A Publication of the Facioscapulohumeral Muscular Dystrophy Society

SPRING 2011

FSH Watch

CONNECTING THE COMMUNITY OF PATIENTS, FAMILIES, CLINICIANS AND INVESTIGATORS

RESEARCH

FSH Society establishes collaboration with Stanford University

An interview with William R. Lewis, Sr., M.D., Chairman of the FSH Society's Board of Directors, by Daniel Perez, President and CEO, of the Society, on a new initiative at Stanford University in facioscapulohumeral muscular dystrophy (FSHD)

In late 2010, Duncan and William R. Lewis, Sr., M.D., Chairman of the Society's Board of Directors, made a gift of $100,000 to the FSH Society, and a challenge to patients, their families, and friends to match this gift and those of other major donors. At the same time, Bill and his wife, Duncan, called to the attention of the Society's Board of Directors and the Scientific Advisory Board, an opportunity to support a research program at Stanford University specifically targeting FSHD. Daniel Perez (DP) asks Dr. Lewis (WL) about the research project and how the work helps fulfill the mission of the FSH Society.

Duncan and William R. Lewis, Sr., M.D., and Michael R. Altherr, Ph.D.

DP: Dr. Lewis, you have lived and worked in California for many years. Can you tell our readers about your life there as well as your connection to Stanford?

WL: When I arrived in California at the Stanford Medical Center in 1960, I had intended to stay for only a few years while I completed my neurosurgical training, thinking at the time that I would return to the South where I had been born and raised, and also where I had hoped to return to Duke Medical School as a member of their neurosurgery department. While at Stanford I was offered a position as a member of the teaching staff in neurosurgery and I then decided to stay at Stanford, at least for a while. Shortly after this decision I was approached by several Monterey physicians who informed me that their beloved previous neurosurgeon, the only one on the Monterey Peninsula and indeed the only neurosurgeon on the California coast between San Jose and Santa Barbara, had recently died prematurely, ostensibly from "overwork." They described a serious need for an immediate replacement since there were many patients for whom there was no specialist in neurology or neurosurgery to assume their care. After site visits and prayerful consideration my wife, Duncan, and I elected to move to Monterey with the understanding that a neurosurgeon from San Francisco was scheduled to replace me

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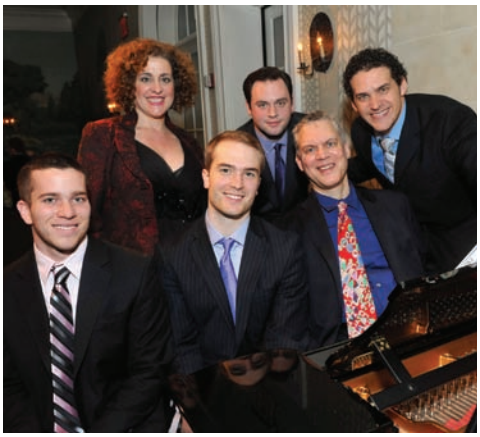
A Festive Evening of Song raises over $200,000 for FSHD research



Andrew Stenval, Mary Testa, John Brancy, Paul Appleby, Steven Blier and Joshua Jeremiah at the New York Botanical Garden, May 19, 2011. More on pages 8 and 9.

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LETTER FROM THE EXECUTIVE DIRECTOR

Dear Friends,

It is good to share news from the FSH Society and the community of FSHD patients in this issue, Spring *Watch*.

Since mid-2010, we have all been buoyed by news of the publication from *Science*, August 19, 2010, that revealed for the first time the biological mechanism causing FSHD. New understanding of a specific genetic "package" of toxic material that causes FSHD means that researchers can focus efforts to test medications and other therapies on this defined target—and other targets that may emerge from continuing investigations. The FSH Society is committed to help investigators carry these findings forward into treatments. On pages 10 and 11, new research awards are announced; in a few weeks the Society's Scientific Advisory Board will meet to consider proposals submitted in the February 2011 cycle.

One of the awards announced within this issue is that of Jean Mah, M.D., Alberta (Canada) Children's Hospital, whose research effort is to better characterize pediatric FSHD. The Society was invited to participate in a meeting of the Cooperative International Neuromuscular Research Group (CINRG) in Washington, D.C., in March. I attended this meeting and heard Dr. Mah present the objectives of the study. We look forward to the natural history data and outcomes measures that will result from this important population.

You support the work of the Society and FSHD research in many ways. We thank all of you who have made membership and other gifts in the first half of 2011. Like you, we are especially grateful to volunteers who have led fundraising events this year. The End of Tax Season Celebration and the Festive Evening of Song brought important philanthropy to the Society, and the events also raised awareness about FSHD among the people who purchased tickets and sponsorships.

Thank you in advance for other initiatives you have planned for later in the year—the Fulmer Family Dinner, the Cape Walk 'n' Roll and the SoCal Walk 'n' Roll, and others. Meanwhile, we are considering locations for the 2012 International Patient/Researcher Network Meeting, and we hope to give you the specifics in the next few months.

All good wishes to you and your families for a safe and productive summer!

Sincerely,

Nancy Van Zant

Nancy Van Zant, *Executive Director*

It is our editorial policy to report on developments regarding FacioScapuloHumeral Muscular Dystrophy (FSHD), but not to endorse any of the drugs or treatments discussed. We urge you to consult with your own physician about the procedures mentioned.

