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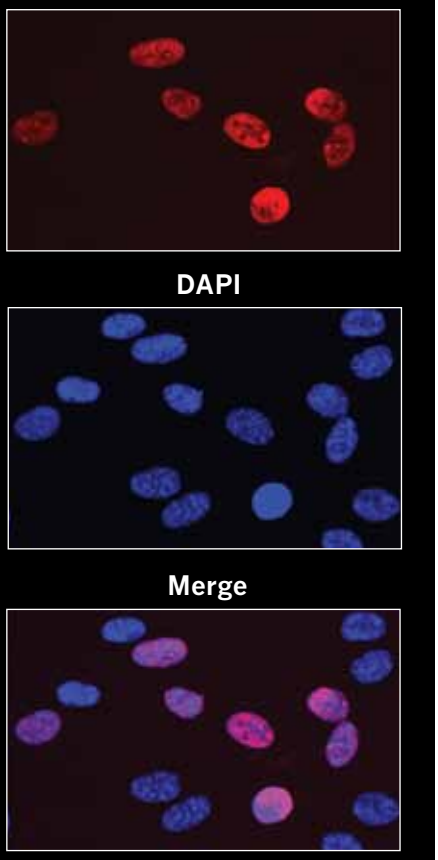
FSH Watch

ISSUE 3 • 2016

FSH SOCIETY
FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY

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

ANNUAL RESEARCH REPORT page 4



These images demonstrate that SMCHD1 (associated with FSHD Type 2, artificially introduced into these cells by a virus) resulted in robust SMCHD1 expression (red) in muscle cell nuclei. The presence of DAPI (blue) confirms these are muscle cell nuclei. Merging the two images shows that SMCHD1 is being expressed in muscle cell nuclei (overlap appears purple). Image courtesy of Yosuke Hiramuki. See story on page 5.

Kathryn Wagner, MD PhD, and Allen Carney in pre-op for bicep muscle biopsy, April 7, 2016, at Johns Hopkins Outpatient Surgery Center, Baltimore, Maryland.

RESEARCH

Informed Consent Authorization

Volunteering for science is a kind of heroism

by **SUSAN W. MAYES**
Fayetteville, Arkansas

The title of my story comes from the 12-page document that my husband typically initials in several places and signs in order to participate in a research project.

Welcome to the world of giving your time and body for research for FSHD! My husband, Allen Carney, has now participated in at least five research projects in three different cities to help researchers investigate facioscapulohumeral muscular dystrophy (FSHD).

Allen has FSHD and, true to his Eagle Scout spirit, he feels compelled to be a part of research projects to try and expedite the eventual development of FSHD treatment. It is one thing to watch and try to understand the research projects (my role). It is an entirely different experience to give samples of blood and tissue for these studies (Allen's role).

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WHAT'S INSIDE

FSH SOCIETY
FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY

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Washington, DC Counsel
Morgan Downey

Chief Science Officer
Daniel Paul Perez
daniel.perez@fshsociety.org

Executive Director & Chief Operating Officer
June Kinoshita
june.kinoshita@fshsociety.org

Director of Finance and Administration
Lisa Schimmel
lisa.schimmel@fshsociety.org

Development Officer
Beth Johnston
beth.johnston@fshsociety.org

Executive Assistant
Robyn O'Leary
robyn.oleary@fshsociety.org

Gifts and Membership
Kathryn Puzzanghera
kathryn.puzzanghera@fshsociety.org

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

Reflecting on the first 25 years

Dear Friends,

Daniel Paul Perez

The FSH Society at the outset was driven by a simple goal: my curiosity to find out what causes FSH muscular dystrophy, learn how it works, and stop or change the course of the disease. I have been interested in FSHD research since 1987, always with the belief that sufficient funding of research on the fundamental molecular biology and genetics of the disease would ultimately lead to treatments and a cure. In my naiveté, I believed this would take five or at most 10 years of fundraising, advocacy to increase NIH funding, and research effort, and then I could get back to my life, scooter free and wheelchair free.

I have served as president and CEO for 25 years now. The Society has provided the funding, stewardship, advocacy, and the foundation to allow us to understand exactly how FSHD works. Since the Society's inception, we have been involved in the evolution and design of FSHD gene mapping and genetics. We have nurtured the relationship between our scientific community and the larger societal context in which FSHD is embedded. Without the Society, there would be no patient advocacy, we would have no say in policy, and the MD-CARE Act would not include adult dystrophies like FSHD.

The Society's work was driven by the passion, dedication, and the extremely long hours of a small group of people committed to change. For several years, it was me and my parents Carol and Charles Perez, working from home in our spare time, who made things happen. Today, we are six employees strong working full-time in our own offices. Today, the FSH Society's work and research funding spans nearly every lab working on the disease, and leads the way on tactical and strategic planning into understanding FSHD and how it might be treated.

Our success is due in large part to the efforts of our Scientific Advisory Board (SAB), led by Professor David Housman of the Massachusetts Institute of Technology, who give selflessly of their knowledge to bring about insight into FSHD. Our Board of Directors is also key to our success and works tirelessly without remuneration to guide the organization and raise funds. Our members each contribute in their own ways, by volunteering for research, donating DNA and muscle tissue, by hosting or participating in fundraisers, or simply by keeping in communication with other members to make the burden of living with FSHD easier to bear.

These successes notwithstanding, it remains a daily challenge to attain the public awareness and funds we need to survive and grow. We must keep research, education, and advocacy moving forward. As a community of individuals living with FSHD, who have lost so many loved ones to FSHD, we honor the memories of those who are no longer with us by moving to a higher level of biological understanding, translation, and treatments for this disease. Our progress is due to the combined efforts we have all made over the past 25 years—efforts that will continue, with your support, until FSHD is solved.

Sincerely,

Daniel Paul Perez
President & CEO

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

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

Look for us on the Internet at:
https://www.fshsociety.org.

EDITORS: June Kinoshita, Daniel Paul Perez
COPY EDITOR: Elaine Alibrandi
EDITORIAL ASSISTANCE: Robyn O'Leary
GRAPHIC DESIGN: Leslie Anne Feagley
PRINTING AND MAILING: ShelDon

Breaking my silence

Learning to live fully with FSHD

by KATIE RUEKERT
Castle Rock, Colorado

We all experience it when diagnosed with a disease that has no treatment or cure—an overwhelming, profound sense of hopelessness. Life will never be the same after you hear a doctor say, "You have FSH muscular dystrophy."

I left that doctor's room in disbelief and tears in March of 2011, at the age of 30. I didn't know where to begin to wrap my head around the fact that there was nothing I could do to make it go away or slow it down. How is this possible? A huge part of my identity resided in physical activity, and now I was told to stop all of that?

My head started to spin in a million different directions. At first I denied it. I tried to convince myself I was different from all the others who have FSHD, and it wouldn't affect me. I told myself, I'll work out harder. But what if working out makes it progress faster, like the doctor had told me? I was in a state of panic, anxiety, and depression. I pleaded to God, the Universe, and my Mom, basically anyone looking over me, to take it away.

I grieved for my passion for long-distance running, an activity that had been like a best friend to me for the past 15 years. Suddenly, it was ripped away from me as my leg muscles became weaker. I was completely lost from the self I once knew. The unenviable began to happen. My body was, in fact, getting weaker, and things that I had once done without even thinking about were becoming more challenging.

I am no different from anyone else living with this disease. I tried to open up about it with family and friends, but oftentimes I would hear, "I don't understand what you are going through," or "You look fine," which only invalidated my reality. Often, the topic was shut down altogether, especially from my very own family.

The standard had been set 10 years earlier when one of my male family members was diagnosed with "FSH" and my family completely swept it under the rug, and it was never discussed. Because of this, I had no clue about the severity of this disease or what it entailed. As far as I knew at 20 years old (and untouchable as many of us think at this age), I should have already been showing symptoms; plus, I was a female and was told this can only happen to males.

Living with FSHD was devastating enough, but not being able to talk about it or have friends and family relate to my experience sent me into a dark depression, so much that I often thought about ending it all. Not only was I starting to feel trapped in my once abled body, but I was also feeling trapped in my emotions centered around FSHD and completely disconnected from friends and family. It was extremely difficult to relay to someone the complexity about something I was still trying to understand myself. I was hitting rock bottom, and felt worthless and constantly questioned my purpose on this earth.

