SMAD3 gene

SMAD family member 3

Normal Function

The *SMAD3* gene provides instructions for making a protein involved in transmitting chemical signals from the cell surface to the nucleus. This signaling pathway, called the transforming growth factor-beta (TGF-β) pathway, allows the environment outside the cell to affect cell function, including how the cell produces other proteins. The signaling process begins when a TGF-β protein attaches (binds) to a receptor on the cell surface, which activates a group of related SMAD proteins (including the SMAD3 protein). These SMAD proteins combine to form a protein complex, which then moves to the cell nucleus. In the nucleus, the SMAD protein complex binds to specific areas of DNA to control the activity of particular genes. Through the TGF-β signaling pathway, the SMAD3 protein also influences many aspects of cellular processes, including cell growth and division (proliferation), cell movement (migration), and controlled cell death (apoptosis).

Health Conditions Related to Genetic Changes

Loeys-Dietz syndrome

At least 35 mutations in the *SMAD3* gene have been found to cause Loeys-Dietz syndrome type III. This disorder affects connective tissue, which gives structure and support to blood vessels, the skeleton, and many other parts of the body. Loeys-Dietz syndrome type III is characterized by abnormal blood vessels, skeletal and joint deformities, and skin abnormalities. Some of the mutations that cause this disorder insert or delete small amounts of genetic material in the *SMAD3* gene, while other mutations result in a change to single protein building blocks (amino acids) in the SMAD3 protein. These mutations lead to the production of a nonfunctional SMAD3 protein. Despite a reduction in SMAD3 function, the TGF-β pathway is overactive. Researchers speculate that the activity of other proteins in this signaling pathway is increased to compensate for the lack of SMAD3 activity; however, the exact mechanism responsible for the increase in signaling is unclear. The overactive signaling pathway leads to dysregulated cell proliferation and gene activation, specifically affecting blood vessel, cartilage, and skin development. These changes lead to the abnormalities typical of Loeys-Dietz syndrome type III.

Familial thoracic aortic aneurysm and dissection

MedlinePlus Genetics provides information about Familial thoracic aortic aneurysm and dissection

Other Names for This Gene

- hMAD-3
- hSMAD3
- JV15-2
- MAD homolog 3
- MAD, mothers against decapentaplegic homolog 3
- mad3
- MADH3
- mothers against decapentaplegic homolog 3
- SMAD, mothers against DPP homolog 3
- SMAD3_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of SMAD3 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4088[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28SMAD3%5BTI%5D%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

- SMAD FAMILY MEMBER 3; SMAD3 (https://omim.org/entry/603109)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/4088)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=SMAD3[gene])

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Genomic Location

The *SMAD3* gene is found on chromosome 15 (https://medlineplus.gov/genetics/chromosome/15/).

Last updated March 1, 2017