MPPH Syndrome

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AKT3 gene

AKT3 gene

AKT serine/threonine kinase 3

Normal Function

The AKT3 gene provides instructions for making a protein that is most active in the nervous system. The AKT3 protein is a key regulator of a chemical signaling pathway called the PI3K-AKT-mTOR pathway. This signaling influences many critical cell functions, including the creation (synthesis) of new proteins, cell growth and division (proliferation), and the survival of cells. The PI3K-AKT-mTOR pathway is essential for the normal development of many parts of the body, including the brain. Studies suggest that the AKT3 protein plays a critical role in determining brain size.

Health Conditions Related to Genetic Changes

Megalencephaly-polymicrogyria-polydactyly-hydrocephalus syndrome

Several mutations in the AKT3 gene have been found to cause megalencephaly-polymicrogyria-polydactyly-hydrocephalus (MPPH) syndrome. This rare condition affects the development of the brain, causing an unusually large brain and head size (megalencephaly) and other abnormalities of the brain's structure.Each of the known mutations changes a single protein building block (amino acid) in the AKT3 protein. These changes are described as "gain-of-function" because they increase the activity of the protein. This enhanced activity increases chemical signaling through the PI3K-AKT-mTOR pathway, which causes excessive cell growth and division. The increased number of cells leads to rapid and abnormal brain growth starting before birth.

More About This Health Condition

Other disorders

Changes involving the AKT3 gene are also involved in other disorders of brain growth. Megalencephaly without the other features of MPPH syndrome (described above) has been associated with gain-of-function AKT3 gene mutations or extra copies (duplication) of the region of chromosome 1 containing the AKT3 gene. These genetic changes increase the amount or activity of the AKT3 protein, which enhances chemical signaling through the PI3K-AKT-mTOR pathway and causes excessive cell growth and division, particularly in the brain.Other genetic changes involving the AKT3 gene are associated with an unusually small brain and head size (microcephaly). These changes include a deletion of the AKT3 gene or a loss of the region of chromosome 1 containing the AKT3 gene. The resulting reduction in AKT3 protein activity likely decreases signaling through the PI3K-AKT-mTOR pathway and restricts cell growth and division in the developing brain.Changes involving the AKT3 gene can also cause a brain malformation called isolated hemimegalencephaly.

This brain abnormality is an enlargement of one of the two major halves (hemispheres) of the cerebrum, which is the large part of the brain that controls most voluntary activity, language, sensory perception, learning, and memory. Like the genetic changes that cause MPPH syndrome and megalencephaly (described above), the AKT3 gene changes that result in isolated hemimegalencephaly are gain-of-function, ultimately leading to increased cell growth and division in the developing brain. However, unlike the mutations that cause those other abnormalities of brain growth, the genetic changes related to isolated hemimegalencephaly are somatic, meaning they occur at some point during embryonic development. As brain cells continue to grow and divide, some of these cells will have the genetic change, and others will not (a situation known as mosaicism). The mosaic nature of these genetic changes helps explain why they cause overgrowth in only one of the two cerebral hemispheres.

Other Names for This Gene

PKB gamma PKB-GAMMA PKBG PRKBG RAC-gamma RAC-gamma serine/threonine protein kinase RAC-PK-gamma STK-2 v-akt murine thymoma viral oncogene homolog 3 (protein kinase B, gamma)

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

Tests of AKT3

Scientific Articles on PubMed

PubMed

Catalog of Genes and Diseases from OMIM

AKT SERINE/THREONINE KINASE 3; AKT3

Gene and Variant Databases

NCBI Gene

ClinVar

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Genomic LocationThe AKT3 gene is found on chromosome 1.

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