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 early 2001, lists 200 HIV-1 mutations, of which 56 occur in protease, 1 in integrase, 107 in reverse transcriptase, and 36 in envelope. Although the tables are quite comprehensive, the reader should be reminded that the mutations described are predominantly found in clade B virus and not in other HIV genotypes. The revised table also includes drug resistance mutations that have been identified for SIV and FIV.

In the table the phrase "Enzyme resist" refers to inhibition assays done just with a mutated enzyme. Instead of introducing the mutations into a virus and testing the susceptibility of the mutant virus to a drug, researchers introduce the mutation(s) into the enzyme and determine their effect by running enzyme activity assays. This type of susceptibility testing does not take into account changes in other viral proteins (like Gag) that would also help confer resistance, which is the reason for distinguishing enzyme resistance from whole virus resistance. In the "Amino Acid Change" column a + means amino acids have been inserted into the sequence, while a Δ indicates a deletion. In the "Class of Drug" column the phrase "Multiple Nucleoside" refers to resistance to combinations of nucleoside RTIs.

All of the information contained in these printed tables and other useful tools are available at our new Web site: `http://resdb.lanl.gov/Resist_DB`.

ACKNOWLEDGMENTS

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Contents

Mutations in HIV RT that confer drug resistance, ordered by position.

Amino Acid Change			Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
M	41	L	ATG to TTG/CTG	Nucleoside RTI	AZT	?	Y	4		M41L/T215Y: 60–70-fold; M41L/ D67N/K70R/T215Y: 180-fold.	Larder89, Larder91, Kellam92
E	44	D	GAA to GAC	HIV-1 Specific RTI	3TC + AZT	N	Y	1.0		Confers moderate levels of resistance to 3TC (4 to 50-fold) when present in an AZT-resistant genetic background without diminishing AZT resistance.	Hertogs00
A	62	V	GCC to GTC	Multiple Nucleoside		N	Y	Nil		A62V alone has no effect, but in combination with mutations at 75, 77, 116, 151 causes multi NRTI resistance.	Iversen96, Shirasaka95
K	65	R	AAA to AGA	Nucleoside RTI	1592U89	Y	N	3		K65R/L74V: 3.6-fold; K65R/M184V: 7-fold; K65R/L74V/M184V: 10.2-fold	Tisdale97
K	65	R	AAA to AGA	Nucleoside RTI	ddC	Y	Y	4–10			Zhang94, Gu94
K	65	R	AAA to AGA	Nucleoside RTI	ddI	Y	Y	4–10	ddC; PMEA; 3TC5	Infrequently observed in patients receiving ddI or ddC	Zhang94
K	65	R	AAA to AGA	Nucleoside RTI	dOTC (BCH-10652)	Y	?			K65R/M184V: 4.2-fold.	Rando99
K	65	R	AAA to AGA	Nucleoside RTI	DXG	Y	?	8	other dioxolane derivatives	Reverses AZT resistance in D67N/ K70R/T215Y/K219Q background	Mellors96
K	65	R	AAA to AGA	Nucleoside RTI	PMEA	Y	N	10–25			Gu95, Foli96
K	65	R	AAA to AGA	Nucleoside RTI	PMPA	Y	?	3.5			Cherrington97
Δ	67		deletion	Multiple Nucleoside	AZT + ddI	N	Y	AZT: 1.2, ddI: 3.8, ddC:18.0		Δ67/T69G/AZT resistance mutations: 445-fold AZT resistance. When NNRTI resistance mutations are also added, AZT resistance increases to 1,813-fold.	Imamichi00a, Imamichi00b, Imamichi01

Mutations in HIV RT that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
D 67 E	GAC to GAG	Multiple Nucleoside		N	Y				Larder99
D 67 G	GAC to GGC	Multiple Nucleoside		N	Y				Larder99
D 67 G	GAC to GAG	HIV-1 Specific RTI	(+)dOTFC	Y	?	4.5	(-)dOTFC: 5.2-fold		Richard00
D 67 N	GAC to AAC	Nucleoside RTI	AZT	Y	Y			D67N/K70R/T215Y/K219Q: 120-fold; M41L/D67N/K70R/T215Y: 180-fold.	Larder89, Larder91, Kellam92
D 67 S		Multiple Nucleoside		N	Y				Larder99
S 68 G	AGT to GGT	Multiple Nucleoside		?	Y			Frequently associated with other multi-ddN resistance mutations V75I, F77L, F116Y and Q151M.	Schmit98
S 68 N	AGT to AAT	Multiple Nucleoside		N	Y				Larder99
S 68 N	AGT to AAT	Multiple Nucleoside		N	Y				Larder99
S 68 S + GGG		Multiple Nucleoside		N	Y				Larder99
S 68 S + SS		Multiple Nucleoside		N	Y				Larder99
S 68 S + SSG		Multiple Nucleoside		N	Y				Larder99
S 68 S + ST		Multiple Nucleoside		N	Y				Larder99
S 68 S + SV		Multiple Nucleoside		N	Y				Larder99
S 68 Y	AGT to TAT	Multiple Nucleoside		N	Y				Larder99
T 69 A	ACT to GCT	Multiple Nucleoside	3TC + d4T	?	Y			Seen in one patient on 3TC + d4T combination therapy.	Lawrence99
T 69 A + SG	ACT to GCT + AGT GGT	Multiple Nucleoside		?	Y	Confers >4-fold resistance to: AZT, ddI, ddC, 3TC and PMEA.		Seen in heavily treated patients.	Winters98
T 69 D	ACT to GAT	Multiple Nucleoside	AZT + 3TC	?	Y			Seen in one patient on AZT + 3TC combination therapy.	Lawrence99
T 69 D	ACT to GAT	Nucleoside RTI	ddC	N	Y	5			Fitzgibbon92
T 69 G	ACT to GGT	HIV-1 Specific RTI	AZT + ddI	N	Y	AZT: 1.5, ddC: 11.0, ddI: 10.0		Δ67/T69G/AZT resistance mutations: 445-fold AZT resistance. When NNRTI resistance mutations are also added, AZT resistance increases to 1,813-fold.	Imamichi00a, Imamichi00b, Imamichi01

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Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
T 69 N	ACT to AAT	Multiple Nucleoside	3TC + d4T	?	Y			Seen in two patients on 3TC + d4T combination therapy.	Lawrence99
T 69 S + RA	ACT to AGT + AGA GCA	Multiple Nucleoside		?	Y	Confers >4-fold resistance to: AZT, ddI, ddC, 3TC and PMEA.		Seen in heavily treated patients.	Winters98
T 69 S + AG		Multiple Nucleoside		N	Y				Larder99
T 69 S + EA	ACT to AGT + AGA GCA	Multiple Nucleoside		?	Y	Confers >4-fold resistance to: AZT, ddI, ddC, 3TC and PMEA.		Seen in heavily treated patients.	Winters98
T 69 S + EE		Multiple Nucleoside		N	Y				Larder99
T 69 S + SA	ACT to AGC + AGC GCT	Multiple Nucleoside		?	Y	Confers >4-fold resistance to: AZT, ddI, ddC and PMEA.		Seen in heavily treated patients.	Winters98
T 69 S + SA	ACT to TCT + AGT GCT	Multiple Nucleoside		?	Y	Confers >4-fold resistance to: AZT, ddI, ddC and PMEA.		Seen in heavily treated patients.	Winters98
T 69 S + SA	ACT to AGT + AGC GCT	Multiple Nucleoside		?	Y	Confers >4-fold resistance to: AZT, ddI, ddC, 3TC and PMEA.		Seen in heavily treated patients.	Winters98
T 69 S + SG	ACT to AGT + AGT GGT	Multiple Nucleoside		?	Y	Confers >4-fold resistance to: AZT, ddI, ddC and PMEA.		Seen in heavily treated patients.	Winters98

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Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
T 69 S + SG	ACT to AGT + AGT GGT	HIV-1 Specific RTI	ddI + hydroxyurea	?	Y			Seen in one patient.	DeAntoni97
T 69 S + SS	ACT to TCT + AGC TCT	Multiple Nucleoside		?	Y	Confers >4-fold resistance to: AZT, ddI, ddC, 3TC and PMEA.		Seen in heavily treated patients.	Winters98
T 69 S + SS	ACT to TCT + AGT TCT	Multiple Nucleoside		?	Y	Confers >4-fold resistance to: AZT, ddI, ddC, 3TC and PMEA.		Seen in heavily treated patients.	Winters98
T 69 S + SS	ACT to AGT + AGT AGT	HIV-1 Specific RTI	ddI + hydroxyurea	?	Y			Seen in one patient.	DeAntoni97
T 69 S + TS	ACT to TCT + ACC TCT	Multiple Nucleoside		?	Y	Confers >4-fold resistance to: AZT, ddI, ddC, 3TC and PMEA.		Seen in heavily treated patients.	Winters98
T 69 S + VG		Multiple Nucleoside		N	Y				Larder99
K 70 E	AAA to GAA	Nucleoside RTI	PMEA	Y	Y	9	3TC (7); PFA: 2-fold hypersusceptibility		Cherrington96, Mulato97
K 70 R	AAA to AGA	Nucleoside RTI	AZT	Y	Y			D67N/K70R/T215Y/K219Q: 120-fold	Larder89, Larder91, Kellam92
K 70 S	AAA to AGA	Multiple Nucleoside	ddI + d4T	?	Y			Seen in one patient on ddC + d4T combination therapy.	
L 74 I	TTA to ATA	HIV-1 Specific RTI	HBY 097	Y	?				Kleim96
L 74 V	TTA to GTA	Nucleoside RTI	1592U89	Y	N	4		K65R/L74V: 3.6-fold; K65R/L74V/M184V: 10.2-fold	Tisdale97
L 74 V	TTA to GTA	Nucleoside RTI	ddI	N	Y	5–10	ddC (4)	Can reverse effect of T215Y AZT resistance mutation	StClair91

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L 74 V	TTA to GTA	Nucleoside RTI	DXG	Y	?	4			Mellors96
L 74 V	TTA to GTA	HIV-1 Specific RTI	HBY 097	Y	?				Kleim96
V 75 I	GTA to ATA	Multiple Nucleoside		N	Y	Nil		V75I alone has no effect, but in combination with mutations at 62, 77, 116, 151 causes multi NRTI resistance.	Iversen96, Shirasaka95
V 75 I	GTA to TTA	HIV-1 Specific RTI	HBY 097	Y	?			Compensates for negative effect of G190E mutation on RT activity	Kleim96
V 75 L	GTA to TTA	HIV-1 Specific RTI	HBY 097	Y	?				Kleim96
V 75 M	GTA to ATG	Multiple Nucleoside	ddC + d4T	?	Y			Seen in one patient on ddC + d4T combination therapy.	Lawrence99
V 75 T	GTA to ACA	Nucleoside RTI	d4T	Y	Y	7	ddI; ddC; d4C; (-)-FTC	Observed with d4T selection in vitro, rarely in patients receiving d4T	Lacey94, Schinazi96
F 77 L	TTC to CTC	Multiple Nucleoside		N	Y	Nil		F77L alone has no effect, but in combination with mutations at 62, 75, 116, 151 causes multi NRTI resistance.	Iversen96, Shirasaka95
W 88 G	TGG to GGG	Pyrophosphate Analogue RTI	Foscarnet (PFA)	Y	Y	5	Hypersusceptibility to AZT	Observed after selection with AZT and PFA; suppresses effects of AZT mutations	Mellors95, Tachedjian95, Tachedjian96
W 88 S	TGG to TCG	Pyrophosphate Analogue RTI	Foscarnet (PFA)	N	Y	2–4	Wild-type susceptibility to AZT.	Partially suppresses effects of AZT resistance mutations	Mellors95, Tachedjian95, Tachedjian96
E 89 G	GAA to GGA	Pyrophosphate Analogue RTI	Foscarnet (PFA)	Y	N	14		Isolated by screening RT clones for ddGTP resistance	Prasad91
E 89 K	GAA to GGA	Pyrophosphate Analogue RTI	Foscarnet (PFA)	Y	N	> 16		Suppresses effects of AZT resistance mutations	Tachedjian95, Tachedjian96
L 92 I	TTA to ATA	Pyrophosphate Analogue RTI	Foscarnet (PFA)	Y	N	8		Partially suppresses effects of AZT resistance mutations	Tachedjian95, Tachedjian96

