Overview

Useful For

Individualizing selection and dosage of medications prescribed for treatment of depression and other psychiatric disorders based on genetic variation

Identifying genetic variation in genes known to be associated with response and/or risk of toxicity with psychotropic medications

Evaluating patients who have failed therapy with selective serotonin reuptake inhibitors (SSRIs)

Evaluating patients with treatment-resistant depression

Predicting response time to improvement with SSRIs

Genetics Test Information

This test includes targeted testing to evaluate the following genes: *ANKK1, ADRA2, CHRNA3, COMT, CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, DRD2, EPHX1, GRIK4, HLA-A*31:01, HLA-B*15:02, HTR2A, HTR2C, MTHFR, OPRM1, SCN1A, SLC6A4 (5-HTT), UGT2B15.*

CYP2D6 testing is done in 2 tiers when needed. Tier 1 uses a PCR-based 5'-nuclease assay to determine the variants present. All samples also have copy number determined by PCR-based 5'-nuclease assay. Testing in tier 1 allows for the detection of all common *CYP2D6* variants (eg, **2, *3, *4, *5, *6, *7, *8, *9, *10, *17, *29, *35, *41*) and rarer alleles such as **11*, **12, *14A, *14B*, and **15*. Duplications and multiplications of alleles are also identified. Unitary and tandem *CYP2D7-2D6* (**13*) alleles and *CYP2D6-2D7* (eg, **4N*, **36*, and **68*) alleles can also be detected. Tier 2 testing involves sequencing using fluorescent dye-terminator chemistry and is only done if an ambiguous phenotype results from tier 1 testing. Approximately 3% of samples require tier 2 testing.

Reflex Tests

Test ID	Reporting Name	Available Separately	Always Performed
2D6S1	CYP2D6 FULL GENE SEQUENCE	No, (Bill Only)	No
2D6S2	CYP2D6 GEN CYP2D6-2D7 HYBRID	No, (Bill Only)	No
2D6S3	CYP2D6 GEN CYP2D7-2D6 HYBRID	No, (Bill Only)	No
2D6S4	CYP2D6 NONDUPLICATED GENE	No, (Bill Only)	No
2D6S5	CYP2D6 5' GENE DUP/MLT	No, (Bill Only)	No
2D6S6	CYP2D6 3' GENE DUP/MLT	No, (Bill Only)	No

Testing Algorithm

If a specimen requires follow-up for *CYP2D6*, then reflex testing will be performed as appropriate at an additional

charge.

See CYP2D6 Comprehensive Cascade Testing Algorithm in Special Instructions.

Special Instructions

- Informed Consent for Genetic Testing
- CYP2D6 Comprehensive Cascade Testing Algorithm
- Pharmacogenomic Associations Tables
- Informed Consent for Genetic Testing (Spanish)

Method Name

Real-Time Polymerase Chain Reaction (RT-PCR) with Allelic Discrimination Analysis

Qualitative Allele-Specific Real-Time Polymerase Chain Reaction (PCR)

PCR Followed by Sizing Analysis

NY State Available

Yes

Specimen

Specimen Type

Varies

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Whole blood

Container/Tube: Lavender top (EDTA)

Specimen Volume: 3 mL

Collection Instructions:

1. Invert several times to mix blood.

2. Send specimen in original tube.

Specimen Stability Information: Ambient (preferred) 9 days/Refrigerated 30 days

Specimen Type: Saliva

Patient Preparation: Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.

Supplies: Saliva Swab Collection Kit (T786)

Specimen Volume: 1 swab

Collection Instructions: Collect and send specimen per kit instructions.

Specimen Stability Information: Ambient 30 days

Additional Information: Due to lower concentration of DNA yielded from saliva, testing cannot proceed to reflex testing for CYP2D6 sequencing and will stop after initial testing is complete.

Specimen Type: DNA

Container/Tube: 2 mL screw top tube

Specimen Volume: 100 mcL (microliters)

Collection Instructions:

1. The preferred volume is 100 mcL at a concentration of 50 ng/mcL.

2. Include concentration and volume on tube.

Specimen Stability Information: Frozen (preferred) 1 year/Ambient/Refrigerated

Forms

New York Clients-Informed consent is required. Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

-Informed Consent for Genetic Testing (T576)

-Informed Consent for Genetic Testing-Spanish (T826)

Specimen Minimum Volume

Blood: 1 mL
Saliva: 1 swab

Reject Due To

Hemolysis	NA
Lipemia	NA
Icterus	NA
Other	NA

Specimen Stability Information

Specimen Type	Temperature	Time
Varies	Varies	

Clinical and Interpretive

Clinical Information

This panel provides a comprehensive analysis for multiple genes that have strong pharmacogenomic associations with medications used in the treatment of psychiatric disorders, including depression. Each sample is tested for specific variations with known functional impact. Pharmacogenomic data for the following specific variants are reviewed and reported (if present):

