids First (GMKF) Data Resource and the NCI's Childhood Cancer Data Initiative (CCDI).

Collaborative biobanking with the CBTN

Patients are consented by one of 32 participating sites and enrolled on a local IRB-approved protocol which includes key language to enable prospective collection of, future research on, and sharing of, de-identified surgical specimens, patient demographics, medical history, diagnoses, treatments, and clinical imaging. CHOP reviews each site's regulatory documents prior to submission and maintains copies along with annual approvals. When possible, site-enabled workflows support the generation of cell lines, organoids, and/or patient-derived orthotopic xenografts from available tissue (Fig. 1A).

In addition, CBTN's cross-disease research platform supports the integration and management of partnered, disease-specific biospecimen and data resources including NF2 Biosolutions (https://nf2biosolutions.org/), the Embryonal Tumor with Multilayered Rosettes One Registry (https://hmh-cdi.org/etmr/), the Chordoma Foundation (https://www.chordomafoundation.org/), and OligoNation (https://www.oligonation.org/). These collaborative efforts advance disease-specific research while harnessing CBTN's operational and research infrastructure.

Creation of the Pediatric Brain Tumor Atlas (PBTA)

Created as a multi-center, multi-omic effort, the CBTN's Pediatric Brain Tumor Atlas (PBTA) includes matched tumor-normal whole genome sequencing (WGS), tumor RNA-Seq, methylation, and proteomics, as well as longitudinal clinical data, images (MRIs, histology slides images, radiology reports), and pathology reports [3]. The first PBTA dataset release of nearly 3000 specimens from 1074 tumors and germline sources occurred in 2018.
(Fig. 1B). A second dataset of nearly 5000 samples including tumor/normal 
WGS and RNA-seq, as well as parental germline WGS, jointly sponsored 
by GMKF and CCDI [4], along with methylation data for > 1700 tumors, 
will be released with no embargo. Additionally, building upon an initial 
proteogenomic PBTA dataset generated in partnership with the NCI’s 
Clinical Proteomic Tumor Analysis Consortium (CPTAC) [5], a large > 400 
sample proteogenomic cohort is underway.

In partnership with CHOP’s Center for Data Driven Discovery 
and Biomedicine (D3b) and the NIH GMKF Data Resource Center, 
the PBTA data has been integrated into cloud-based resources within 
the GMKF portal (http://kidsfirstdrc.org/) enabling cross-disease analysis 
with other GMKF datasets or those hosted by NCI’s cloud resources, 
such as TCGA and TARGET. In 2019, Researchers at D3b and Alex’s 
Lemonade Stand Foundation’s Childhood Cancer Data Lab launched the 
Open Pediatric Brain Tumor Atlas (OpenPBTA). OpenPBTA is a first-in-
kind, open-science, collaborative analysis and manuscript-writing effort to 
comprehensively analyze PBTA tumors [6]. OpenPBTA openly provides 
reproducible workflows and processed data on GitHub, PedBiomarker, 
and CAVITICA supporting multiple research publications as well as informing 
clinical trial decision-making in molecular tumor boards [7]. OpenPBTA’s 
success has paved the way for additional efforts such as OpenPedCan 
[8] currently informing the new pediatric Molecular Targets Platform (https: //moleculartargets.ccdi.cancer.gov/) developed with the CCDo in support of 
the Research to Accelerate Cures and Equity (RACE) for Children Act 
[9] and the Schwannomatosis Open Research Collaborative led by SAGE 
Bioworks [10]. CBTN promotes releasing data without embargo periods, 
allowing near real-time integration, dissemination, processing, and sharing of 
associated petabyte-scale harmonized data.

