Coreceptor Use by Primate Lentiviruses

Christopher C. Broder[1] **and Agnes Jones-Trower**

[1] *Department of Microbiology and Immunology, F. Edward Hébert School of Medicine*
Uniformed Services University of the Health Sciences,
4301 Jones Bridge Road, Bethesda, MD 20814-4799
Phone: 301-295-3401, Fax: 301-295-1545, email: cbroder@mxb.usuhs.mil

The original compilation of the data in the accompanying tables in this section on coreceptor use by HIV-1, HIV-2, and SIV was performed over the past two years by Robert W. Doms and Aimee L. Edinger of the University of Pennsylvania, Department of Pathology and Laboratory Medicine and John P. Moore of The Aaron Diamond AIDS Research Center, The Rockefeller University. This year we have updated and revised the information in these tables for the purpose of maintaining this database on the salient points of virus isolate characteristics and usage of these seven transmembrane domain (7TM) coreceptors. In addition, we have included all HIV-1 isolates and their relevant information from the NIH AIDS Research and Reference Reagent Program that were not already in the existing HIV-1 isolate table. The coreceptor usage data included in this review is included as a searchable field for HIV sequence retrieval at the HIV database web site, http://hiv-web.lanl.gov. Corrections to errors or additional information that would improve these tables are welcome and should be sent by electronic mail to: cbroder@mxb.usuhs.mil.

SUMMARY

Parallel tracks of HIV research began almost simultaneously in two very different arenas, namely immunology and virology. One field focused on the structural and functional characterization of how HIV-1 entered a host cell, with the goal of teasing out the steps and requirements for infection, whereas the other line of research endeavored to define host factors capable of inhibiting HIV-1 replication. For over a decade these lines of research continued but remained essentially separated. Their findings individually built-up our understanding of the biology of HIV until crossovers occurred, shedding light on at least two long-standing unknowns about the virus: (i) some soluble suppressive factors are chemokines and (ii) the tropism-determining/influencing coreceptors for virus entry are chemokine receptors.

A significant part of the overall modulation of HIV-1 replication and the progress of HIV-1-induced disease occurs via a balance of host factors [Fauci(1996), Levy(1998)]. Some of these factors, such as pro-inflammatory cytokines and cellular activation, stimulate viral replication while other inhibitory factors may counteract disease progression. The ligands for the chemokine receptors being utilized as coreceptors for HIV-1 entry and infection are the newly discovered suppressive factors. Further, it has long been noted that there is a temporal change in viral tropism during the course of HIV-1 infection as related to the switch from NSI to SI phenotype and, for the most part, can now be correlated to the specific use of different coreceptors. This switch could be related to colonization of different types of cells rather than escape from immune system pressure. It has been proposed that the antigenic diversity of the HIV-1 envelope glycoprotein could be primarily driven by adaptation to new coreceptors and only secondarily by immune selection [Weiss(1996)] based on these observations: the properties of the HIV-1 coreceptors; the diversity of retrovirus receptors; and the availability of numerous seven transmembrane domain receptors on cell surfaces. It has also been suggested that during the long infection period, the HIV-1 quasispecies has the opportunity to colonize new cell types, thus gradually invading different subsets of hematopoietic and brain cells [Weiss(1996)]. Of further interest, it has also been observed that feline immunodeficiency virus (FIV) can use CXCR4 to infect and fuse in a CD4-independent manner [Willett (1997)]. It appears that chemokine receptors could be a common link between FIV and the primate lentiviruses [Willett (1997)]. It is tempting to speculate that chemokine receptors (or other multiple membrane spanning receptors) were originally used as primary (and possibly exclusive)

receptors by lentiviruses, and that the adaptation to use CD4 was a later event (a notion first proposed by R. Weiss).

Other retroviruses do utilize various multiple membrane-spanning domain proteins (reviewed in [Weiss(1993), Weiss & Tailor(1995)]).In fact, the involvement of a 7TM protein in HIV-1 infection was postulated in 1995 by W. Gallaher, [Gallaher (1995)] in the context of a 'multiple receptor' requirement. Based on the utilization by ecotropic murine leukemia virus of a multiple membrane spanning receptor (but in fact a 14 TM rather than 7TM glycoprotein) [Albritton (1989)] they proposed a structural model in which multiple domains of the gp120 subunit of the envelope glycoprotein would interact with a 7TM host cell molecule in addition to CD4.

Continued progress over the past year has been made detailing coreceptor usage for HIV-1, HIV-2, and SIV strains, and in describing new virus isolates along with their salient features. It was previously proposed that perhaps HIV-1 has developed a dependence on CD4 and CCR5 or CXCR4 because the CD4 and the 7TM receptor(s) are co-localized in the cell membrane [Broder & Dimitrov(1996)]. Indeed, it may be that CD4 and certain 7TM receptors have some, yet to be discovered, functional interacting role in the cells of the immune system. In fact, a constitutive biochemical association between the CD4 and CCR5 receptors which supports such a model has recently been demonstrated [Xiao (1999)]. On the other hand, the endogenous association between CD4 and the CXCR4 coreceptor appears much weaker and is more easily measured only after complexed with HIV-1 gp120 [Lapham (96), Dimitrov (1999)]. The observation that the CCR5-CD4 interaction is stronger than the CXCR4-CD4 interaction may also explain why macrophages expressing both these coreceptors are predominately only a target for M-tropic isolates of HIV-1 [Dimitrov (1999)]. In addition, the important observations of coreceptor use by several virus isolates in the absence of CD4 have suggested new hypotheses concerning the evolution of HIV-1, HIV-2 and SIV, the mechanism of the receptor-induced membrane fusion process, and the structure of the coreceptor molecules. The number of coreceptors used by HIV and SIV is now 14 (CCR5, CXCR4, CCR3, CCR2b, STRL33 (Bonzo), GPR1, GPR15 (BOB), CCR8, CCR9, CCR1, CCR4, CX3CR1 (formerly V28), APJ and US28). This number does not include non-human analogues (other than US28) and is likely to grow. However, it is now well recognized that the principal HIV-1 coreceptors remain the initially discovered CXC chemokine receptor CXCR4 and the CC-chemokine receptor CCR5, and all HIV-1, HIV-2, and SIV strains reported on to date use one or both of these receptors. Unlike HIV-1, it appears that many isolates of HIV-2 and SIV have the added ability to employ alternate coreceptors with efficiencies comparable to that with either CXCR4 or CCR5 depending on the particular isolate, and some can employ the coreceptor in the absence of CD4. It remains an open question as to whether use of alternative coreceptors *in vivo* is an important feature in viral tropism, pathogenesis or other facets of the natural history of these viruses. Indeed, the use of alternate coreceptors other than CCR5 or CXCR4, or their use in a CD4-independent manner, could enable particular virus strains to engage new cellular targets *in vivo*. There have been numerous reviews published on the subject of HIV/SIV and the coreceptors since 1996 which serve as the best source of detailed information and citations for readers of these tables. [Broder & Dimitrov(1996), Moore(1997), Broder & Collman(1997), Dimitrov & Broder(1997), Doranz (1997), Dimitrov (1998), Berson & Doms(1998), Gabuzda (1998), Rucker & Doms(1998), Berger (1999), Clapham (1999), Edinger (1999b), Hoffman & Doms(1999), Michael(1999), Kalinkovich (1999), Ross (1999), Lee & Montaner(1999)] These new data concerning the cellular coreceptors for HIV and the natural chemokine ligands for those receptors continues to advance our understanding of HIV pathogenesis and has offered new therapeutic and preventive strategies.

The coreceptor use tables are updated from last year. The major coreceptor(s) used by each virus strain is listed, as are alternative coreceptors that support virus infection *in vitro* to an extent that is $\sim 10\%$ of the efficiency of the major coreceptor used by each virus strain.

HIV-1

Notes to HIV-1 Coreceptor Use Table.

[a] Accession numbers refer to sequences from the described isolate that contain the longest available sequence including Env (full length genome when avaiable, down to a minimum of the V3 region), but may not pertain directly to the sample used to determine the isolate's phenotype. Accession numbers have been deemed "NA" if there are no related locus names in the HIV Database, or if there is insufficient information to conclude that a similarly named locus in the database is referring to the same isolate.

[b] The tropism for each virus strain is indicated. SI = syncytium inducing; NSI = non syncytium inducing; SI/TCLA = syncytium inducing T-cell line adapted; NA = not available.

[c] As described in the text, we have proposed that viruses which use CCR5 be termed R5 viruses, viruses that use CXCR4 be termed X4 viruses, and viruses that use both be termed R5X4 viruses. For a virus to be termed an R5X4 virus, CXCR4 must be used at $>$ 10% of the efficiency of CCR5 for viruses that use CCR5 as their primary receptor, or CCR5 must be used at $>$ 10% of the efficiency of CXCR4 for viruses that use CXCR4 as their primary receptor.

[d] All virus strains in the Table have been tested for the ability to use CCR5 and CXCR4. The receptors used by each strain are indicated. For both receptors to be listed, the least efficiently used receptor must support virus entry by $>$10% of the levels supported by the most efficiently used receptor. For viruses that use both receptors, CXCR4 is listed first; this does not mean that CXCR4 is used more efficiently than CCR5.

[e] Receptors other than CCR5 or CXCR4 that are used by the indicated strains are listed. Since most viruses have not yet been tested for the ability to use receptors other than CCR5 and CXCR4, the absence of other receptors used in the Table should not be taken to mean that a virus uses only CCR5 or CXCR4. For example, if CCR3 is not listed as being used by a given virus strain, it may be because it has not yet been tested. Receptors that have been shown by experiments not to be used by a given virus strain are not indicated. Occasionally there are discrepancies in the literature concerning the use of one or more receptors. In these cases, we opted for 'majority rules'. If two papers report a positive result and one a negative result, the receptor is shown as being used.

[f] The virus isolate used CCR3 whereas the cloned env from this isolate did not [Bjorndal (1997)]. *Indicates that coreceptor use was determined only by fusion assays rather than by virus infection.

[g] 92HT593.1 (cloned env gene) and 92HA593 (whole virus) come from the same isolate and gave slightly different results in references [Dittmar (1997)] and [Zhang (1996)].

[h] Tybe is a cerebrospinal fluid isolate from an individual with AIDS from the US northeast and likely a clade B isolate.

