

**Testimony of Daniel Paul Perez, President & CEO, FSH Society, Inc.**  
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**United States Senate Appropriations Committee**  
**Subcommittee on Labor, Health and Human Services, Education and Related Agencies on**  
**the Subject of FY2012 Appropriations for National Institutes of Health (NIH) Research on**  
**Facioscapulohumeral Muscular Dystrophy (FSHD) – April 7, 2011**

Honorable Senator Harkin, Mr. Chairman, Honorable Senator Shelby, Ranking Member, Subcommittee members and members of the U.S. Senate Appropriations Committee, Subcommittee on Labor, Health and Human Services, Education and Related Agencies thank you for the opportunity to submit this testimony.

I am Daniel Paul Perez, of Bedford, Massachusetts, President & CEO of the FSH Society, Inc. and an individual who has lived with facioscapulohumeral muscular dystrophy (FSHD) for 48 years. FSHD is also known as facioscapulohumeral muscular disease, FSH muscular dystrophy and Landouzy-Dejerine muscular dystrophy. For hundreds of thousands of men, women, and children the major consequence of inheriting the most prevalent form of muscular dystrophy is a lifelong progressive and severe loss of all skeletal muscles. FSHD is a crippling and life shortening disease. No one is immune, it is genetically and spontaneously (by mutation) transmitted to children and it affects entire family constellations.

My testimony seeks to address the urgent need for NIH to redress and increase funding for research on FSHD.

A consortium of European partners known as Orphanet, led by the French government research agency, INSERM (Insitut National de la Santé et de la Recherche Medicale), that is comparable to the U.S. NIH, which includes both government and private members, has issued new epidemiology and prevalence data for hundreds of diseases that **ranks FSHD as the first and most prevalent muscular dystrophy**. The “Orphanet Series” report November 2010, “Prevalence of Rare Diseases” report can be found at internet web site: ([http://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence\\_of\\_rare\\_diseases\\_by\\_alphabetical\\_list.pdf](http://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_diseases_by_alphabetical_list.pdf)). FSHD is presented as the third most prevalent muscular dystrophy in the Muscular Dystrophy Community Assistance, Research and Education Amendments of 2001 and 2008 (the MD-CARE Act). This new data changes the findings as listed in the MD-CARE Act. FSHD is 40 percent more prevalent than Duchenne muscular dystrophy (DMD), now recognized as the second most prevalent dystrophy.

<b>Estimated Prevalence</b>	<b>(Cases / 100,000)</b>
Facioscapulohumeral muscular dystrophy (FSHD)	7 / 100,000
Duchenne (DMD) and Becker dystrophy (BMD)	5 / 100,000
Steinert myotonic dystrophy (DM)	4.5 / 100,000

Figures from the online NIH database RCDC RePORT and the NIH Appropriations History for Muscular Dystrophy report provided by NIH/OD Budget Office & NIH OCPL show that from the inception of the MD CARE Act 2001, **funding has more than quadrupled from \$21 million to \$86 million in fiscal year 2010 (FY2010) for muscular dystrophy**. In FY2010, total muscular dystrophy funding grew by 3.6% (\$3M / \$83M) over the previous fiscal year.

In FY2010, FSHD funding represented 7% of the NIH-wide muscular dystrophy budget (\$6M / \$86M). In the previous year, FSHD represented 6% of the total muscular dystrophy funding (\$5M / \$83M). **FSHD funding as a percentage of overall NIH muscular dystrophy funding has been level over the last nine years.**

**National Institutes of Health (NIH) FSHD Funding & Appropriations**

Sources: NIH/OD Budget Office & NIH OCPL & NIH RCDC RePORT

<b>Fiscal Year</b>	<b>FSHD Research Dollars (in millions)</b>	<b>FSHD as a Percentage of Total NIH Muscular Dystrophy Funding</b>
2006	\$1.7	4%
2007	\$3	5%
2008	\$3	5%
2009	\$5	6%
2010	\$6	7%

We highly commend the NIH on the ease of use and the continued accuracy of the Research Portfolio Online Reporting Tool (RePORT) report “Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC)” with respect to reporting projects on muscular dystrophy.

