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 updated table lists 143 mutations occurring in the HIV Gag (3), Protease (44), Reverse Transcriptase (69), or Envelope (27) genes. 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 includes for the first time 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. These sort of assays don't 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.

Acknowledgments

The authors would like to gratefully acknowledge their colleagues for assistance in assembling this table. This work was supported in part by the National Institutes of Health, the Department of Veterans Affairs, and the Georgia VA Research Center for AIDS and HIV Infections.

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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-resistance (-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.	(1, 2, 3)
A 62 V	GCC to GTC	Multiple Nucleoside Resistance		N	Y	Nil		A62V alone has no effect, but in combination with mutations at 75, 77, 116, 151 causes multi NRTI resistance.	(4, 5)
K 65 R	AAA to AGA	Nucleoside RTI	ddI	Y	Y	4-10	ddC; PMEA; 3TC(5)	Infrequently observed in patients receiving ddI or ddC	(6)
K 65 R	AAA to AGA	Nucleoside RTI	ddC	Y	Y	4-10			(6, 7)
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	(8)
K 65 R	AAA to AGA	Nucleoside RTI	DXG	Y	?	8	other dioxolane derivatives	Reverses AZT resistance in D67N/K70R/T215Y/K219Q background	(9)
K 65 R	AAA to AGA	Nucleoside RTI	PMEA	Y	N	10-25			(10, 11)
K 65 R	AAA to AGA	Nucleoside RTI	PMPA	Y	?	3.5			(12)
D 67 N	GAC to AAC	Nucleoside RTI	AZT	Y	Y			D67N/K70R/T215Y/K219Q: 120-fold; M41L/D67N/K70R/T215Y: 180-fold.	(1, 2, 3)
T 69 D	ACT to GAT	Nucleoside RTI	ddC	N	Y	5			(13)
K 70 E	AAA to GAA	Nucleoside RTI	PMEA	Y	Y	9	3TC (7); PFA: 2-fold hypersusceptibility		(14, 15)
K 70 R	AAA to AGA	Nucleoside RTI	AZT	Y	Y			D67N/K70R/T215Y/K219Q: 120-fold	(1, 2, 3)
L 74 I	TTA to ATA	HIV-1 Specific RTI	HBY 097	Y	?				(16)
L 74 V	TTA to GTA	Nucleoside RTI	ddI	N	Y	5-10	ddC(4)	Can reverse effect of T215Y AZT resistance mutation	(17)
L 74 V	TTA to GTA	Nucleoside RTI	1592U89	Y	N	4		K65R/L74V: 3.6-fold; K65R/L74V/M184V: 10.2-fold	(8)
L 74 V	TTA to GTA	Nucleoside RTI	DXG	Y	?	4			(9)
L 74 V	TTA to GTA	HIV-1 Specific RTI	HBY 097	Y	?				(16)
V 75 I	GTA to TTA	HIV-1 Specific RTI	HBY 097	Y	?			Compensates for negative effect of G190E mutation on RT activity	(16)

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-resistance (-fold)	Comments	Refs
V 75 I	GTA to ATA	Multiple Nucleoside Resistance		N	Y	Nil		V75I alone has no effect, but in combination with mutations at 62, 77, 116, 151 causes multi NRTI resistance.	(4, 5)
V 75 L	GTA to ATA	HIV-1 Specific RTI	HBY 097	Y	?				(16)
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	(18, 19)
F 77 L	TTC to CTC	Multiple Nucleoside Resistance		N	Y	Nil		F77L alone has no effect, but in combination with mutations at 62, 75, 116, 151 causes multi NRTI resistance.	(4, 5)
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	(20, 21, 22)
W 88 S	TGG to TCG	Pyrophosphate Analogue RTI	Foscarnet (PFA)	N	Y	2-4	Wild-type susceptibility to AZT.	Partially suppresses effects	(20, 21, 22)
E 89 G	GAA to GGA	Pyrophosphate Analogue RTI	Foscarnet (PFA)	Y	N	14		Isolated by screening RT clones for ddGTP resistance	(23)
E 89 K	GAA to GGA	Pyrophosphate Analogue RTI	Foscarnet (PFA)	Y	N	> 16		Suppresses effects of AZT resistance mutations	(21, 22)
L 92 I	TTA to ATA	Pyrophosphate Analogue RTI	Foscarnet (PFA)	Y	N	8		Partially suppresses effects of AZT resistance mutations	(21, 22)
A 98 G	GCA to GGA	HIV-1 Specific RTI	L-697,661	N	Y	8			(24)

