WWP1 gene

WW domain containing E3 ubiquitin protein ligase 1

Normal Function

The *WWP1* gene provides instructions for making a protein that is found is many tissues. This protein has activity known as E3 ubiquitin ligase. Proteins with this activity are involved in the process that targets other proteins to be broken down (degraded) within cells. Protein degradation is a normal process that removes damaged or unnecessary proteins and helps maintain the normal functions of cells.

The WWP1 protein can attach (bind) to various other proteins and mark them for degradation or alteration. In particular, the WWP1 protein binds to an enzyme called PTEN. The PTEN enzyme acts as a tumor suppressor, which means that it helps regulate cell division by keeping cells from growing and dividing (proliferating) too rapidly or in an uncontrolled way. To function, the PTEN enzyme has to bind to another PTEN enzyme (dimerize). Binding of the WWP1 protein to the PTEN enzyme impairs the PTEN enzyme's ability to dimerize, impairing the enzyme's activity.

Health Conditions Related to Genetic Changes

Cowden syndrome

At least 7 variants in the *WWP1* gene have been identified in people with Cowden syndrome or a similar disorder called Cowden-like syndrome. These conditions are characterized by multiple tumor-like growths called hamartomas and an increased risk of developing certain cancers, particularly breast cancer, thyroid cancer, colorectal cancer, and cancer of the uterine lining (endometrial cancer).Other features of Cowden syndrome can include an enlarged head (macrocephaly) and a rare, noncancerous brain tumor called Lhermitte-Duclos disease. People with Cowden syndrome or Cowden-like syndrome and *WWP1* gene variants are more likely to develop colorectal cancer than individuals with Cowden syndrome associated with other genes.

The *WWP1* gene variants associated with Cowden syndrome and Cowden-like syndrome change single amino acids in the WWP1 protein. Researchers describe these variants as "gain-of-function" because they appear to enhance the activity of the WWP1 protein.Studies suggest that the altered protein binds to the PTEN enzyme more often than normal. Excessive binding impairs PTEN enzyme tumor suppressor activity, allowing cells to proliferate unchecked, leading to the formation of tumors.

Cancers

Mutations in the *WWP1* gene are also associated with several types of cancers without the additional features of Cowden syndrome (described above). These include cancers of the prostate, breast, liver as well as other cancers that often occur in Cowden syndrome. Unlike the *WWP1* gene changes in Cowden syndrome, these mutations are somatic, which means they arise during a person's lifetime and are not inherited. These mutations are found only in cells that give rise to cancer.

Similar to those in Cowden syndrome, the *WWP1* gene changes are also known "gain-of-function" mutations as they enhance the activity of the WWP1 protein. As a result, the altered protein is thought to bind to the PTEN enzyme more often than normal. Excessive binding impairs PTEN enzyme tumor suppressor activity, allowing cells to proliferate unchecked, leading to cancer development in affected cells.

Other Names for This Gene

- TGIF-interacting ubiquitin ligase 1
- TIUL1
- WW domain-containing E3 ubiquitin protein ligase 1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of WWP1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=11059[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=WWP1+%5Btiab%5D&filter=lang.english&filter=hum_ani.humans)

Catalog of Genes and Diseases from OMIM

- WW DOMAIN-CONTAINING PROTEIN 1; WWP1 (https://omim.org/entry/602307)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/11059)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=WWP1[gene])

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