

# FSH Watch



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

## Team FSHD Cycling participates in the 36th Race Across America

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### RESEARCH

## Hot off the press: a DUX4 mouse with muscle disease

*Muscles have dystrophic changes; regeneration is impaired*

by **JUNE KINOSHITA**  
FSH Society

The FSH muscular dystrophy scientific literature finally has a publication describing a genetic mouse model that develops skeletal muscle disease. This work comes via the laboratory of Michael Kyba, PhD, at the University of Minnesota's Lillehei Heart Institute. This murine model, called iDUX4 pA, has a number of compelling similarities to the human disease.

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### NEWS AND EVENTS

## Mark A. Stone is new chief executive officer

*Daniel Paul Perez staying on as chief science officer*

by **DANIEL PEREZ**  
FSH Society

William R. Lewis Sr., MD, chairman of the Board of Directors of the FSH Society, has announced that Mark A. Stone has been named president and chief executive officer after a nationwide search.

“Mark brings with him a successful career in making a difference to patients and families suffering with rare diseases, as well

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## Fighting FSHD, together

Family. While I acknowledge this word has different meanings for different people, for me, the word conjures up thoughts of warmth and love, growing and striving, celebrating successes and enduring hardships together. In the few months I've been privileged to be at the FSH Society, I have discovered the richness of "family" infused throughout the organization. I have also felt embraced and welcomed into the family, and for that I'm grateful. In a former position, I was asked if I had the disease in my family, to which I replied, "I do now." Surprisingly, in such a short time, I feel the same regarding the FSHD Family.



Mark A. Stone

Leadership expert Max Dupree stated, "*The first responsibility of a leader is to define reality, and the last is to say, 'Thank you.'* In between, you are both a servant and a debtor." Attempting to define the reality of FSHD research, potential therapeutic developments and activity in our space, I have met with both researchers and teams from the pharmaceutical and biotech industries. I have participated in a conference call with like-minded organizations working on solutions for FSHD worldwide as well as connecting with other organizations in the muscular dystrophy space.

The term "tipping point" continues to surface as a descriptor of where we are on our journey for disease-modifying treatments and, one day, a cure. FSH Society-funded research and advocacy, creating an environment for all interested parties (stakeholders) to work together, has brought us to this point in history. Collectively, we have accomplished much together—and together, we will need to take the same bold steps in seeking to accelerate research toward treatments and a cure!

In addition to defining reality, I realize I am both a servant and a debtor. Great, self-sacrificing individuals have contributed their time, talent, and financial resources to bring us to the place we are today. I am "inheriting" this position from Dan Perez, the co-founder and only president and CEO the Society has had and who has led this organization for 25 years with skill, passion, and unwavering commitment to discovering the cause and cure for FSHD. Wonderfully, Dan is still in a key leadership role as our chief science officer, focusing his knowledge, expertise, and passion to continue moving the science forward. Personally, I value his insight, collegial embrace, and friendship he has graciously extended to me.

Keenly aware of the resources entrusted to us, the wonderfully talented and committed staff at the Society are focusing efforts on investing program and financial resources to expedite research toward treatments and a cure while seeking to enlarge, engage, and empower an active community. We believe these twin focus areas have been the strength of the Society in the past and will be the catalyst to propel us into a future where no one has to suffer the full effects of FSHD.

Additionally, I want to encourage you to save the date for our FSHD Connect conference in Las Vegas on June 9-10, 2018. This is our biennial "Family Gathering"—a reunion of sorts—where the latest in research advancements, technology, and mobility products and insightful seminars will enhance the opportunity to reunite with friends and make new ones.

Finally, allow me to say "Thank you" for your continued support and active participation. What you do matters! I look forward to meeting more of you in the coming months as we work together toward our common goal—working together for the cure!

Mark Stone

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## FSH Watch

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

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# The knee of the curve

*It's time to get in on the action*

by **STUART LAI**

*FSH Society, Board of Directors*

When I graduated in 1990 with a degree in computer science and electrical engineering, I came out to New York City because I had a strong interest in the stock market.



**Stuart Lai**

Amidst the career chaos, every few months I received an FSH Society newsletter in the mail and gave it a casual glance sometimes. My mom, being an occupational therapist, noticed things in my dad, brothers, and me, and found Dr. Steven Jacobsen (the co-founder of the FSH Society along with Dan Perez), so I was fortunate to have an early, accurate diagnosis. Still, I did my very best to ignore the disease and just get on with my life.

Fast forward to 2007. Some of the *FSH Watch* newsletter articles started to catch my eye: DUX4, deletions, activating “junk” DNA. The genetic research and biotechnology industry was starting to feel eerily like the financial tech industry I had experienced a decade earlier where really big things were

starting to happen after years of slow, steady progress. This is the point in a technology revolution known as the knee of the acceleration curve, and I wanted in on the action.

Coming from the financial industry, I thought, okay, let's set up an investment trust. I distinctly remember the feedback from Dan Perez that was something to the effect of, “That's great, but quite frankly we need the money now.” That made immediate sense to me, knowing how critical early investment can be. FSHD is a rare disease with a unique genetic mechanism. There is no riding the coattails of other disease research.

The FSH Society has done an amazing job of seeding FSHD-specific research, which has drawn interest from larger labs and, eventually, now pharma companies. We all must continue to contribute to this mission (through fundraising and more) to keep FSHD research relevant and on the curve.

Fast forward to 2013. I fractured my femur after stumbling on a carpeted office hallway while preoccupied with other things as I was heading out at the end of a long day. I had a year of dedicated rehab with time to think about why I did not know this could

happen to me. (It turns out that bone needs muscle for structural strength.) I came to realize you simply cannot read what you need to know. The different stages of progression and variability of disease severity are simply too great to know what specifically applies to you. I needed to get out of this deal-with-things-as-they-come bubble.

The good news is that the FSH Society sponsors local patient gatherings and recently hosted a flagship FSHD Connect conference in conjunction with the ongoing FSH Society-sponsored international research conferences. My notion of a patient gathering was a circle of chairs in an empty room, and I'd have to introduce myself: “Hi, I'm Stuart, and I have FSHD.” So I was blown away after forcing myself to attend the 2016 FSHD Connect meeting in Boston.

Listening to investigators explain the state of FSHD genetic research and being able to ask questions made understanding of a really complex disease like FSHD possible. And after participating in breakout sessions with fellow patients, researchers, and physical therapists, I became convinced that patients (especially those with FSHD)

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## Carden Wyckoff elected to Board of Directors

### YOUNGEST MEMBER EVER, WITH A PASSION FOR ADVOCACY AND FUNDRAISING

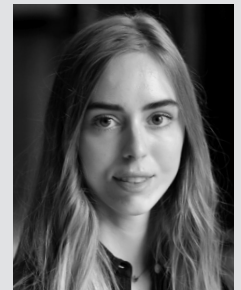
The FSH Society is pleased to announce that Carden Wyckoff was elected to serve on the Board of Directors on September 26, 2017. In joining the Board just two years after graduating from college, she becomes the youngest Board member in the history of the Society.

Carden has been an activist and ambassador for the FSH Society since high school. A 2015 graduate of the University of Georgia, where she earned her BSA in biological sciences, she was a leader among student disability advocates who worked to improve the accessibility of university properties.

As a member of the FSH Society's scientific journal club, she helped to update the Wikipedia entry on FSHD. She has organized many fundraising activities for the FSH

Society, most notably the Piggyback Adventures with her siblings, Spencer and Virginia, to take on physical challenges such as the five-mile Reebok Spartan Run obstacle course and an 82-mile hike on the Appalachian Trail. She also serves as a moderator of the FSHD Teens/Young Adults Facebook community.

Carden was featured in a 2016 episode of *American Ninja Warrior* when Spencer competed in the Atlanta trials for the popular TV show. She lives in the Atlanta area and works at a Fortune 500 tech company.



**Carden Wyckoff**



# Placing a BET on blocking DUX4

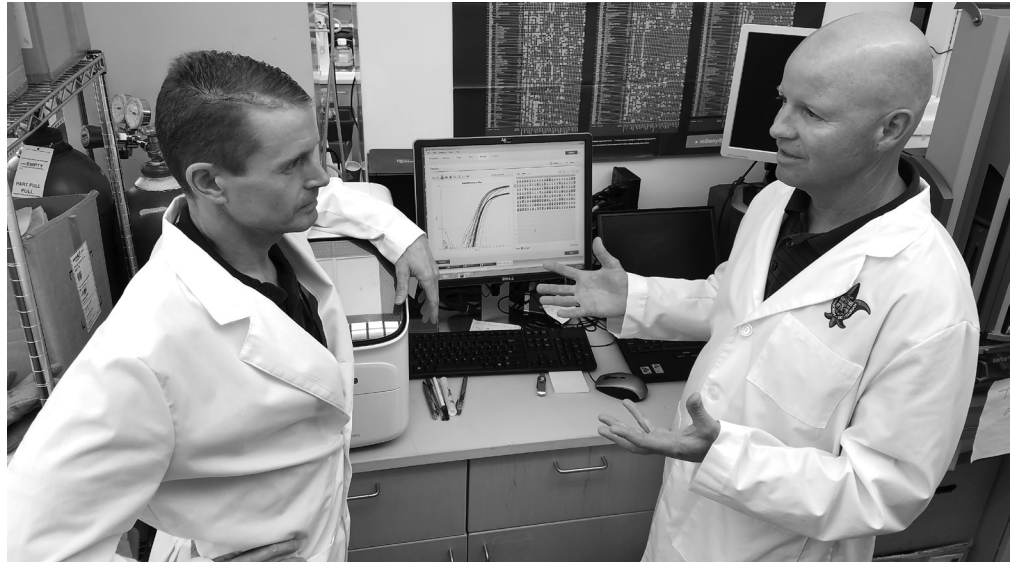
Research points to possible drugs and new targets

by FRAN SVERDRUP, PhD  
St. Louis, Missouri

**D**UX4 is considered to be a key cause of muscle degeneration in FSH muscular dystrophy. This is why we are interested in finding drugs that “turn off” the production of DUX4, which would prevent the many detrimental activities of this toxic protein. Such drugs would potentially provide the first treatment option for slowing or stopping disease progression in FSHD.

