Hematology
Coumadin Treatment
Warfarin Panel: CYP2C9 and VKORC1

The US Food and Drug Administration has mandated changes in the labeling for coumadin that suggest the evaluation of common gene polymorphisms prior to, or in combination with, starting coumadin treatment.

Gene variations that affect the metabolism of coumadin by the liver, as well as the efficacy of a required activating enzyme, have been shown to affect the dose of coumadin required to achieve the target INR in individuals.

The UT Genetics Center Molecular Laboratory offers mutation analysis for both genes identified as contributing to the dosage variation of coumadin.

Possible Test Results

CYP2C9: *1 allele; normal drug metabolism
*2 and *3 alleles: decreased rate of drug metabolism

VKORC1: G allele; normal amount of active enzyme
A allele; decreased amount of active enzyme

Hypercoagulation

Genetic factors contribute to the hypercoagulatory state in a significant percentage of patients. The most common known mutation is in Factor V (Leiden type) while less common gene mutations in Factor II and plasminogen activator inhibitor (PAI) also contribute to the risk for DVT and other coagulation complications. Mutations in the MTHFR gene may also contribute to vascular disease due to the production of increased levels of homocysteine.

Laboratory testing for these common gene variants is available through the UT Genetics Center Molecular Laboratory.

- **Factor V**
- **Factor II**
- **Plasminogen Activator Inhibitor**
- **MTHFR**

The UT Genetics Center laboratories are directed by experienced medical professionals who are board certified by the American Board of Medical Genetics in the specialties of clinical cytogenetics, clinical molecular genetics and clinical biochemical genetics. Genetic counseling/consultation is provided by board certified or board eligible physicians and counselors.

The UT Genetics Center accepts all private and commercial insurance plans, Medicare, and TennCare insurance. Payment in cash or by credit card is also accepted. The Genetics Center participates in the Knoxville Academy of Medicine sponsored program for uninsured patients, and recognizes eligibility evaluations of area hospitals and clinics for sliding scale payments.

Contact the UT Genetics Center Laboratories at 865-305-9449 for information on specific test offerings, specimen requirements, and pick up/delivery options.

The University of Tennessee Genetics Center is supported by:
Tennessee Division of Mental Retardation Services
Tennessee Department of Health
Service Fees and Donations

The University of Tennessee Genetics Laboratories are CLIA licensed and the individual laboratories are directed by board certified clinical genetic specialists.

Genetics Center Laboratories

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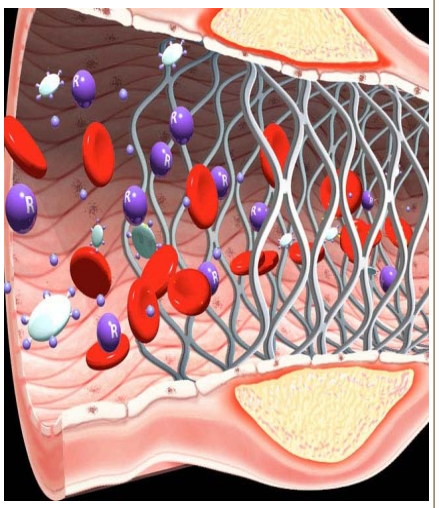
Genetics Center Laboratories

Personalized Anticoagulant Medicine: Predicting the Effectiveness of Treatment Based on Genetic Variants



University of Tennessee Genetics Center Laboratories

Phone: 865-305-9449

How can genetic variants affect Plavix effectiveness?

CYP450 2C19 what is it?

Plavix (clopidogrel) is activated in the body by the CYP4502C19 enzyme and works as an anticoagulant by inhibiting the receptor responsible for physiological activation of the platelet. The Plavix Mutation Panel Test analyzes a patient's DNA for variations in the *CYP4502C19 gene*. In 2009 the Federal Drug Administration approved wording on the drug label encouraging genetic testing for DNA variants based on the following risks:

- Compared to other patients, individuals with these variants are noted to *have an approximate **30% decrease** in active metabolite in plasma*
- Approximately 30% of the US population will carry at least one variant allele at the CYP2C19 locus .
- Patients who have at least one *CYP2C19* variant can experience adverse reactions including serious or life-threatening vascular events when given the usual Plavix dose.
- Compared to other individuals, patients with these variants have an *approximate **50% increase** in risk of stroke, myocardial infarction or death*.
- Compared to other individuals with stent placements, patients with these variants have an *approximate **3 fold increase risk** of stent thrombosis.*

Specimen Submission Requirements

- Collect 5 ml blood from adult
- EDTA anticoagulant tube
- Store at room temperature or refrigerate
- Ship at room temperature
- Receipt by the laboratory within 72 hours of collection

Turn around time: 48-72 hours

The University of Tennessee Genetics Center Laboratories provides pick up services for the Knoxville area, and specimens from offices outside the pick up area can be mailed to the laboratory (see address on reverse side).

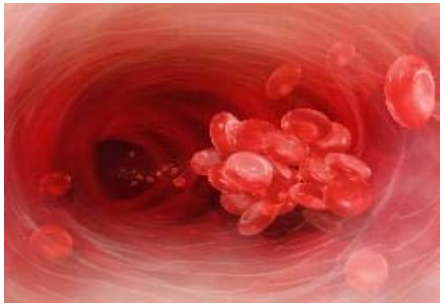
Possible Test Results

CYP4502C19

***1: designates the allele type that provides the expected drug activation**

***2 and *3: designate alleles that result in decreased rate of drug activation**

Patients may have any mix of two alleles such as *1/*1 or *1/*3, or *3/*3, or *2/*1 etc.



At this time there is insufficient information in the literature to indicate what is a fully effective dose of Plavix in patients with one or more variant alleles. Physicians may wish to monitor platelet aggregation characteristics after changes in dosage, or use other drugs or drug combinations to treat patients who do not respond optimally to Plavix due to the presence of variant CYP4502C19 alleles.