[i] Under the new nomenclature proposal, subtype E will be referred to as CRF01(AE)

Strain	Proposed Accession[a]	Primary Clade	Other Tropism[b]	Designation[c]	Main Receptor[d]	Alternate Receptors[e]	References
DJ258	L22939	A	NSI	R5	CCR5		[Trkola (1998)]
92RW026	U13458	A	NSI	R5	CCR5		[Trkola (1998)]
93KE101	NA	A	NSI	R5	CCR5		[Zhang (1996)]
93IN103	NA	A	NSI	R5	CCR5		[Zhang (1996)]
92UG037-8	U51190	A	NSI	R5	CCR5	CCR8*	[Bjorndal (1997), Rucker (1997)]
92RW020-5	U08794	A	NSI	R5	CCR5		[Rucker (1997)]
92UG031	L34667	A	NSI	R5	CCR5		[Dittmar (1997)]
92RW20	U08794	A	NSI	R5	CCR5		[Dittmar (1997)]
92UG029	U13469	A	SI	X4	CXCR4		[Trkola (1998)]
92RW009	U88823	A	SI	R5X4	CXCR4, CCR5		[Zhang (1996)]
JR-FL	U63632	B	NSI	R5	CCR5	CCR3	[Deng (1997), Farzan (1997), Rucker (1997)]
JR-CSF	M38429	B	NSI	R5	CCR5		[Simmons (1996), Trkola (1998), Zhang (1996)]
SF162	M65024	B	NSI	R5	CCR5	STRL33*	[Liao (1997), Rucker (1997)]
YU2	M93258	B	NSI	R5	CCR5	CCR3, GPR15	[Choe (1996), Farzan (1997)]
ADA	AF004394	B	NSI	R5	CCR5	CCR3, GPR15, STRL33*, CCR8	[Choe (1996), Farzan (1997), Rucker (1997)]
Ba-L	M68893	B	NSI	R5	CCR5	CCR3, STRL33*	[Deng (1997), Dragic (1996), Liao (1997), Rucker (1997)]

Strain	Proposed Accession[a]	Primary Clade	Other Tropism[b]	Designation[c]	Main Receptor[d]	Alternate Receptors[e]	References
92US657	U04908	B	NSI	R5	CCR5		[Trkola (1998)]
92US715.6	U08451	B	NSI	R5	CCR5		[Bjorndal (1997)]
92Br20-4	U08797	B	NSI	R5	CCR5	GPR15	[Choe (1996), Rucker (1997), Pohlmann (1999)]
91US005.11	U27434	B	NSI	R5	CCR5	GPR15	[Bjorndal (1997), Rucker (1997), Pohlmann (1999)]
SL-2	NA	B	NSI	R5	CCR5		[Simmons (1996)]
92TH014.12	U08801	B	NSI	R5	CCR5		[Bjorndal (1997)]
M23	NA	B	NSI	R5	CCR5		[Dittmar (1997)]
E80	NA	B	NSI	R5	CCR5		[Dittmar (1997)]
BR92	NA	B	NSI	R5	CCR5		[Dittmar (1997)]
BR49	NA	B	NSI	R5	CCR5		[Dittmar (1997)]
BR53	NA	B	NSI	R5	CCR5		[Dittmar (1997)]
BR90	NA	B	NSI	R5	CCR5		[Dittmar (1997)]
92HA593[g]	U08444	B	SI	R5X4	CXCR4, CCR5		[Zhang (1996)]
92HT593.1[g]	U08444	B	NSI	R5X4	CXCR4, CCR5	GPR15, STRL33	[Bjorndal (1997), Pohlmann (1999)]
2028	NA	B	SI	R5X4	CXCR4, CCR5	CCR3	[Dittmar (1997), Simmons (1996)]
2076	NA	B	SI	R5X4	CXCR4, CCR5		[Dittmar (1997), Simmons (1996), Trkola (1998)]
89.6	U39362	B	SI	R5X4	CXCR4, CCR5	CCR3, CCR2b, CCR8, V28	[Farzan (1997), Rucker (1997)]
DH123	AF069140	B	SI	R5X4	CXCR4, CCR5		[Trkola (1998)]
Isolate C 7/86	NA	B	SI	R5X4	CXCR4, CCR5		[Trkola (1998)]
92HA594	U08445	B	SI	R5X4	CXCR4, CCR5		[Zhang (1996)]
92HA596	U08446	B	SI	R5X4	CXCR4, CCR5		[Zhang (1996)]
M13	NA	B	SI	R5X4	CXCR4, CCR5		[Simmons (1996)]
2006	NA	B	SI	R5X4	CXCR4, CCR5		[Simmons (1996)]
2044	NA	B	SI	R5X4	CXCR4, CCR5		[Simmons (1996)]
2036	NA	B	SI	R5X4	CXCR4, CCR5		[Simmons (1996)]
2005	NA	B	SI	R5X4	CXCR4, CCR5		[Simmons (1996)]
92HT599.24	U08447	B	SI	X4	CXCR4		[Bjorndal (1997)]
BK132	L03697	B	SI	X4	CXCR4	CCR3*, CCR8*	[Rucker (1997), Broder & Collman(1997)]
BR65	NA	B	SI	X4	CXCR4		[Dittmar (1997)]
HC4	NA	B	SI	X4	CXCR4		[Trkola (1998)]
SF2	K02007	B	SI/TCLA	R5X4	CXCR4, CCR5		[Trkola (1998)]
RF	M17451	B	SI/TCLA	R5X4	CXCR4, CCR5		[Alkhatib (1996), Deng (1997), Rucker (1997)]

Strain	Proposed Accession[a]	Primary Clade	Other Tropism[b]	Designation[c]	Main Receptor[d]	Alternate Receptors[e]	References
NL4-3	M19921	B	SI/TCLA	R4,X4	CXCR4		[Zhang (1996), Trkola (1998), Zhang (1998)]
LAI(IIIB)	X01762	B	SI/TCLA	X4	CXCR4		[Trkola (1998)]
HXBc2	K03455	B	SI/TCLA	X4	CXCR4		[Choe (1996)]
GUN-1	D34590	B	SI/TCLA	R5X4	CXCR4, CCR5		[Simmons (1996)]
BH8	K02011	B	SI/TCLA	X4	CXCR4	CCR3*, STRL33*	[Rucker (1997)]
P1 22-211-V4	AF112563	B	NSI	R5	CCR5		[Zhang (1998)]
P2 22-204-V2	NA	B	NSI	R5	CCR5		[Zhang (1998)]
P3 19-245-V6	NA	B	NSI	R5	CCR5		[Zhang (1998)]
P4 03-212-V8	NA	B	NSI	R5	CCR5		[Zhang (1998)]
P5 11-213-V4	NA	B	NSI	R5	CCR5		[Zhang (1998)]
P6 02-217-V3	NA	B	NSI	R5	CCR5	BONZO	[Zhang (1998)]
P7 22-216-V5	NA	B	NSI	R5	CCR5		[Zhang (1998)]
P8 02-236-V6	NA	B	NSI	R5	CCR5		[Zhang (1998)]
P9 22-236-V6	NA	B	NSI	R5	CCR5		[Zhang (1998)]
P10 03-237-V6	NA	B	NSI	R5	CCR5		[Zhang (1998)]
P11 22-202-V3	AF112548	B	NSI	R5	CCR5		[Zhang (1998)]
P13 19-242-V3	AF112542	B	NSI	R5	CCR5		[Zhang (1998)]
P14 22-207-V6	NA	B	NSI	R5	CCR5		[Zhang (1998)]
P15 22-237-V4	AF112565	B	NSI	R5	CCR5		[Zhang (1998)]
301657	NA	B	NSI	R5	CCR5		[Zhang (1998)]
301714	NA	B	NSI	R5	CCR5		[Zhang (1998)]
301073	NA	B	NSI	R5	CCR5		[Zhang (1998)]
301056	NA	B	NSI	R5	CCR5		[Zhang (1998)]
301660	NA	B	NSI	R5	CCR5		[Zhang (1998)]
301727	NA	B	NSI	R5	CCR5		[Zhang (1998)]
MWB	NA	B	NSI	R5	CCR5		[Zhang (1998)]
301593	NA	B	SI	R5X4	CXCR4, CCR5	V28	[Zhang (1998)]
AD73	NA	B	SI	R5X4	CXCR4, CCR5	V28	[Zhang (1998)]
DH123	NA	B	SI	R5X4	CXCR4, CCR5	CCR8	[Zhang (1998)]
P6 02-217-V3-m1	NA	B	NSI	R5	CCR5	BONZO	[Zhang (1998)]
P6 02-217-V4 m2	NA	B	NSI	R5	CCR5	BONZO	[Zhang (1998)]
P6-02-217-V6-m6	NA	B	NSI	R5	CCR5	BONZO	[Zhang (1998)]
P6 02-217-V8-m12	NA	B	NSI	R5	CCR5	BONZO	[Zhang (1998)]
P6 02-217-V9-m18	NA	B	NSI	R5	CCR5		[Zhang (1998)]
M6-V2-m4b	NA	B	SI	R5X4	CXCR4, CCR5	BONZO, V28, APJ	[Zhang (1998)]
M6-V3-m1b	NA	B	SI	R5X4	CXCR4, CCR5	BONZO, V28, APJ	[Zhang (1998)]
M6-V6-m6a	NA	B	SI	R5X4	CXCR4, CCR5	BONZO, V28, APJ	[Zhang (1998)]
EL1	NA	B	SI	X4	CXCR4	APJ, CCR3	[Choe (1998)]

Strain	Proposed Accession[a]	Primary Clade	Other Tropism[b]	Designation[c]	Main Receptor[d]	Alternate Receptors[e]	References
2005	NA	B	SI	X4	CXCR4		[Simmons (1998)]
2044	NA	B	SI	X4	CXCR4		[Simmons (1998)]
2028	NA	B	SI	R5X4	CXCR4, CCR5		[Simmons (1998)]
2076	NA	B	SI	R5X4	CXCR4, CCR5	CCR3, CCR8, STRL33	[Simmons (1998)]
SL-2	NA	B	NSI	R5	CCR5	GPR15	[Simmons (1998)]
92US076	NA	B	SI	R5X4	CCR5, CXCR4	CCR3	[Xiao (1998)]
Tybe		(B)[h]	SI	X4	CXCR4		[Yi (1999)]
92ZW101	NA	C	NSI	R5	CCR5		[Zhang (1996)]
92BR025.9	U52953	C	NSI	R5	CCR5	GPR15	[Bjorndal (1997), Dittmar (1997), Pohlmann (1999)]
BR28	U16217	C	NSI	R5	CCR5		[Dittmar (1997)]
93MW965.26	U08455	C	NSI	R5	CCR5		[Bjorndal (1997)]
BR70	NA	C	NSI	R5	CCR5		[Dittmar (1997)]
JW1	NA	C	NSI	R5	CCR5		[Dittmar (1997)]
JW4	NA	C	NSI	R5	CCR5		[Dittmar (1997)]
92ZW102	NA	C	NSI	R5	CCR5		[Zhang (1996)]
DJ259	L22940	C	NSI	R5	CCR5		[Trkola (1998)]
94ZW103	NA	C	NSI	R5	CCR5		[Trkola (1998)]
94ZW109	NA	C	NSI	R5	CCR5		[Trkola (1998)]
92ZW106	NA	C	SI	X4	CXCR4		[Zhang (1996)]
ZAM20	L22956	C	SI	X4	CXCR4		[Trkola (1998)]
94ZW106	NA	C	SI	X4	CXCR4		[Trkola (1998)]
E3098	NA	C	NSI	R5	CCR5		[Bjorndal (1999)]
E3099	U92051	C	NSI	R5	CCR5		[Bjorndal (1999)]
E3100	NA	C	NSI	R5	CCR5		[Bjorndal (1999)]
E3101	NA	C	NSI	R5	CCR5		[Bjorndal (1999)]
E3347	NA	C	NSI	R5	CCR5		[Bjorndal (1999)]
E3348	NA	C	NSI	R5	CCR5		[Bjorndal (1999)]
E3349	NA	C	NSI	R5	CCR5		[Bjorndal (1999)]
E3350	U45485	C	NSI	R5	CCR5		[Bjorndal (1999)]
E3526	NA	C	NSI	R5	CCR5		[Bjorndal (1999)]
94KE102	NA	D	NSI	R5	CCR5		[Trkola (1998), Zhang (1996)]
94KE103	NA	D	NSI	R5	CCR5		[Trkola (1998), Zhang (1996)]
92UG046	U08737	D	SI	X4	CXCR4		[Trkola (1998)]
UG270	NA	D	SI	X4	CXCR4		[Trkola (1998)]
92UG024.2	U08726	D	SI	X4	CXCR4	CCR8*, V28*, CCR3, GPR15, STRL33[f]	[Bjorndal (1997), Rucker (1997), Trkola (1998), Pohlmann (1999), Broder & Collman(1997)]
92UG021.16	U27399	D	SI	X4	CXCR4		[Bjorndal (1997)]
JW5	NA	D	SI	X4	CXCR4		[Dittmar (1997)]

