Test Definition: HIVPR

HIV-1 Genotypic PR-RT Resistance, P

Overview

Useful For

Identification of genotypic variants associated with viral resistance to HIV-1 nucleotide reverse-transcriptase inhibitors, non-nucleotide reverse-transcriptase inhibitors, and protease inhibitors

Guiding initiation or change of combination antiretroviral therapy in individuals, including children, living with HIV

Testing Algorithm

SeeHIV Treatment Monitoring Algorithmin Special Instructions

Special Instructions

- HIV Treatment Monitoring Algorithm

Method Name

Reverse Transcription Polymerase Chain Reaction (RT-PCR), followed by DNA Sequencing

NY State Available

Yes

Specimen

Specimen Type

Plasma EDTA

Ordering Guidance

This test is intended for monitoring known HIV-positive infections. For primary detection of HIV infections, order HVCOP / HIV-1 and HIV-2 Antigen and Antibody Routine Screen, Plasma.

Shipping Instructions

If shipment will be delayed for more than 24 hours, freeze plasma specimen at -70 degrees C (up to 35 days) until shipment on dry ice.

Specimen Required

Collection Container/Tube: Lavender top (EDTA)

Submission Container/Tube: Plastic vial

Specimen Volume: 2.2 mL

Collection Instructions: Centrifuge and transfer plasma into plastic vial per collection tube manufacturer's instructions (eg, centrifuge and aliquot within 2 hours of collection for BD Vacutainer tubes)

Additional Information: Specimens submitted for HIV-1 genotyping should contain 500 copies/mL or more of HIV-1 RNA.

Specimen Minimum Volume

1.2 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma EDTA	Frozen (preferred)	35 days	ALIQUOT TUBE
	Refrigerated	5 days	ALIQUOT TUBE

Clinical and Interpretive

Clinical Information

Antiviral resistance may compromise highly active antiretroviral therapy (HAART) in HIV-infected patients receiving HAART. When combination therapy fails, detection and analysis of HIV genotypic variants can guide necessary changes to antiretroviral therapy and decrease HIV viral load, thereby improving patient outcome.

HIV-1 is an RNA virus that infects cells and is then converted to complementary DNA (cDNA) by the action of the viral reverse transcriptase (RT) gene product. RT has little proofreading capacity and therefore, incorporates errors in the proviral DNA. These errors are transcribed into infectious viral particles when the proviral DNA is transcribed into RNA. Similarly, the enzyme protease catalyzes a polyprotein to produce peptides necessary for active viral replication. Although HAART (combination of nucleoside analog, nonnucleoside agent and/or protease inhibitor) may be effective in reducing the viral load, genotypic variants arising in the drug-targeted HIV gene loci due to selective pressure from antiviral therapy result in antiviral resistance that may compromise such therapy.

Amplification and analysis of drug-targeted HIV-gene sequence allows identification of changes in nucleotide bases and associated amino acid codons that may cause antiviral drug resistance. Such genotypic changes are deemed as variants by comparing the sequence data of the patient's HIV strain to those of a wild-type HIV strain. The significance of these genotypic variants in relation to antiviral resistance is then determined by a set of interpretive rules developed by a consensus panel of leading experts in the field of HIV resistance. Relevant data presented at a recognized scientific conference or published in peer-reviewed journals are considered by the consensus panel in developing these rules. When necessary, reliable unpublished drug resistance data known to consensus panel members may be considered in the process. The interpretive rules are updated by the consensus panel annually after reviewing newly published data on HIV-1 genotypic drug resistance variants.

Reference Values

Not applicable

Interpretation

Detectable HIV-1 genotypic variants conferring resistance to an antiviral drug are reported as amino acid codon changes (eg, M184V) resulting from the alterations, according to the interpretative algorithm of the Stanford HIV Database program. Genotypic variant codons are categorized and interpreted in relation to previously performed phenotypic antiviral susceptibility tests. Each variant is assigned a drug penalty score and the total score generated from all of the variants relevant to the specific antiviral drug is used to estimate the level of resistance to that drug. These interpretive rules may be updated periodically by the Stanford HIV Database Team after reviewing newly published data on HIV-1 genotypic drug resistance variants.

Susceptible (SUSC) indicates that the genotypic variants present in patient's HIV-1 strain have not been associated with resistance to the specific drug (Stanford HIVdb total score 0 to 9).

Potential Low-Level Resistance (PLR) indicates that genotypic variants detected have been associated with possible reduction in susceptibility to the specific drug (Stanford HIVdb score 10 to 14).

Low-Level Resistance (LR) indicates that genotypic variants detected have been associated with reduction in susceptibility to the specific drug (Stanford HIVdb score 15 to 29).

Intermediate Resistance (IR) indicates that genotypic variants detected have been associated with reduction in susceptibility to the specific drug (Stanford HIVdb score 30 to 59).

High-level Resistant (HR) indicates that genotypic variants detected have been associated with maximum reduction in susceptibility to the specific drug (Stanford HIVdb > or = 60).

Unable to genotype indicates that the sequence data obtained are of poor quality to determine the presence or absence of genotypic resistant variants in the patient's HIV strain. Probable causes of such poor sequence data include polymorphism in the region of the sequencing primers interfering with primer binding and subsequent sequencing reaction, or low viral load (ie, <500 copies/mL).

Inconclusive indicates inability of the assay to reliably determine antiviral resistance because of the presence of PCR inhibitors or ambiguous or incomplete viral target sequences generated from the assay.