When I was six years old, I lost my Mom to ovarian cancer. Growing up, I wanted nothing more than to be the mom that was taken away from me. I have been blessed with two amazing boys. My dream that I longed for for so long had come true.

When FSHD showed up, my older son had just turned three, and my younger was less than a year old. Being a mother, and now knowing I have a horrible genetic disease, brings up a whole other set of deep emotions (a separate topic for a separate blog, indeed).

In my darkest moments with FSHD, the thought of leaving these two was never an option. As badly as I wanted to end my life, I was also more than aware of the challenges of growing up without a mother. These two little angels saved my life, and the fact that I lost my mother early in life was starting to make a bit of sense, perhaps to save me and to do something great in this lifetime.

Rock bottom was an extremely scary place to encounter, but it led to some pretty amazing and unforeseeable outcomes. In the fall of 2014, I decided it was time to meet others living with FSHD. I swallowed the hard fact that my friends and family were not going to be the deep areas of support I so clearly needed.

> *"Rock bottom was an extremely scary place to encounter, but it led to some pretty amazing and unforeseeable outcomes. In the fall of 2014, I decided it was time to meet others living with FSHD."*
>
> KATIE RUEKERT

I wasn't sure how an organization on the other side of the nation was going to provide me support, but I reached out to the FSH Society. To my surprise, one of the Society's board members, Beth Johnston, had just moved back to Colorado and was starting an advocacy group for those living with FSHD in the Denver area. FINALLY, a sign!!!

My husband and our two boys attended our first meeting the next month. I was terrified, but I finally looked fear in the face and was too depleted to focus on the scary "what ifs."

I came home from that first meeting with mixed emotions. Although I met some amazing people and finally started to feel a sense of connection again, I still couldn't believe this was my life. At the time, I would still much rather have been attending a spinning, mountain biking, 14er climbing, skiing, or running group. After all, that was still my identity, and I was having a really tough time making the transition.

I continued to attend the quarterly advocacy meetings and would sometimes

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BASIC SCIENCE AWARDS

Unraveling the enduring mysteries of FSHD

by **JUNE KINOSHITA**
FSH Society

Even as drug companies pursue therapies aimed at the DUX4 gene, a key player in causing FSHD, there is very little that is understood about exactly how the DUX4 gene and protein behave in cells and result in the path of destruction that leads to the symptoms of FSHD. Such knowledge will prove critically important to ensure that future treatments are targeting the right disease-causing processes, avoiding unintended side effects, and inclusive of diverse strategies that could be more practical and safe. The projects described in this annual report are in addition to the newly funded grants listed in the previous issue of *FSH Watch*.

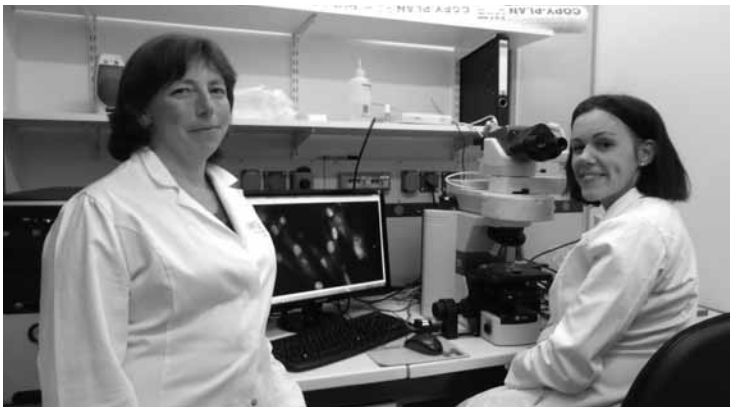
FUNCTIONAL STUDY OF THE DUX4 AND DUX4C DOUBLE HOMEODOMAIN PROTEINS IN SKELETAL MUSCLE

Eugénie Ansseau, with Frédérique Coppée and Alexandra Belayew, Université de Mons, Belgium
$93,450 for one year

The DUX4 protein can kill muscle cells. Researchers investigate DUX4 function in the cell nucleus, where it acts as a crazy chef and activates a number of genes normally only used in testis. A DUX4-like but not toxic protein named DUX4c is also increased in FSHD.

We unexpectedly observed DUX4/4c leave the nucleus for the cytoplasm at the time muscle cells fuse to make fibers. We also identified cytoplasmic proteins binding to DUX4/4c and involved in organizing the cell skeleton, or the structures that mediate muscle contraction.

Genes are recipes to make proteins, and are copied into messenger RNAs (mRNAs) that carry the recipes out of the cell nucleus to the protein building places. Some of the DUX4/4c protein partners we identified are part of granules that contain inactive mRNAs, exit the nucleus, travel along the cell skeleton, and bring their mRNAs



Frédérique Coppée (left) and Eugénie Ansseau (right).

to the cell membrane as needed for protein synthesis during muscle fiber construction.

With FSH Society funding, we have already confirmed the interaction between DUX4/4c and five granule-associated proteins. Our discovery of unexpected functions outside of the nucleus opens new perspectives to understand DUX4 toxicity and the normal role of DUX4c in muscle regeneration, and could suggest new therapeutic strategies.

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

Yosuke Hiramuki; Stephen Tapscott, mentor, Fred Hutchinson Cancer Research Center, Seattle, Washington

$101,132 for two years; FSH Society/FSHD Canada Foundation research fellowship

FSHD has two types: FSHD1 and FSHD2. FSHD1 is caused by contraction of a repeated DNA sequence called D4Z4, whereas FSHD2 is the result of mutations in the SMCHD1 gene. In addition, SMCHD1 modifies disease severity in families affected by FSHD1.

SMCHD1 binds to the D4Z4 region to help repress abnormal expression of the gene called DUX4, which is toxic to skeletal muscle. Two key milestones in this project are to identify how manipulating the level of SMCHD1 could affect the expression of DUX4 in FSHD muscle cells and why SMCHD1 protein decreases in muscle cells.

To study this, I made an engineered virus to introduce SMCHD1 into muscle cells and have confirmed that they are functional. For example, to confirm that a virus expressed the full SMCHD1 protein, I used a microscope to visualize SMCHD1 and showed that there was extra SMCHD1 produced by the virus (see figure on page 1).

As a next step, I am now investigating whether regions of SMCHD1 will suppress DUX4 expression or lead to loss of SMCHD1 in muscle cells. I hope to develop a therapeutic approach to inhibit abnormal DUX4 expression with extra SMCHD1.

▶ PROTEIN CHEMISTRY AND PROTEIN-PROTEIN INTERACTIONS OF DUX4 AND DUX4 FSHD MOUSE

Jocelyn Eidahl; Scott Harper, mentor, Nationwide Children's Hospital, Columbus, Ohio

$70,000 (request one-year extension)

Our lab is dedicated to studying the protein chemistry of DUX4, the molecule that causes muscle damage in people with FSHD.

We first asked whether DUX4 could be modified. Modifications are added by other proteins and can alter how a protein carries out its role in a cell. For example, the presence of modifications could cause the DUX4 protein to move to a different area in a cell or alter how it binds to other proteins or DNA.

Jocelyn Eidahl, PhD

Our lab has first identified that the DUX4 protein has these modifications, and our proposed research plan is to focus on understanding how they could be involved in FSHD progression. If we determine DUX4 needs one of these modifications to cause muscle damage, we can then begin to develop therapies to prevent these from occurring and thus prevent the muscle damage.

A second area of focus has been to identify cofactors of DUX4 that help cause muscle damage. Often, when proteins bind DNA as DUX4 does, they do not bind alone but with the help of other molecules, which are called cofactor proteins. We believe it is important to identify these cofactors and determine whether they are working with DUX4 to cause muscle damage.

The details regarding the physical interaction between DUX4 and cofactor proteins are necessary for successful FSHD drug development. We are hopeful that our research will uncover important details about the role of DUX4 in muscle damage and help aid in developing treatments for FSHD.

