

FSH Watch

A publication of the FacioScapuloHumeral Society

FSH Society Sees Progress in Dollars Earmarked for Research

In 2001 and 2002, the Society reached out to international and government agencies, expressing concerns regarding the paucity of funding for facioscapulohumeral muscular dystrophy (FSHD) research. Our members wrote to their Congressmen and other agencies. We testified before Congress and visited Capital Hill and the National Institutes of Health (NIH) to educate about FSHD. The FSH Society was heard at the highest levels of Congress and at the NIH, emphasizing that not enough is being done to enhance research on FSHD. Finally, there were dramatic gains this past year. In late 2001, the NIH made several announcements for FSHD research and allocated approximately US\$4 million for FSHD. This is a twenty-fold increase over historical funding levels for FSHD at the NIH, and five times the Muscular Dystrophy Association's annual commitment to FSHD research. On December 18, 2001 for the first time in the history of the United States, Public Law 107-84, the Muscular Dystrophy Community Assistance Research and Education Act (MD-CARE Act), mandating research, study and education on muscular

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What can YOU do?

By Edward Schechter, Speaker and Panel member at International Network and Contact Day for FSHD October 13, 2002, Rockville, MD USA.

It is great to be back with you two years after Natick. The same wonderful spirit that pervaded that meeting is very evident here today. I expect this conference to be even more instructive, encouraging and useful.

At Natick, I asked you to do something important for the FSH Society. Today I have another issue to put in your hands. But before I get to that one I have a few words to say about the Natick request. Then, two years ago, I asked you to communicate with your Congressmen and Senators. I said they had to be made aware of what FSHD is, of the existence of our Society, and of the compelling need for the National Institute of Health funds to support FSHD research.

You responded magnificently. I thank you for your effective efforts. As a result of Dan's leadership, Carol's able help and the contacts so many of you made with your Washington representatives, the NIH knows about us now, recognizes our needs, and has begun to open its rich coffers to FSHD research. In the short span of two years we have taken a giant step forward. This has been accomplished within a highly politicized environment not always friendly to this Society, and in spite of

competition from hundreds of other worthy causes.

But with the NIH now directly funding a substantial portion of all types of muscular dystrophy research, an unanticipated difficulty has developed for our Society that we must all understand. The Society needs more staff help. The jobs Dan and Carol are doing on our behalf have grown enormously in scope and in complication. They are working 10 hour days, often seven days a week, month after month. And why is this? We do not have the dollar resources to afford the assistance they need.

Here are some reasons why we don't have those funds. First, although it doesn't sound logical, in spite of all the work Dan and others have done to get research funds, none of the newly freed-up NIH funds go to the FSH Society – the dollars go directly to the researcher or to his or her hospital or research institution. Second, our membership has grown very slowly. We had just 570 dues paying members in 2001; that's only 4% of what we believe are the 14,000 FSHD afflicted persons (without counting their family members) in the US who should be

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From the President

January 7, 2003

The Society plans to produce two types of the *FSH Watch*, resources permitting. The first type, *FSH Watch Newsletter*, will be produced quarterly with information to let people know we are here, what we do and what the needs are of the Society and the FSHD community. The second will be the *FSH Watch Annual Research Report*. It will provide a comprehensive picture of clinical and research happenings across the globe. You are reading the first edition of the newly formatted *FSH Watch Newsletter*; it is quite a bit longer than expected, as we have nearly a year and a half of information to catch up on. The research report will be forthcoming in several months.

As you read this newsletter, I hope you see the extraordinary success the Society has created in FSHD research and you decide to make a firm commitment to significantly financially support the FSH Society in 2003. 2002 was a very tough year for many individuals and charities, and the Society needs your support. If you have FSHD and the resources to back the Society, please do so now. I am impressed with our achievements to date and think you should be too. Over the years, we have advocated for the FSHD research, clinical and patient communities at all levels. We are making a difference!

The FSH Society was key in the drafting, passage, and enhancement of the Muscular Dystrophy Community Assistance Research and Education Act of 2001 (MD-CARE Act). Our efforts and advocacy resulted in a remarkable and comprehensive law. For the first time ever research and investigation into all forms of muscular dystrophy is mandated by law. The FSH Society has been carrying this torch for a decade. With our torch, once and forever, muscular dystrophy has risen out of the shadows and into the light and has become a federal priority. The FSH Society was instrumental in making this law a reality.

The direct result of the FSH Society's work in Washington, DC over the last decade is the National Institutes of Health (NIH) announcement of a series of initiatives to accelerate research on FSHD. All six NIH grantees under a previous contract for research on FSHD were past and present fellows of the Society. I

congratulate Dr. Housman, Chairman, and the FSH Society's Scientific Advisory Board on the tremendous success of its work and counsel. Complementary strands in parallel often yield some of the most profound results in policy, politics and science. The FSH Society's work in Washington, DC and in providing support for new and innovative areas in FSHD research has created a continually growing ladder that FSHD research can climb. We continue to push the envelope by striving to promote four to five new and innovative projects each year. The seeds we plant are growing. We need funds for the continuous demand of research project applications and for the new talented individuals and engaging ideas that come with them.

We ask you to make or increase your donation to the general fund of the Society. We ask you to fundraise for the Society. We ask you to be aware that there is a critical need in the research area for muscle tissue. The researchers have hung out posters ostensibly saying "Wanted Dead or Alive: FSHD muscle biopsies." In this issue we provide ways to help donate muscle tissue. It is a very serious shortage and a barrier to FSHD research moving forward . . . your help is urgently needed. We ask you to register with the NIH FSHD registry. It is imperative to the success of a national clinical and research program on FSHD that individuals with FSHD and their families join the NIH's FSHD registry at the University of Rochester. We ask you to ask your friends, family and employers to support, make and match contributions to the FSH Society's General, and Research and Education funds.

As patients, and we are patient patients, we continually confront the shadowy and terrifying internal reflection of FSHD with its certain destruction, its unending pace, its cruelly casual sadism and concentration of complexities. We find our way from disease to health through the will to achieve well being. We achieve by sharing what we are, who we are, and as we share, we move ultimately towards a healthier status.

Know that the Society, its advisors and fellow individuals with FSHD work diligently day and night to solve FSHD.

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Society Sees Progress, *continued from front page*

dystrophy was enacted. This year there is a Congressional line item in the budget for FSHD and Muscular Dystrophy.

The death of Senator Paul Wellstone was a tremendous loss for the muscular dystrophy community. Senator Wellstone and his staff were crucial in making the MD-CARE Act happen. Senator Wellstone is missed and his passion, candor and forthrightness were uncommon.

In the interim while the MD-CARE Act oversight committee mandated by the act is being formed, the Society has been representing FSHD interests on the NIH MD Task Force. The MD Task Force is an interim committee of experts to outline agendas and direction for muscular dystrophy research at the NIH. The MD-CARE Act coordinating committee will assume much of the work and direction of the task force when it is formed. The FSH Society research programs are yielding enormous insight and being scaled up by other agencies as more and more data flows from the many seeds planted. 2002 has brought several novel areas of investigation that the Society was pleased to begin. 2002 brought several major breakthroughs in the FSHD puzzle and publications in respected journals such as *Cell* and *Nature Genetics*, and many more publications are in press and in review.

President, continued from page 2

Every day we find ourselves standing before the deep mystery of facioscapulohumeral muscular dystrophy and the near and far reality of molecular genetics. The mystery is unfolding, the scientific problem is becoming far more interesting, breakthroughs are happening, more money is making its way into research, our numbers are growing, FSHD is being recognized and documented, and new researchers and clinicians are joining our fight. Last, know that not one cent of the NIH monies that we advocate for go to the Society and that we need money to stay the course and grow.

Thank you for your past and continued support. I am even more optimistic than ever.
Daniel Paul Perez, President & CEO



It is the editorial policy to report on developments regarding FacioScapuloHumeral Muscular Dystrophy (FSHD), but not to endorse any of the drugs or treatments discussed.

We urge you to consult with your own physician about the procedures mentioned.

The *FSH Watch* is published by the *FSH Society* and distributed by mail to its members and supporters. To be placed on the mailing list or to submit an article please write to: Carol Perez, *FSH Society*, 3 Westwood Road, Lexington, MA 02420. Articles may be edited for space and clarity. Every effort has been made to ensure accuracy in the newsletter. If you wish to correct an error, please write to the above address. Look for us on the internet at: www.fshsociety.org

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Lady Hall, In Memoriam

Lady Williams Hall, a long-time FSH Society board member, passed away on October 20, 2001 after a brief illness. We extend our condolences to the family members and to her husband Judge William E. Hall, Jr. who, with Lady, was a founding member. For those of us who had the honor of knowing Lady, she was both friend and mentor and deeply committed to making a difference for those living with facioscapulohumeral dystrophy. We will miss her, and her unwavering support, personally and in our mission. She was truly a woman of uncommon strength and wisdom. We shall miss our "Steel Magnolia."

The Combined Federal Campaign (CFC) #2662 Benefits FSH Society

Federal employees and military personnel can donate to the FSH Society through the Combined Federal Campaign.

Please consider making a contribution to the FSH Society through the CFC. The Combined Federal Campaign or CFC is operated by the United States

Government Office of Personnel Management (OPM). The FSH Society CFC code is #2662. For more information about the CFC you may visit the [OPM website](http://www.opm.gov/cfc/index.htm) at

<http://www.opm.gov/cfc/index.htm>.

Tides Foundation Grant

The Tides Foundation of San Francisco awarded US\$30,000 to the *FSH Society* at the request of a Donor Advised Fund in both 2001 and 2002. The Board of Directors of the FSH Society voted to utilize this award to provide support to the Society's ongoing activities.

The members of the FSH Society express gratitude to the Tides Foundation for this gift that permits the FSH Society to pursue excellence in research and education to support international collaborative efforts.

Marjorie Bronfman Grant for Molecular Genetics Research on FSHD for 2002

The generosity and commitment of Mrs. Marjorie Bronfman to FSHD research started in 1998. To date, the Society has received US\$500,000 of the US\$700,000 pledged through 2004. All of the US\$500,000 has been awarded for two-year research fellowships (US\$30,000/year) for research projects that show extraordinary promise to find the cause of FSHD. This foresighted contribution significantly impacts progress in FSHD research and has already created advances worldwide. The FSH Society is deeply indebted to Mrs. Bronfman and the Marjorie and Gerald Bronfman Foundation for this significant opportunity to advance FSHD research. The FSH Society is pleased to be able to continue the productive collaboration with Mrs. Marjorie Bronfman to advance FSHD research.

What can YOU do?, continued from front page

interested in and supportive of what we are doing. Third, as an “orphan” disease (we are orphans because there are so relatively few of us and we don’t die from our FSHD) we are a poor choice for the pharmaceutical companies that seek profits in exchange for their support of an organization such as ours. Fourth, some former, and some potential new contributors, to the Society have undoubtedly thought that with the NIH now funding the research, there was no longer an imperative need to support the Society. There are lots of other reasons, but four are enough to make my point – we need help.

What is it that demands so much of the time of our limited staff – Dan and Carol and some part time help? To generalize – it is communications – with members, researchers, Congressmen and their staffs, foreign organizations, the Internet, etc. To be specific, Dan and Carol presently perform all the demanding tasks: they maintain budget and financial controls; raise funds; acknowledge receipts; prepare for annual audits; maintain membership and donor lists; pursue grant opportunities; prepare for, attend and write minutes of the FSH Board and the Scientific Advisory Board; manage exhibit booths at two or more professional meetings each year; organize the annual international meeting of the FSHD Work Group at the American Society of Human Genetics meeting; seek new and retain old members; write and edit Society publications and news letters; manage and edit the Society’s Internet domain and chat room; plan and implement effective relationships with federal and state governments; develop FSHD’s research mission; maintain adequate files; respond to information requests; maintain a patient registry; organize and train support groups; organize the bi-annual patient conference; write and edit all Society correspondence; develop and maintain a research library; maintain liaison with US researchers at

various universities and laboratories; maintain liaison with international FSH working groups in England, France, the Netherlands and Japan; and arrange for translation of Society materials in many languages, i.e. Croatian, Spanish, Polish, German, Portuguese and Dutch.

Wow! (Time out to catch my breath!)

It’s obvious now why I told you all of this. The Society needs unrestricted funds (funds not earmarked for a specific purpose, such as genetic research) so that the staff can be enlarged. We need a membership/development person; we need a writer/public relations person. If we can relieve Dan and Carol of these time consuming responsibilities, they will be free to do the things they do best, and to be even more effective than they are today – hopefully even to reduce their work load to a more acceptable level.

And you and me, all of us – what’s our part? Here are four things we can do.

- We can solicit contributions of memberships – from our mothers and fathers, sisters, brothers, aunts and uncles, cousins, close friends, business associates, etc.
- We can make sure our neurologists and physiatrists and therapists receive our literature, are aware of what our Society does, and are given the opportunity to join our Society.
- We can make unrestricted tax free contributions to our Society- contributions that can be used for purposes deemed necessary by our officers and Directors.
- And finally, we can look hard at what we contribute each year for our membership in this Society and then consider making a substantial increase.

If we do our part, when we meet again two years from now, we will have a successful Society leading us with power and assurance towards achieving our research goals – finding the cause of our disease, and finding the means of reducing its effect upon our bodies and our lives. That hope may now be within our grasp. It is up to us to help get our Society there.

Society Presents Fiscal Year 2003 Congressional Testimonies on the need for FSHD Research

In 2002, we again went before Congress on behalf of all concerned with FSHD and submitted two testimonies before the United States House and United States Senate. The Society submitted appropriations testimony before the Senate and House Appropriations Committee, Subcommittees on Labor, Health, Education and Related Agencies regarding appropriations for the National Institutes of Health (NIH) for research on facioscapulohumeral muscular dystrophy on March 31, 2002 and on May 9, 2002. The FSH Society was requested to present testimony before the U.S. House in person. We had the unexpected pleasure of testifying with Julia Roberts who was testifying for Rett’s syndrome. The room was packed, with standing room only.

The Society again acquainted the members of the committee with FSHD and the developments and need for more funding. The salient point of the testimonies is slightly different from most groups requesting money from the Congress for research on a particular disorder. Most volunteer groups educate the Congress on their particular disorder and request money to be given to the NIH for research for that disorder. Congress sees its mission as to give the money to NIH to do the work that it does so well with the hope that the increasing budget levels will have a positive affect on all research areas. We expressed to the committee that despite the passage of the MD-CARE Act, the budget numbers did not reflect a strong commitment from the NIH to muscular dystrophy and that the systems for tracking research areas and budgets were divergent. Last, we made the point that despite the Congressional support to double the NIH budget every five years, clearly not all areas were keeping pace. We asked the Congress to explore why muscular dystrophy has been left behind so many other areas of research at the NIH.

Excerpts from the oral testimony

Your contribution to the FSH Society is tax-deductible and ensures the on-going work of YOUR advocacy group. Please send your donation now. Please see donation form on page 32.

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MD-CARE Act of 2001 Passed - FSHD Research Mandated

On December 18, 2001, "The Muscular Dystrophy Community Assistance, Research and Education Act" (The MD-CARE Act of 2001) was signed by President George W. Bush. The MD-CARE Act of 2001, passed unanimously by both houses of Congress, directs the Public Health Service, including the National Institutes of Health (NIH) and the Center for Disease Control (CDC), to put increased emphasis on muscular dystrophy research. The law enhances ongoing research programs at the NIH and establishes NIH centers of research excellence (COREs) to accelerate muscular dystrophy research. The law also calls for oversight mechanisms and advisory committees.

Progress on the MD-CARE Act of 2001 has been slowed by interplay between the Administration and the NIH and other agencies regarding establishing the MD-CARE Act coordinating committee. The MD-CARE Act requires that a MD coordinating committee be established to coordinate and monitor activities across NIH and other federal agencies involved with MD. Two-thirds of its members must come from government agencies, including NIH, Centers for Disease Control and Prevention (CDC), the Health Resources and Services Administration (HRSA), the Food and Drug Administration (FDA), the Department of Education (DOE) and others; the other third is public members "including a broad cross section of persons affected with muscular dystrophies." The committee falls under the guidelines of the Federal Advisory Committee Act (FACA). The NIH is waiting to hear back from the Bush Administration, including Health and Human Services Secretary Thompson, with permission to move ahead with assembling the committee. The Administration retains final control over the decision on nominees to serve on the committee. As of this writing, all agencies have responded but one and the committee is expected to be formed soon.

In 2001, the FSH Society was crucially involved in the analysis, negotiation and rewriting of the Senate version of the Senate MD-CARE Act draft (S. 805 / H.R.717). It became apparent that the original version was primarily for

Duchenne dystrophy and was inadequate for, and possibly harmful to, FSHD research. We held meetings on the Hill and with the NIH to discuss our concerns about jeopardizing the hard-won but very modest funding we then had for FSHD research. In fact, the proposed bill excluded muscular dystrophies that affect women and adults and incorporated none of the recommendations of the 2000 NIH Research Planning conference.

