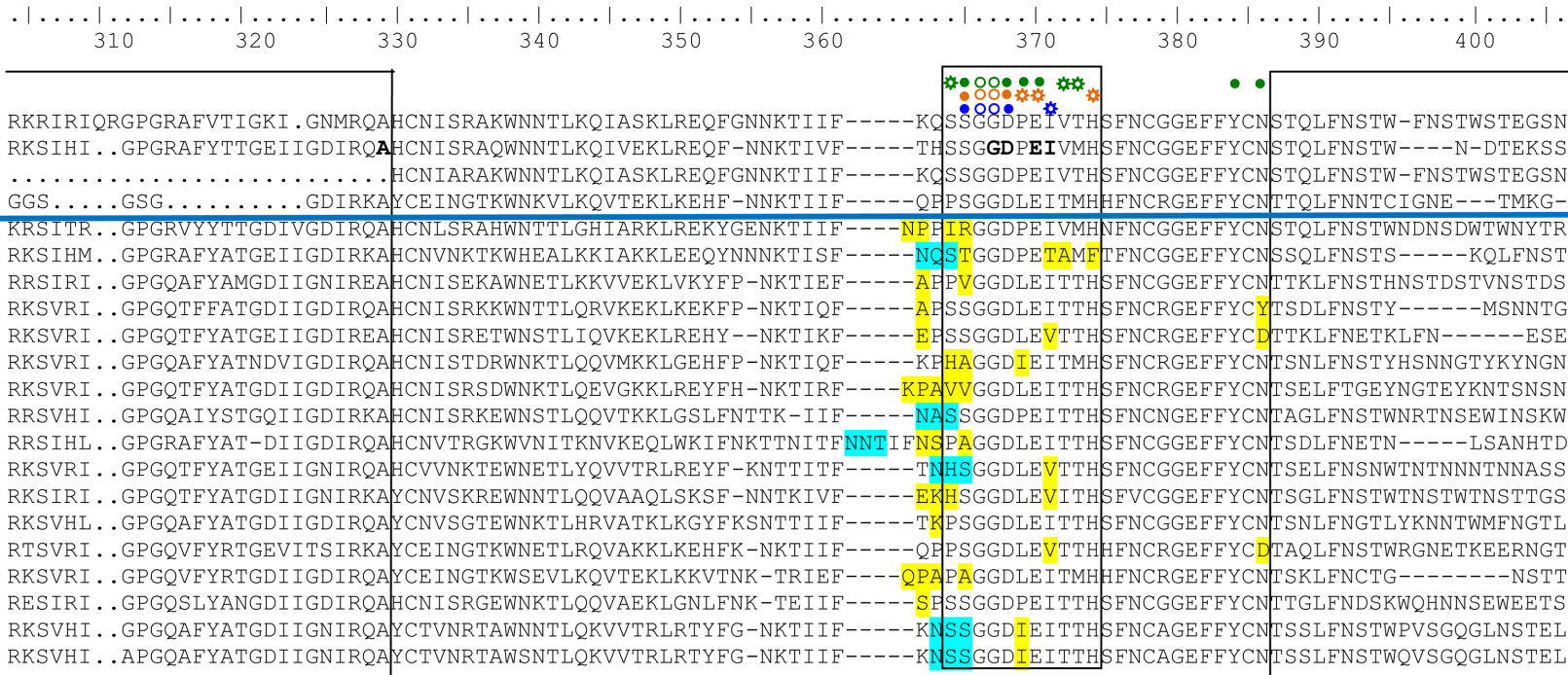
