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THE NATIONAL NEUROFIBROMATOSIS FOUNDATION, INC.

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Scientists Report NF Research Progress

by Dr. Judy A. Small

NNFF Director of Clinical Trials
and Technology Transfer

(Editor's Note: "The NNFF International Consortium for the Molecular Biology of NF1 and NF2 has served as the catalyst for many of the fundamental scientific discoveries in NF1 and NF2. These meetings provide a regular forum to bring together molecular and cell biologists, geneticists, clinicians, and others in and outside the NF field to share their latest findings. The Consortium agenda includes equal time for NF1 and NF2 presentations. The following are highlights of the oral and poster presentations. A copy of the full meeting agenda and presenters can be found at http://www.nf.org/nf_professionals/consortium/2002aspen_summary.pdf)

The pace of research continued to amaze the more than 150 scientists who attended the 2002 meeting of the NNFF International Consortium for the Molecular Biology of NF1 and NF2, held in Aspen, CO, in June. The meeting was chaired and organized by Dr. Peggy Wallace (University of Florida) and Dr. Rick Fehon (Duke University).

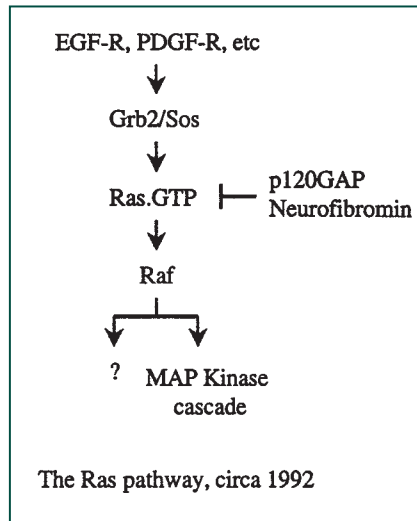
Researchers reported that mouse models have become more sophisticated, and can be programmed to develop tumors specific to NF1 and NF2. Studies are being done using promising new drugs or other treatments using these and other animal or cell models.

While mice serve as one way to help scientists better understand tumor growth, natural history studies are ongoing to study plexiform neurofibromas in people with NF1 and vestibular schwannomas in people with NF2. The results from these studies will provide information critical to assessing the effectiveness of drugs in clinical trials.

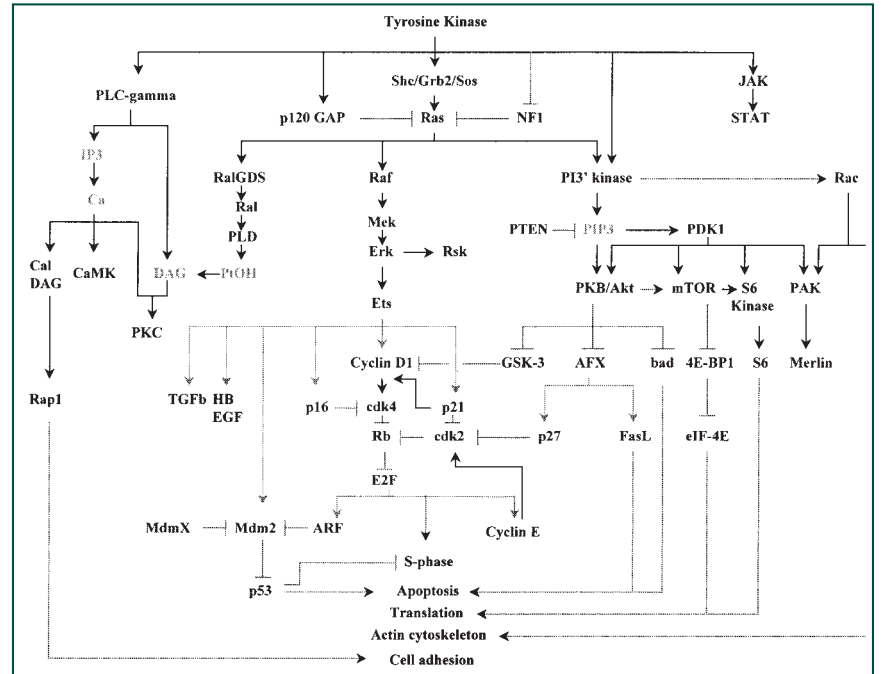
Scientists are also looking at the chain of events that occur in pathways that signal cells to grow and divide to become tumors. Researchers now know more than ever about these signaling pathways and their role in cell growth in both NF1 and NF2.

Results reveal clearer picture about patients' experiences

Dr. Jan Friedman of the University of British Columbia reported results that differ from the conventional wisdom of the clinical picture of NF1— that NF1 largely manifests as a cosmetic problem and that the course of NF1 is not predictable. He dispelled these theories by describing the slightly increased risk for malignancy and the



Dr. Frank McCormick of the UCSF Cancer Center provided this chart (right) illustrating the complexities of what is known today about the Ras oncogene. The chart (above) illustrates what was known in 1992.



shorter life expectancy for the 1300 patients with NF1 whose cases were culled from death certificates. While these death certificates indicate life spans 10 to 15 years shorter than the general population, the findings may represent a biased case ascertainment, where less severely affected individuals may not have been included by this method.

