FSHD Advocate
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FSHD SOCIETY
LIGHTING THE WAY TO A CURE

THE FUTURE IS IN POWERFUL HANDS: YOURS!

ENGAGE & ACTIVATE SPECIAL SECTION

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On the cover, Rod Shuster and Kim Lynch at the 2019 Colorado Walk & Roll
Photo by Marble & Doni Jones Photography, *https://www.donijones.com.*

FSHD Advocate

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

CEO Letter

YOU have the power

"If you want to lift yourself up, lift up someone else." — BOOKER T. WASHINGTON

The stories in this issue represent empowerment and hope. Individuals – patients, families, friends, researchers – in spite of obstacles, coming forward to participate in this life-altering endeavor to deliver treatments for FSHD. These are people who have discovered that as they lift others, they, too, are lifted, and they are in the vanguard of a growing global community of activists and advocates.

As I meet with families across the US and around the world, I am constantly inspired by what they tell me. One individual, discouraged and depressed, stepped forward timidly to start a fundraiser. That simple act of bravery has not only changed her life, but the lives of those around her. A team of committed individuals joined her, and together they have raised hundreds of thousands of dollars, but the best outcome is that her engagement has empowered her in all other areas of her life.

In the year since we launched our national chapter program and Walk & Roll fundraisers, dozens of individuals, like Kristin Zwickau, Dave Lukas, and Meredith Huml, have volunteered to lead the way. In lifting others, they have lifted themselves as they discovered a new sense of purpose and realized the power they have to make a difference.

Some, like Justin Cohen and Anthony Saleh, are applying their scientific talents to find treatments for FSHD. Others, like MDA ambassador Tana Zwart and Facebook activist Alexandrea Comstock, have stepped up as public advocates to raise awareness and empower others to find their own voices.

Mark A. Stone

The FSHD Society's family story book is filled with individuals who have found the strength in themselves to lift others. Some volunteer for clinical studies and drug trials, donating their blood, time, and data so that researchers can unlock clues for future treatments. Others harness their hobbies, activities, and passions to campaign for awareness and funds.

While each person finds his or her own path, all share a common truth. By taking the step to be part of the solution, they have found a sense of purpose and hope that permeates their daily lives.

As you read their stories in these pages, I want to encourage and challenge you to join our community of the powerful. Our goal is to find a cure and break free of the limitations imposed by FSHD, and we'll get there by lifting one another – together.

Mark

Mark Stone
President and CEO
FSHD Society

The FUTURE Is in Powerful Hands — YOURS

BY JUNE KINOSHITA, FSHD SOCIETY

"We are now faced with the fact that tomorrow is today. We are confronted with the fierce urgency of now."

Thus Dr. Martin Luther King Jr. exhorted the nation at the March on Washington on that historic summer day in 1963. While King spoke of long-deferred dreams of equality, today in the FSHD community we are faced with our own pivotal moment.

Long told that "there's no treatment, nothing to be done," many of you supported the Society in a wild leap of faith, hoping that research would – some far-off day – make possible a treatment or cure. Now, that once-distant dream is tantalizingly within reach.

Therapies are being tested in patients, and while many will fail, some will be effective. There are a plethora of promising ideas but not enough funding to propel them forward. We have done a remarkable job with few resources to build a bridge to clinical trials, but we must do more, and faster, to strengthen that bridge and fill in critical gaps. That is why we have launched our Therapeutic Accelerator Initiative and called upon companies to contribute $5 million – to be matched by our leadership donors – to complete the necessary work that will speed more therapies toward the finish line.

But dollars are not enough. FSHD is a uniquely human condition that requires all of you – patients, family members, and those who love you – to activate. We are truly facing the "fierce urgency of now," a call to arms that requires our community to step up as never before.

THE ABC'S OF ACTIVATING

GO DIGITAL

WHY? Email is how we connect with you. If you are not getting our emails, you are missing the latest news, opportunities to volunteer for clinical trials, meet others, and participate in important surveys.
HOW: Visit *www.fshdsociety.org/JoinUs* and share your contact email with us.

TAKE OUR SURVEYS

WHY? Drug companies and regulators turn to the Society to understand how FSHD affects your health and well-being. By taking part in our surveys, you are shaping clinical trials, corporate, and government decisions, and most importantly, making your voice matter.
HOW: Read our emails. Check your spam filter, and make sure FSHD Society emails are not on a blacklist.

Activated patients are the key to progress

BY MEENA UPADHYAYA, PHD OBE, CARDIFF, WALES

Meena Upadhyaya, PhD, OBE

The global FSHD research community is active, collaborative, and innovative, and the patient community has always played an essential part in furthering our knowledge. Patients donating their DNA and data made it possible for researchers to crack the enigma of the molecular genetic basis of facioscapulohumeral muscular dystrophy (FSHD). This breakthrough has driven an extremely exciting time for FSHD research and resulted in a significant increase in our scientific understanding.

I became involved in FSHD research in 1987. My research group made significant contributions to the first international consortium for FSHD held in 1988 in Manchester, UK. I have witnessed marked progress in this field, ranging from mapping of disease genes to the identification of several "causal" genes, molecular diagnoses, understanding of the underlying mechanism of disease, the engineering of animal models, stem cell research, the role of epigenetics, identification of therapeutic targets, and development of clinical trials.

However, there still remain challenges ahead of us. While massive generation of molecular genetic information has provided tangible new targets for therapeutic intervention, there are no treatments yet to slow, stop, or reverse the effects of FSHD.

