

# FSH Watch



CONNECTING THE COMMUNITY OF PATIENTS, FAMILIES, CLINICIANS, AND INVESTIGATORS



## ADVOCACY

### #FSHDstrong

Our next campaign kicks off this August!

by KRISTIN DUQUETTE  
FSH Society

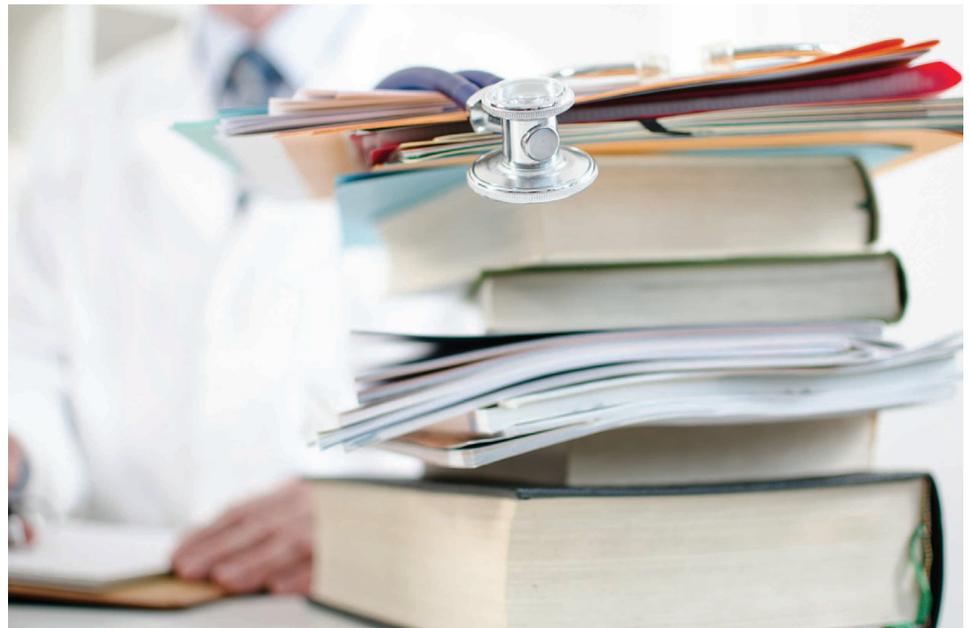
I remember sitting at my new job at the offices of the FSH Society when the idea came to me—to create a T-shirt campaign that could embody not just the condition, but the person, and the strength and courage within each individual. It's not just a condition we want to obliterate; it's a person's life we want to celebrate. And what better way to show the strength of an individual than by wearing a shirt saying, "I am stronger than FSHD"? I imagined the positivity the whole FSHD community could create by embodying those words.

Such a simple phrase, "I am stronger than FSHD," asserts that a person may have this condition but is not defined by it.

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New FSHD T-shirt campaign.



## EDUCATION

### Hot off the press: FSHD care guideline

Evidence-based, if incomplete, new guideline is a major step forward

by JUNE KINOSHITA  
FSH Society

All too often, FSHD patients encounter doctors whose knowledge of the disease seems to be gleaned from dusty textbooks. A patient disabled by pain might be told that "pain is not associated with FSHD." Or a physician may not think to order lung function tests, even though a patient feels too exhausted every morning to get out of bed.

One can hardly blame the doctors. Most have rarely, if ever, seen an FSHD patient, and between 15-minute consultations, they

barely have time to breathe, much less study up on the latest research.

That's why the publication on July 27 of a new care guideline for FSHD by the American Academy of Neurology (AAN) is a big deal. The guideline condenses the results of nearly 80 peer-reviewed studies into a set of recommendations that any doctor can easily follow. The guideline covers evaluating, diagnosing, and managing the care of FSHD patients, and is "evidence based," meaning it takes into account the design and statistical power of each study to evaluate how strong or weak a recommendation should be.

The guideline does have some gaps. It does not mention some widely used interventions, such as orthotics and aquatic therapy, even though many doctors prescribe

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## Hearts and minds

Dear Friends,  
It's hard to believe that I am coming on the third anniversary of my joining the FSH Society as executive director. Only three years? It feels like a lifetime—in a good way. This is a cause that has taken full possession of my heart and mind.



June Kinoshita

Every day, I closely follow the ups and downs that patients and families share with me and our FSH Society team through phone calls, emails, and social media. We do what we can to help, sharing information and emotional support—sometimes simply lending a shoulder to cry on. We take it all in and ask ourselves, Can we do more? Can we do better?

Just sharing stories can be a path to emotional healing. You are not alone. Others have walked and rolled the path you are on, and they are okay. More than okay. In this issue of *FSH Watch*, several teenagers share how they faced their diagnosis. I was struck by the forthright and positive ways in which they have coped and taken charge of the things they can control: telling their peers and teachers, asking for support, and turning a downer into something incredibly uplifting, not just for themselves but for everyone around them. I see them and feel that the future of the FSHD community is in excellent hands.

Sharing images is another powerful way to tell a story. Our portrait project with photographer Romana Vysatova is spreading across the Internet, the Boston transit system, the Indy 500 speedway, biotech company corridors, and beyond. We hope you will share them, too, as a way to open up conversations and promote understanding.

When it comes to sharing experiences, there's nothing like face-to-face meetings. The FSH Society's teams of volunteer organizers are establishing regional patient networks where patients and families can meet several times a year to talk, learn, form friendships, and become advocates and change makers. Our events

calendar on page 28 lists upcoming meetings. If you would like to organize one in your area, please let us know.

Last, but far from least, we are reaching our goals to expand our funding of research. Thanks to so many of you having stepped up to increase your donations, we raised more than \$2 million in 2014, an 11.5 percent growth over the previous year. We have already committed close to \$900,000 to new projects that will blaze trails in deepening our understanding of FSHD and exploring strategies for treatment.

Research on FSHD is advancing at great speed today—never fast enough for patients, we know, yet at a pace that is impressive by any measure. With added resources, we could accelerate that pace. Research leaders know what needs to get done, but they are too often being held back by the lack of funds to pay for a few salaries, house a mouse colony, sequence some genomes, or put a few dozen patients through an imaging scanner. They need us.

That's why it is more important than ever for FSH Society members to step up to the plate. We salute those leaders who organize fundraisers, patients who take the time to volunteer for research studies, and all of you who make sacrifices to contribute to our collective effort.

The world is taking notice. The FSH Society has received its seventh consecutive Charity Navigator four-star award. Fewer than 2 percent of all U.S. charities have accomplished this feat. This achievement belongs to all of us—our hard-working staff, Board of Directors, Scientific Advisory Board, and donors at every level. You help ensure that we are efficient, effective, accountable, and able to grow while keeping our fundraising costs low. For all that you do, we are grateful beyond words.

Sincerely,



June Kinoshita  
Executive Director, FSH Society

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### Executive Director

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Diane Burke

### Office Manager

Doris Walsh

### Administrative Assistant

Kristin Duquette

### FSH Society, Inc.

450 Bedford Street  
Lexington, MA 02420 USA  
(781) 301-6060  
info@fshsociety.org

[www.fshsociety.org](http://www.fshsociety.org)

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

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June Kinoshita, Executive Director  
FSH Society  
450 Bedford Street  
Lexington, MA 02420 USA  
june.kinoshita@fshsociety.org

Look for us on the Internet at [www.fshsociety.org](http://www.fshsociety.org).  
Editors: June Kinoshita, Daniel Paul Perez  
Copy Editor: Elaine Alibrandi  
Editorial Assistance: Howard Chabner, Doris Walsh  
Graphic Design: Leslie Anne Feagley  
Printing and Mailing: Brian Luoma, ShelDon



# Welcome to the new Board of Directors members

*Diverse experiences and expertise enrich the Society*

by JUNE KINOSHITA  
FSH Society

## Stuart Lai

Based in New York City, Stuart is the technology architect for REDI Technologies, a software system provided to professional traders. He managed a 60-person team that originally developed REDI EMS software at Goldman Sachs. The technology was spun out in 2013 into REDI Technologies, where Stuart’s job is to reimagine the REDI system to operate in a faster, better, cheaper modality while retaining the reliability and security standards required for financial trading applications.

“Getting to disease treatment is some time away, just like getting to a fully operational software system. The time to market is never satisfactory to the stakeholders,” Stuart notes. “At Goldman Sachs, we have dealt with this by going after the ‘low-hanging fruit’ ... I believe there is low-hanging fruit to be had for the FSH patient that the FSH Society can bring to market.”

Stuart graduated from UCLA with a bachelor of science in computer science and electrical engineering.



Stuart Lai

## Nancy K. Payton

When her son suffered vision loss from Coats disease and was subsequently diagnosed with FSHD, Nancy committed herself to advocating for patients and families. With a professional background in social work, she is accustomed to helping individuals with complex medical and psychosocial conditions. Until 2014, she worked as a drug addiction treatment counselor for the Tacoma-Pierce County Health Department in Tacoma, Washington.

As an advocate for FSHD, Nancy is interested in raising awareness and funding through patient meetings and events. She serves as a moderator for the FSHD Parents Facebook group. Nancy also sits on the Jack McGovern Coats Disease Foundation Advisory Board.

Nancy is excited and proud to join the Board of the FSH Society, as she has had nothing but positive experiences with the Society since day one. She is honored to know that she can be of help to newly diagnosed families and in guiding families to the resources available at the FSH Society to help answer any questions they may have. She is very much looking forward to working with the diverse and dynamic team on the FSH Society Board of Directors.

One of Nancy’s favorite pastimes is making Coats Monkeys for children affected by Coats disease. She also enjoys spending time with her grown children and grandson, getting together with friends and family, gardening, travel, and music. She lives in Puyallup, Washington, with her husband Norman.



Nancy K. Payton

## Wendy Shack

Among her many talents, Wendy can count “boat builder.” In 2013, she hand-built a traditional wooden Farley boat to sell at auction at Hustle4Muscle, the annual golf tournament she and her family established in 2012. The winner bid nearly \$8,000 for the boat and then immediately donated it back to the auction, where it sold again for the same amount, netting almost \$16,000 for the FSH Society. That is just one example of Wendy’s remarkable fundraising prowess. Over three years, Hustle4Muscle has become a major fundraising event for the Society.

Wendy was a staff associate at American Electric Power in Albany, Texas, where she oversaw and managed many aspects of the business. She and her husband live in Albany. Wendy and her son have volunteered for FSHD research at the Kennedy Krieger Institute, and her daughter will also be participating in that study. “I have the drive and passion that it takes to serve on this great Board,” she says. “But most importantly, I have the heart of a mother, and nothing is more important to me than a cure.” [FSHWatch](#)



Wendy Shack

## Shaking things up with a cocktail

### THE JIZZLE FIZZLE RAISES FUNDS FOR FSHD

Last year at Spicerfest 3, our annual fundraiser for the FSH Society, we introduced a signature cocktail in hopes of generating more research dollars. The “Jizzle Fizzle” was a huge success, and Benny Carter, the owner of Murphy’s Pub, where our event was held, decided to keep the drink on his menu throughout the year.

When I have been asked what a “Jizzle Fizzle” is, I say,

think of it as a Dirty Shirley (Temple). It is a tasty blend of Sprite™, cherry vodka, a splash of grenadine, and a cherry for garnish. People wonder how the cocktail got its name. It came about because “Jizzle” is one of the pet names that my boyfriend, Rudy, calls me, and it seemed to be the perfect fit for this delicious, fizzy drink. We served them again at Spicerfest 4 on June 6, 2015!  
– Jonelle Spicer



# FSH Society Congressional testimony

We request for FY2016 a tripling of the NIH FSHD research portfolio to \$21 million

**Testimony of Daniel Paul Perez, President & CEO, FSH Society, to the United States Senate Appropriations Committee, Subcommittee on Labor, Health and Human Services, Education and Related Agencies on the subject of \$21 million in FY2016 Appropriations for U.S. DHHS National Institutes of Health NIH Research Programs on Facioscapulohumeral Muscular Dystrophy (FSHD), March 31, 2015.**

**Submitted FY 2016 Report Language:** The Committee strongly encourages the NIH to accelerate research efforts and significantly increase projects and funding on what may be the most common form of muscular dystrophy, facioscapulohumeral muscular dystrophy (FSHD). The Committee hopes and recognizes that scientific opportunities and recent epigenetic breakthroughs in FSHD will help advance treatments and access to therapies for this and many other grave diseases.

Honorable Chairman Blunt and Ranking Member Murray, thank you for the opportunity to submit this testimony. Facioscapulohumeral muscular dystrophy (FSHD) is one of the most common adult muscular dystrophies, with a prevalence of 1:8,000.<sup>1</sup> FSHD is a rare disease or an orphan disease (according to U.S. criteria it affects fewer than 200,000 people). For approximately 870,000 men, women, and children worldwide, the major consequence of inheriting this genetic form of muscular dystrophy is a lifelong progressive loss of skeletal muscles. FSHD predominantly initially affects muscles in the face, trunk, and upper extremities. FSHD is a crippling and life-shortening disease. It can affect multiple generations and entire families.

With FSHD, there is a loss of muscle strength that ranges between 1 and 4 percent a year during a lifetime. In terms of functional impairment, 20 percent of FSHD-affected individuals over age 50 will require the use of a wheelchair. FSHD also has very specific non-muscular manifestations: hearing loss, respiratory, cardiac (arrhythmias), and vision. Ninety percent of individuals with FSHD have the FSHD1 (OMIM: 158900) genetic variation—caused by the contraction of DNA macrosatellite repeat units, termed D4Z4 repeats, on chromosome 4, leading to the release of transcriptional repression of a retrogene (DUX4) believed to be associated with the cause of disease. Of the 5 percent of FSHD individuals remaining, 85 percent of those are the FSHD2 (OMIM: 158901) genetic variation—caused by a mutation in the structural maintenance of chromosomes hinge domain 1 (SMCHD1) gene on chromosome 18p that helps to maintain the repressed-state structure of the D4Z4 repeats on the long arm of chromosome 4, which, when mutated, cause unwanted toxic and inappropriate DUX4 gene/protein expression.

The National Institutes of Health (NIH) is the principal source of funding of research on FSHD, currently at the \$7 million level. For nearly two decades, this Committee has supported the incremental growth in funding for FSHD research. I am pleased to report that this modest investment has produced remarkable scientific returns.

**1. Congress has made a major difference.** I have testified many times before Congress, approximately 50. When I first testified, we did not know the genetic mechanism of this disease. Now we

do. Now we can target it. When I first testified, we assumed that FSHD was a rare muscular dystrophy. Now we understand it to be the most prevalent form of muscle disease, based on new ways of evaluating the disease clinically within families. Congress is responsible for this success, through its sustaining support of the NIH and the enactment of the Muscular Dystrophy CARE Act. We are aware that the MD Care Act does not set the amount of spending on FSHD or the other dystrophies at the NIH, and we recognize that funding levels are determined in the appropriations process and the numbers of grant applications received and funded by the NIH on FSHD. Even though it is a technically separate legislative process, the reauthorization of the MD Care Act does raise the visibility of all the muscular dystrophies, which can be of help in the appropriations process—and we thank you for your support of the MD Care Act amendments in 2014. Given these requisites, there are additional efforts and pathways that Congress can request and the NIH can enact to increase the amount of research funding on FSHD in the NIH portfolio that neither increase the NIH budget required nor take money from another area of research, and achieve more efficiency out of a non-growing research budget.

