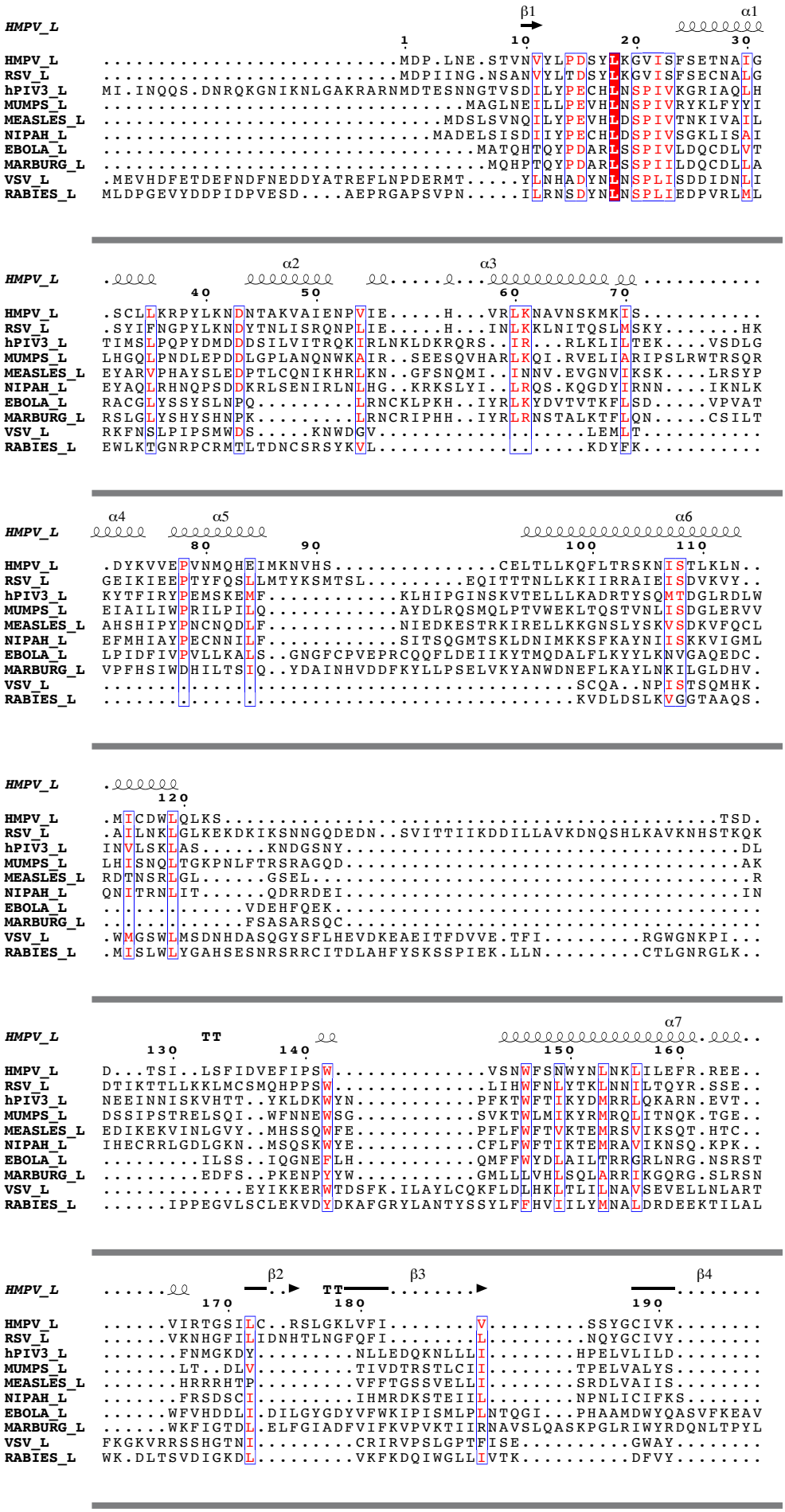
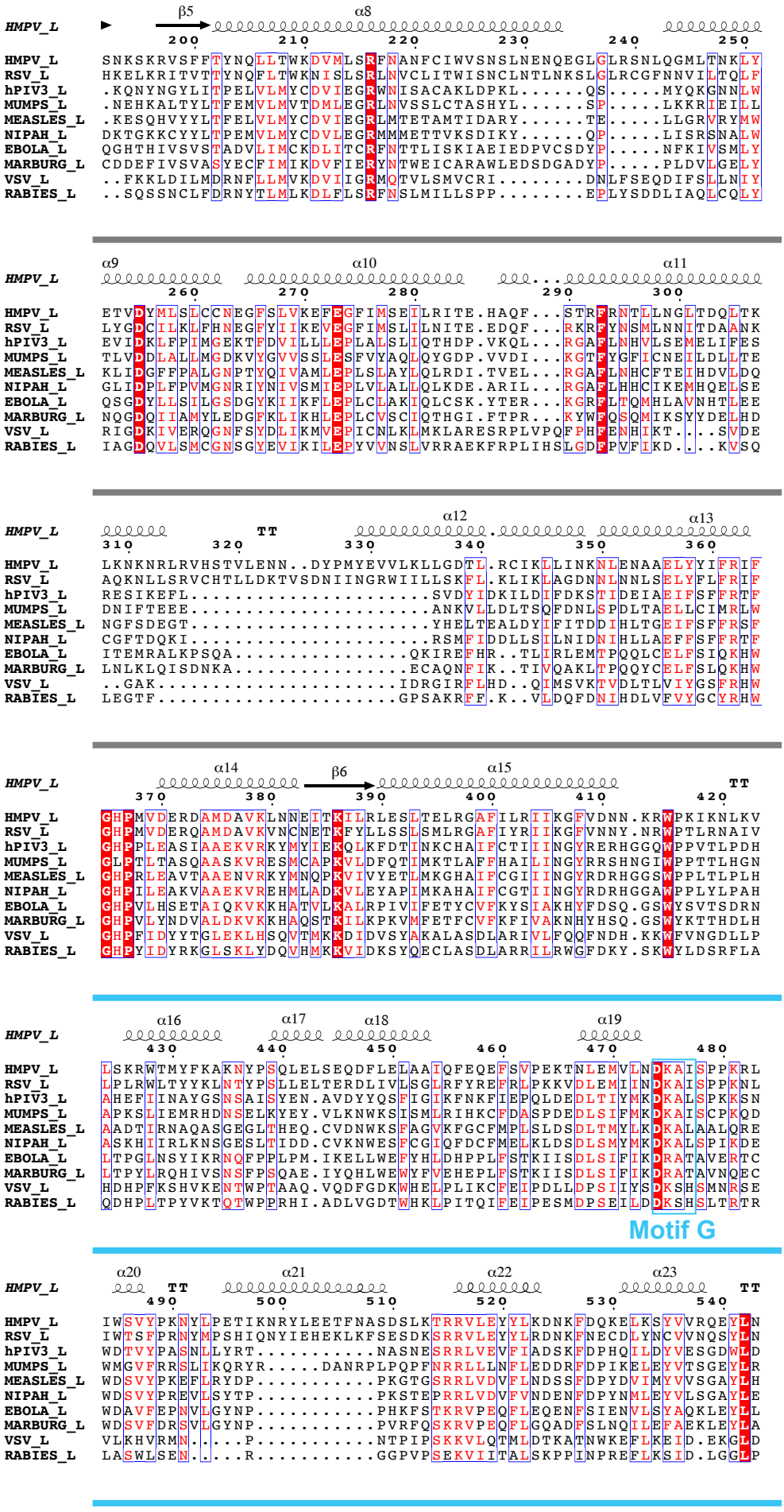
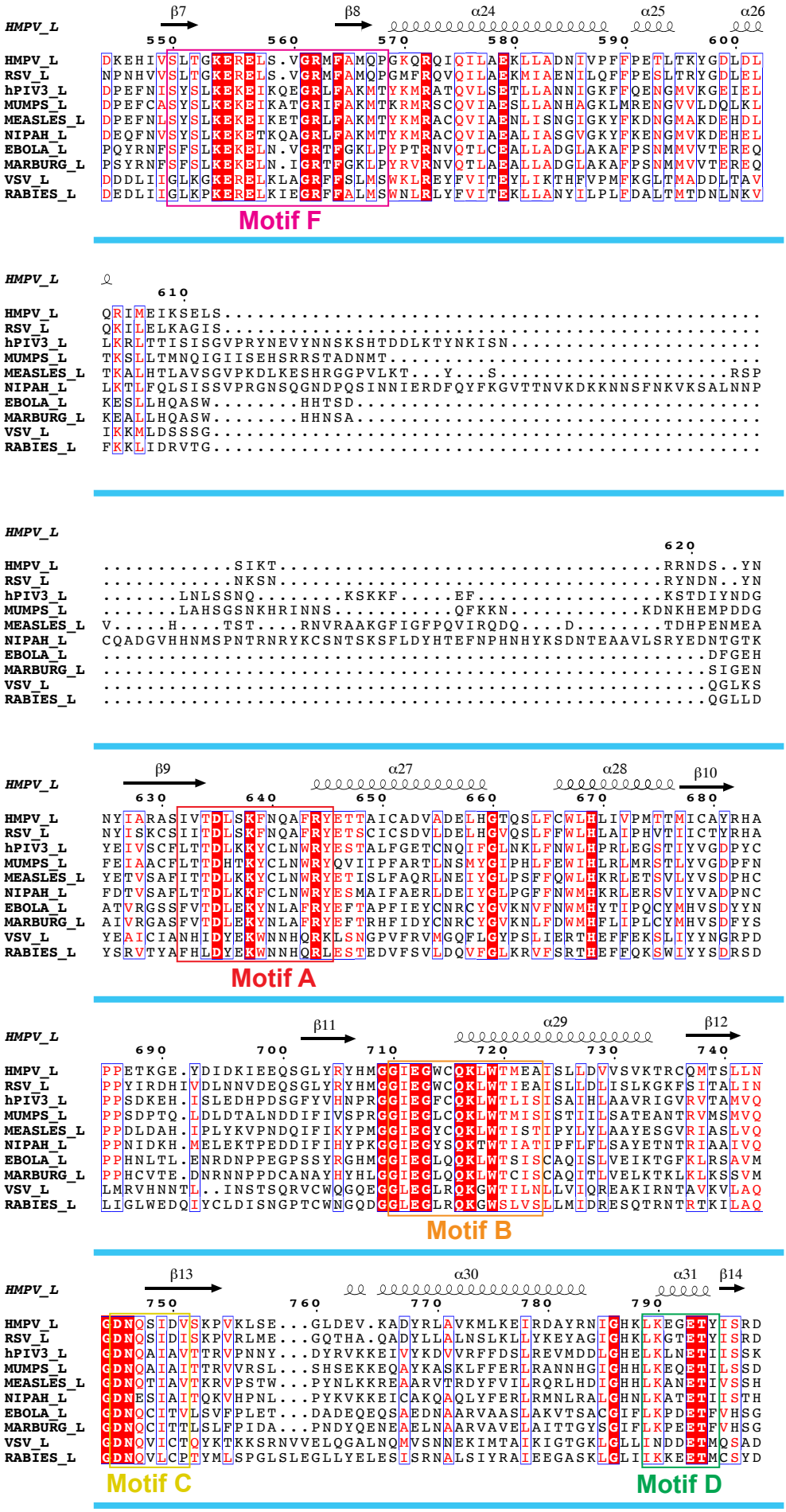
