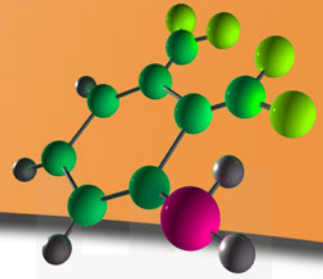




Affiliated with Saint Alphonsus and PAML

TEST UPDATE

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Quick Facts

- ▶ **Order Code: CYP2D6**
- ▶ **CYP2D6 is a highly polymorphic liver enzyme that metabolizes many commonly prescribed drugs.**
- ▶ **Some genetic variants in the *CYP2D6* gene can significantly alter its enzymatic function.**
- ▶ **Altered enzyme function can affect drug efficacy and can induce adverse drug reactions.**
- ▶ **About 5-10% of Caucasians have no CYP2D6 enzyme activity due to mutations in the gene.**
- ▶ **This assay can detect the majority of mutations responsible for the loss of enzyme activity.**

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Cytochrome P450 2D6 Genotyping

CLINICAL APPLICATION

Cytochrome P450 2D6 (*CYP2D6*) genotyping is useful for identifying individuals with altered *CYP2D6* enzyme activity, which increases the risk for reduced drug response and adverse drug reactions. In Caucasians, about 5% to 10% of the population has no *CYP2D6* enzyme activity (also known as poor metabolizers). These individuals are unlikely to achieve a therapeutic response when using drugs like Tamoxifen and Opioids; and may often experience drug-induced adverse reactions with some antidepressants or antipsychotics.

The FDA recommended adding a warning label to the package insert of Tamoxifen and Strattera, which require *CYP2D6* for their metabolism. This label warns of the implications of treating poor *CYP2D6* metabolizers with these drugs.

CLINICAL BACKGROUND

CYP2D6 is a highly polymorphic liver enzyme involved in the metabolism of many therapeutic drugs, including some antidepressants, antipsychotics, antiarrhythmics, antiemetics, b-adrenoceptor antagonists (b-blockers), opioids, and selective estrogen receptor modulators (Tamoxifen).

Genetic variation in the *CYP2D6* gene is common in most ethnic groups and can affect enzyme function and therapeutic response to the drugs it metabolizes. Certain variants completely abolish the enzymatic function of *CYP2D6*; other variants partially disrupt its activity. Therefore, four distinct groups of metabolizer (poor, intermediate, extensive, and ultrarapid) have been defined based on the combination of different alleles of the *CYP2D6* gene.

Genotyping of the *CYP2D6* gene is the most straightforward approach to identifying individuals who may experience adverse drug reactions with conventional doses of certain medications.

TECHNICAL INFORMATION

This assay detects 17 small nucleotide variants found within the *CYP2D6* gene, along with gene rearrangements associated with deletion and duplication genotypes.

This mutation panel identifies about 95% of variants responsible for poor metabolism and has an analytical sensitivity and specificity close to 100%.

Mutation specific regions are PCR amplified from extracted genomic DNA for an allele specific primer extension (ASPE) reaction. Amplicon from the ASPE reaction are then hybridized into a liquid bead array to determine the patient's genotype.

TEST INFORMATION

CYTOCHROME P450 2D6 GENOTYPING	
DESCRIPTION	Cytochrome P450 2D6 Genotyping
METHOD	PCR, ALLELE SPECIFIC PRIMER EXTENSION, AND DETECTION BY LIQUID BEAD ARRAY.
ORDER CODE	CYP2D6
CPT CODE	83891, 83900, 83901X6, 83914X17, 83912, 83892
SPECIMEN REQUIREMENTS	Whole blood (1 mL minimum, 3 mL preferred) in EDTA, sodium citrate, or ACD tube.
RANGES	NORMAL, POOR METABOLIZER

Selected References

1. Cascorbi I. Pharmacogenetic of cytochrome P4502D6: genetic background and clinical implication. Eur J Clin Invest. 2003;33(Suppl.2):17-22
2. Ingelman-Sundberg M. Genetic polymorphisms of cytochrome P450 2D6 (CYP2D6): clinical consequences, evolutionary aspects and functional diversity. Pharmacogenomics J. 2005;5:6-13
3. Neafsey P, Ginsberg G, Hattis D, and Sonawane B. Genetic polymorphism in cytochrome P450 2D6 (CYP2D6): Population distribution of CYP2D6 activity. J Toxicol Environ Health B Crit Rev. 2009;12:334-361
4. Zhou S. Polymorphism of human cytochrome P450 2D6 and its clinical significance, part I. Clin Pharmacokinet. 2009;48(11):689-723

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