By screening thousands of compounds in FSHD cells grown in the laboratory, we have identified two classes of drugs that turn off DUX4. One class is drugs that inhibit bromodomain and extra-terminal (BET) proteins, and the second is beta-2 agonists (drugs used to relax smooth muscle in lungs, blood vessels, etc.). BET inhibitors are in clinical trials for

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Co-authors Matthew Yates (left) and Fran Sverdrup (right)

## New University of Rochester study

### LOOKING AT TESTOSTERONE AND HUMAN GROWTH HORMONE AS POTENTIAL TREATMENT

Researchers at the University of Rochester in New York are conducting a research study to learn more about a potential symptomatic therapy for FSHD. This study may help determine if a combination of drugs (recombinant human growth hormone [rHGH] and testosterone) can be safely given to patients with FSHD and possibly improve walking, strength, muscle mass, quality of life, and functional ability.

The study has recruited 20 men with FSHD between the ages of 18 and 65, who are still able to walk. The volunteers have committed to making five visits (one with an overnight stay) to the University of Rochester. Study procedures include taking the study drugs (testosterone and rHGH), a physical exam, collection of blood samples, muscle strength and function testing, questionnaires, EKGs, and DEXA scans.

According to the NIH Research Portfolio website, the rationale for this study is described as follows: “Large-scale clinical trials have found that testosterone combined with



Chad Heatwole, MD, is lead investigator on the testosterone and rHGH study.

recombinant human growth hormone (rHGH) (combination therapy) is well tolerated and effective in synergistically improving respiratory function, lean body mass, protein synthesis, strength, and aerobic endurance in healthy adult human populations. Both testosterone and rHGH are readily available and approved for human use but have never been formally studied together in a muscular dystrophy population. We propose a 36-week, proof-of-concept clinical study of the safety and tolerability of daily rHGH combined with biweekly testosterone injections in men with FSHD. All participants will be serially and closely monitored during a 24-week period of combination therapy followed by a 12-week washout period.

Safety assessments will include monitoring for medication side effects, laboratory abnormalities, physical exam changes, and EKG alterations. As a secondary objective, we will examine the pharmacokinetic effects of combination therapy on lean body mass and serum biomarkers. Participants will also have serial assessments of their ambulation, strength, physical function, patient-reported disease burden, and respiratory function. Ultimately, this study will generate extensive data regarding the clinical safety, pharmacokinetics, and change in body composition and clinical function associated with combination therapy in a predefined FSHD population.”

# San Francisco FSHD Family Day

*Recurring theme: "Patients are experts"*

by HOWARD CHABNER  
FSH Society, Board of Directors

On July 15, 2017, at the San Francisco Jewish Community Center, the FSH Society convened its first San Francisco Bay Area Family Day Conference. The Fourth Annual Songs in the Key of Steven Blier concert was held that evening after the conference.

Both events were dedicated to the memory of Joyce Hakansson, a longtime supporter of the FSH Society, advocate for patients and families, and an organizer of the Steven Blier concerts. Joyce died in 2016, and the conference and concert were attended by her family.

The free conference was a mini-version of the Society's FSHD Connect meetings, which it has held biannually since the 1990s. We called it a "family day" conference because FSHD occurs in families and affects not only individuals with the disease but their caregivers as well.

There was a good balance between practical, concrete information about living with FSHD and presentations about the latest research and clinical trials. Executive Director June Kinoshita, Board member Neil Solomon, MD, and I kicked off the afternoon with brief welcoming remarks.

John Day, MD PhD, director of the Neuromuscular Division and Clinics at Stanford University School of Medicine, gave an overview of the genetics, diagnosis, and care standards for FSHD. His Stanford colleague physical therapist Richard Gee, PT, presented on physical therapy and exercise. Lee Guion, MA RRT FAARC, neuro-respiratory clinical specialist (retired) at the Forbes Norris Research Center in San Francisco, talked about respiratory care, emphasizing that the issues encountered by many FSHD patients are still not widely known, and offering practical solutions.

Solomon, formerly a medical director for major health insurance companies, and I, a retired attorney, discussed disability rights and insurance, including health insurance, disability insurance, and long-term care insurance, giving tips on how to learn about available resources, navigate an uncertain insurance environment, and advocate for oneself.

In his second talk of the day, Day spoke about the road to clinical trials, underscoring the need to recruit patients and highlighting the critical importance of defining how to measure success. This is especially challenging for a disease like FSHD that is progressive and has wide variation in severity and symptoms. He was followed by Lisa Williams, MD, of UC Davis Medical Center, who described



**The Fourth Annual Songs in the Key of Steven Blier was held in the evening after the Family Day Conference. Our wonderful team (from left) included Ellen Schumm, Robyn O'Leary, Ru Paster, June Kinoshita, Nezha Bennouna, Amanda Lynn Bottoms (soprano), Steven Blier, Dimitri Katotakis (baritone), Christopher Wiseman, and Barbara Kweller.**



Acceleron's ACE-083 clinical trial. ACE-083 is a drug designed to encourage muscle growth. UC Davis is one of the sites of the Acceleron trial.

Peter Jones, PhD, Mick Hitchcock Endowed Chair of Medical Biochemistry at the University of Nevada Reno School of Medicine, gave a spirited presentation on emerging treatment strategies and the relationship between basic scientific research and drug discovery.


A key takeaway from the three speakers is that research truly is accelerating, and the field may be on the cusp of great progress. However, the presenters didn't oversell the current state of affairs or minimize the challenges, stressing

that a Phase 3 clinical trial (the final phase of a human clinical trial and the highest hurdle for FDA approval) requires a large number of research volunteers, much time, and a significant financial investment. A large study is particularly necessary to prove the efficacy of a drug that may have demonstrable but not dramatic results.

June Kinoshita wrapped things up by pointing out that, as knowledgeable, focused, experienced, and committed as researchers and clinicians are, FSHD patients have the greatest personal knowledge and expertise. As such, they must become involved in the campaign for treatments and a cure, and must offer their knowledge to help others live with FSHD and design clinical studies. She suggested many ways to get involved, starting with joining the FSH Society and subscribing to its email alerts.

With about 60 people in the audience, the conference was well attended, with a mixture of newcomers and those who have long been active members of the FSH Society. The presenters were excited about participating, very well received, and energized by their interactions with the attendees. The Society intends to present similar family day conferences regularly in locations around the US in collaboration with FSHD research centers. "With treatments on the horizon, we must strengthen the relationships among all the stakeholders in each region," said Kinoshita.

Videos and slides of the presentations are available at [www.fshsociety.org](http://www.fshsociety.org) (entry dated September 26, 2017) and on the FSH Society's YouTube channel.

We thank each of the speakers, who gave generously and enthusiastically of their time, expertise, and insights. 





# An FSHD antisense therapy primer

Q&A with Dr. Yi-Wen Chen

by JIM ALBERT  
Eldersburg, Maryland

**A**ntisense therapy is a form of treatment for genetic disorders. In the past year antisense drugs have been approved by the FDA for the treatment of two types of muscular dystrophy, some forms of Duchenne muscular dystrophy, and spinal muscular atrophy. While antisense therapy for the potential treatment of FSHD is still in the preclinical stage, we do hear occasional encouraging research results involving antisense technology aimed at FSHD.



Yi-Wen Chen, DVM PhD

My interview with Yi-Wen Chen, DVM PhD, of the Children's National Medical Center and George Washington University in Washington, DC, presents an interesting primer for a basic understanding of antisense technology and the current state of antisense research in fighting FSHD. Thanks to the generosity of our donors, the FSH Society is funding research, described in this article, by Chen's and Toshifumi Yokota's labs, as well as the mouse model developed by Peter Jones' lab.

## Q: What is antisense therapy?

**A:** Antisense therapy is a form of treatment for genetic disorders. One approach is to create a synthetic molecule that will bind to the messenger RNA (mRNA) produced by the target gene, thus inactivating that gene, or turning it "off."

## Q: How does antisense therapy work?

**A:** If you can recall back to high school biology, there are DNA and RNA, which are nucleic acids that play complementary roles in living cells. DNA is what makes up the chromosomes of the cell. A cell's genetic information is transferred between DNA and RNA in a process called *transcription*, where the DNA is used as a template to create a strand of mRNA. In a process called *translation*, the cell uses the mRNA to create proteins. DNA is contained in the cell nucleus, while protein creation via mRNA takes place in the ribosome of the cell with the additional help of ribosomal proteins, ribosomal RNA (rRNA), and transfer RNA (tRNA). You can think of the ribosome as the cell's "protein factory."

You might remember that DNA is made up of the four nucleobases: adenine (A), cytosine (C), guanine (G), and thymine (T). RNA is made up of the four nucleobases: adenine (A), cytosine (C), guanine (G), and uracil (U). In RNA, which is important to antisense therapy particularly for FSHD, A binds to U, and C binds to G.

A given "recipe" for a protein is defined by a sequence of nucleobases. For a very simple example, AAGGUC is referred to as the sense sequence for creating a given protein. We want the complementary, binding, or antisense sequence to bind with that sense sequence and turn it off. In our example, that antisense sequence would be UUCCAG. Since mRNA is single stranded, if we

can bind to it, we can essentially prevent it from doing its job in the ribosome and stop it from making the target protein.

## Q: Aren't most proteins defined by very long strands of nucleobases?

**A:** Yes, they are, often a few thousand as is the case with DUX4. However, we've found that we only need a small antisense sequence to bind with the mRNA to degrade it and turn it off. One of the antisense oligonucleotide molecules studied in our laboratory is called "third-generation antisense (3GA)." This work is in collaboration with Idera Pharmaceuticals in Boston. Idera found that a 19-length set of nucleobases, referred to as a 19-mer, is most effective in shutting down DUX4. In addition, a unique strategy was used to reduce the immune response in mice injected with the 3GA and improve the efficacy of the antisense therapy. This is one of the challenges of antisense therapy. We want the muscle cells to accept the antisense therapy and not reject it, and, in addition, increase the half-life of the therapy while limiting toxicity. (Half-life is the amount of time a molecule stays in the body before it gets degraded.)

## Q: When we read about antisense therapy, we often see the terms oligonucleotide and Morpholino. Can you explain those terms?

**A:** *Oligonucleotide* means short DNA or RNA molecules consisting of a small number of nucleotides (A's, T's, C's, and G's). When we refer to oligonucleotides with regard to antisense therapy, we are referring to *antisense oligonucleotides*. *Antisense oligonucleotides* are the single strands of complementary DNA or RNA that prevent or alter protein translation of a target mRNA. To increase stability and reduce toxicity, chemical modifications of the backbones of the antisense oligonucleotides have been developed. *Morpholino* is one type of antisense oligonucleotide with a specific type of modified backbone. The advantages of *Morpholino* antisense oligonucleotides are long half-life and reduced toxicity. The disadvantage is that it does not enter muscle cells naturally unless the muscle is "leaky," as in Duchenne muscular dystrophy.

