

CYP2C9 gene

cytochrome P450 family 2 subfamily C member 9

Normal Function

The *CYP2C9* gene provides instructions for making an enzyme that is found in a cell structure called the endoplasmic reticulum, which is involved in protein processing and transport. The *CYP2C9* enzyme breaks down (metabolizes) compounds including steroid hormones and fatty acids. The *CYP2C9* enzyme also plays a major role in breaking down the drug warfarin, which thins the blood and prevents blood clots from forming. This enzyme also assists in metabolizing other drugs such as ibuprofen, which reduces inflammation.

Health Conditions Related to Genetic Changes

Warfarin sensitivity

Certain common *CYP2C9* gene variations (polymorphisms) have been associated with warfarin sensitivity, a condition in which individuals require lower doses of the drug warfarin than are usually prescribed. Warfarin is an anticoagulant, which means that it thins the blood, preventing blood clots from forming.

The *CYP2C9* gene polymorphisms associated with warfarin sensitivity change single protein building blocks (amino acids) in the *CYP2C9* enzyme. The altered enzyme slows the breakdown (metabolism) of warfarin, allowing the drug to remain active in the body for a longer period of time. People with warfarin sensitivity take longer than usual to metabolize warfarin and may require lower doses of the drug than are usually prescribed.

The two most common *CYP2C9* polymorphisms in people of European ancestry are known as *CYP2C9*2* and *CYP2C9*3*. Both of these polymorphisms lead to a decrease in warfarin metabolism to such degrees that prescription doses are typically reduced by one-third and one-fifth, respectively. In individuals with African ancestry, the four most common *CYP2C9* polymorphisms associated with warfarin sensitivity are known as *CYP2C9*5*, *CYP2C9*6*, *CYP2C9*8*, and *CYP2C9*11*. These polymorphisms lead to a decrease in warfarin metabolism that would necessitate a reduction in prescription doses by one-third to one-sixth. In other populations, the effects of these polymorphisms are less certain but are an active area of research.

In rare cases in which individuals have more than one *CYP2C9* polymorphisms, the enzyme activity is severely decreased and metabolism of warfarin is very slow. If people with warfarin sensitivity take the average dose (or more) of warfarin, they are at risk of an overdose, which can cause abnormal bleeding in the brain, gastrointestinal tract, or other tissues, and may lead to serious health problems or death.

Other Names for This Gene

- CYP11C9
- cytochrome P-450MP
- cytochrome P450 2C9
- cytochrome P450 MP-4
- cytochrome P450 MP-8
- cytochrome P450 PB-1
- cytochrome P450, family 2, subfamily C, polypeptide 9
- cytochrome P450, family 2, subfamily C, polypeptide 9 gene
- P450 MP-4
- S-mephenytoin 4-hydroxylase
- S-mephenytoin 4-hydroxylase, human
- warfarin-7-hydroxylase, human

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of CYP2C9 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1559\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1559[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28CYP2C9%5BTI%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+720+days%22%5Bdp%5D>)

Catalog of Genes and Diseases from OMIM

- CYTOCHROME P450, SUBFAMILY IIC, POLYPEPTIDE 9; CYP2C9 (<https://omim.org/entry/601130>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/1559>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=CYP2C9\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=CYP2C9[gene]))

References

- Ferder NS, Eby CS, Deych E, Harris JK, Ridker PM, Milligan PE, Goldhaber SZ, King CR, Giri T, McLeod HL, Glynn RJ, Gage BF. Ability of VKORC1 and CYP2C9 to predict therapeutic warfarin dose during the initial weeks of therapy. *J Thromb Haemost*. 2010 Jan;8(1):95-100. doi: 10.1111/j.1538-7836.2009.03677.x. Epub 2009 Oct 30. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19874474>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3718044/>)
- Flockhart DA, O'Kane D, Williams MS, Watson MS, Flockhart DA, Gage B, Gandolfi R, King R, Lyon E, Nussbaum R, O'Kane D, Schulman K, Veenstra D, Williams MS, Watson MS; ACMG Working Group on Pharmacogenetic Testing of CYP2C9, VKORC1 Alleles for Warfarin Use. Pharmacogenetic testing of CYP2C9 and VKORC1 alleles for warfarin. *Genet Med*. 2008 Feb;10(2):139-50. doi:10.1097/GIM.0b013e318163c35f. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18281922>)
- Moyer TP, O'Kane DJ, Baudhuin LM, Wiley CL, Fortini A, Fisher PK, Dupras DM, Chaudhry R, Thapa P, Zinsmeister AR, Heit JA. Warfarin sensitivity genotyping: a review of the literature and summary of patient experience. *Mayo Clin Proc*. 2009 Dec;84(12):1079-94. doi: 10.4065/mcp.2009.0278. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19955245>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2787394/>)
- Perera MA, Cavallari LH, Limdi NA, Gamazon ER, Konkashbaev A, Daneshjou R, Pluzhnikov A, Crawford DC, Wang J, Liu N, Tatonetti N, Bourgeois S, Takahashi H, Bradford Y, Burkley BM, Desnick RJ, Halperin JL, Khalifa SI, Langae TY, Lubitz SA, Nutescu EA, Oetjens M, Shahin MH, Patel SR, Sagreiya H, Tector M, Weck KE, Rieder MJ, Scott SA, Wu AH, Burmester JK, Wadelius M, Deloukas P, Wagner MJ, Mushiroda T, Kubo M, Roden DM, Cox NJ, Altman RB, Klein TE, Nakamura Y, Johnson JA. Genetic variants associated with warfarin dose in African-American individuals: a genome-wide association study. *Lancet*. 2013 Aug 31;382(9894):790-6. doi: 10.1016/S0140-6736(13)60681-9. Epub 2013 Jun 5. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23755828>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3759580/>)
- van der Zee SA, Halperin JL. Anticoagulant therapy: warfarin sensitivity genotyping closer to clinical practice. *Nat Rev Cardiol*. 2010 Oct;7(10):549-50. doi: 10.1038/nrcardio.2010.126. No abstract available. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20865027>)

Genomic Location

The *CYP2C9* gene is found on chromosome 10 (<https://medlineplus.gov/genetics/chrom>)

osome/10/).

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