

Table S1: Trivalent VLP immunization elicits α -EEV mAbs of diverse genetic lineages in NHP, related to Figures 1-3.

IgG heavy and light chain variable region genes of single-specific and triple-specific α -EEV mAbs were amplified, sequenced, codon optimized, synthesized, and cloned into mammalian expression vectors. Included in the table: V-gene and allele, percent V-gene identity, CDR3 length, and CDR3 sequence for both heavy chain and kappa/lambda light chain. If two V genes are shown, it means that the assignment was ambiguous.

Specificity	mAb	IGHV				IGKV/IGLV				Lineage ID
		V-Gene and allele	% SHM	CDRH3	CDR3-IMGT length	V-Gene and allele	% SHM	CDR3-IMGT length	CDRL3	
E	SKE01	IGHV4-NL_42*01_S8550	4.4	CARHAAYCSRGVCYAGLDDAFGFW	22	IGLV3-40*01	5.5	11	CQVWSSSQHSVF	10710.E1
E	SKE02	IGHV4-117*01_S6852	7.1	CATKEGIEYCSGRGCSFNSLDVW	21	IGLV3-40*01	8	11	CQVWSSSYWVWF	10710.E2
E	SKE03	IGHV4-NL_10*01_S4164	7.5	CARGAGTWNTEYFELW	14	IGLV3-40*01	5.9	11	CQVWSSSDHRVF	10710.E3
E	SKE04	IGHV4-NL_5*01_S6960	7	CARGGYTGNYPFDVW	12	IGLV3-40*01	4.5	11	CQVWSSSDHPLF	10710.E4
E	SKE05	IGHV4-NL_5*01_S6960	2.6	CARGGLRGNYPFDVW	12	IGLV3-40*01	2.1	11	CQVWSSSDHPLF	10710.E5
E	SKE06	IGHV4-NL_27*01_S1515	5.7	CARDSTVRGGLDVW	12	IGLV3-40*01	5.2	11	CQVWSDSTSHYIF	10710.E6
E	SKE07	IGHV4-NL_10*01_S4164	1.4	FARGAGTWNTEYFELW	14	IGKV2-72*02	7.6	9	CMQAIQLPLTF	10710.E7
E	SKE08	IGHV4-NL_5*01_S6960	6.6	CAGDRVTASNSLDI	13	IGKV2-72*02	7	9	CMQAIQLPLTF	10710.E8
E	SKE09	IGHV4-NL_5*01_S6960	5.3	CAGDRVTASNSLDI	13	IGKV2-72*02	7.3	9	CMQAIQLPLTF	10710.E8
E	SKE10	IGHV4-NL_5*01_S6960	2.6	CAGDSVTHINSLDVW	13	IGKV2-72*02	4.6	9	CMQGIQLPLTF	10710.E9
E	SKE11	IGHV4-NL_5*01_S6960	7.9	CAGDAVTQYNLSLVW	13	IGKV2-72*02	7.3	9	CMQARQLPLTF	10710.E10
E	SKE12	IGHV4-NL_28*01_S1005	6.1	CARRWSEYCNSTYCTGAFDLW	19	IGKV3-10*02	7.3	8	CFQYHSGWTF	10710.T10
E	SKE13	IGHV4-NL_5*01_S6960, IGHV4-117*01_S7493	12	CARQDYDSEYQGTPELW	16	IGKV3-10*02	7.7	8	CHQYYSGYSF	10710.E11
E	SKE14	IGHV4-NL_5*01_S6960	7.3	CARQDYYSQDYQGAFDLW	16	IGKV3-10*02	4.5	8	CHQYYSGYSF	10710.E11
E	SKE15	IGHV4-NL_5*01_S6960, IGHV4-117*01_S7493	9.9	CARQDYLGVVDYQGAFELW	16	IGKV3-10*02	9.4	8	CHQYYSGHSF	10710.E11
E	SKE16	IGHV4-NL_16*01_S2138	13	CASDRPFDWFASTWFDVW	17	IGLV1-60*01	3	11	CAAWDDSLSGYIF	10710.E12
E	SKE17	IGHV4-NL_13*01_S9273	7.7	CATTEMILSNYYGLDSW	15	IGKV1-43*02	8.7	9	CLQYDIAPWSF	10710.E13
E	SKE18	IGHV4-NL_13*01_S9273	2.7	CATTGVIIITNYGLDSW	15	IGKV1-43*02	8.4	9	CLQYDIAPWSF	10710.E13
E	SKE19	IGHV4-117*01_S7493	8.3	CARGIPDYSGSYYYALDFW	17	IGLV1-72*02+G267T	4.4	11	CSAWDDSLSGPLF	10710.E14
E	SKE20	IGHV4-NL_27*01_S5720	4.7	CASPFPGSGYYVNNFYW	16	IGLV1-64*01	3.7	11	CLSYDVLSAHLF	10710.E15
E	SKE21	IGHV4-NL_27*01_S5720	6.7	CASDWHKWNQNGGYPEFW	16	IGLV3-44*01+70531	3.5	11	CQVWDTSDHVVF	10710.E16
E	SKE22	IGHV4-79*01	4.7	CARDEHYNFWRGFWYW	14	IGLV2-32*02+T122C.C130A	5.4	10	CSYTSDDTGLF	10710.E17
E	SKE23	IGHV4-NL_27*01_S1515	5.4	CVTVGTLPEYALDSW	13	IGLV2S8*01	5.1	10	CFSYTTSRWVWF	10710.E18
