Children's Brain Tumor Project
powered by families

November 2016

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

From the Desk of...
Emmie and Mike Minter

On New Year's Eve 2010 our lives took an unimaginable turn: A doctor told us that our seemingly healthy 19-year-old daughter, Elizabeth, had inoperable brain cancer. We were advised to take her home, find palliative care, and expect her to succumb to her disease within the year. Words cannot describe our devastation, despair, and anger. How is it possible in this day, when we send space probes to the edge of the solar system and develop driverless cars, that there can there be no effective treatment options? There was literally no hope—only prayers for a miracle.

Summer 2011

In November of 2011, while under hospice care, Elizabeth, along with her family and Dr. Jeff Greenfield, launched *Elizabeth's Hope,* an effort to raise funds for research on rare and inoperable pediatric brain tumors—an area of inquiry largely ignored by the pharmaceutical industry and the government. Friends, family, and even strangers responded, and the cornerstone for the Children's Brain Tumor Project was laid.

Five years ago, we hoped that our effort would translate into something meaningful. Thankfully, it has. The Children's Brain Tumor Project is now a well-recognized collaborative leader in the field.

Today, while there are still no cures, I am proud to say that there are real glimmers of hope on the horizon thanks to work of the CBTP. Among the promising new approaches is a novel drug delivery system for pediatric brain tumors pioneered by Dr. Mark Souweidane. In addition, with the move into permanent lab space the doctors are now able to grow pediatric brain cancer cell lines and test different drugs and drug combinations against the tumors in both petri dishes and in mice.

The promise of personalized medicine is becoming a reality. Dr. Greenfield and his team are working closely with the new Precision Medicine Institute at Weill Cornell to sequence every pediatric brain tumor treated there. Samples of these tumors are now implanted into animal

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Laboratory Update

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

There's an old adage that says if you want to go fast, go alone; if you want to go far, go together. Research science rarely adheres to that—investigators spend a lot of lonely hours peering into microscopes and scrolling through endless data points, all in the hope that someday all that solo work will add up to a breakthrough. We often go alone, and go far, but usually not fast.

The Children's Brain Tumor Project has also defied that adage in that we are going fast, but together. This requires teamwork like no other—we need other labs at Weill Cornell, tissue banks around the country, and other scientists comparing notes and sharing findings—because we know we need to move quickly, and get far.

That's what makes 2016 so gratifying to us. We made so much progress this year, from joining the Children's Brain Tumor Tissue Consortium to publishing half a dozen papers to successfully concluding our DIPG clinical trial. Our "summer sprint" laid the groundwork for future trials being planned right now. We've discovered new ways to measure tumor volumes and drug concentrations in brain stem tumors, which will be invaluable in those trials. And we have a partnership with our Precision Medicine Institute that allows us to examine every pediatric tumor we biopsy, not just for research but to actually match individual tumors with the most promising treatment options.

Obstacles remain, and there is still much to be done. The path before us is neither clear nor straight, but we have a dedicated team that allows us to navigate it together. Our team includes not just the researchers, technicians, and students who put in those long hours in the lab, but also the thousands of supporters who run the 5Ks, attend the galas, and buy the raffle tickets that provide funding for our work.

Some of our team's most valued members are the families who know all too well the price of delay. They are the parents, grandparents, siblings, aunts and uncles, cousins, neighbors, friends, and schoolmates of children diagnosed with brain tumors, and who take up this cause for intensely personal reasons. We are so grateful to them for their dedication to this cause, and to their thousands of supporters for their ongoing enthusiasm and loyalty. Know how much we count on your continued gifts to keep our research going. Together, we will go fast—and far.

Onward,

Make a donation today at ChildrensBrainTumorProject.org

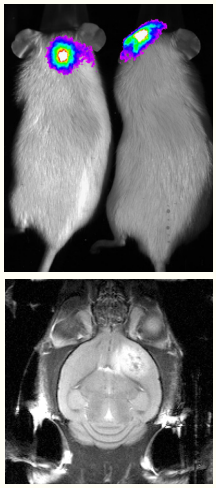
Discover. Share. Repeat.

The Children's Brain Tumor Project made amazing progress this year, not only in terms of what we learned but also in what we shared. The fact is, getting our discoveries out into the scientific community is just as important as making them in the first place. Research is such an iterative process—we make a small but significant finding and share it by publishing an academic paper read by colleagues around the world, which they then use to advance their own work. They publish their new findings, which we then read and use to inspire our next steps. Back and forth, one step at a time, we move the science forward.

First-Ever GC Xenograft Created in CBTP Lab

Perhaps the greatest milestone in 2016 came when Dr. Uday Bhanu Maachani established two gliomatosis cerebri cell cultures from living patients. From one of these lines he created a xenograft: A mouse model with a GC tumor sampled from an actual patient. This is the only animal model anywhere in the world with a GC tumor cultured from a patient.

