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 an anticoagulant, which means that it thins the blood and prevents blood clots from forming. It acts by attaching (binding) to the VKORC1 enzyme and blocking (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, a higher dose of warfarin is needed to inhibit the VKORC1 enzyme and stop the clotting process. If people with warfarin resistance require anticoagulant treatment and take the average warfarin dose (or less), 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 enzyme. 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. This change reduces the amount of VKORC1 enzyme that is available to convert vitamin K into a form that can activate clotting proteins. Because there is a decreased amount of VKORC1 enzyme, a lower dose of warfarin is needed to inhibit the actions of the enzyme, resulting in warfarin sensitivity. If people with warfarin sensitivity take the average warfarin dose (or more), 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

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

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of VKORC1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=79001[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?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)

Catalog of Genes and Diseases from OMIM

- VITAMIN K EPOXIDE REDUCTASE COMPLEX, SUBUNIT 1; VKORC1 (https://omim.org/entry/608547)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/79001)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=VKORC1[gene])

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Genomic Location

The *VKORC1* gene is found on chromosome 16 (https://medlineplus.gov/genetics/chromosome/16/).

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