

RESEARCH MEETINGS

The Foundation organizes and participates in scientific meetings, large and small. To help define current research priorities, we convene workshops where small groups of scientists working in a specific area of NF research can meet, share research findings and develop collaborative efforts. At major conventions with large attendance such as **American Society for Human Genetics**, we organize symposia that highlight NF research and provide an opportunity to attract new researchers to the field. Foundation staff also host information booths at these conventions to promote our research programs and initiatives, highlight funding opportunities, and inform the research community on NF.

We will organize or participate in the following meetings. Look out for reports from these events in future newsletters or on our website.

October 2005

Oct. 25-29 Salt Lake City, UT
American Society of Human Genetics
Annual NF Symposium sponsored by the Foundation; the meeting will highlight the latest on NF research and updates. It is anticipated over 150 researchers will attend the 2005 symposium. Information booth will also be at the convention.

November 2005

Nov. 3-5 Cold Spring Harbor, NY
Use of Mouse Models to Develop Therapies for NF1 and NF2
This Children's Tumor Foundation convened Strategy Workshop, made possible by funds from the *DOD CDMRP Program*, will address how to develop collaborative approaches for pre-clinical screening of therapies for NF.

Nov. 12-16 Washington, DC
Annual Society for Neuroscience Meeting

This major convention attracts over 25,000 neuroscience researchers. The Foundation will have a booth at this meeting for the first time, providing a great opportunity to promote NF research and our funding programs to the extensive research community.

February 2006

Feb 17-19 Los Angeles, CA
Treating NF1 Learning Disabilities
This Children's Tumor Foundation convened Strategy Workshop brings together researchers from around the world to discuss key area of research and how we can develop a framework for screening potential new treatments for NF1-associated learning disorders.

An Update On Molecular Genetic Testing For NF2

By Dr. Mia MacCollin
Harvard University/
Massachusetts General Hospital

Since the cloning of the NF2 gene in 1993, a tangible benefit to the NF community has been the ability to perform molecular genetic testing for some at risk individuals. Unfortunately, technical issues precluded our ability to offer this test to many families because we could not find the exact mutation causing their NF2. Recently, a number of laboratories have reported on the reasons for this technical failure and come up with some ingenious ways around it. In about 25% of founders (persons with unaffected parents), mutations can be best and sometimes only be detected in tumor tissue because non-tumor tissue is predominantly genetically normal or **mosaic** (see *Table A*). Even when mutations cannot be directly found in tumor tissue, a normal chromosome is often lost along with information that can be used to infer diagnosis. Finally, several groups have reported a high percentage of deletions of the NF2 gene that escaped detection by earlier methods. As research labs report these results, clinical labs have stepped up to the plate to plug the gap left by earlier testing techniques and opened the possibility of definitive testing to families for whom it was not previously available.

Why test for NF2?

Molecular testing of at risk adults and children (those individuals who have a parent with known NF2) is a highly personal decision, and every individual and family will come to a slightly different decision based on their experiences and values. For at risk adults, the certainty of a molecular test affords peace of mind that an MRI cannot. For pre-symptomatic children, molecular diagnosis allows the family to consider proactive strategies of monitoring and intervention which may lead to better chances of long term hearing preservation. These benefits must be weighed against the complex psychological, familial, financial and insurance risks that testing entails.

Molecular testing of at risk pregnancies (often in the first trimester by chorionic villus sampling) and **pre-implantation genetic diagnosis (PGD)** (see *Table B and page 7 for complete article on the procedure*) are other important uses of molecular genetic analysis. Such testing needs to be arranged well in advance of a planned pregnancy, and in the case of an NF2 affected mother the risks and

benefits of in vitro fertilization will need to be considered carefully until we have more data regarding its use in women with schwannomas and meningiomas. There are many cases in which molecular genetic testing is possible but not clinically helpful. Molecular testing currently offers little or no direct benefit for an individual known to have NF2 because we do not have exact guidelines about how the mutation that causes a person's NF2 affects the severity or course of the disease.

