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Issue #2 Spring 2008

Clinical Trials Update

By Jennifer Farmer & Ron Bartek

Like everyone in the FA community, FARA is excited about the extremely promising clinical trials that are currently under way or on our doorstep. One such trial is now ongoing while another is expected to begin recruiting patients in late May and others should open later this year. FARA and FA scientists remain confident that these clinical trials will result in the first approved treatments for FA and will begin building the combined or "cocktail" therapy that we all anticipate.

Nearest-Term Clinical Trials:

A phase III study of **Idebenone** is now underway at the Children's Hospital of Philadelphia (CHOP) and the University of California Los Angeles (UCLA) and is based on results of the promising phase II study conducted at the National Institutes of Health (NIH) and published by DiProspero et al in Lancet Neurology. The phase II study showed that high doses of Idebenone were well tolerated and demonstrated a "trend to neurological benefit." Santhera Pharmaceuticals is sponsoring this trial and FARA is working closely with Santhera to help with patient recruitment through our patient registry. Each patient is to be in this trial for only six months. The sooner the full number of patients is enrolled, the sooner the trial will be completed so the FDA can make a decision regarding approval. We need just a few more patients in order to be fully enrolled. Patients from 8 to 17 years of age and able to walk 25 feet without assistance from another person can be enrolled by calling or e-mailing the nearer of the two centers:
CHOP: 267-426-7538 friedmanl@email.chop.edu
UCLA: 310-794-1225 SPerlman@mednet.ucla.edu

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In this issue:

Team Ride Ataxia Completes Cross Country Journey Raising $250,000

The Bryant Family- Steve, Mike, Kyle, Diane, Jina and Collin

By Paul Marcotte

Kyle Bryant and a team of 13 cyclists completed a 650 mile cross-country journey to draw attention and raise $250,000 in research funds seeking a cure for Friedreich's ataxia.

Bryant and five of his Ride Ataxia II teammates Sean Baumstark, Linda Johnson, Beth Bax, Sam Bridgman and David "Spinner" Henry – all live with ataxia.

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What is Friedreich's ataxia?

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

President's Message

U.S. Congressman Recognizes FA Awareness Day

The Honorable Robert E. (Rob) Andrews, who represents the First District of New Jersey, has again made a statement in the U.S. House of Representatives recognizing the third Saturday in May as Friedreich's Ataxia Awareness Day in support of all families dealing with FA and those involved in efforts to raise awareness and the funds needed to advance FA research. The congressman's statement refers to the tremendous progress made in FA research since identification of the FA gene, especially to the extremely promising clinical trials now or soon to be underway. Congressman Andrews characterizes FA researchers and families as not only hopeful but confident that these clinical trials will result in our first approved treatments for FA.

The congressman concludes his statement by saying, "I applaud the Friedreich's Ataxia Research Alliance (FARA) for its contributions to these efforts and ask my colleagues to join me in recognizing May 17, 2008, as Friedreich's Ataxia Awareness Day to show our concern for all those families affected by this disorder and to express our support and encouragement for their efforts to achieve treatments and a cure."

All of your efforts to raise awareness of FA are important, whether they involve helping educate your physicians, families and friends, working with your schools, or working with your colleagues at the office. You never know when something you say or do might help inspire a medical professional to turn additional attention to FA, another patient family to participate in the research, or a prospective donor to make a generous contribution.

We all know how promising the research has become and how much we expect from the clinical trials getting underway. We all know, too, how much those clinical trials depend on each and every one of us. No matter how beneficial each of these drugs might be, all of these trials will fail completely if they do not get enough patients to participate – and the opportunities will be lost forever. The more physicians and families are aware of FA, the more patients will be enrolled in the FARA Patient Registry and the more patients are likely to participate in the clinical trials.

We all know, too, that these clinical trials are far more expensive than the basic research that has led to them. Basic research projects cost tens and hundreds of thousands of dollars. Clinical trials cost millions of dollars. So, raising FA awareness and raising FA funds are both extremely important and go hand in hand. FA families across the United States and around the world continue to put their shoulders to the wheel and use Friedreich's Ataxia Awareness Day as special inspiration and encouragement.

We thank Congressman Rob Andrews for his kindness and leadership in officially recognizing the efforts of FA families and scientists. We thank all of you – not only for your special efforts this month to raise awareness and research funds – but for recognizing that every day is Friedreich's Ataxia Awareness Day for all of us. There are things we can all do every day to work together to get the research done and achieve the treatments and a cure.

Warm regards to you and your families,
Ron

NEW FARA POSITION OPEN
VP/ CHIEF EXECUTIVE FOR SCIENCE

FARA is seeking a Vice-President / Chief Executive for Science to work closely with the President, Executive Director, and the Board of Directors to advance the scientific goals of FARA. We are looking for a goal-oriented professional with a commitment to FA research to oversee and enhance our scientific programs and partnerships and to ensure that our strategic research priorities are efficiently and effectively advanced.

Key responsibilities include: Chairing the FARA Scientific Advisory Board, Overseeing the FARA Grant Program, and Serving as FARA Scientific Ambassador to the larger research community. The ideal candidate will have an MD and/or PhD and a minimum of five years of experience in neurology, neuroscience or neurodegenerative diseases with a track record of grant funding preferred. Knowledge of FA and/or related-disease research and commitment to the values of FARA is essential. The successful candidate will have demonstrated success in networking, collaborative accomplishments and building relationships. The candidate must be able to articulate FARA's mission to scientific community, and possess outstanding written and oral communication skills. An understanding of drug development and pharmaceutical industry is preferred. Travel required. A full position description can be accessed on the FARA website www.cureFA.org.

