KRT14 Gene

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Keratin 14

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1. Introduction

The *KRT14* gene provides instructions for making a protein called keratin 14. 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 14 is specifically produced in cells called keratinocytes in the outer layer of the skin (the epidermis).

Keratin 14 partners with a similar protein, keratin 5 (produced from the *KRT5* 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 14 may also play a role in the formation of sweat glands and the development of patterned ridges on the skin of the hands and feet. These ridges, called dermatoglyphs, are the basis for each person's unique fingerprints.

2. Health Conditions Related to Genetic Changes

2.1. Epidermolysis Bullosa Simplex

More than 60 mutations in the *KRT14* 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 genetic changes alter single protein building blocks (amino acids) used to make keratin 14. The most severe form of epidermolysis bullosa simplex, the Dowling-Meara type, usually results from changes in regions of keratin 14 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.

KRT14 gene mutations change the structure and function of keratin 14, preventing it from working effectively with keratin 5 and interfering with the assembly of the keratin intermediate filament network. Mutations that cause severe forms of the disorder severely 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.

2.2. Naegeli-Franceschetti-Jadassohn Syndrome/Dermatopathia Pigmentosa Reticularis

Several mutations in the *KRT14* gene have been found to cause Naegeli-Franceschetti-Jadassohn syndrome/dermatopathia pigmentosa reticularis (NFJS/DPR). This disorder is a rare form of ectodermal dysplasia, a group of about 150 conditions characterized by abnormal development of ectodermal tissues including the skin, hair, nails, teeth, and sweat glands. NFJS and DPR were originally described as separate conditions; however, they are now often considered forms of the same disorder.

The *KRT14* gene mutations that cause NFJS/DPR most likely reduce the amount of functional keratin 14 in keratinocytes. A shortage of this protein makes these cells more likely to self-destruct (undergo apoptosis). The resulting loss of keratinocytes alters the normal development and structure of ectodermal tissues, which likely underlies most of the skin

and nail problems characteristic of NFJS/DPR. However, it is unclear how a shortage of keratin 14 is related to the net-like pattern of dark skin coloring (reticulate hyperpigmentation) that is also a hallmark of this condition.

3. Other Names for This Gene

- CK14
- cytokeratin 14
- EBS3
- EBS4
- K14
- K1C14_HUMAN
- keratin 14 (epidermolysis bullosa simplex, Dowling-Meara, Koebner)
- keratin 14, type I
- Keratin, type I cytoskeletal 14
- Keratin-14

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