E	SKE24	IGHV4-NL_13*01_S9273	6.4	CASRGGNYGLDSW	11	IGKV1-16*01	4.9	9	CQQYKDAPWTF	10710.E19
E	SKE25	IGHV5-157*01_S8626	11	CARSVWSGYYIGWFDVW	15	IGKV2-72*02	7	9	CMQVLIQVPLTF	10710.E20
E	SKE26	IGHV5-157*01_S8626	6.1	CARSVWSGYYIGWFDVW	15	IGKV2-72*02	7	9	CMQVLIQVPLTF	10710.E20
E	SKE27	IGHV5-157*01_S8626	9.1	CARSVWSGYYIGWFDVW	15	IGKV2-72*02	6.3	9	CMQVLIQVPLTF	10710.E20
E	SKE28	IGHV5-157*01_S8626	8.4	CAMGGYPTYPFDVW	11	IGKV1-28*03	5.6	9	CLQYHTYPPFTF	10710.E21
E	SKE29	IGHV5-157*01_S8626	7.8	CAMGGYPTYPFDVW	11	IGLV5-83*02	2.2	9	CMQWHNNVWVF	10710.E22
E	SKE30	IGHV3-NL_18*01_S7220	3.6	CATAQGPSTVTPDYW	13	IGKV1-43*02	9.1	9	CLQYDSAPWTF	10710.E23
E	SKE31	IGHV3-NL_18*01_S7220	4.3	CATTKGPSTVTPYYW	13	IGKV1-43*02	8.7	9	CLQYDIAPWSF	10710.E23
E	SKE32	IGHV3-73*02_S0606	3	CTRDDYGYSDVW	11	IGKV1-74*01	4.9	9	CQHNSGFPYSF	10710.E24
E	SKE33	IGHV3-36*01_S6650	3	CARLFRGYCSSTFCFKWFDVW	19	IGKV1-32*03+48222	6	9	CQQGHSIPYSF	10710.E25
V	SKV01	IGHV4-NL_30*01_S1240	3.4	CARHAYCTSSGGYPPHNWFDVW	20	IGKV1-66*01	7	9	CQQYDNSPFTF	10710.V1
V	SKV02	IGHV4-NL_5*01_S8913	2	CARDQEPWSGYYTVIHDAFDVW	20	IGKV1-22*01+ A152G.C176A.C237T.T265A	4.5	9	CQQYNSLPFTF	10710.V2
V	SKV03	IGHV4-79*01	7.1	CAKGSCHSRGVCDFVFNWFDVW	19	IGLV7-80*01+C245T.G271T	8.2	9	CLLYYRGVWVF	10710.V3
V	SKV04	IGHV4-NL_27*01_S5720	2	CANSISILGVVITGAFYYW	17	IGKV1-38*01	4.2	9	CQQRHSYPWTF	10710.V4
V	SKV05	IGHV4-NL_27*01_S5720	9.7	CASSNSILGVVIAGAFHFW	17	IGKV1-38*01	11	9	CQQRHAYPWTF	10710.V4
V	SKV06	IGHV4-117*01_S6852	5.4	CAREAHCSDSGCPFPFDVW	17	IGKV1-22*01+87145	3.9	9	CLQDSSPTPLTF	10710.V5
V	SKV07	IGHV4-NL_12*01_S6471	4.7	CAREGGHSSSLDNYGLDWT	17	IGKV1-32*03+48222	5.3	9	CQQGHSFPYSF	10710.V6
V	SKV08	IGHV4-117*01_S6852	4.7	CAREGGYSGSYRPEFW	15	IGKV1-32*03+48222	8.8	9	CQQHYRTPYSF	10710.V7
V	SKV09	IGHV4-NL_42*01_S8550	7.1	CASGSGDWFGYFYRW	13	IGKV1-22*01+ A152G.C176A.C237T.T265A	5.6	9	CQQYISRPWTF	10710.V8
V	SKV10	IGHV4-149*01_S4098	9.1	CAIDGANRYAFDLW	12	IGLV2-23*02	6.4	10	CCSYAGSNPWIF	10710.V9
V	SKV11	IGHV4-NL_5*01_S6960	8.4	CVREAYGTIFYFVW	11	IGKV1-25*02	14	9	CLQHSRHPFSF	10710.V10
V	SKV12	IGHV4-NL_5*01_S6960	7.3	CVREAYGTIFYFVW	11	IGKV1-25*02	12	9	CQHSRHPFSF	10710.V10
V	SKV13	IGHV4-NL_16*01_S2138	1.7	CAREEYWGDPYYW	11	IGKV3S9*01+IGKV3-42*02	5.9	9	CQQYNNWLWTF	10710.V11
V	SKV14	IGHV3-NL_9*01_S6098	6.4	CAKGYPSYLYFW	10	IGLV7-80*01+C245T.G271T	4.4	9	CLLYYSGVHIF	10710.V12
V	SKV15	IGHV3-NL_9*01_S6098	7.1	CAQGFPPYVLFWSW	10	IGLV7-80*01+C245T.G271T	4.8	9	CLLYYGGTQLF	10710.V13
V	SKV16	IGHV3-122*01_S8388	6.1	CARDSPYWGDIYSHSLDVW	16	IGLV3-40*01	4.6	10	CQVWSSSDVLF	10710.V14
V	SKV17	IGHV3-36*01_S6650	13	CVRRDYDGLSLDVW	11	IGLV1-64*01	3.4	11	CLSYDSSLSTHLF	10710.V15
V	SKV18	IGHV3-NL_5*01_S4429	6.3	CTTSVWV	5	IGKV1-66*01	8.7	9	CQQHNSPYNF	10710.V16
V	SKV19	IGHV3-122*01_S8388, IGHV3-94*01	10	CARDPVMTTVATQLLDVW	16	IGLV1-60*01	1.7	11	CAAWDDSLSGYIF	10710.V17
V	SKV20	IGHV2-69*01_S0230	6.3	CAFLVVLTKWFDVW	12	IGLV1-65*01+44178	7.2	11	CGTWDNSLTSVLF	10710.V18

