

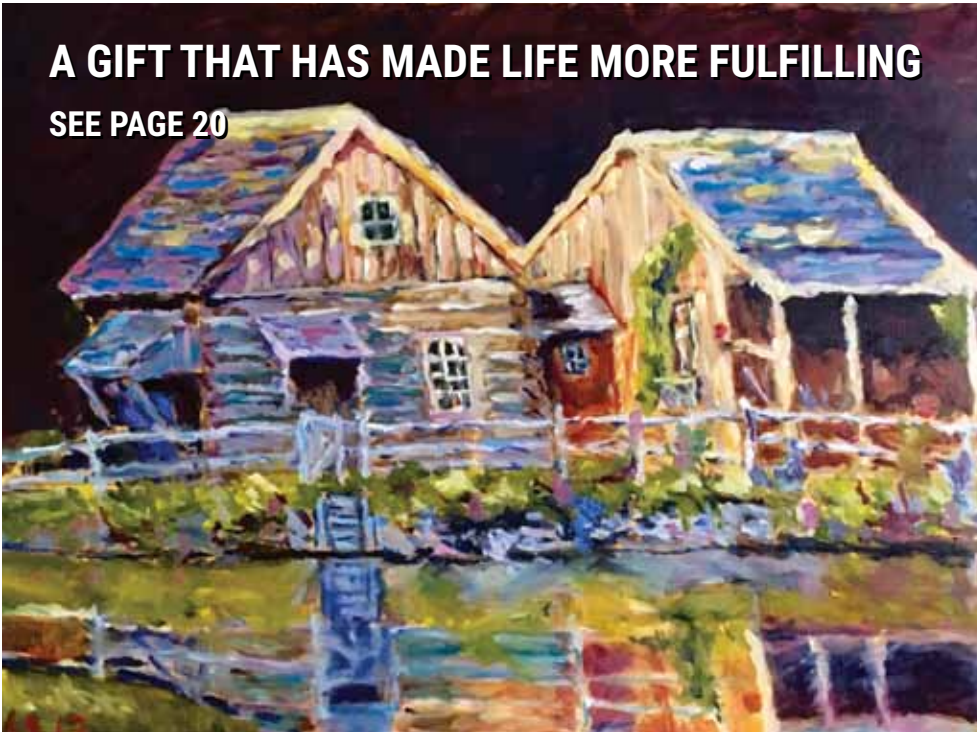
FSH Watch



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

A GIFT THAT HAS MADE LIFE MORE FULFILLING

SEE PAGE 20



RESEARCH

The 2018 FSHD International Research Congress

The field has made astonishingly fast progress

by CHARIS HIMEDA, PhD
University of Nevada, Reno

Nearly 150 researchers, clinicians, patients, and industry partners convened at the FSH Society's 2018 International Research Congress, held in Las Vegas on June 8-9, 2018. The workshop reflected the major focus of the field: building on key discoveries in recent years in an effort to uncover targets for therapy.

Over the past decade, research has shown that FSHD is caused by dysregulation of the disease locus, either by a contraction of the D4Z4 repeat array on chromosome 4 (FSHD1) or by mutations in proteins required for normal silencing of the D4Z4 repeat region (FSHD2).

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NEWS & EVENTS

2018 FSHD Connect Conference

Informative and life changing

by IAN RYS
Port St. John, Florida

As a first-timer, I was very excited to attend the 2018 FSHD Connect Conference held in Las Vegas, Nevada, this year.

As we boarded the plane for Las Vegas I noticed something I wasn't expecting quite so soon—I was feeling waves of emotion that just got bigger with each nearing mile, but I had to stay cool!

This was easy, as our plane kept getting delayed, and my thoughts of meeting another FSHer for the first time kept my mind busy.

When we finally arrived in Vegas, we checked in and got settled. The next day as we approached the El Dorado conference room I saw others. *Others like me!!!* We entered and made our way through the powered chairs and scooters to a table. That ride through the room, with others in chairs and scooters, was awesome! It was almost as if we were a "gang" of sorts, and we were the majority.

We joined a table where we met Carol Chandler, her husband Franco, and her daughter Valerie. This was my first time

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Forward—together

Wow! When I glance back over the past year since I joined the FSH Society community, I am amazed at the progress we have made working together. We are at a tipping point in translating our understanding of FSHD into potential therapies. Your consistent and deepening support over the past quarter-century has catalyzed almost every major discovery in FSHD research and brought us to this remarkable reality. Thank you!



Mark A. Stone

In keeping with our global leadership role, we have reengineered our organization to focus on eliminating the obstacles that slow or prohibit treatments from getting to our families. We have restructured our staff, budget, programs, and governance to better serve our collective mission. Additionally, we have launched FSHD Therapeutics—a therapeutic accelerator initiative to facilitate the work that needs to be done to ensure that promising therapies have a clear regulatory path based on accepted, measurable clinical outcomes.

It's been said, "The power of one, if fearless and focused, is formidable. But the power of many working together is unstoppable." Working together—board and staff, dedicated volunteers, generous donors, researchers, patients, biopharmaceuticals, and governmental agencies—we will achieve our goal of therapies to our families by 2025.

Over this past year, we have been working toward building strong, supportive local communities committed to doing whatever it takes to achieve our collective mission. In pushing this initiative, we have witnessed how unstoppable indeed is the power of all of us working together:

- **Our pioneer leaders are hosting five Walk & Roll fundraiser events** this September and October,

with amazing results already. (See page 10.) In the areas where the Walk & Rolls are being held, our communities are bonding together, tapping into their networks, and leveraging their influence to engage a broader audience and raise significant funds, allowing the Society to go further faster. I applaud the following pioneers for blazing the trail: Susan Aumiller, Nez Bennouna-Nickerson, Ray and Meredith Huml, Nancy Payton, and Katie Ruekert.

- **We launched our national chapter initiative at the recent FSHD Connect Conference.** These are volunteer-led local communities that, with strong support from FSH Society staff, will enable us to have a local presence and a global impact. I celebrate the following chapter directors for leading the way: Susan Aumiller, Kent and Sue Drescher, Karen Dunkerly, Jack Gerblick, Manuel Gomez, Laurie Heyman, Amanda Hill, Dave Lukas, Bill Maclean, Landon and Marie Morrell, Kathy Senecal, and Kristin Zwickau. (See page 3 for details.)

I would be remiss if I didn't highlight all of our faithful volunteers, committed donors, experienced board leadership, and world-renowned researchers and clinicians who host events, give sacrificially, and work diligently toward our common goal of a cure for FSHD.

Thank you for joining your hearts and hands to make us an unstoppable force. Thank you for your continued service and support of the FSH Society. While our "foe" (FSHD) is formidable, working together we will achieve our goal of therapies to our families by 2025.

Working together for a cure.



Mark Stone
President and CEO
FSH Society

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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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National chapter program

Giving a local presence to our global mission

by JUNE KINOSHITA
FSH Society

Big news! The FSH Society has launched a nationwide chapter program. These are volunteer-led local communities that, with strong support from FSH Society staff, will enable us to have a local presence *and* a global impact.



YES! I am interested in getting involved in the new FSH Society Chapter Program!

Each chapter will host two get-togethers a year, including at least one with educational programming, and will organize one fundraiser per year—a Walk & Roll to Cure FSHD (see page 10) or other type of event that fits the capabilities of the chapter.

Fifteen leaders have already responded enthusiastically to our call to action. Each leader has gone through an application process and will receive regular training. We expect additional chapters to be launched through the rest of this year and into next.

Here is our inaugural class of chapter leaders who, by their service and leadership, allow us to multiply our impact while caring for our community. We can't thank them enough!

- Susan Aumiller, Columbus, Ohio
- Kent and Sue Drescher, San Francisco Bay Area
- Karen Dunkerly, Sacramento
- Jack Gerblich, Atlanta
- Manuel Gomez, Mid-Atlantic
- Laurie Heyman, Los Angeles
- Amanda Hill, Colorado
- Dave Lukas, Chicagoland
- Bill Maclean, Philadelphia
- Landon and Marie Morrell, Arizona
- Kathy Senecal, Connecticut
- Kristin Zwickau, Boston/New England

Please visit our website at <https://www.fshsociety.org/connect-locally/fsh-society-chapters> to learn about existing chapters. Are you interested in helping to launch a new chapter? We want to hear from you! Please contact us at <https://www.fshsociety.org/connect-locally/fsh-society-chapters/chapterlaunch/>. **FSH Watch**



Clinical trial readiness study

Now recruiting volunteers with FSH muscular dystrophy

by JIM ALBERT
Eldersburg, Maryland

The FSHD Clinical Trial Research Network (CTRN) is currently recruiting up to 160 FSHD patients across the seven CTRN sites to participate in a study to help standardize a set of tools and measurements for future FSHD clinical drug trials.

Recent genetic advances in the understanding of FSHD have identified possible approaches for future drug therapies. It is important that we have appropriate tools in place to help us measure things like strength, function, and quality of life, which may help us understand if a drug is effective.

The study aims to validate a new FSHD-specific functional rating scale (see story on page 8) made up of activities like walking, getting up from a chair, hand strength, and a new technique for measuring muscle composition called electrical impedance myography (EIM).

EIM is a quick and painless method of measuring muscle composition that can be performed within the clinic. A small meter is placed on the target muscle, and a measurement is recorded within five seconds using a small electrical current. The study measures eight muscles bilaterally for a total of 16 muscles measured. The targets include three muscles in the arm, three in the leg, one in the back and one in the stomach (see photo above).