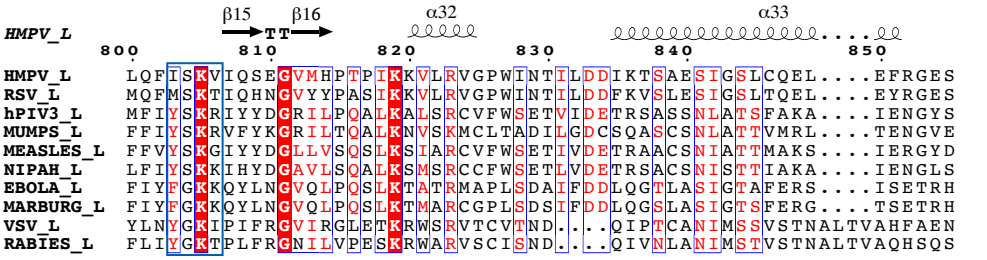
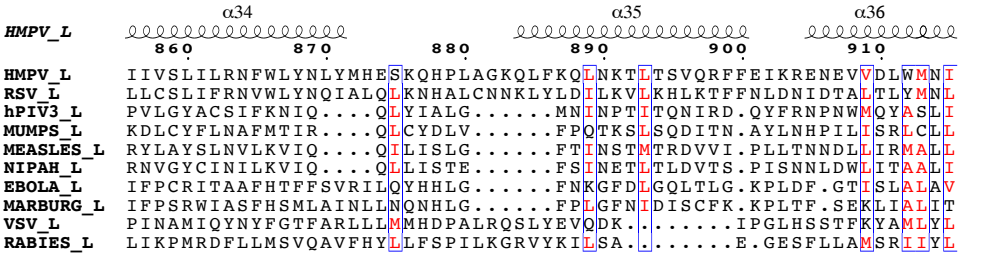

