

FSH Watch



CONNECTING THE COMMUNITY OF PATIENTS, FAMILIES, CLINICIANS AND INVESTIGATORS



RESEARCH

The FSH Society at the cutting edge

Seed grants led to a series of major findings in 2012

by DANIEL PEREZ

President and CEO of the FSH Society, Watertown, MA

A small nonprofit seems like an unlikely place to begin a story about cutting-edge science. Yet that is the story of the FSH Society. Founded 21 years ago by myself and another FSHD patient, Steve Jacobsen, who was also a researcher, the Society's goal was to establish an FSHD research program at a time when virtually no scientists were studying the disease, and no funding was available. We have seen our idea take root, flourish, and start to bear fruit. We were thrilled when a key discovery – which grew in part from seed funding by the Society — landed on the front page of the *New York Times* in 2010, and prompted Francis Collins, Director of the NIH, to proclaim: "If we were thinking of a collection of the genome's greatest hits, this would go on the list."¹

For newcomers to this topic, facioscapulohumeral muscular dystrophy (FSHD) is the most common form of muscular dystrophy. Affecting some 500,000 men, women and children worldwide, FSHD results in a lifelong progressive loss of all skeletal muscles. The disease is crippling and can be life-shortening. It can be either genetically or spontaneously transmitted to children of both sexes and can affect multiple generations and entire family constellations.

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Daive Gabellini, Ph.D., at the FSH Society International Research Consortium workshop with two FSHD researchers, Monica Salani and Angela Zimmerman, see story on page 11.



ADVOCACY

FSHD CHAMPIONS: Achieving faster progress by working more closely together

by DANIEL PEREZ AND KEES VAN DER GRAAF

President and CEO of the FSH Society, Watertown, MA

President of the Stichting FSHD and FSHD Europe, Wassenaar, The Netherlands

In recent years we have seen great progress in several key areas of FSHD research. The emphasis has noticeably begun to shift to translation and developing a therapy. More researchers, clinicians, research institutions, and companies are getting involved in our disease.

Looking at the FSHD-specific patient and fundraising groups, one can only be

impressed by what has been achieved with very limited resources. This is mainly thanks to the passion of a few individuals. Many of the leaders of FSHD groups have met each other on different occasions. But we have never had a formal meeting.

Currently the theater of FSHD research contains small and mid-size FSHD-specific organizations and a few larger funding organizations whose focus is on all of the muscular dystrophies. Alongside these groups there are multiple world-class research groups, some working as a consortium, some cooperating, some working

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Remembering Carol Perez



Remembering why we are here – and those who helped us get here

Dear Friend,

During this past year, we have seen rapid advances and successful treatment of animal models of FSHD. We are very close to clearly mapping out how FSHD works and the prognosis for treatment is quite positive. Through 2011 and into 2012, a continuing series of landmark papers appeared with breakthroughs that were made possible by FSH Society seed grants awarded to researchers who began their careers with FSHD post-doctoral fellowships.



Daniel Paul Perez
 President & CEO

None of this would have happened without expert counsel from the FSH Society Scientific Advisory Board, the Board of Directors and your generosity and sincere wish to make a difference in the lives of family and friends. Thanks to your support, the Society continues its progress in understanding how the disease operates while beginning to lay the foundation needed to commence with clinical trials. As you read about the three recent significant landmark papers in this *FSH Watch*, know that more exciting developments are imminently on the way.

It is also a year of great transition for the Society. Nancy Van Zant announced that she would be retiring. Under Nancy's tenure, with her intensity, dedication and creativity, the FSH Society has accomplished much

towards understanding and treating FSHD. This is part of Nancy's legacy and will live on as she prepares to launch into a well-deserved retirement later this fall. As we wish Nancy well, we introduce you to her successor, June Kinoshita, who began her tenure as the FSH Society's Executive Director in August. June brings her unique signature to the role and a track record of creating ground-breaking philanthropic initiatives in biomedical research. Building on the foundation of Nancy's achievements, through June's commitment to excellence in collaboration, communication and ethics, the FSH Society hopes to attain a new level of support, visibility and impact. June looks forward to getting to know you and working with you as we move forward and continue our progress.

We are deeply saddened by the loss of the following pioneers of FSH Society philanthropy in the past year: Edward Schechter, July 2, 2011, wise mentor of FSH Society CEO and generous funder; Larry Laurello, January 3, 2012, longtime board member who established the Delta Railroad Construction fellowship grants, the Society's first and longest running such program; Carol A. Perez, February 3, 2012, first Executive Director, board member and counselor and friend to many newly diagnosed patients; and Marjorie Bronfman, February 24, 2012, who created the Marjorie and Gerald Bronfman Foundation fellowship grant program. Their collective vision, of offering compassion and counsel to patients and their families while carrying out a sustainable, focused research effort, is one that guides us every day.

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FSH Watch

FALL 2012

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It is our editorial policy to report on developments regarding FSHD but we do not endorse any of the drugs, procedures or treatments discussed. We urge you to consult with your own physician about any medical interventions.

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Articles may be edited for space and clarity. Every effort has been made to ensure accuracy in the newsletter. If you wish to correct an error, please write to the above address.

Look for us on the internet at: www.fshsociety.org
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Having lost my mother Carol, sadly, I truly empathize with those who have lost a loved one to FSHD. As long as we remember them and their efforts, we honor their memory by resolving to work harder today for a better tomorrow. We sincerely appreciate our members and donors and all they do to:

- Hasten the progress of FSHD research
- Continue the good works of the great philanthropists who came before them
- Provide tangible hope to all those living with FSHD

We thank the new generation of philanthropists who honor the memory of these FSHD pioneers and their lives by continuing their work. At this time, with these challenges and great opportunities, please consider becoming a philanthropist, giving even more generously to continue our work to create a unified global front against FSHD. I thank you most sincerely for your support of the Society and our efforts to advance FSHD research and education.

— Daniel Paul Perez
President & CEO



FROM THE FSH SOCIETY EXECUTIVE DIRECTOR

Mission: Make FSHD visible

Dear Friend,

Woody Allen said that 90 percent of life is just showing up. Over the past few months since I joined the FSH Society, I have had the privilege of experiencing several fundraising events, from a family dinner in rural Georgia and a gala concert in New York City, to Walk 'n' Rolls literally spanning the continent, from Cape Cod to Southern California. People showed up by the hundreds, and I want to thank each and every one of them. Because showing up is so very important for FSHD.

I confess that until a few months ago, I had never heard of FSHD. And neither had most of my friends, including many biomedical researchers. This is not good! We must make FSHD visible, because until people see that FSHD is a problem, they will not recognize that it requires a solution.

We need to generate a sense of urgency about FSHD. To do that, we need your help. We need you to proudly wear FSH Society Walk 'n' Roll T-shirts. Speak out about it. Facebook it. Tweet it. Ask your friends to learn about FSHD and attend events. Tell them solutions are in sight. We can get there if we all pull together to raise awareness, gather the resources we need, and volunteer



June Kinoshita, Executive Director

Introducing June Kinoshita, the FSH Society's new Executive Director

It's our pleasure to introduce June Kinoshita, our new Executive Director.

June brings a rich background in biomedical initiatives, notably as the co-founder and Executive Editor of the Alzheimer Research Forum (www.alzforum.org), where she built and managed a multidisciplinary team of editors, writers, knowledge engineers, software developers, database designers and data curators. During her tenure, she worked closely with leaders from academia, industry and federal agencies to position Alzforum as the pre-eminent, game-changing website for the biomedical community.

June has worked closely with a variety of foundations to develop initiatives that resulted in major philanthropic investments in neurodegenerative disease research. As an Advisory Council member for the Harvard-MIT Division of Health Science & Technology, and as a Board member for the American Health Assistance Foundation, she has taken an active role in strategic planning for these organizations. June also has experience as an entrepreneur, having co-founded SocialLife, a start-up in healthcare social networks, and N-of-One, Inc., a pioneering personalized oncology company.

Previously, June pursued a successful career in science journalism, writing for and serving on the editorial board of Scientific American magazine and as a special assignment editor for the journal Science. She also helped create several television documentaries about neuroscience that were broadcast for national PBS audiences.

We look forward to working closely with June during this exciting time for the FSH Society. With her strengths as a science and health communicator and an innovative, strategic thinker, she is a great addition to our leadership team.

June can be reached at 617-658-7878 or june.kinoshita@fshsociety.org. Nancy Van Zant will be with us over the next few months as we transition and she can now be reached at 617-658-7891.

for critically important studies that will lay the foundation for future clinical trials.

So, thank you for your generous contributions. And thank you for showing up.