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Table S1 (continued)

Specificity	mAb	IGHV				IGKV/IGLV				
		V-Gene and allele	% SHM	CDRH3	CDR3- IMGT length	V-Gene and allele	% SHM	CDR3- IMGT length	CDRL3	Lineage ID
W	SKW01	IGHV4-NL_42*01_S8550, IGHV4-117*01_S6852, IGHV4-NL_1*02_S9550	7.4	CARQGLAGTTRDWFVDV	15	IGKV1-38*01	5.9	9	CQHRNDYPFTF	10710.W1
W	SKW02	IGHV4-NL_1*02_S9550, IGHV4-NL_42*01_S8550	6.4	CARQGLAGTTRDWFVDV	15	IGKV1-38*01	4.9	9	CQHRNSYPFTF	10710.W1
W	SKW03	IGHV4-NL_42*01_S8550, IGHV4-NL_1*02_S9550	4.7	CARQGLAGTTRDWFVDV	15	IGKV1-38*01	3.5	9	CQHRNSYPFTF	10710.W1
W	SKW04	IGHV4-NL_1*02_S9550	6.4	CARQGLAGTTRDWFVDV	15	IGKV1-38*01	6.3	9	CQQRNDYPFTF	10710.W1
W	SKW05	IGHV4-NL_42*01_S8550, IGHV4-NL_1*02_S9550	7.4	CARQGLAGTTRDYPVDV	15	IGKV1-38*01	3.5	9	CQQRNSYPFTF	10710.W1
W	SKW06	IGHV4-117*01_S6852, IGHV4-NL_42*01_S8550	10	CARQGLEGTTRDWFVDV	15	IGKV1-38*01	9.4	9	CQQRNDYPFTF	10710.W1
W	SKW07	IGHV4-NL_42*01_S8550, IGHV4-NL_1*02_S9550	7.4	CARQGLEGTTRDWFVDV	15	IGKV1-38*01	6.6	9	CQQRNDYPFTF	10710.W1
W	SKW08	IGHV4-NL_42*01_S8550	7.4	CARQGLPGTTRDWFVDV	15	IGKV1-38*01	7.3	9	CQQRNDYPFTF	10710.W1
W	SKW09	IGHV4-117*01_S6852	7.4	CASRSSVADNWFVDV	13	IGKV1-22*01+ A152G.C176A.C237T.T265A	9.1	9	CQQYDSRPWTF	10710.W2
W	SKW10	IGHV4-117*01_S6852	7.4	CASRSSVADNWFVDV	13	IGKV1-22*01+ A152G.C176A.C237T.T265A	8	9	CQQYDSRPWTF	10710.W2
W	SKW11	IGHV4-117*01_S6852	9.1	CASRTTVADNWFVDV	13	IGKV1-22*01+ A152G.C176A.C237T.T265A	8	9	CQQHDSRPWTF	10710.W2
W	SKW12	IGHV4-117*01_S6852	5.4	CASRTTVADNWFVDV	13	IGKV1-22*01+ A152G.C176A.C237T.T265A	6.3	9	CQQYDSRPWTF	10710.W2
W	SKW13	IGHV4-117*01_S6852	5.4	CASRTTVADNWFVDV	13	IGKV1-22*01+ A152G.C176A.C237T.T265A	6.3	9	CQQFNSRPWTF	10710.W2
W	SKW14	IGHV4-NL_27*01_S5720	6.4	CALAKYSGSPGDY	12	IGLV2-32*02+ T122C.C130A	6.1	12	CSSYSGIDTDYIF	10710.W3
W	SKW15	IGHV4-NL_27*01_S5720	7.4	CALAKYSGSPGDY	12	IGLV2-32*02+ T122C.C130A	8.1	12	CSSYSGSETDYIF	10710.W3
W	SKW16	IGHV4-NL_13*01_S9273	9	CASDENKPYW	8	IGKV4S1*01	4.3	9	CQQYSSPRTF	10710.W4
W	SKW17	IGHV4-NL_13*01_S9273	8.7	CVGDENKIHV	8	IGKV4S1*01	3.9	9	CQQYSSPRTF	10710.W4
