



Children's Brain Tumor Project

powered by families

December 2014



Elizabeth Minter (1991-2012), Founder of Elizabeth's Hope

From the Desk of...
Emma Hill

Michael and I recently spent time traveling in the Southeast, where we had the opportunity to visit some old and historic cemeteries. We were initially startled to see so many graves for young children. It was a reminder that it was not uncommon for parents to lose children a century ago. Indeed, my grandmother lost a 5-year-old daughter to diphtheria and her oldest son was crippled by polio. Medicine has come a long way, but not far enough.

Today the number one killer disease in children is cancer, and the most deadly form is brain cancer. Unfortunately, progress in treating this cancer has been nonexistent. While brain cancer is difficult to treat because of the nature of the organ, the real impediment to progress has been funding for research.

Three years ago Weill Cornell and our daughter, Elizabeth, who was diagnosed with gliomatosis cerebri (GC), a rare and lethal brain cancer, launched *Elizabeth's Hope* to raise funds for research on rare and inoperable pediatric brain cancers. *Elizabeth's Hope* was and is a huge success and became the cornerstone for a bigger and more important effort, the Children's Brain Tumor Project. The premise is to secure more and steady funding through the power of families. Today more than 20 families are supporting the project and have raised nearly \$2.5 million dollars for this critical research. I love the motto of TEAM Sean: Together We Can Achieve Miracles. More families create greater awareness, which helps raise the much-needed research dollars.



Summer 2011

The other major premise of the Children's Brain Tumor Project is collaboration. The CBTP is directed by highly recognized doctors and researchers in the field. Importantly, they know how critical collaboration among doctors and institutions is to achieve the goal of a cure. As an example of leadership in collaboration, this year the CBTP launched the GC International Patient Registry (gcregistry.com). The registry will be a central database of GC cases. In the spring of 2015, Dr. Jeffrey Greenfield, a leader in gliomatosis cerebri research, will be co-chairing the first international GC research conference in Paris, France. This conference will bring together doctors from around the globe to discuss the road map for a cure. Dr. Souweidane, widely recognized for many years as a leader in the collaborative institutional effort to

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Laboratory Update

Dr. Mark Souweidane and
Dr. Jeffrey Greenfield

Co-directors, Children's Brain Tumor Project

November marked the third anniversary of *Elizabeth's Hope*, the effort that quickly grew into the Children's Brain Tumor Project. We had many supporters before then, of course, and we will be forever grateful to the all-important early believers who helped us get started, including the Cristian Rivera Foundation, The Cure Starts Now, the Lyla Nsouli Foundation, St. Baldrick's, Ian's Friends, the Dana Foundation, the Beez Foundation, and the Matthew Larson Foundation.



The launch of *Elizabeth's Hope* created a new momentum, and 2011 became the tipping point for us. Since then the Children's Brain Tumor Project has brought together more than 20 families in a drive to fund our research, raising a combined \$2.5 million from friends and family members who know all too well just how important this work is.

Thanks to our donors, today we are not only conducting important clinical trials, but we are also able to do the lab work necessary to begin new trials in the near future. Keeping that pipeline open is key to maintaining momentum. (See next page for more on that.)

Our deepest thanks to those who believed in us a decade ago, and to those whose ongoing efforts allow us to continue our work. The next three to five years will almost surely produce significant results—and with your continued support, we will find the answers we need.

Onward,

M.M. Souweidane

J. Greenfield

Make a donation today at ChildrensBrainTumorProject.org

3 Years of Progress: What Your Donations Have Done

The end of the year is usually a time for reflection, for looking back over the accomplishments and challenges of the year behind us. We have a lot to be proud of this year, but we are even more excited about our plans for 2015, when all the projects we were able to initiate this year move to their next stage. Here is an overview of our many current initiatives, none of which would have been possible with the support of our generous donors.

LABORATORY INVESTIGATIONS

Mediated Oncogenesis

Dr. Greenfield is working in collaboration with Dr. David Allis at The Rockefeller University as well as with researchers at Memorial Sloan-Kettering on this project investigating how histone H3.3 mutations affect the development of pediatric gliomas. New insights into how pediatric gliomas form may help researchers identify the next generation of treatment options.

Prolonged CED

Under the direction of Dr. Zhiping Zhou, Dr. Souweidane's lab is investigating the feasibility of delivering a weeklong infusion of DIPG-fighting drugs into a tumor instead of a single dose. The procedure has been tested in rats and may hold promise for a future clinical trial.

HDAC Inhibitors

Dr. Souweidane's lab is conducting toxicity testing on targeted compounds (HDAC inhibitors) in search of a new weapon against DIPG. The tests will provide safety data needed to progress to clinical trials, where the compounds may be used in children with DIPG.