As of 2022, CBTN has supported 190 data projects and 111 biospecimen 
projects (Fig. 1C-D) spanning > 25,000 biosamples. CBTN-collected 
biospecimens are available for request via a common approval process by 
both members and non-members. Such common workflows have led to the 
publishation of >100 scientific articles and 25 abstracts in >30 peer-reviewed 
journals.
| Key Strategic Partner | Website | Collaborative Mission |
|-----------------------|---------|-----------------------|
| Australia’s Zero Childhood Cancer | https://www.zerochildhoodcancer.org.au/ | Collaborate and innovate around multi-omic data to personalize treatment for Australian children with cancer |
| Australian BioCommons | https://www.biocommons.org.au/ | Collaboratively create a cloud-based computing infrastructure using CAVATICA |
| Childhood Cancer Data Initiative (CCDI) | https://www.cancer.gov/research/areas/childhood/childhood-cancer-data-initiative | Harmonize pediatric cancer data and develop platform(s) which will help accelerate cures |
| Clinical Proteomic Tumor Analysis Consortium (CPTAC) | https://proteomics.cancer.gov/programs/cptac | Layer proteogenomics into multi-omics analyses of pediatric brain tumors |
| Chordoma Foundation | https://www.pathology.med.umich.edu/ | Invest in research to find better treatments, in patient services to create better services, and in healthcare improvement to drive better care |
| Common Fund Data Ecosystem (CFDE) | https://www.nih-cfde.org/ | Enable broad use of common fund funded data |
| European Union’s Horizon 2020 Individualized Pediatric Cure (iPC) program | https://ipc-project.eu/ | Collaborate and innovate around multi-omic data to personalize treatment for European children with cancer |
| Gift From a Child | https://giftfromachild.org/ | Support families to empower research through end-of-life tissue donation from their child |
| Global Alliance for Genomics and Health (GA4GH) | https://www.ga4gh.org/ | Develop standards for responsible sharing of genomic and health data |
| Human Tumor Atlas Network (HTAN) | https://humanumtumoratlas.org/ | Create a pediatric tumor atlas characterizing cells from pre-cancer through various stages of tumor evolution |
| International Cancer Genome Consortium Accelerating Research in Genomic Oncology (ICGC-ARGO) | https://dcc.icgc.org/ | Develop cloud computing solutions to harness cross-study sample integration |
| INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromeE (INCLUDE) | https://includedcc.org/ | Enable cross-cohort study between Down syndrome and cancer patients |
| Mixhigan Center for Translational Pathology MI-ONCOSEQ Study | https://www.pathology.med.umich.edu/mctp/mi-oncoseq-study | Sequencing study to provide comprehensive landscape of genomic alterations in individual tumors; all brain tumor data deposited into PBTA |
| NF2 Biosolutions | https://nf2biosolutions.org/ | Accelerating gene therapy research for Neurofibromatosis Type 2 |
| NIH Cloud Platform Interoperability effort (NCPI) | https://anvilproject.org/ncpi | Establish and implement cloud-based interoperability across NIH and other platforms |
| NIH Gabriella Miller Kids First Pediatric Research Program (Kids First) | http://kidsfirstdrc.org/ | Integrate PBTA data within Kids First without embargo |
| Oligo Nation | https://www.oligonation.org/ | Develop new treatments for oligodendroglioma |
| Pacific Pediatric Neuro-Oncology Consortium (PNOC) | https://pnoc.us/ | Develop new trials and inform clinical translation |
| Project HOPE (Pediatric and AYA High-grade glioma Omics Project) | https://brain肿瘤.org/research/workshops-meetings/projects-hope-gbm-care/ | Study evolutionary dynamics of high-grade gliomas with single-cell resolution |
| UCSC Treehouse Childhood Cancer Initiative | https://treehousegenomics.ucsc.edu/ | Integrate UCSC as an official data satellite site to enhance data integration |
| International DIPG/DMG Registry | https://www.dipregistry.org/ | Centralize and standardize the collection of clinical data and tumor samples from DIPG and DMG patients |
| International Central Nervous System Pediatric Research Consortium (INSPIRE) | https://commons.cri.uchicago.edu/inspire/ | Collaboratively centralize data resources from pediatric CNS tumor consortia worldwide in the Pediatric Cancer Data Commons (PCDC) |

(continued on next page)
CBTN partners across the globe

Embedded in the mission and vision of CBTN is the notion that collaboration is key for accelerated discoveries required to improve clinical outcomes. CBTN has benefited from many academic, commercial, government, and advocacy partnerships (Table 1), empowering both molecularly-based therapeutic development and decision support as part of drug-repurposing initiatives [7] through institutional initiatives and clinical trials, such as the Pacific Pediatric Neuro-Oncology Consortium (PNOC, https://pnoc.us/).

Discussion

CBTN’s successes to date are empowered by its commitment to partnering with families and advocates supporting the sharing of biospecimens and data on behalf of accelerating clinical translation. CBTN, together with its partners, has developed a combination of open-science governance and platform resources that support the largest, accessible genomic and proteomic pediatric brain tumor data repository annotated with longitudinal clinical data, pathology reports and histologic images, MRI reports and images, and available biospecimens and preclinical models.

