

Children's Brain Tumor Tissue Consortium

The Children's Brain Tumor Tissue Consortium (CBTTC)

Executive Summary

The CBTTC was initiated under a planning grant provided by the Children's Brain Tumor Foundation (CBTF). This support allowed us to develop the concept of a biobanking consortium in which member freely share biospecimens, data and ideas designed to apply the very latest technologies to the understanding of pediatric brain tumors with the goal of developing innovative diagnostic and therapeutic approaches.

CBTF partnered with the Licensing Industry Merchandisers' Association (LIMA), to provide the necessary infrastructure to support the collaboration of leading scientific experts, institutions, innovative informatics platforms, equipment and personnel all essential for realizing the current CBTTC accomplishments while creating a solid foundation for sustainability and growth.

Due to the dedication of the leadership, the efforts of the many volunteers and supporters, we founded the CBTTC with the Ann & Robert H. Lurie Children's Hospital of Chicago, The Children's Hospital of Pittsburg and Seattle Children's Hospital.

The ongoing commitment of donors like the CBTF, LIMA and The Kortney Rose Foundation will safeguard the CBTTC mission and vision to improve testing, treatments and outcomes for children with brain tumors and stands as a model for future development partners. Our intent is to continue to grow the consortium over the next few years to achieve the critical mass and number of biospecimens that will promote scientific discovery even in the rarest of children's brain tumors.

This support has created a growing collection of brain tumor biospecimens and the essential infrastructure to enable a broad range of scientific projects.

This has now been recognized by several other foundations that have provided support for specific research projects in their areas of interest. In this way the investments will be leveraged many-fold as the consortium continues to grow. Thus, the underlying theme of cooperation and sharing is extending beyond the collaboration among the founding members to include additional scientific investigators as well as diverse foundations and fundraising groups. Working together is the key to overcoming these devastating cancers of childhood

CBTTC Facilitating Childhood Brain Tumor Research



The CBTTC is a multi-institutional research program dedicated to the study of childhood brain tumors.

The ultimate goal of the CBTTC is to improve outcomes for children with brain tumors by supporting research on new prognostic biomarkers and therapies.

The CBTTC has made great strides in towards increasing worldwide collaboration and positioning the CBTTC for long term growth and sustainability.

CBTTC Progress

Tumor and Clinical Data Collections

Since the onset of CBTTC enrollment and data collection in December of 2010 at the CHOP location, the CBTTC team members enrolled 457 subjects. Currently, CHOP's contribution to the CBTTC Biorepository includes 387 flash frozen tissue specimens, 171 tissue specimens in freezing and we have obtained 371 separate blood samples.

In addition to the subject's tumors from CHOP, The member sites launched submissions in the Fall of 2013. The University of Pittsburgh Children's Hospital has a submitted 70 specimens, Seattle Children's Hospital has 192 specimens and Lurie Children's Hospital in Chicago has submitted 241 specimens. Therefore, we have over 800 frozen tissue specimens inventoried.

The specimens are annotated with clinical data to further facilitate research projects. Available clinical data is abstracted from medical records, de-identified and presented for query via the CBTTC Data and Specimen Inventory System available online.

Histology subtypes

Medulloblastoma
Supratentorial PNET
Dysembryoplastic neuroepithelial tumor (DNET)
Ependymoma
Pineoblastoma
Craniopharyngioma
Low-grade glioma/astrocytoma (WHO grade I/II)
High-grade glioma/astrocytoma (WHO grade III/IV)
Ganglioglioma
Oligodendroglioma
Brainstem glioma- Diffuse intrinsic pontine glioma
Brainstem glioma- Tectal
Brainstem glioma- NOS
Metastatic secondary tumors
Dysplasia/Gliosis
Primary CNS lymphoma
Atypical Teratoid Rhabdoid Tumor (ATRT)
Neurofibroma/Plexiform
Malignant peripheral nerve sheath tumor (MPNST)
Germinoma
Non-germinomatous germ cell tumor
Teratoma
Choroid plexus papilloma
Choroid plexus carcinoma
Meningioma
Gliomatosis Cerebri
Neurocytoma

Clinical Data

Demographics

Gender
Subject Age at Initial Diagnosis
Ethnicity
Race

Diagnosis and Progression

Initial Pathology Diagnosis
Tumor Primary Location CNS
Metastases at Submission
Pathology Review
Recurrent status
Molecular Testing

History

Cancer Predisposition
Family History
Other Medical Condition

Follow up post TX

Tumor Molecular Test
Tumor Site of Progression
Recurrence Diagnosis
Subject Clinical Status
Tumor Primary Location
Relapse Number
Metastatic Site

Specimen

Pathology Slide Images/Scans
Sample Type
Secondary Sample Type
Remaining volumes

CBTTC Supported Scientific Projects

Currently, the CBTTC is supporting 5 distinct projects focused on the genetic and molecular characterization of specific tumor subtypes. Data is shared in real time with consortium members. Genomic sequencing is performed on site at CHOP by the recently established joint sequencing core, BGI@CHOP.