**2. Quantum leaps in our understanding of FSHD.** The past four and a half years have seen remarkable contributions made by a very small but dedicated tribe of researchers funded by NIH and nonprofits.

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“Mr. Chairman, these major advances in scientific understanding and epidemiological surveillance are not free. They come at a cost. Since Congress passed the MD CARE Act in 2001, research funding at the NIH for muscular dystrophy has increased fourfold.”

DANIEL PAUL PEREZ



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■ On August 19, 2010, American and Dutch researchers published a paper which dramatically expanded our understanding of the mechanism of FSHD.<sup>2</sup> A front page story in *The New York Times* quoted the NIH Director Dr. Francis Collins saying, “If we were thinking of a collection of the genome’s greatest hits, this would go on the list.”<sup>3</sup> “FSHD patients carry specific single-nucleotide polymorphisms in the chromosomal region distal to the last D4Z4 repeat. This FSHD-predisposing configuration creates a canonical polyadenylation

signal for transcripts derived from DUX4, a double homeobox gene of unknown function that straddles the last repeat unit and the adjacent sequence. Transfection studies revealed that DUX4 transcripts are efficiently polyadenylated and are more stable when expressed from permissive chromosomes. These findings suggest that FSHD arises through a toxic gain of function attributable to the stabilized distal DUX4 transcript.”<sup>2</sup>

- Two months later, another paper was published that made a second critical advance in determining the cause of FSHD. The research shows that FSHD is caused by the inefficient suppression of a gene that may be normally expressed only in early development. “The contraction of the D4Z4 repeat in FSHD results in a less efficient suppression of the full-length DUX4 mRNA [DUX4-fl] in skeletal muscle cells. Therefore, FSHD represents the first human disease to be associated with the incomplete developmental silencing of a retrogene array normally expressed early in development.”<sup>4</sup>
- On January 17, 2012, an international team of researchers based out of Seattle discovered that a stabilized form of a normally suppressed gene called DUX4 affects many different germline genes, retro-elements, and immune mediators—all potential targets. “We identify genes associated with germline and early stem cell development as targets of the DUX4 transcription factor, a leading candidate gene for FSHD. The genes regulated by DUX4 are reliably detected in FSHD muscle but not in controls, providing direct support for the model that misexpression of DUX4 is a causal factor for FSHD.”<sup>5</sup>
- Six months later, another high-profile paper produced by a Senator Paul A. Wellstone Cooperative Research Center of the NIH (mandated by the MD CARE Act) used sufficiently “powered” large collections of genetically matched FSHD cell lines generated by the NIH NICHD Wellstone Center, that are both unique in scope and shared with all researchers worldwide, to improve on the Seattle group’s finding by postulating that DUX4-fl expression is necessary but not sufficient by itself for FSHD muscle pathology. “We confirmed that stable DUX4-fl mRNA and protein were expressed in myogenic cells and muscle tissues derived from FSHD-affected subjects, including several 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.”<sup>6</sup>
- On July 13, 2012, a team of researchers from the United States, the Netherlands, and France identified mutations in a gene

causing 80 percent of another form of FSHD called FSHD1B or FSHD2. This paper furthers our understanding of the molecular pathophysiology of FSHD. This work, too, was supported in part by a program project grant from the NIH. “FSHD2 occurs in individuals who inherited both the SMCHD1 mutation and a normal-sized D4Z4 array on a chromosome 4 haplotype permissive for DUX4 expression. Reducing SMCHD1 levels in skeletal muscle results in D4Z4 contraction-independent DUX4 expression. Our study identifies SMCHD1 as an epigenetic modifier of the D4Z4 metastable epi-allele and as a causal genetic determinant of FSHD2 and possibly other human diseases subject to epigenetic regulation.”<sup>7</sup>

- On September 25, 2014, researchers from the United States, France, Spain, the Netherlands, and the United Kingdom narrowed the focus, mechanistically opening the possibility of all types of FSHD having an epigenetic basis. “In FSHD1, for individuals with D4Z4 repeat arrays of 1-6 units, the clinical severity mainly depends on the size of the D4Z4 repeat. However, in individuals with arrays of 7-10 units, the clinical severity also depends on other factors that regulate D4Z4 methylation because affected individuals, but not non-penetrant mutation carriers, have a greater reduction of D4Z4 CpG methylation than can be expected based on the size of the pathogenic D4Z4 repeat array. In FSHD2, this epigenetic susceptibility depends on the nature of the SMCHD1 mutation in combination with D4Z4 repeat array size, with dominant negative mutations being more deleterious than haploinsufficiency mutations. Our study thus identifies an epigenetic basis for the striking variability in onset and disease progression that is considered a clinical hallmark of FSHD.”<sup>8</sup>
- On March 29, 2015, different researchers involved with the NIH Senator Paul A. Wellstone Cooperative Research Center, using its large collection of different FSHD patient samples and various techniques, arrived at the same answer that there is an underlying principle of epigenetics defining asymptomatic or non-manifesting FSHD and playing a role in disease severity. “The epigenetic status of the distal 4qA D4Z4 repeat correlates with FSHD disease; FSHD-affected subjects have hypomethylation, healthy unaffected subjects have hypermethylation, and non-manifesting subjects have characteristically intermediate methylation. Thus, analysis of DNA methylation at the distal D4Z4 repeat could be used as a diagnostic indicator of developing clinical FSHD. In addition, the stability of epigenetic repression upstream of DUX4 expression is a key regulator of disease and a viable therapeutic target.”<sup>9</sup>

Many of these researchers have started their efforts in FSHD with seed funding from the FSH Society and have received continued support from the FSH Society, the NIH, and the Muscular

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## CONGRESSIONAL TESTIMONY

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Dystrophy Association and other partners. In simpler terms, the above research shows that our own genes within us are being inappropriately expressed in tissue at a time and place where they do not normally reside or function by a confluence of events in a variety of ways, giving rise to the decay and destruction of skeletal muscle, and we begin to focus on the very narrow stretch of DNA down to the nucleotide level in an area adjacent to the toxic gene inappropriately turned on, so-named DUX4-fl. You might think of it as the opposite of cancer: rather than runaway genes causing unbridled cell division, runaway genes are causing unbridled cell death. What is fascinating is, though one has all the requisites to have FSHD (e.g., the presence of a chromosome 4qA containing a DUX4 polyadenylation signal, and either a truncation of D4Z4 or a SMCHD1 mutation with a D4Z4 repeat array with array sizes at the lower end of the normal repeat size spectrum), there are modifiers that allow a person to have a severe course of disease whilst other genetically tested positive relatives are spared disease symptoms, for example, methylation. We can see clearly now that the stability of epigenetic repression by the region just upstream of the DUX4 gene on the very last distal D4Z4 repeat, regardless of which route DUX-fl was stabilized and presented (FSHD1, FSHD2, FSHD3, etc.) is a key regulator that can be modified, perhaps via its methylation level/status. We can see clearly that FSHD2 modifies FSHD1 in individuals who carry both mutations, presenting with even more severe disease. More remarkably, we know of and have compounds and techniques to modify and target modifiers and expression of DUX-fl, and still the FSHD research and clinical enterprise is starved for federal funding from NIH! In 2014, the FSH Society funded projects to silence the DUX4 gene using leading-edge genome-editing technologies (CRSPR/Cas9, TALEN), helped support development efforts and models to test antisense oligonucleotide (ASO) and morpholino, and aided the development of animal models and a novel method that we believe will revolutionize FSHD diagnostics. We are thrilled that our grantees and colleagues have data that prove that DUX4-fl and cascading events can be turned off.

**3. We must keep moving forward.** In October, the FSH Society held its annual FSHD International Research Consortium meeting in San Diego, California. The meeting was funded in part by the NIH NICHD University of Massachusetts Medical School Wellstone Center for FSHD. Nearly 80 researchers from around the world

gathered to present the latest data and discuss research strategies. There was considerable progress achieved when compared to the 2013 agenda. The discussion agenda focused on being prepared for intervention development and clinical readiness. To keep the discussion focused, we followed the path: Genetics > Mechanisms and targets > Models > Patients. For each area, an expert moderator was nominated. The priorities stated for 2015 at the October 18, 2014, FSH Society FSHD IRC meetings can be found at <http://www.fshsociety.org/international-research-consortium/>.

Additionally, on March 17, 2015, the FSH Society presented to the federal advisory committee mandated by the MD CARE Act, called the Muscular Dystrophy Coordinating Committee (MDCC), its concern about the small number of NIH grants and that much greater funding is required to address the most pressing challenges for FSHD research, including research on the following topics:

- Mechanisms of DUX4 toxicity.
- More molecular, imaging, and functional markers of disease progression.
- Modifiers of disease: genetic, chemical, and lifestyle.
- Preclinical models validated to represent aspects of FSHD pathophysiology.
- Better animal models based on low expression of DUX4 as seen in patients.
- Mechanisms of pathology in patients' muscles.
- Normal functions of DUX4 in tissues other than muscle.
- Methods of administering anti-DUX4 agents to muscle.
- Muscle regeneration capacity in FSHD muscles.
- Large animal models (monkey, marmoset).
- Biomarkers that can indicate the impact of therapeutic agents.

We need to be prepared for this new era in the science of FSHD. Many leading experts are now turning to work on FSHD because it represents the potential for great discoveries, insights into stem cells, transcriptional processes, new ways of thinking about diseases of epigenetic etiology, and treating diseases with epigenetic origin.

**4. NIH funding for muscular dystrophy.** Mr. Chairman, these major advances in scientific understanding and epidemiological surveillance are not free. They come at a cost. Since Congress passed the MD CARE Act in 2001, research funding at the NIH for muscular dystrophy has increased fourfold (from \$21 million).

### FSHD Research Dollars & FSHD as a Percentage of Total NIH Muscular Dystrophy Funding

Sources: NIH/OD Budget Office & NIH OCPL & NIH RePORT RCDC (e = estimate)

Fiscal Year	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015e	2016e
All MD (\$ millions)	\$38.7	\$39.5	\$39.9	\$47.2	\$56	\$83	\$86	\$75	\$75	\$76	\$78	\$79	\$81
FSHD (\$ millions)	\$2.2	\$2.0	\$1.7	\$3	\$3	\$5	\$6	\$6	\$5	\$5	\$7	\$7	\$7
FSHD (% total MD)	6%	5%	4%	5%	5%	6%	7%	8%	7%	7%	9%	9%	9%

While FSHD research funding has increased 14-fold (from \$0.5 million) during this period, the level of funding is still anemic and, for FSHD, has been astonishingly flat for the past seven years.

Despite the great success of the past four and a half years in the science of FSHD brought about by Congress, we are concerned that under the current funding environment, new research projects

increased from \$39.9 million in 2006 to \$81 million, FSHD increased from \$1.7 million to \$7 million. The economy of scale is so vastly different in particular for FSHD, being equally devastating and burdensome as the disease receiving the most funding in this category called muscular dystrophy, though it functions in the exact same U.S. federal research infrastructure.

**“In the last year alone, incredible opportunities for public, private, and nonprofit entities engaged in FSHD research and clinical research have emerged. Oddly, these discoveries clearly belonging to the leading edge of human genetics and our understanding the epigenome and treating epigenetic diseases are sitting idle at the NIH.”**

DANIEL PAUL PEREZ



will not be funded or existing programs will not be renewed. We are already seeing this play out with some of the larger program projects in FSHD. We have conveyed to the NIH leadership at the Office of the Director, NIAMS, NINDS, NICHD, NHLBI, and the Executive Secretary of the MDCC our grave concern that FSHD research is way too underrepresented in the NIH portfolio and needs a proactive effort on the part of the NIH. At the March 17, 2015, MDCC meeting, we reiterated to Alan E. Guttmacher, MD, Director, NICHD and Chair of the MDCC and all MDCC members that we are fully supportive of his efforts and the Action Plan for Muscular Dystrophy, while at the same time we requested that the NIH redress the imbalance of funding in the muscular dystrophy portfolio by fostering opportunities for multidisciplinary research on FSHD commensurate with its prevalence and disease burden. The future action plan and NIH activity should address this issue head on. We are stunned, if not baffled, that while on one hand, five years ago, NIH Director Dr. Francis Collins said, “If we were thinking of a collection of the genome’s greatest hits, this [FSHD] would go on the list,”<sup>3</sup> on the other hand, the National Human Genome Research Institute (NHGRI) has only one R01 on FSHD!

In the last year alone, incredible opportunities for public, private, and nonprofit entities engaged in FSHD research and clinical research have emerged. Oddly, these discoveries clearly belonging to the leading edge of human genetics and our understanding the epigenome and treating epigenetic diseases are sitting idle at the NIH. The NIH needs to see through the thick fog of flat funding and austerity, and maximize research funding by capitalizing on the low-hanging fruit that FSHD presents as a gateway to treating human epigenetic disease.

There are 26 active projects NIH-wide as of March 12, 2015, according to the NIH Research Portfolio Online Reporting Tools (RePORT; <http://report.nih.gov>); within these 26 are: one F32 training grant, 6 R21, 12 R01, 1 P01, 2 U01, and 2 U54. NHGRI has only one R01. NHLBI has none. NICHD has no R21, no R01. In the last 25 years, NIH has funded 76 grants in FSHD, including only three training grants, 18 R21, and 25 R01. Remarkably, no grants ever on FSHD from key institutes studying heart, lung, blood, hearing, and vision.

While all muscular dystrophy research funding at the NIH

**We request for FY2016 a tripling of the NIH FSHD research portfolio to \$21 million or a level of approximately 25 percent of the total estimated muscular dystrophy funding at NIH.** This will allow an expansion of basic research awards, expansion of postdoctoral and clinical training fellowships, dedicated centers to design and conduct clinical trials on FSHD, and more U.S. DHHS NIH Senator Paul D. Wellstone Muscular Dystrophy Cooperative Research Centers.

We are aware of the great pressures on the federal budget, but the NIH can easily help increase its portfolio on FSHD given the breakneck speed of discovery in FSHD. These are easy ways for the NIH to convey to researchers that it has a revised plan and an interest in funding research in FSHD. There are no quotas on peer-reviewed research above pay line at the NIH, and the NIH can help by issuing written announcements that efforts invested in writing FSHD grant applications will be met with interest.

This is the time to fully and expeditiously exploit the advances and the best scientific opportunities for which the American taxpayer has paid. Thank you for this opportunity to testify before your committee. **FSHWatch**

## Footnotes

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# The decision to stop working

What you need to know

by **HOWARD CHABNER**  
San Francisco, California

As FSHD progresses, some people find that reduced stamina, growing fatigue, and intractable physical problems make it increasingly difficult to continue working. They want to continue but “hit a wall” in their ability to do their job, and they don’t want to risk accelerating the progression of their FSHD by continuing to work in the face of mounting difficulties. The decision to stop working and “go on disability” is one of the most agonizingly difficult decisions one ever has to make—emotionally, practically, and financially.

Making the right decision requires advice and support from one’s spouse or partner, other family members, doctors, and other professionals who might include occupational therapists, social workers, psychologists or psychiatrists, and lawyers. Taking the first step—talking candidly with your spouse or partner, family, and doctor about your difficulties at work—can be especially hard.

