VRK1 gene

VRK serine/threonine kinase 1

Normal Function

The *VRK1* gene provides instructions for making a protein called VRK serine/threonine kinase 1. This protein is active in cells throughout the body.

VRK serine/threonine kinase 1 plays a critical role in directing cell growth and division. This protein regulates several transcription factors, which are proteins that control the activity of genes by attaching (binding) to specific regions of DNA. VRK serine/threonine kinase 1 has a particularly important role in regulating a transcription factor called p53 (which is produced from the *TP53* gene). The p53 protein repairs damaged DNA, regulates cell division, and prevents the formation of cancerous tumors. VRK serine/ threonine kinase 1 stabilizes and activates the p53 protein and controls the levels of p53 in the nucleus.

Studies suggest that VRK serine/threonine kinase 1 has several additional functions. This protein is involved in the assembly of the nuclear envelope, which is a structure that surrounds the nucleus and acts as a barrier between the nucleus and the rest of the cell. The nuclear envelope protects the DNA contained in the nucleus and regulates the movement of molecules into and out of the nucleus. VRK serine/threonine kinase 1 is also thought to play a role in the organization of chromatin. Chromatin is the complex of DNA and protein that packages DNA into chromosomes. Both the assembly of the nuclear envelope and the proper organization of chromatin are necessary for normal cell division.

Researchers speculate that VRK serine/threonine kinase 1 may be involved in the development and maintenance of the nervous system, but its role is not well understood.

Health Conditions Related to Genetic Changes

Pontocerebellar hypoplasia

At least two mutations in the *VRK1* gene have been identified in people with a disorder of brain development called pontocerebellar hypoplasia. The major features of this condition include delayed development, problems with movement, and intellectual disability. *VRK1* gene mutations cause a small percentage of all cases of a form of the

disorder designated pontocerebellar hypoplasia type 1 (PCH1). When PCH1 results from *VRK1* gene mutations, it is sometimes categorized more specifically as PCH1A.

The *VRK1* gene mutations that cause PCH1A significantly reduce the amount of VRK serine/threonine kinase 1 produced in cells. A shortage of this protein prevents it from carrying out its usual functions, including regulating the activity of transcription factors. Although these changes likely affect cell growth and division, it is unknown how they lead to abnormal brain development in people with PCH1A.

Other disorders

At least three mutations in the *VRK1* gene are thought to cause another rare brain disorder that has been described as a form of hereditary motor and sensory neuropathy (HMSN). HMSNs are a group of disorders that affect peripheral nerves, which connect the brain and spinal cord to muscles as well as sensory cells that detect touch, pain, and temperature. Individuals with HMSN resulting from mutations in the *VRK1* gene have weak muscle tone (hypotonia) and delayed development of motor skills such as sitting, standing, and walking. They also have an unusually small head size (microcephaly), but they have normal intelligence.

The *VRK1* gene mutations associated with this disorder change single protein building blocks (amino acids) in VRK serine/threonine kinase 1. Researchers are working to determine how changes in the *VRK1* gene result in the neurological problems associated with this disorder.

One of the mutations associated with HMSN has also been found in an individual with PCH1A (described above). It is unclear why *VRK1* gene mutations can cause different nervous system abnormalities in different people. It is also unknown why the effects of these mutations appear to be limited to the nervous system, as VRK serine/threonine kinase 1 is active in many of the body's cells and tissues.

Other Names for This Gene

- MGC117401
- MGC138280
- MGC142070
- vaccinia related kinase 1
- vaccinia virus B1R-related kinase 1
- vaccinia-related kinase-1
- VRK1_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of VRK1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7443[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28VRK1%5BTIAB%5D%29+OR+%28vaccinia+related+kinase+1%5BTIAB%5D%29%29+OR+%28vaccinia-related+kinase-1%5BTIAB%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+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- VRK SERINE/THREONINE KINASE 1; VRK1 (https://omim.org/entry/602168)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/7443)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=VRK1[gene])

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Genomic Location

The *VRK1* gene is found on chromosome 14 (https://medlineplus.gov/genetics/chromosome/14/).

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