Children's Brain Tumor Network
Until every child is cured

Update Prepared for Lauren's First and Goal Foundation

November 2021

WHY CBTN

Within pediatric illnesses, brain tumors are the leading cause of disease-related death in children in countries around the world. The median age of death is only nine. Despite the high occurrence of this disease, no drug has been developed specifically to treat pediatric brain tumors. We need a new collaborative model of research that serves children *now*.

Bringing the Brightest Minds Together to Advance Brain Tumor Research

Nearly a decade ago, the Center for Data Driven Discovery in Biomedicine (D3b) at Children's Hospital of Philadelphia (CHOP) launched the Children's Brain Tumor Network (CBTN) with one goal in mind — to form a union of forces between clinicians, scientists, patients and foundations from across the globe to address this challenge.

What began as only four member sites devoted to data sharing in 2013 is now a global consortium of 25 institutions throughout Europe, Asia, Australia and the U.S., who together are establishing a new standard of care for patients by sharing data, resources and expertise to accelerate and improve discoveries. Together they created the first, and now largest, clinically annotated biorepository with real-time query abilities. It is also the largest genomic data generation effort of its kind for pediatric brain tumors. CBTN continues to pioneer new digital platforms and exciting ways to approach vast amounts of genomics-based clinical data. We are tireless advocates for pediatric brain tumor research. Our progress to date is a testament to our shared core belief in the power of collaboration and the idea that open access to data can fuel innovation and discovery.

UPDATE

CBTN received exciting news in September 2021 that the National Cancer Institute's Children's Cancer Data Initiative (CCDI) will cover the expenses of molecular profiling the remainder of *all* remaining subjects in the CBTN biobank. This effort, which would have cost CBTN upwards of 40M+ to do on its own, will generate a vast amount of data that, once processed and analyzed, will significantly increase the size and scale of the Pediatric Brain Tumor Atlas (PBTA) and empower translational research for scientists worldwide – making precision treatments a reality for children with brain tumors. The sequencing of these 4,500+ specimens, which includes saliva samples from subjects' parents, represents the largest award of its kind in the history of the NIH's data generation program and will be released without embargo.

Critical NIH Support for Pediatric Brain Tumor Research
Among the samples set to be characterized are 1,025 new low-grade glioma (LGG) samples; currently, CBTN has 300 LGG subjects with associated molecular data in the Pediatric Brain Tumor Atlas. Therefore, this marks a 340% increase to the data available to researchers investigating LGG.

When negotiating with CCDI about the project, they reached out to Dr. Adam Resnick, Director of CBTN, and asked if we would consider excluding the LGG samples from the cohort because, in their words, the cases are not as lethal. Dr. Resnick pushed back, noting how it would not only be unacceptable to us to leave them out because existing treatments have so many long-lasting harmful side effects, but that CBTN represents thousands of patient families who have worked with us over the years, and it is crucial that we find answers for them. They ultimately agreed to profile all of the CBTN's remaining samples, including LGGs.

While the NIH is covering the expenses associated with data generation, they are not able to support the herculean effort required on either end of this process, which will fall on the CBTN infrastructure. Further, CBTN's goal is to accelerate cures, and to do so they must get this data into the hands of as many researchers and data scientists as possible. To that end, we ask your help to work together to ensure that the data is processed quickly, that we have the right resources, and that researchers around the globe can get to work immediately once this new data is available.

PRIORITIES IN THE YEAR AHEAD

In that vein, the CBTN has a range of opportunities and needs around their exciting LGG and NF research, and we would welcome partnership with Lauren's First and Goal Foundation to move any of these efforts forward. The latest CBTN projects and priorities include:

I. **CBTN Infrastructure Support**
The top priority within CBTN is much-needed infrastructure support for the new NIH sequencing opportunity. With these resources, we can scale up necessary positions including new lab technicians, project managers, and bioinformaticians to support the data harmonization and analysis, as well as material costs such as Quia cubes and kits to extract the necessary specimen as well as supplies to ship them safely. These are the most urgent needs as we will need to reallocate our existing efforts in order to meet the aggressive timeline for the sequencing. **A gift of $50,000 for CBTN infrastructure would be utilized immediately to accelerate LGG sequencing efforts.**

II. **LGG Preclinical Model Development**
Another top priority is the development of additional LGG preclinical models. One of the many ways in which CBTN strives to advance its goal of developing new treatments for kids with brain tumors is to advance its preclinical model program. This program provides an opportunity for drug testing and the development of clinical trials. In order to get FDA

approval for a clinical trial, therapies need to be tested to determine if they are safe for use in kids. The best way to test drugs for efficacy and safety is to use tumor samples that are "alive"— on cell lines, organoids, and PDX models – which are grown from tumor tissue samples and behave the way a tumor might inside the body. These tools are a valuable resource and are incredibly labor intensive to develop and maintain.

CBTN currently has over 30 LGG tumor models. This collection consists mostly of cell lines at the various stages of development—from primary cell mixtures to those that have matured in culture cell lines (there are currently 3 cultured cell lines). LGG models present slow growth and decay over time in culture, which makes their use in drug screening a challenge. The lack of long-term growth suggests that the field needs to refine the models. In the year ahead, we are working to expand our cultures using several approaches that appear promising for LGG models. This approach will also include the generation of organoids models, which provide a great alternative and parallel models for both basic biology and translational studies.

