The Advocate

...your connection to the Friedreich's Ataxia Research Alliance

Issue #6 Winter 2006/2007

Scientific Progress and Promise: NIH Conference Research Highlights

NINDS Director Story Landis gives opening remarks at Friedreich's ataxia conference

The Friedreich's Ataxia Research Alliance (FARA) and the National Institutes of Health (NIH) hosted the Third International Friedreich's Ataxia Scientific Conference at the NIH in Bethesda, Maryland, highlighting and advancing the exciting research leading to a variety of clinical trials that show promise of developing treatments for this devastating disorder.

Nearly 150 leading Friedreich's ataxia (FA) scientists from around the world discussed their new insights and findings during four days of meetings at the NIH, November 9-12, 2006. The public-private partnership underlying this progress and highlighted by the conference involved the NIH, patient advocacy foundations, pharmaceutical and biotechnology industry representatives, and scientists from academic institutions. *(Continued on p. 4)*

In this issue:

FARA Fundraising Across the U.S.

Actress Mary Stuart Masterson hosted a fundraiser at the Owenego Inn in Branford, Ct., in September on behalf of Samantha and Alexandria Bode. Also attending was actor Jeremy Davidson. The fundraiser was organized by Mary Caruso on behalf of her two daughters. (L-R) Samantha, Mary Caruso, Jeremy Davidson, Alexandria, Mary Stuart Masterson.

Read *FARA Fundraising Across the U.S.* article on p. 7.

What is Friedreich's ataxia?

Friedreich's ataxia is a life-shortening, debilitating and rare genetic neurodegenerative disorder. Onset of symptoms usually occurs between the ages of 5 and 15. Symptoms include muscle weakness and loss of coordination in the arms and legs; impairment of vision, hearing and speech; aggressive scoliosis (curvature of the spine); diabetes, and a serious heart condition. Most patients need a wheelchair full-time by their late teens or early twenties. There is no cure. Most childhood-onset patients with this disease die in early adulthood. FARA is a 501(c)(3) tax-exempt non-profit organization dedicated to supporting research leading to treatments and a cure for this relentless and devastating disorder.

President's Message

From Hope to Confidence
A Letter from FARA's President

Dear Friends,
Together, we have come a long way. We began together with little more than hope. We are now all confident that we will finish with nothing less than effective treatment.

Friedreich's Ataxia Research Alliance (FARA) was established just over eight years ago – in September 1998. A few months later, we held our first International Friedreich's Ataxia Scientific Conference for which we worked hard to gather 80 interested scientists. No drug companies participated. In November 2006, we held the Third International Friedreich's Ataxia Scientific Conference and had to work hard to limit participation to 150 scientists from all over the world. Six drug companies sent multiple, senior representatives and helped fund the conference.

In its first full year, 1999, FARA raised only $100,000 – almost half of which was from the National Institutes of Health (NIH) grant to support that first international conference; at that time, there was only one, very small clinical trial being conducted for Friedreich's ataxia. By the end of 2006, FARA will have devoted more than $8M to Friedreich's research and will be involved in plans for at least six, very promising clinical trials.

There is no longer ANY doubt about it – working hard together, we WILL get treatments! You are probably accustomed to hearing that kind of confidence from FARA, and now we are all hearing it from those upon whom we all depend - the scientists. During the last few months, and at the November 2006 conference, top leaders of the scientific community began delivering the same message: we will achieve a breakthrough in Friedreich's ataxia; we will develop treatments soon. So soon, that we need to begin developing the mechanisms for newborn screening so treatments can be administered early.

So, the scientists too are confident that they and the rest of the Friedreich's ataxia community will succeed. And, they are confident not just because they "see the data," though that is the most important factor. They are confident, because they have "seen our community." They tell us they are amazed at how the Friedreich's ataxia community pulls together to support their work and to accomplish our mission: to slow, stop, and reverse the damage done by Friedreich's ataxia.

The scientists know better than anyone else that the clinical research of the "treatment era" is a lot more expensive than the basic research that has gotten us here. They also know that the clinical trials will require participation by hundreds – maybe thousands – of Friedreich's patients around the world. Finally, they know that the Friedreich's community has always risen up together to meet the challenge to get the job done. They are confident we will all do so again.

The scientists are right! We WILL succeed! We will ALL have to help. Please help assemble the financial resources needed to support the research that will push treatments across the finish line. Please help by including, in the FARA patient registry, all the patients needed to get the clinical trials on track.

The scientists are confident you will. We all are.

Thank you very much,
Ron

The Importance of Networking -- By Bob, Bridget & Molly Lawson (FA, age 10)

On May 30 of this year, our family received the diagnosis that we had been expecting, but praying not to hear. Our ten year old daughter, Molly, had Friedreich's ataxia.
Among the many feelings that overwhelmed us was the feeling of aloneness. We knew almost nothing about FA. Our friends and family had never heard of it. We turned to the Internet for help. There were multiple Web sites, from as far away as Australia.
The one that proved most helpful was FARA. We learned about FA, read about other parents' experiences, and other children with the disorder. We received helpful advice regarding our daughter's I.E.P.
It was like a whole world opening to us. We met another family, the Wolfsons, whose daughter had also been diagnosed with FA. We talk regularly, and hopefully our daughters will be there for each other through their battles.
I was put in contact with FA experts: genetic counselor Jennifer Farmer, Dr. Susan Perlman, Ron Bartek, Mary Lisa Orth, and many others. All had advice and words of encouragement.
I've only posted one question thus far (on internet discussion boards), and have received several helpful suggestions. I'm sure as Molly's progression continues, I'll rely more and more on the other parents.
We've helped with the Martina McBride concert, learned how to get donations, even offered advice to other parents. The important thing is we're doing something. We're not just sitting back helplessly. Networking with others has helped tremendously. We feel a kinship with other FA families. Together, we are going to win! ■ *More on Martina McBride concert p. 17*

FARA Patient Registry: Facilitating Recruitment for FA Clinical Research Trials

A patient registry is a critical tool for recruiting patients for clinical research. In six short months the FARA patient registry has become the largest FA registry with nearly 500 international registrants. The purpose of this registry is to collect basic information on individuals with Friedreich's ataxia and to share this information with researchers who will be recruiting patients for FA clinical trials. The ultimate goal of the registry is to facilitate and expedite clinical trials.

If you have not joined the FARA Patient Registry, please consider doing so now.

Participation is Simple:

- Go to the FARA Patient Registry Web site www.faresearchalliance.org/registry
- Select the New Registrant button at the top of the screen
- You will be taken through the registry in a series of steps with help and instructions provided as you go

Recruitment for clinical trials can often take a long period of time, especially for a rare disease like FA. Your participation in this registry could help speed up that process considerably. While you are joining the patient registry through an internet Web site, please be assured that your information is stored in a secure database. The database was designed to protect your personal information. If you have questions or concerns, you can visit the registry homepage and review a FAQ (frequently asked questions) link or contact the registry coordinator, Jennifer Farmer at jen.farmer@faResearchAlliance.org.

When FARA recognized the value of having a patient registry process and data repository to collect patient information globally, we called our friends at EDS for a technical solution. A team of EDS volunteers from Rochester, N.Y. turned to their local education partner – Rochester Institute of Technology (RIT) – to see if the project would be a fit for RIT's B. Thomas Golisano College of Computing and Information Sciences Software Engineering Department's senior capstone project. The registry project was selected by RIT students Tracy Rericha, Elaine Simone, Sandy Morris, Steven Coad, and faculty coach, Lei Wu, professor of software engineering. EDS' Steve Baiera, who oversees student projects as part of the RIT/EDS partnership, worked with EDS project mentors, Michelle Whalen and John Manos who ensured that the registry project was completed and launched in May 2006. EDS volunteers, Donald Pecor, Darren Bielby and Julian Pisoni continue to enhance, maintain, and support the FARA registry. We are tremendously grateful to this entire team for sharing their talent and time to bring the FA community closer to a treatment.

Since the launch of the registry many national and international partners have joined to help enhance recruitment and support the registry. We would like to thank MDA®, the Cooperative Ataxia Group, FAPG, Internaf, GoFAR, the Swedish Ataxia Association, the Spanish Ataxia Federation, and FA_babelFAmily for their help with advertisement, recruitment, and increasing accessibility through foreign language translation.

FARA will be using the homepage of the Patient Registry to post communications and advertisements for FA clinical trials. Visit this Web site regularly to get updates on clinical trials. Also, please keep your registry account updated with accurate contact information (address, phone number, and E-mail address).

If you have already registered, thank you for your participation. Please do not register again.

If you have any additional questions, please contact ■ Jennifer Farmer at jen.farmer@faResearchAlliance.org.

Internet Support Groups

Friedreich's ataxia Parents' Group (FAPG)

In September of 1997, a small group of parents with children diagnosed with Friedreich's ataxia began a mailing list in order to share questions, support, and information about Friedreich's ataxia. E-mail is a great forum for support and has remedied the isolation and loneliness many families feel. It provides a way to share unique experiences and knowledge with each other.
Parents interested in subscribing should go to:
http://www.fortnet.org/fapg/subscrib.htm

Internaf - International Network of Ataxia Friends

Ataxia patients and their families are invited to join an internet listserv that provides support and serves as an information exchange vehicle. Subscribers help each other by asking questions, making comments, and providing answers on how to make life with ataxia easier. Subscriptions to INTERNAF are free.

