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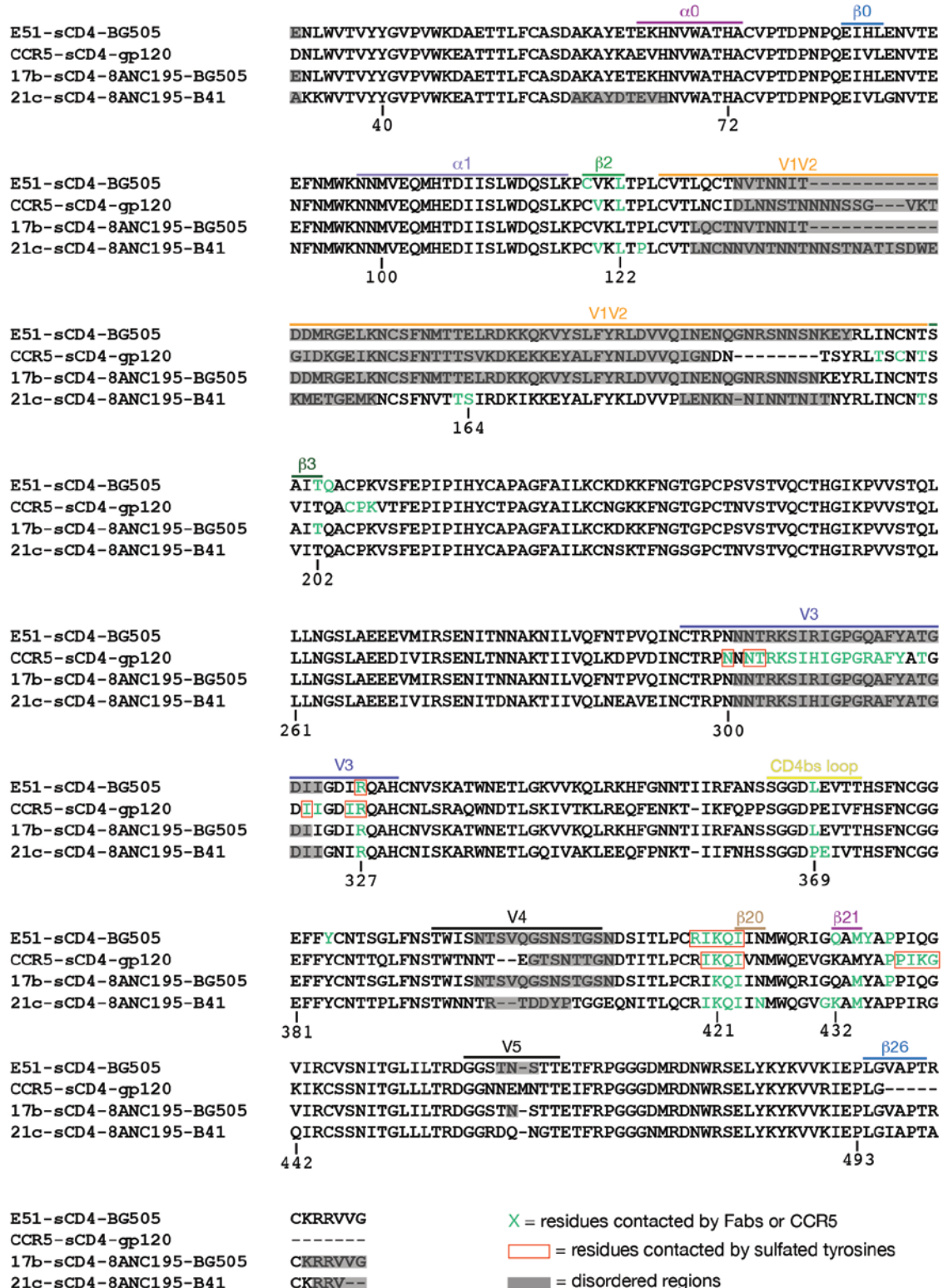
Asymmetric opening of HIV-1 Env bound to CD4 and a coreceptor-mimicking antibody

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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. <i>Cell Host Microbe</i> 24 , 579-592 e4 (2018) |
| 5VN3 | Ozorowski, G. et al. Open and closed structures reveal allostery and pliability in the HIV-1 envelope spike. <i>Nature</i> 547 , 360-363 (2017) |
| 4TVP | Pancera, M. et al. Structure and immune recognition of trimeric pre-fusion HIV-1 Env. <i>Nature</i> 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. <i>Nat Struct Mol Biol</i> 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. <i>Cell</i> 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. <i>Cell</i> 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. <i>Cell</i> 165 , 813-26 (2016) |
| 5I8H | Kong, R. et al. Fusion peptide of HIV-1 as a site of vulnerability to neutralizing antibody. <i>Science</i> 352 , 828-33 (2016) |
| 5JS9 | Kong, L. et al. Uncleaved prefusion-optimized gp140 trimers derived from analysis of HIV-1 envelope metastability. <i>Nat Commun</i> 7 , 12040 (2016) |
| 5JSA | Kong, L. et al. Uncleaved prefusion-optimized gp140 trimers derived from analysis of HIV-1 envelope metastability. <i>Nat Commun</i> 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. <i>Structure</i> 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. <i>Acta Crystallogr D Biol Crystallogr</i> 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. <i>Nat Struct Mol Biol</i> 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. <i>Immunity</i> 43 , 1053-63 (2015) |
| 5CJX | Scharf, L. et al. Broadly Neutralizing Antibody 8ANC195 Recognizes Closed and Open States of HIV-1 Env. <i>Cell</i> 162 , 1379-90 (2015) |
| 5D9Q | Jardine, J.G. et al. Minimally Mutated HIV-1 Broadly Neutralizing Antibodies to Guide |

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|------|--|
| | Reductionist Vaccine Design. <i>PLoS Pathog</i> 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. <i>Science</i> 351 , 1043-8 (2016) |
| 6MDT | Kumar, S. et al. Capturing the inherent structural dynamics of the HIV-1 envelope glycoprotein fusion peptide. <i>Nat Commun</i> 10 , 763 (2019). |
| 6NQD | Ananthaswamy, N. et al. A sequestered fusion peptide in the structure of an HIV-1 transmitted founder envelope trimer. <i>Nat Commun</i> 10 , 873 (2019) |
| 6OKP | Schoofs, T. et al. Broad and Potent Neutralizing Antibodies Recognize the Silent Face of the HIV Envelope. <i>Immunity</i> 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. <i>Nat Commun</i> 9 , 1251 (2018) |
| 6CH7 | Escolano, A. et al. Immunization expands B cells specific to HIV-1 V3 glycan in mice and macaques. <i>Nature</i> 570 , 468-473 (2019) |

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4. Scheres, S.H. RELION: implementation of a Bayesian approach to cryo-EM structure determination. *J Struct Biol* **180**, 519-30 (2012).