Friedreich's Ataxia Research Alliance UPDATE

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FARA's Full-Court Press
Significant Strides in FRDA Research

FARA research grants are enabling significant strides on all fronts - basic science, pre-clinical (translational) research and clinical trials. FARA is implementing a three-pronged, comprehensive research strategy to **SLOW** the progress of disease symptoms, **STOP** the disease in its tracks, **and REVERSE** the damage being done. And, these three objectives are being pursued simultaneously.

FARA's comprehensive research strategy includes:

- **support** of promising research projects worldwide
- **facilitation** of timely collaboration among researchers of diverse, complementary expertise
- **coordination** with the pharmaceutical industry leading to successes in drug discovery, drug development, approval & marketing
- **pursuit** of research opportunities with renowned research institutions at the forefront of biomedical science

FARA will continue to reach out to current and prospective donors and dedicated fundraisers to marshal the resources needed to advance this scientific research strategy. FARA will also go on partnering with major funding sources such as the National Institutes of Health (NIH) and pharmaceutical companies interested in developing treatments. In 2005, FARA will continue this full-court press and build upon the increasing momentum toward treatments and a cure for Friedreich's ataxia (FRDA). *(Cont'd p2)*

FARA Research Grants Approach $2M
$1M Awarded in 2004 alone!!

Thanks to the generosity of donors like you, FARA is nearing the $2 million mark in research funded over the past 6 years, either directly or in partnership with Seek a Miracle/MDA. One financial measure of the accelerating pace of research is the exciting news that half of this amount - $1 million- was funded in 2004 alone!
FARA has developed a well regarded organization that spends 100% of your charitable contributions on research. You have our commitment that FARA will continue its relentless drive to treatments and a cure.

FARA FUNDRAISING ACROSS the NATION
Across the United States, events were held to raise funds for Friedreich's ataxia research. See stories beginning on page 6 to read about the events and gather new ideas for a fundraiser of your own.

Andrew, Sherry, Mitchell, & Dan Daoust - "We held our first fundraiser just two months after receiving our son Andrew's diagnosis of Friedreich's ataxia. Our donation to FARA was more than $12,000. We are simply in awe of the generosity of our family, friends, co-workers, and even strangers."

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. 100% of FARA donations are dedicated to supporting research leading to a treatment or cure for this relentless and devastating disease.

Full-Court Press (Cont'd from p. 1)

Key Research Highlights:
Scientists are now categorizing research into three types – ***basic*** *(lab work exploring genetic causes, underlying mechanisms, etc.),* ***translational*** (*lab work aimed at developing the most promising basic research into therapeutic trials),* and ***clinical*** *(the human trials required to establish treatments).*

FRDA Basic Science *(lab work exploring genetic causes, underlying mechanisms, etc.)***:**
FRDA's ***basic*** research in gene-based approaches has drawn some of the world's finest scientists. Dr. **Robert Wells** at Texas A&M has been awarded three FARA grants and has added significantly to the body of knowledge on the FRDA gene. Dr. **Sanjay Bidichandani** (Oklahoma University) translated FARA grants into a large NIH grant to increase our understanding of the gene and help instruct our search for gene-based therapies. Dr. **Ed Grabczyk,** who works with Dr. **Bronya Keats** at LSU, has been awarded three FARA gene-based grants and has applied for an NIH grant in an exciting new drug-screening program. A new FARA grantee at the University of Illinois in Chicago, Dr. **Maria Krasilnikova**, is further exploring FRDA's triplet-repeat expansion in hopes of shedding new light on a potential therapeutic approach. Dr. **Ian Alexander** and Dr. **Jane Fleming** in Australia have used FARA grants to develop viral delivery vehicles (vectors) for use in gene-based therapies and are testing them in FRDA mouse models. They report: "We have generated **virus vectors that can express normal frataxin protein**. Not only is this frataxin protein expressed in the correct compartment of the cell, but we have also demonstrated that it is functional in patient skin cells (fibroblasts). Our intitial attempts to deliver these vectors to mouse sensory neurons in vivo was not as effective as we had hoped. However, we are continuing to assess these vectors in frataxin-deficient sensory neuron cultures." FARA continues to offer support for this work.


Dr. Sanjay Bidichandani


Dr. Robert Wells

Dr. **Roland Lill** at the University of Marburg in Germany and Dr. **Grazia Isaya** at the Mayo Clinic in Minnesota continue to lead the important effort to nail down the precise function and operating mechanisms of the frataxin protein. The research they and their colleagues around the world are doing is helping point the entire FRDA scientific community in the right direction for taking next steps in protein-based therapies. Dr. Lill's most recent findings, for example, highlight the importance of the frataxin protein in the assembly of iron-sulfur clusters essential to energy production at the mitochondrial walls.

Meanwhile, other FARA-funded researchers are attempting to apply all that has been learned about the FRDA gene and frataxin protein to develop pharmaceutical approaches that result in increased production of frataxin protein and/or improved function of mitochondria (energy factories of the cells) even when frataxin protein levels are low. Dr. **Joel Gottesfeld** of the Scripps Research Institute of La Jolla, California, is using a FARA grant for that purpose, as are Dr. **Barbara Scheiber-Mojdehkar** and Dr. **Brigitte Sturm** at the University of Vienna in Austria. Dr. Gottesfeld, for example, is exploring the potential of carefully designed molecules for addressing the genetic mutation itself and thus increasing frataxin protein production. One such molecule seems to have the ability to bind to and stabilize the FRDA gene's triplet expansion so as to facilitate the gene's expression of the protein. Early findings with this molecule in laboratory cell cultures indicate a several-fold increase in protein production. Other molecules might be able to improve the effectiveness of the limited frataxin protein already at the mitochondrial walls. Other compounds altogether might possibly serve to reduce oxidative stress at the mitochondria and facilitate assembly of the iron-sulfur clusters so important to energy production there. FARA will continue to support these important ***basic*** science projects and to facilitate collaboration among these scientists, knowing that they will yield the next promising candidates for the translational and clinical efforts that will then lead to treatments and a cure.

Full-Court Press (cont'd from p. 2)

FRDA Translational Science (*lab work aimed at "translating" the most promising basic research into therapeutic trials)*:

Dr. Rob Wilson

High-Throughput Screening (HTS) is an extremely important translational device. HTS permits very rapid testing of thousands of drugs at a time against assays (cell cultures or DNA samples, for example) designed to replicate certain aspects of target diseases. For example, a FRDA cell culture could be prepared with an additive that will glow in the presence of increased levels of frataxin protein or increased levels of the messenger RNA needed to assemble frataxin protein. The cell culture could then be placed on 96-well lab plates in sufficient quantities to subject each individual cell culture with a different one of tens of thousands of different drugs. This is a gifted way to test quickly for promising FRDA drugs. The "high scoring" drugs could then be tried in FRDA mouse models or in human trials. A number of FRDA scientists are working hard to develop such assays for HTS. Dr. Helen Puccio has received a FARA grant to run an assay she has developed through 5,000 different compounds. Three other FRDA scientists -- Dr. Rob Wilson, University of Pennsylvania and FARA's Scientific Director; Dr. Panos Ioannou, Murdoch Institute, Australia; and Dr. Ed Grabczyk, Louisiana State University – have applied to submit the assays they have developed to the NIH-wide HTS Center in Birmingham, Alabama, where the assays would be run against more than 120,000 drug compounds.

As promising drug compounds are identified in such High-Throughput Screeing programs, they will join the other drugs being tried in FRDA mouse models and then in human patients. FARA is assisting at each of these steps along the path to treatments. (*Cont'd on p. 4)*

Dr. Panos Ioannou

Dr. Panos Ioannou — Sketch of a Gifted and Dedicated Scientist

Group Leader, Cell and Gene Therapy Research
The Murdoch Children's Research Institute
Royal Children's Hospital
Melbourne, Victoria, Australia

Dr. Ioannou received both his B.Sc. and his Ph.D. in biochemistry from University College, London, with a focus on the molecular mechanisms of memory. While still a student, his keen interest in DNA replication led him to publish a model for the replication mechanism in the highly prestigious medical journal – Nature.

In his native Cyprus, Dr. Ioannou established and ran for almost 15 years a Clinic for Prenatal Diagnosis of Thalassaemia – another disorder, like FRDA, in which iron plays a key role. He later set up the Department of Molecular Genetics in the Cyprus Institute of Neurology and Genetics. In 1992, at the Lawrence Livermore National Laboratory in California, he created the first human P-Artificial Chromosome genomic library, and it was used extensively in the sequencing of the human genome. Dr. Ioannou moved to the Murdoch Children's Research Institute in Melbourne in 1977 and leads the Cell and Gene Therapy Research Group there.

Dr. Ioannou is a FARA and MDA grantee. He has developed a FRDA cell-culture assay designed to detect any increased frataxin protein production resulting from the addition of drug compounds to the cell culture. He has submitted his assay for use in the NIH High-Throughput Screening program. In his excellent lab, Dr. Ioannou has also developed a number of lines of transgenic FRDA mice. He participated actively in both of FARA's international FRDA conferences and is an important leader in FRDA research. The entire FRDA community is indeed fortunate to enjoy the talents, compassion and dedication of this fine scientist.

Full-Court Press (Cont'd from p. 3)

Dr. R. Mark Payne

Dr. Mark Payne's team at Wake Forest University, using a FARA grant, is making progress in another aspect of *translational FRDA science*. Dr. Payne's group, with a technological approach it first developed for a different disorder, is assembling a synthetic frataxin protein and delivering it to mitochondria in cell culture. The delivery technology involves attaching to the synthetic frataxin protein an additional protein fragment (called a TAT) that takes the frataxin into the cell and to the mitochondria. FARA helped Dr. Payne obtain FRDA mice from the Michele Koenig/Helen Puccio team in Strasbourg, France and, in late 2004, awarded Dr. Payne his second FARA research grant. He will use this grant to attempt frataxin protein delivery in the FRDA mice and will breed those mice for use by other scientists as well.

