



Dr. Jeffrey Greenfield and Dr. Mark Souweidane, co-directors of the Weill Cornell Children's Brain Tumor Project

From the Desk of...
Brenda Ries

February has always been special for me...it's the month of my birthday, it's when I met my husband 23 years ago, and on Valentine's Day 2007 my second son, Sean, was born, making our family of four complete. But in 2012, February lost its charm in a way I never could have imagined. Eight days before his fifth birthday, Sean was diagnosed with a dysembryoplastic neuroepithelial tumor (DNET) in the left side of his brain. Told by doctor after doctor that his tumor was inoperable due to its size and location, we were not given many good options for treating Sean: surgery that would likely leave him with a devastating brain injury; chemotherapy that might not even work on his type of tumor; or radiation, which can have devastating long-term side effects on the developing brain of a 5-year-old child.



Sean Ries

But we were also told that we were "lucky," since this wasn't an aggressive tumor and there was an 80% chance he would be alive in five years. Although I wasn't feeling very lucky, that was actually some of the best news we had heard, and yet it made me so mad. I didn't want to talk about Sean maybe being alive in five years...that just wasn't good enough! I have since come to appreciate what "good news" that really was, though, as I know too many parents who would have given anything to get those statistics for their child.

February 2012 is also when we met Dr. Jeffrey Greenfield, the first doctor to give us real hope for Sean. Here was someone who was not just talking about trying to survive five years, but was looking for a solution that would let Sean live a long life. He was committed to finding a safe way to treat his tumor, and was not willing to sacrifice Sean's quality of life to do it. Three risky brain surgeries later, most of Sean's tumor is gone, and he is not just surviving but is thriving thanks to Dr. Greenfield! Fast forward to February 2016: our brave boy turned 9 years old, his 9-month MRI showed that the remaining tumor was still "asleep" and stable, and Sean finally made it one year seizure free, a big first step towards getting off medication. February was a good month for us again!

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Laboratory Update

Prajwal Rajappa, M.D.

Precision Medicine Fellow, Children's Brain Tumor Project

I am very proud to be working in the Children's Brain Tumor Project laboratory, and quite astounded at how fast the initiative has grown. I was appointed as a Fellow in 2012, when I was assigned to work on the role of bone-marrow-derived cells in low-grade glioma transformation. Today, I'm honored to lead the daily operation of our lab's partnership with the Weill Cornell Institute for Precision Medicine (IPM), which allows us to do exactly the sort of personalized medicine that we dreamed about just a few years ago.



Dr. Prajwal Rajappa

Thanks to the IPM, we can now offer genomic sequencing to every single child treated here for a brain or spinal tumor—at no cost to the family. Before surgery (whether it's a biopsy or resection), the patient provides a cheek swab or blood sample to capture data on his or her normal DNA. Then, during surgery, small specimens of any tumor tissue removed are sent to the team at the IPM core facility for further DNA analysis.

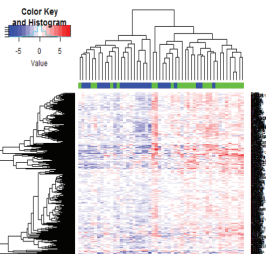
Technical specialists at the IPM extract DNA from these specimens so they can analyze the genome, then screen for mutations among 500 known cancer genes. After they perform the initial sequencing, they generate a report and send it back to me to analyze. It is my responsibility to evaluate the data within this report and search for clues as to how those mutations might best be addressed. I perform extensive research across the scientific literature in search of publications that have identified potential drugs or other treatment options that may be effective in this particular patient against these specific mutations. I also look at specific genomic mutations in each patient and compare them across all cancer cohorts, using new streamlined "big data" portals such as the cBioPortal for Cancer Genomics at Memorial Sloan Kettering, The Cancer Genome Atlas (TCGA) run by the National Cancer Institute, and the U.K.-based COSMIC catalogue.

After a comprehensive chart review of the patient's medical history and disease course, I present the findings to our multidisciplinary tumor board, which consists of scientists, physicians, surgeons, pathologists, and systems biologists. The tumor board reviews the findings from my case presentation and may determine the best treatment options. If there are clinical trials available at any institution across the country that may be appropriate for the patient, we will identify them.