-*ADRA2A* rs1800544

-*ANKK1* (*DRD2* associated) rs1800497

-*CHRNA3* rs1051730

-*COMT* rs4680

-*CYP1A2* *1F, *1K, *6, and *7

-*CYP2B6* *4, *5, *6, *7, *8, *9, *11, *12, *13, *14, *15, *16, *18, *19, *20, *21, *22, *23, *25, *26, *27, *28, *35, *36, and *38

-*CYP2C9* *2, *3, *4, *5, *6, *8, *9, *11, *12, *13, *14, *15, *16, *17, *18, *25, *26, *28, *30, *33, and *35

-*CYP2C19* *2, *3, *4, *5, *6, *7, *8, *9, *10, *17, and *35

-*CYP2D6* *2, *2A, *3, *4, *4N, *5, *6, *7, *8, *9, *10, *11, *12, *13, *14A, *14B,*15, *17, *29, *35, *36, *41, *68, and *CYP2D6* gene duplication; additional *CYP2D6* variants may be detected through the reflex testing process

-*CYP3A4* *8, *11, *12, *13, *16, *17, *18, *22, and *26

-*CYP3A5* *3, *5, *6, *7, *8, and *9

-*DRD2* rs1799978

-*EPHX1* rs2234922

-*GRIK4* rs1954787

-*HLA-A*31:01*

-*HLA-B*15:02*

-*HTR2A* rs7997012

-*HTR2C* rs3813929 and rs1414334

-*MTHFR* rs1801131 and rs1801133

-*OPRM1* rs1799971

-*SCN1A* rs3812718

-*SLC6A4* linked polymorphic region (LPR), a 44-base pair promoter insertion/deletion polymorphism

-*UGT2B15* rs1902023

Based on the results of each assay, a genotype is assigned and a phenotype is predicted for each gene. Assessment of multiple genes may assist the ordering clinician with personalized drug recommendations, avoidance of adverse drug reactions, and optimization of drug treatment.

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided that focuses on medications and genes with published pharmacogenomic practice guidance by the Clinical Pharmacogenetics Implementation Consortium or other professional organizations, where strong FDA guidance has been issued in drug labels, or where peer-reviewed literature strongly suggests that assessment of pharmacogenomic variants may enhance patient care.

For additional information regarding pharmacogenomic genes and their associated medications, see Pharmacogenomic Associations Tables in Special Instructions. This resource also includes information regarding enzyme inhibitors and inducers, as well as potential alternate drug choices.

Cautions

Samples may contain donor DNA if obtained from patients who received heterologous blood transfusions or allogeneic hematopoietic stem cell transplantation. Results from samples obtained under these circumstances may not accurately reflect the recipient's genotype. For individuals who have received blood transfusions, the genotype usually reverts to that of the recipient within 6 weeks. For individuals who have received allogeneic hematopoietic stem cell transplantation, a pretransplant DNA specimen is recommended for testing.

Genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's genetic status for the genes on this panel.

This test is not designed to provide specific dosing recommendations and is to be used as an aid to clinical decision making only. Drug-label guidance should be used when dosing patients with medications regardless of the predicted phenotype.

For additional information, see the following test IDs:

1A2V / Cytochrome P450 *1A2* Genotype, Varies

2C9GV / Cytochrome P450 *2C9* Genotype, Varies

2C19V / Cytochrome P450 *2C19* Genotype, Varies

2D6CV / Cytochrome P450 2D6 (*CYP2D6*) Comprehensive Cascade, Varies

3A4V / Cytochrome P450 *3A4* Genotype, Varies

3A5V / *CYP3A5* Genotype, Varies

CARPB / Carbamazepine Hypersensitivity Pharmacogenomics, Blood

COMTV / Catechol-O-Methyltransferase (COMT) Genotype, Varies

HTR2V / Serotonin Receptor Genotype (*HTR2A* and *HTR2C*), Varies

HTT / Serotonin Transporter Genotype, Blood

Clinical Reference

1. Pharmacogene Variation Consortium database. Accessed September 2018. Available at https://www.pharmvar.org/

2. Clinical Pharmacogenetics Implementation Consortium website. Accessed September 2018. Available at https://cpicpgx.org/

3. DAILYMED. U.S National Library of Medicine listing of FDA approved drug labels. Accessed September 2018. Available at: https://dailymed.nlm.nih.gov/dailymed/index.cfm

4. Hicks JK, Sangkuhl K, Swen JJ, et al: Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther 2017 Jul;102(1):37-44

5. Bradley P, Shiekh M, Mehra V, et al: Improved efficacy with targeted pharmacogenetic-guided treatment of patients with depression and anxiety: A randomized clinical trial demonstrating clinical utility. J Psychiatr Res 2018;96:100-107

6. Brennan FX, Gardner KR, Lombard J, et al: A Naturalistic Study of the Effectiveness of Pharmacogenetic Testing to Guide Treatment in Psychiatric Patients With Mood and Anxiety Disorders. Prim Care Companion CNS Disord 2015 April 16;17(2)

7. Perez V, Salavert A, Espadaler J, et al: Efficacy of prospective pharmacogenetic testing in the treatment of major depressive disorder: results of a randomized, double-blind clinical trial. BMC Psychiatry 2017 Jul 14;17:250

8. Reynolds GP, McGowan OO, Dalton CF: Pharmacogenomics in psychiatry: the relevance of receptor and transporter polymorphisms. Br J Clin Pharmacol 2013;77(4):654-672

Performance

Method Description

Genomic DNA is extracted from the sample.