Look for us on the internet at: *www.fshsociety.org*
Editors: Daniel Paul Perez and Nancy Van Zant
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Introducing Doris Walsh

Doris Walsh joined the FSH Society as Patient Liaison and Office Manager in February 2011. She comes to us with excellent administrative and outreach skills both in non-profit and for profit organizations. Doris can be contacted through the Society's Executive & Development office:

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FSH Friends for the journey

by STEPHANIE STALEY

Neil from United Kingdom: ***Life is about the journey, not about the trips.***
Stephanie from USA: ***But what if you trip right next to the edge of a cliff?***
Carol from Australia: ***splat***

Thus began one of the early threads in the FSH Friends Facebook group I started in February. It has since grown to a thriving social community of over 215 people from around the world. I would like to say the group was a well-planned brain-child, but to be honest, it was an accident. We'll call it a "trip," but not one involving FSHD legs. I blame it on another disability of sorts: my blonde hair. This particular blonde moment was late one night as I was exploring Facebook. I found an icon labeled "Create group..." and had the brilliant idea to organize my friends into categories. I made a "Family" group, a group for old high school chums, a group for church buddies, and a group called "FSH Friends." By the time I realized I wasn't just assigning categories but had invited everyone I knew to private discussion forums, it was too late. There didn't seem to be any way to undo it. I posted an apology, thankful that I had not named the groups anything like "People to Avoid," and went to bed.

In the days that followed, however, something strange happened. All the groups quietly fizzled except one: FSH Friends started to buzz and grow. At first, it was 15 members, then 35, then 50.... People were posting introductions and proposing get-togethers. FSHD jokes began to proliferate. Soon, threads were being hijacked with delightful banter. Sure, there were posts offering helpful tips ("I found this fantastic scooter..."), comparing notes, deeper discussions ("Are you proud of the person you've become?"), candid venting, and impassioned debates on sensitive issues. There were even searching questions about God. Something serendipitous had occurred. The group seemed to be filling a need for Facebooking FSHers everywhere, including myself.

Stephanie (right) at 2010 FSH Society International Patient Researcher Network Meeting, Las Vegas, Nevada, with friends Meg (far left) and Susanna

Getting back to the metaphor of life as a journey, every journey has, yes, trips, but also turning points. You can look back and see the significant bends in the road that got you to where you are. For me, the FSH Friends group is one such turning point. But perhaps I should describe more of my journey with FSHD.

I started out as a tow-head tot with curiously big eyes that would not close all the way and funny full lips--my slobbery attempts to whistle provided much entertainment! Then in high school, my parents noticed me limping. They took me to a doctor at the Naval Hospital in Newport, Rhode Island, who found that I had atrophied calf muscles. He also determined, to my surprise, that I could no longer raise my arms. (Astute readers will conclude that I was not a cheerleader. Indeed, gym class taught me early on that my strengths were not physical!) I recall admitting to the doctor that I was not very active. He laughed, despite his concern, and assured me that inactivity was not to blame. "Something else is going on," he said, "and we are going to figure out what." From there, it was a trip to Tufts New England Medical Center in Boston to see a neurologist who introduced me to electromyograms (who knew EMG Teflon-coated needles could be so fun?!) and a muscle biopsy before making the final diagnosis: a sporadic case of facioscapulohumeral muscular dystrophy.

From there, the journey becomes one of struggle for a while. I have a wonderful, close family and I being the first and only member with FSHD, none of us knew how to navigate this bend in the road. It was a lot to take in for a teenager. I stumbled on "what-ifs" and fears about the future. I had confusion about how this mutation that explained my face re-defined who I was. I worried about passing the gene on. I went to college and started a scientific software career that I love, but FSHD became an isolating condition, as it can be for many, and something I sought to hide. I even went through a period during which I did not want to meet anyone else with it because that would make it more real. Hey, denial is not just a river in Egypt.

But eventually I contacted the FSH Society and attended my first patient researcher conference in Boston organized and sponsored by the Society. Suddenly, I had "siblings," people who looked and walked like me. While a good step, I did react with some blues as I absorbed the reality. My journey continued from there with more reaching out, more muscle loss, and more coming to terms.

Fast forward a decade to last summer, when I attended the FSH Society patient/researcher conference in Las Vegas. This time, no blues! I found I was paying attention to the positives: how devoted the researchers were to finding treatments and a cure, and how encouraging my fellow FSHers were to one another. I made new friends, and we spent a lot of time laughing together.

So when my blonde moment happened, the timing could not have been better. There is a Bible verse often quoted at weddings: "If one person falls, the other can reach out and help. But someone who falls alone is in real trouble." The meaning fits the "life's a journey" metaphor well: we all need companions to help us navigate the road. For me, the Facebook group represented a

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RESEARCH

Toward best practice guidelines for the genetic diagnosis of FSHD

by RICHARD J.L.F. LEMMERS, Ph.D.,
Department of Human Genetics, Leiden University Medical Center, The Netherlands

In June 2010, a meeting was organized at the Leiden University Medical Center (LUMC) in the Netherlands on the Best Practice Guidelines for the genetic diagnosis of FSHD. The meeting was organized by Drs. Lemmers, Rabi Tawil and Silvère van der Maarel of the Fields Center for FSHD and Neuromuscular Research. A total of 39 clinicians and scientists from around the world participated in the course. The FSH Society was one of the sponsors of the meeting together with the Fields Center, the Dutch FSH Foundation, the Muscular Dystrophy Association, Spieren voor Spieren ("Muscles for Muscles"), FSHD Global and Association Française contre les Myopathies.

In most cases, FSHD is caused by a contraction of the repeat array D4Z4 on chromosome 4q (FSHD1) to an array between 1-10 units, while the array size in controls (individuals without FSHD) ranges between 11-100 units. This repeat contraction coincides with the loss of repressive marks in this region and the transcriptional de-repression of the DUX4 gene in skeletal muscle. In some cases, the opening of the chromatin structure is independent from a contraction of the D4Z4 repeat array (FSHD2). The meeting focussed on the detection of the D4Z4 contraction in FSHD1 as the DNA diagnosis of FSHD2 is currently in an exploratory phase.

