

December 2018



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

From the Desk of...

John Jeffers, Samuel Jeffers Foundation



Five years have passed since we lost our son, Sam. He was eight years old. Sam was a bright-eyed, energetic, loving, and highly intelligent little boy. After a brief but brutal fight, we surrounded him with our love as cancer took his life under a full moon at 6:31 am on October 20, 2013.

Sam had a bi-thalamic glioma (TG), a type of brain tumor that could not be surgically removed because of its location and the nature of the cancerous glial cells. Inoperable brain tumors

currently call for treatment either with chemotherapy, radiation, or both. Neither treatment is desirable; each results in terrible side-effects with little to no efficacy for thalamic gliomas in the long term. The families at the Children's Brain Tumor Project are all too familiar with the debilitating effects of cancer, as well as the potentially devastating effects of the cancer treatment itself.

My wife and I have decided to harvest what could be unbearable amounts of negative energy and channel it into a positive avenue—Sam's Foundation. Sam's Foundation is all about searching for and funding better treatment options for children with cancer, helping local families with financial needs, and trying to raise awareness that childhood cancer is a serious problem. Years from now, we hold hope that our fundraising efforts will pay dividends in the number of young lives saved.

There is currently an abysmal amount of money spent on childhood cancer research. Money spent on adult cancer research seldom trickles down to benefit children with cancer, because their cancers are unique to pediatrics and their bodies cannot tolerate the same treatments, yet money spent on childhood cancer research can and often does "trickle up" to benefit adults. When we fund childhood cancer research we are often opening doors that have the potential to benefit other disease types across all age groups.

Dr. Mark Souweidane, head pediatric neurosurgeon at Weill Cornell Medicine and co-director of the Children's Brain Tumor Project, is spearheading our collective efforts to crack the code on thalamic gliomas. Dr. Souweidane has pioneered a drug delivery alternative called convection-enhanced delivery (CED) whereby drugs or other therapeutic agents can be delivered directly into the tumor site,

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A Personalized Approach for Pediatric Brain Tumor Patients

Dr. Prajwal Rajappa knows a lot about brain tumors, especially the rare kinds that tend to strike children. As a physician and scientist passionate about brain tumors, he has worked at the Weill Cornell Medicine Children's Brain Tumor Project (CBTP) for seven years, observing tumors through microscopes, growing them in petri dishes and in animal models. Most recently, he has been working to understand their genomic fingerprints.

Dr. Rajappa has been the Precision Medicine Fellow at the CBTP since 2016, under the mentorship of Dr. Jeffrey Greenfield, Co-Director with Dr. Mark Souweidane of the CBTP. Dr. Rajappa coordinates Dr. Greenfield's innovative program, in which every pediatric brain tumor patient operated on is offered genomic sequencing and a targeted medicine consultation as part of their standard of care. When a tumor is biopsied or removed, samples of the tumor are taken directly from the operating room to the pathology lab for examination, to the CBTP laboratory to grow in dishes and animal models, and to the Englander Institute for Precision Medicine for sequencing and drug screening. This complicated process generates a wealth of data about the tumor, the goal of which is to direct targeted treatment efforts.

Dr. Rajappa is excited to be part of an initiative that could be a game-changer in personalized brain tumor treatment for children. He recently presented the CBTP's Precision Medicine Initiative at a Grand Rounds talk at Nationwide Children's Hospital in Columbus, Ohio. He was invited to present by Elaine R. Mardis, PhD, Nationwide's Chair of Genomic Medicine as well as President-elect of the American Association for Cancer Research.



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A Personalized Approach for Pediatric Brain Tumors (continued)

Dr. Rajappa also spoke and received the Tumor section's Pediatric Brain Tumor Award for best paper, on Dr. Greenfield's behalf, at the CNS annual meeting in Houston last month.

"Precision medicine is the future of cancer care," says Dr. Rajappa. "I was honored to be invited to present our precision medicine program at Nationwide, because I believe we are setting the new standard of care here and it is gratifying that we are being noticed for setting a national standard for excellence. We offer every family whose child has brain tumor surgery here an individual consultation so we can develop a personalized sequencing algorithm based on their specific disease. Once the sequencing is performed, I present these findings to a multi-disciplinary tumor board. Working closely with the surgeons, oncologists, and the computational arm of the Englander Institute for Precision Medicine, the data we analyze from each case is sifted through to find clinically usable data and hopefully inform actual decisions on how to best treat each child's tumor."