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-resistance (-fold)	Comments	Refs
A	98	G	GCA to GGA	HIV-1 Specific RTI	Nevirapine	N	Y				(25)
L	100	I	TTA to ATA	HIV-1 Specific RTI	TIBO R82150	Y	?	> 100		suppresses effects of AZT resistance mutations	(26, 27, 28)
L	100	I	TTA to ATA	HIV-1 Specific RTI	TIBO R82913	Y	?			Found in combination with E138K	(29)
L	100	I	TTA to ATA	HIV-1 Specific RTI	L-697,661	Y	N	2			(24)
L	100	I	TTA to ATA	HIV-1 Specific RTI	Nevirapine	N	Y				(30)
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	(31, 32)
L	100	I	TTA to ATA	HIV-1 Specific RTI	BHAP U-88204E	Y	?				(33, 34)
L	100	I	TTA to ATA	HIV-1 Specific RTI	UC-68 (638532)	Y	?	70			(35)
L	100	I	TTA to ATA	HIV-1 Specific RTI	UC-70 (638534)	Y	?	758			(36)
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	(37, 38)
L	100	I	TTA to ATA	HIV-1 Specific RTI	UC-84 (615985)	Y	?	> 40, > 33			(36, 39)
K	101	E	AAA to GAA	HIV-1 Specific RTI	8-Chloro-TIBO R091767	?	Y				(40)
K	101	E	AAA to GAA	HIV-1 Specific RTI	BHAP U-87201E (atevirdine)	N	Y			K101E, Y188H, E233Y and K238T observed with U-87201E/AZT combination therapy	(41)
K	101	E	AAA to GAA	HIV-1 Specific RTI	DMP 266 (L-743,726)	Y	?	1,000			(32)
K	101	E	AAA to GAA	HIV-1 Specific RTI	L-697,661	N	Y	8			(24)
K	101	E	AAA to GAA	HIV-1 Specific RTI	UC-10 (645129)	Y	?	12		K101E/Y181C: 200-fold	(36, 42, 43)

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-resistance (-fold)	Comments	Refs
K	101	E	AAA to GAA	HIV-1 Specific RTI	UC-38 (629243)	Y	N			K101E/G190E: > 100-fold	(36)
K	101	E	AAA to GAA	HIV-1 Specific RTI	UC-57 (647014)	Y	?			K101E/Y181C: 58-fold	(36)
K	101	E	AAA to GAA	HIV-1 Specific RTI	UC781	Y	?	7	UC040 (18); Nevirapine (15)	V108I/ Y181C: 55-fold; K101E/ V108I/ Y181C: 500-fold.	(37, 43)
K	101	I	AAA to ATA	HIV-1 Specific RTI	UC-16	Y	N	10		K101I/G141E: 10-fold	(36)
K	101	Q	AAA to CAA	HIV-1 Specific RTI	Trovirdine	Y	?			Found in combination with V108I	(44, 45)
K	103	N	AAA to AAC	HIV-1 Specific RTI	8-Chloro-TIBO R091767	?	Y				(40)
K	103	N	AAA to AAC	HIV-1 Specific RTI	BHAP U-87201E (atevirdine)	N	Y			K103N and Y181C observed with monotherapy	(41)
K	103	N	AAA to AAC	HIV-1 Specific RTI	BHAP U-90152 (delavirdine)	?	Y			K103N/Y181C seen separately and in combination in patients	(46)
K	103	N	AAA to AAC	HIV-1 Specific RTI	DMP 266 (L-743,726)	Y	Y	67		Predominant mutation in vivo	(31)
K	103	N	AAA to AAC	HIV-1 Specific RTI	L-697,593	Y	?	20		K103N/Y181C: > 1,000-fold	(47)
K	103	N	AAA to AAC	HIV-1 Specific RTI	L-697,661	Y	Y	8		K103N and Y181C most common with monotherapy	(24, 48)
K	103	N	AAA to AAC	HIV-1 Specific RTI	Loviride (R89439, α-APA)	Y	Y				(49)
K	103	N	AAA to AAC	HIV-1 Specific RTI	MKC442 (I-EBU)	Y	?			predominant mutation in vivo	(50)
K	103	N	AAA to AAC	HIV-1 Specific RTI	Nevirapine	N	Y				(30)
K	103	N	AAA to AAC	HIV-1 Specific RTI	TIBO R82913	Y	?	> 100		K103N/Y181C: > 1,000-fold	(33)
K	103	N	AAA to AAC	HIV-1 Specific RTI	UC-10 (645129)	Y	N	5			(35)
K	103	N	AAA to AAC	HIV-1 Specific RTI	UC-81 (615727)	Y	?	40			

