



From the Desk of...
John "Gungie" Rivera

As a father, you think your biggest worry will be "please let me not drop him" or "let me please not lose him at a toy store." You are never prepared to hear shattering news that makes all your other worries seem small and insignificant.

On January 22, 2007, I received the worst news any parent could ever receive. My entire world seemed to be crashing in on me. Cristian, my handsome son, was sick. The doctor spoke words that seemed to be in a foreign language, a language I had never heard. Diffuse Intrinsic Pontine Glioma, he said. To me those words meant nothing other than: Something is wrong and I have to fix it.

The doctor, seeing my blank and confused face, explained to me that Cristian had an inoperable brain tumor. The average lifespan for a child with a pontine glioma (DIPG) after diagnosis is 3 to 18 months. I remember seeing his mouth move and hearing his words, which were supposed to make sense, but for some reason my brain didn't comprehend what was happening. There was no way that my baby boy had only a few months to live. I refused to accept it.

For two years my brave boy fought a hard battle. For two years I searched high and low for a cure. Unfortunately, that cure never came, and my Cristian passed away on January 25, 2009.

For so long I asked, why? I felt sad and almost defeated. But after countless sleepless nights of anguish I realized that there is an answer to my "why?" It's that Cristian's life has a higher purpose. He truly had a calling. The ever-elusive answer to my "why?" is that my mission now is to make sure no parent suffers what I suffered. It has become my personal mission to be a part of finding a cure for DIPG.



Cristian Rivera

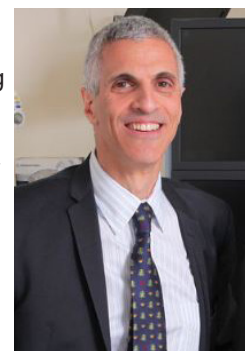
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Laboratory Update

Dr. Mark Souweidane

Co-director, Children's Brain Tumor Project

As I write this, it's hard to believe it's been nearly four years since I received word that the FDA had approved my clinical trial testing the safety of using convection-enhanced delivery (CED) to deliver drugs directly to the site of a DIPG tumor. It seems like the blink of an eye, and in scientific research terms it is. But I know that those four years also represent nearly 800 children who lost their lives to this dreadful disease while we've been searching for a cure.



Keeping those children front and center—in my own mind, in the minds of our lab researchers, and most of all in the minds of our families—is a key driver that keeps this project going, and that creates the momentum we need to keep reaching new milestones.

I reached one of those milestones just today, when I operated on the last patient in the trial to receive dose level six. Nearly two dozen children have been treated, without a single significant adverse effect. We are very close to establishing what I have believed for four years: that CED is safe to use in children, and that it can deliver drugs to a tumor in far greater concentrations than can be achieved using traditional chemotherapy.

Now comes the final stage of this trial: dose level seven. After that we hope to expand the trial to more institutions nationwide—treating more children, with a wider range of drugs and dose levels, using single and combination drug therapies tailored specifically to individual tumors.

The cell lines we have growing right now in our lab are providing us with a wealth of information every day about DIPG (see next page for more on these cell lines). We could not be doing this work if it were not for the collaboration among our peers worldwide, the participation of families who are dedicated to finding new treatments, and the generous donors who keep supporting us. I could not be more proud of where we are today, or more excited about where we are headed.

Onward,

CBTP Using High-Throughput Screening in Search for New DIPG Treatments

By Uday Bhanu Maachani, PhD



Diffuse intrinsic pontine glioma (DIPG) is a complex and challenging tumor. Its location in the brain stem, combined with its diffuse nature, makes it inoperable. No chemotherapy drug has yet been effective against it. Radiation provides only temporary relief before the malignancy returns. And the scarcity of both tumor tissue and research funding has made it difficult for scientists to study it.

Recent advances in the OR and in the lab, however, are starting to change the tumor's grim profile.

For decades, neurosurgeons were reluctant to biopsy pontine gliomas for fear of inflicting devastating neurological harm on their young patients. Stereotactic needle biopsy now makes it possible to biopsy these tumors, not only confirming the diagnosis but also securing tissue samples for research.