Dr. Rajappa notes that some of the lab's most exciting discoveries occur when the genetic data reveal that the tumor is not even the type it had appeared to be under a microscope. "This more accurate molecular diagnosis allows the treating team to re-define and personalize their treatment and allows us to predict prognosis more precisely which is so important for families," he says. "In the best-case scenarios, sequencing identifies a mutation that can be targeted with a treatment known to be effective against that specific alteration. That's the bottom line for the entire precision medicine effort: finding a specific treatment that is effective against an individual tumor."

Dr. Rajappa estimates that through the CBTP's algorithm and tailored treatment plan, as many as 75 percent of genetic mutations found on sequencing are virtually diagnostic, prognostic, or targetable. He says he likes those odds.

"We need to improve the standard of care for high grade, inoperable, and recurrent tumors," Dr. Rajappa emphasizes. That's the promise of precision medicine—improving clinical care based on personalized genomic data that will hopefully help kids defeat brain tumors."



Comedy Night

The room was filled with laughter infused by hope on Tuesday, October 16, at Carolines on Broadway as the Children's Brain Tumor Family Foundation hosted "No Laughing Matter," a night of comedy to benefit the Children's Brain Tumor Project (CBTP) at the Weill Cornell Medicine Pediatric Brain and Spine Center.

Three-time Grammy-nominated comedian Jim Gaffigan performed along with some of the nation's funniest names in comedy today – plus a touching youth performance by the original "Comedy Kids," Max Chwatko and Alex Travin.

The inaugural event raised \$450,000 to benefit the groundbreaking research of Dr. Mark Souweidane and Dr. Jeffrey Greenfield, co-founders of the CBTP.

Performances included Master of Ceremonies Michael Dean Ester,



Introducing "Do Something"

If a child's life was in danger, you would do something... wouldn't you?

Thousands of children are dying each year of brain tumors. Don't look away. Donate right now at childrensbraintumorproject.org.

The Children's Brain Tumor Project Weill Cornell Medicine is proud to team up with DDB Health to present this powerful public service announcement (PSA). The PSA is intended to raise awareness of the traumatic outcomes for far too many children diagnosed with brain tumors every year, and demand action by encouraging viewers to donate.

DDB Health generously donated time, talent and production costs to create this compelling video. Part of the Omnicom Health Group, DDB Health brings together a like-minded community of big thinkers that are passionate about leveraging their creativity to inspire good health. Their dedication is clearly demonstrated by their philanthropic efforts in support of the Children's Brain Tumor Project.

DDB Health is doing something.

You can do something, too.

The generous gifts of our supporters allow our neuroscientist/researchers to continue their important work.

We are asking our followers to share this video and encourage others to do something by donating to the Children's Brain Tumor Project. To view this compelling PSA and/or to make a donation, visit childrensbraintumorproject.org.

Ali Wentworth, Kevin McCaffrey, Kendall Ketchum, Erik Bergstrom, Jessica Kirson, Damien Lemon, Ryan Hamilton, and Jim Gaffigan, all of whom so generously donated their time and talent to support the cause.

"We are so grateful to the Children's Brain Tumor Family Foundation, the dinner committee, the performers, the honorees, the sponsors and the volunteer staff who made this event such a tremendous success. We are so humbled to be the beneficiary and we were completely blown away by the support," said Dr. Jeffrey Greenfield.

Very special thanks to Dinner Chair, Tara Lipton (pictured with 2 of her 4 children, Piper and Walker), for helping to make this vision a reality.

Gliomatosis Cerebri “Letter from the Lab” (volume 2)

Volume 2 - December, 2018: This is the second “Letter from the Lab,” a series of regular lab communications specific to progress being made in studying gliomatosis cerebri (GC)* at the Children’s Brain Tumor Project (CBTP), Weill Cornell Medicine.

Our dedicated lab team has been working with various tissue samples donated by the families of GC patients with the goal of understanding the genetic footprint and identifying mutations that may be better targeted with customized agents. In the first “Letter from the Lab” I was happy to report that our lab team was successful in establishing four differentiated cell lines** derived from these tumor samples, and we identified some targeted drugs in vitro that showed promise. These discoveries continue to be investigated further.