Interested parties should contact Jennifer Farmer, Executive Director, by e-mail, jen.farmer@cureFA.org or by phone (484) 875-3015.

Team Ride Ataxia Completes Cross Country Journey
$250,000 Raised for Friedreich's Ataxia Research

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"We gave inspiration to each other and united as a team. The overwhelming feeling among our entire team was that we did something great for ourselves and others," said Bryant. "Some of these people had never ridden much beyond the end of the block but by the end were all accomplished cyclists."

The riders began their journey March 15 from the California state capital in Sacramento. The first day, approximately 50 riders and 150 supporters participated, and a core group of 15 riders continued on with the cross-country journey. Bryant and the Ride Ataxia team concluded at the National Ataxia Foundation's 51st Annual Meeting at the Flamingo Hotel in Las Vegas on March 27th.

"The high point was coming into Las Vegas," said Bryant. "There were 21 of us. We took a whole lane on the strip and cruised into the Flamingo with crowds cheering us."

Hugs and champagne punctuated the finish, and the arrival was highlighted by a Las Vegas television news crew.

The Ride Ataxia team raised approximately $135,000. The National Ataxia Foundation and Friedreich's Ataxia Research Alliance are providing additional amounts bringing the total to $250,000.

The Friedreich's Ataxia Research Alliance and the National Ataxia Foundation are inviting proposals, under a competitive Request for Applications (RFA) process, to award grants focusing on pre-clinical and clinical investigations that will advance treatments for Friedreich's ataxia. The organizations anticipate funding two one-year awards under this program.

In March 2007, Bryant completed a 2,400 mile bike ride from La Jolla, California to the 50th annual NAF meeting in Memphis. Bryant and his team raised $40,000 during Ride Ataxia I, visiting FA researchers and patient families along his route. NAF and FARA announced at the end of Ride Ataxia I that the two organizations would add sufficient funds to bring the total of the Kyle Bryant Research Award to $100,000.

The 2007 $100,000 Kyle Bryant Award is being provided to translational research being done by Australian researchers and their British collaborators into the catalytic antioxidant CTMIO as a possible treatment for Friedreich's ataxia. Furthermore, this initial Kyle Bryant Award drew such high-quality applications from the scientific community that NAF and FARA have agreed to co-fund three of the other proposals as well.

NAF Executive Director Michael Parent commented, "The National Ataxia Foundation is truly grateful to Kyle Bryant for his courageous 2007 journey to help raise ataxia awareness and needed funds to support promising Friedreich's ataxia research. We're excited that Kyle has decided to continue his initiative in 2008."

FARA President Ron Bartek added, "Kyle's courage, commitment and dedication has inspired and enabled FARA and NAF to collaborate on some very promising research."

"My final thought on the trip is that researchers are going

as fast as they can go," said Bryant. "Everyone is pulling out all the stops for the research. Until there is a cure our team is going to do all we can to fight this disease."

Cyclists who Completed the Entire Journey:

Kyle Bryant
Mike Bryant
Steve Bryant
Collin Bryant
Jina Bryant
Sean Baumstark
Mike Mellott
Travis Cole
Luke Van Sickle
David "Spinner" Henry
Linda Johnson
Andy Johnson
Tess Kretschmann

See more Ride Ataxia II stories and pictures beginning on page 10

Grassroots Fundraising

By Marilyn Downing

Having recently attended the conference in Las Vegas, I was struck by what a powerful group we are – people with FA and their families. The FA community is also a family, sharing the highs and the lows of life with FA. We are a strong force with a single goal, truly helping to drive this research. Some find it therapeutic to plan fundraising events, continuing to raise money to advance research as quickly as possible.

We're all grateful for the efforts made during the first quarter of 2008. We list those people in gratitude for a job well done.

The Kittel Family of Loveland, CO, is raising awareness and garnering funds for research through an online giving campaign. Their fundraising initiative is centered on Aaron and Allie Kittel's Birthday wish to raise money for FA research. The Kittel Family's page is a great example of how to grow an online fundraising effort. They posted their page and alerted family and friends as well as the local media. Through word of mouth and online message forwarding, the Birthday wish reached people the Kittel family didn't know and inspired them to give. Aaron and Allie Kittel's First Giving fundraising page, Have a Heart--Give 1 Buck 4 FA Research (http://www.firstgiving.com/1buck4fa) has successfully raised over $5,000 to date. FARA will be happy to help those families that want to create a similar page on the First Giving website.

Aaron and Allie Kittell

Karla and Dan Wooten recently held their second annual fundraiser in Gainesville, FL, in honor of their son, Josh, who is 11 years old. The February 29th Casino Night, cleverly called "Leaping for a Cure" was held at Sun Country Gymnastics, the co-sponsor of the event. Approximately 200 people attended, bringing in over $8,000 for FA research. Events included casino games, a silent auction and a rock wall with people betting who would climb to the top the fastest. Karla writes, "We had a blast as did everyone who attended. People keep asking me what we are doing next year for FARA so they can mark their calendars!" Thanks to the Sun Country Gymnastics who co-sponsored the event.

There is now an additional $12,000 in research funds thanks to the **family of Jerod Laird from Bakersfield, CA**, who held their second annual event on April 6th. Robin Robinson, from the Canyon Hills Assembly of God with whom this fundraiser was organized, says, "Race 4 Results 5-10k walk/run was an outstanding success! It was a great day of creating awareness and raising funds for research for Friedreich's Ataxia. Several FAers participated in the walk/run either by foot or by wheelchair bringing great motivation and inspiration to everyone around them! It was such a beautiful day in every way! What a privilege it is for us to be able to support Carrie and Jerod and to know that we CAN DO something to help! We can't wait

Above: Participants enjoyed beautiful views as they traveled the route in Bakersfield, CA; Below: Runners trek in honor of Jerod Larid

for next year!" Thanks to all of the FARA supporters in Bakersfield.

