

IF A CHILD'S LIFE WAS IN DANGER, YOU WOULD DO SOMETHING, WOULDN'T YOU?



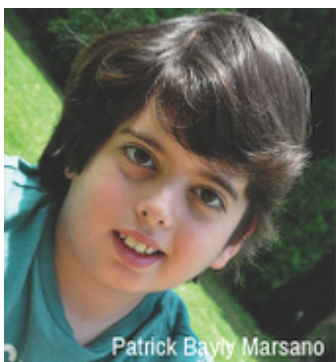
Children's Brain
Tumor Project
powered by families



Weill Cornell
Medicine

May 2019

Patrick Bayly Marsano Foundation Awards \$1M to Fund Precision Medicine for Rare Pediatric Brain Tumors



Patrick Bayly Marsano

Dr. Jeffrey Greenfield, Associate Professor of Neurological Surgery and Pediatrics at Weill Cornell Medicine and co-founder of the Weill Cornell Medicine Children's Brain Tumor Project, was recently awarded \$1.08 million in support of his precision medicine initiative. The generous gift from the Patrick Bayly Marsano Foundation will enable a tremendous increase in defining individualized cancer therapies for children with rare and inoperable pediatric brain tumors.

The gift was made in memory of Patrick, who was ten years old when he lost his life to a rare pediatric brain tumor called gliomatosis cerebri (GC). The two-year initiative will expand the lab's cellular and molecular precision medicine approach to pediatric brain tumor therapy, with a goal of establishing safe and curative patient-specific therapies for devastating pediatric brain tumors, including GC.

Clinicians, computational biologists, neuroscientists, immunologists, biochemists, and stem cell biologists, will work together to conduct next-generation sequencing on every pediatric brain tumor resected at the Weill Cornell Medical Center—an anticipated 50 to 80 children. They will identify new mutations specific to the cell population and to the

patient, and create cell repositories and mouse models to test different targeted therapeutics. Following a comprehensive review of the genetics, cell biology, and pharmacogenomics of patient-specific tumors, a customized therapeutic regimen will be determined for each patient.

Pediatric brain tumors are the most common tumors found in children, and the most fatal. The Children's Brain Tumor Project aims to improve the outcome for children with brain tumors by advancing scientific discovery and clinical research that focuses on targeted therapy, effective drug delivery and low treatment-related toxicity. Gifts such as this brings the team closer to cures.

From the Desk of...

Stefani Healey, Brooke Healey Foundation

My ten year challenge

Earlier this year, there was a blip in time where the social media community was participating in the #tenyearchallenge. The challenge was simple: post a photo of yourself ten years ago, post another recent photo, and comment on the comparison. It's safe to say that the majority of the participants were those who looked "better than ever." Those who were proud of the past decade and how they look like now compared to the person they were ten years ago.

All-in-all, it was an extremely positive campaign. Compliments were flying. Self-confidence dominated my newsfeed. But quietly, I found the entire campaign heartbreaking considering my personal journey over the past ten years.

I don't think there is a person alive who can't reflect on ten years and realize how much life has changed. With every decade we grow and become different versions of ourselves. Time is inevitable, and with it, change.

At the start of this past decade, our beautiful daughter Brooke was

continued on page 4

Monitoring Real-Time Drug Distribution in the Brain

Dr. Souweidane and his tireless lab team recently published new study findings in the esteemed journal, *ACS Chemical Neuroscience*, entitled "Real-Time in Vivo Correlation of Molecular Structure with Drug Distribution in the Brain Striatum Following Convection-Enhanced Delivery."

The findings from this study are of paramount importance as they relate to the team's parallel work studying and fine-tuning the use of convection-enhanced delivery (CED) to treat DIPG, a technique pioneered by Dr. Souweidane using a cannula to deliver drugs directly into the tumor tissue in order to bypass the blood-brain barrier and reduce systemic toxicity.