## Q: How is antisense therapy applicable to FSHD?

**A:** FSHD is believed to be caused by the aberrant expression of the DUX4 gene resulting in the production of DUX4 protein, which is toxic to skeletal muscle. Since antisense therapy can be used to target and remove specific mRNA, the goal is to turn off DUX4 via antisense therapy by degrading the mRNA that is responsible for manufacturing DUX4 protein. If we can do this, we can stop FSHD at what is believed to be the root cause, DUX4 translation, and all subsequent downstream effects of DUX4 would hopefully be relieved.

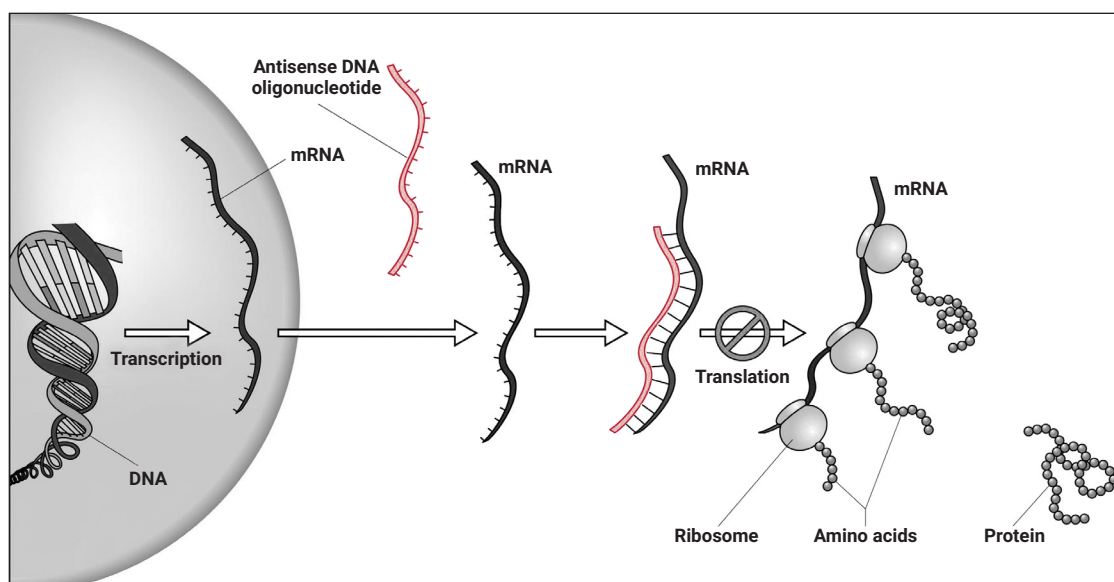
## Q: In theory, could antisense therapy be applicable to both FSHD1 and FSHD2?

**A:** In theory, yes. Antisense therapy could be applicable to both FSHD1 and FSHD2 since, although there are different genetic mechanisms that define FSHD1 and FSHD2, both result in the aberrant expression of DUX4.

**Q: How many different antisense therapies are involved in your research?**

**A:** Idera Pharmaceuticals has tested about 20 different compounds in initial screening studies focusing on DUX4. Of those 20 compounds, five proved effective enough and moved to in vitro and in vivo studies in our lab.

**Q: Speaking of in vivo (in a living organism) studies, what FSHD animal model are you utilizing in your DUX4 antisense in vivo studies?**



DNA inside the cell (left) is transcribed into mRNA, which is recognized and bound by an antisense oligonucleotide (red). This blocks the translation of the mRNA into protein. This method can be used to design a therapy that targets the DUX4 gene, which is thought to cause muscle damage in FSH muscular dystrophy. Image credit: Robinson R. RNAi Therapeutics: How Likely, How Soon? *PLoS Biol.* 2004;2(1):e28.

**A:** We're making use of the FlexD mouse created by Peter Jones, PhD, University of Nevada, Reno School of Medicine. Creating a useful animal model for FSHD has been a challenge to research for quite a while. It's difficult to create a mouse model that expresses DUX4 without the DUX4 becoming lethal to the mouse. The amount of DUX4 expressed in the FlexD mouse can be controlled via exposure to an enzyme, and the amount of "leaky" DUX4 in the mouse is working out well in our in vivo antisense research.

**Q: Does your in vivo DUX4 antisense research involve local or systemic delivery?**

**A:** Both. We are studying delivery of antisense for FSHD via local injection into muscle and systemic delivery via subcutaneous (beneath the skin) injection. We have found subcutaneous injections work well for the antisense therapy to reach muscles, but we may be looking at intravenous delivery as well.

**Q: Are there existing FDA-approved antisense therapies for other forms of muscular dystrophy?**

**A:** Yes. In the past year the FDA has approved eteplirsen for the treatment of some types of Duchenne muscular dystrophy and SPINRAZA® (nusinersen) for the treatment of spinal muscular atrophy (SMA).

**Q: Are you able to learn anything from existing approved muscular dystrophy antisense drugs?**

**A:** There is certainly always something to be learned from previous successes. The strategies developed to increase half-life and reduce toxicity are beneficial to FSHD research. The advancement of delivery methods is critical to developing antisense treatments for FSHD since FSHD patients' muscles are not as "leaky" as in Duchenne. However, there are differences between the approved antisense therapies for Duchenne and SMA and potential antisense drugs for FSHD. The Duchenne and SMA drugs work to improve a faulty protein in patients. In FSHD, we need to stop the creation of a protein.

**Q: The million-dollar question: Do you expect antisense therapy for FSHD to progress to human clinical trials, and if so, how soon might we expect to see that?**

**A:** Based on our current knowledge of antisense oligonucleotide strategies, I am hopeful that antisense therapy for FSHD will progress to human clinical trials soon. The timeline depends on whether we are able to deliver the antisense oligonucleotides systemically and demonstrate efficacy and safety in vivo using animal models. There are several research groups studying different antisense strategies currently, and I believe that we will have promising candidates for clinical trials in the near future. [FSH Watch](#)



# Massachusetts Mom, daughter open up about FSHD and how it affects their lives

*The shared experience deepens their bonds*

by **LARRY LUXNOR**  
*Muscular Dystrophy News*

For years, Lexi Pappas hid the fact that she had facioscapulo-humeral dystrophy (FSHD)—a hereditary muscle-wasting disorder that begins in the face and gradually spreads to the shoulders and upper arms, and sometimes also to the legs.

As the disease took its toll on Lexi—causing her to fall frequently and preventing her from running, rock-climbing, skipping, or even bending over—she began opening up about FSHD. Finally, in 2014, the young woman went public with her condition by starting a blog, and last year, on June 20—World FSHD Day—she announced it to her Facebook friends.

On that day, she posted this online: “In honor of today being World FSHD Day, I want to spread awareness about a huge part of my life. Most of you don’t know this, but I have FSHD, a form of muscular dystrophy. It’s affected my life now for about 10 years. My muscles are deteriorating, and I can no longer do most of the things I could do as a child. From seeing my pictures, you probably can’t tell that I have a disability.”

“I’d been waiting to do it for a long time,” Lexi, 23, said of her Facebook post in an interview with *Muscular Dystrophy News*. “It’s actually really freeing, knowing that all these people know about my disability. It means I don’t have to hide it anymore. The more awareness I can spread, the more research we can get for the FSH Society.”

That Massachusetts organization, which advocates on behalf of Americans with FSHD, is based in the Boston suburb of Lexington—only a 45-minute drive from Gloucester, an old New England fishing port where Lexi lives with her mother, Diane.

The most prevalent of the nine types of muscular dystrophy, FSHD is no stranger to these two women. Diane also has the disease, as did her father, anesthesiologist Edward A. Norris, who died in June 2016. Diane started showing signs of FSHD as a high-school senior in 1981. Her brother, six years older, has it as well, though his symptoms are more mild than Diane’s or her father’s.

Diane, 53, said that, as a mother with FSHD, she can understand Lexi’s frustrations better than a parent without the condition.

“Thank God I do have this disease, so my daughter doesn’t have to face it alone,” she said. “My mom could not relate to me, and



**Lexi and Diane Pappas**

since my dad was a male, he could not really understand my issues of self-esteem, body image, and clothing difficulties. Unfortunately, back in the 1990s, no one had a full understanding of the disease, and gene therapy for FSHD was not available.”

Worldwide, an estimated 870,000 people have FSHD. According to the FSH Society, previous studies had estimated its prevalence at about one in 20,000 people, though a 2014 Dutch study says the prevalence is more like one in 8,000.

With FSHD, muscle weakness often sets in asymmetrically, affecting only one arm or one leg, for

example. Symptoms include an inability to whistle or sip through a straw, eyes that don’t fully close during sleep, difficulty doing sit-ups and pull-ups, shoulder blades that “wing” out, a curved spine (known as lordosis), and difficulty raising one’s arms above shoulder height.

In May 2015, Lexi underwent scapular surgery on her right shoulder and, in December of that year, on her left shoulder as well. This gives her some reassurance that—even if her FSHD progresses—she’ll continue to be able to lift her hand to her face (to eat and drink), “which is something that my grandpa could not do.”

Still, Lexi falls frequently, at least 20 times in the hallway of her former high school, by her own count. She also suffers from lordosis, which gives the appearance of pregnancy.

“I’ve been asked several times if I’m pregnant, and that just takes a toll on me,” she said. “Every single time it brings my confidence down a level. It’s hard to walk around in confidence knowing that everyone thinks you’re pregnant. Also, the comments I get when I park in a handicapped spot are very annoying. People see me and automatically think I am not handicapped. I just wish people knew more about invisible disabilities.”

Lexi considers her blog, “Living With FSHD,” more for herself than for the public at large. But she said she’s been encouraged by the outpouring of support—from her friends, her sorority, even people she’s never met—since launching it.

“This past year, I’ve gotten so many emails from people all around the world. It’s crazy how people find my blog,” she said. “Mostly, I’ve gotten a lot of questions about my surgery. I think people enjoy reading it, and it gives them motivation and hope for themselves. It can teach people to not take what they have for granted.”



Lexi graduated in May from Rhode Island's Bryant University with a degree in marketing. She's now an associate producer and editor with the TV team for the computer company, Dell.