Well before deciding to stop working, you must ask your employer for a “reasonable accommodation.” The Americans with Disabilities Act requires employers to provide a reasonable accommodation for employees with disabilities. The employer must provide an accommodation, but it’s up to the employee to ask. Accommodations could include an evaluation by an occupational therapist or workplace ergonomics expert, assistive technology, changes in furniture, a change in job duties, reduced hours, more frequent breaks, and unpaid time off.

But as people’s FSHD progresses, accommodations that once enabled them to work may no longer be sufficient. They should consider going on disability only after having determined that no further accommodations are available or feasible.

Should you tell your employer that you are considering applying for disability?



Howard Chabner

Obviously, the answer to this question depends on your individual circumstances, but, in general, it’s more prudent not to tell your employer until you’ve made your decision and have your documentation ready. If you consult a lawyer (see below), it’s advisable to discuss this question with him or her.

## Disability insurance

There are two types of disability insurance: Social Security Disability Insurance (SSDI), a program of the Social Security Administration, and long-term disability insurance (LTD), which is issued by insurance companies. Everyone who works and pays Social Security taxes is automatically enrolled in SSDI. Because SSDI will not provide nearly as much income as working, supplementing it with an LTD policy can significantly increase one’s disability income. But it’s not easy to get LTD insurance.

A group LTD policy, where individual underwriting is not required, can be one of the most valuable benefits provided by employers, but many don’t offer it. It may also be possible to enroll in a group LTD policy through a professional organization, alumni association, religious organization, or other group. Individual LTD policies are available but require medical underwriting, making it difficult for most people with FSHD to qualify. Since a group LTD policy does not require underwriting, people with FSHD who have an opportunity to obtain coverage under a group LTD policy are well advised to seize that opportunity. If people have an opportunity to purchase an individual policy because their FSHD symptoms are mild, this is also an opportunity to be seized.

Note that both group and individual policies have a pre-existing condition exclusion period. Typically, a pre-existing condition is one for which the person sought medical advice or treatment within a certain time period before the policy became effective; disability based on that condition is not covered for a specified time duration after the policy’s effective date. The duration

of the look back and exclusion periods varies among policies.

Central to disability insurance is the definition of “disability.” SSDI has a strict, narrow definition of disability, known as an “any occupation” definition. People are not considered disabled if they merely cannot do their current job; they must not be able to perform any other job for which their age, education, training, work experience, and transferable skills would otherwise qualify them. Along with other essential information, the Social Security Administration website has a step-by-step explanation of this definition (<http://www.ssa.gov/dibplan/dqualify4.htm>). A comprehensive brochure about SSDI can be downloaded from the website [www.ssa.gov](http://www.ssa.gov).

LTD policies vary in their definition of disability, ranging from “any occupation” to a more liberal “own occupation” definition, which means people are considered disabled if they are no longer able to perform their current occupation. For example, truck drivers may no longer be able to drive a truck but may be qualified by training and experience for office work. Under an “any occupation” definition, they are not disabled, while under an “own occupation” definition, they are. Surgeons who can no longer perform surgery but are able to teach would be considered disabled under an “own occupation” definition but not under “any occupation.”

The amount of the payment is critical. SSDI is based on average earnings over one’s career, provides a modest fraction of the income earned while working, and has annual cost-of-living increases. LTD policies typically provide 60 percent or two-thirds of the income earned immediately before going on disability (subject to a maximum amount) and may or may not provide inflation protection. Some smaller LTD policies provide a fixed payment amount.

Many LTD policies require the claimant to also apply for SSDI. These policies offset (subtract) the amount of Social Security disability income from the amount they pay; however, cost-of-living increases in Social Security disability income typically are not



**“ Being forced to stop working because of FSHD is difficult, emotionally and socially. It is one of the biggest losses caused by our disease. Mental health professionals and social workers can greatly help those who are faced with the decision to stop working.”**

HOWARD CHABNER

subtracted. Even if you have a generous LTD policy, there are some advantages of making a claim for SSDI. Besides the fact that SSDI cost-of-living increases aren't subtracted from LTD payments, there are possible tax advantages and, very importantly, eligibility for Medicare (see below).

Another important element is the duration of disability payments. SSDI payments continue until normal retirement age (65 or older, depending on the year of birth); thereafter, they are converted to regular Social Security retirement benefits in the same amount. LTD policies vary, ranging from payments for a specified number of years to payments through normal retirement age.

SSDI and LTD insurance both have waiting periods before payments are made. SSDI payments begin on the sixth full month after the date disability began. LTD policies vary in their waiting periods. It's important, therefore, to consider how to replace your lost income, and how to reduce your expenses if need be, during the waiting period. Some employers provide short-term disability benefits to cover part or all of the gap. Some states, including California, have universal short-term disability insurance programs, funded through payroll deductions, that provide some income before SSDI and LTD payments kick in.

#### **Seek expert advice**

It is impossible to overstate the importance of getting professional advice and support. The Social Security Administration and insurance company determinations (both initial and ongoing) about whether or not you are unable to work because of your FSHD will be based on a certification from your doctor and a review of your medical records. (If your claim is approved, the insurance company will require periodic certifications from your doctor that you are still disabled; the Social Security Administration may also require this, but less frequently.)

Having a doctor who knows you well and has been familiar with your FSHD for a long time is extremely advantageous in helping you consider such a difficult decision, and because he or she will have much greater credibility with the Social Security Administration and the insurance company than a doctor who has known you only a short time or who is not very knowledgeable about muscular dystrophy.

Before deciding to apply for disability, it is highly advisable to consult a lawyer who is an expert in disability insurance law—a specialized area of law that is separate from the field of disability civil rights law. (The latter is concerned with discrimination in employment, physical access, government programs, etc.)

Lawyers who are experts in SSDI

tend not to be familiar with LTD law, and vice versa. If you don't have LTD coverage, you would need to consult only with an SSDI lawyer. If you have an LTD policy, it is advisable to consult with two lawyers—one for SSDI and one for LTD. Disability insurance lawyers can advise you about eligibility, what documentation you need, how to fill out the claim forms, policy terms (in the case of LTD), and how to deal with your employer, the Social Security Administration, and your LTD carrier.

Your local bar association probably has a referral service where you can find lawyers with this expertise. Nolo, a publisher of self-help legal guides, publishes a guide to Social Security disability ([www.nolo.com](http://www.nolo.com)). This book is a good place to start, but the fees for a few hours of legal advice before filing a claim will be money well spent.

#### **Tax and medical insurance**

Taxes and medical insurance must be considered. Federal income tax treatment of Social Security benefits is complex and depends on the overall level of income. In many states, including California, SSDI payments and Social Security retirement benefits are exempt from state income taxes.

Generally, federal and state taxability of LTD payments depends on who paid the insurance premium—payments are usually

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## In Brazil for the World Cup

*Scant disabled access, abundant goodwill*

by FRED THYS

WBUR, Boston, Massachusetts

I am not in the habit of seeing the world from the vantage of a moving chair, but after a trip last summer to Brazil to watch the World Cup with my disabled brother, I do now. What I learned during our recent travels can be summed up in two ways:

First, the United States has disability awareness, access, and infrastructure that must be without parallel in the world, thanks in great part to the Americans with Disabilities Act. Second, Brazilians have such goodwill to spare, it almost makes up for how difficult it is to move around that country if your legs don't work.

My brother, Didier, has FSH muscular dystrophy and cannot stand or walk. So we ordered wheelchair-accessible tickets to the World Cup online, through the quadrennial contest's governing body, the Fédération Internationale de Football Association, FIFA. Our first stop upon arriving at Galeão-Antônio Carlos Jobim International Airport in Rio was the FIFA office to pick up our tickets.

There, a FIFA representative asked my brother for proof of his disability. We were a little taken aback. That Didier was in a scooter wasn't proof enough, so my brother offered to fall out of it. No, the FIFA rep said. She needed a document attesting to his disability. I couldn't imagine having been asked for this in the United States.

"In the U.S., the fact of being in a wheelchair or a scooter is proof enough," I said to the FIFA representative. She relented and handed us our tickets, but not before saying, "Don't count on being admitted into the stadiums." It was not the welcome we might have hoped for.

Two days later, the ticket agent's parting words still ringing in my head, we hailed a cab to Rio's Maracanã Stadium, only to find it barricaded by a security perimeter that extended for many blocks. Scooter batteries being fickle, we were worried that Didier's wouldn't make the distance from the cab to the stadium and back again.

Undaunted, our resourceful driver turned around and drove around Rio from newspaper stand to newspaper stand in search of a handicapped parking sticker that could get us inside the barricade. Finding none, he returned to the cab with



a three-by-five-inch index card and a blue magic marker. "What does the handicapped symbol look like?" he asked. We showed him our tickets with the international wheelchair symbol, and the facsimile that he drew, along with his sweet talk, got us past the police roadblock. He dropped us off just two blocks from the stadium, and he was there waiting for us after the match.

Belgium won, but our personal victory was proving the FIFA agent's grim prediction wrong. Not only were Didier and I admitted to the stadium without incident, we were on the receiving end of the kindness of Brazilian volunteers, police officers, ticket takers, and ushers who went out of their way to speed us to our seats just above one of the goal lines.

Goodwill: 1. Uninformed FIFA agent: 0.

In subsequent days, however, I thought of how that ticket agent's attitude was reflected in the country's lack of handicapped-accessible infrastructure, if not in the vast numbers of good Samaritans who came to our aid. It wasn't just tricky access to the arenas—did officials not expect fans with disabilities to want to watch the games in person?—it was airports and planes, subway stations and trains that seemed designed for some pre-wheelchair or scooter age. I wondered: Did people

with physical challenges in Brazil leave their homes? Given the hurdles Didier and I encountered on our way to and from matches across Brazil, I decided that they could be forgiven for not wanting to submit to the indignities of trying.

For example, we had been counting on the relative ease of boarding our domestic Gol flight from Rio to Recife from a jetway ramp, which meant that Didier could ride his scooter to the aircraft door, slide onto an aisle chair, and be wheeled to his seat. But then came word of a gate change and, with it, the news that we would have to board our flight from a staircase on the tarmac. Oh, and the elevator to the

tarmac was out of service.

Didier moved into a wheelchair; I carried his scooter; an airline employee wheeled my brother onto and down an escalator; a handicapped-accessible bus drove us to the plane; I delivered the scooter to the cargo bay for loading; we waited—and waited—for a truck bearing a platform to raise us to the plane and deliver us, its two remaining passengers.

Once boarded, we discovered that Didier could not slide into the bulkhead first row seats we'd been booked into because the arm rests don't lift. This hitch was quickly resolved, thanks to a kind young Brazilian man who offered to switch rows with us.

Three hours later, having landed, we watched as all of our flight's passengers disembarked while we waited—and waited—for the airline to locate an aisle chair with which to transport my brother off the plane. It took so long that the passengers for the next flight were boarding our plane before we were off it.

But once again, it was the goodwill of strangers that made all the difference.

Two days later, it was sad to see the American team fall to Germany at Recife's Arena Pernambuco, and it was sadder still

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# The ticket in the street

## Finding strength in art

by SARAH GEISSLER  
Stowe, New Hampshire

I watched as the cement beneath my feet appeared like the perpetual roll of ocean waves. I thought about how clean it had once been, and how in the matter of a day it had an entirely new appearance. The surface stared back at me unrelentingly, until I was suddenly jerked from my planet and stuck back into reality by a man who appeared to be late for his big city job.

My mother walked beside me; it was warm for late September, and I had to take off my jacket. It had only been a few minutes since we had stepped through the doors of Mass General Hospital, and already we appeared as zombies in a sea of people who always seemed to be late for something. It's strange how, when you learn something about yourself that should be a dramatic change, it doesn't feel like it at first. I found myself feeling like I should be more upset, but I just couldn't get myself to feel that reaction. This was the day I was diagnosed with FSH muscular dystrophy.

Facioscapulohumeral dystrophy (FSHD) is a progressive type of muscular dystrophy that atrophies the skeletal muscles of the body. Before I even knew it existed, this disease had already affected my life. I no longer had the ability to run, and my right arm was dramatically weaker than my left. So I guess I was not too surprised that something was wrong with me. However, it was hard to wrap my head around the fact that, after years of puzzled doctors and negative tests, we had finally found the answer.

This is what was circling my mind when my mother and I were walking down the hectic streets of Boston, Massachusetts. I don't know where we were walking to, but I think it was probably to get our car out of the garage, when a red and white piece of paper found its way into my cement-watching gaze. I still do not know what divine force made me think to pick up that slip of paper that so many people had overlooked and stepped on, but I am thankful it did.

BMFA: admission one. Two corners were ripped and the once white paper was now a dark shade of gray on one side. My eyes shifted to the expiration date on a creased corner of the ticket; the date read that it was good all day. I rushed to catch up with my



Sarah Geissler

mother, who had not noticed that I had stopped, and continued to push her way through the congested sidewalk.

"Mom! Look at this!" I gushed as I fell back in step with her. I handed her the ticket and didn't waste a second before I asked, "Can we go?"

The ticket granted admission to the Boston Museum of Fine Arts. Art had been my savior over the past few years when my passion for sports had been taken away by my failing muscles. We both knew that this was the perfect distraction from the news I had just received, so we began our walk to the home of my golden ticket.

We climbed up the white steps of the museum and were faced with a row of towering pillars. We made our way through the doors and began to weave our way through the rooms of artwork. The paintings were what fascinated me the most. I remember standing alone in a room where one wall was taken up by a single oil painting.

The size of the canvas in front of me captivated my gaze. The feeling was like none I had felt before. A single piece of art, or anything, for that matter, had never made me feel so small and so transfixed at the same time. As I sat there, drawn into the scene by the swords and horses balancing on their hind legs, I realized that I had my own battle to fight, and I wasn't going to lose.

Something as vast as the ocean had not made me feel the way that that painting did. However, it also made me gather strength. Suddenly, I decided that I was not going to let this disease make me feel the way that painting did. I was going to be bigger than it. Standing there in that room with that painting, I knew that even though good luck had not been on my side, I had my own extraordinary force looking out for me. I had found the first surge of strength that would be my weapon in this battle.

My mother and I still frequently talk about how that ticket was placed in my path. It was intended to show up on the cement in front of me, and I was meant to pick it up and be led to the museum.

Whenever I am feeling trapped by my disease, I remind myself about what it felt like to stand in front of that painting. No matter how imbalanced life can seem, it is important to trust that the luck will even out and that we are all being looked after no matter what our beliefs may be. Sometimes, all it takes is a little trust in the universe and the courage to find your strength. [FSHWatch](#)

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## IN BRAZIL FOR THE WORLD CUP

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to be told, upon exiting the arena under torrents of rain, that there were no taxis allowed. This would turn out to be false, but it was too late for us, already making our way on a van to the brand-new subway line a mile and a half away. When we transferred to an old subway line, we were astonished to see that the train was several

inches below and away from the platform. Before we had reason to worry, however, two strangers lifted my brother and his scooter onto the train. My brother, nervous, said, "I don't like this situation." We were now in a subway car looking up at the platform, wondering how we were going to get out.

"Don't worry," the men said. "Someone will help you out."

And someone did. [FSHWatch](#)

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## Newly awarded grants

*Setting a record in our funding of research*

Summaries edited by **JUNE KINOSHITA** and **DANIEL PEREZ**  
FSH Society

This year to date, the FSH Society has awarded \$891,342 in grants to new projects. These projects were among competitive groups that were submitted in August 2014 and February 2015 for review by our Scientific Advisory Board. They include deep dives into how the genetics of FSHD affects the early development of muscle cells and into the lingering and all-important mystery of why muscle weakens in FSHD.

