



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

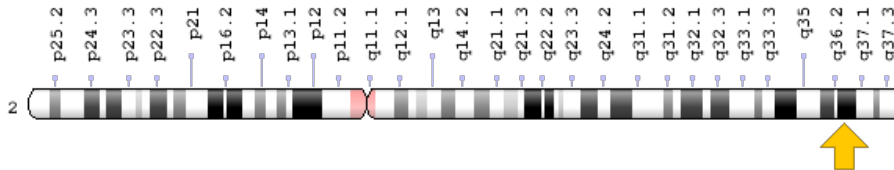
Other disorders

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)



Credit: Genome Decoration Page/NCBI

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

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): A model of the molecular structure of a basal lamina
<https://www.ncbi.nlm.nih.gov/books/NBK26810/?rendertype=figure&id=A3581>
- Molecular Biology of the Cell (fourth edition, 2002): Basal Laminae Perform Diverse Functions
<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
https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:2206
- Monarch Initiative
<https://monarchinitiative.org/gene/NCBIGene:1286>
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/1286>
- UniProt
<https://www.uniprot.org/uniprot/P53420>

Sources for This Summary

- Buzza M, Dagher H, Wang YY, Wilson D, Babon JJ, Cotton RG, Savige J. Mutations in the COL4A4 gene in thin basement membrane disease. *Kidney Int.* 2003 Feb;63(2):447-53.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12631110>
- OMIM: COLLAGEN, TYPE IV, ALPHA-4
<http://omim.org/entry/120131>
- Gregory MC. The clinical features of thin basement membrane nephropathy. *Semin Nephrol.* 2005 May;25(3):140-5. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15880323>
- Gross O, Netzer KO, Lambrecht R, Seibold S, Weber M. Novel COL4A4 splice defect and in-frame deletion in a large consanguine family as a genetic link between benign familial haematuria and autosomal Alport syndrome. *Nephrol Dial Transplant.* 2003 Jun;18(6):1122-7.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12748344>

- Kashtan CE. Alport Syndrome and Thin Basement Membrane Nephropathy. 2001 Aug 28 [updated 2015 Nov 25]. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1207/>
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20301386>
- Kashtan CE. Alport syndrome. An inherited disorder of renal, ocular, and cochlear basement membranes. *Medicine (Baltimore)*. 1999 Sep;78(5):338-60. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/10499074>
- Longo I, Porcedda P, Mari F, Giachino D, Meloni I, Deplano C, Brusco A, Bosio M, Massella L, Lavoratti G, Roccatello D, Frascá G, Mazzucco G, Muda AO, Conti M, Fasciolo F, Arrondel C, Heidet L, Renieri A, De Marchi M. COL4A3/COL4A4 mutations: from familial hematuria to autosomal-dominant or recessive Alport syndrome. *Kidney Int*. 2002 Jun;61(6):1947-56.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12028435>
- Pescucci C, Mari F, Longo I, Vogiatzi P, Caselli R, Scala E, Abaterusso C, Gusmano R, Seri M, Miglietti N, Bresin E, Renieri A. Autosomal-dominant Alport syndrome: natural history of a disease due to COL4A3 or COL4A4 gene. *Kidney Int*. 2004 May;65(5):1598-603.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15086897>
- Rana K, Wang YY, Buzza M, Tonna S, Zhang KW, Lin T, Sin L, Padavarat S, Savige J. The genetics of thin basement membrane nephropathy. *Semin Nephrol*. 2005 May;25(3):163-70. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15880327>
- Slajpah M, Gorinsek B, Berginc G, Vizjak A, Ferluga D, Hvala A, Meglic A, Jaksa I, Furlan P, Gregoric A, Kaplan-Pavlovic S, Ravnik-Glavac M, Glavac D. Sixteen novel mutations identified in COL4A3, COL4A4, and COL4A5 genes in Slovenian families with Alport syndrome and benign familial hematuria. *Kidney Int*. 2007 Jun;71(12):1287-95. Epub 2007 Mar 28.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17396119>
- Tazón Vega B, Badenas C, Ars E, Lens X, Milà M, Darnell A, Torra R. Autosomal recessive Alport's syndrome and benign familial hematuria are collagen type IV diseases. *Am J Kidney Dis*. 2003 Nov;42(5):952-9.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/14582039>

Reprinted from Genetics Home Reference:
<https://ghr.nlm.nih.gov/gene/COL4A4>

Reviewed: December 2013
Published: November 12, 2019

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services