Supplemental Materials

Table S1. Anti-HIV activities of the chimeric inhibitors in R5 cell-cell fusion assay

Inhibitor	5P12	5P12+C37	5P12-linker-C37	C37	5P14	5P14+C37	5P14-linker-C37
IC_{50} (nM)	0.051 ± 0.01	0.044 ± 0.005	0.009 ± 0.003	9.1 ± 4.1	0.03 ± 0.002	0.03 ± 0.01	0.006 ± 0.001

Results are average IC_{50} ± SD (nM) from 4 or more independent experiments in triplicate.
R5 fusion stands for P5L (R5) cells fusion with Hela-ADA cells.

Table S2. Anti-HIV activities of the chimeric inhibitors in X4 cell-cell fusion assay

IC_{50} (nM)	C37	5P12-linker-C37	5P12 + C37	5P14-linker-C37	5P14 + C37
Magi-X4 (X4)	1.5 ± 0.3	4.7 ± 0.9	2.2 ± 0.2	4.3 ± 0.5	2.4 ± 0.7
TZM-bl (R5/X4)	2.1 ± 0.8	0.006 ± 0.003	2.1 ± 0.2	0.005 ± 0.002	2.6 ± 1.0

Results are average IC_{50} ± SD (nM) from 4 or more independent experiments in triplicate.
X4 fusion stands for Magi-X4 cells fusion with HL2/3 cells.
R5/X4 fusion stands for TZM (R5/X4) cells fusion with HL2/3 cells.

Table S3. Anti-HIV activities of 5P12 + C37 and 5P14+ C37 in single-cycle viral assay

HIV virus	Tropism	5P12+C37	5P14+C37
BaL	R5	0.30 ± 0.05	0.16 ± 0.03
SF162	R5	0.61 ± 0.11	0.13 ± 0.08
ADA	R5	0.54 ± 0.06	0.13 ± 0.009
JRFL	R5	0.56 ± 0.05	0.19 ± 0.09
US005	R5	0.28 ± 0.08	0.10 ± 0.01
6535	R5	0.7 ± 0.2	0.08 ± 0.008
HXB2 (Magi-X4)	X4	9.6 ± 1.3	8.5 ± 1.5
HXB2 (TZM)	X4	3.6 ± 0.1	4.6 ± 0.3
VSV-G	> 500	> 500	> 500

Results are average IC_{50} ± SD (nM) from 4 or more independent experiments in triplicate.

Table S4. Anti-HIV activities of 5P12-linker-C37 mutations in cell-cell fusion assay

Tropism	5P12-linker-C37	Mutation in RANTES	Mutation in C37		Change of linker length	
		P2-RANTES-linker-C37	5P12-linker-C37I642D	5P12-linker-C37I656D	5P12-GGS-C37	5P12-$(GGGGS)_4$-C37
R5	0.009 ± 0.003	1.2 ± 0.09	0.06 ± 0.005	0.07 ± 0.003	0.03 ± 0.01	0.01 ± 0.002
X4 (Magi-X4)	4.7 ± 0.9	3.9 ± 0.5	> 500	59.4 ± 15.4	4.1 ± 0.9	6.1 ± 1.7
X4 (TZM-bl)	0.006 ± 0.003	0.2 ± 0.09	> 500	0.05 ± 0.01	0.008 ± 0.003	0.003 ± 0.001

Results are average IC_{50} ± SD (nM) from 4 or more independent experiments in triplicate.

Figure S1. The correlation between the viral sensitivity to C37 and the magnitude of the relative potency enhancement of the chimeric inhibitors over RANTES variants alone. Numbers in parentheses are fold of relative potency enhancement.