"There are so many people I work with, that's it's hard to tell everybody about my disability," Lexi told us. "I don't know when to say it or how to say it, and I'm always worried that there might be things I'm unable to do. Even with business trips, I can't put my carry-on bag in the overhead compartment by myself, so that's always a challenge."

Diane, a certified divorce financial analyst, runs her own business, Solutions for Divorce, as well as her own blog, "Untying the Financial Knot."

"After my divorce, I reinvented my life and went from a stay-at-home mom to a successful, accomplished businesswoman in only six years," she said. "My girls look to me as their role model, which makes me feel incredibly proud and loved."

Meanwhile, Diane says she and her fiancé are building a house with an elevator for herself and Lexi, since both have difficulty walking up and down stairs.

Last November, while attending a patient conference in Boston, she learned that most of the scientific advances in understanding FSHD have been made within the last 10 years.

"My daughter has actually inspired me to be more open about our disease, and she is definitely braver than I ever was growing up," Diane said. "My advice to other parents in this situation is to just support your children, listen to what they have to say, don't make a big deal out of it, show empathy, but do not feel sorry for them or for you. It's not easy to do, but feeling sorry for yourself will not help anyone."

Link to original story: <https://muscular dystrophynews.com/2017/03/23/fshd-interview-diane-lexi-pappas-of-massachusetts-on-living-with-fshd/> **FSH Watch**

## HOT OFF THE PRESS: A DUX4 MOUSE WITH MUSCLE DISEASE

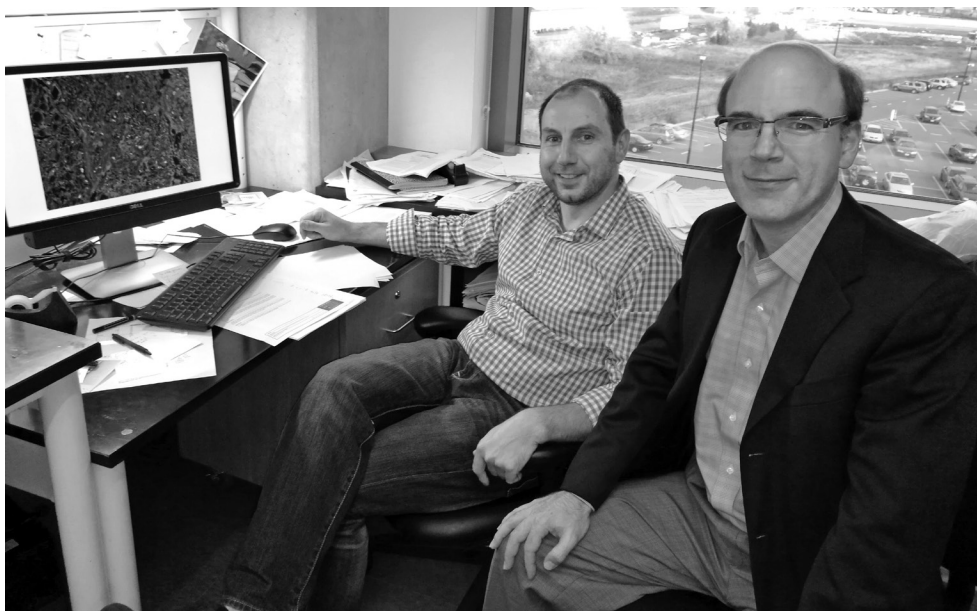
... from page 1

Ever since the genetic mechanism of FSHD, centered on the abnormal expression of the DUX4 gene, was published in 2010, scientists around the world have used genetic engineering to insert DUX4 into various species—many of these efforts funded by the FSH Society—in hopes of recreating key features of FSHD in lab animals.

This turned out to be not as easy as one might have hoped. DUX4, which does not occur naturally in mice, is quite tricky to control. Some initial DUX4 mouse models showed few ill effects. Other efforts led to animals that were so severely affected that they died before birth. It seemed like a Goldilocks dilemma of having too much or too little.

None of these models reflected key aspects of FSHD in humans: the extremely low levels of DUX4 expression, and slow progression leading to dystrophic changes, in which healthy muscle is replaced by scar tissue and fat.

In Kyba's lab, early attempts to create a DUX4-expressing mouse ran into stumbling blocks. DUX4 by itself is an incomplete gene, lacking parts needed for DUX4's genetic code to be transcribed to enable the cell to act on



**Darko Bosnakovski and Michael Kyba**

the genetic information. So when the Kyba lab first tried to engineer an FSHD mouse, it added a piece of genetic material dubbed "SV40 poly A" to DUX4, which permitted the gene to be transcribed. But this system was too efficient. DUX4 is very toxic, so even

when the gene was supposed to be turned off, low levels would still seep out and cause abnormalities and premature death.

Going back to the drawing board, the Kyba team changed out this genetic material

... continued on page 19



# Rediscovering the freedom of bicycling

*Thanks to an adaptive electric-assisted trike*

by MICHELLE CHAUVIN  
Sterling Heights, Michigan

**B**ike riding is something I've always enjoyed. After my husband and I were married, we would drag our bikes down the stairs from our third-floor apartment for a four-mile ride and run every day after work.

Seven years later we had our son, and two years after that our daughter followed. Family bike rides became the norm on the weekends. We would seek out different parks and trails to ride—a great way to spend family time.

It wasn't until the kids were about 10 and eight years old that I noticed a slight decline in my endurance when I rode my bike. It was harder to keep up with my family, and the bike rides were becoming shorter.

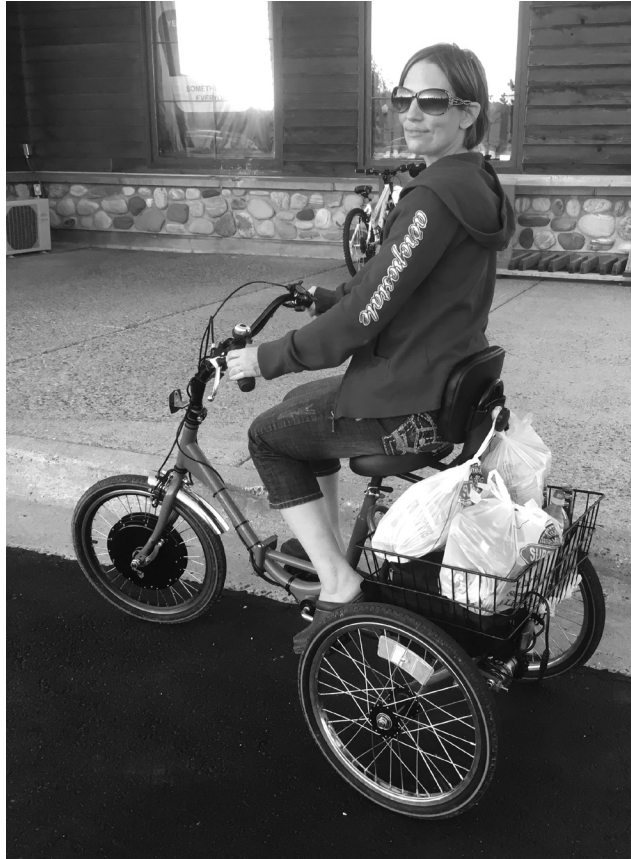
Having been diagnosed at age 12 with FSHD, I felt lucky that I had been able to ride a bike as long as I had, but sad that soon I might not be able to ride with my husband and kids. When I began to need help lifting my feet onto the pedals, I knew that time was probably at hand.

To keep up, I knew I needed a change. At first I tried an electric Razor moped with a seat. That worked fine until my arms collapsed onto the handlebars during a ride, twisting the steering column, and landing me face-first on the asphalt.

About this time, my dad had purchased an electric, two-wheel bike. I thought the idea of a power-assisted bike was great, but I still had the problem of how to balance the bike while lifting my feet onto the pedals when I took off. That's when I thought about a three-wheel, electric-assisted trike.

After doing some research I found a company in New York called Worksmen Cycles. They produce a lightweight, small-wheeled, quality-built electric trike. It's called an electric Port-O-Trike, and this bike isn't your grandpa's bike!

At my age, I really did not want a bike that looked like an old-style trike. With its scaled-down tires, its motor inconspicuously



Michelle Chauvin takes her Port-O-Trike on a shopping expedition.

hidden in the front wheel hub, and a cool choice of colors, I was actually pretty excited to try it out! As an added bonus, this trike folds in half for portability.

No doubt these bikes run a little on the pricey side (an average electric trike runs about \$1,200), but the thought of rejoining the family on bike rides outweighed that hefty price tag. I was ready to put the order in, when I decided I should probably check local online sales first. A local search on Craigslist found the exact same Worksmen Cycle for sale, barely used, for \$900.

My husband and I went to check it out and were pleasantly surprised at its appearance and ease of use. I took it for a test drive, and minutes later we were loading it up into our minivan. The only adjustment I made was to add a backrest for more support.

There are a few other things to consider when thinking about purchasing this bike, like foot straps for the pedals, and whether or not a seatbelt might also be needed. A belt can easily be wrapped around a backrest to keep the rider secure and balanced.

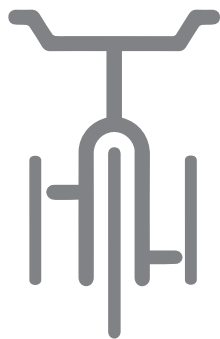
With an electric bike also comes the choice of either a lead acid or lithium ion battery. I have a lead acid battery, which is less expensive but also twice the weight of a lithium ion battery.

In addition to the Port-O-Trike, Worksmen Cycles also sells many other adaptable bicycles, including two-person bikes. The trike easily

handles both paved pathways and dirt roads. As long as the rider feels secure on the trike, he or she should be able to handle both.

In this past year, my trike has seen more than its fair share of mileage—from local trails to Yellowstone, to Colorado Springs. For me, the freedom of jumping back on wheels and being able to once again hit the trails with my family has proved to be priceless.