FA_babelFAmily - multilingual mailing-list with information on research, clinical trials, and fundraising. Provides translations into many languages including Italian, English, Spanish, Portuguese and French. To join, go to:
http://health.groups.yahoo.com/group/FA_babelFAmily/

To subscribe to Internaf, send an E-mail to:
internaf-subscribe@yahoogroups.com

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FA Patient Registry:
http://www.faResearchAlliance.org/registry/
E-Bulletin Sign-up:
http://www.faResearchAlliance.org/news/index.asp

Scientific Progress and Promise: NIH Conference Research Highlights

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The presentations at the November 2006 conference demonstrated clearly how much has been learned about FA since the 1999 conference and how much the research emphasis has shifted from basic science to the tremendous progress being made in translational and clinical science – moving very promising therapeutic discoveries "from bench to bedside." Drug discoveries are moving through a demanding process of drug development and into a growing number of clinical trials, so that drugs determined to be safe and beneficial can be approved for FA patients. Most of these discoveries and advances benefited from FARA grant support – which would not be possible without your commitment to support FA research. Nearly all of the FARA funded scientists in 2005 and 2006 attended the conference and presented their data.

The conference was certainly comprehensive. Leading experts shared insights in full sessions on the FA gene, the frataxin protein, iron metabolism, cellular and mitochondrial pathophysiology, cellular and animal models, therapeutic approaches and clinical trials, the clinical measures needed to monitor progress in clinical trials, and the bio-chemical markers (biomarkers) of the disease. Abstracts from the conference are available on the FARA Web site for a more detailed overview of the sessions and presentations.

The Gene

Scientists believe that about 96% of Friedreich's patients have lengthy triplet expansions (GAA) on both Friedreich's genes – one passed on from the mother and one from the father – with the remainder of patients having a lengthy triplet expansion on one of these two genes and a "point mutation" on the other. In both sets of patients, the genes produce far less of their normal product – the frataxin protein. This low level of protein production might be caused by the formation of "sticky DNA" or "triplexes" when the lengthy triplet expansion supercoils, folding back onto itself. Or, it might result from "gene silencing" caused by changes in the chromatin protein bundles around which the genes are wrapped. Finally, it could result from both, with the "sticky DNA/triplex" causing the changes in the chromatin bundles that, in turn, "silence the gene" and reduce frataxin protein production. In any case, conference presentations outlined several promising approaches to increasing the genes' production of frataxin protein. These approaches will lead to some of the clinical trials described below.

The Protein

Frataxin protein is essential to life. Mice that have no frataxin protein die in embryo. When the Friedreich's gene is correctly read (transcribed), the resulting messenger RNA moves outside the nucleus and assembles amino acids in the sequence and number dictated by the RNA code. That particular bundle of amino acids "folds elegantly" to become frataxin protein. Frataxin then moves to the mitochondria, takes up and "chaperones" iron, participates with other proteins in assembling heme and iron-sulfur clusters. The heme becomes the iron-containing group in hemoglobin, the oxygen-transporting protein in red blood cells. The iron-sulfur clusters become essential to transporting electrons through the mitochondrial complexes so as to produce energy. Healthy mitochondria, with sufficient frataxin, produce abundant cellular energy (ATP). When insufficient frataxin is available, electrons are not transported effectively along the mitochondrial complexes. Instead, they break out of this "circuit" and are taken up in the formation of destructive "free radicals." These unhealthy mitochondria produce much less energy and much more "oxidative stress" leading to cell damage and death. Some of the clinical trials involve attempts to increase the amount of frataxin protein available, while others are aimed at improving mitochondrial function (more energy, less oxidative stress) even in the absence of normal levels of frataxin.

Disease Models in Other Organisms

Significant progress has been made in developing models of FA in other organisms useful in studying the disease and testing therapeutic approaches. Models have been developed, for example, in yeast, fruit flies (drosophila), worms (C. elegans), and mice. All of these models are being used to achieve a better understanding of FA and how best to develop treatments.

Clinical Measures of Disease and Progress

FARA recognized from the beginning that treatments would not be achieved without clinical trials—and clinical trials would not be successful without effective clinical measures to determine, to the satisfaction of the regulatory agencies like the U.S. Food and Drug Administration (FDA)—whether the therapy being tested is actually beneficial. Beginning in 2000, FARA has helped assemble patients and scientists to refine and optimize the available measures or rating scales for FA. For the past three years, FARA and MDA have jointly funded such work at seven centers across the United States. Other scientists, especially in Australia and Europe, have worked hard in the same effort. The Friedreich's Ataxia Rating Scale (FARS), the International Cooperative Ataxia Rating Scale (ICARS), and the Scale for Assessment and Rating of Ataxia (SARA) are currently available. The conference provided an important opportunity for scientists to discuss which scales seem most appropriate to which clinical trials.

Bio-Chemical Markers (Biomarkers) of Disease and Progress

Conference participants included key experts in determining the bio-chemical changes that take place in patient

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FARA Proud and Thrilled to Introduce Jennifer Marie Farmer

Many of you have already had the pleasure of coming into contact with Jennifer Farmer. Jennifer began with FARA in January 2006 and has already been responsible for accomplishments worthy of several people over several years. We wanted to add a face and a background to the name you have already heard.

Jennifer does so much for FARA and for all FA families that it is difficult to construct a simple list of her responsibilities and accomplishments. Jennifer is FARA's Research Grants Administrator. In that capacity, she receives and processes all scientific grant applications. She assigns them to other scientists for peer review, assembles the reviews and the resulting recommendation for consideration by FARA's Board of Directors, notifies applicants regarding the Board's decision, manages FARA's contract with each applicant, monitors progress of each project, and obtains the final progress report for each project. It is also in this capacity that Jennifer is working with volunteers at EDS to develop FARA's Research Portfolio Management Program, which will enable electronic submission and monitoring of all grant proposals from the FARA website.

As many of you know, Jennifer is also FARA's Patient Registry Administrator. When patients submit their information on the FARA Registry page (http://www.faresearchalliance.org/registry/), it is communicated to Jennifer and she ensures that all is in order. It is these submissions that will be reviewed to determine, for each clinical trial, which patients meet the inclusion criteria provided by those conducting the trial. Jennifer worked with volunteers at EDS and a student program at the Rochester Institute of Technology to develop FARA's first-rate Patient Registry. The upcoming clinical trials are far more likely to be successful because of this Registry.

This issue of The Advocate is centered on the invaluable international conference recently completed. Jennifer was the principle organizer of the conference, translating the guidance from the scientific organizing committee into administrative and logistical tasks that she and the FARA team then set about accomplishing. We owe much of the success of the conference to Jennifer.

Jennifer received her Bachelor of Arts degree, Magna Cum Laude, from LaSalle University in Philadelphia and her Master of Science in Genetic Counseling, with Distinction, from Arcadia University in Glenside, PA. She is a Board Certified Genetic Counselor. In addition to her multiple roles with FARA, Jennifer currently serves as a genetic counselor and research coordinator at the Children's Hospital of Philadelphia and the University of Pennsylvania where she was employed prior to joining FARA. Specifically, she has been the study coordinator for the FA Clinical Outcomes Measure study. She is a reviewer for the Journal of Genetic Counseling and has to her credit 25 articles, three book chapters, and numerous abstracts and presentations in the fields of genetics and neurology. She is on the Board of Directors of the Genetic Counseling Foundation and the National Society of Genetic Counselors (NSGC). She is now NSGC's Finance Chair after having already served as its Treasurer.

You can see how much we are all in Jennifer's debt and why FARA is so proud and thrilled to introduce her to you.

Scientific Progress and Promise: NIH Conference Research Highlights

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cells during the natural progression of diseases like FA and the bio-chemical changes in patient cells that will accurately foretell the benefits of therapeutic drugs being tested in clinical trials. These bio-chemical changes are called biomarkers. A biomarker could be a chemical measured from a blood or urine sample, a genetic profile that is expressed, or an MRI or ultrasound measurement.

In regards to the natural progression of the disease, biomarkers could be helpful in assessing the risk of a particular patient developing a particular complication associated with the disease. In several stages of therapeutic development, biomarkers could be tremendously helpful in accelerating progress toward treatments for FA. For example, biomarkers could assist in drug discovery by demonstrating in drug screening which drugs show most promise for further exploration. They could then show in cell cultures and the Friedreich's models listed above which drugs show some indication of being beneficial. Once established as a baseline of disease progression in patients in the absence of treatment, they could be used to show changes more rapidly, more easily, and more accurately than by monitoring the clinical measures of the disease. This will be important in clinical trials to provide rapid assessments to determine when a drug is working. In the earliest stages of human clinical trials, biomarkers will help identify which patients are likely to be most quick to respond to the potential treatment, allowing patient selection for such clinical trials to be more efficient and reducing the number of patients needed for a given trial. Finally, if considered validated by the regulatory agencies like the U.S. FDA, the biomarkers could serve as "surrogate markers" of benefit, replacing the clinical measures or "endpoints" in demonstrating early in a clinical trial that the tested drug will be beneficial so "conditional approval" of the drug could be sought at that point.

Researchers also emphasized how potentially important these same biomarkers, and a number of the drug compounds being developed for FA, will be in advancing treatment options for a number of other, related diseases such as Parkinson's Disease, Huntington's Disease, Alzheimer's Disease, ALS, stroke, diabetes and Spinal Muscular Atrophy, as well as less common diseases such as MELAS and MERFF. These researchers report increasing evidence that the work being done in FA is not only showing tremendous promise of treatments for that disease, but of providing powerful insights into and even treatment options for a growing number of other disorders.

Clinical Trials

The conference culminated in a review of the clinical trials currently being prepared and the clinical tests being refined to measure the therapeutic effects in these trials. The compounds currently involved in clinical trials and those for which clinical trials are in late stages of preparation include those outlined below.