Finally, the results of the sequencing and the recommendations of the tumor
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DIPG Clinical Trial Update

It will be four years in May since Dr. Souweidane treated the very first patient in his clinical trial testing the safety of convection-enhanced delivery (CED) of 124I-8H9 against DIPG. (The 8H9 antibody has been shown to bind to the tumor, and 124I kills cancer cells with radiation.) The trial was originally expected to last for two years and treat 12 DIPG patients at four dose levels; in 2014 the FDA approved an extension of the trial to seven dose levels. Dr. Souweidane is currently treating patients at the seventh dose level, and has re-treated several children. There have been no adverse effects on any child.



A Glimpse of “Big Data”
Mysterious as it may look, this heat map holds a treasure trove of information about 53 DIPG patients. The CBTP is now studying the role of Poly (ADP-ribose) polymerase (PARP) in patients with DIPG; this map shows patients organized by PARP gene expression.

Unlike standard IV or oral chemotherapy, CED delivers the agent directly to the tumor and does not pass through the kidneys, liver, or other organs the drug might damage. It also gets more of the drug directly to the tumor, since it's not blocked by the protective blood-brain barrier. The CED method has been shown to achieve more than 1,000 times the concentration of the drug in the tumor site than other chemotherapy, without the toxicity of other delivery methods.

“Each treatment is a marathon for everyone,” says Dr. Souweidane. “We typically

begin at 7:30 in the morning and often don't finish until 3 or 4 am the following day. That's not only tough on the OR team, but it's also hard on the waiting family. But with each and every child treated we learn something new, and I'm extremely encouraged by the results so far.”

Dr. Souweidane now has extensive data on how the agent penetrated each tumor, what concentrations were achieved, and how long the drug stayed in the tumor. Once the final dose level is complete, Dr. Souweidane expects to move the trial to a multi-site model, in which patients across the country can be treated without having to travel to New York. Not only will more children be treated, but the trial can proceed to the phase in which it is tested for effectiveness and not just safety. Testing other agents, at different dosages, will provide an enormous amount of new data for researchers to plumb for answers.

From Brenda Ries (continued from page 1)

I am reminded every day of what a miracle Sean is, and with every good scan it gets easier to believe he's going to win this fight, but the fear we faced that first day is always lurking. While I know it is great progress that Sean's MRIs will now be annual (in February!) going forward, it scares me. There was a sense of comfort in checking on that tumor every few months to make sure nothing was going on. Instead, I will worry every time Sean has a headache, trips and falls, can't remember something, is overly tired, or is struggling in school—what does it mean? Is the tumor growing? Are the seizures starting again? I'm not complaining, though—it is worry I know I am lucky to have.

It is the hope we first got from Dr. Greenfield that day in February 2012 that drives all I do to support the Children's Brain

Brothers and Sisters

Matthew Bernstein
Youth Volunteer Coordinator, Fly a Kite Foundation

“You have cancer” are three words no child should ever hear. Most people, however, don't realize the impact those words have on the people around the child. It was an odd feeling when the word “cancer” was first used around me. My brother, Zachary, was diagnosed with an inoperable brain tumor called DIPG in 2013 and fought for 9 months, passing in March of 2014.



Matthew Bernstein

Throughout Zachary's illness, I was forced to mature at a rather rapid pace. No one teaches you at 14 how to deal with your sibling having cancer. It was tough going to doctors and hospitals weekly. It was even tougher watching my brother slowly being taken away from me. It all started with radiation, which caused his hair to partially fall out. We had anticipated this, and it made him self-conscious being the only kid in his school with hair loss and physical changes.

My role as his brother was to keep his spirits high and make him feel as normal as possible. I made sure our relationship remained jocular, whether on a good or bad day. As much as my brother was dealing with changes, I too had to deal with unexpected changes. I felt lonely and isolated at times; the opportunity to share my anger with friends was limited because none of them had been through an experience even close to this. I was also concerned bringing up my emotions to my parents for fear it would cause them more heartache and pain.

When my brother passed it was difficult, yet in a way it was somewhat relieving. I felt the weight of responsibility dissipate and relief wash over me. Unfortunately, his passing had several profound effects on my life. I matured more rapidly than I would have hoped, causing me to feel displaced at times. It was a struggle balancing my social life with my personal life, and as a result some of my friendships were damaged.

If I can offer any advice, it would be one thing: have hope. Times will get tough, and you will get down, but hope can provide comfort.

Tumor Project. It's what brought me together with three other families last year to form the Children's Brain Tumor Family Foundation, an organization committed to raising awareness and funding the ground-breaking research underway at the CBTP. I want every child diagnosed with a brain tumor to be given that same hope that we got, to have better/safer treatment options, for parents to be told their child *will* be alive in five years and beyond, and—selfishly—should Sean's tumor ever decide to “wake up,” I want to know there is something that can be done. Our motto is Together Everyone Achieves Miracles, and we will not stop until that miracle cure is there for every child diagnosed with a brain tumor.