HMPV_L
RSV_L
hPIV3_L
MUMPS_L
MEASLES_L
NIPAH_L
EBOLA_L
MARBURG_L
VSV_L
RABIES_L

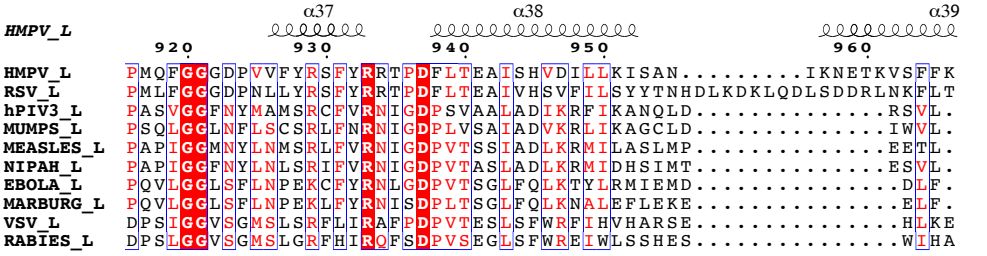

β5
α8
HMPV_L
200 210 220 230 240 250
HMPV_L SNKSKRVSFFTYNQLLTWKDVMLSRFNANFCIWVSNSLNENQEGLGLRSNLQGMLTNKLY
RSV_L HKELKRITVTTYNQFLTWKNISLSRLNVCLITWISNCLNTLNKSLGLRCGFNNVILTQLF
hPIV3_L .KQNYNGYLITPELVLMYCDVIEGRWNISACAKLDPKL......QS.....MYQKGNNLW
MUMPS_L .NEHKALTYLTFEMVLMVTDMLEGRLNVSSLCTASHYL......SP.....LKKRIEILL
MEASLES_L .KESQHVYYLTFELVLMYCDVIEGRLMTETAMTIDARY......TE.....LLGRVRYMW
NIPAH_L DKTGKKCYYLTPEMVLMYCDVLEGRMMMETTVKSDIKY......QP.....LISRSNALW
EBOLA_L QGHTHIVSVSTADVLIMCKDLITCRFNTTLISKIAEIEDPVCSDYP.....NFKIVSMLY
MARBURG_L CDDEFIVSVASYECFIMIKDVFIERYNTWEICARAWLEDSDGADYP.....PLDVLGELY
VSV_L ..FKKLDILMDRNFLLMVKDVIIGRMQTVLSMVCRI........DNLFSEQDIFSLLNIY
RABIES_L ..SQSSNCLFDRNYTLMLKDLFLSRFNSLMILLSPP........EPLYSDDLIAQLCQLY
α9
α10
α11
HMPV_L
260 270 280 290 300
HMPV_L ETVDYMLSLCCNEGFSLVKEFEGFIMSEILRITE.HAQF...STRFRNTLLNGLTDQLTK
RSV_L LYGDCILKLFHNEGFYIIKEVEGFIMSLILNITE.EDQF...RKRFYNSMLNNITDAANK
hPIV3_L EVIDKLFPIMGEKTFDVILLLEPLALSLIQTHDP.VKQL...RGAFLNHVLSEMELIFES
MUMPS_L TLVDDLALLMGDKVYGVVSSLESFVYAQLQYGDP.VVDI...KGTFYGFICNEILDLLTE
MEASLES_L KLIDGFFPALGNPTYQIVAMLEPLSLAYLQLRDI.TVEL...RGAFLNHCFTEIHDVLDQ
NIPAH_L GLIDPLFPVMGNRIYNIVSMIEPLVLALLQLKDE.ARIL...RGAFLHHCIKEMHQELSE
EBOLA_L QSGDYLLSILGSDGYKIIKFLEPLCLAKIQLCSK.YTER...KGRFLTQMHLAVNHTLEE
MARBURG_L NQGDQIIAMYLEDGFKLIKHLEPLCVSCIQTHGI.FTPR...KYWFQSQMIKSYYDELHD
VSV_L RIGDKIVERQGNFSYDLIKMVEPICNLKLMKLARESRPLVPQFPHFENHIKT....SVDE
RABIES_L IAGDQVLSMCGNSGYEVIKILEPYVVNSLVRRAEKFRPLIHSLGDFPVFIKD....KVSQ
α12
α13
HMPV_L
TT
310 320 330 340 350 360
HMPV_L LKNKNRLRVHSTVLENN..DYPMYEVVLKLLGDTL.RCIKLLINKNLENAAELYYIFRIF
RSV_L AQKNLLSRVCHTLLDKTVSDNIINGRWIILLSKFL.KLIKLAGDNNLNNLSELYFLFRIF
hPIV3_L RESIKEFL.....SVDYIDKILDIFDKSTIDEIAEIFSFFRTF
MUMPS_L DNIFTEEE.....ANKVLLDLTSQFDNLSPDLTAELLCIMRLW
MEASLES_L NGFSDEGT.....YHELTEALDYIFITDDIHLTGEIFSFFRSF
NIPAH_L CGFTDQKI.....RSMFIDDLLSILNIDNIHLLAEFFSFFRTF
EBOLA_L ITEMRALKPSQA.....QKIREFHR..TLIRLEMTPQQLCELFSIQKHW
MARBURG_L LNLKLQISDNKA.....ECAQNFIK..TIVQAKLTPQQYCELFSLQKHW
VSV_L ..GAK.....IDRGIRFLHD..QIMSVKTVDLTLVIYGSFRHW
RABIES_L LEGTF.....GPSAKRFF.K..VLDQFDNIHDLVFVYGCYRHW
