THE Morgan Adams FOUNDATION

NEWS

MARCH 2018

RESEARCH:
$625,000 funding 11 projects

PEOPLE:
Dr. Adam Green, DIPG Enemy #1

EVENTS:
ISPNO 2018 and other upcoming events

Denver to Host 18th International Symposium on Pediatric Neuro-Oncology

The 18th International Symposium on Pediatric Neuro-Oncology – a unique forum that brings together leading researchers, physicians, surgeons, nurses, and social workers to exchange information and results and collaborate – is coming to Denver this summer. ISPNO is the major global meeting of the international community of professionals involved in the scientific research, diagnosis, treatment, and rehabilitation of infants, children, and young people with central nervous system (CNS) tumors.

This is the first time the symposium will be held in the U.S. since 2008. Denver being named as a host site marks another recognition of the groundbreaking research being conducted at the University of Colorado and Children's Hospital Colorado.

"The fact that this international, highly regarded conference is being held in Denver speaks directly to the leading edge research being conducted at Children's Hospital Colorado, research that would not have been possible without The Morgan Adams Foundation," said Nick Foreman, MD, ISPNO conference co-chair and Associate Chief of the Center for Cancer and Blood Disorders at Children's Hospital Colorado. "The Symposium is critically important for researchers around the world. It provides a forum for the thoughtful exchange of information and many opportunities to further collaborative efforts, both of which will lead to more promising studies that we can use to help our patients."

The Sympoisum will take place from June 30 to July 3 at the Hyatt Regency Hotel in downtown Denver. It will include plenary and poster sessions, keynote talks, and roundtable discussions about the latest research and clinical care of pediatric CNS tumors.

More than 1,500 pediatric neuro-oncology specialists from around the world will come to Denver to engage in dialogue regarding new treatments, innovative research, and advances in pediatric neuro-oncology. **VOLUNTEERS NEEDED!** Please email joan@morganadamsfoundation.org if you are able to help!

For more information, please visit **ispno2018.com**.

MAF Families and Supporters Invited to Attend ISPNO 2018 Family Day

On June 29th, The Morgan Adams Foundation and other organizations will host Family Day on the University of Colorado Anschutz Medical Campus in Denver.

ISPNO Family Day will include a full day of programs specifically created for families of Central Nervous System tumor patients and will cover a wide range of topics, including research updates, education issues, nutrition and wellness, caregiving, and creating a family's "new normal." A special, specific track for adolescents/young adults battling cancer will be offered, and there will also be a special breakout session for grieving families. The day's sessions will be followed by a cocktail hour and dinner.

Family Day is free for our cancer families - however PLEASE DO REGISTER so we can have an accurate head count for lunch and snacks! We hope to see you there.

For additional information AND TO REGISTER, please visit **ispno2018.com**.

UPCOMING EVENTS:

WHAT'S UP DOC?
April 10

GRACE'S RACE
April 29

SILL-TERHAR MOTORS KENTUCKY DERBY PARTY
May 5

MOTORIZED MADNESS MEDIA CHALLENGE
August 1

RMVR RACE AGAINST KIDS' CANCER
August 4-5

16TH ANNUAL MORGAN ADAMS CONCOURS D'ELEGANCE
September 8

THE MOTORING CLASSIC AT ASPEN SNOWMASS
September 13-16

CVAR RACE AGAINST KIDS' CANCER
November 15-18

FOLLOW US!

We share news and updates about our research, Ambassadors, and events on social media daily!

@MorganAdamsFdn

ABOUT THE MORGAN ADAMS FOUNDATION

The Morgan Adams Foundation is an organization dedicated to improving the quality of life and survival rates of children diagnosed with pediatric cancer. Officially established as a 501(c)(3) in October of 2003, the organization is inspired by the memory of Morgan, whose life was taken in 1998 by a brain tumor when she was 6 years old, and all the children and young adults we have come to know who are bravely battling this disease.

