SUMMER 2012

Children's Tumor Foundation
Ending Neurofibromatosis Through Research

NF NEWS
The Newsletter of the Children's Tumor Foundation

The Children's Tumor Foundation Invites You to Join the NF Registry

The Children's Tumor Foundation is pleased to announce the creation of an online NF Registry. Launched at the 2012 NF Forum in New Orleans, LA, the purpose of the registry is to find people who may be eligible for clinical trials or other research studies being conducted in the field of neurofibromatosis (NF), and to determine the commonality of specific NF characteristics. The NF Registry can be found at **www.nfregistry.org**.

For those who participate in the NF Registry, after entering their information (or their child's information), the Children's Tumor Foundation will look for clinical trials or research studies that are seeking people with the participant's NF characteristics and age. If they find a match, the Children's Tumor Foundation will provide the participant with contact information at the institution conducting the research, so that direct contact can be made.

The information contributors provide about their NF will be summarized along with data from other registry participants so that those researching NF can understand how common specific characteristics of NF are, and what treatments are being used. The Children's Tumor Foundation may share data in the registry with individuals or institutions conducting clinical trials or research studies, companies developing potential drugs or other treatments for NF, or other parties involved in research of patients with NF, but **any information that identifies the participant will be removed**.

To join the NF Registry please go to www.nfregistry.com.

For more information about this important development in the fight against NF, please contact Annette Bakker, Chief Scientific Officer of the Children's Tumor Foundation, at 212-344-6633, ext. 7029 or abakker@ctf.org.

Jim Bob and Laurée Moffett receive an award of recognition at the NF Forum Awards Dinner for their dedication to fighting neurofibromatosis. L-R: Laurée Moffett, Jim Bob Moffett, John Risner, Foundation President, Stuart Match Suna, Chairperson of the Board.

NF Forum 2012: Hope, Help, Heal

The Children's Tumor Foundation's fourth annual NF Forum was convened in New Orleans, LA, June 8-10, 2012, with the theme "Hope, Help, Heal." The largest number of Forum participants thus far, approximately 200, enjoyed a weekend of seminars, question-and-answer sessions, and social events that brought them into contact with the world's foremost NF researchers and gave them the opportunity to build supportive relationships with one another.

The Forum, co-chaired by Amanda Bergner, MS CGC of Johns Hopkins University, Dr. Tena Rosser of the Children's Hospital of Los Angeles, and Murray McCartan, NF Endurance Team Captain of the Twin Cities Marathon,

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NF Conference: The Premier Annual Event in the Neurofibromatosis Research and Clinical Calendar

Children's Tumor Foundation
CONFERENCE

The 2012 NF Conference was held June 9-12 in New Orleans, LA. The NF Conference, founded and hosted by the Children's Tumor Foundation since 1985, is the world's premier gathering of scientists and clinicians dedicated to advancing research and care for individuals living with NF1, NF2, and schwannomatosis. The NF Conference has grown significantly in recent years, which reflects an expanded understanding and interest in neurofibromatosis research and development.

This year's Conference was chaired by two pioneers in NF research and care, Dr. Helen Morrison, a top NF2 scientist from the Fritz-Lipmann Institute in Jena, Germany, and Dr. Brigitte Widemann, a world-class NF clinician from the National Institutes of Health. The agenda featured a balanced collection of basic science, clinical care, and clinical trials presentations regarding NF1, NF2, and schwannomatosis.

Following the Conference, noted experts in the field of NF shared their thoughts on the meeting's highlights.


Dr. Helen Morrison


Dr. Brigitte Widemann

Drs. Helen Morrison and Brigitte Widemann:

"The NF Conference is a unique platform for basic research and clinical work. While growing, the Conference is still small enough that we can communicate, review, and organize efficiently. Below are a few specific examples of the exciting breakthroughs reported at this year's NF Conference:


Dr. Luis Parada

- The first keynote lecture from **Dr. Luis Parada** presented his work which showed that CXCR4 was expressed in MPNST [malignant peripheral nerve sheath tumors – a rare but potentially fatal manifestation of NF1], pointing to the potential benefit of using CXCR4 inhibitors as therapy for MPNSTs.
- **Dr. Rhona Mirsky**, a prominent Schwann cell biologist, delivered an illuminating presentation about the plasticity of Scwhann cells and the molecular pathways present in an injury model. This was Rhona's first time attending the NF Conference, and we're excited about her continued interest in the field.
- **Dr. Gehlhausen**, from **Dr. Wade Clapp**'s lab, presented his work on a novel NF2 animal model in which mice develop hearing loss that correlates with NF2 progression in humans.
  [Ed. Note: CTF is providing funding, through a YIA to Dr. Gehlhausen (see page 3), to expand this research to understand the temporal and anatomical distribution of schwannoma development, functional studies of hearing loss, and vestibular dysfunction that are observed in human progression of NF2.]
- **Dr. Scott Plotkin** gave an informative overview of the REINS [Response Evaluation in NF and Schwannomatosis] initiative.
- **Rene Bernards** delivered an excellent presentation titled "Approaches to Guide us in Choosing Therapies in Cancer." He explored how patients are sometimes enrolled in clinical trials in which the agents do not work and how we may be able to optimize the results of trials.
  [Ed. Note: Dr. Annette Bakker, CTF's Chief Scientific Officer, feels that Rene Bernards presentation underscores the importance of the NF Registry launched by the Children's Tumor Foundation (see page 1). This will help identify patients that should receive clinical benefit from specific agents. To learn more about the registry and to participate, please visit: www.nfregistry.org.]