Here's the link to Worksmen Cycles Port-O-Trike:  
[www.worksmancycles.com/ptcb-hub-eng.html](http://www.worksmancycles.com/ptcb-hub-eng.html)



*“For me, the freedom of jumping back on wheels and being able to once again hit the trails with my family has proved to be priceless.”*

— MICHELLE CHAUVIN



## Giving a piece of me for research

*Hoping to solve FSHD for the next generation*

by HILARY A. C. HOOVER  
Ocala, Florida

I tested positive for the FSHD gene and am currently asymptomatic. Due to my status, I was asked to donate muscle tissue via open muscle biopsy at the Kennedy Krieger Institute (KKI) in Baltimore, Maryland. Knowing that my donated tissue will be used in research to test new treatments made me less nervous about the surgery. I took a silly picture in pre-op and posted it to my Facebook page to raise awareness.

I am very glad that I was able to take part in the research at KKI. My visit opened up an important conversation with two of my brothers who have not been tested at this time. Through them, I have six nieces and nephews. I made my donation for them and for all the children growing up with the potential to carry the FSHD gene. It was important to me to give what I can to be part of the solution. The experience brought me closer to my family and friends, and further opened lines of communication regarding FSHD. [FSH Watch](#)



**Participating in a muscle biopsy to benefit research for facioscapulohumeral muscular dystrophy! As an individual who tests positive for this condition, I am glad my muscle tissue will be used in current and future research to study this debilitating disorder.**

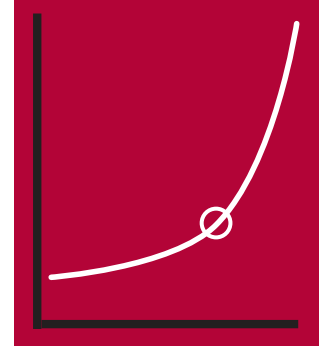
## THE KNEE OF THE CURVE

... from page 3

must direct their own course—absorb the research and experiences of fellow patients, listen to their bodies, and create a dialogue with their physician/physical therapist to apply what works for them.

Fast forward to today. Progress can seem excruciatingly slow when a technology revolution is viewed in real time. And the fact of the matter is, finding a treatment for FSHD is a daunting task for which there are no shortcuts. Do not be disheartened that you don't hear about big clinical trials. It is a heady time for biotechnology in general, and FSHD research in particular, as we approach the knee of the curve.

The very nature of the technology acceleration curve is that the seemingly impossible becomes inevitable if you can keep to the course. I thought it to be impossible before, but my true hope today is that in our lifetime, we will be able to look back and reflect on how we all witnessed and profited from this amazing time of progress and success. So stay tuned in, buckle up, and join us in all ways that you can to keep us all on the acceleration curve! [FSH Watch](#)



## PLACING A BET ON BLOCKING DUX4

... from page 4

cancer and other diseases, while beta agonists are widely used for asthma and chronic obstructive pulmonary disease.

These discoveries are heartening and important for two reasons. First, we can now explore the potential utility of these drug classes in directly treating FSHD. This is a very exciting prospect, but one that must be viewed with caution because significantly more work must be done before we can determine if these potential drugs would be safe and effective.

An equally promising prospect is that studying how these drugs turn off DUX4 is likely to uncover additional drug targets. While the research we have published is preliminary, it raises hope that we will be able to treat FSHD with drugs that prevent or even reverse disease progression.

**Editor's note:** This research received seed funding from the FSH Society, and was subsequently supported by NIH/NIAMS grant R01AR045203 (SJT); NIH/NINDS grant P01NS069539 (RT, SMvdM, SJT, FMS); NIH training grants T32CA009657 (AEC), T32GM007270 (SCS), and T32HG00035 (SCS); Friends of FSH Research (SJT); FSHD Canada Foundation (YH); Prinses Beatrix Spierfonds grant W.OP14-01 (SMvdM); and Spieren voor Spieren (SMvdM).

### Reference

Campbell AE, Oliva J, Yates MP, Zhong JW, Shadle SC, Snider L, Singh N, Tai S, Hiramuki Y, Tawil R, van der Maarel SM, Tapscott SJ, Sverdrup FM. BET bromodomain inhibitors and agonists of the beta-2 adrenergic receptor identified in screens for compounds that inhibit DUX4 expression in FSHD muscle cells. *Skeletal Muscle*. 2017;7:16. doi: 10.1186/s13395-017-0134-x. [FSH Watch](#)





# Nearly \$1.2 million committed in 2017

## Targeting treatment for FSH muscular dystrophy

by **DANIEL PAUL PEREZ** and **JUNE KINOSHITA**  
FSH Society

The FSH Society has awarded grants totaling \$616,476 to seven research projects submitted during the February 2017 grant cycle (see list at right). This brings the Society's total new research commitments to \$1,175,489 for the year. Reviewed by the Society's world-class Scientific Advisory Board, these cutting-edge projects will help to accelerate the development of treatments.

Michael Kyba's project will carry out detailed analyses of a new mouse that expresses very low levels of DUX4 and develops skeletal muscle disease. DUX4 is the gene widely viewed as a key instigator of muscle weakness and degeneration in FSHD. (See story on page 1.)

Projects by Camille Dion, Yosuke Hiramuki, and Sanxiong Liu take aim at the regulation of DUX4. One of the regulators of DUX4 is a gene called SMCHD1. Mutations in SMCHD1 are associated with FSHD Type 2, and also with exacerbating FSHD Type 1. SMCHD1 is thought to normally play a role in repressing DUX4, and the FSHD-associated mutations make the gene less effective at doing its job.

Dion's project will investigate SMCHD1's role in regulating DUX4 and the process by which muscle damage occurs, particularly during the maturation of muscle cells. Hiramuki is exploring ways to make SMCHD1 more effective at repressing DUX4, possibly by blocking enzymes that degrade SMCHD1, which might be targets for new drug development. And Liu will search more broadly for factors that regulate DUX4 expression. All of these efforts aim to uncover potential targets for future drugs.

Angela Lek is harnessing CRISPR gene-editing technology to silence thousands of genes, one by one, in muscle cells that express DUX4. Ordinarily, the expression of DUX4 causes the cells to die. Lek's project aims to find other genes that, when disabled, allow the cells to survive. These genes, as DUX4's accomplices in harming cells, could be keys to unlocking a treatment strategy.

Past investigations have indicated that DUX4 expression can trigger a variety of potentially destructive processes, including oxidative stress and apoptosis ("programmed cell death"). Tissue can also be destroyed through necrosis, a less well-understood biological process commonly found in FSHD biopsies. Julie Dumonceaux's project would, for the first time, investigate the role necrosis plays in FSHD. Her findings might suggest that blocking necrosis could be an avenue for treatment.

Gabsang Lee's project aims to understand how FSHD affects the earliest development of skeletal muscle. Previous research has suggested that DUX4 is expressed in muscle stem cells that also express the PAX7 gene, so Lee proposes to create induced pluripotent stem cells (iPSCs) derived from FSHD patients as well as controls; these cells contain a "reporter" that shows if the cells are expressing PAX7. His goal is to carry out detailed cellular and molecular analysis on these cells as they develop into skeletal muscles. This, he hopes, will provide insight into whether DUX4 affects the early development of skeletal muscle in ways that might predispose it to the disease.



- ▶ **A GENOME-WIDE CRISPR KNOCK-OUT STRATEGY TO IDENTIFY MODIFIERS OF FSHD**  
Angela Lek, PhD, Genetics and Genomics; Louis Kunkel, PhD, Genetics and Genomics, Boston Children's Hospital, Massachusetts, USA.  
\$75,860 for one year
- ▶ **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, (mentor), Fred Hutchinson Cancer Research Center, Seattle, Washington, USA.  
\$53,520 for one year
- ▶ **SMCHD1 AN EPIGENETIC KEY PLAYER OF CHROMATIN REGULATION IN TWO UNRELATED DISEASES: FSHD AND BAMS SYNDROME**  
Camille Dion, PhD student, INSERM UMR\_S910, Aix Marseille Université, FRANCE; Frédérique Magdinier, PhD, (mentor), INSERM UMR S910, Faculté de médecine de la Timone, Aix Marseille Université, FRANCE.  
\$25,000 for six months
- ▶ **SKELETAL MUSCLE DEGENERATION IN THE IDUX4PA MOUSE MODEL**  
Michael Kyba, PhD, University of Minnesota, Minneapolis, USA.  
\$100,000 total (\$50,000 annually) over two years
- ▶ **DERIVATION OF MULTIPLE PAX7:GFP FSHD-SPECIFIC HUMAN IPSC LINES**  
Gabsang Lee, DVM PhD, Johns Hopkins University, Baltimore, Maryland, USA.  
\$94,696 for one year
- ▶ **DUX4 TOXICITY: DECIPHERING NECROTIC PATHWAYS IN FSHD**  
Julie Dumonceaux, PhD, University College London, UK.  
\$142,400 for 18 months
- ▶ **TRANSCRIPTIONAL AND EPIGENETIC REGULATION OF D4Z4 AT CHROMOSOME 4Q35.2**  
Sanxiong Liu, PhD, and Danny Reinberg, PhD, New York University School of Medicine, New York City, USA.  
\$125,000 for one year



# Colorado Walk & Roll fundraiser

*All things are possible*

by **KATIE RUEKERT**  
Castle Rock, Colorado

Our second annual Colorado Walk & Roll to Cure FSHD was another wonderful and successful event, raising \$31,000 to benefit the FSH Society. The day was surrounded by the peaceful Colorado blue sky and sunshine, and the event was overflowing with family, friendship, connection, encouragement, hope, and support.

Our dedicated committee started planning for year 2 with monthly meetings beginning in January, and we made a few changes from our first event. We were able to offer some added fun with live music from a local band, who graciously donated their talents to our

*... continued on page 15*



**Katie Ruekert and the amazing Colorado Walk & Roll Committee and energetic volunteers give an enthusiastic thumbs up to their 2017 efforts.**

## FSHD Canada awards \$20K for FSH Society research grant

### FOUNDATION PROVIDES AN AVENUE FOR CANADIANS TO SUPPORT OUR EFFORTS

The FSH Society is pleased to announce that it has received a grant of \$20,000 from the FSHD Canada Foundation in support of an exciting, treatment-focused project, “Developing LNA-based therapy for facioscapulohumeral muscular dystrophy.”

“We are delighted to help Neil Camarta and his colleagues at FSHD Canada help make a huge impact on FSHD by helping to fund high-quality research, both critical and necessary—in Canada and around the globe,” said Daniel Perez, president, CEO, and CSO of the FSH Society. “Projects as this one are ideal for achieving the purposes of both our organizations and helping to provide insights and hope for the constituents we serve.”