Idebenone's Promising Trial Results

At the conference, NINDS clinical researchers reported on the phase II drug trial of Idebenone. These investigators concluded that Idebenone appears to be safe and well tolerated. They also reported that, although the changes they observed in the patients in this short trial did not achieve the level of "statistical significance," the changes did show "a trend toward dose-dependent effects on neurological outcome measures," suggesting Idebenone has possible therapeutic value in treating FA. This six-month, double-blind, placebo-controlled trial involved 48 Friedreich's patients between 9 and 18 years of age who were given Idebenone three times a day at fixed daily doses of zero and approximately 5, 15, or 45 milligrams per kilogram of body weight. The NINDS clinical trial team plans to publish the data from this trial as soon as possible.

Santhera, the pharmaceutical company that produced the Idebenone for the NINDS phase II trial, is currently conducting an FA phase III trial of Idebenone in Europe. Based on data from the NINDS phase II trial, Santhera is also preparing a protocol to be submitted to the U.S. FDA in hopes of beginning a phase III clinical trial of Idebenone in the United States in 2007.

MitoQ Trial

The mitochondria-targeted antioxidant MitoQ (Mito Quinone) is being evaluated as a possible treatment for FA. Researchers announced at the conference that they have conducted a phase I clinical trial of MitoQ in healthy subjects and hope to begin a phase II trial in FA patients in Australia, New Zealand, and the United States in 2007, after completing discussions with the regulatory agencies. Antipodean Pharmaceuticals, the company developing MitoQ, is also evaluating the drug as a potential treatment for Parkinson's disease and Hepatitis C.

EPI-A0001 Moving Forward

The FDA has granted orphan drug status for mitochondrial dysfunction disorders to Edison Pharmaceutical's compound referred to as EPI-A0001, which targets electron shuttling, energy production, and reduction of oxidative stress in mitochondria. In July 2006, the NIH made EPI-A0001 one of the first compounds to be accepted into the NIH RAID (Rapid Access to Intervention Development) program. This RAID project is intended to move EPI-A0001 from drug discovery through drug development and into clinical trial rapidly as a possible treatment for mitochondrial disorders such as FA. These extremely positive NIH and FDA assessments and substantial support for EPI-A0001 were tremendously affirming of FARA's earlier decisions

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FARA Fundraising Across the U.S.

A runner faced grueling conditions in the Sahara Desert, bicyclists are crossing the U.S., and families around the U.S. have held many events to raise money for Friedreich's ataxia (FA) research during the past year.

Letter Writing Campaigns

There have been a number of fruitful letter writing campaigns this year. This is a very gratifying type of fundraiser that many newcomers take on for their initial attempt at raising money for research. Five families took on the challenge. The Barbush family from Pittsburgh, the Lanes from Orange, CA, the Edwards family of Shelburne, VT, the Wolfson family of Glendale, Arizona, and the Bell family from Salado, TX, all have some generous family and friends who have contributed to FA research this year. Between these five letter writing campaigns, more than $12,500 has been raised for research, and more donations are continuing to come in! Shawna Bell writes, "I know that there are a lot of you out there who feel the same, you feel like you just do not have the time or the energy to do a fundraiser. I am telling you, anyone can do this…I mentioned to one of my friends that we were overwhelmed with the response to our letter and she told me that people ask her all the time how we are doing and how Tye is doing and want to do something, but feel helpless and do not know how to help. She said they feel this is how they can help and are so glad we asked."

Cross Country Cycling for FA

Cyclists are crossing the country to draw awareness and raise funds for FA research.

Frank Wootten of Hooksett, NH is riding his bicycle from St. Augustine, FL to the Scripps Research Institute in La Jolla, CA in December 2006 to raise awareness and research funds to help find a cure for his son's FA. Mr. Wootten's son, Thomas, 28, is confined to a wheelchair. Thomas, nicknamed 'TK' like his grandfather and great-grandfather before him, lives with FA and his service dog James Bond in Columbia, SC. "I am hoping that through my cycling I can help my son and many others who suffer from this horrible disorder," said Frank.

Kyle Bryant, a 2005 graduate of UC Davis, who lives in Sacramento, is planning to ride his cycle from San Diego to Memphis, TN. Kyle, as a teenager, learned he had FA. He is planning to leave San Diego on January 22, 2007, ride 60 miles a day, and arrive at the National Ataxia Foundation meeting in Memphis on March 20, 2007. An Italian cyclist, Alessandro Villa, who also has FA, is planning on flying from Italy to participate in the ride with Kyle.

"At the end of my journey, I plan to have well-defined calves, a tolerance for extremely cold temperatures and, with your help, $30,000 for ataxia research," said Kyle, whose Web site is www.rideataxia.org.

Marathon des Sables

Peter Murakami, a 23-year-old December 2005 graduate of the University of Illinois at Champaign-Urbana, participated in The Marathon des Sables, a grueling 150-mile race over seven days across the Sahara desert in Morocco in April 2006. Peter ran the race on behalf of his friend Garrett who has FA. Garrett started relying on a wheelchair when he was 15. His condition was not diagnosed until he was 20. Garrett has since gone on to earn a degree in finance from the University of Illinois in Champaign-Urbana with the class of 2003.

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Kyle Bryant, Cross Country Cycling for FA

Dr. Massimo Pandolfo

Dr. Massimo Pandolfo discovered the gene responsible for Friedreich's ataxia in 1996. Dr. Pandolfo currently is a Professor of Neurology at the Université Libre de Bruxelles in Brussels, Belgium where he continues to be at the forefront of Friedreich's ataxia research collaborating with his colleagues around the world. Dr. Pandolfo is also a founding member of FARA and remains on its scientific advisory committee. We recently caught up with Dr. Pandolfo at the conclusion of the Third International Friedreich's Ataxia Scientific Conference at the National Institutes of Health in Bethesda, Maryland.

Why did you begin studying Friedreich's ataxia?

It was by chance. I had just started my training in neurology in Milan. My supervisor, Dr. Stefano Di Donato, had developed an interest in FA and was following quite a few patients (about 80). I believe it was because of the Quebec Collaborative Group initiative, prompted by Claude St-Jean and propelled by Prof. Barbeau, that involved some Italians, including Di Donato, but also Prof. Alessandro Filla, who was at the meeting in Bethesda, and who spent some time in Montreal with Prof. Barbeau in the late '70s to be initiated in "ataxiology." When I started, the genetics "explosion" had not happened yet. We used biochemistry to try to understand the basic abnormality in FA. My first studies were on malic enzyme, at that time suspected to be involved in the disease as noted in a few papers from Dr. David Stumpf. It was indeed a mitochondrial enzyme, but whatever abnormality was observed it was clearly not primary. However, that ignited my curiosity and the desire to find the cause of this disease. I was also seeing FA patients and starting to know them. In 1983, after my military service, I started to learn molecular biology and genetics, first in Italy, then at UC Irvine, where I learned linkage analysis and gene mapping, but working on a different disease. I was back in Italy in 1988, just when Sue Chamberlain had mapped FA to chromosome 9, and I decided that finding the gene by making use of what I had learned--and was learning--in molecular genetics was going to be my project for the following years.

How did you discover the gene responsible for Friedreich's ataxia?

It was a very exciting experience that involved lots of exchanges with collaborating groups. Most of the action happened in 1995, after the gene had been mapped to a reasonably small region of chromosome 9, again thanks to the collaborative effort of many groups. I was at Baylor at that time. The group of Michel Koenig in Strasbourg was willing to collaborate for the final effort to find the gene, and I was in close contact with Dr. Sergio Cocozza in Naples. Michel had isolated many putative exons, that is, sequences on genomic DNA that are likely to be part of expressed genes; we also had isolated some. We ran an experiment called RACE-PCR starting from one of Michel's exons and found a transcript, an expressed gene right from the candidate region. Sergio immediately found out that a corresponding sequence was in the database of expressed sequences--what researchers call ESTs. We characterized the expression pattern of this gene and found it to be promising. We then started to look for mutations. After a few months the results were puzzling, to say the least: only three mutations in 186 patients, all heterozygous. What was going on there; was this the good gene? Sergio, Michel, and I met in Strasbourg in September 1995 to discuss it. We planned to follow up this gene a little more but also to look for other genes in the region. When I went back to the lab, I looked at the data with Laura Montermini, my PhD student who had a central role in the discovery, and noticed that, though no mutation was found, patients had much less mRNA from that gene. It looked like it was expressed at a much lower level. We wanted to know why.

I went to the American Society of Human Genetics meeting in Minneapolis that year, discussed the problem with several geneticists, and finally I thought that something similar to fragile X might be going on. In fragile X the gene is normal, but a triplet repeat expansion at the beginning of the gene suppresses its expression. I phoned Laura and suggested an experiment to check whether a similar phenomenon could be occurring in FA. There, serendipity played a role, because we planned to experiment to look for an expansion before, not within the gene, but the DNA fragments we analyzed were large enough to include the FA expansion. When I returned to Houston, Laura had already run the experiment using patient DNAs from Saudi Arabia and from Louisiana. When she came up with the final results, the data looked so weird that she thought the experiment had not worked. It was indeed showing that patients had "extra DNA" within the gene compared to controls, while carriers had one normal and one expanded fragment.

The data was absolutely correct. It took a few days to convince Michel and Sergio that it was true. However, they were eventually convinced, though replication in their labs was not easy. So, the sequencing effort started to find out what this "extra DNA" was. When sequencing data coming from Strasbourg showed a short GAA repeat in that exact spot in control DNA (Michel emailed that to me when it was midnight there), we made a rapid experiment showing that was indeed the sequence to be expanded in patients (I emailed this to him when it was 2 am there, and he was in the lab). At this point, we only had to find a name for the gene and protein and write the paper. I went home; my wife Sabrina suggested we call the protein "frataxin,"since ataxin was already used for the SCA1 protein. I thought the name appropriate, and all collaborators agreed.