Other funded studies will explore novel genetic and biochemical pathways that may be involved in FSHD. A project developed in collaboration with the FSH Society, which will enable FSHD patients and unaffected family members to donate invaluable muscle and other tissue specimens to researchers who need them, was also approved contingent on co-funding from other FSHD funding organizations. In addition, the FSH Society awarded a second year of funding to a genomic engineering project, with half of the money coming from a grant to the Society from the FSHD Canada Foundation.

With these awards, the Society continues to significantly expand funding for FSHD. In 2014, the Society funded a total of \$819,261, a 24 percent increase over total funding in 2013. This year, we aspired to increase our research funding to \$920,000—a goal we hope to attain with the steadfast support of our members, fundraising event organizers, and benefactors. We all owe them a tremendous debt of gratitude for their hard work and generosity.

For full details on our grant awards, please visit [www.fshsociety.org/funded-grants/](http://www.fshsociety.org/funded-grants/).

### February 2014 grant submission cycle awards

#### ► INHIBITED PROTEIN TURNOVER IN FSHD PATHOGENESIS

**Sachiko Homma, PhD, and Jeff Boone Miller, PhD**  
**Boston University, Massachusetts, USA**  
**\$68,920 for one year**

**Summary:** Our lab discovered that the full-length isoform of double homeobox protein DUX4 (DUX4-FL), but not DUX4-S (short isoform of DUX4), inhibits protein turnover and leads to abnormal ubiquitin expression and nuclear aggregation of TDP-43, one of the RNA/DNA-binding proteins previously associated with amyotrophic lateral sclerosis (ALS) and inclusion body myositis (IBM) (Homma et al., 2015). (Protein turnover refers to a process that rids a cell of defective or unneeded proteins. Defects in protein turnover result in the accumulation of “trash” proteins, which can harm or kill cells.) These results identify inhibition of protein turnover as a potential pathological mechanism in FSHD. We propose to identify mechanisms that underlie the DUX4-FL-induced inhibition of protein turnover and promotion of abnormal protein aggregation. We will examine FSHD muscle biopsies to identify if there are signs of dysfunction of the protein degradation system. This new knowledge could lead to potential new therapeutic strategies based on regulating proteasome activities and could identify new clinical biomarker(s) for FSHD.

#### ► DETERMINING THE EFFECTIVENESS OF INCREASED SMCHD1 EXPRESSION TO SUPPRESS DUX4 IN FSHD MUSCLE CELLS AND MODEL MICE

**Yosuke Hiramuki, PhD, and Stephen Tapscott, MD, PhD**  
**Fred Hutchinson Cancer Research Center, Seattle, Washington, USA**  
**\$101,132 for two years**

**Summary:** FSHD1 is caused by contraction of the D4Z4 macrosatellite repeat unit (on chromosome 4), whereas FSHD2 is caused by mutations in SMCHD1 (on chromosome 18). FSHD1 and FSHD2 are furthermore each divided into two classes. D4Z4 macrosatellite repeat size in FSHD1 (1-6 unit and 7-10 unit) is involved in disease severity. Mutations in SMCHD1 are grouped into those that result in disease because one copy of the gene is inactive (“haploinsufficiency”) and those that cause disease through an increase in a disease-causing activity (“dominant negative”). In addition, SMCHD1 modifies disease severity in families affected by FSHD1.

There is no study to test whether SMCHD1 has a possibility of being an effective treatment for FSHD1 and FSHD2. This proposal builds on the hypothesis that SMCHD1 overexpression decreases aberrant DUX4 expression in FSHD1 and FSHD2. The outline of our research plan to test this hypothesis is as follows.

**Aim 1:** We will determine whether increased SMCHD1 expression suppresses DUX4 in FSHD1 and FSHD2 muscle cells. We will also determine which part of SMCHD1 is critical for suppressing DUX4 in muscle cells from different types of FSHD.

**Aim 2:** We will test whether DUX4 can be suppressed by increasing production of SMCHD1, using a virus to deliver SMCHD1 into FSHD muscle cells and model mice.

In this application, Aim 1 will be the proof-of-principle experiments showing that higher SMCHD1 will be effective as a potential therapy, and Aim 2 will develop a method for delivery that might eventually be suitable for preclinical or clinical trials.

#### ► FSH SOCIETY-NDRI TISSUE PROCUREMENT PROJECT

**Jonathan Lonsdale, PhD**  
**National Disease Research Interchange (NDRI), Philadelphia, Pennsylvania, USA**  
**\$265,835 for 3.25 years; was recommended for one year instead of three and, in addition, one-third of the one year at \$30,000 contingent on co-funding from other FSHD funding organizations. Fund if other FSHD research nonprofits and FSHD Champions will co-fund**

**Summary:** In response to a request from the FSH Society, NDRI proposes to develop and implement a resource to recover surgical and postmortem human biospecimens and distribute them to approved investigators. This resource will utilize NDRI’s experience, expertise, and established systems to expand and enhance the type, number, and quality of human tissues available to the FSHD research community.

NDRI's Private Donor Program will collaborate with the FSH Society to recover and distribute tissues from patients who participate in the FSHD Registry and who have provided consent for the recovery of tissues and organs for research. In addition to providing all resources required to recover tissues postmortem and from surgical procedures, NDRI will provide informational materials to the FSH Society for distribution to potential registry participants, as well as IRB-approved templates for obtaining informed consent from patients and authorization to donate from family decision makers.

### ► FUNCTIONAL STUDY OF THE DUX4 AND DUX4C DOUBLE HOMEODOMAIN PROTEINS IN SKELETAL MUSCLE

Eugenie Anseau, PhD, with Frederique Coppee, PhD, and Alexandra Belayew, PhD

University of Mons, Belgium

\$93,450 for one year

**Summary:** The double homeobox (DUX) genes constitute a family with hundreds of members dispersed into the human genome. They have been conserved in evolution, and this argues in favor of a functional role for these genes, although they were long considered as pseudogenes and thus poorly studied. However, several DUX genes are expressed in healthy muscle cells.

Our group has characterized the DUX4 gene that causes FSHD and the homologous DUX4c gene (both located at 4q35). Both encoded proteins are highly similar transcription factors and only differ in the carboxyl-terminal region. DUX4c is expressed in healthy muscle and induced in FSHD and Duchenne muscular dystrophy (DMD). Our previous data suggested a role for DUX4c in normal human muscle regeneration, and its activation (as in FSHD) could impact muscle regeneration in several myopathies. Deciphering the function of unstudied human muscle proteins should increase our understanding of physiological and pathological mechanisms of the skeletal muscle.

A way to decipher new functions for a protein is to go “fishing” for proteins that interact with it. Since many proteins are now well studied, the known functions of the identified partner can help uncover what our mystery protein does. The current project stems from our identification of putative and validated protein partners that hint toward unexpected functions for the DUX4/DUX4c proteins in cell architecture regulation and mRNA translation control.

The mRNA is a copy of the gene that travels from the nucleus to the cytoplasm, where it will give instructions to make the protein (translation). Many mRNAs only get activated at specific times. DUX proteins could be involved in this process. The discovery of partners located in the cytoplasm was unexpected, for DUX proteins are always found in the nucleus. However, we could observe that DUX4c translocated from the nucleus to the cytoplasm in differentiating myoblasts, when they elongate and fuse to make myotubes. To see the same translocation for DUX4, we had to overexpress it because

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**Binding.** The interaction of one molecule to another, which causes a change in the shape and function of the target molecule.

**Biomarker.** An objective measurement that indicates a patient's health status, such as a test of muscle strength, a blood test, imaging, etc. Diagnostic biomarkers show if a person has a disease. Therapeutic biomarkers show if a therapy is having the desired effect.

**Chromosome.** A recognizable organization of chromatin containing genes, regulatory elements, and other nucleotide sequences exploited in the study of cytogenetics. In humans, each cell nucleus contains 23 distinct pairs of chromosomes.

**Clinical trial.** A test of drugs, diagnostics, and other health interventions in human volunteers, conducted to generate safety and efficacy data.

**Cytoplasm.** The jellylike part of the cell lying between the cell membrane and the nuclear membrane.

**D4Z4.** A repeated DNA segment of approximately 3,200 nucleotide bases. The number of repeats can vary significantly in different individuals and can be used to predict FSHD status. Loss of these repeats at chromosome locus 4q35 is associated with FSHD Type 1. Each D4Z4 repeat contains a DUX4 gene.

**Deletion.** Loss of part of a DNA molecule, as in “deletion of D4Z4 repeats at 4q35” associated with FSHD.

**DNA.** The molecule that defines our genetic inheritance. It contains all the instructions for constructing and operating a living organism. DNA is made of four simple units, or “nucleotide bases,” whose specific sequence “spells out” genetic information.

**DUX4 (double homeobox, 4).** A copy of the DUX4 gene is located within each D4Z4 repeat array on chromosome 4. Inappropriate expression of DUX4 in muscle cells is thought to be a contributor to FSHD.

**Gene.** The basic unit of heredity defined by specific segments of DNA. Genes specify the instructions needed to produce an observable trait.

**Gene expression.** The initial step in converting the information contained in a gene, as DNA, to an observable characteristic through an intermediate molecule RNA.

**Genotype.** The actual DNA sequence of a cell, organism, or individual, usually with reference to a specific characteristic under consideration.

**Homeobox.** A DNA sequence found within genes that are involved in the regulation of patterns of anatomical development in organisms.

**Immortalized cells.** Cells that continue to divide indefinitely, unlike normal cells which, with normal aging, cease to divide.

**Methylation.** In biological systems, the addition of a methyl group to DNA, which can regulate the expression of genes. Some methylation changes are heritable.

**Molecular pathway.** A chain of chemical reactions occurring within a cell.

**Mutation.** A change in the nucleotide sequence in the genome of an organism with perceived deleterious effects.

**Myocyte.** A long, tubular cell found in muscle. Myocytes develop from myoblasts to form skeletal muscle fibers (myotubes) in a process known as myogenesis.

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# Advancing Clinical Trial Readiness for FSHD

*International conference brings together key stakeholders*

by **SHIFT COMMUNICATIONS** and the **FSH SOCIETY**

**T**he FSH Society co-funded the second FSHD Trial Preparedness Workshop, held May 29-30, 2015, at the University of Rochester Medical Center in New York. The workshop convened more than 50 stakeholders from around the world, comprising representatives from academic institutes, industry, the Food and Drug Administration, the National Institutes of Health, and patient advocacy groups, including the FSH Society.

The Society and two co-funders, FSHD Stichting of the Netherlands and the FSHD Global Research Foundation from Australia, each donated \$25,000 to cover the costs of the meeting.

“I was happy to see that the FSH Society had also funded many of the studies discussed at the workshop,” said June Kinoshita, who represented the FSH Society at the meeting. “This means that we are doing a good job of identifying and supporting work that is advancing the FSHD field toward treatments.”

“For this year’s workshop, the first objective is to reassess where we are in the process of developing relevant clinical outcome measures, biomarkers, and surrogate outcome measures for future FSHD trials,” said workshop organizer Rabi Tawil, MD, of the University of Rochester. “The second goal is to reach agreement on the most promising outcome measures to be pursued and identify gaps that remain. Finally, we hope to foster collaborations among investigators at different institutions to help accelerate the pace of research to fill those gaps.”

Over the past three years, a scientific consensus has emerged around the central genetic mechanism of FSHD. While many details about the disease process remain to be solved, several labs in both academia and industry have begun to search for potential therapies. In addition, financial incentives to encourage drug development for orphan diseases, combined with advances in tools to track disease progression, have wakened industry interest in FSHD.

Anticipating rapid progress in FSHD drug development, two years ago Tawil,



**Attendees of the second FSHD Trial Preparedness Workshop in Rochester, New York.**

together with Stephen Tapscott of the Fred Hutchinson Cancer Research Center in Seattle, Washington, and Silvere van der Maarel of the University of Leiden in the Netherlands, convened the first FSHD trial preparedness workshop, held in Leiden.

That meeting established working groups to develop recommendations for clinical outcome measures, imaging biomarkers, and molecular biomarkers (molecules that can be detected in tissue and bodily fluids). In addition, the groups developed common protocols to prospectively evaluate and validate the various outcome measures and biomarkers across multiple sites.

Data presented at this year’s workshop showed that researchers had heeded the directives from the 2013 workshop and were making impressive inroads. Notable advances included the following:

- National FSHD patient registries established in the U.K. and France, which are starting to yield useful information. Additional registries are being planned for other countries.
- Investigators are fine-tuning and validating clinical outcome measures such as the FSHD Health Index. Attendees discussed the need to standardize clinical outcome measures and adapt them for worldwide use.
- Preliminary data were presented on blood and tissue biomarkers, which

will need to be validated with larger studies. Discussion ensued on the need to clarify how biomarkers will be used. Some that are not specific for FSHD may still be useful measures of muscle degeneration, while therapies that target a specific mechanism, such as DUX4 gene expression, will require different biomarkers that can show whether a drug has affected the targeted mechanism.

- Magnetic resonance imaging (MRI) studies of patients who are followed over time are showing consistent findings of high water content in specific muscles prior to those muscles undergoing fat infiltration (a sign that muscle has degenerated and been replaced by fat). This seemed to suggest that high water content, interpreted as a sign of inflammation, predicts which muscles are on the verge of degenerating. However, this conclusion has been challenged by other MRI studies that are not seeing such a clear cause-and-effect pattern. An ongoing study is seeking to measure directly whether muscles with high water levels on an MRI also have high levels of immune signaling molecules.
- Electrical impedance myometry (EIM) is currently being explored in a longitudinal study. The method appears to be very reliable in many muscles but

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## NEWLY AWARDED GRANTS

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it is in very low abundance in FSHD cells. As a lot of identified partners are identical for DUX4 and DUX4c, the pathological increase of DUX4/DUX4c proteins in FSHD muscle cells could interfere with the normal DUX4c function in muscle and would contribute to explain why this tissue is particularly sensitive to pathological DUX4 expression (one of the FSH Society research priorities for 2015).

To further investigate these observations, we will 1) monitor DUX4/DUX4c protein trafficking in live muscle cells; 2) produce additional antibodies specifically targeting DUX4c; 3) validate DUX4/DUX4c interactions with partners that play major roles in cell architecture organization or mRNA translation; 4) compare the interactions of selected partners and DUX4/4c in healthy and FSHD-differentiating myoblasts; and 5) map the specific DUX4/DUX4c peptidic domains that interact with validated partners.

We expect this project will help 1) define new functions for DUX4 and the poorly studied DUX4c; 2) discover their putative interactions through shared partners; and 3) bring new light on the mechanisms of DUX4/4c toxicity in FSHD muscle and suggest new therapeutic strategies.