Dr. Friedman also found through *The NNFF International Clinical Database* of patients with NF that there is a correlation between certain features of NF1 among families, including skin pigmentation, tumor burden, and risk for malignancy.

Three other studies looked at variability in familial cases of NF. Dr. Rosemary Foster of Harvard Medical School described a set of identical twins with the same NF1 mutation and very different manifestations, with one sister unaffected except for one

café-au-lait spot, and the other sister's symptoms including multiple neurofibromas and a plexiform neurofibroma. In a poster Dr. Meena Upadhyaya of the University of Wales, UK, described a Portuguese family with three independent mutations in the NF1 gene in different family members. Meanwhile, Dr. Ludwine Messiaen, University Hospital Ghent, Belgium found that in two families with spinal neurofibromatosis, even with the symptoms running true between families, the mutations were not the same.

Several posters addressed the cognitive and behavioral aspects of NF1. Scientists working with Dr. Bartlett Moore at University of Texas MD Anderson Cancer Center suggested the use of visual-spatial performance deficits as a diagnostic indicator in children with questionable diagnosis of

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Mice Provide New Insights into Basis of Tumor Growth

Dr. Luis Parada, a molecular biologist at the University of Texas Southwestern Medical Center at Dallas and colleagues from UT Southwestern and France, reported findings in a May issue of the journal *Science*. Dr. Parada, an NNFF Research Advisory Board Member, and his UT Southwestern colleagues Drs. Yuan Zhu, Pritam Ghosh and Dennis Burns found:

- Genetically engineered mice developed by Dr. Parada et al. had one good and one bad copy of the NF1 gene. The NF1 gene plays an important role in cell growth in everyone. When the NF1 gene functions normally, people have two good copies of the gene. But when the gene is mutated in neurofibromatosis the body's cells carry one good and one bad copy of the gene. If the single good copy of the gene for some reason turns bad, then

tumors can grow. The work was based on studying mouse tumors that were identical to neurofibromas seen in human NF1.

- Schwann cells, cells that insulate the nerve fibers, are the ones that start a tumor growing when there are two bad copies of the NF1 gene.
- Mast cells, which are immune system cells, are partners in the formation of tumors, and migrate to the nerve fibers where there are damaged Schwann cells, even before the tumor starts to grow.
- Tumors formed only when the mast cells also had one bad copy of the NF1 gene, not when they had two good copies. Learning that the genetic makeup of the non-tumor cells also matters provides new information that has never been shown for any other kinds of cancer. **NF**

NNFF Young Investigator Awards Announced

The Foundation has announced the list of Young Investigators it is funding in 2002/03. "This list represents an extraordinary group of young scientists in the fields of NF1 and NF2. Most of them are new to the field," NNFF President Peter Bellermann said, "They came from outstanding laboratories in the United States and abroad, and we hope that many of them will make careers in our field."

2002/2003 Award Projects

"The Role of Genomic Instability in NF2-Related Tumors"

The Richard and Marcy Horvitz Family Fund

Dr. Angela A. G. van Tilborg
Erasmus University Rotterdam,
The Netherlands

"Recruitment of Stem/Progenitor Cells to Brain Tumor Vasculature"

The Edward and Deanne Spiegel Fund

Dr. Kenneth S. Cohen
Harvard Medical School/MGH

"Analysis of Gene Expression in Drosophila NF1 Mutants using DNA Microarrays."

The Kite Foundation

Dr. James Walker
Harvard Medical School/MGH

"Mechanism of Protein 4.1B Growth Suppression"

The Steven and Lottie Walker Family Foundation

Dr. Victoria A. Robb
Washington University School of Medicine

"A Clinical Screening Package for Cognitive Deficits in NF1"

The Barrie and Faith Sommerfield Family Fund

Dr. Shelley Hyman
Children's Hospital Westmead, Australia

"Genetic and Molecular Identification and Characterization of Drosophila Merlin/NF2 Modifiers"

The Adam Goodkind Family Fund

Dr. Sarah Hughes
Duke University

"The Actions of Nerve Growth Factor and Vascular Endothelial Growth Factor on the Function of Haploinsufficient NF1 Sensory Neurons"

The Joseph S. Byrka Medical Research Fund

Dr. Cynthia M. Hingtgen
Indiana University

"Novel Imaging Modalities for Plexiform Neurofibromas"

The Leslie and Bill Griffin Family Fund

Dr. Michael J. Fisher
Children's Hospital of Philadelphia

"Adenovirus Mediated Inhibition of Tumorigenesis in a Neurofibromatosis Type 1 Mouse Model"

The Jaffa Family Fund

Dr. Laura Klesse
University of Texas Southwestern Medical Center at Dallas

"GM-CSF Signaling through the Bc Subunit and Myeloid Leukemia after NF1 Gene Loss"