There's still important basic knowledge to uncover. Effective therapeutic strategies should not focus only on shutting down DUX4, but also on reversing the downstream consequences of DUX4 expression, which could otherwise still be damaging to muscle cells.

I feel this is the most invigorating time in this field, as we are on the verge of delivering long-awaited treatments. But now is not the time to relax. The job is not finished. Indeed, the patient community must become more engaged than ever before.

Donations of blood and tissue by patients will aid in validating therapeutic targets and provide insights into the development of precision medicine. Tissue donations from biopsies, certain types of surgeries (such as scapular fixation), or even in terminal stages of the disease are priceless gifts to research that can lead to treatments and perhaps a cure. There is an urgent need for volunteers for natural history, biomarker, imaging, and "clinical endpoint" studies – all essential stepping stones to clinical trials. The support and collaboration of families are urgently required toward fundraising for cutting-edge research.

Patient advocacy groups like the FSHD Society can answer your questions about how you can help with this landmark progress. There has never been a better time for the community to join in the global campaign to combat FSHD.

EDITOR'S NOTE

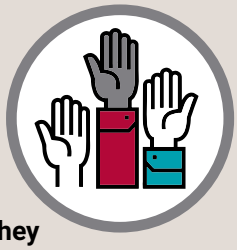
Meena Upadhyaya, PhD OBE, is an Indian-born Welsh medical geneticist and an honorary distinguished professor at Cardiff University. She has made seminal contributions to understanding the genetic basis of FSHD. She received an Order of the British Empire in 2016 for services to medical genetics and the Welsh Asian community.

JOIN A CHAPTER

WHY? There is great power in community. When we come together, each bringing our own unique strengths and skills, we inspire one another to go further and reach higher than we can when we go it alone.

HOW: Visit *www.fshdsociety.org/Chapters* to find a chapter near you. If there isn't one, consider starting one for your region. We'll help you.

REACH OUT



WHY? An estimated 30,000-plus FSHD patients in the US alone have never contacted the Society. The more people are engaged, the more we will be able to do.

HOW: Talk to people about the power they have to lift others and themselves by joining our global movement. Share emails, web pages, social media posts, and publications.

A landmark forum for the patient voice

BY JUNE KINOSHITA, FSHD SOCIETY

Early in 2020, FSHD Society members will have an opportunity to take action by participating – both online and in person – in a pivotal meeting. We have received the green light from the Food and Drug Administration (FDA) to hold an externally led Patient-Focused Drug Development (EL-PFDD) meeting on FSHD. We have invited the Muscular Dystrophy Association and Friends of FSH Research to partner with us. The meeting will be held on April 21 near Bethesda, Maryland.

The PFDD initiative, started in 2012 by the FDA, is used to obtain patient perspectives on specific diseases and their treatments. The demand from disease advocacy groups for PFDD meetings quickly exceeded the agency's capacity, so the FDA set up a mechanism for groups to apply to organize "externally led" PFDDs.

According to the FDA, "PFDD meetings give FDA and other key stakeholders, including medical product developers, health care providers, and federal partners, an important opportunity to hear directly from patients, their families, caregivers, and patient advocates about the symptoms that matter most to them, the impact the disease has on patients' daily lives, and patients' experiences with currently available treatments. This input can inform FDA's decisions and oversight both during drug development and during our review of a marketing application."

The FSHD Society's EL-PFDD meeting will provide individuals with FSHD, caregivers, and other stakeholders an opportunity to share their experiences and preferences so that the FDA and the biopharmaceutical industry can:

- **understand the FSHD patient journey,** and recognize patient preferences and risk tolerance so these may be translated into improved clinical trial designs, selection criteria, and development of outcome measures relevant to FSHD drug development;
- **demonstrate the complexity and heterogeneity of FSHD,** with the end goal of development programs and trial designs that will reflect these aspects of the disease;
- **create a practical, scientifically rigorous framework** that incorporates patient preferences and patient-reported outcomes into FSHD clinical research;
- **better understand patient and caregiver perceptions** about the treatments they are currently using, which treatments are most beneficial, and which ones may have side effects;
- **encourage identification and use of approaches and best practices** to facilitate patient enrollment and minimize the burden of patient participation in clinical trials; and
- **ensure that people with FSHD understand the value of their participation** in the clinical trials, and how their input impacts FDA and biopharmaceutical industry decision-making and outcomes at all levels to both improve their own health-related quality of life as well as that of others with FSHD, now and in the future.

Prior to the meeting, we plan to distribute online surveys to more than 3,000 patients and family members in our contact database, as well as more than 5,000 members of various FSHD-focused Facebook groups. We will collect patient comments over our social media channels. In addition, we will conduct in-person focus group discussions through our national chapter program and Family Day conferences. Data from these surveys and other methods will be used to shape the content and selection of panelists for the April meeting.

Stay tuned!

Do you have questions about the EL-PFDD? Contact June Kinoshita at *june.kinoshita@fshdsociety.org*.

Finding strength in our pain

BY MEREDITH HUML, ANGIER, NORTH CAROLINA

Meredith Huml

The words "no cure" and "no treatment" were dropped casually into my lap after much prodding and poking and examination on the day I was diagnosed with a disease I'd never heard of. I was 12 years old when I was told I had FSHD, and that it was only going to get worse as I got older.

For many years after my diagnosis, I felt very alone. Although FSHD slowly took over my mental health, the disease was something I refused to talk about. I was scared, and often felt ashamed and humiliated. I hurt people who were concerned about me, and I hurt myself.