### August 2014 grant submission cycle awards

#### ► DETAILED TRANSCRIPTIONAL ANALYSIS OF STAGE-SPECIFIC EARLY FSHD MYOGENESIS

Gabsang Lee, PhD, DVM

Johns Hopkins University School of Medicine, Baltimore, Maryland, USA  
\$70,977 for one year

**Summary:** How FSHD unfolds at the level of molecules and cells is complex and not yet fully understood. Recent detailed genetic studies have significantly increased our knowledge of this enigmatic and multifaceted disorder, and suggest that abnormal genetic events occur early during the formation of muscle cells. The Lee lab has developed a novel strategy using human induced pluripotent stem cells (hiPSCs), directing them to develop into myoblasts (precursors to muscle cells). In this new project, the Lee lab proposes to isolate pluripotent cells (cells able to develop into many other types of cells), somite cells (a population of precursor cells), and myoblast cells of FSHD hiPSCs using established techniques, followed by detailed analysis of how the genetic code is transcribed. The proposed studies will shed light on FSHD pathogenesis stage by stage during very early development of human muscles.

#### ► DEVELOPMENT OF A NEW METHYLATION ASSAY FOR FSHD DIAGNOSIS

Giancarlo Deidda, PhD

Institute of Cell Biology and Neurobiology, Rome, Italy  
\$56,000 for 18 months

**Summary:** In both FSHD Type 1 and Type 2, genetic defects result in the D4Z4 repeat units on chromosome 4 becoming depleted in methyl groups ("hypomethylated"). This causes this portion of the chromosome to "relax," resulting in a molecular environment that permits the expression of the DUX4 gene, considered by most researchers to be a key causative gene for FSHD. DUX4 expression also requires the presence of a polyadenylation signal (PAS) distal to the last D4Z4 unit, which stabilizes the DUX4 transcript.

## Glossary of Scientific Terms *continued*

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**Nucleus.** A large, cellular organelle enclosed by a membrane that contains genetic material (DNA).

**Phenotype.** The composite of an organism's observable characteristics or traits, such as its physical form, growth, biochemical and physiological properties, and behavior.

**Pluripotent cell.** A stem cell that has the potential to differentiate into diverse types of cells. Induced pluripotent stem cells (iPS cells or iPSCs) are a type of pluripotent stem cell artificially derived from an adult somatic cell by inducing a "forced" expression of certain genes.

**Protein.** A biological molecule consisting of linear chains of amino acids. Proteins are the principal products of genetic information, and they do the bulk of the work required for life. They perform a vast array of functions within living organisms, including providing cells with structure, mediating biochemical reactions, transmitting biological signals, and transporting molecules from one location to another.

**RNA (ribonucleic acid).** A family of large, biological molecules that perform vital roles in the coding, decoding, regulation, and expression of genes. Like DNA, RNA is assembled as a linear chain of nucleotide "bases" but is usually single stranded.

**Stem cell.** An undifferentiated biological cell that can differentiate into a variety of specialized somatic cells (pluripotent) and divide to produce more stem cells.

**Transcription.** The copying of DNA into messenger RNA in gene expression.

Currently, FSHD diagnosis is based on the identification of a reduction in D4Z4 repeat units on chromosome 4 (in FSHD1) or the presence of mutations in SMCHD1 (in FSHD2), combined with and the assessment of the 4qA polyadenylation signal (PAS). In addition, the D4Z4 repeat units on chromosome 4 are analyzed for hypomethylation.

This project aims to introduce a new assay that combines the different key features found in FSHD patients. The proposed assay will carry out methylation analysis of 10 CpGs within the 3' (3-prime) portion of the distal DUX4 copy (DUX4- $\beta$ ) that is specifically expressed in muscles of FSHD patients. Despite the low complexity and the presence of repetitive elements in the region (pLAM), we were able to design PCR assays on bisulfite-treated DNA that are specific for the presence of PAS sequence in the 4qA allele.

Preliminary results in a subset of FSHD1, FSHD2, and control subjects showed highly significant differences of methylation levels between affected and unaffected subjects in eight out of 10 CpGs tested, strongly supporting the potential usefulness of this assay for FSHD diagnosis. In this project, the investigators propose to:

- develop additional assays to quantify the number of permissive alleles in order to assess whether different allelic combinations are relevant in the identification of diagnostic threshold;
- analyze a large cohort of well-genotyped FSHD patients and normal controls for precise evaluation of methylation threshold between affected and unaffected subjects;

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## RESEARCH STUDIES NEED YOU

Volunteers—individuals with FSHD and unaffected family members—are essential for research. While much progress has been made, many mysteries are still locked up inside patients' genes, bodies, and storehouses of knowledge about symptoms, differences among family members, and the experience of living with FSHD. We cannot guarantee when treatments will arrive, but here's one thing we guarantee: if you volunteer for research, your participation will move us a step closer to that day. Here are studies that are currently recruiting volunteers:

► **SAFETY, TOLERABILITY, PHARMACOKINETICS, AND BIOLOGICAL ACTIVITY OF ATYR1940 IN ADULT PATIENTS WITH MUSCULAR DYSTROPHY**

**Sponsor:** aTyr Pharma, Inc., San Diego, California  
**Contact:** aTyr Pharma, Inc., at +1 (877) 215-5731 or email [clinicaltrials@atyrpharma.com](mailto:clinicaltrials@atyrpharma.com)

This study is recruiting male and female patients aged 18 to 65 years, inclusive, who have an established, genetically confirmed diagnosis of FSHD with clinical findings meeting existing criteria. This is a placebo-controlled, randomized, multiple ascending dose study to evaluate the safety, tolerability, pharmacokinetics, and biological activity of a novel biologic agent, ATYR1940 (trade name Resolaris®). Trial sites in Rochester, New York; Columbus, Ohio; Rome, Italy; Marseille, France; Nijmegen, the Netherlands.

For more information see <https://clinicaltrials.gov/ct2/show/NCT02239224>.

► **THE RELATIONSHIP OF ELECTRICAL IMPEDANCE MYOGRAPHY TO MUSCLE STRUCTURE AND FUNCTION IN FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY (FSHD)**

**Principal Investigator:** Jeffrey Statland, MD, University of Kansas Medical Center, Kansas City  
**Contact:** Melissa Currence at (913) 588-0684 or email [mcurrence@kumc.edu](mailto:mcurrence@kumc.edu)

Recent genetic advances in the understanding of FSHD have identified potential future targets for therapy. Consequently, it is important that we have appropriate tools in place for use in FSHD clinical trials. We are conducting a study to evaluate a new measure of muscle structure, electrical impedance myography. The ability to measure underlying changes in your muscle and understand how those changes relate to your strength or the underlying pathology in FSHD will be of vital importance in designing future FSHD therapeutic clinical trials. We are seeking twenty (20) volunteers to participate in this study. Volunteers will be required to make a single visit lasting approximately six hours. Anyone with a diagnosis of FSHD who is able to walk independently and can travel to and from the University of Kansas Medical Center is eligible for this study.

► **KINECT UO1: DEVELOPMENT OF NOVEL UPPER EXTREMITY OUTCOME MEASURES USING 3-D VISION TECHNOLOGY**

**Principal Investigator:** Jay Han, MD, University of California, Davis  
**Contact:** Research coordinator Alina Nicorici at (916) 734-0968

The purpose of this study is to develop new outcome measures for patients with muscular dystrophy. These outcome measures will focus on upper arm movement and what we call range of motion or reachable workspace. Ultimately, our goal is to develop these new techniques to aid in the development of new therapies and create outcome measures for clinical trials. We would like to see the participant every six months for a total of three visits. Each visit takes about one to one and a half hours. We will also compensate \$20 for each completed visit.

The study will take place at UC Davis Medical Center in PM&R Research, 4860 Y Street, Suite 1113, Sacramento, California 95817.



► **FACIOSCAPULOHUMERAL DISEASE (FSHD) STUDY**

**Principal Investigator:** Kathryn Wagner, MD, PhD, Kennedy Krieger Institute, Wellstone Muscular Dystrophy Cooperative Research Center, Baltimore, Maryland  
**Contact:** Genila Bibat, MD, at (443) 923-2778 or email [bibat@kennedykrieger.org](mailto:bibat@kennedykrieger.org)

Volunteers with FSHD and their immediate family members are needed for a clinical research study. Volunteers will be asked to provide blood and muscle or skin samples to be deposited in a research core facility. Blood, muscle, and skin samples will then be sent to multiple investigators for studies including gene and protein expression analysis and immortalization of muscle cells. Although there is no direct benefit to the volunteer, the samples are anticipated to be a

great asset in multiple studies within the FSHD Wellstone and the larger FSHD research community. The study is especially seeking volunteers with infantile FSHD, families with more than one affected member, ethnic minorities, and people with FSHD-related hearing loss or eye involvement. Volunteers will be reimbursed for travel and lodging costs associated with the study.

► **MYOTONIC DYSTROPHY AND FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY REGISTRY**

**Principal Investigator:** Richard T Moxley, University of Rochester, New York  
**Contact:** Registry Coordinator at (888) 925-4302 or email [dystrophy\\_registry@urmc.rochester.edu](mailto:dystrophy_registry@urmc.rochester.edu)

The purpose of this registry is to connect people with myotonic dystrophy (DM) or facioscapulohumeral muscular dystrophy (FSHD) with researchers studying these diseases. The registry will offer individuals with DM and FSHD an opportunity to participate in research that focuses on their diseases. The registry will also help scientists accomplish research on DM and FSHD and distribute their findings to patients and care providers. For more information, see <https://clinicaltrials.gov/ct2/show/NCT00082108>.

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- assess specificity of this assay for FSHD by testing individuals with unrelated muscular dystrophies;
- analyze the prognostic potential of this assay by correlating methylation levels with different clinical severity scores;
- study possible methylation differences distal to the D4Z4 array between subjects' white blood cells and muscle biopsies.

### ► PHYSIOLOGICAL STUDIES OF MUSCLE WEAKNESS IN FSHD

**Jun Udaka, MD, PhD, and Charles P. Emerson Jr.**  
**University of Massachusetts Medical School, Worcester, USA**  
**\$212,060 for two years**

**Summary:** The pathophysiology of FSHD is poorly understood and understudied. This FSH Society fellowship award will support comprehensive and detailed physiological investigations of force generation and calcium signaling in skinned and permeabilized single fiber preparations of FSHD and unaffected control muscle biopsies. Proposed studies address whether FSHD muscles are defective in: 1) troponin-mediated Ca<sup>2+</sup> signaling for myofibrillar force generation; 2) sarcoplasmic reticulum (SR) calcium release; 3) myosin ATPase activity; and/or 4) contraction fatigue. Additional studies investigate the roles of titin and extracellular matrix (ECM) in muscle fiber elasticity as contributing factors in FSHD disease pathology. Findings will identify muscle proteins and contractile processes that become dysfunctional during FSHD disease progression and reveal the underlying pathophysiology of FSHD muscle weakness to enable the development and evaluation of FSHD therapeutics in preclinical and clinical studies.

### ► IDENTIFICATION OF THE UNDERLYING GENETIC DEFECT IN A FAMILY WITH FSHD-LIKE AND OPTIC ATROPHY PHENOTYPE

**Lionel Van Maldergem, MD, PhD**  
**Université de Franche-Comté, Besançon, France**  
**Björn Fischer-Zirnsak, PhD**  
**Universitätsmedizin Berlin, Germany**  
**\$8,000 for one year**

**Summary:** Some years ago, a consanguineous family from Italy suffering from an FSHD-like phenotype came to our attention. Both parents were unaffected, whereas all four children show a progressive muscle weakness. The patients show facial and upper limb muscular weakness, which became more severe with age. A muscle biopsy from one individual was investigated and showed mild fibrosis, targetoid fibers, and a neurogenic component with increased abundance of Type 1 muscle fibers. Besides muscular features, all affected individuals reported eye abnormalities, such as myopia in early infancy. A detailed investigation of the eye and the eye fundus revealed an atrophy of the optic nerve in all affected individuals, determining progressive blindness.

Furthermore, deep investigation of multiple serum and urine parameters showed an increased level of 3-methylglutaconic acid in the urine and in the serum samples analyzed. Additionally, creatine kinase values are increased in all individuals tested.

The affected individuals from this exceptional family suffer from a disease which combines features known for FSHD and optic nerve atrophy. Furthermore, metabolic alterations which might point to mitochondrial dysfunction were identified which could

lead to a better understanding of the affected gene product. Since the unaffected parents were second cousins, recurrence in sibship strongly suggested autosomal recessive inheritance.

Using various molecular genetic techniques, we were not able to detect the causative genetic defect in our index family. Due to the fact that no deletions and causative coding mutations as well as alterations in regulatory regions around CCDC67 could be identified, it is very likely that a non-coding mutation is the cause of this disease. To identify the causative alteration, whole-genome sequencing (WGS) is the method of choice. Raw data analysis and interpretation may be conducted in the Institute of Human Genetics at Charité (University of Berlin), where both the applicant fellow and his supervisor have acquired an international expertise. Moreover, they collaborate tightly with a strong bioinformatics group which is experienced in the evaluation of large-scale genetic data. We are planning to analyze whether larger genomic rearrangements such as an inversion or translocations are present which could explain, for example, the misexpression of CCDC67. Furthermore, mutations in other intergenic and potential regulatory structures will be investigated.

After the identification of the causative mutation, we plan to perform functional investigations of in vitro and in vivo models. We are experienced in cell culture-driven investigations of genetic disease and in the generation of mouse models using, for example, CRISPR/Cas.

### ► DECIPHERING THE CONTRIBUTION OF FAT1-DEPENDENT PHENOTYPES TO FSHD SYMPTOMS AND RELEVANCE FOR THERAPEUTIC DESIGN

**Françoise Helmbacher, PhD**  
**IBDM, CNRS UMR 7288, Marseille, France**  
**\$138,803 for two years**

**Summary:** This research team previously found that disruption of the Fat1 cadherin gene in mice caused muscular and non-muscular symptoms resembling those of FSHD, and had shown that alterations of the FAT1 locus in humans, located near the FSHD critical region on chromosome 4, were associated with FSHD, identifying FAT1 as a modifier gene in FSHD and as a key player of muscular pathologies.

Removing the Fat1 gene in mice causes abnormalities in the shape of selective groups of muscles and leads to regionalized muscle wasting, the map of affected muscles being highly similar to the map of muscles affected in FSHD. Reduced FAT1 expression levels were seen in muscles of fetal as well as adult FSHD cases. The investigators identified human mutations in the FAT1 locus segregating with FSHD: heterozygous deletions of a putative regulatory enhancer, predicted to cause tissue-specific depletion of FAT1, co-segregate with FSHD, and heterozygous point mutations, either perturbing splicing of FAT1 or leading to deleterious amino acid changes, were found in FSHD-like patients carrying neither chromosome 4 alterations nor mutations in SMCHD1. Thus, FAT1 is a compelling novel FSHD modifier gene.

This collaborative work was the objective of a network grant from FSHD Global, for which Dr. Helmbacher was the coordinator. In addition, part of this work was also supported by the FSH Society through a grant to V. Mariot, working with J. Dumonceaux.

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# Charity Navigator four-star award goes to FSH Society

Society ranks among top 2 percent of all charities in America

by JUNE KINOSHITA

The FSH Society has received its seventh consecutive Charity Navigator four-star rating. Only 2 percent of the charities rated by the Charity Navigator have received at least seven consecutive four-star evaluations. This indicates that the FSH Society outperformed most other charities in America.



Receiving four out of a possible four stars indicates that the FSH Society adheres to good governance and other best practices that minimize the chances of unethical activities and consistently executes its mission in a fiscally responsible way. This rating differentiates the FSH Society from other organizations and demonstrates to the public that it is worthy of their trust.

