

DPYS gene

dihydropyrimidinase

Normal Function

The *DPYS* gene provides instructions for making an enzyme called dihydropyrimidinase. This enzyme is involved in the breakdown of molecules called pyrimidines, which are building blocks of DNA and its chemical cousin RNA. The dihydropyrimidinase enzyme is involved in the second step of the three-step process that breaks down pyrimidines. This step opens the ring-like structures of molecules called 5,6-dihydrothymine and 5,6-dihydrouracil. Further breakdown of these molecules leads to the production of other molecules called beta-aminoisobutyric acid and beta-alanine, which are thought to play roles in the nervous system. Beta-aminoisobutyric acid increases the production and release (secretion) of a protein called leptin, which has been found to help protect brain cells from damage caused by toxins, inflammation, and other factors. Beta-alanine is thought to be involved in sending signals between nerve cells (synaptic transmission) and in controlling the level of a chemical messenger (neurotransmitter) called dopamine.

The dihydropyrimidinase enzyme also helps break down certain drugs called fluoropyrimidines that are used to treat cancer. Common examples of these drugs are 5-fluorouracil and capecitabine.

Health Conditions Related to Genetic Changes

Dihydropyrimidinase deficiency

At least 23 *DPYS* gene mutations have been identified in people with dihydropyrimidinase deficiency, a disorder that can cause neurological and gastrointestinal problems in some affected individuals. Other people with dihydropyrimidinase deficiency have no signs or symptoms related to the disorder, and in these individuals the condition can be diagnosed only by laboratory testing. People with dihydropyrimidinase deficiency, including those who otherwise exhibit no symptoms, may be vulnerable to severe, potentially life-threatening toxic reactions to fluoropyrimidines. These drugs may not be broken down efficiently and can build up to toxic levels in the body (fluoropyrimidine toxicity), leading to drug reactions including gastrointestinal problems, blood abnormalities, and other signs and symptoms.

The *DPYS* gene mutations that cause dihydropyrimidinase deficiency greatly reduce or

eliminate dihydropyrimidinase enzyme function. As a result, the enzyme is unable to begin the breakdown of 5,6-dihydrothymine and 5,6-dihydrouracil. Excessive amounts of these molecules accumulate in the blood and in the fluid that surrounds and protects the brain and spinal cord (the cerebrospinal fluid or CSF) and are released in the urine.

The relationship between the inability to break down 5,6-dihydrothymine and 5,6-dihydrouracil and the specific features of dihydropyrimidinase deficiency is unclear. Failure to complete this step in the breakdown of pyrimidines also impedes the final step of the process, which produces beta-aminoisobutyric acid and beta-alanine. Reduced production of these molecules may impair their function in the nervous system, leading to neurological problems in some people with dihydropyrimidinase deficiency. Because fluoropyrimidine drugs are broken down by the same three-step process as pyrimidines, deficiency of the dihydropyrimidinase enzyme can lead to the drug buildup that causes fluoropyrimidine toxicity.

It is unknown why some people with dihydropyrimidinase deficiency do not develop health problems related to the condition; other genetic and environmental factors likely help determine the effects of this disorder.

Other Names for This Gene

- DHP
- DHPase
- dihydropyrimidine amidohydrolase
- hydantoinase

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of DPYS ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1807\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1807[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28DPYS%5BTIAB%5D%29+OR+%28dihydropyrimidinase%5BTIAB%5D%29%29+OR+%28%28DHP%5BTIAB%5D%29+OR+%28DHPase%5BTIAB%5D%29+OR+%28hydantoinase%5BTIAB%5D%29+OR+%28dihydropyrimidine+amidohydrolase%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D%29>)

Catalog of Genes and Diseases from OMIM

- DIHYDROPYRIMIDINASE; DPYS (<https://omim.org/entry/613326>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/1807>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=DPYS\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=DPYS[gene]))

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Genomic Location

The *DPYS* gene is found on chromosome 8 (<https://medlineplus.gov/genetics/chromosome/8/>).

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