On May 8-9, 2000 The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute of Neurological Disorders and Stroke (NINDS), and the Office of Rare Diseases sponsored a conference on the *Cause and Treatment of Facioscapulohumeral Muscular Dystrophy* in Bethesda, MD (see timeline below for summary information). The Society helped rewrite the bill in person with Senator Paul Wellstone's staff and negotiated a strong bill by coordinating the concerns and input of several large dystrophy and government research agencies, crafting a law that met

the greater interests of the entire muscular dystrophy community. The result of our work is a comprehensive law that addresses the need for research for all of the major muscular dystrophies. It is important to note that the FSH Society pioneered and laid the ground work for this law over a period of ten years and the Parent Project and the Muscular Dystrophy Association brought an enormous amount of energy to Washington, DC. This landmark legislation would not have been a reality without the unprecedented cooperation of all three organizations.

An excerpt of the law follows below. To find the complete text of the MD-CARE Act go online to the Thomas Locator (<http://thomas.loc.gov/home/thomas.html>). Once there, click on "Public Laws by Law Number" under the Legislation link. That will take you to the 107th Congress' public laws. Click on Public Laws 107-51 - 107-100. Then scroll down to Law 84 (H.R. 717). You will find a link to bring up the text or a printable pdf file.

Public Law 107-84

"To amend the Public Health Service Act to provide for research with respect to various forms of muscular dystrophy, including Duchenne, Becker, limb girdle, congenital, facioscapulohumeral, myotonic, oculopharyngeal, distal, and Emery-Dreifuss muscular dystrophies . . . The Director of NIH, in coordination with the Directors of the National Institute of Neurological Disorders and Stroke (NINDS), the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute of Child Health and Human Development (NICHD), and the other national research institutes as appropriate, shall expand and intensify programs of such Institutes with respect to research and related activities concerning various forms of muscular dystrophy, including Duchenne, myotonic, facioscapulohumeral muscular dystrophy (referred to in this section as 'FSHD') and other forms of muscular dystrophy."

Sam E. and Mary F. Roberts Foundation Grant awarded to Study Nutrition and FSHD

The Sam E. and Mary F. Roberts Foundation of Lawrence, Kansas established a fund to study nutrition and FSHD. We are indebted to the Board of the Roberts Foundation and its Chairman Susan Pogany for this opportunity. Dr. Graham Kemp, Department of Musculoskeletal Science, University of Liverpool, United Kingdom is the first recipient of the Roberts Foundation grant for his project, "Muscle damage by reactive oxygen species, muscle atrophy and effects of creatine supplementation in facioscapulohumeral muscular dystrophy."

Congressional Testimony, continued from page 4

before the U.S. House follow:

Facioscapulohumeral muscular dystrophy (FSHD) is the third most prevalent form of muscle disease. FSHD is a neuromuscular disorder that is transmitted genetically and affects 12,500-37,500 persons in the United States. For men and women, the major consequence of inheriting FSHD is progressive and severe loss of skeletal muscle.

The "FSHD mutation" was identified in 1990. Although this molecular genetic defect is now known, there are no genes that have been associated with or linked to FSHD to date. The biochemical mechanism and cause of this common muscle disease remains absolutely unknown and elusive. The same is true for any treatment, therapy or cure — none exist.

For forty years, I have dealt with the continuing, unrelenting and unending loss caused by FSHD. Less than ten years ago, I walked with some difficulty into this very room to testify. Today, I sit before you in a wheelchair because of this disease called FSHD.

Nearly a decade ago, I appeared before this Committee to testify for the first time. Since then, the Congressional Appropriations Committees have repeatedly instructed the National Institutes of Health (NIH) to enhance and broaden the portfolio in FSHD. Due to the Appropriations Committees' interest, FSHD research has begun to take a number of steps forward this past year. I am pleased to report that three major programs to accelerate funding and research on FSHD have been initiated by the NIH.

The FSH Society, incorporated in 1991, solely addresses specific issues and needs regarding FSH muscular dystrophy and has invested more than US\$750,000 into new research initiatives for this common muscle disease. The Society actively represents and educates more than 10,000 patients with FSHD.

Last year, thanks to your efforts, the United States Congress passed the "Muscular Dystrophy Community Assistance, Research and Education Act (The MD-CARE Act) of 2001." The purpose of this law is to rapidly accelerate, develop and broaden the base of research on muscular dystrophy and FSHD and to

bring that research into the clinic.

In spite of all this, the state of research on FSHD is not good. Since 1998, the overall budget for the NIH has increased 70%. The budget for the Arthritis (National Institute of Arthritis and Musculoskeletal and Skin Disease — NIAMS/NIH Arthritis) Institute, has increased 75%. The Neurology (National Institute of Neurological Disorders and Stroke — NINDS/NIH) Institute's budget has increased 70%. Yet, the budget for muscular dystrophy has increased only 49%. In spite of all this, the NIH-funded research on FSHD is minimal at best, and, frankly, we are not sure that the 49% increase for muscular dystrophy figure is reliable. During this period, the total number of grants at the NIH has increased by nearly 30% while grants in muscular dystrophy have barely increased to just over 10%. Budget estimates of increases in future years for muscular dystrophy as indicated by the NIH can only be described as "anemic."

Congress has been very generous with the NIH and has repeatedly expressed its desire to see greater efforts in muscular dystrophy research and FSHD research in particular. This is not happening. This rising tide is not raising all boats.

Thanks to this Committee, the NIH and the FSH Society held a Research Planning Conference in May 2000. Recommendations for future directions included specific projects in basic molecular research, therapeutic candidates, population studies and the creation of new animal models. Today, two years later, that agenda is still in its initial working stages and perhaps 25% complete.

We are very concerned that the enormous scientific progress that is possible for FSHD is not reflected in the budget presented by the NIH.

Mr. Chairman, we trust your judgment on the matter before us. We believe the Committee should explore why muscular dystrophy has been left behind at the NIH. Frankly, we are extremely frustrated that amid a huge increase in funding and strong unambiguous expressions of Congressional support, the NIH commitment in muscular dystrophy continues to be so weak. Only you can answer that question."

International Consortium Research Meeting on FSHD 2002 held in Baltimore, MD

The FSHD International Consortium Research Meeting 2002 was held on Tuesday, October 15, 2002, 3 p.m. - 9 p.m. at the Baltimore Convention Center, MD. Co-Chairs were Rune Frants, Ph.D., Sara Winokur, Ph.D., and Michael Green, Ph.D. The meeting was sponsored by the FSH Society, the Muscular Dystrophy Association (MDA USA), the Stichting FSHD (Dutch FSHD Foundation), Association Française Contre les Myopathies (AFM), the Unione Italiana Lotta alla Distrofia Muscolare (UILDM) - Sezione di Castellammare di Stabia, and Athena Diagnostics. Welcome, opening remarks and keynote were by Daniel Paul Perez, FSH Society, Bill Moore, Muscular Dystrophy Association, and Richard Lymn, NIH, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS/NIH).

The meeting was an extraordinary event with an enormous amount of energy, networking and unprecedented interchange between groups. Kuan Wang, Chief, Laboratory of Muscle Biology, NIH, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS/NIH), Bethesda, MD introduced the research community to resources and programs in muscle biology being done inside the NIH (known in research or NIH jargon as "intramural research") and welcomed collaborations from the external field of researchers (known as "extramural research") in his lecture titled: "NIH Laboratory of Muscle Biology: Introduction, Technical Infrastructure and Extramural Collaboration." It was an unprecedented event and a major step forward for FSHD research. Daniel Paul Perez first met Kuan Wang in July 1999, where the two were panel members at a NIAMS/NIH long range planning session on muscle disease and muscle biology. They discussed the need to bridge the gap between the intramural and extramural communities. In October, 2002, it became reality and collaborations have already come forth from the meeting. We were especially pleased to have a lecture on

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International Consortium Research Meeting, *continued from page 6*

muscle cell differentiation titled "Stage specific modulation of skeletal myogenesis by inhibitors of nuclear deacetylases" by Vittorio Sartorelli, Ph.D., Gene Expression Laboratory, NIH, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS/NIH), Bethesda, MD.

The outline of the meeting, presentations and posters follows. Abstract books are available from the FSH Society by request for a small fee. All research presentations will be elaborated on in the upcoming annual *FSH Watch Annual Research Report*.

GENE EXPRESSION and CELLULAR BIOLOGY

Disease-specific changes in facioscapulohumeral muscular dystrophy by expression profiling

Yi-Wen Chen, Children's National Medical Center, Washington, DC, USA

Inappropriate gene activation in FSHD: A repressor complex binds a chromosomal repeat deleted in dystrophic muscle

Rossella Tupler, University of Massachusetts Medical School, Worcester, MA, USA

Expression profiling in FSHD supports a defect in early stages of Myo-D-regulated myogenic differentiation

Sara Winokur, University of California, Irvine, CA, USA

Facioscapulohumeral dystrophy: Premature activation of the myogenic program?

Denise Figlewicz, University of Rochester Medical Center, Rochester, NY, USA

DISCUSSION

FRG1, FRG2, ANT1 expression in FSHD
Silvère van der Maarel and Michael Green, Moderators

MUSCLE BIOLOGY

Sarcolemmal reorganization in facioscapulohumeral muscular dystrophy
Robert Bloch, University of Maryland, Baltimore, MD, USA

Study of the DUX4 gene and protein in FSHD

Frédérique Coppée, University of Mons-Hainaut, Mons, Belgium

NIH Laboratory of Muscle Biology:

Introduction, Technical Infrastructure and Extramural Collaboration

Kuan Wang, Chief, Laboratory of Muscle Biology, NIH, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS/NIH), Bethesda, MD, USA

Stage specific modulation of skeletal myogenesis by inhibitors of nuclear deacetylases

Vittorio Sartorelli, Gene Expression Laboratory, NIH, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS/NIH), Bethesda, MD, USA

GENOMICS and CHROMATIN STRUCTURE

Facioscapulohumeral muscular dystrophy (FSHD) is uniquely associated with one of the two variants of the 4q subtelomere

Richard J.L.F. Lemmers, Leiden University Medical Center, Leiden, the Netherlands

Evidence consistent with linkage to 15q of a non-chromosome 4 linked FSHD family

Marcy Speer, Duke University Medical Center, Durham, NC USA

Chromatin Structure and DNA Methylation in the FSHD Syndrome-Linked 4q35 Region
Melanie Ehrlich, Tulane Medical School, New Orleans, LA USA

Hypomethylation of the D4Z4 repeat array in Facioscapulohumeral muscular dystrophy alleles

Silvère van der Maarel, Leiden University Medical Center, Leiden, the Netherlands

DISCUSSION

D4Z4 Methylation in FSHD
Alexandra Belayew and Denise Figlewicz, Moderators

GENETICS AND DIAGNOSTICS

Polymorphisms and pathogenic rearrangements at the 4q and 10q loci implicated in FSHD

Luciano Felicetti, Catholic University and Center for Neuromuscular Diseases, Rome, Italy

Southern blot analysis of the parents of 4q35-FSHD patients

Kanako Goto, National Institute of Neuroscience, NCNP, Tokyo, Japan

FSHD in Russian Families: Patterns of muscle involvement, severity of the disease and DNA fragment size correlation.

Valery Kazakov, St. Petersburg Pavlov State Medical University, St. Petersburg, Russia

Evaluation of BglII / BlnI dosage test in a molecular diagnostic testing service for FSHD

Peter Lunt, Clinical Genetics & Regional Molecular Genetics Services, Bristol, United Kingdom

Development of a new analytical test which improves the diagnostic accuracy in facioscapulohumeral muscular dystrophy (FSHD)

Meena Upadhyaya, University of Wales College of Medicine, Cardiff, United Kingdom

DISCUSSION

Genetics and Diagnostics
Antonel Olkers, Luciano Felicetti, Yukiko Hayashi, Moderators

DISCUSSION and FUTURE

DIRECTIONS
Peter Lunt and Rune Frants, Moderators

Do you have a few hours to give to the Society's work? Many things can be done right from where you live. We need you!!

FSH Society Research Fellowship Program Attracts Top Talent & New Ideas

Over the last year, we have again been the advocate for FSHD research, clinical and patient communities at all levels. We are making a difference. The FSH Society research fellowship program was launched in 1998 under the chairmanship of Dr. David Housman of the Massachusetts Institute of Technology (M.I.T.). In a little more than four years, we have received numerous inquiries, requested and reviewed letters of intent and peer-reviewed grant and fellowship applications. We have funded 18 applications and numerous small projects. In four years, we have reviewed numerous high quality applications with extreme relevance to FSHD. We are certain that there is no shortage of excellent personnel and that the research community is extremely interested in FSHD. The Society recruits and makes the NIH aware of researchers expressing interest and data showing scientific promise in FSHD. There are many promising ideas and we are working to see that each request is given an opportunity for success in funding. We are pushing the leading edge of research and fostering tomorrow's leaders in FSHD research. The Society is currently initiating funding for four new exciting projects, which are described below:

Title: *"Muscle damage by reactive oxygen species, muscle atrophy and effects of creatine supplementation in facioscapulohumeral muscular dystrophy."*

Investigator: Graham J. Kemp, M.D.

Institution: University of Liverpool
We are pleased to announce the first FSH Society Sam E. and Mary F. Roberts Foundation grant for research on FSHD and nutrition. "This is a pilot study designed to test the following hypotheses: 1.) that muscle in FSHD shows evidence of damage by reactive oxygen species (ROS) in vivo; 2.) that this is at least due partly to reduced anti-ROS protection; 3.) that this is ameliorated by six months of creatine treatment; 4.) that this also partially alleviates muscle atrophy, even in the absence of training; and 5.) that this results in an increase in muscle strength and clinical indices. This is an open label pre-post protocol examining the effects of creatine supplementation in 10 patients with proven FSHD [and disease controls

and unaffected controls]. ROS protection and damage will be studied in conchotome biopsies of biceps. Muscle atrophy and its effect on body composition will be measured by whole body quantitative magnetic resonance imaging (MRI)." The Society is pleased to have Dr. Kemp and his colleagues at the University of Liverpool, one of the foremost institutions in the world in state-of-the-art MRI and Magnetic Resonance Spectroscopy (MRS), working on FSHD and applying these new methods to examine and quantify critical areas of research

Title: *Tethering Adenine (Dam) Methylase to the 3.3-kb FSHD Repeats to Identify Distant Genes that Physically Come in Contact with the Repeats*

Investigators: York Marahrens/Nieves Embade

Institution: University of California, Los Angeles (UCLA)

The Society is delighted to have Drs. York Marahrens and Nieves Embade of UCLA working on FSHD. This is a fascinating project that is high risk but has a great potential for profound insight into FSHD. "We propose to locate the FSHD gene(s) that interact with the D4Z4 repeats by tethering bacterial adenine methylase to sequences in or near the 3.3kb repeats and then identifying adenine-methylation at distant sites on the same chromosome or different chromosomes." In lay terms, the researchers hope to attach a piece of material to the repeats that is like an ink pad and then watch the chromosome fold up and unfold to see where the ink touches and what it comes in contact with.

Title: *The role of DUX4 in Facioscapulohumeral Muscular Dystrophy*

Investigators: Cecelia Ostlund/Howard J. Worman

Institution: Columbia University
The Society is honored to have Drs. Ostlund and Worman working on FSHD and to have Columbia University on board. This study will "assess the expression of DUX4 from patients with FSHD. Expression of the protein will be assessed by immunoblotting, immunofluorescence microscopy and mass spectroscopy using myoblasts from patients

with FSHD and non-affected controls. In aim 2, the targeting of DUX4 to the nuclear envelope will be examined. Searches for DUX4 binding proteins, including the nuclear envelope proteins lamins and emerin will be performed . . . The results of this project will establish if abnormal expression of DUX4 occurs in FSHD and provide a direction for future studies on its role in disease pathogenesis."

Title: *Mouse models to study candidate genes and epigenetic causes of FSHD*

Investigators: Tonnie Rijkers/Silvère van der Maarel

Institution: Leiden University Medical Center, The Netherlands

Under the direction of Dr. van der Maarel, the Leiden University scientists were able to develop transgenic mouse models with a grant from the Society. Leiden has "generated several transgenic mouse lines in which parts of the human 4q35 region, including 4 FSHD candidate genes and different size D4Z4 repeats, are present." These scientists have successfully spliced lengths of human D4Z4 repeats into the mouse genome and can now study it. Leiden generated several lines with differing lengths of the human D4Z4 repeats. This has already yielded tremendous insights. This project will use these mouse lines to investigate in more detail "the chromatin constitution of the D4Z4 region (through methylation, nuclease and protein binding studies), its effects on expression of the FSHD candidate genes and their biological function. We expect that the interplay between research on human material, in vitro testing and transgenic mice will enhance our understanding of the basic process underlying FSHD."

The Society notes that biological model systems, animal models and human tissue are all an extreme priority for FSHD research. In 2003, we will turn much of our focus towards models and model systems for studying FSHD. We implore those wishing to help research to consider donating living tissue through a biopsy, and to consider tissue and organ donation registry as well. Please contact the FSH Society to let us know your interest.

