

## 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.

## 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

### Tests Listed in the Genetic Testing Registry

- Tests of ADAMTSL4 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=54507\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=54507[geneid]))

### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?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

- ECTOPIA LENTIS ET PUPILLAE (<https://omim.org/entry/225200>)
- ADAMTS-LIKE 4; ADAMTSL4 (<https://omim.org/entry/610113>)

### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/54507>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=ADAMTSL4\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=ADAMTSL4[gene]))

## References

- Chandra A, Aragon-Martin JA, Hughes K, Gati S, Reddy MA, Deshpande C, Cormack G, Child AH, Charteris DG, Arno G. A genotype-phenotype comparison of ADAMTSL4 and FBN1 in isolated ectopia lentis. *Invest Ophthalmol Vis Sci.* 2012 Jul 24;53(8):4889-96. doi: 10.1167/iovs.12-9874. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22736615>)
- Christensen AE, Fiskerstrand T, Knappskog PM, Boman H, Rodahl E. A novel ADAMTSL4 mutation in autosomal recessive ectopia lentis et pupillae. *Invest Ophthalmol Vis Sci.* 2010 Dec;51(12):6369-73. doi: 10.1167/iovs.10-5597. Epub 2010 Aug 11. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20702823>)
- Gabriel LA, Wang LW, Bader H, Ho JC, Majors AK, Hollyfield JG, Traboulsi EI, Apte SS. ADAMTSL4, a secreted glycoprotein widely distributed in the eye, binds fibrillin-1 microfibrils and accelerates microfibril biogenesis. *Invest Ophthalmol Vis Sci.* 2012 Jan 31;53(1):461-9. doi: 10.1167/iovs.10-5955. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/21989719>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3292378/>)
- Hubmacher D, Apte SS. Genetic and functional linkage between ADAMTS superfamily proteins and fibrillin-1: a novel mechanism influencing microfibril assembly and function. *Cell Mol Life Sci.* 2011 Oct;68(19):3137-48. doi:10.1007/s00018-011-0780-9. Epub 2011 Aug 20. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/21858451>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4729447/>)

## Genomic Location

The *ADAMTSL4* gene is found on chromosome 1 (<https://medlineplus.gov/genetics/chromosome/1/>).

**Last updated March 1, 2015**