Multi-drug Therapy for DIPG

Before researchers can test a combination of drugs against a tumor, they must identify (or create) an animal model on which to try it. Our researchers are now working on establishing genetically engineered DIPG rodent models to be used for validating multi-drug therapy using CED of targeted compounds.

Sequencing and Bioinformatics

Elizabeth Minter was the first patient whose GC tumor was sequenced in the search for genetic clues to how the tumor forms and spreads. Many more such tests are needed to establish patterns and commonalities that allow researchers to identify the best approaches to treatment, and we are now sequencing every tumor we treat.

With the addition of the first Ty Louis Campbell Fellow, Sheng Li, in September 2014, we greatly expanded our ability to process all the data generated by each sequencing. By utilizing single-cell gene sequencing technology, we are studying genomic abnormalities and heterogeneity in various types of gliomas. We are exploring the crucial genes and signaling in transformed cells, which make gliomas resistant and cause them to recur after primary therapies.

With advanced cell sorting and RNA sequencing technologies, our researchers are dissecting the glioma microenvironment, including macrophages and endothelial cells at the single-cell level, to reveal their diversified roles during glioma progression.

THE NEUROBANK

Under the supervision of Dr. Yujie Huang, we are bio-banking tumor tissue and blood samples from pediatric brain tumor patients for study by

our precision medicine team. In collaboration with other institutions in the Northeast, we are creating a valuable way for researchers to share data and conclusions, hastening our ability to find answers.

CLINICAL TRIALS

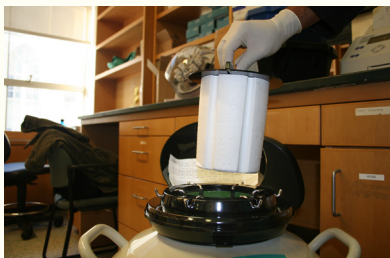
Dr. Souweidane is in the third year of his Phase I trial testing the safety of convection-enhanced delivery (CED) and radioimmunotherapy, which delivers a therapeutic agent directly to a DIPG tumor. With 17 patients treated so far, the trial shows promising results, with no adverse effects reported in any patient. Participants in the trial are now getting the sixth dose level of the seven approved for this trial. As patients are treated, Dr. Souweidane's team is using MRI-based research to monitor the distribution and clearance rates for drugs delivered to the brain stem; they are using

that data to drive their prolonged CED laboratory investigations.

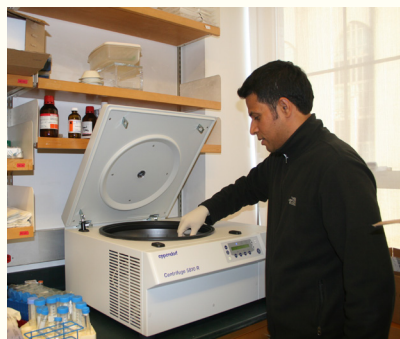
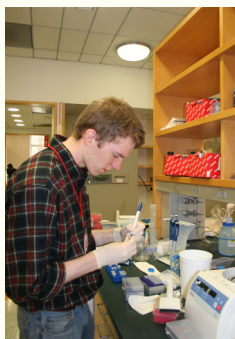
Dr. Greenfield is now enrolling patients in a clinical trial testing the safety and effectiveness of intra-arterial (IA) chemotherapy in children with malignant brain tumors. This approach seeks to avoid the side effects of intravenous chemotherapy and improve the concentration of drugs reaching the tumor itself by delivering them directly into the tumor's blood supply, bypassing the blood-brain barrier. This "super-selective IA cerebral infusion" has been shown to be safe in adults; we hope this trial opens up a new treatment option for children as well.

Moving Day

The year ended with a gratifying new beginning: Dr. Greenfield and his team moved out of their borrowed space into a dedicated laboratory on the sixth floor of the Whitney Pavilion. Thanks to our generous donors, the new lab has some important new equipment and a few new faces, as medical students and research assistants lend a hand.



Clockwise from above left: A compact, portable tank will keep tissue samples in a deep freeze while awaiting study; a brand-new microscope, fresh out of its packing material; and Dr. Prajwal Rajappa tests out the lab's new centrifuge—all three purchases were made possible by CBTP donations. Scott Connors, a medical student who works in the lab, prepares DNA samples taken from bio-banked tumor tissue for genetic sequencing.



Big News!

