DSP Gene

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Desmoplakin: The DSP gene provides instructions for making a protein called desmoplakin.

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1. Normal Function

This protein is found primarily in cells of the heart and skin, where it is a major component of specialized structures called desmosomes. 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).

2. Health Conditions Related to Genetic Changes

2.1 Keratoderma with Woolly Hair

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

The *DSP* gene mutations that cause keratoderma with woolly hair type II lead to the production of an abnormally short version of the desmoplakin protein. The abnormal protein alters the structure of desmosomes, preventing 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 II. Studies suggest that abnormal cell signaling may also contribute to cardiomyopathy in people with this condition.

2.2 Arrhythmogenic Right Ventricular Cardiomyopathy

2.3 Idiopathic Pulmonary Fibrosis

2.4 Other Disorders

DSP gene mutations have also been found to cause a spectrum of signs and symptoms that overlap with those of keratoderma with woolly hair type II (described above). A few families have had similar skin, hair, and heart abnormalities plus missing or unusually small teeth. Other families have had skin and hair abnormalities similar to keratoderma with woolly hair type II but no apparent heart problems. Still others have had palmoplantar keratoderma only, without any other features. *DSP* gene mutations can also cause a potentially life-threatening form of heart disease called arrhythmogenic right ventricular cardiomyopathy (ARVC) without abnormalities of the skin and hair. Although these conditions are all related to impaired function of desmoplakin and abnormal desmosomes, it is unclear how mutations in this gene lead to these different patterns of features.

At least four mutations in the *DSP* gene have been identified in people with a disorder called lethal acantholytic epidermolysis bullosa (LAEB). Features of this condition include very fragile skin that blisters and detaches easily, a complete absence of hair (alopecia), abnormal or missing fingernails, teeth that are present from birth (neonatal teeth), and abnormalities of the heart muscle (cardiomyopathy). The skin abnormalities lead to a severe loss of fluids and death in early infancy. Like the mutations that cause keratoderma with woolly hair type II, the mutations associated with LAEB

lead to an abnormally short version of desmoplakin and impaired function of desmosomes. However, the protein associated with LAEB is missing additional regions, which probably accounts for the more severe signs and symptoms associated with this condition.

3. Other Names for This Gene

- 250/210 kDa paraneoplastic pemphigus antigen
- DCWHKTA
- desmoplakin I
- desmoplakin II
- desmoplakin isoform I
- desmoplakin isoform II
- DP
- DPI
- DPII
- KPPS2
- PPKS2

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