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-resistance (-fold)	Comments	Refs
K	103	Q	AAA to CAA	HIV-1 Specific RTI	L-697,661	N	Y	8			(48)
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	(44, 45)
K	103	R	AAA to AGA	HIV-1 Specific RTI	MKC442(1-EBU)	Y	Y				(51)
K	103	T	AAA to ACA	HIV-1 Specific RTI	BHAP U-90152 (delavirdine)	?	Y				(46)
K	103	T	AAA to ACA	HIV-1 Specific RTI	UC-42	Y	N	100			(36)
V	106	A	GTA to GCA	HIV-1 Specific RTI	BHAP U-88204E	Y	?				(34)
V	106	A	GTA to GCA	HIV-1 Specific RTI	E-EBU-dM	Y	?				(52)
V	106	A	GTA to GCA	HIV-1 Specific RTI	Nevirapine	Y	Y	∼100		No effect on AZT resistance	(25, 29, 30, 33)
V	106	A	GTA to GCA	HIV-1 Specific RTI	TIBO R82913	Y	?	∼100			(29)
V	106	A	GTA to GCA	HIV-1 Specific RTI	UC-69 (646989)	Y	?			V106A/V181C: 166-fold	(36)
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	(37, 38)
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	(53)
V	106	I	GTA to ATA	HIV-1 Specific RTI	HBY 097					Appears under lowered drug concentration selection	(54)
V	108	I	GTA to ATA	HIV-1 Specific RTI	DMP 266 (L-743,726)	Y	?			L100I/V108I: 1,000-fold	(31)
V	108	I	GTA to GCA	HIV-1 Specific RTI	L-697,661	Y	Y	4			(24)
V	108	I	GTA to ATA	HIV-1 Specific RTI	Loviride (R89439, α-APA)	Y	?				(49)
V	108	I	GTA to GCA	HIV-1 Specific RTI	MKC442 (I-EBU)	Y	?				(50)

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-resistance (-fold)	Comments	Refs
V 108 I	GTA to ATA	HIV-1 Specific RTI	Nevirapine	N	Y				(30)
V 108 I	GTT to GAT	HIV-1 Specific RTI	TIBO R82913	N	Y	> 100	R82150 (> 100)		(55)
V 108 I	GTA to ATA	HIV-1 Specific RTI	Trovirdine	Y	?			Found in combination with K101Q	(44, 45)
V 108 I	GTA tO ATA	HIV-1 Specific RTI	UC781	Y	?			V108I/Y181C: 55 fold. K101E/V108I/Y181C: 500 fold.	(43)
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	(8)
F 116 Y	TTT to TAT	Multiple Nucleoside Resistance		N	Y	Nil		F116Y alone has no effect, but in combination with mutations at 62, 75, 77, 151 causes multi NRTI resistance.	(4, 5)
P 119 S	CCC to TCC	Nucleoside RTI	F-ddA	Y	?	4		Found with V179D and/or L214F, which are possibly compensatory	(56)
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	(57, 58, 59)
E 138 K	GAG to AAG	HIV-1 Specific RTI	MKC442 (I-EBU)	Y	N			Obtained in the concomitant presence of low 3TC concentrations	(60)
E 138 K	GAG to AAG	HIV-1 Specific RTI	TIBO R82913	Y	?			Found in combination with L100I	(27)
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	(37, 38)
E 138 K	GAG to AAG	HIV-1 Specific RTI	UC-84 (615985)	Y	?	> 100	TSAOs		(35, 61)
T 139 I	ACA to ATA	HIV-1 Specific RTI	Calanolide A	Y	?	> 70	Not other NNRTIs		(39)
G 141 E	GGG to GAG	HIV-1 Specific RTI	UC-16	Y	N			K101I/G141E: 10-fold	(35)

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-resistance (-fold)	Comments	Refs
Q 151 M	CAG to ATG	Multiple Nucleoside Resistance		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	(4, 5, 62)
S 156 A	TCA to GCA	Pyrophosphate Analogue RTI	Foscarnet (PFA)	Y	N	4.5			(21)
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	(20)
V 179 D	GTT to GAT	HIV-1 Specific RTI	DMP 266 (L-743,726)	Y	?			L100I/V179D/Y181C: 1,000-fold	(31)
V 179 D	GTT to GAT	HIV-1 Specific RTI	L-697,661	N	Y	4			(24)
V 179 D	GTT to GAT	HIV-1 Specific RTI	TIBO R82913	N	Y	20	R82150 (20)		(63)
V 179 D	GTT to GAT	HIV-1 Specific RTI	Trovirdine	Y	?			Found in combination with K103R or Y181C; V179D/Y181C: > 1,000-fold	(44, 45)
V 179 D	GTT to GAT	HIV-1 Specific RTI	UC-10 (645129)	Y	?	16			(35)
V 179 E	GTT to GAG	HIV-1 Specific RTI	L-697,661	N	Y	8			(23)
Y 181 C	TAT to TGT	HIV-1 Specific RTI	α-APA R18893 (loviride analogue)	Y	?				(64)
Y 181 C	TAT to TGT	HIV-1 Specific RTI	BHAP U-87201E (atevirdine)	N	Y			K103N and Y181C observed with monotherapy	(46)
Y 181 C	TAT to TGT	HIV-1 Specific RTI	BHAP U-88204E	Y	?				(34)

