Opioid CYP2D6 Genotyping

2D6 Genotype: *1/*1
2D6 Metabolic Activity: Normal

Cytochrome P450 2D6 is an enzyme involved in the metabolism of many drugs including opioid analgesics such as codeine, hydrocodone, dihydrocodeine, oxycodone, and tramadol. Codeine is O-demethylated to its more active form morphine by CYP2D6 encoded enzymes. Variation in the CYP2D6 gene can result in ultrarapid (UM), normal (EM), intermediate to normal (IM-EM), intermediate (IM) and poor metabolizer (PM) phenotypes.

Ultrarapid metabolizers may experience exaggerated or even potentially dangerous opioid side effects after codeine administration including euphoria, dizziness, epigastric pain, and/or visual disturbance. Duplication of the CYP2D6 gene can cause gene amplification, increased CYP2D6 metabolic activity (ultrarapid metabolizer), and excessive plasma morphine concentrations leading to potentially dangerous side effects. Not all phenotypic ultrarapid metabolizers can be accounted for by gene amplification. A number of other genetic and environmental factors may contribute to an ultrarapid metabolizer phenotype.

Normal metabolizers are anticipated to have normal enzyme activity. For CYP2D6, there is a range of enzyme activity within this category. The distinction between normal and intermediate metabolizer differs between publications and may differ depending on the drug in question.

Intermediate to normal metabolizers are anticipated to have a range of reduced to normal enzyme activity.

Intermediate metabolizers have reduced enzyme activity, and may experience some, or none, of the consequences similar to poor metabolizers.
For poor metabolizers, a reduced analgesic effect may be observed due to insufficient biotransformation of codeine to its more active form, morphine.

The metabolism of drugs is also influenced by race, ethnicity, diet, and other medications. All results must be interpreted in the context of other test results and clinical findings. This testing does not rule out the possibility of variant alleles in other drug metabolism pathways.

**CYP2D6 Information:**

Cytochrome P450 enzymes (including 2D6 and 2C19) are involved in the hepatic metabolism of a large percentage of clinically relevant drugs. Of all drugs, 25-30% are metabolized by CYP2D6.

**Methodology:**

DNA analysis of the Cytochrome P450 2D6 gene (OMIM 124030) is performed using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the variants below. Primer extension then generates a biotin-labeled product to permit flow-sorted detection of both normal and variant sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur.

**Alleles Detected:**

*1,*2,*3,*4,*5,*6,*7,*8,*9,*10,*11,*15,*17,*29,*35,*41, and gene duplications.

Variant *5 is a gene deletion. Copy number of duplicated alleles is not determined. Duplications are often functional (whole gene) but may be nonfunctional (partial gene). It is not always possible to determine which allele is duplicated.

*1 represents detection of the normal sequence for the variant sites tested. This assay does not detect other variants in the CYP2D6 gene that may affect metabolic activity. Copy number of duplicated alleles is not determined, and it is not always possible to determine which allele is duplicated.

**Buccal cells for CYP2D6:** This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

**References:**

TESTS | RESULT | FLAG | UNITS | REFERENCE INTERVAL |
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Director Review:
Annette K. Taylor, M.S., Ph.D., FACMG
Toni R. Prezant, Ph.D.
Samuel H. Pepkowitz, M.D., FAAP
Joseph B. Kearney, Ph.D., FACMG

For inquiries, the physician may contact Branch: 800-222-7566 Lab: 800-282-7300
General Comments & Additional Information
Clinical Info: ABNORMAL REPORT

Ordered Items
Opioid CYP2D6 Genotyping

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<th>REFERENCE INTERVAL</th>
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Interpretation:
Cytochrome P450 2D6 is an enzyme involved in the metabolism of many drugs including opioid analgesics such as codeine, hydrocodone, dihydrocodeine, oxycodone, and tramadol. Codeine is O-demethylated to its more active form morphine by CYP2D6 encoded enzymes. Variation in the CYP2D6 gene can result in ultrarapid (UM), normal (EM), intermediate to normal (IM-EM), intermediate (IM) and poor metabolizer (PM) phenotypes.

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