The "Working for Lindsay Campaign" at Hancock Day School in Savannah was a lesson for many young people. From Lindsay Ashman, 27 with FA: "Months ago my 1st grade teacher sent me an e-mail. She is now vice principal of the grade school I attended 21 years ago, and it seems that once a part of that school, always a part of that school.

Mrs. Brown wrote to me to let me know that she had seen the article in the paper about the '07 FARA fundraiser and the school had their

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Featured Scientist: Grazia Isaya

Grazia Isaya, M.D. Ph.D, of the Mayo Clinic, is one of the world's leading researchers studying Friedreich's ataxia. Her lab pioneered the study of frataxin and was the first to show that frataxin is an iron-binding protein. Her current research focuses on elucidating the mechanism of frataxin and identifying other mitochondrial proteins that cooperate with frataxin and protect the cell from oxidative stress.

How did you first get involved in Friedreich ataxia research?
I trained as a physician and ultimately a neurologist at the University of Padova School of Medicine, Italy, in the early 1980s. During my neurology residency I joined the laboratory of Corrado Angelini, who at the time led one of the first Italian centers for the study of mitochondrial disease. I later decided I wanted to be able to understand mitochondrial disease at the molecular level and joined the laboratory of Leon Rosenberg, a pioneer in the study of mitochondrial protein biogenesis, at Yale University. In the Rosenberg lab I soon realized how much I loved basic mitochondrial research and eventually became one of many Italian "mitochondriacs" doing science in the U.S. When I started my own lab at Yale in 1994 I was interested in identifying mechanisms responsible for the maintenance of oxidative phosphorylation (OXPHOS), the process by which mitochondria provide energy to the rest of the cell. I had chosen to work primarily in yeast and didn't think I would ever again be engaged in clinically relevant research; but I was wrong. While performing a genome wide screening to identify factors involved in mitochondrial DNA integrity, one of my graduate students unexpectedly isolated a protein of unknown function called frataxin. I will always remember the student running into my office excitingly waving the Science issue in which Massimo Pandolfo, Michel Koenig and their colleagues had recently identified frataxin, and linked frataxin deficiency to Friedreich ataxia. At that moment I had come full circle back to studying a mitochondrial disease.

Your lab pioneered the study of frataxin and was the first to show that frataxin is an iron-binding protein. Tell us about that research.
Seminal papers from the labs of Jerry Kaplan, Francois Foury, and Robert Wilson showed early on that frataxin was critical for mitochondrial iron homeostasis and energy production. On the other hand, frataxin looked like no other known protein and there were no clues on how it might be able to accomplish its biological role. We approached this problem biochemically and found that frataxin was not only able to bind iron but could also deliver it to other molecules such as chelators or ferrochelatase, or store it in a mineral core. These initial observations led us to hypothesize that frataxin carried out both iron delivery and iron storage in the mitochondrial matrix. In a figure I made for a review article in the American Journal of Human Genetics back in 2001, I sketched frataxin as a "magic cube" feeding iron into the heme and iron-sulfur cluster biosynthetic pathways, and preventing excess iron from participating in the generation of toxic radicals. This hypothesis was highly controversial for several years but it is standing the test of time and continues to guide our effort to dissect the mechanism of frataxin and understand the biochemical consequences of frataxin deficiency. I am very attached to that old 2001 figure and still use it in my talks, although recently I was happy to replace the "magic cube" with the beautiful 3-dimensional structure of iron loaded frataxin.

How has the field advanced over the years since you first got involved in FA research?
The best way to answer this question is to simply do a PubMed search using Friedreich ataxia and frataxin as key words. In the 12 years that followed the identification of the FA gene and frataxin, over 300 papers have been published with an average of 25 papers per year. This progress is outstanding if one considers that FA has long been regarded as an "orphan" disease, that is, a condition affecting relatively few individuals and expected to provide little incentive for research or drug development. In this respect, I cannot emphasize enough that FARA has been a major driving force behind all the advancements in FA research, from the identification of the molecular defect to the understanding of the disease mechanism to the current race for a cure. I am convinced that little would have happened without the awareness, funding opportunities and spirit of collaboration among scientists that FARA has created and fostered for so many years.

You and your collaborators have recently published papers in Structure and Biochemistry describing the 3-dimensional structure of oligomeric frataxin. What is the significance of this research?
My lab has been very fortunate to publish these two studies in collaboration with my colleague and friend Salam Al-Karadaghi, from the Department of Molecular Biophysics at Lund University, Sweden. At a time when the iron storage function of frataxin was highly controversial, Dr. Al-Karadaghi and his outstanding graduate students accepted the difficult task of characterizing the 3-dimensional structures of two different frataxin oligomers, trimer and 24-mer, in their apo and iron-loaded forms. This research is now helping us to understand how frataxin handles iron at the atomic level and to identify strategies that may be used to enhance the function of frataxin in FA.