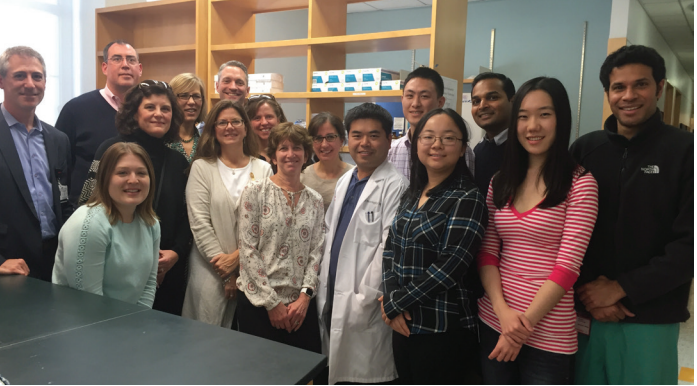
Brenda

Family Update

We are so very grateful to the more than 3,000 supporters who have donated to the CBTP. But we'd like to take this opportunity to offer a special thanks to the donors we *don't* know, the ones who support our families at their events throughout the year. Those generous friends who attend the events, buy the cupcakes, and run the races—those are the people whose dollars add up and allow our families to support us the way they do. Our deepest thanks to the communities who stepped up in 2015 to help our families make these generous contributions:

The **Christian Koehler Foundation** raised \$17,500 for us at its annual lacrosse tournament. We appreciate the gift so much more knowing that the funds come from young athletes and families honoring Christian by playing one of the sports he loved.

The board of the **Team Campbell Foundation** came to visit the new lab, bringing with them a check for \$10,000 to support the research. Board members are pictured below with the CBTP team on their lab tour .



The **McKenna Claire Foundation** donated \$75,000 to the CBTP, the proceeds of their California fund-raising events. We are so very grateful for the gift, and proud to say we represent families from coast to coast.

The **Samuel Jeffers Childhood Cancer Foundation** of Grover Beach, California, chose the CBTP as a beneficiary of its fund-raising efforts. The foundation has set a goal of raising \$75,000 to help establish a Samuel Jeffers Fellowship at the CBTP to research thalamic gliomas.

Elizabeth's Hope donated more than \$100,000, half of which went to support our tumor registries, which are crucial to collecting data about brain tumor patients worldwide. Elizabeth's Hope and the Minter family are responsible for raising more than \$1 million dollars for the CBTP to date.

The **Ty Louis Campbell Foundation** has funded the Ty Louis Campbell Fellowship for the past two years, bringing much-needed bioinformatics talent to the team. The TLC Foundation recently committed to extending the fellowship for a third year.

The **Olivia Boccuzzi Foundation** of Brooklyn donated \$50,000 to the CBTP in 2015, the proceeds of the annual Stomp Out Cancer kids' marathon.

Thanks to Team Little Owl, **Head for the Cure** in Kansas City granted

us \$20,000 for our research. Kyle and Kelly Fisher made the introduction for us and helped secure the gift, for which we are deeply grateful.

The **Cristian Rivera Foundation** raised more than \$100,000 for the CBTP at its superheroes-themed Celebrity Gala in November. The Cristian Rivera Foundation was supporting Dr. Souweidane's research before there even was a Children's Brain Tumor Project and has now raised more than \$550,000 for his DIPG research.



Introducing the Children's Brain Tumor Family Foundation

The **Children's Brain Tumor Family Foundation (CBTFF)** was born in 2015, bringing together several of our families who had been fund-raising independently. The new CBTFF came out of the gate strong, receiving a \$10,000 donation from AT&T, which awarded it on behalf of the winners of its Chairman's Challenge. Thanks to Brenda Ries for leading the winning team, and to Kelly Fisher, Kathleen Clark, and Denise Downing for starting this new initiative.



For 2016, in addition to individual family fund-raisers, the CBTFF has signed on as a charity partner with the Rock'n'Roll Marathon Series and will be recruiting teams in several cities, with the most likely locations this year being Philadelphia, New York, Los Angeles, San Antonio, and St. Louis. If you'd like more information about joining or forming a team in one of those cities, or in one of the other Rock'n'Roll Marathon Series cities, contact the CBTFF at cbtff2015@gmail.com.



