VKORC1 gene

vitamin K epoxide reductase complex subunit 1

Normal Function

The *VKORC1* gene provides instructions for making a vitamin K epoxide reductase enzyme. The VKORC1 enzyme is made primarily in the liver. It spans the membrane of a cellular structure called the endoplasmic reticulum, which is involved with protein processing and transport. The VKORC1 enzyme helps turn on (activate) clotting proteins in the pathway that forms blood clots. Specifically, the VKORC1 enzyme converts one form of vitamin K into a different form of vitamin K that assists in activating clotting proteins.

Health Conditions Related to Genetic Changes

warfarin resistance

Multiple variations (polymorphisms) in the *VKORC1* gene have been associated with warfarin resistance, a condition in which individuals require higher doses of the drug warfarin than are usually prescribed. Warfarin is a blood thinner, which means that it prevents blood clots from forming. It acts by attaching (binding) to the VKORC1 enzyme and preventing (inhibiting) the activation of the clotting proteins.

The most common *VKORC1* gene polymorphism in people with warfarin resistance changes a single protein building block (amino acid) in the VKORC1 enzyme. Specifically, the amino acid aspartic acid is replaced with the amino acid tyrosine at position 36 (written as Asp36Tyr or D36Y). This polymorphism leads to the formation of a VKORC1 enzyme with a decreased ability to bind to warfarin. As a result, more warfarin is needed to inhibit the VKORC1 enzyme and stop the clotting process. If people with warfarin resistance require treatment with warfarin and take the average dose, they will remain at risk of developing a potentially harmful blood clot.

warfarin sensitivity

Multiple polymorphisms in the *VKORC1* gene have been associated with warfarin sensitivity, a condition in which individuals require lower doses of the drug warfarin than are usually prescribed.

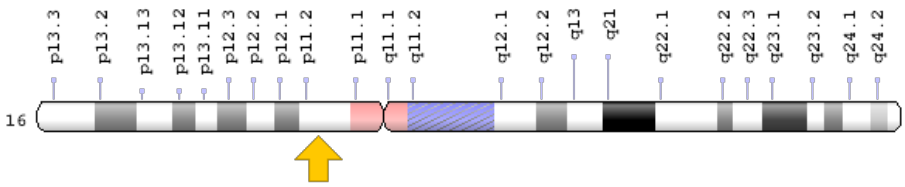
The most common *VKORC1* gene polymorphism in people with warfarin sensitivity, known as VKORC1A, changes a single DNA building block (nucleotide) in an area near the *VKORC1* gene, which controls the production of the complex. Specifically, the nucleotide guanine is replaced with the nucleotide adenine (written as -1639G>A). The VKORC1A polymorphism is particularly common in individuals

of Asian and European descent. The gene change causes less of the enzyme to be produced and reduces the amount of VKORC1 enzyme that is available to convert vitamin K into a form that can help activate clotting proteins. Because there is a decreased amount of VKORC1 enzyme, less warfarin is needed to inhibit the actions of the complex, resulting in warfarin sensitivity. 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.

Chromosomal Location

Cytogenetic Location: 16p11.2, which is the short (p) arm of chromosome 16 at position 11.2

Molecular Location: base pairs 31,090,842 to 31,094,999 on chromosome 16 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- FLJ00289
- vitamin K 1 2,3-epoxide reductase subunit 1
- vitamin K epoxide reductase complex, subunit 1
- VKOR

Additional Information & Resources

<u>Educational Resources</u>

- Biochemistry (fifth edition, 2002): Blood-Clotting Cascade https://www.ncbi.nlm.nih.gov/books/NBK22589/figure/A1401/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28VKORC1%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+1080+days%22%5Bdp%5D

OMIM

- VITAMIN K EPOXIDE REDUCTASE COMPLEX, SUBUNIT 1
  http://omim.org/entry/608547

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_VKORC1.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=VKORC1%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=23663
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/79001
- UniProt
  http://www.uniprot.org/uniprot/Q9BQB6

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