CYP2D6

Last Literature Review: January 2025 Last Update: December 2025

The cytochrome P450 (CYP) isozyme 2D6 is involved in the metabolism of many drugs. Variants in the gene that code for this enzyme may influence pharmacokinetics of the respective medications, and therefore may predict or explain nonstandard dose requirements, therapeutic failure, or adverse reactions.

For more information on pharmacogenetic testing, refer to the ARUP Consult Germline Pharmacogenetics - PGx topic.

Featured ARUP Testing

CYP2D6 3001513

Method: Polymerase Chain Reaction (PCR)/Fluorescence Monitoring/Sequencing

Use to assess genetic variants contributing to risk of abnormal drug metabolism for drugs metabolized by CYP2D6 enzyme coded by the CYP2D6 gene. This test may aid in drug selection and dose planning for many drugs that are either activated or inactivated by CYP2D6 enzyme.

This is a single gene test for CYP2D6. CYP2D6 is also available in panel tests. For more information, refer to the Cytochrome P450 Genotyping and Pharmacogenetics Panel for Psychotropics Test Fact Sheets.

Disease Overview

Treatment Issues

- The actual metabolic phenotype of a drug-metabolizing enzyme is subject to drug-drug interactions, clinical factors, and other nongenetic factors.
- Therapeutic drug monitoring and/or metabolic ratios may be useful for evaluating the pharmacokinetics of a particular drug for a particular patient.
- The Clinical Pharmacogenetics Implementation Consortium (CPIC)[1] and the Food and Drug Administration (FDA)[2] have published clinical associations and dosing guidelines involving *CYP* genotypes.

Genetics

Genes

CYP2D6

Inheritance

Autosomal codominant

Variants Tested

Variants or groups of variants, classified as star (*) alleles, are associated with predicted enzyme function, based on international consensus nomenclature. However, not all variants on a chromosome/allele are interrogated and assumptions about phase are made, as shown below. More details about nomenclature, allele frequencies, and phenotype predictions are available at PharmVar[3] or ClinPGx.[4]

Gene (Transcript)	Alleles	Predicted Allele Function
CYP2D6 **(M33388 sequence)**	*CYP2D6*2*: rs16947, g.2850C>T; rs1135840, g.4180G>C	Functional
	*CYP2D6*2A*: rs1080985, g.-1584C>G; rs16947, g.2850C>T; rs1135840, g.4180G>C	Functional
	*CYP2D6*3*: rs35742686, g.2549delA	No function
	*CYP2D6*4*: rs1065852, g.100C>T; rs3892097, g.1846G>A; rs1135840, g.4180G>C	No function
	*CYP2D6*5*: gene deletion	No function
	*CYP2D6*6*: rs5030655, g.1707delT	No function

