

# Mutations in Retroviral Genes Associated with Drug Resistance

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## Introduction

Drug resistance is the inevitable consequence of incomplete suppression of HIV replication. The rapid replication rate of HIV and its inherent genetic variation have led to the identification of many HIV variants that exhibit altered drug susceptibility. The growing number of drug resistance mutations listed in this revised table stands as a testimony to the genetic flexibility of HIV. This table, updated in September 2005, lists 872 HIV-1 mutation/drug combinations, of which 28 occur in Gag, 298 occur in Protease, 6 in Integrase, 337 in RT, and 203 in Env. Although the tables are quite comprehensive, the reader should be reminded that the HIV-1 mutations described are predominantly found in clade B virus and not in other HIV genotypes. Thirty-one mutations in HIV-2 RT are listed in the table and a new section for HIV-2 Protease containing 27 entries has been added this year. In addition, 2 mutations in SIV RT are listed.

The column “Selected or Cross-R” describes how the mutations have been identified. “Selected” refers specifically to mutations identified by *in vitro* passage of virus in increasing concentrations of a compound, or by sequencing isolates from patients on a specific drug therapy. “Cross-R” (cross-resistance) means that virus with a mutation has been shown to have decreased susceptibility to a compound even though selection of the mutation by the compound has not been reported. The “*in vitro*” column has a “Y” (for yes) when resistance or cross-resistance to the compound is seen using cloned virus or in cell culture studies; the “*in vivo*” column has a “Y” (for yes) when resistance or cross-resistance to the compound is seen in patients.

In the “Amino Acid Change” column a + means amino acids have been inserted into the sequence, while a  $\Delta$  indicates a deletion. In the “Drug Class” column, “NRTI” refers to nucleoside or nucleotide reverse transcriptase inhibitors, while non-nucleoside or HIV-1 specific RT inhibitors are called “NNRTI.” The abbreviation MN stands for “Multiple Nucleoside” and refers to resistance to combinations of NRTIs. “MDR” or multi-drug resistant is noted in the “Compound” column if a mutation causes resistance to multiple compounds. Other abbreviations are listed in a separate Abbreviations Table on page 68. All of the information contained in these printed tables and other useful tools are available at our Web site: [http://resdb.lanl.gov/Resist\\_DB](http://resdb.lanl.gov/Resist_DB).

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## HIV-1 Gag

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
E 12 K	CAG→ATG	Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
E 12 K	CAG→ATG	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?		Gatanaga02
V 35 I	CAG→ATG	Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	?		Gatanaga02
V 35 I	CAG→ATG	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?		Gatanaga02
E 40 K	CAG→ATG	Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	?		Gatanaga02
E 40 K	CAG→ATG	Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
L 75 R	CAG→ATG	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?		Gatanaga02
G 123 E	CAG→ATG	Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	?		Gatanaga02
G 123 E	CAG→ATG	Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
Q 199 H	CAG→ATG	Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
H 219 Q	CAG→ATG	Protease Inhibitor	JE-2147	Selected	Y	?		Gatanaga02
H 219 Q	CAG→ATG	Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	?		Gatanaga02
H 219 Q	CAG→ATG	Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
H 219 Q	CAG→ATG	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?		Gatanaga02
G 381 S	CAG→ATG	Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	?		Gatanaga02
V 390 A	CAG→ATG	Protease Inhibitor	JE-2147	Selected	Y	?		Gatanaga02
V 390 D	CAG→ATG	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?		Gatanaga02
R 409 K	CAG→ATG	Protease Inhibitor	JE-2147	Selected	Y	?		Gatanaga02
R 409 K	CAG→ATG	Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	?		Gatanaga02
R 409 K	CAG→ATG	Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
R 409 K	CAG→ATG	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?		Gatanaga02
G 412 D	CAG→ATG	Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
A 431 V	CAG→ATG	Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	?		Gatanaga02

**HIV-1 Gag**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
L 449 F	CAG→ATG	Protease Inhibitor	JE-2147	Selected	Y	?		Gatanaga02
L 449 F	CAG→ATG	Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
L 449 F	CAG→ATG	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?		Gatanaga02
E 468 K	CAG→ATG	Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
E 468 K	CAG→ATG	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?		Gatanaga02

## HIV-1 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
T 4 P	ACT→CCT	Protease inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	?	Y		Mo05
R 8 K	CGA→AAA	Protease Inhibitor	A-77003	Selected	Y	?	R8K/M46I/G48V: 20-fold	Ho94, Tisdale95
R 8 Q	CGA→CAA	Protease Inhibitor	A-77003	Selected	Y	?	M46I improves replication competency of R8Q mutant. Selected in chronically infected cells at 10 microM.	Ho94, Kaplan94
L 10 F	CTC→TTC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	Y	Y	In vitro, I84V/L10F/M46I: 4 fold I84V/L10F/M46I/T91S; 12 fold I84V/L10F/M46I/T91S/V32I/I47V; 46 fold Passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y: 338 fold (in presence of p7/p1 (AN/F to VN/F) cleavage-site mutation and p1/p6 (F/L to F/F) cleavage-site mutation). In vivo, susceptibility was reduced by mutations at positions 82, 54, 10, 63, 71, 84 (4–10-fold), K20M/R (>20-fold), F53L (>40-fold)	Carrillo98, Kempf01
L 10 F	CTC→TTC	Protease Inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	Y	?	Sequential accumulation of mutations in passage of pNL4-3 in MT4 cells in presence of a LPV/ritonavir ratio of 5:1. Appears second in sequence, in passage 9, after I84V and followed by M46I, V32I, I47V, Q58E.	Mo03
L 10 F	CTC→TTC	Protease Inhibitor	ABT-538 (ritonavir)	Cross-R	Y	?	9-fold resistant to JE-2147-selected virus (L10F/M46I/I47V/I84V)	Yoshimura99
L 10 F	CTC→TTC	Protease Inhibitor	ABT-538 (ritonavir)	Cross-R	Y	?	21-fold resistance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y	Carrillo98
L 10 F	CTC→TTC	Protease Inhibitor	BILA 2185 BS	Selected	Y	?	L10F/L23I/V32I/M46I/I47V/I54M/A71V/I84V: 1,500-fold with associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1'); p7/p1 cleavage site (Q to R (CAG to CGG) at P3', A to V (GCT to CTT) at P2').	Croteau97, Doyon96
L 10 F	CTC→TTC	Protease Inhibitor	BMS-232632 (atazanavir)	Selected	Y	?	V32L/L33F/M46I/A71V/I84V/N88S: 183-fold. L10Y/F/I50L/L63P/A71V/N88S: 93-fold. V32I/M46I/I84V/L89M: 96-fold.	Gong00
L 10 F	CTC→TTC	Protease Inhibitor	DMP 450	Selected	Y	?	Probably compensatory	Hodge96

## HIV-1 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
L 10 F	CTC→TTC	Protease Inhibitor	DMP-323	Selected	Y	?	L10F/V82A: 2-fold; L10F/K45I/I84V: 50-fold	Tisdale95, King95
L 10 F	CTC→TTC	Protease Inhibitor	JE-2147	Selected	Y	?	L10F/I47V/I84V:19-fold. L10F/M46I/I47V/I84V:28-fold. >50 passages required for isolation of resistant virus.	Yoshimura99
L 10 F	CTC→TTC	Protease Inhibitor	KNI-272 (kynostatin)	Cross-R	Y	?	7-fold resistant to JE-2147 selected virus (L10F/M46I/I47V/I184V)	Yoshimura99
L 10 F	CTC→TTC	Protease inhibitor	PNU-140690 (tipranavir)	Selected	Y	?	After 73 passages 9 other mutations accumulated to give 87 fold resistance to tipranavir	Doyon05
L 10 F	CTC→TTC	Protease Inhibitor	SC-55389A	Selected	Y	?	N88S/L10F: 25-fold	Smidt97
L 10 F	CTC→TTC	Protease Inhibitor	TMC114 (UIC-94017)	Cross-R	Y	?	10-fold resistant against aprenavir-selected mutant L10F/V32I/M46I/I54M/A71V/I84V. 73-fold resistant against indinavir-selected L10F/L24I/M46I/L63P/A71V/G73S/N82T	Koh03
L 10 F	CTC→TTC	Protease Inhibitor	UIC-94003	Selected	Y	?	in vitro selection in MT-2 cells, passage 62	Gatanaga02
L 10 F	CTC→TTC	Protease Inhibitor	VB-11,328	Selected	Y	?	L10F/I84V: 8-fold	Partaledis95
L 10 F	CTC→TTC	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?	Selected first	Partaledis95
L 10 I	CTC→ATC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
L 10 I	CTC→ATC	Protease Inhibitor	ABT-538 (ritonavir)	Selected	Y	?	Selected in in vitro passage of NL4-3 in CEMX174 cells in increasing concentrations of ritonavir. Appeared late in selection (passage 44)	Watkins03
L 10 I	CTC→ATC	Protease inhibitor	AG-1343 (nelfinavir)	Selected	?	Y		Matsuoka-Aizawa03
L 10 I	CTC→ATC	Protease Inhibitor	MK-639 (indinavir)	Selected	N	Y		Condra96
L 10 I	CTC→ATC	Protease Inhibitor	Ro 31-8959 (saquinavir) + ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	Y	?	NL4-3 passaged in CEMX174 in presence of SQV+RTV+IDV. Selected mutant had other PI mutations. Used 8-mutant clone for susceptibility assays: L10I, I54V, L63P, A71V, V82T, I84V, M90L.	Watkins03

**HIV-1 Protease**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
L 10 R	CTC→CGC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
L 10 R	CTC→CGC	Protease Inhibitor	MK-639 (indinavir)	Selected	N	Y	L10R/M46I/L63P/V82T: 4-fold; L10R/M46I/L63P/V82T/I84V: 8-fold	Condra96, Condra95
L 10 V	CTC→GTC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
L 10 V	CTC→GTC	Protease inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	?	Y		Mo05
L 10 V	CTC→GTC	Protease Inhibitor	MK-639 (indinavir)	Selected	N	Y		Condra96, Condra95
L 10 Y	CTC→TAC	Protease Inhibitor	BMS-232632 (atazanavir)	Selected	Y	?	V32L/L33F/M46I/A71V/I84V/N88S: 183-fold. L10Y/F150L/L63P/A71V/N88S: 93-fold. V32I/M46I/I84V/L89M: 96-fold.	Gong00
I 11 V	ATC→GTC	Protease Inhibitor	SC-52151 (telinavir)	Selected	Y	?	I11V/M46I/F53L/A71V/N88D: 10- to 20-fold	Smidt97
T 12 K	ACA→AAA	Protease inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	?	Y		Mo05
I 13 V	ATA→GTA	Protease inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	?	Y		Mo05
I 13 V	ATA→GTA	Protease inhibitor	PNU-140690 (tipranavir)	Selected	Y	?	After 73 passages 9 other mutations accumulated to give 87 fold resistance to tipranavir	Doyon05
K 14 R	AAG→AGG	Protease inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	?	Y		Mo05
I 15 V	ATA→GTA	Protease Inhibitor	PNU-140690 (tipranavir)	Selected	?	Y		Rusconi00

## HIV-1 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
G 16 A	GGG→GCG	Protease inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	?	Y	In vitro, Passage 17 virus I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y: reduced susceptibility 338 fold (in presence of p7/p1 (AN/F to VN/F) cleavage-site mutation and p1/p6 (F/L to F/F) cleavage-site mutation). In vivo, susceptibility was reduced 4–10-fold in conjunction with mutations at 82, 54, 10, 63, 71, and 84; >20-fold with K20M/R and >40-fold with F53L.	Mo05 Carrillo08
G 16 E	GGG→GAG	Protease Inhibitor	ABT-378 (lopinavir)	Selected	Y	?		
G 16 E	GGG→GAG	Protease Inhibitor	ABT-538 (ritonavir)	Cross-R	Y	?	21-fold resistance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y	Carrillo08
G 16 E	GGG→GAG	Protease Inhibitor	Ro 31–8959 (saquinavir)	Cross-R	Y	?	4-fold resistance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y	Carrillo08
K 20 I	AAG→?	Protease Inhibitor	ABT-378 (lopinavir)	Selected	?	Y		Parkin03
K 20 I	AAG→ATC	Protease inhibitor	multiple PI	Selected	?	Y		Svicher05
K 20 M	AAG→ATG	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
K 20 M	AAG→ATG	Protease Inhibitor	AG-1343 (nelfinavir)	Selected	N	Y	Seen in two patients following a switch from saquinavir. Associated with reduced susceptibility to both saquinavir and nelfinavir.	Lawrence99
K 20 M	AAG→ATG	Protease Inhibitor	MK-639 (indinavir)	Selected	N	Y		Condra96
K 20 R	AAG→AGG	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01

## HIV-1 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
K 20 R	AAG→AGG	Protease Inhibitor	ABT-538 (ritonavir)	Selected	N	Y	Secondary mutation occurs in combination with mutations at V82, I84, M36, I54, and A71.	Molla96
K 20 R	AAG→AGG	Protease Inhibitor	MK-639 (indinavir)	Selected	N	Y		Condra96
K 20 T	AAG→ACG	Protease inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	?	Y		Mo05
K 20 T	AAG→ACG	Protease inhibitor	AG-1343 (nelfinavir)	Selected	?	Y	Associated with L90M	Svicher05
A 22 V	GCT→GTT	Protease inhibitor	multiple PI	Selected	?	Y		Svicher05
L 23 I	CTA→ATA	Protease Inhibitor	BILA 2185 BS	Selected	Y	?	L10F/L23I/V32I/M46I/I47V/I54M/A71V/I84V: 1,500-fold with associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1'); p7/p1 cleavage site (Q to R (CAG to CGG) at P3', A to V (GCT to CTT) at P2').	Croteau97, Doyon96
L 23 I	CTA→ATA	Protease inhibitor	multiple PI	Selected	?	Y	Mutation selected when either nelfinavir or saquinavir used as sole PI; also selected in patients receiving ritanovir-boosted amprenavir or saquinavir	Johnston04
L 24 I	TTA→ATA	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
L 24 I	TTA→ATA	Protease Inhibitor	ABT-538 (ritonavir)	Selected	Y	?	Selected in in vitro passage of NL4-3 in CEMX174 cells in increasing concentrations of ritonavir.	Watkins03
L 24 I	TTA→ATA	Protease Inhibitor	MK-639 (indinavir)	Selected	N	Y		Condra96, Condra95
L 24 I	TTA→ATA	Protease Inhibitor	Ro, 31-8959 (saquinavir) + ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	Y	?	NL4-3 passaged in CEMX174 in presence of SQV+RTV+IDV. Selected mutant had other PI mutations. Used 8-mutant clone for susceptibility assays: L10I, I54V, L63P, A71V, V82T, I84V, M90L.	Watkins03
L 24 I	TTA→ATA	Protease Inhibitor	TMC114 (UIC-94017)	Cross-R	Y	?	73-fold resistant against indinavir-selected L10F/L24I/M46I/L63P/A71V/G73S/V82T	Koh03



**HIV-1 Protease**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
D 30 N	GAT → AAT	Protease Inhibitor	AG-1343 (nelfinavir)	Selected	N	Y	D30N/A71V: 7-fold; D30N and N88D are most common in vivo after 24 weeks of therapy; they do not cause cross-resistance to other protease inhibitors	Patrick98
V 32 I	GTA → ATA	Protease Inhibitor	A-77003	Selected	Y	?	V32I appears first; occurs with R8Q or V82I/M46L	Kaplan94
V 32 I	GTA → ATA	Protease Inhibitor	ABT-378 (lopinavir)	Selected	Y	?	I84V/L10F/M46I/T91S/V32I/I47V: 46 fold Passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y: 338 fold (in presence of p7/p1 (AN/F to VN/F) cleavage-site mutation and p1/p6 (F/L to F/F) cleavage-site mutation).	Carrillo98
V 32 I	GTA → ATA	Protease Inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	Y	?	Sequential accumulation of mutations in passage of pNL4-3 in MT4 cells in presence of a LPV/ritonavir ratio of 5:1. Appears fourth in sequence, in passage 11, after I84V, L10F and M46I, and followed by I47V, Q58E.	Mo03
V 32 I	GTA → ATA	Protease Inhibitor	BILA 1906 BS	Selected	Y	?	Dominant population at passage 33: V32I/M46I/A71V/I84A: 520-fold resistant. Associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1')	Croteau97
V 32 I	GTA → ATA	Protease Inhibitor	BILA 2185 BS	Selected	Y	?	L10F/L23I/V32I/M46I/I47V/I54M/A71V/I84V: 1,500-fold with associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1'); p7/p1 cleavage site (Q to R (CAG to CGG) at P3', A to V (GCT to CTT) at P2').	Croteau97, Doyon96
V 32 I	GTA → ATA	Protease Inhibitor	BMS-232632 (atazanavir)	Selected	Y	?	V32L/L33F/M46I/A71V/I84V/N88S: 183-fold. L10Y.F/I50L/L63P/A71V/N88S: 93-fold. V32I/M46I/I84V/L89M: 96-fold.	Gong00
V 32 I	GTA → ATA	Protease Inhibitor	JE-2147	Selected	Y	?	in vitro selection in MT-2 cells, passage 33	Gatanaga02
V 32 I	GTA → ATA	Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	N	in vitro selection in MT-2 cells, passage 27	Gatanaga02, Gulmik95
V 32 I	GTA → ATA	Protease Inhibitor	MK-639 (indinavir)	Selected	Y	Y	V32I/M46L/V82A: 3-fold; V32I/M46L/A71V/V82A: 14-fold	Condra96, Condra95
V 32 I	GTA → ATA	Protease inhibitor	PNU-140690 (tipranavir)	Selected	Y	?	After 73 passages 9 other mutations accumulated to give 87 fold resistance to tipranavir	Doyon05

## HIV-1 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
V 32 I	GTA→ATA	Protease Inhibitor	Ro 31-8959 (saquinavir)	Cross-R	Y	?	4-fold resistance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y	Carrillo08
V 32 I	GTA→ATA	Protease Inhibitor	TMC114 (UIC-94017)	Cross-R	Y	?	10-fold resistant against aprenavir-selected mutant L10FV32I/M46I/I54M/A71V/I84V.	Koh03
V 32 I	GTA→ATA	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?	in vitro selection in MT-2 cells, passage 10	Gatanaga02
L 33 F	TTA→TTC	Protease Inhibitor	ABT-538 (ritonavir)	Selected	N	Y	Secondary mutation occurs in combination with mutations at V82, I84, M36, I54, and A71.	Molla96
L 33 F	TTA→TTC	Protease Inhibitor	BMS-232632 (atazanavir)	Selected	Y	?	V32L/L33F/M46I/A71V/I84V/N88S: 183-fold. L10Y,F/I50L/L63P/A71V/N88S: 93-fold. V32I/M46I/I84V/L89M: 96-fold.	Gong00
L 33 F	TTA→TTT	Protease inhibitor	PNU-140690 (tipranavir)	Selected	Y	?	After 73 passages 9 other mutations accumulated to give 87 fold resistance to tipranavir	Doyon05
L 33 I	TTA→ATA	Protease Inhibitor	AG-1343 (nelfinavir)	Selected	N	Y	Associated with Clade E virus	Ariyoshi03
E 34 Q	GAA→CAA	Protease inhibitor	ABT-378 (lopinavir)	Selected	?	Y	Associated with either L33F or F53L	Svicher05
E 34 Q	GAA→CAA	Protease Inhibitor	ABT-378 (lopinavir)	Selected	Y	?	Selected by passage 24 in an In vitro passage of pNL4-3 in MT4 cells in the presence of lopinavir. Genome already had I50V, M46I, L10F and I47V from previous passages. Mutation was seen in combination with V32I, Q61H and E65Q.	Mo03
E 35 D	GAA→?	Protease Inhibitor	PNU-140690 (tipranavir)	Selected	?	Y	Seen in 60% of patients receiving tipranavir therapy.	Rusconi00
E 35 G	GAA→GGA	Protease inhibitor	multiple PI	Selected	?	Y		Svicher05
M 36 I	ATG→ATA	Protease Inhibitor	ABT-538 (ritonavir)	Selected	N	Y	In vivo, V82 occurs first, often followed by changes at 54, 71 and 36	Molla96
M 36 I	ATG→ATA	Protease Inhibitor	AG-1343 (nelfinavir)	Selected	N	Y	D30N/M36I/L63P: 60-fold, although L63P may be a polymorphism.	Patrick98
M 36 I	ATG→ATA	Protease inhibitor	PNU-140690 (tipranavir)	Selected	Y	?	After 73 passages 9 other mutations accumulated to give 87 fold resistance to tipranavir	Doyon05
M 36 L	ATG→CTG	Protease Inhibitor	ABT-538 (ritonavir)	Selected	N	Y	In vivo, V82 occurs first, often followed by changes at 54, 71 and 36	Molla96

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Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
M 36 V	ATG→GTG	Protease inhibitor	ABT-538 (ritonavir)	Selected	?	Y	Seen in 30% of patients receiving tipranavir therapy.	Resch05
N 37 D	ATG→GTG	Protease Inhibitor	PNU-140690 (tipranavir)	Selected	?	Y	These non active site mutations are associated with lower binding affinity of the inhibitors to protease in enzymatic assays Protease containing these mutations were assayed: L10I/M36I/S37D/M46I/R57K/L63P/A71V/G73S/L90M/I93L	Rusconi00
S 37 D	AGT→GAT	Protease Inhibitor	MK-639 (indinavir)	Selected	N	Y	Seen in 20% of patients receiving tipranavir therapy.	Muzammil03, Olsen99
R 41 K	AGA→AAA	Protease Inhibitor	PNU-140690 (tipranavir)	Selected	?	Y	Contrary to selection data, SDM were tested against TMC114 and susceptibility was increased	Rusconi00
R 41 T	AGA→ACA	Protease inhibitor	TMC114 (UIC-94017)	Selected	Y	?	Associated with either I54A or with multi PI resistance mutations V82A, V32I, and I47V	DeMeyer05
K 43 T	AAA→ACA	Protease inhibitor	ABT-378 (lopinavir)	Selected	?	Y	L10F/K45I/I84V: 50-fold	Svicher05
K 45 I	AAA→ATA	Protease Inhibitor	DMP-323	Selected	Y	?	After 73 passages 9 other mutations accumulated to give 87 fold resistance to tipranavir	Tisdale95, King95
K 45 I	AAA→ATA	Protease inhibitor	PNU-140690 (tipranavir)	Selected	Y	?	Associated with D30N and N88D	Doyon05
K 45 R	AAA→AGA	Protease inhibitor	AG-1343 (nelfinavir)	Selected	?	Y	Selected in chronically infected cells at 1 microM	Svicher05
M 46 F	ATG→TTC	Protease Inhibitor	A-77003	Selected	Y	?	No effect on susceptibility but improves replication competency of R8Q mutant; R8K/M46I/G48V: 20-fold	Kaplan94
M 46 I	ATG→ATA	Protease Inhibitor	A-77003	Selected	Y	?	Acquired in conjunction with M46I of in vitro passage of pNL4-3 in MT4 cells, passage 7	Ho94, Kaplan94
M 46 I	ATG→ATA	Protease Inhibitor	ABT-378 (lopinavir)	Selected	Y	?	I84V/L10F/M46I: 4 fold I84V/L10F/M46I/T91S: 12 fold I84V/L10F/M46I/T91S/V32I/I47V: 46 fold Passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y: 338 fold (in presence of p7/p1 (AN/F to VN/F) cleavage-site mutation and p1/p6 (F/L to F/F) cleavage-site mutation).	Mo03
M 46 I	ATG→ATA	Protease Inhibitor	ABT-378 (lopinavir)	Selected	Y	?		Carrillo98