α14
β6
α15
HMPV_L
TT
370 380 390 400 410 420
HMPV_L GHPMVDERDAMDAVKLNNEITKILRLESLTELRGAFILRIIKGFVDNN.KRWPKIKNLKV
RSV_L GHPMVDERQAMDAVKVNCNETKFYLLSSLSMLRGAFIYRIIKGFVNNY.NRWPTLRNAIV
hPIV3_L GHPPLEASIAAEKVRKYMYIEKQLKFDTINKCHAIFCTIIINGYRERHGGQWPPVTLPDH
MUMPS_L GLPTLTASQAASKVRESMCAPKVLDFQTIMKTLAFFHAILINGYRRSHNGIWPPTTLHGN
MEASLES_L GHPRLEAVTAAENVRKYMNQPKVIVYETLMKGHAIFCGIIINGYRDRHGGSWPPLTLPLH
NIPAH_L GHPILEAKVAAEKVREHMLADKVLEYAPIMKAHAIFCGTIINGYRDRHGGAWPPLYLPAH
EBOLA_L GHPVLHSETAIQKVKKHATVLKALRPIVIFETYCVFKYSIAKHYFDSQ.GSWYSVTSDRN
MARBURG_L GHPVLYNDVALDKVKKHAQSTKILKPKVMFETFCVFKFIVAKNHYHSQ.GSWYKTTHDLH
VSV_L GHPFIDYYTGLEKLHSQVTMKKDIDVSYAKALASDLARILVLFQQFNDH.KKWFVNGDLLP
RABIES_L GHPYIDYRKGLSKLYDQVHMKKVIDKSYQECLASDLARRILRWGFDKY.SKWYLDSRFLA
α16
α17
α18
α19
HMPV_L
430 440 450 460 470 480
HMPV_L LSKRWTMYFKAKNYPSQLELSEQDFLELAAIQFEQEFSVPEKTNLEMVLNDKAISPPKRL
RSV_L LPLRWLTYYKLNTYPSLLELTERDLIVLSGLRFYREFRLPKKVDLEMIINDKAISPPKNL
hPIV3_L AHEFIINAYGSNSAISYEN.AVDYYQSFIGIKFNKFIEPQLDEDLTIYMKDKALSPKKSN
MUMPS_L APKSLIEMRHDNSELKYEY.VLKNWKSISMLRIHKCFDASPDEDLSIFMKDKAISCPKQD
MEASLES_L AADTIRNAQASGEGLTHEQ.CVDNWKSFAGVKFGCFMPLSLDSDLTMYLKDKALAALQRE
NIPAH_L ASKHIIRLKNSGESLTIDD.CVKNWESFCGIQFDCFMELKLDSDLSMYMKDKALSPIKDE
EBOLA_L LTPGLNSYIKRNQFPPLPM.IKELLWEFYHLDHPPLFSTKIISDLSIFIKDRATAVERTC
MARBURG_L LTPYLRQHIVSNSFPSQAE.IYQHLWEWYFVEHEPLFSTKIISDLSIFIKDRATAVNQEC
VSV_L HDHPFKSHVKENTWPTAAQ.VQDFGDKWHELPLIKCFEIPDLLDPSIIYSDKSHSMNRSE
RABIES_L QDHPLTPYVKTQTWPPRHI.ADLVGDTWHKLPITQIFEIPESMDPSEILDDKSHSLTRTR
Motif G
α20
α21
α22
α23
HMPV_L
TT
490 500 510 520 530 540
HMPV_L IWSVYPKNYLPETIKNRYLEETFNASDSLKTRRVLEYYLKDNKFDQKELKSYVVRQEYLN
RSV_L IWTSFPRNYMPSHIQNYIEHEKLKFSESDKSRRVLEYYLRDNKFNECDLYNCVVNQSYLN
hPIV3_L WDTVYPASNLLYRT.....NASNESRRLVEVFIADSKFDPHQILDYVESGDWLD
MUMPS_L WMGVFRRSLIKQRYR.....DANRPLPQPFNRRLLLNFLEDDRFDPIKELEYVTSGEYLR
MEASLES_L WDSVYPKEFLRYDP.....PKGTGSRRLVDVFLNDSSFDPYDVIMYVVSGAYLH
NIPAH_L WDSVYPREVLSYTP.....PKSTEPRRLVDVFVNDENFDPYNMLEYVLSGAYLE
EBOLA_L WDAVFEPNVLGYNP.....PHKFSTKRVPEQFLEQENFSIENVLSYAQKLEYLL
MARBURG_L WDSVFDRSVLGYNP.....PVRFQSKRVPEQFLGQADFSLNQILEFAEKLEYLA
VSV_L VLKHVRMN.....P.....NTPIPSKKVLQTMLDTKATNWKEFLKEIDEKGLD
RABIES_L LASWLSEN.....R.....GGPVPSEKVIITALSKPPINPREFLKSIDLGGLP

