



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

Fall 2016

From the Desk of...
Barbara Zak Anderson

*They say that life is a highway and its milestones are the years,
And now and then there's a toll-gate where you buy your way with
tears.*

-Joyce Kilmer ("Roofs," 1917)

September is all about milestones, with its back-to-school firsts and the excitement of new beginnings. This year we have a special milestone: After 40+ years in my childhood home, including 14 years raising our family in it, the Andersons have moved! That house was a home base we had only ever planned on expanding, but Hurricane Irene five years ago, then Sandy a year later, was the beginning of the end. We began to mourn our home then, but we never could have imagined what was yet to come. I've learned a lot in the past five years about "the best laid plans."

On July 1, 2008, Lily LaRue Anderson ("twin B") was born—naturally and epically, butt first and fists flailing—seven minutes after Brady Cooper. I had greeted each of my three prior babies with a proper "Happy Birth Day!" but I asked this one, "who ARE you"? I did not know it then, but this was to be the ride of my life.

Still, it wouldn't be fair to say that this is the date that defines me, since no one ever prepares you for the dates you never knew existed.

The date of diagnosis.

The date of radiation,
chemo, mask fittings...

All the dates of every
single MRI.

The day *something*
changed.

The day she couldn't walk.

The last day she said my
name.

The day she died: April 6, 2015.

All these days make me.

Lily LaRue was diagnosed on May 4, 2014. We were in Hershey, Pennsylvania, celebrating Kentucky Derby weekend (as we always

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Laboratory Update

Mark Souweidane, M.D., and
Jeffrey Greenfield, M.D., Ph.D.

A DIPG Milestone

As many of you probably read about on Facebook, on September 8 we treated the final patient in our Phase I clinical trial of convection-enhanced delivery (CED) for diffuse intrinsic pontine glioma (DIPG). The trial, which had enrolled 27 patients over the past four years, was designed to test the safety of CED as a means of delivering a cancer-fighting drug directly to the site of a DIPG tumor. Four patients received a second infusion, bringing the total number of treatments to 31.

This trial has generated a wealth of information, and we have already started publishing academic papers about it, sharing our discoveries with other researchers in the spirit of collaboration that drives this project. Details of the infusion technique, the imaging studies, and other learning that will assist other researchers worldwide have already appeared in academic journals (see page 4 for a sampling of our recent publications). The "big one," providing data on the safety of the procedure, will probably take a year or more to prepare for publication. But with no dose-limiting toxicity in any patient, we feel confident that the technique is a safe way to deliver cancer-fighting drugs to a DIPG tumor.

The next steps are to identify the most promising drugs to test in future phases of this trial. Fortunately, thanks to our generous donors the legwork on that has already begun. See page 2 of this newsletter for an update on the results of our "summer sprint," the unprecedented effort that brought a dedicated team of young researchers into the lab in July and August to help us lay the foundation for future trials.

These talented young investigators didn't work only on DIPG, however. The drugs they evaluated, the molecular modifications they tested, and the other innovative lines of research they pursued will be of invaluable help as we continue to forge this path. Thank you all, again, for the continued loyal support that allows us to do this important work.

Onward,

Make a donation today at ChildrensBrainTumorProject.org

Exciting Results from the “Summer Sprint”

Thanks to a number of grants and private donations, in July and August the CBTP lab team was joined by several young researchers working on specific projects to advance the field of pediatric neuro-oncology. This “summer sprint” was an unprecedented effort that produced some excellent results.

Umberto Tosi, funded by a POST grant from the Alex’s Lemonade Stand Foundation, worked on a project to improve the measurement of drug delivery to the brain via “theranostic” (therapeutic and diagnostic) agents.

The usual method of determining whether a drug has been successfully delivered is to wait for a clinical response, a “wait-and-see” approach that is neither timely nor precise. If researchers could modify a drug to make it fluorescent—and therefore visible on PET or MRI imaging—they would be able to see in real time whether that drug has reached its target. The key is to make delivery of the drug visible and measurable without reducing its effectiveness.

Working with collaborators at Weill Cornell Medicine’s Molecular Imaging Innovations Institute (MI3), Umberto tested several modified versions of the drug dasatinib both in vitro (in petri dishes) and in vivo (in animal models). Several of them acquired their new imaging potential while retaining their therapeutic properties, and they will advance to further rounds of testing on several different malignancies.

The modification technique was then performed on panobinostat, a drug that has already shown significant promise in the treatment of DIPG. As we had hoped, the modified panobinostat was successfully imaged with PET/CT and its therapeutic properties were not altered. We hope this new compound will allow for a more precise treatment of DIPG.

Raymond Chang tested ways to combine drugs to defeat DIPG, which has defense mechanisms that allow it to evade otherwise effective drugs. Research has identified certain molecular signaling pathways that could be promising targets for drug therapy, but the tumor has alternative pathways that allow it to grow despite use of a single drug.

