Children are our future! They are the rainbow that make our days bright

**HOPE** for more tomorrows for children with Neuroblastoma is the theme of the Neuroblastoma Children's Cancer Society. HOPE stands for the following:

**H**elp for Children and their Families  
**O**ncology Research  
**P**ublic Awareness  
**E**ducation

**In Memory of… Zachary Montell Allen**

- **State:** Illinois  
- **Family:** Sister Kylee Allen, Mom and Dad John and Nikki Leman  
- **Pets:** Dog Spanky (pug); Bearded Dragons Spike and Spikette  
- **Favorite place:** Walt Disney World  
- **Favorite thing:** Disney Cruise  
- **Favorite movie:** Napoleon Dynamite  
- **Favorite song:** Weird Al Yankavich  
- **About Zachary:** Zachary made sure that everyone around him had a smile on his face. He was a comedian. He would make statements that he would grow up to be a comedian to make others smile. He was known as "Teen Wonder" - he turned 13 years old before he went to heaven. He never let NB (fought for 9 years) define who he was.

The Neuroblastoma Children's Cancer Society is a group of volunteers, many with children or relatives who have been both victims and survivors of the disease. The Organization is an advocate for the children and their families and is dedicated to providing support. The primary focus of the Organization is to raise money to assist local research in neuroblastoma cancer and to bring the fight to a national level to try and focus additional research and funding until a cure can be found!
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Those areas in bold will be the focus of our quarterly newsletter. Please send in your ideas, articles, requests, special stories and pictures to: The Neuroblastoma Children’s Cancer Society P. O. Box 957672 • Hoffman Estates, IL 60195

GUIDE TO INTERNET CONNECTIONS
Please note that some of this information is the most current that is available, while some is not always updated regularly, particularly medical information.

AMERICAN BRAIN TUMOR ASSOCIATION HOME PAGE: www.abta.org

AMERICAN SELF-HELP CLEARINGHOUSE, SELF-HELP SOURCE-BOOK ON-LINE: Information on national and model self-help support groups, clearinghouses, organizations, and resources — www.cmhc.com/self-help/

CANCER KIDS WEBSITE: www.cancer.org

CANCERNET and PDQ: This website is managed by the National Cancer Institute and provides information on cancer treatment, supportive care, and advocacy — www.cancernet.nci.nih.gov

CANDLELIGHTERS CHILDHOOD CANCER FOUNDATION: Links to other information and resources on childhood cancer. www.candlelighters.org

CHILDREN’S MEMORIAL HOSPITAL www.childmm.edu/cmhweb/default.htm

UNIVERSITY of CHICAGO COMER CHILDREN’S HOSPITAL www.uchicagokidshospital.org

HISTIOCYTOSIS ASSOCIATION OF AMERICA: The goals of this organization include public and professional education, patient and family support, and stimulation and support of research — www.histio.org

KIDS WITH CANCER — www.kidswithcancer.com


NATIONAL CHILDHOOD CANCER FOUNDATION (NCCF): Describes NCCF and offers a listing of CCG clinical cooperative group protocols — www.nccf.org/

NATIONAL HEALTH INFORMATION CENTER (NHIC): This website is managed by the NHIC, a government sponsored health information referral service. Offers direction to other organizations and resources — http://nhic-lt.health.gov

NEUROBLASTOMA CHILDREN’S CANCER SOCIETY: Provides information on neuroblastoma for families of children diagnosed with this form of cancer — www.neuroblastomacancer.org

PEDIATRIC ONCOLOGY GROUP (POG): www.pog.ufl.edu/main.html


Newsletter Generously Funded by:
We need a sponsor for our newsletter!

NOTE FROM THE EDITOR
The views contained in the articles of this newsletter are the opinions of the authors. The editor and Neuroblastoma Children’s Cancer Society are not in any way affiliated and make no attestation in support (or against) the information supplied in these articles.
October 4, 2010

Neuroblastoma Children's Cancer Society,

I wanted to share two recent research articles that I published in *BMC Cancer* and *Molecular Cancer*, respectively, which highlight two distinct, yet complimentary, research trajectories that my laboratory is pursuing with your support.