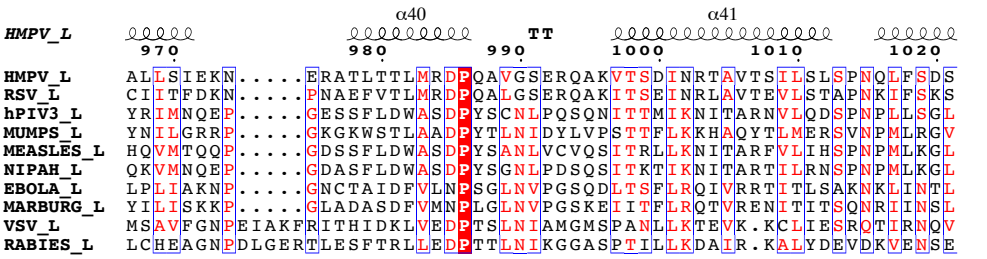

HMPV_L
β7
β8
α24
α25
α26
550
560
570
580
590
600
HMPV_L
RSV_L
hPIV3_L
MUMPS_L
MEASLES_L
NIPAH_L
EBOLA_L
MARBURG_L
VSV_L
RABIES_L
Motif F
610
620
630
640
650
660
670
680
β9
α27
α28
β10
Motif A
690
700
710
720
730
740
β11
α29
β12
Motif B
750
760
770
780
790
β13
α30
α31
β14
Motif C
Motif D