Complete Listing of Past and Present FSH Society, Inc. Fellows

Grant: FSHS-MB-001
Researcher: Silvère M. van der Maarel, Ph.D.
Institution: Leiden University Medical Center
Project Title: "Generation of Transgenic Mouse Models for FSHD."

Grant: FSHS-MB-002
Researcher: Sara T. Winokur, Ph.D.
Institution: University of California Irvine
Project Title: "Analysis of Chromatin Structure and Skeletal Muscle-Specific Gene Expression in Facioscapulohumeral Muscular Dystrophy."

Grant: FSHS-MB-003
Researcher: Denise Figlewicz, Ph.D.
Institution: University of Rochester School of Medicine
Project Title: "Expression of genes proximal to the D4Z4 deletions: a quantitative study in FSHD patients and controls."

Grant: FSHS-MB-004
Researcher: David J. Picketts, Ph.D.
Institution: Ottawa General Hospital
Project Title: "Utilizing an epigenetic approach to identify the FSHD gene."

Grant: FSHS-MB-005
Researcher: Davide Gabellini, Ph.D.
Institution: University of Massachusetts Medical Center

Project Title: "Identification and characterization of a protein interacting with the DNA repetitive element causally related to facioscapulohumeral muscular dystrophy."

Grant: FSHS-MB-006
Researcher: Fern Tsien, Ph.D. / Melanie Ehrlich, Ph.D.
Institution: Tulane Cancer Center
Project Title: "DNA Methylation and Chromatin Structure of FSHD-linked Sequences in FSHD Cells, Normal Cells, and Cells from Patients with the ICF Syndrome."

Grant: FSHS-DR-001
Researcher: Alexandra Belayew, Ph.D., Stephane Plaisance, Ph.D.
Institution: University of Mons-Hainaut, Mons, Belgium
Project Title: "Characterization of a protein expressed from a 3.3 kb element not linked to FSHD."

Grant: FSHS-DR-002
Researcher: Rossella Tupler, M.D., Ph.D.
Institution: University of Massachusetts Medical School
Project Title: "Characterization of differentially expressed genes in facioscapulohumeral muscular dystrophy affected muscles."

Grant: FSHS-DR-003
Researcher: Robert Bloch, Ph.D.
Institution: University of Maryland School of Medicine
Project Title: "Sarcolemmal organization in FSHD and the MYD mouse."

Grant: FSHS-DR-004
Researcher: Jane Hewitt, Ph.D.
Institution: Nottingham University
Project Title: "Fugu rubripes as a model organism for FSHD gene identification."

Grant: FSHS-DR-005
Researcher: Marcy Speer, Ph.D.
Institution: Duke University Medical Center
Project Title: "Genetic Linkage Studies in Non-chromosome 4 FSHD."

Grant: FSHS-TF-001
Researcher: Marcy Speer, Ph.D.
Institution: Duke University Medical Center
Project Title: "Genetic Linkage Studies in Non-chromosome 4 FSHD."

Grant: FSHS-VR-001
Researcher: Robert Bloch, Ph.D.
Institution: University of Maryland School of Medicine
Project Title: "Sarcolemmal organization in FSHD and the MYD mouse."

Grant: FSHS-TG-001
Researcher: Jeanne Lawrence, Ph.D. / Y. Polly Xing, M.D., Ph.D.
Institution: University of Massachusetts Medical Center
Project Title: "Higher level chromatin packaging and nuclear organization of FSHD cell with an emphasis on its 3.3 kb deletion involving high resolution transcript mapping by mRNA in situ and direct visualization of this region of the chromosome via in situ hybridization with loop halo DNA preparations."

Grant: FSHS-SMRF-001
Researcher: Graham J Kemp, M.D.
Institution: University of Liverpool
Project Title: "Muscle damage by reactive oxygen species, muscle atrophy and effects of creatine supplementation in facioscapulohumeral muscular dystrophy."



***Your contribution to the FSH Society is tax-deductible
and ensures the on-going work of YOUR advocacy
group. We need your continued support.***

Please send your donation now.

The donation form can be found on page 32.



The NIH Funds Multiple Research Grants in Facioscapulohumeral Dystrophy

Dr. Richard Lymn of NIAMS/NIH delivered one of the keynotes at the 2001 International Workshop on FSHD in San Diego, CA sponsored by the FSH Society. For the first time, research on FSHD at the NIH received significant increases through the use of a funding mechanism for high risk and innovative research projects. This major investment and infusion of funds into high quality research on FSHD is a big step for NIH. Thirteen proposals were submitted in response to the NIH announcement. Six new grants, solely dedicated to FSHD, were awarded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and the National Institute of Neurological Disorders and Stroke (NINDS) at the NIH. Of the six grantees, five were FSH Society Bronfman grantees, and two were FSH Society Delta Railroad grantees (one was both a Delta and Bronfman team). The total annual NIH award for these six grantees was US\$1,106,291 and is for three years, for a total of US\$3,318,873.

The press release from NIH can be found at http://www.niams.nih.gov/ne/press/2001/12_13.htm. NIAMS Director Stephen I. Katz, M.D., Ph.D. states: "These projects serve to increase the understanding of this disease and to develop better therapies, and ultimately, find ways to prevent the disorder . . . We are encouraged by the hope that they bring to people with facioscapulohumeral muscular dystrophy and their families." The release elaborates on the six projects funded across two Institutes at the NIH. **The new NIAMS/NINDS-funded studies include:**

Molecular Pathophysiology of Facioscapulohumeral Muscular Dystrophy via Genome-Wide Approaches, Yi-wen Chen, Ph.D., Children's Research Institute, Washington, D.C. [Sara Winokur, Ph.D., University of California Irvine, Irvine, CA.] This study will compare clinically affected versus unaffected muscles to help determine the primary cause of FSHD. Disease-specific gene alterations will also be identified using a broad set of genes. Further studies may determine how these gene alterations could affect the severity of the disease.

Llama-Derived Phage Display Antibody

Arrays for FSHD, Silvère M. Van Der Maarel, Ph.D., Leiden University Medical Center, Al Leiden, Netherlands. Muscle-specific animal antibodies will be used to study FSHD pathophysiology in tissues and cell cultures of patients and controls. This project will ultimately attempt to gain insight into the cellular and molecular processes leading to neuromuscular system dysfunction in FSHD patients.

Pathogenesis of Facioscapulohumeral Dystrophy, Denise A. Figlewicz, Ph.D., University of Rochester, Rochester, NY. The aim of this project is to develop a better understanding of the cause of FSHD. The project will seek to determine the abnormal intracellular processes in FSHD muscle cells. Study results may help in the development of intervention strategies for long-term therapeutic effects."

Analysis of the Molecular and Functional Role of D4Z4 in FSHD Pathogenesis, Rossella G. Tupler, M.D., Ph.D., University of Massachusetts Medical School, Worcester, Massachusetts. This project aims to use studies of a specific gene sequence to explain the cause of FSHD. The studies will provide information to

understand the molecular basis of FSHD and to develop effective therapeutic strategies.

The Sarcolemma in FSHD and in the myd Mouse, Robert Bloch, Ph.D., University of Maryland, Baltimore, MD. This study will use animal models and biopsies of human skeletal muscle to better understand the biological changes that occur in FSHD skeletal muscle. These changes will be analyzed to determine if they are related to the pathophysiology of FSHD and will be used in comparison with other human muscular dystrophies. Aims of this research include determining if the biomechanical properties of the membranes that surround muscle fibers are compromised by FSHD.

FSHD Syndrome: DNA Repeats, Methylation, and Chromatin, Melanie Ehrlich, Ph.D., Tulane University Health Science Center, New Orleans, LA. This study will explore whether a change in genetic structure causes inappropriate gene expression in muscle cells affected by FSHD. Researchers hope that this will provide an understanding of the molecular cause of this disease.

Request For Applications (RFA) AR-01-002

Exploratory Research on Facioscapulohumeral Muscular Dystrophy

Type	NIH Grant No.	Researchers	FSH Grant No.
R21	NS43976-01	Robert Bloch	FSHS-DR-003 / FSHS-VR-001
R21	AR48318-01	Yi-Wen Chen, Sara Winokur	FSHS-MB-002
R21	NS43974-01	Melanie Ehrlich	FSHS-MB-006
R21	AR48340-01	Denise Figlewicz	FSHS-MB-003
R21	NS43973-01	Rossella Tupler, Davide Gabellini	FSHS-DR-002 / FSHS-MB-005
R21	AR48327-01	Silvère van der Maarel	FSHS-MB-001
		Total Annual Costs:	US\$1,106,291

Outline Notes on FSHD at the Washington University Neuromuscular Disease Center

The Neuromuscular Disease Center at the Washington University School of Medicine, St. Louis, Missouri <http://www.neuro.wustl.edu/neuromuscular/> has published a nice outline section on disease mechanisms in FSHD at the following internet address: <http://www.neuro.wustl.edu/neuromuscular/musdist/pe-eom.html#fsh>. The page is on Myopathies & Neuronopathies With No EOM Weakness ± Face & Periocular Involvement. It is interesting to note that myotonic dystrophy and oculopharyngeal muscular dystrophy are caused by DNA expansion and FSHD is caused by DNA deletion.

The NIH Announces Contract to Establish Muscular Dystrophy Cooperative Research Centers (MDCRCs) to Increase Research on all Forms of Muscular Dystrophy

According to the NIH, the primary goal of this initiative is to establish two or three research centers, each of which will bring together expertise, infrastructure and resources focused on major questions about muscular dystrophy. Centers of Research Excellence (COREs) are expected to provide an environment and core resources that will enhance collaborations of established basic, clinical, and behavioral science investigators to study muscular dystrophy research questions. Further, the environment should promote cross-disciplinary research training. Each center should develop in accordance with available expertise, interests, and resources, but should also be responsive to national needs related to muscular dystrophy. The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute of Neurological Disorders and Stroke (NINDS), and the National Institute of Child Health and Human Development (NICHD) intend to commit a total of approximately \$4.5 million in FY 2003 to fund two or three new COREs for five years.

MUSCULAR DYSTROPHY
COOPERATIVE RESEARCH CENTERS
RELEASE DATE: September 23, 2002
(see addendum [NOT-AR-03-001](#))
RFA: AR-03-001 [NIAMS, NICHD, NINDS]
LETTER OF INTENT RECEIPT DATE:
January 15, 2003
APPLICATION RECEIPT DATE:
February 24, 2003
RFA uses U54 Grant award mechanism
<http://grants.nih.gov/grants/guide/rfa-files/RFA-AR-03-001.html>

The National Institutes of Health (NIH) recently released an addendum

notice regarding a pre-application meeting for grant applicants on the Muscular Dystrophy Cooperative Research Centers (CORE) contract RFA known as AR-03-001.

The "NIH Guide Archive Ending the Week of December 13, 2002" announces that the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute of Child Health and Human Development (NICHD), and the National Institute of Neurological Disorders and Stroke (NINDS) "have scheduled an informational pre-application meeting at which Program and review staff will make presentations that explain their goals and objectives for the Muscular Dystrophy Cooperative Research Centers described in RFA-AR-03-001." The pre-application meeting is to be held in Bethesda on January 14, 2003.

PRE-APPLICATION MEETING FOR
THE RFA ON MUSCULAR
DYSTROPHY COOPERATIVE
RESEARCH CENTERS (RFA-AR-03-
001)

RELEASE DATE: December 9, 2002

NOTICE: NOT-AR-03-001 [NIAMS,
NICHD, NINDS]

Meeting is: January 14, 2003, 11:00 A.M. -
3:30 P.M. in Room 803, One Democracy
Plaza, 6701 Democracy Boulevard,
Bethesda, MD. Further questions regarding
location may be addressed to Ms. Maureen
Knowles, (telephone: 301-594-5055 or e-
mail: knowlesm@mail.nih.gov).

<http://grants1.nih.gov/grants/guide/2002/02.12.13/index.html>

or <http://grants1.nih.gov/grants/guide/notice-files/NOT-AR-03-001.html>

First Meeting of the NIH Muscular Dystrophy Research Task Force Held

Daniel Paul Perez attended the first meeting of the Muscular Dystrophy Research Task Force on May 16, 2002 along with many other experts in the field of muscular dystrophy. The next meeting of the MDRTF will be in mid-January 2003. The summary of the meeting found at the NIH site follows:

"At this first meeting of the NIH Muscular Dystrophy Research Task Force, the participants agreed that the immediate goal is to add new capabilities to the national effort to understand and treat muscular dystrophies. New support should be used to enhance research efforts and not duplicate existing programs or projects. Participants identified several key issues to be addressed in furthering research and care for muscular dystrophy patients. Efforts must be made to attract talented researchers from very diverse scientific fields and medical specialties, by ensuring that there are career paths and an identifiable muscular disease (myology) expertise and community. There must also be programs to support training that increases exchange of techniques, information, and ideas. The following items were also encouraged: support for research centers that promote side-by-side basic, translational, and clinical research; resources that can be used by the national research community; and training and advice about muscle diseases for researchers and physicians who provide initial diagnosis and treatment." For a complete meeting summary please see Scientific Workshops, Conferences, and Committees Reports at the NIH web site http://www.niams.nih.gov/ne/reports/sci_wrk/2002/mdmeet.htm.

Research Developments for FSHD Families and Individuals whose FSHD is not Linked to Chromosome 4

One of the top priorities identified by the FSH Society Scientific Advisory Board (SAB) and the international community of scientists is research on FSHD patients and families who lack chromosome 4 linkage. These individuals all show classic presentations of FSHD but no evidence of a deletion at 4q35. The Society has funded Dr. Marcy Speer of Duke University to continue to work on this extremely frustrating but most critical aspect of FSHD research. The hope is that a breakthrough may be identified in these rare families that will elucidate what is happening in all FSHD patients. At the October 15, 2002 FSHD workshop, Dr. Speer presented very encouraging data for these families. (See abstract below.) If you are a non-chromosome 4 linked FSHD patient or family member (e.g. your doctor says you have FSHD but the 4q35 DNA test is negative) it is absolutely imperative that you contact the Society and/or Duke University to help accelerate research progress on FSHD. Contact: Dr. Marcy Speer, Duke University Medical Center, Box 3445, Durham, NC 27710 USA, (919) 684-2063.

The abstract of the presentation by Dr. Speer at the October, 15th FSHD

International consortium meeting follows:
Evidence Consistent with Linkage to 15q of a Non-chromosome 4 linked FSHD Family
BL Randolph-Anderson, J Stajich, FL Graham, MA Pericak-Vance, M Speer, JR Gilbert. Duke University Medical Center, Durham, NC 27710

Facioscapulohumeral muscular dystrophy (FSHD; MIM 158900) is a primary disease of muscle with early symptoms including facial or shoulder girdle weakness and subsequent involvement of pelvic girdle and extremity muscles as the disease progresses. The majority of FSHD families are linked to the 4q35-qter region (FSHD1A), although genetic heterogeneity (FSHD1B) has been established within this diagnostic classification. We have identified two FSHD families in which non-linkage to chromosome 4 has been confirmed (DUK1361 and DUK2531). Genomic screening has identified a region on chromosome 15 consistent with linkage. Several markers in an 18cM region on chromosome 15 provided positive lod score values. Multipoint analysis gave supporting evidence for the results revealed in the two point data analysis, with a peak lod score of 3.20 in these

families. While haplotype analysis suggests that the most likely interval spans D15S1004 and D15S536, one individual in family 1361 tentatively classified as affected (individual 9019) in this pedigree excludes the region in its entirety. Initial analysis of the D4Z4 repeat indicates that this affected individual has a repeat length of 30 kb; however, haplotype analysis of the pedigree conclusively eliminates the 4q region in this family. These data raise the possibility that this affected individual may be a phenocopy. A search for candidate genes in the region identified POLG, which encodes the gamma subunit of mitochondrial DNA polymerase. Mutations in this gene are responsible for the myopathic disease progressive external ophthalmoplegia. We have investigated POLG for evidence of mutation by PCR sequence analysis of the 22 coding exons and the promoter region in two affected individuals. To date, these investigations suggest that POLG is not the gene responsible for FSHD1B in this family. Additionally, similar investigations of Desmuslin failed to show evidence of DNA changes implicated in disease. Further investigations of genes in this region are underway.

The NIH Announces Contract for Planning Grant for the Second Wave of Muscular Dystrophy Cooperative Research Centers (MDCRCs) or COREs

The NIH (NIAMS, NINDS and NICHD) seeks "developmental planning grant applications for the establishment of an infrastructure for eventual Muscular Dystrophy Cooperative Research Centers (MDCRCs) . . . These planning grants will enable applicants to effectively organize and integrate multidisciplinary research capacities and core resources to enhance collaborations of basic, clinical, and behavioral science in muscular dystrophy research and to promote cross-disciplinary research training." The NIH hopes to launch a second wave of MDCRCs within the next several years. This contract and application request RFA AR-03-002 will use NIH Exploratory/Developmental Grant R21 award mechanism to commit approximately US\$1,000,000 in FY 2003 to fund four of five new grants in response to this RFA. This will ostensibly give five groups US\$200,000 a year to plan the next round of MD centers.