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Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
A 98 G	GCA to GGA	HIV-1 Specific RTI	L-697,661	N	Y	8			Byrnes93
A 98 G	GCA to GGA	HIV-1 Specific RTI	Nevirapine	N	Y				Richman94
L 100 I	TTA to ATA	HIV-1 Specific RTI	BHAP U-88204E	Y	?				Balzarini93d, Vasudevachari92
L 100 I	TTA to ATA	HIV-1 Specific RTI	DMP 266 (L-743,726)	Y	?	8–11		Combinations of mutations needed for high-level resistance; L100I/V108I: 1,000-fold; L100I/V179D/Y181C: 1,000-fold	Young95, Winslow96
L 100 I	TTA to ATA	HIV-1 Specific RTI	DMP-266 (Efavirenz)	Y	Y				Bacheler00
L 100 I	TTA to ATA	HIV-1 Specific RTI	L-697,661	Y	N	2			Byrnes93
L 100 I	TTA to ATA	HIV-1 Specific RTI	Nevirapine	N	Y				Richman93
L 100 I	TTA to ATA	HIV-1 Specific RTI	TIBO R82150	Y	?	> 100		Suppresses effects of AZT resistance mutations	Mellors93, Balzarini93c, Byrnes93a
L 100 I	TTA to ATA	HIV-1 Specific RTI	TIBO R82913	Y	?			Found in combination with E138K	Larder92
L 100 I	TTA to ATA	HIV-1 Specific RTI	UC-68 (638532)	Y	?	70			Balzarini95
L 100 I	TTA to ATA	HIV-1 Specific RTI	UC-70 (638534)	Y	?	758			Buckheit95a
L 100 I	TTA to ATA	HIV-1 Specific RTI	UC-781	Y	?	20		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 to ATA	HIV-1 Specific RTI	UC-84 (615985)	Y	?	> 40, > 33			Buckheit95a, Buckheit95b
K 101 E	AAA to GAA	HIV-1 Specific RTI	8-Chloro-TIBO R091767	?	Y				Moeremans95
K 101 E	AAA to GAA	HIV-1 Specific RTI	ADAMII	Y	?	30		Not selected for in vitro, resistance determined against a panel of mutants. Viruses with the L100I mutation show an enhanced sensitivity to ADAMII.	Cushman98
K 101 E	AAA to GAA	Multiple Nucleoside	Atevirdine + AZT	?	Y			Seen in one patient on atevirdine + AZT combination therapy. Found in association with K103N.	Demeter98
K 101 E	AAA to GAA	HIV-1 Specific RTI	DMP 266 (L-743,726)	Y	?	1,000			Young95

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K 101 E	AAA to GAA	HIV-1 Specific RTI	DMP-266 (Efavirenz)	Y	Y				Bacheler00
K 101 E	AAA to GAA	HIV-1 Specific RTI	L-697,661	N	Y	8			Byrnes93
K 101 E	AAA to GAA	HIV-1 Specific RTI	UC-10 (645129)	Y	?	12		K101E/Y181C: 200-fold	Buckheit95a, Buckheit97
K 101 E	AAA to GAA	HIV-1 Specific RTI	UC-38 (629243)	Y	N			K101E/G190E: > 100-fold	Balzarini95a, Balzarini95
K 101 E	AAA to GAA	HIV-1 Specific RTI	UC-57 (647014)	Y	?			K101E/Y181C: 58-fold	Buckheit95a
K 101 E	AAA to GAA	HIV-1 Specific RTI	UC-781	Y	?	7	UC040 (18); Nevirapine (15)	V108I/Y181C: 55-fold; K101E/V108I/ Y181C: 500-fold.	Buckheit97
K 101 I	AAA to ATA	HIV-1 Specific RTI	UC-16	Y	N	10		K101I/G141E: 10-fold	Balzarini95
K 101 Q	AAA to CAA	HIV-1 Specific RTI	DMP-266 (Efavirenz)	N	Y				Bacheler00
K 101 Q	AAA to CAA	HIV-1 Specific RTI	Trovirdine	Y	?			Found in combination with V108I	Zhang95, Vrang93
K 103 E	AAA to GAA	Nucleoside RTI	BHAP U-87201E (Atevirdine)	?	Y			Found in association with Y181C in one patient on monotherapy. K103E, K103N and Y181C observed with monotherapy.	Demeter98
K 103 N	AAA to AAC	HIV-1 Specific RTI	8-Chloro-TIBO R091767	?	Y				Moeremans95
K 103 N	AAA to AAC	HIV-1 Specific RTI	ADAMII	Y	?	>28		Not selected for in vitro, resistance determined against a panel of mutants. Viruses with the L100I mutation show an enhanced sensitivity to ADAMII.	Cushman98
K 103 N	AAA to AAC	Nucleoside RTI	BHAP U-87201E (Atevirdine)	?	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 to AAC	HIV-1 Specific RTI	BHAP U-90152 (delavirdine)	?	Y			K103N/Y181C seen separately and in combination in patients	Demeter95
K 103 N	AAA to AAC	HIV-1 Specific RTI	DMP 266 (L-743,726)	Y	Y	67		Predominant mutation in vivo	Winslow96
K 103 N	AAA to AAC	HIV-1 Specific RTI	DMP-266 (Efavirenz)	Y	Y				Bacheler00
K 103 N	AAA to AAC	Nucleoside RTI	GW420867X	Y	?				Kleim99

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K 103 N	AAA to AAC	HIV-1 Specific RTI	L-697,593	Y	?	20		K103N/Y181C: > 1,000-fold	Nunberg91
K 103 N	AAA to AAC	HIV-1 Specific RTI	L-697,661	Y	Y	8		K103N and Y181C most common with monotherapy	Byrnes93, Saag93
K 103 N	AAA to AAC	HIV-1 Specific RTI	Loviride (R89439, α-APA)	Y	Y				Staszewski96a
K 103 N	AAA to AAC	HIV-1 Specific RTI	MKC442 (I-EBU)	Y	?			Predominant mutation in vivo	Seki95
K 103 N	AAA to AAC	HIV-1 Specific RTI	Nevirapine	N	Y				Richman93
K 103 N	AAA to AAC	HIV-1 Specific RTI	TIBO R82913	Y	?	> 100		K103N/Y181C: > 1,000-fold	Balzarini93d
K 103 N	AAA to AAC	HIV-1 Specific RTI	UC-10 (645129)	Y	N	5			Balzarini95
K 103 N	AAA to AAC	HIV-1 Specific RTI	UC-81 (615727)	Y	?				Balzarini95, Yang97
K 103 Q	AAA to CAA	HIV-1 Specific RTI	L-697,661	N	Y	8			Saag93
K 103 R	AAA to AGA	HIV-1 Specific RTI	MKC442 (1-EBU)	Y	Y				BorrotoEsoda97
K 103 R	AAA to AGA	HIV-1 Specific RTI	Trovirdine	Y	?		Nevirapine; 9-chloro-TIBO	K103R/V179D: 500-fold; Found in combination with V179D or Y181C	Zhang95, Vrang93
K 103 T	AAA to ACA	HIV-1 Specific RTI	BHAP U-90152 (delavirdine)	?	Y				Demeter95
K 103 T	AAA to ACA	Nucleoside RTI	S-1153	Y	?				Fujiwara98
K 103 T	AAA to ACA	HIV-1 Specific RTI	UC-42	Y	N	100			Balzarini95
V 106 A	GTA to GCA	HIV-1 Specific RTI	ADAMII	Y	?	7.13		Not selected for in vitro, resistance determined against a panel of mutants. Viruses with the L100I mutation show an enhanced sensitivity to ADAMII.	Cushman98
V 106 A	GTA to GCA	HIV-1 Specific RTI	BHAP U-88204E	Y	?				Vasudevachari92
V 106 A	GTA to GCA	HIV-1 Specific RTI	E-EBU-dM	Y	?				Balzarini93
V 106 A	GTA to GCA	Nucleoside RTI	GW420867X	Y	?			V106A/Y181C: 400-fold resistance	Kleim99
V 106 A	GTA to GCA	HIV-1 Specific RTI	Nevirapine	Y	Y	100		No effect on AZT resistance	Richman94, Larder92, Richman93, Balzarini93d
V 106 A	GTA to GCA	Nucleoside RTI	S-1153	Y	?	4.5		V106A + F227L: 387-fold	Fujiwara98
V 106 A	GTA to GCA	HIV-1 Specific RTI	S-2720 (Quinoxaline)	Y	?			P225H follows V106A. Also seen with L101I and Y181C. Double and triple mutants highly resistant to other NNRTI's, including MKC442	Pelemans97

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V 106 A	GTA to GCA	HIV-1 Specific RTI	TIBO R82913	Y	?	100			Larder92
V 106 A	GTA to GCA	HIV-1 Specific RTI	UC-69 (646989)	Y	?			V106A/V181C: 166-fold	Buckheit95a
V 106 A	GTA to GCA	HIV-1 Specific RTI	UC-82	Y	?	13		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 to ATA	HIV-1 Specific RTI	HBY 097					Appears under lowered drug concentration selection	Kleim97
V 108 I	GTA to ATA	HIV-1 Specific RTI	ADAMII	Y	?	6.74		Not selected for in vitro, resistance determined against a panel of mutants. Viruses with the L100I mutation show an enhanced sensitivity to ADAMII.	Cushman98
V 108 I	GTA to ATA	HIV-1 Specific RTI	DMP 266 (L-743,726)	Y	?			L100I/V108I: 1,000-fold	Winslow96
V 108 I	GTA to ATA	HIV-1 Specific RTI	DMP-266 (Efavirenz)	Y	Y				Bacheler00
V 108 I	GTA to GCA	HIV-1 Specific RTI	L-697,661	Y	Y	4			Byrnes93
V 108 I	GTA to ATA	HIV-1 Specific RTI	Loviride (R89439, α-APA)	Y	?				Staszewski96a
V 108 I	GTA to GCA	HIV-1 Specific RTI	MKC442 (I-EBU)	Y	?				Seki95
V 108 I	GTA to ATA	HIV-1 Specific RTI	Nevirapine	N	Y				Richman93
V 108 I	GTT to GAT	HIV-1 Specific RTI	TIBO R82150	N	Y	> 100	R82150 (> 100)		Vandamme94a
V 108 I	GTA to ATA	HIV-1 Specific RTI	Trovirdine	Y	?			Found in combination with K101Q	Zhang95
V 108 I	GTA to ATA	HIV-1 Specific RTI	UC-781	Y	?		V108I/Y181C: 55 fold. K101E/ V108I/Y181C: 500 fold.		Buckheit97
Y 115 F	TAT to TTT	Nucleoside RTI	1592U89	Y	N	2		K65R/L74V and/or Y115F with M184V: 10 fold; L74V/Y115F/M184V: 11-fold	Tisdale97
F 116 Y	TTT to TAT	Multiple Nucleoside		N	Y	Nil		F116Y alone has no effect, but in combination with mutations at 62, 75, 77, 151 causes multi NRTI resistance.	Iversen96, Shirasaka95

