Children's Brain Tumor Project
powered by families

Summer 2017

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

From the Desk of...
Kathy Arabia

It is always a heartwarming and emotional experience to meet with other families who have lost a child to brain cancer. I had the true pleasure to connect with a group of parents, all of whom had lost a child to the rare brain cancer gliomatosis cerebri, at the Second International Gliomatosis Cerebri Conference, which was recently held at the National Institutes of Health.

The powerful emotions we felt were highlighted by the fact that we were there with a number of the brightest neurosurgeons, neuro-oncologists, researchers, and others who were fully committed to learning more about this cancer, sharing research, and finding effective treatments so no other families would have to go through such a loss.

Top: Anna Yan Ji Arabia. Above: Families and scientists at the Second International GC Conference at the NIH in June

This conference included presentations on GC research from a number of European countries as well as Canada and across the United States. Dr. Jeffrey Greenfield spoke of his research on the invasive growth pattern of gliomatosis cerebri, and the work being done in his lab to test biopsy tissue cells with a number of drugs to find potential treatment options for patients.

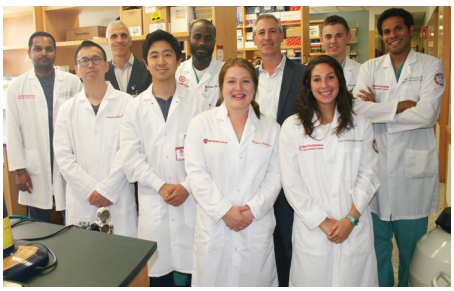
After losing our 16-year-old daughter, Anna Yan Ji, to gliomatosis cerebri, we became committed to supporting research and created the AYJ Fund. We are grateful that Weill Cornell Medicine, Dana-Farber Cancer Institute, National Institutes of Health, and others in the United States as well as a number of hospitals across Europe are now actively studying this disease. This conference brought physicians and researchers together with families from around the world to share their

continued on page 4

Laboratory Update

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

These are exciting times in pediatric neuro-oncology research, and nowhere is that excitement felt more than right here in the CBTP labs. We have recently doubled in size, thanks to the generous support of our families and friends. Where once our two teams worked side by side, taking parallel paths toward our common goal, now we are four. And we couldn't be happier about that.



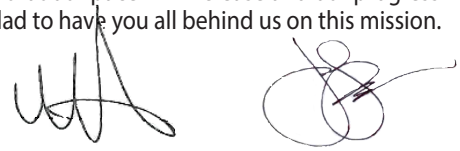
This spring we were honored to welcome Nadia Dahmane, Ph.D., to our team. Dr. Dahmane joined us from the University of Pennsylvania, where she ran an NIH-funded laboratory focused on fetal developmental biology. Her expertise in cell proliferation and differentiation—and how those processes can go wrong and lead to the development of a tumor—is the perfect complement to our work. We have learned that one of the best ways to defeat a disease process is to understand how it begins, then "reverse engineer" that process in an effort to find a way to stop it. We are delighted to have Dr. Dahmane on board, along with Dr. Chaomei Xiang, who will be working alongside her on these important projects.

We are equally excited to welcome Babacar Cisse, M.D., Ph.D., to the CBTP. Until June, Dr. Cisse was Chief Resident in Neurological Surgery here at Weill Cornell Medicine. Upon completion of his residency, Dr. Cisse accepted our offer to join the faculty—and the CBTP.

Dr. Cisse has been working closely with Dr. Greenfield's lab for the past several years, specifically on research into the progression of low-grade gliomas into high-grade malignancies. We are so glad to have him join our laboratory to enhance our investigations into those processes.

This newsletter includes a summary of the new findings and projects your generosity has funded. With a lab full of new investigators and interns, we are confident that our pace will increase and our progress will quicken. We are so glad to have you all behind us on this mission.

Onward,



An Unprecedented Pace

You might think making important scientific discoveries would be accomplishment enough, but getting the word out to a global community of researchers is just as important—maybe even more so, as each publication spreads the knowledge and spurs future investigations. The CBTP lab researchers have been on a bit of a tear lately, publishing some of their most significant finds yet.

In spite of what may seem like esoteric titles, both of the following papers are key to the work done not only in our labs, but in labs around the world:

Malignant Astrocytic Tumor Progression Potentiated by JAK-Mediated Recruitment of Myeloid Cells

Dr. Greenfield made the Weill Cornell home page with his new finding.

This paper from Dr. Greenfield's team, fully five years in the making, details how a specific population of cells that are made in the bone marrow are recruited to the brain to facilitate brain tumor progression; more importantly it shows that inhibiting this process may act as a remote control of sorts to stop tumor progression. JAK inhibitors are compounds that are known to modulate immune responses in other disease states and interrupt signaling pathways involving proteins that have been implicated in cancer.

