MAYO CLINIC LABORATORIES

NEW TEST

Notification Date: May 10, 2021
Effective Date: June 10, 2021

Cytochrome P450 *2D6* Comprehensive Cascade, Varies

Test ID: 2D6Q

Useful for:

Providing information relevant to tamoxifen, codeine, and tramadol, as well as other medications metabolized by cytochrome P450 2D6

Determining the exact genotype when other methods fail to generate this information or if genotype-phenotype discord is encountered clinically

Identifying precise genotype when required (eg, drug trials, research protocols)

Identifying novel variants that may interfere with drug metabolism (when reflex to sequencing is performed)

Genetics Information:

Testing is done in 2 tiers when needed. Tier 1 uses a PCR-based 5'-nuclease assay to determine the variants present. All samples also have copy number determined by PCR-based 5'-nuclease assay. Testing in tier 1 allows for the detection of all common *CYP2D6* variants (eg, *2, *3, *4, *5, *6, *7, *8, *9, *10, *17, *29, *35, *41) and rarer alleles such as *11, *12, *14, *15, and *114. Duplications and multiplications of alleles are also identified. Unitary and tandem *CYP2D7-2D6* (*13) alleles and *CYP2D6-2D7* (eg, *4N, *36, and *68) alleles can also be detected. Tier 2 testing involves sequencing using fluorescent dye-terminator chemistry and is only done if tier 1 testing results are ambiguous. Approximately 3% of samples require tier 2 testing.

Testing Algorithm:

Tier 2 testing will be performed only if an ambiguous phenotype is identified by tier 1 testing. The number of sequencing tests needed to determine the phenotype will vary depending on the tier 1 result

Reflex Tests:

Test ID	Reporting Name	Available Separately	Always Performed
2D61Z	CYP2D6 Full Gene Sequence	No (Bill Only)	No
2D62Z	CYP2D6 GEN CYP2D6-2D7 Hybrid	No (Bill Only)	No
2D63Z	CYP2D6 GEN CYP2D7-2D6 Hybrid	No (Bill Only)	No
2D64Z	CYP2D6 Nonduplicated Gene	No (Bill Only)	No
2D65Z	CYP2D6 5' Gene DUP/MLT	No (Bill Only)	No
2D66Z	CYP2D6 3' Gene DUP/MLT	No (Bill Only)	No

Methods:

Tier 1: Real Time Polymerase Chain Reaction (PCR)
Tier 2: Polymerase Chain Reaction (PCR) followed by DNA Sequence Analysis

Advisory Information:

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This test is not for use in assessing for autoimmune hepatitis. Autoantibodies for the CYP2D6 enzyme are found in many cases of autoimmune hepatitis; order LKM / Liver/Kidney Microsome Type 1 Antibodies, Serum for autoimmune hepatitis assessment.

Testing is available as the single gene assay (this test) and as a part of a psychotropic or focused pharmacogenomics panel.

If multiple pharmacogenomic genotype testing is desired, order PGXQP / Focused Pharmacogenomics Panel, Varies.

If genotype testing for psychotropic medications is desired, order PSYQP / Psychotropic Pharmacogenomics Gene Panel, Varies.

Reference Values:

An interpretive report will be provided.

Specimen Stability Information:

Specimen Type	Temperature	Time
Varies	Varies	

Specimen Requirements:

Multiple genotype tests can be performed on a single specimen after a single extraction.

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

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.
Additional Information: Due to lower concentration of DNA yielded from saliva, testing cannot proceed to tier 2 sequencing and will stop after tier 1 testing is complete.
Specimen Stability Information: Ambient 30 days

Specimen Type: DNA
Container/Tube: 2 mL screw top tube
Specimen Volume: 100 mcL (microliters)
Collection Instructions:
1. The preferred volume is 100 mcL at a concentration of 75 ng/mcL.
2. Include concentration and volume on tube.
Specimen Stability Information: Frozen (preferred)/Ambient/Refrigerated

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.

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Samples may contain donor DNA if obtained from patients who received non-leukoreduced blood transfusions or allogeneic hematopoietic stem cell 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 hematopoietic stem cell transplantation, a pretransplant DNA specimen is recommended for testing.

CYP2D6 genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's CYP2D6 status.

This method may not detect all *CYP2D6* variants that result in altered CYP2D6 activity. Therefore, absence of a detectable variant does not rule out the possibility that a patient has altered CYP2D6 metabolism due to other *CYP2D6* variants that cannot be detected with this method. Furthermore, when 2 or more variants are identified, the cis-/trans- status (whether the variants are on the same or opposite chromosomes) is not always known.

A complicating factor in correlating *CYP2D6* genotype with phenotype is that many drugs or their metabolites are inhibitors of CYP2D6 catalytic activity. Selective-serotonin reuptake inhibitors (SSRI), as well as some tricyclic antidepressants (TCA) and other drugs, may reduce CYP2D6 catalytic activity. Patients in all metabolizer categories, except poor metabolizer, may have CYP2D6 enzyme activity inhibited by a variety of medications or their metabolites. Consequently, an individual may require a lower medication dose than predicted by genotyping alone. It is important to interpret the results of testing in the context of other coadministered drugs.

CYP2D6 alleles with decreased function may metabolize different drugs at different rates, ranging from normal to poor, but the literature on this is incomplete at this time.

This test is not designed to provide specific dosing or drug selection recommendations and is to be used as an aid to clinical decision making only. Drug-label guidance should be used when dosing patients with medications regardless of the predicted phenotype.

CPT Code:
0070U
0071U-0076U (if appropriate)

Day(s) Setup: Monday through Friday **Analytic Time:** 3 days

Questions

Contact your Laboratory Technologist Resource Coordinator Heather Flynn Gilmer at 800-533-1710.

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