MAYO CLINIC LABORATORIES

1-800-533-1710

2D6Q

Cytochrome P450 2D6 Comprehensive Cascade, Varies

Patient ID	Patient Name		Birth Date	Sex	Age
SA00175246	TESTINGRNV, 2D6Q NORMAL		2005-06-06	M	19
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00175246	SA00175246	CLIENT,CLIENT			
Account Information		**Collected**			
C7028846 DLMP Rochester		15 Apr 2025 00:00			

Results

Analyte	Result	Performing Site
CYP2D6 Genotype	*1/*1	MCR
CYP2D6 Phenotype	Normal (extensive) metabolizer	MCR
CYP2D6 Activity Score	2.00	MCR

Interpretation

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Prodrugs are converted to their active metabolite at a normal rate and drugs that are inactivated by CYP2D6 are metabolized at a normal rate.

For tamoxifen: Individuals with this phenotype are expected to reach a therapeutic concentration of the active metabolite, endoxifen. However, CYP2D6 inhibitors should be avoided.

For codeine and tramadol: Codeine is converted to morphine and tramadol is converted to O-desmethyltramadol at a normal rate and good analgesia is expected.

Method

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Genotyping is performed using a PCR-based 5'-nuclease assay. Fluorescently labeled detection probes anneal to the target DNA. PCR is used to amplify the segment of DNA that contains the polymorphism. 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. (TaqMan SNP Genotyping Assays User Guide, Applied Biosystems)

Disclaimer

1 MCR

A two-tiered testing approach was used to identify CYP2D6 variants (including copy number variants). Tier 1 (always performed) consists of targeted variant analysis and a test for copy number variation (CNV) using CYP2D6-specific probes for the promoter, intron 6, and exon 9. Detectable CNVs include duplications, multiplications and deletions (*5) of CYP2D6, as well as CYP2D6::CYP2D7 (i.e. *4N, *36, *68) and CYP2D7::CYP2D6 (i.e. *13) hybrid genes. Tier 2, which is only performed when the phenotype in Tier 1 is ambiguous, consists of comprehensive Sanger sequencing of the CYP2D6 gene and/or CYP2D7::CYP2D6 and CYP2D6::CYP2D7 hybrid genes. If a result from Tier 1 requires additional testing to derive the phenotype, then the sample is reflexed to Tier 2 sequencing. If a result requires no additional testing to derive the phenotype, then testing is stopped and Tier 2 sequencing is not performed.

This assay is designed to detect CYP2D6 (NM_000106.4) *2, *3, *4, *4N, *5, *6, *7, *8, *9, *10, *11, *12, *13, *14,*15, *17, *29, *35, *36, *41, *59, *68, *114, and CYP2D6 gene duplication. Detectable CNVs include duplications, multiplications, and deletions (*5) of CYP2D6, as well as CYP2D6::CYP2D7 (i.e. *4N, *36, *68) and CYP2D7::CYP2D6 (i.e. *13) hybrid genes. Additional CYP2D6 variants may be detected through the cascade testing process. When rare variants are reported, cDNA nomenclature is based on NM_000106.4 and the GRCh37 genome build.

Targeted DNA testing, the CNV detection assay, and Sanger sequencing will not detect all variants that result in decreased or

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MCR	Mayo Clinic Laboratories - Rochester Main Campus	200 First Street SW, Rochester, MN 55905	Nikola Baumann Ph.D.	24D0404292

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increased CYP2D6 enzyme activity. If no detectable CYP2D6 variant is found, a presumed *1 allele is assigned. Absence of a detectable CYP2D6 variant does not rule out the possibility that a patient has altered CYP2D6 activity. CYP2D6 enzyme activity may be inhibited by a variety of medications, or their metabolites.

Based on the test sensitivity and currently available CYP2D6 variant carrier frequencies, individuals of European descent have an approximately 1 percent risk of having an undetected variant which would impact the predicted phenotype if the full CYP2D6 cascade test is done. This risk may be higher or lower in other ancestral groups.

CAUTIONS:

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

The methods used to genotype CYP2D6 may not identify all inactive alleles or the precise configuration of alleles on a patient's chromosomes; therefore, this lab will report the most likely diplotype based upon reported or observed frequencies. Note that this ambiguity does not impact the predicted phenotype and can be clarified by family studies, if desired.

Samples may contain donor DNA if obtained from patients who have recently 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 pre-transplant 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.

Reviewed by MCR

Ann Marie Moyer, M.D., Ph.D.

Received: 15 Apr 2025 10:48 **Reported:** 16 Apr 2025 17:34

Laboratory Notes

1 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.

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