

# The Childhood Brain Tumor Tissue Consortium Annual Report

CBTTC Operations Center

September 1, 2012- June 1st, 2013



# The Childhood Brain Tumor Tissue Consortium Annual Report

## *Executive Summary*

The CBTTC was initiated under a planning grant provided by the Children's Brain Tumor Foundation (CBTF). This support in addition to partnerships with The Lauren's First-And-Goal Foundation allowed us to develop the concept of a biobanking consortium in which members 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 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 CBTF and LIMA 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.

The support from CBTF and LIMA, and Lauren's First-And-Goal Foundation has created a growing collection of brain tumor biospecimens and the essential infrastructure to enable a broad range of scientific projects.

## CBTTC Facilitating Childhood Brain Tumor Research



The CBTTC is a multi-institutional cooperative 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 2012-2013 towards increasing worldwide collaboration and positioning the CBTTC for long term growth and sustainability.



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 investment by CBTF, LIMA and Lauren's First-And-Goal Foundation 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.

This Annual Report describes the current state of the Childhood Brain Tumor Tissue Consortium (CBTTC), metrics of progress together with accomplishments and future planning. Areas of focus include CBTTC; subject recruitment and specimen collection, supported scientific research projects, operations infrastructure development comprising of informatics platform construction and implementation, scaling and outfitting the CHOP Biorepository and overall consortium management with development for sustainability. Overviews are provided from The Children's Hospital of Philadelphia (CHOP) with highlights from the Ann & Robert H. Lurie Children's Hospital of Chicago, The University of Pittsburgh Children's Hospital and Seattle Children's Hospital through June 1st, 2013.

In sum the consortium has remained highly successful in all CBTTC endeavors making great strides in positioning the repository as an international leader for the support of cutting edge pediatric brain tumor research. Successes in the areas of enrolling and consenting patients with the vast compliment of pediatric brain tumor types has begun to provide a comprehensive biorepository of specimen and genomic and molecular analysis data. This foundation will continue to grow facilitating the discovery of new prognostic biomarkers and therapeutic targets to improve outcomes for children with brain tumors. Continued efforts will focus on these core initiatives while looking toward the expansion of facilities, capabilities and infrastructure in support and advancement of the CBTTC vision and mission.

## *CBTTC Consortium Site Administration*

### *Strategic Management*

The CHOP Operations Center works to manage and facilitate all CBTTC activities for the consortium at CHOP and at the member site institutions as agreed upon in the CBTTC Constitution. Using a comprehensive communication strategy the CHOP CBTTC Project Manager works as the site liaison ensuring open and regular communication via; weekly calls, a monthly coordinator WebEx, quarterly investigator calls, a Share Site, annual site visits to each institution and an annual investigator meeting. This strategy in addition to Standard Operating Procedures (SOPs), user guides and training, supports and ensures data and specimen collections and data and specimen submissions are successful. Regulatory compliance is maintained through the same mechanisms, SOPs, user guides, trainings with local IRB applications monitored by the CHOP CBTTC Project Manager and site coordinators. The CHOP Operations Center hosts the informatics platform for CBTTC sites, receives site data



submissions, provides user support, and maintains the data store through monitoring and controlling procedures. Finally, the CHOP CBTTTC Operations Center works as the biorepository and biorepository administrator for the CBTTTC sites, providing specimen collection kits, specimen collection and submission procedures, analysis and storage of all CBTTTC samples.

## *CBTTTC Recruitment, Consenting and Specimen Collection*

### *Process Overview*

Recruitment and consent for data and sample collection is parsed into two groups: prospective subjects and retrospective subjects. Consent of retrospective subjects who had existing samples that were collected under other research studies started in December, 2012 at CHOP. The goals for the consent process for retrospective subjects are to inform the parental guardian of the opportunity to transfer the specimens and explain the objective of the CBTTTC. For those subjects who were lost to follow up, the CHOP IRB issued a waiver of consent to allow the transfer of samples into the CBTTTC repository. The University of Pittsburgh Children's Hospital, Seattle Children's Hospital and Lurie Children's Hospital in Chicago inventoried their applicable retrospective specimens for submission to the CBTTTC following all applicable consenting process and IRB regulations per their institution. Consent of prospective subjects occurs at the time the patient undergoes biopsy and tumor resection. Once the subject is consented, the CBTTTC team is notified for sample collection followed by processing in the laboratory and banking. Prospective subject participation remains successful at CHOP due to the support and collaboration of the Neuro-Oncology surgical physicians, pathology department, adept CBTTTC research coordinator and lab team to create a streamline process facilitating consent and ensure successful collection of data and samples. The CBTTTC sites received IRB approval for consenting prospective subjects in the spring of 2013. Utilizing the CHOP sample collection workflow as a template each sites has developed customized processes customized to maximize consents and collections at their institutions.

### *CBTTTC Specimen Analysis*

#### **BGI@CHOP**

The CBTTTC 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 while strengthening their partnership in January of 2013 to focus on the facilitation of the CBTTTC 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 CBTTTC pediatric brain tumor research worldwide.