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-resistance (-fold)	Comments	Refs
Y	181	C	TAT to TGT	HIV-1 Specific RTI	BHAP U-90152 (delavirdine)	?	Y			K103N/Y181C seen separately and in combination in vivo	(46)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	BM+51.0836	Y	?				(65)
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	(31, 32)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	E-EBU	Y	?				(52)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	E-EPSeU	Y	?	> 50		Y188C confers greater resistance than Y181C	(66)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	E-EPU	Y	?	> 95		Y188C confers greater resistance than Y181C	(66)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	MKC442 (1-EBU)	?	Y				(51)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	L-697,593	Y	?	> 100		K103N/Y181C: > 1,000-fold	(47)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	L-697,661	Y	Y	> 30		K103N and Y181C most common with monotherapy	(24, 48)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	Loviride (R89439, α-APA)	?	Y				(67)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	Nevirapine	Y	Y	> 100	Other NNRTIs	Can suppress effects of AZT mutations	(25, 68, 69)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	NSC 648400 (E-BPTU)	Y	?	160	Other NNRTIs		(70)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	TIBO R82913	Y	?	> 100		K103N/Y181C: > 1,000-fold	(29)
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	(44, 45)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	UC-10 (645129)	Y	?	6		K101E/Y181C: 200-fold	(36, 42)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	UC-32 (645542)	Y	?	38			(36)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	UC-38 (629243)	Y	?	8-149	Other NNRTIs		(36, 71)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	UC-040	Y	?	16			(42)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	UC-57 (647014)	Y	?			K101E/Y181C: 58-fold	(36)

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Amino Acid Change			Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resistance (-fold)	Comments	Refs
Y	181	C	TAT to TGT	HIV-1 Specific RTI	UC-68 (638532)	Y	?	5			(36)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	UC-69 (646989)	Y	?			V106A/V181C: 166-fold	(36)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	UC-80 (639475)	Y	?	18			(36)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	UC-81 (615727)	Y	?	53			(35, 72)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	UC-82	Y	?	5			(42)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	UC-84 (615985)	Y	?	> 118			(36)
Y	181	C	TAT to TGT	HIV-1 Specific RTI	UC781	Y	?	13		V108/ Y181C: 55 fold; K101E/ V108I/ Y181C: 500 fold. (42)	
Y	181	C	TAT to TGT	HIV-1 Specific RTI	1737 (Tetrahydronaphthalene derivative)	Y	?	20		Y181C also confers resistance to numerous other tetrahydronaphthalene derivatives.	(73)
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	(74)
Y	181	I	TAT to ATT	HIV-1 Specific RTI	MKC442 (I-EBU)	Y	N	1,000			(60)
Y	181	I	TGT to ATT	HIV-1 Specific RTI	Nevirapine	N	Y	High-level		Observed in one patient	(75)
M	184	I	ATG to ATA	Nucleoside RTI	3TC (lamivudine)	Y	Y			M184V and M184I can suppress effects of AZT resistance mutations	(76, 77, 78)
M	184	T		Nucleoside RTI	3TC (lamivudine)	Y	?			Reduced replication capacity and RT activity	(79, 80)
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	(76, 77, 78)
M	184	V	ATG to GTG	Nucleoside RTI	(-)-FTC	Y	?	> 100		M184V can suppress effects of AZT mutations	(76, 77)

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-resistance (-fold)	Comments	Refs
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	(8)
M	184	V	ATG to GTG	Nucleoside RTI	ddC	Y	Y	2-5			(81)
M	184	V	ATG to GTG	Nucleoside RTI	ddI	Y	Y	2-5		Rarely observed in patients receiving ddI	(81)
M	184	V	ATG to GTG	Nucleoside RTI	L-FddC	Y	?	> 100			(82)
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	(66)
Y	188	C	TAT to TGT	HIV-1 Specific RTI	E-EPU	Y	?	> 250		Y188C confers greater resistance than Y181C	(66)
Y	188	C	TAT to TGT	HIV-1 Specific RTI	HEPT	Y	?				(52)
Y	188	C	TAT to TGT	HIV-1 Specific RTI	Nevirapine	N	Y				(30)
Y	188	H	TAT to CAT	HIV-1 Specific RTI	BHAP U-87201E (atevirdine)	N	Y			K101E, Y188H, E233Y and K238T observed with U-87201E/AZT combination therapy	(41)
Y	188	H	TAT to CAT	HIV-1 Specific RTI	TIBO R82913	Y	?				(27)
Y	188	H/L	TAT to CAT/CTT	HIV-1 Specific RTI	Loviride (R89439, α-APA)	?	Y				(67)
Y	188	L	TAT to TTA	HIV-1 Specific RTI	DMP 266 (L-743,726)	Y	?	1,000			(31)
Y	188	L	TAT to TTA	HIV-1 Specific RTI	TIBO R82913	N	Y				(63)
V	189	I	GTA to ATA	HIV-1 Specific RTI	HBY 097	Y	?	2	Other NNRTIs (2-6)		(16)
G	190	A	GGA to GCA	HIV-1 Specific RTI	Loviride (R89439, α-APA)	?	Y				(83)
G	190	A	GGA to GCA	HIV-1 Specific RTI	Nevirapine	N	Y				(25)