Several topics were discussed during the meeting. Dr. George Padberg (Nijmegen, the Netherlands) started with the clinical characteristics of FSHD and also focused on the clinical uncertainties and the resemblance of FSHD to other clinical conditions. His presentation highlighted the need for genetic confirmation, especially in new FSHD cases. Dr. Lemmers discussed the current genetic analysis by Southern blotting. Due to the genetic characteristics of the mutation, modern, quicker and less expensive standard methods, like Polymerase Chain Reaction (PCR) cannot be applied to FSHD. Dr. Yukiko Hayashi (Tokyo, Japan) discussed an alternative PCR method to identify D4Z4 contractions, but which cannot be applied to all patients with FSHD. The newest method, molecular combing, was presented by Dr. Nicolas Levy (Marseille, France). This method is based on Fluorescence In Situ Hybridization and allows direct visualization of the mutation on single DNA fibers.

Independent of the disease, the chromosomal region that is associated with FSHD has been subjected to several complex DNA rearrangements that make identification of the FSHD mutation rather challenging in about 10% of the cases. To prevent diagnostic mistakes due to these rearrangements, additional testing methods were discussed. Other topics that were discussed included the homogenization of genetic testing (Dr. Rossella Tupler, Modena, Italy), FSHD2 (Dr. Jessica de Greef, Leiden, the Netherlands), prenatal diagnosis (Dr. Bert Bakker, Leiden, the Netherlands), non-radioactive labeling (Dr. Suzanne O'Shea, Bristol, UK) and whether additional genotyping is required in the standard diagnostics (whole group). The experiences of all participating labs in molecular testing for FSHD were obtained by a questionnaire that was distributed to the participants in advance of the meeting. The results from that questionnaire were discussed by Dr. Peter Lunt (Bristol, UK). During the meeting consensus was reached about the DNA diagnostic criteria for FSHD. FSHWatch

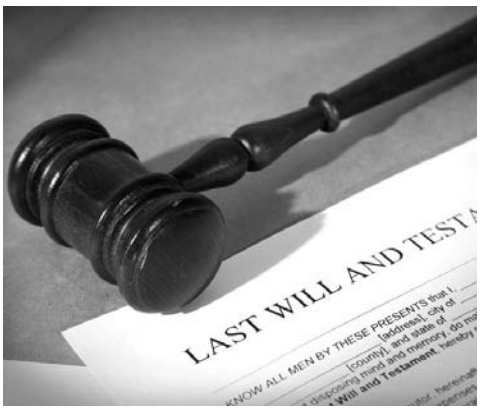
ESTATE PLANNING

You have will power — Join the FSHD Future Fund

Express your appreciation for the Society's leadership in FSHD research and education by directing a portion of your assets to the FSH Society by way of your will. Making a will is an important way to extend your love, care and gratitude to family, friends and the charitable causes you care about.

Members of the FSHD Future Fund are supporters who have remembered the FSH Society through a bequest or other estate planning instrument. FSHD has touched your lives, and that is why your consideration of a bequest to the Society is so important. Please contact the Society to discuss your interest. You can establish one of several types of bequests:

- Unrestricted bequests for the general use of the Society



- Restricted bequests for specific uses, such as patient education and outreach, FSHD research, or another particular program
- Endowed funds

And, any of the above can be named for you, for your family, or in memory of someone.

If you have already included the FSH Society in your will, we hope you will let us know by returning the **enclosed card**. If you will allow the Society to recognize your dedication in our Annual Donor Report, your example might inspire others. If you have questions about your planning and how it can support the work of the Society in the future, or if you would like a copy of the booklet "Questions and Answers about Wills and Bequests," let the Society know by returning the enclosed card.

Always check with your advisors when making or changing a will or before making changes in your plans, and learn how the latest changes in tax laws and other legislation may affect your plans. FSHWatch

International FSH research consortium gathers at the Wellstone Muscular Dystrophy Center

Over 90 scientists, patients, advocates, biotech and pharmaceutical companies, and clinicians from across the United States and throughout the world gathered at Boston Biomedical Research Institute (BBRI) last October to attend the FSH Society 2010 International Research Consortium and Research Planning Meetings for FSHD.

Daniel Paul Perez co-organized the meetings. Rabi Tawil, M.D., University of Rochester Medical Center was clinical chair and Silvère van der Maarel, Ph.D., Leiden University Medical Center was research chair. David Housman, Ph.D., Chairman, FSH Society Scientific Advisory Board (SAB), and many members of the Society's SAB were present and helped moderate the meeting. The meeting was co-hosted by Charles P. Emerson, Jr., Ph.D., Director of the Boston Biomedical Research Institute, and Co-Director, along with FSH Society Board and SAB member Louis Kunkel, Ph.D., of Harvard Medical School and Children's Hospital Boston, of the NIH Eunice Shriver Kennedy NICHD Sen. Paul D. Wellstone MD CRC for FSHD. Also joining the meetings was Ljubisa Vitkovic, Ph.D., program director for the NICHD.

It was a very successful workshop and really was "the place to be" for FSHD research. There was excellent interaction between the BBRI Wellstone MDCRC for FSHD and Fields Center for FSHD, as evidenced by agreements to work jointly and corroboratively on projects.

Given the potential watershed event of the recent DUX4 finding, attendees were encouraged to share their latest data and findings via talks and poster presentations. To read the recommendations and priorities of the group see details at: *http://www.fshsociety.org/assets/pdf/IRCWorkshop2010WorkingConsensusOfPrioritiesGalley.pdf.*

Sponsors for the event included Association Française Contre les Myopathies (AFM), The Fields Center for FSHD and Neuromuscular Research, FSH Society, FSHD Global Research Foundation, NIH Eunice Kennedy Shriver NICHD Boston Biomedical Research Institute Senator Paul D. Wellstone MDCRC, and the Muscular Dystrophy Association (MDAUSA). FSH Watch

University of Rochester Medical Center Neuromuscular Disease Clinic

Editorial note: FSH Watch will occasionally highlight neuromuscular clinics that we believe might be of interest to patients and their families.