FRDA Clinical Science *(the human trials required to establish treatments)***:**

Dr. Kurt Fischbeck

The Idebenone Trial – Phase I of the trial, directed by Dr. Kenneth (Kurt) Fischbeck and Dr. Nick Di Prospero of NIH's Neurological Institute, was designed to test how well tolerated the drug would be at various doses. It was completed in the fall of 2004. In Phase Ia, each patient in three age groups (5-11 years, 12-17 years, 18 and older) took a single dose of Idebenone. The initial patients took a single, very low dose and subsequent patients each took an increasingly high, single dose. In Phase Ib, each patient took the same high dose every day for a month. Phase I demonstrated that the drug is well tolerated, even at high doses, over a month's time. Phase II/III of the trial is being designed to test for safety and efficacy. The Phase II/III team presented the draft Phase II/III design to the Food and Drug Administration (FDA) in early January 2005. After accommodating FDA recommendations, the team plans to begin Phase II in 2005.

Dr. Nick Di Prospero, Keith Andrus, Alison La Pean

The success of Phase II/III will be determined by agreed "end points" or clinical measures designed to show whether the drug has any beneficial effect in the patients. The Phase II/III team is exploring the use of both cardiac measures and neurological measures as end points. The cardiac end points might include such measures as heart muscle mass and agreed parameters of heart function. The neurological end points will likely be centered on the ataxia scales being developed at the seven clinical centers across the United States. (*See story, p.8)* FDA requirements will help determine which type of measures will serve as primary end points and which as secondary end points. Either way, both cardiological and neurological conditions will be fully monitored and the Phase II/III team plans to get the next phase underway in 2005. The Phase II/III team includes a pharmaceutical company that plans to play an active role in this trial and beyond and has secured orphan drug status for Idebenone for potential use in Friedreich's ataxia.

Dr, Martin Delatycki & son Tommy in Sidney

MitoQ Developments - MitoQ (MitoQuinone) is a compound closely related to Coenzyme Q10 and Idebenone. It was developed in New Zealand by Drs. Michael Murphy and Robin Smith and is being taken through preclinical steps in preparation for clinical trials by Dr. Kenneth Taylor. Dr. Taylor writes, "MitoQ has completed preclinical development and we have filed for regulatory approval for phase 1 clinical studies to be carried out in Christchurch, New Zealand. These studies in human volunteers will confirm the MitoQ dose selected for clinical efficacy studies currently scheduled to begin in the second half of 2005. Dr Martin Delatycki, Murdoch Institute, Royal Children's Hospital, Melbourne, will be the Principal Investigator and is currently finalizing the protocol for our clinical study of MitoQ in FA."

FARA's Featured FRDA Scientist

Dr. Bronya Keats

FARA is truly privileged to honor and thank Dr. Bronya Keats in this small way by naming her FARA's Featured FRDA Scientist for the Winter '04-'05 issue. Dr. Keats is a founding member of FARA's Board of Directors and its Scientific Review Committee. As one of the three scientists on that Committee, she has helped oversee the peer- review process for all the research grant applications submitted to the organization. For much of the last couple of years, in fact, she has served as Acting Chairperson of the Scientific Review Committee and has devoted a great deal of her time to managing the peer-review process, assembling its results and making consequent recommendations to the Board of Directors. FRDA families everywhere owe a debt of gratitude to this outstanding scientist and friend.

Born in Adelaide, South Australia, Dr. Keats has made her home in the United States since 1977. She earned both her B.Sc. And Ph.D (Human Population Genetics) from the Australian National University. She is Board certified in Medical Genetics with a specialty in Clinical Molecular Genetics. She is Professor and Head of the Department of Genetics, Louisiana State University Health Sciences Center (LSUHSC), and Director of the Molecular and Human Genetics Center of Excellence, LSUHSC. She is also founding Director of the Center of Acadiana Genetics and Hereditary Health Care, which operates from LSUHSC.

That center was established in 1999 with the help of a federal funding initiative spearheaded by U.S. Congressman Billy Tauzin. The Center provides clinical services needed to address the diseases that especially afflict the Acadian population. For example, "Cajuns" experience Friedreich's ataxia and Usher Syndrome (deaf-blindness) at a rate about two and a half times greater than the general population.

Dr. Keats is President Elect of the Association of Professors of Human and Medical Genetics, and is a Member of the National Advisory Council of the National Institute for Genome Research of the National Institutes of Health (NIH). She is also a former Member of the National Advisory Council of the National Institute on Deafness and Other Communication Disorders.

Dr. Keats has long been a leading scientific investigator in the search for genetic markers for hereditary diseases. She has made significant contributions to such searches in FRDA, Usher syndrome, Tay Sachs disease, and various hearing disorders. She has been awarded research grants by the NIH, the Muscular Dystrophy Association, Howard Hughes Medical Institute, the Marriott Foundation, the Foundation Fighting Blindness, National Ataxia Foundation, Retinitis Pigmentosa Foundation, and the Deafness research Foundation. She serves in important positions of a host of professional organizations and has innumerable publications in the finest medical journals.

Dr. Keats helped immensely in laying the scientific foundation for FARA. She helped get the organization on its "scientific feet," define its mission and set its course. She played a central role in both of the international FRDA scientific conferences (1999 & 2003) FARA co-funded and co-hosted with NIH, chairing critical sessions in both. Her unselfish devotion to the work of FARA's Scientific review Committee in advancing the FRDA research portfolio has been invaluable. She has helped keep FARA's compass set in the direction of the most meritorious science that will lead to treatments and a cure.

Dr. Bronya Keats has earned the respect and gratitude of FRDA families around the world. We are deeply in her debt. She is FARA's Featured FRDA Scientist for 2004-2005.

FARA FUNDRAISING ACROSS THE NATION

Thanks to all the families who hosted events or made donations to help fund Friedreich's ataxia research. Some events were held in conjunction with Friedreich's Ataxia Awareness Day on May 15. Others took advantage of a Valentine's Day Match that raised $35,000. 100% of these donations supported promising research grants approved by FARA's peer-reviews and Board of Directors.

CALIFORNIA

Dinner, Dancing and Tourneys
Starry, Starry Night – Dreams CAN Come True!!

It was a magical atmosphere of candlelight dining and dancing under the stars at the Meridian Rolling Hills Club in Novato, following an afternoon of tennis. Dinner was attended by the Mayor, was catered by the Outback Steakhouse and preceded a highly successful auction. FARA Board Member **BJ Acker-Hittta** organized this fabulous event - another in her series - that will lead ultimately to a "dream come true" through research. The event raised about $48,000.

A Sunset on FRDA… what a vision!
A step in that visionary direction happened on a high hilltop in Fremont! Thanks to a partnership between the MDA and a committee of parents and friends, the "Sunset on Friedreich's Ataxia Dinner Dance" in support of **Phillip Bennett** and his fight against FRDA came to fruition. As more than 200 guests arrived at the five-acre estate perched atop a hill overlooking the South San Francisco Bay and the peninsula to the west, the sky was clear, cooperating fully for the main feature of the evening - dining, dancing and socializing while watching the magnificent view change by the moment, the sun moving down the sky and into the sea behind the peninsula hills. The crowd was regaled by the view, the dinner, the entertainment, and, of course, the live and silent auctions. The **Konanz family** and the **Rupel Family**, also coping with Friedreich's ataxia, enjoyed the event. More than $36,000 was raised—enough to sponsor a research grant!

Phillip Bennett & mom, Valerie Bennett

Bocce Ball

Lisa Carmassi once again scored more research dollars with her annual Bocce Ball Tournament. Bocce is Italian lawn bowling, played on a long, rectangular court, and it contains elements reminiscent of bowling and croquet. Lisa donates her talent and energy in honor of **Aubrey and Nick Olson**, children of **Bruce and Cindy Olson**.

CONNECTICUT

Dinner Dance & Silent Auction
Mary Caruso and her friends organized her annual dance and auction. Mary's two daughters, **Sam and Alex Bode**, get involved in the planning and fun too. "I am very touched each year at the continued support by friends and even strangers! The money goes to such great use and, as the time has gone by, the research is really getting exciting!"

GEORGIA

Letter-writing Campaigns
Georgians conducted two successful letter-writing campaigns. **Lindsay Ashman**, a young woman with Friedreich's ataxia, contacted friends and family asking for donations in support **of FARA research. Dianne Thigpen** spearheaded a letter-writing campaign honoring **Kayla Prather**, her granddaughter.

Neighborhood Walk for Research
Nelda von Schoick organized a walk-a-thon in her neighborhood on Friedreich's Ataxia Awareness Day. She raised $8,000. Seventy-five walkers from the neighborhood, friends and church participated. Donations of visors, balloons and food added to the enjoyment of this neighborhood event.

Car Show - The same **Dianne Thigpen** who did the letter-writing campaign assembled and organized volunteers in April to help conduct the Charity Car Show in North Georgia.

KANSAS

Friends and Family of **Rachel Gill** from Kansas City, KS sent out letters to many folks in support of research dollars. A friend of Rachel's parents, **Jennifer Moen**, conducted a letterwriting campaign as did Rachel's mom. Rachel's grandfather made a monthly pledge to FARA and her aunt's kindergarten class in California contributed too!

MASSACHUSETTS

Food, Fun & Fundraisin' - The **O'Neill family** held a FARA Fundraiser at the American Civic Center in the small town of Wakefield. Two local bands donated the entertainment and the crowd enjoyed buffet-style food (all donated), beer, wine, sodas, and many great raffles.

The O'Neills rally support

Mary Ann O'Neill wrote: "My daughter, Erin, 24, has Friedreich's Ataxia. We raised over $25,000, far surpassing what we had originally expected. We had never done anything like this before, and hated the thought of 'asking for money.' As it turned out, once our local newspapers carried the story, everyone in town wanted to attend. I am so overwhelmed by the love and support we received and, more importantly, the awareness we raised."

Stride & Ride - More than 200 people participated in the **Jaquin family**'s 3rd annual Stride & Ride for Seek a Miracle/MDA According to an article in the Springfield paper, The Republican, **Laura Jacquin**, 16, of Forest Park, "not only talks the talk and walks the walk, but can also raise money - lots of money. 'I'm finally getting to a point where I'm not nervous speaking anymore," she said, after raising a little more than the $16,000 the event raised last year, and more than three times what it raised in its first year.

