

GENOSURE ARCHIVE®

HIV-1 NEXT GENERATION DNA SEQUENCING ASSAY FOR SUPPRESSION MANAGEMENT

Resistance Information In Suppressed Patients

GenoSure Archive® is designed to provide HIV-1 antiretroviral (ARV) drug resistance data when a patient's viral load is suppressed or too low for standard resistance testing. The assay interrogates the viral archive using next-generation sequencing (NGS) to provide a list of the archived mutations and assigns susceptibility calls of *sensitive*, *resistant*, or *resistance possible* based on those mutations.

GenoSure Archive Facilitates Regimen Changes

Advances in ARV drug therapy have resulted in many patients achieving and maintaining full viral suppression. Increasingly common today is the need for "fine tuning" regimens while the patient's virus remains suppressed. Reasons for this include:

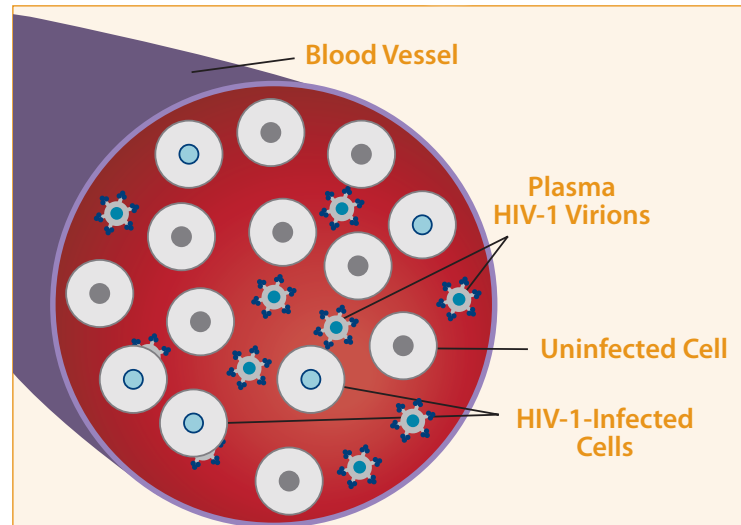
- Side effects
- Adverse events
- Regimen simplification
- Drug-drug interactions
- Concern for long-term toxicities
- Regimen intolerance

GenoSure Archive provides valuable information for nucleoside reverse transcriptase inhibitors (NRTIs), nonnucleoside reverse transcriptase Inhibitors (NNRTIs), integrase inhibitors (INIs) and protease Inhibitors (PIs) when considering regimen switches in virologically suppressed patients:

- Information regarding archived drug resistance mutations and the effectiveness of accompanying ARV drugs is critical when considering regimen switches.¹
- In a 2013 study, patients fully suppressed on an ARV regimen consisting of a boosted protease inhibitor and two NRTIs, were switched to a new single tablet regimen based on historical, pre-suppression, viral RNA resistance data. The study demonstrated favorable concordance between Monogram's HIV-1 DNA resistance profiles and historical plasma viral resistance profiles among enrolled patients.²

Suppression Management

GenoSure Archive is the newest suppression management offering by Monogram Biosciences. In 2010, Monogram launched **Trofile® DNA** to assess HIV-1 tropism when considering a CCR5 antagonist in suppressed patients. Together, **GenoSure Archive** and **Trofile DNA** provide a comprehensive assessment of five ARV drug classes to facilitate regimen simplification or switches in the setting of virologic suppression.





The Viral Archive - A Second Source of Resistance Information

Differences can exist between the viral population circulating in the plasma and the proviral DNA archived in infected cells.

- Viral loads and standard resistance assays analyze viral RNA in plasma. **GenoSure Archive** analyzes archived HIV-1 proviral DNA embedded in host cells during virus replication.
- In the context of emerging treatment failure, ARV drug resistant HIV-1 variants are identified earlier in the plasma compartment relative to infected cells³, but resistant variants may persist longer in the infected cells⁴, especially in the absence of on-going drug pressure.
- **GenoSure Archive** is performed by amplifying cell-associated HIV-1 DNA from infected cells in whole-blood samples then employing NGS technology to analyze the HIV-1 polymerase region, including the full-length protease and integrase coding regions and amino acids 1-400 of reverse transcriptase.