Interaction with a physical therapist is the largest portion of this study. The therapist tests the patient's balance, ability to walk for six minutes, a short walk starting from both standing and sitting, ability to climb a few stairs, and everyday activities such as putting on a coat and picking up a small object off the floor. Manual muscle testing as scored by the therapist is performed as well as more objective muscle strength testing using a myometer and a computer.

A Reachable Workspace Test is performed with the patient sitting in front of a three-dimensional camera and performing a series of sweeping arm movements in order to test range of motion of the upper extremities.

The study also measures lean body mass via a DEXA scan (dual energy X-ray absorptiometry). A set of questionnaires is completed that asks questions ranging from scoring the patient's functional abilities to how FSHD affects the patient's life. Blood samples are drawn for genetic testing and for storage for future research.

Locations for the study include the seven CTRN sites:

- University of California, Los Angeles
- University of Kansas Medical Center in Kansas City
- Kennedy Krieger Institute in Baltimore, Maryland
- University of Rochester Medical Center in New York
- Ohio State University in Columbus
- University of Utah in Salt Lake City
- University of Washington in Seattle

The study involves five visits over a period of 18 months and requires a substantial commitment from the FSHD patient community in order to reach the goal of 160 participants.

If you live near one of these locations or are willing to travel, and you meet the qualifications for the study, please consider participating. Please visit <https://clinicaltrials.gov/ct2/show/NCT03458832?cond=fshd&rank=2> for a description of the study and contact information. **FSH Watch**



An electrical impedance myography (EIM) device in action.



My journey from powerless to powerful

I am stronger than FSHD

by **DAVE LUKAS**

Lake in the Hills, Illinois

Three years ago, my life was changed forever. Three years ago, I walked out of a doctor's office, got into my car, and sobbed. Three years ago, my image of what my future looked like was shattered.

Today, my life is still changed forever. Today, I leave doctors' offices feeling confident and grateful. Today, my image of my future looks uncertain, but there is so much hope.

Three years ago today, I was diagnosed with facioscapulo-humeral muscular dystrophy (FSHD). It took me a long time to remember how to pronounce it, spell it, and for my phone to figure out it wasn't misspelled. It's a rare form of muscular dystrophy I was born with, a genetic disease. My body produces a protein called DUX4, and this protein destroys and kills muscle. And like all forms of muscular dystrophy, it's a progressive disease. I will keep losing more muscles and will not get them back. There is no cure.

But it's not like the muscular dystrophy you know from the Jerry Lewis telethons. FSHD is a much sneakier disease. Most of us get diagnosed in our mid- to late 20s after years of having something just a bit "off" about our bodies that no one seems to be able to explain. Most doctors are mystified.

It's a slow disease that gradually robs people of muscles in their face, shoulders, upper body, core, and legs. It takes away things like being able to reach up and wash your hair, being able to get dishes down from the top shelf, the ability to smile, and other activities most people take for granted. It's a disease people learn to live with by making a series of adjustments to do the random, everyday stuff. For many of us, it progresses to the legs and feet and begins to weaken and kill the muscles there. About a quarter of people with FSHD end up in wheelchairs.

Fun stuff.

But those are the facts. Thankfully, they aren't my reality now, but they are for so many of my friends and others with our disease.

With hindsight, I see that my journey started in my mid-20s when I noticed I couldn't raise my arms completely over my head. Fast forward 16 years, and my wife Brandi (fiancée at the time) kept saying my shoulders just weren't right. The way I took my shirt off wasn't right. The way I reached for things up high wasn't right. So I saw a local orthopedic doctor, and he saw the oddities and thankfully paused long enough to say, "This isn't right. I know a doctor you should go see; she's a friend of mine, and she might know what this is."

Enter Dr. Charulatha Nagar, a neurologist at Northwestern Medicine. Even typing her name makes me cry with gratitude for this woman. She is simply the best doctor I have ever come across. Even my wife, who knows doctors, agrees with me. Dr. Nagar saw me, took a look at me, asked me to do a bunch of random stuff (walk on my heels, push my hand away, purse my lips, to name a few), and then sent me for more bloodwork than I thought was even possible. Even the tech was surprised at the sheer volume of tests Dr. Nagar wanted to run and went to grab extra vials. About a million needle



“Going from powerless to powerful has been quite the journey. I'm not broken. I'm not helpless. I am humbled, honored, and encouraged. I am stronger than FSHD.”

— DAVE LUKAS

and finger pricks later, Brandi and I walked out still unsure of what was going on but confident in Dr. Nagar.

A few weeks later, we had a return visit to go over the results of these tests. That was today, three years ago. She informed me that my muscle protein levels were eight times higher than normal—meaning my muscles were screaming out that they were in trauma. After that result, combined with my physical examination, Dr. Nagar informed me I had facioscapulo-humeral muscular dystrophy. She needed to confirm with a genetic test, but she had studied and worked with patients with FSHD in medical school, so she knew the disease well and was confident I had it. A later genetic test would confirm her diagnosis.

I really don't remember what else we talked about in her office, but I remember walking out to the car with Brandi and feeling overwhelmed with uncertainty. We got back into my car, and I started sobbing! What was my life going to look like now? How soon would I lose all the muscle in my body? Would I die early? What if I couldn't see my kids grow up? What if I became a burden on my future wife? She had already lost one husband to a rare disease. Why does she have to care for another? How was that fair?

Those and many more questions swirled and bounced in my head for what seemed like months. I really struggled to identify as someone who had a disease that would affect me for the rest of my life. I struggled with telling people. I didn't want people to treat me differently. I didn't want people to look at me like I was sick or broken. I kept my diagnosis hidden from everyone except family and close friends.

Which is where everyone else came in somewhere along the path. They either heard my diagnosis from me or heard it from my parents, or read about a random post on Facebook. But not from me directly. And that's not fair. I truly struggled with telling people and to wear the identity as someone who has muscular dystrophy. It was a journey to get to where I am today.

Fast forward three years, and where am I? I've already participated in one clinical research study, and I'm about to start another. I immediately became involved in the biggest and most influential charity and research nonprofit for my disease, the FSH Society. And now I'm taking steps to formally establish a national chapter through the Society here in the Chicagoland.

I have a team of doctors and medical professionals I trust 100 percent, and it brings tears of gratitude simply to think of them. Which then evokes more tears, because I'm one of the lucky ones who didn't have to go through 20 doctors to figure out what I had. I can't tell you the number of stories I've read about people with FSHD who have gone through doctors upon doctors, and they still don't have one who knows how to treat them. I don't have the words to express my gratitude for people like Dr. Nagar. Hence, all the grateful, grateful, grateful tears.

There is hope on the horizon for a cure, as well as treatments to stop the progression of the disease. We know what causes the disease, which is a huge step. There are so many teams all over the world that are working on cures right now. And with the FSH Society leading the way with both their awareness efforts and advancing of research grants, I'm confident we're going to get there.

The Society has a goal of having a disease-modifying drug on the

market by 2025, and is confident that this is achievable. To think that my world was rocked in 2015, and 10 years later we could have a cure or progression stopper for my disease ... holy #%&!

This disease has taught me to be grateful for the little things. There is so much I'm still able to do (like run) that many others with FSHD cannot. There may come a point in my life when I can't do those things anymore. So I do them while I can to the best of my ability.


This isn't a quick story, and it's one I've needed to tell for some time. It's important because while this disease doesn't define me, it's a part of me and my story.

Hard challenges are put in front of us all the time, and we have the choice to look at them as obstacles or as fuel to propel us further on our path. My FSHD diagnosis laid me low for a while. It left me on the side of the road, beat up and broken. But I stood up, dusted myself off, wiped away the tears, and used this diagnosis and this disease as fuel to make me a better person. This disease won't break me. I'm stronger than FSHD.

Three years later, I find myself with a greater sense of power and purpose with FSHD. I may not know what lies ahead for me, but all I have to do is look to my wife and my three children to remember whom else I'm fighting for. All I have to do is reach out and connect to all the friends I've met who have FSHD to remember the collective strength we have.

Going from powerless to powerful has been quite the journey. I'm not broken. I'm not helpless.

I *am* humbled, honored, and encouraged.

I *am* stronger than FSHD. 

Our story corps project

LEND YOUR VOICE TO OUR RADIO PODCASTS



With 14 episodes of our monthly FSH Society Radio show now under our belt, we hope many of you are not only listening but also considering how this medium can give our community a greater voice.

At the FSHD Connect Conference, host Tim Hollenback issued a call to action to the FSHD community. The radio show, which airs live on the last Wednesday of every month at 9 p.m. EST, is "really about all of us who are living with FSHD," he noted. "It's about all of us having a voice," he says. He urged listeners to call in with

questions and stories of their own.

We are also launching our own "story corps" project to gather stories of individuals impacted by FSH muscular dystrophy. Whether you have FSHD yourself, or are a family member or friend, we want to hear from you!

How can you get involved? Simply contact Tim at fshradiohost@gmail.com, or call or text (414) 659-3392. You can message Tim, get your story recorded, and we will air it on an upcoming episode of FSH Society Radio.



Tim Hollenback

2018 FSH Society Awards

Leaders in research and advocacy recognized in Las Vegas

by JUNE KINOSHITA
FSH Society

The 2018 FSH Society awards were presented at the CureFSHD banquet on June 9, 2018, at the Flamingo Resort and Hotel in Las Vegas, Nevada. These awards celebrate individuals who have made exceptional contributions to FSHD research and the community. The recipients were nominated by the community and selected by a jury of their peers.

