COL4A4 gene

collagen type IV alpha 4 chain

Normal Function

The *COL4A4* gene provides instructions for making one piece of a protein called collagen IV. Specifically, this gene makes the alpha4(IV) chain of collagen IV. This chain combines with two other types of alpha (IV) chains (the alpha3 and alpha5 chains) to make alpha345(IV) collagen molecules. These molecules attach to each other to form complex protein networks that make up a large portion of basement membranes, which are thin, sheet-like structures that separate and support cells in many tissues. alpha345(IV) collagen 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

Many variants (also called mutations) in the *COL4A4* gene can cause Alport syndrome, a condition characterized by kidney disease, hearing loss, and eye abnormalities. Most of these variants change single protein building blocks (amino acids) in a region where the alpha4(IV) collagen chain combines with other collagen IV chains. Other variants in the *COL4A4* gene severely decrease or prevent the production of alpha4(IV) chains.

These changes in the structure or amount of alpha4(IV) chains severely impair the formation of alpha345(IV) collagen networks in the basement membranes of the kidney, inner ear, and eye. In the kidney, other types of collagen build up in the basement membranes, eventually scarring the kidneys and leading to kidney failure. Variants in this gene can also lead to hearing loss and changes in the lens of the eye and the light-sensitive tissue at the back of the eye (retina).

Variants in a single copy of the *COL4A4* gene can cause a form of the condition called autosomal dominant Alport syndrome. Individuals with this form typically have the kidney problems that are characteristic of Alport syndrome, including blood in the urine (hematuria), excess amounts of protein in the urine (proteinuria), and a gradual loss of kidney function.

Variants in both copies of the *COL4A4* gene cause autosomal recessive Alport syndrome. Individuals with this form of the condition can have hearing loss and eye

abnormalities in addition to kidney problems.

Keratoconus

MedlinePlus Genetics provides information about Keratoconus

Other disorders

A variant in one of the two copies of the *COL4A4* gene can cause thin basement membrane nephropathy. People with this condition typically 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.

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

Tests Listed in the Genetic Testing Registry

- Tests of COL4A4 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1286[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?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; COL4A4 (https://omim.org/entry/120131)
- HEMATURIA, BENIGN FAMILIAL, 1; BFH1 (https://omim.org/entry/141200)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/1286)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=COL4A4[gene])

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Genomic Location

The *COL4A4* gene is found on chromosome 2 (https://medlineplus.gov/genetics/chromosome/2/).

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