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Clinical Trails Update
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A phase I/II study of **Deferiprone (iron chelator)** was submitted to the FDA last year in hopes of conducting the trial in the United States and Europe. This trial is based on very promising results in a pilot study conducted in France and published last year by Boddaert et al in Blood. Because the FDA requested additional preclinical data prior to a U.S. trial, the pharmaceutical company, ApoPharma, plans now to conduct the phase I/II trial at a number of international sites. Sites in France, Belgium, the UK, Italy and Spain intend to begin patient recruitment this spring or summer. ApoPharma is working with FA clinicians in Canada and Australia regarding additional sites. If this phase I/II study demonstrates safety and benefit, ApoPharma will submit the trial data to the FDA in hopes of including the United States in a phase III trial of Deferiprone. ApoPharma is sponsoring this trial and FARA is working closely with the company to help with patient recruitment through our patient registry.

A0001 (Edison Pharmaceuticals/Penwest Pharmaceuticals) is the compound discovered by Edison Pharmaceuticals that shows such promise of improving mitochondrial function (energy production) in FA patients and other patients with mitochondrial dysfunction disorders. Edison has now partnered with Penwest Pharmaceuticals for the purposes of advancing A0001 through clinical trials. The Edison-Penwest team met with the FDA earlier this year and is preparing to open phase I of the A0001 trial by this summer. Because this phase I will be aimed at dose escalation to the optimum dose, the decision was made to conduct phase I in healthy volunteers in whom the dose escalation can be done much quicker than in FA patients. The plan is then to conduct the phase II in FA patients using the optimum dose.

Erythropoietin (EPO) is a hormone produced in our bodies and is also an approved drug used to increase red blood cells. It is commonly used in dialysis and cancer patients as well as in patients just prior to surgery in which loss of blood is anticipated. Austrian researchers Drs. Scheiber-Mojdehkar and Sturm found that EPO increases frataxin levels and last year completed very promising proof-of-principle studies in FA patients (submitted for publication). Edison Pharmaceuticals is working with the Austrian investigators, our FA clinical research network and the FARA-MDA partnership to initiate an EPO trial later this year.

HDAC (Histone Deacetylase) inhibitors are the compounds discovered for FA by Dr. Joel Gottesfeld of The Scripps Research Institute in La Jolla, California. These HDAC inhibitors act at the DNA/gene level and increase frataxin in cells from FA patients and in FA animal models. The Repligen Corporation has licensed these HDAC inhibitors from Scripps for the purposes of advancing them through preclinical development and clinical trials in FA. Repligen and Dr. Gottesfeld are working very closely together, with the FARA-MDA partnership, and with the FA mouse-model investigators so as to develop the very best HDAC inhibitor for FA, take it to the FDA later this year and into clinical trials as soon as possible thereafter.

Throughout FARA's research pipeline are other early stage studies that are designed to investigate new treatments. We believe that we need multiple shots on goal in various areas to ensure successful treatments are delivered to all patients with FA.

FA scientists and FARA are confident that, WITH YOUR HELP AND PARTICIPATION, these clinical trials will result in approved FA treatments and will put us well on our way to fully effective therapy for FA patients. At the same time, we are certain that, without your help and participation, these trials will fail just like so many others. Please ensure that FA patients sign up on FARA's patient registry (www.curefa.org/registry) so they can be notified regarding clinical trials for which they appear to be eligible. And, please do whatever you can to help raise the awareness and the funds needed to support all this extremely exciting and promising research. ■

Get Signed Up in the Patient Registry Database for Future Clinical Trials:
Visit www.cureFA.org/registry/

Memorial Contributions

All of us in the FA community are grateful when a bereaving family considers having donations given in the name of their loved one earmarked for FA research. FARA sends acknowledgements to the family and to the donors.

If you find you are in need of memorial envelopes please contact Marilyn Downing at 716-626-0274 or e-mail marilyn.downing@cureFA.org

Grassroots Fundraising
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own idea on how to raise some money for this cause. All the students did chores for which their chore money was specifically marked for FARA. Thursday I went to the school … they had raised $2,500!

This was such a beautiful way for the children to raise money because they held the power as to how much they wanted to work for this cause. The parents were awesome because many of them matched what their child earned. This is a feel-good way for anybody to raise attention/money for FARA. Please pass on the idea to other FAers who want to, but don't know how to, be involved in fighting FA!"

Lindsay Ashman

An article about Lindsay and the Hancock Day School was in the Savannah Morning News in March and can be found at http://savannahnow.com/node/471735

On April 26th the **Haldeman family** held their annual event "Haldeman's Hope" for FA research, with the help of their local MDA office. The Haldemans are a very creative group. Penny writes, "We had about 175 people in attendance. Our estimated amount raised is around $10,500. Our theme this year was T.V. Game Shows. Our most popular games were

Steve Haldeman & his neighbor sing karaoke

Price is Right, Card Sharks, and Crosswords. We finished the night with the live auction, raffle drawings and then a "Gong Show Karaoke"($1.00 to sing, $5.00 to have someone else sing, and $10 to not have to sing)." She signs the e-mail, "Exhausted, Penny". Haldemans, and all families who work to raise money for research, we all appreciate your hard work!!

Linda and Dave Zilles held their first Reach for A Cure Wine Tasting Event on April 24th at the W Hotel in Atlanta, with assistance from their local MDA. The format was a business casual event with wine, hors d'oeuvres and a silent auction. A presentation by a local TV personality was followed by Ron Bartek's talk concerning FA and the upcoming clinical trials. There were about 200 in attendance, including more than 16 young adults with FA from the Greater Atlanta area. About $30,000 was raised—and this was a first-time event! Event information is at www.reachforacurefa.org. The Zilles report that they are already planning next year's event.

John Zilles and his dog, Mango

The Starry Night Salon in Venice, Florida held a

Starry Night Salon benefit in honor of Natchez Hanson

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Grassroots Fundraising
(continued from p. 7)

Change Challenge in honor of Natchez Hanson. After reading about fundraising ideas in previous issues of *The Advocate*, Darcy Hanson decided to get involved with the help of her salon colleagues and customers.