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NDK	M27323	D	SI	X4	CXCR4	GPR15	[Deng (1997), Pleskoff (1997)]
93ZR001.3	U27419	D	NA	X4	CXCR4	V28*	[Rucker (1997)]
91ZR001.3	NA	D	SI	R5X4	CXCR4, CCR5		[Bazan (1998)]
SE7076	NA	D	SI	X4	CXCR4		[Vallejo (1998)]
SE8384	NA	D	SI	X4	CXCR4		[Vallejo (1998)]
SE8646	NA	D	SI	R5X4	CCR5, CXCR4		[Vallejo (1998)]
92UG001	U13520	D	SI	R5X4	CCR5, CXCR4	CCR1, CCR2b, CCR3	[Xiao (1998)]
CM235	L03698	E[i]	SI	R5	CCR5		[Trkola (1998), Broder & Collman(1997)]
CM243	L03703	E	NSI	R5	CCR5	GPR15, STRL33	[Rucker (1997), Broder & Collman(1997)]
92TH001	U08742	E	NSI	R5	CCR5		[Trkola (1998)]
M53	NA	E	NSI	R5	CCR5		[Dittmar (1997)]
92TH022	U09131	E	NSI	R5	CCR5		[Dittmar (1997)]
92TH023	U08760	E	NSI	R5	CCR5		[Dittmar (1997)]
C2	NA	E	NSI	R5	CCR5		[Dittmar (1997)]
93TH305	NA	E	NSI	R5	CCR5		[Zhang (1996)]
93TH307	NA	E	NSI	R5	CCR5		[Zhang (1996)]
93TH966.8	U08456	E	NSI	R5	CCR5		[Bjorndal (1997)]
93TH976.17	U08458	E	NA	R5	CCR5		[Bjorndal (1997)]
93TH304	NA	E	SI	R5X4	CXCR4, CCR5		[Zhang (1996)]
SL6	NA	E	SI	X4	CXCR4		[Dittmar (1997)]
SL7	NA	E	SI	X4	CXCR4		[Dittmar (1997)]
SL8	NA	E	SI	X4	CXCR4		[Dittmar (1997)]
94TH304	NA	E	SI	X4	CXCR4		[Trkola (1998)]
CMU02	U48207	E	SI	X4	CXCR4		[Xiao (1998)]
CMU08	U48268	E	SI	X4	CXCR4		AIDS Ref Reag Prog
BR58	NA	F	SI	R5X4	CXCR4, CCR5	CCR3	[Dittmar (1997)]
BZ162	L22084	F	NSI	R5	CCR5		[Trkola (1998)]
R1	NA	F	NSI	R5	CCR5		[Trkola (1998)]
93BR029.2	U27413	F	NA	R5	CCR5		[Rucker (1997)]
RU23	U69657	F	NSI	R5	CCR5		[Vallejo (1998)]
RU29	U69663	F	NSI	R5	CCR5		[Vallejo (1998)]
RU30	U69664	F	NSI	R5	CCR5		[Vallejo (1998)]
93BR020	AF005494	F	SI	R5X4	CCR5, CXCR4, CCR3		[Xiao (1998)]
92UG975.10	U27426	G	NSI	R5	CCR5		[Bjorndal (1997)]
CA9	X96522	O	NSI	R5	CCR5		[Zhang (1996)]
MVP5180	L20571	O	SI	R5X4	CXCR4, CCR5		[Zhang (1996)]

Strain	Proposed Accession[a]	Primary Clade	Other Tropism[b]	Designation[c]	Main Receptor[d]	Alternate Receptors[e]	References
ES1158.1	AF009608	O	NSI	R5	CCR5		[Vallejo (1998)]
ES1159.1	AF009611	O	NSI	R5	CCR5		[Vallejo (1998)]
MD.1	NA	O	NSI	R5	CCR5		[Vallejo (1998)]
MVP-5180	L20571	O	SI	R5X4	CCR1, CCR2b, CCR3, CCR4, CCR5, CXCR4		[Vallejo (1998), Xiao (1998)]
8913-95	NA	O		R5	CCR5		[Dittmar (1999)]
1639-96	NA	O		R5	CCR5		[Dittmar (1999)]
13127-96	NA	O		R5	CCR5		[Dittmar (1999)]
13470-96	NA	O		R5	CCR5		[Dittmar (1999)]
2171-94	NA	O		X4	CXCR4	STRL33, CCR8	[Dittmar (1999)]
2901-94	NA	O		R5	CCR5		[Dittmar (1999)]
4354-94	NA	O		R5	CCR5		[Dittmar (1999)]
6778-94	NA	O		R5	CCR5		[Dittmar (1999)]
8161-94	NA	O		X4	CXCR4		[Dittmar (1999)]
4974-95	NA	O		R5	CCR5		[Dittmar (1999)]
9435-96	NA	O		R5	CCR5		[Dittmar (1999)]
2274-97	NA	O		R5	CCR5		[Dittmar (1999)]

HIV-1 Coreceptor Use Data from the NIH AIDS Research and Reference Reagent Program

The following table is a compilation of HIV-1 isolates from the AIDS Reagent Program. They are ordered by clade (based on env) with their phenotype, coreceptor classification, and main receptor characteristics shown, as in the previous table. These data were derived from the laboratories of Drs. David Ho and Jack Nunberg.

Strain	Proposed Accession[a]	Primary Clade	Other Tropism[b]	Designation[c]	Main Receptor[d]
92RW008	U08762 U08630	A	NSI	R5	CCR5
92RW016	U08633	A		R5	CCR5
92RW021	U08641	A		R5	CCR5
92RW023	U13455	A	NSI	R5	CCR5
92RW024	U08648	A		R5	CCR5
92RW025	U08657	A		R5	CCR5
93RW002	NA	A		R5	CCR5
93RW004	NA	A		R5	CCR5
93RW005	NA	A		R5	CCR5
93RW018	NA	A		R5	CCR5
93RW020	NA	A		R5X4	CXCR4, CCR5
93RW021	NA	A		R5	CCR5
93RW022	NA	A		R5	CCR5
93RW024	NA	A		R5X4	CXCR4, CCR5

Strain	Proposed Accession[a]	Primary Clade	Other Tropism[b]	Designation[c]	Main Receptor[d]
93RW028	NA	A		R5	CCR5
93RW029	NA	A	NSI	R5	CCR5
93RW031	NA	A		R5	CCR5
93RW034	NA	A		R5	CCR5
93RW035	NA	A		R5	CCR5
93RW037	NA	A		R5	CCR5
93UG077	NA	A		R5	CCR5
93UG079	NA	A		R5	CCR5
93UG089	NA	A		R5	CCR5
94UG103	NA	A		R5X4	CXCR4, CCR5
97USSN54	AF096347	A		R5	CCR5
92USSN20	AF096341	A		R5X4	CXCR4, CCR5
96USNG17	NA	A		X4	CXCR4
91US006	U27443	B		R5	CCR5
91US056	U79719	B	NSI	R5	CCR5
91US715	NA	B		R5	CCR5
92BR003	U08771	B	NSI	R5	CCR5
92BR004	U0867	B	NSI	R5	CCR5
92BR014	U08796	B	SI	R5X4	CXCR4, CCR5
92BR017	U08774	B	NSI	R5	CCR5
92BR018	NA	B	NSI	R5	CCR5
92BR019	NA	B		R5	CCR5
92BR021	NA	B	NSI	R5	CCR5
92BR023	U08779	BC	NSI	R5	CCR5
92BR024	NA	B		R5	CCR5
92BR026	NA	B		R5	CCR5
92BR028	U16217	B	NSI	R5	CCR5
92BR030	NA	B	NSI	R5	CCR5
92HT594	U08445	B	SI	R5X4	CXCR4, CCR5
92HT596	U08446	B	SI	R5X4	CXCR4, CCR5
92PR729	U04927	B		R5	CCR5
92TH026	U08802	B	NSI	R5	CCR5
92US076	NA	B	SI	R5X4	CXCR4, CCR5
92US660	U04909	B	NSI	R5	CCR5
92US714	U08450	B	NSI	R5	CCR5
92US723	NA	B		R5X4	CXCR4, CCR5
92US727	U79720	B	NSI	R5	CCR5
93BR008	NA	B		R5	CCR5
93BR009	NA	B		R5	CCR5
93BR011	NA	B		R5	CCR5
93BR012	NA	B		R5	CCR5
93BR013	NA	B		R5	CCR5
93BR015	NA	B		R5	CCR5
93BR017	NA	B		R5	CCR5
93BR021	NA	B		R5	CCR5
93BR022	NA	B		R5	CCR5
93BR023	NA	B		R5	CCR5

Strain	Proposed Accession[a]	Primary Clade	Other Tropism[b]	Designation[c]	Main Receptor[d]
93BR024	NA	B		R5	CCR5
93BR025	NA	B		R5	CCR5
93BR026	NA	B		R5	CCR5
93BR027	NA	B		R5	CCR5
93BR028	NA	B		R5	CCR5
93US073	U79721	B	NSI	R5	CCR5
A17	NA	B		R5X4	CXCR4, CCR5
BZ167	L22087 L11752	B		R5X4	CXCR4, CCR5
ME1	U66221	B		R5	CCR5
ME46	U66222	B		R5X4	CXCR4, CCR5
MN	M17449	B		X4	CXCR4
QZ4589	U32396	B		R5	CCR5
93TH067	U39258 U39259	B		R5	CCR5
93TH074	NA	B		R5	CCR5
93TH080	NA	B		R5	CCR5
96USHIPS4	NA	B		R5X4	CXCR4, CCR5
96USHIPS9	NA	B		R5X4	CXCR4, CCR5
96USHIPS7	NA	B		R5	CCR5
93BR019	U27444 U51289 U27404	BF		X4	CXCR4
93IN101	NA	C	NSI	R5	CCR5
93IN904	AF067157	C		R5	CCR5
93IN905	AF067158	C		R5	CCR5
93IN999	AF067154	C		R5	CCR5
93MW959	U08453 U51292	C	NSI	R5	CCR5
93MW960	U08454 U51293	C	NSI	R5	CCR5
94KE105	NA	C		R5	CCR5
96USNG31	AF096327	C		R5X4	CXCR4, CCR5
96USNG58	AF096329	C		R5	CCR5
97USNG30	AF096349	C		R5	CCR5
98BR004	NA	C		R5	CCR5
98CN006	NA	C		R5	CCR5
98IN022	NA	C		R5	CCR5
98IN026	NA	C		R5	CCR5
98TZ013	NA	C		R5	CCR5
98TZ017	NA	C		R5	CCR5
97ZA003	NA	C		R5	CCR5
97ZA009	NA	C		R5	CCR5
97ZA012	NA	C		R5	CCR5
92UG001	U08721	D	SI	R5X4	CXCR4, CCR5
92UG005	U08803	D		R5	CCR5
92UG035	U36881	AD	NSI	R5	CCR5
92UG038	U08806	D	SI	X4	CXCR4
93UG053	U08738	D	SI	X4	CXCR4
93UG059	U08739	D	SI	X4	CXCR4

