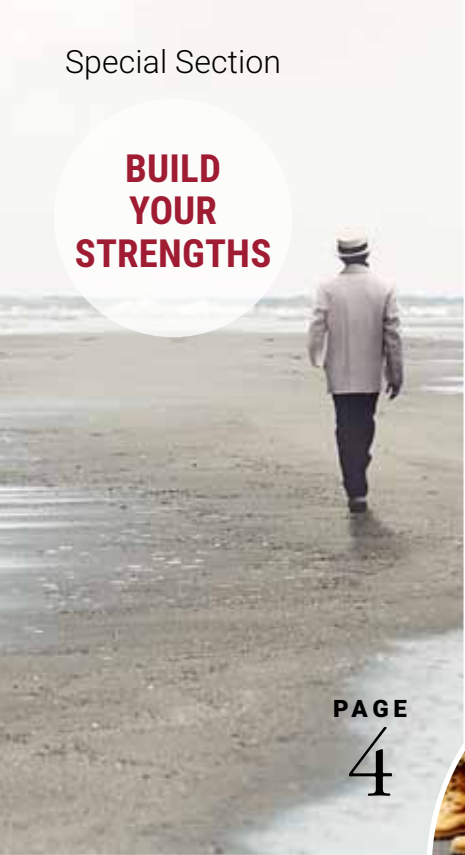




BUILD YOUR STRENGTHS



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FSHD Advocate

The FSHD Society does not endorse any of the drugs, procedures, treatments, or products discussed in its reporting. We urge you to consult your physician about any medical interventions.

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Editor
June Kinoshita
june.kinoshita@fsbdsociety.org

Copy Editor
Elaine Alibrandi

Graphic Design
Leslie Anne Feagley

Look for us on the Internet at fsbdsociety.org. We thank the FSHD Society staff for their editorial assistance.

The power of one

Legendary basketball coach John Wooden would say, “Do not let what you cannot do interfere with what you can do.” These words make me think of you. On a daily basis, the “power of one” is on display throughout the FSHD community. You are incredibly inventive in overcoming obstacles and living full, more empowered lives. With eyes on “what you can do,” you move confidently through your day – living an overcomer’s life.

The real message behind Coach Wooden’s challenge is that a change in focus will foster a change in action and impact every area of your life. The moment you decide to get out of the stands and onto the court, you feel energy and excitement begin to flow through you. Many of you are living examples of this, and I hope that, as you read the articles in this issue of the *FSHD Advocate*, you will discover – or rediscover – the power of a self-activated life.

While the FSHD Society is celebrating 30 years of advancing research toward treatments and a cure, our history is really about



Mark A. Stone

individuals who decided to take action, wherever they were, to bring about needed changes. You can read about some of these people in articles like “The army of everyone” and “My bumpy journey to activism.” Interwoven into our community’s DNA are the passion and persistence in each person who decides to join their abilities with others’ toward our common goal – a cure for FSHD.

As we move forward together, I encourage you to explore the difference the power of self-activation could make in your life. The renewed optimism and energy generated when you “do those things you can do.” The power to help others along their journey. The sense of control as you take steps to make today better than yesterday for yourself and others.

And as you take those steps, be assured that the FSHD Society, a community of thousands of activated individuals, will be there to join you in the journey.



“Do not let what you cannot do interfere with what you can do.”

– JOHN WOODEN

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FSHD Society

(781) 301-6060
info@fsbdsociety.org
fsbdsociety.org

To send general mail:

75 North Main Street, Suite 1073
Randolph, MA 02368
USA

To mail donations:

PO Box 4106
Department 960
Woburn, MA 01888
USA



Developing a resilient mind

Putting mindfulness into action

BY DAVID YOUNGER, AUSTIN, TEXAS

One of the things that stands out to me most vividly about my experience in late adolescence through my 20s and into my 30s was how much I lived at the mercy of my mind. I would wake up one day feeling energetic and optimistic, attractive and alive. The next day I'd wake up feeling small and fearful, insecure and alone. Nothing had changed externally. It was all the product of my fickle mind.

Even though today my body presents a lot more challenges than it did when I was in my 20s and 30s, I no longer live at the mercy of my mind, and for this reason, I am happier and more peaceful in spite of some hefty challenges. This is my “street cred.” What I am sharing with you is my lived experience, not a theory in a textbook.

I first became interested in mindfulness and Eastern philosophy in college. But it's been only in the past decade that I started training formally, and I recently completed a two-year mindfulness and meditation teacher training with Jack Kornfield and Tara Brach, two leaders in the field.

The art of training the mind is quite straightforward in theory, yet it can be elusive in practice. One of the reasons is that it involves a lot of deconditioning and unlearning. This can feel very threatening to a mind that wants to assert control at all costs.

There are a lot of factors that contribute to well-being. I don't want to oversimplify things, but there is a powerful variable that sits at the heart of my message today: Circumstances, including illness, influence, but do not dictate our well-being. It is how we relate to our circumstances that matters most.

Most of us are on autopilot, going through the motions, lost in our thoughts, busy thinking about the past or the future, acting and reacting. We miss the present moment, the only moment we ever have to be alive, to make decisions, to grow, to heal, to be there for the people we love.