— June Kinoshita,
Executive Director

You can always contact me through the Society's Executive and Development Office: FSH Society, 64 Grove Street Watertown, MA 02472 USA 617-658-7878, fax: 617-658-7879 email: june.kinoshita@fshsociety.org

FSHD researchers dig deeper into the story surrounding *DUX4* gene

DUX4 expression is necessary but not sufficient by itself for FSHD

by **DANIEL PEREZ**

President and CEO of the FSH Society, Watertown, MA

Recent studies have proposed that FSHD is caused by the production of an abnormal protein, DUX4-FL. A new high-profile paper published this July reported that while DUX4-FL is indeed significantly over-produced in muscle from FSHD patients, the protein is also found at lower levels in relatives who are genetically unaffected by the disease. This discovery supports that DUX4-FL is necessary to cause FSHD, but other factors regulating the amount of DUX4-FL are involved in determining disease progression. What does this mean for future treatments? “*DUX4* is still a great therapeutic target,” says lead author Peter Jones, “but there are also going to be additional targets. This is great news.”

Facioscapulohumeral muscular dystrophy family studies of *DUX4* expression: Evidence for disease modifiers and a quantitative model of pathogenesis. Takako Iida Jones, Jennifer C. J. Chen, Fedik Rahimov, Sachiko Homma, Patricia Arashiro, Mary Lou Beermann, Oliver D. King, Jeffrey B. Miller, Louis M. Kunkel, Charles P. Emerson Jr, Kathryn R. Wagner, Peter L. Jones. *Human Molecular Genetics* 2012, doi: 10.1093/hmg/dds284

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Abstract: Facioscapulohumeral muscular dystrophy (FSHD), the most prevalent myopathy afflicting both children and adults, is predominantly associated with contractions in the 4q35-localized macrosatellite D4Z4 repeat array. Recent studies have proposed that FSHD pathology is caused by the misexpression of the *DUX4* (double homeobox 4) gene resulting in production of a pathogenic protein, DUX4-FL, which has been detected in FSHD but not unaffected control myogenic cells and muscle tissue. Here we report the analysis of *DUX4* mRNA and protein expression in a much larger collection of myogenic cells and muscle biopsies derived from biceps and deltoid muscles of FSHD affected subjects and their unaffected first-degree relatives. We confirmed that stable DUX4-fl mRNA and protein were expressed in myogenic cells and muscle tissues derived from FSHD affected subjects, including several



Peter Jones and Takako Iida Jones

genetically diagnosed adult FSHD subjects yet to show clinical manifestations of the disease in the assayed muscles. In addition, we report DUX4-fl mRNA and protein expression in muscle biopsies and myogenic cells from genetically unaffected relatives of the FSHD subjects, although at a significantly lower frequency. These results establish that DUX4-fl expression per se is not sufficient for FSHD muscle pathology and indicate that quantitative modifiers of DUX4-fl expression and/or function and family genetic background are determinants of FSHD muscle disease progression. FSH Watch

Carol S. Birnbaum, M.D., joins FSH Society Board of Directors



Carol S. Birnbaum, M.D., is a psychiatrist in private practice in Cambridge, MA. She is a graduate of Bryn Mawr College and the University of Connecticut School of Medicine. She completed her residency in psychiatry and a fellowship in biological psychiatry at Massachusetts General Hospital and is a graduate of the Boston Psychoanalytic Society and Institute. In March 2011, Carol lost her mother Barbara to complications related to FSHD. She is eager to promote the interests of the FSH Society in its search for a cure as well as the Society's support and guidance for patients and their families.

International research team discovers genes and disease mechanisms behind FSH muscular dystrophy

by **DEAN FORBES**
Science writer, Seattle, WA

Continuing a series of groundbreaking discoveries begun in 2010 about the genetic causes of one of the most common forms of inherited muscular dystrophy, an international team of researchers led by a scientist at Fred Hutchinson Cancer Research Center has identified the genes and proteins that damage muscle cells, as well as the mechanisms that can cause the disease. The findings are online and were reported in the January 17 print edition of the journal *Developmental Cell*.

The discovery could lead to a biomarker-based test for diagnosing facioscapulo-humeral muscular dystrophy (FSHD), and the findings have implications for developing future treatments as well as for cancer immunotherapies.

The work establishes a viable roadmap for how the expression of a gene called *DUX4* can cause FSHD. Whether this is the sole cause of FSHD is not known. However, the latest findings “are about as strong evidence as you can get” of the genetic link, said corresponding author Stephen Tapscott, M.D., Ph.D., a member of the Hutchinson Center’s Human Biology Division.

Tapscott and colleagues sought answers to the questions about what the *DUX4* protein does both normally in the body and in the FSHD disease process. In the latest study, they identified that the *DUX4* protein regulates many genes that are normally turned on in the male germ line (sperm cells) but are abnormally activated in FSHD muscle. The genetic material in germ line cells is inherited from parents and passed down to their offspring.

“This study is a significant step forward by solidifying that the *DUX4* transcription factor causes this disease, while offering a number of viable mechanisms for why the muscle is damaged,” Tapscott said. Transcription factors are tools that cells use to control gene expression. Genes are “expressed” in the body when the genetic code written in DNA is “transcribed,” or translated, into proteins. Proteins provide the building blocks of cells, and mistakes in how and when proteins are made can



Dr. Stephen Tapscott, M.D., Ph.D., a member of the Fred Hutchinson Cancer Research Center’s Human Biology Division

*“This study is a significant step forward by solidifying that the *DUX4* transcription factor causes this disease. Transcription factors are tools that cells use to control gene expression.”*

lead to disease.

Now that scientists know that *DUX4* turns on abnormal gene expression in skeletal muscle, a test could be developed to diagnose FSHD by examining muscle tissue for these abnormal RNA or proteins, Tapscott said. Such tests also could be used to determine how well new treatments are working to suppress FSHD.

The study also discovered that *DUX4* regulates cancer/testis antigens. These antigens (proteins on cell surfaces that get

recognized by the immune system) are normally found only in the human germ line, but are also abnormally expressed in various tumor types, including melanoma and carcinomas of the bladder, lung and liver.

“This knowledge now gives us a way to manipulate the expression of cancer/testis antigens, potentially opening the opportunity to use these antigens in a cancer vaccine,” Tapscott said.

Two papers published in 2010 by the same group of researchers established the genetic basis for showing that expression of *DUX4* was necessary for the disease. The previous research also showed that *DUX4* was normally expressed in the germ line, which led to the hypothesis that FSHD is caused by the failure to suppress *DUX4* outside of its normal role.

In addition to Tapscott and other Hutchinson Center researchers, scientists from the University of Washington, Genentech, the University of Rochester, and Leiden University Medical Center in Leiden, The Netherlands, contributed to the study.

The research was supported by grants from the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the National Institute of Neurological Disorders and Stroke, and Friends of FSH Research. [FSHWatch](#)

Adapted with permission from a January 2012 press release from the Fred Hutchinson Cancer Research Center.

FSHD CHAMPIONS: ACHIEVING FASTER PROGRESS BY WORKING MORE CLOSELY TOGETHER

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alone that are in intense competition with one another.

With that in mind Dan Perez, President of the FSH Society, and Kees van der Graaf, President of the Stichting FSHD and FSHD Europe, feel that now is the time to help align professional FSHD research and thera-

peutic efforts by coming together and leading by example to require/enforce a higher degree of sharing, openness and cooperation in the research community.

If all continues to go well, in the next five years we may arrive at the reality where

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Regeneration

by **KAREN MYERS**

Editor, *My Body of Knowledge*, San Francisco, CA

My left thigh is shrinking. I see a new hollow place where it used to be round and strong – or at least stronger. But the muscular dystrophy has sneaked in, shot through my body like an octopus's black ink, and resumed its cruel attack.

I panic every time this happens. Fear wraps around my diaphragm and shows me a slideshow of my worst-case scenario: myself in a wheelchair, dependent on everyone around me, separated from the world by a flight of stairs I can't climb. I don't ever feel the weakness approaching. I just look down at my body one day and see soft sunken skin, that of an old woman in a hospital bed with flabby flesh hanging from her bones. I noticed it in my right calf for the first time seven years ago. I know there is muscle loss all over my body in random spots, but I can't see my own bony back or the lack of firmness in my butt unless I twist into convoluted positions and stare into my full-length mirror. However, when I sit in the bathtub, knees bent, head resting on an inflatable pillow, there is no ignoring that my left thigh now looks nearly half the size of my right.

Thirty-one years ago when I was diagnosed with FSH muscular dystrophy at age 13, I was introduced to the word "degenerative." Every doctor I met told me this was the nature of the disease. Every muscular dystrophy brochure used the word. Even when my neurologist said enthusiastically, "You're doing great. You are degenerating at the speed of a glacier," there was always the understanding that loss of muscle would take place; it was just a matter of how much or how little. I always knew that to some degree my future body would be weaker than the present one.