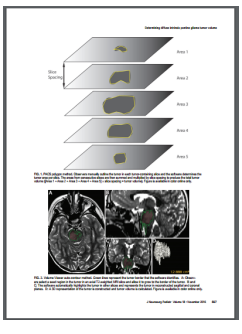
Why is this so exciting?
The promise at the heart of precision medicine is one-to-one matching of disease and cure—creating a xenograft from a patient tissue sample allows us to test promising treatments against that individual's exact tumor in a living model. We are tremendously excited by this advance, even as we face our next hurdle: identifying and gaining access to a drug with the best chance of destroying that tumor.



In August, Dr. Maachani injected mice with tumor cells from a patient with GC; imaging a month later confirmed that he had created the first animal model of an actual patient tumor. At top are bioluminescence images and at bottom is an axial MRI scan that clearly shows the GC tumor as the bright white spot in the striatum (cortex) of the brain.

That's why 2016 was such a big year for us. We made some very interesting findings, but we also concentrated on sharing them. The Internet is a big help here, since it shortens the time it takes to disseminate information. An accepted paper can spend months in the queue for publication, but academic journals now publish electronically in advance of print. That gets our findings into circulation much faster, and it also lets us learn from other labs in a more timely way.

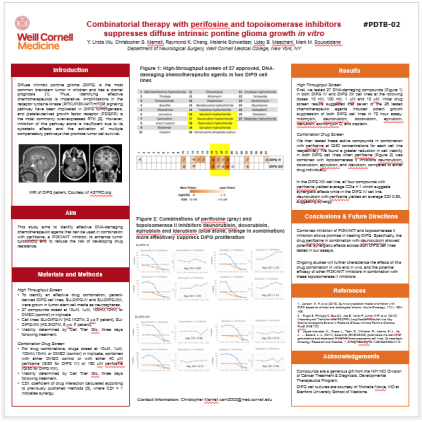
For example, one of our papers appears in the current (November 2016) issue of the *Journal of Neurosurgery: Pediatrics,* but it was made available to other researchers in June. "A novel magnetic resonance imaging segmentation technique for determining diffuse intrinsic pontine glioma tumor volume," by Dr. Souweidane's team, describes an innovative way to measure DIPG tumors. With its irregular borders and diffuse characteristics, a pontine glioma is notoriously difficult to measure. As we move toward finding the right drugs to tackle DIPG, and the right way to deliver them, it becomes very important to know the exact volume of an individual tumor. This new method of measuring a tumor will help establish the best dosage for each patient.



Dr. Souweidane's study showed a way to improve the accuracy of DIPG tumor measurement.

Another milestone paper was released earlier this year in the journal *Critical Reviews in Eukaryotic Gene Expression.* That paper, "Clinical Genomics: Challenges and Opportunities," was published by Dr. Greenfield's team, including Ty Louis Campbell Fellow Sheng Li, and provided an overview of clinical genomics from study design to computational analysis. As the science of genome sequencing races forward, this kind of overview is invaluable to researchers working in the field of precision medicine.

Research presentations are ongoing, as we recognize the importance of sharing information as quickly as we can. As you read this newsletter, Christopher Marnell is attending the 2016 Annual Meeting of the Society for Neuro-Oncology, where he will present findings from his study of drugs with potential against DIPG. Chris started his study with 114 FDA-approved drugs and identified four that blocked the growth of DIPG cells. He is presenting his results on two of those drugs, perifosine and topoisomerase inhibitors, which have suppressed growth of those cells *in vitro* when used in combination.


Weill Cornell Medicine

Combinatorial therapy with perifosine and topoisomerase inhibitors suppresses diffuse intrinsic pontine glioma growth *in vitro*

#PDTB-02

Introduction

Aims

Materials and Methods

Results

Conclusions & Future Directions

References

Acknowledgements

This exciting project is another example of the benefits of collaboration: The DIPG cell cultures Chris tested were provided by Dr. Michelle Monje at Stanford University School of Medicine, and the compounds themselves were a gift from the Developmental Therapeutics Program

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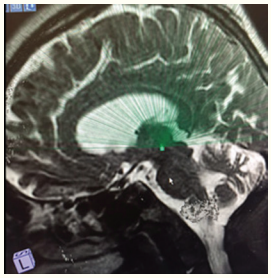
On the Horizon: Focused Ultrasound for Brain Tumors?