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Featured Scientist
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Just one more thing: I wish to remember how supportive Rochelle Litke was at that time, not only financially by starting SAM/MDA, which was very important of course, but also by her frequent phone calls constantly reminding us how important it was to find the gene quickly.

How far has the research progressed since the gene was discovered 10 years ago?

Enormously. Compared to other genetic diseases, our understanding of FA pathogenesis has progressed very very well at all levels. We now have a reasonable understanding of how the GAA expansion silences the gene, of the structure and function of frataxin, of the involved cellular functions, of the abnormalities in the cell that follow frataxin deficiency. And we have identified possible therapeutic targets at all these levels.

What areas of FA research are you currently studying?

We are involved in studying how the GAA expansion silences frataxin gene expression and how to overcome this; we are working on this with Dr. Joel Gottesfeld in La Jolla and Dr. Richard Festenstein in London. This involves collaborating on the development of new therapies acting at this level and testing them in model systems, including animals. We are also resuming the study of frataxin function and interactions, which for various reasons slowed down in our lab for some time; we are starting a collaboration with Dr. Annalisa Pastore in London on this subject. We are looking at the consequences of frataxin deficiency in model systems, and here, too, there is a very important collaboration occurring with Dr. Dan Geschwind at UCLA in microarray studies. On the clinical side, we participate in the Phase III idebenone trial run by Santhera in Europe, and we work on planning trials with other drugs that hopefully will be run in the not-too-distant future. I am also coordinating the creation of a European consortium that aims to gather basic scientists and clinicians together to develop and test treatments for FA. This consortium will apply for European Community funding in 2008; it is now essentially supported by GoFAR and by some national ataxia organizations.

What avenues of research do you find as the most promising in finding effective treatments for Friedreich's ataxia?

All of them, and some we haven't yet thought about. I am personally involved in approaches to restore frataxin expression as well as in approaches acting at the iron/free radical/respiratory chain level. I am open to exploring any new good idea.

How long do you think it will be before there is an effective treatment for Friedreich's ataxia?

I don't know. Of course, I hope it will be soon, and I work for this to happen. By the way, don't you think it was striking that six drug companies were at our meeting? ■

FARA Directors & Officers

Scientific Progress and Promise: NIH Conference Research Highlights

(continued from p. 6)

regarding its own grant and investment aimed at advancing the Edison compounds, and its decision to join Dr. Robert Wilson and Edison as a co-applicant in the RAID proposal. FARA's confidence in the compounds had resulted primarily from the peer reviews of the compounds, including application of the compounds to FA cellular model assays. In these tests, the Edison compounds appeared to improve mitochondrial function in the cell model by about 8-fold and to be about 3-fold better than all other compounds applied to the assay. Edison anticipates having EPI-A0001 in human testing in early 2007.

Edison Pharmaceuticals is also developing a second series ("B series") of related compounds and has recently advanced a compound called EPI-B00072 into formal clinical development. The company anticipates having EPI-00072 in human testing by late 2007 or early 2008. These EPI compounds appear to show real promise, not only in terms of FA, but also in other mitochondrial dysfunction disorders such as Parkinson's disease and Huntington's disease.

HDAC Inhibitors Increase Frataxin Production

Research in cells and mice indicates that Histone Deacetylase (HDAC) inhibitors have potential for therapeutic increases in frataxin protein production, suggesting they could provide a way of slowing or stopping progression of FA. In preliminary tests, particular HDAC inhibitors being developed at the Scripps Research Institute have increased frataxin protein production in affected cells from Friedreich's patients and in Friedreich's mouse models to therapeutic levels. In the affected cells from Friedreich's patients, the HDAC inhibitors have increased frataxin protein production to levels equal to or greater than in the cells of carrier siblings. Ongoing studies of these particular HDAC inhibitors have not revealed any indication of toxicity. If the results of these studies remain positive, these HDAC inhibitors could enter human trials as a Friedreich's ataxia treatment over the next year or so.

EPO in Early Studies

Human Erythropoietin (EPO) is also being studied as a way to raise levels of available frataxin protein in Friedreich's patients. European scientists discovered in 2005 that EPO can raise the frataxin levels in cells from patients. These scientists recently completed a small, 8-week, proof-of-principle trial with about a dozen patients in most of whom frataxin protein levels appeared to be elevated. Discussions are underway as to how best to advance EPO into full-scale clinical trials as quickly as possible.

Iron Chelators are Targeted

It has long been known that iron accumulates in the mitochondria of Friedreich's patients. Scientists in several laboratories are investigating a number of molecules intended to remove such excess iron from mitochondria without depleting the rest of the cell of the iron needed for such important functions as making blood and the iron-sulfur clusters required in mitochondrial production of energy with minimum oxidative stress. If this iron-chelation work continues to progress, clinical trials of such compounds could be anticipated in 2007.

The Treatment Era Needs YOU!

These clinical trials being planned around the world are the vanguards of the treatment era for Friedreich's ataxia and a range of related disorders. We will not be successful in achieving treatments without these clinical trials. These clinical trials will not be successful if we do not all pull together to assemble the funding and the patient participants each trial will require. So, please help by working to get patients registered in the FARA Patient Registry at http://www.faresearchalliance.org/registry; and by helping build the financial resources needed to push these clinical trials across the finish line.

■

The Power of Public-Private Partnership Partnership Essential to Treatment

FARA has always been convinced that rapid, significant progress in Friedreich's ataxia research requires effective public-private partnership, bringing together the forces of government, public foundations, the scientists and representatives of industry – all committed to developing treatments. From the beginning, it was crystal clear that, "Acting alone, there is very little we can accomplish; while, acting together, there is very little we can NOT accomplish."

The Third International Friedreich's Ataxia Scientific Conference certainly illustrated what a powerful public-private partnership has been shaped around the mission of treating Friedreich's ataxia. Both the list of conference participants and the substance of their presentations gave compelling evidence that such a partnership has already fueled tremendous progress and is clearly leading the way to treatments.

The growth and development of this important partnership can be seen across the spectrum of the three international FARA/NIH conferences. The first one was held in the spring of 1999 and involved 80 scientists, a couple of public foundations, and no pharmaceutical companies. The second, held during the Valentine's Blizzard of '03, gathered 100 scientists from 12 countries, representa-

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Scientific Progress and Promise: NIH Conference Research Highlights

(Partnership Essential...continued from p. 10)

tives of four public foundations and four pharmaceutical companies. This third conference brought together 150 scientists (after about 30 others had to be turned away because a larger number would have been difficult to accommodate), seven public foundations and six pharmaceutical companies. The six drug companies are planning Friedreich's ataxia clinical trials or negotiating agreements to advance additional promising drugs. The companies also helped support this conference.

The government sponsors of the conference were the NIH Office of Rare Diseases (NIH/ORD) and the NIH National Institute for Neurological Disorders and Stroke (NINDS). Opening remarks for the conference were provided by NINDS Director Story Landis and NIH/ORD representative Dr. Giovanna Spinella. NINDS is also the Institute, of course, that has conducted both phase I and phase II of the clinical trial of Idebenone in Friedreich's ataxia. It is NINDS, too, that leads the NIH Rapid Access to Intervention Development (RAID) program supporting the drug development of one of the most promising drug compounds for Friedreich's ataxia. About 20 NIH scientists participated in the conference, including Dr. Nicholas Di Prospero, who presented some of the data from the phase II Idebenone trial.

Joining FARA at the conference were representatives from many of the foundations with which FARA is collaborating to support the research. These groups included the Muscular Dystrophy Association (MDA), GoFAR (an Italian FA advocacy and research group), Ataxia UK, the National Ataxia Foundation (NAF), the Friedreich's Ataxia Research Association of Australia/New Zealand, the Spanish Ataxia Federation (FEDAES), and EuroAtaxia. Many of these representatives are participants in web-based communications networks such as the Friedreich's Ataxia Parents Group (FAPG) and the International Network of Ataxia Friends (INTERNAF).

This public-private partnership has been important throughout FARA's eight-year history, helping support and nurture the basic science that has led to the discovery of an increasing number of promising therapeutic approaches. This partnership is now more than important. It is absolutely essential to further progress. The "treatment era" is based on clinical research that is far more expensive than the basic research that led to it. We will succeed in pushing the clinical research across the finish line to treatment but not without full support and collaboration from all the public and private players listed above, as well as the patients needed to participate in the clinical research and the families, friends and donors who support all these efforts. Treatments and a cure for Friedreich's ataxia will require us all.

■

FARA/NIH Conference

Special Thanks

FARA is deeply grateful to Dr. Robert Wilson for organizing all the scientific content and preparing NIH conference applications for all three FARA/NIH International Conferences and for all he does for us and all FA families.

We would also like to thank Dr. Bronya Keats for her invaluable leadership as Chair of FARA's Scientific Review Committee, our wise and constant counselor.

Dr. Keats

Dr. Wilson

Tissue and Organ Donation:

Mary-Lisa Orth had twin sons with FA. After the personal tragedy of losing one of them, Benj, at age 20, she volunteered to become FARA's Organ and Tissue Donation Liaison, bridging another gap between families and researchers. At the recent FARA conference, Dr. Arnulf Koeppen of the VA Medical Center, Albany, presented his important research findings based on tissue and organ donations that included those coordinated by Mary-Lisa.

For more information, contact Mary-Lisa at: rocketmom@att.net

Submitted by Jennifer Farmer and David Lynch, MD

Four years ago researchers at several US medical centers joined forces to begin a long-term study, funded by FARA and the Muscular Dystrophy Association, with the goal of developing and validating clinical outcome measures for FA (FACOM study). Developing those measures was a necessary prerequisite to testing the effectiveness of any possible treatment.