Over a two month period, the salon welcomed donations for FA research from their patrons, and every Wednesday some salon employees contributed money from their gratuity earnings. Collectively, they raised almost $1,250 for Friedreich's ataxia research.

As Nelda Van Schoick says, "It never ceases to amaze me how generous people are." The **Van Schoick family** held their very first fundraiser in their backyard in 2001, raising $1,400. This April 25th they raised over $90,000 with their fundraiser at the Georgia Club in Stratham, GA. Nelda writes, "I am happy to report that our 2008 Benefit Bash for FARA was a success! We had a golf tournament followed by a party with food, drinks, silent auction, raffles, Wii tournament, music and a lot of fun." Her one sentence says it all-- "We had a good time". Imagine raising all of that money for FA research to help her girls (and all of our family members with FA) and having fun at the same time. The Van Schoicks know how to get it done.

Nelda Van Schoick with Vince Palasota, of MedPharmex Animal Health and Performance Awards Center, a generous sponsor of the Van Schoick event.

Jerry Russell and Vince Palasota, of MedPharmex Animal Health and Performance Awards Center, generous sponsors of the Van Schoick event, along with Becca and Robbi Van Schoick, with Ron Bartek of FARA in the center.

Brian Mulvaney's family and friends came out in support of both Brian and the research to help him find a treatment for his FA, by riding in the May 4th Five Borough Bike Tour in New York City. Brian's brother, Kevin, writes, "We raised a little over $10,000 and the donations are still coming in as we speak.

The journey started in Lower Manhattan. We headed north through the heart of Manhattan to Central Park and continued on to historic Harlem and the Bronx, returning south along the East River on the FDR Drive. From there we crossed into Queens and then Brooklyn, where we took over the highway before making the thrilling climb up--and down--the Verrazano-Narrows Bridge to Staten Island. Overall from start to finish, we completed approximately 50 miles along with over 30,000 other cyclists." ■

Kevin Mulvaney, Allison Nelin, Ricky Nelin, Michael Nelin, Karen Nelin and Brian Mulvaney is sitting on his Cattrike 3 wheel bicycle.

See Upcoming Fundraising Events on p. 15

Featured Scientist
(continued from p. 5)

For example, we find that if we increase the speed at which frataxin assembles with itself, yeast cells contain higher levels on enzymatically active aconitase and also become more

resistant to iron overload and different forms of stress. This suggests that the ability to regulate frataxin assembly may provide a means to make frataxin more efficient and ultimately compensate for the lack of frataxin. With this in mind, we are developing assays with which to screening for compounds that promote frataxin assembly.

What other research are you currently doing at the Mayo Clinic?
We are very interested in understanding what are the mechanisms that enable frataxin to interact and donate iron to structurally and functionally different iron-binding proteins. We think that additional factors are involved in these interactions and we are screening for these factors in yeast. Another project stems from our observation that the enzyme dihydrolipoamide dehydrogenase (DLD) has a cryptic proteolytic activity and can cleave the mature form of human frataxin to a shorter form. We are pursuing the possibility that DLD is involved in the regulation of frataxin and possibly other mitochondrial proteins involved in energy metabolism.

What do you see as the most promising FA research currently underway?
I would say that the state of FA research as a whole is extremely promising. Our field is moving forward at a fast pace setting an unprecedented paradigm of how a multidisciplinary approach with integration of basic, translational and clinical research can expedite the understanding of a difficult medical problem and thereby enable a timely development of treatments.

How long do you think it will be before there is an effective treatment for FA?
I think we may be closer than we are willing to admit. What makes me optimistic is the fact that several pharmacological approaches are already in hand or in the pipe line, each targeting different aspects of FA pathophysiology. Thus, even if none of these approaches is sufficient per se to treat FA, combination therapies most likely will be.

In an editorial that appeared in Blood last summer, you wrote about the importance of developing a newborn screening test for FA once effective treatments are in place so that children could be treated for FA before they exhibit any symptoms of the disease. What is the current status of this idea?
Newborn screening is a Public Health program aimed at the identification of conditions for which early intervention can prevent mortality, morbidity, and disabilities. It is typically performed by analysis of diagnostic markers in blood spots collected on filter paper at birth. In recent years, newborn screening has advanced at a very rapid pace and 54 conditions are currently included in a uniform panel of conditions recommended in 2006 by the American College of Medical Genetics. Currently, several other conditions are actively being considered for expansion of the panel. My colleague Piero Rinaldo at Mayo Clinic, Department of Laboratory Medicine and Pathology, has been a driving force behind the creation of the uniform panel. He and the other members of the HHS Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children (http://www.hrsa.gov/heritabledisorderscommittee/) are charged with making recommendations for the panel's expansion when appropriate evidence-based criteria are met. We believe that on the basis of the progressive nature of FA coupled with the therapeutic potential shown thus far by antioxidants, iron chelators, and compounds that increase frataxin expression, a case could already be made to include FA in the uniform panel once a screening method is available. My lab is working in collaboration with Dr. Rinaldo and his colleagues in the Biochemical Genetics Laboratory at Mayo to develop a protein-based method. ■

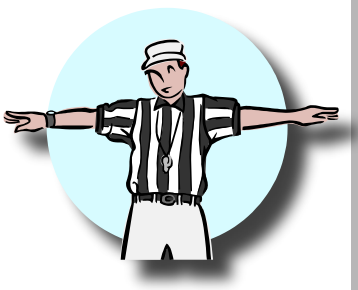
FARA would like to acknowledge and extend a special thank-you to these very generous donors.*

$10,000- $25,000
- Apopharma
- Bridget Moynahan
- DST Systems
- Mr. & Mrs. Herbert Lampert
- MedPharmex Animal Health
- Performance Awards Center
- Andrew & Melora Balson Family Fund

$50,000- $99,000
- Mark Aaron
- Bonefish Grill

$100,000 and Above
- Avery Family Foundation
- Standard Meat Company

*First and second quarter 2008



FARA would also like to thank the National Football League Referees Association for their generous support.