W	SKW18	IGHV4-NL_13*01_S9273	2.3	CATDRNTLAW	8	IGKV4S1*01	3.9	8	CQQYNSRRTF	10710.W5
W	SKW19	IGHV3-76*02_S4190	2.7	CAKVGRSGYCTASGCNALLFDWFDV	24	IGKV2-64*01+ G96A.A162C.G177T	4.6	9	CGQGAHLPPAF	10710.W6
W	SKW20	IGHV3-76*02_S4190	5.8	CAKVGRSGYCTGSGCHALLFDWIDV	24	IGKV2-64*01+ G96A.A162C.G177T	5	9	CGQGAHLPPAF	10710.W6
W	SKW21	IGHV3-76*02_S4190	5.1	CAKVGRSGYCTGTGCVAVLFDWLDV	24	IGKV2-64*01+ G96A.A162C.G177T	3.3	9	CGQGAHLPPAF	10710.W6
W	SKW22	IGHV3-122*01_S8388	5.1	CAREGGYGFY	10	IGLV1-66*01	6.4	11	CETWNSLNAYIF	10710.W7
W	SKW23	IGHV3-122*01_S8388	0.3	CAREVGYGLDSV	10	IGLV1-66*01	4.6	11	CETWNSLNGYIF	10710.W7
W	SKW24	IGHV3-36*01_S6650+16915	1.7	CARVVTESRPPAAWFDV	16	IGLV3-44*01+70531	4.5	12	CQLWDISSDHNLYIF	10710.W8
W	SKW25	IGHV3-76*02_S4190	4.4	CMKDRSSGWYDWLPGERYLEWF	21	IGLV2-32*02+T122C.C130A	3	11	CSSYAGSDTFYIF	10710.W9
W	SKW26	IGHV3-73*02_S0606	1.4	CTREPSWGYSGHRSLDVW	16	IGLV2-32*02+T101C	3.7	9	CSSFAGSNVLF	10710.W10
W	SKW27	IGHV3-73*02_S0606	8.8	CTREPSWGYSRHKSLDVW	16	IGLV2-32*02+T101C	7.7	9	CSSYAGSNVLF	10710.W10
W	SKW28	IGHV3-73*02_S0606	8.4	CVREPSWGHRRHSLDVW	16	IGLV2-32*02+T101C	6.4	9	CSSFVGTNVFF	10710.W10
W	SKW29	IGHV3-76*02_S4190	7.1	CAKEKYSYSSAYGRGYPNSLDVW	21	IGKV2-104*01	5.6	9	CMQPLEYPRTF	10710.W11
W	SKW30	IGHV3-76*02_S4190	8.1	CAKEKYSYSSAYGRGYPNSLDVW	21	IGKV2-104*01	5.3	9	CMQPLEYPRTF	10710.W11
WEV	SKT01	IGHV3-NL_17*01_S0120	4	CTTDDRRTYCSRGVYAAAFYHW	19	IGKV1-43*02	7	9	CLQYNSAPFTF	10710.T1
WEV	SKT02	IGHV3-NL_17*01_S0120	4.3	CTTDDRRTYCSRGVYAAAFYHW	19	IGKV1-43*02	7.3	9	CLQYNSAPFTF	10710.T1
WEV	SKT03	IGHV3-NL_17*01_S0120	2.3	CTTDDRRTYCSRGVYAAAFYHW	19	IGKV1-43*02	7.7	9	CLQYNSAPFTF	10710.T1
WEV	SKT04	IGHV3-NL_17*01_S0120	2.3	CTTDDRRTYCSRGVYAAAFYHW	19	IGKV1-43*02	9.8	9	CLQYNSAPFTF	10710.T1
WEV	SKT05	IGHV3-NL_17*01_S0120	4.6	CTRDDRRTYCSRGVYAAAFYHW	19	IGKV1-43*02	11	9	CLQYNSAPFTF	10710.T1
WEV	SKT06	IGHV3-122*01_S8388	2.4	CARLAGTAHGW	9	IGLV1-64*01	0.7	11	CLSYDSSLSAYIF	10710.T2
WEV	SKT07	IGHV4-149*01_S4098	8.1	CTIGVVAAGLIEYW	14	IGKV2-72*02	4.6	9	CVQAIAPYFSF	10710.T3