These researchers were trying to determine how best to measure neurological dysfunction and progression in patients so that we could answer the ultimate question: Does this drug treat or improve the neurological symptoms of FA? This study involved annual evaluation of a large and diverse group of patients with FA.

What are clinical outcome measures? These are tests or assessments that objectively measure how an individual is functioning at a specific time point. It is important that these measures capture specific aspects of the disease, such as neurological function, and that they are relatively easy and quick to administer.

The development of valid yet sensitive clinical measures is crucial to outcome assessment of patients with FA. The measures assessed in this study include:

- Friedreich's Ataxia Rating Scale (FARS) - this is a detailed neurological exam
- Nine hole peg test (9HPT) - timing someone putting pegs into a board
- Timed 25 foot walk (T25W)
- Speech test
- Vision test
- Health-related quality of life questionnaire (HRQOL)
- Activities of daily living (ADL) questionnaire

Why are studies of outcome measures important? There are two main reasons why these measures are important. First, validated outcome measures in FA are needed for clinical trials. These measures are used to answer the most basic and fundamental question of a clinical trial, Is the patient better? Second, these measures can be used to establish and document the natural history/clinical progression of FA. If you can measure a large group of individuals with FA and follow the group over many years you can make more precise determinations about the variability/severity of the condition, disease progression and full range of FA disease features. Another way of looking at this aspect of the study is to think of this as establishing the FA baseline and long-term controls.

Study Results

More than 200 people (children and adults) have been enrolled into the FACOM study and more than 100 have been followed for 3 years.

Median age at first visit
-- 27 years (year 1), 26.5 years (year 2)
Median shorter GAA repeat
-- 605 repeats (year 1), 635 repeats (year 2)

The initial goals of the study have been accomplished.

Study Findings

- The individual measures (FARS, T25FW, 9HPT, vision, ADL, and HRQOL) were validated in FA.
- A composite measure that consisted of the timed walk, pegboard, vision and FARS performed best compared to just using a single measure. The advantage to the composite is that it allows for different aspects of FA to be assessed by each performance measure. For ex ample, walking, hand coordination, speech, vision and if a patient is not able to perform one of the tasks due to the disease progression this does not limit our ability to determine a measurement and score as the other measures are performed and scored according to ability.
- The FARS and composite measures are both useful and almost equally sensitive.
- While these measures are valid, they don't necessarily measure small/subtle changes in short amounts of time therefore if a clinical trial were to use these measures alone as endpoints the trial would need to be a longer duration 1-2 years depending on the patient group.

While the initial study has reached completion, we need to build on the results and consider next steps that will be optimal for supporting clinical trials. Specifically, we would like to optimize some of the measures so that we can reduce the amount of time needed to demonstrate a neuroprotective effect. Also, clinical trials for FA are coming quickly and we believe that the sites from this study could be leveraged to help conduct clinical trials.

Next Steps Towards Clinical Trials – Collaborative Clinical Research Network in FA

There have been very practical outcomes from the above-described clinical measure study that can be utilized to bring clinical trials in FA to patients quicker and more efficiently. There have now eight centers in the United States with clinical research experience in FA that are ready and eager to participate in clinical trials. There are more than 200 patients with well-documented baseline evaluations.

We propose to create the Collaborative Clinical Research Network in FA to advance clinical care, research and therapeutic approaches in FA.

Primary Functions of the Network

1. Create an expanded network of clinical research centers in FA that will provide quantitative long-term clinical data on patients, and design improved clinical measures. This

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Fundraising Across the U.S.

(continued from p. 7)

Dr. Susan Perlman and Stephanie Magness, A Cure for FA

Phillip and Valerie Bennett, Sunset on FA

Arizona

Martina McBride Phoenix Concert to Help Support Friedreich's ataxia Research – Phoenix, AZ
Country music star Martina McBride was in concert at the US Airways Center in Phoenix, Arizona on Saturday, September 16, 2006 for the 6th annual "Beauty of a Bonzer" event that is sponsored by Outback Steakhouse and Budweiser for the benefit of various charities. This year's charities included FARA. Thanks to all involved, including our own Mary-Lisa Orth! (See related story on p. 2)

California

Sunset on Friedreich's ataxia – San Francisco Bay Area, CA
The third annual Sunset on Friedreich's ataxia (http://www.sunsetonfa.org) was held in the San Francisco Bay area on August 5, 2006. The magical evening included an evening of wine tasting, dinner, silent and live auctions, live music and dancing. The Konanz, Bennett, and Rupel families, plus so many committee volunteers, worked hard on this event and raised a much appreciated $40,000 for FA research, through Seek A Miracle/MDA!!

Stephanie's Hope – A Cure for FA – Valencia, CA
The Magness family of Valencia, CA, held a series of benefits to raise funds and awareness for the Friedreich's Ataxia Research Alliance. Stephanie Magness, age 24, with FA and her family and friends held two dinner/silent auction benefits during the summer of 2006 and a holiday boutique in October, raising more than $16,000. Special guests included Dr. Susan Perlman, FA researcher from UCLA. Sharon writes, "We have learned that there is no such thing as a small event. Anything we do to raise funds makes an impact. We would like to encourage everyone to step out in faith and just do it! It is a little scary at first, but once the momentum starts to build, confidence builds right along side of it. It is truly an unforgettable and remarkable experience. We hope this will be a great encouragement to everyone!"

In addition, the Magness family and friends have formed a team and have begun training for their next fundraiser – a 50-mile bike ride to Palm Springs. The Magness family says they are "hanging on to hope for Stephanie's future and a cure for FA!"

FAITH…
The Rupel family (son Matt, 16 has FA) from Northern California held their FAITH fundraiser on February 11, 2006 and brought in over $31,000 for FA research through Seek A Miracle/MDA. FAITH stands for FA in the Heart. Bart says, "It's a tie in between the heart effects of FA and Valentines' Day". FAITH included a dinner, dance and auction. Thanks, Rupel family, from the heart! The 2nd annual FAITH fundraiser will be held on February 10, 2007 in Sunnyvale, CA. For more information, please visit www.fa-ith.org

Connecticut

Actress Mary Stuart Masterson Hosts Connecticut Fundraiser – Branford, CT
Actress Mary Stuart Masterson hosted a fundraiser September 22, 2006 at the Owenego Inn in Branford, Ct., on behalf of Samantha and Alexandria Bode, to help find a cure for Friedreich's ataxia. Also attending was actor Jeremy Davidson. The fundraiser was organized by Mary Caruso on behalf of her two daughters.

Masterson, who has starred in such movies as "Fried Green Tomatoes," "Bed of Roses," "Benny & Joon," and "Some Kind of Wonderful," was invited to host the event by Mary Caruso. For the past several years, Caruso and her committee have worked hard to put on their annual dinner/auction/dance with the help of the Owenego Inn.

In February, Caruso received a call from Masterson who was preparing her directorial debut in a movie that includes a child with FA. "When I found out it was Mary Stuart Masterson I had been communicating with I almost fell through the floor," said Caruso.

Caruso's daughters Sam and Alex went to New York City

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to meet with Masterson and answer questions about FA and were interviewed on tape. Masterson also arranged for them to attend some of the taping of the movie. "We have had a great time getting to know Mary Stuart," said Alex Bode. This year was the third year for this fundraiser, was entitled "Dream a Little Dream" and raised $25,500 – a record amount for this event.

Colorado

Bro Golf – Denver, CO
This annual event is held in memory of Jeff 'Rosie' Rosenkrantz who died with FA several years ago. This year's tournament in Denver brought together many friends from different parts of the country. The chairman for 2006, Gerald Zaplawa, reports that they raised a record $12,880 for FA research.

One of the former coordinators of the tournament stated, "Our commitment is to continue to fight right along with FARA. We all miss our friend 'Rosie' and through our annual tournament there are now many others that never met him that miss him too…they have been exposed to the legend—and it lives!"

Florida

Church gets involved – Pompano Beach, FL
In September 2006, the First Christian Day School in Pompano Beach, FL where Helen Magnuson of Deerfield Beach works hosted a "Pennies from Heaven" fundraiser for FARA in honor of Helen's daughter, Carly, 15, with FA. In addition, the Christian Women's Fellowship of the First Christian Church hosted a "pot luck" luncheon. The fellowship purchased bookmarks, bracelets, and other items to sell in order to raise funds for FA research. Thank you, good people from Florida!

Georgia

Van Schoick Bash – Bogart, GA
The Van Schoick family (Robbi, 27, FA and Becca, 24, FA) is continuing their annual goal to raise funds for FA research. One night in May 2006 they had two live bands, a silent auction, over one hundred people and "mucho fun". Friends came together, brought food and drinks, decorated the tables, put up lights in the yard and partied until the wee hours of the morning. Nelda said, "I don't know how we could have had more fun." Our researchers received over $16,000 as a result of this very successful evening of enjoyment in Bogart, Georgia.

Experian Walk of Hope – Marietta, GA
The Jacquin family, whose daughter Laura Beth has FA, is now living in Marietta, GA. They were involved once again with the MDA Walk of Hope in Norcross. Supporters in their new community helped to raise nearly $7,000 for Seek A Miracle/MDA. Laura Beth, 19, says of her fundraising, "I want to give those that are affected the hope to keep fighting and looking for a cure because I know that with God's help someday Muscular Dystrophy won't be an issue in anyone's life. And I can't wait for that day."