Parable of the two arrows

My favorite Buddhist teaching is the parable of the two arrows: The first arrow is what life slings at us, things like illness, loss, pain, pandemics. These are outside of our control.

The second arrow is what we shoot at ourselves in response to the first arrow. It includes the clinging, aversion, anxieties, projections, and fears in response to the felt pain of the first arrow. *When will it go away? I don't want to feel this way. Will it last forever? What have I done to deserve this?*

It is the second arrow that turns pain into suffering. It is also the second arrow that we have control over.

We cannot control how the *DUX4* gene impacts our muscles. We do, however, have agency over how we relate to the loss of function and how we relate to the thoughts and feelings that arise in response to the loss.

When we do start to fire the second arrow, we want to become aware that we are doing so, allowing us to turn back to the experience itself, creating the space and openness and compassion for it to run its natural course.

When something happens that makes you feel sadness or pain, it's natural to want to get rid of the pain. Many people are afraid that if they allow themselves to feel the pain, it will be overwhelming and will never go away. The irony is that the opposite is true. When you keep pushing the pain away, it grows, and pressure builds. It rents more

and more space in your head and body, leaving less room for other things.

Mindfulness teacher Shinzen Young created a formula that I love: "Suffering equals pain times resistance."

What happens if you have pain as a constant and there is zero resistance? Zero times something ... what happens to the suffering?

So often, when we suffer from chronic pain, we're really angry at the body because the body has betrayed us. The pain can become emblematic of a narrative that we create about failure and loss, to many deep-seeded emotions connected to the experience of pain.

When we resist pain – by physical tensing, emotional reactivity, judgment, or avoidance – our identity becomes linked with it. We become the victim of pain. It is happening to us. Resisting turns unpleasantness into suffering.

Awareness and attitude are the antidotes to suffering. I do not mean they are the antidotes to pain. They are the antidotes to suffering, which is caused by resistance. When we purposefully bring a kind and mindful attention to pain and the resistance to pain, the identification that creates suffering is dissolved. We become the witness, and not the victim.

Pain and suffering are not the same. Pain is an experience, a feeling, a response that can manifest itself in different ways, including in the body as physical pain and emotionally as psychic pain.

Pain is not the same as suffering, but pain often leads to suffering.

THE GUEST HOUSE

*This being human is a guest house.
Every morning a new arrival.*

*A joy, a depression, a meanness,
Some momentary awareness comes
as an unexpected visitor.*

Welcome and entertain them all!

...

*The dark thought, the shame, the malice,
meet them at the door laughing,
and invite them in.*

*Be grateful for whoever comes,
because each has been sent
as a guide from beyond.*

– RUMI

Tools to cultivate mindfulness

Now, I am going to teach you a powerful tool to overcome the barriers to presence, to catch and break those second arrows, and to help you start to cultivate a mindfulness practice called **RAIN**.

RAIN is an acronym used in the mindfulness community as a tool for practicing mindfulness.

R = Recognize. Attend to whatever is happening in the present moment.

A = Accept. Meet what is occurring right now with an open heart.

I = Investigate. With compassion.

N = Nurture.

Let's start with the **R**, recognizing what is happening. The key is to pay attention. Without judgment, just name things as they happen. You don't have to fix it or change it. Just name it. When you find yourself lost in thought and you become aware of it, you say to yourself "thinking." When you recognize you are feeling something you can say to yourself "feeling," or you can say "sad," "anxious," "afraid."

Recognizing is about stepping back and observing. The hidden power in this is that the more you do this, the more you are distancing yourself from identifying with your thoughts and feelings. When we identify with our thoughts and feelings by clinging to them or fighting them, we are inadvertently giving them much more power.

The next thing to do, after the **R** of recognizing, but before the **A** of acceptance, is to start practicing what is referred to as the sacred pause.

Philosopher Viktor Frankl said, "Between stimulus and response there is a space. In that space is our power to choose our response. In our response lies our growth and our freedom."

The pause allows us to ask ourselves: *What is happening right now? Why am I getting so upset?* Just asking those two questions before responding will provide enough time for the adrenaline to subside a bit and to respond from a different place.

Once we recognize and pause, the next step is the **A** of acceptance.

Acceptance is simply about meeting whatever you are experiencing with an open heart. Some people like to say to themselves, "I consent" or "this, too" or "can I be with this?" Your job is not to change anything or fix anything.

Moving on to the **I** of **RAIN** – investigate.

First, what are you experiencing in the moment in your body? If you're feeling sad, can you locate the sadness in your body? Do you feel a tightness in your chest or throat, heaviness in your stomach? Your job is not to figure out what caused it. It's just about locating it and connecting with how it is living inside you in the moment.

Second, what are you feeling in the moment? Can you categorize it as positive, negative, or neutral? Can you be with it as it is?

Third, what are you thinking about in the moment? Can you be with that as it is?

Fourth, are there beliefs that you hold as a result of what you are experiencing? Are there narratives you have created related to what you are experiencing?

The final step is **N**, nurturing. This is about asking yourself what you need, how to best take care of yourself, meeting your experiences with compassion and an open heart. You don't have to come up with an answer. It's the act of compassion that matters most, saying to the vulnerable part of yourself, "I see you."