COAST TO COAST SUPPORT FOR FRDA RESEARCH

MICHIGAN

"We held our first fundraiser just two months after receiving our son **Andrew**'s diagnosis of Friedreich's ataxia. Our donation to FARA was more than $12,000. We are simply in awe of the generosity of our family, friends, co-workers, and even strangers." **Dan and Sherry Daoust, Andrew, and Mitchell** (photo, p.1)

MINNESOTA

Friends and family gathered at The Olson Annual Seek a Miracle Fundraiser Dinner honoring the **Bruce and Cindy Olson family** of Pine City. Raising over $10,000 this year makes a direct impact on research funding. FARA wishes to thank the many families who have so generously contributed on behalf of the Olson's.

NEW JERSEY

Leo Lazaroupoulous's yard sale is in its 5th year. People now look forward to the sale -- some folks are so concerned for Leo that they come to chat and be welcomed. Others come for the variety, others for the thrill of the hunt. Special thanks to the Lion Design Build Company and Ms. D'Angelo! Leo's mom, **Krissa**, says "I don't think I could stop if I wanted to - I love to see the people; they're so very kind. It really restores your faith in humanity."

Debbie Dalton — United We Stand

Two of **Debbie Dalton**'s three children were recently diagnosed with Friedreich's ataxia. With the help of her energetic friends and colleagues and her "can-do" attitude, she demonstrated a positive way to tackle this disorder—by raising funds that support research leading to a treatment or cure for Friedreich's ataxia.

Kyle & Lindsay, with Keith & Debbie (seated)

Debbie's letter to FRDA Families: "These past six months have been a roller coaster ride for me and my family. At first I just wanted to bury my head in the sand and hope this news would go away. After the initial shock, I decided to put my efforts and emotions into raising money to find a cure for FRDA. My friends volunteered their time and ideas. Our first fundraising effort consisted of sending out an email to friends and family and asking them to forward the letter on to anyone who might make a donation. Our goal was $10,000 and I'm happy to report that we surpassed it. Our second fundraiser came about by friends trying to add laughter to a serious situation by creating Debbie's Can. They made up coffee cans with a poem on the top and handed them out to family and friends. The purpose was the care and feeding of Debbie's Can! Loose change became hundreds of dollars donated for research.

Our third fundraiser became a partnership with a benefit that was created to help the families of the Flight Attendants who lost their lives on September 11, 2001 on United Flight 93 that crashed near Pittsburgh, Pennsylvania. Through the years, this benefit has changed to include making donations to a charitable organization in memory of those lost. Being a United Airlines flight attendant for 35 years, it was an easy fit. That benefit was held in August and raised approximately $10,000 in research money for Friedreich's ataxia. This money was split between FARA and SAM/MDA.

A final gift came just recently from The CAUSE Foundation, an organization that helps flight attendants who are unable to work during times of illness and injury. This organization was started by a woman named Monica Wheat. Since Monica's retirement, the Foundation has set up a $2,500 Founder's Grant in her honor. This year Monica requested the grant go to Friedreich's ataxia research. When I first learned of my children's diagnosis, I was overwhelmed. Through the help of family and friends, I learned I could make a difference in this fight. I found out I had the ability to help and, hopefully, make a difference in the lives of children affected by Friedreich's ataxia.

The extended family of **Dan Eric Olsen,** including the family and friends of **Jim & Lita Ribellino** (his grandparents), held its first FARA fundraiser this year. The family certainly got off to a great start! The 2004 Olsen Family Golf Outing assembled 65 players in the Monroe Township area. A lot of fun and generosity later, they donated $12,500 to the support of FRDA research. That will go a "straight and long" way toward "the pin" of treatments. Thanks to the Bella Vista Country Club of Marlboro, NJ, and thanks to all of you who supported the event!

(Fundraising Cont'd on p. 12)

Closing in on Clinical Measures Needed for Drug Trials

-Seven U.S. Centers Make Strides in FRDA Scales Study-

FRDA patients across the country participate in vital study - As of the time of this publication, the seven centers had **examined and entered data on more than 140 patients at least once. The plan is to have examined at least 100 of those patients twice, with twelve months between the two examinations, by early 2005. The data from all these examinations will provide the basis for validating the clinical measures to be used as end points in the clinical trials being planned for 2005.** We are all grateful to the patient families participating in this important scales study and to the scientists at all seven centers.

With Clinical drug trials for Friedreich's ataxia now underway, it is critically important that ataxia scales be available to determine whether the drugs being tried are effective and document the therapeutic effect of those drugs. Without such clinical measures to demonstrate that a drug has beneficial effect on patients, the Food and Drug Administration (FDA) will not approve the drug, doctors will not be able to prescribe it for Friedreich's ataxia and it will not be covered by U.S. health insurance plans.

The clinical measures being tested and refined in this study include the 9-hole pegboard test, quantitative speech measure, timed 25-foot walk (when possible), quantitative visual function measure, and quality of life measures. The research to date has demonstrated that these measures do correlate with markers of disease severity. The multi-center study is also determining which of the measures are sufficiently sensitive to changes resulting from disease progression and the drugs to be tested in clinical trials.

This multi-center study putting the required ataxia scales in final form is led by **Dr. David Lynch** at the Children's Hospital of Philadelphia and University of Pennsylvania and involves six other centers around the United States –Emory University, UCLA, and the Universities of Iowa, Minnesota, Mississippi, and Texas. In addition to Dr. Lynch in Philadelphia, the study's Investigators are **Dr. George (Chip) Wilmot** (Emory); **Dr. Susan Perlman** (UCLA); **Dr. Henry Paulson** (U. of Iowa); **Dr. Christopher Gomez** (U. of Minnesota); **Dr. S.H. (Sub) Subramony** (U. of Mississippi); and **Dr.Tetsuo (Tee) Ashizawa** (U. of Texas).

Dr. David Lynch

FARA and MDA are cooperating to fund this multi-center study. FARA also funded the research Dr. Lynch conducted to build the preliminary data and structure of the study, as well as the two previous sessions at the National Institutes of Health (NIH) designed to test previously available ataxia scales for potential application to FRDA trials. The current study does not involve the administration of any drugs and does not require participants to alter their current practices regarding drugs and medications they might already be taking.

Dr. Susan Perlman

This large, multi-center effort and the FRDA clinical trials would be far more difficult, time-consuming and error-prone if researchers relied on hand-written data entries. FARA volunteers (see article, p.9) have designed and implemented a computerized solution that will insure that this study and subsequent FRDA clinical trials are "paperless trials" in which data is electronically entered, verified, transmitted and collated, and in which patient registries and databases are generated, secured, maintained, mined and analyzed. FRDA clinical trials will not be successful without the clinical measures to be developed in this study. This study will be successful only with patient participation. Treatments and a cure will be developed only if FRDA patients enroll and participate in this study and subsequent studies and trials. Please see the information on Patient Recruitment *(p.11)* and contact the center nearest you to enroll as soon as possible.

Global Information Technology Excellence Award

FARA *IT* Project Chosen US National Nominee

FARA's Winter '03-'04 Update carried a story about the FARA volunteers who were donating their time, expertise and materials to create a long-awaited and revolutionary change in a critical aspect of FRDA research – a computerized, web-based system in which patient data is electronically entered, verified, transmitted and collated, and in which patient registries and databases are generated, secured, maintained, mined and analyzed. These wonderful volunteers have not only been successful in designing and deploying this Information Technology (IT) solution for "paperless trials" — they were **selected by the Information Technology Association of America as the U.S. public sector nominee for the Global IT Excellence Award** presented every other year by the World Information Technology and Services Alliance.

Alice Bearce, Sherri Stone, Bill Hartnett, Christine Ward, Jill Werner, and Margaret Ferrarone

The following are excerpts from the nomination of the Friedreich's Ataxia Clinical Enterprise (FACE) IT Program :"The FACE IT Program involves a creative technical application of IT software and hardware, and the talents and energies of an all-volunteer IT workforce of EDS, Microsoft and University of Pennsylvania employees.This IT solution is bringing substantial benefits across the United States to individuals, families and the medical research community engaged in the search for treatments and a cure for a devastating neurological disorder – Friedreich's ataxia. Prior to development of the FACE IT Program, research scientists collected data on their patients and entered the data manually into a hard-copy spreadsheet. Complex manual computations were then made to produce summarized statistical data. This time consuming, expensive, error-prone procedure was also followed when recording and assimilating data from patient performance tests and drug administrations. There was no consolidated system or electronic means to collect, validate, archive, preserve, secure, organize, analyze, share, access or mine the precious data. There was no consolidated patient database or patient registry to help manage current clinical studies or plan future clinical efforts. Enter the highly capable, motivated and dedicated IT volunteers who envisioned, created, organized and implemented the FACE IT Program. The leadership, courage, commitment, and talent demonstrated by this all-volunteer team of IT professionals has enabled them to work quickly and successfully with seven diverse clinical centers across the United States as well as the National Institutes of Health (NIH) and a non-profit public charity (FARA) to design, develop, deliver and maintain the IT infrastructure needed to conduct a multi-center 'paperless clinical study' that is the sine qua non for all clinical trials in Friedreich's ataxia and potentially a broad range of other movement disorders."

This project is led by **Bill Hartnett**, FARA Board Member and an extremely generous donor, talented volunteer and leader. The medical-professional coordinator is **Jennifer Farmer**, genetic counselor and FRDA researcher at the University of Pennsylvania. The network engineer at Children's Hospital of Philadelphia is **Erik Witman**. The other volunteers from Electronic Data Systems (EDS) include **Margaret Ferrarone** (a "FRDA mom")**, Marianne Wilcox, Jill Werner, Christine Ward, Leo Bellew, Marty Ohman, Craig Dennstedt, John Young, Rich Dusse, Alice Bearse, Dawn Catanese, Shannon Bielaska, Sheri Stone, Andrei Coler, and Linda Guest.** These EDS professionals led the project design and engineering and a large group of volunteers that contributed to the development and testing of the final application. Kerry Westfall, a Microsoft database engineer and FRDA patient, provided initial project architecture design, set the technology platform, and was able to provide Microsoft products at reduced prices.