The development and maintenance of preclinical models is both time consuming and staff intensive. As the models are, themselves, living organisms, they must be monitored and handled around the clock. **Total cost for the development of additional LGG preclinical models is estimated at $55,000+/year.**

III. **LGG Imaging Trial**

Patients with LGG are closely monitored throughout their treatment, and one primary way to ascertain treatment progress is through imaging, using Magnetic resonance imaging (MRI), to understand the effects of treatment and to monitor size and structure of the tumor. Unfortunately, the changes detected by conventional MRI are often non-specific and slow to change, even in the face of progressing or regressing disease. The Translational Imaging Lab at the Center for Data Driven Discovery at CHOP is working on a more precise, non-invasive technique to assess tumor burden beyond what can be captured by an MRI. Namely, molecular imaging scans, called positron emission tomography (PET), measure tumor cell activity (metabolism) and are helping to identify markers that can better define successful treatment options. The Translational Image Lab is working to initiate a clinical trial that incorporates PET scans into LGG patient monitoring and treatment determinants. All imaging and outcomes will be included in the CBTN dataset (for those already consented onto the CBTN protocol) and thus will be available to inform future research. With a study set to launch for HGG patients as well, there is an opportunity to significantly improve patient monitoring across the pediatric brain tumor landscape. The LGG study will include 30 subjects at CHOP and can launch as soon as funding is secured. **The cost to launch the study is $50,000; the three-year cost is $150,000.**

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ENGAGEMENT

CBTN Executive Council

The CBTN Executive Council (EC) is composed of individuals and organizations committed to supporting and advancing pediatric brain tumor research together. They partner with CBTN leadership and act as the community stakeholder representative to drive global awareness, usage and impact of CBTN, and help to ensure the sustainability of CBTN. Members participate annually in three quarterly calls and attend one in-person meeting. During these sessions, CBTN provides insight and guidance on annual goals; financial, advocacy, NIH collaborations and progress; communications resources and planning; and collaborative goal setting through subcommittees.

Members of the CBTN Executive Council have access to jointly branded collateral succinctly explaining impact to use in fundraising and advocacy efforts, graphics and copy for the organization's website, and collateral recognizing Executive Council participation (this includes logo recognition, a featured story on CBTN.org, and regular emails with concise messaging for organization stakeholders). Members also have the option to request a CBTN spokesperson to provide remarks or presentations at 2 organization events per year, reports in conjunction with each EC call, and budget and communication presentations at the annual in-person CBTN meeting. We would welcome partnership in the Executive Council with Lauren's First and Goal Foundation, and to share more about this wonderful opportunity. Click here to view a list of existing EC members and their collective commitment to pediatric brain tumor research. **By becoming a CBTN Executive Council Member, each organization commits to 2 years of membership and a give/get of $25,000 annually toward CBTN core activities and operations, a $50,000 pledge.**

LGG Working Group

With 27 percent of CBTN biorepository samples allocated for LGG research, CBTN is consistently evaluating, growing and evolving its research efforts and making LGG samples and data available to researchers across the globe. In that spirit, CBTN and the Pacific Pediatric Neuro-Oncology Consortium (PNOC) currently lead a collaborative LGG Working Group, bringing together stakeholders to support translational LGG research through both consortiums with the goal to be forward thinking, strategic, aligned, and efficient in developing clinical trials. The group is led by Dr. Angela Waanders from Lurie Children's, Dr. Sabine Mueller from UCSF, Dr. Pratiti (Mimi) Bandopadhayay from Dana-Farber Cancer Institute and Broad Institute, Dr. Joanna Phillips from UCSF, and Dr. Daphne Haas-Kogan from Dana-Farber Cancer Institute. The group has grown to over 15 members, including scientists and physicians.

Through this LGG Working Group, investigators meet and bring forward their best ideas and strategies for research. Collaborating teams share data on a monthly basis, analyze findings, and share resources to hasten progress. The primary goal is to develop trials through extensive preclinical testing and investigations using imaging, body fluids, and tumor tissue, with additional focus on functional studies (including quality of life and cognitive outcomes collected as part of ongoing trials). Because more trials have been conducted for LGG, the members are very focused on taking the collected data from PNOC and CBTN and using it to inform future trials and research.

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The full list of the PNOC/CBTN Working Groups includes: Low grade Glioma, Diffuse Midline Glioma/High grade Glioma (DMG/HGG), Medulloblastoma, Atypical Teratoid Rhabdoid Tumors (ATRT), Craniopharyngioma, Ependymoma, Germ Cell Tumors, Immunotherapy, Imaging, and Diversity, Equity and Inclusion (DEI).

WITH GRATITUDE

We sincerely thank you for your past support and for considering a continued partnership to support our efforts. Together, we will accelerate the development of new therapies for the children and families who depend on us, and children around the world diagnosed with a brain tumor will be closer to a pathway for customized treatment.

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