Finally, after **RAIN**, we step back and examine our process. What does it mean to not identify with your experience? Recognize that you are not your thoughts or feelings? You can observe them, name them, accept them, understand them, but they do not define you. It's helpful to take stock of how you are feeling before you practice with **RAIN** and then how you are feeling after. This will help you to see how everything is always changing.

I hope my explanation helps to clarify what mindfulness is about and how you can put it into practice. It is about coming off autopilot by cultivating a witness to our experiences. 🧘

Note: A handout for practicing **RAIN** is available on Dr. Younger's blog post at fsbdsociety.org.

AN ACTIVE FORCE FOR FSHD

You can make a difference!

When you first found our website (fshdsociety.org), you may have signed up to receive our emails, and you may, understandably, have thought you were all set. But we still have two vital, unanswered questions:

- Are you a person with FSHD?
- Where do you live?

We must have this information because our clinical trial alerts go out only to patients who live near a study location. To make sure you'll be notified, please fill out the Research Contact Registry form on our website. Your data is safe with us. *You will NOT be contacted directly by companies or automatically enrolled in a study.*

The need is urgent. There could be four or five FSHD clinical trials in the coming year, yet there may not be enough known, email-contactable patients in our database to meet the enrollment goals for these trials. Any delay in enrolling patients slows down the entire clinical trial – and delays promising therapies from reaching our community.

Even if you have been a member of the FSHD Society for many years, or personally know our staff, the fact that you are a patient may not be recorded in our database. To be safe, just point your smartphone at the QR code to get to the online form and fill it out. 📱

Do you have family members with FSHD?

Let them know how important it is for each individual to join the Research Contact Registry.





Regaining the freedom to travel

With folding lightweight power wheelchairs

BY AMY BEKIER, SAN DIEGO CHAPTER DIRECTOR

No one chooses to use a wheelchair. Many who are still mobile opt for a scooter and hope it's not the end of their walking life – and to avoid the perceived stigma of using a chair. Once you have crossed the threshold to purchase a “personal people mover,” however, your world will open.



Amy Bekier

Scooters tend to be heavy and difficult to break apart to put into a car, make a U-turn in an elevator, or navigate in a restaurant. A far better option is the foldable travel electric power wheelchair. This article reviews questions to ask when you are considering this option. It is by no means definitive, as new models are popping up even as I write this.

Think of a folding power wheelchair as a scooter replacement but with a smaller footprint that can turn on a dime. They are usually lighter in weight, ranging from 50 to 65 pounds, whereas a scooter can be 90 to 125 pounds or more.

Folding chairs have drawbacks. They do not elevate, and most do not recline. They cannot be customized (except for accessories), nor are they comfortable enough for full-time use. However, they are ideal for someone who still has some walking ability and is looking for part-time transport. And because they can be folded, they are convenient to take on a trip, including air travel.

Be prepared for a foldable power wheelchair to cost from \$1,500 to



EZ-Lite Cruiser



Bruno Cub-Sider®

Before purchasing a vehicle, I recommend deciding what type of equipment you will want, and visit a mobility specialist to make sure the lift and the chair will fit your car.

\$3,900. Some chairs may be covered by insurance with a doctor's durable medical equipment prescription or through the VA. Ask how to file for insurance and whether there is financing.

The following are questions to consider when contemplating a purchase of a folding power wheelchair.

If you plan to take the chair on a trip, you will want to know:

- What type of battery does it use? Most airlines accept only sealed dry cell batteries. Some may require you carry on the battery before stowing the chair. Check each airline for maximum acceptable wattage.
- Is the charger compatible in other countries?

The next consideration is how to stow it in a vehicle. Is there someone who can lift it in/out? I have a Bruno Curb-Sider® lift in the rear of my SUV.


Until recently I was able to manipulate it quite easily. Now I'm pursuing a ramp or other modification to maintain independence. Before purchasing a vehicle, I recommend deciding what type of equipment you will want, and visit a mobility specialist to make sure the lift and the chair will fit your car.

What did I end up buying?

I decided on the EZ-Lite Cruiser® DX12 for more rugged travel with larger, 12" rear wheels. I named her Corrina. I always name my equipment because they are my friends, allowing me the freedom to roam. Corrina is constructed with airline alloy metal. She weighs 65 pounds and lasted through a South African safari. My only issue is that Corrina does not do well on sharp inclines or cobblestone walkways. The FOLD & GO has received rave reviews from many who have purchased it. It has a magnesium frame, and its website states that it is waterproof. That was my second choice.

A chair's weight may be relevant if you or an aide plan to lift it. Some chairs require both hands to steer. My hands are too weak, and I need a joystick. I decided against brands that could be contacted only via email with no US customer service.

Which one is right for you? The right one is the one you choose to purchase after doing your research.

Editor's note: Visit Amy's blog post on our website for a list of folding wheelchair makers. 