## CBTTTC Informatics Platform

### MRBIG

The CHOP Multidisciplinary Research Biorepository and Informatics Group (MRBIG) is the informatics foundation for the CBTTTC. During this reporting period the MRBIG applications continued development and were placed into production for use by the CBTTTC. MRBIG improves data quality and integrity, facilitates re-use of research data and materials, promotes better research by facilitating data and materials discovery, lowers the barrier to collaborative and interdisciplinary research, increases the competitive viability of research proposals, instills a culture of data transparency, produces efficiencies in resource utilization and minimizes compliance and security risks. MRBIG also unifies, standardizes, and makes interoperable research data across institutions. The CBTTTC applications under the MRBIG umbrella include the Biorepository Portal (BRP), REDCap, Nautilus, eHonestBroker (eHB) Portal and Service and the SHARE, each fully integrated to facilitate compliant and secure data and specimen management with Harvest, the investigator collaboration portal. A development and production site for the Biorepository Portal (BRP) is now live with the Harvest platform to launch in the summer of 2013. The CBTTTC CHOP site is currently entering data into the BRP with the additional consortium sites to beginning data entry in July 2013.

### MRBIG Objectives:

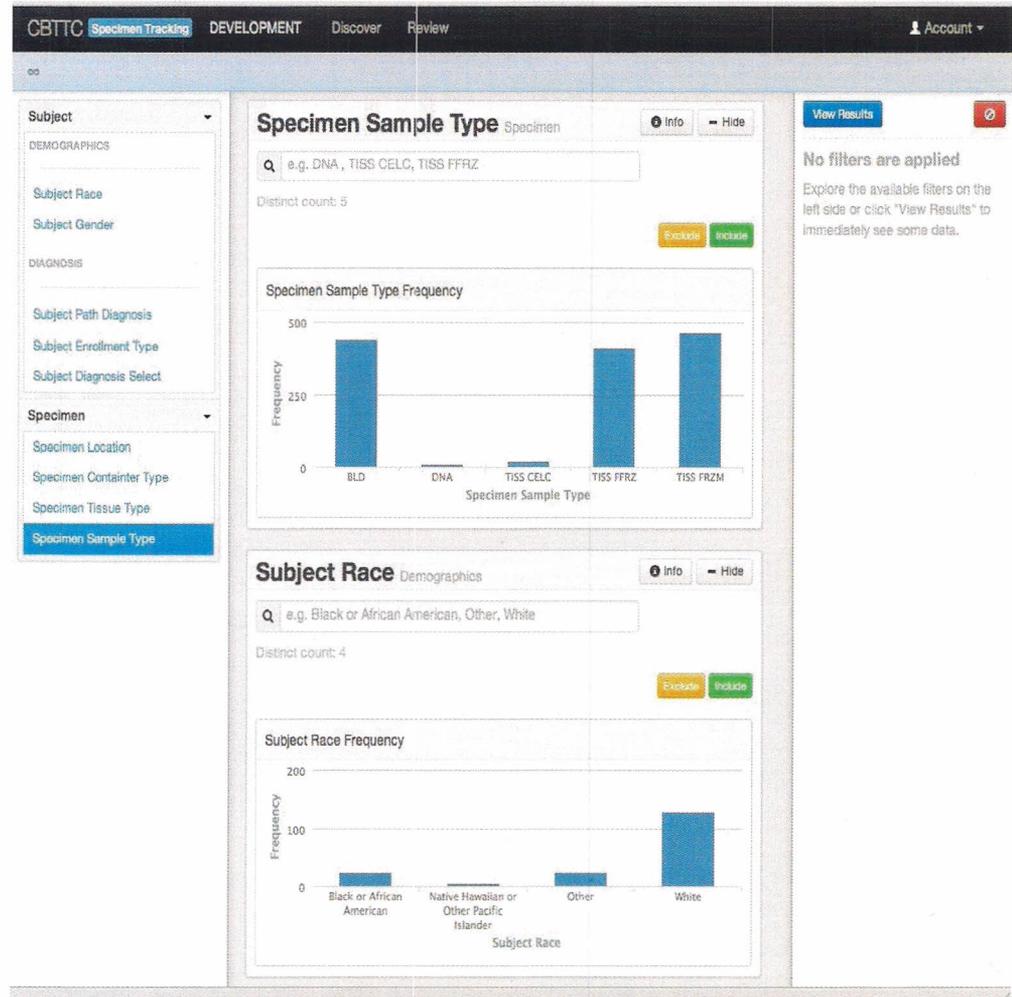
*Data Access:* Provide access to data in a user (scientist/regulatory) friendly fashion that promotes quality control and scientific discovery using the Harvest informatics platform. Harvest allows researchers to query and request de-identified data and or specimens for research purposes. The user friendly platform is accessible via the web 24 hours a day 7 days a week. Functionalities include reports and graphics for data usability.



