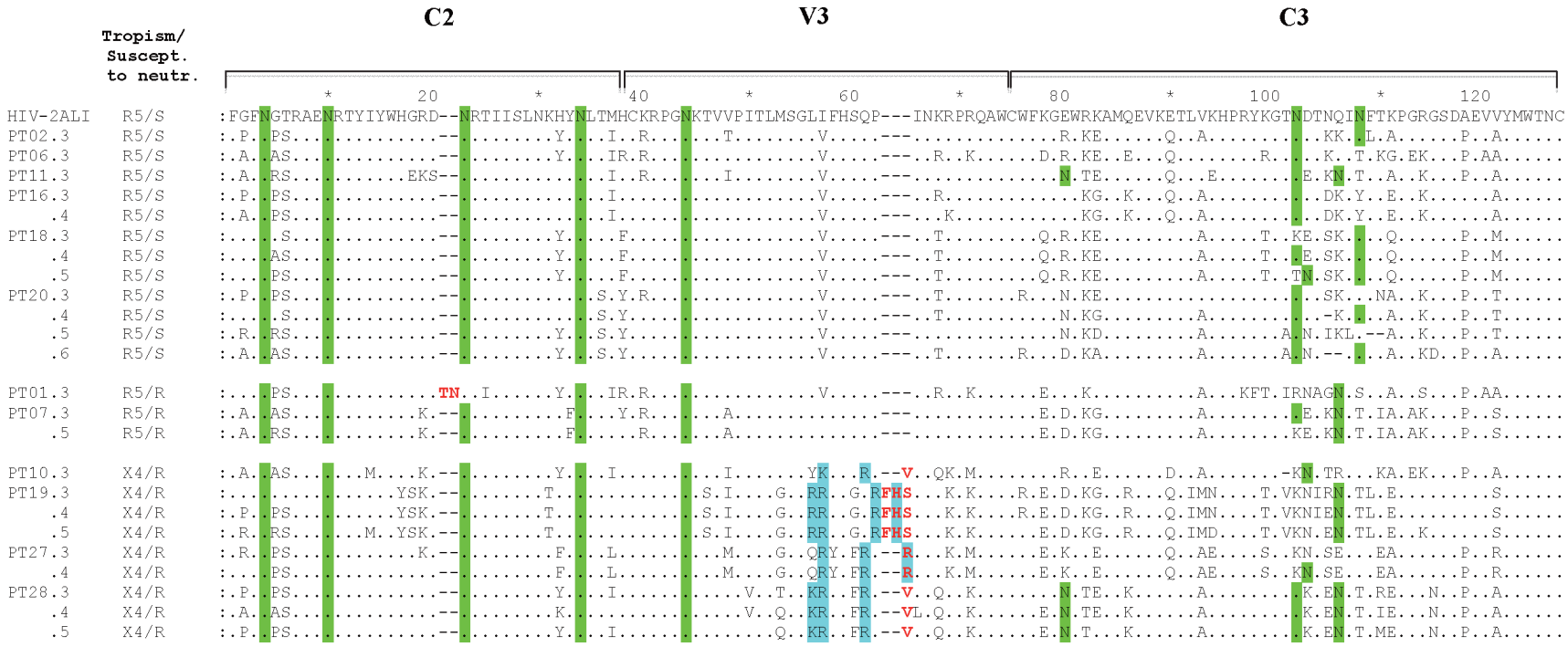
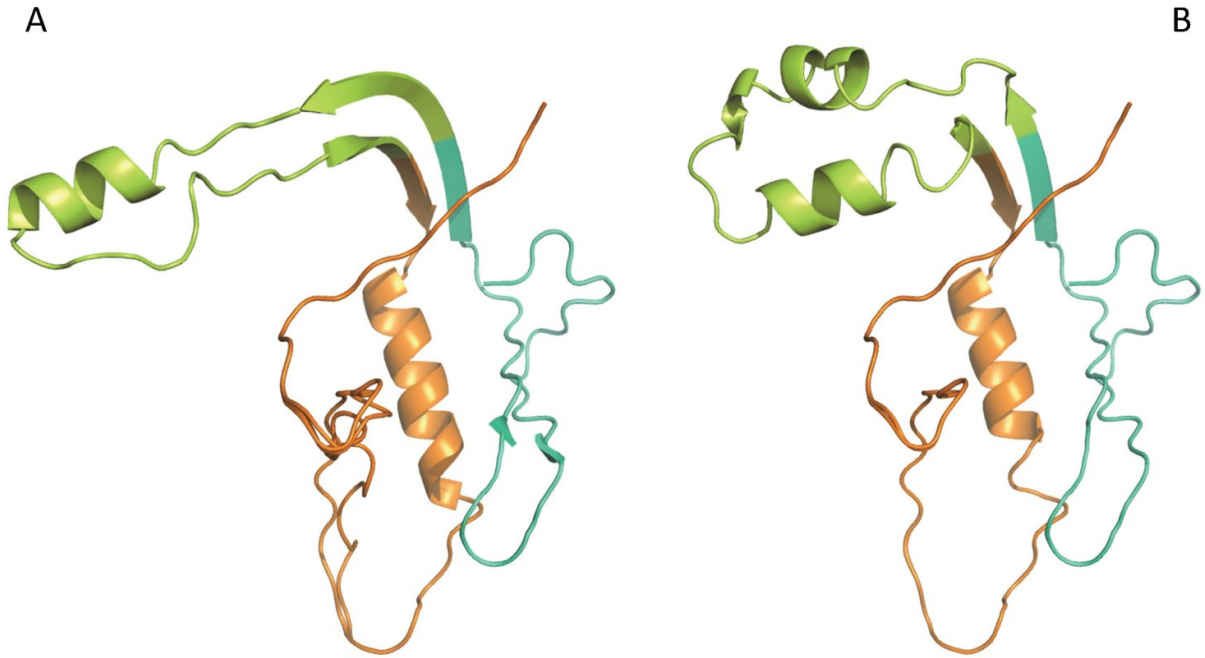


