

**Testimony of Daniel Paul Perez, President & CEO, FSH Society, Inc.**  
**Telephone: (781) 275-7781, e-mail: daniel.perez@fshsociety.org before the Subcommittee**  
**on Labor, Health and Human Services, Education and Related Agencies on the Subject of**  
**FY2011 Appropriations for National Institutes of Health (NIH)**  
**Research on FSHD (Facioscapulohumeral Muscular Dystrophy) -- April 16, 2010**

Mr. Chairman, it is a great pleasure to submit this testimony to you today.

My name is Daniel Paul Perez, of Bedford, Massachusetts, and I am testifying today as President & CEO of the FSH Society, Inc. (facioscapulohumeral muscular dystrophy) and as an individual who has this common and most prevalent form of muscular dystrophy. My testimony is about the profound and devastating effects of a disease known as facioscapulohumeral muscular dystrophy which is also known as facioscapulohumeral muscular disease, FSH muscular dystrophy or FSHD, and the urgent need for increased NIH funding for research on this disorder. For men, women, and children the major consequence of inheriting the most prevalent form of muscular dystrophy, FSHD, is a lifelong progressive and severe loss of all skeletal muscles. FSHD is a terrible, 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.

**Fact1**

**FSHD is The Most Prevalent Form of Muscular Dystrophy**

It is a fact that FSHD is published in the scientific literature as the most prevalent muscular dystrophy in the world. The incidence of FSHD is conservatively estimated to be 1 in 14,000. The prevalence of the disease, those living with the disease, ranges to two or three times as many as that number based on our increasing experiences with the disease and more available and accurate genetic diagnostic tests.

The French government research agency, INSERM (Insitut National de la Santé et de la Recherche Medicale) is comparable to the U.S. NIH, and it recently published prevalence data for hundreds of diseases in Europe. Notable is the "Orphanet Series" reports covering topics relevant to all rare diseases. The "Prevalence or reported number of published cases listed in alphabetical order of disease" November 2008 - Issue 10 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)). This publication contains new epidemiological data and modifications to existing data for which new information has been made available. This new information ranks facioscapulohumeral muscular dystrophy (FSHD) as the most prevalent muscular dystrophy followed by Duchenne (DMD) and Becker Muscular dystrophy (BMD) and then in turn myotonic dystrophy (DM). FSHD is historically 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 ranks FSHD as the first and most prevalent form of muscular dystrophy.

**Estimated Prevalence (Cases / 100,000)**

|  |               |
|--|---------------|
| Facioscapulohumeral muscular dystrophy (FSHD)      | 7 / 100,000   |
| Duchenne (DMD) and Becker Muscular dystrophy (BMD) | 5 / 100,000   |
| Steinert myotonic dystrophy (DM)                   | 4.5 / 100,000 |

## **Fact 2**

### **NIH Muscular Dystrophy Funding Has Quadrupled Since Inception of the MD CARE Act**

Figures from the online RCDC RePORT and the NIH Appropriations History for Muscular Dystrophy report historically provided by NIH/OD Budget Office & NIH OCPL show that from the inception of the MD CARE Act 2001, funding has nearly quadrupled from \$21 million to \$83 million in FY2009 for muscular dystrophy.

## **Fact 3**

### **NIH Funding of FSHD has Remained Level Since the Inception of the MD CARE Act**

In fiscal year 2009, FSHD was 6.02% of the total muscular dystrophy funding (\$5M / \$83M). The previous year FSHD was 5.3% of the total muscular dystrophy funding (\$3M / \$56M). FSHD funding has simply kept its ratio in the NIH funding portfolio and has not grown in the last eight 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 % of MD</b> |
|--------------------|--|---------------------|
| 2002               | \$1.3                                      | 5%                  |
| 2003               | \$1.5                                      | 4%                  |
| 2004               | \$2.2                                      | 6%                  |
| 2005               | \$2.0                                      | 5%                  |
| 2006               | \$1.7                                      | 4%                  |
| 2007               | \$3  | 5%                  |
| 2008               | \$3  | 5%                  |
| 2009               | \$5  | 6%                  |

We highly commend the Director of the NIH on the ease of use and the 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 facioscapulohumeral muscular dystrophy.

## **Fact 4**

### **FSHD: The Most Prevalent Form of Muscular Dystrophy is Drastically Underfunded at NIH**

Now, FSHD is published as the most prevalent muscular dystrophy, and given the extraordinary interest of the scientific and clinical communities in its unique disease mechanism, it defies credibility that it still remains the most prevalent and one of the most underfunded dystrophies at the NIH and in the federal research agency system (CDC, DoD and FDA).

In 2009, the most prevalent muscular dystrophy, FSHD, received \$5 million from NIH. In 2009, the second most prevalent dystrophy, Duchenne (DMD) and Becker Muscular

dystrophy (BMD) type, received \$33 million from NIH. In 2009, the third most prevalent dystrophy myotonic dystrophy (DM), received \$13 million from NIH.

The MD CARE Act 2008, 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 in the last eight years muscular dystrophy has quadrupled to \$83 million and that FSHD has remained on average at five (5) percent of the NIH muscular dystrophy portfolio. FSHD is certainly still far behind when we look at the breadth of research coverage NIH-wide.

It is now time to examine why FSHD receives such a disproportional and inverse level of funding despite its equal burden of disease and highest prevalence. It is crystal clear, if not completely black and white, that we are not achieving the goals of parity in funding as expected by the mandates set forth in the MD CARE Acts 2001/2008 and by the NIH Action Plan for the Muscular Dystrophies as submitted to the Congress by the NIH.