Project 1. Genomic Investigation of Diffuse Fibrillary Astrocytoma. Funded by the PLGA foundation, this project supports the characterization of the genomic landscape of diffuse fibrillary astrocytomas. A major aim of the project is the elucidation of detailed genomic profiles of tumors via whole genome sequence analysis of 12 matched tissue/blood samples at 60x/60x coverage. This project also includes 3 samples provided by the Dana Farber Cancer Institute as part of a joint collaboration.

Project 2. Genomic Investigation of Gangliogliomas. Funded by the Voices Against Brain Cancers foundation, this project supports the characterization of the genomic landscape of gangliogliomas via whole genome sequence analysis of 8 matched tissue/blood samples at 60x/60x coverage.

Project 3. Genomic Investigation of Craniopharyngiomas. This project supports the characterization of the genomic landscape of craniopharyngiomas and is a joint effort between CHOP, Penn, and Dana Farber. The project includes whole genome sequencing of 5 matched pairs of tumor/blood, whole exome sequencing of 7 tumor/blood, and targeted sequencing of 30 additional FFPE samples.

Project 4. A Quantitative Unbiased Proteomics Approach to Decipher The Histone Modification Profiles Of Pediatric And Adult Gliomas. Using tumor-derived glioma stem-like cells, the project aims to profile the histone modifications associated with and contribute to the pathogenesis of adult and pediatric gliomas. This collaborative Penn/CHOP effort will compile data from both adult and pediatric tumor-derived cells. This project is supported by a grant from the Institute for Translational Medicine and Therapeutics (ITMAT) at the University of Pennsylvania.

Project 5. Immunogenomics to Create New Therapies for High-Risk Childhood Cancers. The goal is to rapidly translate promising basic research into transformative, targeted treatments that will improve cure rates in children's cancer. Project is supported by Stand Up To Cancer (SU2C) and the St. Baldrick's Foundation, along with the American Association for Cancer Research (AACR), SU2C's scientific partner.



Immunotherapy: Chimeric Antigen Receptor (CAR). Emily Whitehead

The Consortium Institutions

The Children's Hospital of Philadelphia

*Tom Curran, PhD, FRS, Peter Phillips, MD,
Adam Resnick PhD, Phillip (Jay) Storm, MD*

Since its start in 1855 as the nation's first hospital devoted exclusively to caring for children, The Children's Hospital of Philadelphia has been the birthplace for many dramatic firsts in pediatric medicine. The Children's Hospital of Philadelphia has earned the No. 1 spot on U.S. News & World Report's 2013-14 Honor Roll of the nation's Best Children's Hospitals The Hospital has fostered medical discoveries and innovations that have improved pediatric healthcare and saved countless children's lives. Over 150 years of innovation and service to our patients, their families and our community, reflect an ongoing commitment to exceptional patient care.

Ann & Robert H. Lurie Children's Hospital of Chicago

Stewart Goldman, MD

Ann & Robert H. Lurie Children's Hospital of Chicago is one of the top ten children's hospitals in the country according to U.S. News & World Report. Its Cancer program is ranked number 7 nationally. Lurie Children's is the largest provider of pediatric care in the Midwest region, with more than 600,000 patient visits (including 580,329 outpatient visits, 21,183 surgeries and 13,013 inpatient admission). Its medical staff includes 1,245 physicians in 70 specialties and is the pediatric teaching arm for Northwestern University Feinberg School of Medicine.





Children's Hospital of Pittsburgh of UPMC

Ian Pollack, MD

Renowned for its outstanding clinical services, research programs and medical education, Children's Hospital of Pittsburgh of UPMC has helped establish the standards of excellence in pediatric care. From Ambulatory Care to Transplantation and Cardiac Care, talented and committed pediatric experts care for infants, children and adolescents who make more than 1,000,000 visits to Children's, its many neighborhood locations, and Children's Community Pediatrics practices each year.

Seattle Children's

Russ Geyer, MD, Sarah Leary, MD

Seattle Children's Hospital specializes in meeting the unique physical, emotional and developmental needs of children from infancy through young adulthood. Consistently ranked as one of the best children's hospitals in the country by U.S. News & World Report, Children's serves as the pediatric and adolescent academic medical referral center for the largest landmass of any children's hospital in the country (Washington, Alaska, Montana and Idaho). For more than 100 years, Children's has been delivering superior patient care and advancing new treatments through pediatric research. Children's serves as the primary teaching, clinical and research site for the Department of Pediatrics at the University of Washington School of Medicine.