I am pleased to share that the first article, which appeared in *Molecular Cancer*, illustrates our in vitro and in vivo laboratory experiments which confirmed that the SPARC peptide FSEC has great potential for clinical application in high-risk neuroblastoma patients, more so than any other previously established anti-angiogenic peptides. In fact, FSEC has implications on the treatment of a broad range of pediatric and adult cancers that depend on angiogenesis.

The second article features research in which I collaborated with Lucy Godley, MD, PhD, to better understand the epigenetic underpinnings that are associated with poor outcomes in children with neuroblastoma. Our findings suggest that epigenetic aberrations contribute to neuroblastoma phenotype and that our application of the 5-Aza-dC treatment can reverse epigenetic changes and eradicate a tumor's ability to form and grow.

Both of these lines of research demonstrate noteworthy forward progress in our understanding of the disease, which I aspire to translate into more personalized therapies for each neuroblastoma patient, based on phenotype. Thank you for your support of my efforts and confidence in our work.

Sincerely,

Susan L. Cohn, MD
Professor and Director of Pediatric Clinical Sciences
Section of Pediatric Oncology, Department of Pediatrics
University of Chicago
Due to the rarity of neuroblastoma, research in this field has been hampered, especially among the "high-risk" subset of patients that still experience long-term survival rates of less than 40%. Multi-institutional, cooperative group clinical trials are needed to enroll sufficient numbers of patients for prospective randomized clinical trials, and it has become increasingly apparent that greater international collaboration is needed to conduct research on this rare pediatric cancer to improve survival rates and minimize treatment-related toxicities. Dr. Susan Cohn and her neuroblastoma research colleagues around the world have a long-standing commitment to international collaboration as demonstrated by the recent development of the International Neuroblastoma Risk Group (INRG) Classification System.

To facilitate comparison of clinical trials performed in different regions of the world, Drs. Cohn and Pearson, in collaboration with colleagues across North America, Australia, New Zealand, Europe and Japan, developed the International Neuroblastoma Risk Group (INRG) Classification System. This classification system is based on the statistical analyses of 35 potential prognostic factors in a cohort of 8,800 neuroblastoma patients enrolled on cooperative group studies and is being used to define uniform risk-groups across these geographical areas to ensure the results of clinical trials conducted in different regions of the world can be directly compared.

With Dr. Cohn as co-Chair, the INRG Task Force also developed a mechanism for investigators from around the world to mine the INRG database to advance research with meaningful populations. To date, 20 neuroblastoma research projects have been approved by the INRG Executive Committee, resulting in several abstract presentations, publications, and our improved understanding of the disease. To facilitate expansion of the INRG database and to have the ability to perform analyses with more complex data, from multiple datasets, there is a need for the development of technologies to support and expand the access, management, organization, analysis, and dissemination of these data.

To date, the INRG Task Force has collected data on roughly 11,500 children diagnosed with neuroblastoma between 1980-2002. A number of Society for International Pediatric Oncology Europe Neuroblastoma (SIOPEN) and Children's Oncology Group (COG) cooperative group studies have recently been completed, and we anticipate adding data from over 4,000 new patients treated on these studies within the next two years. This database contains by far, the largest number of neuroblastoma patients ever collected, and significant discoveries have already been made in data mining projects using this unique research. Although the data mining studies have led to a number of seminal discoveries, the current application housing the INRG database has a number of limitations.

**VISION**

Our goal is to harness the outstanding computational infrastructure and expertise at the University of Chicago to develop technology that will facilitate international, multi-institutional, interdisciplinary research in childhood neuroblastoma. Over the long term, this technology will accelerate research efforts for a better understanding of the epidemiology of this disease, the genetic mechanisms that contribute to tumor behavior and development, the long-term consequences of treatment, and new strategies for tumor treatment and prevention.