The project will be carried out by Yi-Wen Chen, PhD, of Children’s National Health System, Washington, DC, and Toshifumi Yokota, PhD, of the University of Alberta Faculty of Medicine and Dentistry. The project was reviewed favorably by the FSH Society’s Scientific Advisory Board and approved by the

boards of the FSH Society and FSHD Canada Foundation. Its total budget of \$179,104 over two years will be jointly funded by the FSH Society and FSHD Canada Foundation.



Chen and Yokota are investigating a promising method for developing a gene therapy to slow down or stop FSH muscular dystrophy (FSHD). They are studying an antisense oligonucleotide (AON) compound called LNA (locked nucleic acid) gapmer to reduce DUX4, a gene widely thought to play a key role in FSHD.

AONs are short, gene-like molecules that bind to and inactivate target gene activities (in this case, DUX4). LNA gapmers are designed to overcome some problems that made earlier AONs unsuitable for use as therapeutics. LNA gapmers are more stable, resistant to

being degraded, more effective, and can penetrate the cell membrane and get inside cells where the target DUX4 messaging molecules (mRNA) reside.

Yokota will continue to improve the anti-DUX4 LNA gapmers, testing them in FSHD cell lines, while Chen will test the safety and efficacy of the molecules in a mouse model of FSHD. If successful, this research could help advance the quest for a gene therapy that can be tried in FSHD patients.

FSHD Canada Foundation was established in 2012 with the assistance of the FSH Society to provide an avenue for Canadians who wish to support FSHD research through tax-deductible donations.

Neil Camarta, CEO, FSHD Canada Foundation, said, “Since its beginning, the partnership with the FSH Society has helped enormously with the inception and development of the FSHD Canada Foundation, and we are effectively serving the needs of Canadians with FSHD—in helping to understand FSHD and find a treatment.”





# Recapping Race Across America

*A life-changing experience for Team FSHD Cycling*

by **GEORGE POLLOCK JR.**  
*Lithia, Florida*

**R**eplacement rider, record heat, flat tire, wheel malfunction at 50 mph, one-hour penalty. This was all in the first day of our adventure to race our bicycles across America from Oceanside, California, to Annapolis, Maryland, in June of this year. We recovered from our initial challenges and then raced through a hailstorm and a tropical storm to complete the race in seven days and seven hours. We had a racer on the road 24 hours a day!

Team FSHD Cycling participated in the 36th running of the Race Across America along with 45 other teams. We were an eight-person team with a mission to raise awareness and funds for the FSH Society. Nearly 400 donors pitched in to raise \$107,000, and all eight riders finished safely together. This was truly a life-changing and inspiring expedition.



## Celebrating Team FSHD Cycling from sea to shining sea

### PARTIES IN CALIFORNIA AND MARYLAND TOAST THE RIDERS

Supporters gathered on June 15 at the Urge Gastropub & Whiskey Bank in Oceanside, California, to give Team FSHD Cycling a rousing send-off for the Race Across America. Team captain George Pollock and the FSH Society's Beth Johnston pose proudly with a poster signed by well-wishers. Amy Bekier, FSH Society Board of Directors member, organized the wonderful party.

Not to be outdone, fans on the East Coast organized a picnic on June 24 to celebrate the completion of the race in Annapolis, Maryland. Weather-related delays kept the team from arriving in time, but George greeted the assembled group via Facetime from the road. Drs. Yi-Wen Chen and Pegah Dehghan spoke about FSHD research and how important donations are to sustaining their efforts.

Team FSHD Cycling was presented with official proclamations from the governor of Maryland and the mayor of Annapolis, and a special cake was devoured by all. We sincerely thank the event organizers, led by Missy Cassidy and Frank and Ann Kolakowski.



Team FSHD Cycling captain George Pollock and FSH Society's Beth Johnston stand with a poster signed by well-wishers (above). A special World FSHD Day cake (left) was waiting at the finish line.





The bicycle race traversed 3,000 miles through 12 states with 170,000 feet of climbing. Most of the climbing was east of the Mississippi River, in West Virginia and Maryland.

What an incredible way to see the country! On our way, we raced down the Glass Elevator descent, a 4,000-foot drop to the desert floor in California, through Monument Valley in Arizona, across the Rocky Mountains, then into the windswept plains of Kansas, into Missouri and across the Mississippi River, over the rolling hills of Ohio and the steep hills of West Virginia, and finally across the hallowed grounds of Gettysburg and into the finish in Annapolis, Maryland, on Saturday evening, June 24.

After recruiting the racers and crew, we spent a year planning for the race—reading books written by racers, studying the rules and the route, creating detailed spreadsheets down to the minute for each rider segment, interviewing former racers, and creating food lists.

All of this planning certainly led to our success, but one does not realize the magnitude of the undertaking until the clock starts and we are racing up the first hill in 110-degree heat and drinking a bottle of water every few minutes and recognizing we have seven days to the finish. Once we all accepted we would be in the same clothes for the week, with very little sleep, we focused on the task at hand and prepared to complete the adventure.

The racers and crew were unbelievable. We had five vehicles, eight racers, and 11 crew members. The racers and crew all volunteered to participate. I cannot thank them enough for their sacrifice and



**“The bicycle race  
traversed 3,000 miles  
through 12 states with  
170,000 feet  
of climbing.”**

efforts to make the race a success. Everyone got along so well. All had such a positive attitude, embraced the opportunity, and stayed focused on our mission of raising awareness and funds to find a cure.

The photos covering our vehicles of families afflicted with this disease were so inspiring and made sure we were thinking about why we made such an effort!

We also met so many great people along the way. We met family members taking care of relatives with muscular dystrophy. They were so thankful for our efforts. We met bicycle racing fans. In Arizona, we met a woman who could recite every winner of the

Tour de France for the past 10 years. In Yates Center, Kansas, we had lunch in a restaurant and sat next to the farmer who raised the beef for our hamburgers. You know it is good when the farmer is eating the same thing! We have dozens of these stories.

I am tired again just reliving the experience!! This was truly one of the most incredible adventures of my life, and I am certainly blessed to share the experience with my family and close friends.

As one who has FSHD, I wanted to show we can take on big challenges and push our bodies to extreme efforts. I certainly recognize I am lucky in that my FSHD is not too debilitating yet. As we all do, I am also experiencing my muscles getting weaker and continuing to impact more muscles.

There may come a time when I cannot pedal a bicycle. Until then, I will continue to ride, and I encourage everyone to enjoy your passions and continue to be positive and be ambassadors for our efforts to find a cure. We will win this fight. FSH Watch

fundraiser. We also made the switch from a raffle drawing to a silent auction. The team was a bit hesitant to take on all the work that goes into organizing a silent auction on top of organizing a Walk & Roll fundraiser, but all the hard work was worth it and brought a great excitement to our event this year. In the end, planning a silent auction truly brought our team closer together, and there was a lot of fun involved.

Year 2 naturally brought a sense of improved organization, and we were able to market ourselves in local online event calendars, which in turn led us to cross paths with local children's book author, Lisa Reinicke. Lisa and her team have been beyond anything we could even imagine possible. Their partnership with us and our cause has touched our committee so deeply, and we are so grateful.

We were also thrilled to meet Mark Stone, the new CEO of the FSH Society, and have him attend our event this year. Mark brought an undeniable uplifted energy and sense of “FSHD Family” to the day. We also had the pleasure of Matt Wicklund, MD, from the University of Colorado attending our event and speaking about the latest FSHD research. There's no question that the future looks bright for FSHers and our generations ahead.

Personally speaking, I went into our second event with the mindset that this year would be a piece of cake since we now knew what we were doing. However, I felt much more drained emotionally and physically afterwards this time around. There was a part of me (a small part) that questioned if all this time and physical effort is worth the strain on someone living with FSHD. My exhausted, fatigued body could easily say, “NO, it's not!” Thankfully, I have been able to tap into my intuition over the past couple of weeks after the fundraiser while seeking recovery from within. My higher self is reconnecting me with my purpose, and I couldn't be more excited for year 3. September 8, 2018, here we come! FSH Watch



## Ask the physical therapist (part 4)

Julie Hershberg answers your questions

*The following is a transcript of a question-and-answer session, conducted over the FSH Society's Facebook page, with Julie Hershberg, PT DPT NCS. Hershberg is a physical therapist who is a board-certified neurologic specialist. She practices at [re+active] physical therapy & wellness and is an instructor in the Doctor of Physical Therapy program at the University of Southern California.*

**Q: I am a 48-year-old man who is asymptomatic. I am still fairly active. Prior to my genetic diagnosis of being positive for FSHD in 2011, I ran two NYC marathons in 2008 and 2009. I am thinking about running another one next year or the year after at a slower pace than I did six years ago. I ran a sub 4:15 in those, and this one would probably be somewhere between 5 and 5.5 hours.**

**Do you foresee any issues or have any concerns if I take up this endeavor? If not, what precautions could or should I take prior to and during the training for the race?**

**A:** Awesome! I think this is an excellent goal! My advice is to proceed with awareness and just an ounce more of caution with your training in general. I would say the same thing to anyone who has not run for a while. Something in particular to think about is that while you may not be aware of any symptoms right now, there may be very subtle areas of weakness or tightness that can predispose you to injury (this is true of the general population). This video, put out by the American Physical Therapy Association, is an excellent resource for things to consider when returning to running: [www.moveforwardpt.com/.../VideoLibrary/detail.aspx](http://www.moveforwardpt.com/.../VideoLibrary/detail.aspx).

I highly recommend a running analysis by a PT (including high-speed camera 2D video analysis) to help identify areas of strength and areas that can be optimized. There also is a free e-book from the American Physical Therapy Association (APTA) on tips for healthy running: [www.moveforwardpt.com/Running/Default.aspx](http://www.moveforwardpt.com/Running/Default.aspx).