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Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
V 118 I	GTT to ATT	Multiple Nucleoside	3TC + AZT	N	Y	2.0		Confers moderate levels of resistance to 3TC (4 to 50-fold) when present in an AZT-resistant genetic background without diminishing AZT resistance.	Hertogs00
P 119 S	CCC to TCC	Nucleoside RTI	F-ddA	Y	?	4.6		Found with V179D and/or L214F, which are possibly compensatory	Tanaka97
I 135 L	ATA to AAA	HIV-1 Specific RTI		N	Y	Nil		Mutation identified by logistic regression analysis. I135L/L283I: 5.0-fold Delavirdine resistance, 4.2-fold Nevirapine resistance, 4.1-fold Efavirenze resistance.	Brown00
I 135 M	ATA to ATG	HIV-1 Specific RTI		N	Y	Nil		Mutation identified by logistic regression analysis. I135L/L283I: 4.0-fold Delavirdine resistance, 4.5-fold Nevirapine resistance, 3.2-fold Efavirenze resistance.	Brown00
I 135 T	ATA to ACA	HIV-1 Specific RTI		N	Y	Nil		Mutation identified by logistic regression analysis. I135L/L283I: 3.4-fold Nevirapine resistance.	Brown00
E 138 A	GAG to GCG	HIV-1 Specific RTI	TSAO	N	Y			Mutation reducing susceptibility to TSAO in TSAO therapy naive patients.	VanLaethem00
E 138 K	GAG to AAG	HIV-1 Specific RTI	MKC442 (I-EBU)	Y	N			Obtained in the concomitant presence of low 3TC concentrations	Balzarini96c
E 138 K	GAG to AAG	HIV-1 Specific RTI	TIBO R82913	Y	?			Found in combination with L100I	Balzarini93c
E 138 K	GAG to AAG	HIV-1 Specific RTI	TSAO	Y	?	> 100		E138A (GAG to GCG) in TSAO-naive patients confers TSAO viral resistance	Balzarini93a, Balzarini93b, Vandamme96
E 138 K	GAG to AAG	HIV-1 Specific RTI	UC-82	Y	?	5		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

Mutations in HIV RT that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
E 138 K	GAG to AAG	HIV-1 Specific RTI	UC-84 (615985)	Y	?	> 100	TSAOs		Balzarini95, Balzarini95b
T 139 I	ACA to ATA	HIV-1 Specific RTI	ADAMII	Y	?	38		Not selected for in vitro, resistance determined against a panel of mutants. Viruses with the L100I mutation show an enhanced sensitivity to ADAMII.	Cushman98
T 139 I	ACA to ATA	HIV-1 Specific RTI	Calanolide A	Y	?	> 70	Not other NNRTIs		Buckheit95c
G 141 E	GGG to GAG	HIV-1 Specific RTI	UC-16	Y	N			K101I/G141E: 10-fold	Balzarini95
Q 151 M	CAG to ATG	Multiple Nucleoside		N	Y	AZT: 10; ddI/ ddC: 5		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	Iversen96, Shirasaka95, Schmit96
S 156 A	TCA to GCA	Pyrophosphate Analogue RTI	Foscarnet (PFA)	Y	N	4.5			Tachedjian95
P 157 S	CCA to TCA	HIV-1 Specific RTI	3TC			5		Mutation increases susceptibility to AZT and PMPA	Smith99
Q 161 L	CAA to CTA	Pyrophosphate Analogue RTI	Foscarnet (PFA)	Y	Y	5		Q161L/H208Y: 9-fold; Q161L/H208Y suppresses effects of AZT mutations	Mellors95
V 179 D	GTT to GAT	HIV-1 Specific RTI	ADAMII	Y	?	28		Not selected for in vitro, resistance determined against a panel of mutants. Viruses with the L100I mutation show an enhanced sensitivity to ADAMII.	Cushman98
V 179 D	GTT to GAT	HIV-1 Specific RTI	DMP 266 (L-743,726)	Y	?			L100I/V179D/Y181C: 1,000-fold	Winslow96
V 179 D	GTT to GAT	HIV-1 Specific RTI	L-697,661	N	Y	4			Byrnes93
V 179 D	GTT to GAT	HIV-1 Specific RTI	QM96521	Y	?	10	Other TDD derivative: 15–140-fold; 8-chloro-TIBO: 10-fold		Witvrouw98

Mutations in HIV RT that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
V 179 D	GTT to GAT	HIV-1 Specific RTI	TIBO R82913	N	Y	20	R82150 (20)		Vandamme94
V 179 D	GTT to GAT	HIV-1 Specific RTI	Trovirdine	Y	?			Found in combination with K103R or Y181C; V179D/Y181C: > 1,000-fold	Zhang95
V 179 D	GTT to GAT	HIV-1 Specific RTI	UC-10 (645129)	Y	?	16			Balzarini95, Balzarini96a
V 179 E	GTT to GAG	HIV-1 Specific RTI	L-697,661	N	Y	8			Byrnes93
Y 181 C	TAT to TGT	HIV-1 Specific RTI	1737 (Tetrahydronaphthalene derivative)	Y	?	20		Y181C also confers resistance to numerous other tetrahydronaphthalene derivatives.	Hara97
Y 181 C	TAT to TGT	HIV-1 Specific RTI	ADAMII	Y	?	>28		Not selected for in vitro, resistance determined against a panel of mutants. Viruses with the L100I mutation show an enhanced sensitivity to ADAMII.	Cushman98
Y 181 C	TAT to TGT	HIV-1 Specific RTI	α-APA R18893 (loviride analogue)	Y	?				deBethune93
Y 181 C	TAT to TGT	HIV-1 Specific RTI	BHAP U-87201E (atevirdine)	N	Y			K103E, K103N and Y181C observed with monotherapy	Demeter95, Demeter98
Y 181 C	TAT to TGT	HIV-1 Specific RTI	BHAP U-88204E	Y	?				Vasudevachari92
Y 181 C	TAT to TGT	HIV-1 Specific RTI	BHAP U-90152 (delavirdine)	?	Y			K103N/Y181C seen separately and in combination in vivo	Demeter95
Y 181 C	TAT to TGT	HIV-1 Specific RTI	BM+51.0836	Y	?				Maass93
Y 181 C	TAT to TGT	HIV-1 Specific RTI	DMP 266 (L-743,726)	Y	?	4		L100I/V179D/Y181C: 1,000-fold; uncommon in vivo	Winslow96, Young95
Y 181 C	TAT to TGT	HIV-1 Specific RTI	E-EBU	Y	?				Balzarini93
Y 181 C	TAT to TGT	HIV-1 Specific RTI	E-EPSeU	Y	?	> 50		Y188C confers greater resistance than Y181C	Nguyen94
Y 181 C	TAT to TGT	HIV-1 Specific RTI	E-EPU	Y	?	> 95		Y188C confers greater resistance than Y181C	Nguyen94

Mutations in HIV RT that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
Y 181 C	TAT to TGT	Nucleoside RTI	GW420867X	Y	?			V106A/Y181C: 400-fold resistance	Kleim99
Y 181 C	TAT to TGT	HIV-1 Specific RTI	L-697,593	Y	?	> 100		K103N/Y181C: > 1,000-fold	Nunberg91
Y 181 C	TAT to TGT	HIV-1 Specific RTI	L-697,661	Y	Y	> 30		K103N and Y181C most common with monotherapy	Byrnes93, Saag93
Y 181 C	TAT to TGT	HIV-1 Specific RTI	Loviride (R89439, α-APA)	?	Y				Staszewski96
Y 181 C	TAT to TGT	HIV-1 Specific RTI	MKC442 (1-EBU)	?	Y				BorrotoEsoda97
Y 181 C	TAT to TGT	HIV-1 Specific RTI	Nevirapine	Y	Y	> 100	Other NNRTIs	Can suppress effects of AZT mutations	Richman94, Richman91, Mellors92
Y 181 C	TAT to TGT	HIV-1 Specific RTI	NSC 648400 (E-BPTU)	Y	?	160	Other NNRTIs		Buckheit95c
Y 181 C	TAT to TGT	HIV-1 Specific RTI	TIBO R82913	Y	?	> 100		K103N/Y181C: > 1,000-fold	Larder92
Y 181 C	TAT to TGT	HIV-1 Specific RTI	Trovirdine	Y	?		Nevirapine; 9-chloro-TIBO	V179D/Y181C: > 1,000-fold; Found in combination with K103R or V179D	Zhang95, Vrang93
Y 181 C	TAT to TGT	HIV-1 Specific RTI	UC-10 (645129)	Y	?	6		K101E/Y181C: 200-fold	Buckheit95a
Y 181 C	TAT to TGT	HIV-1 Specific RTI	UC-32 (645542)	Y	?	38			Buckheit95a
Y 181 C	TAT to TGT	HIV-1 Specific RTI	UC-38 (629243)	Y	?	8–149	Other NNRTIs		Buckheit95a
Y 181 C	TAT to TGT	HIV-1 Specific RTI	UC-57 (647014)	Y	?			K101E/Y181C: 58-fold	Buckheit95a
Y 181 C	TAT to TGT	HIV-1 Specific RTI	UC-68 (638532)	Y	?	5			Buckheit95a
Y 181 C	TAT to TGT	HIV-1 Specific RTI	UC-69 (646989)	Y	?			V106A/V181C: 166-fold	Buckheit95a
Y 181 C	TAT to TGT	HIV-1 Specific RTI	UC-781	Y	?	13		V108/Y181C: 55 fold; K101E/V108I/Y181C: 500 fold. 42	Balzarini98, Buckheit97
Y 181 C	TAT to TGT	HIV-1 Specific RTI	UC-80 (639475)	Y	?	18			Buckheit95a
Y 181 C	TAT to TGT	HIV-1 Specific RTI	UC-81 (615727)	Y	?	53			Balzarini95, Yang97
Y 181 C	TAT to TGT	HIV-1 Specific RTI	UC-84 (615985)	Y	?	> 118			Buckheit95a
Y 181 I	TGT to ATT	HIV-1 Specific RTI	BHAP U-88204E	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	TAT to ATT	HIV-1 Specific RTI	MKC442 (I-EBU)	Y	N	1,000			Balzarini96c
Y 181 I	TGT to ATT	HIV-1 Specific RTI	Nevirapine	N	Y	High-level		Observed in one patient	Shaw94

Mutations in HIV RT that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
M 184 I	ATG to ATA	Nucleoside RTI	3TC (lamivudine)	Y	Y			M184V and M184I can suppress effects of AZT resistance mutations	Schinazi93, Tisdale93, Gao93
M 184 I	ATG to ATA	HIV-1 Specific RTI	QYL-685	Y	?	9	QYL-609	Additional passage of virus did not select M184V	Yoshimura99a
M 184 T	ATG to ACG	Nucleoside RTI	3TC (lamivudine)	Y	?			Reduced replication capacity and RT activity	Larder95, Keulen96
M 184 V	ATG to GTG	Nucleoside RTI	1592U89	Y	N	3		K65R/L74V and/or Y115F with M184V: 10-fold; K65R/M184V: 8-fold; L74V/M184V: 9-fold resistance; L74V/Y115F/M184V: 11-fold	Tisdale97
M 184 V	ATG to GTG	Nucleoside RTI	3TC (lamivudine)	Y	Y	>100	ddI; ddC; (-)-FTC	M184V and M184I can suppress effects of AZT resistance mutations; GTA seen in cell culture	Schinazi93, Tisdale93, Gao93
M 184 V	ATG to GTG	Nucleoside RTI	ddC	Y	Y	2–5			Gu92
M 184 V	ATG to GTG	Nucleoside RTI	ddI	Y	Y	2–5		Rarely observed in patients receiving ddI	Gu92
M 184 V	ATG to GTG	Nucleoside RTI	(-)dOTC	Y	?	nil			Rando99
M 184 V	ATG to GTG	Nucleoside RTI	(+)dOTC	Y	?				Rando99
M 184 V	ATG to GTG	Nucleoside RTI	dOTC (BCH-10652)	Y	?			K65R/M184V: 4.2-fold.	Rando99
M 184 V	ATG to GTG	HIV-1 Specific RTI	(-)dOTFC	Y	?	13			Richard00
M 184 V	ATG to GTG	HIV-1 Specific RTI	(+)dOTFC	Y	?	>15.0			Richard00
M 184 V	ATG to GTG	Nucleoside RTI	(-)-FTC	Y	?	> 100		M184V can suppress effects of AZT mutations	Schinazi93, Tisdale93
M 184 V	ATG to GTG	Nucleoside RTI	L-FddC	Y	?	> 100			Schinazi95
Y 188 C	TAT to TGT	HIV-1 Specific RTI	ADAMII	Y	?	6.07		Not selected for in vitro, resistance determined against a panel of mutants. Viruses with the L100I mutation show an enhanced sensitivity to ADAMII.	Cushman98
Y 188 C	TAT to TGT	HIV-1 Specific RTI	E-EPSeU	Y	?	> 250		Y188C is the predominant mutation for E-EPSeU; Y188C confers greater resistance than Y181C	Nguyen94