WEV	SKT08	IGHV4-NL_13*01_S9273	6	CVDIVGGATDYFEFV	13	IGLV1-72*02+G267T	4.7	11	CSAWDSSVSGRVF	10710.T4
WEV	SKT09	IGHV4-NL_13*01_S9273	6.4	CVDIVGGATDYFEFV	13	IGLV1-72*02+G267T	4.7	11	CSAWDSSVSGRVF	10710.T4
WEV	SKT10	IGHV4-NL_13*01_S9273	5.7	CVNIMGGETDYFEFV	13	IGLV1-72*02+G267T	4.1	11	CSAWDSSVSGRVF	10710.T4
WEV	SKT11	IGHV4-NL_13*01_S9273	2.7	CASIVGGATDYFEFV	13	IGLV1-72*02+G267T	1.4	11	CSAWDSSVSGRVF	10710.T4
WEV	SKT12	IGHV4-NL_13*01_S9273	7.7	CANIVGGATDYFEFV	13	IGLV1-72*02+G267T	2.4	11	CSAWDSSVSGRVF	10710.T4
WEV	SKT13	IGHV4-NL_13*01_S9273	7	CASIVGGATDYFEFV	13	IGLV1-72*02+G267T	2.4	11	CSAWDSSVSGRVF	10710.T4
WEV	SKT14	IGHV3-187*01_S1387	6.3	CVRGWRVYCRNSGCSAFAFDVW	19	IGLV3-44*01+70531	2.1	11	CQVWDISSDHGLF	10710.T5
WEV	SKT15	IGHV4-79*01	5.7	CARQWRTHCTNSGCSRPFYHW	19	IGLV3-40*01	4.8	10	CQVWDSSDRSF	10710.T6
WEV	SKT16	IGHV4-117*01_S6852	5.4	CAREFFREYCNNTGCVGWDNDV	19	IGLV1-72*02+G267T	4.4	11	CSAWDSSVSGRVF	10710.T7
WEV	SKT17	IGHV4-NL_1*02_S9550	2.4	CAKQYCSSTYCYGSLDVG	16	IGKV2-64*01+ G96A.A162C.G177T	3.6	8	CGQGAHLYTF	10710.T8
WEV	SKT18	IGHV4-NL_1*02_S9550	5.1	CAHSYCPGSDCTDAFDV	16	IGKV2-64*01+ G96A.A162C.G177T	3.6	10	CGQGAHLPMYFS	10710.T9
WEV	SKT19	IGHV4-NL_28*01_S1005	7.2	CARRRSEYCNNTYCTGAFDVG	19	IGKV3-10*02	8.4	8	CFQYSSGWF	10710.T10
WEV	SKT20	IGHV4-NL_5*01_S6960	11	CARSHFCNNTFCYGFVDV	17	IGKV2-72*02	3	9	CVQAIAPWTF	10710.T11
WEV	SKT21	IGHV3-187*01_S1387	4	CALRSPGGDW	9	IGLV1-64*01	1.7	11	CLSPDSSLSHFL	10710.T12
WEV	SKT22	IGHV3-187*01_S1387	3.6	CALRSPGGDW	9	IGLV1-64*01	0.7	11	CLSPDSSLSHFL	10710.T12
WEV	SKT23	IGHV3-187*01_S1387	3.6	CALRSPGGDW	9	IGLV1-64*01	1.4	11	CLSPDSSLSHFL	10710.T12
WEV	SKT24	IGHV3-122*01_S8388	2.4	CTRLGGGPIGDFV	12	IGLV1-64*01	2.7	11	CLSPDSRMSGYIF	10710.T13
WEV	SKT25	IGHV4-NL_13*01_S9273	4.7	CASLPNIGGTWGYFYW	15	IGKV1S4*01+11215	1.4	9	CQQHNGYPFTF	10710.T14
WEV	SKT26	IGHV4-NL_13*01_S9273	3	CASAINTHDALDFW	13	IGLV1-64*01	3.4	11	CLSYDSSLNWV	10710.T15
WEV	SKT27	IGHV4-NL_13*01_S9273	3	CASAINTHDALDFW	13	IGLV1-64*01	3.7	11	CLSYDSSLNWV	10710.T15
WEV	SKT28	IGHV4-NL_1*02_S9550	2	CARHFPPGLY	9	IGLV1-64*01	1.7	11	CLSYDSSLNAGLF	10710.T16

