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       37 ▐███████████████████████████████████████████████████████████████████████ 107
B145      VTPYYGPGHI T-SDWCGFGD SRSDCTNPYS PMS-----LD IPQQLC--SK FSSKSSSSMF LSLHWNTSSS FVSYDYFNCG
BRV       VTPYYGPGHI T-FDWCGFGD SRSDCTNPQS PMS-----LD IPQQLC--PK FSSKSSSSMF LSLHWNNHSS FVSYDYFNCG
B150      VTPYYGPGHI T-SDWCGFGD SRSDCNNPYF PSS-----LD IPQQLC--SK FSSKSSSSMF ISLHWNNSVD FVAYNYSNCG
P-MAR     ITPHYGPGHI T-PDWCGFGD SRSDCGNKHT PKS-----LD IPQELC--PK FSSRTGSSMF ISMHWNNGSG FDAFDYSNCG
P10       ITPHYGPGHI T-SDWCGFGD SRSDCGNQHT PKS-----LD IPQELC--PK FSSRTGSSMF ISMHWNNDSD FNAFGYSNCG
P4        ITPHYGPGHI T-SDWCGFGD SRSDCTNPSS PKS-----LD IPQQLC--PK FSSKTGSSMF ISLHWNNSNT FTVFNYSNCG
C/MI/4/93 VKPKAGASVL NQSTWIGFGD SRTDKSNPNF PRS-----AD VSVKTA--NK FRSSTGGSLM LSMF--GPPG KVDYLYQGCG
C/JHG/66  VKPKAGASVL NQSTWIGFGD SRTDKSNSAF PRS-----AD VSAKTA--DK FRFLSGGSLM LSMF--GPPG KVDYLYQGCG
BCoV      NPPTNVVSHL N-GDWFLFGD SRSDCNHVVN TNPRNYSYMD LNPALCDSGK ISSKAGNSIF RSFHF---TD F--YNYTGEG
OC43      NPPTNVVSHV N-GDWFLFGD SRSDCNHIVN INPHNYSYMD LNPVLCDSGK ISSKAGNSIF RSFHF---TD F--YNYTGEG
PHEV      NPPTNVVSHF N-DDWFLFGD SRTDCNHVVK TNPRNYSYMD LNPALCDSGK ISSKAGNSIF RSFHF---TD F--YNYTGEG
ECoV      NPPVNIVSHI N-EDWFLFGD SRSDCNHINT INPRNYSYMD LNPELCNSGK ISSKAGNSLF RSFHF---TD F--YNYTGEG
DVIM      NEPLNVVSHL N-DDWFLFGD SRSDCNHINN LSQQNYNYMD INPELCKSGK ISAKAGNSLF KSFHF---TD F--YNYTGEG
MHV-2     NEPLNTVSHS N-DDWFLFGD SRSDCNHISS LSQQNYKYMD INPELCKSGK ISSKAGNSLF RSFHF---TD F--YNYSGEG
JHM       NEPLNIVSHL N-DDWFLFGD SRSDCTYVEN NGHPKLDWLD LDPKLCNSGK ISAKSGNSLF RSFHF---TD F--YNYTGEG
RCoV      NEPINIVSHL N-DDWFLFGD SRSDCTYVEN NGHPKLDWLD LDPKLCNSGK IAAKSGNSLF RSFHF---TD F--YNYTGEG
PuCoV     NEPLNVVSHL S-DDWFLFGD SRSDCSYVEN NGHPAFDWLD LPQELCNSGK ISAKSGNSLF KSFHF---TD W--YNYTGEG
MHV-S     NEPLNIVSHL N-DDWFLFGD SRSDCTYVEN NGHPKLDWLD LDPKLCNSGR IYAKSGNSLF RSFHF---ID F--YNYSGEG

      108 ███████████████████████████████████████████████████▐██████████████████████ 183
B145      VEKVFYEGVN FSPRRQYSCW DEGVDG-WIE FKTRFYTKLY QMAAASRCIK LIQ-LQPPTS LPALT--AAV CRT---GKQL
BRV       VEKVFYEGVN FSPRKQYSCW DEGVDG-WIE LKTRFYTKLY QMATTSRCIK LIQ-LQAPSS LPTLQ--AGV CRT---NKQL