Now that FSHD has been established as the most prevalent muscular dystrophy, and in light of recent advances in research it makes no sense that FSHD remains the most underfunded dystrophy by the NIH and in the federal research agency system (CDC, DoD and FDA). Given FSHD’s prevalence, disease burden, the overall percentage of funding of the muscular dystrophy research portfolio and major mechanistic breakthroughs on FSHD etiology in 2010 and 2011, we ask Congress to urge NIH to provide a catalyst for scientific opportunity in FSHD.

Inter-dystrophy funding changes and comparisons year after year clearly depicts that NIH FSHD funding needs to be increased and set right. Intra-dystrophy funding changes are misleading as a large change in a small number is still an anemic amount. In FY2010, the most prevalent muscular dystrophy, FSHD, received a one million dollar increase from NIH to \$6 million, up 20 percent from \$5 million. In FY2010, the second most prevalent, Duchenne (DMD/BMD) type, received a five million dollar increase from NIH to \$38 million, up 15 percent from \$33 million. In FY2010, the third most prevalent myotonic dystrophy (DM) type, received one million dollars less from NIH to \$12 million down eight percent from \$13 million. There is an obvious funding disparity as the first and third most prevalent dystrophies combined, each with major breakthroughs in the past two years, are receiving less than half of NIH funding that the second prevalent dystrophy with its disease causing gene being discovered 25 years ago.

The MD CARE Act mandates the NIH Director to intensify efforts and research in the muscular dystrophies, including FSHD, across the entire NIH. **It should be very concerning that: 1). in the last nine years muscular dystrophy has quadrupled to \$86 million and that FSHD has remained on average at five percent of the NIH muscular dystrophy portfolio; 2).** FSHD, the most prevalent muscular dystrophy is far underrepresented based on percentage of overall NIH dystrophy funding given its prevalence and disease burden; and, 3). that both FSHD and DM have had extraordinary major breakthroughs in understanding the disease mechanism in the current and past fiscal years and NIH funding remains level in one and has declined in the other.

Muscular Dystrophy Type	Rank By Prevalence	NIH Funding Dollars in Millions		Percentage of Total MD funding at NIH	
		FY2009	FY2010	FY2009	FY2010
FSHD	1	\$5	\$6	6%	7%
DMD/BMD	2	\$33	\$38	40%	44%
DM	3	\$13	\$12	16%	14%

**Two major breakthroughs on FSHD occurred in FY2010 and FY2011 that make it urgent for the NIH to redress funding for FSHD.** On August 19, 2010, a paper titled, “A Unifying Genetic Model for Facioscapulohumeral Muscular Dystrophy” [*Science* 24 September 2010: Vol. 329 no. 5999 pp. 1650-1653] was published online in the top-rated journal by a group of researchers who started their careers in FSHD research with post-doctoral fellowships from the FSH Society. This paper was a major breakthrough in understanding how FSHD works. It made the front page of the *New York Times* on the following day. The *Times* article “Reanimated ‘Junk’ DNA Is Found to Cause Disease,” quoted Dr. Francis Collins, a human geneticist and Director of the National Institutes of Health saying, “If we were thinking of a collection of the genome’s greatest hits, this would go on the list.” Dr. Collins went on to say, “Well, my gosh, ... here’s a simple disease with an incredibly elaborate mechanism. To come up with this sort of mechanism for a disease to arise — I don’t think we expected that.” Professor David E. Housman, FSH Society Scientific Advisory Committee Chairman and a geneticist at Massachusetts Institute of Technology (M.I.T.), was quoted saying, “Scientists will now be looking for other diseases with similar causes, and they expect to find them. As soon as you understand something that was staring you in the face and leaving you clueless, the first thing you ask is, ‘Where else is this happening?’”

Two months later, another paper was published that originated with seminal funding from the FSH Society that made a second critical advance in determining the cause of FSHD. “Facioscapulohumeral Dystrophy: Incomplete Suppression of a Retrotransposed Gene” was published in *PLoS Genetics*, October 28, 2010, that made a second critical advance in FSHD. The research shows that FSHD is caused by the inefficient suppression of a gene that may be normally expressed only in early development. The international team of researchers led by Stephen Tapscott, M.D., Ph.D., a member of the Hutchinson Center’s Biology Division thinks that the work will lead to new approaches for therapy and new insights into human evolution of disease.

