Test Definition: 2C9GV
CYP2C9 Genotyping Test

Overview

Useful For
Identifying individuals who may be at risk for altered metabolism of drugs that are modified by CYP2C9

Special Instructions
- Informed Consent for Genetic Testing
- Pharmacogenomic Associations Tables
- Multiple Genotype Test List
- Informed Consent for Genetic Testing (Spanish)

Method Name
Real-Time Polymerase Chain Reaction (PCR) with Allelic Discrimination Analysis

NY State Available
Yes

Specimen

Specimen Type
Varies

Advisory Information
If patient is or will be using warfarin, the preferred test is WARSV / Warfarin Response Genotype, which includes testing of CYP2C9, VKORC1, CYP4A2, and rs12777823.

Testing is available as the single gene assay (this test) or as a part of a focused pharmacogenomics panel, which includes testing for the following genes: CYPs 1A2, 2C9, 2C19, 2D6, 3A4, 3A5, 4F2, SLCO1B1, and VKORC1. Order PGXFP / Focused Pharmacogenomics Panel if multiple pharmacogenomic genotype testing is desired.

Specimen Required
Multiple genotype tests can be performed on a single specimen after a single extraction. See Multiple Genotype Test List in Special Instructions for a list of tests that can be ordered together.

Submit only 1 of the following specimens:

Specimen Type: Whole blood

Container/Tube: Lavender top (EDTA)

Specimen Volume: 3 mL

Collection Instructions:
1. Invert several times to mix blood.
2. Send specimen in original tube.

Specimen Stability Information: Ambient (preferred) 9 days/Refrigerated 30 days
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Specimen Type: Saliva

Patient Preparation: Patient should not eat, drink smoke, or chew gum 30 minutes prior to collection.

Supplies: Saliva Swab Collection Kit (T786)

Specimen Volume: 1 swab

Collection Instructions: Collect and send specimen per kit instructions.

Specimen Stability Information: Ambient 30 days

Specimen Type: DNA

Container/Tube: 2 mL screw top tube

Specimen Volume: 100mcL (microliters)

Collection Instructions:

1. The preferred volume is 100 mcL at a concentration of 50 ng/mcL.

2. Include concentration and volume on tube.

Specimen Stability Information: Frozen (preferred)/Ambient/Refrigerated

Forms

1. New York Clients-Informed consent is required. Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

   - Informed Consent for Genetic Testing (T576)
   - Informed Consent for Genetic Testing-Spanish (T826)

2. If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

   - Neurology Specialty Testing Client Test Request (T732)
   - Therapeutics Test Request (T831)

Specimen Minimum Volume

Blood: 0.4 mL
Saliva: 1 swab

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information
Clinical and Interpretive

Clinical Information

Primary metabolism of many drugs is performed by the cytochrome P450 (CYP450) enzymes, a group of oxidative/dealkylating enzymes localized in the microsomes of many tissues, but primarily in the intestines and liver. One of these CYP450 enzymes, CYP2C9, participates in the metabolism of a wide variety of drugs including warfarin and phenytoin.

CYP2C9-mediated drug metabolism is variable among individuals. Some individuals have CYP2C9 genetic variants that lead to severely diminished or absent CYP2C9 catalytic activity (ie, poor metabolizers). These individuals may metabolize various drugs at a slower rate than normal and may require dosing adjustments to prevent adverse drug reactions.

A number of specific CYP2C9 variants have been identified that result in enzymatic deficiencies. The following information outlines the relationship between the variants detected in the assay and their effect on enzyme activity:

<table>
<thead>
<tr>
<th>CYP2C9 Allele</th>
<th>cDNA Nucleotide Change</th>
<th>Effect on Enzyme Metabolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>*1</td>
<td>None (wild type)</td>
<td>Normal activity</td>
</tr>
<tr>
<td>*2</td>
<td>430C-&gt;T</td>
<td>Reduced activity</td>
</tr>
<tr>
<td>*3</td>
<td>1075A-&gt;C</td>
<td>No activity</td>
</tr>
<tr>
<td>*4</td>
<td>1076T-&gt;C</td>
<td>Reduced activity</td>
</tr>
<tr>
<td>*5</td>
<td>1080C-&gt;G</td>
<td>Reduced activity</td>
</tr>
<tr>
<td>*6</td>
<td>818delA</td>
<td>No activity</td>
</tr>
<tr>
<td>*8</td>
<td>449G-&gt;A</td>
<td>Substrate specific</td>
</tr>
<tr>
<td>*9</td>
<td>752A-&gt;G</td>
<td>Reduced activity</td>
</tr>
<tr>
<td>*11</td>
<td>1003C-&gt;T</td>
<td>Reduced activity</td>
</tr>
<tr>
<td>*12</td>
<td>1465C-&gt;T</td>
<td>Reduced activity</td>
</tr>
<tr>
<td>*13</td>
<td>269C-&gt;T</td>
<td>Minimal activity</td>
</tr>
<tr>
<td>*14</td>
<td>374G-&gt;A</td>
<td>Minimal activity</td>
</tr>
<tr>
<td>*15</td>
<td>485C-&gt;A</td>
<td>No activity</td>
</tr>
<tr>
<td>*16</td>
<td>895A-&gt;G</td>
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<td>*17</td>
<td>1144C-&gt;T</td>
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</tr>
<tr>
<td>*18</td>
<td>1190A-&gt;C</td>
<td>No activity</td>
</tr>
<tr>
<td>*25</td>
<td>353_362del</td>
<td>No activity</td>
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<tr>
<td>*26</td>
<td>389C-&gt;G</td>
<td>Minimal activity</td>
</tr>
<tr>
<td>*28</td>
<td>641A-&gt;T</td>
<td>Minimal activity</td>
</tr>
<tr>
<td>*30</td>
<td>1429G-&gt;A</td>
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<table>
<thead>
<tr>
<th>Allele</th>
<th>Description</th>
<th>Activity</th>
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<tr>
<td>*33</td>
<td>395G-&gt;A</td>
<td>Minimal activity</td>
</tr>
<tr>
<td>*35</td>
<td>374G-&gt;T + 430C-&gt;T</td>
<td>No activity</td>
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</table>