For most of my life I have hated my body. It has let me down, taken away my ability to play tennis, go for long walks in the woods, carry a heavy bag of groceries. My body is disappearing on me – so slowly and subtly that I have been lulled into trusting its veneer of strength. I sometimes forget it is filled with invaders ready to attack whenever they see a moment of weakness, whenever they carry out a battle plan I don't understand.

Lately, though, something has shifted. I don't despise my body. I no longer curse its awkward gait or look with disgust at my thin right arm. I don't apologize for a physique that is less physically beautiful than it would have been without muscular dystrophy. Instead, I hate the disease. I hate the misguided group of cells or genetic imprint or chromosomal mishap that beats down my body. I hate that it lives with me. I tell it to leave.

I look at my thigh now and speak to it as if it were a child: "Oh, sweetie, I'm so sorry this is happening to you." I pour vanilla-scented massage oil into my palms and tenderly touch the sunken places of my body, sending them all my warmth. I pet my thigh with the same soft gesture I use on Lucy, the fluffy black cat I adore. I gather all the memories of love I have stored inside – the way I ooze with affection when I spend time with my nieces, the way I feel looking into the eyes of a lover – and I pour them onto myself.

Some months ago, I had abdominal surgery. I prepared for

“As I recovered at home, I watched in awe as my body began to heal. I had only associated my body with degeneration, but here it was mending.”



Karen Myers

it by listening to a meditation tape my mother gave me. A kind woman's voice led me through a series of relaxation techniques. I was guided through every part of my body, slowly softening the places from my head to my fingertips and toes. I imagined myself in my ideal place of relaxation – sometimes staring at the ocean, sometimes lying on a hammock looking up at a sky full of autumn leaves. I visualized my healing taking place.

This was easy to do when I prepared for surgery. I imagined my sweet, skilled surgeon smiling down at me as I lay asleep on the operating table. I imagined all the people praying for me to recover. I said goodbye to my ovary that was to be removed and thanked it for all it had done for me. I imagined waking up easily from my anesthesia, feeling no pain.

I listened to this tape three times a day right up to the moment

I was wheeled into surgery. And, as I had seen in my mind's eye, everything went perfectly.

As I recovered at home, I watched in awe as my body began to heal. I had only associated my body with degeneration, but here it was mending. Initially, I was unable to lie down in bed or sit very long in a chair because of the pain. My stomach was bloated. My incisions were tender and pink. I needed two canes to walk across the room. But every morning I awoke amazed at how much better I felt than the previous day.

I continued to listen to my visualization tape and envision changes taking place in my body. I saw all my beautiful, wise cells going in to repair the damage like a parade of white-uniformed nurses caring for a patient. I felt each breath bring in fresh air, circulation, and comfort. And then I imagined the next stage of my health: me full of energy sitting in a restaurant with my friends laughing and sharing food.

After a couple of months I was back to "normal." I was walking with my usual limp but without the canes. I could sleep in bed without wincing, and my stitches disappeared. But I keep playing that visualization tape.

Now, I imagine regeneration because I've seen it can be done. Instead of surgery scenarios, I lie down in the afternoon, close my eyes, and watch as all my muscles get larger and stronger. They intertwine like fingers until they are thick and solid. I envision a large, metal strainer going down my body removing all the specks of dirty, black disease. Then, I picture myself walking easily on a path by the ocean. I am talking with a friend and not even paying attention to each step I take. Sometimes I turn around and walk backwards as we chat, or I skip like I did as a kid. It is so easy, so effortless I feel it in my roots, down to my core. And as the tape ends, I wake up happy and rejuvenated.

I know my body has the ability to heal itself. I know my muscular dystrophy can be cured. I know this as surely as I know my body is deteriorating and there is nothing I can do. Somehow I can hold the paradox, knowing that both of these things are true. I never say my hopeful words out loud because everyone knows that muscular dystrophy is degenerative. I see it in my shrinking thigh. I feel the weariness in my right arm. And yet, when I close my eyes there is a place just as real where I am as fluid as I want to be. There is a place where my body is whole. [FSH Watch](#)



RESEARCH

FSH Society organizes and funds 18th international research workshop meeting for researchers and clinicians working on FSHD

The FSHD International Research Consortium workshop on Tuesday, November 6, 2012, in San Francisco, CA, brings together clinicians, scientists, patient representatives and policy makers to discuss the latest developments in FSHD. This year's meeting is made possible through generous contributions by The FSH Society, NIH BBRI Senator Paul Wellstone MD Cooperative Research for FSHD, Muscular Dystrophy Association (MDAUSA) and FSHD Global Research.

For eighteen years this workshop has provided the FSHD community with a forum to present and discuss new developments, reinforce collaborative efforts, facilitate new initiatives, and coordinate research and clinical activities. In the past year, there have been breakthrough publications on the molecular pathophysiology of FSHD, the evolving story around *DUX4*, animal and cellular models of FSHD, the use of RNA interference to cure FSHD in

an animal model, and advances in preclinical and clinical measures of FSHD. With so many advances and growing amounts of data and resources from groups around the world, the FSHD field is in greater need than ever for a meeting to disseminate new ideas and discuss new strategies, collaboration and coordination.

To facilitate participation from the U.S., Europe and globally, this year the workshop will be held in conjunction with the American Society for Human Genetics annual meeting. The workshop will pursue five goals:

1. Discuss new data and advances in FSHD;
2. Discuss strategies to verify and independently corroborate the findings;
3. Discuss focusing efforts and resources in the preclinical gap and translational phase of research;
4. Improve diagnostic techniques and criteria for FSHD; and
5. Consider and evaluate with industry new and existing therapies for the disorder.

We expect 90 to 100 attendees, including clinicians, scientists and representatives of funding organizations. Silvère van der Maarel, Ph.D. (Leiden University Medical Center, Leiden, the Netherlands), will be the European research Co-chair. Dr. Rabi Tawil (University of Rochester Medical School, Rochester, NY) will be the American clinical Co-chair. Daniel Perez, President & CEO of the FSH Society, will serve as organizational Chair.

The workshop includes platform, poster presentations and round table discussions. Attendees are requested to submit abstracts in advance. Abstracts are scored on priority and allocated to platform or poster presentations. An abstract booklet will be available at the meeting and will be posted on our website.

Researchers and clinicians interested in attending should contact Daniel Perez (daniel.perez@fshsociety.org). [FSH Watch](#)

Reflections on the Atlanta Patient-Researcher meeting

The state of FSHD research and what patients might expect in the next decade

by VALERIE RENOSTO

Student at University of Cincinnati College of Medicine, Cincinnati, OH



Atlanta skyline

This summer, researchers, FSHD patients and their families and friends met in Atlanta, Georgia for the 12th biennial FHS Society International Patient and Researcher Network Meeting. There were many great talks and a lot of fun as everyone caught up with old friends, made new friends, and learned about the state of FSHD research and what patients might expect in the next decade.

Learning about FSHD research begins with understanding how a genetic disease works. Like all living organisms, people are made of cells and within all cells is DNA that is organized into genes and packed into our chromosomes. When needed, these genes are activated, or “expressed”, to make proteins. Even though all cells have the same DNA, activating different genes in certain cells allows them to develop into different types of cells

such as muscle, bone, or skin. Which genes are activated in a given cell is controlled by many genetic and environmental factors. Activated genes are templates for proteins, so when genes are mutated the proteins made from them may be of the wrong shape, wrong number, or in the wrong place.

Most genetic diseases are caused by a mutated gene that produces a malformed protein, but FSHD is unique because the proteins produced have a normal shape, but there are just too many of them in the wrong place. Whether a gene is active or not depends in part on how much packaging is around it. More packaging makes a gene harder to activate, so that no proteins can be made from that gene. FSHD is linked to a deletion of a segment of chromosome 4 called the D4Z4 microsatellite repeat array. When the D4Z4 segment is deleted some of

the packaging in that area is lost and genes near the deletion are more easily activated and produce proteins when they should not.

Dr. Davide Gabellini described how the first improperly activated gene to be recognized in FSHD patients was FRG1. High levels of FRG1 have been found in the tissues of FSHD patients and more progress has been made with FRG1 than with other genes studied in FSHD. The function of FRG1 is not well understood, but activating FRG1 in mice caused muscular breakdown similar to FSHD. Researchers studying FRG1 have been exploring how to block it by developing molecules called micro-RNAs that keep genes from making proteins. When micro-RNAs were used to block FRG1 in FRG1-active mice, their muscles were able to function as well as unaffected muscles. So far this process has been safe,

effective, potentially applicable to other FSHD genes, and potentially applicable to other genetic disorders as well. There is still a lot of work to be done, but these results are promising.