▶ INHIBITED PROTEIN TURNOVER IN FSHD PATHOGENESIS

Sachiko Homma and Jeffrey Boone Miller, Boston University, Massachusetts

$68,920 for one year

In healthy cells, unnecessary or defective proteins are removed by structures called proteasomes. When proteasomes stop working as they should, however, abnormal proteins can accumulate, sometimes as aggregates. Decreased proteasome function accompanied by abnormal protein accumulation has been implicated in the pathogenesis of many neurodegenerative diseases including amyotrophic lateral sclerosis (ALS).

FSHD is caused by genetic and epigenetic changes that promote aberrant expression of a full-length isoform of DUX4 (DUX4-FL). We are testing the hypothesis that DUX4-FL can cause abnormal protein aggregation and/or decrease proteasome function.

In our studies, we use cultures of muscle cells derived from individuals with FSHD. We discovered that DUX4-FL induced abnormal

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Unraveling the enduring mysteries of FSHD

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aggregation of two proteins called TDP-43 and FUS, both of which are associated with ALS. DUX4-FL also decreased proteasome activity and altered the intracellular distribution of ubiquitin, which binds to abnormal proteins and sends them to the proteasome.

We are now trying to determine 1) if loss of proteasome function contributes to FSHD pathology, and 2) if FSHD muscle biopsies show aggregation of TDP-43 and/or FUS as well as abnormal ubiquitin expression.

Our findings could reveal mechanistic links between FSHD and neurodegenerative diseases such as ALS and could lead to clinical trials for FSHD with available therapeutics.

A GENOME-WIDE CRISPR KNOCK-OUT STRATEGY TO IDENTIFY MODIFIERS OF FSHD

Angela Lek; Louis Kunkel, mentor, Boston Children's Hospital, Massachusetts

$78,000 for one year

Lately I have had my hands full working with an exciting new gene-editing technology called CRISPR that helps me to narrow down which of 20,000 human genes are involved in causing muscle toxicity in FSHD. CRISPR gene editing lets me silence one gene at a time, and then assess whether disease conditions can be improved.

My hope is that this knowledge will help us figure out the genetic changes behind the muscle weakness in FSHD, and why some patients are more affected than others.

I am almost ready to take my cell model findings to a living, breathing model of FSHD—our zebrafish! In our lab, we have spent quite a bit of time tweaking our zebrafish model so that it best mimics the symptoms of human FSHD.

Together with the help of my trusty lab mates, we will gene-edit zebrafish embryos to see if we can eliminate the muscle weakness causing their FSHD-like symptoms. If this works, it means we'll have a potential gene that we can target for therapy in FSHD patients. Fingers crossed!

A day in the life of Angela Lek, PhD: growing, feeding, and performing gene-editing experiments on her cells.

From left: Hernan Paci, Maria Laura Raymond, Julieta Quintero, Alberto Rosa, Sabrina Pagnoni, and Constanza Cioffi.

STUDY OF THE CO-REGULATORY ROLE OF DUX4 ON SEX HORMONE NUCLEAR RECEPTORS AND THE PROTECTIVE EFFECT OF SEX HORMONES ON DUX4-MEDIATED CELL TOXICITY

Sabrina Pagnoni and Constanza Cioffi; Alberto Rosa, mentor Catholic University of Cordoba (UCC)/National Research Council from Argentina (CONICET)

$120,000 for two years

Cumulative research evidence suggests that the muscles from FSHD patients are affected because of the abnormal presence of the protein named DUX4. With the aim to protect muscle cells in FSHD patients, several research laboratories are exploring rational therapeutic strategies based on a biological control of DUX4. Although the normal function of DUX4 is currently unknown, several research groups are shedding light on its various biological roles.

Our laboratory particularly investigates the participation of

DUX4 in the normal human endocrine pathway, a potentially relevant yet unexplored role of DUX4. We have obtained experimental evidence indicating that DUX4 may control the normal activity of specific hormone "receptors" in the cells. Interestingly, we also discovered that some human hormones protect laboratory cultured cells from the dramatic toxic effects of DUX4.

We are currently exploring details of this potential normal function of DUX4 in the endocrine system as well as the potential protective effect of hormones from the toxicity of DUX4.

These studies would contribute to the understanding of the normal role(s) of DUX4, its pathogenic participation in the development of FSHD as well as to the future development of therapeutic strategies for the treatment of FSHD patients.

▶ FSH SOCIETY-NDRI TISSUE PROCUREMENT PROJECT

National Disease Research Interchange (NDRI), Philadelphia, Pennsylvania
$43,943 for first year

Human tissue research is critical to understanding how diseases such as FSHD progress and respond to treatments. Recent researcher surveys conducted by the FSH Society show that investigators studying FSHD request human tissues to support their research studies. Additionally, patient surveys demonstrate an overwhelming willingness to donate tissues and organs for research. Through an FSH Society grant in 2016, the National Disease Research Interchange (NDRI) has been working collaboratively to develop a process where patients have the opportunity to donate tissues for research purposes after surgery or death. These gifts will support research into FSHD and will provide a chance to leave a lasting impact on future generations by helping scientists test breakthrough theories and develop new medications to help treat and ultimately cure FSHD.

Through the "FSH Society-NDRI Tissue Procurement Project," patients now have the opportunity to help further research in order to reach this goal. NDRI's donor registration program allows FSHD patients an opportunity to indicate their wishes and provide consent for donation following a scheduled surgery or after death.

The NDRI and the FSH Society have created a brochure for potential tissue donors which will help you understand the steps necessary to become a FSHD research tissue donor. The NDRI is currently in the process of registering researchers to receive these very important research samples. We are proud to be working to support FSHD patients and researchers on this very important research endeavor. FSHWatch

BREAKING MY SILENCE

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come home in tears, saying I wasn't going back, but not having any family to confide in, and not wanting to burden my friends, I kept on going. I knew I needed to talk about it.

In the meantime, I kept on with my now-modified workout routine. Instead of running, spinning, and weight lifting, my routine was filled with yoga, Pilates, and outdoor walks. As much as I mourned my once-loved passions, at the same time I was beyond grateful that my legs were still strong enough to walk long distances.

Volunteers turned out in force for the Colorado Walk & Roll. A good time was had by all!

I learned to allow my feet to kiss the ground that I was walking on. On my walks, I would often fantasize about all the courses I used to run and even the ones I someday would do should a treatment or cure be found. This eventually led to fantasies about doing something physically active to raise awareness for FSHD, but it was a fantasy that would come and go as I continued to talk myself out of it.

I had a billion excuses. I'm too much of an introvert to do something like this. Nobody would come to my fundraiser. I know nothing about fundraising. It's too much work. I just want to be a "normal" mom and wife. I don't want to fully expose myself to the world. People will judge me. This disease is already humiliating enough. Etc.

However, something inside me kept resurfacing as much as I tried to suppress these feelings about bringing awareness to FSHD. I had already faced so much rejection from wanting to fully talk about FSHD. I didn't want to face it on a much larger scale.

Without being able to explain it, I felt there was a greater force from within, and I could no longer deny my worth and purpose on this earth: I was chosen to have FSHD because I AM capable of stepping outside my fear for the sake of others. I was finally going to come out from hiding and talk about FSHD, and not let a single thing stand in my way. After all, what did I have to lose other than my muscles, which was already happening?

I had become inspired by others living fully with FSHD, such as Daniel Perez, Carden Wyckoff, Doug and Gracie, and Chris Carrino. I showed up to our advocacy meeting in October of 2015 to present my idea to start a fundraiser to raise awareness and funds to help cure FSHD. I was fortunate enough to have some really amazing people from our advocacy group join me.

Our fundraising committee started meeting the following month, and less than a year of hard work and dedication later, the first Colorado Walk & Roll to Cure FSHD was born!

As I mentioned earlier, I knew nothing about fundraising before this. My ambition was driven from passion and a strong de-

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ADVANCING TOWARD TREATMENTS

From molecules and mice to medicine

Your donations are supporting research projects that are advancing the chess pieces toward treatment. A number of projects aim to block expression of the DUX4 gene, which is widely regarded as a key cause of FSHD. Your gifts fund research to develop new experimental models—cell and tissue cultures and animals—that shed light on how FSHD damages muscles, and which can be used to identify drugs and test new treatment strategies. The funds you contribute are also being invested in new tools to measure muscle function and the FSHD Clinical Trial Research Network. Researchers funded by the FSH Society from our 2015 grant cycles share their progress with you below.