Checklist

The following are questions to consider when contemplating a purchase of a folding power wheelchair. Here are the most important questions to ask (if you are in the US):

- Is it FDA cleared?
- Is there US customer service and, if so, where is it located?
- Do they have parts available in a US warehouse?
- What and how long a time does the warranty cover?
- How long has the company been in business?
- What is the projected battery life? Is it lithium ion or equivalent? How fast will it charge? What is the distance that it can travel on a charge?
- What does the chair weigh with/without battery. If it's too light it may take bumps poorly.
- What is the weight-carrying capacity?
- How does it fold/open?
- Does it have a quick joystick release for easier transport?
- Do the armrests lift for easy transfer if necessary?
- Will the footrest flip under the seat instead of swinging away, making it easier to get in/out?
- Are the tires solid so there is no worry about flat tires?
- What is the height of the seat? Can I stand from that height?

Recommended accessories:

- Seat belt
- An extension footrest to accommodate longer legs
- More comfortable cushion
- Drink holder
- Headrest



Asifa Lalji



My bumpy journey to activism

How I became an advocate for universal design

BY ASIFA LALJI, VANCOUVER, CANADA

As my FSHD progressed, I was forced to become less physically active than I had been in the past. However, I found an unexpected gift, almost like a trade-off, from the things I had to give up.

I remember the day well. My husband and I were walking down the boardwalk across from our condo, and I was using my new rollator. I was trying to multitask and was on the phone while I pushed the rollator with one hand. I stepped on some uneven pavement, and down I went. I tried to get up but my body was like jelly, so my husband picked me up. Two more steps and I fell again,

and he picked me up once more. I ignored his pleas to call it a day. Once again, I fell. He finally said, forget it, sat me on the seat of the rollator, and pushed me home.

I had a good cry when I got home because I felt FSHD had won that round. But the next day I called my sister-in-law and made arrangements to borrow her father's power chair. There was no way I was missing a glorious summer by sitting indoors.

I hopped on and pretended I was the Queen of England as I zoomed around. Whatever it takes to make things a positive experience! But as soon as I got to the

boardwalk, I couldn't believe how bumpy the surface was and how challenging for someone relying on a wheelchair. I bounced and shook the length of this boardwalk as I felt every pothole, every uneven plank, and became keenly aware that I should have worn a more structured bra! Where were all the ramps? Was I really expected to go all the way to the next ramp only to reverse direction almost the same distance? And why were these doors so small and so heavy? And the bathroom – impossible to get in and out of easily in a wheelchair.

After just one ride on the boardwalk, my perspective had completely changed. I was enlightened – and ashamed. It made me think about the unconscious bias we all have. While I was still walking, I took for granted the ability to step over the potholes, walk down the steps, not worry about the ramps, never mind the toilet. The more I went out in my wheelchair, the more conscious I became. I was ashamed of my own bias for not considering the challenges of people using wheelchairs, and that I had only encountered their difficulties in my late 40s.

One of the things I learned in my career working with government and corporate organizations is how often the status quo is accepted because no one understands any differently. We may know things in theory, but it's not the same as experiencing them directly.

The day after my first wheeled journey, I contacted our mayor and asked if he would join me on a little tour on wheels on the boardwalk and surrounding areas, with



“Just a couple of hours in a wheelchair was enough for him to understand there needed to be changes to fulfill the mandate of being an accessible and inclusive city.”


– ASIFA LALJI

a photo op, of course. He was willing to join me, and shared the same aha moment. Just a couple of hours in a wheelchair was enough for him to understand there needed to be changes to fulfill the mandate of being an accessible and inclusive city.

Our world is not built in a sustainable way. Anyone can become mobility challenged at any time. City planners should strive to build communities where people can transition seamlessly as they age or as their abilities change. I quickly gravitated toward accessibility through universal design. The basic premise is to design and build in a human-centered approach so it's accessible to all regardless of age, size, ability, or disability.

I started attending meetings, volunteered my time with local businesses, and joined any city committee I could to influence strategy with my personal lived experience. I push my agenda of creating an inclusive, accessible, and sustainable city through

universal design. I've influenced street design and transportation options, forced developers to change sidewalks and ramps, urged city staff to rethink parks and recreation facilities, and have recommended changes to traffic flow during the pandemic to accommodate people with disabilities.

It has been incredibly rewarding to feel that my personal experience and my voice – which I thought had been silenced since I stopped working – was actually sought after and valued. I found great purpose almost by accident, and I couldn't be more grateful. 



The new Early-Onset FSHD Chapter

Supporting parents in their journey

BY LEIGH REYNOLDS, FSHD SOCIETY

Parenting is a huge job and a tremendous blessing. When your child is diagnosed with a chronic health issue like early-onset FSHD, it can be overwhelming and extremely isolating.

Looking for options, seeking expert medical care, maneuvering hurdles within the education system, and wondering if what you are doing is ever enough can be all-consuming. Not having proper connections and resources only makes the isolation even more extreme.

The FSHD Society wants families to connect and thrive. Working with families, led by parents, we have launched the Early-Onset FSHD Chapter. Our volunteer leaders know all too well the challenges of parenting a child with FSH muscular dystrophy, and want to offer support, compassion, and guidance.

If you're looking for a shoulder to lean on or want to help others, plug into the Early-Onset FSHD Chapter today. You can find us at FSHDSociety.org/early-onset or via email at EarlyOnsetChapter@FSHDSociety.org. 📧



Ally Roets (center) and her son Sam Ray (right) are co-leading the Early-Onset FSHD Chapter with Kristin Zwickau.



Calling all GenZ of FSHD

It's time for youth to activate!

