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 February 2007, lists 947 HIV-1 mutation/drug combinations, of which 37 occur in Gag (including this year, 3 in capsid and 3 in SP-1), 321 in Protease, 9 in Integrase, 374 in RT, and 206 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 and 27 in HIV-2 Protease are listed in the table. 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 Δ 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 137. 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`.

The authors gratefully acknowledge their colleagues for assistance in assembling this table. This work was supported in part by Los Alamos National Laboratory.

Contents

HIV-1 Gag

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
E 12 K		Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
E 12 K		Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?		Gatanaga02
V 35 I		Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	?		Gatanaga02
V 35 I		Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?		Gatanaga02
E 40 K		Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	?		Gatanaga02
E 40 K		Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
L 75 R		Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?		Gatanaga02
G 123 E		Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	?		Gatanaga02
G 123 E		Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
Q 199 H		Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
H 219 Q		Protease Inhibitor	JE-2147	Selected	Y	?		Gatanaga02
H 219 Q		Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	?		Gatanaga02
H 219 Q		Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
H 219 Q		Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?		Gatanaga02
G 381 S		Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	?		Gatanaga02
V 390 A		Protease Inhibitor	JE-2147	Selected	Y	?		Gatanaga02
V 390 D		Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?		Gatanaga02
R 409 K		Protease Inhibitor	JE-2147	Selected	Y	?		Gatanaga02
R 409 K		Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	?		Gatanaga02
R 409 K		Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
R 409 K		Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?		Gatanaga02
G 412 D		Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
A 431 V		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
K 436 E		Protease Inhibitor	RO033–4649	Selected	Y		This PI did not select resistance in the protease gene. Sequencing showed that mutations were in the NC/p1 cleavage site.	Nijhuis07
I 437 T		Protease Inhibitor	RO033–4649	Selected	Y		This PI did not select resistance in the protease gene. Sequencing showed that mutations were in the NC/p1 cleavage site.	Nijhuis07
I 437 V		Protease Inhibitor	RO033–4649	Selected	Y		This PI did not select resistance in the protease gene. Sequencing showed that mutations were in the NC/p1 cleavage site.	Nijhuis07
L 449 F		Protease Inhibitor	JE-2147	Selected	Y	?		Gatanaga02
L 449 F		Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
L 449 F		Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?		Gatanaga02
E 468 K		Protease Inhibitor	UIC-94003	Selected	Y	?		Gatanaga02
E 468 K		Protease Inhibitor	VX-478 (amprenavir)	Selected	Y	?		Gatanaga02

HIV-1 CA

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
H 226 Y		Maturation inhibitor	PA-457 (Bevirimat)	Selected	Y		Mutations found near the C terminus of capsid	Adamson06
L 231 F		Maturation inhibitor	PA-457 (Bevirimat)	Selected	Y		Mutations found near the C terminus of capsid	Adamson06
L 231 M		Maturation inhibitor	PA-457 (Bevirimat)	Selected	Y		Mutations found near the C terminus of capsid	Adamson06

HIV-1 SP1

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
A 1 V		Maturation inhibitor	PA-457 (Bevirimat)	Selected	Y		Mutations found in SP-1 peptide	Adamson06
A 3 T		Maturation inhibitor	PA-457 (Bevirimat)	Selected	Y		Mutations found in SP-1 peptide	Adamson06
A 3 V		Maturation inhibitor	PA-457 (Bevirimat)	Selected	Y		Mutations found in SP-1 peptide	Adamson06

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 ration 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 resisance 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/V82T	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, sucepti-bility 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, sucepti-bility 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, sucepti-bility 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 V		Protease Inhibitor	PNU-140690 (tipranavir)	Selected		Y		Baxter06
L 10 Y	CTC→TAC	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 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 accumu-lated 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		Mo05
G 16 E	GGG→GAG	Protease Inhibitor	ABT-378 (lopinavir)	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.	Carrillo98
G 16 E	GGG→GAG	Protease Inhibitor	ABT-538 (ritonavir)	Cross-R	Y	?	21-fold resisance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y	Carrillo98
G 16 E	GGG→GAG	Protease Inhibitor	Ro 31–8959 (saquinavir)	Cross-R	Y	?	4-fold resisance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y	Carrillo98
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, sucepti-bility 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 suscepti-bility to both saquinavir and nelfinavir.	Lawrence99
K 20 M	AAG→ATG	Protease Inhibitor	MK-639 (indinavir)	Selected	N	Y		Condra96
K 20 M		Protease Inhibitor	PNU-140690 (tipranavir)	Selected		Y		Baxter06

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-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, sucepti-bility 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 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 R		Protease Inhibitor	PNU-140690 (tipranavir)	Selected		Y		Baxter06
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
K 20 V		Protease Inhibitor	PNU-140690 (tipranavir)	Selected		Y		Baxter06
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, sucepti-bility 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

HIV-1 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
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
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	Patick98
D 30 N		Protease Inhibitor	TMC-114	Cross-R	Y		Authors use high resoultion crystallography to determine the molecular basis for inhibiton by TMC-114	Kovalevsky06
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 ration 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

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	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, Gulnik95
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
V 32 I	GTA→ATA	Protease Inhibitor	Ro 31–8959 (saquinavir)	Cross-R	Y	?	4-fold resisance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y	Carrillo98
V 32 I	GTA→ATA	Protease Inhibitor	TMC114 (UIC-94017)	Cross-R	Y	?	10-fold resistant against aprenavir-selected mutant L10F/V32I/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

HIV-1 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
E 35 G	GAA→GGA	Protease inhibitor	multiple PI	Selected	?	Y		Svicher05
E 35 G		Protease Inhibitor	PNU-140690 (tipranavir)	Selected		Y		Baxter06
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.	Patick98
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
M 36 V	ATG→GTG	Protease inhibitor	ABT-538 (ritonavir)	Selected	?	Y		Resch05
N 37 D		Protease Inhibitor	PNU-140690 (tipranavir)	Selected	?	Y	Seen in 30% of patients receiving tipranavir therapy.	Rusconi00
S 37 D	AGT→GAT	Protease Inhibitor	MK-639 (indinavir)	Selected	N	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	Muzammil03, Olsen99
R 41 K	AGA→AAA	Protease Inhibitor	PNU-140690 (tipranavir)	Selected	?	Y	Seen in 20% of patients receiving tipranavir therapy.	Rusconi00
R 41 T	AGA→ACA	Protease inhibitor	TMC114 (UIC-94017)	Selected	Y	?	Contrary to selection data, SDM were tested against TMC114 and susceptibility was increased	DeMeyer05
K 43 T	AAA→ACA	Protease inhibitor	ABT-378 (lopinavir)	Selected	?	Y	Associated with either I54A or with multi PI resistance mutations V82A, V32I, and I47V	Svicher05
K 43 T		Protease Inhibitor	PNU-140690 (tipranavir)	Selected		Y		Baxter06
K 45 I	AAA→ATA	Protease Inhibitor	DMP-323	Selected	Y	?	L10F/K45I/I84V: 50-fold	Tisdale95, King95
K 45 I	AAA→ATA	Protease inhibitor	PNU-140690 (tipranavir)	Selected	Y	?	After 73 passages 9 other mutations accumulated to give 87 fold resistance to tipranavir	Doyon05
K 45 R	AAA→AGA	Protease inhibitor	AG-1343 (nelfinavir)	Selected	?	Y	Associated with D30N and N88D	Svicher05

HIV-1 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
M 46 F	ATG⟶TTC	Protease Inhibitor	A-77003	Selected	Y	?	Selected in chronically infected cells at 1 microM	Kaplan94
M 46 I	ATG⟶ATA	Protease Inhibitor	A-77003	Selected	Y	?	No effect on susceptibility but improves replication competency of R8Q mutant; R8K/M46I/G48V: 20-fold	Ho94, Kaplan94
M 46 I	ATG⟶ATA	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
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).	Carrillo98
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	Patick96, Patick98
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

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	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		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 resisance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y	Carrillo98
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, sucepti-bility 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

HIV-1 Protease

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	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		Protease Inhibitor	PNU-140690 (tipranavir)	Selected		Y		Baxter06
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, V82T, I84V, M90L.	Watkins03
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, V82T, 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	Carillo98
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 ration of 5:1. Appears fifth in sequence, in passage 17, after I84V, L10F, M46I and V32I, and followed by Q58E.	Mo03

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	ABT-538 (ritonavir)	Cross-R	Y	?	21-fold resisance 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
I 47 V		Protease Inhibitor	PNU-140690 (tipranavir)	Selected		Y		Baxter06
I 47 V	ATA→GTA	Protease Inhibitor	Ro 31–8959 (saquinavir)	Cross-R	Y	?	4-fold resisance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/ V32I/I47V/V47A/G16E/H69Y	Carrillo98
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 M		Protease Inhibitor	P-1946	Cross-R	Y		Caused 28 fold reduced suscpetibility in conjunction with mutations at 82, 90, 53, and 54	Sevigny06
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

HIV-1 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
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, Colonno04
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		Protease Inhibitor	TMC-114	Cross-R	Y		Authors use high resoultion crystallography to determine the molecular basis for inhibiton by TMC-115	Kovalevsky06
I 50 V	ATT→GTT	Protease Inhibitor	UIC-94003	Selected	Y	?	in vitro selection in MT-2 cells, passage 62	Gatanaga02
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
F 53 L	TTT→?	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, sucepitibility 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		Protease Inhibitor	P-1946	Cross-R	Y		Caused 28 fold reduced suscpetibility in conjunction with mutations at 48,82, 90, and 54	Sevigny06
F 53 L	TTT→?	Protease Inhibitor	SC-52151 (telinavir)	Selected	Y	?	I11V/M46I/F53L/A71V/N88D:10- to 20-fold	Smidt97

HIV-1 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
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 A		Protease Inhibitor	PNU-140690 (tipranavir)	Selected		Y		Baxter06
I 54 L	ATC→CTC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, sucseptibility 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/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 54 M		Protease Inhibitor	PNU-140690 (tipranavir)	Selected		Y		Baxter06
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	Gatanaga02
I 54 S	ATC→AGC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	?	Y		Parkin03
I 54 T	ATC→ACC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, sucseptibility 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
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/F/T/S occurs first, followed by changes at 54, 71 and 36	Molla96
I 54 V		Protease Inhibitor	P-1946	Cross-R	Y		Caused 28 fold reduced suscpetibility in conjunction with mutations at 48, 82, 90, 53, and 54	Sevigny06
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		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 last in sequence, in passage 17, after I84V, L10F, M46I, V32I, and I47V.	Mo03
Q 58 E		Protease Inhibitor	PNU-140690 (tipranavir)	Selected		Y		Baxter06
D 60 E	GAT→GAA	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
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, sucepti-bility 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 K		Protease Inhibitor	PNU-140690 (tipranavir)	Selected		Y		Baxter06
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/p1 (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 resisance 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 resisance 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, sucepti-bility 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, sucepti-bility 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	Patick95
A 71 T	GCT→ACT	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, sucepti-bility 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		Patick98
A 71 T	GCT→ACT	Protease Inhibitor	BMS-186318	Selected	Y	?	A71T/V82A: 15-fold	Patick95
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, sucepti-bility 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	Patick98

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′)	Croteau97, Doyon96
A 71 V	GCT→GTT	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
A 71 V	GCT→GTT	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
A 71 V	GCT→GTT	Protease Inhibitor	KNI-272 (kynostatin)	Selected	Y	N	in vitro selection in MT-2 cells, passage 27, in 30% of clones	Gatanaga02, Gulnik95
A 71 V	GCT→GTT	Protease Inhibitor	MK-639 (indinavir)	Selected	Y	Y	Appears fourth in sequence. Combination V82A/M46L/V32I/A71V: 14-fold	Tisdale95
A 71 V	GCT→GTT	Protease inhibitor	PNU-140690 (tipranavir)	Selected	Y	?	After 73 passages 9 other mutations accumulated to give 87 fold resistance to tipranavir	Doyon05
A 71 V	GCT→GTT	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 in early in passage and was maintained until the appearance of V77I.	Watkins03
A 71 V	GCT→GTT	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
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.	Dulioust99
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 L10F/L24I/M46I/L63P/A71V/G73S/V82T	Koh03
T 74 P		Protease Inhibitor	PNU-140690 (tipranavir)	Selected		Y		Baxter06
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		Patick98
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	Patick95
V 82 A	GTC→GCC	Protease Inhibitor	ABT-378 (lopinavir)	Selected	N	Y	In conjunction with other mutations, sucepti-bility 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	Patick95
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		Protease Inhibitor	P-1946	Cross-R	Y		Caused 28 fold reduced suscpetibility in con-junction with mutations at 48, 90, 53, and 54	Sevigny06
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, sucepti-bility 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/I84V: 97-fold	King95

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	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
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, sucepti-bility 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		Protease Inhibitor	PNU-140690 (tipranavir)	Selected		Y		Baxter06
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
N 83 D		Protease Inhibitor	PNU-140690 (tipranavir)	Selected		Y		Baxter06

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	AG-1343 (nelfinavir)	Selected	Y	?	4-fold resistance when in combination with V32I	Patick96
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
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 ration 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	Patick96

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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	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 84 V	ATA→GTA	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 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	?	10-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

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	VX-478 (amprenavir)	Selected	Y	?	In combination with L10F	Partaledis95
I 85 V	ATT⟶GTT	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Svicher05
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.	Patick98
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		Patick98
N 88 S	AAT⟶AGT	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
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,F/I50L/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, sucepti-bility 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 Patick study; more common in Lawrence study	Patick98, Lawrence99
L 90 M	TTG⟶ATG	Protease Inhibitor	MK-639 (indinavir)	Selected	N	Y		Condra96
L 90 M		Protease Inhibitor	P-1946	Cross-R	Y		Caused 28 fold reduced suscpetibility in con-junction with mutations at 48,82, 53, and 54	Sevigny06

HIV-1 Protease

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
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
L 90 M		Protease Inhibitor	TMC-114	Cross-R	Y		Authors use high resoultion crystallography to determine the molecular basis for inhibiton by TMC-116	Kovalevsky06
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.	Carrillo98
T 91 S	ACT⟶TCT	Protease Inhibitor	ABT-538 (ritonavir)	Cross-R	Y	?	21-fold resisance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y	Carrillo98
T 91 S	ACT⟶TCT	Protease Inhibitor	Ro 31–8959 (saquinavir)	Selected	Y	?	4-fold resisance seen with lopinavir-selected passage 17 virus: I84V/L10F/M46I/T91S/V32I/I47V/V47A/G16E/H69Y	Carrillo98
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;V82A/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		Damond05
V 10 I	GTC→ATC	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Damond05
V 22 I	GTT→ATT	Protease inhibitor	AG-1343 (nelfinavir)	Selected	?	Y		Damond05
A 34 E	GCA→GAA	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Damond05
A 34 S	GCA→TCA	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Damond05
I 36 V	ATT→GTT	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Damond05
L 38 F	TTG→TTT	Protease inhibitor	ABT-538 (ritonavir)	Selected	?	Y		Damond05
I 46 T	ATT→ACT	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Damond05
I 46 V	ATT→GTT	Protease inhibitor	Ro 31–8959 (saquinavir)	Selected	?	Y		Damond05
G 48 R	GGG→CGG	Protease inhibitor	Ro 31–8959 (saquinavir)	Selected	?	Y		Damond05
I 54 L	ATC→CTC	Protease inhibitor	Ro 31–8959 (saquinavir) + MK-639 (indinavir)	Selected	?	Y		Damond05
G 55 R	GGG→CGG	Protease inhibitor	ABT-538 (ritonavir)	Selected	?	Y		Damond05
V 62 A	GTT→GCT	Protease inhibitor	AG-1343 (nelfinavir)	Selected	?	Y		Damond05
E 63 A	GAG→GCG	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Damond05
E 63 Q	GAG→CAG	Protease inhibitor	Ro 31–8959 (saquinavir)	Selected	?	Y		Damond05
T 74 N	ACA→AAT	Protease inhibitor	AG-1343 (nelfinavir)	Selected	?	Y		Damond05
T 77 I	ACT→ATT	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Damond05
G 78 E	GGA→GAA	Protease inhibitor	AG-1343 (nelfinavir)	Selected	?	Y		Damond05
T 80 Y	ACA→TAT	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Damond05
I 82 F	ATT→TTT	Protease inhibitor	ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	?	Y		Damond05
I 82 M	ATT→ATG	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Damond05
I 84 L	ATA→TTA	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Damond05
I 84 V	ATA→GTA	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Damond05

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		Damond05
R 87 K	AGA⟶AAA	Protease inhibitor	AG-1343 (nelfinavir)	Selected	?	Y		Damond05
L 90 M	TTG⟶ATG	Protease inhibitor	ABT-538 (ritonavir) + MK-639 (indinavir)	Selected	?	Y		Damond05
M 95 I	ATG⟶ATC	Protease inhibitor	MK-639 (indinavir)	Selected	?	Y		Damond05

HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
V 35 I		Nucleoside RT Inhibitor (NRTI)		Selected		Y	Increased NRTI susceptibility	Svicher06
T 39 A		Nucleoside RT Inhibitor (NRTI)		Selected		Y		Svicher06
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
M 41 L		RT inhibitor	VRX-329747	Selected	Y			Zhang06
M 41 L		RT inhibitor	VRX-413638	Selected	Y			Zhang06
K 43 E		Nucleoside RT Inhibitor (NRTI)		Selected		Y		Svicher06
K 43 Q		Nucleoside RT Inhibitor (NRTI)		Selected		Y		Svicher06
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
I 50 V		Nucleoside RT Inhibitor (NRTI)		Selected		Y	Increased NRTI susceptibility	Svicher06
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 T		RT inhibitor	VRX-329747	Selected	Y			Zhang06
A 62 T		RT inhibitor	VRX-413638	Selected	Y			Zhang06
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
A 62 V		RT inhibitor	VRX-329747	Selected	Y			Zhang06
A 62 V		RT inhibitor	VRX-413638	Selected	Y			Zhang06
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

HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
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, T215Yand K219Q	Imamichi00
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	Masciari02
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 N		RT inhibitor	VRX-329747	Selected	Y			Zhang06
S 68 N		RT inhibitor	VRX-413638	Selected	Y			Zhang06

HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
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
ins 69 TRVMG	ACT+⟶ACG AGA GTG ATG GGG	Nucleoside RT Inhibitor (NRTI)	1592U89 (abacavir)	Cross-R	Y	Y	32-fold resistance; duplication of 15 mutations of HIV-1 env	Lobato02
ins 69 TRVMG	ACT+⟶ACG AGA GTG ATG GGG	Nucleoside RT Inhibitor (NRTI)	3TC (lamivudine)	Cross-R	Y	Y	84-fold resistance; duplication of 15 mutations of HIV-1 env	Lobato02
ins 69 TRVMG	ACT+⟶ACG AGA GTG ATG GGG	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Cross-R	Y	Y	371-fold resistance; duplication of 15 mutations of HIV-1 env	Lobato02
ins 69 TRVMG	ACT+⟶ACG AGA GTG ATG GGG	Nucleoside RT Inhibitor (NRTI)	d4T (stavudine)	Cross-R	Y	Y	15-fold resistance; duplication of 15 mutations of HIV-1 env	Lobato02
ins 69 TRVMG	ACT+⟶ACG AGA GTG ATG GGG	Nucleoside RT Inhibitor (NRTI)	ddC (zalcitabine)	Cross-R	Y	Y	4-fold resistance; duplication of 15 mutations of HIV-1 env	Lobato02
ins 69 TRVMG	ACT+⟶ACG AGA GTG ATG GGG	Nucleoside RT Inhibitor (NRTI)	ddI (didanosine)	Cross-R	Y	Y	12-fold resistance; duplication of 15 mutations of HIV-1 env	Lobato02
INS 69 TSG	ACT⟶ins	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine) + ddI (didanosine) or ddC (zalcitabine)	Selected	Y	Y	Highly resistant to 3TC, ABC, d4T	Bulgheroni04
T 69 A	ACT⟶GCT	Multiple Nucleoside	3TC (lamivudine) + d4T (stavudine)	Selected	?	Y	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	?	Y	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	?	Y	Seen in one patient on AZT + 3TC combination therapy.	Lawrence99
T 69 D	ACT⟶GAT	Nucleoside RT Inhibitor (NRTI)	ddC (zalcitabine)	Selected	N	Y	5-fold resistance	Fitzgibbon92

HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
T 69 G	ACT→GGT	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine) + ddI (didanosine)	Selected	N	Y	Selected by AZT + ddI. Little effect alone (1.5-fold), but 1813-fold in combination with K103N, L74I, T69G, K70R, T215Yand K219Q	Imamichi00
T 69 G	ACT→GGT	Nucleoside RT Inhibitor (NRTI)	ddC (zalcitabine)	Cross-R	N	Y	Selected by AZT+ddI in patient. Site-directed mutant: 11-fold.	Imamichi00
T 69 G	ACT→GGT	Nucleoside RT Inhibitor (NRTI)	ddI (didanosine)	Selected	N	Y	Selected by AZT+ddI in patient. Site-directed mutant: 10-fold.	Imamichi00
T 69 N	ACT→AAT	Multiple Nucleoside	3TC (lamivudine) + d4T (stavudine)	Selected	?	Y	Seen in two patients on 3TC + d4T combination therapy.	Lawrence99
T 69 S + AG	ACT→ins	Multiple Nucleoside	MDR (multi-drug resistant)	Selected	N	Y		Larder99
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

HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
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
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)	HBY 097	Selected	Y	?		Kleim96
L 74 V	TTA→GTA	Nucleoside RT Inhibitor (NRTI)	1592U89 (abacavir)	Selected	Y	N	K65R/L74V: 3.6-fold; 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)	HBY 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)	HBY 097	Selected	Y	?	Compensates for negative effect of G190E mutation on RT activity	Kleim96

HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
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)	HBY 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
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
R 83 K		Nucleoside RT Inhibitor (NRTI)		Selected		Y	Increased NRTI susceptibility	Svicher06
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, Bacheler00
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

HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
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
K 101 E	AAA→GAA	Multiple Nucleoside	AZT (zidovudine) + BHAP U-87201E (atevirdine)	Selected	?	Y	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	Y	17-fold increase in IC90	Young95, Bacheler00
K 101 E	AAA→GAA	HIV-1 Specific RT Inhibitor (NNRTI)	L-697,661	Selected	N	Y		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	N	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	N	Selected in combination with G141E: 10-fold	Balzarini95
K 101 P	AAA→CCA	HIV-1 Specific RT Inhibitor (NNRTI)	TMC125	Cross-R	Y	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	Y		Bacheler00
K 101 Q	AAA→CAA	HIV-1 Specific RT Inhibitor (NNRTI)	LY-300046 HCl (trovirdine)	Selected	Y	?	Found in combination with V108I	Zhang95, Vrang93

HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
K 103 E	AAA→GAA	HIV-1 Specific RT Inhibitor (NNRTI)	BHAP U-87201E (atevirdine)	Selected	?	Y	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	?	Y		
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 (atevirdine)	Selected	?	Y	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	Y		Richman94
K 103 N	AAA→AAC	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Selected	Y	Y		Young95, Bacheler00
K 103 N	AAA→AAC	HIV-1 Specific RT Inhibitor (NNRTI)	I-EBU (emivirine)	?	Y	?	Predominant mutation in vivo	Seki95
K 103 N	AAA→AAC	HIV-1 Specific RT Inhibitor (NNRTI)	L-697,593	Selected	Y	?	K103N/Y181C: > 1,000-fold	Nunberg91
K 103 N	AAA→AAC	HIV-1 Specific RT Inhibitor (NNRTI)	L-697,661	Selected	Y	Y	K103N and Y181C most common with monotherapy	Byrnes93, Saag93
K 103 N	AAA→AAC	HIV-1 Specific RT Inhibitor (NNRTI)	TIBO R82913	Selected	Y	?	>100-fold alone. K103N/Y181C: > 1,000-fold	Balzarini93d
K 103 N	AAA→AAC	HIV-1 Specific RT Inhibitor (NNRTI)	UC-10	Selected	Y	N	5-fold resistance	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		BorrotoEsoda97
K 103 R	AAA→AGA	HIV-1 Specific RT Inhibitor (NNRTI)	LY-300046 HCl (trovirdine)	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		
K 103 T	AAA→ACA	HIV-1 Specific RT Inhibitor (NNRTI)	S-1153	Selected	Y	?		Fujiwara98
K 103 T	AAA→ACA	HIV-1 Specific RT Inhibitor (NNRTI)	UC-42	Selected	Y	N	100-fold resistance	Balzarini95
V 106 A	GTA→GCA	HIV-1 Specific RT Inhibitor (NNRTI)	ADAMII	Cross-R	Y	?	7.13-fold. Tested against a site-directed mutant.	Cushman98
V 106 A	GTA→GCA	HIV-1 Specific RT Inhibitor (NNRTI)	BHAP U-88204E	Selected	Y	?		Vasudevachari92
V 106 A	GTA→GCA	HIV-1 Specific RT Inhibitor (NNRTI)	BI-RG-587 (nevirapine)	Selected	Y	Y		Larder92, Richman94

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)	E-EBU-dM	Selected	Y	?		Balzarini93
V 106 A	GTA→GCA	HIV-1 Specific RT Inhibitor (NNRTI)	S-1153	Selected	Y	?	V106A + F227L: 387-fold	Fujiwara98
V 106 A	GTA→GCA	HIV-1 Specific RT Inhibitor (NNRTI)	S-2720 (quinoxaline)	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)	TIBO R82913	Selected	Y	?		Larder92
V 106 A	GTA→GCA	HIV-1 Specific RT Inhibitor (NNRTI)	UC-69	Selected	Y	?	Selected in combination, V106A/V181C: 166-fold	Buckheit95a
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)	HBY 097	Selected	Y	?	Appears under lowered drug concentration selection	Kleim97
V 106 I		NNRTI	VRX-480773	Selected	Y			Zhang06b
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)		Y	?	L100I/V108I: 1,000-fold. Observed frequently in patients.	Winslow96, Bacheler00
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 (trovirdine)	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

HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
G 112 S		RT inhibitor	VRX-329747	Selected	Y			Zhang06
G 112 S		RT inhibitor	VRX-413638	Selected	Y			Zhang06
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
V 118 I		RT inhibitor	VRX-329747	Selected	Y			Zhang06
V 118 I		RT inhibitor	VRX-413638	Selected	Y			Zhang06
P 119 S	CCC→TCC	NRTI	4'-Ed4T	Selected	Y	?	selected along with T165A and M184V	Nitanda05
P 119 S	CCC→TCC	Nucleoside RT Inhibitor (NRTI)	F-ddA (lodenosine)	Selected	Y	?	Found with V179D and/or L214F, which are possibly compensatory	Tanaka97
K 122 E		Nucleoside RT Inhibitor (NRTI)		Selected		Y		Svicher06
D 123 G		NNRTI	VRX-480774	Selected	Y			Zhang06b
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

HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
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 L100I	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
E 138 K	GAG→AAG	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
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		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-d4FC (D4FC)	Selected	?	Y		Geleziunas03

HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
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 (tivirapine)	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
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 (trovirdine)	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 tetrahydronaphthalene derivatives.	Hara97
Y 181 C	TAT→TGT	HIV-1 Specific RT Inhibitor (NNRTI)	ADAMII	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

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)	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-EPSeU	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		BorrotoEsoda97
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 (trovirdine)	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
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	?		Balzarini95

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)	UC-84	Selected	Y	?	Passage 5: >118-fold	Buckheit95a
Y 181 C		NNRTI	VRX-480773	Selected	Y			Zhang06b
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	Balzarini94
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		Balzarini96c
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
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	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	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	Y		Gu92

HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
M 184 V	ATG→GTG	Nucleoside RT Inhibitor (NRTI)	ddI (didanosine)	Selected	Y	Y	2–5-fold resistance; Rarely observed in patients receiving ddI	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	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
M 184 V		RT inhibitor	VRX-329747	Selected	Y			Zhang06
M 184 V		RT inhibitor	VRX-413638	Selected	Y			Zhang06
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	Y		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	?		Balzarini93
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		Bacheler00
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		Bacheler00
Y 188 L	TAT→TTA	HIV-1 Specific RT Inhibitor (NNRTI)	TIBO R82913	Selected	N	Y		Vandamme94

HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
V 189 I	GTA→ATA	HIV-1 Specific RT Inhibitor (NNRTI)	HBY 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		Bacheler00
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 hypersuscpetible 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 hypersuscpetible 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 hypersuscpetible to DLV.	Huang03
G 190 E	GGA→GAA	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Selected	N	Y		Bacheler00
G 190 E	GGA→GAA	HIV-1 Specific RT Inhibitor (NNRTI)	HBY 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	Y	Mutation from patient database of isolates >10-fold resistant to NVP and EFV, but hypersuscpetible to DLV.	Huang03
G 190 Q	GGA→CAA	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 hypersuscpetible to DLV.	Huang03
G 190 Q	GGA→CAA	HIV-1 Specific RT Inhibitor (NNRTI)	HBY 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	Y	Mutation from patient database of isolates >10-fold resistant to NVP and EFV, but hypersuscpetible to DLV.	Huang03

HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
G 190 S	GGA→TCA	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Selected	N	Y		Bacheler00
G 190 T	GGA→ACA	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 hypersuscpetible to DLV.	Huang03
G 190 T	GGA→ACA	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 hypersuscpetible to DLV.	Huang03
G 190 T	GGA→ACA	HIV-1 Specific RT Inhibitor (NNRTI)	HBY 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	Y	Mutation from patient database of isolates >10-fold resistant to NVP and EFV, but hypersuscpetible to DLV.	Huang03
G 190 V	GGA→GTA	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 hypersuscpetible 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
E 203 K		Nucleoside RT Inhibitor (NRTI)		Selected		Y		Svicher06
H 208 Y		Nucleoside RT Inhibitor (NRTI)		Selected		Y		Svicher06
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

HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
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 ddI mutation (L74V), NNRTI mutations (L100I;Y181C) or (-)-FTC/3TC mutations (M184I/V)	Larder89, Larder91, Kellam92
D 218 E		Nucleoside RT Inhibitor (NRTI)		Selected		Y		Svicher06
K 219 E	AAA→GAA	Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected	Y	N		Larder89, Larder91, Kellam92
K 219 E	AAA→GAA	NRTI	PMPA (tenofovir)	Selected	?	Y		Wirden05
K 219 N	AAA→AAT	NRTI	PMPA (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) + d4T (stavudine)	Selected	?	Y	Seen in two patient on 3TC + d4T 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) + d4T (stavudine)	Selected	?	Y	Seen in one patient on ddC + d4T combination therapy.	Lawrence99
P 225 H	CCT→CAT	HIV-1 Specific RT Inhibitor (NNRTI)	DMP-266 (efavirenz)	Selected	N	Y	Observed frequently in patients.	Bacheler00
P 225 H	CCT→CAT	HIV-1 Specific RT Inhibitor (NNRTI)	HBY 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
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		Vingerhoets04
F 227 L	TTA→CTC	HIV-1 Specific RT Inhibitor (NNRTI)	S-1153	Selected	Y	?	V106A + F227L: 387-fold. This mutation confers hypersensitivity to delavirdine.	Fujiwara98
F 227 L		NNRTI	VRX-480776	Selected	Y			Zhang06b
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

HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
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		Hachiya04
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
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
E 312 Q		Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected		Y		Nikolenka06
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 (lamivudine)	Cross-R	Y	Y	Facilitates dual resistance to AZT+3TC in association with M184V and standard AZT resistance mutations.	Kemp98