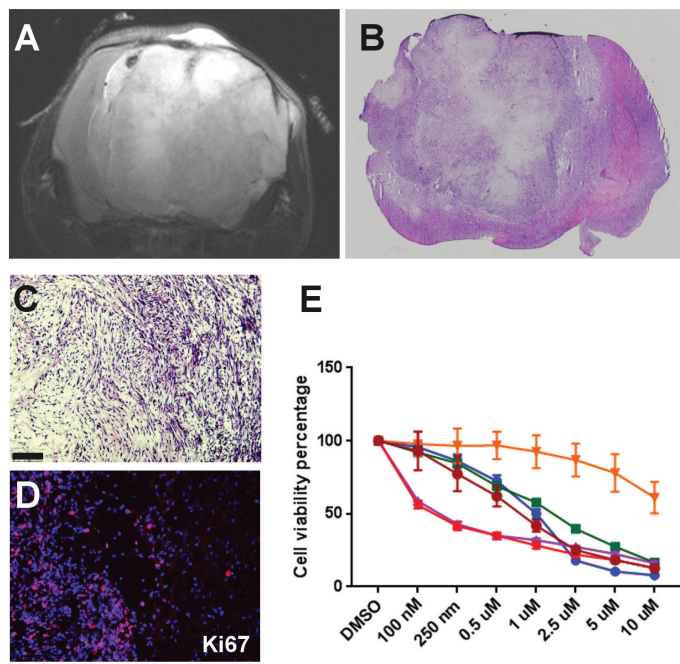
In order to make further progress, the next phase of research requires testing the most promising agents via xenograft mouse models. At the time of the previous letter, we had three mice injected with tumor cells, growing successful flank tumors under the skin, but we had trouble growing a successful tumor in the brain the same way. Instead, the team recently injected cells derived from the flank tumors that were successfully growing subcutaneously, intracranially. This proved to be successful in replicating the GC tumors in the brains of two mice—a tremendous accomplishment—and we are now repeating the process in five more. The CBTP is the only lab that has been successful both in creating differentiated GC cell lines and in growing GC tumors in mouse models.

In order for our research results to best align with what happens in our patients, we need the mouse models to closely represent pediatric GC tumors, both molecularly and histologically. In our case, the two xenograft models described above have been shown to replicate the histological features found in the donor patient. This is an amazing accomplishment because often xenograft models do not completely reflect the tumor of origin. The tumors from the animal models are now under characterization, and our team is defining how these tumor cells migrate and proliferate during the tumor development. The new challenge for the lab is to adjust the number of the tumor cells injected intracranially in the hopes that tumor growth in the animal models can perfectly mimic the one observed in the patients. This achievement will create a solid base for the next in vivo drug screen studies.

In the meantime, we are now characterizing how the GC cells proliferate. Studying tumor growth in vivo helps us track how these cells are invading the tissue, giving us a better understanding of what may trigger growth, why cancer cells are found infiltrating so many parts of the brain, and the paths they take to get there.

Studying drug efficiency on GC cell lines and having the chance to monitor their effect on tumor growth in vivo, thanks to the mouse model, will help us to better identify new treatment options. After completing the first set of in vitro drug screening, we have identified three drugs that are showing efficacy against GC cells, but two out of three of them do not penetrate the blood-brain barrier.

Thanks to the successful development of animal models, our next step is to enhance these drugs with radioactive tags and to inject them into the brain of our mouse model using convection-enhanced delivery (CED). This will allow us to monitor their diffusion into the brain parenchyma and to follow their efficacy on blocking tumor growth and migration. This is not an easy task and carries a \$20,000 to \$30,000 price tag for drug tagging alone, but we are committed to making this happen and hope to secure the support of a pharmaceutical company to offset those costs.



- A. MRI image to assist with studying tumor dimension
- B. Confirmation via tumor histology
- C. Tumor histology clearly resembles the patient tumor, demonstrating successful replication
- D. Tracking and monitoring proliferation to better understand how cancer cells are invading healthy tissue and the pathways to other parts of the brain
- E. Drug matching data shows three viable drugs, two of which we will tag and use with CED

There is still so much to be done, but the progress being made is tangible! The successful creation of animal models is so important as we advance into the next phase of testing new agents against gliomatosis cerebri in order to discover effective new treatment options. Our dedicated team of scientists and clinicians are passionate about finding a cure, and we thank our donors for enabling us to do so. Special thanks to my team who has taken this research so far, including Dr. Carolina Cocito, Meng Huang, and Dr. Uday Maachani.

With deepest gratitude,

Jeffrey P. Greenfield, MD, PhD

*Gliomatosis cerebri (GC) is a rare, highly aggressive brain cancer that is very resistant to treatment. GC is commonly identified by its diffuse infiltration of the brain with thread-like malignancies that spread very quickly, affecting various areas of the cerebral lobes and surrounding brain tissue, making them very difficult to remove with surgery or treat with radiation.

**A cell line is a permanently established cell culture that will proliferate indefinitely given appropriate fresh medium and space, meaning we can replicate tumor growth repeatedly in order to conduct various types of tests.