## Harvest



The Harvest platform is where researchers can view, query and request CBTTTC specimens. To the right is a Harvest screen shot showing the user friendly reporting of specimen sample type inventories.



### MRBIG Functions:

The MRBIG has three functions:

#### *Biospecimen Management and Physical Storage*

This function will provide processing, labeling, storage, retrieval, and QA/QC for a wide variety of specimen types and storage conditions, including -20, -80, -150, and LN<sub>2</sub>. storage. This subgroup develops and implements standard operating procedures for specimen handling, monitoring, auditing, disaster recovery, and quality control following best practices established by the NIH and other relevant agencies.

#### *Informatics and Data Integration*

This function supports and enhances tools and applications that enable:

- Scalable and compliant management of specimens and data
- Appropriate access to both project-specific and enterprise-level integrated data repositories
- Integration of project-specific and enterprise-level data stores



- Buy-in to the informatics model and data integration based on a portal method for utilizing the various tools required to accomplish the data administration, coordination and scientific use.

*Information Systems, Data, and Applications*

This function supports the computing, data storage, and applications infrastructure required to scale-up data acquisition and integration. Existing resources are used will be expanded, including CHOP research Information Management Services (RIS) RIS-managed infrastructure (servers, storage) and multiple existing applications (REDCap, Nautilus LIMS, Oncore, Imaging PACS, electronic honest broker, biorepository portal). This substructure includes a new Research Application support group for RIS.

- Support required software system and applications
- Ensuring a 24/7 nature of the biospecimens informatics resources
- Downtime procedures
- Evaluation to assure systems are fulfilling the latest best practices
- Ensure continued success by Resource Evaluation and Assessment

**MRBIG Applications**

*BRP:* The biorepository portal allows for secure data entry of participant and sample information through a user friendly interface integrated with the eHonestBroker system and multisystem platforms allowing for secure longitudinal data & sample collection.

The screenshot shows a web interface for 'Subject Data'. At the top, there is a table with columns: Project, Last Name, First Name, MRN, Birth Date, and Other Actions. The first row contains: CBTTC-DEV, James, John, 006, Feb. 7, 1960, and a 'Sample Data' button. Below this is a 'Data Collection Instrument' table with columns: Initial, Update 1, Update 2, Update 3, Update 4, Update 5, and Autopsy. The rows include: Initial Data Form (with an 'Edit' button), Updates Data Form (with 'Edit' buttons for each update column), Autopsy Updates Data Form (with an 'Edit' button for the Autopsy column), and Specimen Information Form (with an 'Edit' button for the Initial column). At the bottom, there is a logo for CBMI (The Children's Hospital of Philadelphia Research Institute) and the text 'The Biorepository Portal Project - All rights reserved - The Children's Hospital of Philadelphia'.

*BRP Interface*

Pictured to the left is the BRP interface where CBTTC collaborators enter data into the user-friendly predetermined fields.



## REDCap



The REDCap system works behind the scenes in the BRP to collect and store the data via automatic integration using API technology.

The REDCap database then feeds automatically to the Harvest platform where collaborators can view, query and request samples and data.

**REDCap:** REDCap is an electronic data capture and survey tool with very comprehensive user access to data and data entry. Any and all clinical information required by the CBTTC protocol will reside in a coded manor in REDCap. REDCap is a non-proprietary system supported by a consortium led by Vanderbilt University. The REDCap system pushes the non-protected health information to Harvest for worldwide scientific access and collaboration. MRBIG also establishes a minimum set of common clinical data elements (Id).

**REDCap**  
 Logged in as felmeistere | Log out  
 My Projects  
 Project Home  
 Project Setup  
 Project status: Development

**Data Collection** [Link instruments](#)  
 Record Status Dashboard  
 Add / Edit Records  
 Study Id 522C36Z1R9OYWTF:GQ83OJ03V

**Applications**  
 Calendar  
 Data Export Tool  
 Data Import Tool  
 Data Comparison Tool  
 Logging  
 File Repository  
 User Rights  
 Record Locking Customization  
 E-signature and Locking Mgmt  
 Graphical Data View & Stats  
 Data Quality

**The Children's Hospital of Philadelphia**  
 Hope lives here.  
 Children's Hospital Of Philadelphia  
 Center for Biomedical Informatics (CBMI)

**CBTTC-DEV**

**Event Grid**

The grid below displays the form-by-form progress of data entered into the project for one particular Study Id for all defined events. You may click on the colored buttons to access that form for that event. If you wish, you may modify the events below by navigating to the [Define My Events](#) page.