Gene (Transcript)	Alleles	Predicted Allele Function
	*CYP2D6*7*: rs5030867, g.2935A>C	No function
	*CYP2D6*8*: rs5030865, g.1758G>T; rs16947, g.2850C>T; rs1135840, g.4180G>C	No function
	*CYP2D6*9*: rs5030656, g.2615_2617delAAG	Decreased function
	*CYP2D6*10*: rs1065852, g.100C>T; rs1135840, g.4180G>C	Decreased function
	*CYP2D6*11*: rs1080985, g.-1584C>G; rs201377835, g.883G>C; rs16947, g.2850C>T; rs1135840, g.4180G>C	No function
	*CYP2D6*13*: a CYP2D7-derived exon 1 conversion	No function
	*CYP2D6*14*: rs5030865, g.1758G>A; rs16947, g.2850C>T; rs1135840, g.4180G>C	Decreased function
	*CYP2D6*15*: rs774671100, g.137_138insT	No function
	*CYP2D6*17*: rs28371706, g.1023C>T; rs16947, g.2850C>T; rs1135840, g.4180G>C	Decreased function
	*CYP2D6*29*: rs16947, g.2850C>T; rs59421388, g.3183G>A; rs1135840, g.4180G>C	Decreased function
	*CYP2D6*31:* rs267608319, g.4042G>A; rs16947, g.2850C>T; rs1135840, g.4180G>C	No function
	*CYP2D6*35*: rs1080985, g.-1584C>G; rs769258, g.31G>A; rs16947, g.2850C>T; rs1135840, g.4180G>C	Functional
	*CYP2D6*36*: a CYP2D6*10 carrying a CYP2D7-derived exon 9 conversion	No function
	*CYP2D6*36-*10*: a *CYP2D6*36* and a *CYP2D6*10* in tandem	Decreased function
	*CYP2D6*40*: rs28371706, g.1023C>T; rs72549356, g.1863_1864insTTTCGCCCCTTTCGCCCC; rs16947, g.2850C>T; rs1135840, g.4180G>C	No function
	*CYP2D6*41*: rs16947, g.2850C>T; rs28371725, g.2988G>A; rs1135840, g.4180G>C	Decreased function
	*CYP2D6*42*: rs16947, g.2850C>T; rs72549346, g.3260_3261insTG; rs1135840, g.4180G>C	No function
	*CYP2D6*49*: rs1065852, g.100C>T; rs1135822, g.1611T>A; rs1135840, g.4180G>C	Decreased function
	*CYP2D6*56:* rs72549347, g.3201C>T; rs1135840, g.4180G>C	No function
	*CYP2D6*59:* rs79292917, g.2939G>A; rs16947, g.2850C>T; rs1135840, g.4180G>C	Decreased function
	*CYP2D6*69*: rs1065852, g.100C>T; rs16947, g.2850C>T; rs28371725, g.2988G>A; rs1135840, g.4180G>C	No function
	*CYP2D6*114*: rs1065852, g.100C>T; rs5030865, g.1758G>A; rs16947, g.2850C>T; rs1135840, g.4180G>C	No function
	DUP: complete gene duplication	Varies based on the allele that is duplicated

Sources: PharmVar,[3] ClinPGx[4]

Results

Results are reported according to the Results Reported and Clinical Significance table:

- When appropriate, genetic variant(s) detected are reported as star (*) alleles. Detailed nomenclature for each allele is included in the report.
- The detected combination of alleles (diplotype) is used to predict the metabolizer phenotype and, for CYP2D6, the activity score. These are included in the report.
- Phenotype predictions are subject to change as the scientific and clinical evidence evolves.
- No variants detected is predictive of *1 functional alleles and is reported as “Negative” or “Normal.”
- Functional variants without clinical indication or impact on clinical management may not be reported.

Results Reported and Clinical Significance

CYP2D6 Genotype	Phenotype	Clinical Significance
*1/*1	Normal	Predicts normal CYP2D6 enzymatic activity and a normal metabolizer phenotype
Relevant allele combination	Poor	Predicts low or no CYP2D6 enzymatic activity and a poor metabolizer phenotype
Relevant allele combination	Intermediate	Predicts decreased CYP2D6 enzymatic activity and an intermediate metabolizer phenotype
Relevant allele combination	Ultrarapid	Predicts increased CYP2D6 enzymatic activity and an ultrarapid metabolizer phenotype

Limitations

- Only the targeted genetic variants will be detected by this panel. Assumptions about phase and content are made to assign alleles.
- Diagnostic errors can occur due to rare sequence variations.
- A combination of the *CYP2D6*5* (gene deletion) and a *CYP2D6* gene duplication cannot be specifically identified; however, this combination is not expected to adversely affect the phenotype prediction.
- The assay used to detect the *CYP2D6*40* allele cannot distinguish between insertions of one or two copies; it also cannot distinguish between heterozygous and homozygous mutant samples due to unavoidable cross-reactivity with the wild type sequence. Additional assays will be used to help differentiate the *CYP2D6*40* allele from other *CYP2D6* star alleles.
- Risk of therapeutic failure or adverse reactions with gene substrates may be affected by genetic and nongenetic factors that are not detected by this test.
- The test result does not replace the need for therapeutic drug or clinical monitoring.

References

1. CPIC. Guidelines. Stanford University, St. Jude Children's Research Hospital. Accessed Jun 2025.
2. U.S. Department of Health and Human Services, Food and Drug Administration. Table of pharmacogenetic associations. Updated May 2022; accessed Aug 2022.
3. Pharmacogene Variation Consortium. PharmVar. Updated Nov 2020; accessed Dec 2020.
4. ClinPGx. Accessed Nov 2024.

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