The international FSHD clinical and research community recently came together at the DHHS NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Boston Biomedical Research Institute Senator Paul D. Wellstone MD CRC for FSHD. Almost 90 scientists working on FSHD globally met at the 2010 FSH Society FSHD International Research Consortium, held October 21-22, 2010 to identify **areas of scientific opportunity in FSHD that need funding**. The summary and recommendations of the group state that given the recent developments in our definition of FSHD, that within one to two (1-2) years evidence-based intervention strategies, therapeutics, and trials need to be planned and conducted. Our immediate priorities should be to confirm that the DUX4 gene hypothesis is valid. Then we must understand the normal DUX4 function. Finally, we must understand the naturally occurring variability to enable us to manipulate the disease in our favor. We need to be prepared for this new era in the science of FSHD by accelerating efforts in the following ten areas:

1. Shareable Protocols;
2. Common and shareable materials and data by the whole community;
3. Corroborate and verify DUX4 finding;
4. FSHD alleles in context of population genetics need to be defined;
5. Biomarkers;
6. FSHD clinical evaluation scales/systems need be defined under one agreed standard;
7. Working Groups / animal and mouse model working group consortium;
8. Model systems for mechanistic, intervention work and advancement to clinical trials;
9. Epigenetics / Genetics;
10. Clinical trials readiness.

To read the expanded summary and recommendations of the group please go to on-line file at:  
<http://www.fshsociety.org/assets/pdf/IRCWorkshop2010WorkingConsensusOfPrioritiesGalley.pdf>

It is impossible to justify the current low level of FSHD funding in the current context of muscular dystrophy budget at the NIH. We have worked hard with our scientific colleagues and member patients and families to build the corpus of knowledge to understand FSHD. We have made great progress in understanding our own disease. We have worked side by side with the NIH directors, program and legislative staff the whole distance to these remarkable discoveries. Still, there has been a confounding and recalcitrant lack of traction at NIH for funding in FSHD. Our request to the NIH – increase FSHD funding now!

NIH constantly reminds us that the NIH system of peer-review delivers the best science from investigator initiated grant applications, thus delivering quality science to the American tax-payer. NIH is receiving more and more grant applications on FSHD. As a non-profit volunteer health agency that funds breakthrough research based on peer-review mechanics and on a shoe-string compared to NIH, we appreciate the need for peer review, the need to fund the best science and also the need to recalibrate the process to ensure that pragmatic and necessary choices are being pursued in the advent of paradigmatic changes in a disease. We FSHD patients and fellow citizens appreciate this as tax-payers as well.

What it comes down to is -- the choice of “the best science” in a disease area and how this has been achieved. This is difficult to measure except in hindsight e.g. what hypotheses represent the best science. The Director of NIH said, set this down, take note, this is one of the ten greatest discoveries in human genomics and that we never expected diseases to be caused by unwanted RNA from reanimated junk DNA. The implications are enormous. FSHD has an incredibly elaborate mechanism that we did not expect. We now know that inadvertent expression of DUX4 from a stretch of reactivated “junk-DNA” causes muscle disease known as FSHD. It is clear that this type of research does not and has not done well in peer-review and it is obvious by the fact that funding is dwarfed. Looking back at the recent NIH Request For Proposals (RFAs) that covered FSHD we can see that all of the breakthrough D4Z4 DUX4 gene grant applications went unfunded by NIH. Perhaps the study sections need to be pulled apart and examined in the broader context of muscular dystrophy. Perhaps comparing Duchenne, Myotonic and FSHD is now much akin to determining the best science in computer science and biology combined. Computer science and biology seems an obvious apples to oranges comparison. We are saddened that the most brilliant work on FSHD was turned away by the NIH. It is crystal clear, if not completely black and white, that FSHD is not achieving the goals of parity in funding as set down in mandates set forth in the MD CARE Acts 2001/2008 and by the NIH Action Plan for the Dystrophies submitted to the Congress by the NIH.