Mutations in HIV RT that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
Y 188 C	TAT to TGT	HIV-1 Specific RTI	E-EPU	Y	?	> 250		Y188C confers greater resistance than Y181C	Nguyen94
Y 188 C	TAT to TGT	HIV-1 Specific RTI	HEPT	Y	?				Balzarini93
Y 188 C	TAT to TGT	HIV-1 Specific RTI	Nevirapine	N	Y				Richman93
Y 188 H	TAT to CAT	HIV-1 Specific RTI	ADAMII	Y	?	>128		Not selected for in vitro, resistance determined against a panel of mutants. Viruses with the L100I mutation show an enhanced sensitivity to ADAMII.	Cushman98
Y 188 H	TAT to CAT	Multiple Nucleoside	Atevirdine + AZT	?	Y			Found in two patients on atevirdine + AZT combination therapy.	Demeter98
Y 188 H	TAT to CAT	HIV-1 Specific RTI	DMP-266 (Efavirenz)	N	Y				Bacheler00
Y 188 H	TAT to CAT	HIV-1 Specific RTI	TIBO R82913	Y	?				Balzarini93c
Y 188 H/L	TAT to CAT/CTT	HIV-1 Specific RTI	Loviride (R89439, α-APA)	?	Y				Staszewski96
Y 188 L	TAT to TTA	HIV-1 Specific RTI	DMP 266 (L-743,726)	Y	?	1,000			Winslow96
Y 188 L	TAT to	HIV-1 Specific RTI	DMP-266 (Efavirenz)		Y				Bacheler00
Y 188 L	TAT to TTA	HIV-1 Specific RTI	TIBO R82913	N	Y				Vandamme94
V 189 I	GTA to ATA	HIV-1 Specific RTI	HBY 097	Y	?	2	Other NNRTIs (2–6)		Kleim96
G 190 A	GGA to GCA	HIV-1 Specific RTI	DMP-266 (Efavirenz)	N	Y				Bacheler00
G 190 A	GGA to GCA	HIV-1 Specific RTI	Loviride (R89439, α-APA)	?	Y				Moeremans95
G 190 A	GGA to GCA	HIV-1 Specific RTI	Nevirapine	N	Y				Richman94
G 190 E	GGA to GAA	HIV-1 Specific RTI	AAP-BHAP (U-104489)	Y	?	>100		T139I/G190E/T200A/L214F: >100. Additional mutations possibly restore the replication capacity of the G190E mutant	Olmsted96
G 190 E	GGA to GAA	HIV-1 Specific RTI	DMP-266 (Efavirenz)	N	Y				Bacheler00

Mutations in HIV RT that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
G 190 E	GGA to GAA	Nucleoside RTI	GW420867X	Y	?				Kleim99
G 190 E	GGA to GAA	HIV-1 Specific RTI	HBY 097	Y	?		Other NNRTIs	Reduces enzymatic activity of RT and viral replication competency	Kleim95
G 190 E	GGA to GAA	HIV-1 Specific RTI	S-2720	Y	?				Kleim93
G 190 E	GGA to GAA	HIV-1 Specific RTI	UC-38 (629243)	Y	N			K101E/G190E: > 100-fold; cross resistance to: TSAO-m3T, Nev, TIBO R82913, BHAP U88204; susceptible to L697,661	Balzarini95a
G 190 Q	GGA to CAA	HIV-1 Specific RTI	HBY 097	Y	?		Other NNRTIs	Appears exclusively in connection with V179D	Kleim96
G 190 S	GGA to TCA	HIV-1 Specific RTI	DMP-266 (Efavirenz)	N	Y				Bacheler00
G 190 T	GGA to ACA	HIV-1 Specific RTI	HBY 097	Y	?			Appears during selection with low drug concentrations.	Kleim97
H 208 Y	CAT to TAT	Multiple Nucleoside	AZT + 3TC	?	Y			Polymorphism facilitating AZT+3TC dual resistance	Kemp98
H 208 Y	CAT to TAT	Pyrophosphate Analogue RTI	Foscarnet (PFA)	Y	Y	2		Q161L/H208Y: 9-fold; increased susceptibility to AZT 100-fold), nevirapine (20-fold) and TIBO R82150 (30-fold); Q161L/H208Y suppresses effects of AZT mutations	Mellors95
L 210 W	TTG to TGG	Nucleoside RTI	AZT	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 to AAG	Multiple Nucleoside	AZT + 3TC	?	Y			Polymorphism facilitating AZT+3TC dual resistance in association with M184V and other AZT resistance mutations.	Kemp98
L 214 F	CTT to TTT	Multiple Nucleoside	AZT + 3TC	?	Y			Polymorphism facilitating AZT+3TC dual resistance in association with M184V and other AZT resistance mutations.	Kemp98, Stuyver97

Mutations in HIV RT that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
T 215 F	ACC to TTC	Nucleoside RTI	AZT	?	Y			K67N/K70R/T215Y/K219Q: 120-fold	Larder89, Larder91, Kellam92
T 215 Y	ACC to TAC	Nucleoside RTI	AZT	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
Y 215 C	TTC to TGC	Nucleoside RTI	ddC	N	Y	4		Arises on background of T215Y AZT resistance	Slade93
K 219 E	AAA to GAA	Nucleoside RTI	AZT	Y	N				Larder89, Larder91, Kellam92
K 219 Q	AAA to CAA	Nucleoside RTI	AZT	?	Y			K67N/K70R/T215Y/K219Q: 120-fold	Larder89, Larder91, Kellam92
K 219 R	AAA to AGA	Multiple Nucleoside	3TC + d4T	?	Y			Seen in two patient on 3TC + d4T combination therapy.	Lawrence99
K 219 R	AAA to AGA	Multiple Nucleoside	AZT + 3TC	?	Y			Seen in two patient on AZT + 3TC combination therapy.	Lawrence99
K 219 W	AAA to TGG	Multiple Nucleoside	ddC + d4T	?	Y			Seen in one patient on ddC + d4T combination therapy.	Lawrence99
P 225 H	CCT to CAT	HIV-1 Specific RTI	DMP-266 (Efavirenz)	N	Y				Bacheler00
P 225 H	CCT to CAT	HIV-1 Specific RTI	S-2720 (Quinoxaline)	Y	?	4.0	MKC-442 (5.7); HBY-097 (4.0); UC-781 (3.7)	P225H follows V106A. Also seen with L101I and Y181C. Double and triple mutants highly resistant to other NNRTI's, including MKC442. The presence of P225H in a V106A backgrough restores sensitivity to BHAP U-90152.	Pelemans97, Pelemans98
F 227 L	TTA to CTC	Nucleoside RTI	S-1153	Y	?	nil		V106A + F227L: 387-fold. This mutation confers hypersensitivity to delavirdine.	Fujiwara98

Mutations in HIV RT that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
F 227 L	TTA to CTC	HIV-1 Specific RTI	UC-781	Y	?			V106A/F227L: 10-fold. Found with V106A, K101I, Y181C and L100I. Appears in a V106A background following dose-escalating UC-781 treatment.	Balzarini98
V 233 E	GAA to GTA	HIV-1 Specific RTI	Atevirdine + AZT	N	Y			Seen in 1 patient. K101E, Y188H and K238T also seen in patients on ATV/AZT combination therapy.	Demeter98
L 234 I	CTC to ATC	Nucleoside RTI	S-1153	Y	?	22		This mutation confers hypersensitivity to Loviride.	Fujiwara98
P 236 L	CCT to CTT	HIV-1 Specific RTI	BHAP U-87201E (atevirdine)	Y	N				Dueweke93
P 236 L	CCT to CTT	HIV-1 Specific RTI	BHAP U-90152 (delavirdine)	Y	Y			Sensitizes RT 10-fold to nevirapine, TIBO R82913 and L-697,661	Dueweke93
P 236 L	CCT to CTT	HIV-1 Specific RTI	HEPT	Y	?				Buckheit95c
K 238 T	AAA to ACA	Multiple Nucleoside	Atevirdine + AZT	N	Y			Seen in 1 patient. K101E, K103N, Y188H, and V233E also observed with ATV/AZT combination therapy.	Demeter98
K 238 T	AAA to ACA	Multiple Nucleoside	Atevirdine + AZT	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 to ACT	HIV-1 Specific RTI		N	Y	Nil		Mutation identified by logistic regression analysis. Confers resistance to Delavirdine, Nevirapine, and Efavirenze in conjunction with mutations at codon 135.	Brown00
G 333 D	GGC to GAC	Multiple Nucleoside	AZT+3TC	Y	Y			Facilitates dual resistance to AZT+3TC in association with M184V and standard AZT resistance mutations.	Kemp98
G 333 D	GGC to GAC	Multiple Nucleoside	AZT + 3TC + Abacavir	?	Y				Caride00
G 333 E	GGC to GAG	Multiple Nucleoside	AZT + 3TC	Y	Y			Facilitates dual resistance to AZT+3TC in association with M184V and standard AZT resistance mutations.	Kemp98
G 333 E	GGC to GAG	Multiple Nucleoside	AZT + 3TC + Abacavir	?	Y				Caride00
T 386 I	ACT to ATT	Multiple Nucleoside	AZT + 3TC + Abacavir	?	Y			Abrogates M184V suppression of L210W and L210W/G333D/E	Caride00

Mutations in HIV Protease that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
R 8 K	CGA to AAA	Protease Inhibitor	A-77003	Y	?	10		R8K/M46I/G48V: 20-fold	Ho94, Tisdale94
R 8 Q	CGA to CAA	Protease Inhibitor	A-77003	Y	?	10		M46I improves replication competency of R8Q mutant	Ho94, Kaplan94
L 10 F	CTC to TTC	Protease Inhibitor	ABT-378	Y	?		Passage 17 virus: ritonavir, 21-fold; saquinavir, 4-fold	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
L 10 F	CTC to TTC	Protease Inhibitor	BILA 2185 BS	Y	?		BILA 1906 BS (360)	L10F/L23I/V32I/M46I/I47V/I54M/A71V/I84V: 1,500-fold. 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
L 10 F	CTC to TTC	Protease Inhibitor	BMS-232632	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 to TTC	Protease Inhibitor	DMP 450	Y	?			Probably compensatory	Otto95, Winslow95
L 10 F	CTC to TTC	Protease Inhibitor	JE-2147	Y	?		KNI-272: 7-fold; Ritonavir: 9-fold	L10F/I47V/I84V: 19-fold. L10F/M46I/I47V/I84V: 28-fold. >50 passages required for isolation of resistant virus.	Yoshimura99
L 10 F	CTC to TTC	Protease Inhibitor	SC-55389A	Y	?	2.8	Not SC-52151	N88S/L10F: 25-fold	Potts94, Pillay96, Smidt97
L 10 F	CTC to TTC	Protease Inhibitor	VB 11,328	Y	?			L10F/I84V: 8-fold	Partaledis95
L 10 F	CTC to TTC	Protease Inhibitor	VX-478 (141W94)	Y	?				Tisdale96