Loco's Day to Fight FA – Savannah, GA
Lindsay Ashman once again held her event this past July at Loco's Grill and Pub in Savannah, Georgia. Lindsay writes that "The 2006 Loco's Day to Fight FA was an enormous thrill of a day". From opening till close Loco's donated $1 for each of certain menu items ordered. There was a wing-eating contest, silent auction, a $2 raffle, and a bike run was led by a local chapter of Harley Davidson. Corporate sponsors donated T-shirts and there was some live local music to cap off the night! Local publicity included two local morning shows and an article in the local paper. Lindsay said she "made the most of these appearances, and of course the fundraiser itself, to tell people about FA and how heartbreaking the disorder is, but how normal and capable people who have it actually are – and, of course, how close that cure is. FARA made a decent profit monetarily, and FA'ers got a lot of prayers!"

Smith Family, No More Prisoners

Iowa

No More Prisoners -- Creston, IA
On September 23, 2006, a carnival fundraiser entitled "No More Prisoners" was held in Creston, Iowa, on behalf of Michael Smith a sophomore at Creston High School. It included a street dance, BBQ, face painting, balloon animals, and other events. The very well-received event was sponsored by Leslie's Dance Emporium and will become an annual event in Creston.

Massachusetts

BYSA Family Night at the Revolution – Bridgewater, MA
The Bridgewater Youth Soccer Association (BYSA), in Bridgewater, Massachusetts, held an event on September

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23, 2006 called "BYSA Family Night at the Revolution." The game between the New England Revolution and the Kansas City Wizards was held at Gillette Stadium, home of the New England Revolution soccer team and the New England Patriots football team. Bill Gambill writes, "...we had a tremendous turnout for this event and although we had received many donations of a monetary value we also received tremendous donations of moral support from our many friends and people we do not even know. There is no way you can put a monetary value on that but it showed us that we are so fortunate to live in a caring community that has no boundaries."

The Dalton Family, Rally for the Cure, CAUSE Foundation

Michigan

Haldeman's Hope Dinner Dance – Sterling Heights, MI
This event on March 25, 2006 planned by the Haldeman family (Jesse, 18, FA) with help from their MDA office in Sterling Heights, Michigan, raised $13,600 for FA research through Seek A Miracle. Penny Haldeman reported that this was the second year for their event and it was a rousing success, writing, "We had to turn the lights on and ask people to leave at 12:30 a.m.!"

Minnesota

Minnesota benefit concert – Grand Forks, MN
At the time of printing, a concert was being planned for December 23, 2006, at the Eagles Club in East Grand Forks, MN. Kevin Fuglseth, musician and friend, writes, "And my buddy Aaron, he's twenty-six years old. He has an older brother, Kevin, who also has FA. They both live in St. Paul, MN. They're both sports nuts, and I can't tell you how cool it would be if they could strap on a pair of hockey skates and go out on the ice one day. You guys are doing something so good. Keep it up...since I've started educating myself on the disease and seeing that there is hope, I've wanted to do something, and I'm a musician, so here we are with a benefit show." The show is to include a variety of sounds, with the Rusty Chords Trio, Stompin Tom and the Bad Bananas, Drive O' Dreamer, Rudolph Lives, and Dingus. Thanks to all of you from all of us!

New Hampshire

Fuzzy Buzzy Charity Golf Tournament – Windham, NH
The 20th annual Fuzzy Buzzy was held September 10, 2006 at the Windham Golf and Country Club in Windham, NH. Paul Stanieich, whose niece Erin O'Neil (26) has FA, has chaired his golf tournament for 20 years. This is the 3rd year the event supported the Friedreich's Ataxia Research Alliance (FARA) and a record amount was raised ($11,000). Thank you, Uncle Paul! http://www.fuzzybuzzycharitygolf-tournament.com/

New Jersey

Leo does it again! – Cherry Hill, NJ
Leo Lazaropoulos's annual infamous garage sale in Cherry Hill, NJ must have had some real "finds" this year. His sale brought in $1,000 for FA research. Thanks go out to Leo for hunting for treasures to sell, and to his community for supporting Leo.

Rally for the Cure – Stirling, NJ
The Rally for a Cure was a "drive" to raise funds for FA research and was held May 7, 2006 in Stirling, New Jersey. The CAUSE Foundation, in honor of the Dalton family of Livingston, New Jersey has supported FA research for the past few years. The CAUSE Foundation was established in 1994 by Flight Attendants for Flight Attendants. The foundation assists United Airlines Flight Attendants and their families worldwide. Debbie Dalton is a Newark based flight attendant with two young adult children who have FA. www.thecausefoundation.org

New York

The Voyces sing for Friedreich's Research – New York, NY
Brian Wurscham of The Voyces has planned a concert to be held on January 22, 2007, dedicated to his cousin-in-law John Cernosek (23, FA) from Crofton, Maryland. Held at the Rockwood Music Hall, 196 Allen Street, New York NY, the program will include: Don Freda, Linda Draper, Atoosa, and The Voyces. ALL money made by the artists will go directly to FARA. See www.thevoyces.com for more information.

Good friend runs NYC Marathon – New York, NY
Mark Meadows from Bogart, Georgia ran the New York City marathon on November 5, 2006 in honor of the Van Schoick family. His wife, Melinda, writes that "He was just an hour behind Lance!" Thanks, Mark, from all of us! Checks are still rolling in from his supporters and it looks like they have a quite a generous amount to put toward research to help the Van Schoick girls in their quest for a cure or treatment.

Walk to Seek A Miracle – Pittsford, NY
The Ferrarone family (Laura, 16, FA and Sarah, 20, FA), along with their MDA office, held their 7th annual Walk to Seek A Miracle. The beautiful walk along the old Erie Canal and through the town of Pittsford, accompanied by a delicious lunch provided by Outback Steakhouse netted nearly $50,000 for FA research. *(continued on p. 16)*

Fundraising Across the U.S.
(continued from p. 15)

3rd Annual Westchester Triathlon Fundraiser – Westchester, NY
This year marked Team Donovan's third fundraiser which was held on September 17, 2006. What started out 2 years ago as a friend wanting to do something to support the family after finding out Donovan Simpson,10, had FA has turned out to be a major event with thirty athletes participating for Team Donovan. This year Donovan's mom Debra swam her quickest mile and dad Norm tried out his new hips by doing the 25-mile bike ride. Team Donovan also fulfills a second goal and that is to raise awareness for FA. The race found Donovan at the finish line cheering for each person as they completed the race, knowing that it is one step closer to finding a cure. Norm says, "We survived – and nobody got hurt!"

Ohio

Cincinnati's Race for a Cure – Cincinnati, OH
We're thankful to the Luebbe family who held their second annual "Race for a Cure" on May 20, 2006 on behalf of Evan Luebbe and other children from the Cincinnati area. About 250 people attended the event and 75 volunteers helped organize the walk, run, and family carnival.

Parrish family keeps on fundraising – New Philadephia, OH
The Parrish family (Lindsey, 16, FA) from New Philadelphia, OH, once again got involved with their local MDA office to help raise funds for FA research through Seek A Miracle. Over $27,000 was raised through the Stride-n-Ride, the New Philadelphia Firemen's Golf and a fundraiser at the New Philadelphia High School. Thanks for your ambition, Sandy, and thanks to your community for their continued support.

Toth Elementary Continues to Support Zac – Perrysburg, OH
The student council at Toth Elementary in Perrysburg, OH had a coin challenge, with the students raising $850 for FARA in honor of Zachary Zies. Thanks to the school secretary Kathy Burkey and the principal Dr. Christoff for these efforts!

Many happy returns!
Wedding congratulations to Veronica and Roger Chan of Hong Kong. Veronica, who has FA, is the daughter of Angelo Pepe, a long time supporter of FARA. When Veronica and Roger sent invitations to their friends and relatives they requested that donations be sent to FARA in lieu of wedding gifts. Best wishes to the newlyweds for a healthy and happy future.

Fundraising is a process – a journey. Like any journey, it begins with a plan.

The FARA "Fundraising Made Simple" Kit can be accessed online at http://faresearchalliance.org/fundraising/ or you can contact us for a hard copy. This was created to offer information and advice for families and individuals who are interested in raising funds for FA research.

Evan Luebbe, Race for a Cure

FARA MEMORIALS
Sadly, many of us continue to lose people we love. We are always grateful to the families who think of FARA at such a time and ask that donations be given toward FA research in honor of the deceased. During this year FARA received $17,000 in memorial donations. This is a marvelous tribute to those individuals who passed away in 2006. ■

Quick & Easy Ways to Support FARA Research

Letter Writing Campaigns – A large number of FARA donations come from family and friends. It is one of the easiest ways to raise money. Go to http://faresearchalliance.org/fundraising/ to see a sample fundraising letter you can tailor to your family and friends.

Credit Card Donations by Phone – Quick and easy. You can make a donation by phone using your VISA®, Mastercard®, or AMEX® by calling the FARA office at (703) 426-1576. FARA will take down your credit card information and process your donation. You can designate your donation in honor of a particular person or for a specific purpose (e.g., you can name a certain fundraiser).

Online Credit Card Donations – Network for Good™ (only U.S. donors) – Your transaction is safe, secure, and private. Just follow the directions. You will be asked to type in the amount of your donation, decide if you want to provide FARA with your name and e-mail address, designate your donation for a specific purpose, log on with a password of your choosing, and provide your credit card information. The Network for Good charges 4.75% of your donation for their processing fee. Go to http://www.networkforgood.org/ and type in FARA in the Charity search box. *(continued on p. 17)*

Fundraising Across the U.S.

(Quick & Easy Ways...continued from p. 16)

Corporate Matching Gift Programs – More than 3,000 companies, foundations, and institutions offer their employees the benefits of a "Matching Gift" program. These companies match payroll deductions and other individual gifts of up to a certain amount per employee per year. Contact your personnel office for specific information. Many donors have doubled and tripled their initial donations using this gift program. If you don't work for a company with a charitable program, do you know someone who does and might help?