Pioneer Award

The Pioneer Award was given to Rabi N. Tawil, MD, professor of Neurology, Pathology, and Laboratory Medicine at the University of Rochester School



Rabi N. Tawil, MD

of Medicine, for his seminal, career-long contributions to the field of FSHD research.

Tawil has focused on FSHD research since 1991. His early work led to the completion of the first and only large natural history study of FSHD, an improved understanding of the phenotype-genotype correlation, and the first randomized, placebo-controlled, therapeutic trial in FSHD. Tawil also established one of the largest biorepositories of tissue and cell lines derived from carefully characterized FSHD individuals and has provided these resources to FSHD researchers worldwide.

Together with his collaborators, Tawil used these resources to identify the mis-expression of DUX4 in skeletal muscle as the cause of FSHD, and to identify FSHD2 as a distinct genetic form of FSHD. In addition, Tawil has been a leader in clinical trial preparedness by organizing international workshops to refine studies on natural history and outcomes measurements, biomarkers, and the use of MRI in FSHD. These efforts led to the establishment of the FSHD Clinical Trial Research Network (CTRN), which will facilitate international clinical trials.

Tawil chaired the American Academy of

Neurology's committee to establish the first evidence-based clinical guidelines in FSHD, published in 2015, and he is ranked as the top FSHD expert worldwide by Expertscape.

2018 Young Investigator Award

The 2018 Young Investigator Award was given to Amy E. Campbell, PhD, staff scientist at the Fred Hutchinson Cancer Research Center, and recognizes a scientist in the earlier stages of his or her career who has done exceptional work and shows great promise as a future leader in the FSHD field.



Amy E. Campbell, PhD

As an undergraduate, Campbell studied DNA methylation in repetitive regions of the genome and associated chromatin components. As a graduate student, she determined how mutations in a transcription factor cause human disease with specific characteristics, a study that included analysis of the BET family of chromatin modifiers.

As a postdoctoral fellow, Campbell performed collaborative research that led to the identification of BET proteins as regulators of DUX4 expression and inhibitors of BET proteins as a possible therapeutic for FSHD, as well as identifying a second class of drugs that suppress DUX4 by stimulating a receptor on the surface of muscle cells.

Campbell also used advanced technologies to directly identify proteins involved in regulating DUX4 expression and discovered an entirely new molecular mechanism, which also identified a new target for therapies, for the spread of FSHD pathology through the muscle.

2018 Community Award

The 2018 Community Award recognized an individual or group that has empowered the FSHD community through advocacy

and fundraising. This year's award was presented to Katie Ruekert of Castle Rock, Colorado. Ruekert has been the driving force and face of the Colorado Walk & Roll to Cure FSHD for the past three years.



Katie Ruekert

Starting from scratch with only an idea on how to channel her emotions after receiving a diagnosis of FSHD, Ruekert has expanded the event year after year through her tireless efforts. The Walk & Roll, developed by Ruekert along with earlier fundraising leaders Amy Bekier and Rich Holmes, has inspired the creation of the FSH Society's signature national fundraiser.

As one of the Society's "Pioneer Leaders," Ruekert attends bimonthly training and tests the materials needed to launch the FSH Society's signature Walk & Roll to Cure FSHD. She is inspirational to her family, friends, committee members, and everyone who is affected by a diagnosis of FSHD.

Lifetime Legacy Award

A special Lifetime Legacy Award was presented to Duncan and Bill Lewis Sr. for their game-changing philanthropic support of the FSH Society over the past two-and-a-half decades. Bill Lewis chaired the board of directors until his retirement earlier this year. [FSH Watch](#)



Duncan and Bill Lewis Sr., MD



Don't let this diagnosis limit you

When one path ended, a new one opened up

by **NELSON DRONET**
Sulphur, Louisiana

I would like to take a moment to share my story in the hope that it reaches at least one person and helps him or her understand that a diagnosis of FSHD or any other neuromuscular disease can be transcended.

Growing up, I knew something was slightly off, but my symptoms were not enough to concern doctors. They always told my parents that I grew too fast, and my muscles had to catch up to my 6'2" frame. I graduated from high school and went to work in the chemical refineries, which led to a job in a local shipyard as a ship fitter and welder.

In my early 20s I began to notice that my dominant arm was getting weak. In 1998, after a trip to the neurologist and follow-up visit to a muscular dystrophy specialist, I was diagnosed with FSHD at 24 years old. In 2000, I had to quit working in my chosen field due to the progression of muscle weakness.

I began the fight for disability compensation, which I was finally awarded in 2001. After some soul searching, I realized that this was



Nelson Dronet

not the way I wanted to live. I wanted to stay as active as possible, hopefully to combat some of the progression, and my mind still worked perfectly.

I started researching what kind of jobs I could do with my physical limitations. I contacted Vocational Rehab and began the process to start college. College at age 33 was a scary thought, but I knew I wanted more than what I had. I set out on a path to earn my bachelor's degree in psychology, followed by a master's in psychology, with aspirations of being a counselor for individuals with disabilities.

In the final year of my undergraduate degree, I was introduced to applied behavior analysis, and I knew what I was going to do with the rest of my life. I completed graduate school and went on to begin my career as a behavior analyst, where I work with children

with autism and other developmental disabilities.

I chose to share my story because I want people to understand that these disabilities do not have to limit what you do in life—only the way you must go about doing things. **FSH Watch**

FSH Society testimony to the U.S. Congress

\$28 MILLION REQUESTED FOR NIH FUNDING OF FSHD RESEARCH

As we have been doing since 2008, the FSH Society has submitted written testimony to the U.S. House and Senate appropriations committees detailing the progress being made and the ongoing needs of the FSH muscular dystrophy community. This year's testimony requested \$28 million in fiscal year 2018 appropriations for National Institutes of Health (NIH) research on FSHD.

This House testimony was submitted in March 2018, and the Senate testimony in June 2018. The Senate testimony references recent 2017 publications (first-ever papers on the native function of DUX4 controlling 2C development stage, more nuances at the PAS site DUX4 polyadenylation cleavage site, and respiratory issues/insufficiency warranting clinical monitoring), and

provided updated FSHD grant figures. NIH's funding now stands at \$13.2 million in FY2017.

Our testimony called for more effort on increasing the number of NIH-funded training grants, from exploratory grants (parent R21) and research project grants (parent R01) to larger clinical and therapy-oriented program project/center of research translation (P50) and cooperative clinical research agreements (U01).

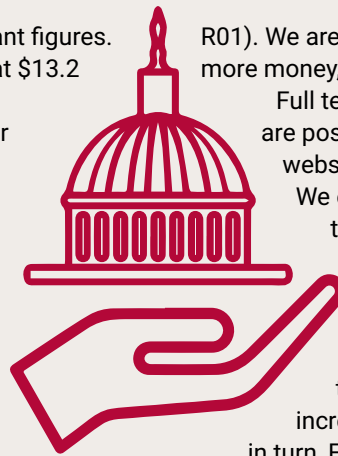
The engine of FSHD basic research runs on the building blocks of workforce training, high-risk research grants (parent R21), and research project grants (parent

R01). We are asking for more grants, more money, and more institutes.

Full texts of our testimonies are posted on the FSH Society website under "Advocacy."

We encourage you to share these testimonies with your congressional representatives via their chiefs of staff or health legislative aides to let them know that increased NIH funding and, in turn, FSHD research funding is important to you. You can locate your senators and congresspersons at Senate.gov or House.gov, and contact them by phone, email, web, or letter.

—Daniel Paul Perez
FSH Society





A new assessment tool for measuring disease burden

FSHD-COM moves closer to validation

by AMANDA HILL

Highlands Ranch, Colorado

FSHD clinical researchers just published what may soon become a standard battery of assessments for use in clinical trials—an exciting and essential milestone for the development of FSHD therapies. Together, the combined assessments are called a “composite outcome measure” (COM) and are designed to more fully capture changes in FSHD progression than any individual measure could on its own.

Researchers at the University of Rochester Medical Center, University of Kansas Medical Center, and Ohio State University Wexner Medical Center collaborated to create the FSHD-COM and published their findings earlier this year in the scientific journal, *Muscle and Nerve*. The FSHD-COM contains 18 individual assessments that were expertly selected to reflect muscle involvement and disease burden as it is actually experienced by FSHD patients.

The FSHD-COM includes tests with which many FSHD patients are likely already familiar, such as the timed sit-to-stand test and the hand grip strength test.

It also includes some more general and practical tasks, like time to pick up a penny from the floor, which was chosen to evaluate trunk strength and balance. The 18 assessments take only 35 minutes to complete and cover five body regions that the researchers determined were most relevant in measuring disease progression: legs, arms and shoulders, trunk, hands, and overall balance.

After creating the FSHD-COM, the researchers launched a clinical trial to begin testing it as a reliable tool to capture changes in disease progression. They administered the FSHD-COM to 41 patients, and then 32 of those same patients came back three weeks later to perform the tests a second time. Researchers used the data collected at both visits to determine that the FSHD-COM was “reliable” and had good “internal consistency,” statistical terms that essentially mean the battery produces stable and corresponding measurements.

In addition, the researchers correlated FSHD-COM scores to measures of clinical severity, such as manual muscle tests, and to patient-reported measures of disease burden and emotional and social well-being. They found that the FSHD-COM also correlated well with measures of clinical severity and with patient-reported

measures of disease burden, further supporting its potential utility.