B150      VEKVFYEGVN FSPHRQYSCY HEGTEG-WVE NKIRFYTQLY KMASTSRCIK LID-LESPSD WPSNR--LGH CLS---GRRI
P-MAR     VEKVFYEGVN FSPHRNYTCY QEGSSG-WVS NKVGFYSKLY SMASTSRCIK LIN-LDPPTN FTNYR--NGT CVGNGGTAKM
P10       VEKVFYEGVN FSPYRNYTCY QEGSFG-WVS NKVGFYSKLY SMASTSRCIK LIN-LDPPTN FTNYR--NGT CTGNGGTAKM
P4        VEKVFYEGVN FSPYRNYTCY HEGSSG-WVN NKAGFYTKLY QMSTTSRCIK LIT-LEPPEN IPSHS--PGM CNPQ--TNKM
C/MI/4/93 KHKVFYEGVN WSPHAAIDCY RKN----WTD IKLNFQKNIY ELASQSHCMS LVNALDKTIP LQATAGVAGN CNNSFLKNPA
C/JHG/66  KHKVFYEGVN WSPHAAINCY RKN----WTD IKLNFQKNIY ELASQSHCMS LVNALDKTIP LQVTAGTAGN CNNSFLKNPA
BCoV      QQIIFYEGVN FTPYHAFKCT TSGSNDIWMQ NKGLFYTQVY KNMAVYRSLT FVN---VPYV YNGSAQSTAL CKSG----SL
OC43      QQIIFYEGVN FTPYHAFKCN RSGSNDIWMQ NKGLFYTQVY KNMAVYRSLT FVN---VPYV YNGSAQATAL CKSG----SL
PHEV      QQIIFYEGVN FTPYHAFKCT SVGNNDIWMQ NKGLFYTQVY KKMAVYRSLT LVN---VPYV YNGSAQPTAL CKSG----SL
ECoV      QQIIFYEGVN FTPNHGFKCT ASGDNAVWMQ NKARFYEIVY RSMAVYRSLT FKT---VAYN YSGTAVATNL CKQS----SL
DVIM      SQIIFYEGVN FTPYVGFKCL NNGDNNRWMG NKARFYTQLY QKMAHYRSLS VIN---ITYT YNGSAGPVSM CKHIANGVTL
MHV-2     SQIIFYEGVN FTPYVGFKCM NNGDNNRWMG NKARFYTQLY QKMAHYRSLS IIN---VTYT YNGNATPVAM CKHTANGVTL
JHM       DQIVFYEGVN FSPNHGFKCL AYGDNKRWMG NKAAFYARVY EKMAQYRSLS FVN---VPYA YGGKAKPTSI CKHK----TL
RCoV      DQIIFYEGVN FSPSHGFKCL VEGDNNKWMG NKARFYALLY KKMAQYRSLS FVT---VPYA YGGNAKPTSI CKDK----TL
PuCoV     DQVIFYEGVN FSPSHGFKCL AEGDNKRWMG NKARFYALVY KKMAYYRSLS FVN---VSYS YGGKAKPTAI CKDN----TL
MHV-S     DQVIFYEGVN FSPSHGFKCL AYGDNKRWMG NKAAFYARVY EKMAQYRSLS FVN---VSYA YGGNAKPTSI CKDK----TL

      184 ████████████████████████████████████████████████████████████████████████ 255
B145      PDNPKFGLLA -DTNPTSVQF -VLPGSSGTT ICTKHLVPFC YL---NRGCF TT-----GGS CLPF-GVSYV SDSFYY--GY
BRV       PDNPRLALLS -DTVPTSVQF -VLPGSSGTT ICTKHLVPFC YL---NHGCF TT-----GGS CLPF-GVSYV SDSFYY--GY
B150      PDNPKLLVLN -SNISTFVQF -QLPSVSGDV RCDKHLVPFC YL---DHGCF TA-----DRY CHPF-GVFYE SSSFYF--GY
P-MAR     PDNPQLVIFD -AVTKLSTQF -VLPNSSDGV SCTKHLVPFC YI---DGGCF EM-----SGV CHPF-GYYYE SPSFYH--GF
P10       PDNPQLVIFN -SVVKVSTQF -VLPSSSDGF SCTKHLVPFC YI---DGGCF EM-----SGV CYPF-GYYYQ SPSFYH--AF