HIV-1 RT

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
G 333 D	GGC→GAC	Multiple Nucleoside	AZT (zidovudine) + 3TC (lamivudine) + 1592U89 (abacavir)	Cross-R	?	Y	found in non-B subtypes	Caride00
G 333 E	GGC→GAG	Multiple Nucleoside	AZT (zidovudine) + 3TC (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 (lamivudine) + 1592U89 (abacavir)	Cross-R	?	Y	found in non-B subtypes	Caride00
G 335 C		Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected		Y		Nikolenka06
G 335 D		Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected		Y		Nikolenka06
N 348 I		Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected		Y		Nikolenka06
A 360 I		Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected		Y		Nikolenka06
A 360 V		Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected		Y		Nikolenka06
V 365 I		Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected		Y		Nikolenka06
T 369 I		NNRTI	VRX-480775	Selected	Y			Zhang06b
A 376 S		Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine)	Selected		Y		Nikolenka06
T 386 I	ACT→ATT	Multiple Nucleoside	AZT (zidovudine) + 3TC (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	In vitro	In vivo	Comments	Refs
I 5 V		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		Nucleoside RT Inhibitor (NRTI)	1592U89(abacavir)+3TC (lamivudine)+AZT (zidovudine)	Selected	?	Y		Brandin03
I 10 V		Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine) + 3TC (lamivudine) + ddI (didanosine)	Selected	?	Y		Brandin03
V 11 I		Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine) + 3TC (lamivudine) + ddI (didanosine)	Selected	?	Y		Brandin03
R 20 K		Nucleoside RT Inhibitor (NRTI)	1592U89(abacavir)+3TC (lamivudine)+AZT (zidovudine)	Selected	?	Y		Brandin03
K 35 R	AAA→AGA	NRTI	multi-nucleoside	Selected	?	Y		Colson05
R 35 K		Nucleoside RT Inhibitor (NRTI)	1592U89(abacavir)+3TC (lamivudine)+AZT (zidovudine)	Selected	?	Y		Brandin03
K 40 R		Nucleoside RT Inhibitor (NRTI)	1592U89(abacavir)+3TC (lamivudine)+AZT (zidovudine)	Selected	?	Y		Brandin03
I 43 I		Nucleoside RT Inhibitor (NRTI)	ABT-538(ritonavir) + AG-1343 (nelfinavir)	Selected	?	Y		Brandin03
K 45 R		Nucleoside RT Inhibitor (NRTI)	ABT-538(ritonavir) + AG-1343 (nelfinavir)	Selected	?	Y		Brandin03
G 48 A		Nucleoside RT Inhibitor (NRTI)	ABT-378 (lopinavir)	Selected	?	Y		Brandin03
I 50 V		Nucleoside RT Inhibitor (NRTI)	ABT-378 (lopinavir)	Selected	?	Y		Brandin03
I 54 M		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		Nucleoside RT Inhibitor (NRTI)	ABT-378 (lopinavir)	Selected	?	Y		Brandin03
K 65 R		Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine) + 3TC (lamivudine) + ddI (didanosine)	Selected	?	Y		Brandin03
N 69 S		Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine) + 3TC (lamivudine) + ddI (didanosine)	Selected	?	Y		Brandin03
K 70 S		Nucleoside RT Inhibitor (NRTI)	1592U89(abacavir)+3TC (lamivudine)+AZT (zidovudine)	Selected	?	Y		Brandin03
V 71 I		Nucleoside RT Inhibitor (NRTI)	ABT-538(ritonavir) + AG-1343 (nelfinavir)	Selected	?	Y		Brandin03
A 92 T		Nucleoside RT Inhibitor (NRTI)	ABT-538(ritonavir) + AG-1343 (nelfinavir)	Selected	?	Y		Brandin03
L 99 F		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		Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine) + 3TC (lamivudine) + ddI (didanosine)	Selected	?	Y		Brandin03
Y 162 H		Nucleoside RT Inhibitor (NRTI)	AZT (zidovudine) + 3TC (lamivudine) + ddI (didanosine)	Selected	?	Y		Brandin03
T 163 A		Nucleoside RT Inhibitor (NRTI)	1592U89(abacavir)+3TC (lamivudine)+AZT (zidovudine)	Selected	?	Y		Brandin03
M 184 V		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		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		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
T 66 I		Integrase Inhibitor	Dihydroxythiophene (DHT)	Cross R	Y		Double mutants T66I/N155S confer 17–25 fold resistance while triple mutants T66I/S153Y/ N155S confers greater than 33 fold resistance. DHTs are a novel series of inhibitors; two are described in this paper DHT-1 and DHT-2.	Kehlenbeck06
G 140 S	GGC⟶AGC	Integrase inhibitor	L-Chicoric Acid	Selected	Y	?	Mutation located in the catalytic core of integrase. Mildly attentuates virus growth.	King98
S 153 Y		Integrase Inhibitor	Dihydroxythiophene	Cross R	Y		Double mutants T66I/N155S confer 17–25 fold resistance while triple mutants T66I/S153Y/ N155S confers greater than 33 fold resistance. DHTs are a novel series of inhibitors; two are described in this paper DHT-1 and DHT-2.	Kehlenbeck06
N 155 S		Integrase Inhibitor	Dihydroxythiophene	Cross R	Y		Double mutants T66I/N155S confer 17–25 fold resistance while triple mutants T66I/S153Y/ N155S confers greater than 33 fold resistance. DHTs are a novel series of inhibitors; two are described in this paper DHT-1 and DHT-2.	Kehlenbeck06
V 165 I		Integrase inhibitor	FZ41	Selected	?	Y	selected in conjunction with V249I; double mutant confers 9 fold resistance	Bonnenfant04
F 185 K		integrase inhibitor	DKA (β-diketo acids)	Cross-R	Y	?	only biochemical studies done to test decrease in susceptibility	Marchand03
V 249 I		Integrase inhibitor	FZ41	Selected	?	Y	selected in conjunction with V165I; double mutant confers 9 fold resistance	Bonnenfant04
C 280 S		integrase inhibitor	DKA (β-diketo acids)	Cross-R	Y	?	only biochemical studies done to test decrease in susceptibility	Marchand03
C 280 Y		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		Fusion/Binding Inhibitor	T20 (pentafuside)	Selected		Y	found in combination with G36D in patients	Wei02
Q 32 R		Fusion/Binding Inhibitor	T20 (pentafuside)	Selected		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		Fusion/Binding Inhibitor	T20 (pentafuside)	Selected		Y		Wei02
V 38 A	GTG→GCG	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		Fusion/Binding Inhibitor	T20 (pentafuside)	Selected		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		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		Fusion/Binding Inhibitor	BMS-488043	Selected	Y	?	Mutation in gp120.	Lin03
V 69 I	GTC→ATC	Fusion/Binding Inhibitor	T20 (pentafuside)	Selected		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/134N/145L/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/134N/145L/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/134N/145L/245I/269E/278H/288V/293D/364–367Deletion/387T:	Schols98
N 106 K	AAT→AAG	Fusion/Binding Inhibitor	SDF-1α	Selected	Y	?	106K/134N/145L/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	Lohrengel05
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	?	106K/134N/145L/245I/269E/278H/288V/293D/ 364–367Deletion/387T: 10 fold	Schols98
S 134 N	AGC→AAC	Fusion/Binding Inhibitor	JM-3100	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/ 364–367Deletion/387T: 10-fold	Schols98
S 134 N	AGC→AAC	Fusion/Binding Inhibitor	Mab 12G5	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/ 364–367Deletion/387T:	Schols98
S 134 N	AGC→AAC	Fusion/Binding Inhibitor	SDF-1α	Selected	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/ 364–367Deletion/387T: 15-fold.	Schols98
F 145 L	TTC→TTA	Fusion/Binding Inhibitor	JM 2763	Cross Resistant	Y	?	106K/134N/145L/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	?	106K/134N/145L/245I/269E/278H/288V/293D/ 364–367Deletion/387T: 10-fold	Schols98
F 145 L	TTC→TTA	Fusion/Binding Inhibitor	Mab 12G5	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/ 364–367Deletion/387T:	Schols98
F 145 L	TTC→TTA	Fusion/Binding Inhibitor	SDF-1α	Selected	Y	?	106K/134N/145L/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
P 203 L		Entry Inhibitor	Amphotericin B Methyl Ester (AME)	Selected	Y		Mutations selected in the cytoplasmic tail of gp41	Waheed06
N 204 K		entry inhibitor	Concanavalin A (ConA)	Selected	Y	?	mutations in gp120	Witvrouw05
S 205 L		Entry Inhibitor	Amphotericin B Methyl Ester (AME)	Selected	Y		Mutations selected in the cytoplasmic tail of gp42	Waheed06
G 237 R		Fusion/Binding Inhibitor	IC9564 (emivirine)	Selected	Y	?	gp-120	Holz-Smith01
F 245 I	TTC→ATC	Fusion/Binding Inhibitor	JM 2763	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/ 364–367Deletion/387T: 10 fold	Schols98
F 245 I	TTC→ATC	Fusion/Binding Inhibitor	JM-3100	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/ 364–367Deletion/387T: 10-fold	Schols98
F 245 I	TTC→ATC	Fusion/Binding Inhibitor	Mab 12G5	Cross Resistant	Y	?	106K/134N/145L/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
F 245 I	TTC→ATC	Fusion/Binding Inhibitor	SDF-1α	Selected	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364–367Deletion/387T: 15-fold.	Schols98
R 252 K		Fusion/Binding Inhibitor	IC9564 (emivirine)	Selected	Y	?	gp-120	Holz-Smith01
S 261 F		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-1α	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 m	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

HIV-1 Env

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	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
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		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		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
S 274 del		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
S 274 del		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
S 274 del		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		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		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
I 275 del		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 275 del		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 275 del		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		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		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	?	106K/134N/145L/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

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→CAC	Fusion/Binding Inhibitor	JM-3100	Selected	Y	?		DeVreese96, DeVreese96a
Q 278 H	CAG→CAT	Fusion/Binding Inhibitor	JM-3100	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364–367Deletion/387T: 10-fold	Schols98
Q 278 H	CAG→CAT	Fusion/Binding Inhibitor	Mab 12G5	Cross Resistant	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364–367Deletion/387T:	Schols98
Q 278 H	CAG→CAT	Fusion/Binding Inhibitor	SDF-1α	Selected	Y	?	106K/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 m	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 mut	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 mutag	Kanbara01
Q 278 T	CAG→ACG	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

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	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 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		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		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		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		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

HIV-1 Env

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
R 279 K		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
R 279 K		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		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		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		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		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

HIV-1 Env

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
A 284 V		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
A 284 V		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		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		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		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		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

HIV-1 Env

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
F 285 L		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
F 285 L		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		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		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		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		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

HIV-1 Env

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
V 286 Y		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
V 286 Y		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-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

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	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 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-1α	Selected	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364–367Deletion/387T: 15-fold.	Schols98
ins 290 T		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		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

HIV-1 Env

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
ins 290 T		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
ins 290 T		Fusion/Binding Inhibitor	T134	Cross Resistant	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
ins 290 T		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		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		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		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
K 290 E		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
K 290 E		Fusion/Binding Inhibitor	T134	Cross Resistant	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
K 290 E		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		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

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	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
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-1α	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-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
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

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	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
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-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
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

HIV-1 Env

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
Q 296 K		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
Q 296 K		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		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		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
Q 296 K		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		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

HIV-1 Env

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
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
H 308 P		Fusion/Binding Inhibitor	AD101	Selected	Y	?	Small molecule entry inhibitor. Mutation in gp120V3. Primary R5 isolate, CC1/85 passaged in PMBC in increasing concentrations of CCR5-inhibitor AD101. When tested in combination with K305R, H308P, A316V and G321E, fold-R was $>5 \times 10^6$	Kuhmann04, Trkola02
T 311 I		entry inhibitor	Concanavalin A (ConA)	Selected	Y	?	mutations in gp120	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		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

HIV-1 Env

Amino Acid Change	Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
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-1α	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
P 385 L	CCA→CTA	Fusion/Binding Inhibitor	JM-3100	Selected	Y	?		DeVreese96, DeVreese96a
R 387 I	AGA→ACA	Fusion/Binding Inhibitor	DS (dextran sulphate)	Selected	Y	?	CD4 binding region; S113N/S134N/K269E/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		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		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		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
Q 574 R		Entry Inhibitor	Retrocyclin-101 (RC-101)	Selected	Y		Substitution in gp160 at position 574, corresponding to the HR1 domain of gp41	Cole06
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

HIV-1 Env

Amino Acid Change			Codon Change	Drug Class	Compound	Selected or Cross-R	In vitro	In vivo	Comments	Refs
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
FNSTW	364–368	Deletion	TTT AAT AGT ACT TGG	Fusion/Binding Inhibitor	DS (dextran sulphate)	Selected	Y			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-1α	Selected	Y	?	106K/134N/145L/245I/269E/278H/288V/293D/364–367Deletion/387T: 15-fold.	Schols98
deletion	364–376			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	phenyalanine
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*R*,5*S*)-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		Tetrahydronapthalene lignan derivative
1592U89	Abacavir, Ziagen, ABC (Glaxo Wellcome)	(1*S*,4*R*)-4-[2-amino-6-cyclopropyl-amino)-9H-purin-9-yl]-2-cyclopentene-1-methanol succinate
3TC	(-)-BCH-189, Lamivudine, Epivir (Glaxo Wellcome)	(-)-β-L-2′,3′-dideoxy-3′-thiacytidine
4′-Ed4T		2′,3′-Didehydro-3′-deoxy-4′-ethynylthymidine
8-chloro-TIBO	RO91767, R86183, tivirapine	(+)-(*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-dimethyl)amino]-2-pyridinyl]amino]piperidine
ABT-378	Aluviran, Lopinavir (Abbott)	N-[(1S,3S,4S)-4-[[2,6-dimethylphenoxy)acetyl]amino]-3-hydroxy-5-phenyl-1-(phenylmethyl)pentyl]tetrahydro-α-(1-methylethyl)-2-oxo-1(2H)-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		Methyl 3′,3″-dichloro-4′,4″-dimethoxy-5′,5″-bis(methoxycarbonyl)-6,6-diphenyl-5-hexenoate
AG1343	Nelfinavir, Viracept (Agouron)	(3*S*,4a*S*,8a*S*)-N-tert-Butyl-2-[(2*R*,3*R*)-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
Amphotericin B Methyl Ester		[2-[[(4E,6E,8E,10E,12E,14E,16E)-38-carboxy-19,25,27,30,31,33,35,37-octahydroxy-18,20,21-trimethyl-23-oxo-22,39-dioxabicyclo[33.3.1]nonatriaconta-4,6,8,10,12,14,16-heptaen-3-yl]oxy]-3,5-dihydroxy-6-methyl-oxan-4-yl]azanium chloride
AZT	zidovudine (Glaxo Wellcome)	3′-azido-3′-deoxythymidine
BHAP U-87201E	Atevirdine (Pharmacia Upjohn)	1-[(5-Methyoxyindol-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)-1H-indol-2-yl-carbonyl)-4-[3-(isopropylamino)-2-pyridinyl]piperazine
BHAP U-90153		bisheteroarylpiperidinyl derivative
BHAP U-90154		bisheteroarylpiperidinyl derivative
BHAP U-90155		bisheteroarylpiperidinyl derivative
BILA 1906 BS	(Bio-Mega/Boehringer Ingelheim)	N-{1*S*-[[[3-[2*S*-(1,1-dimethylethyl)amino]carbonyl-4*R*-]3-pyridinylmethyl)thio]-1-piperidinyl]-2*R*-hydroxy-1*S*-(phenylmethyl)propyl]amino]carbonyl]-2-methylpropyl}-2-quinolinecarboxamide
BILA 2011	Palinavir (Bio-Mega/Boehringer Ingelheim)	N-{1*S*-[[[3-[2*S*-(1,1-dimethylethyl)amino]carbonyl]-4*R*-[4-pyridinylmethyl)oxy]-1-piperidinyl]-2*R*-hydroxy-1*S*-(phenylmethyl)propyl]amino]carbonyl]-2-methylpropyl}-2-quinolinecarboxamide
BILA 2185 BS	(Bio-Mega/Boehringer Ingelheim)	N-(1,1-dimethylethyl)-1-[2*S*-[[2-2,6-dimethyphenoxy)-1-oxoethyl]amino]-2*R*-hydroxy-4-phenylbutyl]4*R*-pyridinylthio)-2-piperidine-carboxamide
BI-RG-587	Nevaripine, Viramune (Boehringer Ingleheim)	11-Cyclopropyl-4-methyl-5,11-dihydro-6H-dipyrido[3,2-b:2′,3′-e]-[1,4]diazepin-6-one
BM+51.0836		thiazolo-isoindolinone derivative
BMS-186318	(Bristol-Myers Squibb)	[1*S*-[1*R**,2*S**(2*S**,3*R**)]]-[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 dipyranocoumarin
Concanavalin A	ConA	plant lectin from *Canavalia ensiformis*
Cyanovirin	CV-N, NSC 682999 (Cellegy Pharmaceuticals)	Protein from cyanobacterium *Nostoc ellipsosporum*

Abbreviations (cont)

Compounds (cont)

cyclo-d4G		β-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
ddC	Zalcitabine, Hivid (Roche)	2′,3′-dideoxycytidine
ddI	Didanosine, Videx (Bristol-Myers Squibb)	2′,3′-dideoxyinosine
Dihydroxythiophene		
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)	[4*R*-(4-α,5-α,6-β,7-β)]-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)	[4*R*-(4-α,5-α,6-β,7-β)]-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	(-)-β-dioxolane-G	(-)-(2*R*,4*R*)-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	4*S*-[8-(28 betuliniyl) aminooctanoylamino]-3*R*-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	(2*S*,3*S*)-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

Abbreviations (cont)

Compounds (cont)

L-FddC		(-)-β-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(1*S*,2*R*),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
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
P-1946		methyl N-[(1S)-1-[[(5S)-5-[(4-aminophenyl)sulfonyl-(2-methylpropyl)amino]-6-hydroxy-hexyl]carbamoyl]-2-(1H-indol-3-yl)ethyl]carbamate
P9941	(Dupont Merck)	[2-pyridylacetyl-IIePheAla-y(CHOH)]$_2$
PA-457	Bevirimat (Panacos)	3-O-(3′, 3′−dimethylsuccinyl)betulinic acid
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)	(6*R*)-3-(1*R*)-1-[3-([Trifluoromethyl)(2-pyridyl)]sulfonylamino)-phenyl]propyl-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
Retrocyclin-101	18-aa peptide GICRCICGKGICRCICGR	
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]-,[3*S*-[2[1*R**(*R**),2*S**],3α,4aβ,8aβ]]-, monomethanesulfonate
RPI-312		1-[(3*S*)-3-(n-alpha-benzyloxycarbonyl)-l-asparginyl)-amino-2-hydroxy-4-phenyl-butyryl]-n-tert-butyl-l-proline amide (peptidyl protease inhibitor)
RPR103611		a triterpene betulinic acid derivative
RO033-4649	(Roche)	
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

Abbreviations (cont)

Compounds (cont)

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-1α		Stromal cell-derived factor 1α
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)	(+)-(5*S*)-4,5,6,7-tetrahydro-5-methyl-6-(3-methyl-2-butenyl)-imidazo[4,5,1-jk][1,4]-benzodiazepin-2(1H)-thione
TIBO R82913	(Janssen)	(+)-(5*S*)-4,5,6,7,-tetrahydro-9-chloro-5-methyl-6-(3-methyl-2-butenyl)-imidazo-[4,5,1-jk]-[1,4]benzo-diazepin-2(1H)-thione
TMC114	UIC-94017, Darunavir, Prezista (Tibotec)	[(1S,5R,8S)-4,6-dioxabicyclo[3.3.0]oct-8-yl] N-[(2S,3R)-4-[(4-aminophenyl)sulfonyl-(2-methylpropyl)amino]-3-hydroxy-1-phenyl-butan-2-yl]carbamate
TMC125		
TSAO		[2′,5′-bis-O-(tert-butyldimethylsilyl)-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

Abbreviations (cont)

Compounds (cont)