“As the nonprofit sector continues to grow at an unprecedented pace, savvy donors are demanding more accountability, transparency, and quantifiable results from the charities they choose to support with their hard-earned dollars,” said John P. Dugan, founder and chairman of the Charity Navigator board. “Our goal in all of this is to provide donors with essential information needed to give them greater confidence in the charitable choices they make.”

The FSH Society has several fundraising events planned around the country. (See our events calendar on page 28.) We are seeking companies, foundations, and individuals to sponsor these occasions, which they can do with confidence knowing that the funds will be well spent. In 2013, 87.4 cents on the dollar went directly to FSH Society programs. We did even better in 2014, directing 91.7 cents on the dollar to programs.

“This four-star rating shines a light on the efforts we put in to ensure that the FSH Society is efficient, ethical, and open,” said Daniel Perez, FSH Society President & CEO. “We are excited and honored to be recognized as one of the top charities in the country.” [FSH Watch](#)



## Fifteen minutes of fame for FSHD!

### #CUREFSHD POSTERS INVADE THE BOSTON METRO TRANSIT SYSTEM

In mid-May of this year, the FSH Society released its first-ever public service message on Boston’s public transit network, the Massachusetts Bay Transit Authority (MBTA). The campaign consists of five images educating commuters about the facts of FSHD and urging them to share images and reach out across social networks to FSHD patients and let them know they are not alone. Thanks to the MBTA’s program to donate free advertising space to nonprofits, we were able to display 250 posters in Boston’s subways, trains, and buses.

One of our portrait subjects is Erin Gullage

of Cambridge, Massachusetts. A few weeks after the campaign began, she posted on Facebook that friends were spotting her photo on the ads.

“I got text messages from three different people who said they were on the train and saw a poster with my picture on it,” she wrote to us. “At first,

I couldn’t figure out why my picture was on the T, and then I remembered the #CureFSHD awareness campaign.

“All of the people who saw the poster said they immediately looked up the meaning of FSHD. I got my 15 minutes of fame and am proud to tell the world about FSHD!”



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The investigators are currently studying the consequences in developing embryos and adult mice of ablating Fat1 in muscle, neurons, and mesenchyme. This work has previously received support from the FSH Society through a postdoctoral fellowship to Angela Zimmermann and is being prepared for publication.

The current project aims to extend this work through the following approaches:

1. Using CRISPR/Cas9 technology in ES cells, generate two mouse models carrying FAT1 alterations found in FSHD-like patients. The investigators will select mutations that altered FAT1 splicing, as these could be corrected (in vitro) with antisense oligonucleotides (AON). Ultimately, the aim is to evaluate the capacity of such splicing-correcting-AON to alleviate muscle symptoms in the resulting humanized mice.
2. Evaluate the relative frequency of any genetic alteration occurring in the FAT1 locus among classical FSHD1 patients, with a particular focus on patients with retinal vascular symptoms, also present in Fat1-deficient mice, to determine whether alteration of FAT1 expression occurs as a result of DUX4 expression or synergizes with DUX4 expression to cause FSHD symptoms. Results of this project will help clarify to what extent the phenotypes caused by perturbations of FAT1 functions contribute to the appearance of FSHD symptoms and will be instrumental in developing novel therapeutic strategies for FSHD patients.

### Ad hoc 2015 grant awards

#### ► EXPLOITING GENOME EDITING TECHNOLOGIES

Michael Kyba, PhD

University of Minnesota, Minneapolis, USA

\$125,000 for one year, jointly funded with FSHD Canada

**Summary:** The past several years have seen tremendous advances in our ability to specifically modify DNA sequences in the human genome. FSHD is caused by the combination of two factors: the contraction of D4Z4 repeat number combined with the presence of a pathogenic sequence downstream of the D4Z4 repeats. Both of these DNA elements are accessible to modification using newly developed genome editing technology. The Kyba lab has developed methods of gene targeting that address both elements and will use these to derive and study genetically corrected FSHD cell lines.

**Aim 1:** To correct the FSHD locus in human stem cells bearing the FSHD mutation. Our work to date has shown that FSHD iPSCs express DUX4 mRNA and suffer from an impaired response to Pax7-induced skeletal muscle differentiation, and that these phenotypes are reverted by genetic removal of the contracted D4Z4 array. These iPSCs were derived from myoblasts; therefore, there is some question of whether these phenotypes represent an epigenetic memory of the pre-iPSC cell type. It will therefore be essential to perform this genetic correction in FSHD human stem cells.

**Aim 2:** To design CRISPRs that target existing and novel sites at 4q35.2. The efficiency of targeted integration with our ZNF reagent is low; therefore, we will test whether our existing genetic repair

method can be made more efficient by CRISPR technology. We will also design and test CRISPRs targeting the pathogenic poly(A) signal, which may allow correction of the locus without elimination of the entire D4Z4 array.

**Aim 3:** To use engineered, sequence-specific DNA-binding tools to target a chromatin nucleation complex to D4Z4. While most enthusiasm around the discovery of TALENs and CRISPRs has concerned their ability to target a nuclease to introduce double-strand breaks in DNA, they can also be used to target other proteins to DNA.

*Dr. Kyba's project is jointly funded through the Society as a result of collaboration and partnership with The FSHD Canada Foundation, Calgary, Alberta.* [FSH Watch](#)

### #FSHDselfies campaign

#### #FSHDSelfies Campaign Takes Top Prize

We have some good news to share! On June 11, members of SHIFT Communications, our pro bono PR/marketing partner, attended the annual Publicity Club of New England's Bell Ringer Awards. The Publicity Club of New England is the region's oldest not-for-profit public relations trade organization. The Bell Ringer Awards honor the superior work done by public relations and communications professionals across New England each year.

SHIFT submitted the #FSHDselfies campaign for the "Non-Profit Communications Campaign" and were the winners of the highest honor in the category—the Gold Bell. We congratulate SHIFT on this prestigious award and couldn't be more proud to be associated with such a stellar team!



Accepting the Gold Bell award for SHIFT are (from left to right) Liz Ianotti, Jennifer Toole, and Annie Perkins.

## Portrait project

Capturing individuals' "FSHD signature" through photography

by ROMANA VYSATOVA  
Cambridge, Massachusetts

Last August at the FSH Society's FSHD Connect meeting in Boston, I photographed volunteers willing to pose to help convey the impact of the disease to the public. This was my first exposure to facioscapulohumeral muscular dystrophy, which I learned is a heritable genetic disorder affecting about one in 8,000 people, causing a progressive weakening of muscles in the upper arms, around the shoulder blades, and in the face. I was told that FSHD is as unique as the individuals who have it, and our goal was to portray how FSHD has affected each one's body and its ability to function.

We weren't sure what to expect and didn't know if anyone would be willing to be photographed. As it turned out, there were many, many people who signed up, each helping me out by exploring poses and movements that are their unique "FSHD signature"—a specific pose, or way of moving, or way they've discovered to enable them to accomplish what has become a difficult task. They generously revealed these things that in daily life they do their best to cover up.

One of the many things that surprised me was how powerfully engaged each person, and their family, was in helping to define FSHD. The conference was about connecting researchers and patients, and it was clear how committed each was to making a contribution by sharing information.



Deborah S. demonstrates her "FSHD signature" move: two-handed lipstick application.

Besides revealing the physical effects, the stories they told were incredible; one man said his grandfather had a particular way of walking which in their family lore was the result of a war injury, but that his grandson now recognizes was a symptom of FSHD that he recognizes in himself now.

After the conference, Deborah S. wrote to me that she had shared a photo with her FSH Facebook group: "The picture of me putting on lipstick with two hands resonated with all the women. And some of my gestures and movements—everyone saw pieces of themselves in those. We ended up discovering that the two-handed thing is because most of us have hand tremors, which all the FSHD neurologists say isn't a part of FSHD. They were wrong about pain, so they could be wrong about this, also."

I guess that is what was most exciting about taking these pictures—besides, of course, working with all these incredible people—the idea that I can help them make a contribution to each other and to science. [FSH Watch](#)

**Editor's note:** Romana Vysatova loves to photograph people doing the things they love. She has worked with nonprofits, schools, companies, and individuals. She also enjoys photographing weddings and other special events. She can be contacted at [romana@romanaphoto.com](mailto:romana@romanaphoto.com).

### #CureFSHD campaign gains exposure

#### FROM THE INDY 500 TO THE BOSTON TRANSIT SYSTEM

The FSH Society's #CureFSHD campaign, which features portraits and facts about FSHD, has been gaining traction. On social media, the images have been shared over 2,630 times and seen by over 15,000 members of the public. The campaign has begun to reach out beyond social media to attract views in new places.

On May 24, the FSH Society showed a new public service announcement at the 99th running of the Indianapolis 500 Mile Race at the Indianapolis Speedway. The 15-second PSA, displayed on a jumbotron to some 500,000 racing fans, featured eye-catching portraits of FSHD patients and families, and encouraged fans to donate in support of finding a cure for FSHD.

During June and July, FSH Society advertisements were seen by thousands of commuters riding subways and buses throughout the Boston transit system, or MBTA. (See story on page 18.)

The MBTA campaign encourages the public to "share an image" and "change a life." The campaign is intended to rouse public curiosity about FSHD as well as reach people with FSHD who may be undiagnosed or who currently lack access to peer support and information. This message is also the focus of the FSH Society's new 60-second PSA, "The #CureFSHD muscular dystrophy campaign," which is now available on YouTube. Please keep sharing campaign images throughout the year. Our mission: to make FSHD a household word!

To find out more about supporting the FSH Society and the #CureFSHD campaign, go to [FSHsociety.org/curefshd](http://FSHsociety.org/curefshd).



# Climbing Mountains

Prologue from a memoir

by SARABIT PARMAR  
Evington, United Kingdom

“Have you managed to walk today?”

This is the usual comment I get from that nosy neighbor (who knows that I can’t walk and have been in a wheelchair since the age of 14).

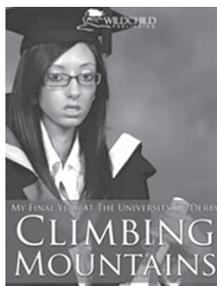
“I only walk at night. Sometimes I even fly down the stairs,” I replied seriously. Her jaw dropped in shock, and she hurried away. Had it been physically possible, a smile would have instantly spread across my face.

Since I was born, I’ve been living with FSHD, a condition that causes speech impairment and prevents me from articulating any facial expressions such as smiling or frowning. You could say I always look like I’m ready to smack someone, but trust me, I’m nice—that’s if you stay on the right side of me.

As a baby I learned to walk and did the usual mischievous things that toddlers do. In fact, I recall a photograph of me as a child eagerly grabbing a bunch of daffodils because apparently I didn’t like them moving in the wind. This just proves my mother’s theory that I always did what I wanted and never let anything get in my way. Some may call it bossy, but I call it determined.

Throughout my childhood, I visited numerous specialists, and at eight years of age I was actually diagnosed with FSHD. The more I grew up, the more my disability progressed. In my early teens, I started walking with a limp, which resulted in my spine developing a curve. Due to this, my ability to walk gradually decreased, and I used to fall flat on my face. Embarrassing at times, but thankfully my nose is still intact.

As a child, I dreamed of being a dancer and owning my own dance school, but that went out of the window when at 14 my backside became best friends with a wheelchair. This was the hardest battle I’ve ever had to fight. My old school friends disappeared, extended family members treated me differently, and my whole world turned upside down. I spent time sulking, being



angry, and trying to make sense of the harsh reality of the situation. I found it extremely tough to adjust, but I soon realized that life stops for no one, and the show goes on.

I toughened up and told myself, “Just get on with it.” I decided that instead of allowing myself to feel restricted by my disability, I had to fight back and use it as a challenge. I became adamant that my wheelchair was not going to change my life, and I refused to become a victim of it. So I did what all young women my age do—shopped ‘til I dropped, partied ‘til dawn, hung out with friends, went to university, and started a career as a writer. People always say I’m fearless, and I guess that’s true. I live life in the fast lane. I grab every opportunity that comes my way, and I won’t stop until I reach my goals.

Going to university and gaining a bachelor of arts honors degree in creative writing and media writing is one of my proudest achievements. Reaching this milestone in my life wasn’t easy, but I realized that the mind is a powerful thing. No matter what adversities you face or how many mountains you have to climb, as long as you have self-belief, stay focused, and work hard, then every dream can become a reality.

Dealing with my condition has given me determination not just to chase my dreams but to damn well make them happen. I’ll

never just talk about the things I want to do, like going to university, traveling the world, holding a snake around my neck. Or tandem-paragliding (for which I had to sign an agreement stating that if I became injured or died, it’s my own fault. But don’t worry. I told the instructor, “Should I meet my death, I’m taking you down with me.”). My actions will always speak louder than words because that’s the way I roll.

*Sarabjit Parmar was born September 2, 1983, in Leicester, England. She lives with her parents, four sisters, and one brother. She is a writer and poet who, since graduating with a BA Joint Honours degree in creative writing and media writing, has contributed to a range of newspapers and magazines. Her memoir of her college experience, Climbing Mountains, is available on Amazon in softcover and Kindle editions. Her next project is a novel, and she’s also working on a children’s book in which a little girl in a wheelchair masters the art of lucid dreaming. When Parmar is not writing, she’s obsessing over chicken dishes, shoes, and lipsticks!* [FSH Watch](#)

To keep up to date with what Sarbs is up to, you can follow her on her Twitter account @Sarbs\_Parmar, or like her on Facebook <https://www.facebook.com/sarabjit1parmar>, or visit her blog <http://sarbzparmar.blogspot>.

## Information at your fingertips

The FSH Society is dedicated to making sure you have accurate, useful information to help improve the quality of your healthcare and daily life. Our publications are created and reviewed by patients and experts. Currently available to download on our website at [www.fshsociety.org](http://www.fshsociety.org):

- About FSHD
- Physical Therapy and FSHD
- FSHD: A Guide for Schools
- FSHD and Social Support: A guide for friends and family

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**FSH Society**  
450 Bedford Street  
Lexington, MA 02420  
Telephone: (781) 301-6060  
Email: [info@fshsociety.org](mailto:info@fshsociety.org)



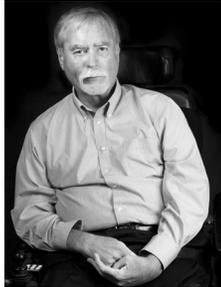


# In memoriam, Robert (“Bob”) Smith, longtime Board member

*Attorney and passionate environmentalist*

by **HOWARD CHABNER**  
*San Francisco, California*

**B**ob Smith, FSH Society Board of Directors member for over 15 years, died on April 7 at age 67 from pneumonia and complications of FSHD. A Massachusetts native, Bob lived in Cape Cod, Massachusetts, for over 40 years, together with his wife Patti. They had been married for 46 years.



**Bob Smith**

Society’s Board, he gave freely of his deep legal experience and keen insight, wisdom, and astute judgment, drafting and reviewing contracts, advising on strategy, and making sure that proper practices were followed. Bob also served as chairman of the nominating committee, recruiting and vetting new Board members, thereby helping to ensure the continuity of the Society.

Bob’s generosity and wisdom extended beyond involvement with FSHD. A proud New Englander, he was the founder and president of the Harwich Conservation Trust (HCT). An early champion of conservation, he recognized the need for land preservation in Harwich and acted on it. Under his leadership, the HCT has saved and preserved over 520 acres—nearly an entire

square mile—in Harwich.