P4        PDNPRLITLT -NNASVSIQF -SLPAEFNGT NCTKHLVPFC YI---DGGCF QT-----SGF CHPF-GYSYS SSAFYY--GF
C/MI/4/93 LYTQEVTPPE -KCCGKENLAF FTLPTQFGTY ECRLHLVASC YFIYDSKEVY NK------RG CDNYFQLIY- -DSSGKVVGG
C/JHG/66  LYTQEVKPSE NKCGKENLAF FTLPTQFGTY ECKLHLVASC YFIYDSKEVY NK-----KRG CDNYFQVIY- -DSFGKVVGG
BCoV      VLNNP-AYIA -REANFGDYY YKVEADFYLS GCDEYIVPLC IF---NGKFL SN-----TKY YDDSQYYFNK DTGVIY--GL
OC43      VLNNP-AYIA -PQANSGDYY YKVEADFYLS GCDEYIVPLC IF---NGKFL SN-----TKY YDDSQYYFNK DTGVIY--GL
PHEV      ILNNP-AYIA -REANVGDYY YKSEADFSLS GCDEYIVPLC IF---NGKFL SN-----TKY YDDSQYYFNK DTGVIY--GL
ECoV      TMNNP-TFIA -KESGFTDYY YTSIANFSLQ GCDEYIIPLC YF---NGKFL SS-----SKY YDDSVYYFNI DTGEVF--GF
DVIM      TLNNP-TFIG -KEVSKPDYY YESEANFTLQ GCDEFIVPLC VF---NGQYL SS-----KLY YDDSQYYNV DTGVLY--GF
MHV-2     TLNNP-TFIG -KETSAPNYY YESEANFTLH GCDEFIVPLC VF---NGQYL SS-----KLY YDDSQYYYNI DTGILY--GF
JHM       TLNNP-TFIS -KESNYVDYY YESEANFTLA GCDEFIVPLC VF---NGHSK GSSSDPANKY YMDSQSYYNM DTGVLY--GL
RCoV      TLNNP-TFIS -KESNYVDYY YVSEANFTLQ GCDEFIVPLC VF---NGHSR GSSSDPANKY YTDSQSYYNI DTGVLY--GF
PuCoV     TLNNP-TFIS -KESNYVDYY YESDANFTLE GCDEFIVPLC VF---NGHSR GSSSDPANKY YMDSQMYYNM DTGVFY--GF
MHV-S     TLNNP-TFIS -KESNYVDYY YESEANFTLQ GCDEFIVTLC VS---NGHSK SSSSDPANKY YTDAQSYYNM DTGVLY--GF

      256 █████████████████████████████████████████████████████▐████████████████████████ 334
B145      YDA--TPQIG ST-EFHDYVC DYLFMEPGTY NASTVGKFLV YPTKSYCMDT MNITVPVQAV QSIWSEQYAS DDAIGQAC-K
BRV       YDA--TPQIG ST-ESHDYVC DYLFMEPGTY NASTVGKFLV YPTKSYCMDT MNITVPVQAV QSIWSEQYAS DDAIGQAC-K
B150      YDN--NKYSG S--EFHNFVC KYLLMEPGVY NASTAGKFLV FPTKSYCMDT INFTVPVQAV QSIWSQTRLS DDAIGLAC-K
P-MAR     YTN--GTA-G ----LHSYIC DYLEMKPGVY NATTFGKFLI YPTKSYCMDT MNYTVPVQAV QSIWSENRQS DDAIGQAC-K
P10       YTN--GTA-G ----LHRYIC DYLEMKPGVY NATTFGKFLI YPTKSYCMDT MNYTVPVQAV QSIWSENRQS DDAIGQAC-K
P4        YTE--GTPVG ----KHNYIC DYLEMKPGVY NATTFGKFLL YPTKTYCMDT MNITVPVQAV QSIWSQSRQS DDAIGMAC-K
C/MI/4/93 LDNRVSPYTG NTGDTPTMQC DMIQLKPGRY SVRSSPRFLL MPERSYCFD- MKEKGPVTAV QSIWGKDRKS DYAVDQACLS
C/JHG/66  LDNRVSPYTG NSGDTPTMQC DMLQLKPGRY SVRSSPRFLL MPERSYCFD- MKEKGPVTAV QSIWGKGRES DYAVDQACLS
BCoV      NST-ETITT- ----GFDFNC HYLVLPSGNY LAISNELLLT VPTKAICLNK RKDFTPVQVV DSRWNNARQS DNMTAVAC-Q