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
VRX-329747		
VX-478	141W94, Amprenavir, Agenerase	Carbamic acid, ((1*S*,2*R*)-3-(((4-aminophenyl)sulfonyl)(2-methylpropyl)amino)-2-hydroxy-1-(phenylmethyl)propyl)-, (3*S*)-tetrahydro-3-furanyl ester
α-APA	R18893, loviride analog	(+)-2,6-Dichloro-α-[(2-acetyl-5-methylphenyl)amino]benzamide

Adamson06 C.S. Adamson, S.D. Ablan, I. Boeras, R. Goila-Gaur, F. Soheilian, K. Nagashima, F. Li, K. Salzwedel, M. Sakalian, C.T. Wild, E.O. Freed, *In vitro* resistance to the human immunodeficiency virus type 1 maturation inhibitor PA-457 (Bevirimat), *J Virol*, **80**(22), 10957–71, 2006, Medline: 16956950

Ariyoshi03 Ariyoshi K, Matsuda M, Miura H, Tateishi S, Yamada K, Sugiura W, Patterns of point mutations associated with antiretroviral drug treatment failure in CRF01_AE (subtype E) infection differ from subtype B infection, *J Acquir Immune Defic Syndr*, **33**(3), 336–42, 2003, Medline: 12843744

Auwerx04 J. Auwerx, M. Stevens, A.R. Van Rompay, L.E. Bird, J. Ren, E. De Clercq, B. Oberg, D.K. Stammers, A. Karlsson, J. Balzarini, The phenylmethylthiazolylthiourea nonnucleoside reverse transcriptase (RT) inhibitor MSK-076 selects for a resistance mutation in the active site of human immunodeficiency virus type 2 RT, *J Virol*, **78**(14), 7427–37, 2004, Medline: 15220416

Bacheler00 Bacheler LT, Anton ED, Kudish P, Baker D, Bunville J, Krakowski K, Bolling L, Aujay M, Wang XV, Ellis D, Becker MF, Lasut AL, George HJ, Spalding DR, Hollis G, Abremski K., Human immunodeficiency virus type 1 mutations selected in patients failing efavirenz combination therapy., *Antimicrobial Agents and Chemotherapy*, **44**, 2475–2484, 2000, Medline: 10952598

Balzarini93 J. Balzarini, A. Karlsson, E. De Clercq, Human immunodeficiency virus type 1 drug-resistance patterns with different 1-[(2-hydroxyethoxy)methyl]-6-(phenylthio)thymine derivatives., *Mol Pharmacol*, **44**, 694–701, 1993, Medline: 94049697

Balzarini93a J. Balzarini, S. Velazquez, A. San-Felix, A. Karlsson, M. J. Perez-Perez, M. J. Camarasa, E. De Clercq, Human immunodeficiency virus type 1-specific [2′,5′-bis-O-(tert- butyldimethylsilyl)-beta-D-ribofuranosyl]-3′-spiro-5′ı-(4′ı-amino-1′ı,2′ı- oxathiole-2′ı,2′ı-dioxide)-purine analogues show a resistance spectrum that is different from that of the human immunodeficiency virus type 1- specific non-nucleoside analogues., *Mol Pharmacol*, **43**, 109–14, 1993, Medline: 93140699

Balzarini93b J. Balzarini, A. Karlsson, E. De Clercq, J. Balzarini, A. Karlsson, A. M. Vandamme, M. J. Perez-Perez, H. Zhang, L. Vrang, B. Oberg, K. Backbro, T. Unge, A. San-Felix, et al, Human immunodeficiency virus type 1 (HIV-1) strains selected for resistance against the HIV-1-specific [2′,5′-bis-O-(tert- butyldimethylsilyl)-3′-spiro- 5′ı-(4′ı-amino-1′ı,2′ı-oxathiole-2′ı,2′ı- dioxide)]-beta-D-pentofurano syl (TSAO) nucleoside analogues retain sensitivity to HIV-1-specific nonnucleoside inhibitors., *Proc Natl Acad Sci U S A*, **90**, 6952–6, 1993, Medline: 93348190

Balzarini93c J. Balzarini, A. Karlsson, M. J. Perez-Perez, L. Vrang, J. Walbers, H. Zhang, B. Oberg, A. M. Vandamme, M. J. Camarasa, E. De Clercq, HIV-1-specific reverse transcriptase inhibitors show differential activity against HIV-1 mutant strains containing different amino acid substitutions in the reverse transcriptase., *Virology*, **192**, 246–53, 1993, Medline: 93297111

Balzarini93d J. Balzarini, A. Karlsson, M. J. Perez-Perez, M. J. Camarasa, W. G. Tarpley, E. De Clercq, Treatment of human immunodeficiency virus type 1 (HIV-1)-infected cells with combinations of HIV-1-specific inhibitors results in a different resistance pattern than does treatment with single-drug therapy., *J Virol*, **67**, 5353–9, 1993, Medline: 93353611

Balzarini94 J. Balzarini, A. Karlsson, V. V. Sardana, E. A. Emini, M. J. Camarasa, E. De Clercq, Human immunodeficiency virus 1 (HIV-1)-specific reverse transcriptase (RT) inhibitors may suppress the replication of specific drug-resistant (E138K)RT HIV-1 mutants or select for highly resistant (Y181C– >C181I)RT HIV-1 mutants., *Proc Natl Acad Sci U S A*, **91**, 6599–603, 1994, Medline: 94294426

Balzarini95 J. Balzarini, M. J. Perez-Perez, S. Velazquez, A. San-Felix, M. J. Camarasa, E. De Clercq, A. Karlsson, Suppression of the breakthrough of human immunodeficiency virus type 1 (HIV-1) in cell culture by thiocarboxanilide derivatives when used individually or in combination with other HIV-1-specific inhibitors (i.e., TSAO derivatives)., *Proc Natl Acad Sci U S A*, **92**, 5470–4, 1995, Medline: 95296332

Balzarini96a J. Balzarini, H. Pelemans, S. Aquaro, C. F. Perno, M. Witvrouw, D. Schols, E. De Clercq, A. Karlsson, Highly favorable antiviral activity and resistance profile of the novel thiocarboxanilide pentenyloxy ether derivatives UC-781 and UC-82 as inhibitors of human immunodeficiency virus type 1 replication., *Mol Pharmacol* , **50**, 394–401, 1996, Medline: 96319790

Balzarini96b J. Balzarini, W. G. Brouwer, D. C. Dao, E. M. Osika, E. De Clercq, Identification of novel thiocarboxanilide derivatives that suppress a variety of drug-resistant mutant human immunodeficiency virus type 1 strains at a potency similar to that for wild-type virus., *Antimicrob Agents Chemother* , **40**, 1454–66, 1996, Medline: 96338367

Balzarini96c Balzarini J, Pelemans H, Perez-Perez MJ, San-Felix A, Camarasa MJ, De Clercq E, Karlsson A, Marked inhibitory activity of non-nucleoside reverse transcriptase inhibitors against human immunodeficiency virus type 1 when combined with (-)2′,3′-dideoxy-3′-thiacytidine. , *Mol Pharmacol* , **49**(5), 882–90, 1996, Medline: 96212950

Baxter06 Baxter J, Schapiro J, Boucher C, Kohlbrenner V, Hall D, Scherer J, Mayers D, Genotypic Changes in Human Immunodeficiency Virus Type 1 Protease Associated with Reduced Susceptibility and Virologic Response to the Protease Inhibitor Tipranavir, *Journal of Virology*, **80**(21), 10794–10801, 2006, Medline: 16928764

Bazmi00 Bazmi HZ, Hammond JL, Cavalcanti SC, Chu CK, Schinazi RF, Mellors JW, *In vitro* selection of mutations in the human immunodeficiency virus type 1 reverse transcriptase that decrease susceptibility to (-)-beta-D-dioxolane-guanosine and suppress resistance to 3′-azido-3′-deoxythymidine, *Antimicrob Agents Chemother*, **44**(7), 1783–8, 2000, Medline: 10858331

Bonnenfant04 S. Bonnenfant, C.M. Thomas, C. Vita, F. Subra, E. Deprez, F. Zouhiri, D. Desmaele, J. D'Angelo, J.F. Mouscadet, H. Leh, Styrylquinolines, integrase inhibitors acting prior to integration: a new mechanism of action for anti-integrase agents, *J Virol*, **78**(11), 5728–36, 2004, Medline: 15140970

Borkow03 Borkow G, Lara HH, Lapidot A, Mutations in gp41 and gp120 of HIV-1 isolates resistant to hexa-arginine neomycin B conjugate, *Biochem Biophys Res Commun*, **312**(4), 1047–52

Borman96 Borman AM, Paulous S, Clavel F, Resistance of human immunodeficiency virus type 1 to protease inhibitors: selection of resistance mutations in the presence and absence of the drug, *J Gen Virol*, **77 (Pt 3)**, 419–26, 1996, Medline: 8601776

BorrotoEsoda97 Borroto-K. Esoda, D.S. Noel, C.P. Moxham, Furman P.A., Preliminary genotypic analysis of HIV-1 in plasma from volunteers receiving repeated multiple doses of MKC-442, *Sixth International Workshop on HIV Drug Resistance St. Petersburg, FL, USA*

Brandin03 Eleonor Brandin, Lena Lindborg, Katarina Gyllensten, Christina Broström, Lars Hagberg,Magnus Gisslen, Björn Tuvesson,Anders Blaxhult, Jan Albert, pol Gene Sequence Variation in Swedish HIV-2 Patients Failing Antiretroviral Therapy, *AIDS Research And Human Retroviruses*, **19**(7), 543–550, 2003, Medline: 12908931

Brenner03 Brenner B, Turner D, Oliveira M, Moisi D, Detorio M, Carobene M, Marlink RG, Schapiro J, Roger M, Wainberg MA, A V106M mutation in HIV-1 clade C viruses exposed to efavirenz confers cross-resistance to non-nucleoside reverse transcriptase inhibitors, *AIDS, 17(1)*, **2003**, 12478089

Brown00 Brown AJ, Precious HM, Whitcomb JM, Wong JK, Quigg M, Huang W, Daar ES, D'Aquila RT, Keiser PH, Connick E, Hellmann NS, Petropoulos CJ, Richman DD, Little SJ., Reduced susceptibility of human immunodeficiency virus type 1 (HIV-1)from patients with primary HIV infection to nonnucleoside reverse transcriptase inhibitors is associated with variation at novel amino acid sites., *Journal of Virology*, **74**, 10269–10273, 2000, Medline: 11044070

Buckheit95a R. W. Buckheit, T. L. Kinjerski, V. Fliakas-Boltz, J. D. Russell, T. L. Stup, L. A. Pallansch, W. G. Brouwer, D. C. Dao, W. A. Harrison, R. J. Schultz, et al, Structure-activity and cross-resistance evaluations of a series of human immunodeficiency virus type-1-specific compounds related to oxathiin carboxanilide., *Antimicrob Agents Chemother*, **39**, 2718–27, 1995, Medline: 96161287

Buckheit95b R. W. Buckheit, V. Fliakas-Boltz, W. D. Decker, J. L. Roberson, T. L. Stup, C. A. Pyle, E. L. White, J. B. McMahon, M. J. Currens, M. R. Boyd, et al, Comparative anti-HIV evaluation of diverse HIV-1-specific reverse transcriptase inhibitor-resistant virus isolates demonstrates the existence of distinct phenotypic subgroups., *Antiviral Res*, **26**, 117–32, 1995, Medline: 95328856

Buckheit95c Buckheit RW Jr, Fliakas-Boltz V, Yeagy-Bargo S, Weislow O, Mayers DL, Boyer PL, Hughes SH, Pan BC, Chu SH, Bader JP, Resistance to 1-[(2-hydroxyethoxy)methyl]-6-(phenylthio)thymine derivatives is generated by mutations at multiple sites in the HIV-1 reverse transcriptase, *Virology*, **210**, 186–193, 1995, Medline: 95313352

Buckheit97 Buckheit RW Jr, Snow MJ, Fliakas-Boltz V, Kinjerski TL, Russell JD, Pallansch LA, Brouwer WG, Yang SS, Highly potent oxathiin carboxanilide derivatives with efficacy against nonnucleoside reverse transcriptase inhibitor-resistant human immunodeficiency virus isolates. , *Antimicrob Agents Chemother*, **41**, 831–837, 1997, Medline: 97242500

Bulgheroni04 Bulgheroni E, Croce F, Citterio P, Vigano O, Visona R, Sala E, Galli M, Rusconi S, Unusual codon 69 insertions: influence on human immunodeficiency virus type 1 reverse transcriptase drug susceptibility, *J Clin Virol*, **29**(1), 27–32, 2004, Medline: 14675866

Byrnes93 V. W. Byrnes, V. V. Sardana, W. A. Schleif, J. H. Condra, J. A. Waterbury, J. A. Wolfgang, W. J. Long, C. L. Schneider, A. J. Schlabach, B. S. Wolanskii, Comprehensive mutant enzyme and viral variant assessment of human immunodeficiency virus type 1 reverse transcriptase resistance to nonnucleoside inhibitors., *Antimicrob Agents Chemother*, **37**, 1576–9, 1993, Medline: 94028780

Caride00 Caride E, Brindeiro R, Hertogs K, Larder B, Dehertogh P, Machado E, de Sa CA, Eyer-Silva WA, Sion FS, Passioni LF,Menezes JA, Calazans AR, Tanuri A., Drug-resistant reverse transcriptase genotyping and phenotyping of B and non-B subtypes (F and A) of human immunodeficiency virus type I found in Brazilian patients failing HAART., *Virology*, **275**, 107–115, 2000, Medline: 11017792

Carrillo98 Carrillo A, Stewart KD, Norbeck DW, Kohlbrenner WE, Leonard JM, Kempf DJ, Molla A., *In vitro* selection and characterization of human immunodeficiency virus type 1 variants with increased resistance to ABT-378, a novel protease inhibitor, *J Virol*, **72**, 7532–7541, 1998, Medline: 98362159

Cherrington96 J. M. Cherrington, A. S. Mulato, M. D. Fuller, M. S. Chen, Novel mutation (K70E) in human immunodeficiency virus type 1 reverse transcriptase confers decreased susceptibility to 9-[2- (phosphonomethoxy)ethyl]adenine *in vitro*., *Antimicrob Agents Chemother*, **40**, 2212–6, 1996, Medline: 97032863

Cole06 A.L. Cole, O.O. Yang, A.D. Warren, A.J. Waring, R.I. Lehrer, A.M. Cole, HIV-1 adapts to a retrocyclin with cationic amino acid substitutions that reduce fusion efficiency of gp41, *J Immunol*, **176**(11), 6900–5, 2006, Medline: 16709850

Colson05 P. Colson, M. Henry, N. Tivoli, H. Gallais, J.A. Gastaut, J. Moreau, C. Tamalet, Polymorphism and drug-selected mutations in the reverse transcriptase gene of HIV-2 from patients living in southeastern France, *J Med Virol*, **75**(3), 381–90, 2005, Medline: 15648062

Condra95 J. H. Condra, W. A. Schleif, O. M. Blahy, L. J. Gabryelski, D. J. Graham, J. C. Quintero, A. Rhodes, H. L. Robbins, E. Roth, M. Shivaprakash, et al, *In vivo* emergence of HIV-1 variants resistant to multiple protease inhibitors, *Nature*, **374**, 569–71, 1995, Medline: 95214785

Condra96 Condra JH, Holder DJ, Schleif WA, Blahy OM, Danovich RM, Gabryelski LJ, Graham DJ, Laird D, Quintero JC, Rhodes A, Robbins HL, Roth E, Shivaprakash M, Yang T, Chodakewitz JA, Deutsch PJ, Leavitt RY, Massari FE, Mellors JW, Squires KE, Steigbigel RT, Teppler H, Emini EA, Genetic correlates of *in vivo* viral resistance to indinavir, a human immunodeficiency virus type 1 protease inhibitor, *J Virol*, **70**(12), 8270–6, 1996, Medline: 97126022

Croteau97 G. Croteau, L. Doyon, D. Thibeault, G. McKercher, L. Pilote, D. Lamarre, Impaired fitness of human immunodeficiency virus type 1 variants with high-level resistance to protease inhibitors., *J Virol*, **71**, 1089–96, 1997, Medline: 97151093

Cushman98 Cushman M, Casimiro-Barcia A, Hejchman E, Ruell JA, Huang M, Schaeffer CA, Williamson K, Rice WG, Buckheit Jr. RW., New alkenyldiarylmethanes with enhanced potencies as anti-HIV agents which act as non-nucleoside reverse transcriptase inhibitors., *J Med Chem*, **41**, 2076–2089, 1998, Medline: 98285673

Damond05 F. Damond, F. Brun-Vezinet, S. Matheron, G. Peytavin, P. Campa, S. Pueyo, F. Mammano, S. Lastere, I. Farfara, F. Simon, G. Chene, D. Descamps, Polymorphism of the human immunodeficiency virus type 2 (HIV-2) protease gene and selection of drug resistance mutations in HIV-2-infected patients treated with protease inhibitors, *J Clin Microbiol*, **43**(1), 484–7, 2005, Medline: 15635022

DeAntoni97 A. De Antoni, A. Foli, J. Lisziewicz, F. Lori, Mutations in the pol gene of human immunodeficiency virus type 1 in infected patients receiving didanosine and hydroxyurea combination therapy, *J Infect Dis*, **176**, 899–903, 97, Medline: 97472322

