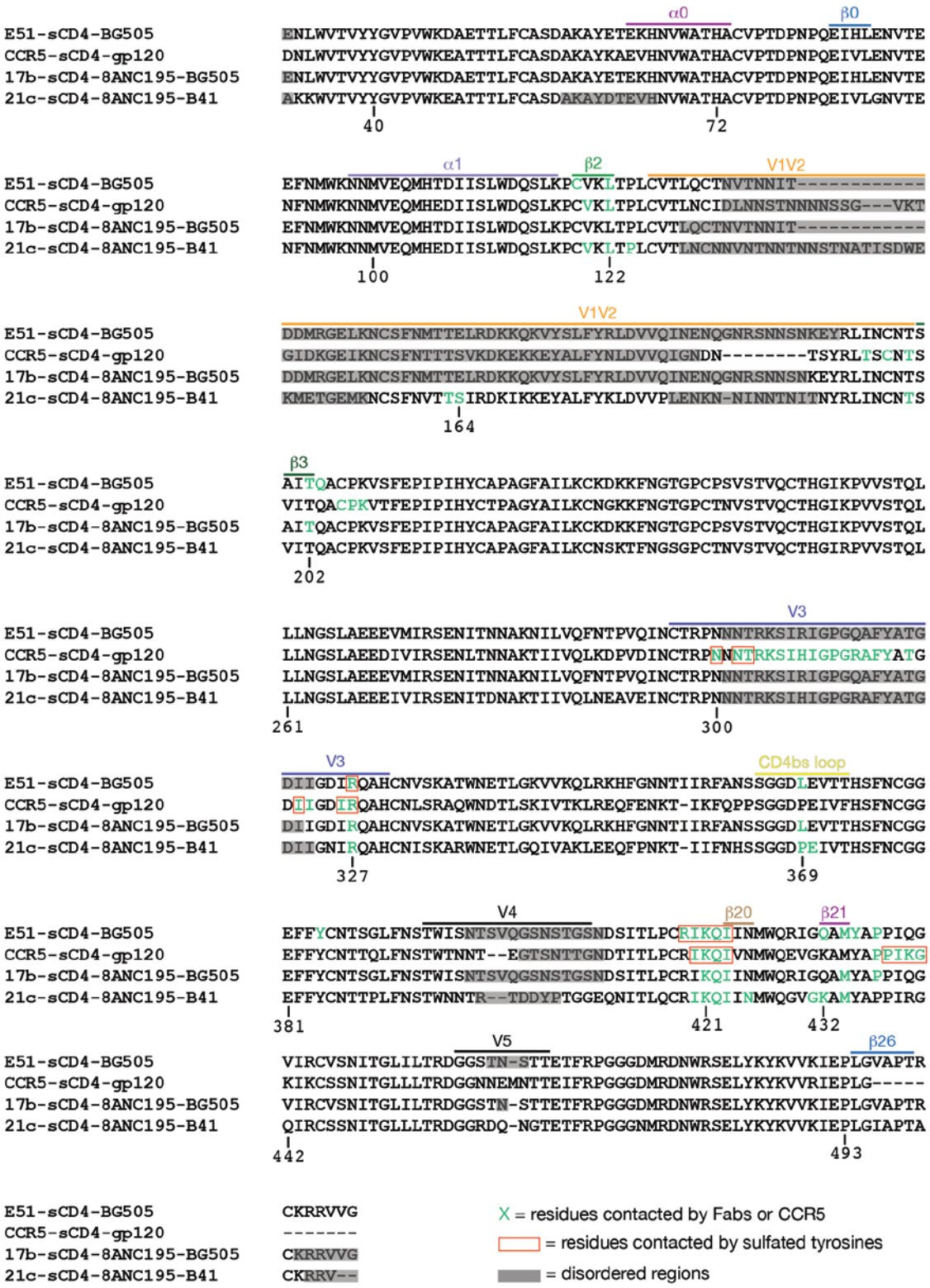
Supplementary Information

Supplementary Note 1. Sequence alignment of gp120s from structures of the indicated complexes demonstrates similarities and differences in interactions.