What You Should Know!

- If you have NF2 and have children or are planning to have children, then defining your NF2 mutation is a reasonable first step towards future genetic diagnosis. Take into account that these tests are complex, have turnaround times of weeks to months and that insurance is frequently not willing to pay for them.
- Many people find it helpful to discuss this decision with a genetic services provider. Should you decide to proceed, a geneticist will be in the best position to determine which type of molecular analysis will be most useful, and to order the test for you. Request a referral from your primary care provider, or visit the CTF website for a list of NF clinics near you.
- If you have previously participated in a genetic study, be sure that your physician or genetic counselor determines if any clinically relevant results were obtained.
- If you are a founder and are planning surgery, request that some tumor tissue is flash frozen for molecular analysis. Tumor tissue frozen at the time of surgery will remain a viable source of material for molecular analysis for decades. Founders who have previously undergone molecular analysis on blood samples which was inconclusive may wish to repeat the study on tumor tissue.
- If you have previously undergone molecular analysis by exon scanning which was negative, you may wish to consider undergoing MPLA analysis.

Meet Foundation's Newly Appointed President: Mr. John W. Risner

“I believe the final piece of the NF puzzle will be solved. My reward will be a cure for NF, it's that simple.”

Mr. John Risner's new position as President of the Children's Tumor Foundation means more than just a new job to him. Mr. Risner will be leading the battle against neurofibromatosis together with the NF community. Learn more about John, his connection with NF, and his goals for the Foundation from the one-on-one interview below.

How did you get involved with the Foundation?

I became involved with the Foundation in the early 1990s, when Dr. Allen Rubenstein, one of the founders of the Foundation, diagnosed my first son with NF1. He put us in touch with Peter Bellermann at the Foundation and we have been active ever since. Before becoming President, I served on the Board of Directors and as Treasurer. My wife, Sharon Parente, has previously served on the Board, and is currently Chair of Council of Fellows and Co-chair of the Annual Gala.

What is your career background and do you think it helps with your current position?

My career background is in investment management. I am a Chartered Financial Analyst and was a Portfolio Manager specializing in high yield bonds. I think I bring a business and a management perspective to the Foundation. The question I am always asking is: are we applying our dollars in the right spots and using technology to achieve our mission as fast as possible? We are fortunate to have an incredibly accomplished and dedicated group of volunteers, researchers, and clinicians on our Research and Clinical Care Advisory Boards. They have done a wonderful job guiding our research efforts.

What do you plan to do differently?

Peter has built a wonderful Foundation and I am happy to be following up his legacy. I think there are ways we can use technology to lower our costs and speed up our response time. For example, electronic submission and peer review of award applications. I also believe we can communicate more often with our members through email and web stories. Strategically, one of the areas Peter began re-focusing in 2003 was our clinical support. I intend to continue the work he started.

What are your short term and long-



term goals for the Foundation?

My short-term goals are to maintain the Federal funding we have been instrumental in securing, and to continue to build on the success of our research programs. This funding is incredibly important to our mission, we would not be as far along as we are today without it. I am very excited over our recent hiring of Kim Hunter-Schaedle Ph.D. as our Chief Scientific Officer. Kim began in August and I am very excited to be working with her. In the medium to long term, I want to see us increase the level of communication to the NF community and to continue to improve the website. Increasing communication between the Foundation and the NF community is critical. This quarterly newsletter is a powerful communication tool but I would like to develop a regular email schedule where we provide news electronically as well. I think the website has strengthened this organization in many ways and with the recent redesign we will continue to make improvements in response to comments and suggestions.

What is your vision for the Foundation?

My vision is not to lose sight of what this Foundation was founded for 26 years ago, to discover effective treatments and cures for the NF. We can all be proud of the progress we have made in those 26 years, but cannot be satisfied until we have a cure. At the same time it is important not to lose focus on the other crucial components of our mission; to continue to improve the health and well-being of individuals and families affected by the NF, and to build on our commitment in supporting and promoting NF research.