Upcoming Events

- April 3:** Muddy Puddles Day Indoor “Mess Fest” (Somers, NY)
- April 9:** TLC Foundation's Share the Love Gala (Greenwich, CT)
- May 21:** 7th Annual Christian Koehler Lacrosse Tournament (East Islip, NY)
- May 22:** Cheering for Caitlin 5K (Oviedo, FL)
- May 22:** BANDs Together Against Brain Tumors Concert (Parsippany, NJ)
- June 4:** McKenna Claire Foundation's “Bootlegger Ball” (Huntington Beach, CA)
- July 30:** Muddy Puddles Annual “Mess Fest” (Camp Kiwi, Mahopac, NY)
- Sept 17-18:** Rock'n'Roll 5K and Half Marathon (Philadelphia, PA)
- Sept 17:** TLC Foundation's TYathlon (Mahopac, NY)
- Oct 8:** Rock'n'Roll Half Marathon (Brooklyn, NY)
- Oct 15-16:** Rock'n'Roll Half Marathon (St. Louis, MO)
- Dec 3-4:** Rock'n'Roll Kids Rock, 5K, 10K, Half Marathon, Relay, and Marathon (San Antonio, TX)

Be sure to check the CBTP calendar for updates to events. If you're planning an event, let us know and we'll add it to the calendar.

Visit: ChildrensBrainTumorProject.org/cbtp/events/

New Publication From the CBTP

Pediatric Suprasellar Tumors

Published in the *Journal of Child Neurology* December 15, 2015

By Heather J. McCrea, MD, PhD; Emilie George, BA; Allison Settler, FNP-BC; Theodore H. Schwartz, MD; and Jeffrey P. Greenfield, MD, PhD

The focus of our research at the Children's Brain Tumor Project is on rare and inoperable pediatric brain tumors, but we are also leaders in the surgical treatment of other brain lesions. In this paper, our team provides a review of childhood suprasellar tumors, meaning tumors that form in the region just below the hypothalamus. Many different tumor types may develop in this region, including craniopharyngioma, chiasmatic glioma, germ cell tumor, Rathke cleft and arachnoid cysts, pituitary adenoma, and histiocytosis. Many of these tumors are benign, but the location—near the optic nerve, pituitary gland, hypothalamus, and third ventricle—can affect vision and cause both endocrine dysfunction and hydrocephalus. This paper provides neurosurgeons with valuable information to help diagnose and treat the various types of suprasellar tumors.



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, neuroscientists 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.



Elizabeth Minter (1991-2012)

Ways to Give

1. By Check

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

Please mail checks to:
Ana Ignat, Dept. Administrator
Weill Cornell Pediatric Brain and 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.



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Laboratory Update *(continued from page 1)*

board are presented to the patient and family by the managing pediatric neuro-oncology team to help guide their decision-making process. As the Pediatric Brain Tumor Precision Medicine Fellow, it is my most important responsibility to make sure the family is informed of all recommendations that may result from the tumor board meeting.

Of course, there is still more progress that needs to be made in this relatively new field of personalized medicine. Many of the tumors that we have sequenced and the mutations we've identified still do not have effective treatments. We need to identify more targetable mutations and more efficacious drugs and/or drug combinations. Once we understand an individual tumor on the molecular level, we will be able to better choose the right agent to utilize for that patient. One thing we have learned from our sequencing efforts is that each tumor is biologically unique, which is crucial to understanding the molecular underpinnings of the disease. This realization also changes our approach to treatment and may ultimately lead to a better outcome for patients in the future.

*"We already have mice models who have brain tumors. But imagine a time when we can say, this mouse has your child's brain tumor, and it responded to this combination of drugs, which we can now offer your child."
- Dr. Jeffrey Greenfield*

We are working hard right now on planning the next steps in this important project. We have just recently injected tumor specimens from select patients into mouse brains. Our goal is to use these mice to model the disease and ultimately test combinatorial agents that may prolong survival in these animals. The agents we identify with the best response in these animals could then be tested for safety and effectiveness in patients.

All of us here at the CBTP are working furiously toward the day when we can apply what we're learning in the lab to our patient population. Our thoughts are always with the children and their families. Every day, even as we get closer to the answers we need, families continue to hear a diagnosis without hope. We know that our job is creating that hope, and we know we could not do it without you and your generous support.

A handwritten signature in blue ink, which appears to read 'Joe Girardi'.

Joe Girardi Lends His Voice to the Cause

New York Yankees manager Joe Girardi recently teamed up with the Fly a Kite Foundation to help raise awareness and funds for DIPG and other pediatric brain tumors. If you haven't yet seen the video featuring Girardi, head over to flyakitefoundation.org to watch.