DEVELOPMENTAL PLANNING GRANTS FOR MUSCULAR DYSTROPHY RESEARCH CENTERS

RELEASE DATE: October 31, 2002

RFA: AR-03-002 [NIAMS, NICHD, NINDS]

LETTER OF INTENT RECEIPT DATE: January 15, 2003

APPLICATION RECEIPT DATE: February 24, 2003

RFA uses R21 Grant award mechanism

<http://grants.nih.gov/grants/guide/rfa-files/RFA-AR-03-002.html>

MD Study Shows Chromosomal Variation

From NIH Spotlight on Research October 2002

<http://www.niams.nih.gov/ne/highlights/spotlight/2002/chromo.htm>

Scientists supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases have found that people with facioscapulohumeral muscular dystrophy (FSHD) have an exclusive association with one of the two different forms, or alleles, of the chromosomal region linked to the disease.

Silvère van der Maarel, Ph.D., and his colleagues at Leiden University Medical Center and University Medical Center Nijmegen in The Netherlands examined the alleles 4qA and 4qB in 80 control individuals and 80 individuals with FSHD. The alleles occurred with roughly equal frequency in the control group, but in the FSHD group, the affected allele was always of the 4qA type. Their work may lead to a better understanding of the instability of FSHD's genetic locus.

Lemmers R, de Kievit P, Sandkuijl L, Padberg G, van Ommen G, Frants R, van der Maarel S. *Facioscapulohumeral muscular dystrophy (FSHD) is uniquely associated with one of two variants of the 4q subtelomere*. Nature Genetics 2002;32(2):235-236.

Fifth FSH Society Delta Railroad Construction Company Research Fellowship Grant Established

Marcy Speer, Ph.D., Duke University Medical Center, Durham, NC has been awarded the fifth FSH Society Delta Railroad Fellowship Grant for research on Facioscapulohumeral Muscular Dystrophy (FSHD) for her project, *Genetic Linkage Studies in Non-chromosome 4 FSHD*. The FSH Society Delta Railroad program continues to help in the FSHD research efforts by awarding research grants that provide needed expansion of current work and innovative approaches in FSHD studies.

The FSH Society is indebted to the Delta Railroad Construction Company of Ashtabula, Ohio, Larry and Ida Laurello and their family for this groundbreaking effort on behalf of the FSHD community. The five Delta Railroad Research Fellowship Grants are yielding tremendous insights in novel areas of FSHD research. We hope that this collaboration will continue and that the members of the Society will consider matching this gift annually.

***Remember the
FSH Society
in your Will!***

Researchers Identify Genetic Switch Mechanism for FSHD

Inappropriate gene activation in FSHD: a repressor complex binds a chromosomal repeat deleted in dystrophic muscle. Gabellini D, Green MR, Tupler R., Howard Hughes Medical Institute, Program in Gene Function and Expression, Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, MA 01605, USA. Cell 2002 Aug 9;110(3):339-48

Facioscapulohumeral muscular dystrophy (FSHD), a common myopathy, is an autosomal dominant disease of unknown molecular mechanism. Almost all FSHD patients carry deletions of an integral number of tandem 3.3 kilobase repeats, termed D4Z4, located on chromosome 4q35. Here, we find that in FSHD muscle, 4q35 genes located upstream of D4Z4 are inappropriately over-expressed. We show that an element within D4Z4 specifically binds a multi-protein complex consisting of YY1, a known transcriptional repressor, HMGB2, an architectural protein, and nucleolin. We demonstrate that this multi-protein complex binds D4Z4 in vitro and in vivo and mediates transcriptional repression of 4q35 genes. Based upon these results, we propose that deletion of D4Z4 leads to the inappropriate transcriptional de-repression of 4q35 genes resulting in disease. PMID: 12176321 [PubMed - indexed for MEDLINE]

Current Happenings - Genetic Research in Leiden, the Netherlands

The following is an extremely significant finding and very substantial addition to solving the FSHD puzzle. The authors acknowledge the FSH Society for supporting the research. The Dutch report that "FSHD is associated solely with the 4qA allele." In layman's terms, the end of the chromosome at the very tip has two variations on chromosome 4 — an A type and a B type. In unaffected individuals both variations are found. FSHD is found to have a 100% association with the A form of the end of the chromosome. This would be distal (toward the end) past the repeats. It is an extremely intriguing finding that there is a sole correlation between the 4qA allele and FSHD. It raises the question whether the B variation provides immunity and the A variation is itself pathogenic (causes the disease) and many other questions as well.

Facioscapulohumeral muscular dystrophy is uniquely associated with one of the two variants of the 4q subtelomere. Lemmers RJ, de Kievit P, Sandkuijl L, Padberg GW, van Ommen GJ, Frants RR, van der Maarel SM. Department of Human Genetics, Center for Human and Clinical Genetics, Leiden University Medical Center, Wassenaarseweg 72, 2333 AL Leiden, The Netherlands. Nature Genetics 2002 Oct; 32(2):235-6

Abstract:

Contractions in the polymorphic D4Z4 repeat array of sub-telomere 4qter cause autosomal dominant facioscapulohumeral muscular dystrophy in humans. A polymorphic segment of 10 kb directly distal to D4Z4 exists in two allelic forms, 4qA and 4qB. Although both alleles are equally common in the general population, we now report that FSHD is associated solely with the 4qA allele. PMID: 12355084 [PubMed - indexed for MEDLINE]

A New Piece of the Genetic Puzzle: Chromosome Structure Implicated in Disease

By Richard Holmes, Staff Writer, *Cape Cod Times*, September 17, 2002 (reprinted with permission)

Genes, little bundles of DNA in our chromosomes that we inherit from our parents, control much of how our bodies develop and work.

The approximately 100,000 human genes operate like little on/off switches for specific traits; they work individually or in combination to determine the color of hair or a predisposition for breast cancer. But research on a form of muscular dystrophy shows that yet another element in our 23 pairs of chromosomes acts like a volume dial, turning up the function of nearby genes above their normal limit.

The discovery confirms a new direction for genetic studies and holds promise for treatment of facioscapulohumeral muscular dystrophy (FSHD) and other inherited diseases.

FSHD, the third most common type of muscular dystrophy, weakens skeletal muscles throughout the body, most noticeably those in the shoulders, upper arms and face. It usually worsens slowly over time, but can rapidly progress. It can cripple or be so slight that it goes undiagnosed. It's autosomal dominant, meaning both sexes get it and each child of a FSHD parent has a 50-50 chance of inheriting the disease.

The newly discovered mechanism implicated in causing FSHD is so-called "junk DNA," repeated sequences of DNA that aren't genes but make up about 40 percent of our chromosomes.

"The term 'junk DNA' just means you don't know what it does," said Dr. Katrina Gwinn-Hardy, a neurologist at the National Institute of Neurological Disorders and Stroke in Bethesda, MD., a branch of the federal government's National Institutes of Health. Her institute has financed some of the research. "This isn't junk, this is cool," she said. "It's a new piece of the puzzle."

Research shows that some "junk DNA" can cause neighboring genes to be over-expressed - their normal function turned up too high.

Now, a Worcester researcher and her colleagues seeking the cause of FSHD have shown that the muscle disease is determined by the amount of "junk DNA"

on one end of a chromosome and not a mutated or missing gene as might be thought.

"That's what's so exciting," said Gwinn-Hardy of the NINDS. The institute has underwritten research being performed by Drs. Rossella Tupler, Davide Gabellini and Michael R. Green at the Howard Hughes Medical Institute at the University of Massachusetts Medical School in Worcester. Gwinn-Hardy said their results have proven for the first time that a human disease can be caused by "junk DNA."

"It's been theorized, but here's hard evidence," she said. "It's a big change for people in the field."

Professor Lee Sweeney, chairman of the physiology department at the University of Pennsylvania Medical School in Philadelphia, PA, who studies muscle diseases, said the cause for FSHD would never have been found by simply mapping the location of genes whose functions had been identified as likely candidates. The answer lay outside the genes themselves and in the structure of the chromosome that contained them.

Such a mechanism had been suspected as FSHD's cause, but never proven, he said.

"Finally, a clear demonstration," he said.

Tupler's work focused on the telomeric end of chromosome 4, a region researchers had identified a decade ago as the probable site of FSHD's genetic basis. It was known that in this region were repeated sequences of DNA, and that people with FSHD had fewer of these repeats. But what this had to do with the muscle-wasting disease was unclear, other than the amount of shortening of the repeat region correlated with the age of onset and severity of the disease.

Tupler and her colleagues showed that genes near this region of repeats were over-expressed. What made these genes function at abnormally high levels?

The researchers proposed and demonstrated that a substance bound to the region of repeats acted to suppress the function of neighboring genes, with those closest to the region being most affected, according to an article in the Aug. 9 issue of *Cell*, a prominent microbiology journal.

They further showed that in individuals with FSHD, because this region is much smaller, the amount of suppression is greatly reduced and the resulting abnormal over-expression of the genes likely causes the disease and controls its progression.

The researchers identified three genes near the shortened region that were over-expressed in muscle cells of FSHD patients. Of these, one gene named ANTI1 was known to cause cells to die when it was over-expressed and had been associated with some illnesses affecting eye and heart muscles. The functions of the other genes were unknown. Tupler's team believes ANTI1's over-expression probably causes cell death in muscle fibers in people with FSH dystrophy.

"They found the switch," said Carol Perez, executive director of the FSH Society, a volunteer network of families affected by FSHD and scientists studying the inherited disease. The organization has funded Tupler's work since 1998 and brought it to the attention of the NIH and the Muscular Dystrophy Association, who gave additional grants.

The model for the cause of FSHD proposed by Tupler paints a complex picture - one that offers an explanation for the disease's variability.

In the normal population, the area of repeats contains 11 to 150 units, but people with FSHD have 10 or fewer. Those with the fewest number of repeats, 1-3, generally have a severe form that begins in childhood. The majority of people with FSHD show symptoms in their teens or early adult years.

The fluctuating nature of the disease means that siblings with it can each have different levels of severity and patterns of progression. This characteristic makes studies of FSHD of especial interest to the NIH.

"It might teach us about variability in other inherited diseases," the Institute's Gwinn-Hardy said. The "junk DNA" mechanism causing FSHD has not been proven to be a cause for any other human disease, she said, although it is suspected.

According to the paper Tupler's team published in *Cell*, a flawed area of variable DNA repeats has been observed in people with Type 1 insulin-dependent diabetes

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and another area has been found near a gene connected to bladder cancer, but whether these regions regulate gene expression has not been proved.

"I think it's a landmark paper," UPenn's Sweeney said. He said that while Tupler's research represents the first time a human disease has been shown to be caused by such a structural mechanism, "I think this is not going to be unique."

He suggested that Tupler's work describes "a new principle that will underlie a number of human diseases."

Gwinn-Hardy said research into the role of variable DNA repeats in the region of a chromosome's telomere may even shed light on the aging process.

"In the telomere (one end) of the chromosome there are lots of repeats," she said, "and as we age, they get shorter and shorter and shorter."

While Tupler's research provides a likely model for FSHD's cause, it is not the complete explanation.

Gender, hormones and environmental factors probably also play a role in the disease's progression, Perez and Tupler said.

Furthermore, while most people with FSHD have fewer DNA sequence repeats on the telomeric arm of chromosome 4, approximately 5 to 10 percent don't. Tupler theorizes that in these cases, mutations may interfere with the repeat region's suppressing effect on neighboring genes.

Once considered rare, FSHD is now recognized as the third most common muscular dystrophy, with an incidence of 1 in 20,000. Only Duchenne and myotonic dystrophies are more common. Development of a DNA test for the disease and greater awareness has led to its increased reporting, according to Perez.

Tupler said her work gives hope to the many FSHD families around the world.

"When you have a genetic disorder, the first feeling you have is you can't do anything."

That was true before Tupler's work; there were no bright spots on the research horizon for treatment of FSHD. But now she and other researchers have a direction to pursue.

UMMS Scientists DISCOVER

Genetic Key to Muscular Dystrophy

Newly identified genetic disorder appears to underlie cause

Contact: Mark L. Shelton, Public Affairs, University of Massachusetts
(reprinted from a press release issued by UMMS on August 9, 2002)

WORCESTER, Mass.—Researchers at the University of Massachusetts Medical School (UMMS) report today [August 9, 2002] on a newly identified genetic cause that underlies a common neuromuscular disorder called facioscapulohumeral muscular dystrophy (FSHD), the third most common of the muscular dystrophies. In the new study, Rossella G. Tupler, MD, Ph.D., and colleagues of the UMMS Programs in Gene Function & Expression and Molecular Medicine, show that a genetic defect called "deletion" of certain repetitive DNA sequences in people with FSHD allows nearby genes to go into overdrive. The finding solves a decade-old riddle about the cause of this disorder and may ultimately lead to the first effective treatments.

The study ("*Inappropriate gene activation in FSHD: A repressor complex binds a chromosomal repeat deleted in dystrophic muscle*," Cell 2002 Aug 9;110(3):339-48.) found that abnormally short strings of repeated DNA sequences on chromosome 4 interfere with the function of a protein complex that controls nearby genes. This leads to over-activity of several genes that appear to play a role in the disorder. This type of genetic problem—a deletion causing repetitive expression—has never before been identified in a human disease.

Scientists first linked the short strings of DNA in this region to FSHD in 1992. People with FSHD typically have fewer than 11 copies of a nucleic acid sequence, called D4Z4, due to a deletion of part of the chromosome. In contrast, people without the disorder usually carry between 11 and 150 copies of the sequence. People with a very small number of copies (three or less) have severe disease symptoms that begin in childhood; those with several more copies typically have milder symptoms that begin in the teens or early adulthood. However, until now, researchers have been unable to determine exactly how the number of DNA sequences influences the disease.

FSHD is the third most common inherited neuromuscular disorder, affecting one in every 20,000 people (only Duchenne muscular dystrophy and myotonic dystrophy are more common). People with FSHD have progressive muscle weakness that primarily affects the face, shoulder blades and upper arms, although other muscles also deteriorate. Despite intensive efforts, researchers have previously been unable to identify any genes that are altered in this disorder.

In this study, Dr. Tupler and colleagues at UMMS and the Universita degli Studi di Pavia in Pavia, Italy, studied human muscle tissue from normal individuals and from people with FSHD as well as several other types of muscular dystrophy. They then analyzed the expression of three genes located near the D4Z4 region and found that activity of all three genes was elevated in the muscle from FSHD patients compared to that of other people. The researchers also analyzed the interaction between the D4Z4 sequence and proteins present in the nucleus of the cell and found that one part of the sequence was necessary to bind a protein complex that normally suppresses gene activity. Deletions of copies of D4Z4 to a critical number reduced the number of these bound protein complexes, which in turn reduced control of genes from nearby parts of the chromosome.

"These findings have specific implications for the disease, and general implications for genetic research," says Dr. Tupler. Knowing how the D4Z4 deletions affect nearby genes points to new strategies for treating the disorder. For example, researchers might be able to find a way to mimic the effect of the protein complex that goes awry in this disorder, thereby reducing the activity of all the affected genes. If a specific gene that causes the disorder can be identified, researchers also might be able to slow or halt its activity with drugs or other treatments. "The mechanism we describe

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continued from page 15

is entirely new and represents an intriguing model for approaching other complex disorders in which the candidate gene approach was not successful," says Tupler.

While most people with FSHD have D4Z4 deletions, about 5 to 10 percent of them do not. These people may have mutations that affect the protein complex, Dr. Tupler says. If researchers can confirm this, it would provide further information about this complex that is central to the development of this disorder, she notes. Researchers have also identified people without FSHD who are missing the entire D4Z4 region and some nearby genes. This suggests that an abnormal D4Z4 region somehow creates havoc in muscle cells and/or that the nearby genes are necessary for development of the disease.

The findings also suggest that repetitive DNA sequences play a previously unsuspected role in human disease by influencing gene activity, Dr. Tupler says. About 40 percent of the human genome is comprised of these repetitive sequences, and they might be linked to other human disorders. For example there are DNA polymorphisms (usually considered normal variations of DNA repetitive sequences) near the insulin gene in Type 1 diabetes that have been linked to insulin levels and birth size. Other DNA repeats have been associated with bladder cancer. Studies of sequences like these could lead to a much better understanding of how gene activity is regulated, Dr. Tupler suggests.

The University of Massachusetts Medical School, one of the fastest growing academic health centers in the country, has built a reputation as a world-class research institution, consistently producing noteworthy advances in clinical and basic research. The Medical School attracts more than US\$131 million in research funding annually, 80 percent of which comes from federal funding sources. Research funding enables UMMS scientists to explore human disease from the molecular level to large-scale clinical trials. Basic and clinical research leads to new approaches for diagnosis, treatment and prevention of disease.