The Barrie and Faith Sommerfield Family Fund

Dr. Kelly Morgan
University of Minnesota

"The NF2 Gene Product- Merlin: Elucidation of Function as a Tumor Suppressor and Its Regulation"

The Adam Goodkind Family Fund

Dr. Joseph Kissil
Massachusetts Institute of Technology

"Functional Analysis of NF1 in Schwann Cell Development and Tumorigenesis"

The Edward and Deanne Spiegel Fund

Dr. Yuan Zhu
University of Texas Southwestern Medical Center at Dallas

"Genetic Mapping of Familial Schwannomatosis"

The Richard and Marcy Horvitz Family Fund

Dr. Sami Gritli
Harvard Medical School/MGH

"Genetic Analysis of NF1 Function in Drosophila"

The Mark B. Wallner Foundation

Dr. Anne Tchoudakova
Harvard Medical School/MGH 

NF Research (continued from page 1)

NF1. The group also confirmed that there is an increase in psychosocial problems in children with NF1.

Touching on another developmental issue, Dr. Gene Fisch of Yale University analyzed age-related characteristics in IQ of children with NF1. He showed that there were no significant age-related declines among children and adolescents with NF1.

Studying The Natural History of Tumors

Technological advances are helping to bring an additional level of knowledge to the Natural History Study of NF1 Plexiform Neurofibromas. In the past, plexiform neurofibromas have been difficult to measure accurately. Dr. Bruce Korf (Harvard Medical School/Partners) described the sophisticated imaging technology that makes it possible to measure the 3-D volume of these tumors, and to follow their progression over time. In addition, Dr. Korf noted that the study is still seeking adults with internal plexiform tumors.

The Natural History Study of NF2 Vestibular Schwannomas recently has been expanded and will now cover NF2 tumors in the entire body, Dr. William Slattery (House Ear Institute) reported. The study will include clinical evaluation, mutation analysis, and tumor growth and pathology.

Managing NF

A number of posters focused on pre-clinical testing and the development of therapies. Several drugs have been identified with potential to treat NF-related tumors and are being tested in animal models or in human tumor cell cultures.

Dr. Dusica Babovic of the Mayo Clinic reported that pirfenidone, an antifibrosis drug, is being tested in clinical trials for plexiform neurofibromas, and in cell models of malignant gliomas. Dr. Victor Mautner, University Hospital Eppendorf and Klinikum Ochsenzoll, Germany is testing Exisulind, a cell death-inducing drug, in cell culture models of MPNST. Dr. Andreas Kurtz, Harvard Medical School/MGH, is testing Oncolytic Herpes Simplex Virus, which targets and kills neurological tumor cells,

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Annual NF Prizes Awarded

The NF Prize was created to stimulate interest among young scientists to make careers in NF research.

Entries are solicited from graduate and post-doctoral students from around the world. A panel of experts selects the winners.




Dr. Scott Boyd

Dr. Scott Boyd, MIT is the winner of the 2002, peer reviewed, worldwide competition for The NF Research Prize. A Canadian hailing from Winnipeg, Manitoba, Dr. Boyd is a Rhodes Scholar working in Dr. Tyler Jacks' laboratory at the MIT Cancer Research Center on. His focus is the regulation and transcriptional targets of the p53 tumor suppressor protein, and related proteins.

Dr. Boyd's prize submission was titled "Mammalian Synthetic Lethal Screens for NF1 Therapeutic Targets". With this submission, Dr. Boyd won the prize, plus a

\$10,000 stipend and also travel expenses to the annual meeting of the NNFF International Consortium For the Molecular Biology of NF1 and NF2.

Second Prize (\$5,000 plus travel expenses to the annual Consortium meeting) went to Dr. Benjamin Braun, UCSF, for "The Use of Conditional Alleles of NF1".

The Third Prize (\$3,000 plus travel to a Consortium meeting) was awarded to Dr. Yuan Zhu, University of Texas, SW for "Identification of the Role of Mast Cells in Neurofibroma Formation". 

Reproductive Issues in NF

The National Neurofibromatosis Foundation regularly receives phone calls and e-mails about reproductive health issues for people with NF. The following is a sample of these commonly asked questions and their answers. Dr. Mia MacCollin of Harvard University and Dr. Peggy Wallace a Professor of Molecular Genetics and Microbiology, and Pediatrics at the University of Florida, Gainesville contributed some of the answers regarding genetic testing. If you have specific questions related to NF and reproductive health, the NNFF recommends you discuss your concerns with a physician and/or genetic counselor at an NF clinic. A list of NF Clinics can be found at http://www.nf.org/us_clinics/

How is NF passed on within families?

Q. If a member of my family has NF is there a possibility that I could have NF too?

A. That depends which family member has NF. When there is a family history of NF it can only be passed directly from parent to child. So if one of your parents has NF, you have a 50% chance of having inherited NF from that parent.