OC43      NST-ETITT- ----GFDLNC YYLVLPSGNY LAISNELLLT VPTKAICLNK RKDFTPVQVV DSRWNNARQS DNMTAVAC-Q
PHEV      NST-ETITT- ----GFDFNC HYLVLPSGNY LAISNELLLT VPTKAICLNK RKVFTPVQVV DSRWNNARQS DNMTAVAC-Q
ECoV      NST-RPTAD- ----GIDFNC FYYRVPSGLY QAISYELMLT VPSKIICLSK PKDFTPVQVV DSRWNSARRS DNMTAIAC-Q
DVIM      NST-LNITS- ----GLDLTC IYLALTPGNY ISISNELLLT VPSKAICLRK PKAFTPVQVV DSRWHSNRQS DNMTAIAC-Q
MHV-2     NSTLNITTG- -----LDLTC IYLSLAPGNY KAILNELLLT IPSKAICLRK PKVFTLVQVV DSRWHSNRQS DNMTAIAC-Q
JHM       NCT-LDVGNT AKDPGLDLTC RYLALTPGNY KAVSLEYLLS LPSKAICLRK PKRFMPVQVV DSRWNSTRQS DNMTAVAC-Q
RCoV      NST-LDVGNT AQNPGLDLTC MYLVLTPGNY KAVSLEYLLT IPSKAICLRK PKRFMPVQVV DSRWNSTRQS DNMTAVAC-Q
PuCoV     NST-LDVGNT AQNPGLDLTC IYYALTPGNY KAVSLEYLLT IPSKAICLRK PKRFMPVQVV DSRWNNAKHS DNMTAVAC-Q
MHV-S     NST-LDVGNT VQNPGLDLTC RYLALTPGNY KAVSLEYLLS LPSKAICLRK PKSFMPVQVV DSRWNSTRQS DNMTAVAC-Q
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          335 ▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆▆ 412
B145       APYCIFYNKT TSYTVTNGSD ANHGDDEVRM MMQGLLRNSS CISPQG-STP LALYSSQMIY LPNYGSCPQY YK--------
BRV        APYCIFYNKT TPYTVTNGSD ANHGDDEVRM MMQGLLRNSS CISPQG-STP LALYSTEMIY EPNYGSCPQF YK--------
B150       APYCIFFNKT HPYLAPNGSD ENHGDDEVRT MMQGLLVNSS CVSPQG-STP LALYSSQMIY SPNYGSCPQY YK--------
P-MAR      SPYCIFYNKT KPYLAPNGAD ENHGDEEVRQ MMQGLLVNSS CVSPQG-STP LALYSSEMIY IPNYGSCPQY YK--------
P10        SPYCIFYNKT KPYLAPNGAD ENHGDEEVRQ MMQGLLVNSS CVSPQG-STP LALYSSEMIY TPNYGSCPQY YK--------
P4         SPYCIFYNKT RPYLAPNGAD GNHGDEEVRQ MMQGLLVNSS CVSPQG-STP LALYSTEMIY TPNYGSCPQY YK--------
C/MI/4/93  TPGCMLIQKQ KPY--TGEAD DHHGDQEMRE LLSGLDYEAR CISQSGWVNE TSPFTEEYLL PPKFGRCPLA AKEESIPKIP
C/JHG/66   TPGCMLIQKQ KPY--IGEAD DHHGDQEMRE LLSGLDYEAR CISQSGWVNE TSPFTEKYLL PPKFGRCPLA AKEESIPKIP
BCoV       PPYCYFRNST TNY-VG-VYD INHGDAGFTS ILSGLLYDSP CFSQQGVFRY DNVSSVWPLY --SYGRCPTA ADINTP----
OC43       PPYCYFRNST TNY-VG-VYD INHGDAGFTS ILSGLLYNSP CFSQQGVFRY DNVSSVWPLY --PYGRCPTA ADINIP----
PHEV       LPYCYFRNST SNY-VG-IYD VNHGDAGFTS ILSGLLYDSP CFSQQGVFRY DNVSTVWPLF --PFGNCPTA ASIISS----
ECoV       LPYCYFRNST SDY-KG-VYD INHGDAGFTS ILSGLLYNSP CFSWQGVYRF DNVSTVWPLY P--FGKCPTA ANLANV----
