ANO5 gene

anoctamin 5

Normal Function

The *ANO5* gene provides instructions for making a protein called anoctamin-5. While the specific function of this protein is not well understood, it belongs to a family of proteins, called anoctamins, that act as chloride channels. Chloride channels, which transport negatively charged chlorine atoms (chloride ions) in and out of cells, play a key role in a cell's ability to generate and transmit electrical signals. Studies suggest that most anoctamin proteins function as chloride channels that are turned on (activated) in the presence of positively charged calcium atoms (calcium ions); these channels are known as calcium-activated chloride channels. The mechanism for this calcium activation is unclear. Anoctamin proteins are also involved in maintaining the membrane that surrounds cells and repairing the membrane if it gets damaged.

The anoctamin-5 protein is most abundant in muscles used for movement (skeletal muscles). For the body to move normally, skeletal muscles must tense (contract) and relax in a coordinated way. The regulation of chloride flow within muscle cells plays a role in controlling muscle contraction and relaxation.

The anoctamin-5 protein is also found in other cells including heart (cardiac) muscle cells and bone cells. Studies have suggested that the anoctamin-5 protein may be important for the development of muscle and bone before birth.

Health Conditions Related to Genetic Changes

Gnathodiaphyseal dysplasia

At least three *ANO5* gene mutations have been identified in people with a bone disorder called gnathodiaphyseal dysplasia, which leads to fragile bones, jaw problems, and other skeletal abnormalities. The *ANO5* gene mutations that cause gnathodiaphyseal dysplasia change single protein building blocks (amino acids) in the anoctamin-5 protein. It is unclear how these mutations lead to the signs and symptoms of gnathodiaphyseal dysplasia, or why they primarily affect bones while other *ANO5* gene mutations cause muscle disorders. Researchers suggest that the mutations may affect the way cells process calcium, an important mineral in bone development and growth.

Limb-girdle muscular dystrophy

More than 40 mutations in the *ANO5* gene have been identified in people with limb-girdle muscular dystrophy type 2L. 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.

The *ANO5* gene mutations identified in people with limb-girdle muscular dystrophy type 2L change single amino acids in the anoctamin-5 protein sequence, disrupt how genetic information is pieced together to make a blueprint for producing the protein, or result in a premature stop signal that leads to an abnormally short protein. One of the mutations adds an extra DNA building block (nucleotide) to the *ANO5* gene (written as 191dupA) and is believed to be a relatively common cause of limb-girdle muscular dystrophy in people with northern European ancestry. This mutation alters the instructions used to make the anoctamin-5 protein, leading to a premature stop signal that would produce an abnormally short protein. Instead, a cellular error-catching mechanism called nonsense-mediated decay prevents the protein from being produced at all.

ANO5 gene mutations that eliminate or impair the role of the anoctamin-5 protein as a chloride channel likely lead to impaired muscle function, resulting in the signs and symptoms of limb-girdle muscular dystrophy.

Miyoshi myopathy

At least 10 mutations in the *ANO5* gene have been found to cause Miyoshi myopathy. When caused by mutations in this gene, the condition is also known as distal anoctaminopathy. Miyoshi myopathy 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 *ANO5* gene mutations identified in people with Miyoshi myopathy change single amino acids in the anoctamin-5 protein or result in the production of an abnormally short protein that is quickly broken down.

These mutations result in the production of little or no anoctamin-5 protein. The effects of the loss of anoctamin-5 are unclear. While chloride is necessary for normal muscle function, it is unknown how a lack of this chloride channel causes the signs and symptoms of Miyoshi myopathy.

The 191dupA mutation that can cause limb-girdle muscular dystrophy (described above) is also a common cause of Miyoshi myopathy in individuals of northern European ancestry. It is not known why the 191dupA mutation can result in different patterns of signs and symptoms. Miyoshi myopathy caused by *ANO5* gene mutations is likely a variation of limb-girdle muscular dystrophy because it is caused by mutations in the same gene, and in some cases even by the same mutation.

Other Names for This Gene

- ANO5_HUMAN
- anoctamin-5
- GDD1

- gnathodiaphyseal dysplasia 1 protein
- integral membrane protein GDD1
- LGMD2L
- TMEM16E
- transmembrane protein 16E

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of ANO5 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=203859[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28ANO5%5BTIAB%5D%29+OR+%28anoctamin+5%5BTIAB%5D%29%29+OR+%28%28GDD1%5BTIAB%5D%29+OR+%28LGMD2L%5BTIAB%5D%29+OR+%28TMEM16E%5BTIAB%5D%29+OR+%28anoctamin-5%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- ANOCTAMIN 5; ANO5 (https://omim.org/entry/608662)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/203859)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=ANO5[gene])

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Genomic Location

The *ANO5* gene is found on chromosome 11 (https://medlineplus.gov/genetics/chromosome/11/).

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