KRT10 Gene

Subjects: Genetics & Heredity
Contributor: Dean Liu

Keratin 10

Keywords: genes

1. Introduction

The *KRT10* gene provides instructions for making a protein called keratin 10. Keratins are a group of tough, fibrous proteins that form the structural framework of cells called keratinocytes that make up the skin, hair, and nails. Keratin 10 is produced in keratinocytes in the outer layer of the skin (the epidermis).

In the fluid-filled space inside these cells (the cytoplasm), the keratin 10 protein partners with a similar protein, keratin 1 (produced from the *KRT1* gene), to form molecules called keratin intermediate filaments. These filaments assemble into strong networks that provide strength and resiliency to the skin and protect it from being damaged by friction and other everyday physical stresses.

2. Health Conditions Related to Genetic Changes

2.1. Epidermolytic Hyperkeratosis

Dozens of mutations in the *KRT10* gene have been found in people with epidermolytic hyperkeratosis. This condition is characterized by red, blistering skin at an early age and thick skin (hyperkeratosis) later in life. People with *KRT10* gene mutations typically have NPS-type epidermolytic hyperkeratosis, which features thick skin on many parts of the body but not the palms of the hands or soles of the feet.

Most *KRT10* gene mutations associated with epidermolytic hyperkeratosis change a single protein building block (amino acid) in the keratin 10 protein. These amino acid changes commonly occur in regions of the protein that play a role in intermediate filament formation. The mutations alter the keratin 10 protein and seem to affect how intermediate filaments interact with each other to form networks. The altered proteins still form intermediate filaments, but the intermediate filament networks are disorganized and do not function normally. Without a strong network, skin cells become fragile and are easily damaged, which can lead to blistering in response to friction or mild trauma. It is unclear how these mutations cause the overgrowth of keratinocytes that results in hyperkeratotic skin.

2.2. Lchthyosis with Confetti

Mutations in the *KRT10* gene can cause another skin disorder known as ichthyosis with confetti (also called congenital reticular ichthyosiform erythroderma), which is characterized by red, scaly skin all over the body with small patches of normal skin that look like confetti. The patches of normal skin increase in number and size with age. The *KRT10* gene mutations involved in this condition, which are initially found in every cell of the body, alter the genetic sequence that is used as a blueprint for protein production, leading to production of abnormal keratin 10 protein. The abnormal protein includes a region at the end with an excess of the amino acid arginine; this arginine-rich region is not found in the normal keratin 10 protein. Researchers believe that this abnormal amino acid sequence directs the protein into the nucleus of the cell, where it cannot form the strong network of intermediate filaments. Loss of this network disrupts the outer layer of skin, contributing to the development of red, scaly skin.

In some abnormal cells, the mutated gene corrects itself through a complex process by which genetic material is exchanged between chromosomes. As a result, normal keratin 10 protein is produced and remains in the cytoplasm. The cell becomes normal and, as it continues to grow and divide, forms patches of normal skin in people with ichthyosis with confetti.

2.3. Other Disorders

Cyclic ichthyosis with epidermolytic hyperkeratosis is another skin disorder caused by mutations in the *KRT10* gene. This condition is similar to epidermolytic hyperkeratosis (described above), but the skin changes disappear for short periods, and then recur. The recurrent skin changes can last for weeks or months.

3. Other Names for This Gene

- CK-10
- CK10
- cytokeratin 10
- K10
- K1C10_HUMAN
- keratin 10, type I
- keratin, type I cytoskeletal 10
- keratin-10

References

1. Chamcheu JC, Siddiqui IA, Syed DN, Adhami VM, Liovic M, Mukhtar H. Keratingene mutations in disorders of human skin and its appendages. Arch BiochemBiophys. 2011 Apr 15;508(2):123-37. doi: 10.1016/j.abb.2010.12.019.
2. Chipev CC, Yang JM, DiGiovanna JJ, Steinert PM, Marekov L, Compton JG, BaleSJ. Preferential sites in keratin 10 that are mutated in epidermolytichyperkeratosis. Am J Hum Genet. 1994 Feb;54(2):179-90.
3. Choate KA, Lu Y, Zhou J, Choi M, Elias PM, Farhi A, Nelson-Williams C,Crumrine D, Williams ML, Nopper AJ, Bree A, Milstone LM, Lifton RP. Mitoticrecombination in patients with ichthyosis causes reversion of dominant mutations in KRT10. Science. 2010 Oct 1;330(6000):94-7. doi: 10.1126/science.1192280.
4. DiGiovanna JJ, Bale SJ. Clinical heterogeneity in epidermolytichyperkeratosis. Arch Dermatol. 1994 Aug;130(8):1026-35.
5. Huber M, Scaletta C, Benathan M, Frenk E, Greenhalgh DA, Rothnagel JA, RoopDR, Hohl D. Abnormal keratin 1 and 10 cytoskeleton in cultured keratinocytes fromepidermolytic hyperkeratosis caused by keratin 10 mutations. J Invest Dermatol.1994 May;102(5):691-4.
6. Rothnagel JA, Dominey AM, Dempsey LD, Longley MA, Greenhalgh DA, Gagne TA,Huber M, Frenk E, Hohl D, Roop DR. Mutations in the rod domains of keratins 1 and10 in epidermolytic hyperkeratosis. Science. 1992 Aug 21;257(5073):1128-30.