Supplementary Tables

Trimer state	Trimer type	Ligand(s)	Method	PDB	Resolution (Å)	Distance(s) between V3 (His330) (Å)	Distance(s) between V1V2 (Pro124) (Å)	Distance(s) between CD4bs (Asp368) (Å)
Closed	BG505 SOSIP.664	8ANC195	X-ray	5CJX	3.6	68	14	54
Closed	BG505 SOSIP.664	PGT122, 35O22	X-ray	4TVP	3.5	69	15	55
Closed	BG505 SOSIP.664	PGT122	X-ray	4NCO	4.7	70	14	56
Closed	BG505 SOSIP.664	3H+109L 35O22	X-ray	5CEZ	3	69	14	56
Closed	BG505 SOSIP.664	IOMA, 35O22	X-ray	5T3Z	3.5	69	14	54
Closed	JR-FL EnvΔCT	PGT151	cryo-EM	5FUU	4.2	69	16	56
Partially open	BG505 SOSIP.664	sCD4, 17b 8ANC195	cryo-EM	6CM3	3.5	76	67	79
Partially open	B41 SOSIP.664	sCD4, 21c 8ANC195	cryo-EM	6EDU	4.1	73	69	79
Open	B41 SOSIP.664	sCD4, 17b	cryo-EM	5VN8	3.6	73	79	84
Open (Class I)	BG505 SOSIP.664	sCD4, E51	cryo-EM	6U0L	3.3	75, 80, 70	67, 75, 70	79, 85, 78
Open (Class II)	BG505 SOSIP.664	sCD4, E51	cryo-EM	6U0N	3.5	81, 73, 70	76, 77, 70	85, 83, 79

Supplementary Table 1. Distance comparisons in Env trimer structures. Structures are grouped into four conformational states: closed (unliganded and bound to Fabs), partially open (bound to 8ANC195, sCD4, and either 17b or 21c), and open (bound to sCD4 and 17b), and the open class I and class II E51-sCD4-BG505 complexes (this study). The PDB identifier is given for each structure. PDB coordinates for gp120 subunits within a trimer were used to measure distances on adjacent protomers between V3 base residue $His330_{gp120}$, V1V2 base residue $Pro124_{gp120}$, and the CD4 binding site residue $Asp368_{gp120}$.

Supplementary Table 2. PDB entries for structures presented in Extended Data Figure 5 and their corresponding references.

