Desmoplakin

Alternative Names
DSP
Desmoplakin I
DSPI
Desmoplakin II
DSPII

Record Category
Gene locus

WHO-ICD
N.B.: Classification not applicable to gene loci.

Incidence per 100,000 Live Births
N/A to gene loci

OMIM Number
125647

Mode of Inheritance
N/A

Gene Map Locus
6p24.3

Description
The DSP gene maps to chromosome 6p24.3, where it encodes a protein of 2,871 amino acids called desmoplakin. This is the most abundant protein of the desmosome proteins. Desmosomes are major protein in cell adhesion junctions, particularly in the epidermis and cardiac tissue and are important for the rigidity and strength of the cells. Desmoplakin plays a role in the organization of the desmosomal cadherin-plakoglobin complexes into discrete plasma membrane domains and in the anchoring of intermediate filaments to the desmosomes. The N-terminus of desmoplakin interacts with the N-terminal region of plakophilin 1 and plakoglobin, and is required for localization to the desmosome, while the C-terminus binds with intermediate filaments. The mid-region of desmoplakin contains a coiled-coiled rod domain, which is responsible for homodimerization.

Defects in this enzyme are the cause of familial arrhythmogenic right ventricular dysplasia/cardiomyopathy type 8 (ARVD/C8) keratoderma, palmoplantar, striate 2 (SPPK2), skin fragility-woolly hair syndrome (SFWHS), epidermolysis bullosa, lethal acantholytic (EBLA) and dilated cardiomyopathy with wooly hair and keratoderma. ARVD/C is an autosomal dominant congenital heart disease characterized by partial degeneration of the myocardium of the right ventricle, electrical instability and sudden death. Dilated cardiomyopathy with woolly hair and keratoderma is an autosomal recessive cardiocutaneous syndrome characterized by dilation of the left ventricle with alterations in muscle contractility, wooly hair, keratotic skin conditions, and sometimes congestive heart failure and death.

Molecular Genetics
The DSP gene contains 24 coding exons and spans around 45 kb genomic distance. Mutations in the DSP gene have been associated with familial arrhythmogenic right ventricular dysplasia/cardiomyopathy type 8 (ARVD/C8) keratoderma, palmoplantar, striate 2 (SPPK2), skin fragility-woolly hair syndrome (SFWHS), epidermolysis bullosa, lethal acantholytic (EBLA) and dilated cardiomyopathy with wooly hair and keratoderma.

Epidemiology in the Arab World
Saudi Arabia
In five members from two related Saudi families diagnosed with skin fragility-woolly hair syndrome, Al-Owain et al. (2011) identified homozygosity for a c.7097G>A transition in the DSP gene, resulting in a p.R2366H substitution. The parents were heterozygous for the mutation, which was not found in 400 chromosomes from healthy control individuals of the same ethnic group. No cardiac symptoms were reported and there was no family history of sudden death. A normal echocardiographic evaluation was found in two of those affected who were 4 and 7 years of age; formal cardiac work-up was refused in the other three affected members, aged 3, 14, and 16 years.

Because cardiomyopathy sometimes occurs later in life in the syndrome of dilated cardiomyopathy with woolly hair and keratoderma, Al-Owain et al. (2011) suggested that the current diagnosis was not beyond doubt.

References

Al-Owain M, Wakil S, Shareef F, Al-Fatani A, Hamadah E, Haider M, Al-Hindi H, Awaji A, Khalifa O, Baz B, Ramadhan R, Meyer B. Novel homozygous mutation in DSP causing skin fragility-woolly hair syndrome: report of a large family and review of the desmoplakin-related phenotypes. Clin Genet. 2011; 80(1):50-8. PMID: 20738328 [FT]

Related CTGA Records

Skin Fragility-Woolly Hair Syndrome

External Links

http://ghr.nlm.nih.gov/gene/DSP
http://www.genecards.org/cgi-bin/carddisp.pl?gene=DSP

Contributors

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