Stanford University

HIV DRUG RESISTANCE DATABASE

A curated public database to represent, store and analyze HIV drug resistance data.

HIV-1 Sequence Analysis Report

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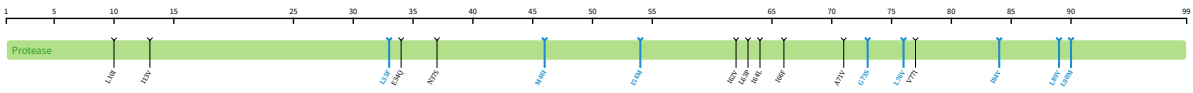
1. HXB2.1

Sequence summary

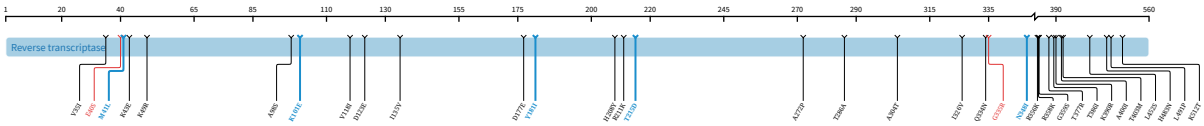
Sequence includes PR:	codons 1 - 99
Sequence includes RT:	codons 1 - 560
Sequence includes IN:	codons 1 - 288
Subtype:	⊞ B (3.84%)
PR SDRMs:	M46I, I54M, G73S, L76V, I84V, L90M
RT SDRMs:	M41L, K101E, Y181I, T215D
IN SDRMs:	None

Sequence quality assessment

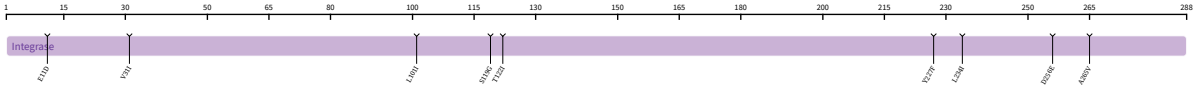
Protease (PR)



Reverse transcriptase (RT)



Integrase (IN)



- **Note**: 173 wildcard notation “N”’s have been removed from the 5’ and/or 3’ ends of the sequence.
- **Note**: There is one unusual mutation at a drug-resistance position in RT: E40S.

Drug resistance interpretation: PR

HIVDB 9.8 (2025-01-05)

PI Major Mutations:	**M46I** • **I54M** • **L76V** • **I84V** • **L90M**
PI Accessory Mutations:	**L33F** • **G73S** • **L89V**
PR Other Mutations:	L10I • I13V • E34Q • N37S • I62V • L63P • I64L • I66F • A71V • V77I

PR comments	Protease Inhibitors	
Major		
atazanavir/r (ATV/r)	High-Level Resistance	
darunavir/r (DRV/r)	High-Level Resistance	
lopinavir/r (LPV/r)	High-Level Resistance	

- **M46I/L** are relatively non-polymorphic PI-selected mutations. In combination with other PI-resistance mutations, they are associated with reduced susceptibility to each of the PIs except DRV.
- **I54M/L** are non-polymorphic mutations selected primarily by FPV and DRV. **I54M/L** reduce susceptibility to LPV, ATV, and DRV.
- **L76V** is a non-polymorphic mutation selected by IDV, LPV and DRV and reduces susceptibility to LPV and DRV.
- **I84V** is a nonpolymorphic substrate-cleft mutation selected by each of the PIs. **I84V** reduces susceptibility to LPV, ATV, and DRV.
- **L90M** is a non-polymorphic PI-selected mutation that reduces susceptibility to ATV and to a lesser extent LPV.

Accessory

- **L33F** is a relatively non-polymorphic accessory mutation selected by each of the PIs. In combination with other PI-resistance mutations, it is associated with reduced susceptibility to LPV, ATV, and DRV.
- **G73S/T/C/A** are common non-polymorphic accessory mutations selected primarily by most PIs. They are associated with minimally reduced susceptibility to each of the PIs.
- **L89V** is a nonpolymorphic accessory mutation weakly selected by each of the PIs. It appears to be minimally associated with reduced PI susceptibility. L89T is an uncommon non-polymorphic PI-selected mutation selected primarily by ATV.

Other

- **L10I/V** are polymorphic, PI-selected accessory mutations that increase the replication of viruses with other PI-resistance mutations.
- **A71V/T** are polymorphic, PI-selected accessory mutations that increase the replication of viruses with other PI-resistance mutations.