My goal in becoming more active in the FSHD community was to find a cure for my younger brother and myself. As I connected with and talked to more people in the community, my goal expanded to finding a cure for them, too, and for their loved ones. An end to this disease is in sight.

Without any conscious effort, this goal led me to also embrace myself and find beauty in my struggles. It has led me to a well of courage to advocate for myself, for others in the FSHD community, and for people with varying disabilities as a whole.

The suffering that FSHD has caused our community has also made us stronger people, and what better people to lead than those who understand pain and can find strength in that pain?

I never would have imagined that being open about my struggles and being vulnerable would have the ability to touch so many others. Sometimes it really is one person who can make a difference. Imagine the difference that thousands together can make.

Save the date!

"The FSHD International Research Congress and FSHD Connect serve a vital role to ensure that all of our stakeholders are working together and speaking with one voice to speed up the delivery of effective treatments to our families."

– MARK STONE, PRESIDENT AND CEO

JUNE 25-26, 2020
27th annual International Research Congress (IRC)

Washington Hilton, Washington, DC. The IRC is the premier global platform for the discussion and dissemination of state-of-the-art research on FSHD.

JUNE 27-28, 2020
FSHD Connect

Washington Hilton, Washington, DC. Leading experts in FSHD clinical care, research, and drug development will share the latest knowledge and answer your questions. There will be workshops to address a wide variety of patient and caregiver concerns.

Registration for the IRC and FSHD Connect will open in January.

Washington Hilton Hotel

Not being involved is not an option

BY KRISTIN ZWICKAU, CHARLESTOWN, MASSACHUSETTS

It was October 2017. I thought I would never find happiness ever again following our daughter Katelyn's diagnosis of FSHD. She was six at the time, and we had never heard of the disease before. Now it is a part of our everyday life. It was overwhelming. During the early days post-diagnosis I kept thinking:

How do we go on?

What other medical punches will we face?

How will she fit in and have friends when she physically can't keep up?

And the list goes on and on ... round and round. All of these questions and more still linger and weigh on us daily, but two years later we have learned to make them background noise and not our main thought process.

We are not willing to let FSHD rule our lives. We have to make it a part of our lives and fight to come out on top. Who knows where our efforts will lead? But if we don't dive in feet first to learn, adjust, and fight, then we are letting FSHD win.

With all we have on our plate – two demanding careers, an almost-nine-year-old who needs so much more than the everyday kid stuff – how and why are we involved with the FSHD community? The answer is simple:

We are the patients and caregivers affected, and who cares more than we do? The FSHD community needs to believe that this is solvable. Be involved. Band together. We're the only ones who can make it happen.

Katelyn and her father, Holger Zwickau

To us, this is solvable, and the time to be involved is now! We have biopharmaceutical companies working on this day in and day out. We have clinical trials now, not just natural history studies gathering basic knowledge. We have scientists working in labs, doctors dedicated to the cause, and the community all working with the FDA to streamline what we need to get drugs over the finish line.

However, success in all of the above hinges on the involvement of the community. In the past two years we have seen so much progress toward a therapy. Involvement means working toward solutions, even if not all of them are known yet. It's better to work toward something than to simply allow FSHD to run its course.

We made the commitment not to sit back and let FSHD determine our daughter's future. A puzzle only gets solved if people care and are determined enough to find the right pieces – and fit them together. We have the pieces to the puzzle. We just need enough people who care to do their part in solving it, and who would that be if not those like us whose lives are affected daily? Sitting by and waiting for others to solve this for us is not a solution.

AFOs with a glittery dress – out and proud with FSHD

BY ALEXANDREA COMSTOCK, LETHBRIDGE, ALBERTA, CANADA

I grew up not knowing what was wrong with me as I faced the consequences of what I eventually learned was early-onset FSHD. I had foot drop. I couldn't close my eyes. I had severe scapular winging, scoliosis, and lordosis. People called me "duck" and would quack at me. I hated gym class and would often be removed for refusing to participate. I knew my limits, but nobody believed me. I played in an all-male lacrosse league for two years, but the bullying because of my body tormented me to the point that I finished my schooling at home at age 17.

I had a daughter when I was 19 years old. When I turned 20, I went to a specialist to inquire about corrective surgery on my spine, but was instead diagnosed with FSHD. I decided to begin modeling, to show the world what FSHD had done to my body. Because of my disease, I was thought unfit to care for my daughter. I fought that charge and won full custody. When I was 21 years old, my daughter was also diagnosed with FSHD.

During those years, I created the Faces of FSHD project on Facebook. It is a place for people to share their selfies, stories, and connect as a community to raise awareness of this condition. We have sold shirts worldwide, held a fundraiser, and we now proudly supply free photography to individuals with disabilities.

Every person I have ever met with FSHD was through Faces of FSHD. This included Mika Mae Jones, a model from Los Angeles. She and I collaborated on Faces of FSHD. Mika was like a sister to me. If I didn't have FSHD I would not have had Mika. Tragically, Mika passed away this past June after she fell and sustained severe brain trauma.

PHOTO BY WILLIAM ZDAN @BILLYZDAN.

Alexandrea Comstock and Mika Mae Jones modeling in Los Angeles

I don't hate FSHD, but it hurts a lot. It is a heavy weight.

My mom was recently diagnosed with FSHD as well. It has been extremely difficult for her psychologically. I grew up watching my mom work hard and provide for everyone around her, no matter how she felt, and that's who I want to be. More than anything, I want my daughter to know that she is supported, loved, and beautiful. I want her to have a community to relate to, talk to, and enjoy.