Society Pulls Off Research Coup

*By Richard Holmes, Staff Writer, Cape Cod Times, September 17, 2002
(reprinted with permission)*

After just four years of funding research, the FSH Society has found a cause for the muscular dystrophy the nonprofit organization is dedicated to.

"It came from the patient community," said Carol Perez, executive director and co-founder of the organization during an interview in Harwich. Her son, Daniel, is FSH Society president and its only full-time paid employee.

Both use wheelchairs as a result of having facioscapulohumeral muscular dystrophy (FSHD), an inherited disease that wastes skeletal muscles throughout the body, but is recognized for weakening those in the shoulders, upper arms and face, as its name suggests. While capable of crippling, this highly variable disease can go undiagnosed in people with mild cases.

Frustrated with the lack of research on the disease, Daniel Perez founded the society in 1991 with Stephen Jacobsen, a researcher with FSHD; Morgan Downey, an attorney and health-care advocate; and his mother, a rehabilitation counselor. They sought to bring together scientists and affected families.

The organization drew on Daniel's scientific knowledge; he studied cell biology [at Harvard] and worked two years on the Human Genome Project, mapping our species' chromosomal blueprint. His association with genetic researchers helped him to assemble a scientific advisory board to guide the organization. In 1998, the society began funding research, and has since awarded more than US\$800,000.

The society last year worked with Massachusetts lawmakers and the Muscular Dystrophy Association to push a research funding bill through Congress and has successfully lobbied the National Institutes of Health (NIH) to support several of its grant projects.

The work determining the likely cause of FSHD was led by Dr. Rossella Tupler, a medical geneticist working at the University of Massachusetts Medical School in Worcester. She received one of

the FSH Society's first grants.

The FSH Society brought her work to the attention of the NIH. Daniel Perez said both the federal institutes and the Muscular Dystrophy Association gave grants to Tupler after his organization persuaded them of her work's value.

Dr. Katrina Gwinn-Hardy, a neurologist at the National Institute of Neurological Disorders and Stroke in Bethesda, Md., a branch of the federal government's National Institutes of Health, said the NIH typically funds research where results are likely to be proven, and said the unconventional approach taken by Tupler made a grant supporting her work "high-risk" but worthwhile.

"This program was done in FSH because we felt there weren't enough people working on it."

She said the FSH Society could be a model for other grassroots organizations seeking research on a specific disease, in contrast with huge charities with large budgets and staffs that raise funds for a number of illnesses.

"It's a nice paradigm for other groups," she said.

The Internet makes much of the society's work possible, said Carol Perez. It allows researchers and FSHD families throughout the world to communicate with each other. She said that through the society's Web site she came into contact with a young person in Eastern Europe who was looking for someone like himself to talk to about the disease. She was able to put him in touch with another young person in a neighboring town.

The Perezes said their organization enters a new phase now that a likely cause has been found: pursuing treatments for FSHD. They predict publication of Tupler's research will attract other researchers to their cause.

"It raises the visibility of FSHD," Daniel Perez said. "Other scientists may be looking at gene silencing but not have a disease (to study)."

New Horizons for FSHD

By Silvère van der Maarel, Ph.D., Leiden University Medical Center, Center of Human and Clinical Genetics

The intensive efforts worldwide to fund FSHD research are starting to pay off. A few years ago, the FSH Society took the initiative to support scientists to specifically study FSHD. Additional efforts of other agencies such as the MDA, the NIH and the FSHD Foundation resulted in a substantial financial support to study FSHD. Now, five years later, two breakthroughs were reported within a time interval of two months.

Already in the early nineties, the chromosomal localization of the genetic defect in FSHD was discovered. Soon afterwards, the basic defect was reported as a partial loss of a repetitive DNA structure at the end of the long arm of chromosome 4. Scientists were optimistic that the exact mechanism was soon to be discovered.

In a scientific struggle of about a decade, enormous progress was made with respect to the genetic diagnosis of FSHD and the basic understanding of the end of chromosome 4 and its homologous region on chromosome 10. It yielded new insights in the peculiar behavior of chromosome ends in general, but the exact molecular mechanism underlying FSHD remained elusive.

In the August 2002 issue of *Cell*, Gabellini, et al. demonstrate in an elegant study that a complex of proteins bind to the repetitive DNA structure that is partially lost in FSHD patients. This complex represses the expression of genes located near the end of chromosome 4. Partial loss of this complex, as observed in FSHD, leads to a loss of control over the expression of these genes. This loss of control may, in turn, cause the disease. For the first time, this report substantiates a hypothesis that was already proposed by many scientists in the field of FSHD.

In a second paper, Lemmers et al., report in September 2002 *Nature Genetics*

that not all ends of chromosome 4 are identical. In fact, two variants exist: 4qA and 4qB. Although both variants are almost equally common in the Dutch population (and likely the Caucasian population), the partial loss of the repetitive DNA structure only on chromosome 4qA causes FSHD. In contrast, partial loss on 4qB ends do not seem to be associated with disease. Apparently, 4qA has, apart from the loss of repetitive DNA, additional features that cause the disease. Conversely, 4qB may contain characteristics that protects against the development of FSHD.

So, are we back where we started? Definitely not! First of all, Gabellini, et al. showed that the principle speculated about for many years may indeed hold true for FSHD. However, the mechanism is not complete and needs to be refined. Obviously, additional features of 4qA are necessary to be incorporated in this model. Nevertheless, for the first time in many years, significant progress has been made in understanding the basic molecular mechanism underlying FSHD.

In the near future, without doubt, progress will be made to refine the molecular cause of FSHD. For the first time in many years, scientists have something to compare: what makes 4qA different from 4qB and how does this relate to the complex that controls the expression of the genes on chromosome 4 and elsewhere in the genome? Are additional genes present on 4qA but not on 4qB, or can additional protein complexes bind to either of the chromosome 4 variants and interfere or co-operate with the proteins just discovered that bind to the repetitive structure?

Eventually, these studies will yield a better understanding of the basic molecular mechanism that causes FSHD, a solid starting point for evidence-based intervention strategies.

New Developments in FSHD Research: Oxidative Stress in FSHD Myoblasts

In Press: *Neuromuscular Disorders*

Sara T. Winokur, Ph.D. University of California, Irvine

Denise A. Figlewicz, Ph.D. and Rabi Tawil, University of Rochester, Rochester, NY *Facioscapulohumeral muscular dystrophy (FSHD) myoblasts demonstrate increased susceptibility to oxidative stress*

Facioscapulohumeral muscular dystrophy (FSHD) is an autosomal dominant disorder resulting from an unusual genetic mechanism. The mutation, a deletion of 3.3 kb subtelomeric repeats, appears to disrupt the regional regulation of 4q35 gene expression. The specific gene(s) responsible for FSHD have not been identified. However, the "vacuolar/necrotic" phenotype exhibited by FSHD myoblasts suggests that aberrant gene expression occurs early in FSHD muscle development. In order to test this hypothesis, global gene expression profiling and in vitro characterization of FSHD and control myoblasts were carried out. Genes involved in several cellular processes such as oxidative stress were found to be dysregulated. In vitro studies confirmed this susceptibility to oxidative stress, as proliferative stage FSHD myoblasts exhibit greatly reduced viability when exposed to the oxidative stressor paraquat. This effect was not seen in either normal or disease control myoblasts, or in any of the cell lines upon differentiation to multinucleated myotubes. Immunocytochemical studies of the cyclin dependent kinase (cdk) inhibitor p21 demonstrated increased expression in FSHD myoblasts, suggesting an early cell cycle arrest. Another process distinguishing FSHD from controls involves the transcription of extracellular matrix (ECM) components. Expression of elastin, decorin, lumican and the ECM remodeling factor TIMP3 were reduced in FSHD myoblasts. These studies suggest that FSHD muscular dystrophy results from a defect in early myogenesis, manifested as increased susceptibility to oxidative stress, morphological aberrations and early cell cycle arrest.

FSH Society Needs Volunteers

The FSH Society is looking for marketing and fund-raising people to continue its work. Please contact Carol Perez at (781) 860-0501 if you have experience in these areas and can lend a hand.

Research Helps Families Plan Healthier Futures

By Richard Holmes, Staff Writer, *Cape Cod Times*, September 17, 2002 (reprinted with permission)

I hadn't expected results to come this soon.

The recent discovery of the cause of FSHD affecting my family thrills me, though I know much work lies ahead.

An expert in muscular diseases, Professor Lee Sweeney of the University of Pennsylvania Medical School, told me the discovery must be frustrating to people with FSHD, because the cause is so complex - actually the first of its kind found among human diseases - and therefore the search for treatments will be that much more difficult.

I saw his point. After all, the gene for Duchenne muscular dystrophy was discovered years ago, and a cure has yet to be found. And the cause of facioscapulohumeral muscular dystrophy (FSHD) is more than just a faulty gene, it's a flawed end of a chromosome that affects several genes, some of which scientists still don't know what they do.

Yet I don't find this depressing; I find it exhilarating. Before the discovery, researchers were looking for a cause; now they have a foundation from which to build.

It means a lot to me. In June, I lost my older brother to the disease. In the space of two years this hard-working, athletic man was reduced to an emaciated invalid who could no longer eat or breathe or talk

without assistance. His rapid decline shocked those around him, and some familiar with the disease questioned whether some other neuromuscular disorder may have been involved. FSHD can cripple, but isn't generally considered fatal. But my brother, a doctor, didn't believe he suffered from a second illness and his doctors never diagnosed one.

I chalk it up to FSHD's maddening variability. Take my fraternal twin brother and myself. As an adult, my twin has slowly developed weakness in his neck and shoulders. But my dystrophy kicked in around puberty. Never as fit as my brothers, I've gradually lost strength in my shoulders, arms, torso and legs, and a little in my face. Now in my mid-40s, I still walk, I talk - indeed, I work, hike and bike, but with some effort and annoying clumsiness. It's been an irritating hindrance, but one I've accepted as I know severe cases rely on wheelchairs and often lose their jobs. I'm not in their situation, and it hasn't looked as if that would ever happen.

It was depressing and scary when my older brother began his downward slide. "I hope this doesn't happen to you," he told me the last time I saw him in his sickroom bed. Those words echo in me.

So I greet this research news as a ray of sunshine. It's not a cure; it's a starting place. But it's something, and there wasn't anything before.

Albuterol Clinical Trial Delayed

By John T. Kissel, MD, Professor of Neurology, Ohio State University

December, 2002: Unfortunately, the start of the clinical trial of albuterol and oxandrolone in FSH dystrophy being performed by the Myopathy Study Group has been delayed. The problem relates to availability of the long-acting albuterol preparation to be used in the study. The company that had originally agreed to provide the drug was shut down by the regulatory arm of the Food and Drug Administration and forbidden from manufacturing the drug. This created two problems for the study. The first is that institutional approval to do a study requires that all medical centers involved depend on a specific drug; all of the paper work has to be redone for each center if a new preparation of the drug is used. The second, and bigger problem, is that there is currently no comparable long-acting preparation of albuterol available. The directors of the study are currently in negotiation with another drug company that is developing a similar preparation. Hopefully, this agent will be approved by the FDA in the near future, and the drug company will make the drug available for the study. Currently, we are hoping to have the study up and running within six months. All of the members of the Myopathy Study Group are committed to the successful completion of this study. Both of the agencies funding the trial (the Food and Drug Administration's Orphan Drug Program and the Muscular Dystrophy Association) are committed to the study, and have guaranteed that the funds will be there for the study when the drug becomes available. We would like to thank the FSH community for their patience during this difficult time.

Update: Gene Expression Studies of FSHD Muscle

By Sara T. Winokur, Ph.D., University of California, Irvine

Global gene expression profiling of muscle tissue in FSHD provides the first insight into a FSHD-specific defect in myogenic differentiation. FSHD expression profiles were compared to those generated from normal muscle as well as other types of muscular dystrophies (DMD, aSGD) in order to determine FSHD specific changes. In addition, matched biopsies (affected and unaffected muscle) from individuals with FSHD served to monitor expression changes during the progression of the disease as well as to diminish non-specific changes resulting from individual variability. Among genes altered in a FSHD specific and highly significant manner, many are involved in myogenic differentiation and suggest a partial block in the normal differentiation program. Indeed, many of the transcripts affected in FSHD represent direct targets of the transcription factor MyoD. As these genes are not affected in the other muscular dystrophies examined, the pathophysiological basis of FSHD may relate to a primary defect in satellite cell differentiation. Additional mis-expressed genes confirm a diminished capacity to buffer oxidative stress demonstrated in FSHD myoblasts. This enhanced vulnerability of proliferative stage myoblasts to reactive oxygen species is also disease-specific, further implicating a defect in FSHD muscle satellite cells.

FSH Society Seeks Web Developers

The FSH Society seeks professional web developers or design firms interested in volunteering time and resources to update and redesign the Society's web site. Please address inquiries to the FSH Society.

Researchers Need You! There are Many Ways to Make a Difference!!

NIH National Registry of Myotonic Dystrophy and Facioscapulohumeral Muscular Dystrophy Patients and Family Members is Enrolling Individuals

By Lynn Cos, RN, CCRC

The University of Rochester Medical Center has been funded by the NIH to establish a registry of patients who have been diagnosed with myotonic dystrophy (DM), FSHD or a related disorder (whose symptoms are identical to those of DM or FSHD). The purpose of the registry is to establish and maintain a comprehensive list of individuals diagnosed with either of the two neuromuscular disorders listed. Participants will fill out a questionnaire to be entered into a data bank. No blood or tissue samples are needed. The registry will assist researchers, from all over the United States, to find and recruit individuals willing to participate in research studies. Currently, the registry is enrolling participants from the United States. For information about FSHD patient participation in the registry contact: Lynn Cos, RN, CCRC Study Coordinator, FSHD (585) 275-7680, (888) 925-4302 toll-free, e-mail: Lynn_Cos@urmc.rochester.edu.

Researchers Need FSHD Patient Volunteers to Help Research Happen

By Dr. Robert Bloch, Ph.D.

Drs. Neil Porter and Robert Bloch, together with Dr. Patrick Reed, of the University of Maryland School of Medicine, have received NIH funding to study FSHD. Their research focuses on the organization and strength of the surface membrane, or covering, of muscle fibers. They are seeking volunteers with FSHD to extend their studies. Each volunteer will undergo a surgical biopsy of the deltoid muscle, located at the junction of the upper arm and shoulder. All volunteers will be compensated. If you are interested in participating or if you have any questions, please contact them by telephone. Dr. Bloch: (410) 706-3020; Dr. Porter: (410) 328-3273 or cell phone, (410) 299-1025; or e-mail: rbloch@umaryland.edu or nport001@umaryland.edu.

Brain and Tissue Banks for Developmental Disorders Enlisting Registered Donors

The Brain and Tissue Banks for Developmental Disorders at the University of Maryland in Baltimore and the University of Miami are tissue resources established to further research aimed at improved understanding, care and treatment of developmental disorders. The Brain and Tissue Banks serve as intermediaries between people who wish to have tissue donated for research upon the time of their death and the researchers who need this tissue for their vital work. Tissues listed on file at the BTB of interest are deltoid, gastrocnemius, wrist flexors (flexor carpi radialis, flexor digitorum superficialis), vastus lateralis, vastus medialis, hamstrings, upper trapezius, biceps, triceps, tibialis anterior, rhomboids, lower trapezius, retina, cochlea, and brain (motor cortex). If you are interested in becoming a registered donor, or if you have any questions or concerns regarding the donation process, please contact Christine Wade, Project Coordinator, (800) 847-1539. Thank you for taking the time to consider the possibilities offered to humanity through the gift of tissue donation. Internet site: www.btbank.org.

Participants Needed for FSHD Muscle Biopsy Study

By Lynn Cos, RN, CCRC

Additional research is being done at the University of Rochester Medical School. Researchers are looking for individuals with FSHD interested in participating in a study to further evaluate the gene causing FSHD. The study involves a one-time visit to obtain a blood sample and a muscle biopsy. Researchers: Denise Figlewicz, Ph.D., Rabi Tawil, M.D. Contact: 601 Elmwood Avenue, Box 673, Rochester, NY 14642. Lynn Cos, RN, Study Coordinator, (585) 275-7680 or email: Lynn_Cos@urmc.rochester.edu.

An Urgent Request from the FSH Society Regarding the NIH National Registry

The NIH and the University of Rochester Medical Center have asked the FSH Society to get the word out about the NIH Registry for FSHD at URMC. It is very important that we all contact the NIH registry. The registry will then send a questionnaire and request medical records for their database. No doctor's visit, blood work or biopsy are required to join. This is a database of contacts for FSHD patients and family members for researchers to access (after approval by a registry oversight committee). It is a very important component of the federal strategy to build the base for research on FSHD at the NIH. Please join and encourage your family members to make an inquiry and join if they have not already done so. It is important that we make a concerted effort to request and fill out the paperwork for the registry. The contact information is provided in the separate article above.

Timeline: Much Progress Made in FSHD Research in 2000-2002

• **May 8-9, 2000**

NIAMS, NINDS, and the Office of Rare Diseases sponsors a conference on the *Cause and Treatment of Facioscapulohumeral Muscular Dystrophy* in Bethesda, MD. A summary of this meeting may be found at: <http://www.nih.gov/niams/reports/fshdsummary.htm>.