Rabi Tawil, M.D., Co-Director

Rabi Tawil, M.D., Co-Director
Emma Ciafaloni, M.D., Co-Director
Rochester, New York

The University of Rochester's Neuromuscular Disease Clinic provides diagnosis and comprehensive management and treatment of adults and children with neuromuscular disorders. The clinic includes nine staff physicians, two nurse practitioners, two physical therapists, a respiratory therapist and a speech pathologist. As this is a Muscular Dystrophy Association clinic, an MDA healthcare coordinator is also present in clinic to help provide patients and families with appropriate information as well as coordinate and facilitate their care. Genetic counseling is provided by a counselor from the Neurogenetics division of the department of Neurology. The clinic includes a diagnostic EMG (electromyography) laboratory as well as facilities to perform diagnostic, minimally invasive muscle biopsies. The availability of these diagnostic facilities allows for an efficient, comprehensive evaluation of patients with neuromuscular diseases. The clinic draws patients from all of the Upstate New York area and Northern Pennsylvania. In addition, for those conditions that the clinic has special expertise in, such as FSHD, myotonic dystrophy and channel disorders, patients are referred from across the United States.

Rabi Tawil, M.D., Director of the Fields Center for FSHD and Neuromuscular Disease Research, has a long standing clinical and research interest in FSHD. The Neuromuscular Center has been actively involved in FSHD clinical care and research dating back to 1988. Clinical work on FSHD has led recently to the development of standards of care for the management of FSHD by a group of international experts in an effort spearheaded by Dr. Tawil. These standards were published in the journal Neuromuscular Disorders in 2010. Shree Pandya, R.P.T., M.S., a research physical therapist is co-author of the FSHD physical therapy guide, an effort sponsored by the FSH Society. Dr. Tawil has also engaged a retina specialist from the University of Rochester's Eye Institute (Dr. Mina Chung), for the clinical evaluation and treatment of retinal vascular disease in FSHD. Finally, as part of the Fields Center outreach program, a full patient day program has been organized yearly since 2007 to offer patients practical information regarding FSHD as well as to provide the most up to date information regarding FSHD research.

Dr. Tawil is currently engaged in both clinical and bench research as part of the Fields Center and is an investigator in an NIH-sponsored program project. This collaborative research draws on the strengths of several institutions to move FSHD research forward and includes the University of Rochester, Leiden University Medical Center (the Netherlands), The University of Washington and the Fred Hutchinson Cancer Research Center in Seattle.

For a clinic appointment: call Gail Bloom at 585-275-2559.

FSH Society submits FY2012 congressional testimonies

In April, the FSH Society submitted testimony to the United States Senate and House Appropriations Committees, Subcommittees on Labor, Health and Human Services, Education and Related Agencies on FY2012 Appropriations for National Institutes of Health (NIH) Research on FSHD.

The two major breakthroughs on FSHD that occurred in FY2010 and FY2011 were described and NIH was asked to redress funding for FSHD to a level of $35 million. The testimony also referred to areas of scientific opportunity in FSHD that were identified by the global community of FSHD researchers as needing funding. To read the entire testimony please visit *www.fshsociety.org*, click "FSH Society" at the top of the page, select "Advocacy" in vertical navigation and then click link to PDF file.

One way to help ourselves is to educate Congress and inform your Senators and Representative on the need for continued research on muscular dystrophy and FSHD in particular by NIH and other Federal agencies. Please read the testimony and contact your representatives to tell them your FSHD story and why continued research is essential to you. Stress the importance of NIH as a job creator, a driver of economic growth, a vital tool in curbing our nation's soaring healthcare costs and as the means to understand and treat FSHD. FSH Watch

FSH SOCIETY ESTABLISHES COLLABORATION WITH STANFORD UNIVERSITY

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in one year, following which I would return to Stanford. Unfortunately that neurosurgeon developed cancer and was unable to make the move. I should note that in those days there was a severe shortage of neurosurgeons so consequently we had little choice but to remain in Monterey where I have now been for the last 48 years, making me one of the longest tenured "medical missionaries" in the record books.

In addition, I have remained active in my relationship with Stanford and have at times held various positions, including an assignment as a "Clinical Professor in Neurosurgery." As the senior member of the "Hanbery Society," which is composed of all of the former neurosurgical chief residents at Stanford, I have continuously followed with great interest all of the many activities of the neurosurgery department as well as many other exceptional medical feats for which Stanford is recognized as a leader. Among the non-neurosurgical innovations was the heart transplant program started while I was at Stanford by my good friend, Dr. Norman Shumway, who was the first surgeon to devise a heart transplant operation which could be implemented safely and effectively.

I hope this answer has not been too long but your question has aroused my interest as well as my recall for some interesting events in my career.

DP: Dr. Lewis, could you tell us about your conversation with Dr. Steinberg and Dr. Rando and their growing interest in FSHD research and therapeutics?
WL: Dr. Gary Steinberg is a long-term friend and Chairman of the Department of Neurosurgery at Stanford as well as a gifted and innovative doctor who has promoted a number of new programs at Stanford. Dr. Tom Rando is an internationally recognized medical neurologist who has been at the forefront in a number of intriguing developments, including an interest in the stem cell field--an area of great interest also for Dr. Steinberg. In one of my continuing discussions with Dr. Steinberg, I noted to him that historically FSHD research had been stronger in other parts of the world than in the United States but that during the past fifteen years or so the FSH Society had led a renewed USA interest in FSHD and that there were now some very enlightening developments and that it would be important to have an institution such as Stanford working on this problem. Furthermore, I pointed out to him that it would be a great favor to me if he would institute a program to explore this disease process. He immediately thought of Dr. Rando as one who was uniquely qualified to begin such work.