**Legend for status icons:**  
 ● Incomplete  
 ● Unverified  
 ● Complete

Data Collection Instrument	Events						
	Initial (1)	Update (2)	Update (3)	Update (4)	Update (5)	Update (6)	Autopsy (7)
Initial Data Form	●						
Updates Data Form		●	●	●	●	●	
Autopsy Updates Data Form							●
Specimen Information Form	●						

[Lock all forms across all Events](#)  
[Unlock all forms across all Events](#)

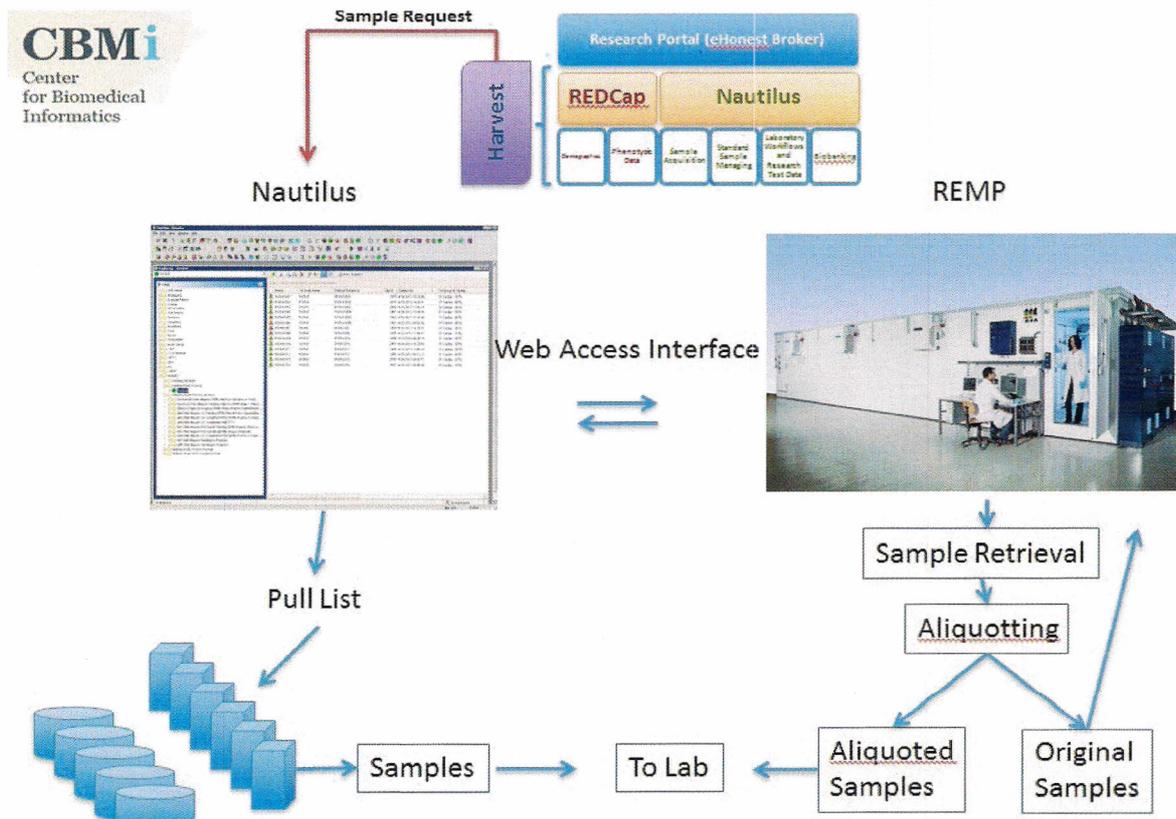
**Nautilus:** The CBTTC specimens within the CHOP Biorepository are tracked through the sophisticated Thermo Nautilus laboratory information management system (LIMS). Nautilus LIMS is an enterprise Oracle database system that facilitates tracking of specimens and specimen data through their functional lifetime, including acquisition, storage, processing, testing, and QC. Nautilus is customizable and able to capture virtually any laboratory workflow, specimen type, test type and result, and provides access to specimen data through a well-developed, secure and user friendly interface. Nautilus is also equipped with a biobanking module that allows for sample request and approval along with order fulfillment and shipping.

**eHonestBroker (eHB) Portal and Service:** In general this software provides the link between the patient and the research record. This link is encrypted and separately maintained in the eHonestBroker



program. The eHB portal also serves as a way for a research coordinator or laboratory technician to deal with longitudinal data, re-identifying the patient to add data and/or specimens to the disparate coded database via software APIs providing communication to the tools which do each portion of the informatics solution best i.e. clinical data capture, specimen tracking.

The CBTTC specimen data within the CHOP Biorepository are coded through Institutional Review Board (IRB) approved coding procedures involving the creation of an encrypted research ID through the use of sophisticated algorithms. The security of the coded data is achieved through the eHonestBroker that holds the encrypted link between direct identifiers and the research ID.





# CBTTC Share Site



This Wiki platform site aids in project management and communication for the CBTTC collaborators by providing a centralized communication hub and knowledge base.

The consortium sites member institutions each have a Wiki page to update their local project status ensuring communication and compliance is maintained at all times.