Table S2: Binding and pseudovirus neutralization of single-specific and triple specific α -EEV mAbs from representative competition binding groups, related to Figures 1-3.

A representative mAb was chosen from each competition group (Figures 2 and S2) for (a) single-specific and (b) triple-specific mAbs. ELISA binding is shown as EC50 values (ng/mL) and pseudovirus neutralization is shown as IC50 and IC80 (μ g/mL).

A

mAb	Specificity	ELISA binding	Pseudovirus neutralization	
		EC50 (ng/mL)	IC50 (μ g/mL)	IC80 (μ g/mL)
SKW11	α -WEEV	3.9	0.05	0.38
SKW14	α -WEEV	4.1	0.01	0.03
SKW17	α -WEEV	3.9	0.02	0.09
SKW19	α -WEEV	2.7	0.03	0.07
SKW24	α -WEEV	3.8	0.04	0.26
SKW27	α -WEEV	8.3	0.03	-
SKE01	α -EEEV	14.1	-	-
SKE13	α -EEEV	2.8	-	-
SKE21	α -EEEV	50.1	2.45	-
SKE22	α -EEEV	15.9	-	-
SKE26	α -EEEV	5.9	0.03	0.07
SKE32	α -EEEV	22.4	1.71	-
SKE33	α -EEEV	21.8	0.07	0.27
SKV05	α -VEEV	29.1	9.51	-
SKV08	α -VEEV	16.8	0.93	4.13
SKV09	α -VEEV	9.2	0.08	0.18
SKV11	α -VEEV	6.6	0.20	0.67
SKV16	α -VEEV	7.6	0.03	0.10
SKV18	α -VEEV	6.1	0.10	0.24
SKV20	α -VEEV	8.5	0.04	0.07

B

mAb	Specificity	ELISA binding	Pseudovirus neutralization	
		EC50 (ng/mL)	IC50 (μ g/mL)	IC80 (μ g/mL)
SKT05	α -WEEV	4.4	0.04	0.07
SKT14	α -WEEV	6.8	0.06	0.24
SKT20	α -WEEV	4.4	-	-
SKT23	α -WEEV	3.4	-	-
SKT05	α -EEEV	6.9	0.04	0.39
SKT20	α -EEEV	2.3	-	-
SKT23	α -EEEV	1.5	-	-
SKT05	α -VEEV	11.5	0.02	0.06
SKT20	α -VEEV	6.2	0.27	1.01
SKT23	α -VEEV	4.9	3.48	15.51

Table S3. Cryo-EM data collection, refinement, and validation statistics for VLPs and VLP-Fab complexes, related to Figures 4-6.

VLP	WEEV (EMD-27389) (PDB 8DEC)	WEEV-SKT05 (EMD-28119)	WEEV-SKW11 (EMD-28118)	WEEV-SKW19 (EMD-28115)	WEEV-SKW24 (EMD-28116)
Data collection and processing					
Magnification	105,000	105,000	105,000	105,000	105,000
Voltage (kV)	300	300	300	300	300
Electron exposure (e-/Å ²)	43.5	46.5	46.5	46.5	46.5
Defocus range (µm)	-0.7 to -2.0	-0.8 to -2.0	-0.8 to -2.0	-0.8 to -2.0	-0.8 to -2.0
Pixel size (Å)	1.245	1.66	1.66	1.245	1.245
Symmetry imposed	Icosahedral	Icosahedral	Icosahedral	Icosahedral	Icosahedral
Init. particle images (no.)	25,165	106,673	53,774	46,554	55,490
Final particle images (no.)	15,890	68,491	34,151	28,914	33,238
Map resolution (Å)	4.7	5.7	6.1	6.3	6.5
FSC threshold	0.143	0.143	0.143	0.143	0.143
Spike					
	WEEV (EMD-27391) (PDB 8DEE)	WEEV-SKT05 (EMD-27722) (PDB 8DUL)	WEEV-SKW11 (EMD-27723) (PDB 8DUN)	WEEV-SKW19 (EMD-27390) (PDB 8DED)	WEEV-SKW24 (EMD-27392) (PDB 8DEF)
Data collection and processing					
Magnification	105,000	105,000	105,000	105,000	105,000
Voltage (kV)	300	300	300	300	300
Electron exposure (e-/Å ²)	43.5	46.5	46.5	46.5	46.5
Defocus range (µm)	-0.7 to -2.0	-0.8 to -2.0	-0.8 to -2.0	-0.8 to -2.0	-0.8 to -2.0
Pixel size (Å)	1.245	1.66	1.66	1.245	1.245
Symmetry imposed	C1	C1	C1	C1	C1
Init. particle images (no.)	15,890	68,491	34,151	28,940	33,238
Final particle images (no.)	953,400	4,109,460	854,520	1,736,400	1,994,280
Map resolution (Å)	3.4	4.2	5.8	4.1	4.2
FSC threshold	0.143	0.143	0.143	0.143	0.143
Refinement					
Model used (PDB code)	7FFE	8DEE	8DEE	8DEE	8DEE
Model resolution (Å)	3.5	4.3		4.2	4.3
FSC threshold	0.143	0.143	0.143	0.143	0.143
Model composition					
Non-hydrogen atoms	30,716	14,203	20,499	20,450	22,071
Protein residues	4,000	1,802	2,876	2,662	2,868
Ligands					
<i>B</i> factors (Å ²)					
Protein	75.8	226.5	481.0	87.2	178.3
Ligand					
R.m.s. deviations					
Bond lengths (Å)	0.004	0.005	0.007	0.007	0.004
Bond angles (°)	0.76	1.27	1.32	0.90	0.84
Validation					
MolProbity score	1.5	1.7	1.7	1.9	1.8
Clashscore	4.0	6.1	5.3	10.0	7.1
Poor rotamers (%)	0.2	0.1	0.0	0.0	0.0
Ramachandran plot					
Favored (%)	95.4	94.7	94.2	94.1	93.8
Allowed (%)	4.5	5.3	5.8	5.8	6.2
Disallowed (%)	0.1	0.0	0.0	0.1	0.0