PDB	Reference
6CM3	Wang, H., Barnes, C.O., Yang, Z., Nussenzweig, M.C. & Bjorkman, P.J. Partially Open HIV-1 Envelope Structures Exhibit Conformational Changes Relevant for Coreceptor Binding and Fusion. *Cell Host Microbe* **24**, 579-592 e4 (2018)
5VN3	Ozorowski, G. et al. Open and closed structures reveal allostery and pliability in the HIV-1 envelope spike. *Nature* **547**, 360-363 (2017)
4TVP	Pancera, M. et al. Structure and immune recognition of trimeric pre-fusion HIV-1 Env. *Nature* **514**, 455-61 (2014)
4ZMJ	Kwon, Y.D. et al. Crystal structure, conformational fixation and entry-related interactions of mature ligand-free HIV-1 Env. *Nat Struct Mol Biol* **22**, 522-31 (2015)
5FYJ	Stewart-Jones, G.B.E. et al. Trimeric HIV-1-Env Structures Define Glycan Shields from Clades A, B, and G. *Cell* **165**, 813-26 (2016)
5FYK	Stewart-Jones, G.B.E. et al. Trimeric HIV-1-Env Structures Define Glycan Shields from Clades A, B, and G. *Cell* **165**, 813-26 (2016)
5FYL	Stewart-Jones, G.B.E. et al. Trimeric HIV-1-Env Structures Define Glycan Shields from Clades A, B, and G. *Cell* **165**, 813-26 (2016)
5I8H	Kong, R. et al. Fusion peptide of HIV-1 as a site of vulnerability to neutralizing antibody. *Science* **352**, 828-33 (2016)
5JS9	Kong, L. et al. Uncleaved prefusion-optimized gp140 trimers derived from analysis of HIV-1 envelope metastability. *Nat Commun* **7**, 12040 (2016)
5JSA	Kong, L. et al. Uncleaved prefusion-optimized gp140 trimers derived from analysis of HIV-1 envelope metastability. *Nat Commun* **7**, 12040 (2016)
5ACO	Lee, J.H., de Val, N., Lyumkis, D. & Ward, A.B. Model Building and Refinement of a Natively Glycosylated HIV-1 Env Protein by High-Resolution Cryoelectron Microscopy. *Structure* **23**, 1943-51 (2015)
5C7K	Kong, L. et al. Complete epitopes for vaccine design derived from a crystal structure of the broadly neutralizing antibodies PGT128 and 8ANC195 in complex with an HIV-1 Env trimer. *Acta Crystallogr D Biol Crystallogr* **71**, 2099-108 (2015)
5T3Z	Gristick, H.B. et al. Natively glycosylated HIV-1 Env structure reveals new mode for antibody recognition of the CD4-binding site. *Nat Struct Mol Biol* **23**, 906-915 (2016)
5CEZ	Garces, F. et al. Affinity Maturation of a Potent Family of HIV Antibodies Is Primarily Focused on Accommodating or Avoiding Glycans. *Immunity* **43**, 1053-63 (2015)
5CJX	Scharf, L. et al. Broadly Neutralizing Antibody 8ANC195 Recognizes Closed and Open States of HIV-1 Env. *Cell* **162**, 1379-90 (2015)
5D9Q	Jardine, J.G. et al. Minimally Mutated HIV-1 Broadly Neutralizing Antibodies to Guide

	Reductionist Vaccine Design. *PLoS Pathog* **12**, e1005815 (2016)
5FUU	Lee, J.H., Ozorowski, G. & Ward, A.B. Cryo-EM structure of a native, fully glycosylated, cleaved HIV-1 envelope trimer. *Science* **351**, 1043-8 (2016)
6MDT	Kumar, S. et al. Capturing the inherent structural dynamics of the HIV-1 envelope glycoprotein fusion peptide. *Nat Commun* **10**, 763 (2019).
6NQD	Ananthaswamy, N. et al. A sequestered fusion peptide in the structure of an HIV-1 transmitted founder envelope trimer. *Nat Commun* **10**, 873 (2019)
6OKP	Schoofs, T. et al. Broad and Potent Neutralizing Antibodies Recognize the Silent Face of the HIV Envelope. *Immunity* **50**, 1513-1529 e9 (2019)
6ORO	Barnes, C.O. et al. Structural characterization of a highly-potent V3-glycan broadly neutralizing antibody bound to natively-glycosylated HIV-1 envelope. *Nat Commun* **9**, 1251 (2018)
6CH7	Escolano, A. et al. Immunization expands B cells specific to HIV-1 V3 glycan in mice and macaques. *Nature* 570, 468-473 (2019)

References

1. Zheng, S.Q. et al. MotionCor2: anisotropic correction of beam-induced motion for improved cryo-electron microscopy. *Nat Methods* **14**, 331-332 (2017).
2. Zhang, K. Gctf: Real-time CTF determination and correction. *J Struct Biol* **193**, 1-12 (2016).
3. Zivanov, J. et al. New tools for automated high-resolution cryo-EM structure determination in RELION-3. *Elife* **7** (2018).
4. Scheres, S.H. RELION: implementation of a Bayesian approach to cryo-EM structure determination. *J Struct Biol* **180**, 519-30 (2012).