Be kind to your referees!

Living With FA

By Linda Johnson

What do you say when someone says "Describe yourself" ??? I guess this is my blurb …

46-year-old woman, wife who is still infatuated with her husband, mother of two fun children, full-time employee at a very accommodating company, world traveler, book club member, dinner club member, church-goer, live in Central New York in a comfortable 100-year old house in the country with my family, dog, cat, rabbit, and chickens … and, oh yeah, I have Friedreich's ataxia.

Life changed when I was diagnosed with FA at the age of 40 … just six years ago. That's when I really started to appreciate the time we have. I have always been a bit "Carpe diem," but there's nothing like being diagnosed with a progressively debilitating disease to get you moving!

I took a new position at work that required/allowed me to travel internationally. On several occasions my family joined me in Europe during the summer break. The motive for traveling internationally was at first pragmatic … I should do it as soon as I can, before my symptoms make it too difficult. But it has proven to be such a positive experience for us all!

Recently, my husband, Andy, and I joined Kyle Bryant and others on Ride Ataxia II. It was certainly a life highlight that I would not have even thought of doing prior to FA! Not only did we all raise a lot of money for FA research, but it was so motivating to physically accomplish so much! We had never done anything like this before, and we were thrilled to be a part of it!

And so I go on, challenging myself in new ways that are more fulfilling than I think I would have if I didn't have FA. My mantra, quoted from Abraham Lincoln, is "And in the end, it's not the years in your life that count. It's the life in your years." I encourage everyone with and without FA to live in this way! ■

Linda and her husband, Andy

REQUEST FOR APPLICATIONS

2008 Kyle Bryant Translational Research Award sponsored by Ride Ataxia, the Friedreich's Ataxia Research Alliance and the National Ataxia Foundation

The Friedreich's Ataxia Research Alliance (FARA) and the National Ataxia Foundation (NAF) invite proposals, under a competitive Request for Applications (RFA) process, focusing on pre-clinical and clinical investigations that will advance treatments for Friedreich's Ataxia. Two awards will be funded under this program, each limited to $125,000 (direct costs only). A full list of proposal guidelines and the application can be accessed at http://www.curefa.org/research/grant_program.asp. Applicants must complete the Kyle Bryant Translational Research Award application form. Applications will be accepted from for-profit organizations, non-profit organizations, public or private institutions, and foreign institutions. A letter of intent is due on June 3rd 2008. The application/proposal is due on June 16th 2008.

Letters of intent and applications are to be submitted electronically to: jen.farmer@cureFA.org and susan@ataxia.org

Carrying the Olympic Torch for FA

By Sean Baumstark

Sean Baumstark was one of 40 people chosen by the City of San Francisco to carry the Olympic flame as it passed through the city in April. Sean's winning essay is below.

Without urgency, desire loses its value.

A year ago, I was diagnosed with a disease called Friedreich's ataxia (FA). A genetic disease, FA took me hostage and has ruled with tyranny over my muscles.

Many people are affected, but my heart sank when I met her. Ashley, an eleven-year old, has chronic fatigue and loss of control and balance. Many children with FA are confined to a wheel chair.

Her altered childhood grips me. She has pushed me to give my life to a cause greater than myself. I established a non-profit organization that is encouraging, motivating, and inspiring for those with rare diseases. I've locked arms with foundations and seen hope for thousands of children with physical and educational needs.

In March, thirty cyclists and I will pedal to Las Vegas from Sacramento; a thirteen-day journey covering over 600 miles. The ride will inspire, inform, motivate, and compel people to action for those who can't take action. Like Ashley.

I want to live life on the edge despite my disease.

I want to give relentlessly so that there can be medical breakthroughs.

I want to carry a torch of hope to illuminate the darkness of disease. ■

Sean with his parents, Elaine and Jack Baumstark.

FARA Fundraising

We need your help!

Families of those with FA—and those closest to them—have the passion to keep the momentum going! You are our best hope. It can be as simple as a letter-writing campaign or as elaborate as a dinner/gala.

Download FARA's Fundraising Made Simple Kit (or email for a hard copy). There are experienced fundraisers in our community who are ready to work with you, offering advice, encouragement or just to brainstorm about some ideas.

Contact FARA at marilyn.downing@cureFA.org

If you can dream it, you can do it!

Sean with some of his fellow torch carriers: Jill Mason, former Olympian and Gold medalist, now in a wheel chair due to a drunk driver, and Annie Chung, appointed to be a torchbearer by the Mayor of SF due to her 30+ years of working with senior citizen health & wellness programs in SF.

See Ride Ataxia II pictures on p. 16

Grants Update

By Jennifer Farmer

In 2008, FARA will be focusing on grant proposals that advance treatments and bring new potential interventions to our research pipeline. We are taking a more proactive approach to facilitating research by taking more of a business approach and contracting for work that answers a specific question, moves a compound through the drug development process or provides infrastructure or research support services. FARA is working to make resources more widely available to accelerate progress and monitor milestones and outcomes on all funded research. FARA is also supporting several conferences and summit meetings in 2008 that will bring researchers together to share information, build collaborations and provide direction for future research. This article highlights a few of the grants, conferences and opportunities supported by FARA's 2008 grant program.

