KRT1 Gene

Subjects: Genetics & Heredity
Contributor: Dean Liu

Keratin 1

Keywords: genes

1. Introduction

The *KRT1* gene provides instructions for making a protein called keratin 1. 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 1 is produced in keratinocytes in the outer layer of the skin (the epidermis), including the skin on the palms of the hands and soles of the feet.

The keratin 1 protein partners with another keratin protein, either keratin 9 or keratin 10, 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 *KRT1* gene have been found in people with epidermolytic hyperkeratosis. This condition is a skin disorder characterized by red, blistering skin at an early age and thick skin (hyperkeratosis) later in life. People with *KRT1* gene mutations typically have PS-type epidermolytic hyperkeratosis, which features thick skin on the palms of the hands and soles of the feet (palmoplantar hyperkeratosis) in addition to other parts of the body.

Most *KRT1* gene mutations associated with epidermolytic hyperkeratosis change a single protein building block (amino acid) in the keratin 1 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 1 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 weaker 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. Other Disorders

KRT1 gene mutations are involved in many other skin disorders. In several of these conditions, there is palmoplantar hyperkeratosis, but the skin on other parts of the body is usually not affected. A condition called epidermolytic palmoplantar keratoderma caused by *KRT1* gene mutations is relatively mild. Affected individuals typically have palmoplantar hyperkeratosis with detachment or loosening of the epidermis (epidermolysis), usually seen as blistering. People with nonepidermolytic palmoplantar keratoderma have palmoplantar hyperkeratosis with no evidence of epidermolysis. In striate palmoplantar keratoderma type 3, the skin thickening on the palms and soles follows a specific pattern.

KRT1 gene mutations are also responsible for a skin disorder called Curth-Macklin ichthyosis hystrix. This condition involves severe hyperkeratosis on the palms and soles and sometimes the skin over large joints or on the torso. This condition is distinguished by specific changes in the keratinocytes.

Another skin condition caused by genetic changes in the *KRT1* gene called cyclic ichthyosis with epidermolytic hyperkeratosis is similar to epidermolytic hyperkeratosis, but the skin changes disappear for short periods, then recur. The recurrent skin changes can last for weeks or months.

3. Other Names for This Gene

- 67 kDa cytokeratin
- CK-1
- CK1
- cytokeratin 1
- cytokeratin-1
- EHK1
- hair alpha protein
- K1
- K2C1_HUMAN
- keratin 1, type II
- keratin, type II cytoskeletal 1
- KRT1A
- type-II keratin Kb1

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, Korge BP, Markova N, Bale SJ, DiGiovanna JJ, Compton JG, SteinertPM. A leucine----proline mutation in the H1 subdomain of keratin 1 causesepidermolytic hyperkeratosis. Cell. 1992 Sep 4;70(5):821-8.
3. DiGiovanna JJ, Bale SJ. Clinical heterogeneity in epidermolytichyperkeratosis. Arch Dermatol. 1994 Aug;130(8):1026-35.
4. 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.
5. Yang JM, Chipev CC, DiGiovanna JJ, Bale SJ, Marekov LN, Steinert PM, ComptonJG. Mutations in the H1 and 1A domains in the keratin 1 gene in epidermolytichyperkeratosis. J Invest Dermatol. 1994 Jan;102(1):17-23.
6. Yang JM, Nam K, Kim HC, Lee JH, Park JK, Wu K, Lee ES, Steinert PM. A novelglutamic acid to aspartic acid mutation near the end of the 2B rod domain in the keratin 1 chain in epidermolytic hyperkeratosis. J Invest Dermatol. 1999Mar;112(3):376-9.