Strain	Proposed Accession[a]	Primary Clade	Other Tropism[b]	Designation[c]	Main Receptor[d]
93UG065	U08740	D	SI	X4	CXCR4
93UG067	U13545	D	SI	R5X4	CXCR4, CCR5
93UG070	U08741	D	SI	X4	CXCR4
93UG082	NA	D	NSI	R5	CCR5
93UG086	NA	D	SI	R5X4	CXCR4, CCR5
94UG105	NA	D	SI	X4	CXCR4
94UG108	NA	D	NSI	R5	CCR5
94UG114	U88824	D	NSI	R5	CCR5
94UG117	AF096328	D	SI	X4	CXCR4
94UG118	NA	D	NSI	R5	CCR5
92TH003	U08743	E[i]	NSI	R5	CCR5
92TH005	U08744	E	NSI	R5	CCR5
92TH006	U08810	EA	NSI	R5	CCR5
92TH007	U08747	E	NSI	R5	CCR5
92TH009	U08748	E	NSI	R5	CCR5
92TH019	U08753	E	NSI	R5	CCR5
92TH020	U08754	E	NSI	R5	CCR5
92TH021	U08724	E	NSI	R5	CCR5
92TH024	U08761	E		R5	CCR5
93TH051	NA	E		R5X4	CXCR4, CCR5
93TH053	NA	E		X4	CXCR4
93TH054	NA	E		R5	CCR5
93TH057	NA	E		R5	CCR5
93TH060	NA	E		R5	CCR5
93TH062	NA	E		R5	CCR5
93TH064	NA	E		R5	CCR5
93TH065	NA	E		R5	CCR5
93TH069A	NA	E		R5	CCR5
93TH072	NA	E		R5	CCR5
93TH073	NA	E		R5	CCR5
93TH078	NA	E		R5	CCR5
CMU02	U48267	E	SI	X4	CXCR4
CMU08	U48268	E	SI	X4	CXCR4
CMU10		E	NSI	X4	CXCR4
93BR020	AF005494	F	SI	R5X4	CXCR4, CCR5
G3	U88825	AG	NSI	R5	CCR5
Jv1083	U88826	G	NSI	R5	CCR5
RU132	NA	G	NA	R5	CCR5
RU570	U08368	G	NSI	R5	CCR5
YBF30	AJ006022	N	NSI	R5	CCR5
BCF01	Y14496	O	NSI	R5	CCR5
BCF02	Y14497	O	NSI	R5	CCR5
BCF03	Y14498	O	NSI	R5	CCR5
MVP5180	L20571	O	SI	R5X4	CXCR4, CCR5
74V				X4	CXCR4
90US144	NA		NSI	R5	CCR5
92US072	NA		NSI	R5	CCR5

Strain	Proposed Accession[a]	Primary Clade	Other Tropism[b]	Designation[c]	Main Receptor[d]
92US077	NA		SI	R5X4	CXCR4, CCR5
93US074	NA		NSI	R5	CCR5
93US075	NA		NSI	R5	CCR5
93US140	NA		NSI	R5	CCR5
93US141	NA		NSI	R5	CCR5
93US142	NA		NSI	R5	CCR5
93US143	NA		SI	R5X4	CXCR4, CCR5
93US149	NA		NSI	R5	CCR5
93US151	NA		SI	R5X4	CXCR4, CCR5
93US155	NA		NSI	R5	CCR5
93US157	NA		NSI	R5	CCR5
93US159	NA		NSI	R5	CCR5
A012	M91819	B	NA	R5X4	CXCR4, CCR5
A018	NA	NA	NA	R5X4	CXCR4, CCR5
ASJM 108	NA			R5	CCR5
ASM 121	NA			R5	CCR5
ASM 3	NA			R5	CCR5
ASM 34	NA			R5	CCR5
ASM 42	NA			R5	CCR5
ASM 44	NA			R5X4	CXCR4, CCR5
ASM 54	NA			R5X4	CXCR4, CCR5
ASM 57	NA			R5	CCR5
ASM 61	NA			R5	CCR5
ASM 71	NA			R5	CCR5
ASM 79	NA			R5	CCR5
ASM 80	NA			R5	CCR5
ASM 93534	NA			R5	CCR5
ASM 93765	NA			R5	CCR5
ASM 94122	NA			R5	CCR5
CC				X4	CXCR4
G910-11	NA			R5X4	CXCR4, CCR5
I391-1	NA			R5X4	CXCR4, CCR5
I391-4	NA			R5X4	CXCR4, CCR5
I495-2	NA			R5X4	CXCR4, CCR5
JC	NA			X4	CXCR4
L10R/M46I/L63P/I84V	NA			X4	CXCR4
LAI-M184V				X4	CXCR4
M46L/L63P/V82T/I84V	NA			R5X4	CXCR4, CCR5
N119				X4	CXCR4
RTMC	NA			R5X4	CXCR4, CCR5
RTMDR1	NA			X4	CXCR4
RTMF	NA			R5X4	CXCR4, CCR5

HIV-2

HIV-2 strains appear to be remarkably promiscuous in their use of coreceptors, with receptors other than CCR5 or CXCR4 often supporting very efficient virus infection in transfected cells. This is obvious from the table, where coreceptors that are used efficiently are listed separately from those that support infection inefficiently. In addition, whenever possible, information is provided about the virus (whether it is a molecular clone, biological clone, or virus swarm, and whether it can infect PBMCs from CCR5-negative individuals) and the clinical stage of the patient from which each virus was isolated.

KEY FOR HIV-2 CORECEPTOR USE TABLE

[a] Δ32 PBMCs Replication

[b] Isolates shown to be capable of CD4-independent cell fusion and/or virus infection

MC = molecular clone

BC = biologic clone

S = virus swarm

ASYMP = asymptomatic

SYMP = symptomatic

DONOR = blood donor

EARLY = isolated at early timepoints

INTERMED = isolated at an intermediate point in disease progression

LATE = isolated late in disease

V28 has been redesignated CX3CR1

( ) indicates results are from cell-cell fusion assays, all other data are from infection assays

Isolate	Proposed Accession	Status	Primary Isolate?	Δ32[a]	Patient Status	Coreceptors	Weak Coreceptors	CD4 independence[b]	References
ST		MC	NO	+	ASYMP	CCR5/GPR15/-STRL33(GPR1/APJ)	CCR1/CCR2b/-CCR3/CXCR4		[Edinger (1997b), Edinger (1998a), Edinger (1998b), Rucker (1997), Hill (1997), McKnight (1998), Deng (1997)]
ST/24.1C#2	M86924	MC				CCR5/GPR15/-STRL33			[Rucker (1997), Hill (1997), Hill (1998), Deng (1997)]
SBL6669	J04498	MC			SYMP	(CCR5/CXCR4/-CCR8/V28)			[Rucker (1997), Chakrabarti (1990), Albert (1987)]
ROD/A	X05291 M15390	MC			AIDS	CCR5/CXCR4/-CCR3/US28/V28		+	[Hill (1997), Sol (1998), Sol (1997), Clavel (1986), Bron (1997), Reeves (1997), Reeves (1999)]
ROD/B		MC	NO			CXCR4	CCR3/V28	+	[Clapham (1992), Reeves (1997), Reeves (1999)]
prCBL-20		MC	YES	+	AIDS	CXCR4	CCR1/CCR2b/-CCR3/CCR5		[McKnight (1998), Schulz (1990)]
CBL-20		MC	NO	+		CXCR4			[McKnight (1998)]
prCBL-23	U05352	MC	YES		SYMP	CXCR4	CCR1/CCR2b/-CCR3/CCR5		[McKnight (1998), Schulz (1990)]

Isolate	Proposed Accession	Status	Primary Isolate?	Δ32[a]	Patient Status	Coreceptors	Weak Coreceptors	CD4 independence[b]	References
UC1	L0965	MC			SYMP	CCR5			[Hill (1997), Evans (1988), Deng (1997)]
UC2	U38293	MC	NO		AIDS	CCR5/CXCR4/-STRL33/GPR15	CCR2b/CCR3		[Hill (1997), Evans (1988), Barnett (1996), Deng (1997)]
MIR		MC		+	AIDS	CXCR4	CCR1/CCR2b/-CCR3/CCR5		[Sol (1997), McKnight (1998), Clavel (1986)]
V9					AIDS	CCR1/CCR2b/-CCR3/CCR5/CXCR4			[McKnight (1998)]
A-ND				+	SYMP	CXCR4	CCR1/CCR2b/CCR3		[McKnight (1998)]
VCP		MC	NO			CXCR4			[Endres (1996)]
F0784	L33083	MC				CCR5/GPR15			[Deng (1997), Gao (1992)]
A195811			YES	-	AIDS	CCR5/GPR15/-STRL33			[Chen (1998a), Owen (1998)]
A227011			YES	-	ASYMP	CCR5/GPR15/-STRL33			[Chen (1998a)]
G0415k			YES			CCR5/GPR15/-STRL33			[Chen (1998a)]
7924A			YES	+	AIDS	CXCR4/CCR2b/-CCR3/CCR5/-STRL33/GPR15			[Chen (1998a)]
JK7312A		MC		+	SYMP	CCR5/GPR15/-CCR4/CXCR4			[Hill (1997), Owen (1998), Gao (1992), Deng (1997)]
310342		S	YES			CCR5/CXCR4/-STRL33/CCR1			[Owen (1998)]
GB87		S	YES	+	SYMP	CCR5/GPR15/-CXCR4/STRL33/-CCR4/CCR2b/CCR1			[Owen (1998)]
310248		S	YES	+		CCR1/CCR4/CCR5/-CXCR4			[Owen (1998)]
310319		S	YES	+		CCR2b/CCR3/-CCR4/CXCR4/-STRL33/GPR15/-CCR5			[Owen (1998)]
77618		S	YES	+	AIDS	CCR2b/CCR3/-CXCR4/GPR15/-STRL33/CCR5			[Owen (1998)]
GB122	L10638	S	YES	+		CCR2b/CCR3/-GPR15	CCR5/CXCR4		[Owen (1998)]
A2267		S	YES	-	ASYMP	CCR5			[Owen (1998)]
SLRHC		S	YES	-	ASYMP	CCR5			[Owen (1998)]
310072		S	YES	-	DONOR	CCR5			[Owen (1998)]
310340		S	YES	-	DONOR	CCR5			[Owen (1998)]
60415k		S	YES	-	ASYMP	CCR5			[Owen (1998)]