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-resistance (-fold)	Comments	Refs
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	(84)
G 190 E	GGA to GAA	HIV-1 Specific RTI	HBY 097	Y	?		Other NNRTIs	Reduces enzymatic activity of RT and viral replication competency	(85)
G 190 E	GGA to GAA	HIV-1 Specific RTI	S-2720	Y	?				(86)
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	(35, 43)
G 190 E	GGA to GAA	HIV-1 Specific RTI	AAP-BHAP (U-95133)	Y	?	>100		T139I/ G190Q/ T200A/ L214F: >100-fold. Additional mutations possibly restore the replication compentency of the G190E mutant.	(84)
G 190 Q	GGA to CAA	HIV-1 Specific RTI	HBY 097	Y	?		Other NNRTIs	Appears exclusively in connection with V179D	(16)
G 190 T	GGA to ?	HIV-1 Specific RTI	HBY 097					Appears under lowered drug concentration selection	(54)
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	(20)
H 208 Y	CAT to TAT	Multiple Nucleoside Resistance	AZT + 3TC	?	Y			Polymorphism facilitating AZT+3TC dual resistance	(87)

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-resistance (-fold)	Comments	Refs
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.	(88, 89, 90)
R 211 K	AGG to AAG	Multiple Nucleoside Resistance	AZT + 3TC	?	Y			Polymorphism facilitating AZT+3TC dual resistance in association with M184V and other AZT resistance mutations.	(87)
L 214 F	CTT to TTT	Multiple Nucleoside Resistance	AZT + 3TC	?	Y			Polymorphism facilitating AZT+3TC dual resistance in association with M184V and other AZT resistance mutations.	(87, 91)
T 215 F	ACC to TTC	Nucleoside RTI	AZT	?	Y			K67N/K70R/T215Y/K219Q: 120-fold	(1, 2, 3)
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)	(1, 2, 3)
Y 215 C	TTC to TGC	Nucleoside RTI	ddC	N	Y	4		Arises on background of T215Y AZT resistance	(92)
K 219 E	AAA to GAA	Nucleoside RTI	AZT	Y	N				(1, 2, 3)
K 219 Q	AAA to CAA	Nucleoside RTI	AZT	?	Y			K67N/K70R/T215Y/K219Q: 120-fold	(1, 2, 3)
P 225 H	CCT to CAT	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.	(53)
E 233 V	GAA to GTA	HIV-1 Specific RTI	BHAP U-87201E (atevirdine)	N	Y			K101E, Y188H, E233Y and K238T observed with U-87201E/AZT combination therapy	(41)
P 236 L	CCT to CTT	HIV-1 Specific RTI	BHAP U-87201E (atevirdine)	Y	N				(93)

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-resistance (-fold)	Comments	Refs
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	(93)
P	236	L	CCT to CTT	HIV-1 Specific RTI	HEPT	Y	?				(70)
K	238	T	AAA to ACA	HIV-1 Specific RTI	BHAP U-87201E (atevirdine)	N	Y			K101E, Y188H, E233Y and K238T observed with U-87201E/AZT combination therapy	(41)
G	333	D	GGC to GAC	Multiple Nucleosides	AZT+3TC	Y	Y			Facilitates dual resistance to AZT+3TC in association with M184V and standard AZT resistance mutations.	(87)
G	333	E	GGC to GAG	Multiple Nucleosides	AZT + 3TC	Y	Y			Facilitates dual resistance to AZT+3TC in association with M184V and standard AZT resistance mutations.	(87)

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

Amino Acid Change			Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resistance (-fold)	Comments	Refs
R	8	K	CGA to AAA	Protease Inhibitor	A-77003	Y	?	10		R8K/ M46I/ G48V: 20-fold	(94, 95)
R	8	Q	CGA to CAA	Protease Inhibitor	A-77003	Y	?	10		M46I improves replication competency of R8Q mutant	(94, 96)
L	10	F	CTC to TTC	Protease Inhibitor	DMP 450	Y	?			Probably compensatory	(97, 98)
L	10	F	CTC to GGC	Protease Inhibitor	VB 11,328	Y	?			L10F/I84V: 8-fold	(99)
L	10	F	CTC to CGC	Protease Inhibitor	VX-478 (141W94)	Y	?				(100)
L	10	F	CTC to CGC	Protease Inhibitor	XM323					L10F/ V82A: 2-fold; L10F/ K45I/ I84V: 50-fold	(101)
L	10	F	CTC to CGC	Protease Inhibitor	SC-55389A	Y	?	2.8	Not SC-52151	N88S/L10F: 25-fold	(102, 103, 104)
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'.	(106)
L	10	I	CTC to ATC	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y				(105)
L	10	I		Protease Inhibitor	Ro 31-8959 (saquinavir)		Y			Found in combination with G48V in vivo	(107)
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	(105)
L	10	V	CTC to GTC	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y		A-80987 (4)		(105)
K	20	M	AAG to ATG	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y		VX-478 (8)		(105)