Mutations in HIV Protease that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
L 10 F	CTC to TTC	Protease Inhibitor	XM323					L10F/V82A: 2-fold; L10F/K45I/I84V: 50-fold	King95
L 10 I	CTC to ATC	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y				Condra96
L 10 I	CTC to ATC	Protease Inhibitor	Ro 31–8959 (saquinavir)		Y			Found in combination with G48V in vivo.	Schapiro96
L 10 R	CTC to CGC	Protease Inhibitor	MK-639 (L-735,524, indinavir)	N	Y		XM-323 (15)	L10R/M46I/L63P/V82T: 4-fold; L10R/M46I/L63P/V82T/I84V: 8-fold	Condra96, Condra95
L 10 V	CTC to GTC	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y		A-80987 (4)		Condra96, Condra95
L 10 Y	CTC to TAC	Protease Inhibitor	BMS-232632	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 15 V		Protease Inhibitor	PNU-140690 (Tipranavir)	?	Y				Rusconi00
G 16 E	GGG to GAG	Protease Inhibitor	ABT-378	Y	?		Passage 17 virus: ritonavir, 21-fold; saquinavir, 4-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
K 20 M	AAG to ATG	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y		VX-478 (8)		Condra96
K 20 M	AAG to ATG	Protease Inhibitor	Nelfinavir	?	Y			Seen in two patients following a switch from saquinavir. Associated with reduced susceptibility to both saquinavir and nelfinavir.	Lawrence99
K 20 R	AAG to AGG	Protease Inhibitor	ABT-538 (ritonavir)	N	Y			K20R/M36I/I54V/V82A: 41-fold	Molla96
K 20 R	AAG to AGG	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y		Ro-31–8959 (8);		Condra96

Mutations in HIV Protease that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
L 23 I	CTA to ATA	Protease Inhibitor	BILA 2185 BS	Y	?		Ro-31–8959 (50); L-735,524 (80); BILA 1906 BS (360)	L10F/L23I/V32I/M46I/I47V/I54M/A71V/I84V: 1,500-fold. 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 24 I	TTA to ATA	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y		SC-52151 (8)		Condra96, Condra95
L 24 V	TTA to GTA	Protease Inhibitor	SC-52151	Y	?	10–20	SC55389A	L24V/G48V/A71V/V75I/P81T: 1000-fold	Potts94, Pillay96
D 30 N	GAT to AAT	Protease Inhibitor	AG1343 (nelfinavir)	Y	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	Patick96, Patick97
V 32 I	GTA to ATA	Protease Inhibitor	A-77003	Y	?	7 (enzyme resist.)		V32I appears first; progression to V32I/M46V and V32I//M46V/A71V/V82A occurs even in the absence of drug	Kaplan94
V 32 I	GTA to ATA	Protease Inhibitor	ABT-378	Y	?		Passage 17 virus: ritonavir, 21-fold; saquinavir, 4-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
V 32 I	GTA to ATA	Protease Inhibitor	ABT-538 (ritonavir)	Y	?	40		V32I and V82I are synergistic mutations yielding 20-fold enzyme resistance	Molla96
V 32 I	GTA to ATA	Protease Inhibitor	BILA 1906 BS	Y	?			V32I/A71V: 3-fold; V32I/M46I,L/A71V/I84V: 5-fold; V32I/M46I,L/A71V/I84A: 520-fold. 32I/46L/71V/84A are functionally impaired. Associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1′)	Lamarre94, Croteau97
V 32 I	GTA to ATA	Protease Inhibitor	BILA 2011 (palinavir)	Y	?	1200	BILA 1906 (1400)	Other mutations found in p1/p6 cleavage site	Lamarre95

Mutations in HIV Protease that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
V 32 I	GTA to ATA	Protease Inhibitor	BILA 2185 BS	Y	?		BILA 1906 (360)	L10F/L23I/V32I/M46I/I47V/I54M/ A71V/I84V: 1,500-fold. 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
V 32 I	GTA to ATA	Protease Inhibitor	BMS-232632	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 to ATA	Protease Inhibitor	KNI-272	Y	?	2		V32I/M46I/I84V: 37-fold; V32I/L33F/ K45I/F53L/A71V/I84V/L89M: 130-fold	Gulnik95
V 32 I	GTA to ATA	Protease Inhibitor	MK-639 (L-735, 524, indinavir)	Y	Y			V32I/M46L/V82A: 3-fold; V32I/M46L/ A71V/V82A: 14-fold	Condra96, Condra95
L 33 F	TTA to TTC	Protease Inhibitor	ABT-538 (ritonavir)	N	Y			M36I/I54V/A71V/V82I: 8-fold; K20R/ M36I/I54V/V82A: 41-fold. In vivo, V82A/F/T/S occurs first, often followed by changes at 54,71 and 36	Molla96
L 33 F	TTA to TTC	Protease Inhibitor	BMS-232632	Y	?			V32L/L33F/M46I/A71V/I84V/N88S: 183-fold., L10Y,F/I50L/L63P/A71V/ N88S: 93-fold., V32I/M46I/I84V/ L89M: 96-fold.	Gong00
E 35 D		Protease Inhibitor	PNU-140690 (Tipranavir)	?	Y			Seen in 60% of patients receiving Tipranavir therapy.	Rusconi00
M 36 I	ATG to ATA	Protease Inhibitor	ABT-538 (ritonavir)	N	Y			In vivo, V82 occurs first, often followed by changes at 54, 71 and 36	Molla96
M 36 I	ATG to ATA	Protease Inhibitor	AG1343 (nelfinavir)		Y				Patick96
N 37 D		Protease Inhibitor	PNU-140690 (Tipranavir)	?	Y			Seen in 30% of patients receiving Tipranavir therapy.	Rusconi00

Mutations in HIV Protease that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
R 41 K		Protease Inhibitor	PNU-140690 (Tipranavir)	?	Y			Seen in 20% of patients receiving Tipranavir therapy.	Rusconi00
K 45 I	AAA to ATA	Protease Inhibitor	XM323					L10F/K45I/I84V: 50-fold	Tisdale94
M 46 F	ATG to TTC	Protease Inhibitor	A-77003	Y	?	4 (enzyme resist.)		Seen with V82A	Kaplan94
M 46 I	ATG to ATA	Protease Inhibitor	A-77003	Y	?			No effect on susceptibility but improves replication competency of R8Q mutant; R8K/M46I/G48V: 20-fold	Ho94, Kaplan94
M 46 I	ATG to ATA	Protease Inhibitor	ABT-378	Y			Passage 17 virus: ritonavir, 21-fold; saquinavir, 4-fold	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 to ATA	Protease Inhibitor	ABT-538 (ritonavir)	Y	Y			M46I/L63P/A71V/V82F/I84V: 27-fold	Molla96
M 46 I	ATG to ATA	Protease Inhibitor	AG1343 (nelfinavir)	Y	Y				Patick96
M 46 I	ATG to ATA	Protease Inhibitor	BILA 1906 BS	Y	?		L 735,524 (60)	V32I/A71V: 3-fold; V32I/M46I,L/A71V/I84V: 5-fold; V32I/M46I,L/A71V/I84A: 520-fold. V32I/M46L/A71V/I84A is functionally impaired. Associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1′)	Croteau97, Doyon96, Lamarre94, Lamarre95
M 46 I	ATG to ATA	Protease Inhibitor	BILA 2185 BS	Y	?		BILA 1906 (360)	L10F/L23I/V32I/M46I/I47V/I54M/A71V/I84V: 1,500-fold. 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

Mutations in HIV Protease that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
M 46 I	ATG to ATA	Protease Inhibitor	BMS-232632	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 to ATA	Protease Inhibitor	DMP 450	Y	?			Probably compensatory	Otto95, Winslow95
M 46 I	ATG to ATA	Protease Inhibitor	JE-2147	Y	?		KNI-272: 7-fold; Ritonavir: 9-fold	L10F/M46I/I47V/I84V: 28-fold. >50 passages required for isolation of resistant virus.	Yoshimura99
M 46 I	ATG to ATA	Protease Inhibitor	MK-639 (L-735,524, indinavir)	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 to ATA	Protease Inhibitor	VB 11,328	Y	?			I50V/M46I/I47V: 20-fold	Tisdale94, Partaledis95
M 46 I	ATG to ATA	Protease Inhibitor	VX-478 (141W94)	Y	?	Nil			Partaledis95
M 46 L	ATG to TTC	Protease Inhibitor	A-77003	Y	?	2–3 (enzyme resist.)			Kaplan94
M 46 L	ATG to TTG	Protease Inhibitor	BILA 1906 BS	Y	?			Associated p1/p6 cleavage site mutation (L to F (CTT to TTT) at P1′)	Croteau97, Doyon96, Lamarre94, Lamarre95
M 46 L	ATG to TTG	Protease Inhibitor	MK-639 (L-735,524, indinavir)	Y	Y			V32I/M46L/A71V/V82A: 14-fold; V32I/M46L/V82A: 3-fold	Tisdale94
M 46 L	ATG to CTG	Protease Inhibitor	XM323	Y	?			V82A/M46L: 7-fold; V82A/M46L/L97V: 11-fold	King95
M 46 V	ATG to GTG	Protease Inhibitor	A-77003	Y	?			V32I appears first; progression to V32I/M46V and V32I/M46V/A71V/V82A occurs even in the absence of drug.	Tisdale94
I 47 V	ATA to GTA	Protease Inhibitor	ABT-378	Y	?		Passage 17 virus: ritonavir, 21-fold; saquinavir, 4-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

Mutations in HIV Protease that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
I 47 V	ATA to CTA	Protease Inhibitor	BILA 2185 BS	Y	?		BILA 1906 (360)	L10F/L23I/V32I/M46I/I47V/I54M/A71V/I84V: 1,500-fold. 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
I 47 V	ATA to CTA	Protease Inhibitor	JE-2147	Y	?		KNI-272: 7-fold; Ritonavir: 9-fold	L10F/I47V/I84V: 19-fold. L10F/M46I/I47V/I84V: 28-fold. >50 passages required for isolation of resistant virus.	Yoshimura99
I 47 V	ATA to CTA	Protease Inhibitor	VB 11,328	Y	?			I50V/M46I/I47V: 20-fold	Partaledis95
I 47 V	ATA to CTA	Protease Inhibitor	VX-478 (141W94)	Y	?	Nil			Partaledis95
V 47 A	GTA to TAT	Protease Inhibitor	ABT-378	Y	?		Passage 17 virus: ritonavir, 21-fold; saquinavir, 4-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
G 48 V	GGG to GTG	Protease Inhibitor	A-77003	Y	?			R8K/M46I/G48V: 20-fold; G48V/I82T: 100-fold	Borman95
G 48 V	GGG to GTG	Protease Inhibitor	MK-639 (L-735,524, Indinavir)	?	Y				Vasudevachari96
G 48 V	GGG to GTG	Protease Inhibitor	MP-167	Y	?	20	MP-134(5) SC-52151(16) Ro31–8959(5) (Fold increase in IC90s).	L10F/G48V: 20-fold	Mo96
G 48 V	GGG to GTG	Protease Inhibitor	Ro 31–8959 (saquinavir)	Y	Y			Found in comb. with L10I in vivo; G48V/I84V/L90M: 30-fold; G48V/L90M: >100-fold enzyme resistance; G48V/L90M/I54V: > 50-fold (subtype B or O)	Jacobsen94, Eberle95
G 48 V	GGG to GTG	Protease Inhibitor	SC-52151	Y	?		Ro 31–8959	G48V/V82A, G48V/L63P/V82A or I54T: 10- to 20-fold; L24V/G48V/A71V/V75I/P81T: 1000-fold	Potts94, Pillay96