As you know, we are impressed with the efforts of NIH staff and Muscular Dystrophy Coordinating Committee (MDCC) on behalf of the community of patients and their families with muscle disease and the research community pursuing solutions for all of us. We recognize in particular the efforts and hard work of the following NIH staff: **Story Landis, Ph.D.** and **John D. Porter, Ph.D.** of National Institute of Neurological Disorders and Stroke (NINDS); **Stephen I. Katz, M.D., Ph.D.** and **Glen H. Nuckolls, Ph.D.** and **Vittorio Sartorelli, Ph.D.**, National Institute of Arthritis and Musculoskeletal and Skin Disease (NIAMS); **James W. Hanson, M.D.** and **Ljubisa Vitkovic, M.D., Ph.D.**, (NICHD).

The pace of discovery and numbers of experts in the field of biological science and clinical medicine working on FSHD are rapidly expanding. Many leading experts are now turning to work on FSHD not only because it is one of the most complicated and challenging problems seen in science, but because it represents the potential for great discoveries, insights into stem cells and transcriptional processes and new ways of treating human disease.

We request this year in FY2012, immediate help for those of us coping with and dying from FSHD. **We ask NIH to fund research on facioscapulohumeral muscular dystrophy (FSHD) at a level of \$35 million in FY2012.** In view of the tremendous breakthroughs in FSHD research that may rewrite genetics, we implore the NIH to immediately address the inadequacy in FSHD muscular dystrophy funding.

We implore the Appropriations Committee to request that the Director of NIH, the Chair, and Executive Secretary of the federal advisory committee MDCC to increase the amount of FSHD research and projects in its portfolios using all available passive and pro-active mechanisms and interagency committees.

We request that **NIH be more proactive in facilitating grant applications** (unsolicited and solicited) from new and existing investigators and through new and existing mechanisms, special initiatives, training grants and workshops – to bring knowledge of FSHD to the next level.

We ask NIH to consider **increasing the scope and scale of the existing DHHS U.S. NIH Senator Paul D. Wellstone Muscular Dystrophy Cooperative Research Centers (U54) to double or triple their size** – they are financially under-powered as compared to their potential. These centers have provided an excellent source of human biomaterials and are a catalyst for research, clinical research and training on muscular dystrophy. We ask NIH to develop funding mechanisms to help expand work from NIH Wellstone Centers outward to address needs and priorities of the scientific communities.

We ask NIH for **more than one Wellstone center solely dedicated to FSHD.** There needs to be one-half dozen groups with six to ten people solely working on FSHD across the U.S. to assure continuity in FSHD efforts.

We strongly support research discovery through the use of post-doctoral and clinical training fellowships -- a model that has worked very effectively for us. It produces results and progeny. Yet, NIH has only a few fellows in dystrophy. We request that NIH issue **an RFA to exclusively fund 12 new post-doctoral fellows and four clinical fellows a year on an ongoing basis for the next five years on FSHD.** We ask that FSHD be the pilot dystrophy for such initiative.

We request that the Director of the **NIH initiate solely for FSHD an RFA for Specialized Centers (P50s)** to encourage multidisciplinary research approaches on the complexity of FSHD.

We request that the Director of the NIH redress the low level of funding in FSHD by issuing an **RFA exclusively for FSHD to allow it to be a prototype disease in the newly forming National Center for Advancing Translational Sciences.** This will help advance the translational science in FSHD and catalyze the development of novel diagnostics and therapeutics for FSHD.

We request that the Directors of the NIH develop, through **an RFA for FSHD, a central place where clinical trials can be designed and run on animal models of FSHD (mouse, dog, sheep, etc.).** It is cost prohibitive to have each U54, P01, P50 funding infrastructure to support these resources. We ask that FSHD be the proof-of-concept disease for such a facility.

Thanks to your efforts and the efforts of your Committee, Mr. Chairman, the Congress, the NIH and the FSH Society are all working to promote progress in FSHD. Our successes are continuing and your support must continue and increase.

Mr. Chairman, thank you for this opportunity to testify before your committee.