At age 23, I'm a single mom, I have 11 rescue animals, I'm an advocate for FSHD, I'm an awareness model, and I am trying to change the world. I hope I can make an impact on this world for my daughter and for everyone with disabilities. I have a loud voice, a big personality, and I intend to demand attention until we have what we need to live a healthy, long life. I will wear AFO foot braces with a sparkly dress without hesitation. I think that's important.

A monument of pearls

BY BELINDA MILLER, MANASSAS, VIRGINIA

Tana Zwart

The United States contains some of the most magnificent monuments in the world, both natural and human-made. But few compare to the state of South Dakota's Mount Rushmore – the massive granite crag sculpted to honor some of our most iconic leaders. A lesser-known South Dakotan, but equally impressive, is Tana Zwart, a member of the FSHD Society and the second adult to serve as a Muscular Dystrophy Association (MDA) national ambassador.

Tana lives in Sioux Falls, South Dakota. Because of her unrelenting volunteer work for the MDA, raising awareness and funds to aid research for finding a cure for FSHD, Tana was honored with an MDA ambassadorship in 2019.

Originally from Minnesota, Tana was diagnosed with FSHD at the age of seven and, like most patients, her diagnosis took time, especially because she is "de novo" – she did not inherit the gene from a family member. Tana and her family worked at turning a negative situation into something positive. They became passionate about working through the MDA, participating in local fundraisers and telethons, and even taking part in the famous annual Sturgis Motorcycle Rally.

In 2012, Tana was crowned Ms. Wheelchair Minnesota, and she competed for the national title, where she gained recognition by receiving the Press Room and Most Photogenic awards. Because of her unwavering volunteerism, she won the MDA's Spirit Award.

For Tana, life has not always been filled with awards and honors. Since her childhood diagnosis, she has had to adapt to the weaknesses in her body from a young age. Although very active as a child, she began to feel the effects of FSHD by the fifth grade. Today, at age 34, she has been wheelchair dependent for half of her life. She has lost her ability to walk, but Tana perceives her wheelchair as an extension of her body.

Definitely a woman of conviction, Tana has not put aside her dreams. She has a strong interest in the fashion field and would like an opportunity to use her ideas in the industry, being involved in its movement of inclusivity to "embrace all bodies." "Fashion is all about uniqueness and individuality," says Tana. "It's about time it started embracing a demographic defined by its physically unique individuals."

Tana will not allow FSHD to define her. Her strength and perseverance have brought her to where she is – the second-ever adult ambassador for the MDA. But her goals do not end there. She sees owning a home, getting married, and writing a book as part of her future.

This young woman does not look at her abilities through rose-colored glasses. "Life with FSHD is hard and unfair," she says. "It's not something I like to readily admit, but it is a truth. For me the reward has always been 10 times greater than the struggle, though. I think that's what pushes me, and what gets me through the harder days. No grit, no pearl, right?"

One thing is for sure: Tana has enough grit to build a monument of precious pearls.

Advocacy in a lab coat

Patients play a role in every aspect of research

BY JUSTIN COHEN, NEW HAVEN, CONNECTICUT

Growing up with a disease for which there is no cure or treatment has meant growing up with endless uncertainty about my future. Will a treatment or cure become available in my lifetime? How severely will my muscles have deteriorated by the time a treatment arises? With these answers a mystery, I realized that if I wanted progress to be made during my lifetime, I needed to advocate for myself and the others affected by this disease. Thus, I decided to pursue my doctorate in molecular biology to further FSHD research and take finding a cure into my own hands.

As I began this journey, I could not ignore the recurring theme of the importance of the FSHD community in all aspects of the research process. Most importantly, due to my limited ability, and thus the need to be within driving distance of family in case of wheelchair breakdowns, it was essential that I find an FSHD lab within the Northeast. Thanks to the network of patients, family members, dedicated scientists, and the FSHD Society, I was able to acquire a postdoctoral position in Monkol Lek's lab at Yale University.

Additionally, the FSHD community has played a significant role in funding the research process. No research can progress without funding, and an overwhelming amount of our monetary support comes from patients and their families. Thanks to donations from people like you, I was able to acquire a grant from the Chris Carrino Foundation to begin my postdoc and further the research in the field.

"Working together with the FSHD community is our best chance for reaching a cure."

— JUSTIN COHEN, PhD

As a patient myself, I value research that has the potential to create the largest impact on others. We are currently testing for drugs that can prevent cell death from DUX4, the toxic protein that causes FSHD. By emphasizing drugs that are already approved for other diseases, we can speed up the time to clinical trials that may lead to faster treatments.

Some of our research utilizes tissues donated by patients; thus, community involvement becomes essential once again. Donating tissue is crucial for progress, and the results can be seen in the advances made in the last decade.

Whether it is donating time, money, tissue samples, or research, being involved and working together with the FSHD community is our best chance for reaching a cure.

PHOTOS BY SCOTT LAUDICK

We are not alone

BY DAVE LUKAS, CRYSTAL LAKE, ILLINOIS

The inaugural Chicagoland Walk & Roll to Cure FSHD exceeded every expectation and goal I had. What an amazing day filled with family, community, music, great food, fun, and perfect weather!

We had **230 walkers** (my goal was 150).

We raised **$42,000** (my goal was $25,000).

But more than anything else, I wanted our Walk & Roll to Cure FSHD to be about family and community. That Saturday I realized that goal when I looked out and saw parents talking and sharing while watching their children play lawn games. I saw picnic tables crowded with people sharing food, stories, and laughter. People didn't simply walk and leave. They stuck around to spend time together. And I started to cry (for the 100th time) because this is what it's all about. It's about connecting, and about family and community.