Do you think that your son being affected by NF gives you extra motivation to do what you do?

My personal connection to NF certainly gives me extra motivation. However, everyday I talk to people and hear stories; two-year olds going through 12 hours of surgery for NF1; adults facing surgeries for NF2, and knowing these surgeries are not a cure but only a slowdown of the progression; and the debilitating pain of Schwannomatosis. We are fighting this battle for all of them.

What is the biggest challenge you have encountered so far?

Doctor Korf Strapped on His Running Shoes for NF Research!



Dr. Bruce Korf, Chair of the Medical Affairs Committee for the Children's Tumor Foundation, ran the **Falmouth Road Race** to help raise awareness for the disorder and to fund research and clinical support for NF patients. The race took place in Cape Cod this past August.

Dr. Korf is a recognized leader in clinical care and research for treatments and a cure for neurofibromatosis world wide. Currently, he is the Chairman of the Department of Genetics, University of Alabama at Birmingham. Dr. Korf has long been involved with the Foundation and Neurofibromatosis research. Prior to his recent appointment in Alabama, Dr. Korf served for nearly two decades at the Harvard Medical School, as a teacher, clinical researcher, physician and author.

"As someone who has dedicated my career to neurofibromatosis research and treatment, I have seen first hand the struggles of families as they try to face the complexities of a life with NF. I have also seen the enormous difference that can be made when people are willing to take the steps to make a difference," said Dr. Korf. "By running the **Falmouth Road Race**, I hope that people will see that the strides we make in the lab are directly supported by the strides made by participation in the NF Marathon Program and other Children's Tumor Foundation programs."

"The **Falmouth Road Race** attracts some of the most elite runners in the world, even though I did not win, I do know that by joining the effort to fund NF Research we all win," said Dr. Korf. This was the 33rd running of the **Falmouth Road Race**. It was a seven-mile race that boasts the largest non-marathon purse in the world at \$112,000.

All money raised from Korf's **Falmouth Road Race** within the states of Tennessee and Alabama went directly to fund an NF Clinic Coordinator at the University of Alabama NF Clinic; funding from around the rest of the country supported NF clinics nationwide and the Young Investigator Awards.

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NF Marathon Team

On November 6th, 2005, a group of dedicated individuals will step up to the starting line of the **ING New York City Marathon**. They are not only stepping up to the challenge of 26.2 miles, but also stepping up to something even greater. These runners hope to raise over \$100,000.00 for NF research - one big step closer to finding a cure for neurofibromatosis.

Long time NF Marathoner, Bob Skold Jr., who has lost most of his hearing due to acoustic neuromas (caused by NF2) will be one of nearly twenty NF Marathon team members running the New York City streets. Bob has



run nine marathons for the Team over the years; his most recent being the **2004 Dublin Marathon**. In addition to raising funds and awareness for the team, Bob is also on the Marathon Advisory Board.

Also on the team this year is another advisory board member, Florence McCarthy, running the **New York Marathon** as her first. Dan Altman and his friends from last year's famed, "*Jessica's Team*" will also be joining in the efforts. The team would not be complete without the many runners from the **McGraw Hill** and **Standard and Poor's Running Club** who have recently joined in our quest to find a cure for NF. Special thanks to runner and supporter, Xavier Cronin, who is calling on the services of his volunteer group within the McGraw Hill companies called "*Writers to the Rescue*" to assist and support the Foundation.

Pictured above: Bob Skold Jr. running the 2004 Dublin Marathon.

The NF Marathon Team would especially like to thank Poland Spring for donating entry slots into the ING New York City Marathon.