## HIV-1 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
M 46 I	ATG→ATA	Protease Inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	Y	?	Acquired in conjunction with I50V in passage 8 (pNL4-3 in MT4 cells, in 1:5 lopinavir/ritonavir)	Mo03
M 46 I	ATG→ATA	Protease Inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	Y	?	Sequential accumulation of mutations in passage of pNL4-3 in MT4 cells in presence of a LPV/ritonavir ration of 5:1. Appears third in sequence, in passage 9 to 11, after I84V and L10F, and followed by V32I, I47V, Q58E.	Mo03
M 46 I	ATG→ATA	Protease Inhibitor	ABT-538 (ritonavir)	Selected	Y	Y	In vitro, occurs after selection of I84V. In vivo, V82A/F/T/S occurs first, followed by changes at 54, 71 and 36	Markowitz95, Molla96
M 46 I	ATG→ATA	Protease Inhibitor	AG-1343 (nelfinavir)	Selected	Y	Y	5-fold resistance in combination with I84V; often seen with D30N in vivo	Patrick96, Patrick98
M 46 I	ATG→ATA	Protease Inhibitor	BILA 1906 BS	Selected	Y	?	Dominant population at passage 33: V32I/M46I/A71V/I84A: 520-fold resistant. Associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1')	Croteau97, Doyon96
M 46 I	ATG→ATA	Protease Inhibitor	BILA 2185 BS	Selected	Y	?	L10F/L23I/V32I/M46I/I47V/I54M/A71V/I84V: 1,500-fold with associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1'); p7/p1 cleavage site (Q to R (CAG to CGG) at P3', A to V (GCT to CTT) at P2').	Croteau97, Doyon96
M 46 I	ATG→ATA	Protease Inhibitor	BMS-232632 (atazanavir)	Selected	Y	?	V32L/L33F/M46I/A71V/I84V/N88S: 183-fold. L10Y,F/I50L/L63P/A71V/N88S: 93-fold. V32I/M46I/I84V/L89M: 96-fold.	Gong00
M 46 I	ATG→ATA	Protease Inhibitor	DMP 450	Selected	Y	?	Probably compensatory	Hodge96
M 46 I	ATG→ATA	Protease Inhibitor	JE-2147	Selected	Y	?	L10F/M46I/I47V/I84V:28-fold. >50 passages required for isolation of resistant virus.	Yoshimura99
M 46 I	ATG→ATA	Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	?	in vitro selection in MT-2 cells, passage 27	Gatanaga02
M 46 I	ATG→ATA	Protease Inhibitor	MK-639 (indinavir)	Selected	N	Y	M46I/L63P/V82T: 4-fold; L10R/M46I/L63P/V82T: 4-fold; L10R/M46I/L63P/V82T/I84V: 8-fold	Condra96, Condra95
M 46 I	ATG→ATA	Protease Inhibitor	Ro 31-8959 (saquinavir)	Cross-R	Y	?	4-fold resistance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y	Carrillo98

## HIV-1 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
M 46 I	ATG→CTG	Protease Inhibitor	SC-52151 (telinavir)	Selected	Y	?	I11V/M46I/F53L/A71V/N88D: 10- to 20-fold	Smidt97
M 46 I	ATG→ATA	Protease Inhibitor	TMC114 (UIC-94017)	Cross-R	Y	?	10-fold resistant against aprenavir-selected mutant L10F/V32I/M46I/I54M/A71V/I84V. 73-fold resistant against indinavir-selected L10F/L24I/M46I/L63P/A71V/G73S/V82T	Koh03
M 46 I	ATG→ATA	Protease Inhibitor	UIC-94003	Selected	Y	?	in vitro selection in MT-2 cells, passage 62	Gatanaga02
M 46 I	ATG→ATA	Protease Inhibitor	VB-11,328	Selected	Y	?	I50V/M46I/I47V: 20-fold	Partaledis95
M 46 I	ATG→ATA	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?	Arose at later passages; L10F/I84V already present	Partaledis95
M 46 L	ATG→TTC	Protease Inhibitor	A-77003	Selected	Y	?		Kaplan94
M 46 L	ATG→TTG	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
M 46 L	ATG→TTG	Protease Inhibitor	ABT-538 (ritonavir)	Selected	Y	?	Selected in in vitro passage of NL4-3 in CEMX174 cells in increasing concentrations of ritonavir. Appeared early in selection.	Watkins03
M 46 L	ATG→CTG	Protease Inhibitor	ABT-538 (ritonavir)	Selected	Y	Y	Secondary mutation occurs in combination with mutations at V82, I84, M36, I54, and A71.	Molla96
M 46 L	ATG→TTG	Protease Inhibitor	BILA 1906 BS	Selected	Y	?	Dominant population at passage 33: M46L/A71V/I84A: 520-fold resistant. Associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1'))	Croteau97, Doyon96
M 46 L	ATG→CTG	Protease Inhibitor	DMP-323	Selected	Y	?	V82A/M46L: 7-fold; V82A/M46L/L97V: 11-fold	King95
M 46 L	ATG→TTG	Protease Inhibitor	MK-639 (indinavir)	Selected	Y	Y	Appears second in sequence. Combination V82A/M46L/V32I/A71V: 14-fold	Tisdale95
M 46 L	ATG→TTG	Protease Inhibitor	Ro 31-8959 (saquinavir) + ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	Y	?	NL4-3 passaged in CEMX174 in presence of SQV+RTV+HDV. Selected mutant had other PI mutations. Used 8-mutant clone for susceptibility assays: L10I, I54V, L63P, A71V, V82T, I84V, M90L.	Watkins03

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Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
M 46 L	ATG → TTG	Protease Inhibitor	Ro 31-8959 (saquinavir) + ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	Y	?	NL4-3 passaged in CEMX174 in presence of SQV+RTV+IDV. Selected mutant had other PI mutations. Used 8-mutant clone for susceptibility assays: L10I, I54V, L63P, A71V, V82I, I84V, M90L.	Watkins03
M 46 L	ATG → CTG	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?	In combination with I50V	Tisdale95
I 47 A	ATA → GCA	Protease inhibitor	ABT-378 (lopinavir)	Selected	Y	Y	Causes hypersusceptibility to saquinavir	Carrillo98
I 47 A	ATA → GCA	Protease inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	?	Y		Mo05
I 47 V	ATA → GTA	Protease Inhibitor	ABT-378 (lopinavir)	Selected	Y	?	I84V/L10F/M46I/T91S/V32I/I47V: 46 fold Passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y: 338 fold (in presence of p7/p1 (AN/F to VN/F) cleavage-site mutation and p1/p6 (F/L to F/F) cleavage-site mutation).	Carrillo98
I 47 V	ATA → GTA	Protease Inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	Y	?	Sequential accumulation of mutations in passage of pNL4-3 in MT4 cells in presence of a LPV/ritonavir ratio of 5:1. Appears fifth in sequence, in passage 17, after I84V, L10F, M46I and V32I, and followed by Q58E.	Mo03
I 47 V	ATA → GTA	Protease Inhibitor	ABT-538 (ritonavir)	Cross-R	Y	?	21-fold resistance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y	Carrillo98
I 47 V	ATA → CTA	Protease Inhibitor	BILA 2185 BS	Selected	Y	?	L10F/L23I/V32I/M46I/I47V/I54M/A71V/I84V: 1,500-fold with associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1'); p7/p1 cleavage site (Q to R (CAG to CGG) at P3', A to V (GCT to CTT) at P2').	Croteau97, Doyon96
I 47 V	ATA → CTA	Protease Inhibitor	JE-2147	Selected	Y	?	L10F/I47V/I84V:19-fold. L10F/M46I/I47V/I84V:28-fold. >50 passages required for isolation of resistant virus.	Yoshimura99
I 47 V	ATA → CTA	Protease Inhibitor	KNI-272 (kynostatin)	Cross-R	Y	?	7-fold resistant to JE-2147 selected virus (L10F/M46I/I47V/I184V)	Yoshimura99

## HIV-1 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
I 47 V	ATA→GTA	Protease Inhibitor	Ro 31-8959 (saquinavir)	Cross-R	Y	?	4-fold resistance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y	Carrillo08
I 47 V	ATA→CTA	Protease Inhibitor	VB-11,328	Selected	Y	?	I50V/M46I/I47V: 20-fold	Partaledis95
I 47 V	ATA→CTA	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?	Arose at later passages; L10F/I84V already present	Partaledis95
G 48 V	GGG→GTG	Protease Inhibitor	A-77003	Selected	Y	N	R8K/M46I/G48V: 20-fold; G48V/I82T: 100-fold	Borman96
G 48 V	GGG→GTG	Protease Inhibitor	MK-639 (indinavir)	Selected	?	Y		Vasudevachari96
G 48 V	GGG→GTG	Protease Inhibitor	MP-134	Cross-R	Y	?	MP-167-selected virus confers 5-fold increase in IC90	Mo96
G 48 V	GGG→GTG	Protease Inhibitor	MP-167	Selected	Y	?	L10F/G48V: 20-fold	Mo96
G 48 V	GGG→GTG	Protease Inhibitor	Ro 31-8959 (saquinavir)	Selected	Y	Y	G48V/L90M: >100-fold enzyme resistance; G48V/L90M/I54V: > 50-fold (subtype B or O). In vivo, also had V82A	Jacobsen95, Eberle95, Winters98a
G 48 V	GGG→GTG	Protease Inhibitor	Ro 31-8959 (saquinavir) + ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	Y	?	NL4-3 passaged in CEMX174 in presence of SQV+RTV+IDV. Selected mutant had other PI mutations. Used 8-mutant clone for susceptibility assays: L10I, I54V, L63P, A71V, V82T, I84V, M90L.	Watkins03
G 48 V	GGG→GTG	Protease Inhibitor	SC-52151 (telinavir)	Cross-R	Y	?	MP-167-selected virus confers 16-fold increase in IC90	Mo96
I 50 L	ATT→CTT	Protease Inhibitor	BMS-232632 (atazanavir)	Selected	Y	Y		Gong00, Colonna04
I 50 L	ATT→CTT	Protease Inhibitor	BMS-232632 (atazanavir)	Selected	Y	?	V32L/L33F/M46I/A71V/I84V/N88S: 183-fold. L10Y/F/I50L/L63P/A71V/N88S: 93-fold. V32I/M46I/I84V/L89M: 96-fold.	Gong00
I 50 V	ATT→GTT	Protease Inhibitor	ABT-378 (lopinavir)	Selected	Y	?	Acquired in conjunction with M46I of in vitro passage of pNL4-3 in MT4 cells, passage 7	Mo03
I 50 V	ATT→GTT	Protease Inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	Y	?	Acquired in conjunction with M46I in passage 8 (pNL4-3 in MT4 cells, in 1:5 lopinavir/ritonavir)	Mo03
I 50 V	ATT→GTT	Protease Inhibitor	UIC-94003	Selected	Y	?	in vitro selection in MT-2 cells, passage 62	Gatnaga02
I 50 V	ATT→GTT	Protease Inhibitor	VB-11,328	Selected	Y	?	I50V/M46I/I47V: 20-fold	Partaledis95
I 50 V	ATT→GTT	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?	Replaced I84V	Partaledis95

**HIV-1 Protease**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
F 53 L	TTT→?	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
F 53 L	TTT→?	Protease Inhibitor	SC-52151 (telinavir)	Selected	Y	?	I11V/M46I/F53L/A71V/N88D: 10- to 20-fold	Smidt97
F 53 Y	TTT→TAT	Protease Inhibitor	Ro 31-8959 (saquinavir) + ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	Y	?	NL4-3 passaged in CEMX174 in presence of SQV+RTV+IDV. Selected mutant had other PI mutations. Used 8-mutant clone for susceptibility assays: L10I, I54V, L63P, A71V, V82T, I84V, M90L.	Watkins03
I 54 A	ATC→GCC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	?	Y		Parkin03
I 54 L	ATC→CTC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
I 54 L	ATT→CTT	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	Y		Maguire02
I 54 M	ATC→ATG	Protease Inhibitor	ABT-378 (lopinavir)	Selected	?	Y		Parkin03
I 54 M	ATT→ATG	Protease Inhibitor	BILA 2185 BS	Selected	Y	?	L10F/L231V/32I/M46I/I47V/I54M/A71V/I84V: 1,500-fold with associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1'); p7/p1 cleavage site (Q to R (CAG to CGG) at P3', A to V (GCT to CTT) at P2').	Croteau97, Doyon96
I 54 M	ATT→ATG	Protease Inhibitor	TMC114 (UIC-94017)	Cross-R	Y	?	10-fold resistant against aprenavir-selected mutant L10F/V32I/M46I/I54M/A71V/I84V.	Koh03
I 54 M	ATC→ATG	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?	in vitro selection in MT-2 cells, passage 31	Gatamaga02
I 54 S	ATC→AGC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	?	Y		Parkin03



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Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
I 54 T	ATC→ACC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
I 54 V	ATC→GTC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
I 54 V	ATC→GTC	Protease Inhibitor	ABT-538 (ritonavir)	Selected	N	Y	In vivo, V82A/FT/S occurs first, followed by changes at 54, 71 and 36	Molla96
I 54 V	ATC→GTC	Protease inhibitor	PNU-140690 (tipranavir)	Selected	Y	?	After 73 passages 9 other mutations accumulated to give 87 fold resistance to tipranavir	Doyon05
I 54 V	ATA→GTA	Protease Inhibitor	Ro 31-8959 (saquinavir)	Selected	Y	?	In subtype O and B	Eberle95
I 54 V	ATA→GTA	Protease Inhibitor	Ro 31-8959 (saquinavir) + ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	Y	?	NL4-3 passaged in CEMX174 in presence of SQV+RTV+IDV. Selected mutant had other PI mutations. Used 8-mutant clone for susceptibility assays: L10I, I54V, L63P, A71V, V82T, I84V, M90L.	Watkins03
K 55 R	AAA→AGA	Protease inhibitor	ABT-378 (lopinavir)	Selected	?	Y	Associated with V82A, I54V, and M46I	Svicher05
K 55 R	AAA→AGA	Protease Inhibitor	AG-1343 (nelfinavir)	Selected	N	Y	Seen in one patient following a switch from saquinavir. Associated with reduced susceptibility to both saquinavir and nelfinavir.	Lawrence99
R 57 K	AGA→AAA	Protease Inhibitor	AG-1343 (nelfinavir)	Selected	N	Y	Seen in one patient following a switch from saquinavir. Associated with reduced susceptibility to both saquinavir and nelfinavir.	Lawrence99
Q 58 E	AGA→AAA	Protease Inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	Y	?	Sequential accumulation of mutations in passage of pNL4-3 in MT4 cells in presence of a LPV/ritonavir ratio of 5:1. Appears last in sequence, in passage 17, after I84V, L10F, M46I, V32I, and I47V.	Mo03
D 60 E	GAT→GAA	Protease Inhibitor	DMP 450	Selected	Y	?	Probably compensatory	Hodge96

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Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
D 60 E	GAT→GAA	Protease Inhibitor	PNU-140690 (tipranavir)	Selected	?	Y	Seen in 30% of patients receiving tipranavir therapy.	Rusconi00
Q 61 H	CAG→?	Protease Inhibitor	ABT-378 (lopinavir)	Selected	Y	?	Selected by passage 24 in an in vitro passage of pNL4-3 in MT4 cells in the presence of lopinavir. Genome already had I50V, M46I, L10F and I47V from previous passages. Mutation was seen in combination with V32I, E34Q, and E65Q.	Mo03
L 63 A	CTC→GCC	Protease inhibitor	ABT-538 (ritonavir)	Selected	?	Y		Resch05
L 63 C	CTC→TGC	Protease inhibitor	ABT-538 (ritonavir)	Selected	?	Y		Resch05
L 63 P	CTC→CCC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
L 63 P	CTC→CCC	Protease Inhibitor	ABT-538 (ritonavir)	Selected	Y	?	Selected in in vitro passage of NL4-3 in CEMX174 cells in increasing concentrations of ritonavir. Appeared early in selection.	Watkins03
L 63 P	CTC→CCC	Protease Inhibitor	BMS-232632 (atazanavir)	Selected	Y	?	V32L/L33F/M46I/A71V/I84V/N88S: 183-fold. L10Y,F/I50L/L63P/A71V/N88S: 93-fold. V32I/M46I/I84V/L89M: 96-fold.	Gong00
L 63 P	CTC→CCC	Protease Inhibitor	MK-639 (indinavir)	Selected	N	Y	M46I/L63P/V82T: 4-fold; L10R/M46I/L63P/V82T/I84V: 8-fold; L10R/M46I/L63P/V82T: 4-fold	Condra96, Condra95
L 63 P	CTC→CCC	Protease Inhibitor	Ro 31-8959 (saquinavir)	Selected	Y	?	Selected by passage 27 of in vitro passage of NL4-3 in CEMX174 cells in increasing concentrations of indinavir.	Watkins03
L 63 P	CTC→CCC	Protease Inhibitor	Ro 31-8959 (saquinavir) + ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	Y	?	NL4-3 passaged in CEMX174 in presence of SQV+RTV+IDV. Selected mutant had other PI mutations. Used 8-mutant clone for susceptibility assays: L10I, I54V, L63P, A71V, V82T, I84V, M90L.	Watkins03
L 63 P	CTC→CCC	Protease Inhibitor	TMC114 (UIC-94017)	Cross-R	Y	?	73-fold resistant against indinavir-selected L10F/L24I/M46I/L63P/A71V/G73S/V82T	Koh03

**HIV-1 Protease**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
L 63 Q	CTC→CAG	Protease inhibitor	ABT-538 (ritonavir)	Selected	?	Y		Resch05
L 63 S	CTC→TCC	Protease inhibitor	ABT-538 (ritonavir)	Selected	?	Y		Resch05
L 63 T	CTC→ACC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	?	Y		Parkin03
I 64 V	ATA→GTA	Protease inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	?	Y		Mo05
E 65 Q	GAA→CAA	Protease Inhibitor	ABT-378 (lopinavir)	Selected	Y	?	Selected by passage 24 in an In vitro passage of pNL4-3 in MT4 cells in the presence of lopinavir. Genome already had I50V, M46I, L10F and I47V from previous passages. Mutation was seen in combination with V32I, E34Q, and Q61H.	Mo03
I 66 F	ATC→TTC	Protease Inhibitor	Ro 31-8959 (saquinavir) + ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	Y	?	NL4-3 passaged in CEMX174 in presence of SQV+RTV+IDV. Selected mutant had other PI mutations. Used 8-mutant clone for susceptibility assays: L10I, I54V, L63P, A71V, V82T, I84V, M90L.	Watkins03
H 69 Y	CAT→TAT	Protease Inhibitor	ABT-378 (lopinavir)	Selected	Y	?	Passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y: 338 fold (in presence of p7/pl (AN/F to VN/F) cleavage-site mutation and p1/p6 (F/L to F/F) cleavage-site mutation).	Carrillo98
H 69 Y	CAT→TAT	Protease Inhibitor	ABT-538 (ritonavir)	Cross-R	Y	?	21-fold resistance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y	Carrillo98
H 69 Y	CAT→TAT	Protease Inhibitor	Ro 31-8959 (saquinavir)	Cross-R	Y	?	4-fold resistance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y	Carrillo98
K 70 E	AAA→GAA	Protease inhibitor	TMC114 (UIC-94017)	Selected	Y	?		DeMeyer05

**HIV-1 Protease**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
A 71 I	GCT→ATT	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
A 71 L	GCT→CTC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
A 71 T	GCT→ACT	Protease Inhibitor	A-77003	Cross-R	Y	?	BMS-186318-selected virus A71T/V82A: 4-fold	Patrick95
A 71 T	GCT→ACT	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
A 71 T	GCT→ACT	Protease Inhibitor	AG-1343 (nelfinavir)	Selected	N	Y		Patrick98
A 71 T	GCT→ACT	Protease Inhibitor	BMS-186318	Selected	Y	?	A71T/V82A: 15-fold	Patrick95
A 71 T	GCT→ACT	Protease Inhibitor	MK-639 (indinavir)	Selected	N	Y		Condra96, Condra95
A 71 T	GCT→ACT	Protease Inhibitor	PNU-140690 (tipranavir)	Selected	?	Y		Rusconi00
A 71 V	GCT→GTC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
A 71 V	GCT→GTT	Protease Inhibitor	ABT-538 (ritonavir)	Selected	Y	Y	Occurred by passage 22 in vitro preceded by I84V, M46I and V82F. In vivo, V82A/F/T/S occurs first, followed by changes at 54, 71 and 36	Markowitz95, Molla96
A 71 V	GCT→GTT	Protease Inhibitor	AG-1343 (nelfinavir)	Selected	N	Y	D30N/A71V: 7-fold; M46I/L63P/A71V/I84V: 30-fold	Patrick98

**HIV-1 Protease**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
A 71 V	GCT→GTT	Protease Inhibitor	BILA 1906 BS	Selected	Y	?	Dominant population at passage 33: V32I/M46I/A71V/I84A or M46L/A71V/I84A: 520-fold resistant. Associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1')/ L10F/L23I/V32I/M46I/I47V/I54M/A71V/I84V; 1,500-fold with associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1'); p7/p1 cleavage site (Q to R (CAG to CGG) at P3', A to V (GCT to CTT) at P2').	Croteau97, Doyon96
A 71 V	GCT→GTT	Protease Inhibitor	BILA 2185 BS	Selected	Y	?	V32L/L33F/M46I/A71V/I84V/N88S: 183-fold. L10Y,F/I50L/L63P/A71V/N88S: 93-fold. V32I/M46I/I84V/L89M: 96-fold.	Croteau97, Doyon96
A 71 V	GCT→GTT	Protease Inhibitor	BMS-232632 (atazanavir)	Selected	Y	?	in vitro selection in MT-2 cells, passage 27, in 30% of clones	Gong00
A 71 V	GCT→GTT	Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	N	Appears fourth in sequence. Combination V82A/M46L/V32I/A71V: 14-fold	Gatanaga02, Gulnik95
A 71 V	GCT→GTT	Protease Inhibitor	MK-639 (indinavir)	Selected	Y	Y	After 73 passages 9 other mutations accumulated to give 87 fold resistance to tipranavir	Tisdale95
A 71 V	GCT→GTT	Protease inhibitor	PNU-140690 (tipranavir)	Selected	Y	?	Selected in in vitro passage of NL4-3 in CEMX174 cells in increasing concentrations of saquinavir. This mutation appeared in early in passage and was maintained until the appearance of V77I.	Doyon05
A 71 V	GCT→GTT	Protease Inhibitor	Ro 31-8959 (saquinavir)	Selected	Y	?	NL4-3 passaged in CEMX174 in presence of SQV+RTV+HDV. Selected mutant had other PI mutations. Used 8-mutant clone for susceptibility assays: L10I, I54V, L63P, A71V, V82T, I84V, M90L.	Watkins03
A 71 V	GCT→GTT	Protease Inhibitor	SC-52151 (telinavir)	Selected	Y	?	I11V/M46I/F53L/A71V/N88D: 10- to 20-fold	Smidt97
A 71 V	GCT→GTT	Protease Inhibitor	TMC114 (UIC-94017)	Cross-R	Y	?	10-fold resistant against aprenavir-selected mutant L10F/V32I/M46I/I54M/A71V/I84V. 73-fold resistant against indinavir-selected L10F/L24I/M46I/L63P/A71V/G73S/V82T	Koh03
A 71 V	GCT→GTT	Protease Inhibitor	UIC-94003	Selected	Y	?	in vitro selection in MT-2 cells, passage 62	Gatanaga02