FSHD brings up a lot of feelings of loneliness. Feelings that no one understands what it's like to have FSHD. There were 16 people with FSHD at the walk, and I took a moment to take a picture with just us. In that moment, for me, I didn't feel alone. I looked around and saw 15 people just like me. Yes, we're each affected differently by it, but we get it.

Then I told our FSHDers to look out at the other 220-plus people looking at us. All those people came out for us. They came because they love us and support us. We are not alone. Not only do we have each other, but we have a small army of people who will show up when we need them. You can't put a price tag on the feeling of being seen.

The other moments that stood out for me were watching people with FSHD finish the walk. Some were in wheelchairs and got up to walk the last stretch to the finish line. Some crossed the finish line in their wheelchairs, with family and friends surrounding them. Some completed the entire walk on their own. We embodied the words on the buttons we wore that day which read, "I have FSHD, but it doesn't have me."

The Walk & Roll to Cure FSHD showcased all the character traits I've come to know and love about all of those affected with FSHD: determination, heart, character, gratitude, love, laughter, positivity, and family.

What's even crazier to think about is that this is just the beginning. We only go up from here. But the foundation we built is a solid one, and I'm excited to see how it grows.

Triumphant FSHDers at the 2019 Chicagoland Walk & Roll

Who will be there to pick up the baton?

BY MARGE SCUDDER BRCHAN, BLAINE, MINNESOTA

A community provides connections to persons who share common life experiences. It is foundational for the achievement of goals. Our FSHD community has blossomed and is strong.

Marge Scudder Brchan

When I was diagnosed 56 years ago, few people had heard of facioscapulohumeral muscular dystrophy. There was little hope that could be shared with patients and their families.

Some 30 years ago, a few individuals with FSHD began to discuss how to bring attention to this poorly understood condition. Steve Jacobsen and Daniel Perez stepped up to envision how to acquire funding that would support research and patient education. They reached out to the few of us they knew and widened the effort.

Look where we are now! We have a dynamic organization that supports patients and families, major research projects, and educational efforts. WOW!!!

This didn't just happen by chance. It has taken the efforts of many who stepped up, joined the community, and volunteered their help. Reaching the goal of a treatment by 2025 will certainly require those of us with FSHD to continue to step up.

Most of us know that stepping up can be a challenge. Every time I visit my daughter's house, I need to climb two sets of stairs to make it to their great room where everyone gathers. I grab, pull, balance, and step. Once I, my walker, and canes have made it to the top, I am able to join the community. My sense of accomplishment and belonging makes the effort worthwhile.

The same is true for the FSHD community. When I organize or participate in an event, it often requires maneuvering schedules, family needs, and travel. The connection with others facing the challenges of FSHD and the sense of belonging make the effort rewarding. I feel nourished and satisfied.

Over the years I have tried to support the Society's efforts in a variety of ways. Sometimes I volunteered; sometimes I could only provide verbal support. My participation depended on my health and energy as well as family and work responsibilities. I have given muscle biopsies, participated in medication trials, taken physical and radiological exams, fundraised, talked to legislators, and organized social and educational events. I believe each step made a difference.

I have a concern. As I age, I have less physical and emotional energy, and my technical skills are becoming out of date. I am less able to lead. I wonder, Who will be there to pick up the baton? Our generation has information and experience that could be transferred to the next generation. We hope they will step up.

All of us need to contribute in our own way. Whether we are raising funds, organizing an event, ordering pizza or baking brownies, conversing with another person with FSHD, or participating in research – it all makes a difference!

Will you step up? Our community needs you.

EDITOR'S NOTE

If you are interested in volunteering to lead a local chapter, please email beth.johnston@fshdsociety.org.

Talk about a miRecule

A family diagnosis prompted a biotech founder to set his sights on FSHD

BY JUNE KINOSHITA, FSHD SOCIETY

In their offices in Maryland, just northwest of Washington, DC, miRecule Inc. and its founder Anthony Saleh, PhD, are hard at work developing a novel treatment for FSHD.

In the early 2000s, Saleh was a graduate student at Johns Hopkins School of Public Health in Baltimore, Maryland, working on a new class of drugs known as RNA therapeutics. He had lost two grandparents to cancer, and he wanted to focus on developing new treatments. "RNA therapeutics were incredibly intriguing," he recalled. "They can be designed to target nearly any gene to tackle the underlying causes of diseases."

All of our genetic information is encoded in our DNA, but DNA's lesser known cousin RNA is an important intermediary messenger that shepherds information encoded in our DNA, so that the cell can create the necessary proteins that perform most of our bodies' functions. When we inherit mutations in our DNA that cause diseases like FSHD, there is also that RNA messenger that orders the cells to create toxic proteins like DUX4, which causes the breakdown of muscles in FSHD. RNA therapeutics can stop those RNA messengers in their tracks, eliminating those specific RNAs and preventing the toxic proteins from ever being made.

After graduating from Johns Hopkins, Saleh went on to a fellowship at the National Institutes of Health (NIH) in Bethesda, Maryland.

miRecule
RNA Therapeutics

It was there, working for about a decade with a large team of experts in cancer biology and treatment, that he helped to develop the underlying technology for miRecule.

"When I started my career, RNA therapeutics were relatively new, and the field ran into some major challenges developing therapeutics that could be safe and effective," Saleh said. "At NIH, our team spent a great deal of time to create a technology platform that could overcome these challenges focusing on RNA therapeutics for cancer. But we also knew what we were learning about RNA therapeutics could be applied to a range of other diseases."