Bob was always ready with a witty remark that put a situation in perspective. His wit was dry and ironic, but always with a generosity of spirit that made his point all the more funny and powerful.

He continued to practice law, served as founder and president of the HCT, and sat on the Society’s Board until his passing. This “triple play” is a remarkable and inspiring feat for an individual with advanced FSHD. He had been diagnosed when he was a teenager and had used a wheelchair for the past 15 years. Bob’s fellow Board members and all who knew him admired him for his generosity, modesty, talent, endurance, strength of character, integrity, and physical courage. [FSHWatch](#)



## ADVOCACY

# Raising awareness about disability

*Massachusetts high school students learn about FSHD*

by **KRISTIN DUQUETTE**

**S**peaking at the Cambridge School of Weston’s Social Justice Day in Weston, Massachusetts, this past April was an incredible experience! Disability awareness was the theme of the day, and it was an honor to engage with students about a topic so close to my heart.

The main points I discussed ranged from disability stereotypes, body image, and disability representation in today’s media, to how we’re all connected. This was also an opportunity to tell them about how FSH muscular dystrophy has affected me.

The main messages I wanted to bring home to students were that disability shouldn’t be feared, and the different ways we can break down this fear from our daily lives. Students were engaged, curious, and some didn’t know what to ask, but the most important takeaway was to have students realize that it’s an incredibly good thing for the world to be filled with diverse and different people.

If we look at our society through a lens of acceptance rather than fear of disability, I truly believe we would live in a more inclusive world. After speaking, I took a selfie with students to show that no matter how diverse we may be or look, we are all connected by just being human.

I was so impressed by how engaging the students were and open to learning a topic that can be uncomfortable for many. Af-

terwards, I got tweets and messages from students with questions and comments. It is great to see students learning about this topic outside of the classroom and connecting it to our world. [FSHWatch](#)



**Kristin (foreground) snaps a selfie with students at Cambridge School of Weston.**

# FSH Society-supported research in print

## Recently published articles

by **JUNE KINOSHITA** and **DANIEL PEREZ**

**T**he following publications were supported by the FSH Society in the form of research fellowships and travel grants. We thank our many donors for providing the funding to advance our scientific and medical understanding of FSHD.

**$\beta$ -catenin is central to DUX4-driven network rewiring in facioscapulohumeral muscular dystrophy.**

Banerji CR, Knopp P, Moyle LA, Severini S, Orrell RW, Teschendorff AE, Zammit PS. *J R Soc Interface*. 2015 Jan 6;12(102):20140797.

**Whole-body magnetic resonance imaging evaluation of facioscapulohumeral muscular dystrophy.**

Leung, D. G., Carrino, J. A., Wagner, K. R. and Jacobs, M. A. *Muscle Nerve*. 2015 Jan 16. doi: 10.1002/mus.24569.

**Expression of FSHD-related DUX4-FL alters proteostasis and induces TDP-43 aggregation.**

Homma S, Beermann ML, Boyce FM, Miller JB. *Ann Clin Transl Neurol*. 2015 Feb;2(2):151-66. doi: 10.1002/acn3.158. Epub 2015 Jan 15.

**miRNA expression in control and FSHD fetal human muscle biopsies.**

Portilho DM, Alves MR, Kratassiouk G, Roche S, Magdinier F, de Santana EC, Polesskaya A, Harel-Bellan A, Mouly V, Savino W, Butler-Browne G, Dumonceaux J. *PLoS One*. 2015 Feb 18;10(2):e0116853. doi: 10.1371/journal.pone.0116853. eCollection 2015.

**Muscle pathology grade for facioscapulohumeral muscular dystrophy biopsies.**

Statland JM, Shah B, Henderson D, van der Maarel S, Tapscott SJ, Tawil R. *Muscle Nerve*. 2015 Feb 23. doi: 10.1002/mus.24621.

**Aberrant splicing in transgenes containing introns, exons, and V5 epitopes: lessons from developing an FSHD mouse model expressing a D4Z4 repeat with flanking genomic sequences.**

Ansseau E, Domire JS, Wallace LM, Eidahl JO, Guckes SM, Giesige CR, Pyne NK, Bellayew A, Harper SQ. *PLoS One*. 2015 Mar 5;10(3):e0118813. doi: 10.1371/journal.pone.0118813. eCollection 2015.

**Reachable workspace reflects dynamometer-measured upper extremity strength in FSHD.**

Han JJ, de Bie E, Nicorici A, Abresch RT, Bajcsy R, Kurillo G. *Muscle Nerve*. 2015 Mar 18. doi: 10.1002/mus.24651.

**Double SMCHD1 variants in FSHD2: the synergistic effect of two SMCHD1 variants on D4Z4 hypomethylation and disease penetrance in FSHD2.**

By van den Boogaard ML, Jfl Lemmers R, Camaño P, van der Vliet PJ, Voermans N, van Engelen BG, Lopez de Munain A, Tapscott SJ, van der Stoep N, Tawil R, van der Maarel SM. *Eur J Hum Genet*. 2015 Mar 18. doi: 10.1038/ejhg.2015.55.

**Individual epigenetic status of the pathogenic D4Z4 macrosatellite correlates with disease in facioscapulohumeral muscular dystrophy.**

Jones TI, King OD, Himeda CL, Homma S, Chen JC, Beermann ML, Yan C, Emerson CP Jr, Miller JB, Wagner KR, Jones PL. *Clin Epigenetics*. 2015 Mar 29;7(1):37. doi: 10.1186/s13148-015-0072-6.

**Respiratory muscle dysfunction in facioscapulohumeral muscular dystrophy.**

Santos DB, Bous-said G, Stojkovic T, Orlikowski D, Letilly N, Behin A, Butel S, Lofaso F, Prigent H. *Neuromuscul Disord*. 2015 Apr 30. pii:

S0960-8966(15)00149-2. doi: 10.1016/j.nmd.2015.04.011.

**Emerging preclinical animal models for FSHD.**

Lek A, Rahimov F, Jones PL, Kunkel LM. *Trends Mol Med*. 2015 May;21(5):295-306. doi: 10.1016/j.molmed.2015.02.011.

**Culture Conditions Affect Expression of DUX4 in FSHD Myoblasts.**

Pandey SN, Khawaja H, Chen YW. *Molecules*. 2015 May 8;20(5):8304-15. doi: 10.3390/molecules20058304.

**Correlation between low FAT1 expression and early affected muscle in facioscapulohumeral muscular dystrophy.**

Mariot V, Roche S, Hourdé C, Portilho D, Sacconi S, Puppo F, Duguez S, Rameau P, Caruso N, Delezoide AL, Desnuelle C, Bessières B, Collardeau S, Feasson L, Maisonobe T, Magdinier F, Helmbacher F, Butler-Browne G, Mouly V, Dumonceaux J. *Ann Neurol*. 2015 May 28. doi: 10.1002/ana.24446. **FSHWatch**

### Liam's science project

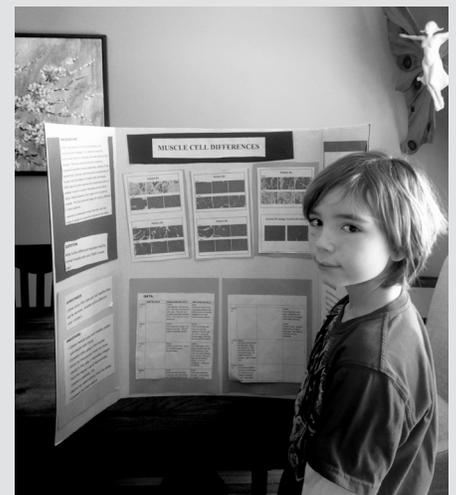
#### WITH A LITTLE HELP FROM AN FSH SOCIETY GRANTEE

**A letter to FSH Society grantee Lindsay Wallace, PhD, Nationwide Children's Hospital, Columbus, Ohio**

**I wanted to send you a picture of my son Liam and his finished science project on the differences between normal muscle cells and FSHD muscle cells. His project included a special thanks to Lindsay from the Harper Lab in his bibliography. Although we couldn't accomplish the actual tests that he wanted to do, I think the project was great and so empowering for him.**

**Liam said that a lot of people in school were asking questions about FSHD and what it means. Since he doesn't have any control over what is happening to his muscle cells, I love that he can control how he feels about his body based on his growing knowledge of it.**

**I can never thank you enough, not only for the day-to-day work you are doing in FSHD research, but for also helping to empower Liam. You are changing his life, and for that I am so grateful!!!**



Liam Eye with his science project!

**—Maureen Eye, Rocky Point, New York**

# Why seek genetic testing for FSHD?

*Even without treatment, a diagnosis is therapeutic*

by **ASIFA LALJI**  
Vancouver, British Columbia

When the Canadian provincial government of British Columbia decided it would not provide national health insurance coverage for genetic testing of FSHD, it triggered this response from a constituent. She raises important arguments that could apply equally well to physicians and insurers elsewhere who do not recognize the medical need for genetic testing.



Asifa Lalji

The guidelines around out-of-province genetic testing state that it can be approved if “the genetic information is medically necessary, as the genetic information may significantly alter current medical treatment for the beneficiary.”

I can tell you unequivocally that an accurate diagnosis of FSH muscular dystrophy is crucial in managing the disease, symptoms, and the quality of life for the patient.

I was diagnosed with FSHD many years ago, and it was covered by the Medical Services Plan (MSP). I was diagnosed when I was 21 after years of misdiagnoses. Those years were filled with confusion, self-doubt, depression, low self-esteem, and increased pain, as I was unable to manage the disease because I didn’t understand what was wrong with me.

I can vividly recall the day I was told about my diagnosis. I was in the neurologist’s office when he told me I had FSH muscular dystrophy. I felt the weight of the world off my shoulders; I was so relieved. After years of being told there was nothing wrong with me or that I was lazy, I finally had a name for my disease.

My neurologist gave me a number of options and resources for managing this disease, which as you know currently has no cure. But knowing what I had empowered me to research what I could do to improve the quality of my life, make decisions around family planning, my career choices, and gave me a support group and research community to understand this disease and what the implications were.

Based on the neurologist’s recommendations, I did undergo a surgical option (scapular fusion) to help improve my mobility. I also qualified for assistance with occupational therapists once I had an official diagnosis.

The genetic testing for diagnosis is not experimental. It is absolutely necessary in managing this disease, and our neurologists conduct diagnostic testing for people showing symptoms.

I know the government and MSP have to make choices. But I think it’s important to note that this test has been funded until very recently. According to neurologists, BC is now the ONLY province in Canada that does not fund this test. The provincial genetics lab was funding this test until about two years ago. What has changed? Why is FSHD no longer tested?

The policy also states that out-of-country testing would be considered if the tests are not available in Canada. As I understand from our neurologists, “provincial genetic labs seem to ‘choose’

which genetic tests they run (maybe based on individual expertise in each lab); this test is not available within British Columbia. However, we are able to diagnose far less common muscular dystrophies in BC, simply because our provincial lab is able to do those tests (i.e., oculopharyngeal muscular dystrophy). There is no more treatment available for these less common muscular dystrophies than there is for FSHD.”

Why can’t testing be done for FSHD when it is the most prevalent form of muscular dystrophy, when the lab can test for other types of muscular dystrophy?

Neurologists have to make individual requests for funding for an FSHD test on each patient. They tell me that the requests have consistently been rejected on the basis that it will not alter treatment. I can tell you from my personal experience (and medical professionals would agree), treatment and medical care are more than just drug therapy. Having a specific diagnosis for one’s symptoms is therapeutic; it is life altering.

It may also help to note, from a neurologist’s perspective, there are a number of implications and long-term costs of not being able to diagnose people showing symptoms, including:

- increased anxiety in those patients, which may lead to additional use of healthcare resources and multiple consultations with specialists trying to get an answer;
- invasive and unnecessary muscle biopsies, which may lead to misdiagnosis and treatment with immunosuppressive drugs that are expensive, and have significant side effects (muscle biopsies in FSHD often demonstrate inflammation which is misinterpreted as being an autoimmune myositis);
- recommendations to screen patients regularly with echocardiograms, EKG, and pulmonary function testing (this is what we recommend in patients with myopathies without a specific diagnosis, as we have no idea if their myopathy will affect cardiac and respiratory systems).

If FSHD could be confirmed, we would not do routine screening, as the heart is not affected in FSHD and the respiratory system is sometimes affected (and we can identify those FSHD patients who are at high risk for respiratory impairment). Thus, access to genetic testing should save money long term.

I believe we have met the criteria of the Medical Services Commission for out-of-province and out-of-country medical care, and that this cost (currently paid by the patient) should be covered by MSP. If those who are responsible for this policy need further evidence, I would appreciate and welcome the opportunity to have our medical specialists in FSHD meet with you and your team.

Thanks again for taking the time to review this information. I look forward to hearing from you soon. 

**Editor’s note:** As this issue of *FSH Watch* goes to press, the provincial government of British Columbia still does not provide health insurance coverage for genetic testing of FSHD.

## Dancers soar for FSHD

*In memory of Cynthia Abelman*

by **STEPHANIE WEIGELT**  
Urbana, Maryland

This spring, the Urbana High School Dance Company, where I serve as company director, produced a dance concert in memory of Cynthia Abelman, the mother of one of our students. Cynthia had been affected by FSHD, as are her daughters, Rebecca and Anna, so we wanted to dedicate our show to raising funds for the FSH Society. Our event on April 16 was awesome, and we raised \$1,500!

The evening was filled with dances from my classes and our dance company. At the end of the evening, we showed one of the videos from the FSH Society's website to educate the audience about FSHD. Rebecca Abelman spoke eloquently about her experience with the disease as well as her hope for a cure.

When speaking to Rebecca's dad, I found out that the FSH Society knows the family well. Rebecca's sister Anna is in my dance class and dance company, so she is the one who inspired my students to choose the FSH Society for the recipient of last night's donations. She is a great kid, and their family's spirit and resilience since her mom's passing has been extraordinary.

After Rebecca spoke, the kids performed a piece featuring Anna that showed the struggles that someone with FSHD goes through and how we can all work together to help and support that individual. The kids did a fabulous job, and Anna was beautiful throughout.

Thanks so much for all you are doing through the FSH Society. We hope our donation will be of some assistance! 



**Urbana High School Dance Company dancers perform a work inspired by the struggles of a person with FSHD.**

## EARN A PERSONAL "THANK YOU" FROM GLEE'S MAX ADLER

**A positive and enthusiastic event for the FSH Society was held on May 6, 2015, at East Brunswick High School in New Jersey. A big "thank you" to Russell Caratenuto, a junior at the school, and his coach, Gregory Rutz, and the team for spreading more awareness about FSHD.**

**The special surprise of the night was actor Max Adler, who thanked Russell, the team, and the school through a heartfelt video. The crowd of students went wild and were touched by his generous words. Students tweeted their appreciation!**



**The East Brunswick High School boys' volleyball team.**

**The event was just as meaningful to Max, who wrote: "Wow! How very moving and inspiring and heartwarming that is to read and to see! Can't thank you enough for including me in this wonderful opportunity and exposing me to the story and allowing me to be a part of it and a part of this young man's journey and his story. Means the world!"**

**Russell was diagnosed with FSHD a year ago. Once he got over the initial shock, he responded by taking positive action—to raise awareness among his fellow students and make a difference. The school embraced Russell and his efforts and wants to make the FSHD Fundraiser an annual event! The volleyball team will be joined during the next academic year by the school's National Honor Society, where Russell will be serving as president.**

**Thank you, Russell, Coach Rutz, and the East Brunswick High School boys' volleyball team for hosting a spectacular event! We send gratitude and good wishes to all of the participants and donors.**

**-Kristin Duquette**

## ADVANCING CLINICAL TRIAL READINESS FOR FSHD

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requires further studies to determine if it is more sensitive to change than clinical outcome measures.