Supplemental Digital Content 1- Co-receptor usage and amino acid sequence of C2, V3 and C3 domains of sequential isolates from HIV-2 infected patients. Potential N-linked glycosilation sites are shaded in green. Charged amino acids that are present in the neutralization resistant isolates and absent from the neutralization sensitive isolates are shaded in blue. Insertions are indicated by bold red letters.

Supplemental Digital Content 2- Susceptibility to antibody neutralization, coreceptor usage and V3 loop charge and size of viruses analyzed in this study.

Viruses	Co-receptor usage	Neutralization	V3 loop	
			Size	Net charge
ALI	R5	Sensitive	34	7
PT18.03	R5	Sensitive	34	6
PT18.04	R5	Sensitive	34	6
PT18.05	R5	Sensitive	34	6
PT02.03	R5	Sensitive	34	6
PT20.03	R5	Sensitive	34	6
PT20.04	R5	Sensitive	34	6
PT20.05	R5	Sensitive	34	7
PT20.06	R5	Sensitive	34	6
PT16.03	R5	Sensitive	34	7
PT16.04	R5	Sensitive	34	7

PT11.03	R5	Sensitive	34	7
PT06.03	R5	Sensitive	34	7
PT07.03	R5	Resistant	34	7
PT07.05	R5	Resistant	34	7
PT01.03	R5	Resistant	34	7
PT10.03	X4	Resistant	35	8
PT27.03	X4	Resistant	35	9
PT27.04	X4	Resistant	35	9
PT28.03	X4	Resistant	35	9
PT28.04	X4	Resistant	35	9
PT28.05	X4	Resistant	35	9
PT19.03	X4	Resistant	37	11
PT19.04	X4	Resistant	37	11
PT19.05	X4	Resistant	37	11



Supplemental Digital Content 3- 3D-structures of C2V3C3 envelope region from X4 isolates. A) Isolates from patients 10, 27 and 28; B) Isolate from patient 19. Structures were generated by homology modelling using consensus C2V3C3 sequences as described in Material and Methods. V3 loop is represented in green, C2 in blue and C3 in orange.

Supplemental Digital Content 4- Percentage of the different elements of secondary structure present in the V3 loop of HIV-2 isolates.

Secondary structure[1]	**X4-R viruses**		**R5-S viruses**		**R5-R viruses**	
	Conformation A	Conformation B	Conformation A	Conformation B	Patient 1	Patient 7
α-helix	23%	35%	0%	15%	15%	15%
Extended β-strand	34%	11%	6%	53%	53%	53%
Irregular	29%	13%	47%	18%	18%	18%
Other	14%	41%	47%	14%	14%	14%

[1]As calculated by homology modeling in Swiss Model for each dataset. Data is arranged according to the major secondary structures: a-helix, beta-strand, irregular and other (includes residues in isolated beta bridges, 3/10 helix, hydrogen bonded turns and bends). X4-R viruses, CXCR4-using viruses that resist antibody neutralization; R5-R viruses, CCR5-using viruses that resist antibody neutralization; R5-S viruses, CCR5-using viruses that are susceptible to antibody neutralization.