At the Children's Brain Tumor Project laboratory, we now have several distinct patient-derived DIPG cell lines growing *in vitro*. Using these cell lines, we can study the molecular

alterations present in these tumors and select effective molecular targeted therapies to test. We are learning more every day about the genetic mutations, epigenetic alterations, and the activation of stem cell pathways that might be causing these malignancies. (We also have gliomatosis cerebri cell lines growing, but GC cells grow more slowly than DIPG cells do, so it will take a bit longer for them to be ready for testing.)

As we learn more about DIPG's molecular characteristics, we can apply newly developed high-throughput

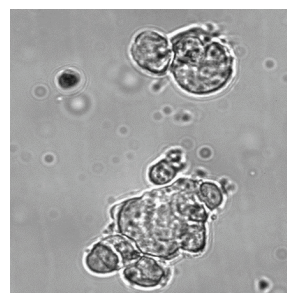
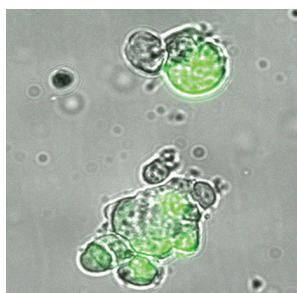
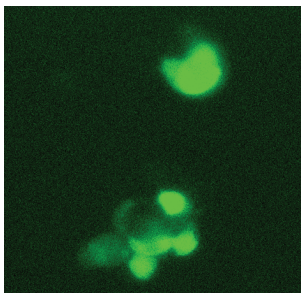
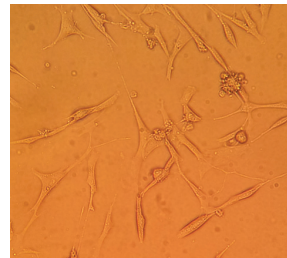
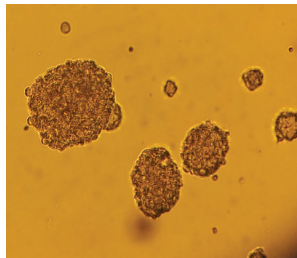
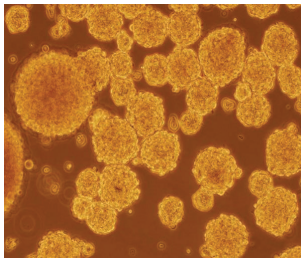
screening (HTS) techniques to try to match those characteristics with existing FDA-approved drugs. Using HTS, we can examine millions of variables in already-approved oncology drugs in search of promising candidates to test against DIPG. These drugs are in clinical use today for other cancers, and we are testing them on our collection of DIPG cell lines. The goal of the initiative is to identify the most potentially effective drugs for DIPG, and then rapidly transition them to clinical trials.

Perhaps even more significantly, HTS allows us to predict which combinations of oncology drugs would make good candidates to use in synergy against DIPG based on the molecular profile of the tumor cells. (In other cancers, synergistic drug combinations have succeeded when single drugs have failed.) Synergistic drug pairs have special potential for success against chemo-resistant cancer cells. Drugs can be specifically paired to attack the cancer cells on parallel paths, so that when the first encounters drug resistance from the tumor, the second is able to continue on its mission. The combinations can also achieve a desired effect at a lower total dosage, usually with fewer side effects.

The next step is to inject our DIPG cells into animal models, then use convection-enhanced delivery (CED, the technique being used in Dr. Souweidane's clinical trial) to deliver specially selected drug pairs into the tumor. Since we'll have very detailed information about the tumor cells, we'll be able

to choose drugs that have the best chance of success against those particular cells. It's a tremendous first step toward developing personalized treatments that will someday allow us to select the most promising drugs to use in children with DIPG.

Dr. Maachani joined the Children's Brain Tumor Project lab this summer as Instructor of Biochemistry in Neurological Surgery. He was previously a post-doc fellow at the National Cancer Institute/NIH, where he studied signal transduction and DNA repair to identify novel chemo and radio sensitizers for effective therapy against glioblastoma multiforme (GBM).