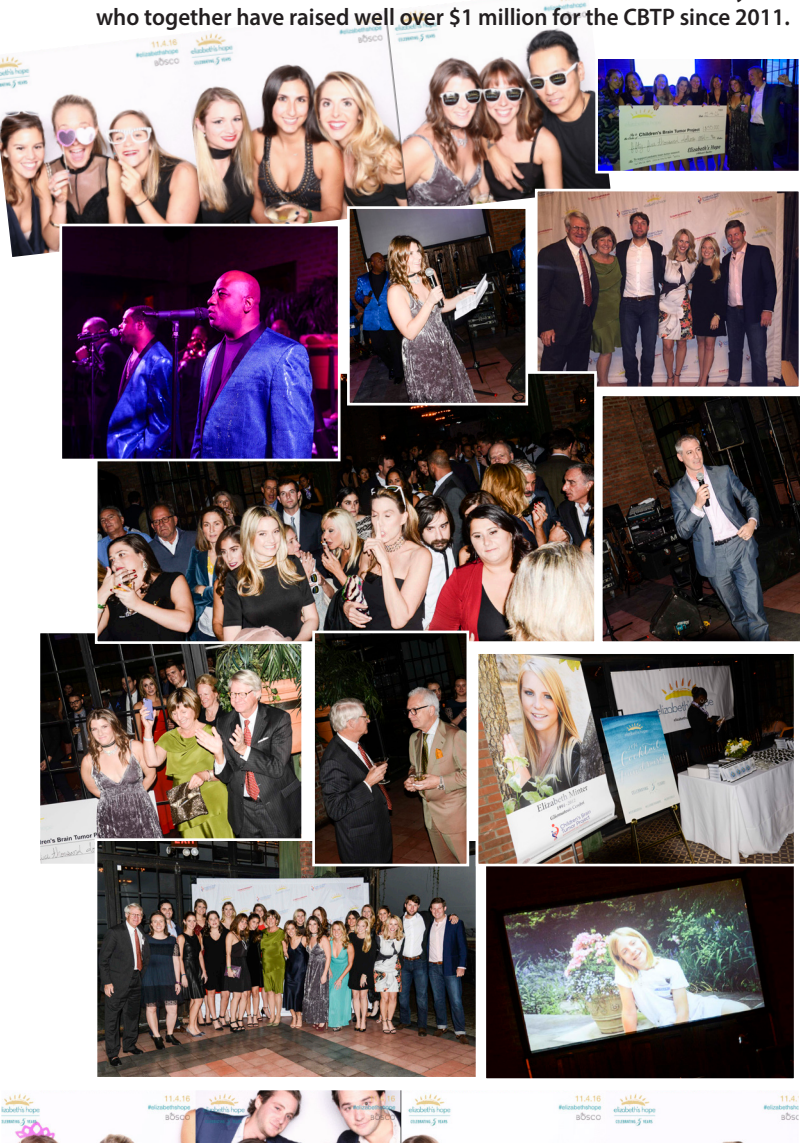


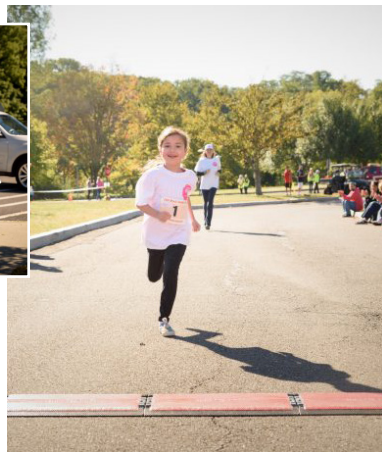
Dr. Michael Kaplitt, our Vice Chair for Research, made news this summer when he became the first in New York to use Magnetic Resonance-guided Focused Ultrasound (MRgFUS) to treat patients with essential tremor, just a week after the technology received FDA approval. The completely non-invasive technique uses 1,000 low-energy ultrasound waves focused on a precise spot in the brain, each individual wave sparing healthy tissue while the combined energy destroys its target.

The potential for using focused ultrasound for other brain disorders is enormous, since the technique temporarily disrupts the blood-brain barrier that keeps chemotherapy drugs away from brain tumors. Dr. Kaplitt and Dr. Souweidane, along with research technician Melanie Schweitzer, are initiating a project that will investigate the use of focused ultrasound combined with an implanted pump to deliver DIPG-fighting drugs to a tumor site. The team theorizes that focused ultrasound may allow doctors to manipulate where drugs are delivered, increasing the precision of that delivery.

Family Update

Elizabeth's Hope celebrated its fifth anniversary this month with a fundraising cocktail party at the Bowery Hotel in New York City. This event has become a must-attend for Elizabeth's friends and family, who together have raised well over $1 million for the CBTP since 2011.





Brooke Blake (right) crossed the finish line at the "Believe in Brooke" 5K in September. Brooke and her family (above) raised nearly $100,000 for the Children's Brain Tumor Project.

Swimmers and runners line up for the start of the Ty Louis Campbell Foundation's 4th Annual "TYathlon" in Mahopac, New York.

The "unicorn bus," honoring Lily LaRue Anderson, made an appearance in this year's Pulaski Day Parade down Fifth Avenue in New York City.