The United Way offers a write-in option for FARA – To find out if your company has a giving campaign through United Way, ask your Human Resources department. FARA has received donations from many states including Massachusetts, New York, Arizona, Connecticut, Michigan, and Pennsylvania.

Combined Federal Campaign – CFC is the annual fundraising drive conducted by federal employees in their workplace each Fall. Each year federal employees and military personnel raise millions of dollars that benefit thousands of non-profit charities through a payroll deduction. FARA's CFC designation number is 7970.

Religious, Professional, and Civic Donations – FARA has received donations from Rotary Clubs and many churches from around the country including Belton Church of Christ (TX), Faith Lutheran Church (Sun City, CA), First United Methodist Church (Pampa, TX), and the Bloomsburg University Rotary (PA). Not a member of such an organization? Maybe a family member or neighbor is and would be happy to support our cause.

In Memoriam Donations – Remember someone close to you by making a gift in his or her memory and help fuel FA research. FARA will send an acknowledgement to the family.

In Honor Donations – Help fund FA research by making a donation in honor of someone who made a difference in your life. Commemorate a birthday, anniversary, wedding or other major event.

Planned Giving – This form of donating to FARA benefits you and your family personally while ensuring that FARA will have the resources to carry out its mission. Speak with your attorney to help you plan a lasting gift to FARA that best suits the needs of you and your family.

If you need any further information regarding ANY of these fundraising ideas, contact FARA at (703) 426-1576. Thank YOU!

■

10 year olds: Alena Wolfson, Ashley Hartigan, and Molly Lawson.

The Ataxia Girls

In September, my daughter, Ashley and I had the pleasure of meeting several families in Arizona when we went to the Martina McBride benefit concert. While the prospect of meeting other families was frightening, it was a huge step in regaining some control over this new world we had been thrown in. Ashley was constantly asking why she was the only one with this disease. She had been to see so many new doctors, dealing with a scoliosis brace and missing a lot of school. I tried to explain to her that there were other ten year olds who also had the disease but without actually meeting those children, it was difficult for her to understand. When she actually met Alena and Molly, she was able to see that there were others out there like her. She knows now that she is no longer the "Lone Ranger", but rather part of a very special group. The girls have dubbed themselves the "Ataxia Girls" although I feel "Ataxia Angels" is more appropriate.

I have also benefited immensely from meeting other families and children who are dealing with this horrific disease. During our trip to Phoenix, Ashley and I had the pleasure of meeting Mary-Lisa, Ron Bartek, the Lawsons, the Wolfsons, the Garcias (Local NAF Chapter), McLaughlins, the Lanes and others. Mary-Lisa made our trip memorable and even arranged for Ashley to have her picture taken with Martina McBride. My husband and I got to meet additional families at the ACARM conference in California. For the first time since the diagnosis, I was able to have a face to face conversation with people who could relate to what I was going through.

I now see that regaining my life following the day that the world fell apart was a two step process: the first step was joining the FAPG and receiving calls from some wonderful people who honestly do understand what I was going through, and just knowing that I was not alone in my pain and fear; the second step is actually meeting the people who I only knew by their E-mails. Without all of you, I would still feel as though there was no hope for my princess' future. Most importantly, however, is that my daughter knows that she is not alone - she is an Ataxia Girl. ■

Moving Towards Clinical Trials

(continued from p. 12)

network will also provide the framework and mechanism for implementing clinical trials more quickly and efficiently.

2. Participate in studies to establish biomarkers for FA. For example, establish a DNA repository for use in large scale translational research such as modifier gene studies and biomarker studies. Biomarkers are biological/chemical measures that can be used for a variety of purposes such as diagnosis of a condition, stratification of patients, inclusion for a specific clinical trials, and determination of change/action of a drug target.

3. Create a mechanism for sharing data and resources with basic and clinical investigators.

By virtue of its existence, this consortium will lead to clinical studies and therapeutic interventions that are more scientifically rigorous and expeditious. Once this network is established we hope to work with similar networks and groups around the world to collaborate on clinical trials at an international level.

Details of the initial study findings can be found in the following scientific publications:

Lynch DR, Farmer JM, Tsou AY, Perlman S, Subramony SH, Gomez CM, Ashizawa T, Wilmot GR, Wilson RB, Balcer LJ. Measuring Friedreich ataxia: complementary features of examination and performance measures. Neurology. 2006 Jun 13;66(11):1711-6.

Lynch DR, Farmer JM, Wilson RB, Balcer LJ. Performance measures in Friedreich ataxia: potential utility as clinical outcome tools. Mov Disord. 2005 Jul;20(7):777-82.

The study sites and physician and coordinators include:

Site	Physician	Coordinator
Children's Hospital of Philadelphia and University of Pennsylvania	Dr. David Lynch	Jennifer Farmer
University of California at Los Angeles	Dr. Susan Perlman	Lyndsay Elliott
Emory University	Dr. George Wilmot	Sue Gronka
University of Mississippi	Dr. Sub Subramony	Leigh Langford
University of Minnesota	Dr. Christopher Gomez and Dr. Khalaf Bushara	Jodi Lowary and Diane Hutter
University of Chicago	Dr. Christopher Gomez	Elizabeth Shaviers
University of Iowa	Dr. Kathy Matthews	Carrie Stephan
University of Texas	Dr. Tetsuo Ashizawa	Penny Stanton

Grants Awarded

FARA Research Portfolio – 2005-2006
Submitted by Jennifer Farmer

To accomplish FARA's mission – to slow, stop and reverse the damage caused by Friedreich's ataxia – FARA funds high quality research through a competitive and growing grants program. Your donations fund the grants awarded.

FARA accepts grant applications on a continuous basis throughout the year. All new grant proposals go through a dual review process: scientific peer-review overseen by FARA's Scientific Review Committee and review by FARA's Board of Directors. Based on the peer review and recommendation of the Scientific Review Committee, FARA's Board makes a funding decision. Grants can vary in size and term:

- small, short-term grants (<$50,000 for one year or less) for seed money for a pilot project, feasibility study, or supplemental support for an existing project
- average grants ($50,000 – $100,000 for 1-2 years) support new/young investigators in the FA field, independent projects, development of new animal models, assay development, drug screening, etc.
- large grants (>$100,000 per year) support established, well-developed projects, drug development, translational and clinical research

We would like to provide a brief overview of FARA grants awarded in 2005 and 2006. Your generosity has enabled FARA to fund so much excellent research that space does not permit detailed explanation of each grant, so we will summarize each in the table below. "Research Area" refers to three broad categories of research -- basic, translational and clinical. Basic research is the most fundamental and explores the underlying causes and mechanisms (pathophysiology) of the disease. Translational (or preclinical) research advances the results of basic research from discovery through development, from "bench to bedside." It involves, for example, testing drug discoveries in animals and human cell cultures in preparation for tests in humans. Clinical research involves trials in humans.

The "Category" column is used to characterize the focus of each research project. The "Outcome" column places the goal or long-term benefit of each project into one of four categories – Determine Pathophysiology, Improve Mitochondrial Function (↑), Reduce Oxidative Stress (↓), or Elevate Frataxin Protein levels (↑). *(continued on p. 19)*

Grants Funded in 2005

Principal Investigator	Project	Research Area	Category	Outcome
Giovanni Coppola	Gene expression study of frataxin deficient mouse	Basic	Microarray analysis/gene expression	pathophysiology
Martin Delatycki	Ataxia Meeting, Nov 3rd-4th 2005, Australia	All	Collaborative Conference	All
Peter Dervan	Gene transcription therapy	Basic	FRDA gene	↑ frataxin
*Edison Pharmaceuticals	Development of drugs that increase mitochondrial function	Translational	Drug development	↑ mito function
Joel Gottesfeld	Polyamides (small molecules)	Basic	FRDA gene	↑ frataxin
Joel Gottesfeld	Chromatin structure and HDAC Inhibitors	Basic	FRDA gene	↑ frataxin
*Michael Hebert	Reporter system to measure transcription of sticky DNA	Basic/Translational	Assay development	↑ frataxin
* Panos Ioannou, Joseph Sarsero	Development of genomic reporter assays and humanized mouse models	Basic/Translational	Assay development	↑ frataxin
Grazia Isaya	Structure/Function studies of frataxin	Basic	Frataxin function	pathophysiology
Filip Lim and Richard Wade Martins	Gene therapy strategies using herpes virus amplicon vectors in transgenic mice	Translational	Gene therapy	↑ frataxin
Arnulf Koeppen	Iron & iron-responsive proteins in FA cardiomyopathy	Basic	Cardiology	pathophysiology
David Lynch, Tetsuo Ashizawa, Christopher Gomez, Susan Perlman, George Wilmot	Friedreich's ataxia clinical outcome measures – multi-center study	Clinical	Clinical outcome measures	All
David Lynch	Speech measures	Clinical	Clinical outcome measures	All
Bogdan Popescu, Wing Hang Tong	Bioiron meeting	All	Iron metabolism	All
Des Richardson	The role of iron and the use of chelation therapy	Basic	Iron metabolism	Pathophysiology ↓oxid stress
*Robert Wilson	Identification of drugs and drug targets	Basic/Translational	Drug screening	All
John Day (NAF)	Ataxia Investigators Meeting, Tampa, FL	Clinical	Collaborative Conference	All

Two-Year Grants Funded in 2005 and 2006

Principal Investigator	Project	Research Area (basic, translational or clinical	Category	Outcome (pathophysiology, ↑ mito function, ↑ frataxin, ↓oxid stress)
*Louise Cahill	Speech as indicator of decline in neurological function	Clinical	Clinical outcome measure	All
**Massimo Pandolfo	Overcoming transcription defect w/ small molecules	Translational	Animal and cellular models	↑ frataxin
*Annalisa Pastore	interaction between frataxin and Isc proteins	Basic	Frataxin function	pathophysiology
Jordi Tamarit	Protein damage induced by iron-overload in the yeast model of FA	Basic	Cell biology	pathophysiology
*Robert Wells	DNAtriplexes in Friedreich's ataxia	Basic	FRDA gene	↑ frataxin