Dr. Stephen Tapscott presented on *DUX4*, a more recently discovered gene that has spurred a lot of interest, and which is also activated by the D4Z4 deletion. *DUX4* is a gene that is present and active in other locations in the human genome, but not normally in muscles. Experiments have shown that when it is activated in muscle cells, it causes the cells to die and blocks defensin, a protein necessary for muscle cell regeneration. Studying *DUX4* has helped scientists propose a possible evolutionary explanation for FSHD: All primates have *DUX4* in this location next to D4Z4, but it's not active in other primates. The current hypothesis is that by reducing muscle mass *DUX4* allows for more expressive facial expressions – something that would have been an important evolutionary step for the social development of humans. Furthermore, the loss of upper body muscle would not have been a big deal to a species that was not swinging or climbing from trees as much.

In addition to looking at genes that cause muscle degeneration, researchers have begun to examine how *DUX4* interacts with genes involved in muscle regeneration. Dr. Michael Kyba explained that when a muscle degenerates, specialized cells called satellite cells replicate and fuse into new fibers that replace the lost muscle fibers. This process is controlled by genes called PAX3 and PAX7, which are turned on in replicating satellite cells but turned off in mature muscle fibers. Having *DUX4* inappropriately activated in a cell is thought to interfere with PAX3 and PAX7 activation, so that the satellite cells are not maintained or do not get signaled to repair the muscle.

There is no single gene that explains whether someone gets FSHD, how early in their life they get it, how severe it is, or which muscles it targets. These are determined by the interaction of many genes in the D4Z4 area and various environmental

factors. However, now that a few candidate genes have been identified, researchers can move on from 'what causes FSHD' to 'what can we do about it.'

There are several things that must be done in the coming decade for research in FSHD to progress. Before developing drugs, researchers must find a way to test them. As Drs. Charles Emerson and Gabellini explained, testing drugs requires a good animal model and good biomarkers. Biomarkers are biological factors that can be measured in mice, other animals or humans before and after an experimental treatment to determine whether a therapy is working. Without biomarkers there is no way to know if an experiment has worked or not. The animal models used right now for FSHD are mice that display FSHD-like muscle degeneration, but not the genetic patterns we see in humans with FSHD. Developing a better mouse model is crucial because the more differences there are between the mouse model of FSHD and human FSHD, the less likely it is that treatments that work in these mice will also work in humans.

Once biomarkers are identified and a

tissues so if blocking it in muscles also blocks it in these tissues there could be problems. Deciding which genes to target is not the only issue. A way to deliver the micro-RNAs into cells will also need to be developed.

How fast research progresses in the coming years will largely depend on how much funding FSHD researchers can get. The disagreement about which FSHD genes to target makes it look like no single idea has the 'best' chance of working, so it can be difficult to get funding. However, developing a mouse model and identifying biomarkers are essential steps for validating potential treatments and will make it easier to attract funding. Also, the fact that some of the work being done on FSHD, such as micro-RNA therapies, can be adapted to other diseases will make it easier to get funding because the research could benefit many more people.

In summary what I took out of the meeting was that a great deal of progress has been made in understanding how FSHD happens and, though there is more work to be done, researchers now have enough information to begin looking at possible treat-



“A great deal of progress has been made in understanding how FSHD happens and, though there is more work to be done, researchers now have enough information to begin looking at possible treatments.”

better mouse model is developed, research on therapies can progress. Researchers are looking at drugs to block a range of steps in the process that turns a normal cell to an FSHD cell, including: keeping genes from being activated, degrading the extra proteins produced, and simply blocking the protein from binding to the cells. Right now the most developed therapy is micro-RNA therapy. This has already been used to block FRG1 and may work for *DUX4*. However, *DUX4* is naturally active in some

tissues. Patients can help out by continuing to donate to the biopsy and cell repositories, by continuing to participate in research studies, and by continuing to raise public and political awareness of FSHD. [FSH Watch](#)

About the author: Valerie has facilitated sessions with young adults at the patient meetings in Las Vegas (2010) and Atlanta (2012). She has FSHD and is a second-year medical student at the University of Cincinnati College of Medicine.



A Guide for Schools is now available

The FSH Society is pleased to announce the publication of *A Guide for Schools*, in the Society's Living with FSHD series. The Guide is available online for download and print at www.fshsociety.org. You can also request a hard copy by emailing your request to info@fshsociety.org.

Created by a team of national experts, this booklet provides information about FSHD and the impact the disease can have on students' experiences during the school day. The goal is to help parents and teachers prepare for some of the challenges faced by students with FSHD, and to facilitate a positive experience for the teacher and the students.

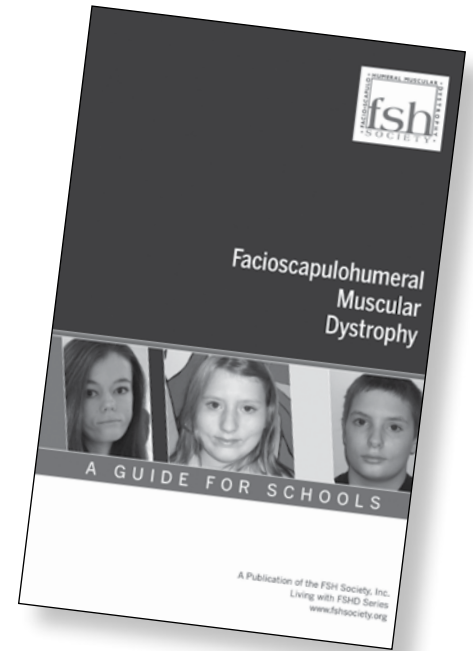
Sample topics:

- Using assistive technology to meet the needs of students
- Using a 504 plan or an Individualized Education Program (IEP) to outline services needed by the student

- The most common problems faced by students at school and strategies to address those problems
- Addressing the social and emotional aspects of living with FSHD
- Participating in physical education and extracurricular activities

The Guide was prepared by the University of Iowa Children's Hospital team of: Shelley R.H. Mockler, PT, MPT, ATP, Senior Physical Therapist; FSH Society Scientific Advisory Board member Katherine D. Mathews, M.D., Professor of Pediatrics and Neurology; and Anne M. Wallace, M.A., CCC/SLP, Clinical Associate Professor. Michelle Hosp, parent of a child with FSHD, also contributed.

The Society thanks the many individuals with FSHD, parents, therapists, teachers, and other school personnel who shared their personal and professional experiences, knowledge, and insight



to make this project possible. We also thank the S & L Marx Foundation for providing a generous grant for the production of the brochure. [FSH+Watch](#)

Get Social



Join our online communities to get news, ask questions, seek advice and support from fellow FSHD patients and family members, and enjoy one another's company. The FSH Society Yahoo! Groups forum, online since the 1990's, has tens of thousands of searchable posts. Bookmark these pages and come back often. To find the FSH Society Facebook page and Yahoo! Groups, go to our homepage at www.fshsociety.org, click on the "Community & Reference" menu tab at the top of the page and select "Online Community" in the left side vertical navigation menu. You'll see links to take you directly to our Facebook page and Yahoo! Group. If privacy is a concern, you can use your account privacy settings to limit who can see your posts. You can also follow us on Twitter @FSHSociety.



FUNDRAISING

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, please let us know by contacting june.kinoshita@fshsociety.org. 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," please contact us.


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 may affect you. [FSH+Watch](#)

Biennial FSHD International patient and researcher network meeting a success!

The 2012 International Patient and Researcher Network Meeting was held at the Atlanta Marriott Marquis, in Atlanta, GA on Saturday-Sunday, June 30-July 1, 2012. This was the twelfth FSHD patient-researcher meeting and it was a resounding success! Over 180 attended, from as far away as Brazil, Canada, Taiwan, and from 23 U.S. states. Thank you to all attendees and presenters for making this the best conference yet. You can view the final program at <http://www.fshsociety.org/assets/pdf/FSHSocietyIPRNTentativeProgram.pdf>.

Leaders in the field of FSHD gave lectures, reported on the latest findings from major clinical and research centers and participated in question and answer sessions with the audience. There were educational sessions on breathing and respiration, and on exercise and physical therapy. Popular breakout sessions included topics that participants have requested as well as those that addressed the interests of teenagers and young adults. If you could not attend, you can listen to and view all of the presentations on the Web:

- Day 1 <http://www.presentationrecreation.com/fsh-society-day-1/>
- Day 2 <http://www.presentationrecreation.com/fsh-society-day-2/>

The FSH Society's biennial International Patient and Researcher Network Meeting is a partnership among patients, families, clinicians and scientists. The Society wishes to thank the Association Française Contre les Myopathies (AFM), Athena Diagnostics/Quest, Cytokinetics, Inc., FSHD Global Foundation, Genzyme, NIH NICHD Boston Biomedical Research Institute Sen. Paul D. Wellstone MD Cooperative Research Center for FSHD Research and Philips Respironics for their generous sponsorship of the 2012 Meeting. We also wish to thank this year's presenters and all attendees for their contributions to the success of this meeting. 