So why is all this important for the development of FSHD therapeutics? Composite measures like the FSHD-COM allow researchers to cast a wider net when they are looking for disease burden improvements in clinical trials. This is especially helpful for a disease like FSHD, whose manifestation and progression are highly variable from one individual to the next.

For example, imagine two patients are taking the same drug in a clinical trial. One patient notices that her balance is improved while walking, while the other notices that he can lift his arms more easily, for example, when taking off his shirt. While very different, both of these improvements are valuable to FSHD patients, and both would be captured by the FSHD-COM.

The FSHD-COM isn't quite ready for its big-screen debut yet. The next step in the development of the battery is a larger clinical trial to further determine its validity and reliability across multiple sites and when administered

by multiple evaluators. This clinical trial is being run by the FSHD Clinical Trial Research Network (CTRN) and is currently recruiting participants (see story on page 3).

If you are interested in volunteering, learn more at ClinicalTrials.gov. The FSH Society has supported the CTRN; Jeffrey Statland, MD; and Rabi Tawil, MD, in the development and ongoing testing of the FSHD-COM. [FSH Watch](#)

Reference

Eichinger K, Heatwole C, Iyadurai S, King W, Baker L, Heininger S, Bartlett A, Dilek N, Martens WB, Mcdermott M, Kissel JT, Tawil R, Statland JM. Facioscapulo-humeral muscular dystrophy functional composite outcome measure. *Muscle Nerve* 2018 Jan 30. doi: 10.1002/mus.26088.

Editor's note: Amanda Hill studied molecular biology at Scripps College and earned an MBA in bioinnovation and entrepreneurship from the University of Colorado, Denver. She is the strategic development manager for the Linda Crnic Institute for Down Syndrome at the University of Colorado Anschutz Medical Campus. Her husband was diagnosed with FSHD in 2016.





Early-onset FSHD

A review of published studies to improve our understanding

by **AMANDA HILL**
Highlands Ranch, Colorado

As many as 20 percent of patients with FSHD have an “infantile” or “early-onset” form, which is generally understood to be more severe and more quickly progressing than typical FSHD. Historically, the criteria that have been used to define early-onset FSHD include facial weakness by the age of five and shoulder weakness by the age of 10. These criteria contrast with the more typical form of FSHD, which is defined by slowly progressing facial and shoulder muscle weakness starting in adolescence or young adulthood, though onset of symptoms may occur as late as 70 years of age.

Despite the fact that up to one in five FSHD patients may have the early-onset form of FSHD (estimates range from 3 to 21 percent), our understanding of the clinical features and prognosis of early-onset FSHD is limited. No large-scale studies have been done to systemically evaluate the features of early-onset FSHD or follow individuals over a period of time to understand how quickly these features change and progress.

A collaborative group of researchers from across the world recently performed a comprehensive review of every single scientific article published about one or more patients with early-onset FSHD since 1970 (see Goselink, et al., 2017).

This massive undertaking is a valuable step forward in improving our understanding of the presentation and progression of early-onset FSHD. It is the first effort to compile all the published data about early-onset FSHD and compare characteristics across all patients.

To do this, the researchers searched scientific publication databases for articles that included observations or data about early-onset FSHD patients. They found usable reports for 227 patients.

Next, they extracted from the publications the same data for all 227 patients, including demographics, clinical severity of disease, wheelchair dependency, pattern of muscle involvement, developmental abnormalities, and other systemic features such as hearing loss, vision

problems, respiratory issues, etc.

Then the researchers used statistical methods to look for relationships among all these variables, asking questions such as, Does wheelchair dependency associate with respiratory issues? Spoiler alert: It does.

The researchers put together a larger picture, backed up by data and statistics, of how early-onset FSHD presents. The 227 reports evaluated were 55 percent female, 45 percent male, 74 percent Caucasian, 25 percent Asian, and 1 percent African.

mobility device by age 50. A majority of the early-onset patients had spinal deformities (70 percent), with lumbar hyperlordosis (aka swayback) being by far the most common (51 percent).

Also interesting was the finding that half of early-onset FSHD patients had one or more systemic features, meaning the FSHD was affecting other bodily systems outside the skeletal muscles. These systemic features included hearing loss (40 percent); retinal damage (37 percent);



“Researchers described early-onset FSHD as having an average age of onset of 2.8 years, with about a quarter of cases showing symptoms in the first year of life, usually facial weakness that resulted in feeding issues and sometimes inadequate eye closure.”

From these data, the researchers described early-onset FSHD as having an average age of onset of 2.8 years, with about a quarter of cases showing symptoms in the first year of life, usually facial weakness that resulted in feeding issues and sometimes inadequate eye closure.

The pattern of muscle involvement was similar to typical FSHD but more severe, and 40 percent of the patients were wheelchair dependent, a much higher figure than for FSHD patients overall, among which 20 to 25 percent become dependent on a

decreased capacity to exhale forcefully, indicating restricted breathing (31 percent); delayed development (15 percent); abnormal electrocardiogram, which measures electrical activity of the heart (9 percent); epilepsy (8 percent); the need for assisted ventilation (8 percent); and vision loss (6 percent).

About one-third of the patients who had systemic involvement have more than one of these symptoms, indicating that it is not uncommon for early-onset FSHD

... continued on page 13

Walk & Roll to Cure FSHD

A life-changing event uniting families, friends, neighbors, and local businesses to forge powerful connections and strengthen our community

by **BETH JOHNSTON AND LEIGH REYNOLDS**
FSH Society

Our first nationally branded event, the Walk & Roll to Cure FSHD, will take place in September and October 2018. This new, signature fundraising event is happening in five locations around the U.S., with additional sites being added in 2019.

Our five brave Walk & Roll “pioneer” volunteers have been taking part in monthly training sessions, testing fundraising materials, reviewing and learning the software platform, and offering valuable feedback and insight as they prepare to host their events. Their participation and leadership are paving the way for a nationwide program in the future, while generating important revenue today. With weeks to go until our first event, we are on track to blow our inaugural fundraising goal out of the water!

The Walk & Roll is first and foremost a fundraiser, generating critical funds to support the search for treatments and a cure. But it is also about so much more:

- **Building community**—On event day, for a few hours, we all join together as one. Living with FSHD can be a lonely road. At the Walk & Roll, we realize no one makes the journey alone.
- **Empowering patients and families**—Knowledge is power. We come together to walk and roll, but we leave with knowledge, connection, inspiration, and new determination to make change happen.
- **Telling the story**—In raising funds, you are challenged to share your story—how FSHD has impacted your family, how the FSH Society has helped, your hope for the future. The Walk & Roll opens the door to that conversation, leaving all of the people you ask more informed and aware about FSHD and its impact.
- **Building programs**—The event will draw a crowd and engage a wide cross-section of people with unique talents and interests that can be activated for other chapter events.
- **Tremendous fundraising potential**—Each person raising a little adds up to a lot. The funds raised through this event may be the ones that fund a cure.

If there is not a Walk & Roll in your area, you can still participate!

- Find a participant from one of our events and show your solidarity by making a gift to support his or her fundraising efforts.
- Share information about the Walk & Roll on your social media accounts.
- Be on the lookout for a Walk & Roll to come to your area in the future, then plan to lead a team and bring others to the event!
- Or make plans to organize a Walk & Roll in your area in 2019!

To learn more, contact Beth Johnston, chief community development officer, at Beth.Johnston@FSHSociety.org. 



NORTH CAROLINA WALK & ROLL TO CURE FSHD

October 7, Cary, NC

fshsocietynorthcarolina.org



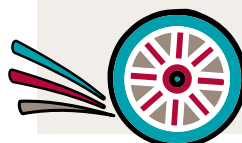
“My hope is that, because of our involvement in the walk, we will raise awareness of FSHD and MD, eventually leading to treatment or a cure. We need a cure, and I am passionate about being a part of finding it in any way I can.”

—MEREDITH HUML AND



“I hope that we raise awareness of FSHD, that families and friends come together to support the participants, and that we raise some money to help folks with FSHD. My hope for the future is a disease-modifying treatment for FSHD by 2025 and, ultimately, a cure.”

—RAYMOND A. HUML



COLORADO WALK & ROLL TO CURE FSHD

September 8, Castle Rock, CO

fshsocietycolorado.org



"It has been truly wonderful and inspirational connecting and empowering other families affected by FSHD in the State of Colorado. My hope is to

see the Colorado Walk & Roll continue to expand and to reach out to more families. My life purpose is that no one else will ever need to hear the words I heard seven years ago: 'You have facioscapulohumeral muscular dystrophy, and there is no treatment and no cure.' The Colorado Walk & Roll won't stop until the cure is found."

—KATIE RUEKERT

TEAM WALK & ROLL TO CURE FSHD

September 16, Alameda, California

fshsocietybayarea.org

"I chose to take on this challenge to launch a Walk & Roll because I'd do anything to help the Society and find a cure. Because of this event, I hope to see more awareness. My hope is that through this event, we will raise the funds needed to find a cure."



—NEZ BENNOUNA-NICKERSON

COLUMBUS WALK & ROLL TO CURE FSHD

September 15, Dublin, OH

fshsocietycolumbus.org



"Our son called in August 2017 to tell us he had been diagnosed with FSHD. Six weeks later my husband was also diagnosed. I'm still in a daze. I want to not only raise money for the FSH Society but raise awareness of a disease

very few people have ever heard of. My ultimate goal is to raise awareness of this disease through the Walk & Roll before having to shut it down in five to seven years because brilliant researchers have found a way to cure it!"