Demeter98 L. M. Demeter, P. M. Meehan, G. Morse, M. A. Fischl, M. Para, W. Powderly, J. Leedom, J. Holden-Wiltse, C. Greisberger, K. Wood, J. Timpone, L. K. Wathen, T. Nevin, L. Resnick, D. H. Batts, R. C. Reichman, Phase I study of atevirdine mesylate (U-87201E) monotherapy in HIV-1-infected patients, *J Acquir Immune Defic Syndr Hum Retrovirol*, **19**, 135–44, 98, Medline: 98439558

DeMeyer05 S. De Meyer, H. Azijn, D. Surleraux, D. Jochmans, A. Tahri, R. Pauwels, P. Wigerinck, M.P. de Bethune, TMC114, a novel human immunodeficiency virus type 1 protease inhibitor active against protease inhibitor-resistant viruses, including a broad range of clinical isolates, *Antimicrob Agents Chemother*, **49**(6), 2314–21, 2005, Medline: 15917527

DeVreese96 K. De Vreese, D. Reymen, P. Griffin, A. Steinkasserer, G. Werner, G. J. Bridger, J. Este, W. James, G. W. Henson, J. Desmyter, J. Anne, I. De Clercq, The bicyclams, a new class of potent human immunodeficiency virus inhibitors, block viral entry after binding., *Antiviral Res*, **29**, 209–19, 1996, Medline: 96315998

DeVreese96a de Vreese K, Kofler-Mongold V, Leutgeb C, Weber V, Vermeire K, Schacht S, Anne J, de Clercq E, Datema R, Werner G, The molecular target of bicyclams, potent inhibitors of human immunodeficiency virus replication, *J Virol*, **70**(2), 689–96, 1996, Medline: 96135175

Doyon05 L. Doyon, S. Tremblay, L. Bourgon, E. Wardrop, M.G. Cordingley, Selection and characterization of HIV-1 showing reduced susceptibility to the non-peptidic protease inhibitor tipranavir, *Antiviral Res*, **68**(1), 27–35, 2005, Medline: 16122817

Doyon96 L. Doyon, G. Croteau, D. Thibeault, F. Poulin, L. Pilote, D. Lamarre, Second locus involved in human immunodeficiency virus type 1 resistance to protease inhibitors., *J Virol*, **70**, 3763–9, 1996, Medline: 96211509

Dueweke93 T. J. Dueweke, T. Pushkarskaya, S. M. Poppe, S. M. Swaney, J. Q. Zhao, I. S. Chen, M. Stevenson, W. G. Tarpley, A mutation in reverse transcriptase of bis(heteroaryl)piperazine- resistant human immunodeficiency virus type 1 that confers increased sensitivity to other nonnucleoside inhibitors., *Proc Natl Acad Sci U S A*, **90**, 4713–7, 1993, Medline: 93281649

Dulioust97 A. Dulioust, S. Paulous, L. Guillemot, F. Boue, P. Galanaud, Clavel F, Selection of saquinavir-resistant mutants by indinavir following a switch from saquinavir, *Sixth International Workshop on HIV Drug Resistance St. Petersburg, FL, USA*

Dulioust99 Dulioust A, Paulous S, Guillemot L, Delavalle AM, Boue F, Clavel F, Constrained evolution of human immunodeficiency virus type 1 protease during sequential therapy with two distinct protease inhibitors, *J Virol*, **73**(1), 850–4, 1999, Medline: 9847401

Eastman98 Eastman PS, Mittler J, Kelso R, Gee C, Boyer E, Kolberg J, Urdea M, Leonard JM, Norbeck DW, Mo H, Markowitz M, Genotypic changes in human immunodeficiency virus type 1 associated with loss of suppression of plasma viral RNA levels in subjects treated with ritonavir (Norvir) monotherapy, *J Virol*, **72**(6), 5154–64, 1998, Medline: 9573287

Eberle95 J. Eberle, B. Bechowsky, D. Rose, U. Hauser, K. von der Helm, L. Gurtler, H. Nitschko, Resistance of HIV type 1 to proteinase inhibitor Ro 31–8959., *AIDS Res Hum Retroviruses*, **11**, 671–6, 1995, Medline: 96078227

el-Farrash94 M. A. el-Farrash, M. J. Kuroda, T. Kitazaki, T. Masuda, K. Kato, M. Hatanaka, S. Harada, Generation and characterization of a human immunodeficiency virus type 1 (HIV-1) mutant resistant to an HIV-1 protease inhibitor., *J Virol*, **68**, 233–9, 1994, Medline: 94076412

Este96 J. A. Este, K. De Vreese, M. Witvrouw, J. C. Schmit, A. M. Vandamme, J. Anne, J. Desmyter, G. W. Henson, G. Bridger, E. De Clercq, Antiviral activity of the bicyclam derivative JM3100 against drug- resistant strains of human immunodeficiency virus type 1., *Antiviral Res*, **29**, 297–307, 1996, Medline: 96316006

Este96a J.A. Este, K. Van Laethem, A.M. Vandamme, J. Desmyter, E. De Clercq, Resistant phenotype of human immunodeficiency virus type 1 to dextran sulfate is conferred by specific amino acid substitutions in the gp120 molecule, *Fifth International Workshop on HIV Drug Resistance Whistler, BC, Canada*

Este97 J.A. Este, D. Schols, K. De Vreese, D. Van Laethem, A.M. Vandamme, J. Desmyter, E. De Clercq, Development of resistance of human immunodeficiency virus type 1 to dextran sulfate associated with the emergence of specific mutations in the envelope gp120 glycoprotein, *Molecular Pharmacology*, **52** , 98–104 , 1997 1997, Medline: 97368051

Fitzgibbon92 J. E. Fitzgibbon, R. M. Howell, C. A. Haberzettl, S. J. Sperber, D. J. Gocke, D. T. Dubin, Human immunodeficiency virus type 1 pol gene mutations which cause decreased susceptibility to 2′,3′-dideoxycytidine., *Antimicrob Agents Chemother*, **36**, 153–7, 1992, Medline: 92272541

Foli96 A. Foli, K. M. Sogocio, B. Anderson, M. Kavlick, M. W. Saville, M. A. Wainberg, Z. Gu, J. M. Cherrington, H. Mitsuya, R. Yarchoan, *In vitro* selection and molecular characterization of human immunodeficiency virus type 1 with reduced sensitivity to 9-[2- (phosphonomethoxy)ethyl]adenine (PMEA)., *Antiviral Res*, **32**, 91–8, 1996, Medline: 97046247

Fujiwara98 T. Fujiwara, A. Sato, M. el-Farrash, S. Miki, K. Abe, Y. Isaka, M. Kodama, Y. Wu, L. B. Chen, H. Harada, H. Sugimoto, M. Hatanaka, Y. Hinuma, S-1153 inhibits replication of known drug-resistant strains of human immunodeficiency virus type 1, *Antimicrob Agents Chemother*, **42**, 1340–5, 98, Medline: 98287568

Gao92 Q. Gao, Z. X. Gu, M. A. Parniak, X. G. Li, M. A. Wainberg, *In vitro* selection of variants of human immunodeficiency virus type 1 resistant to 3′-azido-3′-deoxythymidine and 2′,3′-dideoxyinosine., *J Virol*, **66**, 12–9, 1992, Medline: 92085373

Gao93 Q. Gao, Z. Gu, M. A. Parniak, J. Cameron, N. Cammack, C. Boucher, M. A. Wainberg, The same mutation that encodes low-level human immunodeficiency virus type 1 resistance to 2′,3′-dideoxyinosine and 2′,3′-dideoxycytidine confers high-level resistance to the (-) enantiomer of 2′,3′-dideoxy-3′- thiacytidine., *Antimicrob Agents Chemother*, **37**, 1390–2, 1993, Medline: 93319281

Garcia-Lerma03 Garcia-Lerma JG, MacInnes H, Bennett D, Reid P, Nidtha S, Weinstock H, Kaplan JE, Heneine W, A novel genetic pathway of human immunodeficiency virus type 1 resistance to stavudine mediated by the K65R mutation, *J Virol*, **77**(10), 5685–93, 2003, Medline: 12719561

Gashnikova03 Gashnikova N, Plyasunova O, Kiseleva Y, Fedyuk N, Pokrovsky A, *In vitro* study of resistance-associated genotypic mutations to nucleoside analogs, *Nucleosides Nucleotides Nucleic Acids*, **22(5–8)**, 991–4, 2003, Medline: 14565328

Gatanaga02 Gatanaga H, Suzuki Y, Tsang H, Yoshimura K, Kavlick MF, Nagashima K, Gorelick RJ, Mardy S, Tang C, Summers MF, Mitsuya H, Amino acid substitutions in Gag protein at non-cleavage sites are indispensable for the development of a high multitude of HIV-1 resistance against protease inhibitors, *J Biol Chem*, **277**(8), 5952–61, 2002, Medline: 11741936

Geleziunas03 Geleziunas R, Gallagher K, Zhang H, Bacheler L, Garber S, Wu JT, Shi G, Otto MJ, Schinazi RF, Erickson-Viitanen S, HIV-1 resistance profile of the novel nucleoside reverse transcriptase inhibitor beta-D-2′,3′-dideoxy-2′,3′-didehydro-5-fluorocytidine (Reverset), *Antivir Chem Chemother*, **14**(1), 49–59, 2003, Medline: 12790516

Gong00 Gong YF, Robinson BS, Rose RE, Deminie C, Spicer TP, Stock D, Colonno RJ, Lin PF., *In vitro* resistance profile of the human immunodeficiency virus type 1 protease inhibitor BMS-232632., *Antimicrobial Agents and Chemotherapy*, **44**, 2319–2326, 2000, Medline: 10952574

Gosselin94 Gosselin G, Schinazi RF, Sommadossi JP, Mathe C, Bergogne MC, Aubertin AM, Kirn A, Imbach JL., Anti-Human Immunodeficiency Virus Activities of the beta-L Enantiomer of 2′,3′-Dideoxycytidine and Its 5-Fluoro Derivative *In Vitro*, *Antimicrobial Agents and Chemotherapy*, **38**(6), 292–1297, 1994, Medline: 8092827

Gu92 Z. Gu, Q. Gao, X. Li, M. A. Parniak, M. A. Wainberg, Novel mutation in the human immunodeficiency virus type 1 reverse transcriptase gene that encodes cross-resistance to 2′,3′- dideoxyinosine and 2′,3′-dideoxycytidine., *J Virol*, **66**, 7128–35, 1992, Medline: 93059660

Gu94 Z. Gu, Q. Gao, H. Fang, H. Salomon, M. A. Parniak, E. Goldberg, J. Cameron, M. A. Wainberg, Identification of a mutation at codon 65 in the IKKK motif of reverse transcriptase that encodes human immunodeficiency virus resistance to 2′,3′-dideoxycytidine and 2′,3′-dideoxy-3′-thiacytidine., *Antimicrob Agents Chemother*, **38**, 275–81, 1994, Medline: 94250000

Gulnik95 S. V. Gulnik, L. I. Suvorov, B. Liu, B. Yu, B. Anderson, H. Mitsuya, J. W. Erickson, Kinetic characterization and cross-resistance patterns of HIV-1 protease mutants selected under drug pressure., *Biochemistry*, **34**, 9282–7, 1995, Medline: 95352609

Gurusinghe95 A. D. Gurusinghe, S. A. Land, C. Birch, C. McGavin, D. J. Hooker, G. Tachedjian, R. Doherty, N. J. Deacon, Reverse transcriptase mutations in sequential HIV-1 isolates in a patient with AIDS., *J Med Virol*, **46**, 238–43, 1995, Medline: 96028714

Hachiya04 Hachiya A, Gatanaga H, Kodama E, Ikeuchi M, Matsuoka M, Harada S, Mitsuya H, Kimura S, Oka S, Novel patterns of nevirapine resistance-associated mutations of human immunodeficiency virus type 1 in treatment-naive patients, *Virology*, **327**(2), 215–24, 2004, Medline: 15351209

Hara97 Hara H, Fujihashi T, Sakata T, Kaji A, Kaji H, Tetrahydronaphthalene lignan compounds as potent anti-HIV type 1 agents, *AIDS Res Hum Retroviruses*, **13**, 695–705, 1997, Medline: 97311521

Harrigan02 Harrigan PR, Salim M, Stammers DK, Wynhoven B, Brumme ZL, McKenna P, Larder B, Kemp SD, A mutation in the 3′ region of the human immunodeficiency virus type 1 reverse transcriptase (Y318F) associated with nonnucleoside reverse transcriptase inhibitor resistance, *J Virol*, **76**(13), 6836–40, 2002, Medline: 12050397

Harrigan05 P.R. Harrigan, T. Mo, B. Wynhoven, J. Hirsch, Z. Brumme, P. McKenna, T. Pattery, J. Vingerhoets, L.T. Bacheler, Rare mutations at codon 103 of HIV-1 reverse transcriptase can confer resistance to non-nucleoside reverse transcriptase inhibitors, *AIDS*, **19**(6), 549–54, 2005, Medline: 15802972

Harrigan96 P. R. Harrigan, I. Kinghorn, S. Bloor, S. D. Kemp, I. Najera, A. Kohli, B. A. Larder, Significance of amino acid variation at human immunodeficiency virus type 1 reverse transcriptase residue 210 for zidovudine susceptibility., *J Virol*, **70**, 5930–4, 1996, Medline: 96323108

Hertogs00 Hertogs K, Bloor S, De Vroey V, van Den Eynde C, Dehertogh P, van Cauwenberge A, Sturmer M, Alcorn T, Wegner S, van Houtte M, Miller V, Larder BA., A novel human immunodeficiency virus type 1 reverse transcriptase mutational pattern confers phenotypic lamivudine resistance in the absence of mutation 184V., *Antimicrobial Agents and Chemotherapy*, **44**, 568–573, 2000, Medline: 10681319

Ho94 D. D. Ho, T. Toyoshima, H. Mo, D. J. Kempf, D. Norbeck, C. M. Chen, N. E. Wideburg, S. K. Burt, J. W. Erickson, M. K. Singh, Characterization of human immunodeficiency virus type 1 variants with increased resistance to a C2-symmetric protease inhibitor., *J Virol*, **68**, 2016–20, 1994, Medline: 94149902

Hodge96 Hodge CN, Aldrich PE, Bacheler LT, Chang CH, Eyermann CJ, Garber S, Grubb M, Jackson DA, Jadhav PK, Korant B, Lam PY, Maurin MB, Meek JL, Otto MJ, Rayner MM, Reid C, Sharpe TR, Shum L, Winslow DL, Erickson-Viitanen S, Improved cyclic urea inhibitors of the HIV-1 protease: synthesis, potency, resistance profile, human pharmacokinetics and X-ray crystal structure of DMP 450, *Chem Biol*, **3**(4), 301–14, 1996, Medline: 8807858

Holz-Smith01 Holz-Smith SL, Sun IC, Jin L, Matthews TJ, Lee KH, Chen CH., Role of Human Immunodeficiency Virus (HIV) Type 1 Envelope in the Anti-HIV Activity of the Betulinic Acid Derivative IC9564., *Antimicrobial Agents and Chemotherapy*, **45**, 60–66, 2001, Medline: 11120945

Hooker96 D. J. Hooker, G. Tachedjian, A. E. Solomon, A. D. Gurusinghe, S. Land, C. Birch, J. L. Anderson, B. M. Roy, E. Arnold, N. J. Deacon, An *in vivo* mutation from leucine to tryptophan at position 210 in human immunodeficiency virus type 1 reverse transcriptase contributes to high-level resistance to 3′-azido-3′-deoxythymidine., *J Virol*, **70**, 8010–8, 1996, Medline: 97048084

Huang03 Huang W, Gamarnik A, Limoli K, Petropoulos CJ, Whitcomb JM, Amino acid substitutions at position 190 of human immunodeficiency virus type 1 reverse transcriptase increase susceptibility to delavirdine and impair virus replication, *J Virol*, **77**(2), 1512–23, 2003, Medline: 12502865

Imamichi00 Imamichi T, Sinha T, Imamichi H, Zhang YM, Metcalf JA, Falloon J, Lane HC, High level resistance to 3í-azido-3í-deoxythimidine due to a deletion in the reverse transcriptase gene of human immunodeficiency virus type 1, *J. Virol*, **74**, 1023–1028, 2000, Medline: 10623768

Jacobsen95 Jacobsen H, Yasargil K, Winslow DL, Craig JC, Krohn A, Duncan IB, Mous J, Characterization of human immunodeficiency virus type 1 mutants with decreased sensitivity to proteinase inhibitor Ro 31–8959, *Virology*, **206**(1), 527–34, 1995, Medline: 7831807

Johnston04 E. Johnston, M.A. Winters, S.Y. Rhee, T.C. Merigan, C.A. Schiffer, R.W. Shafer, Association of a novel human immunodeficiency virus type 1 protease substrate cleft mutation, L23I, with protease inhibitor therapy and *in vitro* drug resistance, *Antimicrob Agents Chemother*, **48**(12), 4864–8, 2004, Medline: 15561868