Schwannomatosis

Diagnostic Criteria For Schwannomatosis Published

The first working list of clinical criteria for diagnosing schwannomatosis was published in June in the journal *Neurology*. The landmark publication is the product of collaborative efforts by an international group of clinicians from Japan, Germany, England, Canada and the United States, who were initially convened in 2003 as the '*NNFF International Consensus Conference in Schwannomatosis*'. The definition of these diagnostic criteria marks a significant step toward not only more expedient diagnosis of schwannomatosis, but also establishes measures by which the progress of the disease can be monitored, and therefore by which effectiveness of therapies can be tested in future clinical trials. The research community continues to chase down the schwannomatosis gene itself; identification of this gene will open the door to further refining the clinical diagnostic criteria, as well as informing us on the best drug targeting approaches for the treatment of schwannomatosis. For further information on schwannomatosis, please contact the Foundation.

Highlights from Young Professional Event

An Update On Molecular Genetic Testing For NF2

(continued from page 1)

Persons with a single NF2 related tumor (for example a single vestibular schwannoma or spinal cord tumor) (see table C) do not have NF, and molecular genetic analysis is not helpful in understanding their condition. The diagnosis of persons with related conditions is usually clarified with an MRI scan that is directed towards the skull base (an "internal auditory canal protocol") but occasionally molecular analysis may be helpful following MRI. Use of molecular diagnostics in this context is a complex issue best discussed with a genetics services provider with knowledge of NF.

What methods are available?

Because the gene causing NF2 is known, molecular genetic analysis can be carried out both directly (by finding the exact mutation or misspelling in a person or family) or indirectly (by utilizing anonymous stretches of DNA which provide a unique "fingerprint" of the NF2 region in each family). Each method requires access to different tissue samples, incurs different costs and can be used in different situations.

Indirect methods: Linkage and loss of heterozygosity analysis:

(see table D) Linkage analysis utilizes anonymous stretches of variable DNA in and around the NF2 gene to track which of the two chromosome 22s in a person's body carries the NF2 mutation. Because it is an indirect method, the exact mutation does not need to be found making it relatively fast and inexpensive. Linkage analysis can only be used when more than one individual is known to be affected in the family and certain caveats apply when a founder is used in linkage analysis (see "What is mosaicism") At this point, linkage analysis should not be used for pre-implantation diagnosis.

Loss of heterozygosity analysis or LOH is similar to linkage analysis in that anonymous stretches of variable DNA are used to determine the chromosome affected but not the exact mutation. Unlike linkage analysis, LOH analysis can be used when only a single person is affected, but tumor tissue showing LOH must be available to perform the test.

Direct methods: exon scanning and deletion testing:

The NF2 gene consists of 17 "chapters" or exons interspersed with non-coding areas or introns and covers a total of 35,000 basepairs on chromosome 22. Almost every kindred with NF2 has a different mutation in the NF2 gene shared only amongst other affected members of the same family. Small misspellings such as the substitution of one letter for another are usually detected by examining each of the chapters separately for mistakes, a process termed "exon scanning." The sequence of these "chapters" can also be directly determined. Exon scanning or

Table C: What conditions are related to NF2?

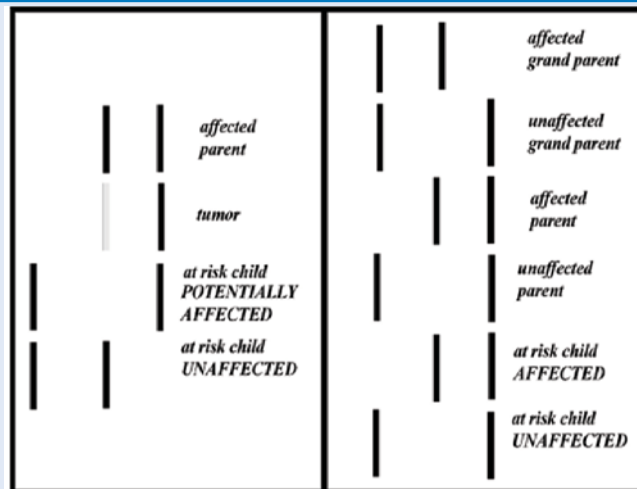
Unilateral vestibular schwannoma: unilateral or single vestibular schwannoma (VS, formally known as acoustic neuroma) are amongst the most common tumors in humans. People with single VS generally develop symptoms later in life and have no risk of passing on a tendency to tumor formation to the next generation.