The paper is a true collaboration, written by Dr. Prajwal Rajappa of the CBTP and co-authored by Dr. David Lyden, professor of Pediatrics and Cell and Developmental Biology at Weill Cornell Medicine and pediatric neuro-oncologist at Memorial Sloan Kettering Cancer Center, and Dr. Jacqueline Bromberg, medical oncologist and researcher at Memorial Sloan Kettering Cancer Center. It was published in the June 2017 issue of the journal *Clinical Cancer Research,* but made available online for other researchers several months earlier.

Biomarker-Based PET Imaging of Diffuse Intrinsic Pontine Glioma in Mouse Models

Dr. Mark Souweidane and co-author Dr. Uday Maachani

This paper, by Dr. Souweidane's team, describes a successful new way to measure and monitor tumor volume in patients with DIPG. DIPG is so infiltrative and amorphous that the tumor itself is nearly impossible to measure, which makes it especially difficult to monitor either its progression or its response to a treatment being tested. Developing a reliable means of measuring the volume of a DIPG tumor is a significant advance that will greatly aid in the assessment of potential new treatments.

The paper will appear in a future issue of *Cancer Research* and has been made available online in advance of publication.

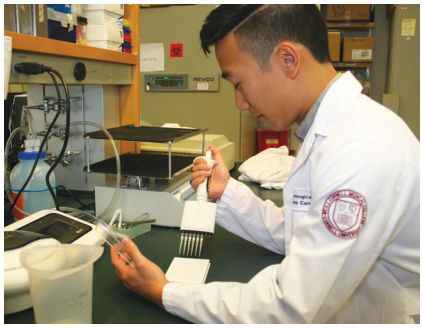
Dr. Souweidane Presents at ASCO

Dr. Souweidane was invited to present results of his groundbreaking clinical trial for DIPG at the annual meeting of the American Society of Clinical Oncology (ASCO), which is the biggest cancer meeting of the year. Dr. Souweidane presented the long-awaited results of his trial testing the safety of convection-enhanced delivery (CED) of a drug directly to the site of the tumor, bypassing the blood-brain barrier.

The results are extraordinarily significant: After 33 infusions (some of which were second infusions in a few of the 25 patients treated), there were zero dose-limiting toxicities. The trial has reopened based on these results, and approval to expand the trial to multiple sites nationwide is now pending.

ABTA Award to Raymond Chang

Weill Cornell medical student Raymond Chang won the American Brain Tumor Association's Lucien Rubinstein Award for his work on the CBTP "summer sprint" in 2016. The annual award is given to the ABTA Medical Student Summer Fellowship recipient whose final report receives the highest score from a panel of scientific reviewers.



Chang spent two months as an ABTA Medical Student Summer Fellow under the mentorship of Dr. Mark Souweidane, researching the effectiveness of pathway inhibitors against DIPG tumors. The goal was to identify potential new drugs to deliver to a brain stem tumor using CED in the next stages of Dr. Souweidane's clinical trial.

Chang tested two PI3K inhibitors and a MEK inhibitor in vitro on patient-derived DIPG cell lines and then in vivo in mouse models. His research uncovered a combination that inhibited DIPG growth in vitro. (Combinations of drugs have been shown to be more effective than single agents, as tumors quickly develop resistance to one drug.) The combination holds promise for use via CED, and Chang is continuing laboratory testing in mice to investigate its safety when infused.

Chang presented his final report, "Synergistic Antineoplastic Activity of PI3K Inhibitor ZSTK474 and MEK Inhibitor Trametinib on Diffuse Intrinsic Pontine Glioma Cells," at the AANS/CNS Section on Pediatric Neurological Surgery.

Family Update

Our families continue to astound us with their loyalty and generosity. From California to New York to Florida, the events kept happening and the funding kept coming. We are so tremendously grateful to all of you!

The Fly a Kite Foundation hosted its first annual HOPE event in May in NYC. David Bernstein presented $10,000 checks to Dr. Oren Becher, Dr. Sharon Gardner, and the CBTP in support of the research.

The annual Cheering for Caitlin 5K and Festival had its largest turnout ever this year, with more than 1,000 participants in Oviedo, Florida, joined by hundreds of others in virtual walks nationwide (including Dr. Souweidane and his family in New York).

The McKenna Claire Foundation hosted its "007th" annual Party with a Purpose at the Huntington Beach Waterfront Beach Resort. This year's event—"A View to a Cure"—raised more than $140,000 for pediatric brain tumor research. (Photo: Kristina Lee)

Upcoming Events

7/15: Freestyle Flashback Benefit Boat Ride (Cristian Rivera Foundation; New York City)

8/1-8/31: Stand Up and Shine Lemonade Stands (nationwide)

8/5: MessFest 2017 (Ty Louis Campbell Foundation; Mahopac, NY)

8/21: 4th Annual Brooke Healey Foundation Golf Outing (Hillsborough, NJ)

8/27: Head for the Cure Metro Kansas City (Overland Park, KS)

9/9: TYathlon 2017 (Ty Louis Campbell Foundation; Mahopac, NY)

10/12: First Annual Hoot Under the Stars (Team Little Owl; Museum at Prairiefire in Overland Park, KS)

10/20: Play It Forward Golf Tournament (Rancho Santa Margarita, CA)

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/

Just missing our last newsletter of 2016, the Cristian Rivera Foundation annual Celebrity Gala in November was once again a sold-out success. With a special appearance from Humans of New York founder Brandon Stanton, this year's event raised $125,000 for the Children's Brain Tumor Project.

