# The Presence of Cytochrome P450 Enzyme 4F2 in the Indian-American Population

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## Background

Pharmacogenomics is the study of how a person's genes influence their response to medications. Genetic variation from person to person can lead to differences in how individuals react to their medications. Cytochrome P450 enzymes have been the focus of pharmacogenomics research for the past several years and have led to advances in drug dosing and monitoring. CYP4F2 specifically has been linked to reduced efficacy of warfarin, leading to sub therapeutic effects and an increased risk of clotting. This clotting can then cause pulmonary embolisms, deep vein thrombosis, and strokes. Specifically CYP4F2 has several variants including *1, *2, and *3. Allele frequencies may differ in various populations. Two large meta-analyses, one on Han Chinese and the other on European ancestry, provide the best estimates for the influence data of CYP4F2*3 on warfarin dose requirements. They suggest statistically significant but modest impacts of 8–11% higher warfarin doses.[1] Looking at various populations including the Indian-American population can be beneficial for identifying variants in CYP4F2 and potential dosing guideline recommendations.

## Potential Impact

Patients can sometimes have a hard time getting to their correct dose of medications, put simply, the Goldie Locks effect. Too little medication and they are not seeing clinical benefit. Too much medication and they see side effects, some of which can be life threatening. For warfarin specifically, too little medication and they can form clots, but too much medication and they can bleed out, both of which can become life threatening situations. There are many factors than can influence the effects of warfarin such as diet and exercise. However, a main factor that influences warfarin concentration is genomics, specifically CYP4F2 and VKORC1, among others. Pharmacogenomics may help prescribers provide an appropriate therapeutic regimen based on a patient's genes and individual variants. Simply put, instead of a guess and check until the patient meets goal INR, we'd be more confident to know what dose to give.

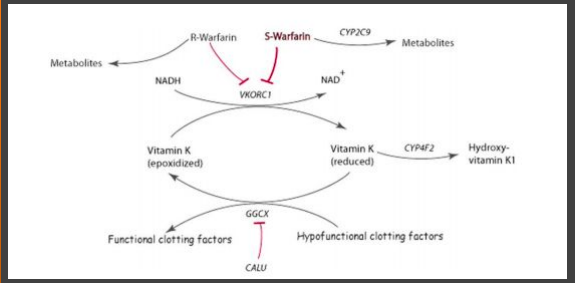


Figure 1: Warfarin MOA

Figure 2: CYP4F2 Allele Sequencing

| GENE:CYP4F2 | | |
|---|---|---|
| Nucleotide change per gene from http://www.cypalleles.ki.se/cyp4f2.htm | 34T>G | 1297G>A |
| Effect on protein (NP_001073.3) | W12G | V433M |
| Position at NC_000019.10 (Homo sapiens chromosome 19, GRCh38.p2) | g.15897578A>C | g.15879621C>T |
| Position at NG_007971.2 (CYP4F2 RefSeqGene; reverse relative to chromosome) | g.5497T>G | g.23454G>A |
| rsID | rs3093105 | rs2108622 |
| CYP4F2 Allele | | |
| *1 | A | C |
| *2 | C | |
| *3 | | T |

## Application

Future studies investigating potential differences in allele frequencies between populations can help provide better therapeutic decisions for individuals. Understanding these differences can lead to better patient-specific dosing and less possibility of subtherapeutic or supratherapeutic effects on the patient. This may in turn lead to less clotting and less bleed risk for patients on warfarin. A limitation to a large scale study as described above would be cost. Genomic testing is not quite at the affordable level as to allow such large scale testing yet, but cost has been steadily decreasing over the past few years, and with the advances of at-home testing, has gained popularity which could help drive the price down even further.

## REFERENCES

1. Johnson JA, Caudle KE, Gong L, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for Pharmacogenetics-Guided Warfarin Dosing: 2017 Update. CPIC. 2017 Sept; 102(3):397-404.

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