Last year, this IT capability was in development — this year, it is in use! FARA funded the three computer servers needed to run this system and pays the annual cost for maintenance and operation. **The time, materials and expertise donated by these internationally recognized FARA volunteers, however, constitute hundreds of thousands of dollars of value and "will probably take two years off the timeline for treatments and a cure." Awesome! Thank you and congratulations!**

Raising Public Awareness — National and Local Efforts

National Friedreich's Ataxia Awareness Day — The third Saturday in May has been recognized as a day on which people around the United States express support for FRDA families and for people like you who are raising funds to support FRDA research. This FARA Press Release and congressional "proclamation" were sent to thousands of print and broadcast media representatives around the country in 2004 to mark the annual event:

Explosion of Research Triggers Hope on Friedreich¹s Ataxia Awareness Day May 15, 2004

May 12, 2004, Washington, D.C. Although there is no effective treatment or cure available, Friedreich's Ataxia patients and families have more reason for real hope as they prepare events around the country for Friedreich's Ataxia Awareness Day on May 15th. The day is recognized in a Congressional proclamation and through various events around the country.

Friedreich's Ataxia is a fatal, hereditary, degenerative, neurological disorder that typically first becomes noticeable when children are in elementary school.

"An extraordinary explosion of research insights has followed the identification of the Friedreich¹s Ataxia gene in 1996," said **U.S. Rep Robert E. Andrews of New Jersey** in introducing the Congressional proclamation. "Growing cooperation among organizations supporting the research and the multidisciplinary efforts of thousands of scientists and health care professionals provide powerful evidence of the increasing hope and determination to conquer Friedreich's Ataxia. There is also a growing conviction that treatments can and will be developed for this disorder and that the resulting insights will be broadly applicable across a wide range of neurological disorders such as Parkinson¹s, Huntington's and Alzheimer's."

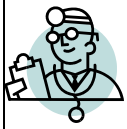
The **Kentucky House of Representatives** passed Resolution 110 recognizing the third Saturday in May as Friedreich's Ataxia Awareness Day. The **Honorable Paul Marcotte**, State Representative, introduced the Resolution in honor of his 8 year-old grandson who is diagnosed with Friedreich's ataxia. State **Senator Dick Roeding**, President Pro-Tem of the **Kentucky Senate**, introduced a companion resolution. California¹s state legislature has also recognized the third Saturday in May as National Friedreich¹s Ataxia Awareness Day.

Additional Congressional Awareness — The **US House of Representatives**, in its FY 2005 appropriations bill for Labor, Health and Human Services and Education recognized the work of the National Institute of Neurological Disorders and Stroke (NINDS) at NIH in conducting a Phase I drug trial in FRDA and co-funding and co-hosting with FARA an international scientific conference on FRDA, thereby facilitating the collaboration so essential in medical research. Congress commended NINDS for these type of efforts in collaborative, translational research.

Other Awareness Raisers

Part time model **Leah Chalcraft and her brother Josh**, both diagnosed with Friedreich's ataxia, are featured in a biology college textbook by Wadsworth Publishing Company.

Jason Antone, here with parents Peter and Najiba, hosts his own TV talk show, the "JROCK Show," on Comcast's Southfield Public Access channel in metro Detroit and in Grand Rapids on GRTV, showing that Friedreich's ataxia is not a showstopper for Jason.



Dr. Paul Donohue, in his nationally syndicated, daily question-and-answer column "To Your Good Health," addressed Friedreich's ataxia. FARA received numerous calls from readers because the article is read in more than 175 newspapers in the US and listed FARA as a source of information.

Blue Bottle Films is producing a video, "Catch You When You Fall," featuring a FRDA patient participating in the Idebenone clinical trial. Award winning producer/director **Elaine Epstein** also interviews the NIH researchers and visits other labs to investigate the latest research. FARA is pleased to help fund this project that will raise awareness about FRDA and NIH's role in FRDA research.

TWO Clinical Trials in Progress— Patient Enrollment Information

FRDA ATAXIA SCALES STUDY — PATIENT RECRUITMENT

The clinical measures to be tested and refined in this study include patient participation in the 9-hole peg-board test, quantitative speech measure, timed 25-foot walk (when possible), quantitative visual function measure, and quality of life measures (see in-depth article, p. 8).

CONTACT A CENTER NEAR YOU FOR INFORMATION**:**

***Philadelphia, PA**: U. of Pennsylvania/Children's Hospital of Philadelphia
Dr. David Lynch, (215)590-2242, lynch@pharm.med.upenn.edu; Jennifer Farmer, (215)614-0937, farmerj@uphs.upenn.edu

***Atlanta, GA**: Emory University– Sue Gronka, (404)778-3075, sgronka@emory.edu

***Los Angeles, CA**: UCLA – Lyndsay Elliott(310)794-1225, lyndsayelliott@aol.com

***Iowa City, Iowa**: U. of Iowa – Dr. Hank Paulson, henry-paulson@uiowa.edu

***Minneapolis, MN** U. of Minnesota – Jodi Lowary, (612)625-0656, jlowary@umphysicians.umn.edu

***Jackson, MS**: U. of Mississippi – Leigh Langford, (601)984-5500, llangford@neurology.umsmed.edu

***Galveston, TX**: U. of Texas – Penny Stanton, (409)747-4567, pstanton@utmb.edu

IDEBENONE CLINICAL TRIAL — PATIENT RECRUITMENT

The National Institutes of Health (NIH) Institute for Neurological Disorders and Stroke (NINDS) is currently recruiting FRDA patients for the Idebenone clinical trial. (See Clinical Research, p. 4).

The Myers - Phase I Participants
Anne & Chris (taller people)
Paige, Puppy Zoe, Jared

Phase I of the Idebenone trial was conducted at the NIH Clinical Center located on the main NIH campus in Bethesda, Maryland, just outside Washington, DC, and was completed in the fall, 2004. Phase I determined that high doses of Idebenone are well tolerated by FRDA patients. Phase II is being planned to begin in 2005.

For further information, please contact:
Ms. Alison La Pean
Email: lapeana@mail.nih.gov
Phone (301) 496-8969
Fax (301) 480-0056

FARA FUNDRAISING ACROSS THE NATION (*Cont'd from p. 7*)

NEW YORK

Donovan Simpson & Jennie

Triathalon

Jennie Casey-Sinnott ran the Westchester Triathalon for FARA It was a beautiful Sunday afternoon in September when Jennie swam one mile, biked 25 miles and ran 6.2 miles, all in honor of **Donovan Simpson,** who is afflicted with Friedreich's ataxia. Joining Donovan in cheering Jennie on were his parents, **Debra and Norman**. Jennie built her support for the Olympic-length event around the faculty and families of the Rye Country Day School, where she worked with Debra. Jennie finished the event strong -- in 3:49:30 and with $27,000 for FRDA research. Jennie wrote to supporters, "This triathlon was an experience I will not soon forget, nor will I ever forget your outpouring of encouraging notes, donations and support that helped me reach the finish line. " She also added, "Debra, Norman and Donovan came to the event to cheer me on, and that was the best part of the whole day."

Sara & Laura

Walk to Seek A Miracle

The **Ferrarone family**—Daughters **Sara and Laura** and parents **Margaret and Bob—** organized their **fifth annual walkathon** in the Rochester area to raise funds for Seek a Miracle/MDA. The event served as a special celebration of the achievements and progress made over the last four years. Margaret hopes that someday Sara, Laura and thousands of others will overcome this disorder. "There's just a lot of phenomenal research going on," she said. We would add that the extraordinary efforts of the Ferrarone family and friends are responsible for funding much of it.

Laura et al

Sold for a Cure!! - the Amherst Auction: Jen's Journey To Seek A Cure was once again held in Amherst. In honor of **Jen**, her aunt had an auction of baskets and has done this event for the past several years raising funds for Seek A Miracle/MDA.

OHIO

The **Parrish family**, in Northeastern Ohio, received their daughter's diagnosis in 2004 and jumped right in to raising research funds. They had a number of events which raised $36,000 for Seek a Miracle/MDA. The majority of their donations came from their Walk-a-thon. They also had a yard sale and their fire department raised money with a number of events. College freshmen of the Kent State University College of Business Colleagues Living/Learning Community made a generous donation honoring **Lindsey Parrish**.

TEXAS

The Bro Golf Assn. again combined passion for golf with a commemoration of dear friend **Jeff Rosenkranz**. This year BGA held a golf tourney in San Antonio, raising about $5,000 and members made many generous donations online from the FARA website.

UTAH

Trisha Hussey, Jon Knight

Jumping for a Cure! Kittel's 2nd Annual Horse Show Doubles Donations

The second annual "Jumping for a Cure" Horse Show was held this year in Sandy, Utah. In the foothills of the Rocky Mountains, **Sue Kittel** and her family held a rated Utah Hunter and Jumper show to benefit FARA research. For the second consecutive year, Sue Kittel's sister, **Trish Hussey** organized the event. Her brother, **Jon Knight**, once again ran the actual horseshow. Her parents donated the facility, ribbons, and mailed premiums. Her dad and sister **Candice** ran the "Ringside Cafe" and prepared all the food for sale. Many friends of her family donated services or items for the raffle. All of the officials and other workers at the horseshow donated their time and services.

WISCONSIN

Family helping Family - In honor of **Bridget Downing**, who has Friedreich's ataxia and is the daughter of **Terry and Marilyn Downing** of Williamsville, New York, her Wisconsin relatives organize an annual golf tournament that raises money for FRDA research. Thank you. We all feel like part of the same family.

2005 Calendar of Fundraising Events

O.C. WALKS THE WALK - Orange County, California declared war on Friedreich's Ataxia six years ago and will host its fifth **Walk for Hope and A Cure** on May 21, 2005, National Friedreich's Ataxia Awareness Day, at St. Norbert's in the city of Orange. The event will again be organized and hosted by the family, friends, church, school and community of the Lanes — Sandy, Steve, Brianna and Chelsea. The past four such events have raised a total of $500,000. As Sandy has said, " Many of you may say, 'I don't know if I could do something like that.' Or, you may be intimidated when you hear the amount of money we have raised. I say to you, please come forward and lend a helping hand. Every dollar raised puts another dollar in our account for finding a cure for Friedreich's Ataxia." To become a volunteer, make a donation, or for more information, please call the Orange County Chapter of FARA at 714/685-0096.