In 2016, Saleh left NIH and recruited Robert Place, PhD, and Ashwin Kulkarni, MS, to co-found miRecule with the goal of translating the NIH work into treatments. "We started the company with money from the founders and an investment from my father," he said. "It took us a couple of years to get the company up and running, and to license our technology from NIH." Once they were organized, they designed a new therapeutic for head and neck cancer, and gained some additional early investment and a grant from the government.

About the time the company was launched, one of Saleh's uncles was diagnosed with FSHD. "It was the first I had ever heard of the disorder, so I started to read the scientific and medical literature on it," he said. Then, in 2017, his father, now in his mid-60s, started to experience symptoms and went to see Dr. Rabi Tawil, an FSHD specialist. Saleh's father was also diagnosed with FSHD.

"As I learned more about FSHD, I realized that an RNA therapeutic that could directly prevent expression of DUX4, the protein which causes the underlying muscle toxicity in the disorder, could potentially be a more effective treatment than traditional therapeutics currently being explored," Saleh said.

By 2018, miRecule was doing well. The company was growing, had found additional funding, and its first therapeutic for cancer was progressing through preclinical development.

Shortly after his father's diagnosis, Saleh read a paper by Kathryn Wagner, MD PhD, at the Kennedy Krieger Institute in Baltimore, Maryland, about testing an RNA therapeutic targeting DUX4. He met with Wagner to discuss her research and get himself tested for FSHD. He indeed tested positive. Saleh also came across the research of Yi-Wen Chen, PhD, at Children's National Hospital in Washington, DC, who is also working on RNA therapeutics targeting DUX4. (Both Wagner and Chen have been supported by FSHD Society grants.)

In discussing FSHD within the company, Saleh learned that his co-founder Rob Place had previously worked on RNA therapeutics for other muscle disorders, and Saleh thought miRecule's technology might also work for FSHD. "I have never experienced such a serendipitous situation," Saleh marveled. "Here I was, diagnosed with FSHD along with multiple members of my family, and the best therapeutic strategy to treat FSHD was a technology I had spent my career working on. Additionally, I had two leading experts in the field working on RNA therapeutics for FSHD less than an hour's drive from my company. How could we not work on this therapy?"

In late 2018, miRecule officially started its FSHD program. By this time several more members of Saleh's family had been diagnosed with FSHD. "My father has 11 siblings, and many of them are positive for FSHD. In retrospect, it is obvious that my grandmother's many physical symptoms as she aged were those of FSHD," Saleh said. "I want to see a therapeutic developed not just for my father and myself, but also for the next generation. As we test our kids, I know some of them will have it as well."

The miRecule team (from left to right): Ashwin Kulkarni, Rob Place, Tishan Williams, Ami Bessell, Anthony Saleh, and Charles Marusak

With a strong resolve to take on FSHD, miRecule raised some initial funding from family members, hired a full-time scientist dedicated to FSHD, and began work designing an RNA therapeutic targeting DUX4. Saleh reports that they already have a dozen compounds that can eliminate DUX4 expression in FSHD patient muscle cells in culture, and he hopes to get proof-of-concept data from mouse models of FSHD in the coming months in his collaborations with Wagner's and Chen's groups.

"With luck in our science, in our fundraising, and through our partnerships with organizations like the FSHD Society," said Saleh, "we hope to have a therapeutic in human clinical trials in a few years."

FSHD gene may help tumors evade the immune system

BY ALEXANDRA BELAYEW, MONS, BELGIUM

DUX4, the gene that plays a key role in facioscapulohumeral muscular dystrophy (FSHD), is gaining unexpected notoriety in cancer research. According to a recent study[1] from the Fred Hutchinson Cancer Research Center in Seattle, Washington, gene mutations in tumor cells can cause a re-expression of DUX4 in malignant tissues. What's more, DUX4 expression in cancer cells helps them to escape detection by the immune system and proliferate.

The link between DUX4 and cancer will undoubtedly generate broader interest.

Why does this matter? Cells of our immune system patrol all over our body to detect and destroy foreign invaders and abnormal cells, including cancer. In this process, the cancer cell presents its ID with proteins on its surface, and T cells of the immune system recognize and kill it. However, some cancer cells manage to hide their ID from the immune system and can thus develop larger tumors.

Novel immunotherapy drugs are being developed with the aim of "waking up" the patient's immune cells and driving them to kill cancer cells. Some patients' tumors shrink very well with such drugs, but unfortunately, after one or two years, some cancers don't respond to these drugs anymore, because their cells have acquired new tricks that enable them to hide their ID from the immune cells. The Seattle team has found that reactivation of the (normally silent) DUX4 gene was one of those hiding tricks, and was frequently used in many different cancer types.

For FSHD researchers, this new report is very intriguing. We know that DUX4 expression is toxic to adult skeletal muscle. We know that DUX4 is important in normal development when the gene is expressed in the four-cell embryo, where it is active briefly and then shuts off. Now comes this finding that DUX4 has a very different impact on cancer cells by helping them hide from immune cells.

What does this mean for the FSHD community? Here are several questions that point to some implications:

Is there a link between FSHD and risk of cancer? Increased cancer incidence has not been reported in FSHD, and there are no data to suggest that individuals with FSHD are at higher risk for developing cancers. However, this concern is a reason to evaluate FSHD registries, which have collected health data on FSHD patients and can be periodically analyzed to identify emerging evidence for altered incidence of any specific associated health event.