From the Desk of John Jeffers

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bypassing the blood-brain barrier and offering a fighting chance for the medicine to have some effect on hard-to-reach tumors. He has currently proven safety in a clinical trial for children with DIPG—a pediatric brainstem tumor with very poor outcomes—and will soon be expanding these efforts to include additional pediatric tumor types and additional institutions.

As wonderful as the direct benefits are to children, the translational benefits of using CED for DIPG and other pediatric brain tumors have the potential to further evolve into a project that Dr. Souweidane expects to define many additional elements of local drug delivery to the brain. Aspects such as device design, dosimetry measurements, drug labeling, monitoring pharmacokinetics, and many others can be applied not only to other brain tumor strategies but to any disease in which drug delivery to the brain is crucial. What this means is that Dr. Souweidane's work on children's brain tumors could eventually affect treatment for a host of other ailments including infections, degenerative diseases like dementia or Alzheimer's, movement disorders, and epilepsy. His clinical trial for DIPG has afforded us the opportunity to translate an innovative and adventurous treatment paradigm for children into an actual clinical tool with widespread potential applications—for children and adults alike—even outside the world of cancer treatment.

This is a powerful example of how helping children with cancer can, in fact, help ourselves. By funding childhood cancer research, not only are we working to save the lives of our precious children, we are also potentially saving the lives of our siblings, parents, grandparents, and ourselves. We believe that's a very wise investment.

When we launched the Samuel Jeffers Foundation, we committed to raise \$75,000 in order to fund the Thalamic Glioma program at Weill Cornell Medicine. I am so proud to share that we have surpassed that goal, and the team at the Children's Brain Tumor Project is in the process of hiring the Samuel Jeffers Fellow at Weill Cornell Medicine, who will be dedicated to better understanding thalamic gliomas at the molecular level in order to aid the discovery of new treatment options for children diagnosed with TG in the future.

While this tremendous accomplishment fills our hearts with purpose, our grief remains ever present. We continue to cling to Sam's old toys and clothes, flip through photographs, and say a little prayer at night asking to dream of him.

We are so incredibly grateful for the community of love and support on behalf of the Samuel Jeffers Foundation. We are honored to have met so many wonderful people and have been lifted by the kind and generous hearts that enable us to honor Sam's memory through helping others.



CBTP "Do Something" Spotlight

Like so many of us, Claudia Amboss and Peggy Theiss have been deeply impacted by cancer. Peggy lost her beloved husband, Cliff, in 2009, and Claudia has seen multiple loved ones undergo treatment, recently losing her dear friend Frederico "Dico" Kowarick. Both Peggy and Claudia also knew and loved young Elizabeth Minter, who lost her life to a rare and incurable pediatric brain tumor called gliomatosis cerebri.

Six years ago Claudia and Peggy decided to do something about it, and they haven't stopped since. Working together, they have planned and executed a flawless Bridge and Tennis fundraiser at the Bronxville Field Club every year, known as the BFC Round Robin for Cancer Research. This year's event took place on September 28, 2018, and paid tribute to Elizabeth Minter by designating Elizabeth's Hope as the beneficiary for the second year in a row.

Elizabeth's Hope was founded in 2011 by Elizabeth and her parents, Mike and Emmie Minter, in order to exclusively fund the research underway at Weill Cornell Medicine (WCM), and it provided the cornerstone for the launch of the Children's Brain Tumor Project. Their fundraising initiatives enabled the Children's Brain Tumor Project at WCM to open its own lab designated to pediatric brain tumor research, which continues to grow in size year over year.



The event theme, Liz Laugh Love, was beautifully depicted on the invitation and décor, photographs of Elizabeth were placed throughout the club, and countless local businesses generously contributed to the corresponding auction that took place during the luncheon. Every event detail was beautifully designed and flawlessly executed, right down to the napkins.

The luncheon was attended by more than 100 people, including Bronxville resident and supporter Patrick McEnroe, who generously donated tennis lessons during the live auction.

"I am deeply touched by how incredibly supportive my friends have been, and the entire Bronxville Community for that matter, for embracing our cause in memory of Elizabeth," said Emmie. "They did such a beautiful job."

Not only was the event a success, but Claudia's outreach while planning the event led to additional support and fundraising opportunities with esteemed shoe designer Alexandre Birman and the Frédéric Fekkai Salon at the Mark Hotel.

The efforts of Claudia and Peggy are an incredible example of two individuals who recognized the tremendous unmet needs facing children with brain tumors, and decided to **do something** about it.



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