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

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resistance (-fold)	Comments	Refs
K 20 R	AAG to AAA	Protease Inhibitor	ABT-538 (ritonavir)	N	Y			K20R/M36I/I54V/V82A: 41-fold	(108)
K 20 R	AAG to AAA	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y		Ro-31-8959 (8);		(105)
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'.	(106, 109)
L 24 I	TTA to ATA	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y		SC-52151 (8)		(105)
L 24 V	TTA to GTA	Protease Inhibitor	SC-52151	Y	?	10-20	SC55389A	L24V/ G48V/ A71V/ V75I/ P81T: 1000-fold	(102, 103)
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	(110, 111)
V 32 I	GTA to ATA	Protease Inhibitor	ABT-538 (ritonavir)	Y	?	40		V32I and V82I are synergistic mutations yielding 20-fold enzyme resistance	(108)
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	(96)

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

Amino Acid Change			Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resistance (-fold)	Comments	Refs
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')	(112, 106)
V	32	I	GTA to ATA	Protease Inhibitor	BILA 2011 (palinavir)	Y	?	1200	BILA 1906 (1400)	Other mutations found in p1/ p6 cleavage site	(113)
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	(114)
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	(105)
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'.	(106)
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	(108)
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	(108)
M	36	I		Protease Inhibitor	AG1343 (nelfinavir)		Y				(110)
K	45	I	AAA to ATA	Protease Inhibitor	XM323					L10F/ K45I/ I84V: 50-fold	(95)
M	46	F	ATG to TTC	Protease Inhibitor	A-77003	Y	?	4 (enzyme resist.)		Seen with V82A	(96)

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

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resistance (-fold)	Comments	Refs
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	(94, 96)
M 46 I	ATG to ATA	Protease Inhibitor	ABT-538 (ritonavir)	Y	Y			M46I/ L63P/ A71V/ V82F/ I84V: 27-fold	(108)
M 46 I	ATG to ATA	Protease Inhibitor	AG1343 (nelfinavir)	Y	Y				(110)
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')	(106, 109, 112, 113)
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'.	(106)
M 46 I	ATG to ATA	Protease Inhibitor	DMP 450	Y	?			Probably compensatory	(97, 98)
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	(105, 115)
M 46 I	ATG to ATA	Protease Inhibitor	VB 11,328	Y	?			I50V/ M46I/ I47V: 20-fold	(95, 99)
M 46 I	ATG to ATA	Protease Inhibitor	VX-478 (141W94)	Y	?	Nil			
M 46 L	ATG to TTC	Protease Inhibitor	A-77003	Y	?	2-3 (enzyme resist.)			(96)
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'	(106, 109, 112, 113)

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

Amino Acid Change			Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resistance (-fold)	Comments	Refs
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	(95)
M	46	L	ATG to CTG	Protease Inhibitor	XM323	Y	?			V82A/ M46L: 7-fold; V82A/ M46L/ L97V: 11-fold	(101)
M	46	V		Protease Inhibitor	A-77003	Y	?			V32I appears first; progression to V32I/ M46V and V32I/ / M46V/ A71V/ V82A occurs even in the absence of drug	(95)
I	47	V	ATA to CTA	Protease Inhibitor	VB 11,328	Y	?			I50V/ M46I/ I47V: 20-fold	
I	47	V	ATA to CTA	Protease Inhibitor	VX-478 (141W94)	Y	?	Nil			
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'.	(106)
G	48	V	GGG to GTG	Protease Inhibitor	A-77003	Y	?			R8K/ M46I/ G48V: 20-fold; G48V/ I82T: 100-fold	(116)
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)	(117, 118)

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

Amino Acid Change			Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resistance (-fold)	Comments	Refs
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	(102, 103)
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	(119)
G	48	V	GGG to GTG	Protease Inhibitor	MK-639 (L-735,524, Indinavir)	?	Y				(120)
I	50	V	ATT to GTT	Protease Inhibitor	VB 11,328	Y	?	3		I50V/ M46I/ I47V: 20-fold	(95)
I	50	V	ATT to GTT	Protease Inhibitor	VX-478 (141W94)	Y	?	3			(121)
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'.	(106)
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	(108)
I	54	V	ATC to GTC	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y				(112)

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

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resistance (-fold)	Comments	Refs
I 54 V	ATA to GTA	Protease Inhibitor	Ro 31-8959 (saquinavir)	Y				In subtype O	
I 54 V	ATC to GTC	Protease Inhibitor	Ro 31-8959 (saquinavir)	Y				In subtype B	(117, 118)
D 60 E	GAT to GAA	Protease Inhibitor	DMP 450	Y	?			Probably compensatory	(97, 98)
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	(105)
A 71 T	GCT to ACT	Protease Inhibitor	BMS 186,318	Y	?			A71T/ V82A: 15-fold	(122, 123)
A 71 T	GCT to ACT	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y				(105)
A 71 V		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	(95, 101)
A 71 V	GCT to GTT	Protease Inhibitor	ABT-538 (ritonavir)	Y	Y				(108)
A 71 V	GCT to GTT	Protease Inhibitor	AG1343 (nelfinavir)	Y	?	5		D30N/ A71V: 7-fold; M46I/ L63P/ A71V/ I84V: 30-fold	
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')	(106, 109, 112, 113)
A 71 V	GCT to GTT	Protease Inhibitor	BILA 2011 (palinavir)	Y	?		BILA 2185: 30-fold		(112)