We would like to commend the program staff at the NIH for the excellent progress made in FSHD and the extraordinary progress made in increasing muscular dystrophy funding. We are very pleased 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.**, Executive Secretary, MDCC and Director, National Institute of Neurological Disorders and Stroke (NINDS); **John D. Porter, Ph.D.**, Executive Secretary, MDCC and Program Director, Neuromuscular Disease, Neurogenetics Cluster and the Technology Development Program, NINDS; **Stephen I. Katz, M.D., Ph.D.**, Director, National Institute of Arthritis and Musculoskeletal and Skin Disease (NIAMS); **Glen H. Nuckolls, Ph.D.**, Extramural Programs, Musculoskeletal Diseases Branch, NIAMS; **James W. Hanson, M.D.**, Director of the Center for Developmental Biology and Perinatal Medicine, Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD); and, **Ljubisa Vitkovic, M.D., Ph.D.**, Mental Retardation and Developmental Disabilities Branch, DHHS NIH NICHD.

Efforts of excellent program staff and leadership at NIH, excellent reviewers and study sections, excellent and outstanding researchers both working on FSHD and submitting applications to the NIH, and extraordinary efforts of the volunteer health agencies working in this area have not yet enabled FSHD funding to increase at the NIH. It is time for requests, contracts and calls for researcher proposals on FSHD to bootstrap existing FSHD research worldwide.

I am here once again to remind you that FSHD is taking its toll on your citizens. FSHD illustrates the disparity in funding across the muscular dystrophies and recalcitrance in growth over twenty years despite consistent pressure from appropriations language and Appropriations Committee questions, and an authorization from Congress mandating research on FSHD.

The pace of discovery and numbers of leading experts in the field of biological science and clinical medicine working on FSHD are very 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.

## **Fact 5**

### **Areas of Scientific Opportunity in FSHD that Need NIH Funding**

The majority of the international FSHD clinical and research community recently came together at the DHHS NIH NICHD Boston Biomedical Research Institute Senator Paul D. Wellstone MD CRC for FSHD. Almost 90 scientists working on FSHD globally met at the 2009 FSH Society FSHD International Research Consortium, held on Monday, November 9, 2009, and Tuesday, November 10, 2009. The summary and recommendations of the group state the following:

During the past two decades, the FSHD research has made steady progress to unravel the molecular basis of this common muscle disease. The main line of research has focused on the extremely complex (epi)genetic enigma. This complexity has fascinated experts involved in related research. At the present moment the FSHD research field is covering a variety of multidisciplinary and complementary approaches. Although the exact details of the molecular genetic basis of FSHD are still not in place, the general picture is coming into focus. Within one to two (1-2) years, evidence-based intervention strategies are on the drawing-board and trials are planned. To be prepared for this new FSHD era, we need to accelerate the efforts in the following areas --

**1. Patients and clinical trials readiness**

There is a need for well-characterized registries with uniform data collection. NIH U54 Wellstone MD CRC, NIH registries, and patient organizations are key to this process. These groups and registry and patient organizations are instrumental for:

- a. Work on natural history – identification of phenotype modifiers (genetic and environmental)
- b. Identification of the FSHD2 gene (contraction-independent FSHD)
- c. Bio-banking (cell lines etc.)
- d. Development of tools and assays to measure clinical trials endpoints

**2. Epigenetics / Genetics**

This line of work will be instrumental to pinpoint the real identity of FSHD1A (chromosome-4-linked cases) and FSHD1B (non-chromosome-4-linked cases). This information will form the basis for evidence-based intervention.

- a. Modifying genes for FSHD1 (large inter-individual variation in symptoms)
- b. Identify the FSHD2 gene (common molecular pathway with FSHD1)
- c. Further work on the chromatin structure / function relationship

**3. Biomarkers for clinical therapy**

There is obvious need for monitoring intervention.

- a. Systems biology approaches
  - i. transcriptomics, proteomics, metabolomics etc.
- b. In situ (RNA, protein) to detect cellular heterogeneity
- c. Non-invasive monitoring (MRI etc.)

**4. Model systems**

Urgent need for more specific model systems for mechanistic, intervention work and advancement to clinical trials.

- a. Cellular models

- i. Biopsies – for well characterized FSHD cell lines
  - ii. Mosaics -- isogenic and clonal lines
  - iii. Induced pleuropotent stem cells (iPS)
- b. Animal
  - i. Mouse – inducible / humanized mouse etc.
  - ii. Other species

## 5. Molecular, Cellular and Genomic

- a. myogenesis in normal and FSHD muscle (myoblasts/myotubes)
- b. Cell cycling
- c. Dynamics of muscle satellite cells
- d. RNA iso-forms and alternative splicing (FRG1, DUX4, others)
  - i. genome wide (normal versus FSHD)
- e. Chromatin structure at 4q35
- f. Downstream gene targets

## Our request to the NIH Appropriations Subcommittee

We request this year in FY2011, 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 \$25 million in FY2011.**

We implore the Appropriations Committee to request that the Director of NIH, the Chair, and Executive Secretary of the federal advisory committee Muscular Dystrophy Coordinating Committee mandated by the MD CARE Act 2008, to increase the amount of FSHD research and projects in its portfolios using all available passive and pro-active mechanisms and interagency committees.

We ask that Congress 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 catalyst for progress in funding and a greater seriousness in the endeavor of treating muscular dystrophy. We ask Congress to request of NIH the development of mechanisms to help expand work from the center of the NIH Wellstone Centers outward to address needs and priorities of the scientific communities.

Given the knowledge base and current opportunity for breakthroughs in treating FSHD it is inequitable that only four of the twelve NIH institutes covering muscular dystrophy have a handful of research grants for FSHD. We request that the Director of the 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.

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 facioscapulohumeral muscular dystrophy. Our successes are continuing and your support must continue and increase.

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