HIV Genotypic Resistance Assay Report

Patient Name:
Specimen Date:
Patient/Location ID #:
Accession #:
Ordering physician:
Tissue analyzed (plasma/PBMC): Plasma viral RNA

Reporting Center:
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Sequence analysis using the ABI-310 was performed on DNA reverse-transcribed from the plasma viral RNA. All mutations that lead to amino acid changes are reported for the patient's specimen when compared to Los Alamos HIV-1 subtype B consensus sequence:

Protease Gene: Amino acids analyzed 1 TO 99
Mutations associated with resistance to protease inhibitors:

Other mutations causing amino acid changes, but not frequently associated with drug resistance:

Reverse Transcriptase Gene: Amino acids analyzed 1 TO 230
Mutations associated with resistance to reverse transcriptase inhibitors:

Other mutations causing amino acid changes, but not frequently associated with drug resistance:

Gp41 Gene: Amino acids analyzed 20 to 70
Mutations associated with resistance to Enfuvirtide

Other mutations causing amino acid changes, but not frequently associated with drug resistance:

Interpretation of resistance profile based on the mutations detected in this patient's HIV-1:

Generic Name	Trade Name			No Evidence of Resistance	Possible Resistance	Low Level Resistance	High Level Resistance
Protease Inhibitors							
Amprenavir	Agenerase	AMP					
Atazanavir		ATV					
Indinavir	Crixivan	IND					
Lopinavir-rit.	Kaletra	LPV					
Nelfinavir	Viracept	NLF					
Ritonavir	Norvir	RIT					
Saquinavir	Invirase	SQV					
Nucloside/Nuclotide Reverse Transcriptase Inhibitors							
Abacavir	Ziagen	ABC					
Didanosine	Videx	ddI					
Lamivudine	Epivir	3TC					
Tenofovir	Viread	TFV					
Stavudine	Zerit	d4T					
Zalcitabine	Hivid	ddC					
Zidovudine	Retrovir	ZDV/AZT					
Non-Nucleoside Reverse Transcriptase Inhibitors							
Delavirdine	Rescriptor	DLV					
Efavirenz	Sustiva	EFV					
Nevirapine	Virammune	NVP					
Entry Inhibitors							
Enfuvirtide	Fuzeon	T20					

HIV Genotypic Resistance Assay Report (continued)

Notes on the interpretation

HIV-1 strain analyzed: subtype B of *pol*.

Legend for the interpretation

No Evidence of Resistance The genotype of the patient's HIV-1 has no known mutations which suggest phenotypic resistance to the anti-retroviral drug noted.

Possible Resistance The genotype of the patient's HIV-1 has mutations which, when associated with other mutations, may cause phenotypic resistance to the anti-retroviral drug noted.

Low Level Resistance The genotype of the patient's HIV-1 has mutations which have been associated with low level phenotypic resistance to the anti-retroviral drug noted.

High Level Resistance The genotype of the patient's HIV-1 has mutations which have been associated with high level phenotypic resistance to the anti-retroviral drug noted.

Note: This interpretation was based on the **29 January 2004** Drug Resistance Key which accompanies this report. The Drug Resistance Key is periodically updated. You may always obtain the most recent version of the Drug Resistance Key (below) to see if new genotype information might alter the interpretation of the patient's HIV.

Guidelines for Interpretation of Results:

1. Please refer to the Drug Resistance Key for more detailed information concerning associations between mutations and HIV-1 resistance. If you do not have a current Drug Resistance Key from this facility, please call Community Services at (phone # 206-598-6066) to obtain one. Information pertaining to HIV-1 drug resistance can also be found in the Los Alamos Database at: http://hiv-web.lanl.gov, on which the Drug Resistance Key is based.
2. In preliminary studies genotypic testing predicted HIV-1 resistance to therapies, but was less predictive of susceptible HIV-1.
3. Specific mutations in the HIV-1 polymerase gene (pol) have been closely associated with a lack of or loss of treatment effect to certain antiretrovirals, e.g.the M184V and T215Y/F mutations are commonly associated with HIV-1 resistance to lamivudine (3TC) and zidovudine (ZDV), respectively. However, HIV-1 resistance to other antiviral drugs is less well understood, either because no single mutation has been identified that confers resistance, or because human cellular factors may contribute to resistance, e.g. by pumping the drug out of the cell.
4. Assessing HIV-1 resistance is complicated by the replication kinetics of resistant mutants. Resistant mutants are often less fit than wild type virus and thus, when the selective pressure of the drug is removed, the mutant population may shrink below the level of detection. Nevertheless, these mutants persist in the patient and when the selective drug pressure is reapplied the mutants replicate and a resistant population quickly predominates.
5. Cross-resistance is common among protease inhibitors and non-nucleoside reverse transcriptase inhibitors. Multi-drug resistance mutations (MDR) have also been found for nucleoside analogs (see Drug Resistance Key).
6. This test was done by consensus sequencing of the patient's HIV-1. The results reflect the predominate genotype of all viral variants in the patient. Variants comprising less than 30 percent of the sample may not be detected.