Cautions

Due to the complexity of the results generated, the International AIDS Society-USA Panel recommends expert interpretation of genotyping and phenotype test results for patient care management. A patient's response to antiviral therapy depends on multiple factors, including the percentage of patient's viral populations that is drug resistant, patient compliance with the prescribed drug therapy, patient access to adequate care, drug pharmacokinetics, and drug interactions. Drug resistance test results should be interpreted only in conjunction with clinical presentation and other laboratory markers when making therapeutic decisions.

Absence of resistance to a drug does not rule out the presence of reservoirs of drug-resistant virus in the infected patient.

The HIV-1 genotypic test is not a direct measure of drug resistance. Although genotypic testing can detect variants in the relevant HIV-1 genome, the significance of these variants requires careful interpretation to predict drug susceptibility. This assay's ability to amplify the target and detect genotypic variants is poor and unreliable when the plasma HIV-1 viral load is less than 500 copies/mL. Specimens submitted for this test should contain greater or equal to 500 copies/mL of HIV-1 RNA.

This assay has been optimized for genotypic analysis and interpretation of HIV-1 group M subtype B, which are the majority of HIV-1 isolates infecting patients in the United States and Europe. The protease and reverse transcriptase gene regions examined in this assay are not well correlated with the envelope gene, which is the defining gene sequence used for subtyping. Other subtypes of group M HIV-1 have been tested and validated to a limited extent by this assay. Therefore, genotypic variants in groups N and O, and some group M non-B subtype HIV-1 isolates may or may not be detected using this assay, and it is not known whether drug resistance variant interpretation for group M subtype B isolates apply to these other groups and subtypes of HIV-1.

The list of drug resistance-associated genotypic variant codons and interpretive rules used by the Stanford HIV database are updated periodically by the Stanford HIV Database team. Therefore, the test results do not necessarily include all of the resistance-associated variant codons described in the current medical literature.

Possible causes of treatment failure other than the development of drug resistance are poor adherence to medication regimen, drug potency, and individual variation in pharmacokinetics (eg, inadequate phosphorylation of nucleosides).

Clinical Reference

1. Gunthard HF, Calvez V, Paredes R, et al: Human immunodeficiency virus drug resistance: 2018 Recommendations of the International Antiviral Society-USA Panel. Clin Infect Dis. 2019 Jan 7;68(2):177-187

2. Wensing AM, Calvez V, Ceccherini-Silberstein F, et al: 2019 Update of the drug resistance mutations in HIV-1. Top Antivir Med. 2019 Sep;27(3):111-121

3. U.S. Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents: Guidelines for the use of antiretroviral agents in adults and adolescents with HIV.. July 10, 2019. Updated August 16, 2021. Accessed October 6, 2021. Available at https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf

Performance

Method Description

This assay utilized a modified method involving the use of the FDA-approved ViroSeq HIV-1 Genotyping System v2.0. HIV-1 RNA in a given human plasma specimen is extracted and purified by a manual method. The entire protease gene from codons 1 to 99 and two-thirds of the reverse transcriptase (RT) gene from codons 1 to 335 of the HIV-1 genome present in plasma are amplified and sequenced with 7 sequencing reactions in forward and reverse directions with the AB 3500xL genetic analyzer. The sequence data generated for the patient's HIV-1 virus are assembled, edited, and analyzed with the ViroSeq HIV-1 Genotyping System Software v3 per manufacturer's instructions. The consensus sequence assembled is compared to a known reference (wild-type) HIV-1 strain sequence to determine the presence of all resistance-related mutation codons using the Stanford HIVdb Program Genotypic Resistance Interpretation Algorithm (http://sierra2.stanford.edu/sierra/servlet/JSierra). The mutation codons observed are compared to the known list of HIV-1 genotypic drug resistance mutations and interpreted for susceptibility to the corresponding antiretroviral drugs.(Package insert: ViroSeq HIV-1 Genotyping System v2.0; Abbott Molecular, Inc., Des Plaines, IL. 04/2016; Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Varies

Report Available

2 to 10 days

Specimen Retention Time

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 has been modified from the manufacturer's instructions. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

87901

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
HIVPR	HIV-1 Genotypic PR-RT Resistance, P	49659-6

Result ID	Test Result Name	Result LOINC Value
37216	HIV-1 Genotypic PR-RT Drug Resistance, P	34700-5
37263	Nucleos(t)ide RT mutations	45175-7
21411	Abacavir	30287-7
21406	Didanosine	30284-4
37285	Emtricitabine	41402-9
37284	Lamivudine	30283-6
21408	Stavudine	30286-9
21530	Tenofovir	41396-3
21405	Zidovudine	30282-8
37264	Nonnucleoside RT mutations	45176-5
604980	Doravirine	91897-9
21414	Efavirenz	30291-9
31267	Etravirine	52749-9
21410	Nevirapine	30289-3
34917	Rilpivirine	68463-9
21400	Protease Mutations	33630-5
28076	Atazanavir + Ritonavir	49618-2
26784	Darunavir + Ritonavir	49630-7
26733	Fosamprenavir + Ritonavir	51409-1
26734	Indinavir + Ritonavir	49619-0
21532	Lopinavir + Ritonavir	42000-0
21416	Nelfinavir	30294-3
26735	Saquinavir + Ritonavir	49621-6

Result ID	Test Result Name	Result LOINC Value
28201	Tipranavir + Ritonavir	49622-4