CED was recently proven safe during the CBTP's ongoing phase 1 clinical trial for DIPG, however, there is still much to understand about the relationship between drug size, charge, and pharmacokinetic behavior in the brain that will help to improve efficacy. Observing drug behavior *in vivo* is essential, and PET imaging of agents delivered via CED allows us to do so.

In this study, researchers modified an existing therapeutic commonly

continued on page 2

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Monitoring Real-Time Drug Distribution in the Brain (continued)

used for leukemia, dasatinib, to monitor the movement of the drug in real time via PET imaging. The team created a panel of significantly improved dasatinib analogues, which can now be observed as they move across the brain and leave the site of injection over time.

In other words, the CBTP research team was able to watch the dissemination of the drug *in vivo* when delivered via CED, and tweak the analogues with the goal of seeing concentrated drug present at the tumor site, extended half-life, and little movement throughout the rest of the body.

As a result, relatively unchanged bioactivity was confirmed in patient- and animal-model-derived cell lines of DIPG. In naïve mice, significant individual variability in CED drug clearance was observed, highlighting a need to accurately understand drug behavior during clinical translation.

These modifications allow researchers to determine what properties a drug should have to be better retained at the CED site (and, theoretically, have a longer therapeutic effect), so that new future drugs can be crafted and optimized for CED.

This publication validates the potential for improved efficacy using CED, and it is only because donors who support the Children's Brain Tumor Project that breakthroughs such as this have been possible.

Match Day 2019

Please join the CBTP in welcoming our new residents in neurological surgery. Congratulations to **Alexandra Giantini Larsen** and **Andrew Garton**, who will join the Neurosurgery team at Weill Cornell Medicine in June to begin their seven-year journey to becoming neurosurgeons.

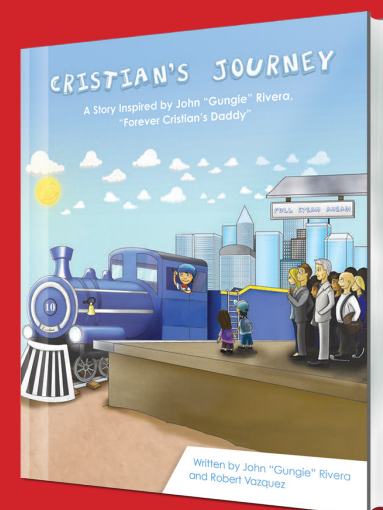
Remembering Dr. Paul Greengard

The entire faculty and staff of the Weill Cornell Medicine Brain and Spine Center mourn the passing of Nobel Prize-winning neuroscientist Paul Greengard, PhD. Dr. Greengard was Vincent Astor Professor and head of the Laboratory of Molecular and Cellular Neuroscience at Rockefeller University as well as the director of the Fisher Center for Alzheimer's Disease Research.

Dr. Jeffrey Greenfield studied under Dr. Greengard during his MD/PhD training and also collaborated on many research papers with him. "His oversight of my scientific training during a critical phase of my career—including a memorable full-day line-by-line review of my PhD thesis shortly after he broke his leg—has been an indelible memory for me, and a powerful reminder for me of the importance of mentorship," said Dr. Greenfield. "No matter how famous and busy he became, he always had time for his students and trainees."



Understanding what's happening at the molecular and cellular level during development to cause the tumor is essential in eventually attempting to prevent or reverse the process in the future.



Cristian's Journey

Cristian's Journey is a beautiful book written by John Rivera, founder of the Cristian Rivera Foundation. It tells the story of his son, Cristian, who loved trains and lived his life by the inspiring motto "full steam ahead," despite his devastating diagnosis. Dr. Mark Souweidane is featured in the book, which delivers messages of love and benevolence. For our families, and for those who may have a nonprofit that provides family resources, Cristian's Journey is a touching tribute. Order yours at cristianriverafoundation.org or on Amazon. Don't forget to use smile.amazon.com!

IronMatt Supports the CBTP

The Children's Brain Tumor Project is proud to announce another project funded by the Matthew Larson Foundation (aka IronMatt) beginning later this year. The research team will be investigating early stages of development in the pons with the hopes of better understanding the mechanisms that control cell development and how they may become deregulated during the process, resulting in the development of tumors such as DIPG.

