Highlights of the 2014 NF Conference

This year’s NF conference, the premier annual event in the neurofibromatosis research and clinical calendar, was held June 6-10 in Washington, D.C. Over 300 people attended from around the world to present the latest developments in NF research and clinical care. The Conference’s theme was “Connecting for a Cure” and included seminars by NF experts, as well as high-profile keynote speakers from related disciplines such as cancer and neuroscience, serving to stimulate thought and build connections between NF and other disorders. Many attendees praised this year’s conference as one of the best NF meetings in years. The 2014 NF Conference Co-Chairs were Dr. Yuan Zhu, PhD of the Gilbert Neurofibromatosis Institute, Children’s National Medical Center and Dr. Bradley Welling, MD, PhD of Massachusetts General Hospital/Harvard University.

It was a pleasure to welcome Dr. Francis Collins, Director of the National Institutes of Health, to this year’s NF Conference. Dr. Collins was a special guest for the Children’s Tumor Foundation; not only has he been a very successful NF doctor, but he discovered the NF1 gene and subsequently donated the patent rights to the Foundation.

All the NF gene masters were present this year: Dr. James Gusella who discovered the NF2 gene, Dr. Theo Hulsebos who discovered the first schwannomatosis gene (SMARCB1), and Dr. Ludwine Messiaen who recently published the discovery of LZTR1 in schwannomatosis. In addition, the Foundation organized the first “Innovative Business Opportunities in NF” meeting for members of the financial, nonprofit, and pharmaceutical industry, as well as clinicians and researchers. (See page 7)

The following are highlights from the 2014 NF Conference.

CLINICAL SCIENCE
A workshop on behavior and cognition in children with NF1, organized by Dr. Maria Acosta, MD, reported that children with NF1 are more likely to have trouble distinguishing subtle facial expressions, which may interfere with social development. (Kristina Hardy, Children’s National Medical Center). Autistic-like behaviors are associated with NF1, but are different than “classic” autism. They can start around ages 8-11 and often involve mainly social communication deficits (John Constantinou, Washington University in St. Louis). Kathryn North, professor of Pediatrics and Health at the University of Sydney, reported that while the IQ of children with NF1 lags behind peers during the childhood years, it seems to “catch up” by age 30. Early diagnosis of cognitive difficulties can be made in children with NF1 as young as 21 months of age. Phonics training is helpful in these children, since many have particular difficulties with sounding out words.
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BASIC SCIENCE

The basic science presented at the meeting highlighted the exciting new advances in the field as a direct result of CTF funding. Using funds provided by CTF’s Young Investigator Award, Dr. Kairong Li developed a completely new class of mouse models mimicking human NF1 mutations. He created mice with mutations like those in NF1 patients in which there is a premature “stop signal.” This type of mutation occurs in approximately 20% of people with NF1. The researchers will study mice with premature stop mutations, and test a group of drugs called “nonsense suppressors” in these mice. These drugs can read through a premature “stop signal,” which would result in normal NF1 protein. The approach of using drugs that “read through” a stop signal, with the goal of restoring gene function, has been feasible in genetic disorders such as cystic fibrosis and Duchenne muscular dystrophy. In this way, CTF funding will lead directly to a completely new class of drugs to treat NF.

Another exciting new technique is being used by CTF-funded scientists to find new treatments for NF2. The innovative technique is called “kinome screening,” and it’s being used in the Synodos Consortium that CTF created. Kinome screening compares NF2 samples with unaffected samples, and searches for a type of gene (kinase genes) changed in NF2. These genes can then potentially be targeted with specific kinase inhibitors to treat NF2. Together with Dr. Gary Johnson’s lab, Dr. Vijaya Ramesh has uncovered several candidate kinase genes. Inhibitors of these kinase genes are now being tested in animal models of NF2. These discoveries may lead to new treatments for NF2, and would not have been possible without the funding from CTF.

