PPM1D gene

protein phosphatase, Mg2+/Mn2+ dependent 1D

Normal Function

The *PPM1D* gene provides instructions for making an enzyme called protein phosphatase 1D. This enzyme plays an essential role in cell division, immune cell development, gene expression, and the process by which cells create energy from food (metabolism). This enzyme is present in many of the body's tissues, including the developing brain.

Protein phosphatase 1D belongs to a group of enzymes known as the PP2C phosphatases, which help regulate cell development in response to environmental stress. The PP2C phosphatases turn on (activate) after attaching (binding) to charged molecules (ions) of manganese or magnesium. The activated enzyme can then regulate the activity of other proteins by removing a cluster of oxygen and phosphorous atoms (phosphate group) from that protein. This regulation helps repair DNA damage and return the cell to its normal state.

Protein phosphatase 1D specifically regulates tumor suppressors, such as tumor protein p53. Tumor suppressors are proteins that keep cells from growing and dividing too fast or in an uncontrolled way. By stopping cells with damaged DNA from dividing, tumor suppressors help prevent the development of tumors. Protein phosphatase 1D turns off proteins such as tumor protein p53 when they are no longer needed, which allows cells to continue growing and dividing.

Protein phosphatase 1D is also thought to play a role in regulating areas of tightly packed DNA called heterochromatin. Because gene expression is lower when DNA is tightly packed than when DNA is loosely packed, protein phosphatase 1D helps to turn off (silence) regions of DNA that are not needed.

Health Conditions Related to Genetic Changes

Jansen-de Vries syndrome

Certain variants (sometimes called mutations) in the *PPM1D* gene can cause Jansen-de Vries syndrome, a developmental disorder that affects many parts of the body. The variants that cause Jansen-de Vries syndrome occur in particular segments of the *PPM1D* gene known as exon 5 or exon 6. These variants disrupt the gene's instructions,

resulting in an enzyme that does not function as it should. Research suggests that this enzyme is not able to reach the cell's nucleus. Without enough functional enzyme, heterochromatin regulation is disrupted, which likely alters gene expression. Altered gene expression may affect the early development of the brain. Researchers are trying to learn exactly how variants in the *PPM1D* gene affect the early development of the brain and other body systems to cause the signs and symptoms of Jansen-de Vries syndrome.

Other Disorders

Variants in the *PPM1D* gene have been found in the tissues of people with various cancers, including breast cancer. These gene variants are known as somatic variants and are acquired during a person's lifetime. The variants are not inherited and are present only in certain cells. Variants in the *PPM1D* gene that are associated with cancer increase the activity of protein phosphatase 1D, which decreases the activity of tumor protein p53 and allows cancer cells to grow and divide.

Other Names for This Gene

- PP2C-DELTA
- protein phosphatase 1D, magnesium-dependent, delta isoform
- protein phosphatase 2C, delta isoform
- wild-type p53-induced phosphatase 1
- WIP1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of PPM1D (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=8493[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=PPM1D+gene&filter=hum_ani.humans&filter=lang.english&filter=years.2018-2024&sort=date)

Catalog of Genes and Diseases from OMIM

- PROTEIN PHOSPHATASE, MAGNESIUM/MANGANESE-DEPENDENT, 1D; PPM1D (https://omim.org/entry/605100)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/8493)

- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=PPM1D[gene])

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