CBTTC Specimen Analysis BGI@CHOP

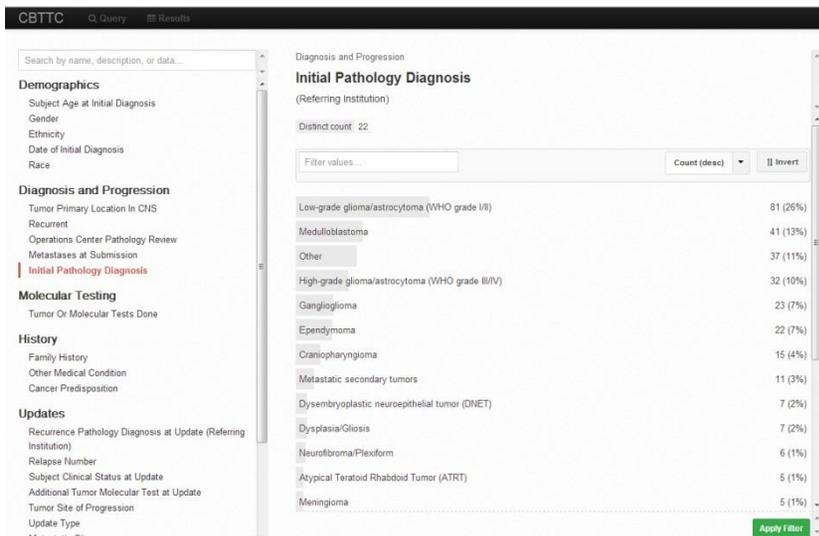
The CBTTC utilizes the expertise of BGI@CHOP Joint Genome Center to research the genetic and molecular characterization of specific tumor subtypes. The Children's Hospital of Philadelphia and the Beijing Genomics Institute (BGI) formed a collaborative genome center entitled BGI@CHOP in 2011 and strengthened their partnership in January of 2013 to focus on the facilitation of the CBTTC mission and vision. BGI@CHOP is a state of the art High-Throughput Sequencing (HTS) Core with increased capacity, expertise and analytical resources for conducting next-generation sequencing studies.

The HTS Core provides automated library construction and high-quality, high-throughput sequencing services for whole genome and whole exome, targeted sequencing, Transcriptome and digital expression profiling (RNA-SEQ), Gene regulation & epigenetic analysis (ChIP-SEQ), Small RNA discovery (smRNA-SEQ), and Multiplex sequencing (multiple samples in one lane) using the Illumina HiSeq 2000 platform. This partnership will ensure the highest quality data, while reducing expenditures and analyses time, facilitating CBTTC pediatric brain tumor research worldwide.



CBTTC Informatics Platform

The CBTTC Biorepository Portal (BRP), developed by the Enterprise Informatics Group (EiG) of CHOP's Center for Biomedical Informatics (CBMi) uses CBMi's Harvest framework to facilitate secure data capture, integration, and specimen management. The Harvest interface enables researchers to query and request de-identified data/specimens and promotes quality control and scientific discovery. Other tools integrated into the CBTTC portal include the Electronic Honest Broker (eHB), REDCap data capture, and Nautilus laboratory information management system (LIMS).



CHOP Center for Biomedical Informatics Enterprise Informatics Group (EiG): The Enterprise Informatics Group (EiG) at The Children's Hospital of Philadelphia Center for Biomedical Informatics (CBMi) works to improve data quality and integrity, facilitate the re-use of research data and materials, and promote better research by supporting data and materials discovery. The EiG also unifies, standardizes, and enables interoperable research data across institutions. CBMi's commitment to data transparency promotes efficiencies in resource utilization and minimizes compliance and security risks.

The Tools

BRP: The Biorepository Portal is the informatics platform for research staff to seamlessly enter data across multiple systems.

Harvest: Harvest is a framework created by CBMi for building highly interactive data-intensive biomedical applications, enabling real-time query and data reporting including custom data sets for exporting.

Electronic Honest Broker: CBMi's DataExpress lets the user quickly and securely move data between two different relational database platforms.

RedCap: Developed by Vanderbilt University, REDCap enables a research team to capture and manage data entirely within the research team.

Nautilus LIMS: CBMi partnered with ThermoFisher Scientific to implement a unique protocol-centered LIMS to specifically support clinical and translational research.