New Grant Awards Funded in 2006

Principal Investigator	Project	Research Area (basic, translational or clinical	Category	Outcome (pathophysiology, ↑ mito function, ↑ frataxin, ↓oxid stress)
Sanjay Bidichandani	DNA repair and GAA triplet-repeat instability	Basic	FRDA gene	pathophysiology
*Sergio Cocozza & Alesandro Filla	Preclinical study of Erythropoietin	Translational	Protein-based	↑ frataxin
Edward Grabczyk	Post Hurricane Katrina – supplement to rebuild research program	Basic	FRDA gene	↑ frataxin
Daniel Harki	Studies of polyamides in living mouse models	Basic/Translational	FRDA gene & drug screening	↑ frataxin
*Emmanuel Lesuisse	Studies of oxidative stress in the yeast model	Basic	Frataxin function	pathophysiology
*John Phillips	Drosophilia Model of FRDA	Basic/Translational	Animal model	pathophysiology
Mark Pook	Epigenetic analysis of the FRDA gene	Basic	FRDA gene	↑ frataxin
*Des Richardson & Erika Becker	Role of Frataxin in iron metabolism	Basic	Frataxin function	pathophysiology
*Pierre Rustin	Identification of new therapeutic compounds	Basic	Drug screening	All
#Roberto Testi	Extramitochondrial function of frataxin	Basic	Frataxin function	pathophysiology

Table notations:
*Funded by FARA and Seek A Miracle
#Funded by FARA and Ataxia UK*Funded by FARA and Seek A Miracle
**Funded by FARA, Seek A Miracle, GoFAR, and Ataxia UK

In summary, the total of grants awarded by FARA and Seek A Miracle in 2005 was $4,395,926 and to date in 2006 was $818,587. Most of the grant recipients attended the 3rd International FA Conference in Nov 2006 and presented data from their research. So, for more information about these projects you can review the submitted abstracts on FARA's website.

FARA is committed to funding a variety of research projects to uncover the disease mechanism and potential therapies. In 2007, we anticipate supporting more translational and clinical research as we have entered the treatment era for FA. However, this type of research is much more expensive. In order to be successful, we need your continued support in donations and fundraising. We will also need to work with our public and private partners, sister organizations and pharmaceutical companies to co-fund and support research.

In 2007, FARA will be launching a new software program that will make our entire grants process electronic. This means that all grants will be received, reviewed, monitored and reported electronically. You will also have access to a part of this program that will give you instant information on the grants funded. This new program is being custom designed and engineered by an all-volunteer software development team at EDS. The generous and talented folks at EDS continue to make enormous contributions to FARA and FA patient families.

Not listed in the tables above are the many cases in which FA research has benefited significantly from additional support from FARA's funding partners. For example:

Government support: NIH co-funded/co-hosted all three

(Continued on p. 21)

Grants Awarded
(continued from p. 20)

International Scientific Conferences; several recipients of FARA "seed grants" (e.g., Drs. Bidichandani, Grabczyk, Payne, Isaya, Wilson and Gottesfeld) have, based on FARA-funded results, secured larger NIH grants to advance their work; NIH/NINDS funded and conducted Phase I and Phase II of the Idebenone clinical trial; FARA, key NIH/NINDS staff and pharmaceutical representatives, served on the steering committee responsible for planning the Idebenone trial and securing the Idebenone supply and required background records; FARA twice served as co-applicant on proposals to the NIH RAID program (Rapid Access to Intervention Development); when one application was successful (with Dr. Robert Wilson and Edison Pharmaceuticals), FARA assisted further to advance the drug candidate – EPI-A0001. For Idebenone and EPI-A0001, FARA and NIH representatives participated in the meetings with the U.S. FDA, seeking FDA approval for clinical trials.

Pharma support: When the other RAID application was not successful (for HDAC inhibitors), FARA looked elsewhere for drug development support, and pharmaceutical companies began positioning themselves eagerly to advance this second drug candidate expeditiously. For each of the other clinical trial drug candidates, FARA has supported pre-clinical research, in many cases with funding partners like Seek A Miracle and MDA, and is currently working closely with the drug companies advancing the drugs. These drug companies are likely to shoulder the bulk of the financial burden for trials.

Non-Profit support: FARA has long worked closely with Seek A Miracle/MDA to fund promising research projects. FARA and MDA met several times during 2006 and issued a joint press release in June announcing they would enhance and accelerate their partnership in funding FA research, recognizing that, "acting together, we will cross the finish line of treatment for Friedreich's ataxia far sooner than would otherwise be possible." FARA has begun co-funding FA research with two European advocacy groups – Ataxia UK and FARA's Italian partner, GoFAR – and with the Friedreich's Ataxia Research Association of Australia/New Zealand. FARA is also working with additional European organizations such as EuroAtaxia, Spanish Ataxia Federation (FEDAES), and organizations in other European countries (e.g., France and Sweden). FARA and the National Ataxia Foundation (NAF) collaborated to support NAF's first Ataxia Investigators Meeting at the 2005 NAF meeting in Tampa, and are exploring prospects for partnering more fully in support of their common mission area – treating FA. Of course, representatives of all these organizations benefit immensely from participating in web-based communications networks such as the Friedreich's Ataxia Parents Group (FAPG) and the International Network of Ataxia Friends (INTERNAF). ■

What Does FA Mean to You?
T-shirt sale

$12 each or 3 for $30 (free shipping)

Sizes XS-XL

Choose your saying:

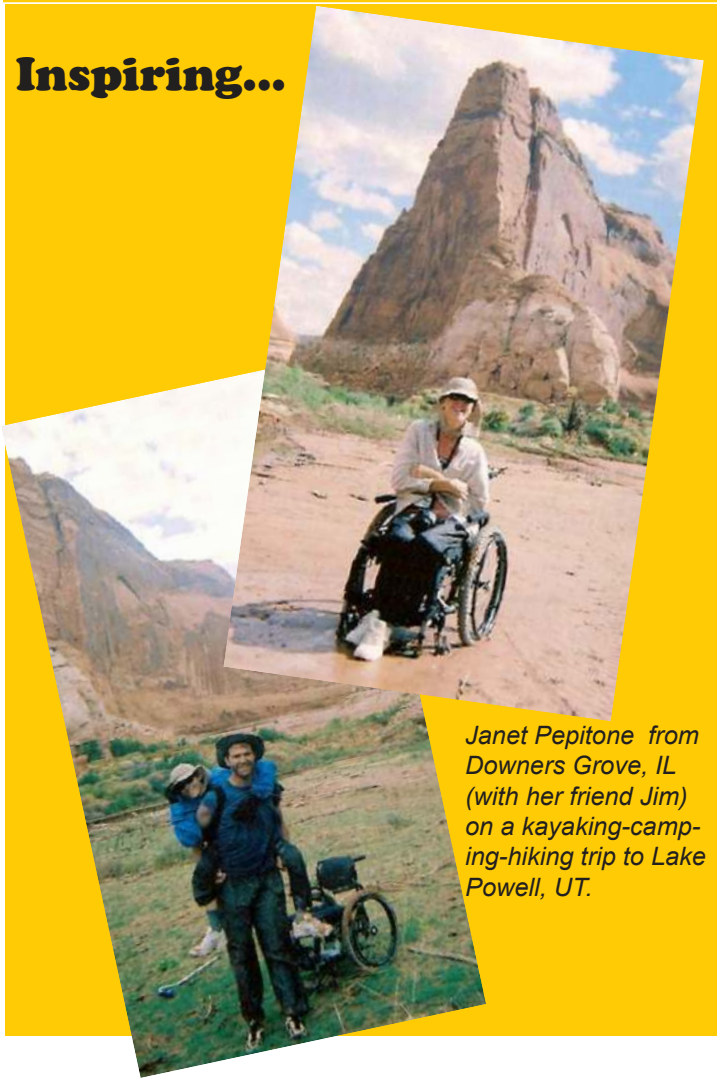
FA- FANTASTIC & AMAZING
FA- FABULOUS & ADORABLE
FA- FREAKIN' AWESOME

All money raised goes to Seek A Miracle/MDA strictly for FA research.

Contact Samantha Litke:
(856) 616-8147 or E-mail:
Samanthalitke@yahoo.com

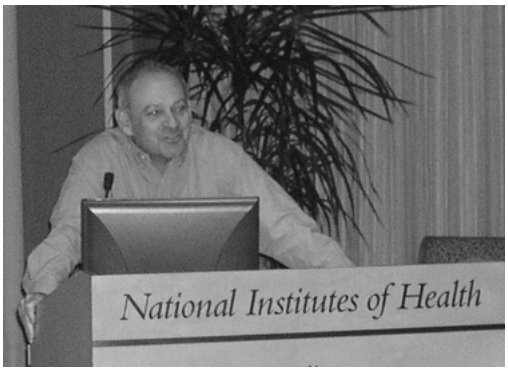
Last Look

Inspiring...



Janet Pepitone from Downers Grove, IL (with her friend Jim) on a kayaking-camping-hiking trip to Lake Powell, UT.

Your generous donations in the past enabled FARA to assemble the fine scientists here so they could share and test their insights into treatments for FA and to initiate and nurture the collaborations needed to achieve them.



Please give generously so that we can continue to accelerate this progress toward treatment and a cure.

Proven courage and strength…….

…in those we love.

Photos taken from FARA website

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