

NEUROtransmitter *Communicating our message.*

2019 Gala / Grants and Sponsorships

Feature Article GALA 2020

On Saturday, November 9, 2019, supporters, friends and families came together to share in gala activities at the Glenview Mansion in Rockville, MD while showing appreciation for our honored guests. A roaring fire in the fireplace warmed the chilly evening adding to the ambiance and good cheer. On behalf of the CBTF Board and Advisors, Jeanne Young, president, expressed appreciation for Jenny Hahn and FD Associates, Inc. our event's Hope for Cures Sponsor in memory of Ian FD Associates, Inc., Prism, Inc. and Whittles Therapeutics were acknowledged for their partnership support

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Grants and Sponsorships

NEW (2019)

- Dana-Farber Cancer Institute, Carl D. Novina, M.D., Ph.D., *Defining LncRNA-Transcription Factor Networks in Diffuse Intrinsic Pontine Gliomagenesis*
- The George Washington University, Huadong Pei, Ph.D., *The Roles of O-GlcNAcylation in the Hedgehog Pathway in Medulloblastoma*
- Massachusetts General Hospital, Jian Teng, M.D., *Repurposing low-dose quinolone methanol derivatives as a novel treatment for pediatric high grade gliomas*

Sponsorships

- *International Symposium on Pediatric Neuro-Oncology (Silver Sponsor)*
- *Society for Neuro-Oncology*

Second-year

- University of Maryland, Baltimore (first-year Children's National), Yin Wang, Ph.D., *A Novel Mechanism and Immediately-Translatable Targeted Therapy Group 3 MB*

CBTF RAISES FUNDS FOR RESEARCH

Funds raised benefit pediatric brain tumor research and other CBTF programs

The Childhood Brain Tumor Foundation

Our mission is to support and fund basic science or clinical research for childhood brain tumors. We are dedicated to heightening public awareness of this devastating disease, and improving the quality of life for those that it affects by funding vital research initiatives.



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Our new website will open before the new year!!

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Johns Hopkins Hospital, Baltimore, MD

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Final Summary-Two-year study

Role of MOS Proto-oncogene in H3.3K27M Diffuse Intrinsic Pontine Glioma Baylor College of Medicine, Texas Children's (one-year study) Stephen C. Mack, Ph.D.

We are grateful for support provided by the CBTF and funders that have allowed us to pursue our project on the characterizing "The Role of MOS Proto-Oncogene in H3.3K27M Diffuse Intrinsic Pontine Glioma". Diffuse intrinsic pontine glioma (DIPG) remains a fatal diagnosis with few experimental therapies available to patients in clinical trials. Advancements are desperately needed to improve our understanding of the molecular basis of DIPG to develop safe and effective treatments. Through work funded by CBTF in the past year we were able to make several key findings: 1) That a protein called MOS is highly essential for DIPG tumor cell growth, and 2) MOS and other related genes and transcripts can be inhibited by drugs called bromodomain inhibitors.

An exciting extension of our work on MOS was an unexpected finding that other transcripts, outside genes, called endogenous retroviruses were also activated. This led us to a new idea that targeting both genes and viral transcripts could be an effective therapeutic approach, which is work we published in May 2019, in a journal called *Cancer Cell*. Our findings have also shed insight into the biology of other aggressive pediatric brain tumors such as ependymoma. Importantly, these findings as a result of CBTF funding have now led to a clinical trial proposal to the pediatric brain tumor consortium as a novel therapy for children with DIPG and ependymoma.

Basic research on brain tumors is an area currently in desperate need for advancements that can help establish and guide clinical trials. Unfortunately, brain tumor research, particularly in children remains a topic that is underfunded, thus posing a challenge for researchers entering the field; as a result, a lack of progress on new treatments for patients. For our lab, CBTF has provided the investment needed to launch a project in an area of high clinical need, yet few available resources to obtain pre-clinical data. We have now used this funding and foundational research to apply for additional resources through the National Institutes of Health.



The 19th International Symposium on Pediatric Neuro-Oncology

The Childhood Brain Tumor Foundation is a sponsor for the 19th International Symposium on Pediatric Neuro-Oncology. Meeting to be held, June 21 to June 24, 2020 in Karuizawa, Nagano, Japan.

As always the ISPNO brings together clinicians, researchers, allied health professionals, and experts.

If you are interested in learning more about the Childhood Brain Tumor Foundation, Inc.,

Please contact: **E-MAIL:** cbtf@childhoodbraintumor.org or jeannyoung@childhoodbraintumor.org (**E-mail preferred due to high volume of robo-calls**)

TELEPHONE: 877-217-4166 or 301-515-2900

Volunteers welcome!