Unilateral vestibular schwannoma with other NF2 related tumors: Some mosaic individuals will develop NF2 only within part of their body resulting in a tumor on one vestibular tumor, sparing of the opposite vestibular nerve, and multiple NF2 related tumors (such as meningiomas) primarily on the same side of the body.

Multiple meningiomas: About 5% of people with meningiomas (tumors of the linings of the central nervous system) have multiple tumors and a tiny proportion of these people will pass along a similar tendency to the next generation. More commonly, people with multiple meningiomas on an MRI scan actually have only a single tumor which has spread through the liquid surrounding the brain and sprouted independent tumors.

Schwannomatosis: Persons with multiple schwannomas that do not have vestibular schwannomas have a condition which is clinically and genetically distinct from NF2.

Table D: Linkage and loss of heterozygosity analysis:



Certain stretches of human DNA are highly variable or polymorphic so that many people will show a difference between the stretch they inherited from their mother and that inherited from their father. Tracking these differences allows us to infer whether an individual is affected or unaffected without knowing the actual mutation in the family. In the top panel, the middle marker went from affected grandparent to parent and this is the

marker that would be passed to an affected child. In the bottom panel, the tumor from an affected parent has lost genetic material when compared to a blood sample. Since the tumor will only lose normal genetic material, an unaffected child can be diagnosed. If the parent is a founder, then passage of the other marker places a child at risk, but the diagnosis cannot be definitive.

direct sequencing is best applied to tumor tissue in founders and is time consuming and expensive. Although methods of exon scanning are well validated, most researchers have found that the small misspellings they detect are present in less than 66% of NF2 patients. Furthermore, the mutations detected by exon scanning are those found in the most severely affected patients, which caused the frustrating situation of a lack of molecular genetic diagnosis for most offspring of mildly affected individuals.

Multiplex ligation-dependent probe amplifi-

cation (helpfully abbreviated MLPA) is a recently developed mechanism of finding deletions that will elude exon scanning because they remove one or more "chapters" of the NF2 gene. Recent work suggests that most non-mosaic individuals whose mutations cannot be found by standard exon scanning will have deletions detectable by MLPA. We do not yet have a good idea about how readily mosaicism will be detected by MLPA so whenever feasible it should be performed on tumor tissue in founders.

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An Update On Molecular Genetic Testing For NF2

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LABORATORIES CURRENTLY OFFERING NF2 TESTING

(Note that costs and turnaround times are subject to change-please contact the laboratory directly for current information):

1 The National Genetics Reference Laboratory, St. Mary's Hospital, Manchester, UK

This lab offers both exon scanning and MPLA analysis. From the states, it is preferred that extracted DNA and not whole blood or tumor samples are shipped. *Insurance is not accepted.*

Current costs:

MPLA on extracted DNA: \$115 (on both first and subsequent samples)
Exon scanning (plus MPLA on extracted DNA): \$1,400

Turnaround time:

MLPA: 4 weeks
Exon Scanning: 4 months

Contact:

Dr. Andrew Wallace,
Email: andrew.wallace@cmmc.nhs.uk
Phone: 44 161 276 6129

2 The Laboratory for Tumor Biology, Hospital Eppendorf, Hamburg, Germany

This lab offers MPLA analysis on both blood and tumor samples. *Insurance is not accepted.*

Current costs:

MLPA (first sample): \$125
Subsequent Analysis: \$60
(Express service with 2 week turnaround available for \$250)
Direct sequencing: \$1,200

Turnaround time:

MLPA: 6 months
Direct sequencing: 2 months

Contact:

Dr. Victor Mautner,
Email: v.mautner@uke.uni-hamburg.de
Phone 49 40 42803 4068

3 The DNA Diagnostic Laboratory, Massachusetts General Hospital, Boston, Massachusetts

This lab offers exon scanning on both tumor and blood samples and LOH and linkage analysis. When frozen tumor tissue is unavailable from founders, the lab will attempt exaction from achieved pathological material. The DNG lab also has extensive experience with prenatal diagnosis, but this should be arranged well in advance of the pregnancy. Insurance is not accepted although some treating institutions have a billing relationship with the lab. (NB: Athena diagnostics sends all samples to this lab)

Current costs:

Exon scanning (first sample): \$1,850
Known mutation: \$250
Linkage Analysis: \$1,100 (up to five samples)
Additional charges apply for working with paraffin embedded tumor specimens and for prenatal samples.

Turnaround time:

Initial sample: 4 to 6 months
Subsequent testing: 4 to 6 weeks

Contact:

Dr. Kathie Sims,
Email: ksims@partners.org or
Dr. Winnie Xin,
Email: xin@helix.mgh.harvard.edu
For more information please visit:
<http://www.dnalab.org>

Table A: What is mosaicism?

Mosaicism results from a mutation that occurs AFTER fertilization of the egg and one or more divisions of the resulting cell. Since the mutation occurs in a single cell out of many in the developing organism, the patient will be a mixture of normal cells and cells carrying the mutation. Mosaic individuals can pass NF2 to the next generation if the germ cells (egg and sperm) are amongst the subpopulation affected by the mutation. Mosaicism can only occur in founders (the first person in a family to have NF2); all subsequent generations will be non-mosaic.

Table B: What is pre-implantation genetic diagnosis?

Pre-implantation genetic diagnosis or PGD involves in vitro fertilization (hormonal treatment of the woman to produce several fertile eggs, surgical extraction of the eggs and fertilization outside the body), with subsequent genetic testing of the cell masses created and re-implantation of only those which test negative for NF2 mutation. PGD offers the advantage of prenatal diagnosis without the potential of termination of an affected pregnancy. PGD is expensive and not yet covered by insurance; in addition the risks of hormonal treatment of women with NF2 are not yet known. For more information:
http://www.givf.com/pgt_sepvcfm

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Meet Foundation's Newly Appointed President: Mr. John W. Risner

(continued from page 2)

I think the solution is to improve communication within the Foundation and the NF community as a whole so that we can examine and embrace the opportunities that will bring us closer to our goal.

What is the most rewarding thing about your new role?

I believe the NF puzzle will be solved. It is a large and complicate puzzle, with many pieces, but we have the corners and borders in place. It won't be all at once, but a process. I know we will get there.

Mr. Risner resides in Larchmont, New York with his wife, Sharon Parente and their two sons. We are excited about the transition and look forward to Mr. Risner's leadership as we push for the discoveries for effective treatments and a cure for NF.

CHAPTER & AFFILIATE NEWS

Waging The Fight Against NF At The Regional Level

Illinois



Members of the Illinois Chapter participated in the **State Fair Parade** held on August 11, 2005. They marched in the parade holding the Children's Tumor Foundation banner. In addition, they represented **Community Health Charities**, an employee giving campaign that represents a partnership of the country's most prestigious health agencies. The Children's Tumor Foundation is a proud member of Community Health Charities, both nationally and regionally in the state of Illinois. Our CFC number is 0550.

Missouri



The Missouri Chapter, in conjunction with **Harry's Restaurant and Bar**, hosted a Golf Tournament on August 23, 2005 at

the **Missouri Bluff's Golf Club**. Twenty-nine foursomes participated in this most successful event that raised over \$12,000 for research. After a beautiful day of golf, the participants enjoyed a steak dinner at **Harry's West**. The Missouri Chapter would like to extend a special thanks to Harry Belli and Tim Pieri for their coordination of the event.

