Cytochrome P450 3A5 (CYP3A5) Genotyping

Disease Overview

CYP3A5 is one of the genes in this super-family encoding enzymes that is responsible for the metabolism of many commonly used drugs.

Uses for Test

- Estimate the genetic risk of abnormal drug metabolism for drugs metabolized by CYP3A5.
- Identify genotypes shown to have a drug-gene variant relationship.
- Pharmacogenomic orders may be reviewed by a pharmacist for clinical appropriateness prior to test completion if clinical data is available.

Therapeutic Implications

To estimate genetic risk of abnormal drug metabolism for drugs metabolized by *CYP3A5*.

Therapeutic drug monitoring should also be used to guide dose adjustments. The actual metabolic phenotype is subject to drug/drug interactions, clinical factors, and other non-genetic factors.

Treatment Guidelines

The Clinical Pharmacogenetics Implementation Consortium (CPIC) has published dosing guidelines for *CYP3A5* genotypes: https://cpicpgx.org/

Test Interpretation

- Clinical sensitivity: drug dependent
- Analytical sensitivity/specificity: > 99%

Results

A detailed report is provided. This report is reviewed and signed out by a Laboratory Director. No mutations detected is predictive for *1 functional alleles.

Test Limitations

- Only the targeted *CYP3A5* variants will be detected.
- Diagnostic errors can occur due to rare sequence variations.
- Risk of therapeutic failure or adverse reactions with *CYP3A5* substrates may be affected by genetic and non-genetic factors that are not detected by this test.
- This result does not replace the need for therapeutic drug or clinical evaluation and monitoring.
- If the DNA is directly sent to the laboratory for analysis by an external laboratory, the Sanford Medical Genetics Laboratory takes no responsibility or liability for sample swaps or extraction errors occurring prior to receipt of the DNA sample by Sanford Medical Genetics Laboratory.

Related Tests

- Multiple genes can be involved in drug metabolism, drug activation and drug action on the target tissue. Additional genotyping tests are available for *CYP2D6, CYP2C9, VKORC1, SLCO1B1, TPMT, IFNL3, CYP4F2, CYP2C cluster, CYP2C19* and *DPYD* as individual tests or as a PGx Panel.
- The panel includes a comprehensive medication report based on the genotypes detected.
- Therapeutic drug monitoring and/or metabolic ratios may be useful for evaluating the pharmacokinetics of a particular drug, for a particular patient.

Sample Requirements

Collection

- Lavender-top tube (EDTA)
- All specimens should be sent in the original container and should not be aliquoted to another tube
- The specimen submitted should only be used for this testing and should not be shared with any other testing that would also utilize this specimen type

Specimen

- Whole Blood, preferred Volume: 2 mL to 4 mL (1mL minimum)

Stability

- Room temp – 72 hours
- Refrigerated – 7 days
- Frozen – 7 days
- Not affected by hemolysis
- Not affected by lipemia

Tests Involved

- CPT code: 81231
- Lab Test ID: LBOR0154

Test Schedule

- Set up Monday to Friday
- Turn Around Time: 5-7 days

Additional information

- These tests are available through the Sanford Imagenetics program. Contact Sanford Laboratories at (605) 328-5464 or (800) 522-2561 for questions regarding this testing.

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References

• Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for CYP3A5 genotypes and dosing, available along with the 2015 supplement and other relevant resources at www.pharmgkb.org • The human cytochrome P450 (CYP) allele nomenclature database, available at http://www.cypalleles.ki.se/ • Barratt DT, Bandak B, Klepstad P, et al. Genetic, pathological and physiological determinants of transdermal fentanyl pharmacokinetics in 620 cancer patients of the EPOS study. Pharmacogenet Genomics. 2014 Apr; 24(4):185-194. • Quaranta S, Chevalier D, Allorge D, Lo-Guidice JM, Migot-Nabias F, Kenani A, Imbenotte M, Broly F, Lacarelle B, Lhermitte M: Ethnic differences in the distribution of CYP3A5 gene polymorphisms. • MacPhee IA. Pharmacogenetic biomarkers: cytochrome P450 3A5. Clin Chim Acta. 2012;413:1312-1317 • Thervet E, Loriot MA, Barbier S, et al: Optimization of initial tacrolimus dose using pharmacogenetic testing. Clin PharmacolTher 2010;87:721-726 • Tucker G. Advances in understanding drug metabolism and its contribution to variability in patients' response. Ther Drug Monitor. 2000;22:110-113. • Jannetto PJ, Bratanow NC. Pain management in the 21st century: utilization of pharmacogenomics and therapeutic drug monitoring. Expert Opin Drug Metab Toxicol. 2011;7:745-752. • Shapiro LE, Shear NH. Drug interactions: Proteins, pumps, and P-450s. J Am Acad Dermatol. 2002;47:467-484. • Lewis DF. 57 varieties: The human cytochromes P450. Pharmacogenomics. 2004;5:305-318. • Zanger UM, Turpeinen M, Klein K, et al. Functional pharmacogenetics/genomics of human cytochromes P450 involved in drug biotransformation. Anal Bioanal Chem. 2008;392:1093-1108. • Ozdemir V, Kalowa W, Tang BK, et al. Evaluation of the genetic component of variability in CYP3A4 activity: a repeated drug administration method. Pharmacogenetics. 2000;10:373-388. • Garsa AA, McLeod HL, Marsh S. CYP3A4 and CYP3A5 genotyping by pyrosequencing. BMC Med Genet. 2005;6:19. doi: 10.1186/1471-2350-6-19. • Lee SJ, Goldstein JA. Functionally defective or altered CYP3A4 and CYP3A5 single nucleotide polymorphisms and their detection with genotyping tests. Pharmacogenomics. 2005;6(4):357-371.

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