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 227,164,559 on chromosome 2 (Homo sapiens Annotation Release 109, GRCh38.p12) (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

  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 and Thin Basement Membrane Nephropathy
  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 Family: Collagens
  https://www.genenames.org/cgi-bin/genefamilies/set/490
- 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
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https://ghr.nlm.nih.gov/gene/COL4A4

Reviewed: December 2013
Published: November 27, 2018

Lister Hill National Center for Biomedical Communications
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