Q. Can I be a carrier for NF and pass it on to my children even if I don't have NF myself?

A. When the NF gene mutates (by a process still unknown), it causes disease. Thus you cannot be a carrier — have the mutated gene — and not have NF. Also, the mutated gene does not skip generations. If you have NF you have a 50:50 chance of passing on the mutant gene with each child.

Q. If I have NF what are the odds that my children will have NF?

A. With each child there is a 50% chance you will pass on the NF to that child.

Q. I have NF1, is it possible for my child to inherit NF2 from me?

A. NF1 and NF2 are two separate genetic disorders caused by two different genes. Therefore, it is not possible to pass NF2 to your child if you have NF1.

Q. I think I have both NF1 and NF2?

A. While NF1 and NF2 share some general characteristics (e.g. spinal and brain tumors, some skin problems), they are distinct and separate conditions and people either have one or the other. Therefore, it is important that a knowledgeable physician determine if you have the more common NF1 or if you have NF2.

Women's Reproductive Health Issues

Q. My fiancée has NF and some day we'd like to have children. Do women with NF have more pregnancy complications?

A. In general, studies indicate that relatively common pregnancy complications are not more frequent among women with NF1 than in the general population. However, there may be a small group of women with NF1 that

are at increased risk because of manifestations of NF that affect their reproductive health. These women may require close monitoring at a high-risk obstetric center. It is also important that anyone with NF who is considering having children discuss the risks and options at least 6-months prior to conception.

Q. I have read that some women with NF get more tumors during pregnancy or when using birth control pills. Is that true?

A. There has been little research done to explain any link between hormones and neurofibroma growth in women. Some women report that they notice an increase in tumor activity during pregnancy. Since there is no evidence that oral contraceptives do not increase NF symptoms, it may be advisable to consider using other forms of contraception, unless medical reasons for using the Pill outweigh the theoretical reasons for not using it.

Genetic Testing

Q. Do I need to have a blood test to tell whether I have NF?

A. An examination by a physician familiar with the signs of NF is the best way available to determine whether NF is present. There is no blood test that can reliably diagnose NF at this time. Blood testing to identify an NF mutation can be done in some circumstances, but it is best used for genetic counseling purposes (see below) rather than diagnostic purposes.

Q. Is there a prenatal test that can be done to see if I have passed NF onto my child?

A. There are two kinds of genetic test that can be used. A pre-natal *linkage analysis* test can be done when there is a family history of NF1 at least two generations available for testing. Blood is collected to get DNA from family members who have NF. Since this method detects a marker for the mutation, rather than the actual NF1-causing mutation, it is extremely accurate but not quite 100%.

Or a *mutational analysis* test can be done when only one family member with NF is available for testing. This test can use either a blood or tumor sample to determine the NF gene sequence. This test has limitations and it is still not possible to find the mutation in every person, even if he has a clinical NF diagnosis.

Once mutational analysis or linkage analysis has been done, testing of a pregnancy may be accomplished by amniocentesis or by chorionic villus sampling.

Q. How long for prior to pregnancy do they have to start the process?

A. The test to find the affected parent's mutation can take a long time to complete.

So, it is best to allow at least six to nine months before becoming pregnant to begin the testing process.

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New Leadership for NNFF Board

After completing two two-year terms, Chairman Bruce Judson, Esq. passed the leadership gavel to Richard A. Horvitz, Esq. at the June 2002 Board of Directors meeting. Mr. Horvitz has been an active Board member for six years, and has previously served as the Foundation's Treasurer.



Richard Horvitz, Esq.


"The NF community is blessed with a terrific board of talented and hard-working individuals, some fighting on behalf of affected family members and some just dedicated to helping others in need," Mr. Horvitz said. "Service on this particular board is more than a fiduciary responsibility—it is a sacred trust. I feel honored by the opportunity to serve as chairman for such a group."

Mr. Horvitz is the CEO of Moreland Management, a family investment office in Cleveland, Ohio. He currently is the Associate Treasurer of Jewish Community Federation of Cleveland, as well as Chairman of their Finance and Investment Committee. Mr. Horvitz is a director of both University Hospitals of Cleveland and University Hospitals Health System, as well as an active member of QualChoice, Inc., their health

insurance subsidiary. He is also a member of the board of University School, a local country day school. He is an Honorary Life Member of the Board of Visitors of Duke University School of Law and is active on their Campaign Planning Committee.

Joel I. Cohen of New York City was named Vice Chairman. Mr. Cohen has been a board member since 1999. He is the Managing Director of Client Advisory Services for Rockefeller & Co. of New York City. Mr. Cohen serves on the Board of Directors of 4Kids Entertainment and Junior Achievement of New York.

John W. Risner, CFA, a resident of Larchmont, New York, was named Acting Treasurer. Mr. Risner is a new Board member and has been active in the foundation for over ten years. Mr. Risner became active with the NNFF after his oldest son was diagnosed with the disease. Mr. Risner is a Chartered Financial Analyst and is a Portfolio Manager specializing in high yield bonds. He is a member of the Association for Investment Management and Research and the New York Society of Security Analysts.