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

Amino Acid Change			Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resistance (-fold)	Comments	Refs
A	71	V	GCT to GTT	Protease Inhibitor	MK-639 (L-735,524, indinavir)	Y	Y			V32I/ M46L/ A71V/ V82A: 14-fold	(95)
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	(102, 103)
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'.	(106)
G	73	S	GGT to GCT	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y			Emerges following a switch from saquinavir to indinavir.	(124)
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	(102, 103)
V	77	I		Protease Inhibitor	AG1343 (nelfinavir)	Y	Y				
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	(102, 103)
I	82	T	ATC to ACC	Protease Inhibitor	A-77003	Y	?			G48V/ I82T: 100-fold (82T was derived from in vitro passage of 82I)	(125)
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	(95, 116, 125)

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

Amino Acid Change			Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resistance (-fold)	Comments	Refs
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	(108)
V	82	A	GTC to GCC	Protease Inhibitor	BMS 186,318	Y	?		A-77003 (4)	A71T/ V82A: 15-fold	(122, 123)
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	(105)
V	82	A	GTC to GCC	Protease Inhibitor	P9941	Y	?	6-8			(126)
V	82	A	GTC to GCC	Protease Inhibitor	SC-52151	Y	?			G48V/ V82A, G48V/ L63P/ V82A or I54T: 10- to 20-fold	
V	82	A		Protease Inhibitor	SKF108922	Y	?				
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	(101)
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.	(127, 128, 129)
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	(108)
V	82	F	GTC to TTC	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y				(99)
V	82	F	GTC to TTC	Protease Inhibitor	XM323	Y	?			V82F/ I84V: 92-fold	(101)
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)	(96)
V	82	I	GTC to ATC	Protease Inhibitor	XM323	Y	?	< 2			(101)
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	(108)

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

Amino Acid Change			Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resistance (-fold)	Comments	Refs
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	(108)
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	(105)
V	82	T		Protease Inhibitor	SKF108842	Y	?				(130)
V	82	T		Protease Inhibitor	SKF108922	Y	?				
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')	(106, 109, 112, 113)
I	84	A	ATG to ATA	Protease Inhibitor	BILA 2011 (palinavir)	Y	?		Ro 31-8959 (400);	I84A is the most common mutation	(112)
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	(108)
I	84	V	ATA to GTA	Protease Inhibitor	AG1343 (nelfinavir)		?			M46I/ L63P/ A71V/ I84V: 30-fold	(110)
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')	(106, 109, 112, 113)

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

Amino Acid Change			Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resistance (-fold)	Comments	Refs
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'.	(106)
I	84	V	ATA to GTA	Protease Inhibitor	DMP 450	Y	?				(97, 98)
I	84	V	ATA to CTA	Protease Inhibitor	MK-639 (L-735,524, indinavir)	N	Y			G48V/ I84V/ L90M: 30-fold; L10R/ M46I/ L63P/ V82T/ I84V: 8-fold	(105)
I	84	V	ATA to GTA	Protease Inhibitor	Ro 31-8959 (saquinavir)	Y	?				(95)
I	84	V	ATA to GTA	Protease Inhibitor	RPI-312	Y	?	5			(131)
I	84	V		Protease Inhibitor	SKF108842	Y	?				
I	84	V	ATA to GTA	Protease Inhibitor	VB 11,328	Y	?			L10F/ I84V: 8-fold	
I	84	V	ATA to GTA	Protease Inhibitor	VX-478 (141W94)	Y	?				
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	(95, 101)
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)		(132)
N	88	D		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	(110)
N	88	D	AAT to GAT	Protease Inhibitor	SC-52151	Y	?			N88D compensatory, no resistance alone	(132)

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

Amino Acid Change			Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resistance (-fold)	Comments	Refs
N	88	S	AAT to AGT	Protease Inhibitor	SC-55389A	Y	?	20	L735,524 (3); not SC-52151	N88S/L10F: 25	(104)
L	90	M	TTG to ATG	Protease Inhibitor	ABT-538 (ritonavir)	N	Y			82A/ 54V/ I/ 71V/ 90L/ M: 7-fold	(108)
L	90	M	TTG to ATG	Protease Inhibitor	AG1343 (nelfinavir)	N	Y			Rare in patients	(110)
L	90	M	TTG to ATG	Protease Inhibitor	MK-639 (L-735,524, indinavir)	?	Y				(105)
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	(117)
L	97	V	TTA to GTA	Protease Inhibitor	XM323	Y	?			No resistance alone; V82A/ L97V: 3-fold; V82A/ M46L/ L97V: 11-fold	(101)