Table S3 (continued)

VLP	EEEV-SKE26 (EMD-28117)	VEEV-SKT05 (EMD-28056)	VEEV-SKV09 (EMD-28187)	VEEV-SKV16 (EMD-28188)	VEEV-SKT20 (EMD-28059)
Data collection and processing					
Magnification	105,000	81,000	105,000	105,000	105,000
Voltage (kV)	300	300	300	300	300
Electron exposure (e ⁻ /Å ²)	58.06	53.8	58.06	58.06	47.6
Defocus range (µm)	-0.7 to -2.0	-0.5 to -2.0	-0.8 to -2.0	-0.8 to -2.0	-0.75 to -2.25
Pixel size (Å)	1.66	1.056	1.245	1.245	1.23
Symmetry imposed	Icosahedral	Icosahedral	Icosahedral	Icosahedral	Icosahedral
Initial particle images (no.)	78,534	172,425	82,810	37,456	36,125
Final particle images (no.)	51,190	67,814	53,462	23,152	11,336
Map resolution (Å)	3.7	4.1	7.0	6.0	4.7
FSC threshold	0.143	0.143	0.143	0.143	0.143
Spike					
	EEEV-SKE26 (EMD-27757) (PDB 8DWO)	VEEV-SKT05 (EMD-28058) (PDB 8EEU)	VEEV-SKV09 (EMD-27395) (PDB 8DEQ)	VEEV-SKV16 (EMD-27396) (PDB 8DER)	VEEV-SKT20 (EMD-28060) (PDB 8EEV)
Data collection and processing					
Magnification	105,000	81,000	105,000	105,000	105,000
Voltage (kV)	300	300	300	300	300
Electron exposure (e ⁻ /Å ²)	58.06	53.8	58.06	58.06	47.6
Defocus range (µm)	-0.7 to -2.0	-0.5 to -2.0	-0.8 to -2.0	-0.8 to -2.0	-0.75 to -2.25
Pixel size (Å)	1.66	1.056	1.245	1.245	1.23
Symmetry imposed	C1	C1	C1	C1	C1
Initial particle images (no.)	51,190	4,068,840	53,462	23,152	680,160
Final particle images (no.)	3,071,400	190,096	83,637	1,389,120	28,235
Map resolution (Å)	3.4	3.5	6.0	3.4	3.6
FSC threshold	0.143	0.143	0.143	0.143	0.143
Refinement					
Initial model used (PDB code)	6XO4	7FFE	7FFE	7FFE	7FFE
Model resolution (Å)	3.5	3.5		3.5	3.6
FSC threshold	0.143	0.143	0.143	0.143	0.143
Model composition					
Non-hydrogen atoms	22,572	19,127	23,306	22,666	21,011
Protein residues	2,916	2,471	3,041	2,921	2,713
Ligands				10	
<i>B</i> factors (Å ²)					
Protein	70.1	73.1	63.4	70.78	70.2
Ligand					
R.m.s. deviations					
Bond lengths (Å)	0.004	0.01	0.006	0.005	0.007
Bond angles (°)	0.802	0.89	1.16	0.86	0.86
Validation					
MolProbity score	1.8	1.77	2.0	1.5	1.84
Clashscore	6.5	4.07	14.6	4.4	4.73
Poor rotamers (%)	0.4	0.05	0.1	0.0	0.0
Ramachandran plot					
Favored (%)	92.4	88.92	95.2	95.8	88.12
Allowed (%)	7.6	10.92	4.7	4.2	11.62
Disallowed (%)	0.0	0.16	0.1	0.0	0.26

Table S4. Epitope characteristics, related to Figure 4.**Heavy chain**

	EEEV-SKE26	VEEV-SKT05	VEEV-SKT20	VEEV-SKV09	VEEV-SKV16	WEEV-SKT05	WEEV-SKW11	WEEV-SKW19	WEEV-SKW24
Sequence variation (BSA weighted average of normalized entropy)	0.37	0.35	0.23	0.73	0.57	0.32	0.33	0.52	0.60
Conformational variability (RMSD, Å)	2.7	2.5	3.0	3.8	4.3	2.5	2.5	5.8	6.5
Surface area (Å ²)	925	520	759	698	656	466	285	615	579
E1/E2 binding(Å ²)	6/919	520/0	464/295	698/0	0/656	466/0	0/285	95/520	58/522
Side chain/main chain recognition(Å ²)	763/162	429/92	698/61	605/93	582/74	376/90	231/54	505/110	516/63