INVESTIGATION OF 4-METHYLUMBELLIFERONE AS A C1QBP-TARGETING FSHD THERAPEUTIC

Alec DeSimone; Charles Emerson, mentor, UMass Medical School, Worcester

$150,000 for two years

My FSH Society-funded project is focused on evaluating the potential for 4-methylumbelliferone, or 4MU, to serve as an FSHD therapeutic. I began my project by searching for cofactors that might affect the function of DUX4, the FSHD disease gene, and that might therefore be targets for FSHD therapeutics.

I identified C1QBP as a protein that physically interacts with

Alec DeSimone, PhD

DUX4, and I recently discovered that it acts as a kind of inhibitor that slows down DUX4 function. This raises the possibility that increasing C1QBP activity might help mitigate the disease-causing effects of DUX4.

C1QBP is an excellent drug target, because the cellular pathways that regulate its function can be affected by exposing cells to 4MU, and I have seen that adding 4MU to cells in culture inhibits DUX4 activity, presumably by increasing the activity of C1QBP.

We are particularly excited by this observation, because 4MU is already an approved drug in Europe (for other indications) and has an established safety record, making it an excellent candidate therapeutic.

My goal for this project is to learn exactly how exposing cells to 4MU affects DUX4 and C1QBP. This will help us determine if 4MU is a suitable FSHD drug, and may also help us develop other therapeutics that affect C1QBP in similar ways. I then hope to use mouse models to determine if 4MU is effective in a living, breathing animal.

▶ DEVELOPMENT OF ANTISENSE OLIGONUCLEOTIDE DRUGS AS THERAPEUTIC AGENTS FOR FSHD

Julie Dumonceaux, Association Institut de Myologie, Paris, France
$94,606 for 1.5 years

Julie Dumonceaux, PhD, currently at University of London.

In 2015, I was lucky enough to obtain a grant from the FSH Society for the research my group is currently carrying out on FSHD in collaboration with George Dickson's lab at Royal Holloway, University of London.

During the last decade, it became more and more evident to the scientific community that the DUX4 protein is aberrantly expressed in FSHD patients and might play a key role in FSHD onset or progression. Therefore, our aim was to develop a new therapeutic approach for FSHD by inhibiting DUX4 synthesis in FSHD muscle.

We have imagined, designed, and set up a new gene-silencing approach targeting DUX4 and made the proof of principle of its efficacy in muscle cells (Marsollier et al., 2016).

As a next step toward a clinical trial, we must test our therapeutic strategy in vivo (in living animals). The grant we received from the FSH Society allows us to pursue this research. We are extremely enthusiastic about this approach and strongly believe in this therapeutic strategy.

Reference

Marsollier AC, Ciszewski L, Mariot V, Popplewell L, Voit T, Dickson G, Dumonceaux J. Antisense targeting of 3' end elements involved in DUX4 mRNA processing is an efficient therapeutic strategy for facioscapulohumeral dystrophy: a new gene-silencing approach. *Hum Mol Genet.* 2016 Apr 15;25(8):1468-78.

▶ CHARACTERIZATION OF A TAMOXIFEN-INDUCIBLE DUX4 KNOCKIN MOUSE

Scott Harper, Nationwide Children's Hospital, Columbus, Ohio
$25,000 for three- to six-month bridge funding

Scott Harper, PhD

FSHD is caused by expression of the toxic DUX4 gene in muscle, and so strategies for treatments should focus on reducing or turning off DUX4.

Before new treatments can be developed for use in humans, they must first be tested in animal models to ensure that they 1) work and 2) are safe. In the case of FSHD, this would ideally mean having an animal model that expresses DUX4 and has diseased muscles, which could then be treated with an anti-DUX4 therapy to determine if muscle damage and weakness can be reduced or prevented.

Mice have been created that contain the human DUX4 gene in their chromosomes, but the ones available now do not develop muscle weakness, or they die before birth.

With seed funding from the Muscular Dystrophy Association, we initiated a project in 2009 to develop a DUX4 mouse model that develops muscle damage and weakness, but we encountered a number of setbacks along the way. One of the problems is that DUX4 is a very toxic gene, and it can interfere with normal

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mouse development, and this fact made it difficult to generate viable animals.

We were unable to produce the mouse in the three-year funding period provided by the MDA, but we persisted and, in December 2015, finally generated the model. The FSH Society then granted us funds to help expand the line, characterize the mice, and eventually distribute it to labs within the FSHD research community who want it for testing therapies or to study DUX4 biology. Importantly, these new mice are viable, and develop obvious muscle weakness and damage. Thanks to the FSH Society, we are now poised to publish the model and make it available to the larger FSHD research community. We hope that this line of mice will help advance therapy development.

EXPLOITING GENOME EDITING TECHNOLOGY TO MODIFY AND REGULATE THE FSHD DISEASE LOCUS

Michael Kyba, Lillehei Heart Institute, University of Minnesota, Minneapolis

$125,000 over one year; FSH Society/FSHD Canada Foundation research fellowship

Michael Kyba, PhD

FSHD is caused by mutations, which are changes to the DNA sequence of the human genome. One approach to reversing FSHD, at least at the cellular level, is to reverse or compensate for the change in the DNA by a further change.

The technology to engineer directed changes to the genome has undergone rapid development over the past decade, and this project focused on using two approaches to "edit" the DNA sequence of cells from FSHD-affected individuals in the petri dish. Since FSHD is caused by large deletions, it is still impractical to put back all of the sequence that is missing; therefore, rather than reverse the mutation, we have focused on alterations that should abolish the effect of the mutation.

In the first approach, we have edited a sequence, downstream of the DUX4 gene, which is necessary for expression of DUX4. We have deleted this important sequence in cells and evaluated the effect on the expression of DUX4.

In the second approach, we have attempted to remove the entire DUX4 gene. Because completely unaffected individuals exist with only one copy of the DUX4 gene locus, the removal of the FSHD-associated copy should not be deleterious.

The project has been successful: We have developed the tools to make these changes and have edited the DUX4 gene in cells. We are now working with these cell lines to understand the effects of these genetic changes.

TO DETERMINE THE INITIAL RESPONSIVENESS TO FSHD DISEASE PROGRESSION OF A SYSTEM OF SYNCHRONIZED WIRELESS MOTION SENSORS

Jeffrey Statland, University of Kansas Medical Center, Kansas City

$39,044 for one year

Jeffrey Statland, MD

Monitoring functional motor tasks such as getting up from a chair and walking may reveal a continuum of motor disability that predicts, only when it reaches a threshold value, future motor disability. This study is designed to test the feasibility, reliability, and association to other measures of FSHD of a commercially available, portable, wireless motion analysis system.

The system measures how fast people walk, how far they go with each step, and the range of motion of their arms, legs, and trunk. Our plan is to follow 20 individuals for one year.

We have tested the system in 20 individuals at baseline, 18 have returned for reliability testing within one week, and 10 have returned for six-month follow-up visits.

So far, the system appears to be reliable, meaning what we measure one day we can measure the next. Simple things like measuring how fast someone walks appear to correspond to overall disease severity and can distinguish someone with mild disease from someone with more severe disease. Such an approach may be useful in a clinical trial where small, incremental changes in motor performance over short timespans like three months might predict further improvement over longer durations like one to two years.

TO EXPEDITE THE DEVELOPMENT OF NEW THERAPIES FOR FSHD BY DEVELOPING A CORE FSHD CLINICAL TRIAL RESEARCH NETWORK (CTRN)

Jeffrey Statland, University of Kansas Medical Center, Kansas City

$121,000 for one year

The overall goal of this project is to expedite the development of new therapies for FSHD by creating a core FSHD Clinical Trial Research Network (CTRN). The network covers a broad geographical region across the United States and includes the following academic centers: University of Kansas, University of

University of Kansas Medical Center, Clinical Research Center, Kansas City

Rochester, Kennedy Krieger Institute, Ohio State University, University of Utah, University of Washington, and University of California, Los Angeles.