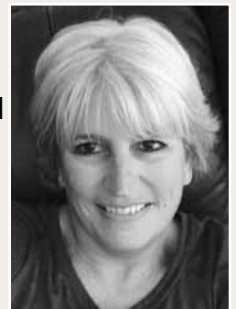
—SUSAN AUMILLER

PACIFIC NORTHWEST WALK & ROLL TO CURE FSHD

September 22, Puyallup, WA

fshsocietynorthwest.org

"My hope is that both patients and our local community have more awareness of FSHD and understand that it takes a community to make a difference. My hope for the future is that this Walk & Roll will outgrow my hometown and become a major event in the Northwest. I took on this challenge because I want to make sure that this mama bear does everything in her power to help find a treatment and cure for FSHD."



—NANCY PAYTON



Managing breathing issues

Webinar with John Bach, MD

by JUNE KINOSHITA
FSH Society

The best practices for managing breathing issues were the subject of the June 19, 2018, FSH Society webinar with John Bach, MD. Bach, of the Rutgers University New Jersey Medical School, is a leading authority on respiratory issues that can arise in individuals with neuromuscular conditions, including FSHD.

In the webinar, Bach recommended that every FSHD patient have respiratory function tested regularly, while noting that standard pulmonary function tests are almost useless for people with FSHD because “they do not measure cough flows, carbon dioxide levels, or lung volume recruitment measures.” FSHD patients should have vital capacity measured, but this must be done with the patient lying down, he said. This is “the most important measurement of all to determine if someone needs nocturnal noninvasive ventilatory assistance/support, or NVS,” he explained.

All FSHD patients should have an oximeter available to monitor their blood oxygen when they are ill, Bach said. He noted that these can be bought for less than \$20 on Amazon. But if oxygen levels drop, “no one with FSHD should ever be given oxygen at home,” he cautioned. “It turns off the drive to breathe, causes carbon dioxide to go up, and patients often need to be intubated and attached to respirators as a result.” NVS and CoughAssist rather than oxygen supplementation should be used to renormalize oxygen levels, he said.

Sleep apnea is typically caused by the brain skipping a breath or the throat obstructing breathing, but according to Bach, sleep apnea is not the primary problem in FSHD. “In FSHD, the problem is hypoventilation caused by weak respiratory muscles (diaphragm), which results in nighttime waking and feeling unrested in the morning. Typical ‘sleep studies’ are not helpful because they do not measure carbon dioxide levels,” he explained. Instead, patients should have oxygen saturation and carbon dioxide (CO₂) levels monitored, he said. CO₂ can now be measured transcutaneously, which is noninvasive and painless.

In patients with hypoventilation, “CPAP (continuous positive airway pressure) is worse than useless,” he said. “BiPAP (bilevel positive airway pressure) is helpful if set at high enough inspiratory pressure, but the expiratory pressure is counterproductive.” He recommended a ventilator such as the Trilogy (made by Philips Respironics), which has more than 10 ventilation modes for NVS that include two for BiPAP.

A CoughAssist device, which he also recommends to keep airways clear and reduce the risk of pneumonia and respiratory failure,



“In FSHD, the problem is hypoventilation caused by weak respiratory muscles (diaphragm), which results in nighttime waking and feeling unrested in the morning. Typical ‘sleep studies’ are not helpful because they do not measure carbon dioxide levels.”

— JOHN BACH, MD

also needs to be set at high enough pressures, i.e., 40 to 60 cm H₂O.

Bach asserted that ventilatory support via tracheostomy tube is never needed for patients with FSH muscular dystrophy and can be avoided by these noninvasive approaches. He noted that after surgery, when the breathing (intubation) tube is removed, an FSHD patient can have weakened breathing, which prompts doctors to put the patient back on the tube. He said that such patients can in fact have the tube removed (extubation) to full noninvasive ventilatory support (NVS)—a process in which his center specializes. Only three or four centers in the United States have this expertise, he noted. They are listed at www.BreatheNVS.com.

These are only a few examples of the wealth of information Bach offered during the webinar. You can watch the one-hour video on the FSH Society’s YouTube channel.

We refer readers to Bach’s website, www.BreatheNVS.com, for extensive, detailed information as well as a list of centers across the U.S. and internationally that specialize in noninvasive ventilatory support. [FSH Watch](#)

patients to have multiple systemic issues.

Next, the researchers performed statistical analyses to determine if each of these disease features associated with any others and, if so, whether that observation was likely due to the FSHD and not random chance.

This exercise resulted in several interesting and, as scientists say, “statistically significant” relationships. For example, in this group of patients, being female was associated with an earlier age of onset, wheelchair dependency, developmental delays, and ECG abnormalities. These observations are intriguing because they deviate from typical FSHD, in which it is generally accepted that males tend to be more affected than females.

Another new and fascinating observation was that ECG abnormalities, epilepsy, and cognitive impairment were all more prevalent in Asian than in Caucasian patients. On the flipside, spinal deformities were more prevalent in Caucasian patients. These geographical differences have not been reported before and will be important for researchers to pursue with additional studies.

Other associations the researchers found confirmed results of previous studies. For instance, a lower number of D4Z4 repeats was associated with higher clinical severity, wheelchair dependency, hearing loss, and epilepsy. Furthermore, an earlier age of onset was associated with higher clinical severity, earlier loss of ambulation, hearing loss, and developmental delays.

Two of the strongest associations were that patients with epilepsy had a very high prevalence of cognitive impairment, and that patients with ECG abnormalities had a high prevalence of assisted ventilation. Other clinically significant associations included: wheelchair dependency with spinal deformities, wheelchair dependency with assisted ventilation, hearing loss with vision loss, and developmental delay with cognitive impairment.

For all of these relationships and associations, it is important to note that the presence of one feature (e.g., developmental delay) does not guarantee that an individual will have or develop the second feature (e.g., cognitive impairment). Instead, based on the data extracted from these 227 cases, we can say, for example, that having developmental delay *increases*

the odds of having cognitive impairment.

Unfortunately, the researchers who compiled these data did not calculate the relative risk in each of these scenarios, so it is difficult to put a quantitative value on the associations.

While incredibly informative and important, this review does have its limitations. For instance, the researchers were only able to look at one point in time for each of the 227 patients. Therefore, these data do not reflect changes in disease progression over time. In addition, the ages of the 227 patients are skewed, with a majority (~70 percent) being between seven and 31 years old. Hence, the observations made here may not as accurately reflect older patients living with early-onset FSHD.

The researchers who authored this report also note that there are many possible selection biases in the scientific articles that they compiled to start with. For example, one article focused on patients in northern Italy because that’s where the scientists were from, and in another article, scientists were specifically looking at patients with hearing loss.

Taken all together, the 227 patients reported in this study probably do not represent a truly normal distribution or random sampling of all early-onset FSHD patients. Consequently, the need for larger, well-designed studies that make observations over a length of time are still desperately needed to improve our understanding of early-onset FSHD.

Thankfully, two such studies are already underway at multiple sites throughout the world, including one supported by the FSH Society in the United States. In fact, just a few months after this review was published, another group of researchers followed up on nine of these early-onset patients who were originally evaluated in 1994 and 1995 as children (see Goselink, et al., 2018). After 22 years of disease progression, the key finding the researchers noted was the variable long-term prognosis and high degree of variability of disease severity. Other findings they noted supported and mirrored the findings explained here by the comprehensive review.

All of this tells us we live in an exciting and fast-paced time for FSHD research. So stay tuned, eager readers; we’ll have more results soon! 

References

Goselink RJM, Voermans NC, Okkersen K, Brouwer OF, Padberg GW, Nikolic A, Tupler R, Dorobek M, Mah JK, van Engelen BGM, Schreuder THA, Erasmus CE. Early onset facioscapulohumeral dystrophy - a systematic review using individual patient data. *Neuromuscul Disord.* 2017 Dec;27(12):1077-1083. doi: 10.1016/j.nmd.2017.09.007. Epub 2017 Sep 21.

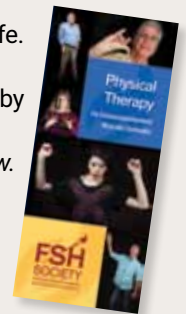
Goselink RJM, van Kernebeek CR, Mul K, Lemmers RJLF, van der Maarel SM, Brouwer OF, Voermans N, Padberg GW, Erasmus CE, van Engelen BGM. A 22-year follow-up reveals a variable disease severity in early-onset facioscapulohumeral dystrophy. *Eur J Paediatr Neurol.* 2018 May 3. pii: S1090-3798(18)30019-9.

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. Visit our website (www.fshsociety.org), and go to Understanding FSHD/Brochures & More to download:

- About FSHD (also in Spanish and Chinese)
- Physical Therapy and FSHD
- FSHD: A Guide for Schools
- FSHD and Social Support: A guide for friends and family
- Evidence-based FSHD care guideline— Summary for clinicians
- Evidence-based FSHD care guideline— Summary for patients & families

You can also request printed copies by mail at FSH Society, 450 Bedford Street, Lexington, MA 02420, or by phone at (781) 301-6060.