Gala continued, In Honor

over the years. Jeanne commented on the honorees heartfelt dedication to the cause.



Citations were presented to all honorees by Maryland State Senator Brian Feldman from his office and U.S. Senator Chris Van Hollen's office. Honorees included medical professionals from Children's National Hospital: Kristina Hardy, Ph.D., Eugene Hwang, M.D., Lindsay Kilburn, M.D., and Karin Walsh, Psy.D. Honorees are carefully selected each year allowing CBTF and its Advisory Board to show appreciation to many deserving individuals. Dedicated to caring for children with brain tumors, Drs. Hardy, Hwang, Kilburn, and Walsh are invaluable assets to the Foundation. They have generously given their time to support our Family Retreat/Conference Day events by sharing knowledge, information, and updates, and Drs. Hwang and Kilburn voluntarily provide support to CBTF by participating as scientific advisors.



Principal Edward Owusu from Clarksburg are High School accepted senatorial citations and a citation from Governor Larry Hogan in recognition of the school's contributions to the Dance Marathon and other activities in memory of Samuel Moore. In addition, three teachers, Jessica and Dave Douglass, and Christina Trumbull were recognized for an event Jess and Dave founded in 2013 in memory of student Samuel Moore who lost his battle to a brain tumor. Christina has continued the event for several years. They have taught students how to organize an event, raise funds, and to value in supporting charity. Sam's dad, John Moore spoke briefly to express his family's appreciation of the Clarksburg team.

As the evening progressed, attendees enjoyed engaging in auction bidding wars, dancing to live music from Steve Young's band, and playing casino games with our entertaining dealers. We hope you will us join us next year! Due to a date conflict, it is possible the event will take place earlier in November or the first weekend in December. Stay tuned!



Please support the Childhood Brain Tumor Foundation

Visit our **GIVE ONLINE** donation button:
<https://www.givedirect.org/donate/?cid=1605>

Be part of the solution in helping fund vital research initiatives cure childhood brain tumors!

*CBTF Advisors
Clarksburg High School
Ella Day
Dave and Jessica Douglass
Jackson Dundon*

*In Honor of
Kristina Hardy
Eugene Hwang
Lindsay Kilburn*

*Roger and Bashi Packer
Coach Jimmy Rizzo
Kathy Triebwasser
Christina Trumbull
Karin Walsh*

MORE RESEARCH SUMMARIES, EVENTS AND UPCOMING EVENTS

New Funding Summary

The Roles of O-GlcNAcylation in the Hedgehog Pathway in Medulloblastoma

Huadong Pei, Ph.D., The George Washington University

Medulloblastoma is the most common and aggressive type of brain tumor in children. It originates in the back part of the brain called the cerebellum. In up to 1/3 of cases, it can spread to other parts of the brain and spinal cord. Most cases are diagnosed before age 10. Perturbation of the Hedgehog (HH) pathway and activation of glioma-associated oncogene (GLI), a dedicated transcription factor in the HH pathway, is responsible for approximately 30% of medulloblastoma. However, incomplete understanding of HH signaling activation represents a significant challenge to designing more effective and personalized treatment for HH-dependent medulloblastoma. The proposed project has the potential to improve public health by elucidating the novel role of O-GlcNAcylation in regulating GLI functions and HH pathway, which will eventually lead to better diagnosis and treatment of medulloblastoma. Treatment for medulloblastoma usually includes surgery followed by radiation or chemotherapy, or both. The proposed work will utilize laboratory-based science to advance strategies for overcoming radiochemoresistance in medulloblastoma.

First-Year Funding Summary going into the second-year

Targeting H3.3 mutations in pediatric HGG

**Brendan D. Price, Ph.D., Dana-Farber Cancer Institute
Department of Radiation Oncology**

Pediatric high-grade gliomas (pHGG) have few treatment options and most children diagnosed only survive for 1-2 years. Identifying new treatments is therefore of the highest priority. Work in the lab is focused on understanding how these brain tumors arise, with the aim of developing new treatments. Pediatric gliomas frequently have mutations in one of the proteins which package the DNA in the cell. This protein, called histone H3.3, plays a very important role in controlling how DNA functions. In pediatric brain tumors, we have found that mutation of a single amino-acid (glycine 34) in H3.3 (called H3.3G34R) blocks one of the cell's DNA repair pathways. This loss of DNA repair has a cascade effect, leading to further genetic changes which ultimately lead to tumor development. However, this makes H3.3G34R pediatric gliomas dependent on other DNA repair pathways to survive. This dependence on a sub-set of DNA repair pathways represents an "achilles heel" which we can exploit to develop new targeted therapies for this disease.