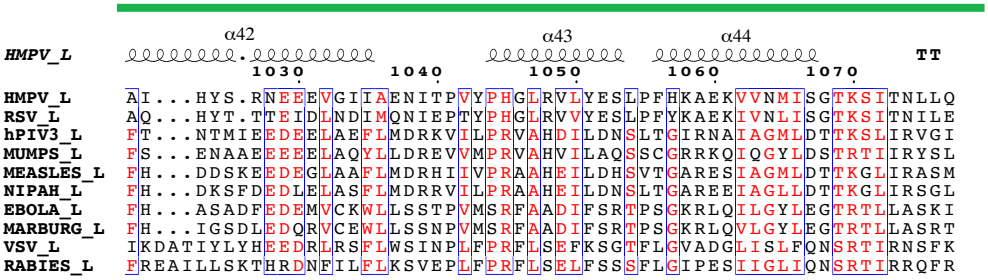

β15 β16 α32 α33
HMPV_L
800 810 820 830 840 850
HMPV_L LQFISKVIQSEGVMHPTPIKKVLRVGPWINTILDDIKTSAESIGSLCQEL....EFRGES
RSV_L MQFMSKTIQHNGVYYPASIKKVLRVGPWINTILDDFKVSLESIGSLTQEL....EYRGES
hPIV3_L MFIYSKRIYYDGRILPQALKALSRCVFWSETVIDETRSASSNLATSFAKA....IENGYS
MUMPS_L FFIYSKRVFYKGRILTQALKNVSKMCLTADILGDCSQASCSNLATTVMRL....TENGVE
MEASLES_L FFVYSKGIYYDGLLVSQSLKSIARCVFWSETIVDETRAACSNIATTMAKS....IERGYD
NIPAH_L LFIYSKKIHYDGAVLSQALKSMSRCCFWSETLVDETRSACSNISTTIAKA....IENGLS
EBOLA_L FIYFGKKQYLNGVQLPQSLKTATRMAPLSDAIFDDLQGTLASIGTAFERS....ISETRH
MARBURG_L FIYFGKKQYLNGVQLPQSLKTMARCGPLSDSIFDDLQGSLASIGTSFERG....TSETRH
VSV_L YLNYGKIPIFRGVIRGLETKRWSRVTCVTND....QIPTCANIMSSVSTNALTVAHFAEN
RABIES_L FLIYGKTPLFRGNILVPESKRWARVSCISND....QIVNLANIMSTVSTNALTVAQHSQS