Raymond tested several drugs, individually and in combination, on DIPG cell lines grown in our lab and discovered one potent inhibitor of DIPG growth in vitro. After combining that drug with several other classes of drugs, he found a MEK-inhibitor that showed substantial synergistic effects. Raymond will continue his work in the lab, where he is now using xenograft mouse models of DIPG to demonstrate that this drug combination will be more effective in reducing tumors than either drug individually. Raymond’s summer assignment was funded by the American Brain Tumor Association.

Emilie George established in vitro cell models of gliomatosis cerebri (GC). Together with the Greenfield lab team, Emilie initiated a drug screening protocol to begin testing chemotherapeutic agents on this newly developed cell model. This project is ongoing and promises to

add important information to our understanding of the best ways to treat this disease.

Emilie also analyzed and interpreted data on all reported cases of gliomatosis cerebri in the peer-reviewed literature to better understand the incidence and outcomes of GC in the past. Emilie’s research was made possible by a grant from the St. Baldrick’s Foundation.

Christopher Marnell, funded by the AANS/NREF, joined our collaboration with MI3 in which we are exploring the use of peptide-based nanofibers (NFP) to extend the length of time a drug is effective when delivered by CED. A big question is whether a drug would retain its anti-cancer effects after being modified and coupled to the nanofiber. Using in vitro techniques, Christopher showed that dasatinib, which is currently used to treat certain types of leukemias and has been explored for use against DIPG, could still block the growth of DIPG cells when added onto the nanofiber. This is an important finding that will enable the nanofiber project to continue.

Christopher also tested 114 drugs that are FDA approved for other cancers with the hope of repurposing some of them to treat DIPG. This was the first time many of these drugs (which were provided by the NCI/NIH) were tested against DIPG patient cells, and the results are very promising. Four drugs commonly used to treat breast and prostate cancer (and that target genes with roles previously unrecognized in DIPG) were found to strongly block the growth of DIPG cells in vitro. Testing in mouse models will soon follow to better characterize these drugs’ potential for use against DIPG.

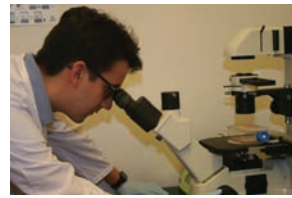
PLUS...

Tina Bharani, a medical student from Qatar Weill Cornell Medical School, joined staffer Rachel Yanowitch to study immunoglobulin superfamily member 3 (IgSF3) and its role in glioma invasiveness. IgSF3 is a novel gene candidate identified by the Greenfield lab and thought to play a role in how tumors spread throughout the brain. High school student **Jared Bassett** assisted. The IgSF3 project is still in its earliest stages and results will be ongoing.

Matthew Bernstein, a high school junior whose work was supported by the Samuel Jeffers Foundation, identified several partner institutions willing to share tissue samples of thalamic glioma. He also conducted a literature search and compiled an overview of the data on thalamic glioma, providing an invaluable resource for our researchers.

Benjamin Shtaynberger helped evaluate data that will form the basis for a new academic paper on gliomatosis cerebri (GC) to be published by Dr. Greenfield’s team. **Kunal Garg** assisted Dr. Greenfield in studying how low-grade gliomas transform into deadly malignancies.

We are grateful not only to the foundations whose grants supported these researchers but also to the private donors, especially those from the Cristian Rivera Foundation, whose generosity provided the drugs, equipment, and supplies they needed to complete their work.



Top: Umberto Tosi. Center: Raymond Chang. Bottom: Rachel Yanowitch, Jared Bassett, Tina Bharani, and Emilie George

Family Update

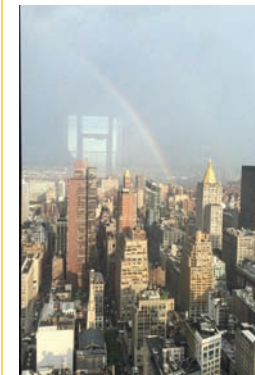


An amazing 334 people ran and walked for Team Little Owl in the August 28 Head for the Cure 5K in Overland Park, Kansas. Many thanks to Kyle and Kelly Fisher, whose supporters came out in such numbers to raise funds for the Children’s Brain Tumor Project.

One of our newest CBTP families, the LyonHearted Foundation, held a kickball tournament that raised \$20,000 for family assistance and research support.



As if the view from The Beatrice isn’t spectacular enough, this year’s Cocktails for Cam provided an extra rainbow treat for party-goers. Thanks to Greg and Robin Hoyt for this elegant annual fund-raiser.



Spectacular weather helped make the Lily LaRue Foundation’s golf outing in Emerson, New Jersey, an early summer success



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



A “dirty dunk,” food fights, and full-body painting were among the messy highlights at the 2016 MessFest at Camp Kiwi, sponsored by the Ty Louis Campbell Foundation/Muddy Puddles Project. Cindy and Lou Campbell throw one heck of a dirty party!

