COL4A1 Gene

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Contributor: Vicky Zhou

collagen type IV alpha 1 chain

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1. 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.

2. Health Conditions Related to Genetic Changes

2.1. 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.

2.2. 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.

2.3. 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.

3. 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

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