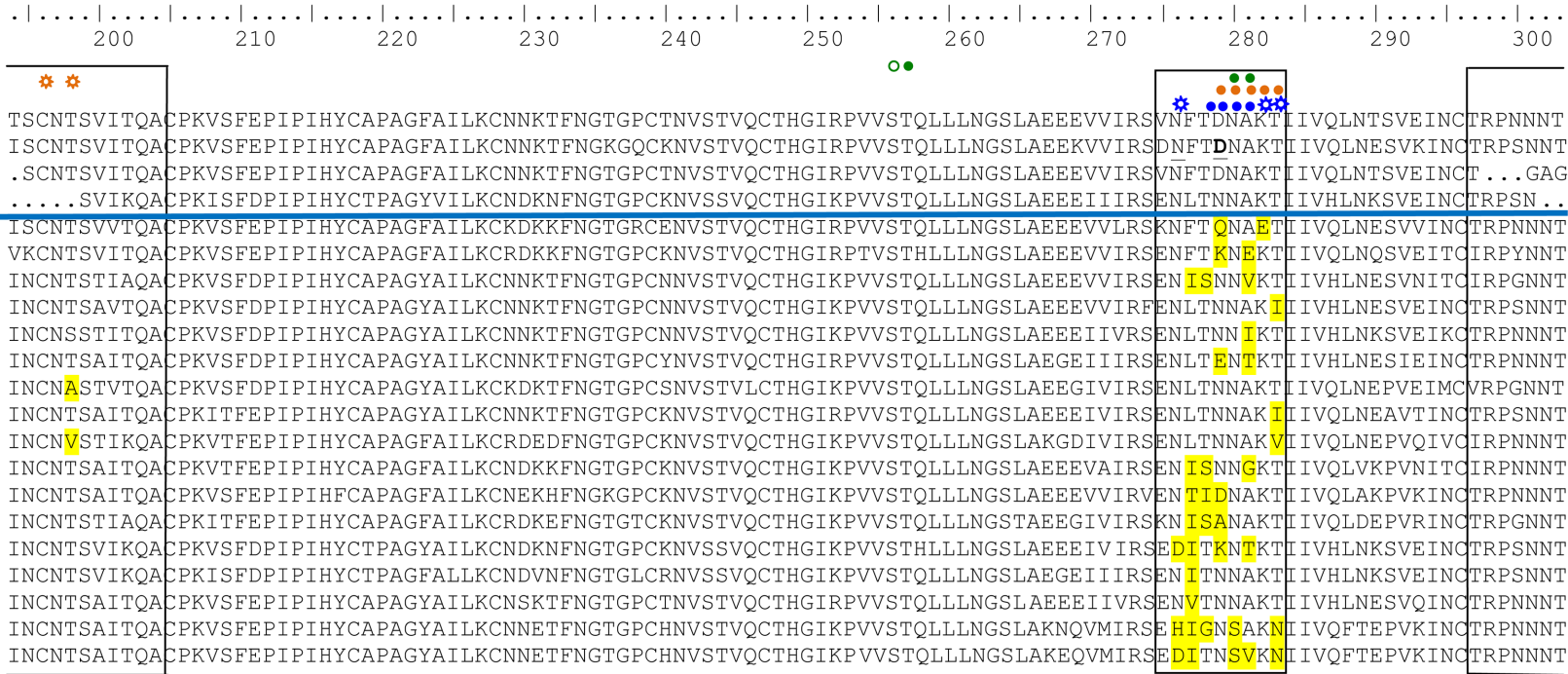


