JUP Gene

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Contributor: Dean Liu

Junction plakoglobin

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1. Introduction

The *JUP* gene provides instructions for making a protein called plakoglobin. This protein is found primarily in cells of the heart and skin, where it is part of two specialized structures called adherens junctions and desmosomes. Both of these structures help hold neighboring cells together, which provides strength and stability to tissues. Desmosomes may also be involved in other critical cell functions, including chemical signaling pathways, the process by which cells mature to perform specific functions (differentiation), and the self-destruction of cells (apoptosis).

Studies suggest that plakoglobin also plays a role in signaling within cells as part of the Wnt pathway. Wnt signaling controls the activity of certain genes and regulates the interactions between cells. This signaling pathway is involved in many aspects of development, including the normal development of the heart, skin, and hair.

2. Health Conditions Related to Genetic Changes

2.1. Keratoderma with Woolly Hair

Several mutations in the *JUP* gene have been found to cause a form of keratoderma with woolly hair classified as type I. This form of the condition is also known as Naxos disease. It is characterized by thick, calloused skin on the palms of the hands and soles of the feet (palmoplantar keratoderma); coarse, dry, fine, tightly curled, and sometimes sparse hair; and a potentially life-threatening form of heart disease called arrhythmogenic right ventricular cardiomyopathy (ARVC).

The *JUP* gene mutations that cause keratoderma with woolly hair type I lead to the production of an abnormally short version of the plakoglobin protein. The abnormal plakoglobin does not interact appropriately with other desmosomal proteins, which alters the structure of desmosomes and prevents cells from attaching to one another effectively. Researchers suspect that the impaired connections between cells make the skin, hair, and heart muscle more fragile. Over time, as these tissues are exposed to mechanical stress (for example, friction on the surface of the skin or the constant contraction and relaxation of the heart muscle), they become damaged and can no longer function normally. This mechanism probably underlies the skin, hair, and heart problems that occur in keratoderma with woolly hair type I.

Studies suggest that the abnormally short plakoglobin also impairs Wnt signaling, which appears to cause heart muscle cells to be replaced with fat cells over time. This abnormal signaling may influence the development of ARVC in affected individuals.

2.2. Other Disorders

JUP gene mutations have also been found to cause a spectrum of signs and symptoms that overlap with those of keratoderma with woolly hair type I (described above). Some affected families have had similar skin and hair abnormalities but no apparent heart problems, while others have had ARVC only, with normal skin and hair. Although these conditions are related to impaired function of plakoglobin and abnormal desmosomes, it is unclear how mutations in this gene lead to these different patterns of features.

At least one mutation in the *JUP* gene can cause a disorder known as lethal congenital epidermolysis bullosa (LCEB). Features of this condition include very fragile skin that blisters and detaches easily, a complete absence of hair (alopecia), and abnormal fingernails. The skin abnormalities lead to a severe loss of fluids and death in early infancy. The mutation found to cause LCEB, written as Gln539Ter or Q539X, prevents the production of any functional plakoglobin. As a result,

the skin has no stable desmosomes, so skin cells are unable to attach to one another effectively. Because affected individuals die before heart disease may become apparent, it is unknown whether a complete loss of plakoglobin also impairs desmosomes in the heart.

3. Other Names for This Gene

- ARVD12
- catenin (cadherin-associated protein), gamma 80kDa
- CTNNG
- desmoplakin III
- desmoplakin-3
- DP3
- DPIII
- PDGB
- PKGB
- plakoglobin

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