## HIV-1 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
A 71 V	GCT→GTT	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?	in vitro selection in MT-2 cells, passage 31	Gatanaga02
G 73 S	GGT→AGT	Protease Inhibitor	AG-1343 (nelfinavir)	Selected	N	Y	Seen in two patients following a switch from saquinavir. Associated with reduced susceptibility to both saquinavir and nelfinavir.	Lawrence99
G 73 S	GGT→GCT	Protease Inhibitor	MK-639 (indinavir)	Selected	N	Y	Emerges following a switch from saquinavir to indinavir.	Duloust99
G 73 S	GGT→GCT	Protease Inhibitor	Ro 31-8959 (saquinavir)	Selected	Y	?	Selected by passage 18 of in vitro passage of NL4-3 in CEMX174 cells in increasing concentrations of indinavir.	Watkins03
G 73 S	GGT→GCT	Protease Inhibitor	Ro 31-8959 (saquinavir) + ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	Y	?	NL4-3 passaged in CEMX174 in presence of SQV+RTV+IDV. Selected mutant had other PI mutations. Used 8-mutant clone for susceptibility assays: L10I, I54V, L63P, A71V, V82T, I84V, M90L.	Watkins03
G 73 S	GGT→GCT	Protease Inhibitor	TMC114 (UIC-94017)	Cross-R	Y	?	73-fold resistant against indinavir-selected L10I/L24I/M46I/L63P/A71V/G73S/V82T	Koh03
T 74 S	ACA→TCA	Protease inhibitor	AG-1343 (nelfinavir)	Selected	?	Y		Svicher05
L 76 V	TTA→GTA	Protease inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	?	Y		Mo05
V 77 I	GTA→ATA	Protease Inhibitor	AG-1343 (nelfinavir)	Selected	N	Y		Patrick98
V 77 I	GTA→ATA	Protease Inhibitor	Ro 31-8959 (saquinavir)	Selected	Y	?	Selected in in vitro passage of NL4-3 in CEMX174 cells in increasing concentrations of saquinavir. This mutation appeared late in the passage and correlated with a reversion of A71V.	Watkins03
V 77 I	GTA→ATA	Protease Inhibitor	Ro 31-8959 (saquinavir) + ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	Y	?	NL4-3 passaged in CEMX174 in presence of SQV+RTV+IDV. Selected mutant had other PI mutations. Used 8-mutant clone for susceptibility assays: L10I, I54V, L63P, A71V, V82T, I84V, M90L.	Watkins03

## HIV-1 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
V 82 A	GTC→GCC	Protease Inhibitor	A-77003	Selected	Y	?	Rare; seen with M46F; V32I appears first; progression to V32I/M46V and V32I/M46V/A71V/V82A occurs even in the absence of drug	Borman96
V 82 A	GTC→GCC	Protease Inhibitor	A-77003	Cross-R	Y	?	BMS-186318-selected virus A71T/V82A: 4-fold	Patrick95
V 82 A	GTC→GCC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
V 82 A	GTC→GCC	Protease Inhibitor	ABT-538 (ritonavir)	Selected	N	Y	In vivo, V82 occurs first, often followed by changes at I54, A71 and M36.	Molla96
V 82 A	GTC→GCC	Protease Inhibitor	AG-1343 (nelfinavir)	Selected	N	Y		Lawrence99
V 82 A	GTC→GCC	Protease Inhibitor	BMS-186318	Selected	Y	?	A71T/V82A: 15-fold	Patrick95
V 82 A	GTC→GCC	Protease Inhibitor	DMP-323	Selected	Y	?	V82A/M46L: 7-fold; V82A/M46L/L97V: 11-fold	King95
V 82 A	GTC→GCC	Protease Inhibitor	MK-639 (indinavir)	Selected	Y	Y	V32I/M46L/V82A: 3-fold; V32I/M46L/A71V/V82A: 14-fold	Condra96, Condra95
V 82 A	GTC→GCC	Protease Inhibitor	P9941	Selected	Y	?	Used plaque assay and endpoint titration to select mutant.	Otto93
V 82 A	GTC→GCC	Protease Inhibitor	Ro 31–8959 (saquinavir)	Selected	N	Y	Follows G48V during saquinavir therapy or after a switch to nelfinavir or indinavir.	Winters98a
V 82 F	GTC→TTC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
V 82 F	GTC→TTC	Protease Inhibitor	ABT-538 (ritonavir)	Selected	Y	Y	In vivo, V82 occurs first, often followed by changes at I54, A71 and M36. Molecular clone of V82F alone: 4–5-fold resistant in vitro.	Markowitz95, Molla96
V 82 F	GTC→TTC	Protease Inhibitor	DMP-323	Selected	Y	?	V82F/84V: 97-fold	King95
V 82 I	GTC→ATC	Protease Inhibitor	A-77003	Selected	Y	?	No resistance alone but V32I and V82I are synergistic mutations yielding 20-fold enzyme resistance.	Kaplan94
V 82 I	GTC→ATC	Protease Inhibitor	JE-2147	Selected	Y	?	in vitro selection in MT-2 cells, passage 33	Gatanaga02

**HIV-1 Protease**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
V 82 I	GTC→ATC	Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	?	in vitro selection in MT-2 cells, passage 27	Gatanaga02
V 82 L	GTC→CTC	Protease inhibitor	ABT-538 (ritonavir)	Selected	?	Y		Resch05
V 82 L	GTC→CTC	Protease inhibitor	PNU-140690 (tipranavir)	Selected	Y	?	After 73 passages 9 other mutations accumulated to give 87 fold resistance to tipranavir	Doyon05
V 82 M	GTC→ATG	Protease inhibitor	ABT-538 (ritonavir)	Selected	?	Y		Resch05
V 82 S	GTC→TCC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	?	Y		Parkin03
V 82 S	GTC→TCC	Protease Inhibitor	ABT-538 (ritonavir)	Selected	N	Y	V82S or T occurs after V82A or F.	Molla96
V 82 T	GTC→ACC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
V 82 T	GTC→ACC	Protease Inhibitor	ABT-538 (ritonavir)	Selected	N	Y	V82S or T occurs after V82A or F.	Molla96
V 82 T	GTC→ACC	Protease Inhibitor	MK-639 (indinavir)	Selected	N	Y	M46I/L63P/V82T: 4-fold; L10R/M46I/L63P/V82T: 4-fold; L10R/M46I/L63P/V82T/I84V: 8-fold	Condra96, Condra95
V 82 T	GTC→ACC	Protease Inhibitor	Ro 31-8959 (saquinavir) + ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	Y	?	NL4-3 passaged in CEMX174 in presence of SQV+RTV+IDV. Selected mutant had other PI mutations. Used 8-mutant clone for susceptibility assays: L10I, I54V, L63P, A71V, V82T, I84V, M90L.	Watkins03
V 82 T	GTC→ACC	Protease Inhibitor	TMC114 (UIC-94017)	Cross-R	Y	?	73-fold resistant against indinavir-selected L10F/L24I/M46I/L63P/A71V/G73S/V82T	Koh03
I 84 A	ATA→GCA	Protease Inhibitor	AG-1343 (nelfinavir)	Selected	Y	?	4-fold resistance when in combination with V32I	Patrick96
I 84 A	ATA→GCA	Protease Inhibitor	BILA 1906 BS	Selected	Y	?	Dominant population at passage 33: V32I/M46I/A71V/I84A or M46L/A71V/I84A: 520-fold resistant. Associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1')	Croteau97, Doyon96



**HIV-1 Protease**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
I 84 A	ATA→GCA	Protease Inhibitor	MK-639 (indinavir)	Selected	Y	?	Selected in in vitro passage of NL4-3 in CEMX174 cells in increasing concentrations of indinavir. This mutation appeared in conjunction with M46I, I54V, L63P and A71V.	Watkins03
I 84 A	ATA→GCA	Protease Inhibitor	Ro 31-8959 (saquinavir) + ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	Y	?	NL4-3 passaged in CEMX174 in presence of SQV+RTV+IDV. Selected mutant had other PI mutations. Used 8-mutant clone for susceptibility assays: L10I, I54V, L63P, A71V, V82T, I84V, M90L.	Watkins03
I 84 V	ATA→GTA	Protease Inhibitor	ABT-378 (lopinavir)	Selected	Y	?	I84V/L10F/M46I: 4 fold I84V/L10F/M46I/T91S; 12 fold I84V/L10F/M46I/T91S/V32I/I47V; 46 fold Passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y; 338 fold (in presence of p7/p1 (AN/F to VN/F) cleavage-site mutation and p1/p6 (F/L to F/F) cleavage-site mutation).	Carrillo98
I 84 V	ATA→GTA	Protease Inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	Y	?	Sequential accumulation of mutations in passage of pNL4-3 in MT4 cells in presence of a LPV/ritonavir ratio of 5:1. Appears first in sequence, in passage 6, followed by L10F, M46I, V32I, I47V, Q58E.	Mo03
I 84 V	ATA→GTA	Protease Inhibitor	ABT-538 (ritonavir)	Selected	Y	?	Selected in in vitro passage of NL4-3 in CEMX174 cells in increasing concentrations of ritonavir. Appeared late in selection (passage 34)	Watkins03
I 84 V	ATA→GTA	Protease Inhibitor	ABT-538 (ritonavir)	Selected	Y	Y	First mutation seen in in vitro passage. Molecular clone 8-10-fold resistant.	Markowitz95, Molla96
I 84 V	ATA→GTA	Protease Inhibitor	AG-1343 (nelfinavir)	Selected	Y	?	M46I/L63P/A71V/I84V: 30-fold	Patrick96
I 84 V	ATA→GTA	Protease Inhibitor	BILA 2185 BS	Selected	Y	?	L10F/L23I/V32I/M46I/I47V/I54M/A71V/I84V; 1,500-fold with associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1'); p7/p1 cleavage site (Q to R (CAG to CGG) at P3', A to V (GCT to CTT) at P2').	Croteau97, Doyon96

**HIV-1 Protease**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
I 84 V	ATA → GTA	Protease Inhibitor	BMS-232632 (atazanavir)	Selected	Y	?	V32L/L33F/M46I/A71V/I84V/N88S: 183-fold. L10Y/F150L/L63P/A71V/N88S: 93-fold. V32I/M46I/I84V/L89M: 96-fold.	Gong00
I 84 V	ATA → GTA	Protease Inhibitor	DMP 450	Selected	Y	?		Hodge96
I 84 V	ATA → GTA	Protease Inhibitor	DMP-323	Selected	Y	?	Occurs with K45I/L10F and V82F; Molecular clone of I84V alone: 50-fold	Tisdale95, King95
I 84 V	ATA → GTA	Protease Inhibitor	JE-2147	Selected	Y	?	L10F/I47V/I84V:19-fold. L10F/M46I/I47V/I84V:28-fold. >50 passages required for isolation of resistant virus.	Yoshimura99
I 84 V	ATA → GTA	Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	N	in vitro selection in MT-2 cells, passage 27	Gatanaga02, Gulnik95
I 84 V	ATA → GTA	Protease Inhibitor	MK-639 (indinavir)	Selected	N	Y	G48V/I84V/L90M: 30-fold; L10R/M46I/L63P/V82T/I84V: 8-fold	Condra96, Condra95
I 84 V	ATA → GTA	Protease Inhibitor	MP-134	Selected	Y	?		Mo96
I 84 V	ATA → GTA	Protease Inhibitor	MP-167	Cross-R	Y	?	MP-134-selected virus confers 5-fold increase in IC90	Mo96
I 84 V	ATA → GTA	Protease inhibitor	PNU-140690 (tipranavir)	Selected	Y	?	After 73 passages 9 other mutations accumulated to give 87 fold resistance to tipranavir	Doyon05
I 84 V	ATA → GTA	Protease Inhibitor	Ro 31-8959 (saquinavir)	Selected	Y	?	In combination with G48V and L90M: 30-fold	Tisdale95
I 84 V	ATA → GTA	Protease Inhibitor	Ro 31-8959 (saquinavir) + ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	Y	?	NL4-3 passaged in CEMX174 in presence of SQV+RTV+IDV. Selected mutant had other PI mutations. Used 8-mutant clone for susceptibility assays: L10I, I54V, L63P, A71V, V82T, I84V, M90L.	Watkins03
I 84 V	ATA → GTA	Protease Inhibitor	RPI-312	Selected	Y	?		el-Farrash94
I 84 V	ATA → GTA	Protease Inhibitor	SC-52151 (telinavir)	Cross-R	Y	?	MP-134-selected virus confers 8-fold increase in IC90	Mo96
I 84 V	ATA → GTA	Protease Inhibitor	TMC114 (UIC-94017)	Cross-R	Y	?	I0-fold resistant against aprenavir-selected mutant L10F/V32I/M46I/I54M/A71V/I84V.	Koh03
I 84 V	ATA → GTA	Protease Inhibitor	VB-11,328	Selected	Y	?	L10F/I84V: 8-fold	Partaledis95
I 84 V	ATA → GTA	Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?	In combination with L10F	Partaledis95
I 85 V	ATT → GTT	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Svicher05

## HIV-1 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
N 88 D	AAT→GAT	Protease Inhibitor	AG-1343 (nelfinavir)	Selected	N	Y	D30N and N88D are most common in vivo after 24 weeks of therapy; they do not cause cross-resistance to other protease inhibitors.	Patrick98
N 88 D	AAT→GAT	Protease Inhibitor	SC-52151 (telinavir)	Selected	Y	?	N88D compensatory, no resistance alone	Smidt97
N 88 G	AAT→GGT	Protease inhibitor	ABT-378 (lopinavir) + ABT-538 (ritonavir)	Selected	?	Y		Mo05
N 88 S	AAT→AGT	Protease Inhibitor	AG-1343 (nelfinavir)	Selected	N	Y		Patrick98
N 88 S	AAT→AGT	Protease Inhibitor	BMS-232632 (atazanavir)	Selected	Y	?	V32L/L33F/M46I/A71V/I84V/N88S: 183-fold. L10Y/F150L/L63P/A71V/N88S: 93-fold. V32I/M46I/I84V/L89M: 96-fold.	Gong00
N 88 S	AAT→AGT	Protease Inhibitor	MK-639 (indinavir)	Cross-R	Y	?	SC-55389A-selected mutant confers 3-fold resistance	Smidt97
N 88 S	AAT→AGT	Protease Inhibitor	SC-55389A	Selected	Y	?	Sufficient to confer resistance alone (19-fold), but 25-fold in combination with L10F	Smidt97
L 89 M	TTG→ATG	Protease Inhibitor	BMS-232632 (atazanavir)	Selected	Y	?	V32L/L33F/M46I/A71V/I84V/N88S: 183-fold. L10Y/F150L/L63P/A71V/N88S: 93-fold. V32I/M46I/I84V/L89M: 96-fold.	Gong00
L 90 M	TTG→ATG	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, susceptibility to lopinavir was reduced by mutations at positions 82,54,10,63,71 and 84 by 4–10-fold, K20M/R by >20-fold and F53L by >40-fold.	Kempf01
L 90 M	TTG→ATG	Protease Inhibitor	ABT-538 (ritonavir)	Selected	N	Y	Secondary mutation occurs in combination with mutations at V82, I84, M36, I54, and A71.	Molla96
L 90 M	TTG→ATG	Protease Inhibitor	AG-1343 (nelfinavir)	Selected	N	Y	Rare in patients in Patrick study; more common in Lawrence study	Patrick98, Lawrence99
L 90 M	TTG→ATG	Protease Inhibitor	MK-639 (indinavir)	Selected	N	Y		Condra96
L 90 M	TTG→ATG	Protease Inhibitor	Ro 31–8959 (saquinavir)	Selected	Y	Y	G48V/L90M: >100-fold enzyme resistance; double mutant rare in vivo; L90M most common in vivo.	Jacobsen95, Eberle95, Winters98a

**HIV-1 Protease**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
T 91 S	ACT→TCT	Protease Inhibitor	ABT-378 (lopinavir)	Selected	Y	?	I84V/L10F/M46I/T91S: 12 fold I84V/L10F/M46I/T91S/V32I/I47V; 46 fold Passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y: 338 fold (in presence of p7/p1 (AN/F to VN/F) cleavage-site mutation and p1/p6 (F/L to F/F) cleavage-site mutation.	Carrillo08
T 91 S	ACT→TCT	Protease Inhibitor	ABT-538 (ritonavir)	Cross-R	Y	?	21-fold resistance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y	Carrillo08
T 91 S	ACT→TCT	Protease Inhibitor	Ro 31-8959 (saquinavir)	Selected	Y	?	4-fold resistance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y	Carrillo08
Q 92 K	CAG→AAG	Protease inhibitor	multiple PI	Selected	?	Y		Svicher05
I 93 L	ATT→CTT	Protease Inhibitor	MK-639 (indinavir)	Selected	N	Y		Muzammil03, Olsen99
C 95 F	TGC→TTC	Protease inhibitor	Ro 31-8959 (saquinavir) + MK-639 (indinavir)	Selected	?	Y	Associated with L90M and I93L	Svicher05
L 97 V	TTA→GTA	Protease Inhibitor	DMP-323	Selected	Y	?	No resistance alone; Y82A/M46L/L97V: 11-fold	King95

## HIV-2 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
K 7 N	AAA→AAT	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Diamond05
V 10 I	GTC→ATC	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Diamond05
V 22 I	GTT→ATT	Protease inhibitor	AG-1343 (nelfinavir)	Selected	?	Y		Diamond05
A 34 E	GCA→GAA	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Diamond05
A 34 S	GCA→TCA	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Diamond05
I 36 V	ATT→GTT	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Diamond05
L 38 F	TTG→TTT	Protease inhibitor	ABT-538 (ritonavir)	Selected	?	Y		Diamond05
I 46 T	ATT→ACT	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Diamond05
I 46 V	ATT→GTT	Protease inhibitor	Ro 31-8959 (saquinavir)	Selected	?	Y		Diamond05
G 48 R	GGG→CGG	Protease inhibitor	Ro 31-8959 (saquinavir)	Selected	?	Y		Diamond05
I 54 L	ATC→CTC	Protease inhibitor	Ro 31-8959 (saquinavir) + MK-639 (indinavir)	Selected	?	Y		Diamond05
G 55 R	GGG→CGG	Protease inhibitor	ABT-538 (ritonavir)	Selected	?	Y		Diamond05
V 62 A	GTT→GCT	Protease inhibitor	AG-1343 (nelfinavir)	Selected	?	Y		Diamond05
E 63 A	GAG→GCG	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Diamond05
E 63 Q	GAG→CAG	Protease inhibitor	Ro 31-8959 (saquinavir)	Selected	?	Y		Diamond05
T 74 N	ACA→AAT	Protease inhibitor	AG-1343 (nelfinavir)	Selected	?	Y		Diamond05
T 77 I	ACT→ATT	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Diamond05
G 78 E	GGA→GAA	Protease inhibitor	AG-1343 (nelfinavir)	Selected	?	Y		Diamond05
T 80 Y	ACA→TAT	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Diamond05
I 82 F	ATT→TTT	Protease inhibitor	ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	?	Y		Diamond05
I 82 M	ATT→ATG	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Diamond05
I 84 L	ATA→TTA	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Diamond05
I 84 V	ATA→GTA	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Diamond05

**HIV-2 Protease**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
F 85 L	TTT→TTA	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Diamond05
R 87 K	AGA→AAA	Protease inhibitor	AG-1343 (nelfinavir)	Selected	?	Y		Diamond05
L 90 M	TTG→ATG	Protease inhibitor	ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	?	Y		Diamond05
M 95 I	ATG→ATC	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Diamond05

## HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
M 41 L	ATG→TTG/CTG	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected	?	Y	M41L/T215Y: 60–70-fold; M41L/D67N/K70R/T215Y: 180-fold.	Larder89, Larder91, Kellam92
E 44 A	GAA→GCA	Nucleoside RT Inhibitor (NRTI)	3TC (lamivudine)	Cross-R	N	Y	Confers moderate resistance in absence of M184V. Development of mutation may be promoted by thymidine analogs.	Montes02
E 44 D	GAA→GAC	Nucleoside RT Inhibitor (NRTI)	3TC (lamivudine)	Cross-R	N	Y	Confers moderate levels of resistance to 3TC (7–32-fold) when present in an AZT-resistant genetic background (41L/67N/210W/215Y)	Hertogs00
P 52 R	CCT→CGT	Nucleoside RT Inhibitor (NRTI)	d4T (stavudine)	Selected	Y	?	Selection of resistant HIV-1EVK passaged in MT-4 cells	Gashnikova03
N 54 D	AAT→GAT	Nucleoside RT Inhibitor (NRTI)	d4T (stavudine)	Selected	Y	?	Selection of resistant HIV-1EVK passaged in MT-4 cells	Gashnikova03
A 62 V	GCC→GTC	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y	A62V alone has no effect, but in combination with mutations at 75, 77, 116, 151 causes multi NRTI resistance.	Shirasaka95
K 65 R	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	1592U89 (abacavir)	Selected	Y	N	K65R/L74V: 3.6-fold; K65R/M184V: 7-fold; K65R/L74V/M184V: 10.2-fold	Tisdale97
K 65 R	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	3TC (lamivudine)	Cross-R	Y	?	>3-fold resistance	Bazmi00
K 65 R	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	BCH-10652 (+/- dOTC)	Selected	Y	?	K65R/M184V: 4.2-fold.	Taylor00
K 65 R	AAA→AGA	NRTI	cyclo-d4G	Cross-R	Y	?	4 fold resistance	Ray05
K 65 R	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	d-d4FC (D4FC)	Selected	Y	?	In vitro selection	Geleziunas03
K 65 R	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	d4T (stavudine)	Selected	Y	?	Selected in 7 viruses (from patient isolates or HXB2) through in vitro selection.	Garcia-Lerma03
K 65 R	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	d4T (stavudine)	Cross-R	Y	?	>3-fold resistance	Bazmi00
K 65 R	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	ddC (zalcitabine)	Selected	Y	Y	4–10-fold resistance	Zhang94, Gu94
K 65 R	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	ddI (didanosine)	Selected	N	Y	Infrequently observed in patients receiving ddI or ddC	Zhang94
K 65 R	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	DXG	Selected	Y	?	8.7-fold resistance	Bazmi00
K 65 R	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	PMEA (adefovir)	Selected	Y	N	10–25-fold resistant	Foli96
K 65 R	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	PMPA (tenofovir)	Selected	Y	?	3.5-fold resistant	Wainberg99
D 67 A	GAC→GCC	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected	Y	?	Selection of resistant HIV-1EVK passaged in MT-4 cells	Gashnikova03
D 67 del	GAC→deletion	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine) + ddI (didanosine)	Selected	N	Y	Selected by AZT + ddI. Little effect alone (1.2-fold), but 1813-fold in combination with K103N, L74I, T69G, K70R, T215Y and K219Q	Imamichi00

## HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R vitro	In vivo	Comments	Refs
D 67 del	GAC→deletion	Nucleoside RT Inhibitor (NRTI)	ddC (zalcitabine)	Cross-R	N	Y Selected by AZT+ddI in patient. Site-directed mutant: 18-fold.	Imamichi00
D 67 del	GAC→deletion	Nucleoside RT Inhibitor (NRTI)	ddI (didanosine)	Selected	N	Y Selected by AZT+ddI in patient. Site-directed mutant: 3.8-fold.	Imamichi00
D 67 del	GAC→del	Nucleoside RT Inhibitor (NRTI)	MDR (multi-drug resistant)	Selected	?	Y 3 nucleotide deletion in multi-treated HIV-1 infected patient	Masciar02
D 67 E	GAC→GAG	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y	Larder99
D 67 G	GAC→GAG	Nucleoside RT Inhibitor (NRTI)	(+)dOTFC	Selected	Y	?	Richard00
D 67 G	GAC→GAG	Nucleoside RT Inhibitor (NRTI)	(+)dOTFC	Cross-R	Y	?	Richard00
D 67 G	GAC→GGC	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y	Larder99
D 67 N	GAC→AAC	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected	Y	Y D67N/K70R/T215Y/K219Q: 120-fold; M41L/D67N/K70R/T215Y: 180-fold.	Larder89, Larder91, Kellam92
D 67 S	GAC→?	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y	Larder99
S 68 G	AGT→GGT	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	?	Y Frequently associated with other multi-ddN resistance mutations V75I, F77L, F116Y and Q151M.	Schmit98
S 68 N	AGT→AAT	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y	Larder99
S 68 N	AGT→AAT	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y	Larder99
S 68 S + GGG	AGT→ins	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y	Larder99
S 68 S + SS	AGT→ins	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y >2500-fold-R to AZT when in combination with 210W, 215Y, 62V	Larder99
S 68 S + SSG	AGT→ins	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y	Larder99
S 68 S + ST	AGT→ins	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y	Larder99
S 68 S + SV	AGT→ins	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y	Larder99
S 68 Y	AGT→TAT	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y	Larder99



## HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R vitro	In vivo	Comments	Refs
ins 69 TRVMG	ACT+→ACG AGA GTG ATG GGG	NTRI	1592U89 (abacavir)	Cross-R	Y	32-fold resistance; duplication of 15 mutations of HIV-1 env	Lobato02
ins 69 TRVMG	ACT+→ACG AGA GTG ATG GGG	NTRI	3TC (lamivudine)	Cross-R	Y	84-fold resistance; duplication of 15 mutations of HIV-1 env	Lobato02
ins 69 TRVMG	ACT+→ACG AGA GTG ATG GGG	NTRI	AZT (zidovudine)	Cross-R	Y	371-fold resistance; duplication of 15 mutations of HIV-1 env	Lobato02
ins 69 TRVMG	ACT+→ACG AGA GTG ATG GGG	NTRI	d4T (stavudine)	Cross-R	Y	15-fold resistance; duplication of 15 mutations of HIV-1 env	Lobato02
ins 69 TRVMG	ACT+→ACG AGA GTG ATG GGG	NTRI	ddC (zalcitabine)	Cross-R	Y	4-fold resistance; duplication of 15 mutations of HIV-1 env	Lobato02
ins 69 TRVMG	ACT+→ACG AGA GTG ATG GGG	NTRI	ddI (didanosine)	Cross-R	Y	12-fold resistance; duplication of 15 mutations of HIV-1 env	Lobato02
INS 69 TSG	ACT→ins	NTRI	AZT (zidovudine) + ddI (didanosine) or ddC (zalcitabine)	Selected	Y	Highly resistant to 3TC, ABC, d4T	Bulgheroni04
T 69 A	ACT→GCT	Multiple Nucleoside	3TC (lamivudine) + d4T (stavudine)	Selected	?	Seen in one patient on 3TC + d4T combination therapy.	Lawrence99
T 69 A + SG	ACT→GCT + AGT GGT	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	?	Seen in heavily treated patients. Confers >4-fold resistance to: AZT, ddI, ddC, 3TC and PMEA.	Winters98
T 69 D	ACT→GAT	Multiple Nucleoside	AZT (zidovudine) + 3TC (lamivudine)	Selected	?	Seen in one patient on AZT + 3TC combination therapy.	Lawrence99
T 69 D	ACT→GAT	NTRI	ddC (zalcitabine)	Selected	N	5-fold resistance	Fitzgibbon92
T 69 G	ACT→GGT	NTRI	AZT (zidovudine) + ddI (didanosine)	Selected	N	Selected by AZT + ddI. Little effect alone (1.5-fold), but 1813-fold in combination with K103N, L74I, T69G, K70R, T215Y and K219Q	Imamichi00
T 69 G	ACT→GGT	NTRI	ddC (zalcitabine)	Cross-R	N	Selected by AZT+ddI in patient. Site-directed mutant: 11-fold.	Imamichi00
T 69 G	ACT→GGT	NTRI	ddI (didanosine)	Selected	N	Selected by AZT+ddI in patient. Site-directed mutant: 10-fold.	Imamichi00
T 69 N	ACT→AAT	Multiple Nucleoside	3TC (lamivudine) + d4T (stavudine)	Selected	?	Seen in two patients on 3TC + d4T combination therapy.	Lawrence99
T 69 S + AG	ACT→ins	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N		Larder99

**HIV-1 RT**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R-vitro	In vivo	Comments	Refs	
T 69 S + EA	ACT→AGT + AGA GCA	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	?	Y	Seen in heavily treated patients. Confers >4-fold resistance to: AZT, ddI, ddC, 3TC and PMEA.	Winters98
T 69 S + EE	ACT→ins	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y		Larder99
T 69 S + RA	ACT→AGT + AGA GCA	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	?	Y	Seen in heavily treated patients. Confers >4-fold resistance to: AZT, ddI, ddC, 3TC and PMEA.	Winters98
T 69 S + SA	ACT→AGC + AGC GCT	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	?	Y	Seen in heavily treated patients. Confers >4-fold resistance to: AZT, ddI, ddC, 3TC and PMEA.	Winters98
T 69 S + SA	ACT→TCT + AGT GCT	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	?	Y	Seen in heavily treated patients. Confers >4-fold resistance to: AZT, ddI, ddC, 3TC and PMEA.	Winters98
T 69 S + SA	ACT→AGT + AGC GCT	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	?	Y	Seen in heavily treated patients. Confers >4-fold resistance to: AZT, ddI, ddC, 3TC and PMEA.	Winters98
T 69 S + SG	ACT→AGT + AGT GGT	Nucleoside RT Inhibitor (NRTI)	ddI (didanosine) + hydroxyurea	Selected	?	Y	Seen in one patient.	DeAntoni97
T 69 S + SG	ACT→AGT + AGT GGT	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	?	Y	Seen in heavily treated patients. Confers >4-fold resistance to: AZT, ddI, ddC, 3TC and PMEA.	Winters98
T 69 S + SS	ACT→AGT + AGT AGT	Nucleoside RT Inhibitor (NRTI)	ddI (didanosine) + hydroxyurea	Selected	?	Y	Seen in one patient.	DeAntoni97
T 69 S + SS	ACT→TCT + AGC TCT	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	?	Y	Seen in heavily treated patients. Confers >4-fold resistance to: AZT, ddI, ddC, 3TC and PMEA.	Winters98
T 69 S + SS	ACT→TCT + AGT TCT	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	?	Y	Seen in heavily treated patients. Confers >4-fold resistance to: AZT, ddI, ddC, 3TC and PMEA.	Winters98
T 69 S + TG	ACT→TCT + ACC GGT	Multiple Nucleoside	MDR (multi drug resistant)	Selected	?	Y		Bulgheroni04
T 69 S + TS	ACT→TCT + ACC TCT	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	?	Y	Seen in heavily treated patients. Confers >4-fold resistance to: AZT, ddI, ddC, 3TC and PMEA.	Winters98

## HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
T 69 S + VG	ACT→ins	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y		Larder99
K 70 E	AAA→GAA	Nucleoside RT Inhibitor (NRTI)	3TC (lamivudine)	Cross-R	Y	?	PMEA-selected virus confers 7-fold resistance.	Cherrington96
K 70 E	AAA→GAA	Nucleoside RT Inhibitor (NRTI)	PMEA (adefovir)	Selected	Y	Y	9-fold in vitro. Also seen in patients on PMEA therapy.	Cherrington96, Miller98
K 70 R	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected	Y	Y	D67N/K70R/T215Y/K219Q: 120-fold	Larder89, Larder91, Kellam92
K 70 S	AAA→AGA	Multiple Nucleoside	ddI (didanosine) + d4T (stavudine)	Selected	?	Y	Seen in one patient on ddC + d4T combination therapy.	Lawrence99
L 74 I	TTA→ATA	HIV-1 Specific RT Inhibitor (NNRTI)	HBV 097	Selected	Y	?		Kleim96
L 74 V	TTA→GTA	Nucleoside RT Inhibitor (NRTI)	1592U89 (abacavir)	Selected	Y	N	K65R/L74V/M184V: 10.2-fold	Tisdale97
L 74 V	TTA→GTA	NRTI	cyclo-d4G	Cross-R	Y	?	2 fold resistance	Ray05
L 74 V	TTA→GTA	Nucleoside RT Inhibitor (NRTI)	ddC (zalcitabine)	Cross-R	N	Y	5–10-fold resistant to ddI-selected virus	StClair91
L 74 V	TTA→GTA	Nucleoside RT Inhibitor (NRTI)	ddI (didanosine)	Selected	N	Y	Can reverse effect of T215Y AZT resistance mutation	StClair91
L 74 V	TTA→GTA	Nucleoside RT Inhibitor (NRTI)	DXG	Selected	Y	?	4-fold resistance	Bazmi00
L 74 V	TTA→GTA	HIV-1 Specific RT Inhibitor (NNRTI)	HBV 097	Selected	Y	?		Kleim96
V 75 I	GTA→ATA	Nucleoside RT Inhibitor (NRTI)	(-)dOTC	Selected	Y	?	1.6-fold after 12 passages, but seen in 5 different clones	Richard99
V 75 I	GTA→TTA	HIV-1 Specific RT Inhibitor (NNRTI)	HBV 097	Selected	Y	?	Compensates for negative effect of G190E mutation on RT activity	Kleim96
V 75 I	GTA→ATA	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y	V75I alone has no effect, but in combination with mutations at 62, 77, 116, 151 causes multi NRTI resistance.	Shirasaka95
V 75 L	GTA→TTA	HIV-1 Specific RT Inhibitor (NNRTI)	HBV 097	Selected	Y	?		Kleim96
V 75 M	GTA→ATG	Nucleoside RT Inhibitor (NRTI)	d4T (stavudine)	Selected	N	Y	Associated with Clade E virus	Ariyoshi03
V 75 M	GTA→ATG	Multiple Nucleoside	ddC (zalcitabine) + d4T (stavudine)	Selected	?	Y	Seen in one patient on ddC + d4T combination therapy.	Lawrence99
V 75 T	GTA→ACA	Nucleoside RT Inhibitor (NRTI)	d4C	Cross-R	Y	N	d4T-selected	Lacey94
V 75 T	GTA→ACA	Nucleoside RT Inhibitor (NRTI)	d4T (stavudine)	Selected	Y	N	Observed with d4T selection in vitro, rarely in patients receiving d4T	Lacey94, Lin99
V 75 T	GTA→ACA	Nucleoside RT Inhibitor (NRTI)	ddC (zalcitabine)	Cross-R	Y	N	d4T-selected	Lacey94
V 75 T	GTA→ACA	Nucleoside RT Inhibitor (NRTI)	ddI (didanosine)	Cross-R	Y	N	d4T-selected	Lacey94
V 75 T	GTA→ACA	Nucleoside RT Inhibitor (NRTI)	(-)-FTC (emtricitabine)	Cross-R	Y	N	d4T-selected	Lacey94

## HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
F 77 L	TTC→CTC	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y	F77L alone has no effect, but in combination with mutations at 62, 75, 116, 151 causes multi NRTI resistance.	Shirasaka95
W 88 G	TGG→GGG	Pyrophosphate Analogue RT Inhibitor	PFA (foscarnet)	Selected	N	Y	Observed after selection with AZT and PFA; suppresses effects of AZT mutations	Mellors95
W 88 S	TGG→TCG	Pyrophosphate Analogue RT Inhibitor	PFA (foscarnet)	Selected	N	Y	Partially suppresses effects of AZT resistance mutations	Mellors95
E 89 G	GAA→GGA	Pyrophosphate Analogue RT Inhibitor	PFA (foscarnet)	Cross-R	Y	N	Isolated by screening RT clones for ddGTP resistance	Prasad91
E 89 K	GAA→GGA	Pyrophosphate Analogue RT Inhibitor	PFA (foscarnet)	Selected	Y	N	Suppresses effects of AZT resistance mutations	Tachedjian95
L 92 I	TTA→ATA	Pyrophosphate Analogue RT Inhibitor	PFA (foscarnet)	Selected	Y	N	Partially suppresses effects of AZT resistance mutations	Tachedjian95
A 98 G	GCA→GGA	HIV-1 Specific RT Inhibitor (NNRTI)	L-697,661	Selected	N	Y		Byrnes93
L 100 I	TTA→ATA	HIV-1 Specific RT Inhibitor (NNRTI)	BHAP U-88204E	Selected	Y	?		Balzarini93d, Vasudevachari92
L 100 I	TTA→ATA	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Selected	N	Y		Richman93
L 100 I	TTA→ATA	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Selected	Y	Y	Combinations of mutations needed for high-level resistance; L100I/V108I: 1,000-fold; L100I/V179D/Y181C: 1,000-fold	Young95, Winslow96, Bachelet00
L 100 I	TTA→ATA	HIV-1 Specific RT Inhibitor (NNRTI)	L-697,661	Selected	Y	N	Not in patients	Byrnes93
L 100 I	TTA→ATA	HIV-1 Specific RT Inhibitor (NNRTI)	TIBO R82150	Selected	Y	?	Suppresses effects of AZT resistance mutations	Mellors93, Balzarini93c
L 100 I	TTA→ATA	HIV-1 Specific RT Inhibitor (NNRTI)	TIBO R82913	Selected	Y	?	Found in combination with E138K	Larder92
L 100 I	TTA→ATA	HIV-1 Specific RT Inhibitor (NNRTI)	UC-68	Selected	Y	?	70-fold resistance	Balzarini95
L 100 I	TTA→ATA	HIV-1 Specific RT Inhibitor (NNRTI)	UC-70	Selected	Y	?	Passage 6: 758-fold	Buckheit95a
L 100 I	TTA→ATA	HIV-1 Specific RT Inhibitor (NNRTI)	UC-781	Selected	Y	?	Activity of UC-781 versus L100I, K103N, V106A, E138K, Y181C and Y188L reduced by 2-, 7-, 1.5-, 1.5-, 5- and 150-fold, respectively, compared to wild type	Balzarini96a, Balzarini96b
L 100 I	TTA→ATA	HIV-1 Specific RT Inhibitor (NNRTI)	UC-84	Selected	Y	?	Passage 6: >333-fold	Buckheit95a
K 101 E	AAA→GAA	HIV-1 Specific RT Inhibitor (NNRTI)	ADAMII	Cross-R	Y	?	>30-fold resistant against a virus isolate, but not resistant against a site-directed mutant.	Cushman98

## HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R vitro	In vivo	Comments	Refs
K 101 E	AAA →GAA	Multiple Nucleoside	AZT (zidovudine) + BHAP U-87201E (ateviridine)	Selected	?	Seen in one patient on atevirdine + AZT combination therapy. Found in association with K103N.	Demeter98
K 101 E	AAA →GAA	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Cross-R	Y	15-fold to UC-781-selected virus	Buckheit97
K 101 E	AAA →GAA	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Cross-R	Y	17-fold increase in IC90	Young95, Bachelet00
K 101 E	AAA →GAA	HIV-1 Specific RT Inhibitor (NNRTI)	L-697,661	Selected	N		Byrnes93
K 101 E	AAA →GAA	noncompetitive RT inhibitor	MSK-076	Selected	Y	HIV-1	Auwerx04
K 101 E	AAA →GAA	HIV-1 Specific RT Inhibitor (NNRTI)	UC-10	Selected	Y	Found in combination, K101E/Y181C: 200-fold	Buckheit95a
K 101 E	AAA →GAA	HIV-1 Specific RT Inhibitor (NNRTI)	UC-38	Selected	Y	Selected In combination with G190E: > 100-fold	Balzarini95
K 101 E	AAA →GAA	HIV-1 Specific RT Inhibitor (NNRTI)	UC-57	Selected	Y	Selected in combination, K101E/Y181C: 58-fold	Buckheit95a
K 101 E	AAA →GAA	HIV-1 Specific RT Inhibitor (NNRTI)	UC-781	Selected	Y	By passage 15: Y181C/V108I/K101E: >500-fold	Buckheit97
K 101 E	AAA →GAA	HIV-1 Specific RT Inhibitor (NNRTI)	UCO40	Cross-R	Y	18-fold to UC-781-selected virus	Buckheit97
K 101 I	AAA →ATA	HIV-1 Specific RT Inhibitor (NNRTI)	UC-16	Selected	Y	Selected in combination with G141E: 10-fold	Balzarini95
K 101 P	AAA →CCA	HIV-1 Specific RT Inhibitor (NNRTI)	TMC125	Cross-R	Y	Clinical isolate with this mutation is associated with decreased phenotypic susceptibility	Vingerhoets04
K 101 Q	AAA →CAA	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Selected	N		Bachelet00
K 101 Q	AAA →CAA	HIV-1 Specific RT Inhibitor (NNRTI)	LY-300046 HCl (troviridine)	Selected	Y	Found in combination with V108I	Zhang95, Vrang93
K 103 E	AAA →GAA	HIV-1 Specific RT Inhibitor (NNRTI)	BHAP U-87201E (ateviridine)	Selected	?	Found in association with Y181C in one patient on monotherapy. K103E, K103N and Y181C observed with monotherapy.	Demeter98
K 103 H	AAA →CAC	NNRTI	NNRTI	Selected	?		
K 103 N	AAA →AAC	HIV-1 Specific RT Inhibitor (NNRTI)	ADAMII	Cross-R	Y	>28-fold. Tested against a site-directed mutant.	Cushman98
K 103 N	AAA →AAC	HIV-1 Specific RT Inhibitor (NNRTI)	BHAP U-87201E (ateviridine)	Selected	?	Found in association with Y181C in several patients on monotherapy. Also seen in patients on ATV + AZT combination therapy.	Demeter98
K 103 N	AAA →AAC	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Selected	N		Richman94

## HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
K 103 N	AAA → AAC	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Selected	Y	Y	Predominant mutation in vivo	Young95, Bachelier00
K 103 N	AAA → AAC	HIV-1 Specific RT Inhibitor (NNRTI)	I-EBU (emivirine)	?	Y	?	K103N/Y181C: > 1,000-fold	Sekt95
K 103 N	AAA → AAC	HIV-1 Specific RT Inhibitor (NNRTI)	L-697,593	Selected	Y	?	K103N and Y181C most common with monotherapy	Nunberg91
K 103 N	AAA → AAC	HIV-1 Specific RT Inhibitor (NNRTI)	L-697,661	Selected	Y	Y	>100-fold alone. K103N/Y181C: > 1,000-fold	Byrnes93, Saag93
K 103 N	AAA → AAC	HIV-1 Specific RT Inhibitor (NNRTI)	TIBO R82913	Selected	Y	?	5-fold resistance	Balzarini93d
K 103 N	AAA → AAC	HIV-1 Specific RT Inhibitor (NNRTI)	UC-10	Selected	Y	N		Balzarini95
K 103 N	AAA → AAC	HIV-1 Specific RT Inhibitor (NNRTI)	UC-81	Selected	Y	?		Balzarini95
K 103 Q	AAA → CAA	HIV-1 Specific RT Inhibitor (NNRTI)	L-697,661	Selected	N	Y		Saag93
K 103 R	AAA → AGA	HIV-1 Specific RT Inhibitor (NNRTI)	I-EBU (emivirine)	?	Y	Y		BorotoEsoda97
K 103 R	AAA → AGA	HIV-1 Specific RT Inhibitor (NNRTI)	LY-300046 HCl (troviridine)	Selected	Y	?	K103R/V179D: 500-fold; Found in combination with V179D or Y181C	Zhang95, Vrang93
K 103 R	AAA → AGA	HIV-1 Specific RT Inhibitor (NNRTI)	O-(2-Phenoxy ethyl)benzoyl (phenyl) thiocarbamate 17c	Cross-R	Y	?	Low potency also against K103N/Y181C	Ranise03
K 103 S	AAA → AGT	NNRTI	NNRTI	Selected	?	Y	clinical isolates as well as site-directed mutants tested in vitro	Harrigan05
K 103 T	AAA → ACA	NNRTI	NNRTI	Selected	?	Y		Fujiwara98
K 103 T	AAA → ACA	HIV-1 Specific RT Inhibitor (NNRTI)	S-1153	Selected	Y	?		Balzarini95
K 103 T	AAA → ACA	HIV-1 Specific RT Inhibitor (NNRTI)	UC-42	Selected	Y	N	100-fold resistance	Cushman98
V 106 A	GTA → GCA	HIV-1 Specific RT Inhibitor (NNRTI)	ADAMII	Cross-R	Y	?	7.13-fold. Tested against a site-directed mutant.	Vasudevachari92
V 106 A	GTA → GCA	HIV-1 Specific RT Inhibitor (NNRTI)	BHAP U-88204E	Selected	Y	?		Larder92, Richman94
V 106 A	GTA → GCA	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Selected	Y	Y		Balzarini93
V 106 A	GTA → GCA	HIV-1 Specific RT Inhibitor (NNRTI)	E-EBU-dM	Selected	Y	?	V106A + F227L: 387-fold	Fujiwara98
V 106 A	GTA → GCA	HIV-1 Specific RT Inhibitor (NNRTI)	S-1153	Selected	Y	?	P225H follows V106A. Also seen with L101I and Y181C. Double and triple mutants highly resistant to other NNRTI's, including MKC442	Pelemans97
V 106 A	GTA → GCA	HIV-1 Specific RT Inhibitor (NNRTI)	S-2720 (quinoxaline)	Selected	Y	?		Larder92
V 106 A	GTA → GCA	HIV-1 Specific RT Inhibitor (NNRTI)	TIBO R82913	Selected	Y	?	Selected in combination, V106A/V181C: 166-fold	Buckheit95a
V 106 A	GTA → GCA	HIV-1 Specific RT Inhibitor (NNRTI)	UC-69	Selected	Y	?		