Access to Experimental Drugs for Single-Patient Use Shows Promise in Pediatrics

A recent study, "Use, Safety, and Efficacy of Single-Patient Use of the US Food and Drug Administration Expanded Access Program," published in *JAMA Oncology*, has shown that a small but meaningful number of patients appeared to benefit upon accessing experimental therapies through compassionate use—pediatric patients, in particular. The Weill Cornell Medicine Children's Brain Tumor Project is hopeful that single-patient use will work seamlessly in conjunction when designing patient-specific protocols based on genetic findings.

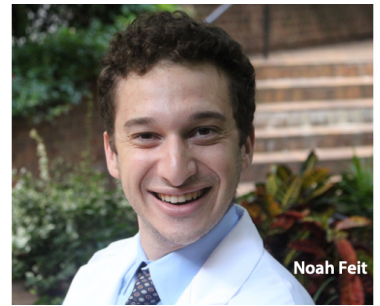
The federal "Right to Try" law now permits manufacturers to provide experimental therapies to terminally ill patients without FDA authorization. Prior to this bill, the FDA had traditionally granted significant flexibility to physicians pursuing access to experimental products through a mechanism called Expanded Access (otherwise known as "Compassionate Use").

The Compassionate Use program has two major access routes: single-patient use (SPU) and intermediate to wide patient population. Generally, the single-patient use mechanism is used to obtain products that may or may not have demonstrated safety or efficacy toward the particular indication requested.

Under the direction of Dr. Jeffrey Greenfield, Noah Feit, MD candidate in the Class of 2020 at Weill Cornell Medical College, dedicated countless hours toward the research effort that leveraged the FDA Expanded Access program to give access to investigational products to patients of all ages with a variety of cancer types. The team reviewed all investigational drugs that were accessed for SPU at Memorial Sloan Kettering Cancer Center over a six-year period. The aim of the project intended

to: 1) describe the characteristics of patients for whom this tool is used, and 2) describe outcomes including safety and efficacy associated with use.

Although patients were heavily pretreated, the team observed benefit among the cohort of participants, of whom children represented 34.1% despite representing only ~2% of the patients seen at the center in 2017, suggesting SPUs may provide an important means of pediatric drug access.



SPU has the potential to be of special use to pediatric cancer patients, in whom access to experimental therapies has been particularly limited. The SPU mechanism provides a potentially useful outlet for flexibility for pediatric patients who have exhausted the standard of care and/or who do not qualify for clinical trials.

"My background in public policy and my family's experience with cancer made this an especially meaningful endeavor for me," said Noah. "In the era of precision medicine and enhanced connectivity, policy must work to connect people with cures, and the SPU mechanism provides clinicians with a tool to customize cancer care even when clinical trials are out of the question."

This research was supported by the St. Baldrick's Foundation Summer Fellowship.

Save the Dates

MAY 19 - Cheering for Caitlin 5K (Oviedo, FL and Succasunna, NJ)

JUNE 1 - Run 4 Kids Children's Marathon benefitting the Olivia Boccuzzi Foundation (Brooklyn, NY)

JUNE 8 - Cristian Rivera Foundation 5K Walk/Run (New York, NY)

JUNE 22 - Head for the Cure/CBTP 5K (Bronxville, NY)

JUNE 24 - Tee'd Off - Driving Out DIPG (Ann Arbor, MI)

AUGUST 3 - Muddy Puddles Mess Fest (Carmel, NY)

AUGUST 17 - Dingers for DIPG (Battle Creek, MI)

AUGUST 25 - Head for the Cure 5K/Team Little Owl (Kansas City, KS)

SEPTEMBER 14 - TYathlon Sprint Triathlon and 5K (Mahopac, NY)

SEPTEMBER 16 - Brooke Healey Golf Outing (Bedminster Twp, NJ)

OCTOBER 22 - No Laughing Matter 2019 (New York, NY)

OCTOBER 18 - Play it Forward Golf Tournament (Huntington Bch, CA)

NOVEMBER 3 - NYC Marathon with the Children's Brain Tumor Family Foundation (New York, NY)

NOVEMBER 13 - Cristian Rivera Fdn. Celebrity Gala (New York, NY)

Run for Research

The Children's Brain Tumor Family Foundation (CBTFF) is an official charity partner for the TCS New York City Marathon. Marathon fundraising for Team CBTF directly benefits the Children's Brain Tumor Project lab. Contact Brenda Ries to inquire about joining the team! brenda@cbtff.org.