Mutations in HIV Protease that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
I 50 L	ATT to CTT	Protease Inhibitor	BMS-232632	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 to GTT	Protease Inhibitor	VB 11,328	Y	?	3		I50V/M46I/I47V: 20-fold	Tisdale94, Partaledis95
I 50 V	ATT to GTT	Protease Inhibitor	VX-478 (141W94)	Y	?	3			Partaledis95, Rao96
G 52 S	GGT to AGT	Protease Inhibitor	Nelfinavir	?	Y			D30N/G52S: 93-fold	Patick98
I 54 M	ATT to ATG	Protease Inhibitor	BILA 2185 BS	Y	?		BILA 1906 (360)	L10F/L23I/V32I/M46I/I47V/I54M/ A71V/I84V: 1,500-fold. 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
I 54 V	ATC to GTC	Protease Inhibitor	ABT-538 (ritonavir)	N	Y			I54V/V82T: 9-fold; K20R/M36I/I54V/ V82A: 41-fold; M36I/I54V/A71V/ V82T: 8-fold; I54V/A71V/V82A/L90N: 7-fold; In vivo, V82A/F/T/S occurs first, followed by changes at 54, 71 and 36	Molla96
I 54 V	ATC to GTC	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y				Lamarre94
I 54 V	ATA to GTA	Protease Inhibitor	Ro 31–8959 (saquinavir)	Y				In subtype O and B	Jacobsen94, Eberle95
K 55 R	AAA to AGA	Protease Inhibitor	Nelfinavir	?	Y			Seen in one patient following a switch from saquinavir. Associated with reduced susceptibility to both saquinavir and nelfinavir.	Lawrence99

Mutations in HIV Protease that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
R 57 K	AGA to AAA	Protease Inhibitor	Nelfinavir	?	Y			Seen in one patient following a switch from saquinavir. Associated with reduced susceptibility to both saquinavir and nelfinavir.	Lawrence99
D 60 E	GAT to GAA	Protease Inhibitor	DMP 450	Y	?			Probably compensatory	Otto95, Winslow95
D 60 E	GAT to GAA	Protease Inhibitor	PNU-140690 (Tipranavir)	?	Y			Seen in 30% of patients receiving Tipranavir therapy.	Rusconi00
L 63 P	CTC to CCC	Protease Inhibitor	BMS-232632	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 to CCC	Protease Inhibitor	MK-639 (L-735,524, indinavir)	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 to CCC	Protease Inhibitor	Nelfinavir	?	Y			D30N/M36I/L63P: 60-fold	Patick98
H 69 Y	CAT to TAT	Protease Inhibitor	ABT-378	Y	?		Passage 17 virus: ritonavir, 21-fold; saquinavir, 4-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
A 71 T	GCT to ACT	Protease Inhibitor	BMS 186,318	Y	?			A71T/V82A: 15-fold	Patick95, Rose94
A 71 T	GCT to ACT	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y				Condra96, Condra95
A 71 T	GCT to ACT	Protease Inhibitor	PNU-140690 (Tipranavir)	?	Y				Rusconi00
A 71 V	GCT to GTT	Protease Inhibitor	A-77003	Y	?			V32I appears first; progression to V32I/M46V and V32I/M46V/A71V/V82A occurs even in the absence of drug; M46I/L63P/A71V/V82F/I84V: 27-fold	Tisdale94, King95
A 71 V	GCT to GTT	Protease Inhibitor	ABT-538 (ritonavir)	Y	Y				Molla96

Mutations in HIV Protease that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
A 71 V	GCT to GTT	Protease Inhibitor	AG1343 (nelfinavir)	Y	?	5		D30N/A71V: 7-fold; M46I/L63P/A71V/I84V: 30-fold	Patick98
A 71 V	GCT to GTT	Protease Inhibitor	BILA 1906 BS	Y	?			V32I/A71V: 3-fold; V32I/M46I,L/A71V/I84V: 5-fold; V32I/M46I,L/A71V/I84A: 520-fold. 32I/46L/71V/84A are functionally impaired. Associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1′)	Croteau97, Doyon96, Lamarre94, Lamarre95
A 71 V	GCT to GTT	Protease Inhibitor	BILA 2011 (palinavir)	Y	?		BILA 2185: 30-fold		Lamarre94
A 71 V	GCT to GTT	Protease Inhibitor	BILA 2185 BS	Y	?		BILA 1906 (360)	L10F/L23I/V32I/M46I/I47V/I54M/A71V/I84V: 1,500-fold. 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
A 71 V	GCT to GTT	Protease Inhibitor	BMS-232632	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 to GTT	Protease Inhibitor	MK-639 (L-735,524, indinavir)	Y	Y			V32I/M46L/A71V/V82A: 14-fold	Tisdale94
A 71 V	GCT to GTT	Protease Inhibitor	SC-52151	Y	?		Not L-735,524	A71V/V75I/P81T: 20- to 30-fold; L24V/G48V/A71V/V75I/P81T: 1000-fold; N88D or I11V/M46I/F53L/A71V/N88D:10- to 20-fold	Potts94, Pillay96
G 73 S	GGT to GCT	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y			Emerges following a switch from saquinavir to indinavir.	Dulioust97
G 73 S	GGT to AGT	Protease Inhibitor	Nelfinavir	?	Y			Seen in two patients following a switch from saquinavir. Associated with reduced susceptibility to both saquinavir and nelfinavir.	Lawrence99
V 75 I	GTA to ATA	Protease Inhibitor	SC-52151	Y	?			L24V/G48V/A71V/V75I/P81T: 1000-fold; A71V/V75I/P81T: 20- to 30-fold; L24V/G48V/A71V/V75I/P81T: 1000-fold	Potts94, Pillay96

Mutations in HIV Protease that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
V 77 I	GTA to ATA	Protease Inhibitor	AG1343 (nelfinavir)	Y	Y				Patick98
P 81 T	CCT to ACT	Protease Inhibitor	SC-52151	Y	?			A71V/V75I/P81T: 20- to 30-fold; L24V/G48V/A71V/V75I/P81T: 1000-fold	Potts94, Pillay96
I 82 T	ATC to ACC	Protease Inhibitor	A-77003	Y	?			G48V/I82T: 100-fold 82T was derived from in vitro passage of 82I)	Swanstrom94
V 82 A	GTC to GCC	Protease Inhibitor	A-77003	Y	?			Rare; seen with M46F; V32I appears first; progression to V32I/M46V and V32I//M46V/A71V/V82A occurs even in the absence of drug	Tisdale94, Borman95, Swanstrom94
V 82 A	GTC to GCC	Protease Inhibitor	ABT-538 (ritonavir)	N	Y	2		In vivo, V82 occurs first, often followed by changes at I54, A71 and M36	Molla96
V 82 A	GTC to GCC	Protease Inhibitor	BMS 186,318	Y	?		A-77003 (4)	A71T/V82A: 15-fold	Patick95, Rose94
V 82 A	GTC to GCC	Protease Inhibitor	MK-639 (L-735,524, indinavir)	Y	Y			V32I/M46L/V82A: 3-fold; V32I/M46L/A71V/V82A: 14-fold	Condra96, Condra95
V 82 A	GTC to GCC	Protease Inhibitor	Nelfinavir	?	Y				Lawrence99
V 82 A	GTC to GCC	Protease Inhibitor	P9941	Y	?	6–8			Otto93
V 82 A	GTC to GCC	Protease Inhibitor	Ro 31–8959 (saquinavir)	?	Y			Follows G48V during saquinavir therapy or after a switch to nelfinavir or indinavir.	Winters97, Eastman97, Schapiro97
V 82 A	GTC to GCC	Protease Inhibitor	SC-52151	Y	?			G48V/V82A, G48V/L63P/V82A or I54T: 10- to 20-fold	Potts94, Pillay96
V 82 A	GTC to GCC	Protease Inhibitor	SKF108922	Y	?				Shao95
V 82 A	GTC to GCC	Protease Inhibitor	XM323	Y	?			V82A/M46L: 7-fold; V82A/M46L/L97V: 11-fold; L10F/V82A: 2-fold; ; V82A/L97V: 3-fold	King95
V 82 F	GTC to TTC	Protease Inhibitor	ABT-538 (ritonavir)	Y	Y			V82F/I84V: 8- to 10-fold; M46I/L63P/A71V/V82F/I84V: 27-fold	Molla96

Mutations in HIV Protease that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
V 82 F	GTC to TTC	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y				Partaledis94
V 82 F	GTC to TTC	Protease Inhibitor	XM323	Y	?			V82F/I84V: 92-fold	King95
V 82 I	GTC to ATC	Protease Inhibitor	A-77003	Y	?			No resistance alone but V32I and V82I are synergistic mutations yielding 20-fold enzyme resistance 82T was derived from in vitro passage of 82I)	Kaplan94
V 82 I	GTC to ATC	Protease Inhibitor	XM323	Y	?	< 2			King95
V 82 S	GTC to TCC	Protease Inhibitor	ABT-538 (ritonavir)	N	Y	6		In vivo, V82 occurs first, often followed by changes at I54, A71 and M36	Molla96
V 82 T	GTC to ACC	Protease Inhibitor	ABT-538 (ritonavir)	N	Y	3		In vivo, V82 occurs first, often followed by changes at I54, A71 and M36; V82T has reduced replication efficacy in natural background	Molla96
V 82 T	GTC to ACC	Protease Inhibitor	MK-639 (L-735,524, indinavir)	N	Y			M46I/L63P/V82T: 4-fold; L10R/M46I/L63P/V82T: 4-fold; L10R/M46I/L63P/V82T/I84V: 8-fold	Condra96, Condra95
V 82 T	GTC to ACC	Protease Inhibitor	SKF108842	Y	?				Shao95
V 82 T	GTC to ACC	Protease Inhibitor	SKF108922	Y	?				Shao95
I 84 A	ATA to GCA	Protease Inhibitor	BILA 1906 BS	Y	?		BILA 2185 BS (200)	V32I/A71V: 3-fold; V32I/M46I,L/A71V/I84V: 5-fold; V32I/M46I,L/A71V/I84A: 520-fold. 32I/46L/71V/84A are functionally impaired. Associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1′))	Croteau97, Doyon96, Lamarre94, Lamarre95
I 84 A	ATG to ATA	Protease Inhibitor	BILA 2011 (palinavir)	Y	?		Ro 31–8959 (400);	I84A is the most common mutation	Lamarre94