One of the challenges in our work is that there are few cell lines available which we can use to study this disease. Funding from the Childhood Brain Tumor Foundation has allowed us to create cell lines expressing tumor derived mutations in histone H3.3. To achieve this, we have used the new genome engineering method, called CRISPR, to insert point mutations in histone H3.3 which are the same as those found in pediatric patients. This has allowed us to generate paired cell lines which are either normal or mutated for histone H3.3. We are using these cell lines to identify the key DNA repair pathway which is inactivated in pHGG with the H3.3G34R mutation. With support from the Childhood Brain Tumor Foundation, we are carrying a small screen for potential new drugs which can specifically kill these tumor cells. By understanding how these mutations contribute to altered DNA repair in pHGG, we can develop new approaches to treat this intractable disease.

(continued on page 5)

Thank you so much!

FD Associates, Inc.
Roger and Bashi Packer
John Paul II School

Recent Events

2019 Casino Gala

CBTF Sponsorship:

2020 -19th International Symposium on Pediatric Neuro-Oncology
2019-2020 Society for Neuro-Oncology International

Upcoming Events

Family Day
Education and Updates: Childhood Brain Tumors
Saturday, Spring 2020

CBTF Party 2020
TBD Glenview Mansion, Rockville

**Annual Superheroes 5K and Kids Run—Sligo Creek Pkwy
Spring, Sunday, April 19, 2020 (registration to open on the
Potomac River Running website)**

(Contact us if you are interested in helping with any of our events)

RESEARCH SUMMARIES, Give2Charity

Rapid Development of Chimeric Antigen Receptors (CARs) for DIPG

Daniel W. Lee, MD

University of Virginia Cancer Center Charlottesville
(one-year study)

Dr. Lee and his lab set out to develop a brand new tool to effectively treat children with DIPG. Using Chimeric Antigen Receptor (CAR) T cells, a therapy he helped pioneer in children with refractory leukemia, Dr. Lee's lab designed, built, and implemented a new CAR T cell therapy that rapidly and effectively kills multiple types of DIPG tumors in the culture dish as well as in mice with human DIPG tumors in their brains. Importantly, the cured mice do not exhibit any side effects including neurologic effects.

They are on the verge of publishing this data, which is only possible through the help and funding by the generous donors to the Childhood Brain Tumor Foundation. Dr. Lee aims to open a clinical trial of this new CAR T cell therapy for DIPG at the University of Virginia using a new, recently opened clinical-grade cell manufacturing facility.

Defining LncRNA-Transcription Factor Networks in Diffuse Intrinsic Pontine Glioma

Carl D. Novina, M.D., Ph.D.

Dana-Farber Cancer Institute (first of two-years)

"The central organizing idea of biology (dogma) is that DNA (the blueprint of a cell), makes RNA (a messenger of information contained in the DNA) which in turn makes proteins (which carry out the activities of a cell).

Whereas most scientists and physicians study changes in the genes which make proteins, the Novina laboratory is studying a special class of genes which only make RNAs but do not make proteins. These long non-coding RNAs (a.k.a. lncRNAs) were only recently described and very little is understood about how they work. The Novina laboratory has developed a novel platform to identify which proteins bind to disease-relevant lncRNAs. Many lncRNAs frequently alter the activity of the proteins that are bound to them. The Novina laboratory was funded by the Childhood Brain Tumor Foundation to identify how lncRNAs are altered function in Diffuse Intrinsic Pontine Glioma. Dr. Novina hopes that this work will significantly advance the field of lncRNA biology and accelerate the development of RNA-directed therapeutics."

A Novel Mechanism and Immediately-Translatable Targeted Therapy Group 3 MB

First-year Children's National, DC; Second-year University of Maryland, Baltimore

Yin Wang, Ph.D. (two-year study)

Dr. Wang's group has made significant progress for their project, "A Novel Mechanism and Immediately-Translatable Targeted-Therapy for Group 3 Medulloblastoma". Their completed studies have demonstrated that [HIF1 \$\alpha\$](#) is a driver for infant Group 3 medulloblastoma (G3MB) by reciprocal positive regulation with MYC. They found that HIF1 α enhances MYC expression through transcriptional and post-transcriptional mechanisms. In turn, MYC enhances HIF1 α stability via inhibiting the E3 ligase VHL, which otherwise targets HIF1 α for proteasome-mediated degradation. Thus, targeting HIF1 α with liposomal echinomycin, an HIF1 α specific inhibitor, efficiently dampens the oncogenic drivers, HIF1 α and MYC, thereby effectively restraining primary G3MB growth and significantly extending the survival of mice xenografted with primary G3MB. Dr. Wang's group is currently conducting studies to demonstrate the preclinical efficacy of liposomal echinomycin in G3MB mouse models. They have analyzed the dose response of PDX-F211, Icb-1299, and Icb-1459 primary cells to liposomal echinomycin *in vitro* and *in vivo*, and found that these cells are very sensitive to the drug. Furthermore, they are optimizing the liposomal formulation to include targeting ligand for selective uptake by brain tumor cells and thus maximize therapeutic index for pediatric therapeutic applications in infantile G3MB. They have tested the improved brain tumor-specific liposomal echinomycin in mice bearing PDX-F211 xenografts and found that the new formulation further increased survival rates compared to the prior formulation.