"Junk" DNA actions may explain FSHD

by **DEBORAH HALBER**
Science writer, Cambridge, MA

A never-before-seen defect in gene regulation underlies FSHD, one of the most common but little-understood forms of muscular dystrophy, Milan researchers reported in the May 7, 2012, issue of *Cell*.


The study also identified a potential therapeutic target--a long non-coding RNA (lncRNA) the researchers dubbed DBE-T. The work may explain how "junk" DNA, which makes up more than half of our genome but does not code for proteins, may come into play in other diseases, including

some forms of diabetes and cancer.

In 1992, FSHD was traced to a deletion in a region of chromosome 4. Scientists assumed that FSHD would follow the classic pattern: mutation of a gene and loss of its corresponding protein.

The Milan researchers found that, instead, FSHD is caused by a lncRNA attaching at a specific "junk" DNA address on chromosome 4 known as D4Z4, that in turn recruits a suite of proteins that cause nearby genes on the chromosome 4 to be disregulated.

This in turn results in excess production of apparently toxic proteins, leading to FSHD. Examining muscle biopsies, the team saw DBE-T RNA transcripts binding to a section of "junk" DNA exclusively in FSHD patients and not in healthy subjects.


They also demonstrated that blocking the production of DBE-T normalized gene expression in the FSHD region of the genome, suggesting that DBE-T may be a promising therapeutic target for controlling the disease. 

FSHD CHAMPIONS: ACHIEVING FASTER PROGRESS BY WORKING MORE CLOSELY TOGETHER

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clinical trials with patients will commence. To have successful trials, we need to be prepared. There are multiple things that will need to happen that will only be achieved by working together and leveraging our resources. More importantly we need to ensure that the rights of the people with FSHD are respected.

Messrs. Perez and van der Graaf have co-organized a meeting titled "FSHD Champions" to be held alongside the FSHD International Research Workshop in early November in San Francisco, CA,

USA. One to three members from each organization will attend. Thus far executive staff from Association Française contre les Myopathies – AFM, Carrino Foundation, FSHD Canada, FSHD Europe, FSHD Global Research Ltd, Stichting FSHD, FSH Society, Muscular Dystrophy Association (MDA), National Institutes of Health, Pacific Northwest Friends of FSHD, Shaw Fischer families, and VSN Netherlands will attend to discuss how to achieve faster progress by working more closely together. 

The FSH Society funds advances in understanding and treating FSHD

Grant Awards for the February 2012 Cycle

The FSH Society Scientific Advisory Board (SAB) met in June 2012 to review grant applications received for the February 2012 round of FSH Society grants funding.

Since 1998, the FSH Society has transformed FSHD research. The field is on the verge of significant breakthroughs. It is essential to fund new ideas and support new investigators and new lines of investigation when tackling a disease as complex as FSHD.

The scientific engine of the FSH Society is its Scientific Advisory Board. Scientific progress requires having the most qualified panel of experts who not only evaluate the merit of new proposals they receive, but are also actively engaged in thinking proactively and comprehensively about the scientific problem. Peer-reviewed science is key to research success, and the peer review must be just that — review by scientists and doctors who have comprehensive, up to date command of the science and can evaluate the proposed investigations in light of the science. [FSHWatch](#)

We are very pleased to announce the following grantees funded in the February 2012 cycle:

- ▶ **A transgenic model of DUX4-mediated FSHD**
 Peter Jones, Ph.D.
 Boston Biomedical Research Institute
 Watertown, MA
 \$105,000 over 2 years, \$60,000 year 1, \$45,000 year 2
- ▶ **Expression of human DUX4 in zebrafish development**
 Hiroaki Mitsuhashi, Ph.D. / Louis Kunkel, Ph.D.
 Children's Hospital Boston
 Boston, MA
 \$60,000 over 1 year
- ▶ **FAT1 roles in muscular physiology and FSHD onset**
 Virginie Mariot, Ph.D. / Julie Dumonceaux, Ph.D. and Gillian Butler-Browne, Ph.D.
 Thérapie maladies du muscle strié / Institut de myologie
 Paris, France
 \$68,000 over 1 year
- ▶ **A humanized mouse model for investigations of FSHD pathology and therapeutic development**
 James Windleborn, Ph.D. / Charles Emerson, Ph.D.
 Boston Biomedical Research Institute
 Watertown, MA
 \$60,000 over 1 year
- ▶ **Tri-dimensional organization of the FSHD locus during proliferation and differentiation of muscle cells in FSHD patients and controls**
 Marie Gaillard, M.S. / Frederique Magdinier, Ph.D.
 INSERM UMR_S 910, Epigenetics, chromatin & diseases team
 Faculté de Médecine de la Timone Marseille, FRANCE
 \$30,000 over 1 year

How the FSH Society awards grants

Since 1998, the FSH Society has transformed FSHD research by providing vital start-up funding for investigators and research projects. The milestones and insights gained have been significant. The program allows innovative and entrepreneurial research to develop, prove successful, and ultimately attract funding from major sources such as the US National Institutes of Health (NIH) and large private philanthropies.

The FSH Society has two rounds of grant applications each year, with deadlines in February and August. Grant applications are reviewed by the Society's Scientific Advisory Board (SAB), whose members serve without pay.

Investigators submit an initial letter of intent, which is reviewed by Professor David Housman, Chair of the SAB. If a letter of intent is accepted, the applicant submits a full application, which includes detailed description of the proposed work and workflow. Professor Housman assigns teams of two or more SAB members to critique each proposal. SAB members who may have a conflict are not assigned to review, and do not vote on, the particular proposal.

The reviewers read the application in depth and provide a detailed written description and recommendation to the other members. Grant applications are reviewed and voted upon by the entire SAB (except any who may have a potential conflict). Applications that the SAB recommends for approval are then sent to the Society's Board of Directors for a vote. When the SAB declines an application, it provides the applicant with a detailed description of the reasons, and the applicant may resubmit the application for consideration in a later round.

Investigators must report satisfactory progress every six months in order to receive subsequent installments of the grant funding.



THE FSH SOCIETY AT THE CUTTING EDGE

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The genetic mechanism of FSHD is unlike any previously reported in human disease. The gene defect underlying FSHD occurs in part of the genome commonly known as “junk” DNA. Unlike the genes we learned about in high school biology, this type of DNA tells our cells not what protein to make, but when and where. In FSHD, a defect in “junk” DNA causes a protein that is normally not active in muscle to be produced at high levels. This protein is suspected of causing muscles to degenerate. The Herculean effort to crack open the genetic origins of FSHD is now paving the way to an entirely new understanding how genes work.

FSH Society funding has allowed researchers to characterize FSHD, first in the cell, then at the chromosome level, where the disease-causing defect was pinpointed to a specific address on the chromosome called 4q35. This then led to the discovery that a repetitive DNA pattern at 4q35, called D4Z4, is truncated in FSHD patients. Normally, people have between 11 and 150 D4Z4 repeats, but FSHD patients usually have fewer than 11.

In the past two years, research initiatives fueled by funding from the FSH Society and others have begun to shed light on how the loss of D4Z4 may drive the development of FSHD. In August 2010, Dutch and American researchers published a paper that dramatically expanded our understanding of the mechanism of FSHD.² Two months later, a paper published in *PLoS Genetics* made a second critical advance in determining the cause of FSHD.³ This research showed that FSHD is caused by a gene that is normally expressed only during very early embryonic development, as well as in the male germ (sex cell) line.

In January of this year, an international team of researchers led by Stephen J. Tapscott, M.D., Ph.D., of the Seattle Fred Hutchinson Center, published a third major advance further elucidating the mechanisms that can drive the disease genes and proteins that damage FSHD muscle cells. The researchers also discovered that one of the genes required for FSHD, called *DUX4*, regulates cancer/testis antigens.⁴ Cancer and testis antigens are abnormally expressed in various tumor types, including melanoma and carcinomas of the bladder, lung and liver. These antigens may be attractive targets for new cancer vaccines.

In April, researchers who began their careers with FSH Society fellowships published a paper in *Cell* which for the first time reported that a long non-coding RNA (lncRNA) regulates gene expression and may be involved in FSHD.⁵ Two FSH Society fellows, Daphne Cabianca, Ph.D., and Davide

factors governing the amount of *DUX4*-fl expression and/or function are the determinants of muscle disease progression.⁶

What does this mean for future treatments? “*DUX4* is still a great therapeutic target,” says lead author Peter Jones, “but there are also going to be additional therapeutic

“In the past two years, research initiatives fueled by funding from the FSH Society and others have begun to shed light on how the loss of D4Z4 may drive the development of FSHD.”