Dr. Scott Plotkin


Dr. Roger J. Packer

Dr. Roger J. Packer, *Senior Vice President, Center for Neuroscience and Behavioral Medicine, and member of the Foundation's Medical Advisory Committee:*

"For me, the overwhelming highlight of the meeting was how quickly the field of neurofibromatosis has transformed itself into a therapeutic one. Multiple sessions, both for children and adults with NF1 and NF2, highlighted the rapid progress that has been made in the molecular understanding of the disease and how these understandings have already resulted in the development of multiple clinical studies. Working groups and established consortiums now exist to perform these studies. The next greatest challenge is how to make these studies even more biologically informed, evaluating enriched patient populations with the type of molecular and clinical characteristics most likely to benefit from therapy. Another major challenge remains in designing these trials so as to not put patients at undue risk for complications that are significant but, unlike the situation in many diseases, are chronic."

Dr. Bruce Korf

Dr. Bruce Korf, ***Chairman of the Children's Tumor Foundation's Medical Advisory Committee:***

"The most salient aspect of the Conference for me was the discussion of treatment endpoints for the various forms of NF and the consideration of candidate therapeutics."

Dr. Karen Cichowski

Additionally, **Karen Cichowski**, the Director of the Foundation's NF Preclinical Consortium, delivered a presentation at the Conference about the Consortium and its impressive progress.

NEXT STEPS

Following each NF Conference, the Foundation, the Conference Chairs, and the session Chairs publish a report outlining the presentations made throughout the week. This report, published in top medical journals, informs a broad spectrum of the research and clinical communities about important advances in NF research, improvements in care, and next steps that need to be taken in the search for treatments and a cure.

Dr. Cristina Fernandez-Valle and Alejandra Petrilli

YOUR INVESTMENT AT WORK

Drug Discovery Initiative Research Yields Encouraging Results, Receives Follow-On Funding

Dr. Cristina Fernandez-Valle, an NF2 researcher in the Burnett School of Biomedical Sciences at the College of Medicine at the University of Central Florida, received two grants from CTF in 2011. A pre-doctoral student in her laboratory, **Alejandra Petrilli**, received a Young Investigator Award (YIA) and Dr. Fernandez-Valle received a Drug Discovery Initiative (DDI) grant. The goal of the projects was to establish protocols for using mouse merlin-null schwannoma cells in a high-throughput screening format. Once this primary objective was met, the team conducted a screening of the Library of Pharmacologically Active Compounds (LOPAC) in conjunction with the Sanford-Burnham Medical Research Institute (SBMRI) located in Orlando, Florida. The results identified 40 molecules in the 1284 compound library that slowed the growth of merlin-null Schwann cells. The results of this pilot study were used as preliminary evidence in three grant applications made to the National Institutes of Health and the Congressionally Directed Medical Research Program funded through the U.S. Department of Defense. The million dollar proposals, if funded, will use this new approach to screen two larger compound libraries, again in conjunction with the experts at SBMRI. In addition, CTF is funding a follow-up project in Dr. Fernandez-Valle's laboratory to confirm and validate the initial "compound hits" from the LOPAC library. The overall hope with this project is that compounds will be identified that are already in clinical use for other conditions and which could be "fast-tracked" into clinical use for NF2.

Dr. Marco Giovannini

Children's Tumor Foundation Funds the First Schwannomatosis Animal Model

The laboratory of **Dr. Marco Giovannini** is interested in the genetic events that contribute to tumor development. Using advanced gene targeting methods, generating mouse models of cancer that accurately reproduce the genetic alterations present in human tumors is now relatively straightforward. The challenge is to determine to what extent such models faithfully mimic human disease with respect to the underlying molecular mechanisms that accompany tumor initiation and progression. Using conventional and conditional loss-of-function and gain-of-function mutations, scientists in Dr. Giovannini's lab have generated several mouse models of neurofibromatosis type 2 and, more recently, of schwannomatosis. Interestingly, although initiated by a Smarcb1 mutation, molecular analysis of peripheral nerve tumors in the schwannomatosis mouse model showed a profile of cell signaling pathway activation similar to that of NF2-associated schwannomas. In addition to the mice, cells derived from mutant animals are used to study the function of these genes in cell culture models. These represent excellent model systems for investigating the molecular mechanisms that underlie schwannomatosis and its relationship with NF2. "Our mouse models should be suitable to further dissect pathways critically important in schwannoma development and serve as invaluable tools to test new intervention strategies. We have also derived a series of cell lines that reproduce the disease when grafted into peripheral nerves. These may also facilitate design of better therapies for schwannomatosis patients," concludes Dr. Giovannini. *[Ed. Note: These studies were supported by CTF Schwannomatosis Awards, in 2007, 2008, and 2011.]*

PROFILES

The Children's Tumor Foundation is excited to announce the recent addition of Marco Nievo and Kathleen Berentsen as consultants to the Foundation.

Dr. Marco Nievo

Marco Nievo is a PhD in biological chemistry and a certified patent attorney. He will provide the professional Intellectual Property and competitive services necessary to adapt the Foundation's business model where necessary.

Kathleen Berentsen

Kathleen Berentsen, a Certified Genetic Counselor and Clinic Coordinator with long-standing experience in neurofibromatosis, will work on improving care and coordinating best practices in the Foundation's NF Clinic Network.