Me and my cowboy boots

From the department of silver linings

by **JEFF GIBLER**
Humble, Texas

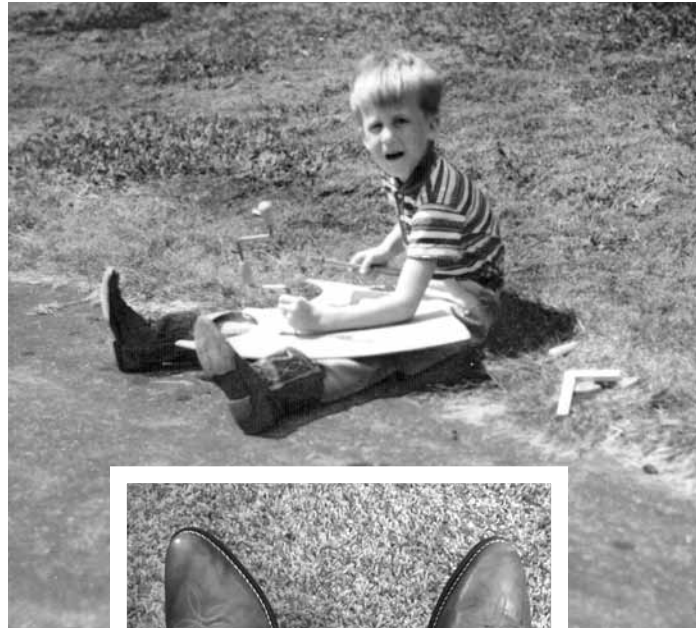
When I was a kid we would come to the United States during the summer to visit my paternal grandparents in Houston. It was also when we got to do our annual visits to the dentist, and I, having been born cross-eyed and undergone three eye surgeries, got to see the eye doctor.

Invariably, before going back home to Venezuela, my mother took us clothes shopping at the big mall for the coming school year. Along with my new shirts and jeans (jeans that never seemed to be long enough to last through the year without me getting teased about puddle jumping) and socks and underwear, if I was lucky, there would be a new pair of cowboy boots. After all, my dad was from Houston, he grew up on a ranch in Mexico, and we were visiting Texas. It just seemed natural that I would go home with a new pair of cowboy boots. And I loved my boots!

I was diagnosed with FSH muscular dystrophy in 1994, just before my 34th birthday. It was a little ironic. I had had symptoms all my life without a diagnosis, but that was not why I went to the doctor this time. I had a pinched nerve in my wrist that was causing me occasional sharp pain, which forced me to drop anything that I might have in my hand when the pain occurred.

Needless to say, after spilling a couple of cups of hot coffee in my lap, I decided to go to the doctor. I did mention to the doctor that I was concerned that there were certain tasks at my job as an airplane mechanic that seemed to be getting difficult for me to perform. I had always had problems raising my arms above my head, but now it felt like my upper body strength was rapidly deteriorating, and I'll be darned if the doc didn't say that she wanted to refer me for some tests because she thought I might have muscular dystrophy. They did the tests, and the rest is history.

I think it was around 1999 or so that my doctor told me I would have to start wearing an AFO (ankle-foot orthosis) on my right foot. The AFO goes inside the shoe. My foot-drop had become bad enough that if I was not paying close attention when walking (you know, like chewing gum and walking at the same time) I would often stub my toe on the ground and trip over myself. I had fallen



Jeff Gibler modeling his cowboy boots as a child (above) and now (below).

and hurt myself several times.

The first AFO I got was custom made. It was molded to my foot and calf, and had a Velcro strap that wrapped around my leg. It was plastic and rigid and big. It fit under my foot and went up the back of my leg. It kept my foot from dropping. Did I mention the AFO goes inside the shoe? It did not fit in my boot! Eventually, I started wearing an AFO on my left foot, too. Although the new AFOs were better, smaller, and lighter carbon fiber ones, they still went inside the shoe. And they still did not fit in a boot!

When I first began wearing the AFOs, I would occasionally forgo them and wear my boots.

However, it has been more than 17 years since I wore boots. I gave away my last pair to a man from Canada in 2005. He was visiting Houston and said that he wanted to buy a pair of "real" Texas cowboy boots before he went back to Canada. I told him that I just happened to have a practically brand-new pair that I had barely broken in. They had been sitting in my closet for several years. He was happy to have them.

When I was diagnosed with FSHD in 1994, I was terrified by the thought that I might have to use a wheelchair someday. But it also happened that I knew a little girl with cerebral palsy who was in a wheelchair. Courtney always made me smile when I saw her. She always made everyone who saw her smile. So that terror was fleeting.

It occurred to me that if I did end up in a wheelchair, if I could make just one person smile the way Courtney made me smile, I would be okay. That's not to say that I welcomed the idea of ending up in a wheelchair, but knowing Courtney made it so that I was no longer terrified by the thought.

The day did come. In May 2017, my doctor told me she wanted me to start using a wheelchair. It took me a little bit to get over the hurdle. I'd had several falls in the last year, and walking had become extremely difficult and precarious.

She wrote the prescription, and I got the chair in July. I made all kinds of excuses for not using it. I would go places and not take it with me. I would tell myself that I wasn't going too far. Then in August I fell in my driveway (yeah ... not going too far!) and suf-



Why I made the FSH Society a beneficiary in my will

Because if not us, then who?

by **DEBORAH SCHWARTZ**

New York, New York

ferred a very bad concussion. I've been using the chair pretty consistently since then.

There is a bright side to all of this—to needing a wheelchair. I don't have to worry about foot-drop and tripping over myself in the wheelchair! So I don't need to wear the AFOs. Did I tell you the AFOs go inside the shoes? They don't fit in boots. My wife took me to buy a new pair of boots today. FSH Watch

Many ways to engage

NOT GETTING FSH SOCIETY EMAILS?

Check your spam folder! Don't miss out on important news and current events. Sign up by clicking "JOIN" on our website. If you're already a member, check your spam folder!



GET SOCIAL!

Find our Facebook, Twitter, and Yahoo! Groups by visiting www.fshsociety.org and clicking on the logos

at the foot of the page. Our online communities are great sources of news, advice, and social support.

HAVE YOU MADE A GIFT TO THE SOCIETY IN 2018?

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. Thank you!

COMMIT TO THE FUTURE

Take your support to the next level by including 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.

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.

I was clinically diagnosed with FSHD two years before the FSH Society came into being. Mine is a spontaneous mutation. I always had winged shoulder blades and rounded shoulders, and had started falling. As I knew no one who had this and there was no available research—this was before the Internet—I did what any normal person would do: I panicked.

I earned my living as a commercial designer. At 37, I could no longer hold a paintbrush or a pen. Then one day, my neurologist gave me a number to call. The FSH Society had just been formed, and I spoke to Carol Perez, one of the most remarkable women I have ever met.

Carol invited me and my father up to Lexington, Massachusetts, to a conference. As a friend who also attended that event recently recalled, "You were terrified, and your father was not much better, and he was trying to be strong for you." Carol spoke to both of us, and we felt much calmer afterward. I had found a place that was home. The emotional support was amazing.

I volunteered for a DNA study with Dr. Rabi Tawil at the University of Rochester. I turned out to have FSHD Type 2. Every time bodies are needed for research, I volunteer blood and guts, because if not us, then who?

I've seen incredible leaders rise through the FSHD community. When one passes, another steps forward to take his or her place. We have a legacy of helping each other up.

I am eternally grateful to my father for giving me the financial means to take care of myself and to help others. The FSH Society has supported me, so I have supported the Society. I have designated it as a beneficiary in my will, to ensure that there will be treatments for this disease. I want to make sure there will always be someone to help the next person up.

To learn more about joining the Legacy Circle through a planned gift, please visit <https://www.fshsociety.org/planned-giving/>. FSH Watch



Deborah Schwartz



Stance control braces

This orthotic has been a great solution for me

by **KATHY SENECA**
Cromwell, Connecticut

As a wearer of a stance control brace for three years, I became aware that I have not yet met another individual with FSHD wearing one. After doing a little research, I discovered a lack of information and/or access, resulting in this type of brace being underutilized.

First developed in 1989 by Nils Van Leedam, PhD, of the Netherlands, the stance control brace is a full leg brace (KAFO: knee-ankle-foot orthosis, or SCO: stance control orthosis) that allows the knee joint to lock and unlock during walking, providing stability, safety, and range of motion. This style of brace became available in the U.S. in the late 1990s through the early 2000s, so although it has been available for about 20 years, this proven technology is considered relatively new.

There are approximately 10 styles of SCOs (all but one being a full leg brace), as well as seven mechanical models covered by insurance in the U.S., available through three main manufacturers. Each manufacturer provides a trial unit to assist the patient in determining a proper match.

The first question one may have is, How do I know if this would benefit me? One indication is falling, walking with a stiff knee for fear of falling, making unhealthy compensatory movements, turning sideways to go down a hill, and noticing other behavioral changes that are limiting your access to activities in the community.

