

## AN ANIMAL MODEL FOR FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY

**Researchers at the Howard Hughes Hospital in Massachusetts, USA have identified a gene which plays a strong role in causing facioscapulohumeral muscular dystrophy (FSH), a muscle weakening and wasting disease affecting approximately 1 in 20,000 people in Britain. Currently there is no cure for this disease and the genetic mechanism which leads to the disease is not fully understood. The breakthrough was achieved by generating an animal model for the disease – the genetic defect was introduced into the DNA of mice. The generation of animal models for a certain disease is an extremely valuable way to gain vital clues for the understanding of genetic diseases. In these animals the DNA is altered so they carry a disease which is similar to the human counterpart. This gives the researchers the opportunity to study a disease in great detail in a living organism. The fact that there are mice available that carry the disease is a huge step forward to understand why the muscles become gradually weaker in patients with FSH. The discovery of the gene that is responsible for causing FSH presents a fantastic starting point for the development of a treatment for this muscle wasting disease. However, a lot more research needs to be done before a therapy will be available to individuals with FSH.**

In a paper published in the journal *Nature*, Davide Gabellini and Rosella Tupler et al. at the Howard Hughes Hospital in Massachusetts, USA describe the successful generation of a mouse model which shows a similar disease pattern to patients with facioscapulohumeral muscular dystrophy (FSH). The analysis of this mouse model has not only helped to identify a gene involved in the pathology of the disease, but might also provide essential knowledge to help develop and evaluate potential approaches to treatments.

Facioscapulohumeral muscular dystrophy is the third most common inherited muscular dystrophy and affects approximately 1 in every 20,000 people in Britain. The disease is characterized by progressive weakness and wasting of facial, shoulder and upper-arm muscles. In most of the familial cases, FSH is caused by a deletion of part of chromosome 4 and the extent of the deletion correlates with the severity of the symptoms. Previous studies revealed that the deleted DNA on chromosome 4 does not code for a gene, a discovery that has made it extremely difficult to find an explanation for the underlying molecular defect. Instead, the deletion comprises repeating blocks of DNA with the same sequence – called tandem repeat units. However, in the vicinity of these tandem repeat units researchers identified three genes that are

shown to be abnormally active in patients with FSH. Hence, the hypothesis was that the tandem repeat units interact somehow with these genes and regulate their activity. If the tandem repeats are not present the genes run riot and produce far too much protein – a situation described as overexpression. But, up until now, the scientists did not know which one of those genes might cause the muscle wasting associated with FSH.

In this paper, Gabellini et al. report the results of experiments in which they add the three human genes separately into the genome of mice - called transgenic mice - and screen the mice for symptoms that are seen in FSH. They discovered that one gene alone, termed FRG1, was implicated in the pathology of FSH. It causes the muscles to waste and weaken and the mice also show kyphosis, the typical curvature of the spine. First analysis into the function of the gene shows that it is involved in the maturation of proteins which are specifically required for normal muscle function.

These results are of particular importance because the generation and analysis of this animal model did not only contribute to the identification of a gene responsible for FSH, but will provide further insight into the molecular basis and pathogenesis of the disease. The findings might also present the basis for the development and evaluation of successful treatment strategies.

The article can be found in ***Nature*, Vol. 439, 973-977 (2006)** under the following website address: **<http://www.nature.com>**.

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