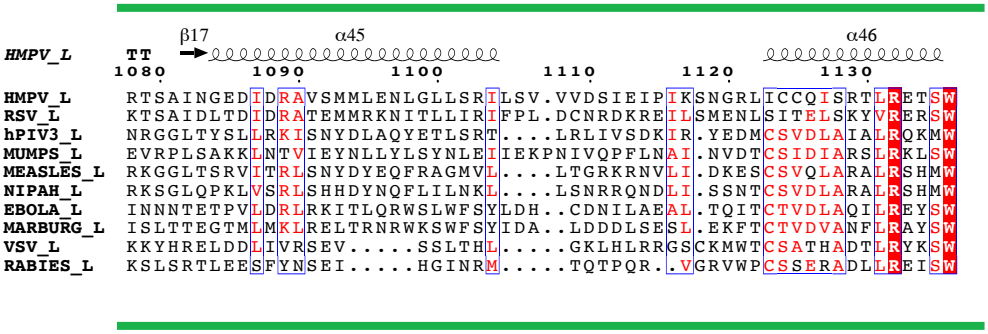
Motif E

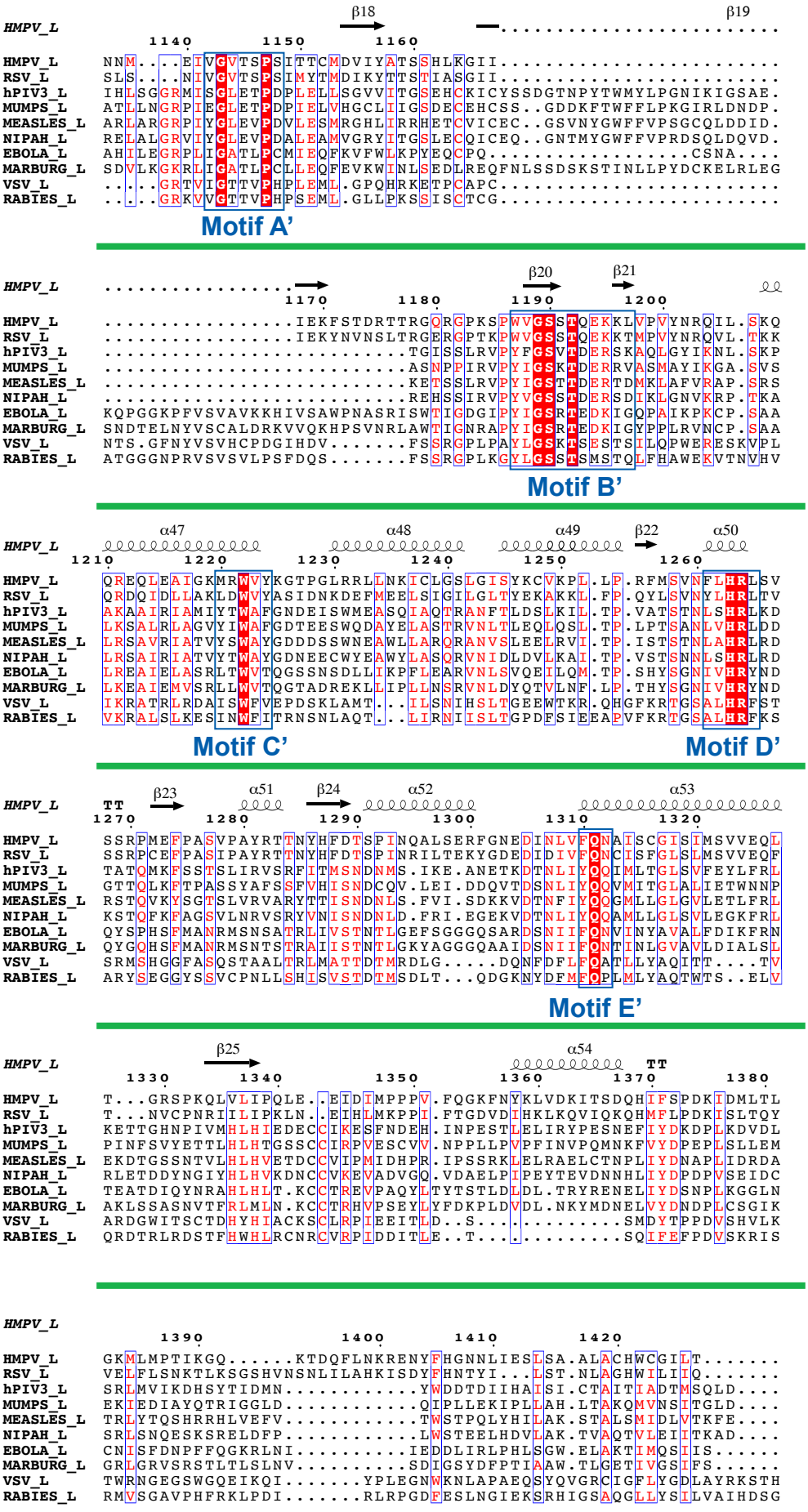

α34 α35 α36
HMPV_L
860 870 880 890 900 910
HMPV_L IIVSLILRNFWLYNLYMHESKQHPLAGKQLFKQLNKTLTSVQRFFEIKRENEVVDLWMNI
RSV_L LLCSLIFRNVWLYNQIALQLKNHALCNNKLYLDILKVLKHLKTFFNLDNIDTALTLYMNL
hPIV3_L PVLGYACSIFKNIQ....QLYIALG......MNINPTITQNIRD.QYFRNPNWMQYASLI
MUMPS_L KDLCYFLNAFMTIR....QLCYDLV......FPQTKSLSQDITN.AYLNHPILISRLCLL
MEASLES_L RYLAYSLNVLKVIQ....QILISLG......FTINSTMTRDVVI.PLLTNNDLLIRMALL
NIPAH_L RNVGYCINILKVIQ....QLLISTE......FSINETLTLDVTS.PISNNLDWLITAALI
EBOLA_L IFPCRITAAFHTFFSVRILQYHHLG......FNKGFDLGQLTLG.KPLDF.GTISLALAV
MARBURG_L IFPSRWIASFHSMLAINLLNQNHLG......FPLGFNIDISCFK.KPLTF.SEKLIALIT
VSV_L PINAMIQYNYFGTFARLLLMMHDPALRQSLYEVQDK.......IPGLHSSTFKYAMLYL
RABIES_L LIKPMRDFLLMSVQAVFHYLLFSPILKGRVYKILSA.......E.GESFLLAMSRIIYL


α37 α38 α39
HMPV_L
920 930 940 950 960
HMPV_L PMQFGGGDPVVFYRSFYRRTPDFLTEAISHVDILLKISAN.........IKNETKVSFFK
RSV_L PMLFGGGDPNLLYRSFYRRTPDFLTEAIVHSVFILSYYTNHDLKDKLQDLSDDRLNKFLT
hPIV3_L PASVGGFNYMAMSRCFVRNIGDPSVAALADIKRFIKANQLD..............RSVL.
MUMPS_L PSQLGGLNFLSCSRLFNRNIGDPLVSAIADVKRLIKAGCLD..............IWVL.
MEASLES_L PAPIGGMNYLNMSRLFVRNIGDPVTSSIADLKRMILASLMP..............EETL.
NIPAH_L PAPIGGFNYLNLSRIFVRNIGDPVTASLADLKRMIDHSIMT..............ESVL.
EBOLA_L PQVLGGLSFLNPEKCFYRNLGDPVTSGLFQLKTYLRMIEMD..............DLF.
MARBURG_L PQVLGGLSFLNPEKLFYRNISDPLTSGLFQLKNALEFLEKE..............ELF.
VSV_L DPSIGGVSGMSLSRFLIRAFPDPVTESLSFWRFIHVHARSE..............HLKE
RABIES_L DPSLGGVSGMSLGRFHIRQFSDPVSEGLSFWREIWLSSHES..............WIHA


α40 α41
HMPV_L
970 980 990 1000 1010 1020
HMPV_L ALLSIEKN.....ERATLTTLMRDPQAVGSERQAKVTSDINRTAVTSILSLSPNQLFSDS
RSV_L CIITFDKN.....PNAEFVTLMRDPQALGSERQAKITSEINRLAVTEVLSTAPNKIFSKS
hPIV3_L YRIMNQEP.....GESSFLDWASDPYSCNLPQSQNITTMIKNITARNVLQDSPNPLLSGL
MUMPS_L YNILGRRP.....GKGKWSTLAADPYTLNIDYLVPSTTFLKKHAQYTLMERSVNPMLRGV
MEASLES_L HQVMTQQP.....GDSSFLDWASDPYSANLVCVQSITRLLKNITARFVLIHSPNPMLKGL
NIPAH_L QKVMNQEP.....GDASFLDWASDPYSGNLPDSQSITKTIKNITARTILRNSPNPMLKGL
EBOLA_L LPLIAKNP.....GNCTAIDFVLNPSGLNVPGSQDLTSFLRQIVRRTITLSAKNKLINTL
MARBURG_L YILISKKP.....GLADASDFVMNPLGLNVPGSKEIITFLRQTVRENITITSQNRIINSL
VSV_L MSAVFGNPEIAKFRITHIDKLVEDPTSLNIAMGMSPANLLKTEVK.KCLIESRQTIRNQV
RABIES_L LCHEAGNPDLGERTLESFTRLLEDPTTLNIKGGASPTILLKDAIR.KALYDEVDKVENSE