Susan Harvey of Seattle, Washington, a board member since 1999, continues as the Foundation's Secretary. Mr. Judson will continue to serve as a Director of the Foundation. 

CHAPTER NEWS

WAGING THE FIGHT AGAINST NF AT THE GRASSROOTS

California



Movie Town Makes Way for NNFF Fundraisers

Top Left: Over 500 people made their way to the Egyptian Theater in Hollywood to recognize guest of honor Tom Hansen during the NNFF California Chapter's 2002 Hero for a Cure Award and Movie Spectacular. The event featured Mr. Hansen's favorite movie "The Adventures of Robin Hood" starring Errol Flynn.

Above: Co-Chairs of the event Rick Jaffa and Amanda Silver took a break from the festivities to pose with Heroes for a Cure award recipient Tom Hansen, CA Regional VP Stuart Rogoff and NNFF President Peter Bellermann.

Left: A fashion show by a local boutique wrapped up the festivities during NNFF California Chapter's First Annual "Chari-Tea" Luncheon / Fashion Show held at The Reef Restaurant in Long Beach, CA. The California Chapter sends a big thanks to Patti Montemer, who spearheaded this event.

Want to participate? Contact NFCAL@aol.com

Connecticut



Fairway Fundraising in CT

The Byrka Family hosted friends to a day of golf during their 12th annual Friends of NF Celebrity Golf Classic in Ellington, CT. The event brought together long time supporters and sports and TV personalities including Pete Johnson (former Cincinnati Bengal), John Davidson (MSG, NY Rangers and NHLTV), Olivia Brown (Miami Vice) and Art Still (former Kansas City Chief). To learn more about this event, log onto www.nf.golf.com

Colorado



CO Goes Bowling for Bucks

The NNFF Colorado chapter hosted their 2nd Annual Bowl-A-Thon at the Arapahoe Bowling Center in Englewood, CO. The event, which was co-sponsored by South Metro Fire District firefighters, was a great success for adults and kids alike. The Colorado Chapter looks forward to the 2003 season with many great fundraising events on the horizon. To learn more about Colorado's upcoming events, please contact the Colorado Chapter at bkhnn1@aol.com

Maryland



MD Moves to Speed NF Research

Jeff Robertson and the Robertson/Cashour families hosted the 2nd Annual JARC Tournament at Whiskey Creek Golf Club in Ijamsville, MD. The event began two years ago in honor of Jeff's sister Julie Ann Robertson Cashour and the legacy of her struggle against NF. For more information on this event, please contact Jeff Robertson at 301-607-8001

Missouri



Show Me State Says Show Me the Money

NNFF Missouri Chapter enjoys great food, dancing and the company of good friends during the 6th Annual Patio Extravaganza at Harry's Restaurant and Bar in St. Louis, MO. To learn more about this event contact the NNFF MO office at Nfmissouri@aol.com

New Jersey



New Jersey Marches to Awareness

Adults and children, police officers and mayors all joined together at the NNFF Tri-state Chapter's Annual New Jersey NF Walk during May's NF Awareness Month. Interested in learning more about New Jersey's activities, contact DonnaNF@aol.com

Oregon



Spring Fling Sends Oregon Around the Maypole

Oregon's Governor and the Mayor of Portland declared May - NF Awareness Month. The month also kicked off with a Spring Fling event complete with a Maypole. To learn more about Oregon's activities, please contact Walktours@aol.com

New York



The Big Apple Takes Tea (Tee) Three Ways

Above Left: Posing in designs by April Cornell, friends and members of the Tri-State Tea Party Committee gathered at the first Annual Mother Daughter Tea Party in New York City's Historic Puck Building.

Above Right: The LoPrimo family hosted an early kick off to the spring golfing season with the 3rd Annual NNFF Benefit Golf Classic at the Silver Lake Course in Staten Island.

Right: Celebrating its 5th year, The Jerry Shannon Memorial Golf Tournament once again brought people from around the country to share good times on the course and raise money for the NNFF.

To learn more about New York events, contact plinton@nf.org



Pennsylvania



PA Goes Hog Wild for NF

Top and Bottom Left: Kim Sloop of Carlisle, PA organized the 1st Annual Jordan's Ride for Research in which motorcycle riders went to the open road to help raise funds for NF. A second Ride for Research will be happening in October of 2002.

Bottom Right: An NF Patient and Family Picnic was held in Carlisle, PA thanks to event coordinator, Kim Sloop. People came from Ohio, Pennsylvania and North Carolina to participate in PA's first get to know you event.

For more details on PA happenings, contact Kim Sloop at nfpennsylvania@msn.com

Washington



Fundraising Efforts in Washington State Take Root

Buying and selling plants was the activity of the day during the 15th Annual Garden Sale hosted by the NNFF Washington Chapter. Other NF Washington happenings during the past few months include the 6th Annual NF Golf Outing, a Racquetball Tournament and a Spring Education Workshop. To find out more about these events, contact the NNFF WA office at nf@nffwa.org

NF Research (continued from page 2)

in cell culture models of MPNST.