New Chapter/Affiliate

Having a local volunteer presence throughout the United States is crucial in helping to carry out the mission of the Foundation. A total of 11 Chapters and 14 Affiliates have been active in providing patient support through support groups, medical symposia and informal information sharing; public awareness campaigns; and fundraising efforts for research to find effective treatments and a cure. Within the past months we have greatly increased our efforts throughout the United States.

The Utah Affiliate has upgraded to a Chapter. Six new Affiliates have been formed: Arizona; NW Arkansas; Indiana; Las Vegas, Nevada; Nebraska; and North Carolina. We now have 12 Chapters and 19 Affiliates, a total of 31 regional volunteer groups nationwide. Congratulations to all of our volunteers and welcome to our new Chapter and Affiliates!

The contact information for each is listed below as well as on the "Activities by State" section of the www.ctf.org web site. For assistance or to volunteer, please contact your local Chapter or Affiliate.

UTAH CHAPTER

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LAS VEGAS, NEVADA AFFILIATE

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NEBRASKA AFFILIATE

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NORTH CAROLINA AFFILIATE

Erika Jepsen Robertson,
Representative
3605 Melinda Drive
Wilmington, NC 28409
Phone: (910) 297-4708
Email: erika_robertson@bellsouth.net

For additional information on Chapters and Affiliates, and volunteering in general, please contact Cathy Silberstein, Director of Volunteer Training and Development at csilberstein@ctf.org or (800) 323-7938 ext. 239.

Oregon

The Oregon Affiliate held its annual **Summer Picnic** on June 25, 2005 in McMinnville, Oregon. However, this year it was far more than a picnic. **It was a wedding!**



The bride and groom, Randy and Peaches Riddell, met through their work environment. Randy has NF and is a member of the Affiliate. As their relationship progressed, Peaches joined him at the meetings. So when it came time to plan their wedding they decided what better place than with their NF family. The minister who married them, Daniel Kempton, also has NF. It was a day filled with joy. All of us at the Children's Tumor Foundation wish Randy and Peaches a lifetime of happiness!



Pictured above: Bride Peaches and groom Randy with minister Daniel Kempton.

PGD (Preimplantation Genetic Diagnosis) in NF

By Susan Conradi Toomey, M.S.
Genetic Counselor

A new procedure allows couples at risk of having a child with neurofibromatosis the ability to screen an embryo for the defective NF gene, prior to a pregnancy being achieved. The procedure is called Preimplantation Genetic Diagnosis (PGD), a technique that can be used during in vitro fertilization (IVF) to test embryos for a variety of genetic disorders. PGD testing is done before the embryo is transferred to the uterus. Initial PGD research was performed in the UK during the late 1980s. Since then, there have been thousands of births resulting from this new technology.

Prenatal diagnosis (amniocentesis or CVS) has been available for decades allowing at-risk couples to diagnose neurofibromatosis in an ongoing pregnancy. If a fetus was found to have NF, the couple faced the agonizing decision to continue or terminate the pregnancy. PGD is a valid alternative for couples wishing to avoid decisions about pregnancy termination by providing the opportunity to know that any pregnancy achieved should be unaffected, thus negating the ethical-moral problems associated with pregnancy termination.

Just as with prenatal testing, mutation or linkage analysis must be performed in advance and be informative. Direct Mutation Analysis will detect up to 95% of mutations responsible for NF1 and up to 60% of mutations in NF2. For both NF1 and NF2, linkage analysis can be performed with greater than 95% accuracy in families with two or more affected individuals. Once mutation or linkage testing is complete, PGD can be offered.

Couples who choose PGD undergo an in

vitro fertilization (IVF) cycle which entails removing eggs from the woman's body and fertilizing them with the man's sperm in a laboratory setting. In an incubator, the fertilized eggs develop into embryos. At approximately the 8-cell stage, a single cell is biopsied from each embryo and sent for analysis while the developing embryo remains in the incubator to continue to grow. The cells removed from each individual embryo are sent to a specialized laboratory and quickly analyzed by genetic testing using PCR-based DNA amplification. Those embryos considered to be unaffected are selected for transfer into the woman's uterus while the embryos considered to be affected are discarded.