• **October 3, 2000**

FSH Society sponsors the International Consortium on Facioscapulohumeral Muscular Dystrophy (FSHD) held as a satellite meeting to the American Society of Human Genetics (ASHG) in Philadelphia, Pennsylvania.

• **November 8, 2000**

NIH issues AR-01-002 FSHD Research Contract for Exploratory Research on Facioscapulohumeral Muscular Dystrophy. NIAMS/NINDS makes direct request to FSHD researchers for grant applications. Contract uses NIH Exploratory/Developmental Grant R21 award mechanism for high risk and innovative research areas.

• **December 11, 2000**

NIH announces the establishment of a National Patient Registry at the University of Rochester Medical School for FSHD under a contract program numbered N01-AR-02250. Approximately US\$400,000 is awarded annually to establish the NIH Registry called the "National Registry of Myotonic and Facioscapulohumeral Muscular Dystrophy Patients and Family Members" at the University of Rochester, NY. (Please see article on page 19 in this newsletter.)

• **January 4, 2001**

NIH issues PAS-01-041: Therapeutic and Pathogenic Approaches for the Muscular Dystrophies. The funding mechanism is research project grant (R01) and the program project grant (P01). The NIH earmarked approximately US\$5.0 million in total costs during fiscal years 2002-2004. See NIH web site http://www.niams.nih.gov/rtac/funding/grants/pas_01_041.pdf.

• **September 6, 2001**

FSH Society sponsors multiple speakers on FSHD at the 6th World Muscle Society Congress held in Snowbird, UT. The Society awards a travel grant to Richard Festenstein, Ph.D., Gene Control Mechanisms and Disease, Department of Medicine, Hammersmith Hospital, London for his keynote lecture for the day series on FSHD research titled: "Chromatin structure, gene expression, and disease." The Society also helps with travel for other FSHD researchers needing assistance to make the meeting.

• **October 14, 2001**

NIH announces grant awards for RFA AR-01-002: FSHD Research Contract for Exploratory Research on Facioscapulohumeral Muscular Dystrophy. Thirteen applications were submitted by FSHD researchers and six were funded at a total of over US\$1,100,000 annually for three years. (Please see article on page 10 in this newsletter.)

• **October 14, 2001**

FSH Society sponsors international workgroup meeting on FSHD in San Diego. Nearly all FSHD researchers attend except researchers from countries that would not allow travel in the aftermath of September 11, 2001. Two significant findings are reported. First, the nature of the chromosome structure and chromatin formation in FSHD is fast becoming understood. Second, scientists now see many biochemical and cellular pathways indicating significant overlap with respect to cellular oxidative stress and muscle cell differentiation issues in FSHD.

• **December 18, 2001**

United States Public Law 107-84, the Muscular Dystrophy Community Assistance Research and Education Act (MD-CARE Act), a law mandating research, study and education on muscular dystrophy, is signed by President Bush. The law mandates the NIH Director to convene an oversight committee and report back with progress in one year. (Please see article on page 5 of this newsletter.)

• **January 16, 2002**

FSH Society meets with directors and program staff of three of the NIH institutes (NINDS, NIAMS, and NICHD) and colleagues at the Muscular Dystrophy Association (MDA) and the Parent Project for Duchenne Muscular Dystrophy (PPMD) to discuss muscular dystrophy research issues and opportunities and strategies for the year ahead relating to the MD-CARE Act.

• **March 1, 2002**

FSH Society helps establish the "FSHD-Research ListServ" at the University of California, Irvine to facilitate interchange and communication of ideas in the international research community.

• **March 23, 2002**

FSH Society presents U.S. Senate testimony submitted in written format before Senators Specter and Harkin. To view the complete testimony, please check the FSH Society internet web site, or contact the FSH Society for a written copy.

• **May 9, 2002**

FSH Society recognized and named to the "Fleet Top 100" as part of Small Business Leadership Awards 2002 by Fleet Bank. (Please see article on page 24 in this newsletter.)

• **May 9, 2002**

FSH Society presents oral and written testimony before the U.S. House Committee on Appropriations, Subcommittee on Labor, HHS, Education and Related Agencies, chaired by Representative Ralph Regula. To view the complete testimony, please check FSH Society web site, or contact the FSH Society for a written copy. (Please see article on page 4 in this newsletter.)

• **May 10, 2002**

FSH Society meets with the director and program staff of three of the NIH institutes (NINDS, NIAMS, and NICHD) in Bethesda, MD to discuss FSHD research issues and opportunities.

Timeline, continued from page 20• **May 15-16, 2002**

NIAMS, NINDS, and NICHD bring together a Muscular Dystrophy Research Task Force to identify ways to increase the level of understanding of muscular dystrophies and improve diagnosis and treatment approaches. A summary of the first meeting of the Task Force is available at: http://www.niams.nih.gov/ne/reports/sci_wrk/2002/mdmeet.htm. Among other suggestions, the Task Force recommends support for research centers (COREs) to promote the exchange of ideas and information between basic and clinical investigators. Daniel Paul Perez participates as a member of the Task Force on behalf of the FSHD community.

• **August 9, 2002**

Italian Researchers Drs. Tupler and Gabellini at University of Massachusetts Medical School announce major breakthrough in FSHD genetic research. For the first time ever in human disease, a novel genetic switch mechanism is seen in FSHD. (Please see articles on pages 13-15 in this newsletter.)

• **September 23, 2002**

Drs. Lemmers, van der Maarel and Frants of Leiden University, the Netherlands, announce a major breakthrough in allelic differences seen in FSHD and a chromosomal variation seen 100% of the time in FSHD. For the first time an absolute is found in FSHD without any exceptions to the rule. (Please see article on page 13 in this newsletter.)

• **September 23, 2002**

The NIH announces contract RFA AR-03-001 requesting applications on Muscular Dystrophy Cooperative Research Centers. Letters of Intent are due January 15, 2003; applications are due February 24, 2003. RFA uses U54 Grant award mechanism and will award approximately US\$4.5 million for five years to be distributed to two or three CORES. See NIH site <http://grants.nih.gov/grants/guide/rfa-files/RFA-AR-03-001.html>. (Please see article on page 11 in this newsletter.)

• **October 12-13, 2002**

International Network and Contact Day for FSHD held in Rockville, MD. This day is designed for patients, families and caregivers, and covers topics such as *Clinical, Therapeutic and Orthopedic Issues; Orthopedics and Scapular Fixation; Genetic and Research Issues; and Physical Therapy*. (Please see article on page 22 in this newsletter.)

• **October 15, 2002**

FSHD International Consortium Research Meeting 2002 is attended by renowned scientists from around the world. Some of the topics of discussion are: Facioscapulohumeral dystrophy: Premature activation of the myogenic program?; Sarcolemmal reorganization in facioscapulohumeral muscular dystrophy; and Hypomethylation of the D4Z4 repeat array in Facioscapulohumeral muscular dystrophy alleles. (Please see article on page 6 in this newsletter.)

• **October 31, 2002**

The NIH announces contract RFA AR-03-002 requesting applications on developmental planning for Muscular Dystrophy Cooperative Research Centers. Letters of Intent are due January 15, 2003; applications are due February 24, 2003. The letter of intent for this grant application is due at the NIH the same day as the previous announcement for the Muscular Dystrophy Cooperative Research Centers requested under AR-03-001. RFA uses R21 Grant award mechanism and will award approximately US\$1 million for five grants for two years. See NIH <http://grants.nih.gov/grants/guide/rfa-files/RFA-AR-03-002.html>. (Please see article on page 12 in this newsletter.)

• **December 9, 2002**

The NIH (NIAMS, NICHD, NINDS) schedules an informational pre-application meeting at which program and review staff make presentations that explain their goals and objectives for the Muscular Dystrophy Cooperative Research Centers described in RFA-AR-03-001. The pre-application meeting is held in Bethesda on January 14, 2003 (the day before letter of intent is due). See NIH for more information on this notice NOT-AR-03-001 at <http://grants1.nih.gov/grants/guide/notice-files/NOT-AR-03-001.html>

Using GenBank Online to Find Important DNA Sequence for FSHD

“What is GenBank? GenBank® is the NIH genetic sequence database, an annotated collection of all publicly available DNA sequences (Nucleic Acids Research 2002 Jan 1;30(1):17-20). There are approximately 22,617,000,000 bases in 18,197,000 sequence records as of August 2002 (see GenBank growth statistics). As an example, you may view the record for a *Saccharomyces cerevisiae* gene. The complete release notes for the current version of GenBank are available. A new release is made every two months. GenBank is part of the International Nucleotide Sequence Database Collaboration, which is comprised of the DNA DataBank of Japan (DDBJ), the European Molecular Biology Laboratory (EMBL), and GenBank at NCBI. These three organizations exchange data on a daily basis.” See internet hyperlink <http://www.ncbi.nlm.nih.gov/Genbank/GenbankOverview.html> for more information.

For more information, go to the “Submit to Genbank” internet page at the following location: <http://www.ncbi.nlm.nih.gov/Genbank/index.html>. The search box should be set to “nucleotide.” In the “for” box try searching for any of the accession numbers for FSHD sequence as follows:

Genbank accession numbers

4qA distal sequence:

U74496 and U74497

4qB distal sequence:

AF017466

D4Z4 repeat array sequence:

AF117653

Distal 10q sequence:

AF538960

The FSH Society is making great strides toward finding a cure. We need your help! Consider donating both financially and with your time!

FSH Society 2002 International Network and Contact Day for FSHD a Success!

The Bi-Annual International Network and Contact Day for Facioscapulohumeral Muscular Dystrophy (FSHD) was held as a meeting of the FSH Society on October 12-13, 2002, in Rockville, MD. Despite the DC-area sniper, almost all who registered – over 140 people – attended. It was quite remarkable considering the tension, fear and uncertainty in Rockville

during those days. Attendees came from Australia, Canada, France, Russia and across the U.S. Saturday, October 12, 2002 was informally structured with four discussion groups for people to come together to meet one another, get acquainted and find common ground and mutual support. The four discussion groups were: Getting to Know You/Express

Yourself; Significant Others/Care Givers; Taking Care of Ourselves; and Legal, ADA and Patient Advocacy. Discussion groups were moderated by Karen Johnsen and Carol Perez, Dean Johnsen and Dawn Young, Robert and Patti Smith, and Howard Chabner, respectively. All were well received and extraordinarily helpful for all attendees.

Keynote Address

By Daniel Paul Perez, President and CEO, FSH Society

Welcome to the 5th International Patient Network Day for facioscapulohumeral muscular dystrophy (FSHD). My name is Daniel Paul Perez, founder, President and CEO of the FSH Society. I thank you for coming, and you are truly the bravest people I know. We realize that the lives of FSHD patients and their caregivers are nothing short of heroic.

A few weeks back, I saw a cartoon in the New Yorker. For a thousand different reasons and on a hundred different levels, I liked it. One fish out of water, standing on land with newly found legs, says to another fish in the water, "In order to be free I had to make certain adjustments." It speaks exactly to what the FSH Society is and to what we do.

Remarkable progress has been made in FSHD . . . thanks to your guidance, backing, and the persistence and tenacity of the FSH Society.

What has happened?

The Society has made FSH dystrophy visible.

The Society has educated both houses of the U.S. Congress on FSHD research.

The Society has advised and educated the federal body responsible for doing biomedical research, called the National Institutes of Health (NIH), on FSHD.

The Society has recruited and implored people to work on FSHD.

The Society initiated nearly a dozen research projects that are pioneering breakthroughs in FSHD and we are closing in on understanding this disease. We can now begin to build the bridge connecting research to treatments.

The NIH has established a National Registry for FSHD patients and their families.

The NIH issued contracts and programs for FSHD in the millions of dollars and continues to do so.

A law of the land was written and passed mandating research on FSHD.

The NIH has begun to establish large scale muscular dystrophy research centers.

The FSH Society is reversing decades of neglect of FSHD by the American medical establishment and is gaining strength and credibility.

The FSH Society is now the voice for two thousand families strong.

The Society continues to challenge those who choose to ignore the issue of FSHD.

Carol, Stephen and I have typed and spoken the word facioscapulohumeral no less than a hundred thousand times.

The FSH Society has changed the perception of just how competent and able folks with FSHD are.

And, the FSH Society has helped countless numbers of people worldwide.

You should know that the FSH Society corporation is an independent organization and does not receive one penny from the government or the NIH. The FSH Society has been the impetus behind the increase in national spending on FSHD research from US\$450,000 to US\$2.4M annually. We have done this on a shoestring budget on which we still struggle to function. The pendulum must swing in the other direction, given the laws of gravity. It is now necessary for us to build the Society itself. Your concerted help to give us the resources needed to continue this mission is critical. It is wonderful to see these remarkable successes. There are many stories behind the scene. I know who did heavy lifting and how and when the events transpired. The Society is less interested in claiming credit than in getting solutions for FSHD. We need capital to stay with this necessary and focused program.

Sunday, October 13, 2002, the main education day, began with keynote and kick-off speeches by Daniel Paul Perez, President & CEO, and Carol A. Perez, Executive Director. Dan Perez emphasized the remarkable work that the Society has done in the two years since the last patient meeting and the immediate and urgent need for funds to grow the Society.

The morning session, "Clinical, Therapeutic and Orthopedic Issues in Facioscapulohumeral Muscular Dystrophy (FSHD)" was chaired by Rabi Tawil, M.D., Neurologist, FSH Society Scientific Advisory Board Member, Associate Professor of Neurology, Department of Neurology, University of Rochester School of Medicine, Rochester, NY, USA. Dr. Tawil lectured on the clinical aspects of FSHD and overall developments in FSHD. The highlight was a timeline slide detailing major events in FSHD since its discovery/classification in 1864 and the remarkable progress in the last ten years.

Wendy King, Physical Therapist, Adjunct Assistant Professor, Department of Neurology, Ohio State University, Columbus, OH lectured on "Maintenance and Treatment Aspects of FSHD Physical Therapy." This was very informative and explained from a clinical perspective what losses occur and where they occur and how to diagnose FSHD and how to distinguish it from diseases that appear clinically similar. Attendees expressed the need to see and learn more about exercises and stretching routines.

Anthony Romeo, M.D., Orthopedic Surgeon, Director, Shoulder Section, Assistant Professor of Orthopaedics, Rush Presbyterian St. Lukes Medical Center, Chicago, IL lectured on "Orthopedics and Scapular Fixation in FSHD." We were able to see for the very first time a movie of an actual scapular fixation operation. It was truly impressive to see the surgery

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Contact Day, continued from page 22

documented so well and to see such training materials being developed for surgeons. Dr. Romeo presented the advantages, risks and rehabilitation aspects of the surgery so that persons with FSHD who are considering having the surgery can make well-informed decisions. The morning ended with a good discussion with the three presenters and the audience of more than 140.

The afternoon session, "Genetic and Research Issues in Facioscapulohumeral Muscular Dystrophy (FSHD)" was chaired by Denise Figlewicz, Ph.D., Researcher, Associate Professor of Neurology, Department of Neurology, University of Rochester School of Medicine, Rochester, NY. Dr. Figlewicz started with a comprehensive lecture and overview on "Genetic and Cellular Research on FSHD." The next lecture was "Genetic Research on FSHD" by Rossella Tupler, M.D., Ph.D., University of Massachusetts Medical School, Howard Hughes Medical Institute, Worcester, MA on the recent work on the repression complex and gene regulation switch found in FSHD. "Genetic Research on FSHD" was presented by Silvere M. van der Maarel, Ph.D., Leiden University Medical Centre, Leiden, the Netherlands. Dr. van der Maarel discussed the latest results, breakthroughs and findings in FSHD from one of the world's foremost laboratories on FSHD. The last presentation was a much different and unique area of research in FSHD titled "Cellular Biology Research on FSHD" by Patrick Reed, Ph.D. (with his colleagues Robert Bloch, Ph.D. and Neil Porter, M.D. in the audience), University of Maryland, Medical School, Baltimore, MD. The work shows the insights gained in the muscle membrane and the sarcolemmal membrane in FSHD. The

afternoon session concluded with a brief panel/audience discussion. The presenters were impressed with the nature and qualities of the questions. Attendees requested a primer of the scientific terms used throughout the talks. The late afternoon was structured with two rounds of four workshops to explore further issues and questions raised during the day.

The concluding remarks, "The FSH Society: Looking Ahead" were presented by Mr. Edward Schechter. (Please see article beginning on the front cover of this newsletter for the text of Mr. Schechter's speech.) Mr. Schechter's impromptu speech at the Natick Patient Conference in 2000 moved many people to action. The FSH Society is indebted to Mr. Schechter and the significant contributions he has made towards progress on FSHD and in the development of the Society.

Sunday's events were digitally recorded on video and audio and the Society will shortly begin editing the eight ninety minute tapes. We hope to complete this process by mid-February, 2003. Please contact the Society if you wish copies of the conference tapes for a nominal fee.