NF2 in children is more easily diagnosed with better imaging techniques and molecular diagnostics. Surgical treatment, however, results in less favorable outcomes in children compared to adults according to Dr. Fabio Nunes, Harvard/MGH. Dr. Clemens Hanemann, University of Ulm, Germany reported that patients may suffer from peripheral neuropathy. An analysis of peripheral nerves in patients with NF2 found multiple tumorlets along the length of peripheral nerves, which may cause compression of adjacent nerves.

There were two posters with information on surgical interventions in young patients with NF1. Dr. Tena Rosser, Children's National Medical Center, found that the most common surgery was for plexiform neurofibromas, followed by orthopedic procedures for scoliosis and pseudoarthrosis. Dr. G. Tirino of the Second University of Naples, Italy found that reduction of optic gliomas by chemotherapy did not improve symptoms, and tumor growth did not necessarily involve visual impairment.

Better Mouse Models Yield NF Insights

In the past it has been difficult to do preliminary research about NF tumors and potential treatments because it was not possible to produce the tumors seen in humans in NF affected mice. Dr. Kevin Shannon of the University of California, San Francisco reported on the NF Mouse Models Consortium, which the NNFF initiated. This group of the world's leading mouse model scientists has made possible model systems for NF that more closely approximate the tumors that occur in NF1 and NF2. In addition, these mice have provided new data on the biochemical actions of the NF proteins.

The mice have also yielded new data about the role of NF1 in the formation of cardiac cells. Dr. Aaron Gitler of University of Pennsylvania presented data that the mice showed some cardiac abnormalities, which suggests that NF1 is controlling some types of non-nerve related cells.

God's Caregivers: A Journey of Faith by Robert V. Weeber

Soft Cover—136 pages
published by iUniverse
\$12.95

In 1962 Robert and Jane Weeber became parents of twin boys, Bobby and Nicky. Both boys were born with NF1 and have experienced some less common and severe manifestations of the disorder. *God's Caregivers: A Journey Of Faith* is Robert Weeber's first per-



son account of the issues the family dealt with from the time the twins were born.

son account of the issues the family dealt with from the time the twins were born.

Weeber splits his time chronicling the family's interaction with the health care system from diagnosis to hospital stays to home care and insights culled from their experiences with schools, insurers and social services. Weeber brings the fresh, less often articulated, perspective of a father dealing with a child's NF.

Weeber is brutally honest about the issues faced by his twin sons, including Bobby's death in 1993. Even though Bobby and Nicky's cases are more severe than most, Weeber's book hits on themes central to any parent's experience while raising a child with NF – fear of NF's unpredictability, frustrations with the health and educational systems, stress

NF In The News: Parade Magazine

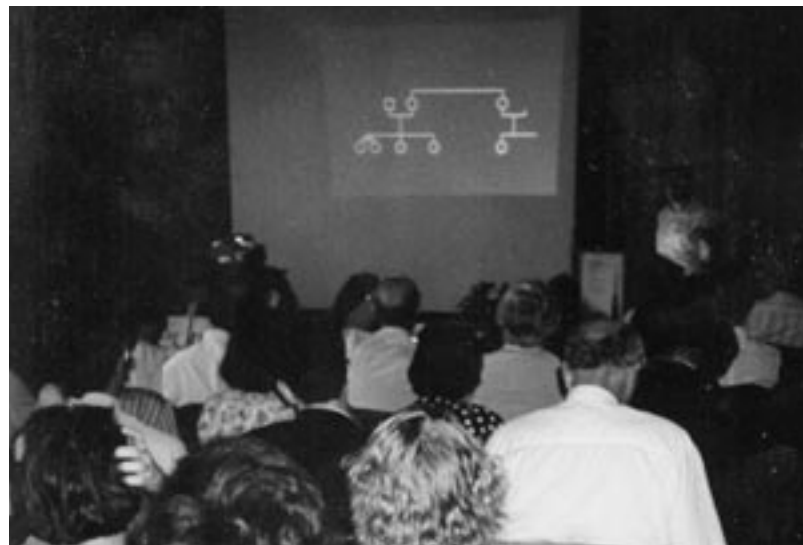
Neurofibromatosis was in the national spotlight in June with a two-page spread in *Parade*, a magazine supplement to daily newspapers around the country. The article was a profile of NNFF Board member, former astronaut and retired Sen. Jake Garn of Utah and his son, Matthew, who has NF1. NNFF Medical Affairs Director Dr. Allan Rubenstein was also interviewed for the article.

The article was the result of work by the National Neurofibromatosis Foundation and two of its families who have connections to *Parade*. *Parade* reaches 75 million readers. The Garns had never spoken to the media about their family's experience with NF before this article. The article's impact was felt immediately as NNFF received hundreds of calls from *Parade* readers. **NF**

In NF1 mice with leukemia, Dr. Richard Chao of the University of California, San Francisco, found that NF1 affected mice developed more treatment-induced malignancies after radiation and chemotherapy when compared with non-NF1 mice.