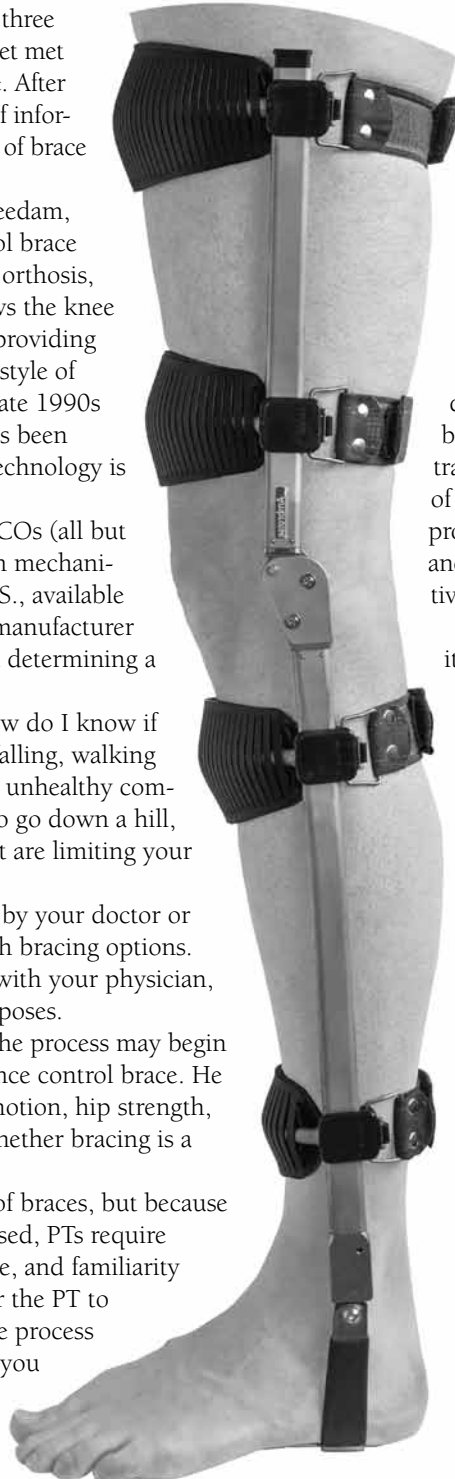
The process begins with an evaluation by your doctor or physical therapist (PT) who is familiar with bracing options. You will need a face-to-face appointment with your physician, as well as a prescription for insurance purposes.

If you are already working with a PT, the process may begin with the therapist evaluating you for a stance control brace. He or she will look for appropriate range of motion, hip strength, and other elements that would indicate whether bracing is a viable option.

PTs have basic training in other types of braces, but because stance control braces are not commonly used, PTs require additional training. Knowledge, experience, and familiarity with FSHD are also important qualities for the PT to have. If you are not working with a PT, the process should begin with your doctor evaluating you for a stance control brace.

Once bracing is prescribed by your doctor, and the patient is interested in pursuing that option, the next step is seeing an orthotist trained specifically in stance control orthoses.

Specific elements help the orthotist



UTX®-SWING stance-control knee-ankle-foot orthosis is the most popular and is essentially the base/primary model for the entire UTX line from Becker Orthopedic.

select the best type of brace for you. Some of those include strength and weight of the patient, ability to move the hip, cognition, occupational and environmental needs, and willingness to work with a PT to achieve the best possible benefits from wearing a KAFO. The orthotist then does further evaluation to select the best brace for your needs.

Once a brace is selected, it is custom-made for your leg. Following a fitting and any possible adjustments done by the orthotist, collaborative teamwork begins with the patient, the PT, and the orthotist.

These braces are passive mechanical devices and don't walk for you. Once you're established in the brace, the PT and orthotist will work with you for gait training, functional activities, learning the mechanics of the brace, and problem solving. This is not a simple process, so it is very important that a knowledgeable PT and orthotist work in tandem with you to ensure a positive outcome.

I can personally attest that the effort is well worth it. Once I got the hang of walking with this device, I noticed some positive results: less fatigue; more stability and confidence; the adjacent joints (ankle and hip) operating in a more normal fashion, thus allowing a better gait; the ability to do more; and the freedom to get around more easily. Coupled with a pole or poles to help with balance, this comfortable brace has become a natural part of my everyday life.

Best of luck, and Happy Trails! FSH Watch

For more information

I cannot stress enough the importance of a competent, collaborative team to ensure success and encourage you not to shy away from the length of the brace. If this is of interest to you, here are the websites for the three manufacturers:

- Becker Orthopedic:
www.beckerorthopedic.com
- Ottobock:
<https://www.ottobockus.com>
- Fillauer:
fillauer.com/Orthotics/index.html

Each company is happy to receive inquiries if you would like guidance in finding the right team to help you achieve your walking goals.

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Both cases lead to aberrant expression of the DUX4 gene, which is stably expressed from the distal-most repeat unit of the array. The DUX4 protein, in turn, activates a host of genes normally expressed in early development, which cause pathology when expressed in adult skeletal muscle. This model of FSHD pathogenesis has achieved widespread consensus in the field, stimulating the search for therapeutic targets both upstream and downstream of DUX4.

Indeed, several companies have been aggressively pursuing DUX4-based targets for several years. Following up on large-scale screens for drugs that inhibit DUX4 activity, Fulcrum Therapeutics, Novartis, and Genia Biocells are now engaged in preclinical validation of their small molecule targets.

While unbiased screens can be profitable, more specific targets might be revealed through a better understanding of the factors controlling DUX4 expression in both health and disease. To this end, Amy Campbell, PhD, and Stephen Tapscott, MD PhD, of the Fred Hutchinson Cancer Research Center in Seattle have analyzed the host of proteins binding D4Z4 repeats and identified the Nucleosome Remodeling Deacetylase and Chromatin Assembly Factor 1 complexes as normal repressors of DUX4 expression in healthy muscle cells.

Scott Harper, PhD, and his group at Nationwide Children's Hospital in Columbus, Ohio, is identifying the proteins that interact with DUX4, and the ways in which DUX4 is modified inside cells. In an effort to understand the series of events leading to muscle pathology, Silvere van der Maarel, PhD, and colleagues at the Leiden University Medical Center in the Netherlands have examined the spectrum of mRNA transcripts in single muscle cells from patients. They have found a small population of cells with an FSHD-specific gene expression signature and developed a way to model changes in this signature over time.

Animal models

Studying the biology of primary muscle cells is very informative, but these cells can only be grown in a culture dish, away from the normal physiological signals and connections that researchers would see inside a patient. Fortunately, there are now several animal models of FSHD in which levels of DUX4 expression can be controlled by the investigators (Jones, Harper, and Kyba labs), or in

which patient cells have been xenografted into mouse limbs (Bloch and Emerson labs).

Importantly, every disease model comes with its own set of advantages and limitations, but each is capable of great utility when used to answer appropriate questions. For example, human xenografts in mice contain a patient's cells with endogenous D4Z4 arrays, making them well suited

are not distinct, but form a genetic continuum in which molecular defects correlate with disease severity. In a study of a subgroup of these patients, Richard Lemmers, PhD, of Leiden University Medical Center demonstrated that for FSHD2 patients with unusually long repeat lengths, small D4Z4 array duplications explain the increased susceptibility to disease.



Nearly 150 scientists and patients crowded into the Flamingo resort ballroom for the FSH Society's 2018 International Research Congress in Las Vegas, Nevada.

to address the regulation of these arrays in the context of living tissue. However, xenografted mice are immunocompromised and thus not equipped to provide information relating to the effects of DUX4 on the immune system, or vice versa.

Genetics and improved diagnostics

In the realm of diagnostics, Frank Baas, MD PhD, and colleagues at Leiden University Medical Center, along with Frédérique Magdinier and colleagues at Marseille Medical Genetics, have validated and used an enhanced molecular combing technique for visualizing the FSHD locus. Giancarlo Deidda, PhD, and colleagues at the Institute of Cell Biology and Neurobiology, National Research Council of Italy (CNR), Rome, are integrating sequence information with DNA methylation—a repressive mark which is lost at the disease locus in FSHD—for more precise genotyping.

Sabrina Sacconi, MD PhD, and colleagues at Nice University Hospital in France are continuing their study comparing patients with FSHD1 and FSHD2, showing that the two forms of the disease

FSHD2 is commonly caused by mutations in SMCHD1, a protein that silences repetitive DNA. Interestingly, mutations in this protein can also lead to arhinia, a rare developmental disorder characterized by the complete absence of an external nose. Several groups (Shaw, Talkowski, Van der Maarel, Van Engelen, and Blewitt labs) are now investigating how similar mutations in the same gene can lead to strikingly different diseases. Their findings should aid the understanding and treatment of both forms of FSHD.

Progress toward clinical trials

Meanwhile, the search for robust and reliable biomarkers and outcome measures continues. In collaboration with Fulcrum Therapeutics, the FSHD Clinical Trial Research Network is now using a 3D camera to document “reachable workspace” (volume of space people can reach with their arms) as a measure of upper body function.

Baziel van Engelen, MD PhD, and colleagues at Radboud University Medical Centre in the Netherlands showed that muscle MRI and ultrasound are promising

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meeting another person affected by FSHD. I embraced my emotions and was living in the moment from then on. This was great as I took it all in, but in retrospect I wish I had thought to take more photos with those in my tribe. But enough of that. On to the conference!

We were welcomed as the FSH Society's top brass introduced themselves, gave a quick summary of what's going on in today's research, and what we could expect from the experts that joined us from around the world. FSH Society Board Chair Jim Chin, President and CEO Mark Stone, and Chief Strategic Programs Officer June Kinoshita kicked things off, and their passion was contagious.

No time was wasted, as there was a lot to tell. The first day was very educational and scientific. At first, I was concerned that I wouldn't understand the language being used, but I was surprised to find that the presenters did a great job in breaking it down for us all. There were only a few points that, no matter how hard I tried, I just couldn't keep up, but that may have been my own excitement overwhelming me. There was so much wonderful information.

Alexandra Belayew, PhD, started off with an explanation of the role DUX4 plays in FSHD: how it operates, and what we know about it. Then Rabi Tawil, MD, from the University of Rochester spoke about genetic testing as well as answering some questions I'd always had regarding heart and respiratory involvement. I also learned that we should exercise if we can and that scapula wiring does not work (bone grafting is the recommended method for stabilizing the scapula). I hope to meet with Dr. Tawil in August so I can get genetic testing and see about getting into the very promising Acceleron trial.