*SHARE:* The CHOP Research Institute user-centric Wiki maintains real-time CBTTC feeds of information from the informatics resources for administration and QA/QC purposes. *SHARE* is the go-to source for appropriate QA/QC documentation on all MRBIG user, technical processes and team collaboration. The CBTTC Share Site is currently fully operational and accessible by all consortium members and works as the project management communication hub to facilitate project status updates, discussions and acts as a CBTTC knowledge base.

**CBTTC Home Page**

Added by Administrator, last edited by Lilly, Jena V on Jun 14, 2013 (view change)

**Welcome to the CBTTC Wiki Share**

This site is for CBTTC collaborators and partners to share information, discuss topics and work towards achieving the objectives, mission and vision of the CBTTC. Please comment, add pages and edit content. Please remember NO PHI. Contact Lilly, Jena V

Expand all Collapse all

- Consortium Sites
- Meetings
- CBTTC CHOP Operations Center
- About the CBTTC

**Recruitment**

Date	Sites	Total Evaluable Subjects
1/31/13	CHOP	305

**Chilhood Brain Tumor Tissue Consortium (CBTTC)**

The CBTTC is a multi-institutional cooperative research program dedicated to the study of childhood brain tumor outcomes for children with brain tumors by supporting research on new prognostic biomarkers and therapies

**Project Status Updates**

Projects	Status
Recruitment & Sample Collection	Recruitment ongoing at CHOP. Recruitment to launching at CBTTC sites. Retros after launch
CBTTC Biorepository	Implementation ongoing
BRP	The Biorepository portal is set to launch prior to the Fall of 2013. Currently worki
Harvest	Harvest is in development. Looking to launch prior to Fall of 2013
Consortium sites	Next coordinator call 6/14/13. The consortium sites are set to launch prior to Fall BRP, specimen kits and bar code scanners to be shipped to the sites.
CBTTC External Website	The CBTTC External Website is set to launch in the Nov/Dec 2013

**CBTTC Consortium Sites Status**

	Specimen Supplies	IRB Approved	IRB Pending	IP	Access to BRP	Retro Histology	Comments	Status
<a href="#">University of Pittsburgh</a>	<ul style="list-style-type: none"> <li># initial kits</li> <li># monthly kits</li> <li>shipping schedule</li> </ul>	<ul style="list-style-type: none"> <li>Prospective</li> </ul>	<ul style="list-style-type: none"> <li>Retrospective</li> <li>AMD 1 Forms</li> </ul>	Y	6.4.13 RSA Requested	Received		Good
<a href="#">Seattle Children's</a>	<ul style="list-style-type: none"> <li># initial kits</li> <li># monthly kits</li> <li>shipping schedule</li> </ul>	<ul style="list-style-type: none"> <li>Prospective</li> </ul>	<ul style="list-style-type: none"> <li>Retrospective</li> <li>AMD 1 Forms</li> </ul>	Y	6.4.13 RSA Requested	Received	<ul style="list-style-type: none"> <li>is currently accruing and holding</li> <li>need to address relabeling samples</li> </ul>	Good
<a href="#">CBTTC @ Lucie Children's Hospital</a>	<ul style="list-style-type: none"> <li># initial kits</li> <li># monthly kits</li> <li>shipping schedule</li> </ul>	<ul style="list-style-type: none"> <li>Prospective</li> </ul>	<ul style="list-style-type: none"> <li>AMD 1 Forms</li> </ul>	Y	6.4.13 RSA Requested	Received	<ul style="list-style-type: none"> <li>need instructions for processing blood</li> </ul>	Good
<a href="#">Children's Hospital of Philadelphia</a>		<ul style="list-style-type: none"> <li>Prospective</li> <li>Retrospective</li> </ul>	<ul style="list-style-type: none"> <li>Approved</li> </ul>	Y				Good



## CBTTC Biorepository @ CHOP

The CHOP Biorepository core will serve to collect and organize biospecimens from CBTTC investigators. 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 N<sub>2</sub> 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.

**Tissue Storage and Requests:** In general questions regarding prioritization of biospecimens use from the CHOP biorepository are handled by appropriate tissue banking committees consisting of users and experts. The tissue committees have responsibility for determining which materials should be deposited, the appropriate storage conditions, the proposed period of storage, and prioritization of access. The tissue committees will also receive and consider petitions from outside groups for deposits and access to materials. The CBTTC Scientific Committee reviews all CBTTC specimen requests providing the CHOP biorepository with approval releases.

**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 stores' temperature. Electrical power is ensured through the CTRB's emergency power system. A UPS backup is also on-line to bridge the two systems during an electrical emergency and the facility is equipped with a wireless system for monitoring equipment status.