DP: The Society's gift is also being matched by Stanford, is it not? How did you make this happen?
WL: I then told Dr. Steinberg that I would like to accelerate the Stanford interest and that I would make a monetary contribution with the hope that Stanford would match that amount. He responded favorably to this suggestion. Dr. Rando promptly proposed a specific project which I found to be worthy of our support through the FSH Society, and Duncan and I then agreed to a two-year sponsorship.

DP: Could you tell us about the new initiative at Stanford called the Stanford Institute for Neuro-Innovation and Translational Medicine?
WL: The newly formed Stanford Institute for Neuro-Innovation and Translational Neurosciences (SINTN), led by Dr. Steinberg, has as its primary focus the unification of the efforts of clinicians and basic scientists in various fields working collaboratively toward solving some of the many remaining mysteries in medicine. Since Stanford has traditionally been blessed with a series of great minds, including several Nobel prize winners, the hope is that these individuals will stimulate one another and collectively they will be more productive working in a group setting rather than individually.

DP: What problems are they working on and what biomedical research questions can they answer? Please tell our readers about the FSH Society-funded research initiative.

Greetings from AMIS FSH and Manuel Cabral, President

AMIS FSH is an association of FSHD patients and their families founded in 2002 around a small group of patients who met on an internet forum. We are primarily French speakers from France, Belgium and Switzerland, but we also have members in Italy, Spain and Portugal. Our association is based around three major objectives:

- To break the isolation of families by sharing information and experience,
- To raise awareness with public authorities of the need for research and care for this disease, and,
- To promote research aimed at understanding the mechanisms to develop treatments.

In addition, we organize two meetings annually between FSHD patients and researchers. We distribute a quarterly newsletter devoted to the latest research and community life. We offer briefs:

physiotherapy, nutrition, pre-implantation genetic diagnosis and prenatal(PND/PGD), arthrodesis scapulothoracic, etc. AMIS FSH is a founding member of the FSHD-Europe consortium, established in 2009, which brings together European FSH associations: Stichting FSHD (Netherlands), UILDM-(Italy) and AMIS FSH: *www.fshd-europe.org*. You can find us on Facebook. FSH Watch

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WL: Currently there are about 150 neuroscientists working with the Institute. Dr. Steinberg has recently received a grant of twenty million dollars from the California Institute of Regenerative Medicine (CIRM), to study the use of stem cells in the restoration of function in stroke patients. I have attended two seminars led by SINTN scientists and they have discussed there a variety of profoundly complex issues including the specific role of glial cells in the brain as they may relate to Alzheimer's disease, the molecular mechanisms of aging and longevity, the neural mechanisms underlying visual perception and simple forms of decision making, the basic principles of early brain development, and other bed-time stories. The FSHD project is taking a new approach to the recent work with DUX4 product in the hope that it will lead to a definitive biochemical intervention of potentially curative nature.

DP: How is this work at Stanford different from other anti-DUX4 therapeutic-research strategies?

WL: Dr. Rando has been previously involved in other unrelated projects and saw in FSHD a potential biochemical site at which he could utilize his past work to bring an innovative mechanism into play with FSHD. Only time will tell how effective this may be but I am impressed with the possibilities.

DP: Do you think it is possible for these seed funds to grow into larger stem cell projects funded by CIRM?

WL: The current funding is not intended at this stage to be stem cell related but in time it could develop into some variation of stem cell therapy depending on preliminary findings. Certainly, Stanford will be the place to be if and when stem cell expertise is needed. I am intrigued by the use of Gelfoam material, as a possible platform to sustain individual stem cells as on-lay grafts over diseased muscle should we get to the point that "replacement" tissue becomes feasible.

DP: You have been involved in the FSH Society for twenty years. What is your vision for the community of FSHD researchers? What gives you hope? What has been discouraging to you?

WL: The brightest hope for all of us in this field comes from the realization that we are now working with and supported by a small "army" of researchers who are truly dedicated to our cause. This point has been reached only after much frustration primarily relating to underfunding and the lack of even a "clue" as to how this genetic dysregulation could lead to muscle loss. The recent DUX4 findings appear to give that vital clue and now we must continue with the hard task of more precisely defining and correcting the underlying flaws.

DP: It is excellent to hear about FSH Society funds being matched by Stanford. Could you also speak about your challenge to the FSHD community? How does the challenge help the FSH Society and its research programs? What does this mean for FSHD research?

WL: Unfortunately, as with virtually all else in life, there is a price to be paid to keep the show going. We have been blessed to have had the strong support of our entire membership with an occasional boost by our "challenge" campaigns. Of course we will continue to seek NIH, MDA, and all other potential funding wherever it may be found. In the end, it is important that we be seen as having made a sincere effort to "help ourselves" through our own fundraising efforts rather than be seen as only standing around waiting for a handout. Each of us should plan to be as generous as possible and to "dig deep" when called upon for support. I can assure you that our ultimate goal of a "cure" is almost solely dependent upon the funding available to continue and to amplify vital research. We thank all who have given and ask that you continue to make that effort.

DP: Thank you, Bill and Duncan Lewis for your care, your concern and your gifts to the FSHD community. FSH Watch

A Festive Evening of Song raises over $200,000 for FSHD research

Over 250 concert goers enjoyed a splendid evening to benefit the FSH Society on May 19, at the New York Botanical Garden, Bronx, New York. Steven Blier, co-founder and artistic director, New York Festival of Song, with vocalists Paul Appleby, John Brancy, and Joshua Jeremiah and Mary Testa, and percussionist Andrew Stenval played and sang a wonderful concert: A Vaudeville Entertainment. Steve delighted the concert goers with humor, good spirit and commentary in his introductions.

A silent auction and dinner preceded the concert and a dessert buffet followed it. Special thanks from all the FSH Society to these wonderful musicians, to Judy Seslowe and Beth Johnston, co-chairs of the concert; to Bob and Abigail Kirsch for enabling the use of the Garden Terrace Room at the Botanical Garden and to their fine staff for wonderful food and service, and to the concert committee for making this the most successful evening to date for the Society in New York.