Isolate	Proposed Accession	Status	Primary Isolate?	Δ32[a]	Patient Status	Coreceptors	Weak Coreceptors	CD4 independence[b]	References
BAJE (B)		S	YES	-	ASYMP	CCR5/CCR3			[Sol (1998)]
BATI (A)		S	YES	-	ASYMP	CCR5	CCR3		[Sol (1997)]
BAPA (C)		S	YES	+	ASYMP	CCR5	CCR3		[Sol (1997)]
DESY (E)		S	YES		ASYMP	CCR5	CCR3		[Sol (1997)]
BAYO (G)		S	YES	+	AIDS	CXCR4			[Sol (1997)]
B3		S	YES			CCR5			[Heredia (1997)]
B4		S	YES			CCR5			[Heredia (1997)]
B7		S	YES			CCR5			[Heredia (1997)]
B8		S	YES			CCR5			[Heredia (1997)]
B9		S	YES			CCR5			[Heredia (1997)]
B2		S	YES			CCR1/CCR2b/-CCR5/CXCR4			[Heredia (1997)]
B5		S	YES			CCR1/CCR2b/-CCR5/CXCR4			[Heredia (1997)]
B10		S	YES			CCR1/CCR2b/-CCR5/CXCR4			[Heredia (1997)]
RH-2-1		S	YES		EARLY	CCR5			[Guillon (1998)]
PH-2-1 C1		BC	YES		INTERMED	CCR5			[Guillon (1998)]
PH-2-1 C12		BC	YES		INTERMED	CCR5/CCR1/CCR3			[Guillon (1998)]
PH-2-1 E6		BC	YES		INTERMED	CCR5/CXCR4/-CCR3/CCR1			[Guillon (1998)]
PH-2-1 H8		BC	YES		INTERMED	CCR5/CCR3/CCR1			[Guillon (1998)]
PH-2-1 D5		BC	YES		INTERMED	CCR5	CCR3/CXCR4/CCR1		[Guillon (1998)]
PH-2-1 H12		BC	YES		INTERMED	CCR5/CCR3/CCR1	CXCR4		[Guillon (1998)]
RH-2-5 A10		BC	YES		INTERMED	CCR5	CCR3		[Guillon (1998)]
RH-2-5 E4		BC	YES		INTERMED	CCR5/CCR3/CCR1	CXCR4		[Guillon (1998)]
RH-2-5 E11		BC	YES		INTERMED	CCR5/CCR3/CCR1	CXCR4		[Guillon (1998)]
RH-2-5 F7		BC	YES		INTERMED	CCR5/CCR3/CCR1/-CXCR4			[Guillon (1998)]
RH-2-5 G7		BC	YES		INTERMED	CCR5	CXCR4/CCR1/CCR3		[Guillon (1998)]
RH-2-7 A5		BC	YES		INTERMED	CCR5/CCR3	CCR1/CXCR4		[Guillon (1998)]
RH-2-7 C9		BC	YES		INTERMED	CCR5/CCR1/CCR3/-CCR2b/CXCR4			[Guillon (1998)]
RH-2-7 C12		BC	YES		INTERMED	CCR5	CCR3/CXCR4/CCR1		[Guillon (1998)]
RH-2-7 D7		BC	YES		INTERMED	CCR5/CCR3/CCR1	CXCR4/CCR2b		[Guillon (1998)]
RH-2-7 G12		BC	YES		INTERMED	CCR5/CCR3/CCR1	CXCR4/CCR2b		[Guillon (1998)]
RH-2-2		S	YES		LATE	CCR3/CCR1/-CXCR4/CCR5	CCR2b		[Guillon (1998)]
RH-2-6		S	YES		LATE	CXCR4			[Guillon (1998)]
MLC			yes		symp	CCR5	CCR1, CCR3		[Reeves (1999)]
TER			YES		AIDS	CCR5, CCR1, CCR3		+	[Reeves (1999)]

Isolate	Proposed Accession	Status	Primary Isolate?	$\Delta 32$[a]	Patient Status	Coreceptors	Weak Coreceptors	CD4 independence[b]	References
ALI			YES		AIDS-rel-compx	CCR5	CCR1, CXCR4	+	[Reeves (1999)]
ETP			YES		symp	CCR5, CXCR4, CCR1, CCR2b, CCR3		+	[Reeves (1999)]
JAU			YES		AIDS	CCR5, CXCR4, CCR1, CCR2b, CCR3		+	[Reeves (1999)]
MIL			YES		AIDS	CXCR4		+	[Reeves (1999)]
SAB			YES		AIDS	CXCR4	CCR3	+	[Reeves (1999)]
1010			YES		AIDS	CCR1, CCR2b, CCR3, CCR5, CXCR4	gpr15, STRL33		[Morner (1999)]
1654			YES		AIDS	CCR5	CCR1, CCR3, gpr15, STRL33		[Morner (1999)]
1682			YES		asymp	CCR1, CCR3, CCR5	CCR2b, gpr15, STRL33		[Morner (1999)]
1808			YES		asthenia	CCR1, CCR3, CCR5	gpr15, STRL33		[Morner (1999)]
1812			YES		AIDS	CCR5	gpr15		[Morner (1999)]
1816			YES		AIDS	CCR5	CCR1, CCR2b, gpr15, STRL33		[Morner (1999)]
2297			YES		asthenia	CCR5, gpr15	CCR1, STRL33		[Morner (1999)]
2298			YES		asymp	CCR5	CCR2b, gpr15, STRL33		[Morner (1999)]
2300			YES		AIDS	CCR1, CCR3, CCR5	gpr15, STRL33		[Morner (1999)]
6669			YES		AIDS	CCR3, CXCR4	gpr15, STRL33		[Morner (1999)]
1653			YES		AIDS	CCR5	gpr15		[Morner (1999)]

SIV

SIV strains are also rather promiscuous in their use of coreceptors. SIV strains use CCR5 with few exceptions, while CXCR4 is only rarely used, even by laboratory-adapted viruses, a feature that distinguishes them from HIV-1 strains. The Table indicates the tropism of the virus (when known) as well as whether the data were derived from a molecular clone or virus swarm.

KEY FOR SIV CORECEPTOR TABLE

[a] Isolates shown to be capable of CD4-independent cell fusion and/or virus infection

S = uncloned virus swarm

MC = molecular clone

M = macrophage tropic, Md = delayed infection kinetics in macrophages, (M) = probably M-tropic, T = T-tropic

( ) indicate fusion results, all other data from infection assays

Strain	Accession	Status	Tropism	Coreceptors	CD4 independence[a]	References
SIVmac251	U62334	S	M	CCR5/GPR15/STRL33		[Chen (1997), Chen (1998a), Kuhmann (1997), Luciw (1992)]
SIVmac251 (BK28 clone)		MC		CCR5/GPR15/STRL33/-GPR1		[Edinger (1997b), Edinger (1999a)]
SIVmac251 (v194 clone)		MC		(CCR5/STRL33/GPR1/-GPR15)		[Rucker (1997), Edinger (1997a), Edinger (1997b), Koenig (1989)]
SIVmac239	M33262	MC	T	CCR5/STRL33/GPR15/-GPR1/(ChemR23)		[Edinger (1997a), Edinger (1997b), Edinger (1999a), Choe (1998), Rucker (1997), Chen (1997), Chen (1998a), Hill (1997), Hill (1998), Kirchhoff (1997), Marcon (1997), Samson (1998), Farzan (1997), Deng (1997)]
SIVmac316		MC	M	CCR5/STRL33/GPR15/-APJ/CCR8/GPR1/-(ChemR23)	+	[Edinger (1997a), Edinger (1997b), Choe (1998), Rucker (1997), Kirchhoff (1997), Samson (1998), Farzan (1997)]
SIVmac316mut		MC	Md	CCR5/(STRL33/GPR1/-GPR15/ChemR23/APJ)		[Edinger (1997a), Edinger (1997b), Edinger (1998b), Rucker (1997), Kirchhoff (1997), Kirchhoff (1994), Samson (1998)]
SIVmac316EM		MC	M	CCR5/GPR15/STRL33		[Chen (1997), Chen (1998a)]
SIVmac32H				CCR5, CCR1, gpr15, STRL33	+	[Reeves (1999)]
SIVmac1A11		MC	M	CCR5/STRL33/GPR15		[Edinger (1997b), Edinger (1999a), Chen (1997), Chen (1998a), Hill (1997), Banapour (1991a), Banapour (1991b), Deng (1997), Chen (1998a), Chen (1998b)]
SIVmac/17E-Fr		MC	M	CCR5/STRL33/GPR15/-APJ/(ChemR23/CCR8)	+	[Edinger (1997a), Edinger (1997b), Edinger (1998b), Edinger (1999a), Rucker (1997), Flaherty (1997)]
SIVmac/17E-Cl		MC	M	(CCR5/GPR1/STRL33/-GPR15)		[Edinger (1998a), Flaherty (1997)]

Strain	Accession	Status	Tropism	Coreceptors	CD4 independence[a]	References
SIVmacCP-MAC		S		CXCR4		[Endres (1996)]
SIVmacCP-MAC		MC		CCR5/STRL33/GPR15/APJ		[Edinger (1997b), Edinger (1998b), Edinger (1999a)]
SIVmac(mne)				CCR5/GPR15		[Chen (1998a)]
SIVsmΔB670 clone 3		MC		CCR5/GPR15/STRL33	+	[Edinger (1997a), Edinger (1997b), Rucker (1997)]
SIVsmΔB670 clone 12		MC	(M)	CCR5/GPR15	+	[Edinger (1997b), Edinger (1999a), Amedee (1995)]
SIVsm62A		MC	T	(CCR5/GPR1/GPR15/-STRL33/ChemR23)	+	[Edinger (1997b), Hirsch (1994)]
SIVsm62B	SIU04983	MC		(CCR5)	+	[Edinger (1997b), Hirsch (1994)]
SIVsm62D	SIU04987	MC	M	CCR5		[Edinger (1997b), Hirsch (1994)]
SIVsmE543/3		MC	M	CCR5/GPR15		[Edinger (1997b), Hirsch (1997)]
SIVsmE543/B10		MC		(CCR5/GPR15/GPR1/-STRL33)		[Edinger (1997b), Hirsch (1997)]
SIVsmPBj6.6		MC		(STRL33/CCR5/GPR1/-GPR15)		[Edinger (1998a), Novembre (1993)]
SIVsmSL92a	U48818	S		CCR5/GPR15/STRL33		[Chen (1997), Chen (1998a)]
SIVsmSL92b	U48819	S		CCR5/GPR15/STRL33		[Chen (1998a)]
SIVsmLib-1	U48824	S		CCR5/GPR15/STRL33		[Chen (1997), Chen (1998a)]
SIVsmFNS		S		CCR5/GPR15/STRL33		[Chen (1998a)]
SIVagmSab1.4		MC		(CCR5/GPR15/GPR1/-STRL33)		[Edinger (1997b)]
SIVagm9063-2		MC	M	(CCR5)		[Edinger (1997b), Hirsch (1995)]
SIVagmTYO	X07805	MC		CCR5/GPR15/STRL33		[Deng (1997), Chen (1998a), Chen (1998b)]
SIVmneCl8		MC		CCR5		[Chackerian (1997)]
SIVrcm				CCR2b/STRL33		[Marx & Chen(1998)]
SIVcpzGAB	X52154	S		CCR5		[Chen (1997), Marx & Chen(1998)]
SIVmnd(GB-1)		S		CXCR4		[Schols & De Clercq(1998)]

REFERENCES

[Albert (1987)] J. Albert, U. Bredberg, F. Chiodi, B. Bottiger, E. M. Fenyo, E. Norrby, & G. Biberfeld. A new human retrovirus isolate of West African origin (SBL-6669) and its relationship to HTLV-IV, LAV-II, and HTLV-IIIB. *AIDS Res Hum Retroviruses* **3**:3–10, 1987. (Medline: 87299193).

