COL4A4 gene
collagen type IV alpha 4 chain

Normal Function

The *COL4A4* gene provides instructions for making one component of type IV collagen, which is a flexible protein. Specifically, this gene makes the alpha4(IV) chain of type IV collagen. This chain combines with two other types of alpha (IV) chains (the alpha3 and alpha5 chains) to make a complete type IV collagen molecule. Type IV collagen molecules attach to each other to form complex protein networks. These networks make up a large portion of basement membranes, which are thin sheet-like structures that separate and support cells in many tissues. Type IV collagen alpha3-4-5 networks play an especially important role in the basement membranes of the kidney, inner ear, and eye.

Health Conditions Related to Genetic Changes

**Alport syndrome**

More than 20 mutations in the *COL4A4* gene have been found to cause Alport syndrome. Most of these mutations change single protein building blocks (amino acids) in a region where the alpha4(IV) collagen chain combines with other type IV collagen chains. Other mutations in the *COL4A4* gene severely decrease or prevent the production of alpha4(IV) chains. As a result, there is a serious deficiency of the type IV collagen alpha3-4-5 network in the basement membranes of the kidney, inner ear, and eye. In the kidney, other types of collagen accumulate in the basement membranes, eventually leading to scarring of the kidneys and kidney failure. Mutations in this gene can also lead to abnormal function in the inner ear, resulting in hearing loss.

**Keratoconus**

**Other disorders**

Mutations in the *COL4A4* gene have been found to cause thin basement membrane nephropathy. This condition typically causes people to have blood in their urine (hematuria) but no other signs or symptoms of kidney disease. In the past, this condition was often called benign familial hematuria. Thin basement membrane nephropathy rarely progresses to kidney failure.
**Chromosomal Location**

Cytogenetic Location: 2q36.3, which is the long (q) arm of chromosome 2 at position 36.3

Molecular Location: base pairs 226,970,293 to 227,164,482 on chromosome 2 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)

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**Other Names for This Gene**

- alpha 4 type IV collagen
- CA44
- CO4A4_HUMAN
- Collagen IV, alpha-4 polypeptide
- collagen of basement membrane, alpha-4 chain
- collagen type IV alpha 4
- collagen, type IV, alpha 4

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**Additional Information & Resources**

**Educational Resources**

  https://www.ncbi.nlm.nih.gov/books/NBK26810/?rendertype=figure&id=A3581
  https://www.ncbi.nlm.nih.gov/books/NBK26810/#A3583

**Clinical Information from GeneReviews**

- Alport Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1207
Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28COL4A4%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+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- COLLAGEN, TYPE IV, ALPHA-4
  http://omim.org/entry/120131
- HEMATURIA, BENIGN FAMILIAL
  http://omim.org/entry/141200

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_COL4A4.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=COL4A4%5Bgene%5D
- HGNC Gene Symbol Report
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:1286
- NCBI Gene
- UniProt
  https://www.uniprot.org/uniprot/P53420

Sources for This Summary

- OMIM: COLLAGEN, TYPE IV, ALPHA-4
  http://omim.org/entry/120131
Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301386

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https://ghr.nlm.nih.gov/gene/COL4A4

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