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RESEARCHER SPOTLIGHT:

Adam Green, MD, Assistant Professor of Pediatrics

Attending Physician in Pediatric Neuro-Oncology/Oncology

Dr. Adam Green joined the neuro-oncology group at Children's Hospital Colorado in 2014. He has a dual role – caring for patients at Children's Hospital Colorado in the pediatric neuro-oncology department and conducting research for The Morgan Adams Foundation Pediatric Brain Tumor Research Program. His goal is to develop better treatments, and ultimately a cure, for rare brain tumors that have low survival rates. Diffuse Intrinsic Pontine Glioma (DIPG), which has a 0% survival rate, is at the top of his list. The tumor is rare: about 200 patients, mostly between the ages of five and nine, are diagnosed each year in the U.S. The sole treatment option for DIPG is radiation, which only serves to slow the tumor's progression, not stop it.

WHY STUDY DIPG?

I planned to become a pediatrician when I was in high school and I was a neurobiology major in college. I became interested in pediatric brain tumors in medical school and then specifically in DIPG because of a patient I treated during my first year of fellowship. It felt unacceptable to me that we still have a disease in our field for which we can offer patients and families no hope for cure, unlike every other cancer we treat. I felt compelled to try to change this through research.

RESEARCH FOCUS:

In my work on DIPG to this point, we have used cell culture and lab models of the disease, created directly from patient tumor samples, to identify new weaknesses in these tumors and try to exploit those weaknesses through new treatments. We have been able to bring two of these treatments into clinical trials.

GETTING CHEMO TO THE TUMOR:

One trial is designed to determine whether chemotherapy delivered orally or by IV can penetrate to DIPG tissue enough to have an effect. The trial arose from work conducted in our lab as part of the Morgan Adams Foundation Pediatric Brain Tumor Research Program and is currently expanding to other hospitals. The trial will help us decide whether we should continue to investigate new medicines delivered by these routes or focus on delivering chemotherapy directly to the tumor. I am confident we'll be able to answer this question.

ONE TRIAL COMING UP:

Dr. Green and his colleagues will present findings from this clinical trial at the International Symposium on Pediatric Neuro-Oncology, taking place this July in Denver. (See article on Page 1.)

2018 FUNDING:
$625k to Support 11 Research Projects!

The Morgan Adams Foundation Board of Directors has granted $625,000 to fund 11 research projects and equipment in The Morgan Adams Pediatric Brain Tumor Research Program at Children's Hospital Colorado in 2018. This brings the total amount of research dollars we've funded since our inception in 2001 to more than $4.7 million dollars.

"The crucial support from Morgan Adams continues to fund all those high-risk, high-reward studies that would otherwise not be possible," said Rajeev Vibhakar, MD, PhD and Program Leader of Pediatric Neuro-Oncology at the University of Colorado School of Medicine and Children's Hospital Colorado. "It is these studies that often lead to novel, groundbreaking research projects and subsequent therapeutic interventions." (Below is a summary of the research projects funded in 2018. We'll tell you more about these projects and the equipment in upcoming newsletters.)

2018 PROJECTS FUNDED

The RNASeq transition: Creation of a pediatric brain tumor RNAseq reference database (year 2 of 2)

Andrew Donson, Nick Foreman, Rajeev Vibhakar

Through 15 years of using gene chip technology ("chipping") to analyze tissues of brain tumor samples, The Morgan Adams lab now houses one of the largest pediatric brain tumor gene expression databases in existence. This resource has been an essential reference set for state-of-the-art diagnosis, allowing researchers to assign children's brain tumors into newly described and clinically relevant pediatric brain tumor subgroups. RNA sequencing provides amplified data, giving researchers the unprecedented opportunity to identify the DNA mutations underlying tumor growth. Identification of tumor mutations will allow more definitive identification of tumor types so that more effective chemotherapy can be selected to specifically target these tumors.

Chipping "in the round." Extension of tumor characterization to include mutational and fusion data on all new patients

Nick Foreman, Andrew Donson, Rajeev Vibhakar

Researchers will use RNA sequencing to analyze new tumors, as well as tumor samples from the last 30 years. This project will extend the analysis to identifying whether tumors result from gene mutations or fusions of existing genes. This improved characterization of tumor samples provides additional information to help determine the best treatment for each tumor.

High throughput next-gen sequencing and analysis of CRISPR-Cas9 mediated gene knockout system

Sujatha Venkataraman, Rajeev Vibhakar

This project will perform sequencing and analysis of different brain tumor cells based on CRISPR/Cas9 platforms from two companies. CRISPR/Cas9 is a technology that enables researchers to edit parts of the genome by removing, adding, or altering sections of the DNA sequence. (Paid for by The Adam Crocker Fund for Cancer Research.)