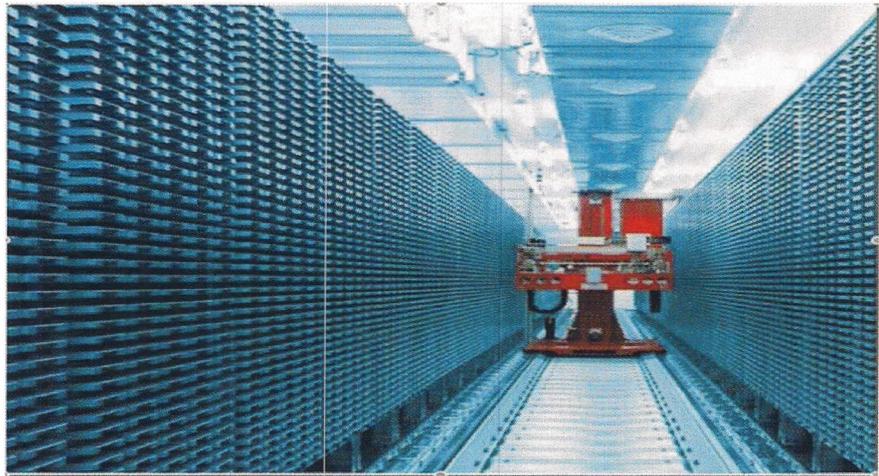
**REMP:** The REMP stores and retrieves samples by use of a sophisticated robotic system that travels up and down the central corridor on a rail system. Racks of plates and trays are stored in shelves on both sides of the store. The robot is capable of scanning barcodes, cherry-picking tubes, and running 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 N<sub>2</sub> storage for up to 400,000 samples and -80°C storage for up to 1.2 million samples.



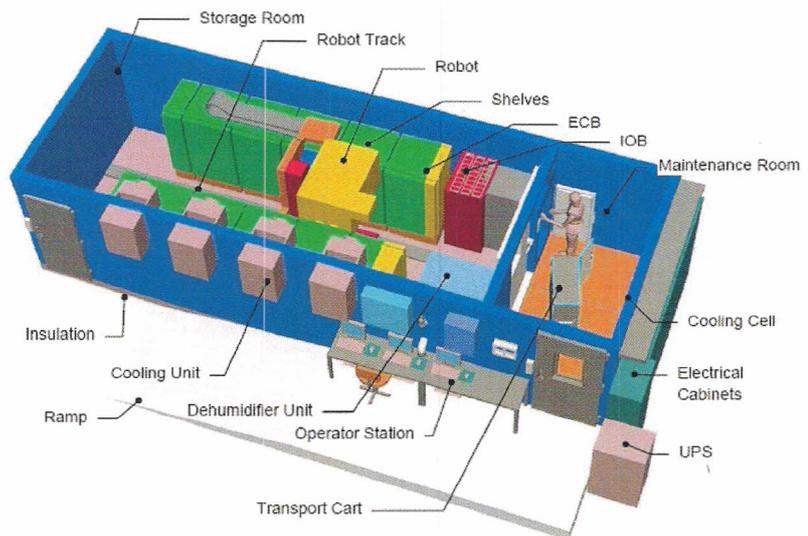
## REMP



Pictured to the right is a photo of the REMP Robot used for automated sample storage and retrieval.



Also pictured is a diagram of the REMP Layout within the CHOP Biorepository.



## CBTTC Communication Platform

To promote the CBTTC mission and vision initial planning for outreach began during this reporting period. The communications outreach plan is comprised of branding the CBTTC for digital and print mediums to address the variety of CBTTC audiences identified including, healthcare professionals, research investigators and teams, patients, their families and sponsors. Through this strategy the CBTTC will support its foundation for sustainability and growth.

The cornerstone of the communication strategy is a CBTTC website. The website is undergoing initial planning and will be designed and developed using CHOP internal resources. The objectives of the



website are to educate the public, identify new investigator collaborations, support existing collaborators, specimen donors, and communicate CBTTTC milestones, successes and publications. The website will have full integration with CHOP's Facebook and Twitter account.

The project plan for the website will occur in 3 phases, design, implementation and monitoring. Phase I is extensive and will entail development of the wire frame; all design elements, the writing of all content, identifying user needs and functionality, programming and testing. The website will be designed in collaboration with the CHOP Research IS and Communications Department. Phase II, implementation, will include, hosting and the launch of the site. Phase III, monitoring and oversight, will entail ensuring functionality, ease of use, updates for new capabilities as needed and content updates. The website is anticipated to launch in the latter part of fall 2013.

Additionally, the CHOP CBTTTC Operations Center will implement email and snail mail campaigns to inform the CBTTTC audiences of updates. These activities will include letters, newsletters, and meeting materials (agendas, logistic information and minutes) mailed and emailed. Mobile technologies will also be integrated throughout the plan to provide a supportive framework for communication while minimizing the burden of the audience.

A few examples of print collateral in support of consenting efforts may include a CBTTTC branded educative subject folder including the Informed Consent booklet(s), informational trifold written for potential subjects to learn about the process of donating blood and tissue and a letter of thank you from the investigators. Other potential projects include targeted materials by audience, trifold(s), poster presentations and customize reports.