FARA has been working with The Jackson Laboratory, who are experts in mouse breeding and research services, and FA researchers who have created FA mouse models (Dr. Mark Pook, Dr. Helene Puccio, Dr. Massimo Pandolfo, and Dr. Joseph Sarsero) to make FA mouse models more available to the research community. Having JAX provide these services provides several benefits:

- FA mouse models are accessible to the greater biomedical research community without distracting their creators from their other important research and
- JAX will do additional studies to characterize FA mouse models and ensure quality of the colonies.

FARA believes in supporting and mentoring new/young researchers who have new ideas and competencies, technological skills, enthusiasm for science and a strong interest in FA research to our scientific community. Each year FARA awards grants to new/young investigators who have demonstrated a strong interest in pursuing their career in FA research. These awards help the investigator to establish an independence, credibility, and begin to identify their area of expertise.

Recent FARA New/Young Investigator Awardees:
2006 – Dr. Erika Becker, University of Sydney, Australia
2007 – Dr. Marek Napierala, University of Texas, MD Anderson, United States
2008 – Dr. Alain Martelli, INSERM, Institut de Génétique et de Biologie Moléculaire et Cellulaire, France

FARA awarded a conference grant to the National Ataxia Foundation to support the Ataxia Investigator's Meeting in March 2008. This conference brought together researchers from various backgrounds to share insights and plan future direction of research across the ataxias.

FARA and MDA are co-hosting a Mitochondrial Summit meeting in May 2008 at the Biodesign Institute in Tempe, AZ. The goals of this meeting are:

- advancing the understanding of how mitochondrial dysfunction can cause various neurodegenerative diseases,
- sharing and discussing approaches, insights, and mechanisms that suggest new therapeutics for mitochondrial neurodegenerative diseases, and
- promoting collaboration among mitochondrial researchers across various specialty areas, and coordination and support from the public sector for mitochondrial advancements.

FARA's competitive research grant program accepts grants on a continuous basis throughout the year from FA scientists around the world. All grant applications go through a scientific peer-scientific review process to ensure that we fund the best research. We are currently accepting applications in response to a specific request for proposals – Kyle Bryant Translational Research Award.

Our ability to fund research is directly dependent on your active support through donations and participation in fundraising. FARA partners are also committed to advancing FA research and we have been able to partner with them in making several of these grant awards. We would like to recognize our 2008 funding partners:
Muscular Dystrophy Association
National Ataxia Foundation and
Friedreich's Ataxia Research Alliance – Australia/New Zealand.

Acting alone there is little we can accomplish but working together there is little we will NOT accomplish.

See Grants Funded in 2008 table on page 13

The FARA eAdvocate is brought to you by:

Editors: Ron Bartek, Felicia DeRosa, Marilyn Downing, Jennifer Farmer, Mary Beth Kosmicki, Paul Marcotte
Advisor: Bill Hartnett
Design/Layout: Meg Giaconia

Grants Funded in 2008

Principal Investigator	Project	Research Area	Category	Outcome
David Lynch	Mitochondrial protein levels as biomarkers in Friedreich Ataxia	Translational/ Clinical	Biomarker	All
Alain Martelli	Iron Metabolism in FA: from the fundamental understanding of iron dysregulation to the therapeutic potential of iron chelators	Basic/ Translational	Iron Metabolism	↓ oxidative stress and ↑ mitochondrial function
Sidney Hecht	Analysis and restoration of Mitochondrial Function	Basic	Mitochondrial	↓ oxidative stress and ↑ mitochondrial function
Jackson Laboratories	FA Mouse Models	Translational	Animal Models	All
John Day/ National Ataxia Foundation	Ataxia Investigator's Meeting, LasVegas, NV, March 2008	All	All	All
*David Lynch	Collaborative Clinical Research Network for Friedreich's Ataxia	Clinical	Clinical Outcome Measures, Biomarkers and Trials	All
Bernard Ravina	Supplement Clincal Research Network for Friedreich's Ataxia – Data Coordination Center	Clinical	Clinical Outcome Measures, Biomarkers and Trials	All
*Grazia Isaya	Modulators of frataxin assembly: assay development for high throughput screening	Translational	Drug Screening	All
Marek Napierala	Influence of chlorambucil-conjugated GAA-TTC sequence-specific polyamides and Histone Deacetylase Inhibitors (HDACI) on repeat instability and frataxin expression	Basic/ Translational	FRDA Gene	↑ frataxin
Tracey Rouault and Richard Holms	Development and use of synthetic iron-sulfur clusters in therapy of Friedreich ataxia	Translational	Iron-Sulfur Cluster assembly	↓ oxidative stress and ↑ mitochondrial function

* grants co-funded with MDA, # grant co-funded with NAF, ^ grant co-funded with FARA-Australia

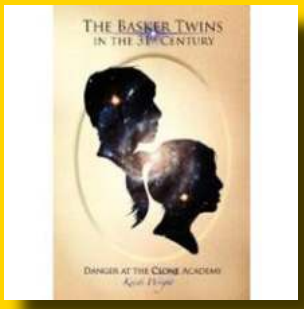
"Research Area" refers to three broad categories of research -- basic, translational and clinical. Basic research is the most fundamental and explores the underlying causes and mechanisms (pathophysiology) of the disease. Translational (or preclinical) research advances the results of basic research from discovery through development, from "bench to bedside." It involves, for example, testing drug discoveries in animals and human cell cultures in preparation for tests in humans. Clinical research involves trials in humans. The "Category" column is used to characterize the focus of each research project. The "Outcome" column places the goal or long-term benefit of each project into one of four categories – Determine Pathophysiology, Improve Mitochondrial Function (↑), Reduce Oxidative Stress (↓), or Elevate Frataxin Protein levels (↑).