BY JACOB DUNN, HELOISE HOFFMANN, ALENA JONES, AND LEXI PAPPAS

Join the GenZ of FSHD group to connect with other youth affected by FSHD. Connect with us to hear others' stories, stay updated on information and upcoming events, share tips and tricks, and more. We are here to serve as the voice of GenZ with FSHD and help you stay in the loop. Our generation has the power to make a difference, and we want to help you find your voice to speak up about FSHD. Raising awareness about our rare disease is half the battle, and staying informed can help you have an impact. We understand the struggles faced as young people living with FSHD, but we believe you can use these roadblocks to excel. Led by youth with FSHD for youth with FSHD, GenZ of FSHD aims to create a group of young activists who will join the march for a cure. You are not alone – together, we will beat FSHD! Follow us on Instagram at [@genz_of_fshd](https://www.instagram.com/genz_of_fshd). 📸





BUILD YOUR STRENGTHS



The army of everyone

There's a role for every person – so join us!

BY BETH JOHNSTON AND LEIGH REYNOLDS, FSHD SOCIETY

In an army, everyone has a role to play. From top generals to the humblest potato peeler, everyone contributes to the battle. It's the same with our fight to bring awareness and treatments for FSHD. And the way we have grown our army is through the FSHD Society chapter program. With the mission to enlarge, engage, and empower an active global community, today we have 33 chapters across the US and Canada, and are adding more. This incredible expansion has been fueled by the passion and commitment of the individuals who have stepped up to lead each chapter. We salute you!

Why are chapters so important?

- They provide FSHD families with local hands and hearts, so that no one need ever face this disease alone.
- They connect people to local and regional resources, enabling families to be their own best advocates when it comes to physical and mental well-being.
- They activate the patient community more deeply, because an active patient community is critical to accelerating research that will deliver treatments and a cure.

This past year, when we could not gather in person, our volunteer leaders made it possible for our communities to stay connected.

- They quickly adopted Zoom and hosted countless virtual chapter meetings and educational events.
- The FSHD Radio podcast, hosted by Tim Hollenback, increased its broadcast from monthly to weekly in a live format, bringing people online into a shared experience.
- They joined our mental health task force and helped

launch our Wellness Hour and Sharegiver Hour meetings.

- In a year when fundraising seemed impossible and in-person Walk & Roll events could not happen, chapters raised more than half a million dollars through 25 virtual Walk & Roll to Cure FSHD fundraisers.

Recalibrate. Reconnect. Recommit.

Now, we are focused on the road ahead.

Time to recalibrate... As the world reopens, we know there is no going back; we are on a new path. Chapters worked together to bring new and exciting ideas to the table, and we want to continue to foster that collaboration and creativity. Many people benefited from and prefer a virtual setting, so as we return to in-person programs, we know we need to continue to offer meaningful and effective virtual options.

Time to reconnect... As we slowly emerge from our isolation, we know that direct, personal connection is one of the most powerful components of chapter membership. At the right time in each area, chapter leaders are planning re:Connect parties and in-person Walk & Roll celebrations. We can't wait to see you there.

Time to recommit... Accelerating the delivery of FSHD therapies and bringing us closer to a cure is the focus of all we do. We simply cannot do it without you. Each and every one of us has a part to play. Little by little, our efforts add up to a force that can't be stopped. 🇺🇸

Attendees at the 2021 FSHD Society Volunteer Leadership Summit



ReDUX4 trial results exceed expectations

“Positive benefit/risk supports losmapimod’s potential to be a transformative therapy for the treatment of FSHD.” –Fulcrum Therapeutics

BY JUNE KINOSHITA, FSHD SOCIETY

Fulcrum Therapeutics announced on June 24 that losmapimod, the company’s experimental therapy for facioscapulohumeral muscular dystrophy, produced statistically significant improvements in function and decreased fatty infiltration of muscle in its ReDUX4 clinical trial. ReDUX4 was a randomized, double-blind, placebo-controlled Phase 2b clinical trial in 80 participants. The trial was conducted at multiple sites internationally and designed to investigate the efficacy and safety of losmapimod taken in 15-mg pills twice per day. Based on today’s results, Fulcrum said it “plans to meet with health authorities, including the U.S. Food and Drug Administration (FDA), in the second half of 2021 to determine the regulatory path for losmapimod in FSHD.

ReDUX4 looked at a variety of indicators of patient physiology and function, including muscle biopsies, magnetic resonance imaging (MRI), muscle strength and function, and patient questionnaires. Some of these measures included tools, such as MRI-informed biopsies to look for genes activated by *DUX4* (the gene that causes FSHD), whole-body MRI, reachable workspace (RWS), and FSHD timed-up-and-go (FSHD TUG), which were developed in preparation for this trial. The COVID pandemic forced Fulcrum to extend its trial from 24 to 48 weeks – enabling the collection of additional data that allowed these positive outcomes to be more clearly demonstrated.

Other companies will be keenly



Fulcrum employees mark World FSHD Day with orange-slice smiles.

interested in Fulcrum’s data because they indicate which outcome measures are the most robust for future FSHD clinical trials. They will also help trial researchers model the number of patients and duration of trials needed to demonstrate the effects of future drug candidates.