We are working to create a system, the Interactive International Neuroblastoma Information Network (IININ), which will provide physicians, scientists, and other members of the INRG community with access to high-quality health and research related information resources and services. We intend to integrate data from multiple datasets pertaining to childhood neuroblastoma, including biological data, phenotypic measures, and clinical outcomes. By leveraging the current data collection and sharing procedures developed by the INRG community, we will be positioned to expand the connections to additional datasets, introduce tools for facilitating data requests and data sharing, and create interfaces for data visualization and basic statistical analysis. This infrastructure is likely to provide a distinctive advantage to scientists involved in neuroblastoma research and thus enable new perspectives, collaborations and knowledge. The specific aims of the proposed 2-year project are:

1. **To assess the information needs of researchers, biostatisticians, and clinicians.** We will use an adaptation of the Critical Incident Technique and survey instruments to analyze and understand the information and data needs of researchers in the INRG Task Force. These studies will explore issues related to data governance, data sharing, and application functionality.

2. **To develop an architecture for the ININ database.** We will develop database models and web applications to support research in neuroblastoma. We will evaluate the INRG data set and additional clinical, biological, genomic, outcomes, imaging, and survivorship data. We will leverage the interaction of clinicians, researchers, and biostatisticians to clarify and refine the models and applications.

3. **To assess the ease-of-use of the application in a pilot study.** We will use a pilot study and standardized instruments to measure the perceived ease of use, usefulness, functionality and satisfaction of the application. We will conduct usability studies to analyze the process of users performing a task, and the ease with which they can do this. These studies will be instrumental for guiding our future developments.

(continued on page 7)
NCCS Awards $50,000 Neuroblastoma Research Grant

September 25, 2010
Dr. Susan Cohn
University of Chicago

Dear Dr. Cohn:

The 9th Annual 'Friends of Michael Williams' Fund Raiser is expected to raise over $25,000. 'Friends of Michael Williams' is a chapter of the Neuroblastoma Children's Cancer Society. NCCS matched the proceeds in the amount of $25,000.

We are pleased to announce that you, in connection with the University of Chicago Hospital, are the recipient of our annual research grant for neuroblastoma research totaling $50,000! We want this to help support the International Neuroblastoma Information Network directed by Dr. Cohn.

We appreciate your dedicated work and support of neuroblastoma research. It is our hope that our grant will give you the financial means to support the research that will lead to a cure for neuroblastoma! Best of Luck!

Warmest Regards,
James F. Sexton Dori Sexton
Chairman Executive Director

October 4, 2010
Mr. and Mrs. James and Dori Sexton
The Neuroblastoma Children’s Cancer Society

Dear Dori and Jim:

Thank you for directing the Neuroblastoma Children's Cancer Society's generous match of the 'Friends of Michael Williams' gift to support my neuroblastoma research at the University of Chicago. Your partnership has allowed me to work in collaboration with investigators around the world to better understand and more effectively treat this devastating disease.

As you well know, one of my top priorities is to build an online database to facilitate data sharing and international, interdisciplinary research in neuroblastoma. With your support, we are already harnessing the outstanding computational infrastructure and expertise at the University of Chicago to develop this Interactive International Neuroblastoma Information Network (IININ), which, over the long term, will accelerate research efforts for a better understanding of the disease and strategies for tumor treatment and prevention.

This database is likely to provide a distinctive advantage to scientists involved in neuroblastoma research and thus enable new perspectives, collaborations and knowledge. We anticipate that this technology will also serve as a model for other pediatric cancer registries. It is a truly revolutionary tool that holds great promise improving the way we identify and treat neuroblastoma.

Such ground-breaking collaboration is possible only through your and the 'Friends of Michael Williams' generosity and continued partnership. Dr. Sam Volchenboum and I both look forward to updating you on the progress of the IININ and to what we can accomplish together. In the meantime, thank you for your hard work on behalf of patients and families with neuroblastoma.