Dr. Laura Klesse of University of Texas Southwestern used cells from NF1 mutant mice to study cell signaling pathways. By treating the cells with a chemical compound she was able to inhibit the cell pathway to prevent tumor growth.

Mast cells are a cell type associated with inflammation. They move into an area where the body perceives trauma. These cells are among several cell types found in neurofibromas. Dr. David Ingram of Indiana University described experiments investigating the role of mast cells in NF1 tumor formation. He found that mast cells increase the signaling pathway activity and, therefore, may signal the cells to keep growing.



Scientists from around the globe listen to an NF research update at "The NNFF International Consortium for the Molecular Biology of NF1 and NF" held in June.

Fruit flies provide new pieces of NF puzzle

In addition to mouse models, studies are also being done in the common fruit fly (*Drosophila melanogaster*). In the NNFF Newsletter (Winter/Spring 2002) the work of several fruit fly scientists who presented at the Consortium was previewed. Specifically, Dr. Andre Bernards of Harvard Medical School/MGH Cancer Center demonstrated that NF1 mutant flies are reduced in size and have defects in learning, and Dr. Amita Sehgal of University

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the illness creates within the family.

While a single Chapter focuses on the power of faith, this is not a theme throughout the book. In fact, the title *God's*

Weeber brings the fresh, less often articulated, perspective of a father dealing with a child's NF.

Caregivers is not a pronouncement of the Weeber's faith, but instead is a term a minister used to describe the Weeber's role in caring for Nicky and Bobby. The minister told the Weebers that they were "his heroes as you are doing God's Work".

This straightforward, plainspoken book can provide reassurance to all parents that they are not alone trying to navigate the challenges of raising a child with NF. **NF**

New Additions to The NF Web Site

Two new forums have been added to the NNFF Bulletin Board (<http://www.nf.org/cgi-bin/bb2-cgi/ultimatebb.cgi>).

Memorials: This section of the NF Website's Bulletin Board gives members the opportunity to post messages in memory of family members, friends and loved ones.

Birthday Calendar: A new feature where members of our bulletin board community can post their birthdays, anniversaries, and other special days.

NF en Espanol: Several significant additions have been made to the "Espanol" section of the NF web site (<http://www.nf.org/espanol/>).

- Spanish Chat Room
- 8 NF Pamphlets written completely in Spanish
- Online Book on NF (In Spanish) by Dr. Ignacio Pascual Castroviejo

New book at the NF Bookstore: Click on the "NF Books" button at (https://secure.nf.org/cgi-bin/web_store/web_store.cgi)

God's Caregivers: A Journey of Faith by Robert V. Weeber
Soft Cover — 199 pages
\$12.95

The NF Bear has a new look!

The NF bear is now new and improved! This cute little messenger will spread NF awareness everywhere he goes. Get yours online at (https://secure.nf.org/cgi-bin/web_store/web_store.cgi). Click on the "NF Bear" button. 

NEUROFIBROMATOSIS PROFILE

Shedding Light on NF in Land of the Midnight Sun

In late 2000, when Anchor Point, Alaska resident Denise Ogle's then two-year-old son, Leo, was diagnosed with NF she felt that there was nothing that she could do to help. Then she discovered The NF Marathon Team. Denise contacted Marathon Team Director Anita Carter and decided to train for and run in the Anchorage Mayor's Midnight Sun Marathon. Instead of waiting and worrying, Denise focused on fund raising and marathon training.

Knowing that she was working toward a goal, Denise found the training therapeutic. She was surprised how easy it was to raise the money she needed for her Marathon Team commitment. The support from her community was tremendous and she found that people were willing to give. As she logged more miles, she saw her fundraising efforts pay off when she received letters from Carter, updating her on the funds she raised. Knowing that her hard work was for Leo kept her on the treadmill, running nowhere for countless hours, and running during the cold, dark Alaskan Winter.

Denise's sister, Beth Baggett, and Denise's friend, Angela McKinney, ran with Denise in her first marathon in June of 2001. In December, Denise ran in the Honolulu Marathon. This time her team was three people stronger as Denise's husband, John, John's 71-year-old Uncle, Ephraim Romesberg, and Ephraim's daughter, Laura Romesberg, joined the team. On June 22, 2002 Denise Ogle ran her third marathon in a year, the 2002 Mayor's

Midnight Sun Marathon. Denise recruited nine other runners to the team, including Ephraim and Laura, and 30 people to cheer them on.


Besides the fulfillment of crossing the finish line marathon running gives Denise

4-year-old Leo Ogle (right) is proud of his mom Denise who triumphantly completed the Anchorage Mayor's Midnight Sun Marathon in his honor, winning him a medal (below).



the opportunity to run alongside strangers and educate them about NF. "People would come along and ask what NF (printed on The Marathon Team shirt) was and I could spend the next mile telling them about NF."