[Albritton (1989)] L. M. Albritton, L. Tseng, D. Scadden, & J. M. Cunningham. A putative murine ecotropic retrovirus receptor gene encodes a multiple membrane-spanning protein and confers susceptibility to virus infection. *Cell* **57**:659–66, 1989. (Medline: 89249329).

[Alkhatib (1996)] G. Alkhatib, C. Combadiere, C. C. Broder, Y. Feng, P. E. Kennedy, P. M. Murphy, & E. A. Berger. CC CKR5: a RANTES, MIP-1alpha, MIP-1beta receptor as a fusion cofactor for macrophage-tropic HIV-1. *Science* **272**:1955–8, 1996. (Medline: 96275693).

[Amedee (1995)] A. M. Amedee, N. Lacour, J. L. Gierman, L. N. Martin, J. E. Clements, R. Bohm, R. M. Harrison, & M. Murphey-Corb. Genotypic selection of simian immunodeficiency virus in macaque infants infected transplacentally. *J Virol* **69**:7982–90, 1995. (Medline: 96079048).

[Banapour (1991a)] B. Banapour, M. L. Marthas, R. J. Munn, & P. A. Luciw. In vitro macrophage tropism of pathogenic and nonpathogenic molecular clones of simian immunodeficiency virus (SIVmac). *Virology* **183**:12–9, 1991a. (Medline: 91272471).

[Banapour (1991b)] B. Banapour, M. L. Marthas, R. A. Ramos, B. L. Lohman, R. E. Unger, M. B. Gardner, N. C. Pedersen, & P. A. Luciw. Identification of viral determinants of macrophage tropism for simian immunodeficiency virus SIVmac. *J Virol* **65**:5798–805, 1991b. (Medline: 92015471).

[Barnett (1996)] S. W. Barnett, H. S. Legg, Y. Sun, J. Klinger, D. J. Blackbourn, C. P. Locher, & J. A. Levy. Molecular cloning of the human immunodeficiency virus subtype 2 strain HIV-2UC2. *Virology* **222**:257–61, 1996. (Medline: 96400130).

[Bazan (1998)] H. A. Bazan, G. Alkhatib, C. C. Broder, & E. A. Berger. Patterns of CCR5, CXCR4, and CCR3 usage by envelope glycoproteins from human immunodeficiency virus type 1 primary isolates. *J Virol* **72**:4485–91, 1998. (Medline: 98216824).

[Berger (1999)] E. A. Berger, P. M. Murphy, & J. M. Farber. Chemokine receptors as HIV-1 coreceptors: roles in viral entry, tropism, and disease. *Annu Rev Immunol* **17**:657–700, 1999. (Medline: 99286823).

[Berson & Doms(1998)] J. F. Berson & R. W. Doms. Structure-function studies of the HIV-1 coreceptors. *Semin Immunol* **10**:237–48, 1998. (Medline: 98317010).

[Bjorndal (1997)] A. Bjorndal, H. Deng, M. Jansson, J. R. Fiore, C. Colognesi, A. Karlsson, J. Albert, G. Scarlatti, D. R. Littman, & E. M. Fenyo. Coreceptor usage of primary human immunodeficiency virus type 1 isolates varies according to biological phenotype. *J Virol* **71**:7478–87, 1997. (Medline: 97456513).

[Bjorndal (1999)] A. Bjorndal, A. Sonnerborg, C. Tscherning, J. Albert, & E. M. Fenyo. Phenotypic characteristics of human immunodeficiency virus type 1 subtype C isolates of Ethiopian AIDS patients. *AIDS Res Hum Retroviruses* **15**:647–53, 1999. (Medline: 99260286).

[Broder & Collman(1997)] C. C. Broder & R. G. Collman. Chemokine receptors and HIV. *J Leukoc Biol* **62**:20–9, 1997. (Medline: 97369500).

[Broder & Dimitrov(1996)] C. C. Broder & D. S. Dimitrov. HIV and the 7-transmembrane domain receptors. *Pathobiology* **64**:171–9, 1996. (Medline: 97183186).

[Bron (1997)] R. Bron, P. J. Klasse, D. Wilkinson, P. R. Clapham, A. Pelchen-Matthews, C. Power, T. N. Wells, J. Kim, S. C. Peiper, J. A. Hoxie, & M. Marsh. Promiscuous use of CC and CXC chemokine receptors in cell-to-cell fusion mediated by a human immunodeficiency virus type 2 envelope protein. *J Virol* **71**:8405–15, 1997. (Medline: 98001362).

[Chackerian (1997)] B. Chackerian, E. M. Long, P. A. Luciw, & J. Overbaugh. Human immunodeficiency virus type 1 coreceptors participate in postentry stages in the virus replication cycle and function in simian immunodeficiency virus infection. *J Virol* **71**:3932–9, 1997. (Medline: 97248442).

[Chakrabarti (1990)] S. Chakrabarti, T. Mizukami, G. Franchini, & B. Moss. Synthesis, oligomerization, and biological activity of the human immunodeficiency virus type 2 envelope glycoprotein expressed by a recombinant vaccinia virus. *Virology* **178**:134–42, 1990. (Medline: 90357756).

[Chen (1998a)] Z. Chen, A. Gettie, D. D. Ho, & P. A. Marx. Primary SIVsm isolates use the CCR5 coreceptor from sooty mangabeys naturally infected in west Africa: a comparison of coreceptor usage of primary SIVsm, HIV-2, and SIVmac. *Virology* **246**:113–24, 1998a. (Medline: 98321155).

[Chen (1998b)] Z. Chen, D. Kwon, Z. Jin, S. Monard, P. Telfer, M. S. Jones, C. Y. Lu, R. F. Aguilar, D. D. Ho, & P. A. Marx. Natural infection of a homozygous delta24 CCR5 red-capped mangabey

with an R2b-tropic simian immunodeficiency virus. *J Exp Med* **188**:2057–65, 1998b. (Medline: 99059829).

[Chen (1997)] Z. Chen, P. Zhou, D. D. Ho, N. R. Landau, & P. A. Marx. Genetically divergent strains of simian immunodeficiency virus use CCR5 as a coreceptor for entry. *J Virol* **71**:2705–14, 1997. (Medline: 97213934).

[Choe (1998)] H. Choe, M. Farzan, M. Konkel, K. Martin, Y. Sun, L. Marcon, M. Cayabyab, M. Berman, M. E. Dorf, N. Gerard, C. Gerard, & J. Sodroski. The orphan seven-transmembrane receptor apj supports the entry of primary T-cell-line-tropic and dualtropic human immunodeficiency virus type 1. *J Virol* **72**:6113–8, 1998. (Medline: 98285773).

[Choe (1996)] H. Choe, M. Farzan, Y. Sun, N. Sullivan, B. Rollins, P. D. Ponath, L. Wu, C. R. Mackay, G. LaRosa, W. Newman, N. Gerard, C. Gerard, & J. Sodroski. The beta-chemokine receptors CCR3 and CCR5 facilitate infection by primary HIV-1 isolates. *Cell* **85**:1135–48, 1996. (Medline: 96270515).

[Clapham (1992)] P. R. Clapham, A. McKnight, & R. A. Weiss. Human immunodeficiency virus type 2 infection and fusion of CD4- negative human cell lines: induction and enhancement by soluble CD4. *J Virol* **66**:3531–7, 1992. (Medline: 92260623).

[Clapham (1999)] P. R. Clapham, J. D. Reeves, G. Simmons, N. Dejucq, S. Hibbitts, & A. McKnight. HIV coreceptors, cell tropism and inhibition by chemokine receptor ligands. *Mol Membr Biol* **16**:49–55, 1999. (Medline: 99265141).

[Clavel (1986)] F. Clavel, D. Guetard, F. Brun-Vezinet, S. Chamaret, M. A. Rey, M. O. Santos-Ferreira, A. G. Laurent, C. Dauguet, C. Katlama, & C. Rouzioux. Isolation of a new human retrovirus from West African patients with AIDS. *Science* **233**:343–6, 1986. (Medline: 86261773).

[Deng (1997)] H. K. Deng, D. Unutmaz, V. N. KewalRamani, & D. R. Littman. Expression cloning of new receptors used by simian and human immunodeficiency viruses (see comments). *Nature* **388**:296–300, 1997. (Medline: 97373958).

[Dimitrov & Broder(1997)] D. S. Dimitrov & C. C. Broder. In *HIV and Membrane Receptors*, Austin, TX. Landes Bioscience, 1997.

[Dimitrov (1999)] D. S. Dimitrov, D. Norwood, T. S. Stantchev, Y. Feng, X. Xiao, & C. C. Broder. A mechanism of resistance to HIV-1 entry: inefficient interactions of CXCR4 with CD4 and gp120 in macrophages. *Virology* **259**:1–6, 1999. (Medline: 99294885).

[Dimitrov (1998)] D. S. Dimitrov, X. Xiao, D. J. Chabot, & C. C. Broder. HIV coreceptors. *J Membr Biol* **166**:75–90, 1998. (Medline: 99058164).

[Dittmar (1997)] M. T. Dittmar, G. Simmons, S. Hibbitts, M. O'Hare, S. Louisirirotchanakul, S. Beddows, J. Weber, P. R. Clapham, & R. A. Weiss. Langerhans cell tropism of human immunodeficiency virus type 1 subtype A through F isolates derived from different transmission groups. *J Virol* **71**:8008–13, 1997. (Medline: 97456582).

[Dittmar (1999)] M. T. Dittmar, L. Zekeng, L. Kaptue, J. Eberle, H. G. Krausslich, & L. Gurtler. Coreceptor requirements of primary HIV type 1 group O isolates from Cameroon. *AIDS Res Hum Retroviruses* **15**:707–12, 1999. (Medline: 99284358).

[Doranz (1997)] B. J. Doranz, J. F. Berson, J. Rucker, & R. W. Doms. Chemokine receptors as fusion cofactors for human immunodeficiency virus type 1 (HIV-1). *Immunol Res* **16**:15–28, 1997. (Medline: 97200271).

[Dragic (1996)] T. Dragic, V. Litwin, G. P. Allaway, S. R. Martin, Y. Huang, K. A. Nagashima, C. Cayanan, P. J. Maddon, R. A. Koup, J. P. Moore, & W. A. Paxton. HIV-1 entry into CD4+ cells is mediated by the chemokine receptor CC- CKR-5 (see comments). *Nature* **381**:667–73, 1996. (Medline: 96260018).

