
Lab Dept: Microbiology/Virology

Test Name: HIV-1 ULTRASENSITIVE GENOTYPIC DRUG RESISTANCE MUTATION ANALYSIS

General Information

Lab Order Codes: GHIVS

Synonyms: HIV -1 Resistance; HIV-1 Genotyping for Drug Resistance; HIV-1 Genotypic Protease & Reverse Transcription Inhibitor Drug Resistance

CPT Codes: 87901 – Infectious agent genotype analysis by nucleic acid (DNA or RNA); HIV 1, reverse transcriptase and protease

Test Includes: Amplification and analysis of drug-targeted HIV-1 gene sequences.

Logistics

Test Indications: Identification of HIV-1 genotypic variants associated with 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.

Lab Testing Sections: Microbiology/Virology – Sendouts

Referred to: Mayo Medical Laboratories (MML: HIVPR)

Phone Numbers: MIN Lab: 612-813-6280

STP Lab: 651-220-6550

Test Availability: Daily, 24 hours

Turnaround Time: 2 – 4 days

Special Instructions: Plasma specimens submitted for this test should contain > or =500 copies per/mL of HIV-1 RNA.

Specimen

Specimen Type: Blood

Container: Lavender top (EDTA) tube

Draw Volume:	6.6 mL (Minimum 3.6 mL) blood
Processed Volume:	2.2 mL (Minimum: 1.2 mL) EDTA plasma
Collection:	Routine blood collection, invert tube several times to mix so no clots form. Send to Children's laboratory as soon as possible for shipping to the reference lab facility.
Special Processing:	Lab Staff: Immediately centrifuge blood (within 6 hours of collection). Immediately remove plasma from cells and transfer to a plastic screw-capped tube. Store frozen and ship at frozen on dry ice. If shipment is delayed for >24 hours, freeze specimen at -70°C (up to 35 days) until shipment with dry ice.
Patient Preparation:	None
Sample Rejection:	Collected in wrong tube; specimen thawed; mislabeled or unlabeled specimens

Interpretive

Reference Range: Not applicable

Interpretation: Detectable HIV-1 genotypic mutations to an antiviral drug are reported as amino acid codon changes (eg, M184V) resulting from 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 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 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 mutations in the patient's HIV strain. Possible causes of such poor sequence data include poor sequence data include polymorphism in the region of the sequencing primers interfering with primer bonding 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.

Critical Values: N/A

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

The 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 mutations 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 mutation 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 drug-related mutations described in 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).

Methodology: Reverse transcription-polymerase chain reaction (RT-PCR) followed by DNA sequencing

References: [Mayo Medical Laboratories](#) January 2018

Updates: 6/25/2015: Method update, specimen volume update, test code update.
12/3/2019: Updated to include Stanford HIVdb scores and TAT update