The FSH Society wishes to thank the 2002 Network Conference speakers; the 2002 Network Conference Committee: Stephen J. Jacobsen, Ph.D., Karen and Dean Johnsen, Cheryl Olds, Judy and Don Lockerson, Carol A. and Charles Perez; the members of the Mid-Atlantic FSH Society Support Group under Karen Johnsen's leadership; the staff and owners of the Rockville Doubletree Hotel; and all attendees, especially those who traveled far under difficult circumstances, for their contributions to the success of this meeting.

Researching FSHD at the NCBI NIH NLM Online Mendelian Inheritance in Man Database

The National Center for Biotechnology Information (NCBI) at the NIH National Library of Medicine (NLM) maintains a database called "Online Mendelian Inheritance in Man" (OMIM). OMIM describes itself as "a catalog of human genes and genetic disorders authored and edited by Dr. Victor A. McKusick and his colleagues at Johns Hopkins and elsewhere, and developed for the World Wide Web by NCBI, the National Center for Biotechnology Information. The database contains textual information and references. It also contains copious links to MEDLINE and sequence records in the Entrez system, and links to additional related resources at NCBI and elsewhere."

You can do a search on FSHD and its associated syndromes by going to <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM>, entering "FSHD" in the text search box and pressing the go button. At the next page, click on *158900 FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY 1A; FSHMD1A.

The New York Community Trust Foundation Grant to the FSH Society, Inc.

Since 2000, at the request of an anonymous donor, The New York Community Trust has awarded an annual grant of US\$50,000 for five years to the FSH Society. The Society is grateful for the continued generosity and respect demonstrated by this gift. We express our gratitude to our anonymous donor. Due to our anonymous donor and the New York Community Trust, these funds provide resources to develop our organization into a responsive Society.

***The FSH Society has been instrumental
in the giant advances in research
to find a cure for FSH.***

***We need your donations to continue the
fight! Please see donation form on page 32.***

FSHD and Genetic Testing Information Available at GeneClinics

A half dozen years ago the Society started working with GeneClinics to help raise the visibility of FSHD. GeneClinics, a non-profit organization, receives funding support from the National Institutes of Health (NIH), the Health Resources and Services Administration, and the US Department of Energy. Technical support for the www.geneclinics.org website is by the University of Washington and administrative support is provided by the University of Washington School of Medicine and Children's Hospital Regional Medical Center, both of which are in Seattle, WA. GeneClinics describes its web site on the home page as a "publicly funded medical genetics information resource developed for physicians, other healthcare providers and researchers, at no cost to all interested persons."

GeneClinics asked the Society to help with its last grant application by providing written letters of support for grant applications by the GeneClinics organization to government funding agencies. This led to increased interest in FSHD at the University of Washington and is helping to shore up FSHD research in the northwest and on the west coast of the U.S. For more information, follow the GeneReviews link on the www.geneclinics.org website and search for FSHD; this will lead to a summary page on

FSHD that contains a section called "Testing;" under "test availability" there is a hyperlink called "testing" that leads to the GeneTest lab search results.

The section will provide details for physicians and genetic counselors on diagnostic and pre-natal testing. The laboratories that conduct clinical testing for FSHD shown on GeneTest-GeneClinics are:

- Alberta Children's Hospital, Molecular Diagnostic Laboratory, Calgary, Alberta, Canada
- Athena Diagnostics, Inc., Reference Lab, Worcester, MA
- Children's Hospital of Eastern Ontario, DNA Diagnostic Laboratory, Ottawa, Ontario, Canada
- Leiden University Medical Center, DNA Diagnostic Lab/KGCL, Leiden, Netherlands
- New York University School of Medicine, Neurogenetics Laboratory, NY, NY
- University Hospital of Umea, Department of Clinical Genetics, Umea, Sweden
- University of Antwerp, Department of Medical Genetics, Antwerp, Belgium
- University of Iowa Health Care, Department of Pathology, Iowa City, IA
- Wolfson Medical Center, Molecular

Genetics Laboratory, Holon, Israel

In addition, the Department of Medical Genetics and Neurology, University of Washington, Seattle, WA has posted a web site at <http://depts.washington.edu/neurogen/> called "Genetic Testing for Neurological Conditions" that has informational materials on genetic testing for several diseases. One of the brochures found at this site is called "Facioscapulohumeral Muscular Dystrophy: Making an Informed Choice about Genetic Testing." The FSH Society Scientific Advisory Board (SAB) has not reviewed this document for accuracy. The University of Washington brochure on FSHD is a good read although it has several minor errors. The brochure covers some general concepts in genetic testing and may give the impression that pre-implantation genetic (PGD) diagnosis is available for FSHD. PGD is not yet technically feasible for FSHD according to the top experts in FSHD genetic testing. The FSH Society, through the SAB, continues its work on a brochure for the complex testing aspects of FSHD. The Society hopes to have a definitive and authoritative document for patients and professionals by mid-2003.

About the FSH Society

The Facioscapulohumeral Society (FSH Society) is an independent, 501(c)(3) non-profit and tax-exempt U.S. corporation organized to address issues and needs specifically related to Facioscapulohumeral Muscular Dystrophy (FSHD). Papers certifying its incorporation, bylaws and tax-exempt status are deposited at the Corporation's East and West Coast offices and the office of its General Counsel in Washington, D.C.

The FSH Society was created because of a need for a comprehensive resource for FSHD individuals and families. Purposes of the organization are:

- to encourage and promote scientific and clinical research and development through education of the general public, governmental bodies and the medical profession;
- to support such research and

development through solicitation of grants and contributions from individuals, private foundations, the pharmaceutical industry and others;

- to accumulate and disseminate information about FSHD;
- to actively cooperate with related organizations and foster communication among all interested parties; and
- to represent individuals and families with FSHD.

The Society invites contact from any interested individuals, families, physicians, caregivers, charitable organizations, government agencies, industry, scientific researchers and academic institutions. Any inquiries regarding membership, charitable donations, purposes and goals or other issues pertaining to the Society and FSHD, should be addressed to the Boston or San Diego offices.

Society Receives Award

On May 9, 2002 the FSH Society was recognized and named to the "Fleet Top 100" as part of the Small Business Leadership Awards 2002 by Fleet Bank. The Society was selected for demonstrating leadership and exemplary business practices from 1,500 nominations and applications. Fleet Bank recognized the FSH Society for its contributions to the community, for our passion for success and for dedication to our business.

FSH Society Seeks Director of Development

The FSH Society seeks a professional with 5-10 years experience with non-profits in public relations, membership development, all aspects of fundraising and planned giving. This is a part-time salaried position two-three days per week. Please address inquires and send resume or c.v. to the FSH Society, Inc.

NIH Continues Program Announcement for Therapeutic and Pathogenic Approaches for the Muscular Dystrophies

The National Institutes of Health (NIH) has an ongoing program announcement with funds set aside (a PAS) called Therapeutic and Pathogenic Approaches for the Muscular Dystrophies PAS-01-041. This PAS was a renewal of the PA offered in 1998: PA-98-044; and hopefully after three years the new PAS will be renewed. The FSH Society was instrumental in bringing about the prior 1998 announcement after many years of work in Washington, DC and at the NIH. The mechanisms of support will be the individual research project grant (R01) and the program project grant (P01). The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and National Institute of Neurological Disorders and Stroke (NINDS) intend to commit approximately US\$5.0 million in total costs to fund competing applications submitted in response to this announcement during fiscal years 2002- 2004. One project has already been funded under this program in

the US\$1 million dollar range that covers, in part, gene expression in FSHD muscle tissue.

Several examples of research requested for study under this announcement are:

- Determine basis of differential involvement of muscles, reflected by the regional pattern of disease. Comparison of muscle groups might show the cause of relative specificity of affected muscles. Comparing expression patterns of RNA and protein in affected and non-affected muscle will provide insights into alterations occurring as the disease progresses.
- Explore the role of inflammation in FSHD. While FSHD has been described as the most inflammatory form of muscular dystrophy, there is no evidence that disease severity is lessened by administration of the anti-inflammatory drug prednisone. It is necessary to explore the relationship between inflammatory

cells, muscle cell death, and blood vessels.

- Study properties of muscle cells derived from affected tissue. Cells cultured from FSHD muscle show increased sensitivity to oxidative stress. This needs to be followed up by studies verifying that this occurs in vivo and establishing how this cellular phenotype develops.

THERAPEUTIC AND PATHOGENIC APPROACHES FOR THE MUSCULAR DYSTROPHIES

Release Date: January 4, 2001

PA NUMBER: PAS-01-041

National Institute of Arthritis and Musculoskeletal and Skin Diseases
National Institute of Neurological Disorders and Stroke

PAS uses R01 and P01 Grant award mechanisms. http://www.niams.nih.gov/rta/funding/grants/pa/pas_01_041.pdf.

FSH Society Board of Directors and Staff Update

The FSH Society Board of Directors established a Board Member Emeritus position to acknowledge the extraordinary contributions of former members who wish to continue to serve the Society.

Theodore L. Munsat, M.D., of Boston, Massachusetts, and **Paul Schultz, M.D.**, of San Diego, California, are now serving in this capacity. Drs. Munsat and Schultz were founding board members and Scientific Advisory Board members. We are indebted to Dr. Schultz for his tireless efforts and work as the first chairman of the Scientific Advisory Board. We are grateful for their significant contributions, both past and present, to FSHD research and patients, the FSH Society and the field of neurology.

The Board has expanded its membership with the election of **C. Larry Laurello** and **Howard L. Chabner** in 2001. In addition, the Society has added staff to help with operations in the administrative office. Elizabeth Merkle joined the staff of the Society in 2001. We

are pleased to have Mrs. Merkle with us in our administrative office.

C. Larry Laurello, P.E.: A partner in the Delta Railroad Construction Company, Ashtabula, Ohio, Mr. Laurello has been instrumental in providing the annual Delta Fellowship grant since 1997. Active in the FSH Society Michigan/Ohio Support Group, Mr. Laurello has devoted his time to increasing knowledge of FSHD at all levels and providing strong leadership in the FSHD community. As a concerned FSHD patient, parent and grandparent, Mr. Laurello is committed to FSHD research worldwide.

Howard L. Chabner, J.D.: A graduate of Harvard Law School and a former corporate attorney in San Francisco, California, Mr. Chabner, an FSHD patient, is a disability rights advocate who successfully challenged the life insurance industry for individuals with FSHD.

Elizabeth T. Merkle, Pharm. B.S.: Lexington, Massachusetts. A native of The Netherlands, she came to the United

States in 1955 where she held the position of Administrative Officer at MIT, Cambridge, Massachusetts until her retirement in 1983. Since January 2001, she has been assisting the Society's Director, Carol A. Perez, with administrative, clerical and general activities on a part time basis. She routinely translates FSHD-related Dutch publications for incorporation into *The Watch* and, in November 2002, represented the Society at the VSN [Vereniging Spierziekten Nederland — Organization Muscle Diseases Netherlands] patient day in Baarn, The Netherlands. Mrs. Merkle developed and maintains a library system for FSHD related reprints and pamphlets. In addition to her work with the Society, Mrs. Merkle actively volunteers as a tax counselor for the elderly in the IRS/AARP tax assistance program and is a volunteer money manager for low income elderly and disabled.

FSH Society Works with Human Genome Project to Sequence 4q35

Given the location of the FSHD deletion near the tip end of chromosome 4, it has been a top priority of the Society to facilitate the sequencing of the adjacent region. Daniel Paul Perez worked on the Human Genome Project for several years in the late 1990's helping with the efforts on chromosome 10. For some years, the Society's Scientific Advisory Board stated that the sequencing of the end of chromosome 4 from the end of chromosome 4 to a distance of 5 million to 10 million base pairs towards the center was a top priority for FSHD research. The reason for this is simple - the need is to identify genes or genetic apparatus adjacent to the deletions in D4Z4. The Society made numerous inquiries and had numerous meetings with U.S. and foreign government research agencies to help complete the 4q35 band of the human chromosome 4. Although the Human

Genome Project had stated that the first pass of the Human Genome Sequence was complete, this was far from the case for the very complicated region of 4q35. Much of this region was incomplete and had gaps or holes. In fact, at the beginning of 2002 several million (2-3M) base pairs of genetic DNA sequence were missing from the map of chromosome 4. The Society inquired about sequencing the region completely but the cost would have been prohibitively expensive for the Society and so we pursued the agencies in charge of the task.

The Society funded a little-publicized but incredibly critical project under the direction of Jane Hewitt, Ph.D., Nottingham University, Division of Genetics, Queen's Medical Centre, Nottingham, England titled "Fugu rubripes as a model organism for FSHD gene identification." The project ran from

7/1/2000 - 6/30/2001 and was funded under a Delta Railroad grant to promote high risk and necessary projects for one year. The theory behind the project was that genes are conserved across the species in evolution (otherwise know as evolutionary breakpoints) and that evolutionary important genes would stay clustered together over evolution. Fugu Rubripes is the well-known puffer fish. Over evolution the genetic material has expanded and thus sequencing the region on the fugu containing the same genes of interest would be significantly smaller than the human region. Dr. Hewitt is one of the leading genomic experts in the world and one of only several individuals eminently qualified in FSHD genomics. The research yielded an enormous amount of information regarding the genetic architecture of the region.

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Figure: Tiling Path of Clones for 4q35

1646.5	4016	M	AC131943	AC084844	3	CTD-2242C10	137070	WIBR	+++	
1648	4016	M	AC093601		3	RP11-338P22	?	WUGSC	?	replacement clone,
1649	4016	M	AC109353	AC021002	3	RP11-521B22	151332	WIBR	+0+	
1650	4016	M	AC105288	AC060763	3	RP11-554F9	144721	WIBR	+0+	
1651	4016	M	AC079226		3	RP11-18D7	177064	WUGSC	+0+	?
1652	4016	M	AC114798		?	RP11-713K18	?	WUGSC	?	new spanner
1652.5	4016	M	AC079766		3	RP11-188P17	139249	WUGSC	+0+	?
1653	4016	?	AC019193		3	RP11-335L23	176034	WUGSC	+++	?
1654	4016	M	AC099397		3	RP11-247K9	?	WUGSC	?	RFP, ESF less than,
1655	4016	M	AC093844	AC046164	3	RP11-451F20	187956	WIBR	+++	
1655.5	4016	M	AC112698		3	RP11-692E14	?	WUGSC	?	new spanner
.										
.										
1693	4016	M	AC079092		1	RP11-237D3	163116	WUGSC	+++	will finish 4kb to
1695	4016	M	AC097521	AC027414	3	RP11-565A3	182556	WIBR	+++	
1696.2	4016	M	AC113157		3	RP11-799E7	?	WUGSC	?	new spanner
1696.5	4016	M	AC115540		3	RP11-629I23	?	WUGSC	?	new spanner
1697.5	4016	O	gap-type-2		?	?	?	?	?	#GAP H_NH0366H04-
1698	4016	O	AC110789		3	RP11-516D7	?	WUGSC	?	minimal o/l btw
1701	4016	M	AC093789	AC046187	3	RP11-219G10	194254	WIBR	+0+	
1703	4016	M	AC114759		3	RP11-347K3	?	WUGSC	?	replacement clone,
1704	4016	M	AC093909	AC021748	3	RP11-756P10	178028	WIBR	+++	
1705	4016	M	AC017063		3	RP11-354H17	190538	WUGSC	+00	Right 4020
1706	4016	M	AC122138	AC025844	3	RP11-818C3	175347	WIBR	+00	
1707	4016	M	AC107391		3	RP11-545D9	?	WUGSC	?	new spanner
1707.5	4016	?	AC105924		3	RP11-706F1	?	WUGSC	?	new spanner
1708	4016	P	AC020698		3	RP11-45F23	148418	WUGSC	+++	?
1709	4016	?	AC018687		3	RP11-462G22	181585	WUGSC	+++	o/l's AF250324
1710.6	4016	?	AF250324		3	RPCL-11-463J17	?	NA	ALL	o/l's RP11-
1710.61	4016	?	AF146191		3	?	?	OTHER	0+0	from Harold's map
1710.63	4016	?	U85056		3	?	?	?	?	from Harold's map
1710.64	4016	?	AC126281		?	XXcos-2173C8	?	?	?	should contain

Human Genome Project, continued from page 26

In early 2002, Daniel Paul Perez looked at the Human Genome Map and recognized that it was still in poor shape. Dan called his old colleagues from the Human Genome Project at the Whitehead Institute for Genomic Research at Massachusetts Institute of Technology (M.I.T.) and asked which laboratory would be completing the sequencing of chromosome 4. He was told that Whitehead and Washington University Genome Sequencing Center (WashU GSC) would be responsible for chromosome 4 and that WashU GSC would be doing the work to finish and sequence chromosome 4. The Society called Bob Waterston, Director of the WashU GSC, to discuss the 4q35 region on the human genome map/sequence. The Society asked for resources in the GSC to work with FSHD genomic experts to help finish what is called the physical map of the region, which is essentially a path of overlapping clones, and then to sequence the path to help close the numerous holes in the map. Dr. Waterston connected the Society with Robert Fulton and Tina Graves in sequencing operations and clone management at WashU GSC. Robert Fulton expressed great enthusiasm and immediate support for working together to finish this portion of chromosome 4.