Golf, Charity and a Bloomin' Good Time

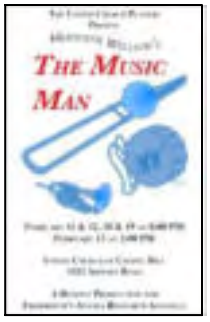
Outback Steakhouse Pro-Am Champions Tour Golf Tournament
February 21-27, Tampa Bay, FL

"Outback Steakhouse is committed to giving back to our communities. Through the Pro-Am tournament we have a unique opportunity to present an exciting, fan-friendly golf event that raises awareness and funds for area charities," said Outback Steakhouse CEO Chris Sullivan. FARA is thrilled to have been chosen as one of the four charities to receive the donations from this tournament. Past champions include Dave Stockton, Jack Nicklaus, Bruce Fleisher (2000, 2003) and Mark McNulty (2004), who became the 11th player to win in his Champions Tour debut.

Tournament Ticket Packages - These are collections of really cool activities at the tournament and at other times of the year at the TPC world-class course. The package includes all the best access to the course during the tournament, including the best of the "watering holes" for refreshments and the best views of the play. It also includes a weekday foursome of golf at the TPC later in the year. GREAT GIFT FOR A GOLFER: The actual value of these ticket packages is listed at $3,250. FARA has ten tickets available for $1,000 each. If you know a company, colleague or a friend who would be interested in buying a ticket, contact FARA at fara@frda.org or (703)413-4468. For more information visit the tournament Web site at www.outbackproam.com or contact the tournament office at (813) 265- GOLF (x4653).

The "Music Man" blows his horn to lead the research parade!

Feb 11,12,13 and 18,19, United Church of Chapel Hill
Chapel Hill, NC



"The Music Man" is scheduled as the 3rd theatrical event the **Barnett family** has organized. This Terriffic Troupe also staged "Fiddler on the Roof" and "Anything Goes" which, together, raised more than $100,000. For "Music Man," the royalties are paid, the leads are cast and rehearsal is ongoing! Daughter **Carrie** is choreographing the show as part of her Girl Scout Gold Award. This wonderful community has set the goal at another $76,000 — "a thousand dollars for every one of those blasting trombones that led the big parade." Put this on your calendar!! For further information contact **Paige** at pbarnett2@nc.rr.com.

Fresh Fish Daily & Charity Night for FRDA Research

Ashburn, VA, Jan. 29, 2005

The Bonefish Grill has generously offered to support FRDA research by providing all the proceeds of its pre-opening Charity Night at the Bonefish Grill located at 43135 Broadlands Center Plaza, Ashburn, VA. Admission will be $20 per person for all the super-fresh delicacies you can eat. If you can make it, please contact us at fara@frda.org. All the proceeds from this event will be presented to Seek A Miracle/MDA in memory of the SAM/MDA founder, Rochelle Litke (see commemoration, p.16).

Race For A Cure


Evan Luebbe


Jessica Jones


Brandon Emerson

May 21, 2005, National Friedreich's Ataxia Awareness Day
Shawnee Elementary School, 9394 Sterling Drive, Cincinnati, Ohio
5K Walk / Run, Silent Sale Raffle, Lunch
This event will rally "**Cincy Families Fighting FA**" and is being organized by the family of **Evan Luebbe** with the families of **Jessica Jones** and **Brandon Emerson.** Contact Tammy Luebbe at TAMMYLUEBBE@aol.com or (513) 755-6396 to participate, contribute, help or inquire.

Running for FARA

January 16, 2005
Evangelische Kirchengemeinde, Köln-Pesch, Germany

Warmhearted and generous German friends of the **Barnetts** have, once again, volunteered to help the Barnetts meet their "Music Man" fundraising goal (see p. 13) by inviting people to find sponsors for every kilometer they want to walk, run or hike around a course of about 11 kilometers at the church in Pesch. The Trans-Atlantic Partnership is alive and well.

The Frozen Chosen Open

Tee it Up for a Cure this winter in Atlanta, Ga. Being organized by friends and colleagues of the **Nelda Van Schoick family**. Contact steve.curvey@merial.com

Letter-Writing Campaign

One family raised over $10,000 for research in a single letter-writing campaign. This is the easiest way to raise funds and can be extremely successful. This enables you to inform people -- family, friends, colleagues, and community about Friedreich's ataxia. You might consider including on your mailing list special sets of people such as your high school or college classmates, the families of classmates of students with Friedreich's ataxia, and other members of civic organizations to which you belong. FARA will gladly provide you copies of letters other people have used successfully or you can see samples at http://www.fortnet.org/fapg/sample.htm or email FARA at fara@frda.org

MAKING A DIFFERENCE TOGETHER - dozens of ways to donate & raise funds for FRDA research

No one alone can solve the puzzle of Friedreich's ataxia, nor can we wait for someone else to solve this one for us. Acting alone, there is little we can do. Acting together, there is little we can NOT do! Please consider making a tax-deductible contribution to FARA today. You might even consider holding a fundraising event and giving your community the opportunity to express its support for your family and the research that offers us all such hope. Every dollar donated goes to support that research.

CREDIT CARD DONATIONS - QUICK & EASY
Donate to FARA online through Network for Good. Your transaction is safe, secure, and private. You can donate on FARA's website (www.frda.org). Go to the homepage just below the "Welcome paragraph and click on the banner that reads, "Donate Now through Network for Good." Then, click on, "Donate Now." 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 email address to FARA, designate your donation for a specific purpose (you can type in "research"), dedicate your donation (in honor of a particular person, for example), login with a password of your choosing, and provide your credit card information.

WORKPLACE GIVING

Corporate Matching Gift Programs 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 to FARA with corporate matching gifts. If you don't work for a company with a charitable program or do not work outside the home, do you know someone who does and might help?

The **United Way** offers a write-in option. You can direct your donation to the "Friedreich's Ataxia Research Alliance." To find out if your company has a giving campaign through United Way, ask your Human Resources department. FARA has received United Way donations from many states, including Arizona, Connecticut, Louisiana, Massachusetts, New York, and Pennsylvania.

United Way

Combined Federal Campaign (CFC) is the annual fund-raising 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 the CFC. FARA is listed in the CFC of the National Capital Area. FARA's CFC designation number is 7970.

Religious, Professional and Civic Donations: the list of religious, professional and community organizations that give to nonprofits is never-ending. FARA has received donations from Rotary Clubs, for example, and many churches from around the country. Not a member of any such organization? Maybe a family member or neighbor is and would be happy to support our cause.

Foundations support nonprofits such as FARA with generous donations. Do you know of a foundation that might be sympathetic to our cause? Please explore that possibility. Some corporate matching gifts are made through foundations. Sincere thanks to the foundations listed below who have already contributed to FARA:

Bank of America, Capital Group Companies, Cisco Foundation, Community Foundation of Central Illinois Depository, Deutsche Foundation, DST Systems, Grinnell Corporation, eBay Foundation, IBM, Illinois Tool Works, KTLA Inc., Merrill Lynch, Landamerica Foundation, Microsoft, Nordson-EFD Inc., Pepsico; Sara Lee Foundation, and Times Mirror.

Always Seeking A Miracle, She Performed Them

On December 23, 2004, we all lost a friend, an ally, a champion and an inspiration. Rochelle Litke lived her life with passion, dedication and determination. For many years, she devoted countless hours to fundraising for charitable causes such as The Rainbow and United Friends of the Children. In 1995, not long after her daughter, Samantha, was diagnosed with Friedreich's ataxia, Rochelle established Seek A Miracle (SAM) in coordination with the Muscular Dystrophy Association (MDA). She set about gathering others around her and raising funds that were then allocated by MDA to Friedreich's ataxia research. Since then, SAM has been responsible for funding $1.3 million in scientific research projects aimed at developing treatments and a cure for Friedreich's ataxia. Rochelle was very proud of that, and rightfully so.

In 1998, Rochelle and her husband, Marty Litke, agreed to join with ten others to form the Board of Directors of FARA, which was established that year. A few years later, Rochelle agreed to have the SAM funds she worked so hard to raise used to co-fund with FARA the scientific research grants that bring us all so much hope for treatments and a cure. That wonderful collaboration is still working extremely well to this day and will be continued in her honor until her goal — that we all share — is accomplished. As one small tribute to Rochelle's tireless spirit and tremendous accomplishments, FARA has arranged with the management of the Bonefish Grill to have all the proceeds of its Charity Night on January 29, 2005, in Ashburn, Virginia, go to Seek A Miracle in Rochelle's honor.

Rochelle Litke will be greatly missed. Her legacy to us, though, lives on and her spirit will be there with us when we cross the finish line together.

FARA and Seek A Miracle/MDA Collaboration

FARA and Seek A Miracle/MDA (SAM/MDA) have established an arrangement whereby they draw from the resources of both organizations to award peer-reviewed grants to FRDA scientists. WHY? "Two pots of money are better than one!" More research funds available through FARA and SAM/MDA mean more and larger grants for promising scientific research. WHEN? Researchers can apply for a grant at ANY time—not just several times per year as with most other non-profit organizations. The FARA grant mechanism accelerates the funding of qualified grants. Time is valuable to patients fighting the battle of progression and to researchers who are ready to proceed with promising avenues of research.

For those who donate to MDA, please consider making your donations payable to "Seek A Miracle/MDA," so your donations go to fund FRDA research in this collaborative way.

RESEARCHERS - A Summary of the FARA — SAM/MDA Collaborative Grant Process:

FARA receives grant applications at any time during the year from FRDA scientists around the world and submits them to FARA's Scientific Review Committee for peer review. If the scientific peer review results in a favorable recommendation, that recommendation is submitted to FARA's Board of Directors, which includes the three scientists serving on the Scientific Review Committee and about a dozen lay Members.

If FARA's Board of Directors votes to award the grant, it can request that SAM/MDA provide a portion of the funds required. In most such cases, SAM/MDA has agreed and has provided up to half the total funds for the grant. FARA's Board of Directors includes the founders of SAM/MDA, who were instrumental in concluding and implementing this arrangement that significantly increases the resources being devoted to promising FRDA research around the world. For further information contact Ron Bartek at fara@frda.org or Marilyn Downing at mdown4@aol.com.