Mutations in HIV Protease that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
I 84 V	ATA to GTA	Protease Inhibitor	ABT-378	Y	?		Passage 17 virus: ritonavir, 21-fold; saquinavir, 4-fold	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 to GTA	Protease Inhibitor	ABT-538 (ritonavir)	Y	Y			M46I/L63P/A71V/V82F/I84V: 27-fold; V82F/I84V: 8- to 10-fold; M46I/L63P/A71V/V82F/I84V: 27-fold	Molla96
I 84 V	ATA to GTA	Protease Inhibitor	AG1343 (nelfinavir)		?			M46I/L63P/A71V/I84V: 30-fold	Patick96
I 84 V	ATA to GTA	Protease Inhibitor	BILA 1906 BS	Y	?		BILA 2185 BS(200)	V32I/A71V: 3-fold; V32I/M46I,L / A71V/I84V: 5-fold; V32I/M46I,L/A71V/I84A: 520-fold. 32I/46L/71V/84A are functionally impaired. Associated Gag mutations: p1/p6 cleavage site (L to F (CTT to TTT at P1′)	Croteau97, Doyon96, Lamarre94, Lamarre95
I 84 V	ATA to GTA	Protease Inhibitor	BILA 2185 BS	Y	?		BILA 1906 BS(360)	L10F/L23I/V32I/M46I/I47V/I54M/A71V/I84V: 1,500-fold. 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
I 84 V	ATA to GTA	Protease Inhibitor	BMS-232632	Y	?			Minor resistance mutation for BMS-232632.	Gong99
I 84 V	ATA to GTA	Protease Inhibitor	BMS-232632	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 to GTA	Protease Inhibitor	DMP 450	Y	?				Otto95, Winslow95
I 84 V	ATA to GTA	Protease Inhibitor	JE-2147	Y	?		KNI-272: 7-fold; Ritonavir: 9-fold	L10F/I47V/I84V: 19-fold. L10F/M46I/I47V/I84V: 28-fold. >50 passages required for isolation of resistant virus.	Yoshimura99

Mutations in HIV Protease that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
I 84 V	ATA to GTA	Protease Inhibitor	MK-639 (L-735,524, indinavir)	N	Y			G48V/I84V/L90M: 30-fold; L10R/M46I/L63P/V82T/I84V: 8-fold	Condra96, Condra95
I 84 V	ATA to GTA	Protease Inhibitor	MP-134	Y	?	10	MP-167(5) ABT-538(10) MK-639(8) SC-52151(8) Ro31–895(2) (IC90 data)		Mo96
I 84 V	ATA to GTA	Protease Inhibitor	Ro 31–8959 (saquinavir)	Y	?				Tisdale94
I 84 V	ATA to GTA	Protease Inhibitor	RPI-312	Y	?	5			el-Farrash94
I 84 V	ATA to GTA	Protease Inhibitor	SKF108842	Y	?				Shao95
I 84 V	ATA to GTA	Protease Inhibitor	VB 11,328	Y	?			L10F/I84V: 8-fold	Partaledis95
I 84 V	ATA to GTA	Protease Inhibitor	VX-478 (141W94)	Y	?				Partaledis95
I 84 V	ATA to GTA	Protease Inhibitor	XM323	Y	?	12	P9941; not A-77003 or Ro 31–8959	V82F/I84V: 92-fold; L10F/K45I/I84V: 50-fold	Tisdale94, King95
N 88 D	AAT to GAT	Protease Inhibitor	AG1343 (nelfinavir)	Y	Y			D30N and N88D are most common in vivo after 24 weeks of therapy; they do not cause cross-resistance to other protease inhibitors.	Patick96
N 88 D	AAT to GAT	Protease Inhibitor	SC-52151	Y	?			N88D compensatory, no resistance alone	Potts94, Pillay96
N 88 S	AAT to AGT	Protease Inhibitor	Amprenavir	Y	Y			Confers >2.5-fold hypersusceptibility to Amprenavir.	Ziermann00
N 88 S	AAT to AGT	Protease Inhibitor	BMS-232632	Y	?			Major resistance mutation for BMS-232632.	Gong99
N 88 S	AAT to AGT	Protease Inhibitor	BMS-232632	Y	?			V32L/L33F/M46I/A71V/I84V/N88S: 183-fold., L10Y,F/I50L/L63P/A71V/N88S: 93-fold., V32I/M46I/I84V/L89M: 96-fold.	Gong00

Mutations in HIV Protease that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
N 88 S	AAT to AGT	Protease Inhibitor	SC-55389A	Y	?	20	L735,524 (3); not SC-52151	N88S/L10F: 25	Smidt97
L 89 M		Protease Inhibitor	BMS-232632	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 to ATG	Protease Inhibitor	ABT-538 (ritonavir)	N	Y			82A/54V/I/71V/90L/M: 7-fold	Molla96
L 90 M	TTG to ATG	Protease Inhibitor	AG1343 (nelfinavir)	N	Y			Rare in patients	Patick96
L 90 M	TTG to ATG	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y				Condra96
L 90 M	TTG to ATG	Protease Inhibitor	Ro 31–8959 (saquinavir)	Y	Y			G48V/L90M: >100-fold enzyme resistance; double mutant rare in vivo; L90M most common in vivo; G48V/I84V/L90M: 30-fold	Jacobsen94
T 91 S	ACT to TCT	Protease Inhibitor	ABT-378	Y	?		Passage 17 virus: ritonavir, 21-fold; saquinavir, 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
L 97 V	TTA to GTA	Protease Inhibitor	XM323	Y	?			No resistance alone; V82A/L97V: 3-fold; V82A/M46L/L97V: 11-fold	King95

Mutations in HIV Integrase that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
G 140 S	GGC to AGC	Integrase inhibitor	L-Chicoric Acid	Y	?	156-fold		Mutation located in the catalytic core of integrase. Mildly attentuates virus growth.	King98

Mutations in HIV Env that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
R 22 A	AGG to AGA	Fusion/Binding Inhibitor	RPR103611	Y	?				Labrosse97
G 36 S	GGT to AGT	Fusion/Binding Inhibitor	DP178 (T20)	Y	?			Both G36S and V38M mutations must be present to confer resistance.	Rimsky98
V 38 M	GTG to ATG	Fusion/Binding Inhibitor	DP178 (T20)	Y	?			Both G36S and V38M mutations must be present to confer resistance.	Rimsky98
I 84 S	ATC to AGC	Fusion/Binding Inhibitor	RPR103611	Y	?				Labrosse97
L 91 H	to	Fusion/Binding Inhibitor	RPR103611	Y	?				Labrosse00
N 106 K	AAT to AAG	Fusion/Binding Inhibitor	SDF-1α	Y	?		SDF-1β: 15-fold; AMB2763: 3-fold.	106K/134N/145L/245I/269E/278H/ 288V/293D/364–367Deletion/387T: 15-fold.	Schols98
S 113 N	AGT to AAT	Fusion/Binding Inhibitor	Dextran sulphate (DS)	Y	?			S113N/S134N/K269E/Q278E/N293D/ N323S/R387I: 250-fold; 113 is in the V1 loop region	Este96a, Este97
S 134 N	AGC to AAC	Fusion/Binding Inhibitor	Dextran sulphate (DS)	Y	?			V2 loop region; S113N/S134N/K269E/ Q278E/N293D/N323S/R387I: 250-fold	Este97, Este96a
S 134 N	AGC to AAC	Fusion/Binding Inhibitor	SDF-1α	Y	?		SDF-1β: 15-fold; AMB2763: 3-fold.	106K/134N/145L/245I/269E/278H/ 288V/293D/364–367Deletion/387T: 15-fold.	Schols98
F 145 L	TTC to TTA	Fusion/Binding Inhibitor	JM-3100 (SID791)	Y	?			Combination of mutations: 2- to 100-fold	DeVreese96, DeVreese96a
F 145 L	TTC to TTA	Fusion/Binding Inhibitor	SDF-1α	Y	?		SDF-1β: 15-fold; AMB2763: 3-fold.	106K/134N/145L/245I/269E/278H/ 288V/293D/364–367Deletion/387T: 15-fold.	Schols98
N 188 K	AAT to AAA	Fusion/Binding Inhibitor	Siamycin I	Y	?			N188K/G332E/N351D/A550T/N633D/ L762S: 9-fold	Lin96
I 228 V	ATA to GTA	Fusion/Binding Inhibitor	JM-2763	Y	?			Combination of mutations	DeVreese96a

Mutations in HIV Env that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
G 237 R	to	Fusion/Binding Inhibitor	IC9564	Y	?				Holz-Smith01
F 245 I	TTC to ATC	Fusion/Binding Inhibitor	SDF-1α	Y	?		SDF-1β: 15-fold; AMB2763: 3-fold.	106K/134N/145L/245I/269E/278H/288V/293D/364–367Deletion/387T: 15-fold.	Schols98
R 252 K	to	Fusion/Binding Inhibitor	IC9564	Y	?				Holz-Smith01
K 269 E	AAA to GAA	Fusion/Binding Inhibitor	Dextran sulphate (DS)	Y	?			V3 loop region; S113N/S134N/K269E/Q278E/N293D/N323S/R387I: 250-fold	Este97, Este96a
N 269 E	AAC to GAA	Fusion/Binding Inhibitor	SDF-1α	Y	?		SDF-1β: 15-fold; AMB2763: 3-fold.	106K/134N/145L/245I/269E/278H/288V/293D/364–367Deletion/387T: 15-fold.	Schols98
N 270 S	AAT to AGT	Fusion/Binding Inhibitor	JM-3100 (SID791)	Y	?				DeVreese96, DeVreese96a
R 272 T	AGA to ACA	Fusion/Binding Inhibitor	JM-3100 (SID791)	Y	?				DeVreese96, DeVreese96a
S 274 R	AGT to AGA	Fusion/Binding Inhibitor	JM-2763	Y	?			Combination of mutations: 95- to 792-fold	DeVreese96, DeVreese96a
S 274 R	AGT to AGA	Fusion/Binding Inhibitor	JM-3100 (SID791)	Y	?	DS (> 7 to 6,667)			DeVreese96, DeVreese96a
Q 278 H	CAG to CAT	Fusion/Binding Inhibitor	Dextran sulphate (DS)	Y	?			V3 loop region; S113N/S134N/K269E/Q278E/N293D/N323S/R387I: 250-fold	Este97, Este96a
Q 278 H	CAG to CAT	Fusion/Binding Inhibitor	JM-2763	Y	?				DeVreese96, DeVreese96a
Q 278 H	CAG to CAC	Fusion/Binding Inhibitor	JM-3100 (SID791)	Y	?				DeVreese96, DeVreese96a
Q 278 H	CAG to CAT	Fusion/Binding Inhibitor	SDF-1α	Y	?		SDF-1β: 15-fold; AMB2763: 3-fold.	106K/134N/145L/245I/269E/278H/288V/293D/364–367Deletion/387T: 15-fold.	Schols98
I 288 V	ATA to GTA	Fusion/Binding Inhibitor	JM-3100 (SID791)	Y	?				DeVreese96, DeVreese96a

Mutations in HIV Env that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
I 288 V	ATA to GTC	Fusion/Binding Inhibitor	SDF-1α	Y	?		SDF-1β: 15-fold; AMB2763: 3-fold.	106K/134N/145L/245I/269E/278H/ 288V/293D/364–367Deletion/387T: 15-fold.	Schols98
N 293 D	AAT to GAT	Fusion/Binding Inhibitor	Dextran sulphate (DS)	Y	?			V3 loop region; S113N/S134N/K269E/ Q278E/N293D/N323S/R387I: 250-fold	Este97, Este96a
N 293 D	AAT to GAT	Fusion/Binding Inhibitor	SDF-1α	Y	?		SDF-1β: 15-fold; AMB2763: 3-fold.	106K/134N/145L/245I/269E/278H/ 288V/293D/364–367Deletion/387T: 15-fold.	Schols98
N 293 H	AAT to CAT	Fusion/Binding Inhibitor	JM-3100 (SID791)	Y	?				DeVreese96, DeVreese96a
A 297 T	GCA to ACA	Fusion/Binding Inhibitor	JM-2763	Y	?				DeVreese96, DeVreese96a
A 297 T	GCA to ACA	Fusion/Binding Inhibitor	JM-3100 (SID791)	Y	?				Este97, Este96a
N 323 S	AAT to AGT	Fusion/Binding Inhibitor	Dextran sulphate (DS)	Y	?			C3 region; S113N/S134N/K269E/ Q278E/N293D/N323S/R387I: 250-fold	Este97, Este96a
G 332 E	GGA to GAA	Fusion/Binding Inhibitor	Siamycin I	Y	?			N188K/G332E/N351D/A550T/N633D/ L762S: 9-fold	Lin96
N 351 D	AAT to GAT	Fusion/Binding Inhibitor	Siamycin I	Y	?			N188K/G332E/N351D/A550T/N633D/ L762S: 9-fold	Lin96
ΔFNSTW 364–368	Deletion	Fusion/Binding Inhibitor	SDF-1α	Y	?		SDF-1β: 15-fold; AMB2763: 3-fold.	106K/134N/145L/245I/269E/278H/ 288V/293D/364–367Deletion/387T: 15-fold.	Schols98
P 385 L	CCA to CTA	Fusion/Binding Inhibitor	JM-2763	Y	?				DeVreese96, DeVreese96a
P 385 L	CCA to CTA	Fusion/Binding Inhibitor	JM-3100 (SID791)	Y	?				DeVreese96, DeVreese96a