Could this line of research be beneficial for FSHD? Possibly. Most pharmaceutical companies have very active programs to develop better treatments for cancer. The link between DUX4 and recurring solid tumors will undoubtedly generate interest and lead to additional research funding in this area. These activities may ultimately lead to a cancer therapy targeting DUX4 that could then be adapted for FSHD. More specifically, PRPF8, a novel repressor of the DUX4 gene that was identified in this study, could constitute a new drug target.

Could any of the pending FSHD treatments in development also serve to treat recurring forms of cancer? Possibly. Treatments specifically designed to lower DUX4 in FSHD may have beneficial effects in recurring cancers. Notably, a number of cancer drugs are now being investigated as potential FSHD therapies. These oncology drugs may need to be reexamined in the context of DUX4-expressing tumors.

In addition, new studies could investigate why DUX4 expression doesn't kill cancer cells, while it causes cell death in FSHD muscle. This would identify a protection mechanism that might be of interest in FSHD treatment.

EDITOR'S NOTE

Welcome to our series in which we invite experts to provide fair and balanced commentary on new research. Our stories will appear in FSHD Advocate *and on our blog, and explain why the findings matter to patients and families.*

REFERENCES

1 Chew G-L et al. DUX4 Suppresses MHC Class I to Promote Cancer Immune Evasion and Resistance to Checkpoint Blockade. *Developmental Cell*. 2019;50:1-14.

Newly funded grants

Four novel paths to outwitting FSHD

BY JAMSHID ARJOMAND, JUNE KINOSHITA, AND DANIEL PEREZ, FSHD SOCIETY

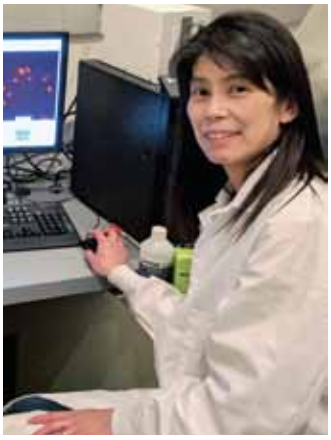
Research funding approved by the FSHD Society board of directors includes $448,000 for four projects from the February 2019 grant cycle.

- **Identification and testing of DUX4 inhibitory compounds**
  Angela Lek, PhD, Yale University, Hartford, Connecticut, USA, and Louis Kunkel, PhD, Boston Children's Hospital, Massachusetts, USA
  $110,000 for one year

Angela Lek, PhD

Harnessing CRISPR technology, Lek found molecular pathways that rescued FSHD muscle cells (in a test tube) from the deadly effects of the DUX4 gene. She identified drugs that mimic this protective effect and is planning to test them in a mouse model of FSHD. "Our aim will be to identify and prioritize testing of compounds with minimal side effects, that are suitable for long-term dosing, and have FDA approval [for other conditions] to ensure a fast route to a clinical trial in patients," she said.

- **Mechanisms of DUX4-induced muscle atrophy**
  Sachiko Homma, PhD, Boston University School of Medicine, Massachusetts, USA
  $158,000 for two years



Sachiko Homma, PhD

The ubiquitin-proteasome system (UPS) is responsible for degrading 80 to 90 percent of proteins in cells, and has been shown to play an important role in mediating muscle atrophy. DUX4 expression in muscle cells changes the expression of many genes involved in the UPS. Homma proposes to identify the possible mechanisms by which DUX4 may promote muscle atrophy. Results of this project might reveal therapeutic targets for DUX4-induced muscle atrophy.

- **New compound discovery targeting ASH1L for FSHD**
  Peter Jones, PhD, University of Nevada, Reno, USA
  $120,000 for one year

Peter Jones, PhD

The Jones lab recently confirmed that the epigenetic regulator ASH1L is a key driver of pathogenic DUX4 expression, and showed that even modest reductions in ASH1L levels greatly reduced DUX4 expression without significantly altering expression of other genes. "We propose that ASH1L is an outstanding FSHD therapeutic target," said Jones. The lab intends to identify promising lead inhibitors of ASH1L activity.

- **Study of the coregulatory role of DUX4 on sex hormone nuclear receptors and the protective effect of sex hormones on DUX4-mediated cell toxicity**
  Sabrina Pagnoni, PhD candidate, and Alberto Rosa, MD PhD, IRNASUS, Catholic University of Cordoba, Argentina
  $60,000 for one year

Sabrina Pagnoni, PhD candidate

Female FSHD patients are clinically less affected than males and represent a higher proportion of asymptomatic carriers. Progesterone is a key female hormone involved in regulating the uterine lining. The lab found that DUX4 is a co-repressor of the progesterone nuclear receptor (NR) in various cell models. These results suggested that DUX4 could indirectly modulate gene expression by repressing the activity of the progesterone NRs, a previously unrecognized role for DUX4.

My journey to become a forensic psychologist

A former singer, model, and interior designer, Heather Green embarked on a new career when her diagnosis with FSHD forced her to reassess her future. Childhood memories of a small-town murder mystery reawakened her fascination with crime, and Heather decided to pursue degrees in forensic sciences and psychology. She has researched stalkers, worked on high-profile cases, and is counseling violent offenders in a California state prison. You won't want to miss her incredible blog post.
https://www.fshdsociety.org/2019/08/forensic/

Heather Green

Tips & tricks: Travel Scoot

A few years ago, Bill Maclean purchased a Travel Scoot, and says it has been an excellent investment. He has traveled the world with it and uses it for any type of event that requires some walking. The Travel Scoot is fully qualified for airline travel. It can be gate-checked, and the battery can be carried onto the plane. Fully assembled, the current version weighs about 35 pounds. The body can be collapsed, so it can fit in a standard vehicle trunk. Bill shares his experiences and product details on our blog.
https://www.fshdsociety.org/2019/08/travel-scoot-2/

What's at *www.fshdsociety.org*?

