COL4A1 gene  
collagen type IV alpha 1 chain

Normal Function

The COL4A1 gene provides instructions for making one component of type IV collagen, which is a flexible protein important in the structure of many tissues throughout the body. Specifically, this gene makes the alpha1(IV) chain of type IV collagen. This chain combines with another alpha1 chain and a different type of alpha (IV) chain called alpha2 to make a complete type IV collagen alpha1-1-2 molecule. Type IV collagen molecules attach to each other to form complex protein networks. These protein networks are the main component of basement membranes, which are thin sheet-like structures that separate and support cells in many tissues. Type IV collagen alpha1-1-2 networks play an important role in the basement membranes in virtually all tissues throughout the body, particularly the basement membranes surrounding the body’s blood vessels (vasculature). The type IV collagen network helps the basement membranes interact with nearby cells, playing a role in cell movement (migration), cell growth and division (proliferation), cell maturation (differentiation), and the survival of cells.

Health Conditions Related to Genetic Changes

COL4A1-related brain small-vessel disease

Mutations in the COL4A1 gene have been found to cause COL4A1-related brain small-vessel disease. This condition is part of a group of conditions called COL4A1-related disorders that have overlapping signs and symptoms involving fragile blood vessels. COL4A1-related brain small-vessel disease is characterized by stroke and eye abnormalities. Most of the identified COL4A1 gene mutations that cause COL4A1-related brain small-vessel disease change one of the protein building blocks (amino acids) used to make the alpha1(IV) chain of type IV collagen. Specifically, the mutations replace the amino acid glycine with a different amino acid at one of various places in this collagen chain. The substitution of another amino acid for glycine in the alpha1(IV) chain prevents this chain from combining with other chains to form a complete type IV collagen molecule. This alteration in type IV collagen prevents protein networks from forming and basement membranes from developing properly, which causes the tissues they support to weaken. Blood vessels throughout the body become fragile, leading to the signs and symptoms of COL4A1-related brain small-vessel disease.

It is unclear how mutations in the COL4A1 gene can lead to different disorders. It is likely that mutations in different regions of this gene play a role in the development of the various signs and symptoms of the COL4A1-related disorders. Other genetic
changes as well as environmental factors may also contribute to the features of the different *COL4A1*-related disorders.

**Familial porencephaly**

Mutations in the *COL4A1* gene have been found to cause familial porencephaly, another member of the group of vascular conditions called *COL4A1*-related disorders. Familial porencephaly is characterized by early stroke and brain cysts. Most of the identified *COL4A1* gene mutations that cause familial porencephaly change one of the amino acids used to make the alpha1(IV) chain of type IV collagen. Specifically, the mutations replace the amino acid glycine with a different amino acid at one of various places in this collagen chain. The substitution of another amino acid for glycine in the alpha1(IV) chain prevents this chain from combining with other chains to form a complete type IV collagen molecule. This alteration in type IV collagen prevents protein networks from forming and basement membranes from developing properly, which causes the tissues they support to weaken. Blood vessels in the brain become fragile, leading to the signs and symptoms of familial porencephaly.

**Hereditary angiopathy with nephropathy, aneurysms, and muscle cramps syndrome**

Mutations in the *COL4A1* gene have been found to cause hereditary angiopathy with nephropathy, aneurysms, and muscle cramps (HANAC) syndrome, a third member of the group of conditions called *COL4A1*-related disorders. HANAC syndrome is characterized by weakened blood vessels in the brain and throughout the body, kidney disease, muscle cramps, and eye abnormalities. Most of the identified *COL4A1* gene mutations that cause HANAC syndrome change one of the amino acids used to make the alpha1(IV) chain of type IV collagen. Specifically, the mutations replace the amino acid glycine with a different amino acid at one of various places in this collagen chain. The substitution of another amino acid for glycine in the alpha1(IV) chain prevents this chain from combining with other chains to form a complete type IV collagen molecule. This alteration in type IV collagen prevents protein networks from forming and basement membranes from developing properly. As a result, the tissues they support weaken, particularly in the eyes and kidneys. Fragile blood vessels and weakened basement membranes lead to the signs and symptoms of HANAC syndrome.
Chromosomal Location

Cytogenetic Location: 13q34, which is the long (q) arm of chromosome 13 at position 34.

Molecular Location: base pairs 110,148,958 to 110,307,157 on chromosome 13 (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)

Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- arresten
- CO4A1_HUMAN
- COL4A1 NC1 domain
- collagen alpha-1(IV) chain
- collagen alpha-1(IV) chain preproprotein
- collagen IV, alpha-1 polypeptide
- collagen of basement membrane, alpha-1 chain
- collagen type IV alpha 1
- collagen, type IV, alpha 1

Additional Information & Resources

Educational Resources


Clinical Information from GeneReviews

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28COL4A1%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- COLLAGEN, TYPE IV, ALPHA-1
  http://omim.org/entry/120130

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_COL4A1.html
- ClinVar
- HGNC Gene Symbol Report
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:1282
- NCBI Gene
- UniProt
  https://www.uniprot.org/uniprot/P02462

Sources for This Summary

- OMIM: COLLAGEN, TYPE IV, ALPHA-1
  http://omim.org/entry/120130


Reprinted from Genetics Home Reference:

Reviewed: September 2011
Published: June 11, 2019

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