Gabellini, Ph.D., of the San Raffaele Scientific Institute, in Milan, Italy, and their colleagues in Milan and Tokyo, Japan, reported that this lncRNA behaves as a “master switch” to unleash *DUX4* and other genes in the 4q35 region associated with FSHD. This discovery opens the possibility of controlling FSHD by going after this master switch.

In July, another high-profile paper was released online in the journal *Human Molecular Genetics*. The paper comes from researchers working at the NIH-funded Wellstone Muscular Dystrophy Cooperative Research Center for FSHD based out of the Boston Biomedical Research Institute, in Watertown, MA. Takako I. Jones, Ph.D., and Peter L. Jones, Ph.D., first and last authors on this paper, are past and current FSH Society grant recipients and the Society is acknowledged in the paper. The study analyzed the large collection of muscle precursor cells and muscle biopsies derived from FSHD affected volunteers and their unaffected first-degree relatives.

The Wellstone researchers confirmed that stable *DUX4*-fl mRNA and protein were expressed in cells derived from muscle tissues of FSHD-affected subjects. However, *DUX4*-fl expression was also detected in several volunteers who carry the FSHD1 genetic mutation but do not yet show clinical symptoms or weakness in the muscles that were analyzed. In addition, they reported *DUX4*-fl mRNA and protein expression in muscle biopsies and myogenic cells from genetically unaffected relatives of the FSHD subjects, although in a significantly smaller percentage of cells. These results establish that *DUX4*-fl expression per se is not sufficient for FSHD muscle pathology and indicate that other

targets. This is great news.”

The FSH Society is pleased that, with the ongoing generous donations from Society members, it can continue to support both “mainstream” research objectives and well-founded alternative hypotheses. FSH Society SAB member, Dr. Michael R. Altherr of the Los Alamos National Laboratory in New Mexico, sums it up by saying: “These funds have served as a catalyst to support a diverse portfolio of scientifically based research endeavors that are expediting our understanding of the molecular pathology of FSHD. Only after we understand the genetic consequences of the FSHD mutation will we be able to design strategies to ameliorate the consequences of the genetic aberration.” FSH Watch

¹ Kolata, G. Reanimated ‘Junk’ DNA Is Found to Cause Disease. *New York Times*, August 19, 2010. <http://www.nytimes.com/2010/08/20/science/20gene.html>

² Lemmers, RJ, et al. A Unifying Genetic Model for Facioscapulohumeral Muscular Dystrophy. *Science*, September 24, 2010. Vol. 329, no. 5999, pp. 1650-1653.

³ Snider, L., et al. Facioscapulohumeral dystrophy: incomplete suppression of a retrotransposed gene. *PLoS Genetics*, October 28, 2010.

⁴ Geng, LN, et al. *DUX4* Activates Germline Genes, Retroelements, and Immune Mediators: Implications for Facioscapulohumeral Dystrophy. *Developmental Cell*, December 29, 2011. Vol. 22, no. 1, pp. 38-51. doi:10.1016/j.devcel.2011.11.013.

⁵ Cabianca, DS, et al. A Long ncRNA Links Copy Number Variation to a Polycomb/Trithorax Epigenetic Switch in FSHD Muscular Dystrophy. *Cell*, April 26, 2012. Vol. 149, No. 4, pp. 819-831. doi:10.1016/j.cell.2012.03.035.

⁶ Jones, TI, et al. Facioscapulohumeral muscular dystrophy family studies of *DUX4* expression: Evidence for disease modifiers and a quantitative model of pathogenesis. *Hum. Mol. Genet.*, published online July 13, 2012. doi: 10.1093/hmg/dds284.



Remembering Carol Perez

by ANN BIGGS-WILLIAMS

FSH Society Board member, Brewton, AL

“We are fam-i-ly” sang Carol Perez from her motorized scooter as she bravely led fellow attendees of an FSH Patient Conference, over dinner at a restaurant in Rockville, MD, in 2002, amid the height of the sniper scare. If those of us with FSHD are a family, then Carol Perez served as the matriarch. I often called her “Mama” Perez and phoned Carol with some of those questions one might only ask one’s Mother.

Carol Perez, who served as the first Executive Director of the FSH Society, was truly patient-oriented. Carol had that wonderful ability to listen, really listen, and wanted to hear everyone’s FSHD “story.” We now know that it is therapeutic to tell your story. When you are diagnosed with a disorder like FSHD, it is important to have someone to listen to your questions, who will give you positive steps to take. For many years, when someone phoned the FSH Society, Carol was the voice on the other end. I think many people who phoned never knew that Carol was affected with the disease. Certainly after knowing Carol, the scooter became invisible and there was just Carol, a complete encyclopedia of knowledge about FSHD. Carol never used her disability as an excuse and stayed involved with the Society, serving as Secretary of the FSH Society’s Board of Directors at the time of her death. Carol was excited and optimistic about recent research.

In the early days of the FSH Society, Carol and her husband Charles operated the East Coast office of the Society from their home. Charles was the wind beneath her wings. The Perez duo worked diligently to support son Dan’s efforts in the founding of an



Carol and Charles Perez

organization dedicated to Facioscapulo-humeral Muscular Dystrophy.

As an after-dinner activity at one FSH Patient Conference, we invited audience participation in a “You might have FSHD if...” activity. One popular response that garnered audience approval was: “You might have FSHD if you have Carol Perez on speed dial!”

One of those panicked times I phoned Carol Perez was on a Friday afternoon in February of 2007. I experienced a sudden change in vision and was told by an eye specialist that it was a vitreous detachment, just a part of growing older and not to worry about it. The very next day while taking a photograph midday, I only saw glare reflecting from a tin roof with my right eye through the camera lens. In a few hours, I could not read the letters on a stop sign with my right eye. I phoned Carol to ask about retinal problems with FSHers and Carol said, “Get to a retina specialist now!” So I drove to the nearest town and got to a specialist at about 5 p.m. on a Friday afternoon. The retina

specialist immediately did laser surgery on what was a tear in my retina. Needless to say, I credit Carol’s urgent advice with saving my vision in that eye.

One might search online for information on Facioscapulo-humeral Muscular Dystrophy but the Internet can’t hold a candle to what Carol Perez knew about FSHD.

Carol, you are part of us and we are part of you. We are family and we miss your physical presence, but your spirit abides with us.

We continue this journey towards a cure to honor your memory. [FSH Watch](#)

In Memory of Carol A. Perez, 1935–2012

Carol Anne Perez, 76, died on February 3, 2012, in Lexington, MA, from respiratory complications of FSHD. Carol was a founding member of the FSH Society, its first Executive Director and served as Secretary for many years. For hundreds of newly diagnosed FSHD patients, she was the first other person with FSHD they met, and the first person they turned to for moral support and practical advice to help them confront their diagnosis. Prior to serving the FSH Society, Carol was Area Director for the Massachusetts Rehabilitation Commission. Born and raised in Queens, New York, she earned a Master’s in Education from Northeastern University. She was an authority on vocational rehabilitation and leaves behind a legacy of assisting

countless numbers of people with disabilities and diseases to lead better lives. She sought to see the best in every individual and was tireless in the battle against injustice to the ill and disabled. She lived her final days with dignity in her own home surrounded by loved ones. She is survived by her devoted husband of 55 years, Charles; son Daniel and his wife Susan; daughter Rosanne Sterne and her husband Ned; and grandchildren Annelise and Clifton Dawson and Gabriella and Camilla Sterne.

Those wishing to honor Carol’s memory may make a donation to the FSH Society, 64 Grove Street, Watertown, MA 02472 or online at www.fshsociety.org.

MAZEL TOV ALEX! WE'RE GRATEFUL FOR YOUR GENEROSITY



For his Bar Mitzvah in March, Alex Whitman raised funds for the FSH Society. His friends made gifts in his honor and he also sold popcorn at his synagogue. Alex's effort, totaling more than \$1,600, was a tribute to his grandfather, who is affected with FSHD.

FSHD CANADA FOUNDATION — NOW OFFICIAL!

Great news for Canadians who wish to support FSHD research! The FSHD Canada Foundation has received tax-exempt status from the Canadian tax authorities. This means that Canadians can now donate funds directly towards FSHD research — and get a tax deduction. The FSHD Canada Foundation website is at www.fshd.ca. If you have questions, please feel free to contact the President of FSHD Canada, Neil Camarta, at neil@camarta.ca or 403-470-0141.