CBTN’s support of > 300 research projects generated reagents, models, data, and publications that have, in turn, enriched the CBTN’s offerings. Likewise, consortium-wide efforts towards foundational data generation like the OpenPRTA, in combination with cloud-based platforms, support a dynamic research ecosystem that continually increases the volume and rate of brain tumor research, accelerates the development of clinical trials, and provides decision support resources to improve the outcomes of children diagnosed with CNS tumors. Importantly, CBTN is also poised to help support enforcement of the RACE Act [9], which requires companies to test cancer drugs in children that are used in adults when there is a shared molecular target. The CBTN collaborative framework of governance and paired technology advances rapid data sharing and clinical translation, defining a new model for research that breaks the traditional mold of siloed, individual achievement. Together with the many institutions, patient families, foundations, and community stakeholders, CBTN will improve the outcomes for children affected with brain cancer.

Children’s Brain Tumor Network members

Past and present members of CBTN’s Executive Council and CHOP’s Brain Tumor Board of advisors who inspired the creation and ensured the sustainability of CBTN are Alan Stallng, Jr., Al Gustafson, Al Musella, Amanda Haddock, Amy Summy, Amy Weinstein, Amy Wood, Andrea Gorsegner, Anita Nirenberg, Ann Friedholm, Bob Budlou, Caroline Court, Carrie Ann Stallings, Charles Genuardi, Jr., Daniel Hare, Daniel Lipka, David Bovard, Dean Crowe, Deborah Eise, Eliza Greenbaum, Gerald Kilhefner, Geralyn Ryerson, Ginny McLean, Graham Cox, Heather Ward, Hank Summy, James Blauvelt, James Minnick, James Yeager, Jeanne Norris, Jessica Kilhefner, John Nilson, Kevin Eise, Kim Hare, Kim MacNeil, Kim Wark, Kristen Gillette, Laura Cooke, Leigh Anna Lang, Lisa Ward, Liz Dawes, Mario Lichtenstein, Mark Mosier, Meghan Gleeson, Meghan Gould, Nancy Minnick, Nicole Giroux, Patri Gustafson, Patricia Genuardi, Paul Olson, Paul Touhey, Peter Norris, Richard Haddock, Robert Martin, Sarah Lilly, Scott Perricelli, Stacia Wagner, Stephanie Strotbeck, Stephanie Marvel, Stephan Ward, Sue Perricelli, Susan Funck, Timothy Court, Toni HeadTrisha Danze, W. Craig Marvel, and Wendy Payton.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] Curtin SC, Minino AM, Anderson RN. Declines in Cancer Death Rates Among Children and Adolescents in the United States, 1999-2014. *NCHS Data Brief* 2016(257):1–8.

[2] Learned K, Durbin A, Currie R, Kephart ET, Beale HC, Sanders LM, et al. Barriers to accessing public cancer genomic data. *Sci Data* 2019;6(1):98.

[3] Pediatric brain tumor atlas [Internet]. [cited 2022 Oct 2]. Available from: https://cbtn.org/pediatric-brain-tumor-atlas

[4] Gabriella miller kids first [Internet]. 2021 [cited 2022 Oct 2]. Available from: https://commonfund.nih.gov/kidsfirst/2021X01projects

[5] Petralia F, Tignor N, Reva B, Koppyra M, Chowdhury S, Rykunov D, et al. Integrated Proteogenomic Characterization across Major Histological Types of Pediatric Brain Cancer. *Cell* 2020;183(7):1962–85 e31.

[6] Shapiro JA, Gaonkar KS, Savonen CL, Spielman SJ, Bethell CJ, Jin R, et al. OpenPRTA: An Open Pediatric Brain Tumor Atlas [Internet]. bioRxiv; 2022. 2022 [cited 2022 Oct 1] 09.13.507832. Available from: https://www.biorxiv.org/content/10.1101/2022.09.13.507832v1.

[7] Kline C, Jain P, Kilburn L, Bonner ER, Gupta N, Crawford JR, et al. Upfront biology-guided therapy in diffuse intrinsic pontine glioma: therapeutic, molecular, and biomarker outcomes from PNOC003. *Clin Cancer Res [Internet]* 2022 Available from: doi:10.1158/1078-0432.CCR-22-0803.

[8] Jin R, Zhang Y, Gaonkar K, Rathk K, Rokita JL, Wafula E, et al. PediatricOpenTargets/OpenPedCan-analysis: Release v1.0.0 [Internet]. 2022. Available from: https://zenodo.org/record/6473913.

[9] RACE Act Poised to Advance Pediatric Cancer Research. *Cancer Discov* 2020;10(10):1434.

[10] SageBionetworks. Schwannomatosis Open Research Collaborative [Internet]. [cited 2022 Oct 2]. Available from: https://www.synapse.org/Synapse/syn28545963/wiki/617092