Kanbara01 Kanbara K, Sato S, Tanuma J, Tamamura H, Gotoh K, Yoshimori M, Kanamoto T, Kitano M, Fujii N, Nakashima H., Biological and genetic characterization of a human immunodeficiency virus strain resistant to CXCR4 antagonist T134., *AIDS Res Hum Retroviruses*, **17**(7), 615–22, 2001, Medline: 11375057

Kaplan94 A. H. Kaplan, S. F. Michael, R. S. Wehbie, M. F. Knigge, D. A. Paul, L. Everitt, D. J. Kempf, D. W. Norbeck, J. W. Erickson, R. Swanstrom, Selection of multiple human immunodeficiency virus type 1 variants that encode viral proteases with decreased sensitivity to an inhibitor of the viral protease., *Proc Natl Acad Sci U S A*, **91**, 5597–601, 1994, Medline: 94261633

Kehlenbeck06 S. Kehlenbeck, U. Betz, A. Birkmann, B. Fast, A.H. Goller, K. Henninger, T. Lowinger, D. Marrero, A. Paessens, D. Paulsen, V. Pevzner, R. Schohe-Loop, H. Tsujishita, R. Welker, J. Kreuter, H. Rubsamen-Waigmann, F. Dittmer, Dihydroxythiophenes are novel potent inhibitors of human immunodeficiency virus integrase with a diketo acid-like pharmacophore, *J Virol*, **80**(14), 6883–94, 2006, Medline: 16809294

Kellam92 P. Kellam, C. A. Boucher, B. A. Larder, Fifth mutation in human immunodeficiency virus type 1 reverse transcriptase contributes to the development of high-level resistance to zidovudine., *Proc Natl Acad Sci U S A*, **89**, 1934–8, 1992, Medline: 92179296

Kemp98 S. D. Kemp, C. Shi, S. Bloor, P. R. Harrigan, J. W. Mellors, B. A. Larder, A novel polymorphism at codon 333 of human immunodeficiency virus type 1 reverse transcriptase can facilitate dual resistance to zidovudine and L-2′,3′-dideoxy-3′-thiacytidine., *J Virol*, **72**, 5093–8, 1998, Medline: 98241751

Kempf01 Kempf DJ, Isaacson JD, King MS, Brun SC, Xu Y, Real K, Bernstein BM, Japour AJ, Sun E, Rode RA., Identification of genotypic changes in human immunodeficiency virus protease that correlate with reduced susceptibility to the protease inhibitor lopinavir among viral isolates from protease inhibitor-experienced patients., *J Virol.*, **75**(16), 7462–9, 2001, Medline: 11462018

Keulen96 W. Keulen, A. van Wijk, C. Boucher, B. Berkhout, Initial appearance of 184Ile variant in 3TC-treated patients can be explained by the mutation bias of the HIV-1 RT enzyme, *Fifth International Workshop on HIV Drug Resistance Whistler, BC, Canada*

Keulen97 Keulen W, Back NK, van Wijk A, Boucher CA, Berkhout B, Initial appearance of the 184Ile variant in lamivudine-treated patients is caused by the mutational bias of human immunodeficiency virus type 1 reverse transcriptase, *J Virol*, **71**(4), 3346–50, 1997, Medline: 9060708

King95 R.W. King, S. Garber, D.L. Winslow, C. Reid, L.T. Bacheler, E. Anton, M.J. Otto, Multiple mutations in the human immunodeficiency virus protease gene are responsible for decreased susceptibility to protease inhibitors., *Antiviral Chemistry and Chemotherapy*, **669**(9), 80–88

King98 P.J. King, W. E. Robinson Jr. , Resistance to the anti-human immunodeficiency virus type 1 compound L-chicoric acid results from a single mutation at amino acid 140 of integrase., *Journal of Virology*, **72**, 8420–8424

Kleim93 J. P. Kleim, R. Bender, U. M. Billhardt, C. Meichsner, G. Riess, M. Rosner, I. Winkler, A. Paessens, Activity of a novel quinoxaline derivative against human immunodeficiency virus type 1 reverse transcriptase and viral replication., *Antimicrob Agents Chemother*, **37**, 1659–64, 1993, Medline: 94028795

Kleim95 J. P. Kleim, R. Bender, R. Kirsch, C. Meichsner, A. Paessens, M. Rosner, H. Rubsamen-Waigmann, R. Kaiser, M. Wichers, K. E. Schneweis, et al, Preclinical evaluation of HBY 097, a new nonnucleoside reverse transcriptase inhibitor of human immunodeficiency virus type 1 replication., *Antimicrob Agents Chemother*, **39**, 2253–7, 1995, Medline: 96109422

Kleim96 J. P. Kleim, M. Rosner, I. Winkler, A. Paessens, R. Kirsch, Y. Hsiou, E. Arnold, G. Riess, Selective pressure of a quinoxaline nonnucleoside inhibitor of human immunodeficiency virus type 1 (HIV-1) reverse transcriptase (RT) on HIV- 1 replication results in the emergence of nucleoside RT-inhibitor- specific (RT Leu-74–>Val or Ile and Val-75–>Leu or Ile) HIV-1 mutants., *Proc Natl Acad Sci U S A*, **93**, 34–8, 1996, Medline: 96133872

Kleim97 J. P. Kleim, I. Winkler, M. Rosner, R. Kirsch, H. Rubsamen-Waigmann, A. Paessens, G. Riess, *In vitro* selection for different mutational patterns in the HIV-1 reverse transcriptase using high and low selective pressure of the nonnucleoside reverse transcriptase inhibitor HBY 097., *Virology*, **231**, 112–8, 1997, Medline: 97288331

Kleim99 J-P. Kleim, V. Burt, M. Maguire, R. Ferris, R.J. Hazen, G. Roberts, M. St. Clair. , NNRTI GW420867X: Comparative evaluation of the *in vitro* resistance profile. , *6th Conference on Retroviruses and Opportunistic Infections, Chicago, IL, USA.* , Abstract 600

Koh03 Koh Y, Nakata H, Maeda K, Ogata H, Bilcer G, Devasamudram T, Kincaid JF, Boross P, Wang YF, Tie Y, Volarath P, Gaddis L, Harrison RW, Weber IT, Ghosh AK, Mitsuya H, Novel bis-tetrahydrofuranylurethane-containing nonpeptidic protease inhibitor (PI) UIC-94017 (TMC114) with potent activity against multi-PI-resistant human immunodeficiency virus *in vitro*, *Antimicrob Agents Chemother*, **47**(10), 3123–9, 2003, Medline: 14506019

Kovalevsky06 A.Y. Kovalevsky, Y. Tie, F. Liu, P.I. Boross, Y.F. Wang, S. Leshchenko, A.K. Ghosh, R.W. Harrison, I.T. Weber, Effectiveness of nonpeptide clinical inhibitor TMC-114 on HIV-1 protease with highly drug resistant mutations D30N, I50V, and L90M, *J Med Chem*, **49**(4), 1379–87, 2006, Medline: 16480273

Kuhmann04 Kuhmann SE, Pugach P, Kunstman KJ, Taylor J, Stanfield RL, Snyder A, Strizki JM, Riley J, Baroudy BM, Wilson IA, Korber BT, Wolinsky SM, Moore JP, Genetic and phenotypic analyses of human immunodeficiency virus type 1 escape from a small-molecule CCR5 inhibitor, *J Virol*, **78**(6), 2790–807, 2004, Medline: 14990699

Labrosse00 Labrosse B, Treboute C, Alizon M., Sensitivity to a nonpeptidic compound (RPR103611) blocking human immunodeficiency virus type 1 Env-mediated fusion depends on sequence and accessibility of the gp41 loop region., *Journal of Virology*, **74**(5), 2142–50, 2000, Medline: 10666243

Labrosse97 B. Labrosse, O. Pleskoff, N. Sol, C. Jones, Y. Henin, M. Alizon, Antiviral and resistance studies of RPR103611, an inhibitor of HIV replication, *Sixth International Workshop on HIV Drug Resistance, St. Petersburg, FL, USA*

Lacey94 S. F. Lacey, B. A. Larder, Novel mutation (V75T) in human immunodeficiency virus type 1 reverse transcriptase confers resistance to 2′,3′-didehydro-2′,3′- dideoxythymidine in cell culture., *Antimicrob Agents Chemother*, **38**, 1428–32, 1994, Medline: 94379807

Larder89 B. A. Larder, S. D. Kemp, Multiple mutations in HIV-1 reverse transcriptase confer high-level resistance to zidovudine (AZT)., *Science* , **246**, 1155–8, 1989, Medline: 90069587

Larder91 B. A. Larder, K. E. Coates, S. D. Kemp, Zidovudine-resistant human immunodeficiency virus selected by passage in cell culture., *J Virol*, **65**, 5232–6, 1991, Medline: 91374572

Larder92 B. A. Larder, 3′-Azido-3′-deoxythymidine resistance suppressed by a mutation conferring human immunodeficiency virus type 1 resistance to nonnucleoside reverse transcriptase inhibitors., *Antimicrob Agents Chemother*, **36**, 2664–9, 1992, Medline: 93128874

Larder95 B. A. Larder, S. D. Kemp, P. R. Harrigan, Potential mechanism for sustained antiretroviral efficacy of AZT-3TC combination therapy., *Science*, **269**, 696–9, 1995, Medline: 95350663

Larder99 Larder BA, Bloor S, Kemp SD, Hertogs K, Desmet RL, Miller V, Sturmer M, Staszewski S, Ren J, Stammers DK, Stuart DI, Pauwels R., A family of insertion mutations between codons 67 and 70 of human immunodeficiency virus type 1 reverse transcriptase confer multinucleoside analog resistance., *Antimicrobial Agents and Chemotherapy*, **43**, 1961–1967, 1999, Medline: 10428920

Lawrence99 J. Lawrence, J. Schapiro, M. Winters, J. Montoya, A. Zolopa, R. Pesano, B. Efron, D. Winslow, T. C. Merigan, Clinical resistance patterns and responses to two sequential protease inhibitor regimens in saquinavir and reverse transcriptase inhibitor- experienced persons, *J Infect Dis*, **179**, 1356–64, 99, Medline: 99246335

Li03 Li F, Goila-Gaur R, Salzwedel K, Kilgore NR, Reddick M, Matallana C, Castillo A, Zoumplis D, Martin DE, Orenstein JM, Allaway GP, Freed EO, Wild CT, PA-457: a potent HIV inhibitor that disrupts core condensation by targeting a late step in Gag processing, *Proc Natl Acad Sci U S A*, **100**(23), 13555–60, 2003, Medline: 14573704

Lin03 Lin PF, Blair W, Wang T, Spicer T, Guo Q, Zhou N, Gong YF, Wang HG, Rose R, Yamanaka G, Robinson B, Li CB, Fridell R, Deminie C, Demers G, Yang Z, Zadjura L, Meanwell N, Colonno R, A small molecule HIV-1 inhibitor that targets the HIV-1 envelope and inhibits CD4 receptor binding, *Proc Natl Acad Sci U S A*, **100**(19), 11013–11018, 2003, Medline: 12930892

Lin04 P F Lin, H T Ho, Y F Gong, I Dicker, N Zhou, L Fan, B McAuliffe, B Kimmel, B Nowicka-Sans, T Wang, J Kadow, G Yamanaka, Z Lin, N Meanwell, and R Colonno, Characterization of a Small Molecule HIV-1 Attachment Inhibitor BMS-488043: Virology, Resistance and Mechanism of Action, *Abstract 534 11th Conference on Retroviruses and Opportunistic Infections, San Francisco, CA*

Lin96 P. F. Lin, H. Samanta, C. M. Bechtold, C. A. Deminie, A. K. Patick, M. Alam, K. Riccardi, R. E. Rose, R. J. White, R. J. Colonno, Characterization of siamycin I, a human immunodeficiency virus fusion inhibitor., *Antimicrob Agents Chemother*, **40**, 133–8, 1996, Medline: 96379881

Lin99 Lin PF, Gonzalez CJ, Griffith B, Friedland G, Calvez V, Ferchal F, Schinazi RF, Shepp DH, Ashraf AB, Wainberg MA, Soriano V, Mellors JW, Colonno RJ, Stavudine resistance: an update on susceptibility following prolonged therapy, *Antivir Ther*, **4**(1), 21–8, 1999, Medline: 10682125

Lobato02 Lobato RL, Kim EY, Kagan RM, Merigan TC, Genotypic and phenotypic analysis of a novel 15-base insertion occurring between codons 69 and 70 of HIV type 1 reverse transcriptase, *AIDS Res Hum Retroviruse*, **18**(10), 733–6, 2002, Medline: 12167282

Lohrengel05 S. Lohrengel, F. Hermann, I. Hagmann, H. Oberwinkler, L. Scrivano, C. Hoffmann, D. von Laer, M.T. Dittmar, Determinants of human immunodeficiency virus type 1 resistance to membrane-anchored gp41-derived peptides, *J Virol*, **79**(16), 10237–46, 2005, Medline: 16051817

Maass93 G. Maass, U. Immendoerfer, B. Koenig, U. Leser, B. Mueller, R. Goody, E. Pfaff, Viral resistance to the thiazolo-iso-indolinones, a new class of nonnucleoside inhibitors of human immunodeficiency virus type 1 reverse transcriptase., *Antimicrob Agents Chemother*, **37**, 2612–7, 1993, Medline: 94153035

Maguire02 Maguire M, Shortino D, Klein A, Harris W, Manohitharajah V, Tisdale M, Elston R, Yeo J, Randall S, Xu F, Parker H, May J, Snowden W, Emergence of resistance to protease inhibitor amprenavir in human immunodeficiency virus type 1-infected patients: selection of four alternative viral protease genotypes and influence of viral susceptibility to coadministered reverse transcriptase nucleoside inhibitors, *Antimicrob Agents Chemother*, **46**(3), 731–8, 2002, Medline: 11850255

Marchand03 Marchand C, Johnson AA, Karki RG, Pais GC, Zhang X, Cowansage K, Patel TA, Nicklaus MC, Burke TR Jr, Pommier Y, Metal-dependent inhibition of HIV-1 integrase by beta-diketo acids and resistance of the soluble double-mutant (F185K/C280S), *Mol Pharmacol*, **64**(3), 600–9, 2003, Medline: 12920196

Masciari02 Masciari R, Cosco L, Diaco MC, Della DN, Ferraro T, Raimondi T, Ruperti B, Santandrea E, HIV-1: a case of RT67 deletion in a multi-treated non responder patient, *New Microbiol*, **25**(1), 83–8, 2002, Medline: 11837395

Matsuoka-Aizawa03 S. Matsuoka-Aizawa, H. Sato, A. Hachiya, K. Tsuchiya, Y. Takebe, H. Gatanaga, S. Kimura, S. Oka, Isolation and molecular characterization of a nelfinavir (NFV)-resistant human immunodeficiency virus type 1 that exhibits NFV-dependent enhancement of replication, *J Virol*, **77**(1), 318–27, 2003, Medline: 12477837

Mellors92 J. W. Mellors, G. E. Dutschman, G. J. Im, E. Tramontano, S. R. Winkler, Y. C. Cheng, *In vitro* selection and molecular characterization of human immunodeficiency virus-1 resistant to non-nucleoside inhibitors of reverse transcriptase [published erratum appears in Mol Pharmacol 1992 Jul;42(1):174], *Mol Pharmacol*, **41**, 446–51, 1992, Medline: 92186808

Mellors93 J. W. Mellors, G. J. Im, E. Tramontano, S. R. Winkler, D. J. Medina, G. E. Dutschman, H. Z. Bazmi, G. Piras, C. J. Gonzalez, Y. C. Cheng , A single conservative amino acid substitution in the reverse transcriptase of human immunodeficiency virus-1 confers resistance to (+)-(5S)-4,5,6,7-tetrahydro-5-methyl-6-(3-methyl-2-butenyl)imidazo[4,5, 1- jk][1,4]benzodiazepin-2(1H)-thione (TIBO R82150). , *Mol Pharmacol*, **43 192** , 11–6 246–53 , 1993 1993 1993, Medline: 93140700

Mellors95 J. W. Mellors, H. Z. Bazmi, R. F. Schinazi, B. M. Roy, Y. Hsiou, E. Arnold, J. Weir, D. L. Mayers, Novel mutations in reverse transcriptase of human immunodeficiency virus type 1 reduce susceptibility to foscarnet in laboratory and clinical isolates. , *Antimicrob Agents Chemother*, **39**, 1087–92, 1995, Medline: 95351747

Menzo04 Menzo S, Castagna A, Monachetti A, Hasson H, Danise A, Carini E, Bagnarelli P, Lazzarin A, Clementi M, Resistance and replicative capacity of HIV-1 strains selected *in vivo* by long-term enfuvirtide treatment, *New Microbiol*, **27 (2 Suppl 1)**, 51–61, 2004, Medline: 15646065

Mo03 Mo H, Lu L, Dekhtyar T, Stewart KD, Sun E, Kempf DJ, Molla A, Characterization of resistant HIV variants generated by *in vitro* passage with lopinavir/ritonavir, *Antiviral Res*, **59**(3), 173–80, 2003, Medline: 12927307

Mo05 Mo H, King MS, King K, Molla A, Brun S, Kempf DJ, Selection of Resistance in Protease Inhibitor- Experienced, Human Immunodeficiency Virus Type 1-Infected Subjects Mailing

Lopinavir- and Ritonavir-Based Therapy: Mutation Patterns and Baseline Correlates, *J Virol*, **79**(6), 3329–3338, 2005, Medline: 15731227