Dosage

- There is evidence for high-level **DRV** resistance. If **DRV** is administered it should be used twice daily.

Mutation scoring: PR

HIVDB 9.8 (2025-01-05)

Drug resistance mutation scores of PI:

Rule	ATV/r	DRV/r	LPV/r
L33F	5	5	5
M46I	10	0	10
M46I + I84V + L90M	5	0	5
M46I + L90M	10	0	5
I54M	15	20	20
I54M + L90M	10	0	5
G73S	10	0	5
G73S + L90M	10	0	0
I84V	60	15	30
L90M	20	0	10
I54M + I84V	0	5	5
I54M + L89V	0	5	5
L76V	0	20	30
L89V	0	5	0
M46I + L76V	0	0	10
Total	155	75	145

Drug resistance interpretation: RT

HIVDB 9.8 (2025-01-05)

NRTI Mutations: **M41L** • **T215D**

NNRTI Mutations: **K101E** • **Y181I** • **N348I**

RT Other Mutations: V35I • E40S • K43E • K49R • A98S • V118I • D123E • I135V • D177E • H208Y • R211K • A272P • T286A • A304T • I326V • Q334N • G335R • R356K • R358K • G359S • T377R • T386I • K390R • A400I • T403M • L452S • H483N • L491P • K512T

Nucleoside Reverse Transcriptase Inhibitors		Non-nucleoside Reverse Transcriptase Inhibitors	
abacavir (ABC)	Susceptible	**doravirine (DOR)**	Low-Level Resistance

zidovudine (AZT)	Intermediate Resistance	**efavirenz (EFV)**	Intermediate Resistance
emtricitabine (FTC)	Susceptible	**etravirine (ETR)**	High-Level Resistance
lamivudine (3TC)	Susceptible	**nevirapine (NVP)**	High-Level Resistance
tenofovir (TDF)	Susceptible	**rilpivirine (RPV)**	High-Level Resistance

RT comments

NRTI

- **M41L** is a TAM that usually occurs with T215Y. In combination, **M41L** plus T215Y confer intermediate / high-level resistance to AZT and d4T and contribute to reduced ddI, ABC and TDF susceptibility.
- T215Y/F are TAMs that causes intermediate/high-level resistance to AZT and potentially low-level resistance to ABC and TDF. **T215S/C/D/E/I/V/N/A/L** do not reduce NRTI susceptibility but arise from viruses that once contained T215Y/F. The presence of one of these revertant mutations suggests that the patient may have once been infected with a virus containing T215Y/F.

NNRTI

- **K101E** is a non-polymorphic accessory mutation that confers intermediate resistance to NVP and RPV and low-level reductions in susceptibility to EFV, ETR, and DOR when it occurs with other NNRTI-resistance mutations.
- **Y181I/V** are 2-base pair non-polymorphic mutations selected by NVP and ETR. They cause high-level resistance to NVP, ETR, and RPV but not EFV. Their effects on DOR have not been well-characterized.
- **N348I** is a non-polymorphic accessory mutation selected by NVP and EFV and the NRTIs AZT and D4T. Alone it reduces AZT and NVP susceptibility by about 3-fold and EFV susceptibility by 2-fold.

Other

- **V118I** is a polymorphic accessory NRTI-resistance mutation that often occurs in combination with multiple TAMs.

Mutation scoring: RT — HIVDB 9.8 (2025-01-05)

Drug resistance mutation scores of NRTI:

Rule	ABC	AZT	FTC	3TC	TDF
M41L	5	15	0	0	5
M41L + T215D	0	10	0	0	0
T215D	0	10	0	0	0
Total	5	35	0	0	5

Drug resistance mutation scores of NNRTI:

Rule	DOR	EFV	ETR	NVP	RPV
K101E	10	15	10	30	45
Y181I	10	30	60	60	60
N348I	0	0	0	15	0
Total	20	45	70	105	105

Drug resistance interpretation: IN — HIVDB 9.8 (2025-01-05)

INSTI Major Mutations:	None
INSTI Accessory Mutations:	None
IN Other Mutations:	E11D • V31I • L101I • S119G • T122I • Y227F • L234I • D256E • A265V

Integrase Strand Transfer Inhibitors

bictegravir (BIC)	Susceptible
cabotegravir (CAB)	Susceptible
dolutegravir (DTG)	Susceptible
elvitegravir (EVG)	Susceptible
raltegravir (RAL)	Susceptible

Mutation scoring: IN — HIVDB 9.8 (2025-01-05)

No drug resistance mutations were found for INSTI.