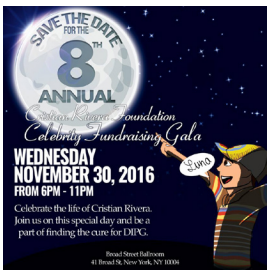
The annual Allie's Sale in Overland Park, Kansas, has grown from a neighborhood rummage sale into a veritable shopping mall. This year's three-day sale, the fourth annual event, raised $46,000 to support our research. Allie's Sale was begun in honor of Allie Fisher, and the CBTP is so grateful to Kyle and Kelly, and all of Team Little Owl, for making us its beneficiary.

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

Upcoming Events

November 19: Poker by the Beach: 2nd Annual Charity Poker Tournament
(Paséa Hotel, Huntington Beach, CA)

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—we'd love to include it!
ChildrensBrainTumorProject.org/cbtp/events/

Second International GC Conference Set

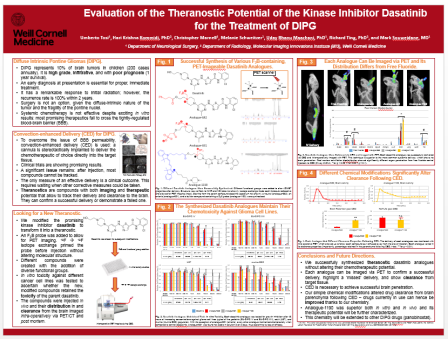
June 22–23, 2017
National Institutes of Health, Washington, DC

We are delighted to announce that planning is now under way for the second International Gliomatosis Cerebri Conference. The first conference (below), held in Paris in 2015, was generously funded by families dedicated to curing GC and included scientists, foundations, and families from around the world. That first meeting laid the groundwork for international collaboration to advance GC research, and set a goal for establishing patient and tissue referral centers in London, Heidelberg, and New York.

Many of the families and foundations who attended have held monthly international phone calls and communicate regularly via email and social media, and they are committed to helping fund this next important session. Please reach out to the AYJ Fund, Elizabeth's Hope, or the Joshua Bembo Project in the United States, or Izas la Princesa Guisante (in Spain) or Franck un rayon de soleil (in France) if you are interested in providing support. Contact information for all these groups can be found at childrensbraintumorproject.org.

Discover. Share. Repeat. *(continued from page 2)*

of the NIH's National Cancer Institute, Division of Cancer Treatment & Diagnosis.


Evaluation of the Theranostic Potential of the Kinase Inhibitor Dasatinib for the Treatment of DIPG

Next month, Umberto Tosi will present his findings at the annual meeting of the Joint Pediatric Section of the AANS/CNS. Umberto has been working on modifying a promising drug, the kinase inhibitor dasatinib, to make it visible on PET scans as it enters, affects, and clears a DIPG tumor. His presentation will focus on one of several dasatinib variations, or analogues, he created; these analogues retain their effectiveness against tumors, but unlike the original dasatinib they can be seen and monitored on scans. This allows a neurosurgeon administering the drug via convection-enhanced delivery (CED) to confirm successful dosing, spot a missed delivery, and monitor the rate at which the drug clears the tumor. The most promising of the analogues will now undergo further testing, and the modification will also be attempted in another drug, panobinostat.

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From Emmie and Mike Minter *(continued from page 1)*

models, meaning a mouse can have not just *a* brain tumor but a *specific* child's *actual* brain tumor (see page 2 for more on that). That mouse could then be treated with the most promising drug based on genomic testing, and if it proved effective the child could receive that same drug. We are not there yet, and many obstacles remain, but it's exciting to see the promise of personalized medicine developing right before our eyes.

Over the last 15 years there have been dramatic improvements in the treatment of other childhood cancers, namely leukemia. It is our expectation that the same will be true of brain cancer in the coming years.


Fall 2012

Importantly, the donor base of the CBTP continues to grow as more families—in grief or hope—commit to the effort. The work truly is "powered by families." In fact, over the last five years, we have grown to nearly 30 families and well over 3,000 supporters, who together have raised three and a half million dollars to power the research.

The groundbreaking discoveries of the doctors and researchers are the direct results of the generosity of you, the donors, who make the work possible. This is the good news. The new challenge is to keep the dollars coming so that existing research projects can be completed and new lines of inquiry can be explored.

Five years ago friends, family, and strangers responded to Elizabeth's request and helped launch this significant project. Today we ask you to continue to support the CBTP, as we are on the cusp of bringing real, tangible hope to young brain cancer patients and their families.

The Minter family is forever humbled by the generosity and love bestowed on us and thankful for the many courageous brain cancer families who are taking a lead in ensuring the continued success of the CBTP. Please consider making another gift today.

Mike Emmie

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


Elizabeth Minter (1991-2012)

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.