Mo96 H. Mo, M. Markowitz, P. Majer, S. K. Burt, S. V. Gulnik, L. I. Suvorov, J. W. Erickson, D. D. Ho, Design, synthesis, and resistance patterns of MP-134 and MP-167, two novel inhibitors of HIV type 1 protease., *AIDS Res Hum Retroviruses*, **12**, 55–61, 1996, Medline: 96423018

Moeremans95a M. Moeremans, M. De Raeymaeker, R. Van den Broeck, P. Stoffels, K. Andries, Genotypic analysis of HIV-1 isolates from patients receiving loviride alone or in combination with nucleoside reverse transcriptase inhibitor, *Fourth International Workshop on HIV Drug Resistance Sardinia, Italy*

Molla96 A. Molla, M. Korneyeva, Q. Gao, S. Vasavanonda, P. J. Schipper, H. M. Mo, M. Markowitz, T. Chernyavskiy, P. Niu, N. Lyons, A. Hsu, G. R. Granneman, D. D. Ho, C. A. Boucher, J. M. Leonard, D. W. Norbeck, D. J. Kempf, Ordered accumulation of mutations in HIV protease confers resistance to ritonavir., *Nat Med*, **2**, 760–6, 1996, Medline: 96266327

Montes02 Montes B, Segondy M., Prevalence of the mutational pattern E44D/A and/or V118I in the reverse transcriptase (RT) gene of HIV-1 in relation to treatment with nucleoside analogue RT inhibitors., *J Med Virol.*, **66**(3), 299–303, 2002, Medline: 11793380

Muzammil03 Muzammil S, Ross P, Freire E, A major role for a set of non-active site mutations in the development of HIV-1 protease drug resistance, *Biochemistry*, **42**(3), 631–8, 2003, Medline: 12534275

Nguyen94 M. H. Nguyen, R. F. Schinazi, C. Shi, N. M. Goudgaon, P. M. McKenna, J. W. Mellors, Resistance of human immunodeficiency virus type 1 to acyclic 6- phenylselenenyl- and 6-phenylthiopyrimidines., *Antimicrob Agents Chemother*, **38**, 2409–14, 1994, Medline: 95142586

Nijhuis07 M. Nijhuis, N.M. van Maarseveen, S. Lastere, P. Schipper, E. Coakley, B. Glass, M. Rovenska, D. de Jong, C. Chappey, I.W. Goedegebuure, G. Heilek-Snyder, D. Dulude, N. Cammack, L. Brakier-Gingras, J. Konvalinka, N. Parkin, H.G. Krausslich, F. Brun-Vezinet, C.A. Boucher, A Novel Substrate-Based HIV-1 Protease Inhibitor Drug Resistance Mechanism, *PLoS Med*, **4**(1), e36, 2007, Medline: 17227139

Nikolenko07 Nikolenko GN, Delviks-Frankenberry KA, Palmer S, Maldarelli F, Fivash MJ Jr, Coffin JM, Pathak VK., Mutations in the connection domain of HIV-1 reverse transcriptase increase 3′-azido-3′-deoxythymidine resistance, *PNAS*, **104**(1), 317–322, 2007, Medline: 17179211

Nitanda05 T. Nitanda, X. Wang, H. Kumamoto, K. Haraguchi, H. Tanaka, Y.C. Cheng, M. Baba, Anti-human immunodeficiency virus type 1 activity and resistance profile of 2′,3′-didehydro-3′-deoxy-4′-ethynylthymidine *in vitro*, *Antimicrob Agents Chemother*, **49**(8), 3355–60, 2005, Medline: 16048947

Nunberg91 J. H. Nunberg, W. A. Schleif, E. J. Boots, J. A. O'Brien, J. C. Quintero, J. M. Hoffman, E. A. Emini, M. E. Goldman, Viral resistance to human immunodeficiency virus type 1-specific pyridinone reverse transcriptase inhibitors., *J Virol*, **65**, 4887–92, 1991, Medline: 91333034

Ochoa de Echaguen05 de Echaguen AO, Arnedo M, Xercavins M, Martinez E, Roson B, Ribera E, Domingo P, Gonzalez A, Riera M, Llibre JM, Gatell JM, Dalmau D, for the Nevirapine, Efavirenz and Abacavir (NEFA) Resistance Substudy Team, Genotypic and phenotypic resistance patterns at virological failure in a simplification trial with nevirapine, efavirenz, or abacavir, *AIDS*, **19**(13), 1385–1391, 2005, Medline: 16103769

Olmsted96 R. A. Olmsted, D. E. Slade, L. A. Kopta, S. M. Poppe, T. J. Poel, S. W. Newport, K. B. Rank, C. Biles, R. A. Morge, T. J. Dueweke, Y. Yagi, D. L. Romero, R. C. Thomas, S. K. Sharma, W. G. Tarpley, (Alkylamino) piperidine bis(heteroaryl)piperizine analogs are potent, broad-spectrum non-nucleoside reverse transcriptase inhibitors of drug- resistant isolates of human immunodeficiency virus type 1 (HIV-1) and select for drug-resistant variants of HIV-1IIIB with reduced replication phenotypes., *J Virol*, **70**, 3698–705, 1996, Medline: 96211502

Olsen99 Olsen DB, Stahlhut MW, Rutkowski CA, Schock HB, vanOlden AL, Kuo LC, Non-active site changes elicit broad-based cross-resistance of the HIV-1 protease to inhibitors, *J Biol Chem*, **274**(34), 23699–701, 1999, Medline: 10446127

Otto93 M. J. Otto, S. Garber, D. L. Winslow, C. D. Reid, P. Aldrich, P. K. Jadhav, C. E. Patterson, C. N. Hodge, Y. S. Cheng, *In vitro* isolation and identification of human immunodeficiency virus

(HIV) variants with reduced sensitivity to C-2 symmetrical inhibitors of HIV type 1 protease., *Proc Natl Acad Sci U S A*, **90**, 7543–7, 1993, Medline: 93361483

Paolucci03 Paolucci S, Baldanti F, Tinelli M, Maga G, Gerna G, Detection of a new HIV-1 reverse transcriptase mutation (Q145M) conferring resistance to nucleoside and non-nucleoside inhibitors in a patient failing highly active antiretroviral therapy, *AIDS*, **17**(6), 924–7, 2003, Medline: 12660544

Paolucci04 S. Paolucci, F. Baldanti, G. Maga, R. Cancio, M. Zazzi, M. Zavattoni, A. Chiesa, S. Spadari, G. Gerna, Gln145Met/Leu changes in human immunodeficiency virus type 1 reverse transcriptase confer resistance to nucleoside and nonnucleoside analogs and impair virus replication, *Antimicrob Agents Chemother*, **48**(12), 4611–7, 2004, Medline: 15561833

Parkin03 Parkin NT, Chappey C, Petropoulos CJ, Improving lopinavir genotype algorithm through phenotype correlations: novel mutation patterns and amprenavir cross-resistance, *AIDS*, **17**(7), 955–61, 2003, Medline: 12700444

Partaledis95 Partaledis JA, Yamaguchi K, Tisdale M, Blair EE, Falcione C, Maschera B, Myers RE, Pazhanisamy S, Futer O, Cullinan AB, Stuver CM, Byrn RA, Livingston DJ., *In vitro* selection and characterization of human immunodeficiency viru type 1 (HIV-1) isolates with reduced sensitivity to hydroxyethylamino sulfonamide inhibitors of HIV-1 aspartyl protease., *J Virol*, **69**(9), 5228–5235, 1995, Medline: 95363927

Patick95 A. K. Patick, R. Rose, J. Greytok, C. M. Bechtold, M. A. Hermsmeier, P. T. Chen, J. C. Barrish, R. Zahler, R. J. Colonno, P. F. Lin, Characterization of a human immunodeficiency virus type 1 variant with reduced sensitivity to an aminodiol protease inhibitor., *J Virol*, **69**, 2148–52, 1995, Medline: 95190985

Patick96 A. K. Patick, H. Mo, M. Markowitz, K. Appelt, B. Wu, L. Musick, V. Kalish, S. Kaldor, S. Reich, D. Ho, S. Webber, Antiviral and resistance studies of AG1343, an orally bioavailable inhibitor of human immunodeficiency virus protease [published erratum appears in Antimicrob Agents Chemother 1996 Jun;40(6):1575], *Antimicrob Agents Chemother*, **40**, 292–7, 1996, Medline: 96431786

Patick98 Patick AK, Duran M, Cao Y, Shugarts D, Keller MR, Mazabel E, Knowles M, Chapman S, Kuritzkes DR, Markowitz M, Genotypic and phenotypic characterization of human immunodeficiency virus type 1 variants isolated from patients treated with the protease inhibitor nelfinavir, *Antimicrob Agents Chemother*, **42**(10), 2637–44, 1998, Medline: 98443459

Pelemans97 H. Pelemans, R. Esnouf, A. Dunkler, M.A. Parniak, A-M. Vandamme, A. Karlsson, E. De Clercq, J-P. Kleim, J. Balzarini. , Characteristics of the Pro225His mutation in human immunodeficiency virus type 1 (HIV-1) reverse transcriptase that appears under selective pressure of dose-escalating quinoxaline treatment of HIV-1., *J Virol*, **71**(11), 8195–8203, 1997, Medline: 98001335

Prasad91 V. R. Prasad, I. Lowy, T. de los Santos, L. Chiang, S. P. Goff, Isolation and characterization of a dideoxyguanosine triphosphate- resistant mutant of human immunodeficiency virus reverse transcriptase., *Proc Natl Acad Sci U S A*, **88**, 11363–7, 1991, Medline: 92107950

Ranise03 Ranise A, Spallarossa A, Schenone S, Bruno O, Bondavalli F, Vargiu L, Marceddu T, Mura M, La Colla P, Pani A, Design, synthesis, SAR, and molecular modeling studies of acylthiocarbamates: a novel series of potent non-nucleoside HIV-1 reverse transcriptase inhibitors structurally related to phenethylthiazolylthiourea derivatives, *J Med Chem*, **46**(5), 768–81, 2003, Medline: 12593657

Ray05 A.S. Ray, B.I. Hernandez-Santiago, J.S. Mathew, E. Murakami, C. Bozeman, M.Y. Xie, G.E. Dutschman, E. Gullen, Z. Yang, S. Hurwitz, Y.C. Cheng, C.K. Chu, H. McClure, R.F. Schinazi, K.S. Anderson, Mechanism of anti-human immunodeficiency virus activity of beta-D-6-cyclopropylamino-2′,3′-didehydro-2′,3′-dideoxyguanosine, *Antimicrob Agents Chemother*, **49**(5), 1994–2001, 2005, Medline: 15855524

Resch05 W. Resch, N. Parkin, T. Watkins, J. Harris, R. Swanstrom, Evolution of human immunodeficiency virus type 1 protease genotypes and phenotypes *in vivo* under selective pressure of the protease inhibitor ritonavir, *J Virol*, **79**(16), 10638–49, 2005, Medline: 16051856

Richard00 Richard N, Salomon H, Rando R, Mansour T, Bowlin TL, Wainberg MA., Selection and characterization of human immunodeficiency virus type 1 variants resistant to the (+) and (-) enantiomers of 2′-deoxy-3′-oxa-4′-thio-5-fluorocytidine., *Antimicrobial Agents and Chemotherapy*, **44**, 1127–1131, 2000, Medline: 10770740

Richard99 Richard N, Quan Y, Salomon H, Hsu M, Bedard J, Harrigan PR, Rando R, Mansour T, Bowlin TL, Wainberg MA, Selection and characterization of HIV-1 variants resistant to the (+) and (-) enantiomers of 2′-deoxy-3′-oxa-4′-thiocytidine (dOTC), *Antivir Ther*, **4**(3), 171–7, 1999, Medline: 12731757

Richman91 D. Richman, C. K. Shih, I. Lowy, J. Rose, P. Prodanovich, S. Goff, J. Griffin, Human immunodeficiency virus type 1 mutants resistant to nonnucleoside inhibitors of reverse transcriptase arise in tissue culture., *Proc Natl Acad Sci U S A*, **88**, 11241–5, 1991, Medline: 92107925

Richman93 D. D. Richman, Resistance of clinical isolates of human immunodeficiency virus to antiretroviral agents., *Antimicrob Agents Chemother*, **37**, 1207–13, 1993, Medline: 93319246

Richman94 D. D. Richman, D. Havlir, J. Corbeil, D. Looney, C. Ignacio, S. A. Spector, J. Sullivan, S. Cheeseman, K. Barringer, D. Pauletti, et al, Nevirapine resistance mutations of human immunodeficiency virus type 1 selected during therapy., *J Virol*, **68**, 1660–6, 1994, Medline: 94149857

Rimsky98 Rimsky LT, Shugars DC, Matthews TJ., Determinants of human immunodeficiency virus type 1 resistance to gp41-derived inhibitor peptides., *J Virol*, **72**(2), 986–993, 1998, Medline: 98105736

Rose94 B. Rose, J. Greytok, C. Bechtold, M. Alam, B. Terry, Gong Y.F. DeK. Vore, A. Patrick, R. Colono, Lin P, Combination therapy with two protease inhibitors as an approach to antiviral therapy, *Third International Workshop on HIV Drug Resistance Kauai, HI, USA*

Rusconi00 Rusconi S, La Seta Catamancio S, Citterio P, Kurtagic S, Violin M, Balotta C, Moroni M, Galli M, d'Arminio-Monforte A., Susceptibility to PNU-140690 (Tipranavir) of human immunodeficiency virus type 1 isolates derived from patients with multidrug resistance to other protease inhibitors., *Antimicrobial Agents and Chemotherapy*, **44**, 1328–1332, 2000, Medline: 10770770

Saag93 M. S. Saag, E. A. Emini, O. L. Laskin, J. Douglas, W. I. Lapidus, W. A. Schleif, R. J. Whitley, C. Hildebrand, V. W. Byrnes, J. C. Kappes, et al, A short-term clinical evaluation of L-697,661, a non-nucleoside inhibitor of HIV-1 reverse transcriptase. L-697,661 Working Group., *N Engl J Med*, **329**, 1065–72, 1993, Medline: 93382466

Schinazi93 R. F. Schinazi, R. M. Lloyd, M. H. Nguyen, D. L. Cannon, A. McMillan, N. Ilksoy, C. K. Chu, D. C. Liotta, H. Z. Bazmi, J. W. Mellors, Characterization of human immunodeficiency viruses resistant to oxathiolane-cytosine nucleosides., *Antimicrob Agents Chemother*, **37**, 875–81, 1993, Medline: 93263665

Schmit98 J. C. Schmit, K. Van Laethem, L. Ruiz, P. Hermans, S. Sprecher, A. Sonnerborg, M. Leal, T. Harrer, B. Clotet, V. Arendt, E. Lissen, M. Witvrouw, J. Desmyter, E. De Clercq, A. M. Vandamme, Multiple dideoxynucleoside analogue-resistant (MddNR) HIV-1 strains isolated from patients from different European countries, *AIDS*, **12**, 2007–15, 98, Medline: 99030034

Schols98 Schols D, Este JA, Cabrera C, Cabrera C, De Clercq E., T-cell-line-tropic human immunodeficiency virus type 1 that is made resistant to stromal cell derived factor 1a contains mutations in envelope gp120 but does not show a switch in coreceptor use., *J Virol*, **72**(5), 4032–4037, 1998, Medline: 98216769

Seki95 M. Seki, Y. Sadakata, S. Yuasa, M. Baba , Isolation and characterization of human immunodeficiency virus type-1 mutants resistant to the non-nucleoside reverse transcriptase inhibitor MKC-442, *Antiviral Chemistry and Chemotherapy*, **6**, 73–9

Sevigny06 G. Sevigny, B. Stranix, B. Tian, A. Dubois, G. Sauve, C. Petropoulos, Y. Lie, N. Hellmann, B. Conway, J. Yelle, Antiviral activity and cross-resistance profile of P-1946, a novel human immunodeficiency virus type 1 protease inhibitor, *Antiviral Res*, **70**(2), 17–20, 2006, Medline: 16473417

Shaw94 G. Shaw, X. Wei, Johnson V, M. Taylor, J. Decker, M. Kilby, J. Lifson, B. Hahn, Saag M, Nucleotide sequence analysis of HIV-1 RNA and DNA from plasma and PBMCs of patients treated with ZDV, ddI and nevirapine: rapid turnover and resistance development *in vivo*, *Third International Workshop on HIV Drug Resistance Kauai, HI, USA*

Shirasaka95 T. Shirasaka, M. F. Kavlick, T. Ueno, W. Y. Gao, E. Kojima, M. L. Alcaide, S. Chokekijchai, B. M. Roy, E. Arnold, R. Yarchoan, et al, Emergence of human immunodeficiency virus type 1 variants with resistance to multiple dideoxynucleosides in patients receiving therapy with dideoxynucleosides., *Proc Natl Acad Sci U S A*, **92**, 2398–402, 1995, Medline: 95199357

Smidt97 M. L. Smidt, K. E. Potts, S. P. Tucker, L. Blystone, T. R. Stiebel, W. C. Stallings, J. J. McDonald, D. Pillay, D. D. Richman, M. L. Bryant, A mutation in human immunodeficiency virus type 1 protease at position 88, located outside the active site, confers resistance to the hydroxyethylurea inhibitor SC-55389A., *Antimicrob Agents Chemother*, **41**, 515–22, 1997, Medline: 97209043

