DYSF Gene

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Dysferlin: The DYSF gene provides instructions for making a protein called dysferlin.

genes

1. Normal Function

This protein is found in the thin membrane called the sarcolemma that surrounds muscle fibers. Dysferlin is thought to aid in repairing the sarcolemma when it becomes damaged or torn due to muscle strain. Researchers suggest that dysferlin may also be involved in the formation of new muscle fibers (regeneration) and in inflammation, but little is known about these functions.

2. Health Conditions Related to Genetic Changes

2.1 Limb-Girdle Muscular Dystrophy

More than 140 mutations in the *DYSF* gene that can cause limb-girdle muscular dystrophy type 2B have been identified. Limb-girdle muscular dystrophy is a group of related disorders characterized by muscle weakness and wasting (atrophy), particularly in the shoulders, hips, thighs, and upper arms. Muscle problems caused by *DYSF* gene mutations, such as limb-girdle muscular dystrophy type 2B and others (see below), are called dysferlinopathies.

DYSF gene mutations may disrupt the function of the dysferlin protein and interfere with the muscle repair process. Studies suggest that inefficient repair of damaged muscle fibers may lead to inflammation and degeneration of muscles, resulting in muscle weakness.

2.2 Miyoshi Myopathy

More than 100 mutations in the *DYSF* gene have been found to cause Miyoshi myopathy. This condition is a muscle disorder that is characterized by progressive weakness and atrophy of muscles that are away from the center of the body (distal muscles), particularly those in the legs. The *DYSF* gene mutations identified in people with Miyoshi myopathy change single amino acids in the dysferlin protein, which impairs the protein's function or results in the production of a nonfunctional protein. A common cause of the condition in people of Japanese ancestry is a mutation that replaces the amino acid tryptophan with the amino acid cysteine at position 999 in dysferlin (written Trp999Cys or W999C).

A lack of normal dysferlin leads to a reduced ability to repair damage done to the sarcolemma of muscle fibers. As a result, damage accumulates and leads to atrophy of the muscle fiber. It is unclear why the *DYSF* gene mutations that cause Miyoshi myopathy lead to the specific pattern of weakness and atrophy that is characteristic of this disorder.

Some researchers consider Miyoshi myopathy to be a variant of limb-girdle muscular dystrophy (see above) rather than a separate disorder because they are caused by mutations in the same gene and have overlapping signs and symptoms.

2.3 Other Disorders

DYSF gene mutations also cause another dysferlinopathy called distal myopathy with anterior tibial onset. In this condition, the muscle weakness is most apparent in the muscles of the lower legs. This condition first becomes apparent in a muscle called tibialis anterior, which is located at the front of the lower leg and helps to flex the foot. Distal myopathy with anterior tibial onset later affects the muscles of the upper leg, and affected individuals eventually require wheelchair assistance.

3. Other Names for This Gene

- DYSF_HUMAN
- dysferlin, limb girdle muscular dystrophy 2B (autosomal recessive)
- dystrophy-associated fer-1-like 1
- fer-1-like protein 1
- FER1L1
- FLJ00175
- FLJ90168
- LGMD2B

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