COL8A2 Gene

Subjects: Genetics & Heredity
Contributor: Vicky Zhou

collagen type VIII alpha 2 chain

Keywords: genes

1. Normal Function

The *COL8A2* gene provides instructions for making a component of type VIII collagen called alpha 2(VIII) collagen. Type VIII collagen is largely found within the front surface of the eye, called the cornea. Type VIII collagen is a major component of Descemet's membrane, which is a tissue at the back of the cornea. This membrane is a thin, sheet-like structure that separates and supports corneal endothelium cells. These cells regulate the amount of fluid inside the cornea. An appropriate fluid balance in the cornea is necessary for clear vision.

To construct type VIII collagen, one subunit of the alpha 2(VIII) collagen protein interacts with two subunits of another protein called alpha 1(VIII) collagen. These three proteins twist together to form a triple-stranded, rope-like molecule known as procollagen. Procollagen molecules are secreted by the cell and processed by enzymes to remove extra protein segments from the ends. Once these molecules are processed, they arrange themselves into long, thin bundles of mature type VIII collagen.

2. Health Conditions Related to Genetic Changes

Fuchs Endothelial Dystrophy

At least two mutations in the *COL8A2* gene have been found to cause a variant of Fuchs endothelial dystrophy, an eye disorder characterized by progressively blurry vision and sensitivity to bright light. *COL8A2* gene mutations are associated with the rare, early-onset variant of Fuchs endothelial dystrophy, in which vision problems typically begin in a person's twenties.

The *COL8A2* gene mutations that cause the early-onset variant of Fuchs endothelial dystrophy replace single protein building blocks in alpha 2(VIII) collagen. One mutation replaces the amino acid leucine with the amino acid tryptophan at position 450 (written as Leu450Trp or L450W). Another mutation replaces the amino acid glutamine with the amino acid lysine at position 455 (Gln455Lys or Q455K). These mutations impair the structure of alpha 2(VIII) collagen, probably preventing the abnormal protein from being incorporated into type VIII collagen fibers. As a result, there is a reduced amount of type VIII collagen in the cornea, specifically in Descemet's membrane. This abnormal Descemet's membrane leads to the death of the corneal endothelial cells, causing the cornea to become swollen with fluid. Corneal endothelial cells continue to die over time, which causes the vision problems in people with the early-onset variant of Fuchs endothelial dystrophy.

3. Other Names for This Gene

- CO8A2_HUMAN
- collagen alpha-2(VIII) chain
- collagen alpha-2(VIII) chain precursor
- collagen type VIII alpha 2
- collagen VIII, alpha-2 polypeptide
- collagen, type VIII, alpha 2
- endothelial collagen

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