Upcoming Events

- September 17:** TLC Foundation’s TYathlon (Mahopac, NY)
- September 24:** Long Beach Luau (Long Beach, NY)
- September 25:** Believe in Brooke Defeat DIPG 5K (Ridgefield, CT)
- September 30:** Rockin’ for SuperTy benefit concert (Upton, MA)
- October 6-8:** Allie’s Sale (Overland Park, KS)
- October 8:** Rock’n’Roll Half Marathon (Brooklyn, NY)
- October 14:** McKenna Claire Foundation Play It Forward Golf Tournament (Huntington Beach, CA)
- November 4:** Elizabeth’s Hope Fifth Anniversary Cocktail Party (Bowery Hotel, NYC)
- November 30:** Cristian Rivera Foundation Annual Gala (Broad Street Ballroom, NYC)



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

ChildrensBrainTumorProject.org/cbtp/events/

New Publications From the CBTP

"Exploring the role of inflammation in the malignant transformation of low-grade gliomas." *Journal of Neuroimmunology*, 2016 Aug 15;297:132-40. Epub 2016 May 25.

"A novel magnetic resonance imaging segmentation technique for determining diffuse intrinsic pontine glioma tumor volume." *Journal of Neurosurgery, Pediatrics*, 2016 Jul 8:1-8. [Epub ahead of print]

"A Novel Methodology for Applying Multivoxel MR Spectroscopy to Evaluate Convection-Enhanced Drug Delivery in Diffuse Intrinsic Pontine Gliomas." *AJNR American Journal of Neuroradiology*, 2016 Jul;37(7):1367-73. Epub 2016 Mar 3.

"Gliomatosis cerebri: A consensus summary report from the First International Gliomatosis cerebri Group Meeting, March 26-27, 2015, Paris, France." *Pediatric Blood Cancer*, 2016 Jul 28. [Epub ahead of print]

"Convection-Enhanced Delivery for Diffuse Intrinsic Pontine Glioma Treatment." *Current Neuropharmacology*, 2016 Jun 13. [Epub ahead of print]

"Clinical Genomics: Challenges and Opportunities." *Critical Reviews in Eukaryotic Gene Expression*, 2016;26(2):97-113.

You can find summaries of these papers on PubMed.com

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.



Follow the CBTP on Facebook

From Barbara Zak Anderson (continued from page 1)

did) and she fell at the pool. We wanted to make sure she could go on roller coasters the next day, so we took her to the hospital. (We hoped no one would think we were silly, overly cautious parents, and the irony of that is NOT lost on me.) It was there that we were introduced to "the room."

The room may be different for everyone in its geography, smell, or shape, but we all know that room. It's where they took us to tell us they'd found a lemon-sized mass in Lily's brainstem. No, there were no symptoms. No, she was FINE. No, do it again, you're wrong...

We traveled thousands of miles in her remaining 337 days seeking a cure, and we would have traveled a million more. We researched and reached out from a place of acute and overwhelming confusion and knowledge, in a place and time we never knew existed. Pediatric cancer. Brain tumor. Cannot remove.

"Cannot cure it, Mrs. Anderson..."

Yet somehow we never lost hope, and in our travels we came across the people who were "right" for the time. I had been asked to speak at a brain tumor foundation gala, and Jeff Greenfield came up to me in the parking lot later and said, "I think we can do something." In the days that followed, I found myself



in correspondence with Mark Souweidane and his office. Mark and Jeff may not even recall all the moments and conversations, but I remember everything, and my loyalty and support will always be fast and firm. Always.

I would be lying if I did not acknowledge the milestone that changed me forever, and that stays with me always. With all my days and dates and moments, all profound and impactful on my heart and soul, there will always be one day, hour, and minute that severed me from my "before." All those other dates I keep in my heart merely shadow the framework of April 6, 2015, at 7:01 am. The day that marks me, that represents all my sad, worst days of remembrance and memory, has made me better.

How is that possible? How did I not die, too? But is HAS helped me help. Has made me see my path. No, I am NOT "okay." Time hasn't healed a thing. But...somehow, somehow, I AM *better* because of her. Her example, her essence. Her story in my life. Her everything... My unicorn. My Lily LaRue.

September is *not* just back-to-school anymore for some of us, those with one less backpack to shop for. Now it is #gogold and Pediatric Cancer Awareness Month (which, before cancer, I never realized existed). And now we LIVE and FIGHT for this. Now and ALWAYS. Broken, as only parents who have been through this can be or understand, yet better and stronger together than apart. We ARE the Children's Brain Tumor Project. We are proud and honored to be with you, "Powered by Families." Always. I use her #yellyvoice to continue and be THE change.