The primary aims of the network are to 1) establish a common regulatory, data, and biostatistical infrastructure; 2) engage patients and industry to ensure all major stakeholders have a voice in CTRN activities; and 3) develop clinical trial strategies to improve the efficiency and reduce the burden on patients for future clinical trials.

So far, the FSHD CTRN has achieved a number of year 1 milestones, including the following: 1) we convened a national conference of clinical evaluators to develop standard procedures for common FSHD strength and functional outcome assessments; 2) we have assembled an advisory board which includes clinical trialists, representatives from industry, and patient representatives; 3) we have started the process of streamlining regulatory oversight by leveraging initiatives like the National Center for Advancing Translational Science IRB Reliance Platform; and 4) we have submitted grant proposals to help refine FSHD clinical trial strategies and validate new clinical outcome assessments.

▶ TO COVER THE REMAINING MONTHS OF GRADUATE STUDENT YUANFAN "TRACY" ZHANG IN THE KATHRYN WAGNER LAB

Tracy Zhang; Kathryn Wagner, mentor, Kennedy Krieger Institute, Baltimore, Maryland

FSH Society Musclepalooza graduate research award; $21,592 for three months

Tracy Zhang, PhD

Our lab has piloted development of a human muscle xenograft model for FSHD[1]. By transplanting patient muscle into the front part of mice hind limbs, we generated a xenograft. (The mice had deficient immune systems that won't reject the foreign tissue.)

The human muscle regenerates itself from the stem cells in the muscle. It is functional with the blood supply and nervous system from the mouse. Furthermore, gene expression in the xenograft mirrored that of the patient donor muscle, which is crucial to be a disease model.

This FSH Society grant helped support my work validating a potential therapeutic for FSHD in our human muscle xenografts. The drug is a small piece of chemically modified nucleic acid that recognizes and knocks down a potential causal gene, DUX4. We were able to achieve significant knockdown not only in the target gene but also other disease markers with treatment of the drug in xenografts.

We have shown proof of concept to use xenografts to model FSHD and test therapies. This could help bridge the gap in developing therapies for FSHD. This work is published in the journal *Molecular Therapy*[2]. This project was a collaborative effort among the Kennedy Krieger Institute, the Senator Paul D. Wellstone Muscular Dystrophy Cooperative Research Center for FSHD at the University of Massachusetts, and Sanofi Genzyme, and it could not have been possible without the support from the FSH Society and many FSHD families. FSHWatch

[1] Zhang Y, King OD, Rahimov F, Jones TI, Ward CW, Kerr JP, Liu N, Emerson CP, Jr., Kunkel LM, Partridge TA, et al. Human Skeletal Muscle Xenograft as a New Preclinical Model for Muscle Disorders. *Human Molecular Genetics.* 2014;23(12):3180-8.

[2] Chen JC, King OD, Zhang Y, Clayton NP, Spencer C, Wentworth BM, Emerson CP, Jr., Wagner KR. Morpholino-Mediated Knockdown of DUX4 Toward Facioscapulohumeral Muscular Dystrophy Therapeutics. *Molecular Therapy: the journal of the American Society of Gene Therapy.* 2016;24(8):1405-11.

Ask the physical therapist (part 1)

Julie Hershberg answers your questions

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

Julie Hershberg, PT, DPT, NCS (standing, center) works with neuromuscular clients.

Q. My son has FSHD. Has there been research done in using braces or taping techniques to assist weak muscles or improve posture to then decrease the stress on other compensatory muscles? If so, what are your recommendations for how to get these braces?

A. There is not research in FSHD on particular braces, but there is clinical expertise that has recommended specific bracing depending on your son's problems. (Wendy King and Katy Eichinger are great resources and PTs with a lot of experience in this area.) Abdominal bracing and leg orthotics are two of the most common forms. General abdominal braces can be found online, and I often recommend the least restrictive and most comfortable ones to start, which are essentially soft elastic. I also recommend custom AFOs for the legs, made by an orthotist.

Q. My husband has FSHD, and his shoulder blade is hanging on by the muscle by the clavicle, and is on the verge of dislocating. He is constantly in pain, and stretching is difficult. Do you have any suggestions on this?

A. I recommend a couple of options: **1)** evaluation by an orthopedic MD with consideration of surgical management; **2)** evaluation by a PT. There are many people who prefer to avoid surgery, and there are some shoulder braces that can be helpful, but it is difficult to make a specific recommendation without analyzing his particular case. Non-surgical options using braces (scapular retraction orthosis) have provided limited benefit because the pressure needed to keep the scapula fixed is not tolerable for extended periods of time. It may be an option for specific activities or limited time periods only.

Q. What kind of shoes are good for people who have very high arches and the top of their foot has begun to arch?

A. Rather than a specific recommendation for shoes, I often recommend customized orthotics by a PT or podiatrist that people can wear in any shoe that can accommodate the high arch, provide support, and help avoid pain and injury.

Q. I am 69 and was diagnosed with FSHD 10 years ago after back surgery proved ineffective. I am blessed to have trainers as well as gym and pool facilities to provide a balanced, vigorous exercise program of weights, aerobics (bike and arc trainer), swimming, plus stretch meditation and wellness. Nevertheless, as with most muscular dystrophies, the deterioration continues with recent dramatic declines in mobility, strength, and posture. I find very little literature on best practices for exercise therapy and wellness for FSHD. Could you suggest readable, up-to-date literature?

A. Thanks for the great question. This is the most recent care guideline that is available, and admittedly is not very detailed: *https://www.aan.com/Guidelines/Home/GetGuidelineContent/703*.

Another resource that I recommend is a recent Cochrane review: *http://www.ncbi.nlm.nih.gov/pubmed/23835682*.

And here is another recent exercise study: "Both aerobic exercise and cognitive-behavioral therapy reduce chronic fatigue in FSHD: an RCT by Voet et al. This is a link to the abstract article: *http://www.ncbi.nlm.nih.gov/pubmed/25339206*.

Q. Do you recommend on-ground or in-water exercises?

A. Great question! This is very specific to what you like the best! Water exercises have been very beneficial in my experience because

of the unweighting and the ability to get a nice aerobic workout even with little muscle strength. However, some people just don't like the water and no need to force it! I think people are best off performing the exercises that they most enjoy because they are more likely to stick with them.

Q. My father-in-law has FSHD. Could you give some insight on the early stages? My husband is 38 and doesn't appear to have any symptoms, but our son is two and has been diagnosed with high-frequency hearing loss in the left ear and weak facial muscles, and has to go for motor speech therapy. Neither has been genetically tested.

A. I definitely recommend a medical evaluation to look into potentially early signs and testing if that is something you are interested in. The disease is so variable that there is not one way it presents. The materials from the FSH Society resource page are amazing, and I have used these a lot in my own practice to help people understand the presentation and testing: *https://www.fshsociety.org/resources/*.

There is a pediatrician who did a talk for the FSH Society who may be a good resource: *https://www.youtube.com/watch?v=zQGi9CM6gwA*.

Q. How do you encourage adult patients to understand how important exercise is? My son is 21 and has the winging and noticeable arm strength loss as well as his core muscles.

A. I spend a lot of time with people really trying to understand what they like doing and how we can incorporate that into exercise and healthy living. We are not all natural exercisers, but we can often find various means to stay healthy and active that are not traditional.

I like to educate people about the importance of maintaining muscle strength and mobility for as long as possible to prevent problems such as postural deformity—and sometimes this is a big motivator.

The APTA "Find a PT" is a great resource: *http://www.apta.org/apta/findapt/index.aspx*.

Q. If joining an Osteofit class or shallow water exercise class (at a local recreation center), how do I know what exercises are beneficial and if maybe there are some that wouldn't be good to do, given my FSHD? Also, what information should I share with an instructor of such classes?

A. I am so glad you are joining a class—this is a great way to exercise! A physical therapist would be able to help direct you to some exercises that are most beneficial (and keep you from doing the ones that are harmful). Within the class, it is important to really listen to your body and pay close attention to the way your arms and legs are moving to notice if you might be compensating. (This admittedly is very difficult to do on your own body!) For the most part, if you are able to exercise without pain or discomfort or extreme fatigue afterward, you are probably safe.