Genotyping for the following genes is performed using a PCR-based 5'-nuclease assay. Fluorescently labeled detection probes anneal to the target DNA: *ANKK1*, *ADRA2, CHRNA3, COMT, CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, DRD2, EPHX1, GRIK4, HTR2A, HTR2C, MTHFR, OPRM1, SCN1A,* and *UGT2B15.* PCR is used to amplify the section of DNA that contains the variant. If the detection probe is an exact match to the target DNA, the 5'-nuclease polymerase degrades the probe, the reporter dye is released from the effects of the quencher dye, and a fluorescent signal is detected. Genotypes are assigned based on the allele-specific fluorescent signals that are detected.(Instruction manual: TaqMan SNP Genotyping Assay, Applied Biosystems Revision A.0 January 2014)

Amplification for the *HLA-B*15:02* and *HLA-A*31:01* alleles and an internal control gene is performed by real-time PCR in the presence of SYBR Green, which fluoresces when bound to double-stranded DNA. A genotype is assigned based on the allele-specific SYBR Green fluorescent signals that are detected.(Unpublished Mayo method)

SLC6A4 is performed utilizing PCR amplification of the region surrounding the polymorphism followed by size separation of the products.(Lesch KP, Bengel D, Heils A, et al: Association of anxiety-related traits with a polymorphism in the serotonin transporter gene regulatory region. Science 1996;274:1527-1530)

CYP2D6 Copy Number Assay:

This assay utilizes a duplex real-time PCR, which includes 1 copy number probe and a reference assay per reaction. Each copy number probe detects the genomic sequence of interest and the reference assay detects a sequence that is known to be present in 2 copies in a diploid genome. Relative quantitation is used to determine the relative copy number of the target of interest in a genomic DNA (gDNA) sample normalized to10 ng/mcL for each probe. Each probe is normalized to the known copy number of the reference sequence, and compared to a calibrator sample with known copies of the target sequence included with each run.(Package insert: Taqman Copy Number Assays Revision B, Applied Biosystems, Carlsbad, CA)

2D6 Sequencing Assays (Tier 2, as needed):

The *CYP2D6* allele of interest is amplified by PCR. The PCR product is then purified and sequenced in both directions using fluorescent dye-terminator chemistry. Sequencing products are separated on an automated sequencer and trace files analyzed for variations in the exons and intron/exon boundaries of all 9 exons using mutation detection software and visual inspection.(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Thursday; 8 a.m.

Analytic Time

3 days (not reported Saturday or Sunday)

Maximum Laboratory Time

14 days

Specimen Retention Time

Whole Blood/Saliva Swab: 2 weeks; Extracted DNA: 2 months

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

81479

81226

81225

81227

81230

81231

81291

81381 x 2

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
PSYGP	Psychotropic PGx Panel	In Process

Result ID	Test Result Name	Result LOINC Value
602687	ADRA2A rs1800544 Genotype	In Process
602707	ANKK1 rs1800497 Genotype	In Process
602689	CHRNA3 rs1051730 Genotype	In Process
602691	COMT rs4680 Genotype	74511-7
602692	CYP1A2 Genotype	72884-0
602693	CYP1A2 Phenotype	In Process
602694	CYP2B6 Genotype	72511-9
602695	CYP2B6 Phenotype	79720-9
602696	CYP2C19 Genotype	57132-3
602697	CYP2C19 Phenotype	79714-2
602698	CYP2C9 Genotype	46724-1
602699	CYP2C9 Phenotype	79716-7
602700	CYP2D6 Genotype	40425-1
602701	CYP2D6 Phenotype	79715-9
602702	CYP3A4 Genotype	81139-8
602703	CYP3A4 Phenotype	In Process
602704	CYP3A5 Genotype	81140-6
602705	CYP3A5 Phenotype	79717-5
602706	DRD2 rs1799978 Genotype	In Process
602708	EPHX1 rs2234922 Genotype	In Process
602709	GRIK4 rs1954787 Genotype	In Process
602776	HLA-A*31:01 Genotype	79712-6
602777	HLA-B*15:02 Genotype	57979-7
602710	HTR2A rs7997012 Genotype	93190-7

Result ID	Test Result Name	Result LOINC Value
602711	HTR2C rs3813929 Genotype	75732-8
602712	HTR2C rs1414334 Genotype	93192-3
602713	MTHFR Genotype	38415-6
602715	OPRM1 rs1799971 Genotype	In Process
602716	SCN1A rs3812718 Genotype	41765-9
602779	SLC6A4 5HTTLPR Genotype	50330-0
602717	UGT2B15 rs1902023 Genotype	72881-6
602718	Interpretation	69047-9
602719	Additional Information	48767-8
602720	Method	85069-3
602721	Disclaimer	62364-5
602722	Reviewed by	18771-6