KRT5 Gene

Subjects: Genetics & Heredity
Contributor: Dean Liu

Keratin 5

genes

1. Introduction

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).

2. Health Conditions Related to Genetic Changes

2.1. 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.

2.2. 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.

3. Other Names for This Gene

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

- Keratin-5
- KRT5A

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