After the break, the presenters dove deeper into the therapies being developed to target muscle growth and regeneration, and how important it is for us patients to participate in these clinical trials. (Join the National Registry of Myotonic Dystrophy and FSHD Patients and Family members for information about research studies and how to participate.) This is history being made and we are a part of it.

The afternoon continued with presenters covering their work on developing therapies. I also learned a bit about DUX4 and its behavior in relation to FSHD. This was all new and very exciting for me as a patient.

Many researchers from all over the world were gathered in this one room, at this moment, and they were sharing the very latest drug development research with us. I could tell that they live and breathe this work. It is their passion, and I believed it was transferred to us all in that room.

As the first day of the conference came to an end, I was hoping for some social "face time" with new friends. After dinner we got to



Mark Stone and Ian Rys

do just that—finally meeting friends who had been acquaintances for years through FSH Today's Facebook page. It was awesome!

Day two started with a great breakfast provided by the FSH Society. President and CEO Mark Stone addressed us all and shared his vision for the future. As I watched and listened to Mark speak, I was so proud that he is our fearless leader. He has such a warm personality, I felt as if he was talking directly to me.

On to the breakout sessions. I think this was my favorite part of the conference. I found my way to five different breakout groups and walked away from each one with something I will use in my daily life. It was during these sessions that I was able to listen to others talk about their experiences, their progression, concerns, and fears, and share mine as well.

Another highlight for me was getting a few minutes between sessions to introduce myself to the presenters and chat some more. I really enjoyed the way things were going when it came time for Nate Phipps from Harvard Medical School to show the latest in soft textile robotics. It was very interesting to see how this technology might be used in the future of assistive devices for FSHD. This was a genuine information gathering session for both Nate and us as patients, and I was honored to be in attendance.

The conference came to an end on a very high note for me.

I am a more informed patient.

I feel I am a better reference for others seeking information.

I now have information to advocate for myself.

For the first time, I learned about my disease from people I trust.


FSHD has taught me many lessons over the years. I have learned gratitude and compassion. I have learned to accept myself and that FSHers are all people who share common human interests. We all want to get through life with hope for a treatment or even, dare I say, a cure.

We are all unique not only in our personal battles with FSHD but as human beings trying to do the right thing for ourselves the best way we can so we can make the most of this beautiful life.

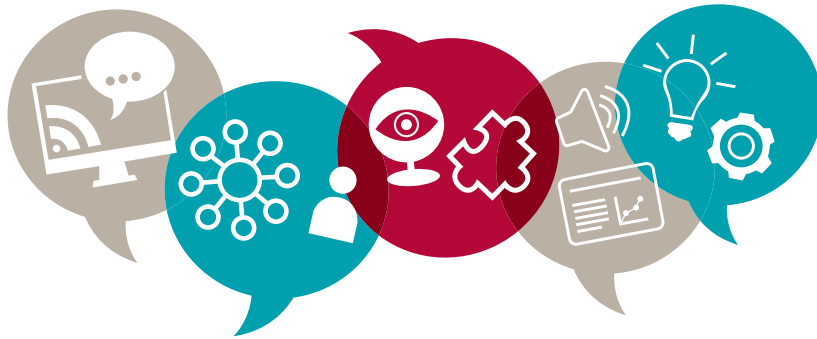
I highly recommend attending a conference or a Family Day or any other FSH Society gathering. The connections we made are priceless.

My wife and I agree that, not only was this conference informative, but it was life changing. Thirty-five years after my diagnosis, I met another person with FSHD.

I'd like to thank the FSH Society for making this event possible. I'd also like to thank all of the researchers and presenters who contributed as well.

Last but definitely not least, June Kinoshita. You are my hero! Without you, I don't think I would have ever found my tribe. 

Events calendar



FUNDRAISING EVENTS

September 8—Castle Rock, CO
2018 Colorado Walk & Roll to Cure FSHD

September 15—Dublin, OH
2018 Columbus, OH, Walk & Roll

September 16—Alameda, CA
Bay Area Walk & Roll to Cure FSHD

September 22—Puyallup, WA
2018 Pacific Northwest Walk & Roll to Cure FSHD

October 7—Cary, NC
North Carolina Walk & Roll to Cure FSHD

October 21—Los Angeles, CA
Ghostly Gala to Vanish FSHD

CONFERENCES

September 30—Baltimore, MD
Mid-Atlantic FSHD Family Day Conference

November 10—Kansas City, KS
Midwest FSHD Family Day Conference

CHAPTER AND LOCAL MEETINGS

July 26—Columbus, OH
Columbus Chapter Launch

August 4—Clarksburg, MD
Mid-Atlantic Chapter Launch

August 19—Los Angeles, CA
Los Angeles Chapter Launch

September 18—Sacramento, CA
Sacramento Chapter Launch

September 29—Blue Bell, PA
Pennsylvania Chapter Launch

October 13—Denver, CO
Colorado Chapter Launch

October 27—Chicago, IL
Chicagoland Chapter Launch

October 27—Dallas, TX
Dallas Member Meeting

October 28—Austin, TX
Austin Member Meeting

November 3—New York City
NYC Member Meeting

December 1—Los Angeles, CA
Los Angeles Chapter Meeting

December 2—Palo Alto, CA
Bay Area Chapter Meeting

December 2—San Diego, CA
San Diego Member Meeting

VIRTUAL MEETINGS: Open to all!

FSH Society Talk Radio broadcasts live on the last Wednesday of every month at 9 p.m. EST (8 p.m. CST). 2018 dates: August 29, September 26, October 31, November 28, December 26.

Connecticut Connections meets via webinar on the first Thursday of each month (except in summer), 7-8:30 p.m. EST. 2018 dates: September 6, October 4, November 1, December 6.

Western Washington FSH Community meets via Skype on the fourth Saturday of each month, 10-11 a.m. PST. 2018 dates: August 25, September 22, October 27, November 24.

WEBINARS

All webinars are noon–1 p.m. US EST. Register online via our event calendar.

August 1—Doris Leung, MD PhD. Dr. Leung is a neurologist at Kennedy Krieger Institute Center for Genetic Muscle Disorders. She is the principal investigator of an ongoing research study using whole-body magnetic resonance imaging (MRI) to evaluate patterns of muscle involvement and changes over time in people with FSHD, with the aim of developing noninvasive imaging biomarkers for FSHD clinical trials.

November 7—Stephen Tapscott, MD PhD. Dr. Tapscott's lab studies gene transcription and expression in normal development and disease, including FSHD. Other research interests include gene and cell therapies for muscular dystrophy. Tapscott is a professor of neurology at the University of Washington School of Medicine and has an appointment at the Fred Hutchinson Cancer Research Center.

2018 FSHD INTERNATIONAL RESEARCH CONGRESS

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biomarkers of disease severity, with the ability to detect muscle dysfunction prior to the appearance of symptoms. Electrical impedance myography (Rabi Tawil, MD; Jeffrey Statland, MD PhD; and colleagues), expression of DUX4 target genes (Fulcrum Therapeutics), and the myostatin pathway (Julie Dumonceaux, PhD, and colleagues) are also potential biomarkers, once drug candidates are ready for clinical trials.

In the clinical trial arena, Statland presented the positive results of a Phase 2 trial on ACE-083, a myostatin inhibitor developed by Acceleron that increases muscle mass and may improve patient strength in multiple diseases of muscle weakness.

Understanding and curing a disease requires tremendous work on multiple fronts. Once the root cause is identified, many hurdles must be overcome before a treatment reaches the clinic. With this in mind, we are astonished at how far FSHD research has progressed in a relatively short amount of time. Ten years ago, the cause of FSHD was still unknown, and now we have an established model of pathogenesis, and many viable therapeutic candidates.

Although the life cycle of DUX4 in FSHD is being revealed—from the failure of its upstream regulatory mechanisms, through its expression and activation of an abnormal program of gene expression, to how that program causes muscle disease—many questions remain. Why is FSHD a late-onset disease? What causes the variability in disease manifestation, severity, and progression? Why aren't all muscles affected equally? Answering these and other questions will surely uncover better and more specific targets for therapy. FSH Watch

Editor's note: Charis Himeda, PhD, is a research assistant professor in the Department of Pharmacology at the University of Nevada, Reno, School of Medicine.



A gift that has made life more fulfilling

TV and film producer finds creative outlet in painting

by **BRIDGET WINGERT**
Editor, Bucks County Herald

Doylestown, Pennsylvania's Alan Brown, who has a form of muscular dystrophy named FSH dystrophy, has worked for 30 years in television and film. He said the artistic process intrigued him, but the passion lay dormant until 2013, after the progress of the disease left him "quite isolated and unproductive."

"[Painting] was a way of bringing beauty into my world and also attempting to contribute something beautiful that would enable me to feel productive about my existence," he explained.

Brown credits Lambertville, New Jersey, artist Robert Beck for helping him get started. "One thing led to another, and one day the doorbell rang," Brown wrote. "It was Robert Beck dropping



Spring Vegetables by Alan Brown. On the cover of this issue is Brown's Cuttolossa Farm.

off all the things I would need to start painting. I will never forget that generosity and also the challenge he presented me with.

"Painting has changed my view of the world. I see things I have never seen before. I see colors in things that I never noticed before. It really is a gift, and it has made my

life much more fulfilling.

"I hope that at the very least, my paintings allow you to see that I am a person who needs to produce and who wishes to share how I see the world with you." **FSH Watch**

Editor's note: Reprinted with permission and edited for timeliness.