α42 α43 α44
HMPV_L
1030 1040 1050 1060 1070
HMPV_L AI...HYS.RNEEEVGIIAENITPVYPHGLRVLYESLPFHKAEKVVNMISGTKSITNLLQ
RSV_L AQ...HYT.TTEIDLNDIMQNIEPTYPHGLRVVYESLPFYKAEKIVNLISGTKSITNILE
hPIV3_L FT...NTMIEEDELAEFLMDRKVILPRVAHDILDNSLTGIRNAIAGMLDTTKSLIRVGI
MUMPS_L FS...ENAAEEEELAQYLLDREVVMPRVAHVILAQSSCGRRKQIQGYLDSTRTIIRYSL
MEASLES_L FH...DDSKEEDEGLAAFLMDRHIIVPRAAHEILDHSVTGARESIAGMLDTTKGLIRASM
NIPAH_L FH...DKSFDEDLELASFLMDRRVILPRAAHEILDNSLTGAREEIAGLLDTTKGLIRSGL
EBOLA_L FH...ASADFEDEMVCKWLLSSTPVMSRFAADIFSRTPSGKRLQILGYLEGTRTLLASKI
MARBURG_L FH...IGSDLEDQRVCEWLLSSNPVMSRFAADIFSRTPSGKRLQVLGYLEGTRTLLASRT
VSV_L IKDATIYLYHEEDRLRSFLWSINPLFPRFLSEFKSGTFLGVADGLISLFQNSRTIRNSFK
RABIES_L FREAILLSKTHRDNFILFLKSVEPLFPRFLSELFSSSFLGIPESIIGLIQNSRTIRRQFR


β17 α45 α46
HMPV_L
1080 1090 1100 1110 1120 1130
HMPV_L RTSAINGEDIDRAVSMMLENLGLLSRILSV.VVDSIEIPIKSNGRLICCQISRTLRETSW
RSV_L KTSAIDLTDIDRATEMMRKNITLLIRIFPL.DCNRDKREILSMENLSITELSKYVRERSW
hPIV3_L NRGGLTYSLLRKISNYDLAQYETLSRT....LRLIVSDKIR.YEDMCSVDLAIALRQKMW
MUMPS_L EVRPLSAKKLNTVIEYNLLYLSYNLEIIEKPNIVQPFLNAI.NVDTCSIDIARSLRKLSW
MEASLES_L RKGGLTSRVITRLSNYDYEQFRAGMVL....LTGRKRNVLI.DKESCSVQLARALRSHMW
NIPAH_L RKSGLQPKLVSRLSHHDYNQFLILNKL....LSNRRQNDLI.SSNTCSVDLARALRSHMW
EBOLA_L INNNTETPVLDRLRKITLQRWSLWFSYLDH..CDNILAEAL.TQITCTVDLAQILREYSW
MARBURG_L ISLTTEGTMLMKLRELTRNRWKSWFSYIDA..LDDDLSESL.EKFTCTVDVANFLRAYSW
VSV_L KKYHRELDDLIVRSEV.....SSLTHL.....GKLHLRRGSCKMWTCSATHADTLRYKSW
RABIES_L KSLSRTLEESFYNSEI.....HGINRM.....TQTPQR.VGRVWPCSSERADLLREISW



Supplementary figure 2 -Structure-based alignment of L from HMPV, RSV, human parainfluenza virus 3 (hPIV3), Mumps virus, Measles virus, Nipah virus, Ebola virus, Marburg virus, VSV and Rabies Virus. Accession codes for the sequences included in the alignment are: HMPV_L: Q6WB93.1; RSV_L: NP_044598.1; hPIV3: ACJ70091.1; MUMPS_L ACH78356.1; MEASLES_L: AAF85706.1; NIPAH_L: NP_112028.1; EBOLA_L: Q05318.2; MARBURG_L: ABA87130.1; VSV-L: Q98776.1 and Rabies_virus L: BAA24082.1. Secondary structures of HMPV-L (this work) are displayed above the alignment. The domains of L are indicated by a colored bar below the alignment (NTD, grey; RdRp, aquamarine and capping domain, green). Evolutionary conserved motifs of the RdRp and capping domains are boxed. Polymerase motifs A-G were defined according to previous work[40-43]. In particular, we made use of the structure-based sequence alignment of HMPV-L (this work) with the poliovirus polymerase (PDB code: 1RA6). The five capping motifs are labeled A'-E'. The r.m.s.d. between the structure of HMPV_L and RSV_L[16] is 1.21 Å over 1282 residues.