The FSHD community owes thanks to the Fulcrum team and to the patients, caregivers, researchers, clinicians, funders, and advocacy groups that have brought us to this milestone.

What does this mean for people with FSHD?

There are still hoops to jump through before people will be able to get a prescription for losmapimod. Fulcrum needs to meet with regulators and determine its path forward. The FDA (and in Europe, the EMA)

must review the data and make a decision on whether to grant an accelerated approval or require additional clinical trials before allowing losmapimod onto the market. The fact that losmapimod has been given a Fast Track designation is like getting TSA Pre to get through airport security screening faster.

Fulcrum also said that it is evaluating all populations, including children and individuals who were excluded from the ReDUX4 trial, and “working with regulators to find the best path forward to get losmapimod to patients as quickly as possible,” said Michelle Mellion, senior medical director at Fulcrum.

For further details about the clinical trial data, read the blog post “ReDUX4 trial result exceeds expectations” on the FSHD Society website.

28th annual International Research Congress

Shining a spotlight on therapy development

BY JUNE KINOSHITA, FSHD SOCIETY



The FSHD Society's 28th annual International Research Congress (IRC), conducted entirely online, brought 350 attendees together virtually on June 24 and 25. The two-day conference is the premier global platform for the discussion and dissemination of cutting-edge research on facioscapulohumeral muscular dystrophy (FSHD).

This annual meeting, started in 1994, has catalyzed fundamental discoveries and helped to bring the field to its current state, with 25 biopharmaceutical companies and an international array of academic labs actively developing treatments that target the root genetic cause of FSHD. The dominantly inherited condition, which affects about one in 8,000 people in the general population, causes muscle weakness and wasting, leading to significant disability.

The 2021 International Research Congress included a highly anticipated presentation by Fulcrum Therapeutics of the data from its ReDUX4 Phase 2b clinical trial (see story on page 14). The trial was designed to evaluate the safety and efficacy of losmapimod, an investigational selective p38 α / β MAPK inhibitor, in addressing the underlying cause of FSHD. It is the first disease-modifying drug for FSHD to advance this far in the clinical trial process. To conduct the trial, Fulcrum measured multiple clinical and patient-reported outcome assessments and broke new ground in the use of muscle biomarkers and magnetic resonance imaging as outcome measures, both areas that are of keen interest to all drug developers in this space.


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The congress also convened a panel to discuss antisense strategies to treat FSHD, with seven industry and academic speakers presenting various approaches to silence the target gene, called *DUX4*, and deliver their candidate molecules into muscle safely at therapeutically relevant levels.

Keynote talks highlighted topics that promise to lead to important new insights and therapeutic targets. Russell Butterfield, MD PhD, of the University of Utah, spoke about an 80-year study of a large Utah kindred with hundreds of FSHD cases, which continues to provide insight into factors that influence the severity of disease symptoms. Stephen Tapscott, MD PhD, of the Fred Hutchinson Cancer Research Center, addressed aspects of the immune response in FSHD, a subject that had been largely overlooked until very recently.

A growing number of companies sponsored the FSHD International Research Congress as they entered the field of FSHD diagnostics and therapy development. This year's foundation and industry supporters included: AMRA, Armatus Bio, Arrowhead Pharmaceuticals, Association Française Contre

les Myopathies, Avidity Biosciences, Bionano Genomics, Dyne Therapeutics, Facio Therapies, Fulcrum Therapeutics, Genomic Vision, miRecule, Muscular Dystrophy Association, National Institutes of Health, PerkinElmer Genomics, Ultragenyx, and the University of Nevada, Reno.

"Although current circumstances prevent us from hosting an in-person meeting, we are delighted by the incredible number of researchers and clinicians who were able to advance the field during these challenging times," said Jamshid Arjomand, PhD, chief science officer of the FSHD Society. "We are grateful for the tremendous support from our sponsors and families, without whom none of this would be possible." 



Adding an arrow to the quiver

New biopharma enters the FSHD space

BY JUNE KINOSHITA, FSHD SOCIETY

Arrowhead Pharmaceuticals, Inc., a Pasadena, California, company, has announced that it is developing a therapy for FSH muscular dystrophy (FSHD). Called ARO-DUX4, it is Arrowhead's first muscle-targeted investigational RNAi therapeutic candidate. Using the company's proprietary Targeted RNAi Molecule (TRIM™) platform, ARO-DUX4 is designed to target the gene *DUX4*, which is thought to be the root cause of FSHD.


Arrowhead presented its preclinical data on ARO-DUX4 at the 28th annual FSHD Society International Research Congress, which was held virtually on June 24-25, 2021. The data showed that ARO-DUX4 is highly effective in suppressing the expression of *DUX4* in mice that have been engineered to express *DUX4*.

"In our various animal models, ARO-DUX4 reduced *DUX4* expression by greater than 70%, prevented body weight loss associated with tamoxifen-induced *DUX4* expression, and prevented loss of muscle function," said Chris Anzalone, PhD, president and chief executive officer at Arrowhead. (In these studies, tamoxifen, a drug used to treat tumors, is employed as an artificial switch to turn on the *DUX4* gene in mice that have been genetically engineered to respond in this way. Switching on *DUX4* in the mice leads to muscle degeneration and weakness, similar to those seen in the human disease. Normally, tamoxifen does not affect *DUX4* expression, so individuals with FSHD should not be concerned that taking tamoxifen might trigger the progression of symptoms.)



