TP63 gene

tumor protein p63

Normal Function

The *TP63* gene provides instructions for making a protein called tumor protein p63 (also known simply as p63). The p63 protein functions as a transcription factor, which means it attaches (binds) to certain regions of DNA and controls the activity of particular genes.

The p63 protein interacts with other proteins to turn many different genes on and off at different times. The action of p63 helps regulate numerous cell activities, including cell growth and division (proliferation), cell maintenance, the process by which cells mature to carry out specific functions (differentiation), the ability of cells to stick to one another (cell adhesion), and the orderly self-destruction of cells (apoptosis).

The p63 protein plays a critical role in early development. It is especially important for the normal development of ectodermal structures, such as the skin, hair, teeth, and nails. Studies suggest that it also plays essential roles in the development of the limbs, facial features, urinary system, and other organs and tissues. In addition to its roles in development, the p63 protein appears to be necessary for the maintenance of various cells and tissues later in life.

Health Conditions Related to Genetic Changes

Ankyloblepharon-ectodermal defects-cleft lip/palate syndrome

At least 40 mutations in the *TP63* gene have been identified in people with ankyloblepharon-ectodermal defects-cleft lip/palate (AEC) syndrome. This condition is a form of ectodermal dysplasia, which is a group of disorders characterized by abnormal development of the skin, hair, nails, teeth, and sweat glands. Other characteristic features of AEC syndrome include partial or complete fusion of the upper and lower eyelids (ankyloblepharon filiforme adnatum) and an opening in the roof of the mouth (a cleft palate), a split in the lip (a cleft lip), or both.

Most of the *TP63* gene mutations responsible for AEC syndrome occur in regions of the p63 protein known as the sterile alpha motif (SAM) domain and the transactivation inhibitory (TI) domain. Mutations in these regions interfere with the ability of p63 to turn target genes on and off at the right times. However, it is unclear how these changes lead to abnormal ectodermal development and the specific features of AEC syndrome.

Other disorders

Mutations in the *TP63* gene cause several additional ectodermal dysplasias with features that overlap those of AEC syndrome. These conditions include ectrodactyly, ectodermal dysplasia, clefting (EEC) syndrome; acro-dermato-ungual-lacrimal-tooth (ADULT) syndrome; and limb-mammary syndrome (LMS). This group of disorders is characterized by varying combinations of ectodermal abnormalities (which affect the skin, hair, nails, teeth, and sweat glands), cleft lip and/or cleft palate, and malformations of the hands and feet.

Mutations in the *TP63* gene have also been found to cause split hand/foot malformation type 4 (SHFM4), a condition involving hand and foot malformations without any other signs or symptoms. Additionally, *TP63* gene mutations are a rare cause of cleft lip and/ or cleft palate that occur without features affecting other parts of the body.

The *TP63* gene mutations responsible for these conditions occur in various regions of the *TP63* gene and affect the function of the p63 protein in different ways. Some of the known mutations may give the p63 protein a new, abnormal function (described as "gain-of-function" mutations) or lead to a version of the p63 protein that interferes with normal cell activities (described as "dominant-negative" mutations). These changes alter the ability of p63 to interact with other proteins, to turn target genes on and off at the right times, or both. It is unclear how abnormal p63 activity disrupts ectodermal development and leads to the specific features of the *TP63*-related conditions.

Other Names for This Gene

- AIS
- amplified in squamous cell carcinoma
- chronic ulcerative stomatitis protein
- CUSP
- KET
- NBP
- p40
- p51
- p51A
- p51B
- p53CP
- p63
- P63_HUMAN
- p73L
- TP53CP
- TP53L
- TP73L

- transformation-related protein 63
- tumor protein 63
- tumor protein p53-competing protein

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of TP63 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=8626[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28TP63%5BTIAB%5D%29+OR+%28p63%5BTI%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- ADULT SYNDROME (https://omim.org/entry/103285)
- SPLIT-HAND/FOOT MALFORMATION 4; SHFM4 (https://omim.org/entry/605289)
- ECTRODACTYLY, ECTODERMAL DYSPLASIA, AND CLEFT LIP/PALATE SYNDROME 3; EEC3 (https://omim.org/entry/604292)
- TUMOR PROTEIN p63; TP63 (https://omim.org/entry/603273)
- LIMB-MAMMARY SYNDROME; LMS (https://omim.org/entry/603543)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/8626)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=TP63[gene])

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Genomic Location

The *TP63* gene is found on chromosome 3 (https://medlineplus.gov/genetics/chromosome/3/).

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