Mutations in HIV Env that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
R 387 I	AGA to ACA	Fusion/Binding Inhibitor	Dextran sulphate (DS)	Y	?			CD4 binding region; S113N/S134N/ K269E/Q278E/N293D/N323S/R387I: 250-fold	Este97, Este96a
R 387 T	AGA to ACA	Fusion/Binding Inhibitor	SDF-1α	Y	?		SDF-1β: 15-fold; AMB2763: 3-fold.	106K/134N/145L/245I/269E/278H/ 288V/293D/364–367Deletion/387T: 15-fold.	Schols98
Q 410 E	CAA to GAA	Fusion/Binding Inhibitor	JM-3100 (SID791)	Y	?				DeVreese96, DeVreese96a
S 433 P	TCC to CCC	Fusion/Binding Inhibitor	JM-3100 (SID791)	Y	?				DeVreese96, DeVreese96a
V 457 I	GTA to ATA	Fusion/Binding Inhibitor	JM-3100 (SID791)	Y	?				DeVreese96, DeVreese96a
A 550 T	GCC to ACC	Fusion/Binding Inhibitor	Siamycin I	Y	?			N188K/G332E/N351D/A550T/N633D/ L762S: 9-fold	Lin96
N 633 D	AAT to GAT	Fusion/Binding Inhibitor	Siamycin I	Y	?			N188K/G332E/N351D/A550T/N633D/ L762S: 9-fold	Lin96
L 762 S	TTG to TCG	Fusion/Binding Inhibitor	Siamycin I	Y	?			N188K/G332E/N351D/A550T/N633D/ L762S: 9-fold	Lin96

Mutations in SIVRT that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
K 65 R	AAA to AGA	SIV Nucleoside RT Inhibitor	PMPA	?	Y	5	3TC (80); ddI; ddC; d4T; PMEA	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 to ATG	SIV Nucleoside RT Inhibitor	AZT	?	Y	>100	ddI; ddC; d4T; 3TC		VanRompay97
M 184 V	ATG to GTG	SIV Nucleoside RT Inhibitor	(-)-FTC	Y	?				Schinazi95

Mutations in FIVRT that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resist (-fold)	Comments	Refs
D 3 H	GAT to CAT	FIV Nucleoside RT Inhibitor	ddC	Y	?	4	ddI; PFA		Medlin96, Zhu96
V 47 I	GTA to ATA	FIV Nucleoside RT Inhibitor	d4T	Y	?	4-6	PFA (>50); AZT; ddI; PMEA		Smith96
P 156 S	CCA to TCA	FIV Nucleoside RT Inhibitor	3TC	Y	?	7	AZT (4), AZT + 3TC (6)		Smith98
M 183 T	ATG to ACG	FIV Nucleoside RT Inhibitor	(-)-FTC	Y	?	10	ddC	Corresponds to 184 in HIV; M183V recombinant displays 10-fold resistance to 3TC or (-)-FTC.	Smith97

Abbreviations

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

Compounds

1592U89	(1*S*,4*R*)-4-[2-amino-6-cyclopropyl-amino)-9*H*-purin-9-yl]-2-cyclopentene-1-methanol succinate (a carbovir analogue, Glaxo Wellcome)
3TC	(-)-β-L-2′,3′-dideoxy-3′-thiacytidine (Glaxo Wellcome)
1737	Tetrahydronapthalene lignan derivative
α-APA R18893	α-nitro-anilino-phenylacetamide
A-77003, A-75925 and A-80987	C2 symmetry-based protease inhibitors (Abbott Laboratories)
AAP-BHAP	bisheteroarylpiperazine analogue (Pharmacia & Upjohn)
ABT-378	Protease inhibitor
ABT-538	C2 symmetry-based protease inhibitor (Abbott Laboratories)
ADAMII	Methyl 3′,3″-dichloro-4′,4″-dimethoxy-5′,5″-bis(methoxycarbonyl)-6,6-diphenyl-5-hexenoate. (An alkenyldiarylmethane).
AZdU	3′-azido-2′,3′-dideoxyuridine
AZT	3′-azido-3′-deoxythymidine (Glaxo Wellcome)
AZT-p-ddI	3′-azido-3′-deoxythymidilyl-(5′,5′)-2′,3′-dideoxyinosinic acid (Ivax)
BHAP	bisheteroarylpiperazine
BILA 1906	*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 (Bio-Mega/Boehringer Ingelheim)

Abbreviations (cont)

Compounds (cont)

BILA 2185	*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 (Bio-Mega/Boehringer Ingelheim)
BM+51.0836	thiazolo-isoindolinone derivative
BMS 186,318	aminodiol derivative HIV-1 protease inhibitor (Bristol-Myers Squibb)
BMS-232632	An azapeptide protease inhibitor
d4API	9-[2,5-dihydro-5-(phosphonomethoxy)-2-furanel]adenine (Gilead Sciences)
d4C	2′,3′-didehydro-2′,3′-dideoxycytidine
d4T	2′,3′-didehydro-3′-deoxythymidine (Bristol-Myers Squibb)
ddC	2′,3′-dideoxycytidine (Roche)
ddI	2′,3′-dideoxyinosine (Bristol-Myers Squibb)
DMP 266	a 1,4-dihydro-2*H*-3,1-benzoxazin-2-one
DMP 450	[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)-2*H*-1,3-diazepin-2-one-bismesylate (Avid Therapeutics)
DP178	Synthetic peptide containing amino acids 127–162 of HIV-1 gp41
DXG	(-)-β-D-dioxolane-guanosine
EBU-dM	5-ethyl-1-ethoxymethyl-6-(3,5-dimethylbenzyl)uracil
E-EBU	5-ethyl-1-ethoxymethyl-6-benzyluracil
DS	dextran sulphate
E-EPSeU	1-(ethoxymethyl)-(6-phenylselenyl)-5-ethyluracil
E-EPU	1-(ethoxymethyl)-(6-phenyl-thio)-5-ethyluracil
F-ddA	2′-fluoro-2′,3′-dideoxyadenosine
(-)-FTC	(-)-β-L-2′,3′-dideoxy-5-fluoro-3′-thiacytidine (Triangle Pharmaceuticals)
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(1*H*)-thione
HEPT	1-[(2-hydroxyethoxy)methyl]6-(phenylthio)thymine
JE-2147	An allophenylnorstatine-containing dipeptide protease inhibitor
JM2763	1,1′-(1,3-propanediyl)-bis-1,4,8,11-tetraazacyclo-tetradecane (Johnson Matthey)
JM3100	1,1′-[1,4-phenylenebis-(methylene)]bis-(1,4,8,11-tetraazacyclotetradecane) octahydrochloride dihydrate (Johnson Matthey)
KNI-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(1*H*)-one
L-697,661	3-[(-4,7-dichloro-1,3-benzoxazol-2-yl)methyl]amino-5-ethyl-6-methylpyridin-2(1*H*)-one
L-chichoric acid	Integrase inhibitor
L-FDDC	(-)-β-L-5-fluoro-2′,3′-dideoxy-cytidine
L-FDOC	(-)-β-L-5-fluoro-dioxolane cytosine
MK-639	hydroxy-aminopentane amide HIV-1 protease inhibitor (Merck & Co)
MKC442	6-benzyl-1-ethoxymethyl-5-isopropyluracil (I-EBU, Triangle Pharmaceuticals/Mitsubishi)
MP-134	C2 symmetry-based protease inhibitor
MP-167	C2 symmetry-based protease inhibitor

Abbreviations (cont)

Compounds (cont)

nevirapine	11-cyclopropyl-5,11-dihydro-4-methyl-6*H*-dipyridol[3,2-b:2′,3′-e] diazepin-6-one (Boehringer Ingelheim)
NNRTI	non-nucleoside reverse transcriptase inhibitor
NSC648400	1-benzyloxymethyl-5-ethyl-6-(alpha-pyridylthio)uracil (E-BPTU)
P9941	[2-pyridylacetyl-IIePheAla-y(CHOH)]$_2$ (Dupont Merck)
PFA	phosphonoformate (foscarnet, Astra)
PMEA	9-(2 phosphonylmethoxyethyl)adenine (Gilead Sciences)
PMPA	(*R*)-9-(2-phosphonyl-methoxypropyl)adenine (Gilead Sciences)
QM96521	1,1,3-trioxo-2H,4H-thieno[2,4-3][1,2,4]thiadiazine derivative (TTD)
Ro 31-8959	hydroxyethylamine derivative HIV-1 protease inhibitor (Roche)
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	
RT	reverse transcriptase
S-1153	5-(3,5-dichlorophenyl)thio-4-isopropyl-1-(4-pyridyl)methyl-1H-imidazol-2-yl methyl carbamate
S-2720	6-chloro-3,3-dimethyl-4-(isopropenyl-oxycarbonyl)-3,4-dihydro-quinoxalin-2(1*H*)thione
SC-52151	hydroxyethylurea isostere protease inhibitor (Searle)
SC-55389A	hydroxyethyl-urea isostere protease inhibitor (Searle)
SDF-1α	Stromal cell-derived factor 1α
SDF-1β	Stromal cell-derived factor 1β
TIBO R82150	(+)-(5*S*)-4,5,6,7-tetrahydro-5-methyl-6-(3-methyl-2-butenyl)-imidazo[4,5,1-*jk*][1,4]-benzodiazepin-2(1*H*)-thione (Janssen)
TIBO 82913	(+)-(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(1it H)-thione (Janssen)
TSAO-m^{3}T	[2′,5′-bis-*O*-(tert-butyl-dimethylsilyl)-3′-spiro-5′-(4′-amino-1′,2′-oxathiole-2′,2′-dioxide)]-β-D-pentofuranosyl-N^3-methylthymine
U-90152	1-[3-[(1-methylethyl)-amino]-2-pyridinyl]-4-[[5-[(methylsulphonyl)-amino]-l*H*-indol-2yl]carbonyl]-piperazine
U-95133	(Alkylamino)piperidine bis(heteroaryl) piperizine analog
U-104489	(Alkylamino)piperidine bis(heteroaryl) piperizine analog
UC-040	thiocarboxanilide derivative (Uniroyal Chemical Co)
UC	thiocarboxanilide derivatives (Uniroyal Chemical Co)
UC-781	*N*-[4-chloro-3-(3-methyl-2-butenyloxy)phenyl]-2-methyl-3-furan-carbothioamide
UC-82	*N*-[4-chloro-3-(3-methyl-2-butenyloxy)phenyl]-2-methyl-3-thiophene-carbothioamide
VB 11,328	hydroxyethyl-sulphonamide protease inhibitor (Vertex Pharmaceuticals)
VX-478	hydroxyethylsulphonamide protease inhibitor (Vertex Pharmaceuticals)
XM 323	cyclic urea protease inhibitor (Dupont Merck)

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