Arrowhead CEO Chris Anzalone

Arrowhead is currently conducting toxicology studies and intends to file for regulatory clearance in the third quarter of 2021 to begin Phase 1 clinical studies, with the aim of establishing the safety and tolerability of ARO-DUX4 in healthy humans.

Interested in receiving e-alerts about FSHD clinical trials? Join our Research Contact Registry (see page 7). 

The search for circulating blood biomarkers in FSHD

Filling a critical gap in clinical trial readiness

BY JAMSHID ARJOMAND, PHD, CHIEF SCIENCE OFFICER, FSHD SOCIETY

What are biomarkers? Briefly, they are measurable indicators of a biological function. For example, cholesterol levels (HDL, LDL, triglycerides) measured in the blood serve as an indicator of vascular health. In cases of high cholesterol, statins (along with diet and exercise) may be prescribed to reduce the risk of heart attacks or strokes.

There are many different types of biomarkers in medicine. Some are used to report on an organ's function or size (PSA levels for prostate cancer), or an organ's health (CK levels for muscle damage), or even as a surrogate measure of a drug's effectiveness (dystrophin levels in Duchenne muscular dystrophy).

In FSHD, because current therapeutic approaches are targeting *DUX4*, the toxic gene that causes the disease, drug researchers would find it very useful to have a biomarker that can measure *DUX4* levels. Unfortunately, *DUX4* itself is very difficult to measure directly. However, because *DUX4* is normally not active at all in muscle, and because when it is active, it is a master switch that activates a series of other genes, these "*DUX4*-regulated" genes could potentially be used to report on *DUX4* levels indirectly.

This is, in fact, what researchers currently do, by analyzing muscle biopsies to monitor *DUX4*-regulated genes as a proxy for *DUX4* levels and activity. But muscle biopsies are not ideal. Not only are they invasive, but



Amy Campbell and Suja Jagannathan

a needle biopsy only reports on a very small muscle region. We know that in FSHD, muscle fibers with activated *DUX4* can lie right next to others that are inactive, so a needle biopsy is a hit-or-miss method. But if muscle fibers with activated *DUX4* are secreting a unique set of proteins into the blood, it may be possible to measure them in a blood test. This "blood biomarker" would indicate *DUX4* activity throughout the body and be a more reliable measure of a drug's impact on *DUX4* level.

In June of 2020, the FSHD Society convened a workshop to identify possible *DUX4*-regulated genes that might be detectable in blood. The workshop reviewed the published research data on downstream genes that are activated by *DUX4* in

muscle. The analysis also included a review of existing commercial tests, or "assays," that could be used to measure these candidate biomarkers. Since developing assays can be complicated and take years, making use of any ready-made assays would significantly speed up the biomarker discovery process.

Amazingly, three different commercial assays were found, and experiments were quickly designed to test whether they are sensitive enough. Dr. Amy Campbell and Dr. Suja Jagannathan at the University of Colorado used a series of muscles-in-a-dish models to quickly help rule candidate biomarkers in or out. Of the three potential biomarkers, two failed, but one candidate was not only detected

Continued on page 19...

FSHD University Webinar: Dynamic Sitting

We've all heard how important a well-tailored exercise program is for people with FSH muscular dystrophy. This is easier said than done, especially if you have difficulty standing up or worry about falling during exercise. In our July 15 webinar, Dr. Nikia Stinson discusses upper body weakness and pain that are frequently experienced by people with FSHD, and describes exercises that can be done from a seated position to help address these issues. Dr. Stinson is at the Kennedy Krieger Institute's Center for Genetic Muscle Disorders, where she works with patients with hereditary muscle diseases, including FSHD. As a physical therapist and lead clinical evaluator, Dr. Stinson participates in ongoing clinical research at the Institute.



Dr. Nikia Stinson

Educating doctors about FSHD on August 12

Spread the word! The FSHD Society is offering its first-ever CME-accredited masterclass on facioscapulohumeral muscular dystrophy (FSHD). This course, which will be held live virtually on August 12, is of interest to any physician and allied health professional who sees adult and pediatric neuromuscular patients. Attendees will be able to earn up to 4.25 continuing medical education (CME) credits – a great incentive for doctors who need CME credits to maintain their medical licenses and/or credentials.

This masterclass offers comprehensive, authoritative updates on diagnosis, genetic testing, symptom management, therapeutic strategies, and anticipated clinical trials. Held virtually, it will include live, interactive sessions with ample time for questions and discussion.

If you know any medical providers who would be interested in updating their knowledge of FSHD, please let them know.

Visit our blog for details, registration information, and a template for a letter to send to your doctor.



What is FSHD 360?

After decades of incremental progress, we are in a transformed world. Every few months, a new pharmaceutical company enters the FSHD field. Clinical trials are coming. How can you keep up, while taking the best possible care of yourself and your loved ones?

The FSHD Society is joining forces with the Clinical Trial Research Network (CTRN) sites to provide you with a well-rounded education on FSH muscular dystrophy through our "FSHD 360" meetings.

