KRT5 gene

keratin 5

Normal Function

The *KRT5* gene provides instructions for making a protein called keratin 5. Keratins are a group of tough, fibrous proteins that form the structural framework of certain cells, particularly cells that make up the skin, hair, and nails. Keratin 5 is produced in cells called keratinocytes in the outer layer of the skin (the epidermis).

Keratin 5 partners with a similar protein, keratin 14 (produced from the *KRT14* gene), to form molecules called keratin intermediate filaments. These filaments assemble into strong networks that help attach keratinocytes together and anchor the epidermis to underlying layers of skin. The network of keratin intermediate filaments provides strength and resiliency to the skin and protects it from being damaged by friction and other everyday physical stresses.

Researchers believe that keratin 5 interacts with pigment-producing cells called melanocytes to transport melanosomes, which are cellular structures within melanocytes that carry pigment called melanin. The transport of these structures from melanocytes to keratinocytes is important for the development of normal skin coloration (pigmentation).

Health Conditions Related to Genetic Changes

Dowling-Degos disease

At least five mutations in the *KRT5* gene have been found to cause Dowling-Degos disease. This condition results in various skin abnormalities, including a characteristic lacy pattern of abnormally dark skin coloring (hyperpigmentation) that occurs mostly in the body's folds and creases. Most *KRT5* gene mutations that cause Dowling-Degos disease lead to the production of a keratin 5 protein that is abnormally small and nonfunctional or prevent any protein from being produced from the gene. A shortage (deficiency) of functional keratin 5 impairs the formation of keratin intermediate filaments. As a result, the organization of the epidermis is altered, leading to the development of different types of skin abnormalities. Additionally, a deficiency of keratin 5 may disrupt the movement of pigment-carrying melanosomes into keratinocytes, where they are needed for the development of normal skin pigmentation. This disruption of melanosome transport is thought to cause the pigmentation abnormalities seen in individuals with Dowling-Degos disease.

Epidermolysis bullosa simplex

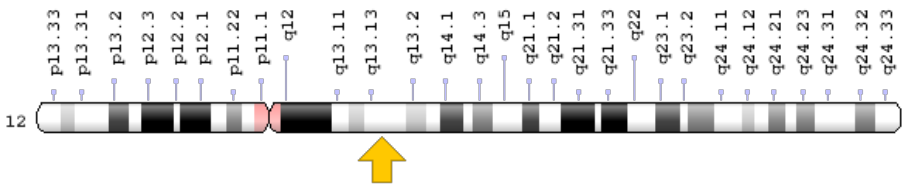
More than 130 mutations in the *KRT5* gene have been identified in people with epidermolysis bullosa simplex, a condition that causes the skin to be very fragile and to blister easily. Most of these mutations alter single protein building blocks (amino acids) used to make keratin 5. The most severe form of epidermolysis bullosa simplex, the Dowling-Meara type, usually results from changes in regions of keratin 5 that are essential for the normal assembly of keratin intermediate filaments. Milder forms of the disorder, including the localized type (formerly called the Weber-Cockayne type) and a form known as the other generalized type (formerly called the Koebner type), are often caused by changes affecting less critical regions of the protein. Another form of the disorder called epidermolysis bullosa simplex with mottled pigmentation typically results from a particular *KRT5* mutation. This mutation replaces the amino acid proline with the amino acid leucine at protein position 25 (written as Pro25Leu or P25L).

The *KRT5* gene mutations responsible for epidermolysis bullosa simplex change the structure and function of keratin 5, preventing it from partnering effectively with keratin 14 and interfering with the assembly of the keratin intermediate filament network. Mutations that cause severe forms of the disorder badly disrupt the assembly of keratin intermediate filaments, while mutations that result in milder forms impair keratin filament assembly to a lesser degree. A disruption in this network makes keratinocytes fragile and prone to rupture. Minor trauma to the skin, such as rubbing or scratching, can cause these cells to break down, resulting in the formation of painful, fluid-filled blisters.

Chromosomal Location

Cytogenetic Location: 12q13.13, which is the long (q) arm of chromosome 12 at position 13.13

Molecular Location: base pairs 52,514,575 to 52,520,459 on chromosome 12 (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- 58 kda cytokeratin
- CK5
- cytokeratin 5
- EBS2
- K2C5_HUMAN
- K5
- Keratin-5
- keratin 5, type II
- keratin, type II cytoskeletal 5
- KRT5A

Additional Information & Resources

Educational Resources

- Madame Curie Bioscience Database: Epidermal Blistering Caused by Keratin Mutations
  https://www.ncbi.nlm.nih.gov/books/NBK6247/#A49044
- Molecular Cell Biology (fourth edition, 2000): Intermediate Filaments
  https://www.ncbi.nlm.nih.gov/books/NBK21560/