I recommend the Physical Therapy brochure from the FSH Society—I hand it out to everyone I come into contact with! It is found on the resource page: *https://www.fshsociety.org/resources/*.

Q. I am going to PT (water) once a week. I wanted to know what is the best course of action: maintain the same level of difficulty on the water treadmill and go longer each time, or increase the level of difficulty (adding jets, increasing speed of treadmill) and keep the same length of time for the exercise?

A. This is an awesome question! I think of three things when progressing exercise: **1)** endurance (time or duration of training); **2)** intensity (level of difficulty); **3)** frequency (how many times per day or week); and probably most important, **4)** quality. I would keep those four things in mind here.

As far as duration, frequency, and intensity, we don't have definitive evidence for one or the other at this time, but the results of the FAST trial indicate that moderate aerobic exercise (50-65 percent of heart rate reserve, 12-14 on the Borg, ability to keep a conversation going) is beneficial to decrease fatigue, and it is safe!

In this trial the participants worked at 30 minutes with an additional warmup and cooldown. I would recommend getting to that level and then working with your PT to both progress endurance and resistance together—always keeping in mind your movement quality. For example, you don't want to increase the resistance of the exercise if you end up compensating or using poor form—which would potentially lead to injury. With most people, I tend to ramp up the endurance and the resistance very slowly (even by a 0.5 lb.) in order to ensure that we don't overdo it. FSH Watch

"Water exercises have been very beneficial in my experience because of the unweighting and the ability to get a nice aerobic workout even with little muscle strength."

JULIE HERSHBERG

Little stories about my life

Adapting to my "defect"

by CHRISTER OLDENHOV
Malmö, Sweden

Christer Oldenhov

> *"My family takes it harder than me that I have FSHD. It is probably normal that family members do take stuff like this harder. But I always say to them—which is from the bottom of my heart—it could always be worse!"*
>
> CHRISTER OLDENHOV

I was born in June, 1976, and live in the southern part of Sweden. I was diagnosed with FSHD sometime in 2005, but the dystrophy started much earlier than that. My memory says sometime in the fourth grade, which would make me 10 years old. Back then, absolutely no one in Sweden knew what I had, and we never tried to do anything about it.

I was one of the strongest and fastest kids during school, too, running, arm wrestling, and so on. From fourth to sixth grade, I practiced kung fu, and from seventh to ninth grade, I switched to tae kwon do. I just loved it, but I was affected in my upper body and arms, which meant that I was unable to do the correct movements in blocking techniques. When you are advancing in belt grades, you often do katas, which are choreographed movements. I explained to my instructor about my issues, and we solved it by doing a slightly different movement.

In addition, I regularly practiced spinning, the off-road motorcycle sport called enduro, and also just running. My legs were never affected before my thirtieth birthday.

Today, I'm unable to run or practice spinning, or other, tougher sports. I also don't want to stress my body that much. But to compensate, I exercise my stomach and back, and I do the "Nordic walking," which is great. They say that the older you get, the wiser you are, and what muscle I have left in my body I intend to keep as long as I can. Nowadays I do my exercise with caution.

There is a visible difference in the muscularity in my legs, and my left thigh is thinner. When it comes to my face, I can still smile without any problem, but I'm unable to blow up a balloon, and my eyelids stay open during sleep. My upper body has the typical attributes of FSHD.

I have a very small family: only a grandmother, mom, and a big sister, and none of them have FSHD. I do not have a father. I actually don't care where this disease comes from. If it's a new mutation or inherent, it would not change my situation.

Luckily, I have a great job as an information technology technician. I started in 1997, and of course this line of work suits my body perfectly. I also have the opportunity to take my bicycle to work, which I do regularly.

My family takes it harder than me that I have FSHD. It is probably normal that family members do take stuff like this harder. But I always say to them—which is from the bottom of my heart—it could always be worse! I mean, my life works super fine, and I'm in no need for assistance. And everyday stuff works fine even though to take a glass from a shelf above my shoulder, I have to throw my arm up in the air and then lean it toward a shelf, grab the glass, and concentrate on the return so I don't break the glass or hit my elbow on the way back down.

I have had a serious relationship of a few years, and a year ago I told my girlfriend about my defect (which I actually prefer to call it). I explained to her that I will never ever be able to take the little baby up in my arms if we had children, and that they would have a 50-50 risk of inheriting FSHD. I could see her genuine facial expression, which said, "Do you really think I would leave you because of this?!" In this scenario, I was the one building up the big problem.

Anyway, I wanted to share these little stories about my life and living with the defect.

By the way, I saw the news about the biotech company Acceleron Pharma's upcoming Phase 2 test in 2016. I'm probably not eligible to participate since I'm in Sweden, but this kind of news keeps up the good spirits in you! FSHWatch

Rollin' through life on wheels

OVERCOMING FEAR AND FINDING FREEDOM

Carden Wyckoff

My 14-year-old self didn't believe it when a physician told me I would become reliant on a mobility scooter or wheelchair by age 25. I laughed it off, reassuring myself I was different from the rest.

My FSH muscular dystrophy progression wasn't as noticeable; I could still run and play competitive sports, so surely my physical state wouldn't succumb to this condition. But many nights were spent bawling my eyes out, scared that I would be defined by an assistive device. I refused to accept reality, was blind to what all the research said.

Why was I so afraid of wheels as legs? I would become another statistic, another box checked off on the researcher's list, another burden to the able-bodied. Something about being labeled "disabled" or "handicapped"—all these things my core being rebelled against.

The best decision my 22-year-old self has made was to face this ugly monster of a mental obstacle and purchase a three-wheeled, red, shiny scooter. The last nine months have been the antithesis of everything I expected. I am alive, inspired, and ebullient. My scooter takes me places I would never have considered in a million years.

No longer do I count steps, look for places to sit and rest, worry about keeping up with friends, or tripping and falling; I am no longer afraid of living life.

There are tons of perks with wheels: people holding doors open for you, front row seats, free parking, and people in general lending a hand.

This is not to say getting wheels has been all kittens and rainbows. Scooters require regular maintenance, and parts break or loosen from regular wear and tear. It's a machine, and machines break. Downtime can be weeks or months, depending on the part. Being 100 percent reliant on electronics for mobility is scary when insurance is not able to supply a backup.

Now that I'm rollin' (not hatin'), I'm even more aware of uneven surfaces, curb cuts, ramps, elevators, and overall ADA accessibility.

My scooter takes a hard beating in the city of Atlanta, so I dedicate my free time to advocate for change. The way I advocate is by wandering around the city, taking pictures/videos of areas that need improvement, and submitting claims through the Department of Public Works.

The 2010 ADA Standards for Accessible Design notes that there must be an accessible path of travel. We are at a pivotal point in architectural history where we are required to start designing for wheels first. If we design for wheels first, we are saying yes to inclusion. If we design for wheels first, we believe in equality.

— Carden Wyckoff, Atlanta, Georgia

Our experience with NeuroPhysics

Therapy has improved strength and function for our son

by MICHELLE DODD
Melbourne, Australia

My son Matt, who is 12 years old, has FSHD. He was diagnosed in 2014. We live in Melbourne, Australia, and have just recently been to Queensland to try NeuroPhysics Therapy to see if it would help with Matt's symptoms. He was having difficulties lifting his arms above his head. He was having frequent falls when walking and felt fatigued when standing for a long period of time.

I first discovered NeuroPhysics a couple of months ago after stumbling across a video online of Michelle Mackay, who also has FSHD and has had success with the therapy. After doing a bit more research online, we decided to fly to Queensland and start the therapy.

Matt was quite excited to get started. We met with Nickie Ware, his neurotricionist, and began! The therapy is done mostly on pin weight machines focusing on correct positioning of the body and slow, precise movements. Some exercises are also done with light free weights.

Nickie was fantastic. She went at a pace that suited Matt and made it a lot of fun. I also committed to doing the program so that I could fully understand how the therapy works. Now that we have returned to Melbourne, we are continuing the program together at home and at the local gym.