Workshop participants also touched on clinical outcome measures for early-onset, or infantile, FSHD. While iFSHD is defined by onset of symptoms before age 5 or 10 (definitions vary), the national registries showed that many patients who typically are diagnosed in their late teens or twenties report having had classic symptoms, such as the inability to smile or close the eyelids fully, and weakness in the arms, legs, or abdominal muscles, at a much younger age. Should these patients be reclassified as early-onset FSHD? In addition, recent data suggest that retinal vascular disease and hearing loss are restricted to early-onset FSHD patients who have only one to three D4Z4 repeat units. This suggests that separate outcome measures may be required for this subgroup of early-onset patients.

"The FSH Society is proud to help fund and advise this important workshop," said Daniel Paul Perez, FSH Society President & CEO. "Meetings like this will help all future developers of FSHD treatments design good clinical trials—and help avoid costly failures. We are very pleased that organizers, at the behest of the meeting sponsors, improved on the proposal by including industry, a biostatistician, international trial sites, NIH, and the Food and Drug Administration (FDA), who gave excellent input.

"We are investing in rigorous science, collaboration, and open discussion involving all stakeholders. That's the way to move us forward toward treatments and a cure." 

# A call to awareness

Breathing issues that every patient needs to understand

by DANIEL PEREZ  
FSH Society

I used to think that if you had FSHD, it was less likely than likely that breathing and respiratory issues might occur. I had not learned that it can happen ever so gradually and that it could take years to surface, either as a long-standing chronic issue needing to be addressed and managed or, as in some cases, precipitated by an event rather suddenly and acutely. At first, I thought FSHD individuals needing pulmonary and respiratory support were few and far between—but after 30 years I have run into this issue again and again, and there you are, with individuals working hard for a sense of survival against respiratory issues.

Yes, respiratory involvement can occur. Every individual with FSHD should be aware of issues and symptoms that arise from respiratory insufficiency that may be associated with muscle weakness caused by the disease.

Patients with moderate to severe FSHD should have their respiratory function evaluated during periodic clinic visits. Regular monitoring of respiratory function is also suggested, as one might experience insufficiency over a long period of time without presenting signs.

It is important to be aware that respiratory compensatory mechanisms can allow one to adapt to functioning with high levels of carbon dioxide (CO<sub>2</sub>) in the blood—levels that doctors would not expect to permit normal function. This is known as hypercarbia and is dangerous in the long term.

You should discuss breathing tests with your doctor if you experience any of the following:

- Feeling generally fatigued in the morning.
- Never feeling rested after a full night's sleep.
- Morning headaches.
- Snoring loudly or in a different pattern than usual.
- Labored and interrupted breathing while lying down.
- Fatigue and daytime sleepiness.

Because many doctors—even experienced neurologists—do not associate FSHD with respiratory problems, your doctor may be reluctant to order respiratory tests. Insist on respiratory tests if you feel the symptoms described above.

Fortunately, there are concerned, dedicated, and talented individuals working hard to understand respiratory issues in FSHD. Two recent papers published are noteworthy. The first is an



excellent case study of a 68-year-old man with FSHD who had symptoms of nocturnal hypoventilation such as morning headache, fatigue, and daytime sleepiness, and after an adequate assessment of his diaphragm and breathing, he improved by using non-invasive positive pressure ventilation.<sup>1</sup> The article is three pages long and free to download from PubMed at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4356051/pdf/main.pdf>. It nicely illustrates what the nighttime pattern of carbon dioxide and oxygen saturation looked like before this individual started ventilation and how this picture improved after ventilation (Fig 1, Fig 2, pp. 38-39).

The second paper compared two age- and sex-matched groups of 29 patients, with and without respiratory issues. Tests in the patients with respiratory dysfunction suggested predominant expiratory muscle dysfunction.<sup>2</sup> This is one of the first papers I can recall that

mentions respiratory dysfunction in FSHD being “predominantly related to expiratory muscle weakness.” This is at the heart of what causes hypercarbia (elevated CO<sub>2</sub>).

If you have questions, please contact the FSH Society at (781) 301-6060 or [info@fshsociety.org](mailto:info@fshsociety.org). FSHWatch

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- 1 Facioscapulohumeral muscular dystrophy and respiratory failure; what about the diaphragm? Hazenberg A, van Alfen N, Voet NB, Kerstjens HA, Wijkstra PJ. *Respir Med Case Rep*. 2014 Dec 29;14:37-9. doi: 10.1016/j.rmcr.2014.12.006. eCollection 2015.
- 2 Respiratory muscle dysfunction in facioscapulohumeral muscular dystrophy. Santos DB, Bous-said G, Stojkovic T, Orlikowski D, Letilly N, Behin A, Butel S, Lofaso F, Prigent H. *Neuromuscul Disord*. 2015 Aug;25(8):632-9. doi: 10.1016/j.nmd.2015.04.011. Epub 2015 Apr 30.

## #FSHDSTRONG

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The T-shirts, designed by Convey360, will be available at [teespring.com](http://teespring.com), with 100 percent of the profits donated to the FSH Society. The more we sell, the larger the percentage the Society will earn. Go to [teespring.com/FSHDbestrong](http://teespring.com/FSHDbestrong) to get your shirt today!

Visit the FSH Society's Facebook page to share images of the campaign. A new one will be posted every day for 21 days to increase awareness, spread our empowerment message, and raise funds! FSHWatch

## HOT OFF THE PRESS: FSHD CARE GUIDELINE

... from page 1

them and patients find them beneficial. This is not because these interventions are useless, but simply because their benefits have not yet been studied in a controlled trial.

**For a copy of the AAN's summary created for patients and families, please contact the FSH Society. The Society will also produce web conferences and other forums for educating patients and physicians about the guideline.**

The new AAN FSHD guideline is a result of the FSH Society's advocacy efforts in Washington, DC, over the past 20 years and the Society's role in the writing and passage of the Muscular Dystrophy Community Assistance Research and Education Act (MD CARE Act 2001, 2008, and 2014). That law mandated the U.S. Centers for Disease Control to increase its efforts on adult muscular dystrophy and now, specifically, FSHD.

"Before this publication, there were no evidence-based care guidelines for FSHD," said Julie Bolen, PhD, MPH, epidemiologist,

National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention (CDC). "We expect that this guideline will fill that evidence gap for both the people who live with these rare disorders and the healthcare professionals who treat them."

"We are pleased to have been a part of the process of developing an evidence-based care guideline for patients with FSHD and their families," remarked Daniel Perez, President & CEO of the FSH Society. The guideline "represents a solid foundation and competent standard on which to begin to standardize and improve on care given to FSHD patients.

"The Society was especially pleased to see the thoughtfulness and care given to creating a clear picture and highlighting key issues in FSHD care, though sometimes a paucity of publications was present," Perez noted. "We thank the CDC, the AAN, the AANEM, Boards of Directors of the AANEM

and the AANI, authors of the guideline published in *Neurology*<sup>®</sup>, and the review and dissemination panels for their efforts to include the patient at all levels of the process, and in improving lives for all affected with and by FSHD."

Funding for this publication was made possible (in part) by grant DD10-1012 from the Centers for Disease Control and Prevention. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. The remaining funding was provided by the American Academy of Neurology. **FSHWatch**

### Reference

"Evidence-based Guideline: Evaluation, Diagnosis, and Management of Facioscapulohumeral Muscular Dystrophy," a report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the Practice Issues Review Panel of the American Association of Neuromuscular & Electrodiagnostic Medicine.

## THE DECISION TO STOP WORKING

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taxable if the employer paid the premium and tax exempt if the employee paid it. Also, if you are receiving LTD payments, you may still be eligible to contribute to an IRA; eligibility depends on the amount and nature of your LTD payments. The IRS website ([www.irs.gov](http://www.irs.gov)) has comprehensive information. See Publication 907 (Tax Highlights for Persons with Disabilities), Publication 575 (Pension and Annuity Income), and Publication 590 (Individual Retirement Arrangements).

Everyone who receives SSDI payments is automatically eligible for Medicare beginning two years after the date of disability. "Traditional" or "original" Medicare is fee-for-service and includes Parts A and B. Medicare Part A (hospital insurance) is free for most people. Most have to pay for Part B (medical insurance), and premiums are deducted from monthly SSDI payments. An alternative to traditional Medicare is Medicare Advantage, which is typically provided as an HMO or PPO.

Parts A and B do not cover everything, so most people on traditional Medicare also choose to get Medicare supplemental insurance—Medigap—which is provided by private insurance companies and paid for by the insured. People who are on Medicare

because they are receiving retirement benefits have an automatic right to purchase Medigap insurance from any company serving their geographic area. But the situation is different for those on Medicare because of disability. State law, not federal, governs whether or not private insurers are required to offer Medigap insurance for people who are on Medicare because of disability; some states (including California) require it, and others do not.

One must also consider how to maintain health insurance coverage from the last day of work until the beginning of Medicare coverage. Possible options include continuation of your employer's insurance through COBRA (although this can be expensive), obtaining insurance through your spouse's employer, and coverage under the Affordable Care Act.

California Health Advocates (CHA) ([www.cahealthadvocates.org](http://www.cahealthadvocates.org)) and the Kaiser Family Foundation (KFF) ([www.kff.org](http://www.kff.org)) offer comprehensive information about Medicare. Although CHA is geared toward California consumers, much of the information applies to residents of all states. Besides information about Medicare, KFF has lots of useful information about health insurance and healthcare policy in general.

### Planning for post-work life

Working gives us creative fulfillment, intellectual stimulation, social camaraderie, and a sense of accomplishment. It fills our waking hours and is an important part of our identity. Being forced to stop working because of FSHD is difficult, emotionally and socially. It is one of the biggest losses caused by our disease. Mental health professionals and social workers can greatly help those who are faced with the decision to stop working.

Finally, if you do decide it's time to stop working, it's also time to start planning your post-work life. Don't put this off until after your disability claim is settled. There are many fulfilling, productive ways to spend your time without overdoing it physically. One door closes and another opens. **FSHWatch**

**Author's note:** This article is provided for general informational and educational purposes only. *Neither the author nor the FSH Society provides medical, legal, financial, or other advice or recommendations.* People who are considering filing a claim for disability should consult their professional advisors. Moreover, the information in this article is subject to change.



## June-December 2015 FSH Society events

Volunteer organizers are having an impact coast to coast

For updates, details, and registration, please check the FSH Society website at [www.fshsociety.org](http://www.fshsociety.org). Interested in organizing an event of your own? Please contact Executive Director June Kinoshita at [june.kinoshita@fshsociety.org](mailto:june.kinoshita@fshsociety.org) or (781) 301-6649.

**June 6**—Fourth Annual Spicerfest benefit concert. Memphis, TN.

**June 13**—New England FSH Society members meeting. Boston, MA.

**June 20**—North Carolina FSH Society members meeting. Winston-Salem, NC.

**June 27**—Mid-Atlantic FSH Society members meeting. Kennedy Krieger Institute, Baltimore, MD.

**July 11**—Third Annual Lake Party for FSHD. Hickory Corners, MI.

**July 17**—Songs in the Key of Steven Blier. San Francisco, CA.

**July 18**—LA Connects, FSH Society members meeting. Los Angeles, CA.

**July 18**—FSH Society members meeting. Waterford, MI.

**July 22**—FSH Society members meeting. Denver, CO.

**July 25**—Western Washington FSH Community. Renton, WA. Meets last Saturday of each month.

**August 19**—FSH Society members gathering at Mimi's Café. Sacramento, CA.

**September 4**—Any Body Can Dance. Ballroom danceathon, Brandon, FL.

**October 3**—Mid-Atlantic FSH Society members meeting. Home of Lileen Walters, Leesburg, VA.

**October 3**—Musclepalooza, music benefit. Doylestown, PA.

**October 4**—Second Annual Cosie Laurello Memorial 5K and 10K Run. Ashtabula, OH.

**October 5-6**—FSH Society International Research Consortium and Research Planning Meeting (a meeting for research professionals). Boston, MA.

**October 18**—A Ghostly Gala to Vanish FSHD. Halloween costume ball. Los Angeles, CA.

**October 20**—Denver FSH Society members meeting. Denver, CO.

**October 24**—North Carolina FSH Society members meeting. Durham, NC.

**November 8**—New England members network meeting, Tuckerman Brewing. Conway, NH.



### GIVE WITH A SMILE THROUGH AMAZON



your choice, please explore it. This is a great way to double, triple, or even quadruple your gift.

Amazon will donate 0.5 percent from your eligible AmazonSmile purchases to the FSH Society whenever you shop on AmazonSmile. To get started, register at <http://smile.amazon.com/ch/52-1762747>.

### RAZOO ONLINE FUNDRAISING



Razoo provides an easy way for you to create an online campaign. Your donors will enjoy the convenience of giving online and knowing that their gifts will go directly to the FSH Society. Razoo has built-in social media sharing, so you and your friends can help spread the word over Facebook, Twitter, and other social media (<http://www.razoo.com/story/Facioscapulohumeral-Society>).

### OUR EBAY CHARITY AUCTION SITE



The FSH Society is registered (as the "FSH Muscular Dystrophy Society") on eBay's charity auction site. If you have an eBay seller's account, you can put items up for auction and direct from 10 to 100 percent of the proceeds to the Society (<http://givingworks.ebay.com/charity-auctions/charity/fsh-muscular-dystrophy-society/76296/>).

### COMBINED FEDERAL CAMPAIGN (CFC), 2015

Pledges made by federal, civilian, postal, and military donors during the campaign season (September 1 to December 15) support our mission. Enroll using the FSH Society's identification number 10239.



### EMPLOYER MATCHING GIFTS

If your employer offers you options for directing the company's funds to a charitable organization of

### GET SOCIAL!

Join our online communities to get news, ask questions, and seek advice and support from fellow FSHD patients and family members. The FSH Society Yahoo! Groups forum, online since the 1990s, has tens of thousands of searchable posts. Bookmark these pages and come back often. To find our Facebook, Twitter, and Yahoo! Groups, go to [www.fshsociety.org](http://www.fshsociety.org).



org and click on the logos in the right-hand margin. If privacy is a concern, you can use your account privacy settings to limit who can see your posts.

### HAVE YOU MADE A GIFT TO THE SOCIETY IN 2015?

Thanks to the support from members like you, the FSH Society is a world leader in combating muscular dystrophy. Your donations are tax deductible, and they make a real difference. Please send your gift in the enclosed envelope. Or contribute online at [www.fshsociety.org](http://www.fshsociety.org). Thank you!

### CHARITY NAVIGATOR TOP PERFORMER



The FSH Society has been awarded its seventh consecutive 4 Stars by Charity Navigator, placing us among the top 2 percent of U.S. charities for fiscal responsibility and governance.

### NOT GETTING OUR EMAIL NEWS?

Sign up right on our website at [www.fshsociety.org](http://www.fshsociety.org) by clicking "JOIN." If you are certain you are on our email list, please check your spam or junk folder.