Clinical Information from GeneReviews

- Epidermolysis Bullosa Simplex
  https://www.ncbi.nlm.nih.gov/books/NBK1369

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28KRT5%5BTIAB%5D%29+OR+%28keratin+5%5BTIAB%5D%29%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

- KERATIN 5, TYPE II
  http://omim.org/entry/148040

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_KRT5.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=KRT5%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:6442
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:3852
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/3852
- UniProt
  https://www.uniprot.org/uniprot/P13647

Sources for This Summary

- Arin MJ, Grimberg G, Schumann H, De Almeida H Jr, Chang YR, Tadini G, Kohlhase J, Krieg T, Bruckner-Tuderman L, Has C. Identification of novel and known KRT5 and KRT14 mutations in 53 patients with epidermolysis bullosa simplex: correlation between genotype and phenotype. Br J Dermatol. 2010 Jun;162(6):1365-9. doi: 10.1111/j.1365-2133.2010.09657.x. Epub 2010 Feb 25.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20199538
- Betz RC, Planko L, Eigelshoven S, Hanneken S, Pasternack SM, Bussow H, Van Den Bogaert K, Wenzel J, Braun-Falco M, Rutten A, Rogers MA, Ruzicka T, Nöthen MM, Magin TM, Kruse R. Loss-of-function mutations in the keratin 5 gene lead to Dowling-Degos disease. Am J Hum Genet. 2006 Mar;78(3):510-9. Epub 2006 Jan 19.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16465624
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1380294/
- Bolling MC, Lemmink HH, Jansen GH, Jonkman MF. Mutations in KRT5 and KRT14 cause epidermolysis bullosa simplex in 75% of the patients. Br J Dermatol. 2011 Mar;164(3):637-44. doi: 10.1111/j.1365-2133.2010.10146.x. Epub 2011 Feb 17.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21375516
- Hanneken S, Rütten A, Pasternack SM, Eigelshoven S, El Shabrawi-Caelen L, Wenzel J, Braun-Falco M, Ruzicka T, Nöthen MM, Kruse R, Betz RC. Systematic mutation screening of KRT5 supports the hypothesis that Galli-Galli disease is a variant of Dowling-Degos disease. Br J Dermatol. 2010 Jul;163(1):197-200. doi: 10.1111/j.1365-2133.2010.09741.x. Epub 2010 Mar 5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20222933
- Li M, Wang J, Zhang J, Ni C, Li X, Liang J, Cheng R, Li Z, Yao Z. Genome-wide linkage and exome sequencing analyses identify an initiation codon mutation of KRT5 in a unique Chinese family with generalized Dowling-Degos disease. Br J Dermatol. 2016 Mar;174(3):663-6. doi: 10.1111/bjd.14178. Epub 2015 Dec 26.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/26440693

- Müller FB, Küster W, Wodecki K, Almeida H Jr, Bruckner-Tuderman L, Krieg T, Korge BP, Arin MJ. Novel and recurrent mutations in keratin KRT5 and KRT14 genes in epidermolysis bullosa simplex: implications for disease phenotype and keratin filament assembly. Hum Mutat. 2006 Jul;27(7): 719-20.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16786515
- Pfendner EG, Bruckner AL. Epidermolysis Bullosa Simplex. 1998 Oct 7 [updated 2016 Oct 13]. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from http://www.ncbi.nlm.nih.gov/books/NBK1369/
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301543
- Pfendner EG, Sadowski SG, Uitto J. Epidermolysis bullosa simplex: recurrent and de novo mutations in the KRT5 and KRT14 genes, phenotype/genotype correlations, and implications for genetic counseling and prenatal diagnosis. J Invest Dermatol. 2005 Aug;125(2):239-43.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16098032
- Planko L, Böhse K, Höhfeld J, Betz RC, Hanneken S, Eigelshoven S, Kruse R, Nöthen MM, Magin TM. Identification of a keratin-associated protein with a putative role in vesicle transport. Eur J Cell Biol. 2007 Dec;86(11-12):827-39. Epub 2007 Mar 29.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17397964
- Schuilenga-Hut PH, Vlies Pv, Jonkman MF, Waanders E, Buys CH, Scheffer H. Mutation analysis of the entire keratin 5 and 14 genes in patients with epidermolysis bullosa simplex and identification of novel mutations. Hum Mutat. 2003 Apr;21(4):447. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12655565
- Verma S, Pasternack SM, Rütten A, Ruzicka T, Betz RC, Hanneken S. The First Report of KRT5 Mutation Underlying Acantholytic Dowling-Degos Disease with Mottled Hypopigmentation in an Indian Family. Indian J Dermatol. 2014 Sep;59(5):476-80. doi: 10.4103/0019-5154.139884.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25284854
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4171917/

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/KRT5

Reviewed: August 2017
Published: June 11, 2019

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services