The whole experience was amazing. For Matt and myself, the NeuroPhysics Therapy Institute is such a positive and inspiring place to learn this therapy. Matt's walking, strength, and posture are a lot better, and he can complete the exercises more easily. He feels stronger and more energized, and with continued work we hope to see further improvements. Our experience is presented in this video: *https://vimeo.com/183750187*. FSHWatch

Matt Dodd

INFORMED CONSENT AUTHORIZATION

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The most recent study in which he participated consisted of giving 11 vials of blood to be sent to different studies in Iowa, Massachusetts, and Maryland, and to have a skeletal muscle biopsy. Muscle collected during the biopsy, a form of minor surgery, could be used to implant into a laboratory mouse to analyze how novel therapeutics could improve FSHD muscle.

The muscle tissue could also be stored in a repository that can provide characterized FSHD cells or be used as control muscle cells by labs studying FSHD. One important difference in this study is that the muscle cells obtained from volunteers are "immortalized" so that they will reproduce in a laboratory dish nearly indefinitely and not be exhausted. Biomaterials contributed to this program will therefore advance the research of investigators around the world.

Our most recent experience was with Kathryn R. Wagner, MD PhD, a principal investigator for a National Institutes of Health-sponsored project called "Facioscapulohumeral Disease Biomaterial for Wellstone Core." Dr. Wagner and her highly sophisticated team of researchers are located at the Center for Genetic Muscle Disorders at the Kennedy Krieger Institute as a part of Johns Hopkins Medicine in Baltimore, Maryland.

Allen also sees Dr. Wagner as a patient in her clinical practice. Allen understands he is working with a cutting-edge researcher in a first-rate facility. Dr. Wagner has multiple research projects ongoing in FSHD as well as other forms of muscular dystrophy.

From the minute we walked into Kennedy Krieger Institute (KKI) Center for Genetic Muscle Disorders, we had the feeling that we were a part of something much bigger than MD. We felt we were part of a consortium of medical "think tankers" who will someday develop a viable treatment plan for those individuals who have FSHD.

The feeling of hope at KKI is tremendous, and the appreciation of our help was overwhelming. These professionals are way beyond seeing my husband as just another person with a disability; they see my husband as someone for whom they will be able to stop the progression of his degenerating disease!

As Allen's wife, I just can't tell you how proud I am of his willingness to be part of the bigger picture of research in FSHD. Is it fun to have 11 vials of blood taken? (Actually, the phlebotomist was so interesting and kind!) Is it an everyday event to have a muscle biopsy (minor surgery) and be told not to move your arm for 48 hours?

Allen Carney and Susan Mayes during their visit to the Kennedy Krieger Institute in Baltimore, Maryland.

> *"From the minute we walked into Kennedy Krieger Institute Center for Genetic Muscle Disorders, we had the feeling that we were a part of something much bigger than MD. We felt we were part of a consortium of medical "think tankers" who will someday develop a viable treatment plan."*
>
> SUSAN W. MAYES

I personally would answer "no" to the above two questions. However, Allen knows his DNA is being protected for further research projects in the U.S. and abroad. He hopes his efforts as a research subject will improve the quality of life for those individuals who also share his pain, inconveniences, and downright nastiness—the byproducts associated with genetic muscle disease.

Wow, Allen, you are my hero!

Please consider the possibility of participating in a clinical research project. Your study may be the one that leads to a pharmaceutical treatment plan to reduce or stop muscle degeneration and promote healthy muscle growth! I am confident this will happen!

Visit the FSH Society website *(https://www.fshsociety.org/find-a-clinical-trial/)* or *https://clinicaltrials.gov/* and search for "facioscapulohumeral" to find a research project in which you can participate.

Visit *https://www.kennedykrieger.org/patient-care/faculty-staff/kathryn-r-wagner* for more information about Dr. Wagner and her research. FSHWatch

Editor's note: The author received permission to use personal references and images as well as editorial suggestions from Allen Carney, Missy Carney Cassidy, and Dr. Kathryn Wagner. The FSH Society created legislation that resulted in Senator Paul D. Wellstone Cooperative Centers for Muscular Dystrophy Research and has funded research at the Kennedy Krieger Institute (a Wellstone center member), and provides travel reimbursement to study volunteers.

North Carolina member meeting

Join us for our next get-together!

by RAY HUML and DEBORAH WOOLARD
Durham and Winston-Salem, North Carolina

Fourteen North Carolina FSH Society members and family attended the meeting on September 24 hosted by the Humls at the Triangle Presbyterian Church in Durham, North Carolina.

Two speakers from Duke University Hospital attended our meeting: Edward Smith and Laura Case. Both doctors have worked with Raymond Huml's son, Jonathan R. Huml, who has FSHD and is now a freshman at the University of North Carolina at Chapel Hill.

Dr. Smith's muscular dystrophy expertise comes from working with patients with Duchenne muscular dystrophy through the MDA clinic at Duke. His group sees about 80 patients with FSHD. Three are children with FSHD, and the rest are adults. He provided a short overview and answered questions from the group. He wishes to learn more about FSHD and was advised to reach out to Dr. Kathryn Wagner from the Kennedy Krieger Institute in Baltimore, Maryland, and the FSH Society.

Dr. Case's expertise is with orthotic devices, wheelchairs, and physical therapy (PT). Dr. Case is very knowledgeable on supports and devices that may benefit those of us with FSHD. She brought samples of orthotic devices and pictures of equipment to share with the group.

Those with FSHD and their family members provided introductions and updates on their status, and shared suggestions and ideas that might be helpful to others.

Our next meeting is on Saturday, February 25, 2017, at Parkway United Church of Christ, 2151 Silas Creek Parkway, Winston-Salem, North Carolina. We plan to meet at our usual time, 11 a.m. to 2 p.m. with lunch. Hope to see everyone there. If you are interested in joining this group, please contact Deborah Woolard at *dgwoolard@gmail.com.*

We thank Drs. Smith and Case for making the time to meet with our group. They kindly provided their contact information:

- **Edward Smith, MD**
  Pediatric Neurologist
  Lenox Baker Children's Hospital
  Duke University Hospital
  3000 Erwin Road
  Durham, NC 27705
  (919) 668-0477 and
  (919) 684-6669
  Edward.smith@duke.edu

- **Laura Case, PhD**
  Board-Certified Clinical Specialist in Pediatric Physical Therapy
  Lenox Baker Children's Hospital
  Duke University Hospital
  (919) 681-9930
  Laura.case@duke.edu FSH Watch

Many ways to support us!

OUR EBAY CHARITY AUCTION SITE

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

RAZOO ONLINE FUNDRAISING

Razoo makes it easy to create an online campaign. Your donors will enjoy the convenience, knowing that their gifts will go directly to the FSH Society. With Razoo you can easily promote your campaign over Facebook, Twitter, and other social media.
http://www.razoo.com/story/Facioscapulohumeral-Society

FREE MONEY!

Many organizations will match employees' charitable donations, or will donate if employees volunteer their time to a charity. Don't leave this money on the table! Ask your employer about their charitable gift programs.

COMBINED FEDERAL CAMPAIGN (CFC)

Federal employees can enroll in workplace giving from September 1 to December 15. The FSH Society's CFC identification number is 10239.

GIVE WITH A SMILE THROUGH AMAZON

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

BREAKING MY SILENCE

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sire to not allow FSHD to be swept under the rug any longer. I was tired of hiding, and I knew there were others out there living with FSHD and feeling the same way.

I'm proud to say that because of our first fundraiser, we were able to connect with a couple of new people in the area living with FSHD. The day was absolutely spectacular, as we raised more than $20,000 for the FSH Society! You can check out our blog and pictures from our event here: *https://www.fshsociety.org/2016/09/walk-roll-to-cure-fshd/.*

I personally believe FSHD is much more common than 870,000 people worldwide. As someone living with FSHD, I feel it is my responsibility, my purpose,

. . . continued on page 19

Why we meet

Mid-Atlantic meeting hits a grand slam!

by DON BURKE
Alexandria, Virginia

On September 17, 2016, about 15 people from the Mid-Atlantic area met at Children's National Medical Center in Washington, DC, to hear from researchers and share experiences with FSH muscular dystrophy.