OFFICIAL CHARITY PARTNER

**TCS
NEW YORK CITY
MARATHON**

From the Desk of Stefani Healey

continued from page 1



born. She was the sweetest addition to our then 15-month-old son. We settled into what was supposed to be the next chapter in our lives, raising a family. A few short years later, Brooke was diagnosed with a terminal brain tumor at the age of 4. I cared for her day and night as she suffered from the debilitating disease for 8 months. My husband and I held her when she died just days after her fifth birthday. In this decade, we buried our daughter. We gained tremendous love and support from our community, but also lost many friends along the way. My #tenyearchallenge is very different than the positivity that has otherwise flooded my newsfeed.

I am a different person than I was ten years ago. I'm raising a family that is missing a child, and my other children will never be the same, just as I am missing a piece of myself that I can never get back. Brooke has given more empathy and compassion than I could have imagined, and her suffering and death have caused more pain than can be explained.

With the help of a friend, I decided to participate in the #tenyearchallenge to share my perspective on the campaign. The picture we posted speaks so clearly...Even if you didn't know Brooke, even if you don't understand what our family had to endure, you can understand what is missing.

I dream that 2029 will look different for other families battling cancer. That over the next decade we will see tremendous progress in research, and more children will be cured.

Fundraising is hard work, and I have been fundraising to support the Brooke Healey Foundation ever since losing her in 2013. I look forward to the 2029 #tenyearchallenge where I hope to look well rested and relieved. I hope to find my new passion because we don't have to fundraise anymore. I hope our hard work will have made an impact in the lives of other children, and we can finally rest because a cure has been found.

CBTP "Do Something" Spotlight The Magic of a Blue Lollipop

"I started the Blue Lollipop Project because when I heard Ty's story, I knew I had to do something," said Riley Damiano. "I learned so much about childhood cancer and I couldn't just walk away from it."

Riley is not your typical 16-year-old. When Riley was just nine years old, she was touched by the story of a child in her community who was battling brain cancer named Ty Campbell. She related to his love for blue lollipops and the smile they could bring to his face when sharing the color transformation on his lips and tongue. She too, was always inclined to choose a blue lollipop over all other colors for that same reason. For Ty, it was such a small and simple thing, but it brought a smile to his face when there wasn't much else to smile about.

Riley has since launched the Blue Lollipop Project in his memory, and she has been running this campaign for more than five years. What started as a Bat Mitzvah project in 2013 has become a nationwide fundraising campaign most recently recognized by Ashoka for her social entrepreneurship.



The concept is wonderful. For every dollar donated, the donor walks away with a blue lollipop knowing that a blue lollipop will also be sent to a child with cancer. At the same time, the money donated benefits childhood cancer research, much of which funded the Children's Brain Tumor Project at Weill Cornell Medicine through the Ty Louis Campbell Foundation.

Riley is now 16 years old and plans to study biology in college. She has visited the lab at Weill Cornell Medicine for inspiration, and she is most interested in pursuing a career in research. People who meet Riley always comment on how she is wise beyond her years.

Kids go through a lot of changes from nine years old to sixteen, yet Riley has never lost momentum for this initiative. In fact, she is now more passionate than ever. Riley's social media is filled with little kids showing off their blue tongues, children in treatment opening her care packages, and inspirational messages—not selfies. That's because she is, indeed, a most selfless person.

In a recent interview, Riley said "If I could change one thing, I wish that I had started earlier. There is no age that's too young to be a changemaker."

Riley is doing something.



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