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

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resistance (-fold)	Comments	Refs
R 22 A	AGG to AGA	Fusion/ Binding Inhibitor	RPR103611	Y	?				(132)
I 84 S	ATC to AGC	Fusion/ Binding Inhibitor	RPR103611	Y	?				(132)
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	(132, 133)
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	(133, 134)
F 145 L	TTC to TTA	Fusion/ Binding Inhibitor	JM-3100	Y	?			Combination of mutations: 2- to 100-fold	(135, 136)
N 188 K	AAT to AAA	Fusion/ Binding Inhibitor	Siamycin I	Y	?			N188K/ G332E/ N351D/ A550T/ N633D/ L762S: 9-fold	(137)
I 228 V	ATA to GTA	Fusion/ Binding Inhibitor	JM-2763	Y	?			Combination of mutations	
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	(133, 134)
N 270 S	AAT to AGT	Fusion/ Binding Inhibitor	JM-3100	Y	?				
R 272 T	AGA to ACA	Fusion/ Binding Inhibitor	JM-3100	Y	?				
S 274 R	AGT to AGA	Fusion/ Binding Inhibitor	JM-2763	Y	?			Combination of mutations: 95- to 792-fold	(135, 136)
S 274 R	AGT to AGA	Fusion/ Binding Inhibitor	JM-3100	Y	?	DS (> 7 to 6,667)			
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	(133, 134)
Q 278 H	CAG to CAT	Fusion/ Binding Inhibitor	JM-2763	Y	?				
Q 278 H	CAG to CAC	Fusion/ Binding Inhibitor	JM-3100	Y	?				
I 288 V	ATA to GTA	Fusion/ Binding Inhibitor	JM-3100	Y	?				
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	(133, 134)

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

Amino Acid Change			Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resistance (-fold)	Comments	Refs
N	293	H	AAT to CAT	Fusion/ Binding Inhibitor	JM-3100	Y	?				
A	297	T	GCA to ACA	Fusion/ Binding Inhibitor	JM-2763	Y	?				
A	297	T	GCA to ACA	Fusion/ Binding Inhibitor	JM-3100	Y	?				
N	323	S	AAT to AGT	Fusion/ Binding Inhibitor	Dextran sulphate (DS)	Y	?			C3 region; S113N/ S134N/ K269E/ Q278E/ N293D/ N323S/ R387I: 250-fold	(133, 134)
G	332	E	GGA to GAA	Fusion/ Binding Inhibitor	Siamycin I	Y	?			N188K/ G332E/ N351D/ A550T/ N633D/ L762S: 9-fold	(137)
N	351	D	AAT to GAT	Fusion/ Binding Inhibitor	Siamycin I	Y	?			N188K/ G332E/ N351D/ A550T/ N633D/ L762S: 9-fold	(137)
P	385	L	CCA to CTA	Fusion/ Binding Inhibitor	JM-2763	Y	?				
P	385	L	CCA to CTA	Fusion/ Binding Inhibitor	JM-3100	Y	?				
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	(133, 134)
Q	410	E	CAA to GAA	Fusion/ Binding Inhibitor	JM-3100	Y	?				
S	433	P	TCC to CCC	Fusion/ Binding Inhibitor	JM-3100	Y	?				
V	457	I	GTA to ATA	Fusion/ Binding Inhibitor	JM-3100	Y	?				
A	550	T	GCC to ACC	Fusion/ Binding Inhibitor	Siamycin I	Y	?			N188K/ G332E/ N351D/ A550T/ N633D/ L762S: 9-fold	(137)
N	633	D	AAT to GAT	Fusion/ Binding Inhibitor	Siamycin I	Y	?			N188K/ G332E/ N351D/ A550T/ N633D/ L762S: 9-fold	(137)
L	762	S	TTG to TCG	Fusion/ Binding Inhibitor	Siamycin I	Y	?			N188K/ G332E/ N351D/ A550T/ N633D/ L762S: 9-fold	(137)

Mutations in SIV Reverse Transcriptase that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resistance (-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.	(138, 139, 140)
Q 151 M	CAG to ATG	SIV Nucleoside RT Inhibitor	AZT	?	Y	>100	ddI; ddC; d4T; 3TC		(141)
M 184 V	ATG to GTG	SIV Nucleoside RT Inhibitor	(-)-FTC	Y	?				(82)

Mutations in FIV Reverse Transcriptase that confer drug resistance, ordered by position.

Amino Acid Change	Codon Change	Class of Drug	Compound	In vitro	In vivo	-Fold -resistance	Cross-resistance (-fold)	Comments	Refs
D 3 H	GAT to CAT	FIV Nucleoside RT Inhibitor	ddC	Y	?	4	ddI; PFA		(142, 143)
V 47 I	GTA to ATA	FIV Nucleoside RT Inhibitor	d4T	Y	?	4-6	PFA (>50); AZT; ddI; PMEA		(144)
P 156 S	CCA to TCA	FIV Nucleoside RT Inhibitor	3TC	Y	?	7	AZT (4), AZT + 3TC (6)		(145)
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.	(146)

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-538	C2 symmetry-based protease inhibitor (Abbott Laboratories)
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)
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)

Abbreviations (cont)

Compounds (cont)

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)
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)
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
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-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
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)
Ro 31-8959	hydroxyethylamine derivative HIV-1 protease inhibitor (Roche)

Abbreviations (cont)

Compounds (cont)

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-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)
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^3T	[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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