**HIV-1 RT**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
V 106 A	GTA → GCA	HIV-1 Specific RT Inhibitor (NNRTI)	UC-82	Selected	Y	?	Activity of UC-82 versus L100I, K103N, V106A, E138K, Y181C and Y188L reduced by 2-, 6-, 1.5-, 2-, 4- and 200-fold, respectively, compared to wild type	Balzarini96b, Balzarini96a
V 106 I	GTA → ATA	HIV-1 Specific RT Inhibitor (NNRTI)	HBV 097	Selected	Y	?	Appears under lowered drug concentration selection	Kleim97
V 106 M	GTG → ATG	HIV-1 Specific RT Inhibitor (NNRTI)	BHAP U-90152 (delavirdine)	Cross-R	Y			Brenner03
V 106 M	GTG → ATG	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Cross-R	Y			Brenner03
V 106 M	GTG → ATG	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Selected	Y	Y	selected in vitro under efavirenz pressure in Clade C virus. Also developed in 3/6 efavirenz-treated patients with Clade C infection.	Brenner03
V 108 I	GTA → ATA	HIV-1 Specific RT Inhibitor (NNRTI)	ADAMII	Cross-R	Y	?	6.74-fold. Tested against a site-directed mutant.	Cushman98
V 108 I	GTA → ATA	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Selected	N	Y		Richman94
V 108 I	GTA → ATA	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Selected	Y	?	L100I/Y108I: 1,000-fold. Observed frequently in patients.	Winslow96, Bachelor00
V 108 I	GTA → GCA	HIV-1 Specific RT Inhibitor (NNRTI)	I-EBU (emivirine)	?Selected	Y	?		Seki95
V 108 I	GTA → GCA	HIV-1 Specific RT Inhibitor (NNRTI)	L-697,661	Selected	Y	Y		Byrnes93
V 108 I	GTA → ATA	HIV-1 Specific RT Inhibitor (NNRTI)	LY-300046 HCl (troviridine)	Selected	Y	?	Found in combination with K101Q	Zhang95, Vrang93
V 108 I	GTT → GAT	HIV-1 Specific RT Inhibitor (NNRTI)	TIBO R82913	Selected	N	Y	>100-fold	Vandamme94a
V 108 I	GTA → ATA	HIV-1 Specific RT Inhibitor (NNRTI)	UC-781	Selected	Y	?	By passage 10: 55-fold-R, in combination with Y181C	Buckheit97
Y 115 F	TAT → TTT	Nucleoside RT Inhibitor (NRTI)	1592U89 (abacavir)	Selected	Y	N	K65R/L74V and/or Y115F with M184V: 10 fold; L74V/Y115F/M184V: 11-fold	Tisdale97
F 116 Y	TTT → TAT	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y	F116Y alone has no effect, but in combination with mutations at 62, 75, 77, 151 causes multi NRTI resistance.	Shirasaka95
V 118 I	GTT → ATT	Nucleoside RT Inhibitor (NRTI)	3TC (lamivudine)	Cross-R	N	Y	Confers moderate levels of resistance to 3TC (7-32-fold) when present in an AZT-resistant genetic background (41L/67N/210W/215Y)	Hertogs00
P 119 S	CCC → TCC	NRTI	4'-E44T	Selected	Y	?	selected along with T165A and M184V	Nitanda05

**HIV-1 RT**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
P 119 S	CCC→TCC	Nucleoside RT Inhibitor (NRTI)	F-ddA (Iodenosine)	Selected	Y	?	Found with V179D and/or L214F, which are possibly compensatory	Tanaka97
I 135 L	ATA→AAA	HIV-1 Specific RT Inhibitor (NNRTI)	BHAP U-90152 (delavirdine)	Cross-R	N	Y	Identified by logistic regression analysis, confirmed by mutagenesis studies. I135L/L283I: 5.0-fold resistance.	Brown00
I 135 L	ATA→AAA	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Cross-R	N	Y	Identified by logistic regression analysis, confirmed by mutagenesis studies. I135L/L283I: 4.2-fold resistance.	Brown00
I 135 L	ATA→AAA	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Cross-R	N	Y	Identified by logistic regression analysis, confirmed by mutagenesis studies. I135L/L283I: 4.1-fold resistance.	Brown00
I 135 M	ATA→ATG	HIV-1 Specific RT Inhibitor (NNRTI)	BHAP U-90152 (delavirdine)	Cross-R	N	Y	Identified by logistic regression analysis, confirmed by mutagenesis studies. I135M/L283I: 4.0-fold resistance.	Brown00
I 135 M	ATA→ATG	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Cross-R	N	Y	Identified by logistic regression analysis, confirmed by mutagenesis studies. I135M/L283I: 4.5-fold resistance.	Brown00
I 135 M	ATA→ATG	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Cross-R	N	Y	Identified by logistic regression analysis, confirmed by mutagenesis studies. I135M/L283I: 3.2-fold resistance.	Brown00
I 135 T	ATA→ACA	HIV-1 Specific RT Inhibitor (NNRTI)	BHAP U-90152 (delavirdine)	Cross-R	N	Y	Identified by logistic regression analysis, confirmed by mutagenesis studies. I135T/L283I: 2.8-fold resistance.	Brown00
I 135 T	ATA→ACA	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Cross-R	N	Y	Identified by logistic regression analysis, confirmed by mutagenesis studies. I135T/L283I: 3.4-fold resistance.	Brown00
I 135 T	ATA→ACA	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Cross-R	N	Y	Identified by logistic regression analysis, confirmed by mutagenesis studies. I135T/L283I: 2.5-fold resistance.	Brown00
E 138 A	GAG→GCG	HIV-1 Specific RT Inhibitor (NNRTI)	TSAO	Selected	N	Y	Mutation reducing susceptibility to TSAO in TSAO therapy naive patients.	VanLaethem00
E 138 K	GAG→AAG	HIV-1 Specific RT Inhibitor (NNRTI)	I-EBU (emivirine)	Selected	Y	N	Obtained in the concomitant presence of low 3TC concentrations	Balzarini96c
E 138 K	GAG→AAG	HIV-1 Specific RT Inhibitor (NNRTI)	TIBO R82913	Selected	Y	?	Found in combination with L1001	Balzarini93c
E 138 K	GAG→AAG	HIV-1 Specific RT Inhibitor (NNRTI)	TSAO	Selected	Y	?	E138A (GAG to GCG) in TSAO-naive patients confers TSAO viral resistance	Balzarini93a, Balzarini93b



## HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
E 138 K	GAG→AAG	HIV-1 Specific RT Inhibitor (NNRTI)	UC-82	Selected	Y	?	Activity of UC-82 versus L1001, K103N, V106A, E138K, Y181C and Y188L reduced by 2-, 6-, 1.5-, 2-, 4- and 200-fold, respectively, compared to wild type	Balzarini96b, Balzarini96a
E 138 K	GAG→AAG	HIV-1 Specific RT Inhibitor (NNRTI)	UC-84	Selected	Y	?		Balzarini95
T 139 I	ACA→ATA	HIV-1 Specific RT Inhibitor (NNRTI)	ADAMII	Cross-R	Y	?	38-fold resistant against a virus isolate, but not tested against a site-directed mutant.	Cushman98
T 139 I	ACA→ATA	HIV-1 Specific RT Inhibitor (NNRTI)	Calanolide A	Selected	Y	?	>70-fold resistance but not cross-resistant to other NNRTIs	Buckheit95c
G 141 E	GGG→GAG	HIV-1 Specific RT Inhibitor (NNRTI)	UC-16	Selected	Y	N	Selected in combination with K101I: 10-fold	Balzarini95
P 143 S	GGG→GAG	Nucleoside RT Inhibitor (NRTI)	ddI (didanosine)	Selected	Y	?	Selection of resistant HIV-1EVK passaged in MT-4 cells	Gashnikova03
Q 145 L	CAG→TTG	NRTI/NNRTI	multi-nucleoside	Cross-R	Y	Y	Resistance levels similar to Q145M	Paolucci04
Q 145 M	CAG→ATG	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	Y	Y	confers multi drug resistance to both NRTI and NNRTI; mutation selected in patient on multidrug therapy	Paolucci03
Q 151 M	CAG→ATG	Nucleoside RT Inhibitor (NRTI)	d-44FC (D4FC)	Selected	?	Y		Gelezianas03
Q 151 M	CAG→ATG	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y	Pivotal multi nucleoside RTI resistance mutation (first to occur), found in association with combinations of four other mutations: A62V/V75I/F77L/F116Y/Q151M: AZT >190-fold; ddI 50-fold; ddC 20-fold; d4T > 10-fold	Shirasaka95
S 156 A	TCA→GCA	Pyrophosphate Analogue RT Inhibitor	PFA (foscarnet)	Selected	Y	N		Tachedjian95
P 157 S	CCA→TCA	Nucleoside RT Inhibitor (NRTI)	3TC (lamivudine)	Cross-R	Y	N	Found from selection experiments with FIV (P156S); made mutant of corresponding change in HIV.	Smith99
Q 161 L	CAA→CTA	Pyrophosphate Analogue RT Inhibitor	PFA (foscarnet)	Selected	Y	Y	5-fold alone; Q161L/H208Y: 9-fold; suppresses effects of AZT mutations	Mellors95
T 165 A	ACA→GCA	NRTI	4'-Ed4T	Selected	Y	?	selected along with P119S and M184V	Nitanda05
V 179 D	GTT→GAT	HIV-1 Specific RT Inhibitor (NNRTI)	8-chloro-TIBO (tivrapipe)	Selected	Y	?	Tested against QM96521-selected virus. 10-fold.	Witvrouw98
V 179 D	GTT→GAT	HIV-1 Specific RT Inhibitor (NNRTI)	ADAMII	Cross-R	Y	?	28-fold. Tested against a site-directed mutant.	Cushman98
V 179 D	GTT→GAT	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Selected	Y	?	11-fold alone; L100I/V179D/Y181C: 1,000-fold	Winslow96

## HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
V 179 D	GTT→GAT	HIV-1 Specific RT Inhibitor (NNRTI)	L-697,661	Selected	N	Y		Byrnes93
V 179 D	GTT→GAT	HIV-1 Specific RT Inhibitor (NNRTI)	LY-300046 HCl (troviridine)	Selected	Y	?	Found in combination with K103R or Y181C; V179D/Y181C: > 1,000-fold	Zhang95, Vrang93
V 179 D	GTT→GAT	HIV-1 Specific RT Inhibitor (NNRTI)	QM96521	Selected	Y	?	10-fold resistant. Other TTD-derivatives are 15–140 fold-R.	Witvrouw98
V 179 D	GTT→GAT	HIV-1 Specific RT Inhibitor (NNRTI)	TIBO R82913	Selected	N	Y	20-fold	Vandamme94
V 179 D	GTT→GAT	HIV-1 Specific RT Inhibitor (NNRTI)	UC-10	Selected	Y	?		Balzarini96a
V 179 E	GTT→GAG	HIV-1 Specific RT Inhibitor (NNRTI)	L-697,661	Selected	N	Y		Byrnes93
V 179 F	GTT→TTT	HIV-1 Specific RT Inhibitor (NNRTI)	TMC125	Cross-R	Y	Y	Fold-change tested using double mutant V179F+Y181C	Vingerhoets04
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	1737	Selected	Y	?	Y181C also confers resistance to numerous other tetrahydrophthalene derivatives.	Hara97
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	ADAMIII	Cross-R	Y	?	>28-fold. Tested against a site-directed mutant.	Cushman98
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	α-APA (loviride)	Selected	?	Y		Staszewski96
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	BHAP U-87201E (atevirdine)	Selected	?	Y	K103E, K103N and Y181C observed with monotherapy	Demeter98
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	BHAP U-88204E	Selected	Y	?		Vasudevachari92
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Selected	Y	Y		Richman94, Richman91, Mellors92
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	BM+51,0836	Selected	Y	?		Maass93
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Selected	Y	?	L100I/V179D/Y181C: 1,000-fold; uncommon in vivo	Winslow96
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	E-BPTU	Selected	Y	?	160-fold resistant	Buckheit95c
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	E-EBU	Selected	Y	?		Balzarini93
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	E-EPSU	Selected	Y	?	Y188C confers greater resistance (>250-fold) than Y181C (>50-fold)	Nguyen94
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	E-EPU	Selected	Y	?	Y188C (>250-fold) confers greater resistance than Y181C (>95-fold)	Nguyen94
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	I-EBU (emivirine)	?	?	Y		BorotoEsoda97
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	L-697,593	Selected	Y	?	K103N/Y181C: > 1,000-fold	Nunberg91
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	L-697,661	Selected	Y	Y	K103N and Y181C most common with monotherapy	Byrnes93, Saag93
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	LY-300046 HCl (troviridine)	Selected	Y	?	V179D/Y181C: > 1,000-fold; Found in combination with K103R or V179D	Zhang95, Vrang93
Y 181 C	TAT→TGT	noncompetitive RT inhibitor	MSK-076	Selected	Y	?		Auwerx04

## HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	O-(2-Phenoxy ethyl)benzoyl (phenyl) thiocarbamate 17c	Cross-R	Y	?	Low potency also against K103N/Y181C	Ranise03
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	TIBO R82913	Selected	Y	?	K103N/Y181C: > 1,000-fold	Larder92
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	UC-10	Selected	Y	?	Found in combination, K101E/Y181C: 200-fold	Buckheit95a
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	UC-32	Selected	Y	?	Passage 6: 38-fold	Buckheit95a
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	UC-38	Selected	Y	?	By passage 6: 8–149-fold	Buckheit95a
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	UC-57	Selected	Y	?	Selected in combination, K101E/Y181C: 58-fold	Buckheit95a
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	UC-581	Selected	Y	?	Passage 6: 53-fold	Buckheit95a
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	UC-68	Selected	Y	?	Passage 6: 5-fold	Buckheit95a
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	UC-69	Selected	Y	?	Selected in combination, V106A/V181C: 166-fold	Buckheit95a
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	UC-781	Selected	Y	?	By passage 5: 50-fold-R	Buckheit97
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	UC-80 (NSC 639475)	Selected	Y	?	Passage 6: 18-fold	Buckheit95a
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	UC-81	Cross-R	Y	?		Balzarin95
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	UC-84	Selected	Y	?	Passage 5: >118-fold	Buckheit95a
Y 181 I	TGT→ATT	HIV-1 Specific RT Inhibitor (NNRTI)	BHAP U-88204E	Selected	Y	Y	Appeared after treatment of Y181C-mutated virus with BHAP; high-level resistance to BHAP, nevirapine and TIBO; observed in one nevirapine-treated patient	Balzarin94
Y 181 I	TGT→ATT	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Selected	N	Y	Observed in one patient	Shaw94
Y 181 I	TAT→ATT	HIV-1 Specific RT Inhibitor (NNRTI)	I-EBU (emivirine)	Selected	Y	N		Balzarin96c
Y 181 I	TAT→ATT	HIV-1 Specific RT Inhibitor (NNRTI)	TMC125	Cross-R	Y	Y	Clinical isolate with this mutation is associated with decreased phenotypic susceptibility	Vingerhoets04
Y 181 V	TAT→GTT	HIV-1 Specific RT Inhibitor (NNRTI)	TMC125	Cross-R	Y	Y		Vingerhoets04
M 184 I	ATG→ATA	Nucleoside RT Inhibitor (NRTI)	3TC (lamivudine)	Selected	Y	Y	M184V and M184I can suppress effects of AZT resistance mutations	Schinazi93, Tisdale93, Gao93
M 184 I	ATG→ATA	Nucleoside RT Inhibitor (NRTI)	(+)dOTC	Selected	Y	?	Selected in <10 passages	Taylor00
M 184 I	ATG→ATA	Nucleoside RT Inhibitor (NRTI)	(+)dOTFC	Cross-R	Y	?		Richard00
M 184 I	ATG→ATA	Nucleoside RT Inhibitor (NRTI)	(-)dOTFC	Cross-R	Y	?		Richard00
M 184 I	ATG→ATA	Nucleoside RT Inhibitor (NRTI)	(-)FTC (emtricitabine)	Selected	Y	?		Schinazi93
M 184 I	ATG→ATA	HIV-1 Specific RT Inhibitor (NNRTI)	QYL-609	Cross-R	Y	?	QYL-selected virus.	Yoshimura99a

## HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R vitro	In vivo	Comments	Refs
M 184 I	ATG→ATA	HIV-1 Specific RT Inhibitor (NNRTI)	QYL-685	Selected	Y ?	9-fold. Additional passage of virus did not select M184V	Yoshimura99a
M 184 I	ATG→ATG	HIV-1 Specific RT Inhibitor (NNRTI)	QYL-685	Cross-R	Y ?	Additional passage of virus did not select M184V, but infectious clone was resistant.	Yoshimura99a
M 184 T	ATG→ACG	Nucleoside RT Inhibitor (NRTI)	3TC (lamivudine)	Selected	Y	Reduced replication capacity and RT activity	Keulen97, Larder95
M 184 V	ATG→GTG	Nucleoside RT Inhibitor (NRTI)	1592U89 (abacavir)	Selected	Y N	K65R/L74V and/or Y115F with M184V: 10-fold; K65R/M184V: 8-fold; L74V/M184V: 9-fold; L74V/Y115F/M184V: 11-fold	Tisdale97
M 184 V	ATG→GTG	Nucleoside RT Inhibitor (NRTI)	3TC (lamivudine)	Selected	Y	M184V and M184I can suppress effects of AZT resistance mutations; GTA seen in cell culture	Schinazi93, Tisdale93, Gao93
M 184 V	ATG→GTG	NRTI	4'-Ed4T	Selected	Y ?	selected at day 26 while P119S and T165A added at day 81	Nitanda05
M 184 V	ATG→GTG	Nucleoside RT Inhibitor (NRTI)	BCH-10652 (+/- dOTC)	Selected	Y ?	K65R/M184V: 4.2-fold.	Taylor00
M 184 V	ATG→GTG	Nucleoside RT Inhibitor (NRTI)	ddC (zalcitabine)	Cross-R	Y		Gu92
M 184 V	ATG→GTG	Nucleoside RT Inhibitor (NRTI)	ddl (didanosine)	Selected	Y	2-5-fold resistance; Rarely observed in patients receiving ddl	Gu92, Gao92
M 184 V	ATG→GTG	Nucleoside RT Inhibitor (NRTI)	(-)dOTC	Selected	Y ?	Selected in 15-20 passages	Taylor00
M 184 V	ATG→GTG	Nucleoside RT Inhibitor (NRTI)	(+)dOTC	Selected	Y ?	6-7-fold resistance	Richard99
M 184 V	ATG→GTG	Nucleoside RT Inhibitor (NRTI)	(-)dOTFC	Selected	Y ?	high level resistance	Richard00
M 184 V	ATG→GTG	Nucleoside RT Inhibitor (NRTI)	(+)dOTFC	Cross-R	Y ?	high level resistance	Richard00
M 184 V	ATG→GTG	Nucleoside RT Inhibitor (NRTI)	(-)FTC (emtricitabine)	Selected	Y	>100-fold resistance. M184V can suppress effects of AZT mutations	Schinazi93, Tisdale93
M 184 V	ATG→GTG	Nucleoside RT Inhibitor (NRTI)	L-FddC	Cross-R	Y ?	>100-fold resistant to 3TC-resistant virus	Gosselin94
Y 188 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	ADAMII	Cross-R	Y ?	6.07-fold. Tested against a site-directed mutant.	Cushman98
Y 188 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Selected	N		Richman94
Y 188 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	E-EPSeU	Selected	Y ?	Y188C is the predominant mutation for E-EPSeU; Y188C confers greater resistance than Y181C	Nguyen94
Y 188 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	E-EPU	Selected	Y ?	Y188C confers greater resistance than Y181C	Nguyen94
Y 188 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	HEPT	Selected	Y ?		Balzarin93

**HIV-1 RT**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
Y 188 H	TAT→CAT	HIV-1 Specific RT Inhibitor (NNRTI)	ADAMII	Cross-R	Y	?	>128-fold resistant against a virus isolate, but not tested against a site-directed mutant.	Cushman98
Y 188 H	TAT→CAT	Multiple Nucleoside	AZT (zidovudine) + BHAP U-87201E (atevirdine)	Selected	?	Y	Found in two patients on atevirdine + AZT combination therapy.	Demeter98
Y 188 H	TAT→CAT	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Selected	N	Y		Bachelor00
Y 188 H	TAT→CAT	HIV-1 Specific RT Inhibitor (NNRTI)	TIBO R82913	Selected	Y	?		Balzarini93c
Y 188 H/L	TAT→CAT/CTT	HIV-1 Specific RT Inhibitor (NNRTI)	α-APA (loviride)	Selected	?	Y		Staszewski96
Y 188 L	TAT→TTA	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Cross-R	Y	?	1000-fold increase in IC90	Young95
Y 188 L	TAT→?	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Selected	Y	Y		Bachelor00
Y 188 L	TAT→TTA	HIV-1 Specific RT Inhibitor (NNRTI)	TIBO R82913	Selected	N	Y		Vandamme94
V 189 I	GTA→ATA	HIV-1 Specific RT Inhibitor (NNRTI)	HBV 097	Selected	Y	?	2-fold resistant	Kleim96
G 190 A	GGA→GCA	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Selected	N	Y		Richman94
G 190 A	GGA→GCA	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Selected	N	Y		Bachelor00
G 190 C	GGA→?	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Cross-R	Y	Y	Mutation from patient database of isolates >10-fold resistant to NVP and EFV, but hy-persusceptible to DLV.	Huang03
G 190 C	GGA→?	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Cross-R	Y	Y	Mutation from patient database of isolates >10-fold resistant to NVP and EFV, but hy-persusceptible to DLV.	Huang03
G 190 E	GGA→GAA	HIV-1 Specific RT Inhibitor (NNRTI)	AAP-BHAP (U-104489)	Selected	Y	?	T139I/G190E/T200A/L214F: >100. Additional mutations possibly restore the replication capacity of the G190E mutant	Olmsted96
G 190 E	GGA→GAA	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Cross-R	Y	Y	Mutation from patient database of isolates >10-fold resistant to NVP and EFV, but hy-persusceptible to DLV.	Huang03
G 190 E	GGA→GAA	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Selected	N	Y		Bachelor00

## HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R vitro	In vivo	Comments	Refs
G 190 E	GGA →GAA	HIV-1 Specific RT Inhibitor (NNRTI)	HBV 097	Selected	Y ?	Reduces enzymatic activity of RT and viral replication competency	Kleim95
G 190 E	GGA →GAA	HIV-1 Specific RT Inhibitor (NNRTI)	S-2720 (quinoxaline)	Selected	Y ?		Kleim93
G 190 E	GGA →GAA	HIV-1 Specific RT Inhibitor (NNRTI)	UC-38	Selected	Y N	Selected In combination with G190E: > 100-fold	Balzarini95
G 190 Q	GGA →CAA	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Cross-R	Y	Mutation from patient database of isolates >10-fold resistant to NVP and EFV, but hy-persusceptible to DLV.	Huang03
G 190 Q	GGA →CAA	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Cross-R	Y	Mutation from patient database of isolates >10-fold resistant to NVP and EFV, but hy-persusceptible to DLV.	Huang03
G 190 Q	GGA →CAA	HIV-1 Specific RT Inhibitor (NNRTI)	HBV 097	Selected	Y ?	Appears exclusively in connection with V179D	Kleim96
G 190 R	GGA →AGA	noncompetitive RT inhibitor	MSK-076	Selected	Y ?		Auwerx04
G 190 S	GGA →TCA	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Cross-R	Y	Mutation from patient database of isolates >10-fold resistant to NVP and EFV, but hy-persusceptible to DLV.	Huang03
G 190 S	GGA →TCA	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Selected	N		Bachelier00
G 190 T	GGA →ACA	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Cross-R	Y	Mutation from patient database of isolates >10-fold resistant to NVP and EFV, but hy-persusceptible to DLV.	Huang03
G 190 T	GGA →ACA	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Cross-R	Y	Mutation from patient database of isolates >10-fold resistant to NVP and EFV, but hy-persusceptible to DLV.	Huang03
G 190 T	GGA →ACA	HIV-1 Specific RT Inhibitor (NNRTI)	HBV 097	Selected	Y ?	Appears during selection with low drug concentrations.	Kleim97
G 190 V	GGA →GTA	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Cross-R	Y	Mutation from patient database of isolates >10-fold resistant to NVP and EFV, but hy-persusceptible to DLV.	Huang03
G 190 V	GGA →GTA	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Cross-R	Y	Mutation from patient database of isolates >10-fold resistant to NVP and EFV, but hy-persusceptible to DLV.	Huang03
G 196 E	GGG →GAG	NNRTI	BI-RG-587 (nevirapine) or DMP-266 (efavirenz)	Selected	Y ?	mutation selected in conjunction with K103N in one patient and V108I and Y181C in another	Ochoa de Echaguen05

## HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
H 208 Y	CAT→TAT	Multiple Nucleoside	AZT (zidovudine) + 3TC (lamivudine)	Cross-R	?	Y	Polymorphism facilitating AZT+3TC dual resistance	Kemp98
H 208 Y	CAT→TAT	Pyrophosphate Analogue RT Inhibitor	PFA (foscarnet)	Selected	Y	Y	2-fold alone; Q161L/H208Y: 9-fold; suppresses effects of AZT mutations	Mellors95
L 210 W	TTG→TGG	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected	Y	Y	210W/215Y: 42-fold 41L/210W/215Y: 49-fold 41L/67N/70R/210W/215Y: 366-fold Mutation arises after prolonged AZT therapy.	Gurusinghe95, Harrigan96, Hooker96
R 211 K	AGG→AAG	Multiple Nucleoside	AZT (zidovudine) + 3TC (lamivudine)	Cross-R	?	Y	Polymorphism facilitating AZT+3TC dual resistance in association with M184V and other AZT resistance mutations.	Kemp98
L 214 F	CTT→TTT	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected	Y	?	Selection of resistant HIV-1EVK passaged in MT-4 cells	Gashnikova03
L 214 F	CTT→TTT	Nucleoside RT Inhibitor (NRTI)	ph-AZT	Selected	Y	?	Selection of resistant HIV-1EVK passaged in MT-4 cells	Gashnikova03
T 215 F	ACC→TTC	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected	?	Y	K67N/K70R/T215Y/K219Q: 120-fold	Larder89, Larder91, Kellam92
T 215 Y	ACC→TAC	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected	Y	Y	M41L/T215Y: 60-70-fold; K67N/K70R/T215Y/K219Q: 120-fold. Effect of T215Y is reversed by a ddl mutation (L74V), NNRTI mutations (L100I;Y181C) or (-)-FTC/3TC mutations (M184I/V)	Larder89, Larder91, Kellam92
K 219 E	AAA→GAA	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected	Y	N		Larder89, Larder91, Kellam92
K 219 E	AAA→GAA	NRTI	PMFA (tenofovir)	Selected	?	Y		Wirden05
K 219 N	AAA→AAT	NRTI	PMFA (tenofovir)	Selected	?	Y		Wirden05
K 219 Q	AAA→CAA	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected	?	Y	K67N/K70R/T215Y/K219Q: 120-fold	Larder89, Larder91, Kellam92
K 219 R	AAA→AGA	Multiple Nucleoside	3TC (lamivudine) + ddT (stavudine)	Selected	?	Y	Seen in two patient on 3TC + ddT combination therapy.	Lawrence99
K 219 R	AAA→AGA	Multiple Nucleoside	AZT (zidovudine) + 3TC (lamivudine)	Selected	?	Y	Seen in two patient on AZT + 3TC combination therapy.	Lawrence99
K 219 W	AAA→TGG	Multiple Nucleoside	ddC (zalcitabine) + ddT (stavudine)	Selected	?	Y	Seen in one patient on ddC + ddT combination therapy.	Lawrence99
P 225 H	CCT→CAT	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Selected	N	Y	Observed frequently in patients.	Bachelet00
P 225 H	CCT→CAT	HIV-1 Specific RT Inhibitor (NNRTI)	HBV 097	Cross-R	Y	?	S-2720-selected double mutant V106A/P225H: 4.0-fold	Pelemans97
P 225 H	CCT→CAT	HIV-1 Specific RT Inhibitor (NNRTI)	I-EBU (emivirine)	Cross-R	Y	?	S-2720-selected double mutant V106A/P225H: 5.7-fold	Pelemans97