A greeting from Steven Blier, from the evening's program

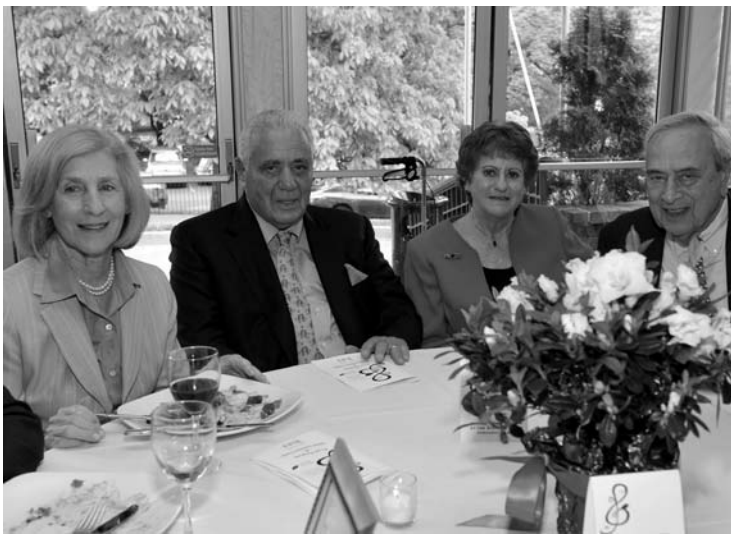
We are celebrating three miracles tonight, and the first of them is the miracle of song. I never cease to be amazed at the way words and music can coalesce a chaotic roomful of people into a community of rapt dreamers. I am also awed by the way song brings me close to my colleagues, with whom I share an almost indescribable intimacy of vibration and emotion as we make music together. Häagen-Dazs® cannot come close to matching the intense sweetness of those collaborations.

There are other miracles at work. It takes a mysterious synergy of brains, muscles, and nerves to play the piano. We pianists start with an idea of a sound we want to make, and (on a good day) that idea travels with the speed of thought down to our fingertips, which seem to divine the exact speed and force they need to make the sound emerge into the room. My brains aren't bad for my age, but FSH Dystrophy has surely tried to have its way with my muscles and nerves. Through enormous luck and quiet force of will, I've managed to fight back to keep the channels open. I'm no Samson, but my hands are like meathooks and my forearms are like clubs. They just won't take no for an answer. They are the Ted Kheel of my body, negotiating between all the stubbornly warring factions and striking under-the-table deals with my shoulders and torso, so that I can still play a little Gershwin.

The third miracle? Well, because of Judy Seslowe, Nancy Van Zant, and Beth Johnston, I got involved with fundraising for the FSH Society. It finally occurred to me that I could abandon my many decades of brave, passive stoicism and actually do something to help myself and my FSHD brothers and sisters. Now, I know that everyone in this room was exhilarated last August when we learned that our researchers had found the genetic cause of FSH dystrophy, the elusive "junk gene" that springs into action like a dybbuk and makes all kinds of inroads on our mobility. But the child within me couldn't help seeing this confluence of events as a miracle: when I took action, the scientists finally cracked the code. In reality, of course, this potentially life-changing breakthrough was the end product of years of fundraising and research, not merely the result of a few concerts. But its strange synchronicity empowered me in a profound way: I played some songs, and the next thing I knew, we had an enormous scientific advance. If I didn't have enough reasons already to make music, I now have another. Music lifts our spirit, but I now think music might actually lift me out of this wheelchair. I shall keep the faith. FSH Watch

Good friends enjoy the party

Garrison Keillor enjoys the concert



Bob Kirsch, second from left, with friends

Judy and Kenneth Seslowe, M.D.

Research Grant

2011 Delta Railroad Construction research fellowship grants

The FSH Society Delta Railroad Construction Company fellowship program continues to help FSHD research by awarding grants that provide needed expansion of current work and innovative new work. The FSH Society is indebted to the Delta Railroad Construction Company of Ashtabula, Ohio, and to Larry and Ida Laurello and their family for this groundbreaking effort on behalf of the FSHD community. For more information about research fellowships, please contact Daniel Paul Perez at daniel.perez@fshsociety.org.

FSH SOCIETY ACHIEVES CHARITY NAVIGATOR'S COVETED 4-STAR RATING

The FSH Society has earned Charity Navigator's third consecutive 4-star rating for its ability to efficiently manage and grow its finances. Only 13% of charities rated have received this highest rating. This 'exceptional' designation from Charity Navigator differentiates FSH Society from its peers and demonstrates to the public it is worthy of their trust. See *www.charitynavigator.org*.

COMBINED FEDERAL CAMPAIGN (CFC) 2011 CAMPAIGN—CONTRIBUTE TO THE FSH SOCIETY

The FSH Society has been approved by the Office of Personnel Management for the 2011 campaign. Pledges made by federal civilian, postal and military donors during the campaign season (September 1 to December 15) support eligible non-profit organizations that provide health and human service benefits throughout the world. The FSH Society's identification number is 10239.

DO YOU FOLLOW THE SOCIETY'S FACEBOOK AND YAHOO! GROUPS PAGES?

You can access the FSH Society Facebook page and Yahoo! Groups forum by going to *www.fshsociety.org* and clicking on the "Community & Reference" menu tab at the top of the page and then selecting "Online Community" in the vertical navigation menu.

HAVE YOU MADE A GIFT TO THE SOCIETY IN 2011?

The FSH Society is a world leader in combating muscular dystrophy. It has provided over $2.9 million in seed grants for pioneering research worldwide and has developed an international collaborative network of patients and researchers. Please return your membership gift, or another gift, in the enclosed envelope. Or contribute online at *www.fshsociety.org*. Go to Contribute, and select the gift category you wish to make. Thank you.