CBTTC Biorepository @ CHOP

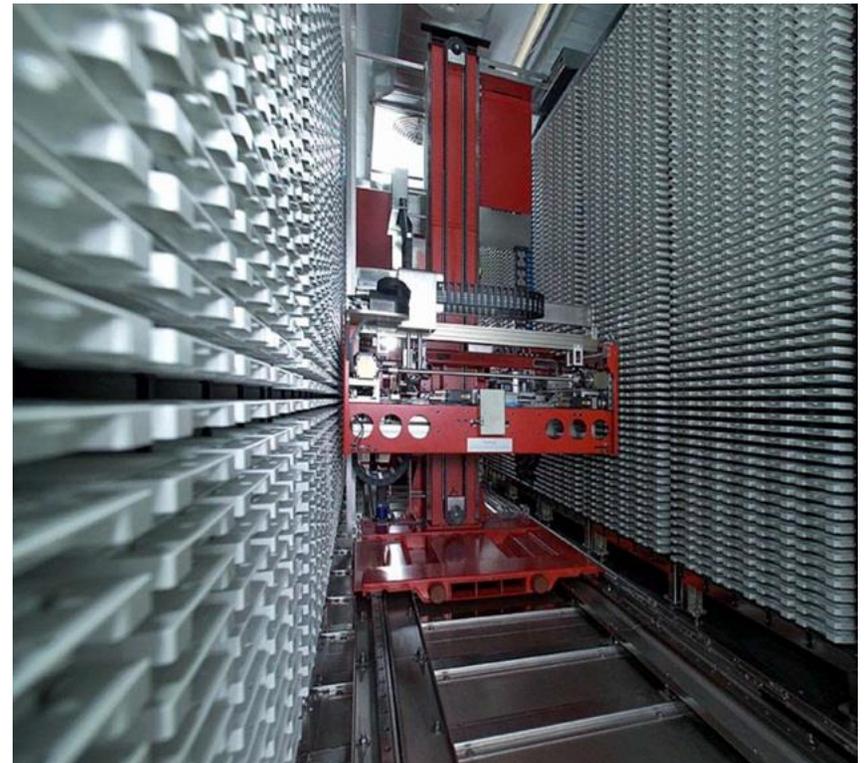
The CHOP Biorepository core will serve to collect and organize biospecimens from the CBTTC. With a capacity for approximately 8.6 million samples, the facility is designed to serve all of the CBTTC's biobanking needs, avoiding specimen duplication, preserving precious materials, and providing broad access to data and materials.

Initial sample collection has focused on DNA samples, however, additional resources are in place (-80°C freezers and liquid N2 storage) to safely store fluids, RNA, tissue samples, cells, and a number of other biospecimens.

The CBTTC at CHOP is collaborating with the CHOP Biorepository to facilitate the operational launch of the facility. The Biorepository uses Nautilus and the eHonestBroker to manage the specimen inventories.

Facility: The Biorepository is located in a 2956 sqft, temperature controlled, card access facility on the A-Level of the CHOP Colket Translational Research Building (CTRB) in Philadelphia, Pennsylvania. The heart of the Biorepository core is the REMP Mid-size Store (MSS). The store holds up to 17,472 plates (96 or 384 well or matrix tube format, 1.7-6.7 million samples) in a carefully monitored -20°C temperature and humidity-controlled environment. The REMP MSS operates with four redundant cooling systems however, only two of the cooling units are needed at any given time to maintain the store's temperature. Electrical power is ensured through the CTRB's emergency power system.

REMP: The REMP stores and retrieves samples by use of a sophisticated robotic system that travels up and down the central corridor on a rail system. The robot is capable of scanning barcodes, cherry-picking tubes, and running automated sample consolidation routines during downtime to maximize storage efficiency. The REMP MSS keeps track of sample location within the store itself through an integrated sample administration system and an Oracle database. Samples and plates are tracked within REMP via 1D and 2D barcodes. Currently, the Biorepository is also outfitted to accommodate liquid N2 storage for up to 400,000 samples and -80°C storage for up to 1.2 million samples.



CBTTC 2013-2014 & Beyond

The integration of the CBTTC Institutional collaborations, operations, Biorepository and informatics platforms provides extensive support to launch new innovative, pediatric brain tumor scientific research projects.

Continuing to build on our successful foundation positions the consortium to achieve the long-term goal of actively stimulating tissue-based research and increasing worldwide access to the molecular analysis of large numbers of brain tumor specimens.

Together, our efforts are poised to identify new childhood brain tumor therapeutic targets and biologically-based prognostic factors essential to inform therapeutic decisions and improve patient outcomes.

Development Team

Lynn Salvo at 267-425-2086 or salvol@email.chop.edu

Dan Agoglia at 267-426-6461 or agogliad@email.chop.edu

CBTTC Operations Center Manager

Jena V. Lilly at 267-425-3137 or lillyj@email.chop.edu

Address:

CBTTC Operations Center
Colket Translational Research Building
The Children's Hospital of Philadelphia
3501 Civic Center Blvd
Philadelphia, Pa 19104

WEB:

CBTTC.ORG

Facebook:

<https://www.facebook.com/CHOPBTP>