**HIV-1 RT**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
P 225 H	CCT→CAT	HIV-1 Specific RT Inhibitor (NNRTI)	S-2720 (quinoxaline)	Selected	Y	?	P225H follows V106A. Also seen with L101I and Y181C.	Pelemans97
P 225 H	CCT→CAT	HIV-1 Specific RT Inhibitor (NNRTI)	UC-781	Cross-R	Y	?	S-2720-selected double mutant V106A/P225H: 3.7-fold	Pelemans97
F 227 C	TTC→TGC	HIV-1 Specific RT Inhibitor (NNRTI)	TMC125	Cross-R	Y	Y	V106A + F227L: 387-fold. This mutation confers hypersensitivity to delavirdine.	Vingerhoets04
F 227 L	TTA→CTC	HIV-1 Specific RT Inhibitor (NNRTI)	S-1153	Selected	Y	?		Fujiwara98
V 233 E	GAA→GTA	Multiple Nucleoside	AZT (zidovudine) + BHAP U-87201E (atevirdine)	Selected	N	Y	Seen in 1 patient. K101E, Y188H and K238T also seen in patients on ATV/AZT combination therapy.	Demeter98
L 234 I	CTC→ATC	HIV-1 Specific RT Inhibitor (NNRTI)	S-1153	Selected	Y	?	This mutation confers hypersensitivity to loviride.	Fujiwara98
P 236 L	CCT→CTT	HIV-1 Specific RT Inhibitor (NNRTI)	BHAP U-87201E (atevirdine)	Selected	Y	?	Sensitizes RT 10-fold to nevirapine, TIBO R82913 and L-697,661	Dueweke93
P 236 L	CCT→CTT	HIV-1 Specific RT Inhibitor (NNRTI)	BHAP U-90152 (delavirdine)	Selected	Y	?	Sensitizes RT 10-fold to nevirapine, TIBO R82913 and L-697,661	Dueweke93
P 236 L	CCT→CTT	HIV-1 Specific RT Inhibitor (NNRTI)	HEPT	Selected	Y	?		Buckheit95c
K 238 S	AAA→AGT	NNRTI	BI-RG-587 (nevirapine)	Cross-R	Y	Y		Hachiyu04
K 238 T	AAA→ACA	Multiple Nucleoside	AZT (zidovudine) + BHAP U-87201E (atevirdine)	Selected	N	Y	Seen in 1 patient. K101E, K103N, Y188H, and V233E also observed with ATV/AZT combination therapy.	Demeter98
K 238 T	AAA→ACA	Multiple Nucleoside	AZT (zidovudine) + BHAP U-87201E (atevirdine)	Selected	N	Y	Seen in 1 patient. K101E, K103N, Y188H and E233V also seen in patients on ATV/AZT combination therapy.	Demeter98
L 283 I	CTT→ACT	HIV-1 Specific RT Inhibitor (NNRTI)	BHAP U-90152 (delavirdine)	Cross-R	N	Y	Identified by logistic regression analysis, confirmed by mutagenesis studies. Confers resistance in conjunction with mutations at codon 135.	Brown00
L 283 I	CTT→ACT	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Cross-R	N	Y	Identified by logistic regression analysis, confirmed by mutagenesis studies. Confers resistance in conjunction with mutations at codon 135.	Brown00



**HIV-1 RT**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
L 283 I	CTT→ACT	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Cross-R	N	Y	Identified by logistic regression analysis, confirmed by mutagenesis studies. Confers resistance in conjunction with mutations at codon 135.	Brown00
Y 318 F	TAT→TTT	HIV-1 Specific RT Inhibitor (NNRTI)	BHAP U-90152 (delavirdine)	Cross-R	Y	Y	This mutation also acts synergistically with K103N and Y181C to confer higher levels of resistance to DLV and EFV than seen with either of these mutations alone	Harrigan02, Pelemans98
Y 318 F	TAT→TTT	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Cross-R	Y	Y	This mutation also acts synergistically with K103N and Y181C to confer higher levels of resistance to DLV and EFV than seen with either of these mutations alone	Harrigan02, Pelemans98
G 333 D	GGC→GAC	Multiple Nucleoside	AZT (zidovudine) + 3TC Cross-R (lamivudine)	Cross-R	Y	Y	Facilitates dual resistance to AZT+3TC in association with M184V and standard AZT resistance mutations.	Kemp98
G 333 D	GGC→GAC	Multiple Nucleoside	AZT (zidovudine) + 3TC Cross-R (lamivudine) + 1592U89 (abacavir)	Cross-R	?	Y	found in non-B subtypes	Caride00
G 333 E	GGC→GAG	Multiple Nucleoside	AZT (zidovudine) + 3TC Cross-R (lamivudine)	Cross-R	Y	Y	Facilitates dual resistance to AZT+3TC in association with M184V and standard AZT resistance mutations.	Kemp98
G 333 E	GGC→GAG	Multiple Nucleoside	AZT (zidovudine) + 3TC Cross-R (lamivudine) + 1592U89 (abacavir)	Cross-R	?	Y	found in non-B subtypes	Caride00
T 386 I	ACT→ATT	Multiple Nucleoside	AZT (zidovudine) + 3TC Cross-R (lamivudine) + 1592U89 (abacavir)	Cross-R	?	Y	Abrogates M184V suppression of L210W and L210W/G333D/E	Caride00

**HIV-2 RT**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R vivo	In vitro	In vivo	Comments	Refs
I 5 V	ATG→ATC	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine) + 3TC (lamivudine) + ddI (didanosine)	Selected	?	Y		Brandin03
I 5 V	ATT→GTT	NRTI	multi-nucleoside	Selected	?	Y		Colson05
I 10 V	ATT→GTT	Nucleoside RT Inhibitor (NRTI)	I592U89(abacavir)+3TC (lamivudine)+AZT (zidovudine)	Selected	?	Y		Brandin03
I 10 V	ATT→GTT	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine) + 3TC (lamivudine) + ddI (didanosine)	Selected	?	Y		Brandin03
V 11 I	ATT→GTT	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine) + 3TC (lamivudine) + ddI (didanosine)	Selected	?	Y		Brandin03
R 20 K	ATT→GTT	Nucleoside RT Inhibitor (NRTI)	I592U89(abacavir)+3TC (lamivudine)+AZT (zidovudine)	Selected	?	Y		Brandin03
K 35 R	AAA→AGA	NRTI	multi-nucleoside	Selected	?	Y		Colson05
R 35 K	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	I592U89(abacavir)+3TC (lamivudine)+AZT (zidovudine)	Selected	?	Y		Brandin03
K 40 R	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	I592U89(abacavir)+3TC (lamivudine)+AZT (zidovudine)	Selected	?	Y		Brandin03
I 43 I	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	ABT-538(ritonavir) + AG-1343 (nelfinavir)	Selected	?	Y		Brandin03
K 45 R	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	ABT-538(ritonavir) + AG-1343 (nelfinavir)	Selected	?	Y		Brandin03
G 48 A	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	ABT-378 (lopinavir)	Selected	?	Y		Brandin03
I 50 V	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	ABT-378 (lopinavir)	Selected	?	Y		Brandin03
I 54 M	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	ABT-538(ritonavir) + AG-1343 (nelfinavir)	Selected	?	Y		Brandin03

**HIV-2 RT**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
I 64 V	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	ABT-378 (lopinavir)	Selected	?	Y		Brandin03
K 65 R	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine) + 3TC (lamivudine) + ddI (didanosine)	Selected	?	Y		Brandin03
N 69 S	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine) + 3TC (lamivudine) + ddI (didanosine)	Selected	?	Y		Brandin03
K 70 S	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	I592U89(abacavir)+3TC (lamivudine)+AZT (zidovudine)	Selected	?	Y		Brandin03
V 71 I	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	ABT-538(ritonavir) + AG-1343 (nelfinavir)	Selected	?	Y		Brandin03
A 92 T	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	ABT-538(ritonavir) + AG-1343 (nelfinavir)	Selected	?	Y		Brandin03
L 99 F	AAA→AGA	Nucleoside RT Inhibitor (NRTI)	ABT-538(ritonavir) + AG-1343 (nelfinavir)	Selected	?	Y		Brandin03
A 101 P	GCC→CCC	noncompetitive RT inhibitor	MSK-076	Selected	Y	?	Mutation found in HIV-2 at a position equivalent to the NNRTI binding site in HIV-1	Auwerx04
G 112 E	GGG→GAG	noncompetitive RT inhibitor	MSK-076	Selected	Y	?	Mutation found close to the HIV-2 active site	Auwerx04
Q 151 M	GGG→GAG	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine) + 3TC (lamivudine) + ddI (didanosine)	Selected	?	Y		Brandin03
Y 162 H	GGG→GAG	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine) + 3TC (lamivudine) + ddI (didanosine)	Selected	?	Y		Brandin03
T 163 A	GGG→GAG	Nucleoside RT Inhibitor (NRTI)	I592U89(abacavir)+3TC (lamivudine)+AZT (zidovudine)	Selected	?	Y		Brandin03
M 184 V	GGG→GAG	Nucleoside RT Inhibitor (NRTI)	3TC (lamivudine)	Selected	?	Y		Brandin03

**HIV-2 RT**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
F 214 L	GGG→GAG	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine) + 3TC (lamivudine) + ddI (didanosine)	Selected	?	Y		Brandin03
F 214 L	TTT→CTT	NRTI	multi-nucleoside	Selected	?	Y		Colson05
E 219 D	TTT→CTT	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected	?	Y		Brandin03
K 223 R	AAA→AGA	NRTI	multi-nucleoside	Selected	?	Y		Colson05

**SIV RT**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
K 65 R	AAA→AGA	SIV Nucleoside RT Inhibitor	PMPA (tenofovir)	Selected	?	Y	K65R appears first, followed by N69S and I118V. Observed changes at N69S and I118V do not result in increased resistance.	VanRompay96, Cherrington96a, VanRompay97a
Q 151 M	CAG→ATG	SIV Nucleoside RT Inhibitor	AZT (zidovudine)	Selected	?	Y		VanRompay97

**HIV-1 Integrase**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
G 140 S	GGC→AGC	Integrase inhibitor	L-Chicoric Acid	Selected	Y	?	Mutation located in the catalytic core of integrase. Mildly attenuates virus growth.	King98
V 165 I	GGC→AGC	Integrase inhibitor	FZ41	Selected	?	Y	selected in conjunction with V249I; double mutant confers 9 fold resistance	Bonnenfant04
F 185 K	GGC→AGC	integrase inhibitor	DKA ( $\beta$ -diketo acids)	Cross-R	Y	?	only biochemical studies done to test decrease in susceptibility	Marchand03
V 249 I	GGC→AGC	Integrase inhibitor	FZ41	Selected	?	Y	selected in conjunction with V165I; double mutant confers 9 fold resistance	Bonnenfant04
C 280 S	GGC→AGC	integrase inhibitor	DKA ( $\beta$ -diketo acids)	Cross-R	Y	?	only biochemical studies done to test decrease in susceptibility	Marchand03
C 280 Y	GGC→AGC	Integrase inhibitor	FZ41	Selected	?	Y	confers 5 fold resistance	Bonnenfant04

## HIV-1 Env

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
Q 32 H	CAG→ATG	Fusion/Binding Inhibitor	T20 (pentafuside)	Selected	Y	Y	found in combination with G36D in patients	Wei02
Q 32 R	CAG→ATG	Fusion/Binding Inhibitor	T20 (pentafuside)	Selected	Y	Y	found in combination with G36D in patients	Wei02
L 33 S	TTA→TCA	fusion inhibitor	M87	Selected	Y	?	Enhances viral fitness	Lohrengel05
G 36 D	GGT→GAT	Fusion/Binding Inhibitor	T20 (pentafuside)	Selected	Y	Y	Resistance lost when R122G substitution is present in HR2 domain	Wei02
G 36 S	GGT→AGT	Fusion/Binding Inhibitor	T20 (pentafuside)	Selected	Y	?	Both G36S and V38M mutations must be present to confer resistance.	Rimsky98
G 36 V	GGT→GTT	fusion inhibitor	T20 (enfuvirtide)	Selected	?	Y		Menzo04
I 37 V	GGT→GTT	Fusion/Binding Inhibitor	T20 (pentafuside)	Selected	Y	Y		Wei02
V 38 A	GTG→CGG	Fusion/Binding Inhibitor	T20 (pentafuside)	Selected	Y	Y		Wei02
V 38 M	GTG→ATG	Fusion/Binding Inhibitor	T20 (pentafuside)	Selected	Y	?	Both G36S and V38M mutations must be present to confer resistance.	Rimsky98
Q 39 R	GTG→ATG	Fusion/Binding Inhibitor	T20 (pentafuside)	Selected	Y	Y	found in combination with G36D in patients	Wei02
N 42 D	AAC→GAC	fusion inhibitor	T20 (enfuvirtide)	Selected	?	Y		Menzo04
N 42 T	AAC→ACC	fusion inhibitor	T20 (enfuvirtide)	Selected	?	Y		Menzo04
N 43 D	AAT→GAC	fusion inhibitor	T20 (enfuvirtide)	Selected	?	Y		Menzo04
L 44 M	TTG→ATG	fusion inhibitor	T20 (enfuvirtide)	Selected	?	Y		Menzo04
L 45 M	TTG→ATG	fusion inhibitor	T20 (enfuvirtide)	Selected	?	Y		Menzo04
R 46 M	AGG→ATG	Fusion/Binding Inhibitor	T20 (pentafuside)	Selected	Y	Y		Wei02
I 48 V	ATT→GTT	fusion inhibitor	M87	Selected	Y	?	Double mutant I48V/N126K results in strong reduction of viral fitness	Lohrengel05
V 68 A	ATT→GTT	Fusion/Binding Inhibitor	BMS-488043	Selected	Y	?	Mutation in gp120.	Lin03
V 69 I	GTC→ATC	Fusion/Binding Inhibitor	T20 (pentafuside)	Selected	Y	Y	represents a conservative change that is present in the HIV-1 LAI consensus sequence	Wei02
I 84 S	ATC→AGC	Fusion/Binding Inhibitor	RPR103611	Selected	Y	?		Labrosse97
N 106 K	AAT→AAG	Fusion/Binding Inhibitor	JM 2763	Cross Resistant	Y	?	106K/I34N/I45L/245I/269E/278H/288V/293D/364-367Deletion/387T: 10 fold	Schols98
N 106 K	AAT→AAG	Fusion/Binding Inhibitor	JM-3100	Cross Resistant	Y	?	106K/I34N/I45L/245I/269E/278H/288V/293D/364-367Deletion/387T: 10-fold	Schols98
N 106 K	AAT→AAG	Fusion/Binding Inhibitor	Mab 12G5	Cross Resistant	Y	?	106K/I34N/I45L/245I/269E/278H/288V/293D/364-367Deletion/387T.	Schols98
N 106 K	AAT→AAG	Fusion/Binding Inhibitor	SDF-1 $\alpha$	Selected	Y	?	106K/I34N/I45L/245I/269E/278H/288V/293D/364-367Deletion/387T: 15-fold.	Schols98
S 113 N	AGT→AAT	Fusion/Binding Inhibitor	DS (dextran sulphate)	Selected	Y	ND	V1 Loop Region	Este96a, Este97

## HIV-1 Env

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
N 126 K	AAT→AAA	fusion inhibitor	M87	Selected	Y	?	Double mutant I48V/N126K results in strong reduction of viral fitness	Lohregel05
S 134 N	AGC→AAC	Fusion/Binding Inhibitor	DS (dextran sulphate)	Selected	Y	?	V2 loop region: S113N/S134N/K269E/Q278E/N293D/N323S/R387I: 250-fold	Este97, Este96a
S 134 N	AGC→AAC	Fusion/Binding Inhibitor	JM 2763	Cross Resistant	Y	?	I06K/I34N/I45L/245I/269E/278H/288V/293D/364-367Deletion/387T: 10 fold	Schols98
S 134 N	AGC→AAC	Fusion/Binding Inhibitor	JM-3100	Cross Resistant	Y	?	I06K/I34N/I45L/245I/269E/278H/288V/293D/364-367Deletion/387T: 10-fold	Schols98
S 134 N	AGC→AAC	Fusion/Binding Inhibitor	Mab 12G5	Cross Resistant	Y	?	I06K/I34N/I45L/245I/269E/278H/288V/293D/364-367Deletion/387T:	Schols98
S 134 N	AGC→AAC	Fusion/Binding Inhibitor	SDF-1 $\alpha$	Selected	Y	?	I06K/I34N/I45L/245I/269E/278H/288V/293D/364-367Deletion/387T: 15-fold.	Schols98
F 145 L	TTC→TTA	Fusion/Binding Inhibitor	JM 2763	Cross Resistant	Y	?	I06K/I34N/I45L/245I/269E/278H/288V/293D/364-367Deletion/387T: 10 fold	Schols98
F 145 L	TTC→TTA	Fusion/Binding Inhibitor	JM-3100	Selected	Y	?	Combination of mutations: 2- to 100-fold	DeVreese96, DeVreese96a
F 145 L	TTC→TTA	Fusion/Binding Inhibitor	JM-3100	Cross Resistant	Y	?	I06K/I34N/I45L/245I/269E/278H/288V/293D/364-367Deletion/387T: 10-fold	Schols98
F 145 L	TTC→TTA	Fusion/Binding Inhibitor	Mab 12G5	Cross Resistant	Y	?	I06K/I34N/I45L/245I/269E/278H/288V/293D/364-367Deletion/387T:	Schols98
F 145 L	TTC→TTA	Fusion/Binding Inhibitor	SDF-1 $\alpha$	Selected	Y	?	I06K/I34N/I45L/245I/269E/278H/288V/293D/364-367Deletion/387T: 15-fold.	Schols98
N 188 K	AAT→AAA	Fusion/Binding Inhibitor	siamycin I	Selected	Y	?	N188K/G332E/N351D/A550T/N633D/L762S: 9-fold	Lin96
N 204 K	AAT→AAA	entry inhibitor	Concanavalin A (ConA)	Selected	Y	?	mutations in gp120	Witvrouw05
G 237 R	AAT→AAA	Fusion/Binding Inhibitor	IC9564 (emivirine)	Selected	Y	?	gp-120	Holz-Smith01
F 245 I	TTC→ATC	Fusion/Binding Inhibitor	JM 2763	Cross Resistant	Y	?	I06K/I34N/I45L/245I/269E/278H/288V/293D/364-367Deletion/387T: 10 fold	Schols98
F 245 I	TTC→ATC	Fusion/Binding Inhibitor	JM-3100	Cross Resistant	Y	?	I06K/I34N/I45L/245I/269E/278H/288V/293D/364-367Deletion/387T: 10-fold	Schols98
F 245 I	TTC→ATC	Fusion/Binding Inhibitor	Mab 12G5	Cross Resistant	Y	?	I06K/I34N/I45L/245I/269E/278H/288V/293D/364-367Deletion/387T:	Schols98
F 245 I	TTC→ATC	Fusion/Binding Inhibitor	SDF-1 $\alpha$	Selected	Y	?	I06K/I34N/I45L/245I/269E/278H/288V/293D/364-367Deletion/387T: 15-fold.	Schols98
R 252 K	TTC→ATC	Fusion/Binding Inhibitor	IC9564 (emivirine)	Selected	Y	?	gp-120	Holz-Smith01



**HIV-1 Env**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
S 261 F	TTC→ATC	entry inhibitor	Concanavalin A (ConA)	Selected	Y	?	mutations in gp120	Witvrouw05
K 269 E	AAA→GAA	Fusion/Binding Inhibitor	DS (dextran sulphate)	Selected	Y	?	V3 loop region; S113N/S134N/K269E/Q278E/N293D/N323S/R387I: 250-fold	Este97, Este96a
N 269 E	AAC→GAA	Fusion/Binding Inhibitor	JM 2763	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T: 10 fold	Schols98
N 269 E	AAC→GAA	Fusion/Binding Inhibitor	JM-3100	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T: 10-fold	Schols98
N 269 E	AAC→GAA	Fusion/Binding Inhibitor	Mab 12G5	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T:	Schols98
N 269 E	AAC→GAA	Fusion/Binding Inhibitor	SDF-1 $\alpha$	Selected	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T: 15-fold.	Schols98
N 269 K	AAC→?	Fusion/Binding Inhibitor	ALX40-4C	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 145-fold cross-resistant to ALX40-4C. Role of each mutation not confirmed by site-directed mut	Kanbara01
N 269 K	AAC→?	Fusion/Binding Inhibitor	AMD3100	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 15-fold cross-resistant to AMD3100. Role of each mutation not confirmed by site-directed mut	Kanbara01
N 269 K	AAC→?	Fusion/Binding Inhibitor	SDF-1	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 26-fold cross-resistant to SDF-1. Role of each mutation not confirmed by site-directed mutag	Kanbara01
N 269 K	AAC→?	Fusion/Binding Inhibitor	TI34	Selected	Y	N	In vitro selected virus (p145 of HIV-INL4-3, contains mutations N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 15-fold resistant to TI34. Role of each mutation not conf	Kanbara01

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Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
N 269 K	AAC→?	Fusion/Binding Inhibitor	T140	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 21-fold cross-resistant to T140. Role of each mutation not confirmed by site-directed mutag	Kanbara01
N 269 K	AAC→?	Fusion/Binding Inhibitor	vMIP-II	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 42-fold cross-resistant to vMIP II. Role of each mutation not confirmed by site-directed mut	Kanbara01
N 270 S	AAT→AGT	Fusion/Binding Inhibitor	JM-3100	Selected	Y	?		DeVreese96, DeVreese96a
R 272 T	AGA→ACA	Fusion/Binding Inhibitor	JM-3100	Selected	Y	?		DeVreese96, DeVreese96a
S 274 del	AGA→ACA	Fusion/Binding Inhibitor	ALX40–4C	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 145-fold cross-resistant to ALX40–4C. Role of each mutation not confirmed by site-directed m	Kanbara01
S 274 del	AGA→ACA	Fusion/Binding Inhibitor	AMD3100	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 15-fold cross-resistant to AMD3100. Role of each mutation not confirmed by site-directed mut	Kanbara01
S 274 del	AGA→ACA	Fusion/Binding Inhibitor	SDF-1	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 26-fold cross-resistant to SDF-1. Role of each mutation not confirmed by site-directed mutag	Kanbara01