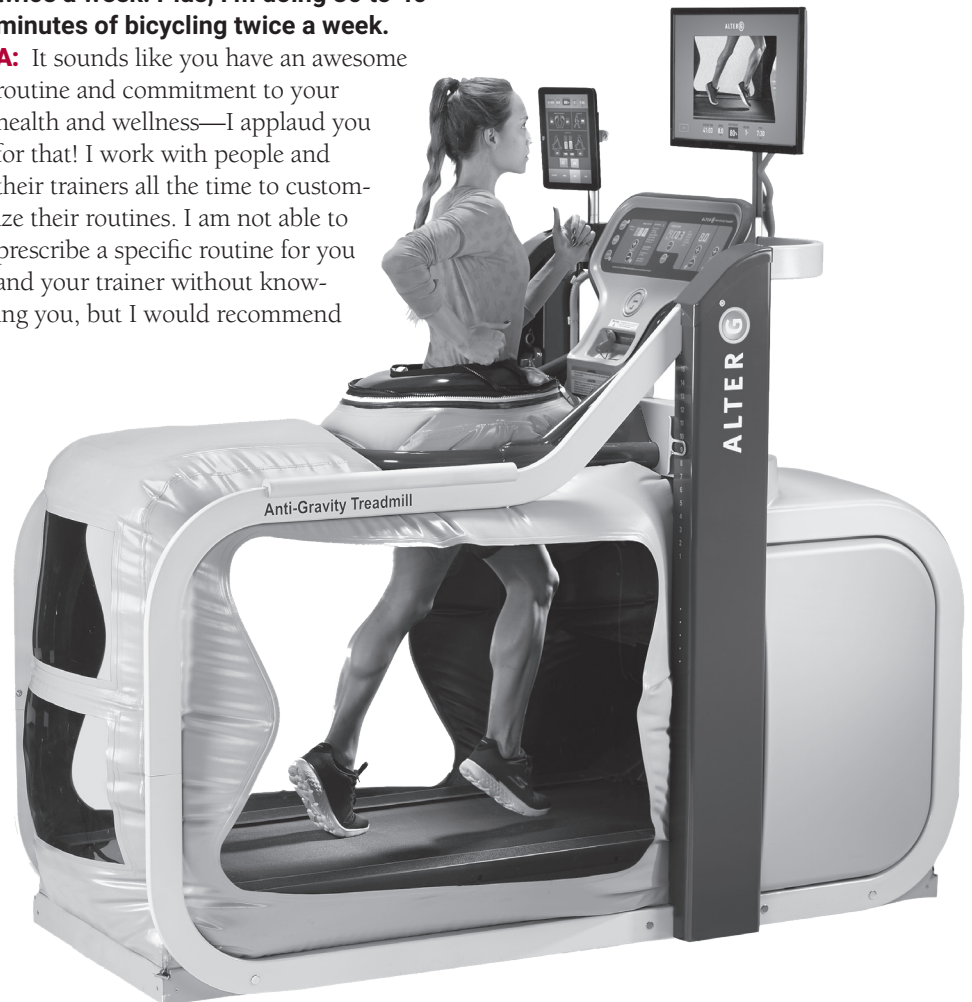
Some great nuggets of information from that e-book that I think you may want to consider: "Recovery time isn't a break from

training; it is part of it. Runners, particularly those at the Master's (40+) level, can consider taking recovery time every third week instead of every fourth week during a marathon training program. Consider using cross training, such as the elliptical or bike, to substitute for recovery runs to give your legs a break. This allows you to rest your legs while remaining on track for a successful race."

**Q: I would like to know what type of exercise I can do at the gym. My trainer gave me a good program, but I would like to have your opinion so that I'll be able to ask my trainer to do a specific program for me. One thing that is very important for me is to continue training at least twice a week. Plus, I'm doing 30 to 40 minutes of bicycling twice a week.**

**A:** It sounds like you have an awesome routine and commitment to your health and wellness—I applaud you for that! I work with people and their trainers all the time to customize their routines. I am not able to prescribe a specific routine for you and your trainer without knowing you, but I would recommend

that you work with a PT who can create an individualized routine for you to carry out with your trainer. When I do this, I create videos and take pictures of clients doing the exercises so they can share this with the trainer—I highly recommend that for you if that is possible. Also, I highly recommend that the trainer pay close attention to your movement as you do the exercises—always quality before quantity. Finally, I recommend a very thorough assessment and training routine that includes key areas such as scapular and shoulder strength, abdominals (deep abdominals and back muscles—not just crunches or sit-ups), hip strength (especially gluts), and knee and lower leg strength. In general, I am a proponent of functional



The AlterG anti-gravity treadmill is gaining popularity among people with FSHD.

strengthening done in upright positions (doing as much as you can while standing or sitting) and in many planes (not just straight up and down but rotation and diagonals).

**Q: I have been recently diagnosed. I have always been quite active. However, I have been told to stop my kettlebell class, as well as using any free weights, and go swimming instead. Is this something you agree with?**

**A:** The general thought in the past is that strength training was harmful for FSHD—that is not the case now. Moderate-intensity strength and aerobic exercises have been found to be safe. So the answer is not a universal recommendation to stop strength training! However, it would be important to know how you are performing the exercises so that you are using the appropriate amount of resistance and not compensating or hurting yourself. I recommend a physical therapist to help give you guidance in this area!

A Cochrane review article published in 2013 compares evidence from all qualified studies and found that moderate strength-training is not harmful. The article title is “Moderate-intensity strength training appears not to do harm, but there is

insufficient evidence to conclude it offers benefit.” I also have a presentation that I have done summarizing the literature for exercise and strengthening that I would be happy to pass on to you: [www.ncbi.nlm.nih.gov/pubmed/23835682](http://www.ncbi.nlm.nih.gov/pubmed/23835682).

**Q: Someone told me about a zero-gravity treadmill. Would you recommend exercising on one of these for someone with FSHD?**

**A:** Yes—I do love the AlterG anti-gravity treadmill for people who are able to walk. It is a supported treadmill that supports you with air (like water but without the resistance of water). I use this in my clinic, and now many gyms and physical therapy practices have them available: [www.alterg.com](http://www.alterg.com).

**Q: My son, age 36, has FSHD. His general doctor was concerned about his marked lordosis and his chronic back pain, and sent him to a spine specialist. The general doc said she hoped there would be a brace that would improve the lordosis and pain. However, the spine specialist examined my son for a fair amount of time and determined that he would “fall**

... continued on page 19

Available now!

## GET YOUR UPDATED PHYSICAL THERAPY FOR FSHD BROCHURE

Co-written by leading FSHD experts Katy Eichinger, PhD; Shree Pandya, PT DPT MS; and Wendy King, PT, the brochure provides an excellent review of the literature on physical therapy and exercise, with practical guidelines for patients and therapists.



To order copies, please email your postal address to [kathryn.puzzanghera@fshsociety.org](mailto:kathryn.puzzanghera@fshsociety.org). You can also download the brochure from [www.fshsociety.org](http://www.fshsociety.org), but it's worth having hardcopies on hand to share with your PT, family members, and others.

## Ask Beth

### DONATE YOUR OLD CAR TO THE FSH SOCIETY!

A few weeks ago, a member called the office and asked “... can we accept cars as donations?” The answer: “Heck, yeah!” (Well, maybe not in those exact words.)

The FSH Society recently partnered with Vehicles for Charity (VFC) to accept many types of vehicles as donations. A nonprofit itself, VFC manages the entire process of arranging a FREE pickup of your vehicle, auctioning it off, sending the proceeds of the sale to the FSH Society, and providing you with the appropriate tax documentation—all at no charge to you! It accepts cars, trucks, vans, recreational vehicles, motorcycles, dirt bikes, tractors, boats, and trailers.

I spoke with Majella, who recently donated her car to us through VFC. “I would do it again in a moment—it was the



**Beth Johnston, Chief Community Development Officer at the FSH Society**

easiest donation I've ever made! I completed a simple form online that had some basic questions, they called to confirm, then within four days they came to pick it up at a time that was convenient for me. Everyone was so very professional and courteous, from the office staff to the tow truck driver ... it was really a no-brainer—SO easy!”

Do you have a vehicle you'd like to get rid of? Donating it to the FSH Society is convenient, easy, and may qualify you for a tax deduction. Best of all, your vehicle donation will make a big difference in supporting the mission of the FSH Society!

To get all the details and find out more, visit our website at [www.fshsociety.org/donate-car-fsh-society](http://www.fshsociety.org/donate-car-fsh-society). More questions? You can call VFC directly at (866) 628-2277.





# 2018 IRC Workshop and FSHD Connect

*Las Vegas is site of next worldwide gathering*

by JUNE KINOSHITA  
FSH Society

Join us for the FSH Society's 2018 International Research Consortium Workshop and FSHD Connect conference, from June 8 to 10 at the Flamingo Las Vegas.

From June 8 through noon on June 9, scientific and medical researchers from academia and industry will convene for the FSH Society's 23rd annual International Research Consortium (IRC) Workshop. This invitation-only workshop is the premier annual platform for clinicians, medical researchers, and basic scientists to present and discuss new developments in FSHD research, reinforce collaborative efforts, and facilitate new initiatives.

On the afternoon of June 9 through June 10, hundreds of patients, family members, researchers, physicians, and health experts will gather for a day-and-a-half of immersive learning and community building. Our 2018 meeting will feature talks by thought leaders on the latest in scientific research and medical management of FSHD, living with FSHD, and raising "an army of activists." Breakout sessions will address topics to help you cope and live better with FSHD, including exercise and physical therapy, strategies for dealing with practical and emotional transitions, caregiving, "life hacks," and much more.

A highlight of the conference is the CureFSHD banquet on the evening of Saturday, June 9, to celebrate the FSHD community. Banquet tickets are included with registration.



Additional details and registration for the IRC Workshop and FSHD Connect are available at [www.fshsociety.org](http://www.fshsociety.org). The deadline for registration is Friday, May 25, 2018. We are offering a limited number of scholarships to help defray costs of registration and travel. Applications can be downloaded from our website. The deadline for scholarship applications is March 1, 2018.

## CONFERENCE HOTEL INFORMATION

Overnight accommodations for the IRC and FSHD Connect are available at the Flamingo Las Vegas hotel. The FSH

Society has a special conference rate of \$154 per night (single or double occupancy), not including a \$30 resort fee and taxes. As of this time, the hotel guarantees 50 accessible rooms with roll-in showers. For the best selection of accessible rooms, please reserve early.

## FLAMINGO LAS VEGAS RESERVATIONS

Visit <https://aws.passkey.com/go/SFFSH8> or call the Reservation Center at (888) 373-9855 to secure a reservation in our FSH Society Connect conference room block (group code SFFSH8). Please be aware that a processing fee of \$15.00 + tax per reservation will be incurred if you choose to call rather than use the dedicated weblink. The closing date for the Society's block of rooms is May 18, 2018.

## Ways to engage

### #GIVINGTUESDAY IS NOVEMBER 28!

Make an online donation on this day, and a group of generous benefactors will match it dollar for dollar up to \$11,500!