Fig. S1. Amino acid sequence alignment of 16 VRC1-resistant viruses. The VRC01-sensitive HXBc2 and JRCSF gp120 virus envelope sequences are shown as references. In addition, the HXBc2 and 93TH057 core protein sequences are shown, as these proteins were used to solve the liganded crystal structures of b12 and VRC01, respectively. The gp120 contacts with VRC01, CD4, or b12 are indicated in blue, gold, or green, respectively. Open circles (○) denote gp120 main-chain-only contacts, open circles with rays (☼) denote gp120-side-chain-only contacts, and filled circles (●) denote both main-chain and side-chain contacts. Residues that vary from the reference sequence are highlighted in yellow. Residues that showed a significant change in VRC01 binding when mutated are shown in bold; the residue is underlined if the mutant virus displayed neutralization resistance to VRC01. Variations within the CD4 binding loop and its proximal region that contains the NXS/T motif resulting in additional N-glycosylation sites are highlighted in blue.



V2

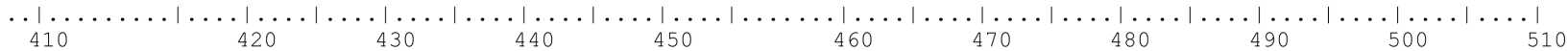
Loop D

V3

V3

CD4 Binding Loop

V4



HXB2R-K03455	TEG-----SDTITLPCRIKQIINMWQKVGKAMYAPPISGQIRCSSNITGLLLTRDGG---NSNNESEIEIFRPGGGDMRDNWRSELYKYKVKVIEPLGVAPTAKARRVQREKR
JR_CSF	TEG-----NDTIILPCRIKQIINMWQEVGKAMYAPPKQIRCSSNITGLLLTRDGG---KNESEIEIFRPGGGDMRDNWRSELYKYKVKVIEPLGVAPTAKARRVQREKR
HXBc2 Core	TEG-----SDTITLPCRIKQIINMWQKVGKAMYAPPISGQIRCSSNITGLLLTRDGG---NSNNESEIEIFRPGGGDMRDNWRSELYKYKVKVIE.....
93TH057 Core	-----CNGTITLPCRIKQIINMWQGTQAMYAPPIDGKINCVSNITGILLTRDGG---ANNTSNETFRRPGGGNIKDNWRSELYKYKVVQIE.....
AY124970_BL01	TYNP----NDTITLPCRIKQIINLWQKVGKAMYAPPVIRGQIRCSSNITGLLLTRDGGK---NGTEGTEIEIFRPGGNMRDNWRSELYKYKVKVIEPLGVAPTAKARRVQREKR
EF210732_H086_8	NNT-----NANIELPCRIQIVNMWQRIGKAMYAPPISGQINCTSNTGLLLTRDGG---KNNKSTEVFRPIGGEMRDNWRSELYKYKVVQIEPLGVAPTAKARRVQREKR
CAP210_2_00_E8	AETG---NSTNTNITLPCRIQIINMWQEVGRAMYAPPISGQINCTSNTGLLLTRDGGENKTE NNDEIFRPGGGDMKDNWRSELYKYKVVIEKPLGVAPTAKARRVQREKR
Du172_17	-----ANITLQCRIKQIINMWQGVQAMYAPPVIRGQIRCSSNITGLLLTRDGG---KEKNDTETFRRPGGGDMRDNWRSELYKYKVVIEKPLGIAPDKARRVQREKR
Du422_1	VDN-----KTIIILPCRIKQIINMWQEVGRAMYAPPVIRGQIRCSSNITGLLLTRDGG---ENSTEGVFRPGGGDMKDNWRSELYKYKVVIEKPLGVAPTAKARRVQREKR
TV1_29	S-----LPITLQCRIKQIVRMWQGVQAMYAPPVIRGQIRCSSNITGLLLTRDGG---FNNTTNETFRPGGGDMRDNWRSELYKYKVVIEKPLGIAPTAKARRVQREKR
TZA125_17	-----NITLPCRIKQIVNMWQEVGRAMYAPPVIRGQIRCSSNITGLLLTRDGG---NNTNGTETFRRPGGGDMRDNWRSELYKYKVVIEKPLGIAPTAKARRVQREKR
57128_02	NKTE----DVNITLQCRIKQIINMWQGVGKAMYAPPVIRGQIRCSSNITGLLLTRDGGGA---DNNRQNETFRPGGGDMRDNWRSELYKYKVVIEKPLGIAPTAKARRVQREKR
EU885764_x2088_9	N-----ENITLQCRIKQIVRMWQEVGQAMYAPPVIRGQIRCSSNITGLLLTRDGGVN---DTHDKENETFRTGGDMRDNWRSELYKYKVKVIEKPLGVAPTARRRRVQREKR
242_14	ANG-----NITLTCKIKQIINMWQVVGQAMYAPPVIRGQIRCSSNITGLLLTRDGGFRNDTNETYEAFRPGGGDMRDNWRSELYKYKVKVIEPLGVAPTHAKARRVQREKR
T250_4	GTES----NDTITLQCEIKQFINMWQVGRAMYAPPVIRGQIRCSSNITGLLLTRDGGP---NSTQNETFRPGGGDMRDNWRSELYKYKVVQIEPLGVAPTAKARRVQREKR
T278_50	NNTNESSTSGTITIKCRIKQIINMWQIVGQAMYAPPVIRGQIRCSSNITGLLLTRDGGEG---DEKANETFRTGGDMRDNWRSELYKYKVKVIEPLGVAPTAKARRVQREKR
620345_C1	N-----DIIILPCRIKQIVRMWQGVQSMYAPPVIRGQIRCSSNITGLLLTRDGGD---GPTADNETFRPAGGDMRDNWRSELYKYKVVQIEPLGIAPTAKARRVQREKR
CNE28	CNG-----TIILPCRIKQIINMWQEVGQAMYAPPISGQIRCSSNITGILLTRDGGAN---SSQSNEIFRPGGGDMKDNWRSELYKYKVVQIEPLGVAPTAKARRVQREKR
3817_V2_C59	RMNS---PEANITLQCRIKQIVNMWQVGRAMYAPPVIRGQIRCSSNITGLLLTRDGG---LNTSNNETFRPGGGDMRDNWRSELYKYKVVQIEPLGLAPTAKARRVQREKR
6540_V4_C1	-----DTITLQCRIKQIINMWQRAAQAIYAPPVIRGQIRCSSNITGLLITSDYG---NNNSDNEIFRRTGGDMRDNWRSELYKYKVKVIEPIGVAPTAKARRVQREKR
6545_V4_C1	-----DTITLQCRIKQIINMWQRAAQAIYAPPVIRGQIRCSSNITGLLITSDYG---NRSSDNETFRRTGGDMRDNWRSELYKYKVKVIEPIGVAPTAKARRVQREKR

V4

β20 / β21

V5 / β24

β24 / α5
Connection