In addition to running 78.6 miles and dropping an hour from her time in the last year Denise has also been instrumental in laying the groundwork for an Alaska Chapter. Working with NNFF President Peter Bellermann, Denise and other Alaskans have met with Senator Ted Stevens (R-AK) to garner his support for the U.S. Army NF Research Program funding and to talk about the chapter. Denise will continue her work on behalf of Leo. She has set several goals for herself, including bringing a stronger voice to Alaskan families with NF who are spread out all over the state, running two marathons a year, and adding more people to The NF Marathon Team.

For more information on The NNFF Marathon Team please contact Anita Carter toll free at 1-800-NF RACES (637-2237) or visit the NF Website at www.nf.org. 

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NF Marathon Team

— racing for research

Upcoming Marathons — next 6 months

- 9/01/02 Rock N Roll Marathon, Virginia Beach, VA*
- 9/22/02 Maui HI*
- 10/06/02 Portland, OR*
- 10/13/02 Chicago, IL*
- 10/13/02 Long Beach, CA*
- 10/20/02 St Louis 10K, MO
- 10/28/02 Dublin, Ireland*
- 12/1/02 Seattle, WA
- 12/08/02 Honolulu, HI
- 1/12/03 Disneyworld, Orlando, FL
- 02/22/03 Myrtle Beach, SC
- 3/2/03 Los Angeles, CA
- 3/23/03 Rome, Italy
- 4/6/03 Paris, France
- 4/6/03 St Louis, MO
- 4/13/03 London, UK
- 4/21/03 Boston, MA
- 4/26/03 Country Music, Nashville, TN
- 05/04/03 Vancouver, BC
- 05/18/03 Prague, Czech Republic
- 6/1/03 Rock N' Roll, San Diego, CA
- 6/21/03 Mayor's Midnight Sun, Anchorage, AK
- 9/28/03 Berlin, Germany

Marathon applications no longer accepted for marathons marked with "." volunteer participation only. Some Marathons have registration deadlines many months in advance. Therefore, apply as early as possible for each Marathon.

Pen Pals

Miriam Deegan, Leaberg, Ballycumber, County Offaly, Ireland seeks Pen Pals with NF.

Joan Campbell is looking for pen pals to write her at 743 Mauro Circle, #6, Warren, OH 44484

Tara Hathaway a divorced mother of two with NF2 is seeking Pen Pals who have NF2 or have family members with NF2. Please write her at 223 Spruce, Caddo, OK 74729.

NF Research (continued from page 6)

of Pennsylvania described the role for the NF1 gene in regulating circadian rhythms. Dr. Frances Hannan from Cold Spring Harbor Laboratory described her studies on an NF1-regulated pathway in fruit flies. She showed how the normal human NF1 gene is able to prevent the size and learning defects in NF1 mutant flies.

More Answers and More Questions

While tremendous progress is being made, Dr. Frank McCormick of the University of California, San Francisco Cancer Center provided a take-home message about the recent pace and advances in research. He noted that the knowledge is good, but complexities arise as the search for answers continues to yield more questions. Scientists must continue working together across fields of expertise if all the answers are to be found. **NF**

Reproductive Issues (continued from page 3)

Q. How would I go about getting the test done?

- A. The test should be discussed with your doctor, including the cost and insurance coverage issues involved. Your doctor can arrange for the test through the following labs:

NF1

Linkage Testing
University of Utah School of Medicine
Diagnostic Lab
(801) 585-1134

Mutational Analysis

University Hospital Ghent, Belgium
Dr. Ludwine Messiaen
Ludwine.messaien@rug.ac.be

NF2

Linkage Testing and Mutational Analysis
MGH Developmental Neurogenetics
DNA Diagnostic Laboratory
(617) 726-5721

Q. Can the test results tell me anything about severity?

- A. Genetic tests cannot detect anything specific to the types of manifestations a child will have or the severity of the disorder.

Q. Is there any way to prevent me from passing NF to my baby?

- A. The use of pre-implantation diagnosis is a way to prevent passing NF on to your child. Pre-implantation diagnosis is highly specialized, done by only a few centers. This requires a woman to undergo an in vitro fertilization procedure. It is expensive and is usually not covered by insurance. It is very important that the

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On the Web: www.nf.org

Guest Editor: Suzanne J. Cohen

The purpose of the National Neurofibromatosis Foundation, Inc. (NNFF) is to improve the well-being of patients and families affected by NF1 and NF2. The Foundation therefore sponsors scientific research aimed at finding the causes and cures for the neurofibromatoses, promotes the development of clinical activities, works to create public awareness and provides patient support services.

The National Neurofibromatosis Foundation is a founding member of the International Neurofibromatosis Association.

couple meet with a genetic counselor or geneticist to discuss all the ramifications of this procedure. It also should be noted that pre-implantation technology only can be used when a parent's mutation has already been identified. This identification can take months of laboratory work so advanced planning is needed. **NF**

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