CYP2C9 drug metabolism is dependent on the specific genotype detected, and also on the number and type of drugs administered to the patient. Individuals without a detectable CYP2C9 variant will have the predicted phenotype of an extensive drug metabolizer and are designated as CYP2C9 *1/*1. If an individual is homozygous or compound heterozygous for an allele with no activity, the individual is predicted to be a poor metabolizer. If an individual is heterozygous for an allele with no activity, the individual is predicted to be an intermediate metabolizer. In some cases, a range of potential phenotypes may be given, depending on the combination of alleles identified.

Patients who are poor metabolizers may benefit from dose alteration or selection of a comparable drug that is not primarily metabolized by CYP2C9. It is important to interpret the results of testing in the context of other coadministered drugs.

**Reference Values**

An interpretive report will be provided.

**Interpretation**

An interpretive report will be provided.

The genotype, with associated star alleles, is assigned using standard allelic nomenclature as published by the Pharmacogene Variation (PharmVar) Consortium.(1)

For additional information regarding pharmacogenomic genes and their associated drugs, see Pharmacogenomic Associations Tables in Special Instructions. This resource also includes information regarding enzyme inhibitors and inducers, as well as potential alternate drug choices.

Drug-drug interactions and drug/metabolite inhibition must be considered in the case of all metabolizer categories except poor metabolizer.

It is important to interpret the results of testing and dose adjustments in the context of hepatic and renal function and patient age.

**Cautions**

Rare variants may be present that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings (phenotype), additional testing should be considered.

Samples may contain donor DNA if obtained from patients who received heterologous blood transfusions or allogeneic blood or marrow transplantation. Results from samples obtained under these circumstances may not accurately reflect the recipient's genotype. For individuals who have received blood transfusions, the genotype usually reverts to that of the recipient within 6 weeks. For individuals who have received allogeneic blood or marrow transplantation, a pretransplant DNA specimen is recommended for testing.

CYP2C9 genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's CYP2C9 status.

This method may not detect all variants that result in altered CYP2C9 activity. Therefore, absence of a detectable variant does not rule out the possibility that a patient has altered CYP2C9 metabolism due to other CYP2C9 variants that cannot be detected with this method. Furthermore, when 2 or more variants are identified, the cis-/trans- status...
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(whether the variants are on the same or opposite chromosomes) is not always known.

**Clinical Reference**


**Performance**

**Method Description**
Genomic DNA is extracted from whole blood or saliva. Genotyping for the CYP2C9 alleles is performed using a PCR-based 5’-nuclease assay. Fluorescently labeled detection probes anneal to the target DNA. PCR is used to amplify the section of DNA that contains the variant. If the detection probe is an exact match to the target DNA, the 5’-nuclease polymerase degrades the probe, the reporter dye is released from the effects of the quencher dye, and a fluorescent signal is detected. Genotypes are assigned based on the allele-specific fluorescent signals that are detected. (User Guide: TaqMan SNP Genotyping Assay, Applied Biosystems Revision A.0 January 2014)

**PDF Report**
No

**Day(s) and Time(s) Test Performed**
Monday through Friday; 8 a.m.

**Analytic Time**
3 days (Not reported Saturday or Sunday)

**Maximum Laboratory Time**
8 days

**Specimen Retention Time**
Whole Blood/Saliva swab: 2 weeks Extracted DNA: 2 months

**Performing Laboratory Location**
Rochester

**Fees and Codes**

**Fees**
- Authorized users can sign in to Test Prices for detailed fee information.
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- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
81227

LOINC® Information

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