Yes, we do mean BIG: Thanks to a \$500,000 grant that Dr. Souweidane received from the **Rudin Foundation**, one medical student per year will be awarded a pediatric brain tumor research fellowship. Each fellow will take a year off from school to focus on CBTP research. The grant will allow us to hire a Rudin Fellow every year for the next ten years. We are so very grateful for this commitment, which allows us to initiate longer-term projects in the lab.

PLUS... the **Lyla Nsouli Foundation** has approved a grant in the amount of \$266,400 to Dr. Souweidane, allowing him to complete his DIPG clinical trial. This extraordinary gift allows Dr. Souweidane to treat patients at dose levels 6 and 7. On behalf of the children who will join the trial because of this gift, our deepest thanks to Nadim and Simone Nsouli for their generosity.

RECENT PUBLICATIONS

The Children's Brain Tumor Project researchers are conducting the investigations needed to understand tumor growth in children, reporting on the application of minimally invasive surgical techniques to improve outcomes, and working on research projects that will pave the way for our next generation of clinical trials. Here is a sampling of results published in the past year.

October 2014, **Journal of Neurosurgery** (published online in advance of print): Dr. Souweidane co-authored a new report on neuroendoscopic biopsies of brain tumors, which showed that minimally invasive approaches can produce accurate results with less intrusive surgery.

October 2014, **Child's Nervous System**: Dr. Souweidane's team published the results of a study on rats that tested "prolonged CED," which builds on the current clinical trial of single-treatment CED for DIPG. Prolonged CED is one potential way to prevent the rapid drop-off in drug concentrations in a tumor that happens after a single CED infusion.

June 2014, **Neurosurgery**: Drs. Souweidane and Greenfield published the results of a study of endoscopic endonasal surgery in children, whose smaller nasal passages were thought to make the approach impossible. Pediatric patients may be subjected to open brain surgery if doctors don't have good information about when the minimal-access alternative is appropriate; the measurements reported in this paper should make it easier for neurosurgeons to select which children could benefit from the minimally invasive alternative.

February 2014, **Cancer Research**: Dr. Greenfield's team published the results of an investigation into the role of certain progenitor cells in forming new blood vessels that encourage the growth of gliomas, and defined a signaling axis that drives the tumors to progress. Learning how to slow or stop this process could help us prevent the progression or recurrence of these brain tumors.



Holiday Gifts That Give Back

Don't forget to order your glassy-baby votive holders—10 percent of the purchase price comes to the CBTP. Choose the *Elizabeth's Hope* set or the *Family* set. Find them at: glassybaby.com/shop/sets/family
glassybaby.com/shop/sets/love-4-liz



Brothers and Sisters

When a child is diagnosed with a brain tumor, an entire family is affected. We asked some of the children's siblings to share their unique perspective on having a brother or sister diagnosed.



Gavin Campbell

Gavin was a toddler when his brother, Ty, was diagnosed with AT/RT, and just three and a half when Ty passed away. Now in kindergarten, Gavin made a drawing that shows Ty in a wheelchair and himself as Spiderman. "I got in a fight on the bus because the kids told me I don't have a brother," he says. "I yelled at them and said 'Yes I DO!' I hate the bus."



Brian Ries

Brian was 8 when his little brother Sean was diagnosed with a benign but dangerous brain tumor. Dr. Greenfield removed most of it and Sean is doing well—but Brian, now 11, remembers it as a frightening time. "I was scared because I was with my grandmother and only knew a little bit of what was going on. I knew it was something bad, but I didn't know much else. My parents didn't get many trips back to say hi or even just to see me. We were experiencing different lives, unlike the life we usually had. I knew that whether he survived or not, it would never be the same life."



Jordan Wetzel

Jordan's younger sister, McKenna Claire, was diagnosed with DIPG at age 7 and was gone before her next birthday. Jordan was 12 at the time. Now 16, Jordan says that "people tried their best to treat my sister just as they had before she was diagnosed and didn't talk to her about her illness. But with siblings, people say things like, 'I know how you feel.' I have never hated a phrase so much in my entire life."



Trey Minter

Trey and Will's little sister, Elizabeth, was 19 when she was diagnosed with GC in December 2010; she became extremely ill the following year. "A part of my childhood story died with Elizabeth," Trey says. "When I find myself lamenting my loss, when I dwell on all the experiences cancer robbed us of, I drift back to the winter of 2011 and to the lessons she taught me. Elizabeth battled unspeakable adversity, but somehow found purpose, humor, and joy in the most dire circumstances. I will not get to see her walk down the aisle and will miss her laughter at the holiday table, but she is with me in what she taught me during her struggle."