TOP ROW: Left and center, two of the patient-derived DIPG cell lines now growing in the CBTP lab; right, a GC cell line growing *in vitro*. **MIDDLE ROW:** Patient-derived DIPG cells are engineered to express green fluorescent protein (GFP) and luciferase, making it possible to monitor tumor progression in animal models when the cells are injected. **Left:** Dr. Maachani examines DIPG cells under a microscope to monitor their growth.

Event Update

Bronxville Road Race 2015



TLC Foundation MessFest and Luau



TEAM Sean Goes Gold



Team Campbell Foundation's Cocktails for Cam



Team Little Owl's Allie's Sale



CBTP Ice Cream Social at A La Mode Shoppe

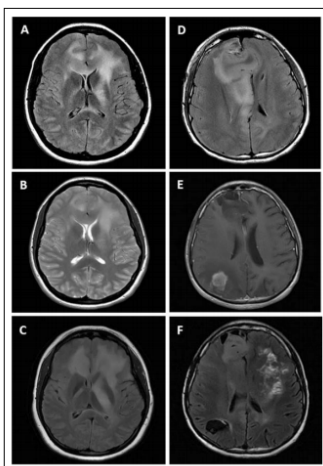
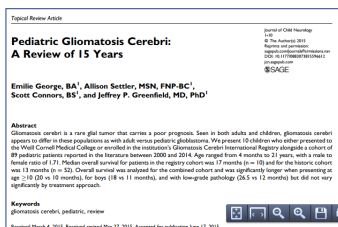
Fly a Kite Foundation's Brunch and Beyond



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

New GC Publication From the CBTP

Shortly after our summer issue went to press, Dr. Greenfield and CBTP researchers published a 15-year review of gliomatosis cerebri cases in the *Journal of Child Neurology*. The paper examined the cases of 10 children seen at Weill Cornell or enrolled in our GC International Registry, alongside 89 children diagnosed with GC reported in the literature between 2000 and 2014. The review documents the kinds of molecular changes seen in gliomatosis cerebri and paves the way for future research. Retrospective reviews like these are invaluable to the research community, as they painstakingly gather data that others can use to initiate new lines of investigation.



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.



Ways to Give

1. By Check

You may make your gift by check, payable to Weill Cornell Medical College. Please indicate "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 John Rivera (continued from page 1)

In June 2009 I founded the Cristian Rivera Foundation, a New York 501(c)(3), in the hopes of finding a cure for DIPG. During these past six years the foundation has already contributed more than half a million dollars to the research of Dr. Mark Souweidane of Weill Cornell and Dr. Oren Becher of Duke University. Their cutting-edge research is bringing us closer every day to finding a cure. We know that the strides we are making to find a cure are grand.

On Tuesday, November 17, 2015, we will be celebrating our 7th Annual Celebrity Fundraising Gala. This year our theme is "Heroes." This year we want to honor the memory of all our Angels who will forever be heroes in our hearts. The Heroes theme is truly symbolic. We hope to really thank and honor the members of the Cristian Rivera Foundation and Dr. Mark Souweidane, who are everyday heroes.



Heroes who put on their invisible capes every day and lend their voices and hearts to this cause. With their dedication and commitment, we get closer and closer every day to our mission of finding a cure.

There is not a day that goes by where I don't wake up and think of Cristian. There is not a moment that goes by where I don't close my eyes and see his smile. There isn't a night where I don't meet him in my dreams. But one thing has changed. Now the sadness and loneliness my heart felt doesn't consume me—now it fuels me. Every day I wake up more and more certain that I am on the right path. Every day I wake up, I smile, and I thank Cristian for filling me with the strength to keep fighting his fight, for filling me with strength to never give up. Every night I thank my personal hero, Cristian, for teaching me the true meaning of Hero.

John "Gungie" Rivera
Founder of the Cristian Rivera Foundation
& "Forever Cristian's Daddy"

Upcoming Events

November 17: Cristian Rivera Foundation Gala (New York)

December 5: Joshua Bembo Project Annual Raffle

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/