Lab model to investigate nanoparticle-mediated brain drug delivery (year 3 of 3)

Krishna Madhavan, Rajeev Vibhakar

Many of the drugs used in chemotherapy to treat brain tumors perform very well in the laboratory settings, but they fail to cross the blood-to-brain barrier in direct clinical applications, meaning the chemotherapy doesn't reach the tumor. This project will study the delivery of drugs using gold nanoparticles into brain tumor cells in lab models to evaluate the effectiveness of delivery routes and the drug dosage required to be effective.

Pre-clinical modeling of drug efficacy in pediatric brain tumors

Angela Pierce, Rajeev Vibhakar

Development of novel drugs to treat pediatric brain tumors is often complicated by a lack of robust pre-clinical data and lab modeling of drugs. This frequently results in phase 1 clinical trials that fail. To avoid situations like this, we have established pre-clinical models of a range of brain tumors (funded by MAF in 2015) and we can test multiple drugs using this platform. These studies will leverage data from all MAF-funded research from the past 7 years to test novel therapeutics and combinations.

High-throughput drug screening in pediatric brain tumors for rapid clinical translation

Andrew Donson, Nick Foreman, Katie Dorris

This project will systematically test more than 100 FDA-approved oncology drugs on all pediatric tumor types, using an established process that allows testing to be done quickly, using tumor samples obtained from Children's Hospital Colorado patients. Previous analysis by researchers led to the identification of novel therapeutic approaches for a patient with an Ependymal tumor.

By specifically testing FDA-approved compounds that already have known treatment effects in adults and often children, the results of testing can be rapidly applied to patients without the need for time-consuming drug development and safety testing.

Disease progression model for H3K27M-mutant DIPG: Determining downstream effects of effective treatment

Sujatha Venkataraman, Adam Green

Diffuse intrinsic pontine gliomas (DIPG) are aggressive tumors at the base of the brain that typically are untreatable. In the past several years, major sequencing projects have

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found most of these tumors harbor a mutation in histone 3 called H3K27M, which is unique in human disease. Histones are proteins around which DNA folds and mutations in these proteins have major implications for which genes are turned on and off. We believe that a better understanding of the H3K27M mutation's effects will allow us to target DIPG treatments against the combination of genetic changes truly driving the tumor.

The oncogenic role of the SEC in H3K27M-mutant DIPG

Nathan Dahl, Rajeev Vibhakar

This project seeks to understand secondary factors, in addition to mutations in the histone 3 gene (H3K27M), that lead to growth of the DIPG tumor. Completion of this project will bring new understanding of the mechanisms by which H3K27M mutations drive the formation of DIPGs and lay the groundwork for a novel therapeutic approach in treating these tumors.

Use of pluripotent stem cells (hiPSCs) to model DIPG cell formation and radio-resistance

Sujatha Venkataraman, Rajeev Vibhakar

This project will use stem cells to create lab models of DIPG tumors and better understand the biology of this tumor, including how tumor cells form and how they develop resistance after radiation. Understanding the biology of a tumor is the best way to target the tumor effectively. This will ultimately result in new therapies for DIPG patients.

Analysis of paired BRAF V600E mutant glioma patient samples to identify novel resistance mechanisms to targeted BRAF inhibition

Jean Mulcahy-Levy, Theodore Nicolaides (University of California San Francisco)

BRAF V600E mutations occur in a variety of gliomas, and the development of targeted therapies has provided a new treatment option for some patients. However, research shows that these mutations are likely to develop a resistance to these therapies. This project seeks to identify molecular and pathway alterations driving resistance to BRAF V600E inhibitors in central nervous system tumors. This will provide tools to identify patients who will need additional therapies to treat their tumors.

Oncogenesis caused by loss of SMARCB1 tumor suppressor is dependent on the activity of SIRT2

Rajeev Vibhakar

This project seeks to determine the molecular mechanisms by which the SIRT2 gene drives atypical teratoid/rhabdoid (AT/RT) tumor progression and to provide pre-clinical validation that using the drug TM is a worthwhile therapeutic approach. It is expected that this will then progress to a phase 1 clinical trial for treating AT/RT patients.

THE Morgan Adams FOUNDATION
Funding Kids' Cancer Research
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