To seek our miracle, FARA and SAM/MDA are working together to make a difference more quickly.

REQUEST FOR APPLICATIONS

FARA will accept applications at any time from US & International Researchers

FARA has organized, co-hosted and co-funded two international scientific workshops with the National Institutes of Health (NIH) at which leading scientists from all over the world shared their findings and vision regarding Friedreich's ataxia, explored prospects for treatments, and identified the most promising avenues of research. FARA is also accelerating progress on these research avenues by providing direct financial support for promising, peer-reviewed research projects, and by helping assemble patients to participate in them.

Research Grants. FARA awards grants across a wide spectrum of basic, translational and clinical science. FARA also awards grants across a moderate financial spectrum from 1) "seed" grants to "grow the field" by supporting post-doctoral fellows, equipment and supplies, and development of preliminary data required for larger grant applications to, e.g., NIH, to 2) larger, multi-year grants to principal investigators well established in the field.

Workshop Grants. FARA supports scientific workshops designed to advance the research into treatments and cures for Friedreich's ataxia and the related sporadic ataxias. These workshops will be of two types - full-scale workshops and project-specific workshops. Full-scale workshops bringing together leading FRDA researchers from around the world will continue to be held at intervals determined by the pace of progress. Project-Specific Workshops will be arranged on shorter notice for small groups of investigators when face-to-face collaboration on a specific approach or insight promises a significant advance in FARA's mission. In such cases, the workshop site will be selected so as to optimize collaboration and minimize costs.

Application Submission. Applications accepted at any time from anywhere in the world. Applications are to be submitted in electronic or paper form to FARA at the addresses below. Electronic submissions are preferred because they help expedite the review process. FARA's two-tier review process is modeled on that of NIH. All applications are first subjected to a peer-review led by FARA's Scientific Review Committee. The Committee seeks reviews by scientists especially well qualified in the particular area involved in each application. The Scientific Review Committee reports the results of peer reviews, along with its recommendations, to FARA's Board of Directors. If the peer review is favorable and the Scientific Review Committee recommends approval, the Board of Directors can vote to approve the grant and determine the amount to be awarded. FARA undertakes to complete this process within 60 days of each grant's submission.

Grant applications can be submitted to:

Friedreich's Ataxia Research Alliance (FARA)
Electronic applications are encouraged and will be accepted at fara@frda.org

Paper copies are not required but can be mailed to:
FARA
2001 Jefferson Davis Highway; Suite 209
Arlington, Virginia 22202 USA

FARA Research Grants Reach 2-Million-Dollar Mark

FARA was established in September of 1998 and gave its first research grant in April of 1999. As a result of the generosity of donors, the tireless commitment of the people conducting fundraisers, co-funding by Seek A Miracle/MDA, and the increasing tempo of FRDA scientific progress, **FARA has awarded research grants that now total about <u>two million dollars</u>**. The FARA Update of 2003, available on FARA's website (www.frda.org) gave a summary of the research grants FARA awarded from 1999 through 2003, amounting to about $1M. The following is a list of FARA research grants awarded in 2004:

- Dr. Michel Baudry* U of S.Cal, Superoxide Dismutase,Catalase Mimetics in FRDA Mice
- Dr. Louise Cahill* U of Queensland, Australia, Speech Function in FRDA
- Dr. Giovanni Coppola* U of Cal, LA, Antioxidants in FRDA Mice
- Dr. Martin Delatycki Murdoch Inst., Australia, Cardiac Measures in FRDA
- Dr. Martin Delatycki Murdoch Inst., Australia, Clinical Measures and Clinical Trial
- Dr. Peter Dervan Cal Tech, Small Molecules to Redress FRDA Genetic Mutation
- Elaine Epstein Blue Bottle Films, Video on FRDA family & Clinical Trial
- Dr. Joel Gottesfeld Scripps, Small Molecules to Redress FRDA Genetic Mutation
- Dr. Joel Gottesfeld* Scripps, Equipment for Small Molecule FRDA Research
- Dr. Grazia Isaya* Mayo Clinic, Function of Frataxin Protein
- Dr Arnulf Koeppen * Albany Research Inst., Dentate Nucleus in FRDA
- Dr Maria Krasilnikova* U of Ill, Chicago, Triplet Repeat Expansion in FRDA
- Dr. Filip Lim U of Madrid, Gene Therapy in FRDA Mice
- Dr. David Lynch U of Penn, Ops & Maintenance, FARA IT solution for trials *(see p. 8)*
- Dr. Massimo Pandolfo U of Brussels-Erasmus Hospital, Basic & Cinical Studies of FRDA
- Dr. Mark Payne Wake Forest U, Frataxin Protein Delivery in FRDA Mice
- Dr. Helene Puccio* IGBMC, Strasbourg, Drug Trials and Screening in FRDA Mice
- Dr. Barbara Scheiber-Mojdehkar* Medical U of Vienna, Drug to Elevate Frataxin Expression

*Jointly funded by FARA and Seek A Miracle/MDA

At the time of this publication, a number of excellent and promising research grant applications were under review and were likely to be awarded very early in 2005. New grant applications are arriving at an ever-increasing pace.

FARA uses the two-tiered NIH model of grant review. FARA's Scientific Review Committee (**Drs. Rob Wilson, Bronya Keats and Massimo Pandolfo**) leads the peer-review process and reaches out to additional scientists for particular expertise, especially to members of FARA's Scientific Advisory Board (**Drs. Henry Paulson, Robert Wells, and Arnie Koeppen**) and to previous recipients of FARA grants. Based on the peer review, the Scientific Review Committee makes a recommendation to FARA's Board of Directors, which includes the three scientists on the Scientific Review Committee. The Board of Directors then votes and grants are awarded if approved. The Board of Directors can approve a grant only if the Scientific Review Committee, based on the peer review, recommends approval. If the Board of Directors approves a grant, it takes into account FARA's available resources and determines the level of funding to be awarded.

Availability of FRDA Cell Lines

The Coriell Cell Repositories provide essential research reagents to the scientific community by establishing, maintaining, and distributing cell cultures and DNA derived from the cell cultures. These collections are supported by funds from the National Institutes of Health (NIH) and several foundations. Coriell maintains and provides lymphoblast and fibroblast samples obtained from FRDA patients. These samples are reasonably priced and used by scientists around the world studying FRDA. To view the collection or place an order, visit the Coriell website at http://locus.umdnj.edu/

Internaf-Pro Invitation to health professionals
International Network of Ataxia Friends

Internaf, an internet listserv supporting the ataxia community, is very privileged to have noted researchers in the field of hereditary ataxia, along with many other medical professionals, who participate via an anonymous invitation-only list which runs in tandem to the main Internaf list which serves patients and families coping with "an ataxia." If you are a health professional with an interest in ataxia and would like further details or an invitation to join, please email internaf-pro-owner@yahoogroups.com

The NIH Office of Rare Diseases (ORD) stimulates and coordinates research on rare diseases and supports research to respond to the needs of patients who have any one of the more than 6,000 rare diseases known today. ORD has been a principal funder of the 2 FARA/NIH international FRDA scientific research conferences held at NIH. ORD has also established The **Rare Disease Clinical Research Network (RDCRN)** that "will focus on identifying biomarkers for disease risk, disease severity and activity, and clinical outcome, while encouraging development of new approaches to the diagnosis, prevention, and treatment of rare diseases." ORD funds 9 centers of excellence for this rare disease clinical research. The clinical research performed is primarily small interventional trials and some longitudinal studies of single patients.

FARA President Ron Bartek has been **appointed to the RDCRN Data Safety Monitoring Board (DSMB).** The DSMB will: 1) review the study/trial protocol, consent form, monitoring plan and data table for each RDCRN study/trial prior to patient enrollment and advise NIH of any concerns, and 2) examine endpoints, toxicity and safety data of ongoing RDCRN studies/trials and make recommendations to NIH concerning continuation, modification or termination of such studies/trials.

Ron also has the privilege of serving on the **National Advisory Council** of the NIH's **National Institute of Neurological Disorders and Stroke (NINDS).** The Council advises the NINDS Director on matters of Institute policy and helps provide the second layer of review (following peer review) of all research grant proposals submitted to NIND.

Spanish Ataxia Federation Conference

The Spanish Ataxia Federation hosted a scientific conference on ataxia in Madrid, Spain, June 4-5, 2004. The conference provided scientists from a number of countries the opportunity to share insights into ataxia research. FARA President Ron Bartek was invited to speak about the organization of FARA and the avenues FARA uses to finance research into Friedreich's ataxia in the United States and elsewhere. FARA was pleased to participate and continues to work with the Spanish Ataxia Federation and Spanish scientists identifying, developing and funding collaborative FRDA research projects in Spain.

The Heart and Friedreich's Ataxia - A Beginner's Primer and Introduction

According to the National Institutes of Health, "Most people with Friedreich's ataxia die in early adulthood if there is significant heart disease, the most common cause of death."
The FARA website now has a Beginner's Primer and Introduction to FRDA heart conditions **to assist families** trying to understand the science and the treatments available**. It is also helpful to medical professionals**, especially if they have not examined patients with Friedreich's ataxia. The Primer draws from many medical resources, as well as a patient family's perspective. **Visit the FARA website at http://www.frda.org/education/beginners-primer.shtml** to learn more about:
What is Hypertrophic cardiomyopathy (HCM) or left ventricular hypertrophy?
What are Arrhythmias? Types of Arrhythmias? Common Treatments for Arrhythmias?
Anti-arrhythmic medications
Anti-coagulant (anti-clotting) medications
Electronic devices
Cardiac pacemakers
Implantable cardioverter-defibrillators (ICDs)
Catherization
Chart with Types of Medications/How it Works/Examples/Generic (Brand Name)
An Appointment with the Cardiologist - Physical Exam
An Appointment with the Cardiologist - Diagnostic Testing (ECG/Echo/Holter/Event Monitors)
Preparing for the Cardiology Appointment
Suggested Questions to Ask the Cardiologist
A Trip to the Emergency Room!
Warning Signs and Tips
Genetically Speaking, Why does FRDA damage the Heart?
Cardiac Function - Different Rates of Progression
Variations of cardiac involvement - Research Abstracts
Idebenone or CoQ10/Vitamin E - Helpful in Controlling Cardiac Hypertrophy?
Participation in the Idebenone Clinical Trial in the US
Dictionary of Heart Definitions and Terms

WHAT THE NEWLY DIAGNOSED REALLY WANT TO KNOW

Most patients and families had never heard the words "Friedreich's ataxia" until a loved one received the diagnosis. Many families enter into a very confusing and emotionally draining time, coupled with an intense desire to learn as much as possible about what to expect and what to do. **Patients, families and their medical providers now have understandable and helpful information to address their concerns**. Written by a patient family in collaboration with the scientific and medical community, the topics include:
Receiving the Diagnosis/Telling Your Child
Could My Other Children Have Friedreich's ataxia ?
What do the two numbers on the FRDA genetic test mean?
Genetically speaking, what happens in the body due to FRDA?
School - Your Child's Education
Telling Your Child's Classmates
Medical Care for Your Child
Coping - Where can I turn?
"A Message to the Newly Diagnosed" can be found on the FARA website at http://www.frda.org/education/message.htm.

