

Rippling Muscle Disease

Subjects: **Genetics & Heredity**

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Rippling muscle disease is a condition in which the muscles are unusually sensitive to movement or pressure (irritable).

genetic conditions

1. Introduction

The muscles near the center of the body (proximal muscles) are most affected, especially the thighs. In most people with this condition, stretching the muscle causes visible ripples to spread across the muscle, lasting 5 to 20 seconds. A bump or other sudden impact on the muscle causes it to bunch up (percussion-induced muscle mounding) or exhibit repetitive tensing (percussion-induced rapid contraction). The rapid contractions can continue for up to 30 seconds and may be painful.

People with rippling muscle disease may have overgrowth (hypertrophy) of some muscles, especially in the calf. Some affected individuals have an abnormal pattern of walking (gait), such as walking on tiptoe. They may experience fatigue, cramps, or muscle stiffness, especially after exercise or in cold temperatures.

The age of onset of rippling muscle disease varies widely, but it often begins in late childhood or adolescence. Rippling muscles may also occur as a feature of other muscle disorders such as limb-girdle muscular dystrophy.

2. Frequency

The prevalence of rippling muscle disease is unknown.

3. Causes

Rippling muscle disease can be caused by mutations in the *CAV3* gene. Muscle conditions caused by *CAV3* gene mutations are called caveolinopathies. The *CAV3* gene provides instructions for making a protein called caveolin-3, which is found in the membrane surrounding muscle cells. This protein is the main component of caveolae, which are small pouches in the muscle cell membrane. Within the caveolae, the caveolin-3 protein acts as a scaffold to organize other molecules that are important for cell signaling and maintenance of the cell structure. It may also help regulate calcium levels in muscle cells, which play a role in controlling muscle contraction and relaxation.

CAV3 gene mutations that cause rippling muscle disease result in a shortage of caveolin-3 protein in the muscle cell membrane. Researchers suggest that the reduction in caveolin-3 protein disrupts the normal control of calcium levels in muscle cells, leading to abnormal muscle contractions in response to stimulation.

In addition to rippling muscle disease, CAV3 gene mutations can cause other caveolinopathies including CAV3-related distal myopathy, limb-girdle muscular dystrophy, isolated hyperCKemia, and a heart disorder called hypertrophic cardiomyopathy. Several CAV3 gene mutations have been found to cause different caveolinopathies in different individuals. It is unclear why a single CAV3 gene mutation may cause different patterns of signs and symptoms, even within the same family.

Some people with rippling muscle disease do not have mutations in the CAV3 gene. The cause of the disorder in these individuals is unknown.

3.1. The Gene Associated with Rippling Muscle Disease

- CAV3

4. Inheritance

Rippling muscle disease is usually inherited in an autosomal dominant pattern, but it is occasionally inherited in an autosomal recessive pattern.

Autosomal dominant inheritance means that one copy of an altered CAV3 gene in each cell is sufficient to cause the disorder. In most cases, an affected person has one parent with rippling muscle disease or another caveolinopathy. Rare cases result from new mutations in the gene and occur in people with no history of caveolinopathies in their family.

Autosomal recessive inheritance means that both copies of the CAV3 gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition. People with autosomal recessive rippling muscle disease generally have more severe signs and symptoms than do people with the autosomal dominant form.

5. Other Names for This Condition

- rippling muscle syndrome
- RMD

References

1. Aboumoussa A, Hoogendijk J, Charlton R, Barresi R, Herrmann R, Voit T, Hudson J, Roberts M, Hilton-Jones D, Eagle M, Bushby K, Straub V. Caveolinopathy--new mutations and additional symptoms. *Neuromuscul Disord*. 2008 Jul;18(7):572-8. doi:10.1016/j.nmd.2008.05.003.
2. Betz RC, Schoser BG, Kasper D, Ricker K, Ramírez A, Stein V, Torbergson T, Lee YA, Nöthen MM, Wienker TF, Malin JP, Propping P, Reis A, Mortier W, Jentsch TJ, Vorgerd M, Kubisch C. Mutations in CAV3 cause mechanical hyperirritability of skeletal muscle in rippling muscle disease. *Nat Genet*. 2001 Jul;28(3):218-9.
3. Gazzero E, Bonetto A, Minetti C. Caveolinopathies: translational implications of caveolin-3 in skeletal and cardiac muscle disorders. *Handb Clin Neurol*. 2011;101:135-42. doi: 10.1016/B978-0-08-045031-5.00010-4. Review.
4. Gazzero E, Sotgia F, Bruno C, Lisanti MP, Minetti C. Caveolinopathies: from the biology of caveolin-3 to human diseases. *Eur J Hum Genet*. 2010 Feb;18(2):137-45. doi: 10.1038/ejhg.2009.103. in: *Eur J Hum Genet*. 2009 Dec;17(12):1692.
5. Kubisch C, Schoser BG, von Düring M, Betz RC, Goebel HH, Zahn S, Ehrbrecht A, Aasly J, Schroers A, Popovic N, Lochmüller H, Schröder JM, Brüning T, Malin JP, Fricke B, Meinck HM, Torbergson T, Engels H, Voss B, Vorgerd M. Homozygous mutations in caveolin-3 cause a severe form of rippling muscle disease. *Ann Neurol*. 2003 Apr;53(4):512-20.
6. Lamb GD. Rippling muscle disease may be caused by "silent" action potentials in the tubular system of skeletal muscle fibers. *Muscle Nerve*. 2005 May;31(5):652-8. Review.
7. Traverso M, Bruno C, Broccolini A, Sotgia F, Donati MA, Assereto S, Gazzero E, Lo Monaco M, Modoni A, D'Amico A, Gasperini S, Ricci E, Zara F, Lisanti M, Minetti C. Truncation of Caveolin-3 causes autosomal-recessive Rippling Muscle Disease. *J Neurol Neurosurg Psychiatry*. 2008 Jun;79(6):735-7. doi:10.1136/jnnp.2007.133207.
8. Ullrich ND, Fischer D, Kornblum C, Walter MC, Niggli E, Zorzato F, Treves S. Alterations of excitation-contraction coupling and excitation coupled Ca^{2+} entry in human myotubes carrying CAV3 mutations linked to rippling muscle. *Hum Mutat*. 2011 Mar;32(3):309-17. doi: 10.1002/humu.21431.
9. Woodman SE, Sotgia F, Galbiati F, Minetti C, Lisanti MP. Caveolinopathies: mutations in caveolin-3 cause four distinct autosomal dominant muscle diseases. *Neurology*. 2004 Feb 24;62(4):538-43. Review.

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