VOLUNTEERS ARE STILL NEEDED FOR MUSCLE BIOPSY STUDY

To date, approximately 60 individuals in 26 groups of FSHD-affected volunteers and their unaffected relatives have participated in the FSHD-NIH-Wellstone Muscular Dystrophy Cooperative Research Center's research study. Muscle samples are in extremely short supply and tissue donors are most needed. The study is in particular need of patients with suspected FSHD-related hearing and retinal involvement, and from minority races and ethnicities, but all are welcome. In order to determine eligibility, you will need to provide a copy of your gene test result and medical records indicating FSHD diagnosis. For more information, please contact Doris Walsh at the FSH Society 617-658-7877 or *doris.walsh@fshsociety.org* or Genila Bibat, M.D., Johns Hopkins, 443-923-2778.

DOES THE SOCIETY HAVE YOUR CURRENT E-MAIL ADDRESS?

If we do not have your current e-mail address and if you want to be sure of receiving up-to-the-minute information from the Society as news breaks, please send your e-mail address to us at info@fshsociety.org. Thank you.

FSH Society grants recently awarded

Since 1998, the FSH Society has transformed FSHD research by providing research grants for vital start-up funding for investigators studying FSHD. We are pleased to list the grantees funded in the August 2010 cycle. You can also read more about FSH Society funded research projects by going to *www.fshsociety.org*, clicking on the "Research" menu tab at top of the page and then selecting "Research Fellows & Grantees" in the vertical navigation menu.

▶ **Small Molecule Screen to Identify Inhibitors of DUX4-mediated Toxicity, Therapeutic Approach for FSHD**
Darko Bosnakovski, D.V.M., Ph.D.
University "Goce Delcev" Stip
R. MACEDONIA
$90,000 over 2 years

Summary: The goal of this proposal is to discover a chemical compound that efficiently inactivates the DUX4 protein and to work towards a drug for a therapeutic approach to FSHD. The aims of the proposed study target the most crucial topic and urgent needs of FSHD patients: specific and direct pharmacological therapy. First, the project helps to narrow focus from 82 potential compounds to inactivate DUX4, implicated as necessary to cause FSHD, as a result of high-throughput screening to the most promising direct DUX4 inhibitors. Second, scientists will evaluate effectiveness of DUX4 inhibition and study the properties of the selected compounds.

▶ **Toward Therapeutics for FSHD: Understanding mRNA Processing**
Thomas A. Rando, M.D., Ph.D./Antoine de Morree, Ph.D.
Department of Neurology and Neurological Sciences
Stanford University School of Medicine
Stanford, California
$200,000 over 2 years
This research project is being matched dollar for dollar up to $100,000 over two years by the Stanford Institute for Neuro-Innovation and Translational Medicine (SINTN).

Summary: Recently, the group of Dr. van der Maarel reported in the journal *Science* their findings of the high resolution haplotype mapping of patients and unaffected individuals with D4Z4 contractions. Their findings provide evidence that the disease develops in individuals who have BOTH a D4Z4 repeat contraction AND a specific sequence in the pLAM domain at the 3' end of the D4Z4 array. The D4Z4 repeat contraction results in "relaxed chromatin", and allows the transcription of the DUX4 gene in the final D4Z4 repeat. However, it is the sequence in the pLAM domain that creates a site that is recognized by the cellular machinery allowing cleavage of the mRNA and the addition of a poly(A) tail. Without a poly(A) tail in the 3' untranslated region (3' UTR), transcripts are rapidly degraded and never translated into proteins. With these tails, transcripts are stabilized and appropriately localized in the cell, allowing for protein translation. In individuals who have D4Z4 contractions but a single base change in the distal sequence, the cell does not recognized it as a "polyadenylation signal" (PAS) site, no poly(A) tail is added to the 3'UTR of the transcript, the DUX4 transcript is unstable, no DUX4 protein is made, and the individuals are protected from getting the disease. Within this cascade are several opportunities, at least theoretically, to treat or even prevent FSHD in susceptible individuals. Any intervention that prevents the addition of the poly(A) tail to the DUX4 transcript is a potential therapeutic approach for FSHD.

The research project aims for a direct line to a novel therapeutic approach. The toxicity leading to FSHD depends on effective mRNA processing in which the DUX4 transcript is cleaved and modified by the addition of a poly(A) tail. If one of these processes could be blocked, then the mRNA would be destabilized and the FSHD genotype would yield a normal phenotype. Clearly, it is untenable to interfere with mRNA processing in general because of the toxicity to the cell. Therefore, understanding the mechanisms by which a cell can bypass a specific PAS site would suggest a mechanism for selectively blocking the PAS site in the pLAM domain in the DUX4 gene without generally affecting cellular mRNA processing. This would be an effective treatment for patients with FSHD.

▶ **Defining the Tissue and Cell Specificity of the Human DUX4 Promoter in Mice**
Scott Harper, Ph.D.
Center for Gene Therapy
The Research Institute at Nationwide Children's Hospital
The Ohio State University
Columbus, Ohio
$50,000 over 1 year

Summary: Since animal models, particularly mice, are crucial tools for studying disease pathogenesis and developing potential therapeutics, the absence of an FSHD mouse model is a fundamental problem in the FSHD field. The goal of this project is to generate an FSHD mouse model expressing a single FSHD-permissive human D4Z4 repeat, and to use this model to understand the role of the D4Z4-resident gene, DUX4, in FSHD pathogenesis, and develop RNAi therapeutics targeting DUX4. This project will carefully define the developmental and cell specific expression patterns of DUX4p-GFP mice, and develop an AAV vector to determine whether a viral-mediated vascular delivery approach can produce the same expression patterns. These studies are important first steps toward developing an AAV-mediated D4Z4 mouse model.