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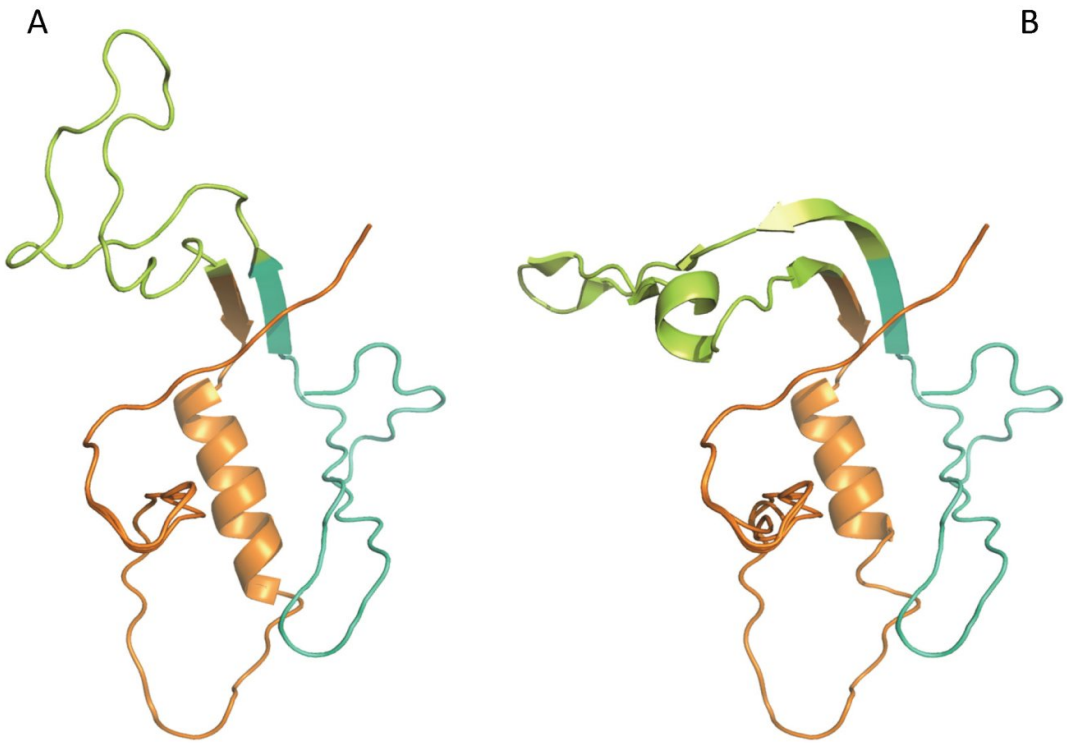
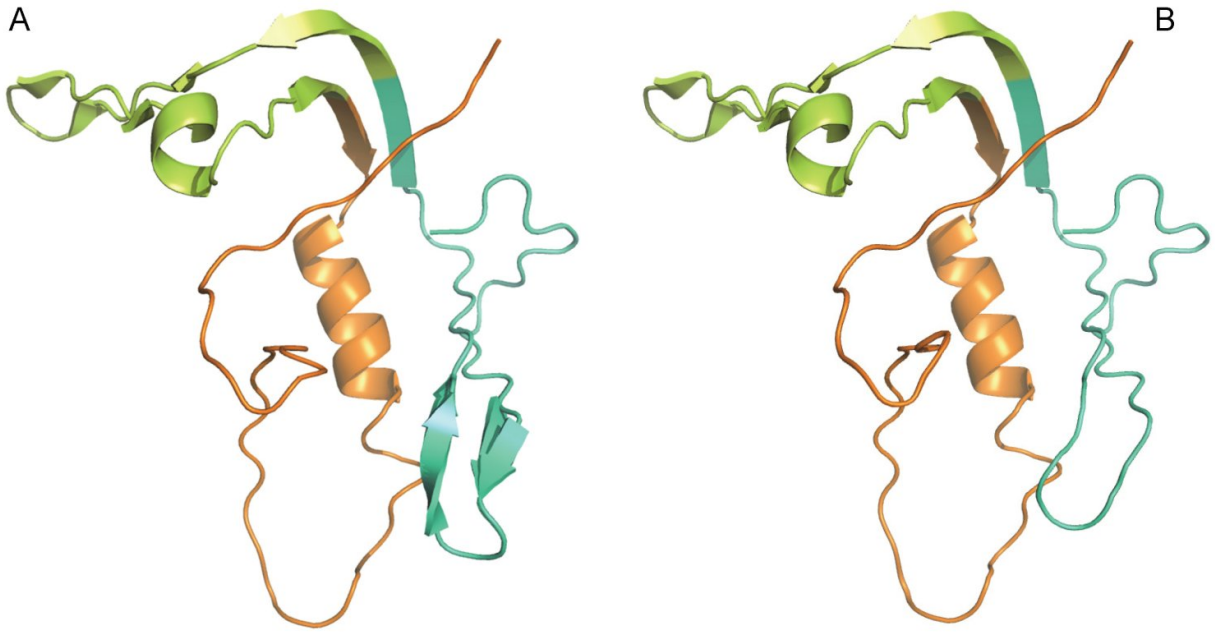


Supplemental Digital Content 5- 3D-structures of C2V3C3 envelope region from neutralization-sensitive R5 isolates. A) Isolates from patients 2, 18 and 20; B) Isolates from patients 6, 11 and 16. Structures were generated by homology modelling using consensus C2V3C3 sequences as described in Material and Methods. V3 loop is represented in green, C2 in blue and C3 in orange



Supplemental Digital Content 6 - 3D-structures of C2V3C3 envelope region from neutralization-resistant R5 isolates. A) Structure derived from 14 clonal C2V3C3 sequences obtained from patient 1 in 2003. B) Structure derived from 15 clonal C2V3C3 sequences obtained from patient 7 in 2003. Structures were generated by homology modelling as described in Material and Methods. V3 loop is represented in green, C2 in blue and C3 in orange.