- What are the basic facts that every family should know?
- How can you best take care of your health and well-being?
- What's going on at the frontiers of research?
- How soon can you expect clinical trials and treatments?
- What can you do to help?

FSHD 360 meetings will give you a comprehensive, 360-degree overview of the latest in healthcare and research for the FSHD community. Check our Events Calendar and newsletters for an FSHD 360 near you.

Thank you to our FSHD 360 sponsors:




... From page 17

The search for circulating blood biomarkers in FSHD

in the muscle cells, but it was also measurable in the liquid that bathes the cells in the dish – a good proxy for blood. More importantly, the levels of the candidate biomarker could be reduced when the cells in the dish were exposed to compounds that have been shown to lower *DUX4* levels in the lab.

Additional studies have since been carried out to test this assay with patient blood samples. Unfortunately, these experiments did not detect the biomarker in the patient blood samples at any levels higher than control samples. This could be due to the assay not being sufficiently sensitive, the biomarker itself not being sufficiently stable in circulating blood, or a combination of both.

As with the drug discovery process, the search for biomarkers is difficult and labor intensive. These initial candidate biomarkers were the proverbial “low-hanging fruit,” primarily because there were existing commercial assays to detect them. The Society’s aim is to speed up the development of essential tools, such as biomarkers, through pragmatic and fast steps. The effort may not always pan out – that’s science – but the idea is to test all good ideas quickly.

Several other groups are now testing a variety of candidate biomarkers and actively working on developing assays to measure *DUX4* activity in blood. Given the importance biomarker assays play in drug development, the FSHD Society is committed to working with all researchers, clinicians, and companies to help identify and develop a reliable and sensitive *DUX4* biomarker assay for the clinic. 

Visit our Events Calendar for updates and to register for events (fshdsociety.org/fshd-events-calendar/).

FUNDRAISERS & WALK & ROLLS



Visit the Walk & Roll to Cure FSHD page for a complete list (FSHDSociety.org/WalkRoll).

September 11: Walk & Rolls in Columbus, Chicago, and Dallas

September 12: Walk & Rolls in Colorado and South Carolina

September 18: Walk & Rolls in 19-plus locations plus International Walk & Roll Live-Stream Celebration

September 19: Walk & Roll in Minnesota

October 2: Targeting a Cure in Tampa, FL

November 6: Western PA Drum & Roll

FSHD 360



Register in advance.

August 28: University of Colorado

September 25: UCLA

October 30: Virginia Commonwealth University

WEBINARS



All webinars at 1 p.m. ET.

Register in advance.

July 15: *Dynamic Sitting*, with Nikia Stinson, DPT, Kennedy Krieger Institute

August 19: *Sleep, Pain, and FSHD: Uncovering the Missing Link*, with Heloise Hoffmann

September 23: *The Mattering Effect: How Feeling Valued and Adding Value Shape Our Lives*, with Isaac Prilleltensky, PhD, and Ora Prilleltensky, PhD

October 21: *Pregnancy and Reproductive Genetic Counseling*, with Sanne Vincenten, MD, and Nicol Voermans, MD PhD, of Radboud University Medical Center, and Jacinda Sampson, MD PhD, of Stanford University Medical Center

November 18: *Drug Development panel*, with speakers from companies working on FSHD therapies

December 16: *Orthotics for FSHD*, Speakers TBD

FSHD SOCIETY RADIO



--All shows at 9 p.m. ET, 8 p.m. CT, 7 p.m. MT, 6 p.m. PT

August 10

September 14

October 12

November 9

CHAPTER MEETINGS



For virtual meetings, anyone can join from anywhere. Please pay attention to the time zones.

July 18: 1:30 p.m. PT – Pacific Northwest re:Connect

July 24: 10 a.m. ET – Ontario Virtual Chapter Meeting

July 27: 5 p.m. CT or 6 p.m. ET – CenTex, Dallas, and South Carolina virtual meeting with Dr. Jamshid Arjomand

September 14: 11:30 a.m. PT – San Diego re:Connect

October 5: 8 p.m. ET – South Carolina

October 7: 7 p.m. – New England Connections (virtual)

WELLNESS HOUR



Second Monday of every month at 5 p.m. ET

August 9

September 13

October 11

November 8

SHAREGIVER HOUR



Last Tuesday of every month at 8 p.m. ET

July 27

August 31

September 28

October 26

November 30

Moving together toward a cure

Virtual or in-person, in a small group or a large crowd, this year you can Walk & Roll your way!

The Walk & Roll to Cure FSHD is the only national event focused solely on funding progress for FSH muscular dystrophy. Led entirely by dedicated volunteers, and supported by the FSHD Society staff, these events will take place all over the US and Canada this fall.

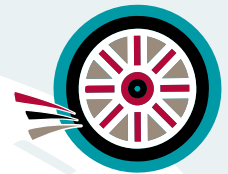
Since 2018, the Walk & Roll has had life-changing impact. It has united families, friends, neighbors, and local businesses to forge powerful connections and strengthen our families and our community.

Learn more and join us at FSHDSociety.org/WalkRoll. 🇺🇸



TO CURE FSHD

SEPTEMBER 2021



Together, we move closer to a cure.
Virtual or in-person, in a small group or
a large crowd, this year you can
Walk & Roll Your Way.