The Childhood Brain Tumor Foundation is dedicated to funding research for all pediatric brain tumor types. Please contact us if you have any questions:



cbtf@childhoodbraintumor.org

To make a donation to our cause, visit our secure website: www.childhoodbraintumor.org

HELPFUL RESOURCE LINKS

Thoughts Can Fuel Some Deadly Brain Cancers (paper in Cell), Michelle Monje

"The discovery of a link between tumor growth and brain activity "has opened up a window into potential therapeutic interventions," says Bachelor

Follow the link for more information:
<http://www.npr.org/blogs/health/2015/04/23/401723235/thoughts-can-fuel-some-deadly-brain-cancers>



GRACIOUS GIVING

(continued from page 6)

Repurposing low-dose quinolone methanol derivatives as a novel treatment for pediatric high grade gliomas (one-year)

Jian Teng, Ph.D., Massachusetts General

I want to take this opportunity to sincerely thank CBTF for your funding to my proposal of using a subset of quinoline methanol anti-malaria agents in killing pediatric brain cancer cells. This funding helps us get one step closer to our goal. With the funding from CBTF, I tested several mefloquine analogs in cultured cells and in mouse models, and generated enough preliminary results to initiate two important collaborations, each with proposal to apply funding from NIH or DOD.

1. With Broad Institute at MIT, which can provide all the cutting-edge technologies to support this project.
2. With the Walter Reed Army Institute of Research (WRAIR), which is the original developer of mefloquine and they have more than 300,000 analogs available and agreed to provide any promising compounds for us to test in treating pediatric brain cancers.



There are two easy ways to make a donation:

GIVE ONLINE: Visit our secure website:
www.childhoodbraintumor.org

Go to our **Support page** and click on the **Give2Charity button**.

(Accepts Discover, MC, VISA, and AE).

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20312 Watkins Meadow Drive
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THANK YOU FOR YOUR SUPPORT!

Campaign donations may be made for the United Way (**UW**) through the "donor option" or "donor choice." Please check with your employer in reference to **UW** campaigns.

Thank you donors!



Thank you to our friends who donated through workplace charitable giving campaigns this year, inclusive of the **CFC, Maryland**

The Childhood Brain Tumor Foundation, friends and families are very appreciative of your support. (National) **CFC 12035**

Maryland Charity Campaign

Charity Campaign and other independent campaigns.

The Childhood Brain Tumor Foundation participates in the **Combined Federal Campaign (CFC) and Maryland Charities**.

Check our Website in the late summer or fall for our confirmed designated numbers. Check your campaign pamphlet for our **United Way number or write us in**.

Vehicle Donation Program



CBTF accepts vehicle donations. Help make a difference, donate online or call 877-999-8322 and designate the Childhood Brain Tumor Foundation as your charity of choice.

The service is totally free and includes convenient pick-up of your car, truck, or RV anywhere in the U.S.

Stock Donations

If you would like to make a stock donation, contact us: cbtf@childhoodbraintumor.org

Our treasurer will provide you with the necessary details to proceed with your donation.
Thank you.

Gift Matching Opportunities

Many companies offer a matching gifts program to support charitable organizations.

Your human resources department can tell you if such a program exists at your company. Ask them about the form that can be sent to the Childhood Brain Tumor Foundation reporting a contribution (donation or event contribution). The form states that they will match your contribution.

We return the form to the employer with the proper acknowledgment and information required.
Our website: www.childhoodbraintumor.org

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together, reaching for a cure!



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 Sligo Creek Parkway
 Registration will be on the Potomac River Running website!

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The Childhood Brain Tumor Foundation

Email preferred

cbtf@childhoodbraintumor.org

Telephone: (301) 515-2900

Toll Free: (877) 217-4166

www.childhoodbraintumor.org

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 IRS 501(C)(3) WHOSE MISSION IS TO RAISE MONEY TO IMPROVE
 PROGNOSIS AND QUALITY OF LIFE FOR CHILDREN SUFFERING FROM
 BRAIN TUMORS. EVERY YEAR THE REQUESTS CONTINUE TO GROW,
 WE NEED YOUR SUPPORT.