[Edinger (1997a)] A. L. Edinger, A. Amedee, K. Miller, B. J. Doranz, M. Endres, M. Sharron, M. Samson, Z. H. Lu, J. E. Clements, M. Murphey-Corb, S. C. Peiper, M. Parmentier, C. C. Broder, & R. W. Doms. Differential utilization of CCR5 by macrophage and T cell tropic simian immunodeficiency virus strains. *Proc Natl Acad Sci U S A* **94**:4005–10, 1997a. (Medline: 97268687).

[Edinger (1999a)] A. L. Edinger, C. Blanpain, K. J. Kunstman, S. M. Wolinsky, M. Parmentier, & R. W. Doms. Functional dissection of CCR5 coreceptor function through the use of CD4-independent simian immunodeficiency virus strains. *J Virol* **73**:4062–73, 1999a. (Medline: 99214345).

[Edinger (1999b)] A. L. Edinger, J. E. Clements, & R. W. Doms. Chemokine and orphan receptors in HIV-2 and SIV tropism and pathogenesis. *Virology* **260**:211–21, 1999b. (Medline: 99348505).

[Edinger (1998a)] A. L. Edinger, T. L. Hoffman, M. Sharron, B. Lee, B. O'Dowd, & R. W. Doms. Use of GPR1, GPR15, and STRL33 as coreceptors by diverse human immunodeficiency virus type 1 and simian immunodeficiency virus envelope proteins. *Virology* **249**:367–78, 1998a. (Medline: 99009390).

[Edinger (1998b)] A. L. Edinger, T. L. Hoffman, M. Sharron, B. Lee, Y. Yi, W. Choe, D. L. Kolson, B. Mitrovic, Y. Zhou, D. Faulds, R. G. Collman, J. Hesselgesser, R. Horuk, & R. W. Doms. An orphan seven-transmembrane domain receptor expressed widely in the brain functions as a coreceptor for human immunodeficiency virus type 1 and simian immunodeficiency virus. *J Virol* **72**:7934–40, 1998b. (Medline: 98406195).

[Edinger (1997b)] A. L. Edinger, J. L. Mankowski, B. J. Doranz, B. J. Margulies, B. Lee, J. Rucker, M. Sharron, T. L. Hoffman, J. F. Berson, M. C. Zink, V. M. Hirsch, J. E. Clements, & R. W. Doms. CD4-independent, CCR5-dependent infection of brain capillary endothelial cells by a neurovirulent simian immunodeficiency virus strain. *Proc Natl Acad Sci U S A* **94**:14742–7, 1997b. (Medline: 98070822).

[Endres (1996)] M. J. Endres, P. R. Clapham, M. Marsh, M. Ahuja, J. D. Turner, A. McKnight, J. F. Thomas, B. Stoebenau-Haggarty, S. Choe, P. J. Vance, T. N. Wells, C. A. Power, S. S. Sutterwala, R. W. Doms, N. R. Landau, & J. A. Hoxie. CD4-independent infection by HIV-2 is mediated by fusin/CXCR4. *Cell* **87**:745–56, 1996. (Medline: 97083584).

[Evans (1988)] L. A. Evans, J. Moreau, K. Odehouri, D. Seto, G. Thomson-Honnebier, H. Legg, A. Barboza, C. Cheng-Mayer, & J. A. Levy. Simultaneous isolation of HIV-1 and HIV-2 from an AIDS patient. *Lancet* **2**:1389–91, 1988. (Medline: 89069975).

[Farzan (1997)] M. Farzan, H. Choe, K. Martin, L. Marcon, W. Hofmann, G. Karlsson, Y. Sun, P. Barrett, N. Marchand, N. Sullivan, N. Gerard, C. Gerard, & J. Sodroski. Two orphan seven-transmembrane segment receptors which are expressed in CD4-positive cells support simian immunodeficiency virus infection. *J Exp Med.* **186**:405–11, 1997. (Medline: 98105758).

[Fauci(1996)] A. S. Fauci. Host factors and the pathogenesis of HIV-induced disease. *Nature* **384**:529–34, 1996. (Medline: 97113407).

[Flaherty (1997)] M. T. Flaherty, D. A. Hauer, J. L. Mankowski, M. C. Zink, & J. E. Clements. Molecular and biological characterization of a neurovirulent molecular clone of simian immunodeficiency virus. *J Virol* **71**:5790–8, 1997. (Medline: 97366637).

[Gabuzda (1998)] D. Gabuzda, J. He, A. Ohagen, & A. V. Vallat. Chemokine receptors in HIV-1 infection of the central nervous system. *Semin Immunol* **10**:203–13, 1998. (Medline: 98317007).

[Gallaher (1995)] W. R. Gallaher, J. M. Ball, R. F. Garry, A. M. Martin-Amedee, & R. C. Montelaro. A general model for the surface glycoproteins of HIV and other retroviruses. *AIDS Res Hum Retroviruses* **11**:191–202, 1995. (Medline: 95260528).

[Gao (1992)] F. Gao, L. Yue, A. T. White, P. G. Pappas, J. Barchue, A. P. Hanson, B. M. Greene, P. M. Sharp, G. M. Shaw, & B. H. Hahn. Human infection by genetically diverse SIVSM-related HIV-2 in west Africa. *Nature* **358**:495–9, 1992. (Medline: 92350299).

[Guillon (1998)] C. Guillon, M. E. van der Ende, P. H. Boers, R. A. Gruters, M. Schutten, & A. D. Osterhaus. Coreceptor usage of human immunodeficiency virus type 2 primary isolates and biological clones is broad and does not correlate with their syncytium-inducing capacities. *J Virol* **72**:6260–3, 1998. (Medline: 98285800).

[Heredia (1997)] A. Heredia, A. Vallejo, V. Soriano, J. S. Epstein, & I. K. Hewlett. Chemokine receptors and HIV-2 [letter]. *AIDS* **11**:1198–9, 1997. (Medline: 97377877).

[Hill (1997)] C. M. Hill, H. Deng, D. Unutmaz, V. N. Kewalramani, L. Bastiani, M. K. Gorny, S. Zolla-Pazner, & D. R. Littman. Envelope glycoproteins from human immunodeficiency virus types 1 and 2 and simian immunodeficiency virus can use human CCR5 as a coreceptor for viral entry and make direct CD4-dependent interactions with this chemokine receptor. *J Virol* **71**:6296–304, 1997. (Medline: 97404634).

[Hill (1998)] C. M. Hill, D. Kwon, M. Jones, C. B. Davis, S. Marmon, B. L. Daugherty, J. A. DeMartino, M. S. Springer, D. Unutmaz, & D. R. Littman. The amino terminus of human CCR5 is required for its function as a receptor for diverse human and simian immunodeficiency virus envelope glycoproteins. *Virology* **248**:357–71, 1998. (Medline: 98389855).

[Hirsch (1997)] V. Hirsch, D. Adger-Johnson, B. Campbell, S. Goldstein, C. Brown, W. R. Elkins, & D. C. Montefiori. A molecularly cloned, pathogenic, neutralization-resistant simian immunodeficiency virus, SIVsmE543-3. *J Virol* **71**:1608–20, 1997. (Medline: 97151152).

[Hirsch (1995)] V. M. Hirsch, G. Dapolito, P. R. Johnson, W. R. Elkins, W. T. London, R. J. Montali, S. Goldstein, & C. Brown. Induction of AIDS by simian immunodeficiency virus from an African green monkey: species-specific variation in pathogenicity correlates with the extent of in vivo replication. *J Virol* **69**:955–67, 1995. (Medline: 95115151).

[Hirsch (1994)] V. M. Hirsch, J. E. Martin, G. Dapolito, W. R. Elkins, W. T. London, S. Goldstein, & P. R. Johnson. Spontaneous substitutions in the vicinity of the V3 analog affect cell tropism and pathogenicity of simian immunodeficiency virus. *J Virol* **68**:2649–61, 1994. (Medline: 94187106).

[Hoffman & Doms(1999)] T. L. Hoffman & R. W. Doms. HIV-1 envelope determinants for cell tropism and chemokine receptor use. *Mol Membr Biol* **16**:57–65, 1999. (Medline: 99265142).

[Kalinkovich (1999)] A. Kalinkovich, Z. Weisman, & Z. Bentwich. Chemokines and chemokine receptors: role in HIV infection. *Immunol Lett* **68**:281–7, 1999. (Medline: 99351719).

[Kirchhoff (1994)] F. Kirchhoff, K. Mori, & R. C. Desrosiers. The "V3" domain is a determinant of simian immunodeficiency virus cell tropism. *J Virol* **68**:3682–92, 1994. (Medline: 94246713).

[Kirchhoff (1997)] F. Kirchhoff, S. Pohlmann, M. Hamacher, R. E. Means, T. Kraus, K. Uberla, & P. Di Marzio. Simian immunodeficiency virus variants with differential T-cell and macrophage tropism use CCR5 and an unidentified cofactor expressed in CEMx174 cells for efficient entry. *J Virol* **71**:6509–16, 1997. (Medline: 97404658).

[Koenig (1989)] S. Koenig, V. M. Hirsch, R. A. Olmsted, D. Powell, W. Maury, A. Rabson, A. S. Fauci, R. H. Purcell, & P. R. Johnson. Selective infection of human CD4+ cells by simian immunodeficiency virus: productive infection associated with envelope glycoprotein- induced fusion. *Proc Natl Acad Sci U S A* **86**:2443–7, 1989. (Medline: 89184643).

[Kuhmann (1997)] S. E. Kuhmann, E. J. Platt, S. L. Kozak, & D. Kabat. Polymorphisms in the CCR5 genes of African green monkeys and mice implicate specific amino acids in infections by simian and human immunodeficiency viruses. *J Virol* **71**:8642–56, 1997. (Medline: 98001387).

[Lapham (96)] C. K. Lapham, J. Ouyang, B. Chandrasekhar, N. Y. Nguyen, D. S. Dimitrov, & H. Golding. Evidence for cell-surface association between fusin and the CD4-gp120 complex in human cell lines. *Science* **274**:602–5, 96. (Medline: 97002453).

[Lee & Montaner(1999)] B. Lee & L. J. Montaner. Chemokine immunobiology in HIV-1 pathogenesis. *J Leukoc Biol* **65**:552–65, 1999. (Medline: 99260325).

[Levy(1998)] J. A. Levy. In *HIV and the Pathogenesis of AIDS*, Washington, DC. ASM Press, 1998.

[Liao (1997)] F. Liao, G. Alkhatib, K. W. Peden, G. Sharma, E. A. Berger, & J. M. Farber. STRL33, A novel chemokine receptor-like protein, functions as a fusion cofactor for both macrophage-tropic and T cell line-tropic HIV-1. *J Exp Med* **185**:2015–23, 1997. (Medline: 97311099).

[Luciw (1992)] P. A. Luciw, K. E. Shaw, R. E. Unger, V. Planelles, M. W. Stout, J. E. Lackner, E. Pratt-Lowe, N. J. Leung, B. Banapour, & M. L. Marthas. Genetic and biological comparisons of pathogenic and nonpathogenic molecular clones of simian immunodeficiency virus (SIVmac). *AIDS Res Hum Retroviruses* **8**:395–402, 1992. (Medline: 92239216).