**HIV-1 Env**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
S 274 del	AGA → ACA	Fusion/Binding Inhibitor	T134	Selected	Y	N	In vitro selected virus (p145 of HIV-INL4-3, contains mutations N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275 in V3 loop of gp120 ) 15-fold resistant to T134. Role of each mutation not conf	Kanbara01
S 274 del	AGA → ACA	Fusion/Binding Inhibitor	T140	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 21-fold cross-resistant to T140. Role of each mutation not confirmed by site-directed mutag	Kanbara01
S 274 del	AGA → ACA	Fusion/Binding Inhibitor	vMIP-II	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 42-fold cross-resistant to vMIP II. Role of each mutation not confirmed by site-directed mut	Kanbara01
S 274 R	AGT → AGA	Fusion/Binding Inhibitor	JM-2763	Selected	Y	?	Combination of mutations: 95- to 792-fold	DeVreese96, DeVreese96a
S 274 R	AGT → AGA	Fusion/Binding Inhibitor	JM-2763	Selected	Y	?		DeVreese96, DeVreese96a
S 274 R	AGT → AGA	Fusion/Binding Inhibitor	JM-3100	Selected	Y	?		DeVreese96, DeVreese96a
I 275 del	AGT → AGA	Fusion/Binding Inhibitor	ALX40-4C	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 145-fold cross-resistant to ALX40-4C. Role of each mutation not confirmed by site-directed m	Kanbara01
I 275 del	AGT → AGA	Fusion/Binding Inhibitor	AMD3100	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 15-fold cross-resistant to AMD3100. Role of each mutation not confirmed by site-directed mut	Kanbara01

## HIV-1 Env

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
I 275 del	AGT→AGA	Fusion/Binding Inhibitor	SDF-I	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 26-fold cross-resistant to SDF-1. Role of each mutation not confirmed by site-directed mutag	Kanbara01
I 275 del	AGT→AGA	Fusion/Binding Inhibitor	T134	Selected	Y	N	In vitro selected virus (p145 of HIV-1NL4–3, contains mutations N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275 in V3 loop of gp120 ) 15-fold resistant to T134. Role of each mutation not conf	Kanbara01
I 275 del	AGT→AGA	Fusion/Binding Inhibitor	T140	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 21-fold cross-resistant to T140. Role of each mutation not confirmed by site-directed mutag	Kanbara01
I 275 del	AGT→AGA	Fusion/Binding Inhibitor	vMIP-II	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 42-fold cross-resistant to vMIP II. Role of each mutation not confirmed by site-directed mut	Kanbara01
Q 278 H	CAG→CAT	Fusion/Binding Inhibitor	DS (dextran sulphate)	Selected	Y	?	V3 loop region: S113N/S134N/K269E/Q278E/N293D/N323S/R387I: 250-fold	Este97, Este96a
Q 278 H	CAG→CAT	Fusion/Binding Inhibitor	JM 2763	Cross Resistant	Y	?	I06K/I34N/I45L/245I/269E/278H/288V/293D/364–367Deletion/387T: 10 fold	Schols98
Q 278 H	CAG→CAT	Fusion/Binding Inhibitor	JM-2763	Selected	Y	?		DeVreese96, DeVreese96a
Q 278 H	CAG→CAC	Fusion/Binding Inhibitor	JM-2763	Selected	Y	?		DeVreese96, DeVreese96a
Q 278 H	CAG→CAC	Fusion/Binding Inhibitor	JM-3100	Selected	Y	?		DeVreese96, DeVreese96a
Q 278 H	CAG→CAT	Fusion/Binding Inhibitor	JM-3100	Cross Resistant	Y	?	I06K/I34N/I45L/245I/269E/278H/288V/293D/364–367Deletion/387T: 10-fold	Schols98
Q 278 H	CAG→CAT	Fusion/Binding Inhibitor	Mab 12G5	Cross Resistant	Y	?	I06K/I34N/I45L/245I/269E/278H/288V/293D/364–367Deletion/387T:	Schols98

**HIV-1 Env**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
Q 278 H	CAG→CAT	Fusion/Binding Inhibitor	SDF-1 $\alpha$	Selected	Y	?	I06K/134N/145L/245I/269E/278H/288V/293D/364–367Deletion/387T: 15-fold.	Schols98
Q 278 T	CAG→ACG	Fusion/Binding Inhibitor	ALX40–4C	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 145-fold cross-resistant to ALX40–4C. Role of each mutation not confirmed by site-directed mutagenesis	Kanbara01
Q 278 T	CAG→ACG	Fusion/Binding Inhibitor	AMD3100	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 15-fold cross-resistant to AMD3100. Role of each mutation not confirmed by site-directed mutagenesis	Kanbara01
Q 278 T	CAG→ACG	Fusion/Binding Inhibitor	SDF-1	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 26-fold cross-resistant to SDF-1. Role of each mutation not confirmed by site-directed mutagenesis	Kanbara01
Q 278 T	CAG→ACG	Fusion/Binding Inhibitor	T134	Selected	Y	N	In vitro selected virus (p145 of HIV-INL4–3, contains mutations N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 15-fold resistant to T134. Role of each mutation not confirmed	Kanbara01
Q 278 T	CAG→ACG	Fusion/Binding Inhibitor	T140	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 21-fold cross-resistant to T140. Role of each mutation not confirmed by site-directed mutagenesis	Kanbara01

**HIV-1 Env**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
Q 278 T	CAG→ACG	Fusion/Binding Inhibitor	vMIP-II	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 42-fold cross-resistant to vMIP II. Role of each mutation not confirmed by site-directed mut	Kanbara01
R 279 K	CAG→ACG	Fusion/Binding Inhibitor	ALX40-4C	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 145-fold cross-resistant to ALX40-4C. Role of each mutation not confirmed by site-directed m	Kanbara01
R 279 K	CAG→ACG	Fusion/Binding Inhibitor	AMD3100	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 15-fold cross-resistant to AMD3100. Role of each mutation not confirmed by site-directed mut	Kanbara01
R 279 K	CAG→ACG	Fusion/Binding Inhibitor	SDF-1	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 26-fold cross-resistant to SDF-1. Role of each mutation not confirmed by site-directed mutag	Kanbara01
R 279 K	CAG→ACG	Fusion/Binding Inhibitor	T134	Selected	Y	N	In vitro selected virus (p145 of HIV-INL4-3, contains mutations N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 15-fold resistant to T134. Role of each mutation not conf	Kanbara01
R 279 K	CAG→ACG	Fusion/Binding Inhibitor	T140	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 21-fold cross-resistant to T140. Role of each mutation not confirmed by site-directed mutag	Kanbara01

**HIV-1 Env**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
R 279 K	CAG→ACG	Fusion/Binding Inhibitor	vMIP-II	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 42-fold cross-resistant to vMIP II. Role of each mutation not confirmed by site-directed mut	Kanbara01
A 284 V	CAG→ACG	Fusion/Binding Inhibitor	ALX40–4C	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 145-fold cross-resistant to ALX40–4C. Role of each mutation not confirmed by site-directed m	Kanbara01
A 284 V	CAG→ACG	Fusion/Binding Inhibitor	AMD3100	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 15-fold cross-resistant to AMD3100. Role of each mutation not confirmed by site-directed mut	Kanbara01
A 284 V	CAG→ACG	Fusion/Binding Inhibitor	SDF-1	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 26-fold cross-resistant to SDF-1. Role of each mutation not confirmed by site-directed mutag	Kanbara01
A 284 V	CAG→ACG	Fusion/Binding Inhibitor	T134	Selected	Y	N	In vitro selected virus (p145 of HIV-INL4–3, contains mutations N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 15-fold resistant to T134. Role of each mutation not conf	Kanbara01
A 284 V	CAG→ACG	Fusion/Binding Inhibitor	T140	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 21-fold cross-resistant to T140. Role of each mutation not confirmed by site-directed mutag	Kanbara01

**HIV-1 Env**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
A 284 V	CAG→ACG	Fusion/Binding Inhibitor	vMIP-II	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 42-fold cross-resistant to vMIP II. Role of each mutation not confirmed by site-directed mut	Kanbara01
F 285 L	CAG→ACG	Fusion/Binding Inhibitor	ALX40-4C	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 145-fold cross-resistant to ALX40-4C. Role of each mutation not confirmed by site-directed m	Kanbara01
F 285 L	CAG→ACG	Fusion/Binding Inhibitor	AMD3100	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 15-fold cross-resistant to AMD3100. Role of each mutation not confirmed by site-directed mut	Kanbara01
F 285 L	CAG→ACG	Fusion/Binding Inhibitor	SDF-1	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 26-fold cross-resistant to SDF-1. Role of each mutation not confirmed by site-directed mutag	Kanbara01
F 285 L	CAG→ACG	Fusion/Binding Inhibitor	T134	Selected	Y	N	In vitro selected virus (p145 of HIV-INL4-3, contains mutations N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 15-fold resistant to T134. Role of each mutation not conf	Kanbara01
F 285 L	CAG→ACG	Fusion/Binding Inhibitor	T140	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 21-fold cross-resistant to T140. Role of each mutation not confirmed by site-directed mutag	Kanbara01



**HIV-1 Env**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
F 285 L	CAG→ACG	Fusion/Binding Inhibitor	vMIP-II	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 42-fold cross-resistant to vMIP II. Role of each mutation not confirmed by site-directed mut	Kanbara01
V 286 Y	CAG→ACG	Fusion/Binding Inhibitor	ALX40-4C	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 145-fold cross-resistant to ALX40-4C. Role of each mutation not confirmed by site-directed m	Kanbara01
V 286 Y	CAG→ACG	Fusion/Binding Inhibitor	AMD3100	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 15-fold cross-resistant to AMD3100. Role of each mutation not confirmed by site-directed mut	Kanbara01
V 286 Y	CAG→ACG	Fusion/Binding Inhibitor	SDF-1	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 26-fold cross-resistant to SDF-1. Role of each mutation not confirmed by site-directed mutag	Kanbara01
V 286 Y	CAG→ACG	Fusion/Binding Inhibitor	T134	Selected	Y	N	In vitro selected virus (p145 of HIV-INL4-3, contains mutations N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 15-fold resistant to T134. Role of each mutation not conf	Kanbara01
V 286 Y	CAG→ACG	Fusion/Binding Inhibitor	T140	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 21-fold cross-resistant to T140. Role of each mutation not confirmed by site-directed mutag	Kanbara01

**HIV-1 Env**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
V 286 Y	CAG→ACG	Fusion/Binding Inhibitor	vMIP-II	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 42-fold cross-resistant to vMIP II. Role of each mutation not confirmed by site-directed mut	Kanbara01
I 288 T	ATA→ACA	Fusion/Binding Inhibitor	ALX40-4C	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 145-fold cross-resistant to ALX40-4C. Role of each mutation not confirmed by site-directed m	Kanbara01
I 288 T	ATA→ACA	Fusion/Binding Inhibitor	AMD3100	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 15-fold cross-resistant to AMD3100. Role of each mutation not confirmed by site-directed mut	Kanbara01
I 288 T	ATA→ACA	Fusion/Binding Inhibitor	SDF-1	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 26-fold cross-resistant to SDF-1. Role of each mutation not confirmed by site-directed mutag	Kanbara01
I 288 T	ATA→ACA	Fusion/Binding Inhibitor	T134	Selected	Y	N	In vitro selected virus (p145 of HIV-INL4-3, contains mutations N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 15-fold resistant to T134. Role of each mutation not conf	Kanbara01
I 288 T	ATA→ACA	Fusion/Binding Inhibitor	T140	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 21-fold cross-resistant to T140. Role of each mutation not confirmed by site-directed mutag	Kanbara01

## HIV-1 Env

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
I 288 T	ATA→ACA	Fusion/Binding Inhibitor	vMIP-II	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 42-fold cross-resistant to vMIP II. Role of each mutation not confirmed by site-directed mut	Kanbara01
I 288 V	ATA→GTC	Fusion/Binding Inhibitor	JM 2763	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T; 10 fold	Schols98
I 288 V	ATA→GTA	Fusion/Binding Inhibitor	JM-2763	Selected	Y	?	Combination of mutations	DeVreese96a
I 288 V	ATA→GTA	Fusion/Binding Inhibitor	JM-3100	Selected	Y	?		DeVreese96, DeVreese96a
I 288 V	ATA→GTC	Fusion/Binding Inhibitor	JM-3100	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T; 10-fold	Schols98
I 288 V	ATA→GTC	Fusion/Binding Inhibitor	Mab 12G5	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T;	Schols98
I 288 V	ATA→GTC	Fusion/Binding Inhibitor	SDF-1 $\alpha$	Selected	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T; 15-fold.	Schols98
ins 290 T	ATA→GTC	Fusion/Binding Inhibitor	ALX40-4C	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 145-fold cross-resistant to ALX40-4C. Role of each mutation not confirmed by site-directed m	Kanbara01
ins 290 T	ATA→GTC	Fusion/Binding Inhibitor	AMD3100	Selected	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 15-fold cross-resistant to AMD3100. Role of each mutation not confirmed by site-directed mut	Kanbara01
ins 290 T	ATA→GTC	Fusion/Binding Inhibitor	SDF-1	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 26-fold cross-resistant to SDF-1. Role of each mutation not confirmed by site-directed mutag	Kanbara01

**HIV-1 Env**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
ins 290 T	ATA→GTC	Fusion/Binding Inhibitor	T134	Cross Resistant	Y	N	In vitro selected virus (p145 of HIV-INL4-3, contains mutations N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 15-fold resistant to T134. Role of each mutation not conf	Kanbara01
ins 290 T	ATA→GTC	Fusion/Binding Inhibitor	T140	Selected	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 21-fold cross-resistant to T140. Role of each mutation not confirmed by site-directed mutag	Kanbara01
ins 290 T	ATA→GTC	Fusion/Binding Inhibitor	vMIP-II	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 42-fold cross-resistant to vMIP II. Role of each mutation not confirmed by site-directed mut	Kanbara01
K 290 E	ATA→GTC	Fusion/Binding Inhibitor	ALX40-4C	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 145-fold cross-resistant to ALX40-4C. Role of each mutation not confirmed by site-directed m	Kanbara01
K 290 E	ATA→GTC	Fusion/Binding Inhibitor	AMD3100	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 15-fold cross-resistant to AMD3100. Role of each mutation not confirmed by site-directed mut	Kanbara01
K 290 E	ATA→GTC	Fusion/Binding Inhibitor	SDF-1	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 26-fold cross-resistant to SDF-1. Role of each mutation not confirmed by site-directed mutag	Kanbara01

**HIV-1 Env**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
K 290 E	ATA→GTC	Fusion/Binding Inhibitor	T134	Cross Resistant	Y	N	In vitro selected virus (p145 of HIV-INL4-3, contains mutations N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 15-fold resistant to T134. Role of each mutation not confirmed	Kanbara01
K 290 E	ATA→GTC	Fusion/Binding Inhibitor	T140	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 21-fold cross-resistant to T140. Role of each mutation not confirmed by site-directed mutag	Kanbara01
K 290 E	ATA→GTC	Fusion/Binding Inhibitor	vMIP-II	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 42-fold cross-resistant to vMIP II. Role of each mutation not confirmed by site-directed mut	Kanbara01
N 293 D	AAT→GAT	Fusion/Binding Inhibitor	ALX40-4C	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 145-fold cross-resistant to ALX40-4C. Role of each mutation not confirmed by site-directed m	Kanbara01
N 293 D	AAT→GAT	Fusion/Binding Inhibitor	AMD3100	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 15-fold cross-resistant to AMD3100. Role of each mutation not confirmed by site-directed mut	Kanbara01
N 293 D	AAT→GAT	Fusion/Binding Inhibitor	DS (dextran sulphate)	Selected	Y	?	V3 loop region; S113N/S134N/K269E/Q278E/N293D/N323S/R387I: 250-fold	Este97, Este96a
N 293 D	AAT→GAT	Fusion/Binding Inhibitor	JM 2763	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T: 10 fold	Schols98
N 293 D	AAT→GAT	Fusion/Binding Inhibitor	JM-3100	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T: 10-fold	Schols98

## HIV-1 Env

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
N 293 D	AAT→GAT	Fusion/Binding Inhibitor	Mab 12G5	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364–367Deletion/387T;	Schols98
N 293 D	AAT→GAT	Fusion/Binding Inhibitor	SDF-1	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 26-fold cross-resistant to SDF-1. Role of each mutation not confirmed by site-directed mutag	Kanbara01
N 293 D	AAT→GAT	Fusion/Binding Inhibitor	SDF-1 $\alpha$	Selected	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364–367Deletion/387T; 15-fold.	Schols98
N 293 D	AAT→GAT	Fusion/Binding Inhibitor	T134	Selected	Y	N	In vitro selected virus (p145 of HIV-INL4–3, contains mutations N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275 in V3 loop of gp120 ) 15-fold resistant to T134. Role of each mutation not conf	Kanbara01
N 293 D	AAT→GAT	Fusion/Binding Inhibitor	T140	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 21-fold cross-resistant to T140. Role of each mutation not confirmed by site-directed mutag	Kanbara01
N 293 D	AAT→GAT	Fusion/Binding Inhibitor	vMIP-II	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 42-fold cross-resistant to vMIP II. Role of each mutation not confirmed by site-directed mut	Kanbara01
N 293 H	AAT→CAT	Fusion/Binding Inhibitor	JM-3100	Selected	Y	?		DeVreese96, DeVreese96a
M 294 I	ATG→ATC	Fusion/Binding Inhibitor	ALX40–4C	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 145-fold cross-resistant to ALX40–4C. Role of each mutation not confirmed by site-directed m	Kanbara01

**HIV-1 Env**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
M 294 I	ATG→ATC	Fusion/Binding Inhibitor	AMD3100	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 15-fold cross-resistant to AMD3100. Role of each mutation not confirmed by site-directed mut	Kanbara01
M 294 I	ATG→ATC	Fusion/Binding Inhibitor	SDF-1	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 26-fold cross-resistant to SDF-1. Role of each mutation not confirmed by site-directed mutag	Kanbara01
M 294 I	ATG→ATC	Fusion/Binding Inhibitor	T134	Selected	Y	N	In vitro selected virus (p145 of HIV-INL4–3, contains mutations N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275 in V3 loop of gp120 ) 15-fold resistant to T134. Role of each mutation not conf	Kanbara01
M 294 I	ATG→ATC	Fusion/Binding Inhibitor	T140	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 21-fold cross-resistant to T140. Role of each mutation not confirmed by site-directed mutag	Kanbara01
M 294 I	ATG→ATC	Fusion/Binding Inhibitor	vMIP-II	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 42-fold cross-resistant to vMIP II. Role of each mutation not confirmed by site-directed mut	Kanbara01
Q 296 K	ATG→ATC	Fusion/Binding Inhibitor	ALX40–4C	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274–275) 145-fold cross-resistant to ALX40–4C. Role of each mutation not confirmed by site-directed m	Kanbara01

**HIV-1 Env**

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
Q 296 K	ATG→ATC	Fusion/Binding Inhibitor	AMD3100	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 15-fold cross-resistant to AMD3100. Role of each mutation not confirmed by site-directed mut	Kanbara01
Q 296 K	ATG→ATC	Fusion/Binding Inhibitor	SDF-1	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 26-fold cross-resistant to SDF-1. Role of each mutation not confirmed by site-directed mutag	Kanbara01
Q 296 K	ATG→ATC	Fusion/Binding Inhibitor	T134	Selected	Y	N	In vitro selected virus (p145 of HIV-INL4-3, contains mutations N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275 in V3 loop of gp120 ) 15-fold resistant to T134. Role of each mutation not conf	Kanbara01
Q 296 K	ATG→ATC	Fusion/Binding Inhibitor	T140	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 21-fold cross-resistant to T140. Role of each mutation not confirmed by site-directed mutag	Kanbara01
Q 296 K	ATG→ATC	Fusion/Binding Inhibitor	vMIP-II	Cross Resistant	Y	N	T134-resistant virus (selected in vitro, contains N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; 290Tins, D274-275) 42-fold cross-resistant to vMIP II. Role of each mutation not confirmed by site-directed mut	Kanbara01
A 297 T	GCA→ACA	Fusion/Binding Inhibitor	JM-2763	Selected	Y	?		DeVreese96, DeVreese96a
N 302 K	AAA	entry inhibitor	Concanavalin A (ConA)	Selected	Y	?	mutations in gp120	Witvrouw05
N 302 K	AAA	entry inhibitor	Cyanovirin (CV-N)	Selected	Y	?	mutations in gp120	Witvrouw05



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Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
H 308 P	AAA	Fusion/Binding Inhibitor	AD101	Selected	Y	?	Small molecule entry inhibitor. Mutation in gp120V3. Primary R5 isolate, CCI/85 passaged in PMBC in increasing concentrations of CCR5-inhibitor AD101. When tested in combination with K305R, H308P, A316V and G321E, fold-R was $>5 \times 10^6$ mutations in gp120	Kuhmann04, Trkola02
T 311 I	AAA	entry inhibitor	Concanavalin A (ConA)	Selected	Y	?		Witvrouw05
N 323 S	AAT→AGT	Fusion/Binding Inhibitor	DS (dextran sulphate)	Selected	Y	?	C3 region; S113N/S134N/K269E/Q278E/N293D/N323S/R387I: 250-fold	Este97, Este96a
G 332 E	GGA→GAA	Fusion/Binding Inhibitor	siamycin I	Selected	Y	?	N188K/G332E/N351D/A550T/N633D/L762S: 9-fold	Lin96
I 339 T	ATT→ACT	Fusion/Binding Inhibitor	NeoR6	Selected	Y	?	Mutation in gp120. Found in combination with S372L, Q395K, S668R, F672Y.	Borkow03
I 339 T	ATT→ACT	Fusion/Binding Inhibitor	R3G	Cross-R	Y	?	Mutation in gp120. Tested against NeoR6-resistant virus passaged in vitro. Virus contains mutations I339T, S372L, Q395K, S668R and F672Y.	Borkow03
N 351 D	AAT→GAT	Fusion/Binding Inhibitor	siamycin I	Selected	Y	?	N188K/G332E/N351D/A550T/N633D/L762S: 9-fold	Lin96
S 372 L	TCA→TTA	Fusion/Binding Inhibitor	NeoR6	Selected	Y	?	Mutation in gp120. Found in combination with I339T, Q395K, S668R, F672Y.	Borkow03
S 372 L	TCA→TTA	Fusion/Binding Inhibitor	R3G	Cross-R	Y	?	Mutation in gp120. Tested against NeoR6-resistant virus passaged in vitro. Virus contains mutations I339T, S372L, Q395K, S668R and F672Y.	Borkow03
S 375 W	TCA→TTA	Fusion/Binding Inhibitor	BMS-488043	Selected	Y	?	Mutation in CD4 contact site.	Lin03
R 378 T	AGA→ACA	Fusion/Binding Inhibitor	JM 2763	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T: 10 fold	Schols98
R 378 T	AGA→ACA	Fusion/Binding Inhibitor	JM-3100	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T: 10-fold	Schols98
R 378 T	AGA→ACA	Fusion/Binding Inhibitor	Mab 12G5	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T.	Schols98
R 378 T	AGA→ACA	Fusion/Binding Inhibitor	SDF-1 $\alpha$	Selected	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T: 15-fold.	Schols98
P 385 L	CCA→CTA	Fusion/Binding Inhibitor	JM-2763	Selected	Y	?		DeVreese96, DeVreese96a