Susan L. Cohn, MD, Professor and Director
Clinical Sciences • Department of Pediatrics
Section of Pediatric Hematology/Oncology
University of Chicago

SAVE THIS DATE
SEPTEMBER 24, 2011
10th Annual Friends of Michael Williams Golf Outing
Epigenetic Alternations (continued from page 3)

**Methods:** Two NB cell lines (tumorigenic LA1-55n and non-tumorigenic LA1-5s) that differ in their ability to form colonies in soft agar and tumors in nude mice were used. Quantitative RNA expression analyses were performed on seven genes in LA1-5s, LA1-55n and 5-Aza-dC treated LA1-55n NB cell lines. The methylation status around *THBS-1, HIN-1, TIG-1* and *CASP8* promoters was examined using methylation specific PCR. Chromatin immunoprecipitation assay was used to examine histone modifications along the *THBS-1* promoter. Luciferase assay was used to determine *THBS-1* promoter activity. Cell proliferation assay was used to examine the effect of 5-Aza-dC on NB cell growth. The soft agar assay was used to determine the tumorigenicity.

**Results:** Promoter methylation values for *THBS-1, HIN-1, TIG-1, and CASP8* were higher in LA1-55n cells compared to LA1-5s cells. Consistent with the promoter methylation status, lower levels of gene expression were detected in the LA1-55n cells. Histone marks associated with repressive chromatin states (H3K9ME3, H3K27ME3, AND H3K4ME3) were identified in the *THBS-1* promoter region in the LA1-55n cells, but not the LA1-5s cells. In contrast, the three histone codes associated with an active chromatin state (acetyl H3, acetylH4, and H3K4Me3) were present in the *THBS-1* promoter region in LA1-5s cells, but not the LA1-55n cells, suggesting that an accessible chromatin structure is important for *THBS-1* expression. We also show that 5-Aza-dC treatment of LA1-55n cells alters the DNA methylation status and the histone code in the *THBS-1* promoter modifies cell morphology, and inhibits their ability to form colonies in soft agar.

**Conclusion:** Our results suggest that epigenetic aberrations contribute to NB phenotype, and that tumorigenic properties can be inhibited by reversing the epigenetic changes with 5-Aza-dC.

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**Memorial or Honor Gift Request**

Your Name: ____________________________
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☐ In Memory Of  ☐ In Honor Of  ☐ On the Occasion Of

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City: ____________________________ State: _____ Zip: _____

I would like an acknowledgement gift card sent to: ____________________________

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Send form and payment to: NCCS, P. O. Box 957672 • Hoffman Estates, IL 60195

Donations also can be made online through PayPal. Go to our web site at www.neuroblastomacancer.org.

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United Way is not just about giving ... it's about caring

You can designate that your contribution be given to NCCS.

Call us at our office for details (800) 532-5162.

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Save The Date

Michael James Sexton Memorial 5K Run/Walk

Saturday, Sept. 10, 2011 a.m.

Busse Woods Forest Preserve Elk Grove Village, IL

All proceeds will go to neuroblastoma research

More information to come at www.neuroblastomacancer.org

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(1-800-422-6237)

☐ Tips to prevent cancer
☐ Informational Materials
☐ Answers to questions about cancer
☐ Other Resources

www.cancer.gov/publications

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Fund-Raisers
HOW
The IININ will be an internet-based initiative designed to stimulate research and accelerate progress on epidemiology, prognosis, treatment, and outcome of neuroblastoma in children. The main goal is to serve as the international resource for researchers in the neuroblastoma community, providing an environment that would include phenotypic, genotypic, and environmental data from patients of multiple backgrounds, gender, race and ethnicity. A secondary goal is to facilitate local, regional, and international collaboration among researchers, clinicians, research institutes, and national organizations.

To ensure that we have the ability to collect more complex patient data and that investigators have access to high-quality health and research related information resources, we plan to develop technologies to support the INRG database’s expansion into the IININ. The IININ will provide unparalleled opportunities for investigators focused on studying this rare cancer, and we anticipate this research will ultimately direct us to a better understanding of neuroblastoma genomics, epidemiology, therapeutic strategies, and long-term outcome. We anticipate that this technology will also serve as a paradigm for other pediatric cancer registries.