Canada



Greetings from Distrofia Muscular FSH en Chile

Distrofia Muscular FSH en Chile (FSHD in Chile), is an association founded by Roberto Alvarez, who has FSHD, and his friend Andrea Cid. It was established in 2009 on the Internet, with the intention of providing a meeting place for other people with FSHD. Roberto and Andrea did not know anyone else who had FSHD, and the information provided by the doctors at the hospital where Roberto goes was insufficient. At the beginning, their goal was to bring together people with FSHD and their families and friends. Subsequently, they started to exchange information between the other members, with the aim to help each other. They started with only five members, and now they have more than 150, from many countries. Most of the members are from Chile, followed by Spain, Argentina and Uruguay, among others.



The group's principal objectives are to learn about:

- Research on FSHD
- Nutrition in FSHD
- How each member copes with FSHD
- Assistive technology
- Potential therapies

You can find this association on Facebook:

<http://www.facebook.com/groups/37192057832/> (group)

<http://www.facebook.com/pages/Distrofia-muscular-facioescapulo-humeral-en-Chile/296547130360560> (fan page)



Andrea Cid and Roberto Alvarez



Remembering Cosmo (“Larry”) Laurello

by LARRY, MICKEY AND PAUL LAURELLO
Sons of Larry Laurello, Saybrook, OH

There comes a time in our lives when we have to celebrate someone’s life because they have passed into another place. When we wish we had one more moment, one more kiss, one more hug, and in our case one more talk. Our father was the most amazing man we have ever known and probably will ever know. He was a husband, a father, a grandfather, a friend, and a teacher. He taught his family how to love, how to laugh, how to cry, how to be humble, and how to live life every day. When we think of our father we are flooded with the most amazing memories, stories, and lectures that made us who we are today. His life is a legacy that we can all learn from and never forget.

Our father taught all of us how to have empathy for others. He would always say to us “try and put yourself in someone else’s shoes when making any kind of decision. If after you do that, your decision is the same then you have made the right choice.” The most important thing he taught all of us is that perception is key. How others perceive you is the key that unlocks all doors. Although today things are not done with handshakes anymore because of the loss of trust among people, Dad was a man of his word, and he taught his entire family to be the same. If he said he would do something, there were no questions asked because everyone trusted him. He lived his life this way always.

He was the first person we went to with a problem, as many of you probably did. His intelligence astounded us; he was a wealth of knowledge and insight, always knowing what to say. The way he spoke and what he said always seemed to be the right thing, because after we were done talking to him, we couldn’t even remember what we were upset about in the first place.

Even though he had an incredibly difficult handicap, he took lemons as they say and made lemonade, and it was always sweet. He took his disability and instead of making it a curse made it one of the blessings of our family, because without his disability our family would not be as close as we are. Ida and Larry are the foundation of our family and from them we grew. Many of you know that the Laurello family does not just extend to blood relatives. We have a huge family. Everyone at Delta was loved by Larry and is still loved by all of us. If you wanted to be a part of our family there were no questions asked, Larry welcomed everyone with open arms, and that is how he taught all of us.

Although he could not walk, he had a passion for life like no other. He loved living through what his family did. We can remember the countless number of times that we would be at Mom and



Mr. Larry Laurello (second from right, seated) and sons

Dad’s house talking about everything. The stories that were told and still will be told in their house could fill a library. This brought the most joy to Dad.

You have to believe that in the balance of life, things always come full circle. That we are all in so much pain right now just means that his life was so great and brought so much to each one of us. It is only fair that the gifts we received from him during his life are matched by

“ Try and put yourself in someone else’s shoes when making any kind of decision. If after you do that, your decision is the same then you have made the right choice. ”

the pain we feel now. So celebrate life now, because the pain you go through when you lose someone is worth it. Although we wanted to keep Dad on earth as long as we could, I guess God and all the angels needed an engineer in heaven more than we needed him here. When we meet again, we expect that we will see the most amazing place you can imagine because Dad is there. FSHWatch

Editor’s note: After Larry’s passing, his widow Ida kindly agreed to join the FSH Society’s Board of Directors. Larry’s sister JoAnn Forance also serves on the Board.



Origami hearts for FSHD

by MIMI GARCIA

FSH Society member, Calabasas, CA

I have been looking for an opportunity for my son Damien to get involved with FSHD awareness and fund raising at Calabasas High School (CHS) in California. With the great help of my older son Sixto, I decided to write an article about my two sons with FSHD for the local newspaper, *The Acorn*, and to get in touch with Sixto's former French teacher at CHS, Madame Bogoshian. She put me in contact with the Associated Student Body advisor, who supported my wish that students participate in a fundraiser for the benefit of the FSH Society.

Derek Shui, the Origami Club advisor in Calabasas High School, was willing to help me find a way of raising the funds. I did not want an event of the bake-sale variety. So, I made a presentation about FSHD at CHS in Madame's class during lunch time to about 40 students (some of them club advisors), and at the end of the presentation we came up with an idea. We decided that we would run an Origami project for the fundraiser, and we would have it during the month of March while calling it the "Month for FSHers". With the leadership of Derek, his team of about a dozen students started to make small Origami hearts.

The first 200 hearts were made and sold in honor of Carol Perez who passed away in February and also in honor of the late Larry Laurello, who left us in January. Derek had no idea how many hearts to make. On March 15, I joined the team during lunchtime in the main court where we had a table displaying information about FSHD, brochures, and even a poster on muscular dystrophy that one of the students had made for a project. We went table to table explaining the reason for the fundraiser and selling hearts at \$1 each.

By the end of the month of March, Derek's team of about 24 students as well as Madame's had raised \$1,700. Madame had also made a couple of trays of baklava which she sold with great success. To thank all participants of CHS for helping to raise funds and promoting awareness about FSHD, I presented a plaque of gratitude to Derek and his team at a general assembly at CHS on April 25. I also gave them the



Raising FSHD awareness at Calabasas High School (CHS) in California



Damien and Sixto Garcia

new *Guide for Schools*, written by Katherine D. Mathews, M.D., and her expert team at the University of Iowa Children's Hospital. CHS runs a few charity fundraisers every year; we are now one of them that I hope Damien will run with his new peers again

next year.

Middle schools and high schools are great places for promoting awareness about FSHD. Should you want to follow this effort, start by contacting your local schools and present the *Guide* as a first step. [FSH Watch](#)



In Memory of Marjorie Bronfman and Edward Schechter

by **CORINNE BRONFMAN**

FSH Society member

Two strong long-term supporters of the FSH Society died this past year: Edward Schechter (died July 2, 2011) and Marjorie Bronfman (died February 24, 2012). They were brother and sister. When Ed became aware of the Society in 1996, it was the first time he had met others with the disease that was increasingly disabling him. He got his sister and the Marjorie and Gerald Bronfman Foundation interested in supporting the work of the FSH Society. Marjorie herself was affected with a milder form of the condition, but her generosity came from her dismay at how the disease was affecting her brother and its potential impact for generations to come.

Both were strong supporters of communal activities — Ed in Shavertown, Pennsylvania, Marjorie in Montreal, Quebec — but it is their support of the FSH Society that we recognize here.

Ed cared deeply about the FSH Society, patients and their families. He eagerly awaited the reports that showed membership growing and funds increasing. He used his experience as a business executive to guide his efforts on behalf of the FSH Society. He knew that the long-term viability of the Society required a strong base of support. Marjorie and Ed cared deeply about the quality of the research and the support of the researchers whom the Society identified. The thoroughness of the Society's reporting allowed them to be excited about the research and therefore to encourage the Society to focus on its organization and strength. (For more about Ed, see the Summer 2011 *Watch*, page 4.)

With their deaths, the FSH Society is deprived not only of their committed support but also of their wise counsel. [FSH Watch](#)

At the wishes of Ed's family and friends, the FSH Society has established the Ed Schechter Fund for FSHD, an endowment fund to recognize his many years of care and concern not only for the FSH Society and FSHD research, but also his keen interest in the individuals carrying out this research. When you make your 2012 gift at this time, please join with others in remembering Marjorie Bronfman and Edward Schechter and make a gift to the FSH Society's Ed Schechter Fund for FSHD to support research.



Marjorie Bronfman



Edward Schechter

Grants funded by the Marjorie and Gerald Bronfman Foundation

These are the 19 FSH Society fellowships/grants funded with gifts from the Marjorie and Gerald Bronfman Foundation over the years. Nearly all of these studies have formed the basis of the breakthrough research going on today with many resulting in landmark publications.