## HIV-1 Env

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
P 385 L	CCA → CTA	Fusion/Binding Inhibitor	JM-3100	Selected	Y	?	CD4 binding region; S113N/S134N/K269E/	DeVreese96, DeVreese96a
R 387 I	AGA → ACA	Fusion/Binding Inhibitor	DS (dextran sulphate)	Selected	Y	?	Q278E/N293D/N323S/R387I: 250-fold	Este97, Este96a
Q 395 K	CAG → AAG	Fusion/Binding Inhibitor	NeoR6	Selected	Y	?	Mutation in gp120 Found in combination with I339T, S372L, S668R, F672Y.	Borkow03
Q 395 K	CAG → AAG	Fusion/Binding Inhibitor	R3G	Cross-R	Y	?	Mutation in gp120. Tested against NeoR6-resistant virus passaged in vitro. Virus contains mutations I339T, S372L, Q395K, S668R and F672Y.	Borkow03
Q 410 E	CAA → GAA	Fusion/Binding Inhibitor	JM-3100	Selected	Y	?		DeVreese96, DeVreese96a
N 418 S	CAA → GAA	entry inhibitor	Cyanovirin (CV-N)	Selected	Y	?	mutations in gp120	Witvrouw05
M 426 L	ATG → TTG	Fusion/Binding Inhibitor	BMS-488043	Selected	Y	?	Mutation in gp120.	Lin04, Lin03
W 427 V	ATG → TTG	Fusion/Binding Inhibitor	BMS-488043	Selected	Y	?	Mutation in CD4 contact site.	Lin03
S 433 P	TCC → CCC	Fusion/Binding Inhibitor	JM-3100	Selected	Y	?		DeVreese96, DeVreese96a
M 434 I	ATG → ?	Fusion/Binding Inhibitor	BMS-488043	Selected	Y	?	Mutation in gp120.	Lin04, Lin03
S 440 R	ATG → ?	Fusion/Binding Inhibitor	BMS-488043	Selected	Y	?	Mutation in gp120.	Lin03
V 457 I	GTA → ATA	Fusion/Binding Inhibitor	JM-3100	Selected	Y	?		DeVreese96, DeVreese96a
M 475 I	ATG → ?	Fusion/Binding Inhibitor	BMS-488043	Selected	Y	?	Mutation in gp120.	Lin04, Lin03
A 550 T	GCC → ACC	Fusion/Binding Inhibitor	siamycin I	Selected	Y	?	N188K/G332E/N351D/A550T/N633D/L762S: 9-fold	Lin96
N 633 D	AAT → GAT	Fusion/Binding Inhibitor	siamycin I	Selected	Y	?	N188K/G332E/N351D/A550T/N633D/L762S: 9-fold	Lin96
S 668 R	AGT → AGA	Fusion/Binding Inhibitor	NeoR6	Selected	Y	?	Mutation in gp41. Found in combination with I339T, S372L, Q395K, F672Y.	Borkow03
S 668 R	AGT → AGA	Fusion/Binding Inhibitor	R3G	Cross-R	Y	?	Mutation in gp41. Tested against NeoR6-resistant virus passaged in vitro. Virus contains mutations I339T, S372L, Q395K, S668R and F672Y.	Borkow03
F 672 Y	TTT → TAT	Fusion/Binding Inhibitor	NeoR6	Selected	Y	?	Mutation in gp41. Found in combination with I339T, S372L, Q395K, S668R.	Borkow03
F 672 Y	TTT → TAT	Fusion/Binding Inhibitor	R3G	Cross-R	Y	?	Mutation in gp41. Tested against NeoR6-resistant virus passaged in vitro. Virus contains mutations I339T, S372L, Q395K, S668R and F672Y.	Borkow03
L 762 S	TTG → TCG	Fusion/Binding Inhibitor	siamycin I	Selected	Y	?	N188K/G332E/N351D/A550T/N633D/L762S: 9-fold	Lin96

## HIV-1 Env

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## Drug Resistance Mutations in HIV-1 Env

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
FNSTW 364-368 Deletion	TTT AAT AGT ACT TGG	Fusion/Binding Inhibitor	DS (dextran sulphate)	Selected	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T: 10 fold	Este97
FNSTW 364-368 Deletion	Deletion	Fusion/Binding Inhibitor	JM 2763	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T: 10 fold	Schols98
FNSTW 364-368 Deletion	Deletion	Fusion/Binding Inhibitor	JM-3100	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T: 10-fold	Schols98
FNSTW 364-368 Deletion	Deletion	Fusion/Binding Inhibitor	Mab 12G5	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T:	Schols98
FNSTW 364-368 Deletion	Deletion	Fusion/Binding Inhibitor	SDF-1 $\alpha$	Selected	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364-367Deletion/387T: 15-fold.	Schols98
deletion 364-376	Deletion	entry inhibitor	Cyanovirin (CV-N)	Selected	Y	?	mutations in gp120	Witvrouw05

## Abbreviations used in tables

### Amino acids

A	alanine
C	cysteine
D	aspartate
E	glutamate
F	phenylalanine
G	glycine
H	histidine
I	isoleucine
K	lysine
L	leucine
M	methionine
N	asparagine
P	proline
Q	glutamine
R	arginine
S	serine
T	threonine
V	valine
W	tryptophan
Y	tyrosine

### Drug class

F/BI	Fusion/Binding Inhibitor
II	Integrase Inhibitor
MN	Multiple Nucleoside
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NNRTI	HIV-1 Specific Nonnucleoside RT Inhibitor
PI	Protease Inhibitor
PARTI	Pyrophosphate Analogue RTI
SIV RTI	SIV Nucleoside RTI

## Compounds

Compound	Other Names (Company)	Chemical Name or Description
(-)-dOTC	BCH-10652	(-)-2'-deoxy-3'-oxa-4'-thiocytidine
(-)-dOTFC		(-)-2'-deoxy-3'-oxa-4'-thio-5-fluorocytidine
(-)-FTC	Emtricitabine, Coviracil (Triangle Pharmaceuticals)	(-)-(2 <i>R</i> ,5 <i>S</i> )-5-fluoro-1-[2-(hydroxymethyl)-1,3-oxathiolan-5-yl]cytosine
(+)-dOTC		(+)-2'-deoxy-3'-oxa-4'-thiocytidine
(+)-dOTFC		(+)-2'-deoxy-3'-oxa-4'-thio-5-fluorocytidine
1737		Tetrahydronaphthalene lignan derivative
1592U89	Abacavir, Ziagen, ABC (Glaxo Wellcome)	(1 <i>S</i> ,4 <i>R</i> )-4-[2-amino-6-cyclopropyl-amino)-9 <i>H</i> -purin-9-yl]-2-cyclopentene-1-methanol succinate
3TC	(-)-BCH-189, Lamivudine, Efavir (Glaxo Wellcome)	(-)- $\beta$ -L-2',3'-dideoxy-3'-thiacytidine
4'-Ed4T		2',3'-Didehydro-3'-deoxy-4'-ethynylthymidine
8-chloro-TIBO	RO91767, R86183, tivrapipe	(+)-(S)-4,5,6,7-Tetrahydro-8-chloro-5-methyl-6-(3-methyl-2-butenyl)imidazol[4,5,1-jk][1,4]benzodiazepine
A-77003	C2 symmetry-based protease inhibitor (Abbott)	2PyridCH2NCH3CO-Val-NHCH(Bz)]CHOHCHOH
AAP-BHAP	U-104489 (Pharmacia & Upjohn)	1-[(5-Methanesulfonamidoindol-2-yl)carbonyl]-4-[N-ethyl-N-[3-(1,1-dimethylamino)-2-pyridinyl]amino]piperidine
ABT-378	Aluviran, Lopinavir (Abbott)	N-[(1 <i>S</i> ,3 <i>S</i> ,4 <i>S</i> )-4-[[2,6-dimethylphenoxy)acetyl]amino]-3-hydroxy-5-phenyl-1-(phenylmethyl)pentyl]tetrahydro- $\alpha$ -(1-methylethyl)-2-oxo-1(2 <i>H</i> )-pyrimidineacetamide
ABT-538	Ritonovir, Norvir (Abbott)	10-Hydroxy-2-methyl-5-(1-methylethyl)-1-[2-(1-methylethyl)-4-thiazolyl]-3,6-dioxo-8,11-bis(phenylmethyl)-2,4,7,12-tetraazatridecan-13-oic acid, 5-thiazolylmethyl ester

## Abbreviations (cont)

## Compounds (cont)

AD101		
ADAMII		
AG1343	Nelfinavir, Viracept (Agouron)	Methyl 3',3''-dichloro-4',4''-dimethoxy-5',5''-bis(methoxycarbonyl)-6,6-diphenyl-5-hexenoate (3 <i>S</i> ,4 <i>aS</i> ,8 <i>aS</i> )- <i>N</i> -tert-Butyl-2-[(2 <i>R</i> ,3 <i>R</i> )-3-(3,2-cresotamido)-2-hydroxy-4-(phenylthio)butyl]decahydro-3-isoquinoline-carboxamide monomethanesulfonate
ALX40-4C		a polypeptide of nine d-Arg residues
AMD3100		octahydrochloride dihydrate of 1,19-[1,4-phenylene-bis-(methylene)]-bis-1,4,8,11-tetra-azacyclotetradecane
AZT	zidovudine (Glaxo Wellcome)	3'-azido-3'-deoxythymidine
BHAP U-87201E	Ateviridine (Pharmacia Upjohn)	1-[(5-Methoxyindol-2-yl)carbonyl]-4-[3-(ethylamino)-2-pyridyl]piperazine
BHAP U-88204E		1-(Indolyl-2-carbonyl)-4-[3-[(1-methylethyl)amino]pyridyl]-piperazine
BHAP U-90152	Delavirdine, Rescriptor (Pharmacia Upjohn)	1-(5-Methanesulphonamido)-1 <i>H</i> -indol-2-yl-carbonyl)-4-[3-(isopropylamino)-2-pyridinyl]piperazine
BHAP U-90153		bisheteroaryl piperidinyl derivative
BHAP U-90154		bisheteroaryl piperidinyl derivative
BHAP U-90155		bisheteroaryl piperidinyl derivative
BILA 1906 BS	(Bio-Mega/Boehringer Ingelheim)	<i>N</i> -{1 <i>S</i> -[[[3-[2 <i>S</i> -(1,1-dimethylethyl)amino]carbonyl]-4 <i>R</i> -3-pyridinylmethyl]thio]-1-piperidinyl]-2 <i>R</i> -hydroxy-1 <i>S</i> -(phenylmethyl)propyl]amino]carbonyl]-2-methylpropyl}-2-quinolinecarboxamide
BILA 2011	Palinavir (Bio-Mega/Boehringer Ingelheim)	<i>N</i> -{1 <i>S</i> -[[[3-[2 <i>S</i> -(1,1-dimethylethyl)amino]carbonyl]-4 <i>R</i> -[4-pyridinylmethyl)oxy]-1-piperidinyl]-2 <i>R</i> -hydroxy-1 <i>S</i> -(phenylmethyl)propyl]amino]carbonyl]-2-methylpropyl}-2-quinolinecarboxamide
BILA 2185 BS	(Bio-Mega/Boehringer Ingelheim)	<i>N</i> -(1,1-dimethylethyl)-1-[2 <i>S</i> -[[2-2,6-dimethylphenoxy)-1-oxoethyl]amino]-2 <i>R</i> -hydroxy-4-phenylbutyl]4 <i>R</i> -pyridinylthio)-2-piperidine-carboxamide
BI-RG-587	Nevaripine, Viramune (Boehringer Ingleheim)	11-Cyclopropyl-4-methyl-5,11-dihydro-6 <i>H</i> -dipyrido[3,2- <i>b</i> :2',3'- <i>e</i> ]-[1,4]diazepin-6-one
BM+51.0836		thiazolo-isoindolinone derivative
BMS-186318	(Bristol-Myers Squibb)	[1 <i>S</i> -[1 <i>R</i> *,2 <i>S</i> *(2 <i>S</i> *,3 <i>R</i> *)]]-[3-[[[3-[(1,1-Dimethylethoxy)-carbonyl]amino]-2-hydroxy-4-[4-[2-(4-morpholinyl)-2-oxoethoxy]phenyl]butyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]carbamic Acid, 1,1-dimethylethyl-ester
BMS-232632	Atazanavir	azapeptide protease inhibitor
BMS-488043		
Calanolide A	NSC675451	a dipyrancoumarin
Concanavalin A	ConA	plant lectin from <i>Canavalia ensiformis</i>
Cyanovirin	CV-N, NSC 682999 (Cel- legy Pharmaceuticals)	Protein from cyanobacterium <i>Nostoc ellipsosporum</i>
cyclo-d4G		$\beta$ -D-6-cyclopropylamino-2',3'-Didehydro-2'3'-Dideoxyguanosine
d-d4FC	D4FC, DPC 187	2'3'-Didehydro-2' 3' dideoxy -5-fluorocytidine
d4C		Didehydro-2' 3' dideoxy cytidine
d4T	Stavudine, Zerit (Bristol- Myers Squibb)	2',3'-didehydro-3'-deoxythymidine

## Abbreviations (cont)

## Compounds (cont)

ddC	Zalcitabine, Hivid (Roche)	2',3'-dideoxycytidine
ddI	Didanosine, Videx (Bristol-Myers Squibb)	2',3'-dideoxyinosine
DKA		beta-diketo acids
DMP-266	Efavirenz, Sustiva (Dupont Merck)	(-)-6-Chloro-4-cyclopropylethynyl-4-trifluoromethyl-1,4,-dihydro-2H-3,1-benzoxazin-one
DMP-323	XM-323 (Dupont Merck)	[4R-(4- $\alpha$ ,5- $\alpha$ ,6- $\beta$ ,7- $\beta$ )]-hexahydro-5,6-dihydroxy-1,3-bis[(4-hydroxymethyl)phenyl]methyl]-4,7-bis(phenylmethyl)-2H-1,3-diazepin-2-one
DMP-450	(Avid Therapeutics)	[4R-(4- $\alpha$ ,5- $\alpha$ ,6- $\beta$ ,7- $\beta$ )]-hexahydro-5,6-bis(hydroxy)-1,3-bis(3-amino)phenyl]methyl]-4,7-bis(phenylmethyl)-2H-1,3-diazepin-2-onebismesylate
(+)dOTFC	(+)-dOTFC	(+)-2'-Deoxy-3'-oxa-4'-thio-5'-fluorocytidine
DS		dextran sulfate
DXG	(-)- $\beta$ -dioxolane-G	(-)-(2R,4R)-9-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]guanine
E-BPTU	NSC 648400	1-benzyloxymethyl-5-ethyl-6-(2-pyridylthio)uracil
EBU-dM		5-ethyl-1-ethoxymethyl-6-(3,5-dimethylbenzyl)uracil
E-EBU		5-ethyl-1-ethoxymethyl-6-benzyluracil
E-EPSeU		1-(ethoxymethyl)-(6-phenylselenyl)-5-ethyluracil
E-EPU		1-(ethoxymethyl)-(6-phenyl-thio)-5-ethyluracil
F-ddA	Lodenosine	2'-fluoro-2',3'-dideoxyadenosine
FZ41		styrylquinoline
GW420867X		S-3-ethyl-6-fluoro-4-isopropoxycarbonyl-3,4-dihydro-quinoxalin-2(1H)-one
HBY 097		(S)-4-isopropoxycarbonyl-6-methoxy-3-(methylthio-methyl)-3,4-dihydroquinoxalin-2(1H)-thione
HEPT		1-[(2-hydroxyethoxy)methyl]6-(phenylthio)thymine
IC9564	Betulinic acid derivative	4S-[8-(28 betuliniyl) amino-octanoylamino]-3R-hydroxy-6-methylheptanoic acid
I-EBU	MKC-442, emivirine, coactinon (Triangle Pharmaceuticals)	6-benzyl-1-ethoxymethyl-5-isopropyluracil/
JE-2147		an allophenylnorstatine-containing dipeptide protease inhibitor
JM-2763	(Johnson Matthey)	1,10-(1,3-propanediyl)-bis-1,4,8,11-tetraazacyclo-tetradecane
JM-3100	SID791 (Johnson Matthey)	1,10-[1,4-phenylenebis-(methylene)]bis-(1,4,8,11-tetraazacyclotetradecane)octahydrochloride dihydrate
KNI-272	Kynostatin 272	(2S,3S)-3-amino-2-hydroxy-4-phenylbutyric acid-containing tripeptide
L-697,593		5-ethyl-6-methyl-3-(2-phthalimido-ethyl)pyridin-2(1H)-one
L-697,661		3-[-(4,7-dichloro-1,3-benzoxazol-2-yl)methyl]amino-5-ethyl-6-methylpyridin-2(1H)-one
L-Chicoric acid		[S-(R*,R*)]-2,3-Bis[[3-(3,4-dihydroxyphenyl)-1-oxo-2-propenyl]oxy]butanedioic acid
L-FddC		(-)- $\beta$ -L-5-fluoro-2',3'-dideoxy-cytidine
LY-300046 HCl	Trovirdine (Lilly/Medivir/Abbott)	N-[2-(2-pyridylethyl)-N'-[2-(5-bromopyridyl)thiourea,hydrochloride
M87		membrane anchored gp41 derived peptide
MK-639	Indinavir, Crixivan, L735,524 (Merck)	[1(1S,2R),5(S)]-2,3,5-Trideoxy-N-(2,3-dihydro-2-hydroxy-1H-inden-1-yl)-5-[2-[[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-D-erythro-pentonamide sulfate

## Abbreviations (cont)

## Compounds (cont)

MP-134		C2 symmetry-based protease inhibitor
MP-167		
MSK-076	(Medivir AB)	phenylmethylthiazolythiourea (PETT) derivative
NeoR6	hexa-arginine neomycin B conjugate	
no name		O-(2-Phenoxy ethyl)benzoyl (phenyl) thiocarbamate 17c
P9941	(Dupont Merck)	[2-pyridylacetyl-IlePheAla-y(CHOH)] <sub>2</sub>
PFA	Foscarnet (Astra)	phosphonoformate
ph-AZT	5'-phosphit 3' azido-2'3'-dideoxythymidine	
PMEA	adefovir (Gilead Sciences)	9-(2 phosphonylmethoxyethyl)adenine
PMPA	tenofovir (Gilead Sciences)	(R)-9-(2-phosphonyl-methoxypropyl)adenine
PNU-140690	Tipranavir, U-140690 (Pharmacia & Upjohn)	(6R)-3-(1R)-1-[3-([Trifluoromethyl](2-pyridyl)]sulfonylamino)-phenylpropyl-4-hydroxy-6-(2-phenylethyl)-6-propyl-5,6-dihydro-2H-pyran-2-one
QM96521		1,1,3-trioxo-2H,4H-thieno[2,4-3][1,2,4]thiadiazine derivative (TTD)
QYL-609		
QYL-685		methylenecyclopropane nucleoside analog with a phenylphosphoralaninate moiety
R3G		tri arginine gentamicin C conjugate
Ro 31-8959	Saquinavir, Invirase, Fortovase (Roche)	N(1)-[3-[3-[[[(1,1-dimethylethyl)amino]carbonyl]octahydro-2(1H)-isoquinolinyl]-2-hydroxy-1-(phenylmethyl)propyl]-2-[(2-quinolinylcarbonyl)amino]-, [3S-[2[1R*(R*),2S*],3 $\alpha$ ,4 $\alpha$ , $\beta$ ,8 $\alpha$ , $\beta$ ]]]-, monomethanesulfonate
RPI-312		1-[(3S)-3-(n-alpha-benzyloxycarbonyl)-1-asparginyl]-amino-2-hydroxy-4-phenyl-butyl]-n-tert-butyl-1-proline amide (peptidyl protease inhibitor)
RPR103611		a triterpene betulinic acid derivative
S-1153		5-(3,5-dichlorophenyl)thio-4-isopropyl-1-(4-pyridyl)methyl-1Himidazol-2-yl methyl carbamate
S-2720		6-chloro-3,3-dimethyl-4-(isopropenyl-oxycarbonyl)-3,4-dihydroquinoxalin-2(1H)thione
SC-52151	Telinavir	N-tert-butyl-N'-isobutyl-N'-[2(R)-hydroxy-4-phenyl-3(S)-[4-amino-1,4-dioxo-2(S)-(2-quinolinylcarboxamido)butyl-amino]butyl]urea
SC-55389A	(Searle)	hydroxyethyl-urea isostere protease inhibitor
SDF-1		Stromal cell-derived factor 1
SDF-1 $\alpha$		Stromal cell-derived factor 1 $\alpha$
Siamycin I		21-residue tricyclic peptide
SKF108842		protease inhibitor
T134		[Tyr5,12, Lys7]-polyphemusin II-derivative with amino acid sequence R-R-W-C-Y-R-K-DK-P-Y-R-Ci-C-R-COOH
T140		[Tyr5,12, Lys7]-polyphemusin II-derivative
T20	DP-178, Pentafuside (Trimeris)	Ac-YTSLIHSLIEESQNQQEKNEQELLELDKWASLWNWF-NH2
TIBO R82150	(Janssen)	(+)-(5S)-4,5,6,7-tetrahydro-5-methyl-6-(3-methyl-2-butenyl)-imidazo[4,5,1-jk][1,4]-benzodiazepin-2(1H)-thione

## Abbreviations (cont)

## Compounds (cont)

TIBO R82913	(Janssen)	(+)-(5 <i>S</i> )-4,5,6,7,-tetrahydro-9-chloro-5-methyl-6-(3-methyl-2-butenyl)-imidazo-[4,5,1- <i>jk</i> ]-[1,4]benzo-diazepin-2(1 <i>H</i> )-thione
TMC114	UIC-94017	
TMC125		
TSAO		[2',5'-bis-O-(tert-butyl dimethylsilyl)-3'-spiro-5''-(4''-amino-1'',2''-oxathiole-2'',2''-dioxide)]-β-D-pentofuranosyl derivative
UC-10	NSC 645129 (Uniroyal Chemical Co)	thiocarboxanilide derivative
UC-16	(Uniroyal Chemical Co)	thiocarboxanilide derivative
UC-32	NSC 645542 (Uniroyal Chemical Co)	thiocarboxanilide derivative
UC-38	NSC 629243 (Uniroyal Chemical Co)	4-chloro-3-(isopropoxycarbonyl)phenylcarbamothioic acid, O-isopropyl ester
UC-42	(Uniroyal Chemical Co)	thiocarboxanilide derivative
UC-57	NSC 647014 (Uniroyal Chemical Co)	thiocarboxanilide derivative
UC-68	NSC 638532 (Uniroyal Chemical Co)	thiocarboxanilide derivative
UC-69	NSC 646989 (Uniroyal Chemical Co)	thiocarboxanilide derivative
UC-70	NSC 638534 (Uniroyal Chemical Co)	thiocarboxanilide derivative
UC-80	NSC 639475 (Uniroyal Chemical Co)	thiocarboxanilide derivative
UC-81	NSC 615727 (Uniroyal Chemical Co)	thiocarboxanilide derivative
UC-82	(Uniroyal Chemical Co)	N-[4-chloro-3-(3-methyl-2-butenyloxy)phenyl]-2-methyl-3-thiophenecarbothioamide
UC-84	NSC 615985 (Uniroyal Chemical Co)	thiocarboxanilide derivative
UC-581	NSC 645727 (Uniroyal Chemical Co)	
UC-781	(Uniroyal Chemical Co)	N-[4-chloro-3-(3-methyl-2-butenyloxy)phenyl]-2-methyl-3-furancarbothioamide
UCO40	NSC650065	
UIC-94003		
VB 11,328	(Vertex)	Carbamic acid, [3-[[[(4-methoxyphenyl)sulfonyl](cyclopentylmethyl)amino]-2-hydroxy-1-(phenylmethyl)propyl]-,tetrahydro-3-furanyl ester
vMIP-II		viral macrophage inflammatory protein II
VX-478	141W94, Amprenavir, Agenerase	Carbamic acid, ((1 <i>S</i> ,2 <i>R</i> )-3-(((4-aminophenyl)sulfonyl)(2-methylpropyl)amino)-2-hydroxy-1-(phenylmethyl)propyl)-,(3 <i>S</i> )-tetrahydro-3-furanyl ester
α-APA	R18893, loviride analog	(+)-2,6-Dichloro-α-[(2-acetyl-5-methylphenyl)amino]benzamide



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