▶ **Identification of a Novel FSHD Biomarker [an unknown 50 kDa polypeptide highly expressed in FSHD samples**
Jessica Sun, Ph.D./Peter Jones, Ph.D.
Boston Biomedical Research Institute
Watertown, Massachusetts
Partial funding for more preliminary data $10,000 over 1 year

Summary: Screening FSHD patient-derived myoblasts, control myoblast, and muscle samples for expression changes at the proteomic level produced an unknown 50 kDa polypeptide highly expressed in FSHD samples compared to controls. Interestingly, this polypeptide is equally expressed in both normal and FSHD-patient derived

myoblasts and early myotubes, however, unlike in control cells where its expression decreases, this unknown polypeptide remains highly expressed in differentiated muscle suggesting it is developmentally regulated and this regulation is disrupted in FSHD. Identifying this protein will provide insight into FSHD pathophysiology, will be a useful FSHD biomarker, and may be one of the first proteins consistently and specifically upregulated in viable FSHD muscle.

▶ **A Multicenter Collaborative Study on the Clinical Features, Expression Profiling, and Quality of Life of Pediatric FSHD**
Jean Mah, M.D.
Alberta Children's Hospital
Calgary, Alberta
CANADA
US$96,669 over two years; the project is being co-funded by the Muscular Dystrophy Canada FSHD Fund at CDN$65,000.

Summary: FSHD is one of the most common types of muscular dystrophy. The prevalence, clinical variability, cross cultural presentation, and psychosocial impact of FSHD on affected individuals constitute a significant public health concern. Emerging therapeutic trials will benefit from the availability of natural history data and reliable outcome measures for both children and adults with FSHD. The main objectives of this study are: 1) to establish a standardized muscle testing protocol for use in children and youth with FSHD; 2) to describe the clinical phenotypes of pediatric onset FSHD; 3) to evaluate the impact of FSHD on health-related quality of life and disability across different age groups; and 4) to explore potential genetic modifiers of clinical phenotypes and disease progression in FSHD. FSH Watch

FSH FRIENDS FOR THE JOURNEY

. . . from page 3

FSHD community, something I was ready to embrace. Not to say that our "traveling companions" must have everything in common with us. In fact, FSHD is pretty much the only thing we all have in common (and I should be clear that the group includes all whose lives are touched by it, "unaffected" friends and family too). There is also a surprising variance among our FSHD experiences, depending on age of onset, severity, etc. However, what we do have in common is deep enough that, for the most part, we "get it"--the hopes, fears, triumphs, and frustrations--without a need to justify or explain. Understanding is such an empowering, un-isolating force.

The FSH Friends "traveling companions" have also opened my eyes to possibility. Among the members are successful go-getters, talented artists, dedicated students, proud parents, loving partners, people of strong convictions and faith ... even athletes who give their all to compete! I am daily reminded that though we grieve our losses, we also adapt. Despite the profound impact of our common bond, FSHD does not define us. There is so much more to who we are and to what we can become.

Some of the group's "deeper discussions" have been about the question of suffering and the nature of happiness versus more lasting joy. They have helped me verbalize a realization about my own journey: if it isn't just about getting from start to finish with the most fun, but is actually about the deeper joys of growing and contributing and loving, then my struggles are not just obstacles that have gotten in my way. Instead, in a sense, they are my way; they teach me compassion and help me not to cling to what is external, physical and temporary (because FSHD or not, these bodies are not built to last), but to seek what is internal, intangible and eternal. Having others with me on this journey is essential to contributing and to expressing love and compassion and to letting others do the same. So although I would not wish FSHD on anyone, and am committed to supporting research to find a cure, I can see, for myself, how it has helped me become the person I am today and enabled me to meet some wonderful, inspiring friends along the way. And for this turning point of realization, I am thankful.

> ***"Getting back to the metaphor of life as a journey, every journey has, yes, trips, but also turning points. You can look back and see the significant bends in the road that got you to where you are. For me, the FSH Friends group is one such turning point. But perhaps I should describe more of my journey with FSHD."***

I can also be thankful for the blonde hair. Without it, I would not have made my Facebook faux pas! My hope is that this happy accident continues to grow and thrive as a place for FSHers from around the world to connect, laugh about life's "trips," and live out our journeys together. Please join us! According to the privacy settings of the group, you aren't able to search for it on Facebook, but if you would like to join, just send an e-mail to me at *stefstaley@gmail.com*. My FSH Friends and I look forward to meeting you.

The FSH Society's Facebook page has been up since 2008 and attracts hundreds of viewers and fans. Accessing Facebook is free and easy. Go to www.facebook.com and sign up. Search on 'FSH Society' and join. If you are already on Facebook please visit, say hello and click 'like' this site. Bookmark it and come back often. FSH Watch

End of Tax Season Celebration for FSH Muscular Dystrophy raises over $30,000 for Society

Christopher and Ellen Stenmon hosted the 13th annual End of Tax Season Celebration, a very successful fundraiser, on April 16, at Florian Hall in Dorchester, Massachusetts. Guests enjoyed good food and drink, music, dancing, a door prize, a silent auction and a raffle. They had great fun and supported a great cause. Chris is a member of the Society's Board of Directors.

Takako Jones, Ph.D., and Peter Jones, Ph.D., Boston Biomedical Research Institute, spoke about FSHD research. FSH Watch

Chris Stenmon, left, and the Stenmon family

Ellen Stenmon, second from right, and her family, the Webers

This must be the Mahoneys!

Murphy family and other relatives

Ellen and Chris Stenmon, co-chairs

Save the Date!

October 1
Annual Walk 'n' Roll
Cape Cod, Massachusetts

October 9
Annual Walk 'n' Roll
Irvine, California

Summer 2012
FSH Society International Patient Researcher Network Meeting

Interested in participating? Want more information?
Go to *www.fshsociety.org*, or *e-mail info@fshsociety.org*