It is best to think of PGD as a screening tool, which greatly reduces the risk of an affected pregnancy occurring. Prenatal testing is still recommended, as a way to confirm the results of PGD.

Typically, the accuracy of PGD is between 90-98% depending upon the exact laboratory methods utilized. PGD does not replace the need for prenatal testing, as PGD is a research-based test with limitations in accuracy. It is best to think of PGD as a screening tool which greatly

reduces the risk of an affected pregnancy occurring. Prenatal testing is still recommended, as a way to confirm the results of PGD.

Like all genetic screening, PGD has risks and limitations. When mutation or linkage analysis is uninformative, PGD (and prenatal diagnosis) can not be offered. An IVF cycle with PGD can be rather expensive and insurance companies rarely cover the cost of IVF. The technology adds about \$3,000 to the cost of in vitro fertilization. Some patients, however, have been successful in obtaining insurance coverage for the PGD portion of the cycle. PGD cannot predict the potential severity of NF in the embryo and, at this time, cannot rule out additional genetic defects in the embryo. There is a 1% risk of accidental damage to an embryo during the biopsy; and if damaged, the embryo (even if unaffected) would typically stop growing and would not be suitable for transfer into the uterus. Recent reports have revealed a potential link between IVF procedures and a slight increased risk for certain birth defects. And finally, for some couples, ethical concerns may still arise when discarding affected embryos.

In the last several years, PGD has been successfully implemented in families with both NF1 and NF2, resulting in the birth of healthy unaffected babies. If you are interested in discovering whether PGD is an option, ask your OB/GYN or NF Clinic to refer you to an IVF center that offers PGD. Many IVF/PGD centers have trained genetic professionals who can counsel patients regarding the risks, benefits, and limitations of PGD.



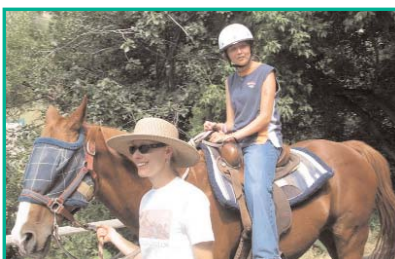
International NF Summer Camp

Every year kids and teens look forward to summer vacation. The time away from school is a welcome break and a time to socialize with friends. But for one group of teens that share a bond through NF, a more exciting time to them than summer vacation is the **International NF Camp!**

The International NF Camp is not just about meeting people, it's about taking advantage of a unique summer opportunity and creating memorable experiences that will last a lifetime.

Here are some pictures for this year's camp, to see more photos please visit: <http://www.ctf.org/camp/>.

Campers are already counting the days to the next International NF Camp!



Fun Walk and Festival!!



The *Barron Chiropractic and Rehabilitation P.C.* in Mattapan, MA organized a **5K Fun**

Walk and Festival that raised \$8,000 for the Children's Tumor Foundation this past August. The inspiration of the event comes from Michelle Barron, daughter of Dr. Philip Barron, who suffers from NF1.

HIGHLIGHTS:

- An Update On Molecular Genetic Testing For NF2
- Meet Foundation's Newly Appointed President...
- Highlights From The Young Professional Event
- PGD (Preimplantation Genetic Diagnosis) in NF

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The mission of the Children's Tumor Foundation, Inc. is to improve the well-being of patients and families affected by NF1, NF2, and Schwannomatosis. The Foundation 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 Children's Tumor Foundation is a founding member of the International Neurofibromatosis Association.

An update to an event we featured from the last newsletter!



The 2nd Annual Jovani Cruz Garcia Family Fund Benefit Luncheon raised more than \$12,000 toward NF research!

From left to right: Julie Molina, Ana D'Aguiar, Emily Ann Garcia, Emilia Garcia and Margaret Redman