The CHOP CBTTTC Operations Center will track key metrics associated with the communication plan, including website traffic, mailing responses, Facebook comments and Twitter reposts. This data will be analyzed to monitor the feasibility, acceptability and success of the communication plan. All identified trends will be reviewed for action plans to ensure continued process improvement.

## *CBTTTC Regulatory Oversight & Compliance*

### *IRB Management*

The CHOP CBTTTC continues to ensure IRB approval by the CHOP IRB and Consortium sites. During this reporting period one amendment was submitted and approved to update data collection forms. Once approved the forms were sent to the consortium sites for submittal to their IRBs. All CBTTTC site protocol approval expirations will be monitored by the site coordinators and the CHOP CBTTTC Project Manager. All protocol changes will receive IRB approval prior to execution in the field.



## IP

All Intellectual Property agreements (IP) for the Consortium sites remain active and approved during this reporting period. The CBTTC IP will be monitored and maintained by the CHOP CBTTC Project Manager. Reviews will be conducted as required.

## MTA

All material transfer agreements (MTA) for the Consortium sites are currently being executed. The CBTTC MTA will be monitored and maintained by the CHOP CBTTC Project Manager. Reviews will be conducted as required and copies provided as needed in all shipments.

## *The CBTTC Team*

To complement our existing CHOP CBTTC team a new clinical research coordinator Ratnakar Patti joined the CHOP team allocating a portion of his fulltime efforts to the project. Mr. Patti has extensive experience in oncology clinical research at CHOP. Additionally, Tyler Rivera (informatics) and Jena Lilly (project manager) joined the CHOP CBTTC team in June 2013. Mr. Rivera will focus his expertise on the informatics platforms, integrations and systems management for the CBTTC. Mrs. Lilly will manage the consortium sites, data, biorepository, pathology and communication teams, all operations and associated projects. This brings the CHOP CBTTC team to 8 members. Each investigator at the CBTTC member site institutions has identified a clinical research coordinator to provide, data, specimens, IRB coordination, reporting information and to work as a liaison with the CHOP CBTTC Project Manager.

## *CBTTC Data Quality Assurance (QA) Program*

The CHOP CBTTC initiated and continues to develop for process improvement the CBTTC Data Quality Assurance (QA) and Quality Control (QC) program. This Data QA program will attempt to identify problem trends using QC techniques including but not limited to the subject enrollment and consenting, data submission, data quality, specimen submission and specimen quality and the CBTTC informatics systems. Metrics will be tracked for trending with all issues to be addressed as appropriate with supplemental training for CBTTC team members and or updates to SOPs, training guides and the informatics platform as applicable.

## *2012-2013 CBTTC Advancements*

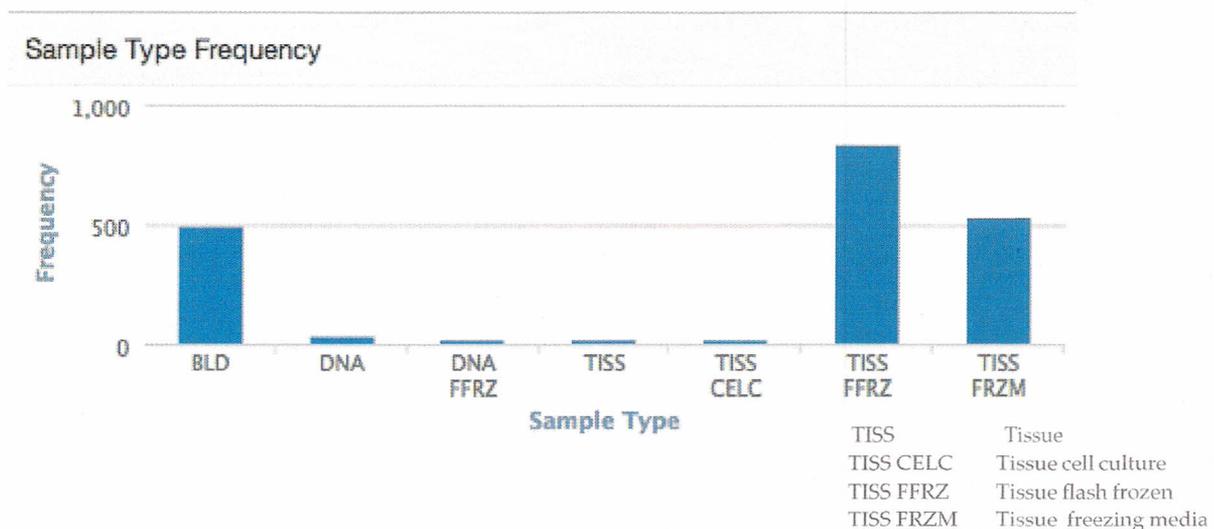
### *Tumor Collections and Current Status*

Since the onset of CBTTC enrollment and data collection in December of 2010 at the CHOP location, CBTTC team members enrolled 370 subjects. Of the 370 subjects, 361 have available samples and 9 subjects were withdrawn due to specimen ineligibility. 136 tissue samples were collected prior to the CBTTC and consent was originally obtained under a separate protocol. These samples have now been



transferred to the CBTTC, are being re-consented under IRB-approved CBTTC consents and are termed retrospective subjects. 234 tumors were obtained under CBTTC consents directly and are termed prospective subjects. Currently CHOP's contribution to the CBTTC biorepository is 1,922 separate samples obtained from the 361 subjects. These include 836 separate flash frozen tissue vials, 531 separate tissue vials in freezing media and 19 different tissue cell cultures. In addition we have obtained 491 separate blood samples.