We would love to hear from other siblings who would like to share their experiences. Please email your stories to info@childrensbraintumorproject.org

From Emma Hill

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find better treatment options and a cure for diffuse intrinsic pontine glioma (DIPG), has been invited to speak about his clinical trial at the 2015 DIPG Symposium in Chicago next April. That meeting of the DIPG Collaborative brings together all the top researchers in the field in an effort to share learning and advance the science. The CBTP truly is led by some of the best minds in the field.

The families of the CBTP are grateful for your support. In three short years, thanks to your dollars, Weill Cornell has become established as a leader and innovator in pediatric brain cancer research. Thanks to the broadening support the team is able to accelerate and expand its research projects. As Proverbs 29 says, "Where there is no vision, the people will perish." We—along with the other CBTP patients, families, doctors, and researchers—all share the vision of a cure.

Thanks again for believing in our vision. Michael and I hope you will include the Children's Brain Tumor Project in your year-end giving plans.

With love,
Emma

Elizabeth's Hope and the Children's Brain Tumor Project

The CBTP was founded in 2011 when the dedication of Dr. Mark Souweidane and Dr. Jeffrey Greenfield, neuro-scientists at Weill Cornell Pediatric Brain and Spine Center, met up with the determination of Elizabeth Minter, a remarkable young woman diagnosed with gliomatosis cerebri. Inspired by Elizabeth, Drs. Souweidane and Greenfield joined forces on a monumental task: Finding new treatment options for rare and inoperable brain tumors that strike children, adolescents, and young adults. These tumors strike "only" a few hundred patients a year, so they don't get federal funding or support from larger foundations. That's why we say the CBTP is "powered by families"—because families know all too well that even one child is too many to lose.



Ways to Give

1. By Check

You may make your gift by check, payable to Weill Cornell Medical College. Please indicate "Children's Brain Tumor Project" in the memo area.

Please mail checks to:

Ana Ignat, Dept. Administrator
Weill Cornell Pediatric Brain & Spine Center
525 East 68th Street, Box 99
New York, NY 10065

2. By Credit Card

Visit childrensbraintumorproject.org to use a credit card to make a secure online donation or a monthly pledge.

3. Stock, Matching Gifts, and Other Options

To discuss corporate matching programs, donations of securities, or other options, please contact Ana Ignat, Department Administrator, at ani7003@med.cornell.edu.



Follow the CBTP on Facebook

Event Highlights

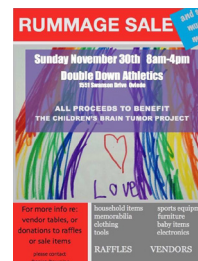
The Sixth Annual **Cristian Rivera Foundation Gala**, held at the Broad Street Ballroom, honored Dr. Souweidane for his continuing work to find a cure for DIPG. John "Gungie" Rivera, one of Dr. Souweidane's earliest supporters, presented him with a check for \$100,000 to help fund his research.



Maria Gratton organized two fundraising events for the Children's Brain Tumor Project last month: a Tastefully Simple house party and a Paint Social Art evening at Angellino's Restaurant in Mansfield, Connecticut. Many thanks to Paint Social Art and Angellino's, and thanks to Maria for working so hard on both events!



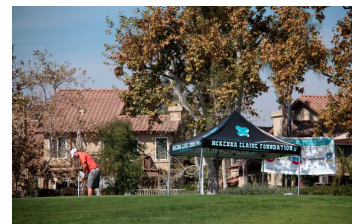
The second annual Rummage Sale hosted by **Denise Downing** required a rented storage locker to hold all the goods that were donated for it! The event brought out what seemed to be all of Oviedo, Florida, on Thanksgiving weekend to have fun and raise money for the Children's Brain Tumor Project. Many thanks to the Downings and all the rummagers!



The second annual Allie's Sale, hosted by **Team Little Owl** in Overland Park, Kansas, raised an amazing \$24,000 for the Children's Brain Tumor Project. Many thanks to Kyle and Kelly Fisher for supporting us as they honor Allie.



The **McKenna Claire Foundation** had a perfect day for the third annual Play It Forward golf tournament in Rancho Margarita, California. On December 2, Kristine Wetzal presented Dr. Souweidane with a check for \$30,000 to support the Children's Brain Tumor Project. We are grateful to David and Kristine for their generosity, and proud to have become a coast-to-coast movement!



Save the Dates: 2015

March 14: TLC Casino Night, Hyatt Regency (Greenwich, CT)

May 1: Elizabeth's Hope cocktail party (Bowery Hotel, NYC)

August 8: Muddy Puddles MessFest (Mahopac, NY)

September 12 (tentative): Bronxville Road Race (Bronxville, NY)

REMEMBER: If you hold an event, email details and photos to info@childrensbraintumorproject.org so we can include you in our next newsletter