This test was developed and it performance characteristics determined by University of Washington Academic Medical Centers, Department of Laboratory Medicine. It has not been cleared or approved by the U. S. Food and Drug Administration.

UW Clinical Virology Drug Resistance Key for HIV-1 Genotypic Analysis

Protease Inhibitors: HIV-1 resistance to PI increases with the number of mutations in the gene encoding protease; ***unshaded mutations confer resistance, and shaded mutations increase viral replication capacity***

A.A. WildType Mutation	**10** L> F/ I/R/V	**20** K> M/R	**23** L> I	**24** L> I	**30** D> N	**32** V> I	**33** L> F/V	**36** M> I	**46** M> I/L	**47** I> V	**48** G> V	**50** I> V	**50** I> L	**54** I> L/M/V	**71** A> V/T	**73** G> S/T	**82** V>A/F L/S/T	**84** I> V	**88** N> D/S/T	**90** L> M
Amprenavir Fosamprenavir	+					+			+	+	+^	+++		++^	+		+^	+++		++^
Atazanavir						+			++		++^		+++	++^	+		++^	++^	++	++^
Indinavir	+	+		+		+		+	+		+^	+		+^	+	+	+++	+++		++^
Lopinavir-	+	+		+		+	+		+	++	+^	++		+^	+		++^	+^		+^
Nelfinavir	+		++		+++			+	+		+^	+		++^	+		++^	+++	+++	+++
Ritonavir	+	+				+	+	+	+		+^	++		++^	+		+++	+++		++^
Saquinavir	+								+		+++	+		+^	+	+	+^	+++		+++

Nucleoside/Nucleotide Reverse Transcriptase Inhibitors

A.A. WildType Mutation	**41** M> L	**44** E> D/K	**62** A> V	**65** K> R	**67** D> N	**69** T>D /N	**69** T>S xx	**70** K> R	**74** L> V/I	**75** V>T M/A	**75** V> I	**77** F> L	**115** Y> F	**116** F> Y	**118** V> I	**151** Q> M	**184** M> V/I	**208** H> Y	**210** L> W	**215** T> Y/F	**219** K> Q/E	**333** G> D/E
Abacavir	++	+	*	++	+		***	+	++		*	*	++	*	+	+++*	++		+	++	++	
Didanosine			*	++		++	***		+++	+	*	*		*		+++*	+			+		
Lamivudine Emtricitabine		**	*	++			***				*	*		*	**	+++*	+++	**				**
Stavudine	++		*	++	+	+	***	+		+++	*	*		*		+++*	#		+	++	++	
Tenofovir	^^			+++			***									+*	#		^^	^^	+	
Zalcitabine			*	+++		++	***		++	+	*	*		*		+++*	+			+		
Zidovudine	+++		*	+	++		***	++			*	*		*		+++*	#	**	+	+++	+++	**

Non-Nucleoside Reverse Transcriptase Inhibitors

A.A WildType Mutation	**100** L> I	**103** K>N S/T	**106** V> M/A	**108** V> I	**181** Y> C/I	**188** Y>L/ H/C	**190** G> A/S	**225** P> H	**236** P> L
Delavirdine	+++	+++	+++	+	+++	++	+	+	++
Efavirenz	+++	+++	+++	++	++	+++	+++	++	+
Nevirapine	+++	+++	+++	++	+++	+++	+++	+	+

Entry Inhibitors

A.A WildType Mutation	**36** G> D/S	**37** I> V	**38** V> A/M	**39** Q> R	**42** N> T	**43** N> D
Enfuvirtide	+++	+++	+++	+++	+++	+++

Legend:

+++ Indicates major mutation, frequently observed with high-level resistance to the drug.

++ Indicates mutation that is frequently observed with low-level resistance to the drug.

+ Indicates mutation which may cause resistance to the drug, usually in combination with other resistance mutations.

^ Any combination of 3 the following mutations likely confer multi-drug PI resistance: 46I/L; 54V/M/L; 82A/F/T/S; 84V; 90M

******* Mutation of T69S followed by the insertion of any two amino acids confers low-level resistance to the NRTI; w/ ZDV-resistance mutations confers moderate to high level resistance

****** H208Y, R211K, F214L, and G333D/E facilitate dual resistance to ZDV and LMV in association with mutation at M184V/I. E44D/K and V118I facilitate resistance to LMV when accompanied by ZDV resistance mutations (M41L, K70R, T215Y/F).

***** Q151M is the pivotal mutation in a multi-drug complex which includes amino acids (AA) 62, 75, 77, and 116, that confers high-level resistance to all nucleoside RT inhibitors

M184V has been reported to increase susceptibility to ZDV, TFV and STV when co-existing with M41L and/or T215F/Y

^^ M41L + L210W + T215Y/F facilitate resistance to tenofovir

These tables are based on data from the Los Alamos Database (http://hiv-web.lanl.gov), the Stanford HIV Database (http://hivdb.stanford.edu), and available presented or published clinical and laboratory studies.