Stay Connected Via the Internet

Helpful sites for patients, families and the medical community

Friedreich's Ataxia Parents' Group - FAPG

Are you are a parent coping with a child diagnosed with childhood onset ataxia? ***This forum is a MUST!***
In September 1997, a small group of FRDA parents began a mailing list to share questions, support and information about Friedreich's ataxia. This online support group, FAPG, has grown to an international list of about **300 families in 21 countries around the world**! The list now includes parents of other childhood-onset ataxias as well. "E-mail is a great way to give and receive support and has remedied the isolation and loneliness many of us feel dealing with the challenges of raising children with these degenerative diseases. This website provides another forum for parents to share our unique experiences and knowledge of how we've learned to cope with ataxia in our family." (FAPG Homepage) To join, visit http://www.fortnet.org/fapg or email Sue Kittel at kittel@webaccess.net

International Network of Ataxia Friends (INTERNAF)

Ataxia patients of all ages & Family - Internet mailing list
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. There are currently over 400 subscribers from more than 40 countries worldwide. Subscriptions to INTERNAF are free and the list is unmoderated.
To subscribe to INTERNAF, send an email to internaf-subscribe@yahoogroups.com

Visit the FARA Website at **www.frda.org**

The website is full of helpful information on research, education and advocacy. At the bottom of the "Welcome" paragraph is a link to an excellent collection of information explaining the basic aspects of FRDA, the "letter to newly diagnosed families." http://www.frda.org/education/message.shtml (see facing page) This letter contains helpful information on medical, education, and coping issues, outlined especially to help newly diagnosed families searching for answers, explanations and support. The letter was written by a parent from the personal experience of one FRDA family. It might also prove helpful to the medical community in understanding the patients' needs.

A **new homepage section displays links to all the most recent FARA publications and press releases** - a great way to catch up on the latest developments. The website also includes, "The Heart and Friedreich's Ataxia - A Beginner's Primer" http://www.frda.org/education/beginners-primer.shtml (see facing page) Comprehensive Information has been compiled to aid in understanding the cardiac problems associated with Friedreich's ataxia, as well as offering tips and advice regarding cardiology appointments and care. You might even discover that your cardiologist appreciates reading this portion of the website.

For researchers and the scientifically oriented, the website includes a summary of scientific developments in FRDA and the abstracts of all presentations made at the 1999 and 2003 international scientific conferences.

PLEASE HELP FARA

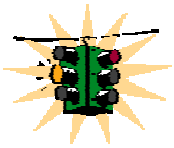
Support research aimed at a treatment for Friedreich's Ataxia. Your donation promises a new legacy of scientific advancement and gives families genuine hope for the future. **NO overhead costs** --100% of your donation is **tax-deductible** and 100 % funds research. Donors receive this Update. Thank you.
Yes, I would like to help FARA with the enclosed tax-deductible donation in the amount of $_____.

Use enclosed envelope or mail to FARA, 2001 Jefferson Davis Hwy, Suite 209, Arlington, VA 22202
Your name: **Address:**

Mail to: FARA **2001 Jefferson Davis Highway, Suite 209** **Arlington, VA 22202**

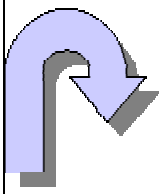
The Road Ahead — FARA's Vision for Progress

Together, we are engaged in a determined effort - a full-court press - **to slow, stop and reverse** the damage done by **Friedreich's ataxia**. FARA is supporting promising research in each of these three mission areas simultaneously because it would take far too long to take them one step at a time. Those three mission areas provide a helpful structure for considering the research we are currently pursuing as well as a strategy for the research we need to encourage, nurture and develop in order to achieve the objective in all three.



The foundation for progress in all three mission areas, of course, is laid by the advances we are enjoying in basic science. We are deeply indebted to the scientists that have identified the FRDA gene, deciphered its mutations, analyzed the composition and function of its protein, and sorted out the mechanism of the damage being done. None of the progress being made in slowing, stopping or reversing this disease would be possible without the marvelous advances in such basic understanding. More needs to be done in this basic science arena but, based on the giant steps taken to date, promising research is underway in all three mission areas.

For the most part, the research being conducted on antioxidant therapies (Idebenone, CoQ10, MitoQ, etc.) we can consider in the first mission area—**slowing** the disease progression and providing our scientists and our patients more time to make advances in the other two mission areas. We are supporting a wide spectrum of research aimed at **stopping** the disease. The common ground shared in most of these investigations is the attempt to increase the availability of the frataxin protein. Some scientists are pursuing that goal with gene-based approaches to delete, repair or stabilize the mutation so that more of the protein is produced. Others are working to synthesize the protein and deliver it to the mitochondria directly. In whatever way it is accomplished, making more of the frataxin protein available in the right place holds the promise of stopping the disease in its tracks. In both of these first two mission areas, we support a variety of promising approaches and monitor progress closely, looking for the optimum approach or combination of approaches that will take us to treatments.



The third mission - **reversing** the damage, regenerating lost capabilities - seems to present considerable challenges. We do anticipate that a small amount of reversal will be achieved when we are able to slow and stop the disease, because some "sick" cells will be rescued in the process. However, scientists do not yet know how to rescue the cells that are already dead, so more significant reversal will await a different approach. Currently, the approach that seems most promising in that regard is stem-cell research.

FARA will leave no stone unturned in its commitment to accomplish all three missions. Much progress has been made and continues to be made in the projects we are all supporting around the world. Especially in slowing the disease, antioxidants and other drugs are moving from drug screening to animal models and the large human trials needed to obtain approved therapies. We need to continue accelerating that process by working closely with the NIH, the other scientists preparing the drug screenings, animal experiments and clinical trials, and with the pharmaceutical companies interested in supporting clinical trials and developing additional drugs. **As that "slowing" process advances, we need to take the "stopping" and "reversing" research to the next level. To go to the next level in the gene therapy and protein therapy, for example, needed to stop the disease and the stem-cell research needed to reverse it, our strategy is to get excellent scientists, who develop such therapeutic technologies and approaches for a living, together with our excellent scientists who know enough about FRDA to determine how to apply**

Dr. Rob Wilson and Dr. Jeff Kelly at Scripps

Ron Bartek, Rob Wilson, Sandy Lane, & Paul Avery at Scripps

those technologies and approaches to FRDA. We need to continue to **encourage the best minds to think about FRDA and to do research on FRDA, because no single scientist or group of scientists has a monopoly on good ideas and no single group of scientists can "do it all."** We have therefore begun establishing fruitful collaborations with key institutions accomplished in the types of scientific endeavor needed **to stop and reverse FRDA**.


Dr. Joel Gottesfeld

For example, FARA has awarded one grant to an excellent scientist at the **Scripps Research Institute** in La Jolla, California, **Dr. Joel Gottesfeld**. Dr. Gottesfeld's findings thus far are extremely encouraging, showing the possibility that a particular drug molecule may be effective in increasing production of the frataxin protein. FARA met recently with Dr. Gottesfeld and, at FARA's encouragement, he and his collaborator at the California Institute of Technology, **Dr. Peter Dervan**, have applied for additional support. We also met with the Scripps Research Institute's Vice President and Director of Research, **Dr. Jeff Kelly**, to discuss expanding the work Scripps does in FRDA and facilitating collaboration with other experienced FRDA investigators. While in La Jolla, we also met with leading investigators at the **Burnham Institute**, which led the California consortium instrumental in passage of the California referendum that is to bring up to $3 billion over a ten-year period to embryonic-stem-cell research in that state. FARA will continue to collaborate with such accomplished institutions capable of helping accomplish our three missions.

Another key area of collaboration is with elements of the pharmaceutical community. As FRDA scientists continue their promising progress toward therapeutic discovery, we need to put in place the support structure we will need to take such discoveries through subsequent steps. For example, when our scientists discover a drug that is beneficial, we need to accelerate the drug through pre-clinical research and clinical trials, drug development and making it available to patients. FARA has helped make giant strides in establishing the required clinical structure. NIH has conducted Phase I of the Idebenone trial and is prepared to play a leading role in Phase II. FARA is working closely with a pharmaceutical company that has the rights to Idebenone in North America and Europe and is also prepared to play a leading role in Phase II. FARA is supporting the seven centers across the United States that are refining the ataxia scales required for FRDA clinical trials. **FARA is also consulting with experienced experts in drug discovery, drug development and drug marketing to ensure that the appropriate mechanisms are in place to take beneficial therapies to patients when the time comes**.

This comprehensive research strategy is ambitious, but we need to be ambitious to slow, stop and reverse this disease. With your continued, generous support, this strategy will be successful. FRDA scientists are increasingly certain they will conquer Friedreich's ataxia. They are convinced **it is no longer a question of "if" but, rather, a question of "when."** They tell us, too, that **what we have all done together already has taken years off the road to "when."** We need to continue to build our momentum and drive this research across the finish line of treatments and a cure.

The Gift that Keeps on Giving

Personal Story by Mary-Lisa J. Orth

In 2003 I needed to modify my home to accommodate my twin boys in wheelchairs. My twins, Alex and Benj, were diagnosed with FRDA in January 2000. When I contacted a builder, we were shocked to find that both of us had kids with FRDA. Bill's daughter was in her early thirties, while my twins were in their late teens. As my home modifications preceded, Bill and I became friends and I spent time with his daughter, Kelley, who had some speech problems, diabetes and used a wheelchair full time, but had not shown the heart problems typical of FRDA.

