MAP3K1 gene

mitogen-activated protein kinase kinase kinase 1

Normal Function

The *MAP3K1* gene provides instructions for making a protein that helps regulate signaling pathways that control various processes in the body, including the processes of determining sex characteristics before birth. The MAP3K1 protein attaches (binds) to other molecules called RHOA, MAP3K4, FRAT1, and AXIN1. The binding of MAP3K1 to these molecules, which are called cofactors, helps MAP3K1 control the activity of the signaling pathways.

Health Conditions Related to Genetic Changes

Swyer syndrome

Variants (also called mutations) in the *MAP3K1* gene are thought to account for up to 18 percent of cases of Swyer syndrome, also known as 46,XY complete gonadal dysgenesis or 46,XY pure gonadal dysgenesis. Swyer syndrome is a condition that affects sex development.

Sex development usually follows a particular pattern based on an individual's chromosomes. People usually have 46 chromosomes in each cell. Two of the 46 chromosomes, known as X and Y, are called sex chromosomes because they help determine whether a person will develop male or female sex characteristics. Girls and women typically have two X chromosomes (46,XX karyotype), while boys and men typically have one X chromosome and one Y chromosome (46,XY karyotype). However, individuals with Swyer syndrome have a male-typical chromosome pattern (46,XY karyotype), but they develop female-typical sex characteristics.

The *MAP3K1* gene variants that cause Swyer syndrome result in production of MAP3K1 proteins that attach to cofactors more readily than usual. Enhanced binding reduces signaling that leads to male-typical sex development and increases signaling that leads to female-typical sex development. As a result, affected individuals with a 46,XY karyotype will not develop male gonads (testes) but will develop female reproductive structures (a uterus and fallopian tubes).

Breast cancer

MedlinePlus Genetics provides information about Breast cancer

Langerhans cell histiocytosis

MedlinePlus Genetics provides information about Langerhans cell histiocytosis

Other disorders

MAP3K1 gene variants have also been identified in people with 46,XY disorder of sex development, which is also known as partial gonadal dysgenesis. These variants likely have similar but less severe effects on signaling pathways involved in sex development than those that cause Swyer syndrome (described above). Affected individuals may have external genitalia that do not look clearly male or clearly female or other abnormalities of the genitals and reproductive organs.

Other Names for This Gene

- M3K1_HUMAN
- MAP/ERK kinase kinase 1
- MAPK/ERK kinase kinase 1
- MAPKKK1
- MEK kinase 1
- MEKK
- MEKK 1
- MEKK1
- mitogen-activated protein kinase kinase kinase 1, E3 ubiquitin protein ligase
- SRXY6

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of MAP3K1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4214[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28MAP3K1%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+1440+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- MITOGEN-ACTIVATED PROTEIN KINASE KINASE KINASE 1; MAP3K1 (https://omim.org/entry/600982)
- 46,XY SEX REVERSAL 6; SRXY6 (https://omim.org/entry/613762)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/4214)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=MAP3K1[gene])

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Genomic Location

The *MAP3K1* gene is found on chromosome 5 (https://medlineplus.gov/genetics/chromosome/5/).

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