Drs. Susan Cohn, Eneida Mendonca, and Wendy London co-direct this project because their expertise is synergistic. Dr. Cohn is a pediatric oncologist who has devoted her career to the care of children with NB and to understanding the molecular pathogenesis of the disease through the investigations of her laboratory.

Dr. Mendonca is Board-certified in pediatrics and intensive care with a doctoral degree in biomedical informatics. A member of the University of Chicago Computation Institute, she has expertise in user needs assessment and the development and evaluation of clinical and research systems. Her research interests lie in using computational methods and informatics techniques to analyze large biomedical data sources for patterns and new knowledge. As Director of Informatics for the New York-Presbyterian Hospital from 2002-2007, Dr. Mendonca led the development of a web-based registry which currently includes more than 140,000 children has been used by inpatient and outpatient clinics associated with both the Weill Medical College at Cornell University and Columbia University.

IMPACT: ONE EXAMPLE
Less than 5% of localized neuroblastomas are MYCN amplified, a genetic marker that is strongly associated with aggressive behavior and poor outcome in advanced-stage disease. Because of the rare nature of this finding in localized disease, it has been difficult to develop an evidence-based therapeutic strategy for this group. Because of the large numbers of patients included in the current INRG database, it presents a unique opportunity to study rare subgroups of patients, including those with unusual combinations of clinical and biological features. Our current database includes 87 patients with low-stage, MYCN amplified neuroblastoma, more than three-fold the number of patients ever previously reported with these clinical and biological features.

Although tumor cell genetics was associated with outcome in this cohort of patients, more modern genome-wide molecular studies are likely to reveal the genes and cellular pathways that distinguish the tumors that will be cured from surgery alone from the ones that will require additional treatment. This is an intriguing set of tumors to analyze because by definition, they all have MYCN amplification, yet only a subset behave aggressively, suggesting that the MYCN targets are not universally activated. Genome-wide molecular studies of neuroblastoma tumors are being conducted in laboratories around the world, and these data are largely available to the public. Linkage of the clinical and biological data in the IININ database with publicly available genomic data will provide an unprecedented resource for analyzing neuroblastoma biology and determining risk. Our long-term goal is to improve the outcome for all children with neuroblastoma using an evidence-based approach. For rare cohorts of patients such as those with MYCN-amplified localized neuroblastomas, large databases, like the proposed IININ database, with detailed clinical and biological information are essential.
NEW NCCS WEBSITE NOW LIVE

CURRENT FEATURES EXPANDED
- Links to Vital Resources
- Legislation Update
- Fund-raising Opportunities
- Resource Handbook

NEW FEATURES INCLUDE...
- Contact with Medical Advisors
- Postings of Current Research and Treatment
- YouTube Video of Our Special Kids
- Facebook and Family Communications

PLUS MUCH MORE!

Please update your child’s profile on WALL OF FAME

http://www.neuroblastomacancer.org

WALL OF FAME SPONSORS

Please help us by sponsoring one of our children and build our WALL OF FAME!! The response to our survey and WALL OF FAME has been overwhelming. We have had over 200 families respond with pictures, drawings, surveys, etc. and they are still rolling in. Come visit our internet WALL OF FAME being built and see our little celebrities, our children. Now we need your help to complete this project. The wall is now complete and we have over 200 children who represent the thousands of U.S. families affected by neuroblastoma. Please help by sponsoring or finding sponsors for these children. If we can raise $2,500 for each child, we will have raised over $250,000, 100% of which will be used for a neuroblastoma research grant.

Let us build this WALL OF FAME and provide HOPE for these children! Together we can make a difference!

My tax deductible contribution is enclosed:
- $25,000
- $2,500
- $1,000
- $500
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- Other $___________________________

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Child’s Name________________________________________

Donations can be made online through PayPal. Go to our web site at www.neuroblastomacancer.org.

For all donations: My name is____________________________________

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