DVIM       LPYCYFRNTT SDY-NG-VYD SHHGDAGFTS ILAGLMYNVS CLAQQGAFVY NNVSSSWPQY --PYGHCPTA ANIVFM----
MHV-2      LPYCYFRNAS NDY-NG-IYD SHHGDAGFTS ILSGLLYNVS CIAQQGAFLY NNVSASWPVF --GYGHCPTA ANIGYM----
JHM        LPYCFFRNTS ADY-SGGTHD VHHGDFHFRQ LLSGLLLNVS CIAQQGAFLY NNVSSSWPAY --GYGQCPTA ANIGYM----
RCoV       LPYCFFRNTS ADY-SGDTHD VHHGDFYFRQ LLSGLLYNVS CIAQQGAFLY NNVSSIWPVY --GYGHCPTA ANIGYM----
PuCoV      TPYCLFRNTS SGY-NGSTHD VHHGGFHFRK LLSGLLYNVS CIAQQGAFFY NNVSSQWPVL --GYGQCPTA ANIEFI----
MHV-S      LPYCFFRNTS ADY-SGGTHD VHHGDFHFRQ LLSGLLYNVS CIAQQGAFVY NNVSSSWPAY --GYGHCPTA ANIGYM----


          413 ▆▆▆▆▆▆▆▆▆▆▆▆▆▆ 424
B145       ---LFETSSD EN
BRV        ---LFDTSGN EN
B150       ---LFETSSD EN
P-MAR      ---LFETSSD EN
P10        ---LFETSSD EN
P4         ---LFEISSD EN
C/MI/4/93  DGLLIPTSGT DT
C/JHG/66   DGLLIPTSGT DT
BCoV       ---DVPICVY DP
OC43       ---DLPICVY DP
PHEV       ---DLPICVY DP
ECoV       ---DGPICVY DP
DVIM       ---A-PVCMY DP
MHV-2      ---A-PVCMY DP
JHM        ---A-PVCIY DP
RCoV       ---A-PVCLY DP
PuCoV      ---A-PVCLY DP
MHV-S      ---A-PVCIY DP
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Suppl. Fig. 1

Suppl. Fig. 1. Structure-based alignment of orthomyxo- and nidoviral HE proteins. Receptor-binding (R), fusion (F), and esterase domains (E) as identified for HEF by Rosenthal *et al.* (1998) are indicated by green, blue and red bars, respectively. The numbering of amino acid residues corresponds to that of HEF of Influenza C virus strain Johannesburg/66. Active site residues are shown in red. Residues, thought to form the oxyanion hole (corresponding to Gly^{85}, Asn^{117} and Arg^{322} of HEF), are shown in blue. BCoV: bovine coronavirus; OC43: human coronavirus OC43; PHEV: porcine hemagglutinating encephalomyelitis virus; ECoV: equine coronavirus; MHV: murine hepatitis virus (strains JHM, DVIM, -2 and -S; RCoV: rat sialodacryoadenitis coronavirus; PuCoV: puffinosis virus; C/MI/4/93: influenza C virus strain Miyagi; C/JHG/66: influenza C virus strain Johannesburg; BRV, B145, B150: bovine torovirus strains Breda, B145 and B150; P-MAR, P10, P4: porcine torovirus strains Markelo, P10 and P4.