There were also presentations about advances in the field of impaired fracture healing and reduced muscle strength in NF1. Fractures often require multiple surgeries and potential amputation, and children with NF1 may have low muscle tone and coordination difficulties. The groups of Dr. Aaron Schindeler and Dr. Kate Quinlan in Australia, both recipients of CTF Drug Discovery Initiatives, have developed exciting new mouse models to further study these features of NF1 and screen for compounds to treat these aspects of the disease. Dr. Quinlan’s group developed muscle-specific NF1 mutant mice and Dr. Schindeler’s group developed a mouse model in which NF1 is mutated at the site of the tibial fracture. Using this model of tibial fracture, they found a very promising combination of drugs that heals the fractures and will soon lead to clinical trials. These mouse models will be available to the NF community of scientific researchers through the CTF Drug Discovery Initiative Toolbox, which was created in order to foster collaboration and accelerate drug discovery for the treatment of NF.

Another exciting advance in the field is the discovery of biomarkers for MPNSTs. Researchers have long wondered how to tell if a plexiform neurofibroma would turn into an MPNST. To identify key gene signatures of MPNST, Dr. Karen Cichowski has used “transcriptional profiling,” which is a comparison of genes that are expressed in plexiform neurofibromas compared to genes expressed in MPNSTs. She has identified biomarkers that could potentially be used to screen plexiform neurofibromas and identify which might be at risk for developing into an MPNST. This groundbreaking discovery would not have been possible without CTF funding.

THOUGHTS ON THE 2014 NF CONFERENCE

Dr. Bruce Korf, MD, PhD, of the University of Alabama at Birmingham and Chair of CTF’s Medical Advisory Committee:
“Two things stood out to me at the recent NF Conference and NF Forum: First is the dramatic increase in the number of drugs that are being validated in animal models and may be ready for clinical trials; second is the energy that resulted from having NF scientists as well as patients and families in the same room for the symposium dinner. I have no doubt that the scientific community was greatly inspired by this event, and by the meeting as a whole.”

Mr. Randall Stanicky, Managing Director of RBC Capital Markets and CTF Board Member:
“It was inspiring to see the interest expressed during the ‘Innovative Business Opportunities in NF’ session as the potential for additional capital to come into NF research to help find new therapies...
This year’s NF Conference hosted a satellite meeting outlining innovative business opportunities in the field of neurofibromatosis, including a presentation of the NF market model. Foundation President Annette Bakker opened the meeting by highlighting the various CTF initiatives aimed at bringing treatments to patients through industry involvement. She explained that all drugs currently under clinical investigation for NF are repurposed medications that were initially developed for other more lucrative diseases, (most notably cancer), and that drugs that are conceived specifically for NF should soon appear in the global research pipeline.

David Lapidus, a Principal at LapidusData, gave a presentation on the hard numbers of the NF market value, a CTF-commissioned study which is based on the epidemiologic data of NF and analyzed according to the various segments of the NF market (i.e. plexiform neurofibromas, optic pathway gliomas, MPNSTs, etc.)

These presentations served as grounds for a panel discussion led by Randall Stanicky, CTF Board Member and Managing Director at RBC Capital Markets. Panelists included representatives from clinical care, (Dr. Scott Plotkin of Massachusetts General Hospital), the venture capital world, (Sara Nayeem of New Enterprise Associates and Isai Peimer of MedImmune Ventures Inc.), the industry sector, (Mark DeSouza of desouzatech and Gideon Bollag of Plexxikon), the non-profit arena, (Margaret Anderson of FasterCures), and the healthcare market, (David Lapidus of LapidusData). These discussions highlighted a growing interest from industry in NF and a strong incentive for companies to invest in this sector.

INNOVATIVE BUSINESS OPPORTUNITIES IN NF

Dr. Karen Cichowski, PhD, of Brigham and Women’s Hospital and Harvard Medical School: “The best aspect of CTF’s NF Conference is that the basic scientists and clinicians get the opportunity to really interact. As a consequence, basic discoveries are now being translated into clinical trials, and new discoveries keep fueling new ideas.”

UPCOMING EVENTs:

September 4-7, 2014:
16th European Neurofibromatosis Meeting,
Barcelona
www.nfbarcelona2014.org

October 10-12, 2014:
Annual NF2 Ohio Gathering
www.ohiogathering.com

UPCOMING AWARD APPLICATION DUE DATES:

Clinical Research Awards LOI (CRA)
August 4, 2014

Schwannomatosis Awards
September 1, 2014

Drug Discovery Initiative (DDI) Awards “B”
September 2, 2014

NF Clinic Stipend Awards
November 20, 2014

For more details visit www.ctf.org/research