Artists Use Their Talents to Help FA Research

by Felicia DeRosa

FARA is honored to have been the charity of choice among several accomplished artists across the country including a car builder in Illinois, Troy Trepanier, a writer in California, Kristi Wright, a band in New York City, *The Voyces*, and a crochet hook carver in Washington, Jim Price.

Award winning hot rod builder, TroyTrepanier and his team at Rad Rides by Troy, were invited by Ford Motor Company to build a pedal car based on the 1932 Ford roadster in celebration of the car's 75th anniversary year. Troy and his team customized a one of kind car for Ford's charity auction event titled "Hot Rod Heroes," and Troy's team designated FARA as the charity recipient of proceeds from the sale of their car. Troy's car is pictured above. Special thanks to Annette for helping to select FARA as a charity of choice. To learn more about Rad Rides by Troy visit www.radrides.com.



Author, Kristi Wright, published her latest book, The Basker Twins in the 31st Century and generously designated FARA as the recipient of 75% of her royalties from the book. The story is a futuristic, science fiction adventure of twin siblings at their uncle's clone academy. The book is said to be targeted to a younger audience, but several adults are known to have enjoyed it too. The cover features the silhouettes of Kristi's close friends Matt and Katie Rupel, whose family is very active in fundraising for FA research. To read an excerpt from The Basker Twins or to purchase a copy visit www.baskertwins.com.

In March, musical group, *The Voyces* played to packed crowd at New York City's Rockwood Music Hall. Attendees enjoyed lead singer Brian Wurschum's sense of humor and the harmonizing sound of *Voyces* favorites such as *Kissing Like It's Love* and *Where Little Girls Throw Roses*. The benefit performance also featured music from Deborah T and Toby Goodshank as well as raffled prizes. To listen to a sample of *The Voyces* music or view their tour schedule visit www.thevoyces.net.

Helping to "Axe Ataxia" is Jim (aka "Jimbo") Price's mission. He's raising money for ataxia research in honor of his friends, the Austins, from Spokane, WA, whose daughter Jessica has FA. Jimbo is busily making chophooks (proceeds go to FARA) for crocheting, and he has been able to get a number of people in the community of crocheters to take on this cause. There is a Traveling Hook project underway, and many are putting the "axe ataxia" badge up in their blogs. The Traveling Hook, organized by Bonnie J, will send one of Jimbo's hooks through the crocheting community to create squares for afghans to be auctioned for research. To find out more about Jimbo or The Traveling Hook project, visit www.jimbosfrontporch.blogspot.com/ or www.travelinghook3.blogspot.com/

Art is a powerful medium by which to reach an audience, and FARA is grateful to Troy, Kristi, *The Voyces* and Jim for using their talents to contribute to the advancement FA research initiatives. ■

Fundraising Across the U.S.
(continued from p. 8)

2008 FUNDRAISING EVENTS
(2nd & 3rd Quarter)

Wing Night- May 9, 2008
Buffalo Wild Wings-The Pointe; Pittsburgh, PA
abwst4@mail.rmu.edu

Ferrarone Walk - May 17, 2008
Nazareth College; Rochester, NY
rochesterdistrict@mdausa.org

4th Annual Race for the Cure- May 18, 2008
Independence Elementary School; Liberty Twp., Ohio
tammyluebbe@aol.com

Play for FA- Game Night - May 21, 2008
Hilton School District, NY
KBELLNIER@hilton.k12.ny.us

Peters Golf Tournament- May 29, 2008
Peoria, Illinois
rick@callenderco.com

FA-ith (FA- in the Heart) Dinner Dance - May 31, 2008
Sunnyvale Community Center; Sunnyvale, California
www.fa-ith.org

People and Puppies for a Cure/MDA Stride & Ride
June 14, 2008
Tukwila, WA
http://home.comcast.net/~hhespelt/index.htm

BRO Golf Tournament – June 19- 21, 2008
Washington, D.C.
amartinezcpa@gmail.com

FA Fighters 5K Walk- June 28, 2008
Harrisburg, PA
davidanddanielle@netzero.com

Fuzzy Buzzy Golf Tournament- September 7, 2008
Windham, NH
MDay485@aol.com

Dream a Little Dream Dinner Dance – September 5, 2008
North Branford, CT
meirbode@aol.com

Simpson Triathlon- September 21, 2008
Rye, New York
simpson4us@mac.com

FARA Board, Directors & Advisors

FARA Advisors

Ride Ataxia II Photos

(continued from p. 11)

A triumphant Ride Ataxia II team in Las Vegas, NV

Ride Ataxia II cyclists working hard on the open road

Sam Bridgman, Kyle Bryant, and Steve Bryant

Linda Johnson, David "Spinner" Henry, Paul Konanz, and Angela Lacativo-Greene

Ride Ataxia II Photos

(continued from p. 16)

Linda Johnson

"A bicycle built for two"- Mike and Steve Bryant

Back row: Steve, Mike, Max, Tess; Front row: Sam and Kyle

After a tough day of cycling, Travis, Libby, Neil, Mike, and Sean relax in the hot tub.

Bart, Travis, Sean, Luke and Mike also known as "The Speedy Boys."

Kyle and Sean, co-organizers of Ride Ataxia II

Contact Us

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