Dr. Uday Maachani of Dr. Souweidane's lab stood in for his boss at the Olivia Boccuzzi Run 4Kids event in Brooklyn in June. As the Boccuzzis presented the CBTP with a $50,000 check, Dr. Souweidane was presenting his clinical trial results at ASCO in Chicago.

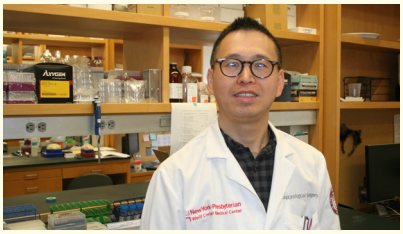
Team Little Owl hosted the "Volley to Beat Pediatric Brain Tumors" at Volleyball Beach in Kansas City, Missouri, in June.

The founders of the Children's Brain Tumor Family Foundation presented Dr. Greenfield and Dr. Souweidane with the proceeds from their events at the 2017 Family Council Meeting of the CBTP. From left to right: Dr. Greenfield, Brenda Ries, Denise Downing, Kyle and Kelly Fisher, and Dr. Souweidane. Not able to attend from the CBTFF was co-founder Kathleen Clark.

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 Faces in the CBTP Laboratories

We recently welcomed two new researchers to the staff. Both will be working with Dr. Nadia Dahmane to advance her work in understanding how fetal development can lead to pediatric brain tumors.



Chaomei Xiang, Ph.D., who joined the team earlier this year, has focused his research career on the fetal developmental aspects and genetics of pediatric brain tumors. His current investigation at the Children's Brain Tumor Project is linked to understanding how glioma progression is controlled by transcription factors.

Victoria D'Acunto graduated from Haverford College in May and joined Dr. Dahmane's laboratory at the CBTP in June. She is working in collaboration with Dr. Xiang on a project investigating the role of the RP58 gene during brain development in mice. Tori will also be working on projects aimed at understanding the mechanisms controlling brain tumor progression.

A New Sprint for Summer '17

Building on the success of last year's "Summer Sprint," the Children's Brain Tumor Project has initiated several new projects that take advantage of summer grants as well as the additional resources we now have available through Dr. Dahmane's laboratory.

Dennis Lee joins Dr. Souweidane's team thanks to a summer grant from the Alex's Lemonade Stand Foundation. Dennis will be investigating drugs that are known to work against androgen-receptor and aromatase-driven prostate and breast cancers, and that show surprising promise against DIPG. Dennis will focus on understanding why these drugs work, since there has not been any previous link between DIPG and androgen-receptor and aromatase. If successful, this work would validate the drugs for further study and could make FDA-approved drugs available for clinical trials for children with DIPG.

Jared Bassett returns to the lab this year to continue the work he started with Dr. Greenfield last summer on immunoglobulin superfamily member 3 (IgSF3) and its role in glioma invasiveness. IgSF3 has been identified by the Greenfield lab as possibly playing a role in how tumors spread throughout healthy tissue in the brain. Dr. Greenfield's lab is engaged in a number of projects to investigate the function of this gene in invasive brain cancers like gliomatosis cerebri.

Staff researcher **Melanie Schweitzer** was awarded a POST grant from the Alex's Lemonade Stand Foundation in support of her current project. Melanie is working with members of Dr. Michael Kaplitt's molecular neurosurgery lab testing the use of focused ultrasound to sculpt the infusion pattern of drugs delivered via convection enhanced delivery (CED). This strategy may prove helpful in achieving better drug coverage of highly diffuse and infiltrative tumors such as DIPG. The ability to alter the drug distribution pattern once an infusion catheter has been placed may allow a surgeon to encapsulate a diffuse tumor in a patient who might otherwise require multiple catheters or additional surgery. Melanie has already acquired some exciting preliminary results and she is working hard this summer to collect and analyze more data.

Second International GC Conference

continued from page 1

research, collaborate on projects, and to identify a plan to move GC research further.

Thanks to Elizabeth's Hope, The Children's Brain Tumor Family Foundation, Kelly and Kyle Fisher, the Joshua Bembo Foundation, and the AYJ Fund, as well as foundations from Peru and across Europe, for sponsoring this important conference.

The challenges are many, and more funding is critical, but research is moving forward and we are grateful to be part of this important team making a difference for gliomatosis cerebri.

Kelly Arabia

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

Elizabeth Minter (1991-2012)

The CBTP was founded in 2011 when the dedication of Drs. Mark Souweidane and Jeffrey Greenfield, neuroscientists at Weill Cornell Medicine 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.

Follow the CBTP on Facebook