DSG4 Gene

Subjects: Genetics & Heredity
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Desmoglein 4: The DSG4 gene provides instructions for making a protein called desmoglein 4 (DSG4).

Keywords: genes

1. Normal Function

This protein is found in specialized structures called desmosomes that are located in the membrane surrounding certain cells. Desmosomes help attach cells to one another and play a role in communication between cells. The DSG4 protein is found in cells in certain regions of hair follicles, including the inner compartment of the hair strand (shaft) known as the cortex. Hair growth occurs at the hair follicle when cells divide and the hair shaft is pushed upward and extends beyond the skin.

Desmosomes provide strength to the hair and are involved in signaling between neighboring cells within the hair shaft. The DSG4 protein may play a role in communicating the signals for cells to mature (differentiate) and form the hair shaft. In addition, the DSG4 protein is found in the upper layers of the skin where it provides strength and communicates signals for the skin cells to mature.

2. Health Conditions Related to Genetic Changes

2.1 Autosomal Recessive Hypotrichosis

At least 10 mutations in the *DSG4* gene have been found to cause autosomal recessive hypotrichosis, a condition that results in sparse hair growth (hypotrichosis) on the scalp, and less frequently, other parts of the body. A particular mutation that deletes a piece of genetic material in the *DSG4* gene (written as Ex5_8) is a common cause of the condition in individuals of Pakistani ancestry. This mutation impairs the protein's ability to help cells attach to one another. Other *DSG4* gene mutations result in the production of abnormal DSG4 proteins that cannot communicate signals between cells within hair follicles or skin. As a result, hair follicles are structurally abnormal and often underdeveloped. Irregular hair follicles alter the structure and growth of hair shafts, leading to fragile hair that breaks easily. A lack of normal DSG4 protein function may weaken the skin and contribute to the skin problems sometimes seen in individuals with autosomal recessive hypotrichosis.

2.2 Monilethrix

Mutations in the *DSG4* gene have been found in people with monilethrix, a hair condition characterized by strands of hair with a beaded appearance. The hair is also short, brittle and breaks easily. The mutations associated with this condition can affect any part of the DSG4 protein, but these changes typically alter the extracellular domain, which is the region of the protein outside the cell that interacts with other cells. In people with monilethrix, the cortex of the affected hair shaft appears abnormal. However, it is unclear how mutations in the *DSG4* gene are related to the abnormality in the cortex or the beaded appearance of the hair.

It is unknown why some individuals with *DSG4* gene mutations develop monilethrix and others develop autosomal recessive hypotrichosis (described above). These conditions may represent different forms of the same disorder.

3. Other Names for This Gene

- cadherin family member 13
- CDGF13
- CDH family member 13

- CDHF13
- desmoglein-4
- DSG4_HUMAN
- LAH

References

1. Bazzi H, Getz A, Mahoney MG, Ishida-Yamamoto A, Langbein L, Wahl JK 3rd,Christiano AM. Desmoglein 4 is expressed in highly differentiated keratinocytesand trichocytes in human epidermis and hair follicle. Differentiation. 2006Mar;74(2-3):129-40.
2. Farooq M, Ito M, Naito M, Shimomura Y. A case of monilethrix caused by novelcompound heterozygous mutations in the desmoglein 4 (DSG4) gene. Br J Dermatol.2011 Aug;165(2):425-31. doi: 10.1111/j.1365-2133.2011.10373.x.
3. John P, Tariq M, Arshad Rafiq M, Amin-Ud-Din M, Muhammad D, Waheed I, Ansar M,Ahmad W. Recurrent intragenic deletion mutation in desmoglein 4 gene underliesautosomal recessive hypotrichosis in two Pakistani families of Balochi and Sindhiorigins. Arch Dermatol Res. 2006 Aug;298(3):135-7.
4. Kljuic A, Bazzi H, Sundberg JP, Martinez-Mir A, O'Shaughnessy R, Mahoney MG,Levy M, Montagutelli X, Ahmad W, Aita VM, Gordon D, Uitto J, Whiting D, Ott J,Fischer S, Gilliam TC, Jahoda CA, Morris RJ, Panteleyev AA, Nguyen VT, ChristianoAM. Desmoglein 4 in hair follicle differentiation and epidermal adhesion:evidence from inherited hypotrichosis and acquired pemphigus vulgaris. Cell. 2003Apr 18;113(2):249-60.
5. Messenger AG, Bazzi H, Parslew R, Shapiro L, Christiano AM. A missensemutation in the cadherin interaction site of the desmoglein 4 gene underlieslocalized autosomal recessive hypotrichosis. J Invest Dermatol. 2005Nov;125(5):1077-9.
6. Rafiq MA, Ansar M, Mahmood S, Haque S, Faiyaz-ul-Haque M, Leal SM, Ahmad W. A recurrent intragenic deletion mutation in DSG4 gene in three Pakistani familieswith autosomal recessive hypotrichosis. J Invest Dermatol. 2004 Jul;123(1):247-8.
7. Shimomura Y, Sakamoto F, Kariya N, Matsunaga K, Ito M. Mutations in thedesmoglein 4 gene are associated with monilethrix-like congenital hypotrichosis. J Invest Dermatol. 2006 Jun;126(6):1281-5.
8. Wajid M, Bazzi H, Rockey J, Lubetkin J, Zlotogorski A, Christiano AM.Localized autosomal recessive hypotrichosis due to a frameshift mutation in thedesmoglein 4 gene exhibits extensive phenotypic variability within a Pakistanifamily. J Invest Dermatol. 2007 Jul;127(7):1779-82.
9. Zlotogorski A, Marek D, Horev L, Abu A, Ben-Amitai D, Gerad L, Ingber A,Frydman M, Reznik-Wolf H, Vardy DA, Pras E. An autosomal recessive form ofmonilethrix is caused by mutations in DSG4: clinical overlap with localizedautosomal recessive hypotrichosis. J Invest Dermatol. 2006 Jun;126(6):1292-6.