### GET SOCIAL!

Find our Facebook, Twitter, and Yahoo! Groups by visiting [www.fshsociety.org](http://www.fshsociety.org) and clicking on the logos in the right-hand margin. Our online communities are great sources of news, advice, and social support. Bookmark these pages and visit often. Use your account privacy settings to limit who can see your posts.

### HAVE YOU MADE A GIFT TO THE SOCIETY IN 2017?

You can count on us to invest your donation for maximal impact on FSH muscular dystrophy! Send your tax-deductible gift in the enclosed envelope, or contribute online at [www.fshsociety.org](http://www.fshsociety.org). Thank you!

### COMMIT TO THE FUTURE

Include the FSH Society in your will. Your bequest sustains our work for future generations. Questions? Please contact June Kinoshita at (781) 301-6649 or [june.kinoshita@fshsociety.org](mailto:june.kinoshita@fshsociety.org). Always check with your financial advisor when making a change in your will or estate plans, and learn how current tax laws and other legislation may affect your plans.

### DON'T LEAVE MONEY ON THE TABLE!

Many companies will match employees' charitable donations, or will donate if employees volunteer their time to a charity. Find out if your employer matches donations at [doublethedonation.com/fshsociety](http://doublethedonation.com/fshsociety).

### COMBINED FEDERAL CAMPAIGN (CFC)

Federal employees can enroll in workplace giving from October 2 to January 12, 2018. The FSH Society's CFC identification number is 10239.

## HOT OFF THE PRESS: A DUX4 MOUSE WITH MUSCLE DISEASE

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for sequences downstream of the DUX4 gene which were predicted to be equivalent but turned out to be actually much weaker, and this did the trick. With the new mouse, called “DUX4 polyA,” pups are born looking fairly normal but go on to develop a slow, progressive degenerative myopathy. It appears that they have, à la Goldilocks, gotten the DUX4 dose “just right.”

Intriguingly, the muscle degeneration in the DUX4 polyA mice involves inflammation and stimulates certain cells to form scar tissue (fibrosis). While inflammation has not been widely seen as a cardinal feature of FSHD, studies of patients have reported evidence of inflammation, and some researchers think it may play a more important role than previously acknowledged. “Inflammation could be a response to damaged muscle,” noted Kyba, “or it could be a response to some factor that DUX4 is activating.”

Another interesting feature of these mice is that they have high-frequency hearing loss—a symptom seen in 50 percent of FSHD patients. This hearing loss is subtle, so although it can be detected by hearing tests, many affected individuals don’t realize they have it.

In addition, when their skeletal muscles are injured, the DUX4 polyA mice are less able to regenerate healthy new muscle. “Immature muscle fibers may be more vulnerable to DUX4,” Kyba suspects. This is one of the questions he will be investigating with funding from an FSH Society grant awarded this year. (See related story on page 12.)

In future mouse work, Kyba would like to lower DUX4 levels even further in hopes of “finding levels of DUX4 expression and rates of muscle deterioration as similar as possible to the human disease.”

In addition to probing for insights into the disease process, Kyba’s ultimate aim is to be able to screen drugs in a mouse model—particularly at approaches that “go after the DUX4 protein directly,” which he thinks are likely to have fewer side effects than approaches that alter gene expression. [FSH Watch](#)

**Editor’s note:** Other research teams are also making progress in regulating DUX4 expression in ways that allow mice to develop FSHD-like muscle weakness. These studies have been presented at scientific meetings and are being prepared for publication. See *FSH Watch* 2017 Issue 1, pages 12 and 17.

### Reference

Bosnakovski D, Chan SSK, Recht OO, Hartweck LM, Gustafson CJ, Athman LL, Lowe DA, Kyba M. Muscle pathology from stochastic low level DUX4 expression in an FSHD mouse model. *Nat Commun.* 2017;(8):550. Published online 2017 Sep 15. doi: 10.1038/s41467-017-00730-1. PMID: PMC5601940.

## ASK THE PHYSICAL THERAPIST (PART 4)

... from page 17

**over” if he wore a brace because it would throw off his way of walking. He seemed to be saying that our son’s lordosis and his peculiar center of gravity have forced him to adapt his walk in order to remain upright. A brace to alter the lordosis would throw off his equilibrium, causing him to fall. I realize you have not seen our son, but, in general, do you agree that a back brace could cause this kind of outcome?**

**A:** The simple answer is that no one brace is a one-size-fits-all solution for lordosis and back pain, and it really does take some trying different types of braces to see if a type of brace might be helpful. It is true that biomechanically the hyperlordosis can provide people hip and knee stability in stance and can be a compensation for weak hip extensors. It is possible that altering the alignment may make a person feel more unstable. However, I am not sure that an abdominal brace would particularly alter the alignment enough to cause a problem. [FSH Watch](#)

## MARK A. STONE IS NEW CHIEF EXECUTIVE OFFICER

... from page 1

as fine executive leadership skills in nonprofit health care and policy management,” said Lewis. “Mark will certainly help the FSH Society navigate the new challenges of translational research and enter into the business of supporting clinical trials while maintaining a solid basic research platform.”



Mark A. Stone

Stone, a leading executive in health care-related nonprofit organizations, has served as an executive leader of research-focused patient advocacy groups for the past 13 years, his most recent assignment being the chief executive officer of NephCure Kidney International. During his tenure at NephCure, Stone launched the NephCure Accelerating Cures Institute (NACI), a drug discovery initiative anchored by a clinical trial network comprising more than 35 sites, which seeks to expedite potential treatments for nephrotic syndrome.

“I am looking forward to bringing my experience to the FSH Society. The Society’s track record of success in advancing research initiatives in facioscapulohumeral muscular dystrophy (FSHD) is unmatched, and I am excited about working collaboratively with the founder, our involved and dedicated Board, Advisory Board, donors, volunteers, and staff to accelerate promising treatments to families impacted by this debilitating disease,” said Stone.

Stone is passionate about helping organizations work to expedite treatments and cures in diseases that are both rare and of a genetic origin. He has successfully engaged patients, families, and friends in raising up an “army of activists” while advocating with pharmaceutical companies, the National Institutes of Health (NIH), and the FDA to increase funding levels and enlarge the pipeline of potential therapies. Individuals and families impacted by FSHD will remain the FSH Society’s core focus and priority.

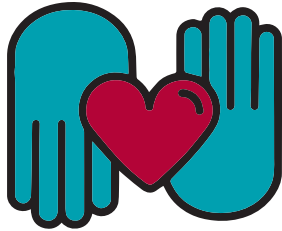
“Mark embodies the qualities of a leader of nonprofits and passionate causes—he is visionary, entrepreneurial, and has been instrumental in achieving strong growth. Mark’s experience in strategic planning, implementation, and successful fundraising is key at this critical juncture. He has compassion, and his empathy is evident. He is an excellent communicator—and this will help FSHD become a known disease. Mark will be an outstanding CEO of the FSH Society,” said Daniel Paul Perez, co-founder, chief science officer, and outgoing CEO. [FSH Watch](#)

## It is up to all of us

*FSH Society Board challenges you to match their \$370,000 pledge*

by MARK A. STONE  
FSH Society

### “IF NOT US—WHO? IF NOT NOW—WHEN?”




We have entered a convergence zone—a “tipping point”—of activity in the FSHD field. More pharmaceutical companies are working to find solutions, the global FSHD environment has deepened with new discoveries, and through your continued support, we are funding cutting-edge research and initiatives to accelerate research toward treatments.

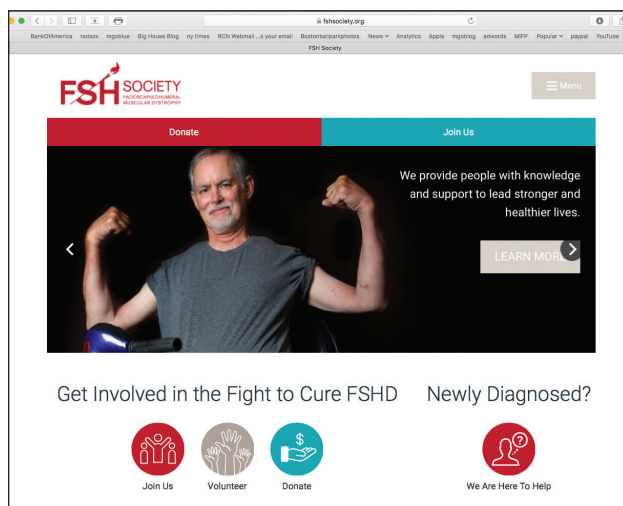
We ask you to join with hundreds of individuals and families like yours and make a gift in this year. If all of us push together, we will move the needle on FSHD research and therapeutic development in the next few years. We know that a cure is out there, and we together must be responsible for finding it.

From now through December 31, 2017, your gift will be counted dollar for dollar toward our year-end challenge.

It's easy to donate:

- Mail a check using the enclosed envelope to the FSH Society, 450 Bedford Street, Lexington, MA 02420. This will save us credit card processing fees.
- Give online at [www.fshsociety.org](http://www.fshsociety.org).
- Call Kathryn Puzanghera at (781) 301-7301. 

### CHECK OUT OUR NEW WEBSITE!



We've redesigned our website so that the information you're looking for is at your fingertips. The latest news, events, resources for living with FSHD, doing research, and calls to action—it's all on the homepage. Please visit [www.fshsociety.org](http://www.fshsociety.org) and let us know how you like it!

### SUPER BOWL TICKET AUCTION!

We are holding a virtual auction for two pairs of tickets (four total) to Super Bowl LII, which takes place at U.S. Bank Stadium in Minneapolis, Minnesota, on February 4, 2018. These tickets are being provided by our connection at NFL Films. The exact seat locations will be known about two weeks before the game. Bid on one—or both—pairs of these guaranteed tickets knowing that your purchase will help support life-saving research on FSH muscular dystrophy!

For a bid form, contact: [robyn.oleary@fshsociety.org](mailto:robyn.oleary@fshsociety.org).

Deadline: Friday, December 8, 2017, noon EST.

Starting bid per pair: \$4,000.



### BARTENDING FOR A CAUSE



I was a volunteer bartender for a few hours at McGreevy's in Boston on July 14. I invited a lot of my friends and family members to come, and even had some wonderful unexpected guests show up. One hundred percent of my tips and 10 percent of total sales went to the FSH Society. It was a lot of fun, and I am hoping to make it an annual activity!

—Lexi Pappas  
Gloucester, Massachusetts