ADAMTSL4 gene

ADAMTS like 4

Normal Function

The *ADAMTSL4* gene provides instructions for making a protein that is found throughout the body. The ADAMTSL4 protein is released from cells into the extracellular matrix, which is an intricate lattice of proteins and other molecules that forms in the spaces between cells. In this matrix, the ADAMTSL4 protein attaches (binds) to another protein called fibrillin-1. Fibrillin-1 proteins bind to each other and other proteins to form threadlike filaments called microfibrils. It is likely that the binding of ADAMTSL4 to fibrillin-1 promotes microfibril assembly. Microfibrils provide support to many tissues, including the lenses of the eyes, which are held in their central position by these filaments.

Health Conditions Related to Genetic Changes

Isolated ectopia lentis

At least 15 mutations in the *ADAMTSL4* gene have been found to cause isolated ectopia lentis. In this condition, the lens in one or both eyes is off-center (displaced), which leads to vision problems. An *ADAMTSL4* gene mutation that is frequently found in affected individuals of European ancestry deletes 20 DNA building blocks (nucleotides) from the gene (written as 767_787del20). This mutation leads to the production of a protein that is abnormally short and nonfunctional. A lack of functional ADAMTSL4 protein likely diminishes the ability of fibrillin-1 to effectively form microfibrils. As a result, there is a reduction in filaments to anchor the lens in its central position at the front of the eye, leading to its displacement and the vision problems characteristic of isolated ectopia lentis. While the ADAMTSL4 protein is found throughout the body, it is thought that other proteins can compensate for its function in tissues other than the eyes, which likely explains why only the eyes are affected in this condition.

Other disorders

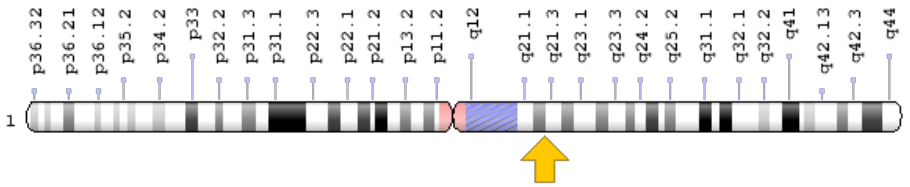
Some *ADAMTSL4* gene mutations cause an eye condition called ectopia lentis et pupillae. In this condition, both the lenses and the pupils are off-center; they are usually displaced in opposite directions. People with ectopia lentis et pupillae have eye and vision problems similar to those with isolated ectopia lentis (described above), including nearsightedness (myopia), farsightedness (hyperopia), or an irregular curvature of the front of the eye (astigmatism). They may also develop clouding of the lenses (cataracts) or increased pressure in the eyes (glaucoma) at an early age. Similar to isolated ectopia lentis, the *ADAMTSL4* gene mutations that

cause ectopia lentis et pupillae lead to decreased production of microfibrils or the formation of impaired microfibrils, which prevents the proper anchoring of certain structures in the eyes. It is unclear why some *ADAMTSL4* gene mutations affect only the lenses and others also affect the pupils.

Chromosomal Location

Cytogenetic Location: 1q21.2, which is the long (q) arm of chromosome 1 at position 21.2

Molecular Location: base pairs 150,549,369 to 150,560,937 on chromosome 1 (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ADAMTS-like 4
- ADAMTS-like protein 4
- ADAMTSL-4
- ATL4_HUMAN
- ECTOL2
- thrombospondin repeat-containing protein 1
- TSRC1

Additional Information & Resources

Educational Resources

- Madame Curie Bioscience Database: Assembly of Microfibrils https://www.ncbi.nlm.nih.gov/books/NBK5960/

Clinical Information from GeneReviews

- ADAMTSL4-Related Eye Disorders https://www.ncbi.nlm.nih.gov/books/NBK84111

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28ADAMTSL4%5BTIAB%5D%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

- ADAMTS-LIKE 4
  http://omim.org/entry/610113
- ECTOPIA LENTIS ET PUPILLAE
  http://omim.org/entry/225200

Research Resources

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=ADAMTSL4%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:19706
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:54507
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/54507
- UniProt
  https://www.uniprot.org/uniprot/Q6UY14

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