Silvere M. van der Maarel, Ph.D., "Generation of Transgenic Mouse Models for FSHD." 1998 - 2002

Sara T. Winokur, Ph.D., "Analysis of Chromatin Structure and Skeletal Muscle-Specific Gene Expression in FSHD." 1998 - 2001

Denise Figlewicz, Ph.D., "Expression of genes proximal to the D4Z4 deletions: a quantitative study in FSHD patients and controls." 1999 - 2000

David J. Picketts, Ph.D., "Utilizing an epigenetic approach to identify the FSHD gene." 1999 - 2001

Davide Gabellini, Ph.D., "Identification and characterization of a protein interacting with the DNA repetitive element causally related to FSHD." 2000 - 2002

Fern Tsién, Ph.D. and Melanie Ehrlich, Ph.D., "DNA Methylation and Chromatin Structure of FSHD-linked Sequences in FSHD Cells, Normal Cells, and Cells from Patients with the ICF Syndrome." 2001 - 2003

Tonnie Rijkers, Ph.D. and Silvere M. van der Maarel, Ph.D., "Mouse models to study candidate genes and epigenetic causes of FSHD." 2003 - 2005

Cecilia Ostlund, Ph.D. and Howard Worman, Ph.D., "The role of *DUX4* in FSHD." 2003 - 2005

Alberto Luis Rosa, M.D., Ph.D., "Role of nuclear localization signal (NLS) and H1/H2 motifs in *DUX4*-mediated cell death." 2004 - 2006

Richard Lemmers, MSc., Ph.D., "Refinement of the FSHD critical region on 4qA chromosomes." 2005 - 2009

Yi-Wen Chen, D.V.M., Ph.D., "Molecular Mechanisms of Muscle Atrophy in FSHD." 2006

Davide Gabellini, Ph.D., "Development of an Animal Model of FSHD." 2006

Melanie Ehrlich, Ph.D., "Finding the 4q35 FSHD Gene." 2006 - 2008

Patrick Reed, Ph.D., "Analysis of Changes in the Proteome in FSHD." 2007 - 2009

Yvonne Meijer-Krom, Ph.D., "Towards the Discovery of Early Developmental Defects in FSHD." 2007 - 2009

Darko Bosnakovski, D.V.M., Ph.D., "Molecular Analyses of *DUX4* and Interaction with Myogenic Regulators in FSHD." 2007 - 2008

Paola Picozzi, Ph.D. and Davide Gabellini, Ph.D., "Functional characterization of D4Z4 in FSHD." 2007 - 2009

Alberto Luis Rosa, M.D., Ph.D., "Analyses of functional domains in the pro-apoptotic protein *DUX4*" 2009-2011

Richard J.L.F. Lemmers, Ph.D. and Silvere van der Maarel, Ph.D., "Identification of the epigenetic mechanisms that regulate *DUX4* activity in skeletal muscle." 2011-2013

Hot 'Lanta and the 'Rents

by **CHRISTIANE WYCKOFF**
Teacher, Atlanta, GA

It was a typical summer day in Hot 'Lanta, high humidity and 100 plus degrees, when 200 people gathered for the FSH Society Biennial Conference in downtown Atlanta. Thank heavens for air conditioning!

The event was a first for our family of five, but it will certainly not be our last. As a mother of one daughter with FSHD, Carden, 19 years old, I anxiously anticipated the opportunity to learn about the latest research, therapies, and meet other parents whose journey was similar to mine. I was not disappointed.

After the learned physicians and clinicians presented their findings, we broke into small groups to share on a more intimate level our experiences, concerns and questions. Our small group was comprised of about 28 parents who had children with FSHD, and was beautifully spearheaded by Jeff and Barbara Bache. Some of the attendees were parents whose child had recently been diagnosed while others were clearly veterans. Some parents travelled from Venezuela, Brazil, Taiwan and Canada, but most were from the U.S. Each brought a unique version of their trials and celebrations to our group and shared their journey.

One of the most positive side effects of the parent group meeting happened by accident and was, in reality, totally selfish on my part. It occurred to me that once the 48-hour conference was over, I would return to my very frustrated and lonely place living in



The Wyckoff family

Atlanta without a support group or medical care that understood FSHD and being the only parent I knew with a child/young adult with the disease. I would still be isolated, patiently awaiting an FSH Watch or news tidbit. So, the Parent FSH Email list was created in a grassroots effort to link parents together to provide a means for support, advice, comic relief, opinions, fundraising ideas, sense of community, and friendship.

Although I recognize that social networking sites are wonderful tools for our children, email is still the preferred method to use for

the parent generation. Perhaps that will change in the future. At present, we are 18 strong and growing. So, if you are interested in joining the FSH Parent Group please contact June Kinoshita (june.kinoshita@fshsociety.org). It would be helpful to include where you live, email address, phone number, child/young adult/adult child's name and age, as some of us contact the entire list while others direct their emails to individuals with similarly aged children or geographic location.

Hot 'Lanta certainly lived up to its name and the conference was wonderful, but my new parent friends are priceless! I no longer feel the isolation and fear that I did prior to the meeting. There is hope and most importantly, strength in numbers! We look forward to having you join our group! [FSH Watch](#)



NEWS AND EVENTS

We need volunteers for the 2012 Combined Federal Campaign (CFC)

The CFC is the world's largest and most successful annual workplace charity campaign, with more than 300 CFC campaigns throughout the country and internationally to help to raise millions of dollars each year. Pledges made by Federal civilian and military donors during the campaign season (September 1st to December 15th) support eligible non-profit organizations that provide health and human service benefits throughout the world. We need volunteers to represent the FSH Society at CFC fairs around the country, to hand out our information to potential donors. It's a great way to raise awareness and engage a larger community in supporting FSHD research! Please email june.kinoshita@fshsociety.org if you are interested in volunteering. The FSH Society's CFC identification number is 10239. [FSH Watch](#)



SWIM LIKE A FSH!



Haviva Ner-David, an FSHD patient, participated in the Israel Women's Triathlon in June to raise money for the FSH Society. Family and friends contributed nearly \$7,000 in Haviva's honor. Thank you, Haviva and supporters! (Haviva is being helped out of the water by a volunteer, left.)

New books



You're not alone with FSHD
 By Anke Lanser
 Translated from Dutch
 \$17, including postage and shipping

This book illustrates what it is like living with FSHD. It includes stories, poems and photos of people with FSHD, as well as general information about the disease. People speak movingly about their life with this difficult disorder. All profits go to FSHD Europe and our fight against FSHD. Go to <http://www.fshd-europe.org/index.php/bookshop.html> for ordering details or to preview parts of the book.



Still Walking
 By Bill Moss
 Sydney, 2011
 \$45 US, plus shipping
 To purchase, email info@fshsociety.org
 To read about, www.stillwalking.com.au

"These memoirs are the inspirational, moving, blunt and at times very funny account of how a senior and seemingly all-powerful Macquarie banker struggled for years through physical discomfort, pain and the many barriers thrown in the path of people with physical disabilities...to come to terms with his disability." The author is affected with FSHD and is the founder of FSHD Global Research Foundation, Australia. He has generously offered net profits from books purchased by FSH Society supporters, to the FSH Society. FSH Watch

14th Annual Friends Supporting Hope Fundraiser for FSH Muscular Dystrophy raises over \$38,000

Christopher and Ellen Stenmon hosted the 14th Annual Friends Supporting Hope (formerly End of Tax Season Celebration) on April 28 at Florian Hall in Dorchester, MA. Guests enjoyed good food and drink, music, dancing, a door prize, and silent and live auctions. They had great fun and supported a great cause. Thanks to the Stenmons, their families and friends for the most successful event in 14 years! Chris is a member of the Society's Board of Directors. FSH Watch



Christopher Stenmon



Chris Stenmon's grandmother, mother and friend at the 14th Annual Friends Supporting Hope Fundraiser for FSH Muscular Dystrophy

MATCHING GIFTS AND OTHER WORKPLACE GIVING

Many employers offer workers options for directing the company's funds to a charitable organization of their choice. When this opportunity is available to you, please consider how your workplace might make a gift to the FSH Society.

HAVE YOU MADE A GIFT TO THE SOCIETY IN 2012?

Please help now. The FSH Society is a world leader in combating muscular dystrophy. It has provided over \$3.6 million in seed grants for pioneering research worldwide and has developed an international collaborative network of patients and researchers. If you are not already a member, won't you join in this effort? Please return your 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!

UNITED WAY COMMUNITY CAMPAIGNS, FALL 2012

You may have an opportunity to support the FSH Society this fall when you make a United Way pledge for 2012. Check with your human resources department at work for more information.

DOES THE SOCIETY HAVE YOUR CURRENT EMAIL ADDRESS?

If you want to be sure to receive breaking news and other up-to-the-minute information from the Society, please send your email address to us at info@fshsociety.org. Thank you.

FSH SOCIETY WINS AWARD

The FSH Society has been awarded its fourth consecutive 4 Star rating by Charity Navigator.