The Gift *(Cont'd from p.23)*

In January 2004, Kelley aspirated something she had eaten. Eventually she was hospitalized and the doctors realized an infection had invaded her entire body. While I was visiting Kelly at the hospital one evening, her mother, Robin, said Kelley wanted to be an organ donor. That got me thinking about a doctor who spoke at the NAF Conference several years earlier and showed slides of the effect of FRDA on a portion of the brain.

Kelly Lannom
(1972-2004)

Over the next few days, Kelley's condition worsened and I began to track down the speaker from the conference. I was looking both for medical advice for Kelley's doctors and information for organ and tissue donation if Kelley lost her battle for life. Eventually, I found the researcher - Dr. Arnulf Koeppen. Once contact was established between Dr. Koeppen and Kelley's family, arrangements for the donation went well. When Kelley lost her battle and died in January 2004, her donation became a selfless and wonderful gift to all of us, so typical of Kelley and her family.

My son Benj had spinal fusion surgery about two months later. Benj seemed to come through the surgery with no problem but, about 3 days later, he began multi-organ shutdown. There was no indication prior to the surgery that he would have any problems. We had obtained approval from all the appropriate specialists, including the cardiologist. Unfortunately, though, Benj continued his downward spiral for approximately ten days before dying. Due to my experience with Kelley's passing, I knew some of what to expect and what needed to be done to arrange for the donation of Benj's organs for FRDA research. The PICU physician was aware of my intention to donate Benj's body for research and, immediately following Benj's death, arranged the details with the pathologist. I had one form to sign and called Dr. Koeppen in Albany. The doctors arranged all the details for harvesting the organs and tissue samples and transporting them from Tucson to New York. I believe they removed Benj's brain, spinal cord, heart and other tissues. Dr. Koeppen stores such donations, distributing them to FRDA scientists as needed in research.

Dr. Koeppen later gave me the following update:

Benj Orth
(1983-2004)

"Various researchers are studying the donated tissues of Kelley and Benj. Through them, we have been able to confirm some of our previous findings. Friedreich's ataxia mostly affects the spinal cord and the heart. However, there is also one iron-rich area in the brain that suffers, that is, the dentate nucleus of the cerebellum. It is named after its appearance (like growing, still irregular, very young teeth). Magnetic resonance imaging of the brain shows the iron in the dentate nucleus quite well, and at least one investigator reported that iron is increased. I have analyzed the iron in this structure and find it at normal levels. However, iron undergoes an abnormal shift from cells that nurture nerve cells to scavenger cells and ultimately into glial cells that make up a brain scar. The iron does not increase or decrease, it only shifts to an abnormal location. Study of iron is important because one of the proteins that is necessary for the maintenance of iron in the proper location is frataxin, the very protein that is in short supply in FRDA patients."

Dr. Koeppen can be contacted at the following address:Arnulf H. Koeppen, M.D.; Chief Neurologist; VA Medical Center; 113 Holland Avenue; Albany, N.Y. 12208; Tel. 518-626-6373; FAX 518-626-6369; Arnulf.Koeppen@med.va.gov

I will never believe that Benj's death was pre-ordained, or happened for a reason, but in order to help his twin brother Alex and everyone else with FRDA, I took lemons and made bittersweet lemonade. There is some solace in knowing that part of Benj lives on and is an active part of finding a cure for FRDA. I sincerely hope that we find a cure soon, but it can only be done with help from all of us. If you would like to contact me, Mary-Lisa Orth, e-mail me at Rocketmom@att.net, with FARA included in the subject line.

FARA's Organizational Structure

FARA's Board of Directors currently consists of 15 people. Three of them are leading FRDA scientists who constitute FARA's Scientific Review Committee and guide the peer-review process for research grant applications. The other 12 serve in the capacities listed below. In addition, a number of scientists have agreed to serve on FARA's Scientific Advisory Committee and to assist in guiding the peer-review process.

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Bronya Keats, Ph.D
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Massimo Pandolfo, MD
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Of Counsel
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Washington, DC

Milton Cerny, Attorney at Law
Washington, DC

SCIENTIFIC ADVISORY COMMITTEE - Dr. Robert Wells, Texas A&M; Dr. Henry Paulson, University of Iowa; and Dr. Arnulf Koeppen, Albany Medical College & Albany VA Medical Center. These scientists assist in identifying the scientific expertise appropriate to the peer review of each grant application

A RARE DISEASE WITH ORPHAN DRUG STATUS

Friedreich's Ataxia - Genetics and Population

FRDA is defined as a rare disorder in the United States based on the estimated number of FRDA patients in the country. That estimated number is arrived at statistically as follows:

What are the odds of being a carrier of the defective FRDA gene?

Approximately 1 in 100 among those with ancestry in Europe and West Asia, including the Indian subcontinent and Middle East (some argue about 1 in 90)

What are the odds that two FRDA carriers will meet and have children?

Approximately 1 in 10,000 (100 x 100)

What are the odds that a child of such a union of two FRDA carriers will have FRDA?

Because FRDA is a recessive (rather than dominant) trait, each child of such a union has, independent of siblings' status, a one-in-four chance of having FRDA.

What are the overall odds, then, that two carriers will meet, have children and give birth to a child with FRDA?

Approximately 1 in 40,000 (10,000 x 4)

What is the statistical estimate, then, of how many citizens in the US are afflicted with FRDA?

Approximately 7,000 to 8,000 U.S. citizens are estimated to have Friedreich's ataxia. (U.S. population divided by 40,000). The estimate would rise to 9,000 to 10,000 if 1 in 90 were carriers, so it would be fair to estimate that 7,000 to 10,000 U.S. citizens have FRDA.

Any disease or disorder that is known to affect fewer than 200,000 people in the United States is considered a "rare disease". This is the definition used by the U.S. Food and Drug Administration (FDA) to determine whether a treatment may be eligible for "orphan" drug status. **FRDA, therefore, is well within the definition of a "rare disease" and is, in fact eligible for "orphan drug" status in the pursuit of treatments.**

Ancestry and the "Founder Effect" in Friedreich's Ataxia

The statistical estimates above do not seem to be uniformly applicable across all areas of the pertinent populations. For example:

Dean et al. (1988) found a particularly high frequency of FRDA in **Cyprus**.

A relatively high frequency of Friedreich's ataxia has been found in the Rimouski area of the Province of **Quebec** (Barbeau et al, 1978). Also, Friedreich's ataxia in 'typical' French-Canadian patients (i.e., those in the province of Quebec) shows clinical differences from FRDA in the Acadian population of **Louisiana**, which likewise came originally from France. Following an initial period of parallel development of the dis

A Rare Disease *(Cont'd from p. 26)*

ease, the latter exhibits a more slowly progressive peripheral involvement (muscle weakness and loss of vibratory perception) and a lower incidence or absence of cardiomyopathy leading to a longer life span than commonly found among FRDA patients (Barbeau et al., 1984).

In **Italy**, the estimated incidence of FRDA is 1 in 22,000 to 1 in 25,000 due to the frequency of parental consanguinity (Romeo et al.,1983). (The definition of consanguinity is "related by blood.")

In a nationwide survey of **Japanese** patients, Hirayama et al. (1994) estimated the prevalence of all forms of spinocerebellar degeneration to be 4.53 per 100,000. Of these, 2.4% had Friedreich's ataxia, though the definition of FRDA in this study was somewhat different than used elsewhere.

Juvonen et al. (2002) 'dissected' the epidemiology of Friedreich's ataxia in **Finland** by combining results from a nationwide clinical survey and a molecular carrier testing study. In the general population of Finland, the carrier frequency was estimated to be only 1 in 500, corresponding to a birth incidence of 1 in a million. In the more sparsely populated northern Finland, the carrier frequency was 5 times higher and 4 of the 7 Finnish FRDA patients originated from this region. Haplotype analysis revealed the major universal risk haplotype in all of the investigated patients. Alleles in the uppermost end of the normal variation (28-36 GAA) were totally missing in the Finnish population. The relative enrichment of the FRDA mutation in the north was thought to date back to the internal migration movement and the settling of northern Finland in the 1500s. The missing reservoir of expansion-prone large normal alleles in the frataxin gene found in this study was thought to be one explanation for the rarity of Friedreich's ataxia in Finland. The same phenomenon had been seen in Huntington disease, which is rare in Finland and is associated with a low frequency of large normal CAG repeats.

"Genetic studies on the origin of the FRDA gene major mutation (the GAA trinucleotide repeat expansion mutation) have revealed that over 95 per cent of the patients of Caucasian ancestry (including the Europeans and most populations of the Arabic countries) received the mutations from a **single ancestor who lived tens of thousands of years ago** (Cossee, et al.,1997). The study revealed that the common ancestor (called **the founder**) did not pass an expansion mutation to his descendants but a frataxin GAA repeat longer (presumably around 18 GAA) than the GAA repeat prevailing at that time (presumably around 9 GAA). However, **the longer GAA repeat happened to be more unstable** (as is usually the case for the simple nucleotide repeats) **and gave rise to GAA repeat expansions (disease causing) by successive enlargement over centuries, even millennia."** (Excerpted from "Our Common Ancestry: The origin of the Friedreich's ataxia GAA repeat expansion"; by Michel Koenig; Euro-Ataxia Newsletter No. 13-August 1997.)

PubMed — Keeping up with FRDA Science Online

PubMed, a service of the National Library of Medicine, includes over 15 million citations for biomedical articles back to the 1950's. These citations are from MEDLINE and additional life science journals. PubMed includes links to many sites providing full text articles and other related resources. You can read research abstracts and more, by going to the website http://www.pubmed.gov and searching for Friedreich's ataxia.

You can also read all the research abstracts summarizing the findings of the scientists that participated in the FARA-NIH international FRDA scientific conferences of 2003 and 1999 by going to the FARA website homepage (www.frda.org) and, under "Research," clicking on "2003 FARA-NIH Conference Research Abstracts (pdf)" and "1999 FARA-NIH Conference Research Abstracts (pdf)."

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