Cytochrome P450 Genotyping

Last Literature Review: September 2021 Last Update: March 2025

The cytochrome P450 (CYP) isozymes 2B6, 2C19, 2C8, 2C9, 2D6, 3A4, and 3A5 are involved in the metabolism of many drugs. Variants in the genes that code for these enzymes 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.

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.
  - Refer to the ARUP Laboratory Test Directory for a list of available drug-gene specific testing (search by test name or number).
- 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

CYP2B6, *CYP2C19*, *CYP2C8*, *CYP2C9*, *CYP2C* rs12777823, *CYP2D6*, *CYP3A4*, *CYP3A5*

Inheritance

Autosomal codominant

Variants Tested

Variants or groups of variants are classified as “star” (*) alleles, that 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 PharmGKB.[4]

Featured ARUP Testing

Cytochrome P450 Genotyping Panel 3001524

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

Use to assess genetic variants contributing to risk of abnormal drug metabolism for drugs metabolized by enzymes coded by *CYP2B6*, *CYP2C19*, *CYP2C8*, *CYP2C9*, *CYP2D6*, 2C cluster variant (rs12777823), *CYP3A4*, and *CYP3A5*. This test may aid in drug selection and dose planning for many drugs that are either activated or inactivated by one or more CYP450 enzymes.

Cytochrome P450 Genotyping Panel, with GeneDose Access 3004255

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The report may include comprehensive medication guidance based on the genotypes detected and access to GeneDose Live, a cloud-based medication management and risk mitigation tool.

Gene (Transcript)	Alleles	Predicted Allele Function
CYP2B6 (NM_000767)	*CYP2B6*4*: rs2279343, c.785A>G	Increased function
	*CYP2B6*6*: rs3745274, c.516G>T; rs2279343, c.785A>G	Decreased function
	*CYP2B6*7*: rs3745274, c.516G>T; rs2279343, c.785A>G; rs3211371, c.1459C>T	Decreased function
	*CYP2B6*9*: rs3745274, c.516G>T	Decreased function
	*CYP2B6*18*: rs28399499, c.983T>C	No function
	*CYP2B6*22*: rs34223104, c.-82T>C	Increased function
	*CYP2B6*36*: rs34223104, c.-82T>C; rs3745274, c.516G>T; rs2279343, c.785A>G	Decreased function
CYP2C19 (NM_000769)	*CYP2C19*2*: rs4244285, c.681G>A; rs12769205, c.332-23A>G	No function
	*CYP2C19*3*: rs4986893, c.636G>A	No function
	*CYP2C19*4A*: rs28399504, c.1A>G	No function
	*CYP2C19*4B*: rs28399504, c.1A>G; rs12248560, c.-806C>T	No function
	*CYP2C19*5*: rs56337013, c.1297C>T	No function
	*CYP2C19*6*: rs72552267, c.395G>A	No function
	*CYP2C19*7*: rs72558186, c.819+2T>A	No function
	*CYP2C19*8*: rs41291556, c.358T>C	No function
	*CYP2C19*9*: rs17884712, c.431G>A	Decreased function
	*CYP2C19*17*: rs12248560, c.-806C>T	Increased function
	*CYP2C19*35*: rs12769205, c.332-23A>G	No function
CYP2C8 (NM_000770)	*CYP2C8*2*: rs11572103, c.805A>T	Unassigned function
	*CYP2C8*3*: rs10509681, c.1196A>G	Unassigned function
	*CYP2C8*4*: rs1058930, c.792C>G	Unassigned function
CYP2C cluster	*CYP2C* cluster: rs12777823, g.96405502 G>A	Unclassified[a]
CYP2C9 (NM_000771)	*CYP2C9*2*: rs1799853, c.430C>T	Decreased function
	*CYP2C9*3*: rs1057910, c.1075A>C	No function
	*CYP2C9*4*: rs56165452, c.1076T>C	Decreased function
	*CYP2C9*5*: rs28371686, c.1080C>G	Decreased function
	*CYP2C9*6*: rs9332131, c.818delA	No function
	*CYP2C9*8*: rs7900194, c.449G>A	Decreased function
	*CYP2C9*11*: rs28371685, c.1003C>T	Decreased function
	*CYP2C9*12*: rs9332239, c.1465C>T	Decreased 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

Gene (Transcript)	Alleles	Predicted Allele 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
	*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
CYP3A4 (NM_017460)	*CYP3A4*22*: rs35599367, c.522-191C>T	Decreased function
CYP3A5 (NM_000777)	*CYP3A5*3*: rs776746, c.219-237A>G	No function
	*CYP3A5*6*: rs10264272, c.624G>A	No function
	*CYP3A5*7*: rs41303343, c.1035dupT	No function

Gene (Transcript)	Alleles	Predicted Allele Function

[a]The *CYP2C* cluster variant is associated with a decreased warfarin dose requirement in some people of African descent.

Sources: PharmVar,[3] PharmGKB[4]

Results

- Genetic variant(s) detected: alleles detected are reported. The combination of alleles detected or diplotype is used to predict metabolizer phenotype, and in the case of *CYP2D6*, the activity score. Phenotype predictions are subject to change as the scientific and clinical evidence evolves.
- Samples where *CYP2D6* copy number testing reveals a duplication and where there are two alleles of different activity scores, will be reflexed to LR-PCR for additional testing to reveal which allele is duplicated.
- No variants detected is predictive of **1* functional alleles.
- Functional variants without clinical indication or impact on clinical management may not be reported.

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. Clinical Pharmacogenetics Implementation Consortium. CPIC guidelines. Updated Mar 2021; accessed Oct 2021.

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. PharmGKB. Last updated 2024; accessed Nov 2024.

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