[Marcon (1997)] L. Marcon, H. Choe, K. A. Martin, M. Farzan, P. D. Ponath, L. Wu, W. Newman, N. Gerard, C. Gerard, & J. Sodroski. Utilization of C-C chemokine receptor 5 by the envelope glycoproteins of a pathogenic simian immunodeficiency virus, SIVmac239. *J Virol* **71**:2522–7, 1997. (Medline: 97184592).

[Marx & Chen(1998)] P. A. Marx & Z. Chen. The function of simian chemokine receptors in the replication of SIV. *Semin Immunol* **10**:215–23, 1998. (Medline: 98317008).

[McKnight (1998)] A. McKnight, M. T. Dittmar, J. Moniz-Periera, K. Ariyoshi, J. D. Reeves, S. Hibbitts, D. Whitby, E. Aarons, A. E. Proudfoot, H. Whittle, & P. R. Clapham. A broad range of chemokine receptors are used by primary isolates of human immunodeficiency virus type 2 as coreceptors with CD4. *J Virol* **72**:4065–71, 1998. (Medline: 98216773).

[Michael(1999)] N. L. Michael. Host genetic influences on HIV-1 pathogenesis. *Curr Opin Immunol* **11**:466–74, 1999. (Medline: 99379882).

[Moore(1997)] J. P. Moore. Coreceptors: implications for HIV pathogenesis and therapy. *Science* **276**:51–2, 1997.

[Morner (1999)] A. Morner, A. Bjorndal, J. Albert, V. N. Kewalramani, D. R. Littman, R. Inoue, R. Thorstensson, E. M. Fenyo, & E. Bjorling. Primary human immunodeficiency virus type 2 (HIV-2) isolates, like HIV- 1 isolates, frequently use CCR5 but show promiscuity in coreceptor usage. *J Virol* **73**:2343–9, 1999. (Medline: 99139017).

[Novembre (1993)] F. J. Novembre, P. R. Johnson, M. G. Lewis, D. C. Anderson, S. Klumpp, H. M. McClure, & V. M. Hirsch. Multiple viral determinants contribute to pathogenicity of the acutely lethal simian immunodeficiency virus SIVsmmPBj variant. *J Virol* **67**:2466–74, 1993. (Medline: 93233209).

[Owen (1998)] S. M. Owen, D. Ellenberger, M. Rayfield, S. Wiktor, P. Michel, M. H. Grieco, F. Gao, B. H. Hahn, & R. B. Lal. Genetically divergent strains of human immunodeficiency virus type 2 use multiple coreceptors for viral entry. *J Virol* **72**:5425–32, 1998. (Medline: 98285695).

[Pleskoff (1997)] O. Pleskoff, N. Sol, B. Labrosse, & M. Alizon. Human immunodeficiency virus strains differ in their ability to infect CD4+ cells expressing the rat homolog of CXCR-4 (fusin). *J Virol* **71**:3259–62, 1997. (Medline: 97214002).

[Pohlmann (1999)] S. Pohlmann, M. Krumbiegel, & F. Kirchhoff. Coreceptor usage of BOB/GPR15 and Bonzo/STRL33 by primary isolates of human immunodeficiency virus type 1. *J Gen Virol* **80 (Pt 5)**:1241–51, 1999. (Medline: 99281902).

[Reeves (1999)] J. D. Reeves, S. Hibbitts, G. Simmons, A. McKnight, J. M. Azevedo-Pereira, J. Moniz-Pereira, & P. R. Clapham. Primary human immunodeficiency virus type 2 (HIV-2) isolates infect CD4- negative cells via CCR5 and CXCR4: comparison with HIV-1 and simian immunodeficiency virus and relevance to cell tropism in vivo. *J Virol* **73**:7795–804, 1999. (Medline: 99370224).

[Reeves (1997)] J. D. Reeves, A. McKnight, S. Potempa, G. Simmons, P. W. Gray, C. A. Power, T. Wells, R. A. Weiss, & S. J. Talbot. CD4-independent infection by HIV-2 (ROD/B): use of the 7-transmembrane receptors CXCR-4, CCR-3, and V28 for entry. *Virology* **231**:130–4, 1997. (Medline: 97288333).

[Ross (1999)] T. M. Ross, P. D. Bieniasz, & B. R. Cullen. Role of chemokine receptors in HIV-1 infection and pathogenesis. *Adv Virus Res* **52**:233–67, 1999. (Medline: 99312231).

[Rucker & Doms(1998)] J. Rucker & R. W. Doms. Chemokine receptors as HIV coreceptors: implications and interactions. *AIDS Res Hum Retroviruses* **14 Suppl 3**:S241–6, 1998. (Medline: 99030115).

[Rucker (1997)] J. Rucker, A. L. Edinger, M. Sharron, M. Samson, B. Lee, J. F. Berson, Y. Yi, B. Margulies, R. G. Collman, B. J. Doranz, M. Parmentier, & R. W. Doms. Utilization of chemokine receptors, orphan receptors, and herpesvirus encoded receptors by diverse human and simian immunodeficiency viruses. *J Virol* **71**:8999–9007, 1997. (Medline: 98037607).

[Samson (1998)] M. Samson, A. L. Edinger, P. Stordeur, J. Rucker, V. Verhasselt, M. Sharron, C. Govaerts, C. Mollereau, G. Vassart, R. W. Doms, & M. Parmentier. ChemR23, a putative chemoattractant receptor, is expressed in monocyte- derived dendritic cells and macrophages and is a coreceptor for SIV and some primary HIV-1 strains. *Eur J Immunol* **28**:1689–700, 1998. (Medline: 98264639).

[Schols & De Clercq(1998)] D. Schols & E. De Clercq. The simian immunodeficiency virus mnd(GB-1) strain uses CXCR4, not CCR5, as coreceptor for entry in human cells. *J Gen Virol* **79 (Pt 9)**:2203–5, 1998. (Medline: 98418501).

[Schulz (1990)] T. F. Schulz, D. Whitby, J. G. Hoad, T. Corrah, H. Whittle, & R. A. Weiss. Biological and molecular variability of human immunodeficiency virus type 2 isolates from The Gambia. *J Virol* **64**:5177–82, 1990. (Medline: 90376478).

[Simmons (1998)] G. Simmons, J. D. Reeves, A. McKnight, N. Dejucq, S. Hibbitts, C. A. Power, E. Aarons, D. Schols, E. De Clercq, A. E. Proudfoot, & P. R. Clapham. CXCR4 as a functional coreceptor for human immunodeficiency virus type 1 infection of primary macrophages. *J Virol* **72**:8453–7, 1998. (Medline: 98406265).

[Simmons (1996)] G. Simmons, D. Wilkinson, J. D. Reeves, M. T. Dittmar, S. Beddows, J. Weber, G. Carnegie, U. Desselberger, P. W. Gray, R. A. Weiss, & P. R. Clapham. Primary, syncytium-inducing human immunodeficiency virus type 1 isolates are dual-tropic and most can use either Lestr or CCR5 as coreceptors for virus entry. *J Virol* **70**:8355–60, 1996. (Medline: 97126031).

[Sol (1997)] N. Sol, F. Ferchal, J. Braun, O. Pleskoff, C. Treboute, I. Ansart, & M. Alizon. Usage of the coreceptors CCR-5, CCR-3, and CXCR-4 by primary and cell line-adapted human immunodeficiency virus type 2. *J Virol* **71**:8237–44, 1997. (Medline: 98001340).

[Sol (1998)] N. Sol, C. Treboute, E. Gomas, F. Ferchal, B. Shacklett, & M. Alizon. The rhesus macaque CCR3 chemokine receptor is a cell entry cofactor for HIV-2, but not for HIV-1. *Virology* **240**:213–20, 1998. (Medline: 98118446).

[Trkola (1998)] A. Trkola, W. A. Paxton, S. P. Monard, J. A. Hoxie, M. A. Siani, D. A. Thompson, L. Wu, C. R. Mackay, R. Horuk, & J. P. Moore. Genetic subtype-independent inhibition of human immunodeficiency virus type 1 replication by CC and CXC chemokines. *J Virol* **72**:396–404, 1998. (Medline: 98080427).

[Vallejo (1998)] A. Vallejo, A. Heredia, A. Mas, S. F. Lee, J. S. Epstein, V. Soriano, & I. K. Hewlett. Tropism, coreceptor use, and phylogenetic analysis of both the V3 loop and the protease gene of three novel HIV-1 group O isolates. *J Acquir Immune Defic Syndr Hum Retrovirol* **18**:417–25, 1998. (Medline: 98379694).

[Weiss(1993)] R. A. Weiss. In J. A. Levy, editor, *The Retroviridae*, pages 1–108, New York. Plenum Press, 1993.

[Weiss(1996)] R. A. Weiss. HIV receptors and the pathogenesis of AIDS [see comments]. *Science* **272**:1885–6, 1996. (Medline: 96275680).

[Weiss & Tailor(1995)] R. A. Weiss & C. S. Tailor. Retrovirus receptors. *Cell* **82**:531–3, 1995. (Medline: 95393464).

[Willett (1997)] B. J. Willett, M. J. Hosie, J. C. Neil, J. D. Turner, & J. A. Hoxie. Common mechanism of infection by lentiviruses [letter]. *Nature* **385**:587, 1997. (Medline: 97177102).

[Xiao (1998)] L. Xiao, S. M. Owen, I. Goldman, A. A. Lal, J. J. deJong, J. Goudsmit, & R. B. Lal. CCR5 coreceptor usage of non-syncytium-inducing primary HIV-1 is independent of phylogenetically distinct global HIV-1 isolates: delineation of consensus motif in the V3 domain that predicts CCR-5 usage. *Virology* **240**:83–92, 1998. (Medline: 98110142).

[Xiao (1999)] X. Xiao, L. Wu, T. S. Stantchev, Y. R. Feng, S. Ugolini, H. Chen, Z. Shen, J. L. Riley, C. C. Broder, Q. J. Sattentau, & D. S. Dimitrov. Constitutive cell surface association between CD4 and CCR5. *Proc Natl Acad Sci U S A* **96**:7496–501, 1999. (Medline: 99307438).

[Yi (1999)] Y. Yi, S. N. Isaacs, D. A. Williams, I. Frank, D. Schols, E. De Clercq, D. L. Kolson, & R. G. Collman. Role of CXCR4 in cell-cell fusion and infection of monocyte-derived macrophages by primary human immunodeficiency virus type 1 (HIV-1) strains: two distinct mechanisms of HIV-1 dual tropism. *J Virol* **73**:7117–25, 1999. (Medline: 99370151).

[Zhang (1996)] L. Zhang, Y. Huang, T. He, Y. Cao, & D. D. Ho. HIV-1 subtype and second-receptor use (letter). *Nature* **383**:768, 1996. (Medline: 97048157).

[Zhang (1998)] Y. J. Zhang, T. Dragic, Y. Cao, L. Kostrikis, D. S. Kwon, D. R. Littman, V. N. Kewal-Ramani, & J. P. Moore. Use of coreceptors other than CCR5 by non-syncytium-inducing adult and pediatric isolates of human immunodeficiency virus type 1 is rare in vitro. *J Virol* **72**:9337–44, 1998. (Medline: 98440604).