The Society then contacted FSHD researchers intimately familiar with the genomics of FSHD and asked them to help WashU construct the region of 4q35. The genomics and complexity of the DNA in this region is extraordinarily complex and at the limits of what a large-scale

sequencing lab can handle in terms of assembling all of the pieces (clones) in the right order to be sequenced. Much of the DNA in this region can be found all over the chromosomes (known as the genome). Dr. Hewitt was able to piece together the right human clones needed for sequencing 4q35 based on her insights from the work on the puffer fish. As well, Drs. Lemmers, van der Maarel and van Geel (Leiden and Nijmegen) and Drs. Tupler and Gabellini (UMass Medical) and Dr. Altherr (Los Alamos National Laboratory) and Dr. Harold Reithman (UPenn Wistar) helped in a very substantial manner with the effort to piece together 4q35. A year later the 4q35 region is nearly completely sequenced with the exception of one gap. The figure on page 26 shows the tiling path and associated notes for the clones needed to be sequenced for 4q35 that the group has put together. The first line is the beginning of the 4q35 region and the last line is the tip of chromosome 4 at 4q35. Each line (clone) connects to the following line (or next clone). The gap in the map is at position 1697.5

Difficulties still remain with sequencing each of the repeats in 4q35 region known as D4Z4. Dr. Altherr (LANL) has undertaken this initiative but has been slowed by the loss of the laboratory personnel working on the project. There are now two variations to the end of the chromosome (4q35A, 4q35B) and we are working with Leiden to isolate the much needed pathogenic 4q35A tip. WashU can sequence the DNA in a matter of a day. The difficulty remains

with the isolation of the DNA and insertion into a suitable clone vector for sequencing. Leiden has proposed a strategy to isolate and WashU has said it will sequence the provided set of clones. According to the UCSC browser (see below), 4q35 starts at accession AC084844 (clone name CTD-2242C10) then continues to the end of the chromosome. There is only one sequence gap in this region, for which WashU has clones in the pipeline. There are only two clones that are not finished. The clones not yet finished are RP11-713K18, which is in finishing, and XXcos-2173C8, which is a cosmid at the very telomeric end of 4q.

This is one of the many examples of the work that the FSH Society does to promote solutions for FSHD and how your donations and dollars are so valuable to help the Society continue its work.

For the interested reader, the ongoing genome map and sequence can be browsed at the Human Genome Browser Gateway Web tool at the University of California Santa Cruz (UCSC). Go to the UCSC Genome Browser at <http://genome.ucsc.edu/cgi-bin/hgGateway?org=human>. At this page "Human Genome Browser Gateway" type "4q35" in the position box, and press the submit button. On the bottom of the next page switch "Map Contigs" by drop down box to full, and switch "Assembly" by drop down box to full and hit the refresh button. You will then see the path above displayed.

Thelma B. Green Memorial Fellowship Grant Awarded

In loving memory of Thelma B. Green (1909-2001), family and friends established a one-year US\$30,000 FSH Society Fellowship Grant for research on FSHD. In honoring Thelma through this memorial, family and friends are continuing her efforts to provide encouragement and support for her great granddaughter, Jessica Smith Ryley. By funding this research, the family hopes to help find a cure for Jessica and all others living with Facioscapulohumeral Muscular Dystrophy.

In January 2002, Dr. Polly Xing, University of Massachusetts Medical Center, was awarded the FSH Society Thelma B. Green Fellowship Grant for her project: "Higher level chromatin packaging and nuclear organization of FSHD cell with an emphasis on its 3.3 kb deletion involving high resolution transcript mapping by mRNA in situ and direct visualization of this region of the chromosome via in situ hybridization with loop halo DNA preparations." The work is continuing under Dr. Jeanne Lawrence's direction.

Visit us @ www.fshsociety.org

By Daniel Paul Perez, President & CEO,
FSH Society

Be sure to bookmark the FSH Society at its Internet location www.fshsociety.org. We are seeing a tremendous increase in domestic and international traffic, and our home page receives more than 3,500 hits weekly. We are getting the word out about FSHD!

The home page at www.fshsociety.org contains a rich resource of material for those interested in FSHD. The FacioScapuloHumeral Muscular Dystrophy Society home page contains the following:

- Information on the FSH Society, including an introduction to the FSH Society and FSHD, the FSH Society membership application and donation form and an on-line form to request membership materials;
- A comprehensive patient brochure on FSHD. We will have a brochure on genetic testing for FSHD available soon;
- Information and links to the FSH Society online resources conferences that include bulletin board and chat room software by O'Reilly. The O'Reilly WebBoard product allows you to share information by posting messages directly to conferences (and reading and replying to responses). The bulletin board is a moderated board; all approved messages will appear after approval by a moderator. WebBoard's java-enabled chat provides instant

interaction via your web browser without needed internet relay chat software. Just click and go. The chat room and BBS are open 24 hours a day, 7 days a week (24x7) and we have regular chat session times at 2pm EST and 9pm EST on Sundays. We use the 2pm EST Sundays to make it easier for international users of the system;

- FSH Society publications and information, including all back issues of the FSH Watch from the first issue (Vol. 1, No. 1, Spring 1994).

Please be sure to get the word out about this rich resource of information on FSHD to your family, friends, doctors, and anyone who may have an interest in FSHD. We encourage you to refer new members and individuals to the BBS, the chat room and to the home page.

We need and invite ideas and suggestions for a new site design. To date, we have chosen simplicity, speed and search engine compatibility/performance over graphics. Professional web designers and web architects who would like to volunteer their time and services are encouraged to contact us. Given the amount of time and resources needed to maintain and monitor this site, we sincerely appreciate the contributions and donations made to the Society to support this important and timely resource. Please consider making a donation to the FSH Society Internet fund.

We look forward to seeing you on-line!

Support Groups

FSH SOCIETY GROUPS WELCOME NEW MEMBERS AND OFFER NEW RESOURCES

Support groups in the Arizona, Colorado, Gulf Area (Alabama, Louisiana and Mississippi), Michigan/Ohio, Mid-Atlantic, Minnesota, New England, and North-West (including Canada) offer the unique opportunity to meet others to discuss FSHD issues. Meetings are generally held every other month covering topics specific to FSHD. Groups meet in accessible locations. Experts address clinical, research, genetics, nutrition, exercise and coping strategies for FSHD. Individuals, family members and professionals concerned with FSHD are welcome to attend. Information about support groups and networks will be posted on the FSH Society website: www.fshsociety.org. Please call **Karen Johnsen**, FSH Society Support Group Coordinator, (301) 262-0701 or email: kjohnsen5@msn.com, with any questions or interest in a local group, telephone network or pen pal group.

We have requests to form groups in San Diego, San Francisco and Los Angeles, CA; Palm Beach, FL; and Philadelphia, PA. Please contact Karen for new group information. In order to preserve confidentiality, the FSH Society contacts members directly to inform them of group meetings in their areas.



FSH SOCIETY'S FSHD CHATROOM IN CYBERSPACE

On Sundays at 2 and 9 p.m. Eastern Time (USA), the Society hosts chats that include our network members worldwide. Ready-to-use java chat software is available at www.fshsociety.org by clicking on hyperlink "FSHD Bulletin Board and Chat" or use your own Internet Relay Chat (IRC) software or mIRC via the IRC FSHD channel ([#fsh_society](http://webboard.novatech.net:7000)).



ADDITIONAL RESOURCES

Videotapes of selected meetings from the Mid-Atlantic FSHD Support Group and New England FSHD Support Group

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***Would you like to support
the efforts of the FSH Society?
Pull out the envelope from the middle
of this newsletter,
fill it out and send it in today!***

Support Groups & Acknowledgements, continued from page 28

are available on loan. In addition, videotapes of the FSH Society 2002 Network Conference are available. Contact the office of the FSH Society for further details.

Pen pal network for our teens

Please contact **Karen Johnsen**, (301) 262-0701 for names of those interested in receiving correspondence.

Network for the Partners and Family Members: please contact **Dean Johnsen** at (301) 262-0701



INTERNATIONAL FSH SOCIETY NETWORK CONTACTS

Australia-Ray Jordan, 86 Barry Street, Reservoir, Victoria 3073, Australia, Phone: 03 9460 2559, Email:

rrev@optusnet.com.au. MDA Victoria coordinator for FSHD group. **Update:** Ray attended the 2002 International Conference on FSHD and FSH Society Conference in October 2002 in Maryland.

Canada-Dawn Young, New coordinator for Canada. Email: dadayoung@shaw.ca

England-FSHMD Support Group, 2, Hamlyn Close, Edgware, Middlesex, HA8 8DB, England, Phone: 0181-958-788, Fax: 0181-958-2198, Holds annual meeting for FSHMD. Web Site:

<http://www.btinternet.com/~fsh>

France-Daniel Mennetret, e-mail: daniel.mennetret@libertysurf.fr, liaison to Friends (**Amis**) of FSHD, **Association Française contre les Myopathies (AFM)**, 1 Rue de l' Internationale, 91002 Evry Cedex, France. **Update:** The French Delegation, Martine Devillers, M.D., Direction Recherche & Therapeutiques, Claude and Christie Martelet and Mr. and Mrs. Daniel Mennetret attended the 2002 FSH Society Conference.

Netherlands-Dutch FSHD Foundation (Stichting FSHD): Kees C. J. van der Graaf, President and Founder, **Stichting FSHD**, Kievitslaan 34, 2243 GD Wassenaar, The Netherlands. Phone: 31 70 511 8466 Fax: 31 70 511 0041. The purpose of the foundation is to stimulate, facilitate and fund scientific (genetic and clinical) research into the causes and etiology of FSHD. The Foundation works closely with the FSH Society on scientific issues.

The Netherlands-VSN (Muscular Disease Society Netherlands): VSN FSHD Working Group, Gortstraat 115, 3905 BD Veenendaal, The Netherlands: **Frank van Zimmeren**, e-mail: frank_van_zimmeren@hotmail.com, liaison with VSN.

South Africa-Mr. Honiball, FSHD Coordinator, **Muscular Dystrophy Foundation SA**, P O Box 1535, Pinegowrie 2123 South Africa, e-mail: mdsa@megaweb.co.za



THANK YOU!

The FSH Society wishes to acknowledge the following for their contributions to our efforts:

2002 CONFERENCE

Mid Atlantic Support Group; **Discussion Group Leaders:** Michele DeSha and Howard Chabner; Patti and Bob Smith; Dean Johnsen and Dawn Young; Karen Johnsen and Carol Perez. **Faculty:** Chair, Rabi Tawil, M.D.; Dr. Robert Bloch and Patrick Reed; Denise Figlewitz, Ph.D.; Wendy King, P.T.; Anthony Romeo, M.D.; Rossella Tupler, M.D., Ph.D.; Silvere van der Maarel, Ph.D.; Cheryl Olds and Edward Schechter. **Accommodations:** Thomas Kammerer and the staff, Rockville Doubletree Hotel.

The AFM for funding the participation of the French delegation to the 2002 FSH Society Conference.

Paul Closson, host of the FSH Society web board and chat room.

Colorado FSH Society support group for their work at the American Academy of Neurology meeting in Denver, CO.

Drs. Rune Frants, Michael Green and Sara Winokur for hosting the 2002 ASHG FSHD Work Group.

Mid-Atlantic FSH Society support group as well as Don Burke, Linda Hoover, Dawn Young, Janine and Alain Thys for their work at the American Society for Human Genetics meeting in Baltimore, MD.

Ardeth Millner and Charles Perez, Lexington, MA, for continued support to the FSH Society office.

Support Group Leaders: Ann Biggs-Williams; Jeri Blom; Lori Heater; Catherine l'Heureux; Linda Hoover; Karen Johnsen; Meg Morris-Aabakken; Carol Perez; Peg Powers; Joanne Smith; Stephanie Staley; Dawn Young.

Bev and Jim Weyenberg, Kaukauna, WI for membership and newsletter mailings.



FUNDRAISING EVENTS

- **Bear Creek Elementary School**, Baltimore, Maryland 2001 and 2002 Read-A-Thon Fundraiser. The Bear Creek Elementary School held the 2001 and 2002 Read-A-Thon Fundraiser to support the FSH Society and educate their community about FSHD. 2002 was the sixth annual Read-A-Thon honoring Arlene Endres, mother of Jessica Ryley and teacher at the Bear Creek School

- **Friends of Christopher Stenmon - End of Tax Season Events in Quincy, MA** to support the activities of the FSH Society 2000, 2001 & Fourth Annual 2002: Alba Bar and Grill; Jason M. Alwardt in memory of Madison Alwardt, Sr.; Erica L. Art NH; Bad Abbots; Gloria Andersen; Jignesh Amin; Nathan Auclair; Lillian P. Battles; Joe Bryson; Sheri Buckingham; John D. Butters, Jr.; Club 58; Steven J. Cohen; Irene M. Connolly; Corporate Staffing; Kevin R. Danehy; Erin L. Delaney; Steven Deroian; Eileen Dunning; Kimberly Eddy; Kimberley Ennis; Eight Ball Billiard Parlor, Inc.; Andrew W. Fink; Bernadette Finneran; Jason Forish; Fours Boston; John Gregorio; Carrie Hartman; Thomas P. Hennigan; Eric A. Heshion; Anne Higgins; Kate Hurley NY; Steven Ialuna; Shirley Inbar; Shirley Judice; Ulrike Kjellberg; Bettina Landgraf; Francis P. Leone; Lauren Liberman; Joseph Marnikovic; Jennifer Maya-Salamone; Jennifer McCarthy; Alison McLaughlin; Fiona McDonagh; Anne McDonnell; Carol Murphy; Mystic Lounge; Jennifer Maya-Salome; Richard Nelson; O'Connor & Drew, P.C.; Mary Oldmixon; Paddy Barrys; Erin Parks;

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Acknowledgements, continued from page 29

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• High Woods Sportsman's Club

Second Annual (2001) and Third Annual (2002) FSH Society Benefit Archery Shoot, Saugerties, NY. Proceeds from the archery shoots were donated to the FSH Society. With special thanks to John and Denise Van Etten for their good work on our behalf.



ORGANIZATIONAL DONORS

• Athena Diagnostics – Worcester, MA; Association Française Contre les Myopathies (AFM) - Paris, France; Gerald Norton Memorial Foundation – Northfield, IL; U.I.L.D.M – Naples, Italy



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The following individuals have requested to be acknowledged in the FSH Watch Newsletter as of September 30, 2002:



NEW & RENEWING MEMBERS

Jeffrey & Barbara Bache MD; Sanford L. Batkin NY; E. A Biggs-Williams AL; Barbara Birnbaum CT; Jerilyn Blom MN; Ms. Lisa Brouillette WI; Lori Calandro Janice Caldwell MI; Howard Chabner & Michele DeSha CA; Mr. & Mrs. Stuart J. Cohen NY; Leandra Dean CO; Larry Dressler WA; Leonard Gilman FL; Hyman L. Hillson FL; Susan Holic CA; Mr. & Mrs. Gerald Isaacson NJ; John & Donna E. Kirtz TX; Russell W. Lai CA; Stuart A. Lai NY; Sharon Larson MN; Gabriele Lieb – Germany; Dr. David Lokerson MD; Mr.

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PROFESSIONAL MEMBERSHIPS

• William Herzberg, M.D., Portland, OR *Neurologist with Special Interest in FSHD
• Anthony A. Romeo, M.D., S.C., Chicago, IL *Orthopedic surgeon with a special interest in scapular fixation and FSHD.
• Vicki Tuschak, NJ



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• Ms. Janet Brennan FL

RESEARCH AND EDUCATION FUND

Mrs. Leonard Schwartz NY; Joanne & Gerry Smith honoring granddaughter, Jessica Ryley

IN HONOR OF

• Kaleb Bates Wolcott: Grandmother, Nan Wolcott Ph.D. NY
• Marjorie Bronfman: Mr. & Mrs. Marvyn Kussner, Town of Mont Royal, Canada
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Grandmother, Rose Kanter NY honoring 11th birthday; Caryn Stoner NJ

- Sean Fitzmaurice's graduation: "Continued Prayers" CA
- Cindy Gilman: Elaine Disick MA
- Joseph Grech: Sister, Rosina Grech CA
- Richard A. Lefebvre's Birthday: Marie Bortone MA
- William G. Michael's kindness: Henry T. Wiggin MA
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- Emily K. Tucker: Grandparents Ralph & Jane Stephens FL

IN MEMORY

- John Leon Biggs: Stephanie Biggs Rentfro, JD GA
- Josephine Berg Blier at age 86: Malcolm and Vicki Blier MA "she was valiant and loving and very involved with the world to the end."
- Clay Boisvert: Brenda Novoson MA
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We appreciate all of those who make the work of the Society possible. It is an honor to serve and represent you. Please call if there is anything we can do for you. Together, we can make a difference!

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