RESOURCES TO DOWNLOAD:

- About FSHD
- Physical Therapy and Exercise
- A Guide for Schools
- An Overview of Anesthetic Concerns

YOUTUBE HITS:

- Muscle activation, massage, and Rolf technique
- CBD and medical marijuana
- Facial surgery methods for FSHD
- Scapulothoracic surgery for FSHD

ABLE accounts

Some consider the Stephen Beck Jr. Achieving a Better Life Experience (ABLE) Act to be the most significant federal legislation for disabled individuals since the Americans with Disabilities Act (ADA) of 1990. Signed into law by President Obama in December 2014, the ABLE Act established tax-advantaged savings accounts that enable eligible individuals to set aside funds to cover the significant costs of living with a disability without incurring taxes on income earned by the fund. Learn whether you are eligible by reading our article by Chris Stenmon, CPA.
https://www.fshdsociety.org/2019/10/able/

ABLE
Achieving a Better Life Experience

Acceleron halts ACE-083 for FSHD

Acceleron Pharma Inc. announced on September 16, 2019, that treatment with ACE-083 in patients with facioscapulohumeral muscular dystrophy (FSHD) did not achieve functional secondary endpoints in the Phase 2 trial.

"Although ACE-083 demonstrated a robust, statistically significant increase in mean total muscle volume, the primary endpoint of the trial, the increase failed to translate to statistically significant improvements in functional tests," the company reported. "As a result, Acceleron will not conduct further clinical trials of ACE-083 in FSHD."

We are grateful to all patients who volunteered. The speed with which Acceleron was able to complete the trial is encouraging for other companies that are thinking about developing FSHD treatments. A well-run trial with good data adds to scientific knowledge and speeds up progress across the board, even if specific trial results may be disappointing.

Medicare coverage for maintenance physical therapy

A common misconception is that Medicare will only cover physical therapy (PT) when a patient is improving (getting stronger, moving more independently, gaining flexibility). Often physical therapists discharge patients because they do not realize that ongoing skilled maintenance therapy is covered by Medicare. If your therapist feels that PT is needed to maintain your current function and slow your decline, Medicare will cover it. Melissa Fox, PT DPT, of the University of Virginia Health System provides a useful guide to getting the coverage you need. *https://www.fshdsociety.org/2019/05/maintenance_pt/*

Upcoming

Visit *www.fshdsociety.org/events/events-calendar/* for details and updates.

CONFERENCES

November 16, New York, NY
New York City FSHD Family Day Conference

June 25-26, 2020, Washington, DC
27th annual FSHD International Research Congress

June 27-28, 2020, Washington, DC
FSHD Connect

FUNDRAISERS

November 16, Greenville, SC
2019 FSHD fundraiser in honor of Zachary

July 11, 2020, San Diego, CA
San Diego Walk & Roll

October 22-November 24
Win a VIP trip to experience pop-up sets from the hit show *Schitt's Creek,* in NYC. Look for star Dan Levy's Omaze campaign on our Facebook page.

CHAPTER AND LOCAL MEETINGS

November 2, Naples, FL
Southwest Florida chapter launch meeting

November 2, Austin, TX
Austin support group meeting

November 4, web conference
Dr. David Younger on CT Connections

November 9, Barrington, IL
Chicagoland chapter meeting

November 9, Durham, NC
North Carolina chapter meeting

November 9, Lone Tree, CO
Colorado chapter meeting

November 10, Fairway, KS
Kansas City chapter meeting

December 7, Daytona Beach, FL
Daytona Beach chapter meeting

WEBINARS

December 7, The ABC's of Clinical Trials
With Rabi Tawil, MD, University of Rochester

VIRTUAL MEETINGS

FSHD Society Radio
Broadcasts on Facebook Live are usually on the last Wednesday of every month at 9 p.m. EST (8 p.m. CST). Podcasts are recorded and available in the video section of the FSHD Society Facebook page.

Connecticut Connections
Open to all New Englanders (and beyond), this chapter meets via web conference on the first Thursday of each month (except in summer), 7–8:30 p.m. EST.

Wisconsin Chapter Virtual Meetings
Serving not only Wisconsin but also Michigan and Minnesota, this chapter meets via web conference on the first Monday of each month at 8–9:30 p.m. CST.

Western Washington FSHD Community
Meets via web conference on the fourth Saturday of each month (except in December), 10 a.m. PST.

FSHD Advocate

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THE. FUTURE. IS. NOW.

This year, the FSHD Society — **empowered by you** — launched an aggressive plan to accelerate therapeutic development for FSHD. We have brought together pharmaceutical companies, researchers, government agencies, and families in a working collaborative with the goal of **delivering disease-modifying therapies by 2025.**

Yes, the future is now. And the future is in powerful hands…yours. While we are confident that together we are strong enough, our goals will take the best of us and the best from us over the next three years. Our board of directors has risen to the task, pledging $500,000 toward our year-end goal and challenging the rest of the community to match it. Will you deepen your commitment to our collective mission by considering an "over and above" gift to help us reach this goal?

One Million Dollar Goal
Your year-end donation counts toward our $500,000 matching gift challenge!

- Donate at: *fshdsociety.org*
- Mail a check to:
  FSHD Society
  450 Bedford Street
  Lexington, MA 02420
- Call 781.301.7301