COL7A1 gene

collagen type VII alpha 1 chain

Normal Function

The *COL7A1* gene provides instructions for making proteins that are used to assemble type VII collagen. Collagens are a family of proteins that strengthen and support connective tissues, such as skin, bone, tendons, and ligaments, throughout the body. In particular, type VII collagen plays an essential role in strengthening and stabilizing the skin.

The proteins produced from the *COL7A1* gene, called pro-α1(VII) chains, are the components of type VII collagen. Three pro-α1(VII) chains twist together to form a triple-stranded, ropelike molecule known as a 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 VII collagen.

Type VII collagen is the major component of structures in the skin called anchoring fibrils. These fibrils are found in a region known as the epidermal basement membrane zone, which is a two-layer membrane located between the top layer of skin, called the epidermis, and an underlying layer called the dermis. Anchoring fibrils hold the two layers of skin together by connecting the epidermal basement membrane to the dermis.

Health Conditions Related to Genetic Changes

**Dystrophic epidermolysis bullosa**

More than 400 mutations in the *COL7A1* gene have been identified in people with dystrophic epidermolysis bullosa. These mutations alter the structure or disrupt the production of type VII collagen, which impairs the ability of anchoring fibrils to connect the epidermis to the dermis. When type VII collagen is abnormal or missing, anchoring fibrils cannot form properly. As a result, friction or other minor trauma can cause the two skin layers to separate. This separation leads to the formation of blisters, which can result in extensive scarring as they heal.

The autosomal recessive types of dystrophic epidermolysis bullosa (RDEB) result from mutations in both copies of the *COL7A1* gene in each cell. The most severe, classic form of this disorder is known as the Hallopeau-Siemens type (RDEB-HS). Most of the *COL7A1* mutations responsible for RDEB-HS significantly reduce or eliminate the production of type VII collagen. As a result, few or no anchoring fibrils are present to connect the epidermis with the dermis. This lack of anchoring fibrils causes the severe signs and symptoms of RDEB-HS. A somewhat less severe
form of autosomal recessive dystrophic epidermolysis bullosa, known as the non-
Hallopeau-Siemens type (Non-HS RDEB), is caused by other types of mutations.
These genetic changes allow a small amount of normal or partially functional type VII
collagen to be produced.

A milder, autosomal dominant form of dystrophic epidermolysis bullosa (DDEB)
results from mutations in one copy of the COL7A1 gene in each cell. In many cases,
these mutations occur in a part of type VII collagen known as the collagenous region.
This region gives type VII collagen its usual triple-stranded structure. It is made up
of a pattern of protein building blocks (amino acids) in which every third amino acid
is a glycine. Mutations that substitute other amino acids for glycine in this region can
disrupt the triple-stranded structure of type VII collagen. When the abnormally shaped
collagen molecules are incorporated into anchoring fibrils, they interfere with the
fibrils’ normal function and prevent them from effectively connecting the epidermis
and the dermis. DDEB can also be caused by other types of mutations, particularly
changes that affect the folding of type VII collagen.

It is unclear how COL7A1 mutations are associated with an increased risk of certain
cancers, particularly squamous cell carcinoma, in people with severe types of
dystrophic epidermolysis bullosa. Some research has suggested that abnormal forms
of type VII collagen that retain a fragment called the NC1 domain may increase the
risk of tumor formation. Other studies, however, have not found this association.

Chromosomal Location

Cytogenetic Location: 3p21.31, which is the short (p) arm of chromosome 3 at position
21.31

Molecular Location: base pairs 48,564,073 to 48,595,302 on chromosome 3 (Homo
sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- alpha 1 type VII collagen
- CO7A1_HUMAN
- collagen type VII alpha 1
• collagen VII, alpha-1 polypeptide
• collagen, type VII, alpha 1
• collagen, type VII, alpha 1 (epidermolysis bullosa, dystrophic, dominant and recessive)
• EBD1
• EBDCT
• EBR1
• LC collagen
• long chain collagen

Additional Information & Resources

Educational Resources
• Molecular Biology of the Cell (fourth edition, 2002): Collagens Are the Major Proteins of the Extracellular Matrix
  https://www.ncbi.nlm.nih.gov/books/NBK26810/#A3551

Clinical Information from GeneReviews
• Dystrophic Epidermolysis Bullosa
  https://www.ncbi.nlm.nih.gov/books/NBK1304

Scientific Articles on PubMed
• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28COL7A1%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 VII, ALPHA-1
  http://omim.org/entry/120120

Research Resources
• Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_COL7A1.html
• ClinVar
• HGNC Gene Symbol Report
Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10367730

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17425959

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12485454

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9375848

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16484981

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15774758

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301481

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17495952
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