FSHD 101:
AN UPDATE ON CAUSES & TREATMENTS

Facioscapulohumeral dystrophy (FSHD) is the most common form of muscular dystrophy that effects both adults and children and there is a good chance you haven't heard of it. It is our mission at the FSHD Global Research Foundation to put FSHD on the map, to fund medical research and work towards a time when FSHD is treatable, curable and even preventable.

MDNSW have about 70 people with FSHD who they support. However, the hundreds of contacts in the Foundation database suggests that the numbers in NSW are much more than this. The estimated prevalence of FSHD is about one in 7500, or about 3000 people in Australia. This is probably lower than the real estimate. FSHD, like many muscular dystrophies, often goes undiagnosed or misdiagnosed.

FSHD is commonly associated with progressive weakening of facial, shoulder and upper arm muscles. However, this explanation does little justice to a disease that can rob people of their ability to walk, talk, smile or even eat. The progression often comes in bursts with sudden deterioration followed by periods of no change.

Genetic mechanism of FSHD

FSHD is one of the most complex genetic conditions currently known. FSHD involves a complicated interplay between genes and proteins in the muscle cell. FSHD is caused by mutations that actually increase the expression of a toxic protein that destroys muscle cells in the body. Currently there are two types of FSHD, type 1 and type 2 although the number of subtypes is likely to increase as more becomes known about this condition.

FSHD type 1

About 95% of FSHD cases are type 1 (FSHD1) and are associated with a mutation on chromosome 4. Chromosome 4 contains a series of repeated pieces of DNA, so called D4Z4 units. People without FSHD1 have 11 - 100 D4Z4 units. In people with FSHD 1 the D4Z4 array is shortened to 1 - 10 units.

The D4Z4 units act like a lock for this region of the genome. With fewer repeats a gene embedded in this region called DUX4 is expressed. DUX4 is a toxic protein that kills muscle cells.

FSHD type 2

The defect in FSHD2 was found to be in a gene called Structural Maintenance of Chromosomes Hinge Domain Containing 1 (SMCHD1). This gene acts as a lock for regions on the genome, in people without FSHD this protein is keeping regions like the one that contains the DUX4 protein, closed. Mutations in SMCHD1 lead to a smaller amount of this protein being produced. Less protein means less repression on the D4Z4 region causing DUX4 expression.

Management

Like most of the other neuromuscular conditions there is currently no treatment and no cure for FSHD. However, this does not mean that there aren't options for management.

Exercise

The old thinking that exercise should be avoided has been replaced by a cautious optimism that exercise may help people with FSHD maintain muscle function, prevent falls and delay the use of mobility aids. Experts in this field suggest that moderate aerobic exercise (eg. 15 – 30 minutes on a stationary bike 3 times a week) is not harmful and may be beneficial.

It's important to consult a health professional before engaging in exercise. It may be most helpful to find a physiotherapist or exercise physiologist who has experience in neuromuscular conditions who you can work with to develop an exercise program that suits your unique needs and goals.

Surgery, massage and other management techniques

There are a number of options for surgical management of FSHD. The main one is scapula (shoulder blade) fixation to help with shoulder function. Surgery doesn't work for everyone, but it can be very helpful for people with poor shoulder function.

Respiratory support is usually not recommended for people with FSHD because they do not experience the same reductions in lung function that the other dystrophies do. However, the Foundation has reports that people with FSHD do have issues with breathing, particularly at night time and we will be exploring mechanical support as a potential clinical intervention.

Other strategies such as hydrotherapy and massage may help managing pain and function. Orthotics and mobility aids can also help you get around and prevent injury.

On the horizon: progress on treatments and a cure

It is an exciting time for FSHD research. Our most recent funding round received 22 high quality applications on diagnostics, therapeutics and infantile FSHD (a severe form of FSHD that manifests in childhood). The amount of research that is starting to bridge the gap from bench to bedside is impressive.

There are three main areas where efforts are focussing at the moment; gene therapy, small molecules and biologicals.

FSHD Global is currently funding projects in all three of these areas. Some are focussing on gene silencing technology to try and switch off DUX4, others are screening vast libraries of small molecules to find ones that prevent the expression of DUX4.

One area that is receiving a great deal of attention at the moment is myostatin inhibitors. Myostatin is a protein that inhibits muscle growth. Interrupting its activity increases muscle size and strength. The Foundation is exploring variations on myostatin inhibitors to promote muscle growth for people with FSHD. It is likely that there will be a clinical trial in Australia in the very near future.

For more information on causes and treatments for FSHD see our recent clinical consensus statement published in a leading neuromuscular journal http://www.nmd-journal.com/article/S0960-8966(16)30096-7/abstract

Fast facts about FSHD and the Foundation

- FSHD is the most common form of Muscular Dystrophy affecting both adults and children
- FSHD affects men and women equally and can manifest at any point in your life from infancy to late adulthood. Infantile FSHD is particularly severe
- FSHD can affect all the skeletal muscles in the body
- At the moment there are no treatments and no cure for FSHD
- FSHD Global is the largest funder of medical research into FSHD outside the USA government
- In eight years FSHD Global has raised over $7.5 million for research
- The Foundation has funded 34 medical research grants in 9 countries and supports 59 scientists including 18 Australians
- FSHD Global receives no government funding

FSHD Global Research Foundation: working hard to find a cure

The Foundation was formed in 2008 by Bill Moss AO. Bill has FSHD and has made it a life goal to find treatments and a cure for this condition. In just 8 years the Foundation has grown exponentially and is the largest funder worldwide of medical research into FSHD outside the US government. From creating the first FSHD stem cells to planning some of the first clinical trials into FSHD the Foundation has made, and will continue to make, a significant and lasting contribution to FSHD research.

Do you want to know more?

This year three of the world's leading scientists and clinicians will be joining us in Australia for a country wide tour. Our NSW event will be held on the evening of Monday 5th September. Join us at the Garvan Institute of Medical Research in Darlinghurst for an evening of science and debate. We would love to see you there. We will also be in Melbourne on the 6th of September, Brisbane on the 7th of September and Perth on the 8th of September.

For more information on this event see https://fshdglobal.org/news-events/ or email admin@fshdglobal.org

MUSCULAR DYSTROPHY NSW BUILDING STRENGTH REACHING POTENTIAL

FSHD Global Research Foundation Ltd