DC FSH Society members, Manuel Gomez (left), and Don Burke (right), with executive director June Kinoshita (center).

I've had the great privilege of attending these networking events in the DC area since 1988, when Karen Johnsen first started the group. Since then, the group has ebbed and flowed as people come and go, when we lost Karen too early, and as the nature of FSHD advocacy in the area waxed and waned.

The gathering in September reminded me again why we meet.

This meeting included three elements that would each be powerful on its own, but when combined left a real impression.

First, I heard the clearest and most understandable explanation yet of FSHD's genetics as we know it today.

Second, I learned about emerging research into stopping FSHD that left us wowed and excited.

Third, the meeting offered the chance for a new family to come out of the wilderness, and meet and learn from others with FSHD for the first time.

It was a grand slam meeting in my book. A special shout-out as well to Kelly Mahon and her fiancé for bringing food.

Yi-Wen Chen, PhD, gave a two-part talk. She first provided the group with a very clear and understandable overview of FSHD from a genetics perspective, which is no small feat given the complex and multifaceted nature of the disease. We hope to have Dr. Chen make a recording of this presentation so it can be made more widely available.

Dr. Chen then transitioned into an overview of her research using a compound from Idera Pharmaceuticals called 3GA that seeks to interfere with the ability of muscle cells to create the DUX4 protein. In a cell, genes determine what proteins get produced. In our case, that is the DUX4 gene. Genes then send signals out into the cell so that the cell will actually produce the protein. Dr. Chen's research focuses on an approach called antisense therapy, which works to block that signal. 3GA is the compound that does the blocking so the cell can't actually create the DUX4 protein.

In a scientist's typically understated manner, Dr. Chen matter-of-factly walked through the research and the results. She focused on detailing how 3GA knocks down the level of DUX4 protein in muscle cells and how the cells react to that change.

Several of us who were listening had a reasonable grasp of science and FSHD research; when we saw her graphs and statistics, our jaws were on the floor because the data look so promising. Her research appears to show that it is possible to knock down DUX4 and, even more shockingly, that affected muscle cells appear to get healthier as a result.

It's important to keep in mind that Dr. Chen's work is still preclinical trial basic research. Much more work will be needed to confirm the results and undertake clinical trials before there is real confidence that this research isn't an aberration. Regardless, we all left feeling like we'd just heard about an extremely promising avenue for altering the direction of FSHD.

While hearing new and exciting presentations is always a great part of support group meetings, it is the people who attend that make the gatherings so special.

Every so often someone new shows up, and those days are really impactful. So it was for this meeting.

A wonderful lady with FSHD attended for the first time with her son and friends. She'd never before met anyone with FSHD and, like so many of us, had gone through a long and tortured journey to diagnosis. After introducing ourselves, we shared stories and answered her many questions. Many of us recounted our own journeys with the disease. We were so happy she found her way to our meeting.

I've been lucky enough to be in the room many times when someone with FSHD first meets others with the disease. The sense of relief that "I'm not alone" and that there are others who understand what their day is like is almost overwhelming. That is why we meet. FSH Watch

Thanks to Ann Biggs-Williams

Stepping down after 17 years of service on the Board

by HOWARD CHABNER
FSH Society Board of Directors

Ann Biggs-Williams, one of the longest-serving Board members in the history of the FSH Society, retired from the Board of Directors in September. Ann and her husband Mike attended the organizational meeting of the Society in San Diego, and she began serving on the Board in 1999.

A resident of Brewton, Alabama, Ann led the Gulf FSHD Support Group for many years. Covering Alabama, Florida, Louisiana, and Mississippi, the group connected many people with FSHD who had never met anyone else with the condition, giving them hope, enabling them to discover strength they hadn't known they possessed, and generating enthusiasm for the Society. The group met in all of the states for many years.

Beginning with the first conference in San Diego, Ann attended all of the Society's biennial patient conferences except Iowa in 2008 and Boston in 2014. Over the years, she led sessions on women's issues and FSHD, caregiving, and practical tips for dealing with FSHD. She's remembered, among other things, for trying to give all first-time attendees a welcoming Southern hug. (Some repeat attendees were also fortunate to receive hugs from Ann!)

For many years, Ann volunteered in the Society's peer-to-peer counseling program, giving newly diagnosed FSHD patients practical advice and letting them know they would never be alone.

She and Mike sponsored two boat trips on the Mobile Tensaw River Delta to raise money for the FSH Society. She represented the Society in many events over the years, most recently in 2016 in Pensacola, Florida, by greeting Diane Lea on behalf of the Society at the Grand Finale Party at the culmination of Ms. Lea's 50-day bicycle ride from San Diego to Pensacola that raised money and awareness for 50 causes, including FSHD.

Ann Biggs-Williams proudly sports her "I am STRONGER THAN FSHD" T-shirt.

As the Society grew in fundraising and size, Ann never let her fellow board members lose sight of the fact that, as important as the scientific research is, and as necessary as dollars are in making that research possible, the Society is about people first and foremost: about connecting, educating, supporting, and giving hope to people of all ages, all backgrounds, and all places who have FSHD or whose family members or friends do.

Ann was head librarian at Jefferson Davis Community College in Brewton, Alabama, where she worked for 24 years. After retirement, she volunteered with the Escambia County Historical Society in Alabama, which maintains a local history archive at the museum at the same college. She served as president of the Historical Society and is now a trustee. Since retirement, she has also been renovating the family home, which was built in 1896 and is listed on the Alabama Register of Landmarks and Heritage, and has led several local history projects.

The Society's unofficial historian, Ann put her professional skills to use by documenting the patient conferences and the history of the Society through photos, documents, and other memorabilia. A labor of love, this work began before it was made easier by digital images, email, social media, and other technologies that we take for granted today. Ann educates new members and others about the history and achievements of the Society.

The Society and her fellow board members thank Ann for everything she has done, and hope that she will continue to spread the word about FSHD and the Society. Known by all for her charm, her warmth, her graciousness, her welcoming spirit, and her optimism, Ann truly will be missed. FSH Watch

BREAKING MY SILENCE

. . . from page 17

to provide a platform for others affected by this devastating disease to be able to live fully with FSHD. Breaking my silence has provided me with an unexpected sense of freedom, peace, control, and confidence.

This is not to say that I'm okay living with this disease or that I'm okay with others having to live with this disease, but at least I no longer feel trapped in my emotions with FSHD.

My hope is to inspire others to break their silence and to show them how much beauty the other side possesses. I truly believe there will be a day soon that I and all those living with FSHD will be able to live fully without FSH muscular dystrophy, and I will spend my lifetime making sure it becomes a reality. FSH Watch

Invest in our future

Join thousands of supporters and rise to the challenge!

by JUNE KINOSHITA
FSH Society

Your gift matters more than ever. Our entire Board of Directors has pledged a total of **$400,300** and challenges you to match this. From now through December 31, 2016, your gift will be counted toward our year-end challenge. Please stretch a little—13 percent over last year's gift—so we can achieve our goals!

Information at your fingertips

The FSH Society is dedicated to making sure you have accurate, useful information to help improve the quality of your healthcare and daily life. Our publications are created and reviewed by patients and experts. Visit our website (*www.fshsociety.org*), and go to Understanding FSHD/Brochures & More to download:

- **About FSHD**
- **Physical Therapy and FSHD**
- **FSHD: A Guide for Schools**
- **FSHD and Social Support: A guide for friends and family**
- **Evidence-based FSHD care guideline—Summary for clinicians**
- **Evidence-based FSHD care guideline—Summary for patients & families**

You can also request printed copies by contacting us at:
FSH Society
450 Bedford Street
Lexington, MA 02420
Telephone: (781) 301-6060
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HAVE YOU MADE A GIFT TO THE SOCIETY IN 2016?

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

CHARITY NAVIGATOR TOP PERFORMER

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

COMMIT TO THE FUTURE

Consider taking your gift to the next level by making a planned gift. A bequest or endowed fund helps to ensure that the FSH Society has the long-term support to sustain its mission. Questions? Please contact June Kinoshita at (781) 301-6649 or *june.kinoshita@fshsociety.org*. Always check with your advisors when making changes in your will or estate plans, and learn how current tax laws and other legislation may affect your plans.