GenoSure Archive® Sample Report







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Client: _____ Project: _____
Phone: _____ Fax: _____

Patient Name	DOB	Patient ID/Medical Record #	Gender	Monogram Accession #
Date Collected	Date Received	Date Reported	Mode	Report Status FINAL
Referring Physician			Reference Lab ID/Order #	
Comments HIV-1 Subtype: B				

Generic Name	Brand Name	Assessment	Drug Resistance Associated Mutations Detected	Comments
NRTI	Abacavir	Resistance Possible	T69T/N, M184M/V	
	Didanosine	Resistance Possible	M184M/V	
	Emtricitabine	Resistant	M184M/V, K219K/E	
	Lamivudine	Resistant	M184M/V, K219K/E	
	Stavudine	Sensitive	T69T/N	
	Tenofovir	Sensitive	None	
	Zidovudine	Sensitive	None	
NNRTI	Efavirenz	Resistant	L100L/I, K103K/N	
	Etravirine	Resistant	L100L/I, V179I/T	
	Nevirapine	Resistant	L100L/I, K103K/N, V179I/T	
	Rilpivirine	Resistant	L100L/I, K103K/N	
INSTI	Dolutegravir	Sensitive	None	
	Evitegravir	Sensitive	None	
	Raltegravir	Sensitive	None	





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Date Collected	Date Received	Date Reported	Mode	Report Status FINAL

* Assessment of drug susceptibility is based upon detected mutations and interpreted using an advanced proprietary algorithm (version 16).
 * Interpretation algorithms for ritonavir-boosted protease inhibitors appropriate for the following dosages: AMP/r 600mg/100mg BID; IDV/r 800mg/200mg BID; LPV/r 400mg/100mg BID; SQV/r 1000mg/100mg BID; TPV/r 500mg/200mg BID; and DRV/r 600mg/100mg BID.
 * Mixtures are indicated by amino acids separated by a slash. Deletions in the amino acid sequence are indicated by a ^ symbol.

RT									
PI									

Summary of Mutations Observed

RT V35L, T69T/N, R83K, L100L/I, Q102K, K103K/N, K122P, C162D, E189K, F171Y, D177E, I178M, V179I/T, M184M/V, G196G/E, T200T/A, R211K, K219K/E, V245E, A272P, K275R, R277K, Q278H, T286T/A, V293I, E297E/K, S322T, G335C, M357T, K358R, A360T, A376T, T377K, T386I, A400T

IN D6E, V37I, V72V/I, T124N, T125A, G163E/Q, V201I, V234L

PR I15I/V, L33L/I, E35E/D, R57K, D60E, Q61E, L63P, V77I

Genotype Comments (clinical significance may vary)

- Assessment for this drug was derived considering the sensitizing effect of mutation M184V.
- Assessment for this drug was derived considering the sensitizing effect of mutations L100I and M184V.

For more information on interpreting this report, please visit www.MonogramBio.com or call Customer Service at 800-777-0177 between the hours of 6:30am to 5:00pm PT Monday through Friday.

GenoSure Archive is a DNA sequencing assay that uses next-generation sequencing to analyze the protease (amino acids 1-99), reverse transcriptase (amino acids 1-400) and integrase (amino acids 1-288) coding regions derived from HIV-1 cell associated DNA. Subtype is determined using the protease and reverse transcriptase sequence information. This assay meets the standards for performance characteristics and all other quality control and assurance requirements established by the Clinical Laboratory Improvement Amendments. The results should not be used as the sole criteria for patient management. The results have been disclosed to you from confidential records protected by law and are not to be disclosed to unauthorized persons. Further disclosure of these results is prohibited without specific consent of the persons to whom it pertains, or as permitted by law.

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References

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- White KL, Toma J, Napolitano LA, et al. Genotypic Analyses of Pre-Existing HIV-1 Drug Resistance in Provirial HIV-1 DNA from PBMCs in Suppressed Patients Switching to RPV/FTC/TDF. 2013; International Workshop on HIV & Hepatitis Virus Drug Resistance and Curative Strategies. Poster 67.
- Simmonds P, Zhang LQ, McOmish F, et al. Discontinuous sequence change of human immunodeficiency virus (HIV) type 1 env sequences in plasma viral and lymphocyte-associated proviral populations in vivo: implications for models of HIV pathogenesis. *J Virol*. 1991; 65(11):6266-76.
- Vandamme A-M, Camacho RJ, Ceccherini-Silberstein F, et al. European Recommendations for the Clinical Use of HIV Drug Resistance Testing: 2011 Update. *AIDS Rev*. 2011; 13:77-108.

Test Name	GenoSure Archive®	GenoSure Archive® Plus Trofile® DNA
Test Number	551776	552020
Specimen Collection	4 mL lavender-top (EDTA) whole blood, frozen	8 mL lavender-top (EDTA) whole blood, frozen
Limitation	This procedure should be used for patients with documented HIV-1 infection and undetectable viral load or low level viremia.	This procedure should be used for patients with documented HIV-1 infection and undetectable viral load or low level viremia.