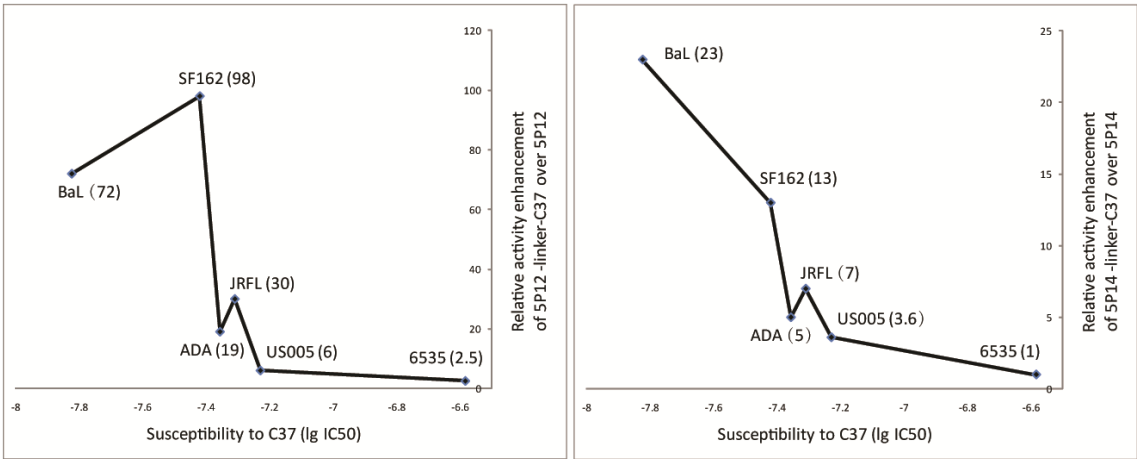

Figure S2 CCR5 receptor density comparison by flow cytometry. The CCR5 receptor expression levels on HeLa-TZM-bl cells and HeLa-P5L cells were compared using flow cytometry.

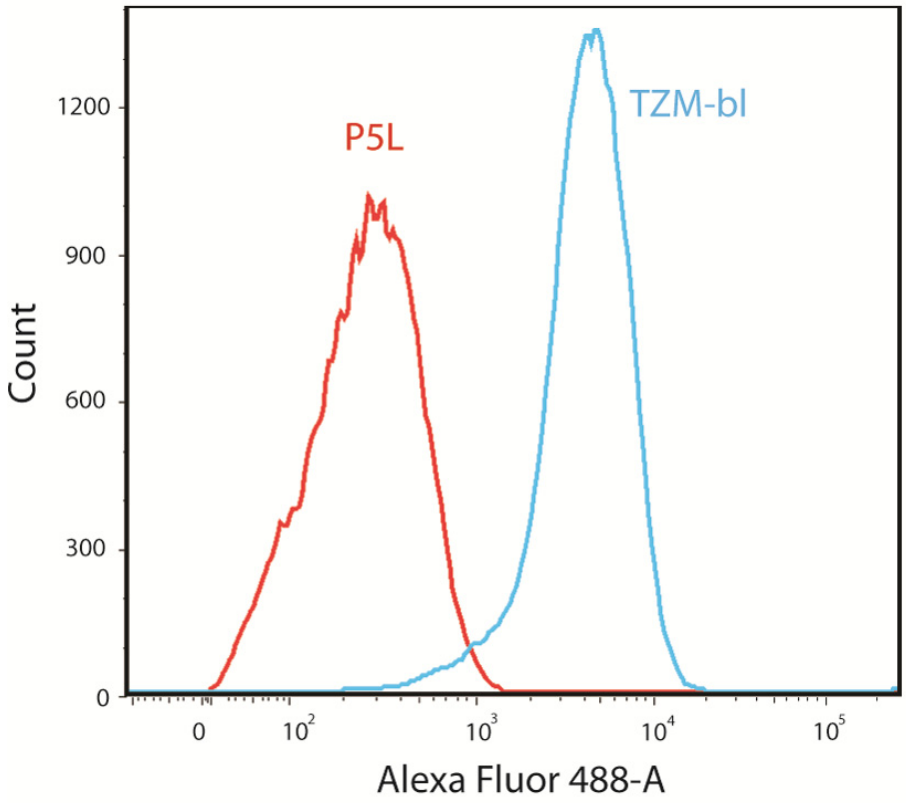

Table S5. Anti-HIV activities of the chimeric inhibitors in R5 tropic fusion assays with P5L and TZM-bl as target cells.

Cell lines CCR5 density	Hela-P5L Low	TZM-bl High
5P12	0.051 ± 0.01	14 ± 1.4
5P12+C37	0.044 ± 0.005	7.0 ± 1.3
5P12-linker-C37	0.009 ± 0.003	0.8 ± 0.2
C37	9.1 ± 4.1	340 ± 80
5P14	0.03 ± 0.002	11 ± 2.4
5P14+C37	0.03 ± 0.01	4.8 ± 0.2
5P14-linker-C37	0.006 ± 0.001	0.6 ± 0.02

Results are average IC_{50} ± SD (nM) from 4 or more independent experiments in triplicate.