Light chain

	EEEV-SKE26	VEEV-SKT05	VEEV-SKT20	VEEV-SKV09	VEEV-SKV16	WEEV-SKT05	WEEV-SKW11	WEEV-SKW19	WEEV-SKW24
Sequence variation (BSA weighted average of normalized entropy)	0.58	0.29	0.0	0.66	-	0.29	0.54	-	0.58
Conformational variability (RMSD, Å)	4.7	2.2	4.4	3.5	-	2.3	3.7	-	4.0
Surface area (Å ²)	325	465	211	464	-	617	343	-	338
E1/E2 binding(Å ²)	0/325	439/26	211/0	464/0	-	617/0	0/343	-	0/338
Side chain/main chain recognition(Å ²)	290/35	430/34	210/1	399/65	-	539/79	275/67	-	311/27

Table S5. Contribution of residues to binding surface for VEEV-SKT05 (top) and WEEV-SKT05 (bottom), related to Figures 5-6.

SKT05			VEEV		
Residue	Bond	BSA Å ²	Residue	Bond	BSA Å ²
Heavy chain					
H:ASP 31		16.07	A:SER 65		22.16
H:SER 32		4.93	A:GLN 66		7.52
H:TRP 33		0.89	A:GLU 67	HS	112.51
H:ASP 53		4.79	A:CYS 68	H	44.03
H:ARG 94	HS	16.05	A:THR 69		3.67
H:ASP 95		3.19	A:PRO 70		61.43
H:ASP 96		32.05	A:TYR 72		22.87
H:ARG 97	HS	83.01	A:ARG 73		0.49
H:THR 98	H	47.36	A:PRO 74		0.67
H:SER 99		29.64	A:ASP 75	HS	28.50
H:CYS 100	H	68.35	A:GLU 76	H	43.34
H:ARG 100A		39.84	A:GLN 77		40.56
H:ARG 100B	HS	114.84	A:CYS 78	H	34.57
H:GLY 100C		38.70	A:LYS 79		20.01
H:CYS 100E		10.09	A:VAL 80	H	32.39
H:HIS 101		11.59	A:TYR 214		7.76
			A:ALA 215	H	11.85
			A:ASN 216		10.34
			A:ASN 218		4.79
			A:VAL 220		3.52
Light chain					
L:PHE 31		30.28	A:GLY 64		1.10
L:ARG 46		1.17	A:SER 65		3.68
L:TYR 49		54.92	A:LYS 79	S	59.76
L:ASP 50		12.08	A:VAL 80		34.14
L:SER 52		8.83	A:PHE 81		13.22
L:GLU 53	S	82.07	A:THR 82	H	75.90
L:LEU 54	H	32.81	A:THR 98		47.28
L:GLN 55		0.50	A:GLU 99		45.85
L:GLY 56		42.61	A:ARG 223		27.89
L:GLY 57		25.94			
L:VAL 58		9.85			
L:SER 60		13.95			

SKT05			WEEV		
Residue	Bond	BSA Å ²	Residue	Bond	BSA Å ²
Heavy chain					
H:ASP 31		10.62	F:SER 65	H	37.65
H:SER 32		2.52	F:LEU 66		2.82
H:ARG 94		8.16	F:GLU 67	HS	91.97
H:ASP 95		1.96	F:CYS 68		36.12
H:ASP 96	H	29.53	F:LYS 69		5.02
H:ARG 97	HS	75.92	F:ALA 70		59.41
H:THR 98	H	48.35	F:SER 71		6.99
H:SER 99		31.42	F:ASP 75	HS	22.29
H:CYS 100	H	63.17	F:TYR 76		37.16
H:ARG 100A		26.54	F:THR 77		21.65
H:ARG 100B	HS	103.81	F:CYS 78	H	38.79
H:GLY 100C		28.93	F:ARG 79		19.02
H:CYS 100E		8.77	F:VAL 80	H	36.07
H:HIS 101		16.05	F:MET 195		1.51
			F:ALA 215	H	7.60
			F:ARG 216		27.88
			F:ASP 218		10.99
			F:ILE 219		1.72
Light chain					
L:PHE 31		39.87	F:CYS 63		1.72
L:TYR 32		5.93	F:SER 65		10.54
L:ARG 46		2.19	F:ARG 79		65.11
L:TYR 49		43.29	F:VAL 80		45.04
L:ASP 50		25.48	F:PHE 81		8.05
L:SER 52		19.95	F:GLY 82		31.14
L:GLU 53		59.66	F:GLY 83		4.51
L:LEU 54		27.07	F:SER 98		15.47
L:GLY 56		41.39	F:GLU 99	H	65.74
L:GLY 57	H	19.92	F:ASN 100		8.29
L:VAL 58		7.51	F:THR 101		17.59
L:SER 60		4.03	F:LEU 221		0.12
			F:LYS 223		31.34

BSA: Buried Surface Area, Å²
HSDC: Residues making Hydrogen/Disulphide bond, Salt bridge or Covalent link
|||: Buried area percentage, one bar per 10%