Smidt97 Smidt ML, Potts KE, Tucker SP, Blystone L, Stiebel TR Jr, Stallings WC, McDonald JJ, Pillay D, Richman DD, Bryant ML, A mutation in human immunodeficiency virus type 1 protease at position 88, located outside the active site, confers resistance to the hydroxyethylurea inhibitor SC-55389A, *Antimicrob Agents Chemother*, **41**(3), 515–22, 1997, Medline: 9055985

Smith99 Smith RA, Klarmann GJ, Stray KM, von Schwedler UK, Schinazi RF, Preston BD, North TW., A new point mutation (P157S) in the reverse transcriptase of human immunodeficiency virus type 1 confers low-level resistance to (-)-beta-2′,3′-dideoxy-3′-thiacytidine., *Antimicrobial Agents and Chemotherapy*, **43**, 2077–2080, 1999, Medline: 10428942

Staszewski96 S.Staszewski, V. Miller, A. Kober, R. Colebunders, B. Vandercam, J. Delescluse, N. Clumeck, F. VanWanzeele, M. De Brabander, J De Cree, M. Moeremans, K. Andries, C. Boucher, P. Stoffels, P.A.J. Janssen, Evaluation of the efficacy and tolerance of RO18893, RO89439 (loviride) and placebo in asymptomatic HIV-1-infected patients, *Antiviral Therapy*, **42–50**

StClair91 M. H. St Clair, J. L. Martin, G. Tudor-Williams, M. C. Bach, C. L. Vavro, D. M. King, P. Kellam, S. D. Kemp, B. A. Larder, Resistance to ddI and sensitivity to AZT induced by a mutation in HIV-1 reverse transcriptase., *Science*, **253**, 1557–9, 1991, Medline: 91376665

Svicher05 V. Svicher, F. Ceccherini-Silberstein, F. Erba, M. Santoro, C. Gori, M.C. Bellocchi, S. Giannella, M.P. Trotta, A. Monforte, A. Antinori, C.F. Perno, Novel human immunodeficiency virus type 1 protease mutations potentially involved in resistance to protease inhibitors, *Antimicrob Agents Chemother*, **49**(5), 2015–25, 2005, Medline: 15855527

Svicher06 Svicher V, Sing T, Santoro MM, Forbici F, Rodriguez-Barrios F, Bertoli A, Beerenwinkel N, Bellocchi MC, Gago F, d'Arminio Monforte A, Antinori A, Lengauer T, Ceccherini-Silberstein F, Perno CF., Involvement of novel human immunodeficiency virus type 1 reverse transcriptase mutations in the regulation of resistance to nucleoside inhibitors, *Journal of Virology*, **80**(14), 7186–7198, 2006, Medline: 16809324

Tachedjian95 G. Tachedjian, D. J. Hooker, A. D. Gurusinghe, H. Bazmi, N. J. Deacon, J. Mellors, C. Birch, J. Mills, Characterisation of foscarnet-resistant strains of human immunodeficiency virus type 1., *Virology*, **212**, 58–68, 1995, Medline: 95407116

Tanaka97 M. Tanaka, R. V. Srinivas, T. Ueno, M. F. Kavlick, F. K. Hui, A. Fridland, J. S. Driscoll, H. Mitsuya, *In vitro* induction of human immunodeficiency virus type 1 variants resistant to 2′-beta-Fluoro-2′,3′-dideoxyadenosine., *Antimicrob Agents Chemother*, **41**, 1313–8, 1997, Medline: 97316916

Taylor00 Taylor DL, Ahmed PS, Tyms AS, Wood LJ, Kelly LA, Chambers P, Clarke J, Bedard J, Bowlin TL, Rando RF, Drug resistance and drug combination features of the human immunodeficiency virus inhibitor, BCH-10652 [(+/-)-2′-deoxy-3′-oxa-4′-thiocytidine, dOTC], *Antivir Chem Chemother*, **11**(4), 291–301, 2000, Medline: 10950391

Tisdale93 M. Tisdale, S. D. Kemp, N. R. Parry, B. A. Larder, Rapid *in vitro* selection of human immunodeficiency virus type 1 resistant to 3′-thiacytidine inhibitors due to a mutation in the YMDD region of reverse transcriptase., *Proc Natl Acad Sci U S A*, **90**, 5653–6, 1993, Medline: 93296196

Tisdale95 Tisdale M, Myers RE, Maschera B, Parry NR, Oliver NM, Blair ED, Cross-resistance analysis of human immunodeficiency virus type 1 variants individually selected for resistance to five different protease inhibitors, *Antimicrob Agents Chemother*, **39**(8), 1704–10, 1995, Medline: 7486905

Tisdale97 M. Tisdale, T. Alnadaf, D. Cousens, Combination of mutations in human immunodeficiency virus type 1 reverse transcriptase required for resistance to the carbocyclic nucleoside 1592U89., *Antimicrob Agents Chemother*, **41**, 1094–8, 1997, Medline: 97291261

Trkola02 Trkola A, Kuhmann SE, Strizki JM, Maxwell E, Ketas T, Morgan T, Pugach P, Xu S, Wojcik L, Tagat J, Palani A, Shapiro S, Clader JW, McCombie S, Reyes GR, Baroudy BM, Moore JP, HIV-1 escape from a small molecule, CCR5-specific entry inhibitor does not involve CXCR4 use, *Proc Natl Acad Sci U S A*, **99**(1), 395–400, 2002, Medline: 11782552

Vandamme94 A. M. Vandamme, Z. Debyser, R. Pauwels, K. De Vreese, P. Goubau, M. Youle, B. Gazzard, P. A. Stoffels, G. F. Cauwenbergh, J. Anne, et al, Characterization of HIV-1 strains isolated from patients treated with TIBO R82913., *AIDS Res Hum Retroviruses*, **10**, 39–46, 1994, Medline: 94235372

Vandamme94a A.-M. Vandamme , Polymerase chain reaction (PCR) as a diagnostic tool in HIV infection, *Verhandelingen van de Koninklijke Academie voor Geneeskunde van Belgie*, **56**, 231–265

VanLaethem00 Van Laethem K, Schmit JC, Pelemans H, Balzarini J, Witvrouw M, Perez-Perez MJ, Camarasa MJ, Esnouf RM, Aquaro S, Cenci A, Perno CF, Hermans P, Sprecher S, Ruiz L, Clotet B, Van Wijngaerden E, Van Ranst M, Desmyter J, De Clercq E, Vandamme AM., Presence of 2′,5′-Bis-O-(tert-butyldimethylsilyl)-3′-spiro-5”-(4”-amino-1”,2”-oxathiole-2”,2”-dioxide) (TSAO)-resistant virus strains in TSAO-inexperienced HIV patients., *AIDS Research and Human Retroviruses*, **16**, 825–833, 2000, Medline: 10875608

VanRompay96 K. K. Van Rompay, J. M. Cherrington, M. L. Marthas, C. J. Berardi, A. S. Mulato, A. Spinner, R. P. Tarara, D. R. Canfield, S. Telm, N. Bischofberger, N. C. Pedersen, 9-[2-(Phosphonomethoxy)propyl]adenine therapy of established simian immunodeficiency virus infection in infant rhesus macaques., *Antimicrob Agents Chemother*, **40**, 2586–91, 1996, Medline: 97070544

VanRompay97 Van Rompay KK, Greenier JL, Marthas ML, Otsyula MG, Tarara RP, Miller CJ, Pedersen NC, A zidovudine-resistant simian immunodeficiency virus mutant with a Q151M mutation in reverse transcriptase causes AIDS in newborn macaques, *Antimicrob Agents Chemother*, **41**, 278–83, 1997, Medline: 97173274

VanRompay97a K. Van Rompay, J. Cherrington, M. Marthas, E. Agatep, Z. Dehqanzada, P. Lamy, C. Berardi, N. Bischofberger, N. Pedersen, Therapeutic efficacy of PMPA treatment for infant macaques infected with PMPA-resistant simian immunodeficiency virus, *Sixth International Workshop on HIV Drug Resistance St. Petersburg, FL, USA*

Vasudevachari92 Vasudevachari MB, Battista C, Lane HC, Psallidopoulos MC, Zhao B, Cook J, Palmer JR, Romero DL, Tarpley WG, Salzman NP, Prevention of the spread of HIV-1 infection with nonnucleoside reverse transcriptase inhibitors, *Virology*, **190**(1), 269–77 , 1992, Medline: 92410603

Vasudevachari96 M. B. Vasudevachari, Y. M. Zhang, H. Imamichi, T. Imamichi, J. Falloon, N. P. Salzman, Emergence of protease inhibitor resistance mutations in human immunodeficiency virus type 1 isolates from patients and rapid screening procedure for their detection., *Antimicrob Agents Chemother*, **40**, 2535–41, 1996, Medline: 97070533

Vingerhoets04 J Vingerhoets, I De Baere, H Azijn, T Van den Bulcke, P McKenna, T Pattery, R Pauwels, and M-P de BÈthune, Antiviral Activity of TMC125 against a Panel of Site-directed Mutants Encompassing Mutations Observed *in vitro* and *in vivo*, *Abstract 621 11th Conference on Retroviruses and Opportunistic Infections, San Francisco, CA*

Vrang93 L. Vrang, C. Rydergard, C. Ahgren, P. Engelhardt, M. Hogberg, N.G. Johansson, J. Kangasmetsa, P. Lind, R. Noreen, C. Sahlberg, X. X. Zhou, A. Karlsson, C. Lopez, J.M. Morin, R.J. Ternansky, F.W. Bell, C.L. Jordan, M.D. Kinnick, J.A. Palkowitz, C.A. Parrish, P. Pranc, R.T. Vasileff, S.J. West, B.Oberg, Comparative rates of *in vitro* resistance development of HIV-1 to non-nucleoside analog RT inhibitors, *Antiviral Res*, **20 (S1)**, 77

Waheed06 A.A. Waheed, S.D. Ablan, M.K. Mankowski, J.E. Cummins, R.G. Ptak, C.P. Schaffner, E.O. Freed, Inhibition of HIV-1 replication by amphotericin B methyl ester: selection for resistant variants, *J Biol Chem*, **281**(39), 28699–711, 2006, Medline: 16882663

Wainberg99 Wainberg MA, Miller MD, Quan Y, Salomon H, Mulato AS, Lamy PD, Margot NA, Anton KE, Cherrington JM, *In vitro* selection and characterization of HIV-1 with reduced susceptibility to PMPA, *Antivir Ther*, **4**(2), 87–94, 1999, Medline: 10682153

Watkins03 Watkins T, Resch W, Irlbeck D, Swanstrom R, Selection of high-level resistance to human immunodeficiency virus type 1 protease inhibitors, *Antimicrob Agents Chemother*, **47**(2), 759–69, 2003, Medline: 12543689

Wei02 Wei X, Decker JM, Liu H, Zhang Z, Arani RB, Kilby JM, Saag MS, Wu X, Shaw GM, Kappes JC, Emergence of resistant human immunodeficiency virus type 1 in patients receiving fusion inhibitor (T-20) monotherapy, *Antimicrob Agents Chemother*, **46**(6), 1896–905, 2002, Medline: 12019106

Weinheimer04 S. Weinheimer, L. Dicotto, J. Friborg, R. Colonno, Recombinant HIV Gag-Pol Proteins Display the Unique I150L Phenotype of Selective Atazanavir Resistance and Increased Susceptibility to Other PIs, *Abstract 625 11th Conference on Retroviruses and Opportunistic Infections, San Francisco, CA*

Winslow96 D. L. Winslow, S. Garber, C. Reid, H. Scarnati, D. Baker, M. M. Rayner, E. D. Anton, Selection conditions affect the evolution of specific mutations in the reverse transcriptase gene associated with resistance to DMP 266., *AIDS*, **10**, 1205–9 , 1996, Medline: 97037953

Winters98 M. A. Winters, K. L. Coolley, Y. A. Girard, D. J. Levee, H. Hamdan, R. W. Shafer, D. A. Katzenstein, T. C. Merigan, A 6-basepair insert in the reverse transcriptase gene of human immunodeficiency virus type 1 confers resistance to multiple nucleoside inhibitors, *J Clin Invest*, **102**, 1769–75, 98, Medline: 99038179

Winters98a Winters MA, Schapiro JM, Lawrence J, Merigan TC, Human immunodeficiency virus type 1 protease genotypes and *in vitro* protease inhibitor susceptibilities of isolates from individuals who were switched to other protease inhibitors after long-term saquinavir treatment, *J Virol*, **72**(6), 5303–6, 1998, Medline: 9573309

Wirden05 Wirden M, Marcelin AG, Simon A, Kirstetter M, Tubiana R, Valantin MA, Paris L, Bonmarchand M, Conan F, Kalkias L, Katlama C, Calvez V, Resistance mutations before and after tenofovir regimen failure in HIV-1 infected patients, *J Med Virol*, **76**(3), 297–301, 2005, Medline: 15902696

Witvrouw05 M. Witvrouw, V. Fikkert, A. Hantson, C. Pannecouque, B.R. O'keefe, J. McMahon, L. Stamatatos, E. de Clercq, A. Bolmstedt, Resistance of human immunodeficiency virus type 1 to the high-mannose binding agents cyanovirin N and concanavalin A, *J Virol*, **79**(12), 7777–84, 2005, Medline: 15919930

Witvrouw98 Witvrouw M, Arranz ME, Pannecouque C, Declercq R, Jonckheere H, Schmit J-C, Vandamme A-M, Diaz JA, Ingate ST, Desmyter J, Esnouf R, Van Meervelt L, Vega S, Balzarini J, De Clercq E., 1,1,3-Trioxo-2H,4H-thieno[3,4-e][1,2,4]thiadiazine (TDD) derivatives: a new class of nonnucleoside human immunodeficiency virus type 1 (HIV-1) reverse transcriptase inhibitors with anti-HIV-1 activity., *Antimicrob Agents Chemother*, **42**(3), 618–623, 1998, Medline: 98177121

Yoshimura99 K. Yoshimura, R. Kato, K. Yusa, M. F. Kavlick, V. Maroun, A. Nguyen, T. Mimoto, T. Ueno, M. Shintani, J. Falloon, H. Masur, H. Hayashi, J. Erickson, H. Mitsuya, JE-2147: a dipeptide protease inhibitor (PI) that potently inhibits multi-PI-resistant HIV-1, *Proc Natl Acad Sci U S A*, **96**, 8675–80, 99, Medline: 99342077

Yoshimura99a Yoshimura K, Feldman R, Kodama E, Kavlick MF, Qiu YL, Zemlicka J, Mitsuya H., *In vitro* induction of human immunodeficiency virus type 1 variants resistant to phosphoralaninate prodrugs of Z-methylenecyclopropane nucleoside analogues., *Antimicrobial Agents and Chemotherapy*, **43**, 2479–2483, 1999, Medline: 10508028

Young95 S. D. Young, S. F. Britcher, L. O. Tran, L. S. Payne, W. C. Lumma, T. A. Lyle, J. R. Huff, P. S. Anderson, D. B. Olsen, S. S. Carroll, et al, L-743, 726 (DMP-266): a novel, highly potent nonnucleoside inhibitor of the human immunodeficiency virus type 1 reverse transcriptase., *Antimicrob Agents Chemother*, **39**, 2602–5, 1995, Medline: 96161265

Zhang06 Zhang Z, Walker M, Xu W, Shim JH, Girardet JL, Hamatake RK, Hong Z, Novel nonnucleoside inhibitors that select nucleoside inhibitor resistance mutations in human immunodeficiency virus type 1 reverse transcriptase, *Antimicrobial Agents Chemotherapy*, **50**(8), 2772–2781, 2006, Medline: 16870771

Zhang06b Zhang Z, Xu W, Koh YH, Shim JH, Girardet JL, Yeh LT, Hamatake, RK, Hong Z, A Novel nonnucleoside analogue that inhibits human immunodeficiency virus type 1 isolates resistant to

current nonnucleoside reverse transcriptase inhibitors, *Antimicrobial Agents Chemotherapy*, **51**(2), 429–437, 2007, Medline: 17116677

Zhang94 D. Zhang, A. M. Caliendo, J. J. Eron, K. M. DeVore, J. C. Kaplan, M. S. Hirsch, R. T. D'Aquila, Resistance to 2′,3′-dideoxycytidine conferred by a mutation in codon 65 of the human immunodeficiency virus type 1 reverse transcriptase., *Antimicrob Agents Chemother*, **38**, 282–7, 1994, Medline: 94250001

Zhang95 H. Zhang, L. Vrang, K. Backbro, P. Lind, C. Sahlberg, T. Unge, B. Oberg, Inhibition of human immunodeficiency virus type 1 wild-type and mutant reverse transcriptases by the phenyl ethyl thiazolyl thiourea derivatives trovirdine and MSC-127., *Antiviral Res*, **28**, 331–42, 1995, Medline: 96264013

Ziermann00 Ziermann R, Limoli K, Das K, Arnold E, Petropoulos CJ, Parkin NT., A mutation in human immunodeficiency virus type 1 protease, N88S, that causes *in vitro* hypersensitivity to amprenavir., *Journal of Virology*, **74**, 4414–4419, 2000, Medline: 10756056