In addition to the 361 subject's tumors from CHOP, The University of Pittsburgh Children's Hospital has a total of 191 eligible subject tumors banked as retrospective samples, Seattle Children's Hospital has 277 banked as all retrospective samples and Lurie Children's Hospital in Chicago has 430 tumor samples. Therefore, when all retrospective and CHOP prospective tumors are combined, the CBTTC currently has access to 1259 childhood brain tumors.



The histological subtypes within the CBTTC repository include the following:

Medulloblastoma / PNET	165 Subjects
Atypical Teratoid / Rhabdoid Tumor	33 Subjects
Low Grade Astrocytoma	301 Subjects
High Grade Glioma	120 Subjects
Ependymoma	170 Subjects
Germ Cell Tumors	18 Subjects



Other tumor types include the following: craniopharyngiomas; choroid plexus tumors, mixed histology glial tumors, pinealoblastoma, neurocytoma, meningioma, schwannomas, sarcomas, and dysembryoplastic neuroepithelial tumors, and various others.

### CBTTC Supported Scientific Projects

Currently, the CBTTC is supporting 4 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 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 the 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 contribute to the pathogenesis of adult and pediatric gliomas. This is collaborative Penn/CHOP effort that 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.

### Looking Forward: CBTTC 2013-2014

Numerous projects will continue, expand and initiate in the coming year around tissue and specimen acquisition, specimen analysis, scientific research collaborations, consortium site operations, data and specimen management, regulatory oversight, training, reporting and strategic communications and informatics.

All CBTTC sites will be submitting prospective samples in a real-time fashion continually increasing the repository holding. The launch of real time submission will begin starting the end of July into early



August of 2013. Each CBTTTC member site will initiate specimen submission once certification to submit specimens and data per the CBTTTC procedures is obtained. Through collaboration the consortium sites will work to enact constant and regular submissions. Submission metrics will be reviewed to ensure the agreed upon annual volume is met and will be used to set future goals and projections. The transfer of all retrospective samples on a research specific basis into the CBTTTC repository will also be completed in 2013-2014 growing the biorepository holdings for use in scientific endeavors. Strategic planning to add additional primary CBTTTC will also begin in the next reporting period to facilitate the continued growth of the repository.

BGI@CHOP is poised to handle the increase specimen volume analysis anticipated in 2013-2014 while the informatics platform and the CHOP biorepository will continue to develop in tandem to store the specimens and analyzed data. Informatics enhancements will include tissue slide imaging, improved data fields for specimen status, downloading functionality, online tutorials and streamlined accessibility. The informatics team will continue to integrate the specimen information for sharing and collaborative research, monitor promising technologies for systemic advancements and tackle continuing topics of data standardization, storage and sharing. The CHOP biorepository will expand programing technologies to interface systems and equipment, monitor storage and begin planning to launch services including, blood and specimen processing.

The CBTTTC will also develop in 2013-2014 a strategic, branded, comprehensive, communication strategy for the broad spectrum of CBTTTC audience members to assist in recruitment, sample collection, scientific research and new collaborations as mentioned previously. The cornerstone will be a user friendly, interactive website promoting and supporting the CBTTTC vision and mission. From this cornerstone addition digital media collateral will be cross marketed in social media platforms and print media will launch to ensure a successful contact algorithm to keep the audience informed and interacting with the CBTTTC. The website will also work with investigator teams as a portal to internal systems for submission of data and specimen, supply user guides, training information and CBTTTC annual conference coordination.

The culmination of the CBTTTC Institutional collaborations, operations, Biorepository and informatics platforms will provide extensive support to launch new pediatric brain tumor scientific research projects in the next reporting period. The CBTTTC Institutions and Scientific Committee (SC) will review proposals in the fall of 2013 and meet in early 2014 to support the scientific progress of the CBTTTC. The SC will work during the new reporting period to approve all proposed abstracts, posters and publications supported by the CBTTTC while ensuring transparency to further research initiatives.

The CBTTTC institutions and teams are devoted to the mission of collecting high-quality brain tumor biospecimens with associated clinical data, facilitating genomic analysis of biospecimens, developing cell lines and transplantable tumor models from submitted biopsy specimens, and sharing results from



these efforts with CBTTC member institutions and the world-wide scientific community. Due to the exceptional work accomplished in 2012-2013 the CBTTC mission is now a reality.

Continuing to building on this 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 decisions and improve patient outcomes.

