Supplementary Fig. S1a

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                        10        20      80        90      100 110      120 190       200       210
                  ....|....|....|....|....|//|....|....|....|....|//|....|....|//|....|....|....|....|//
BOT72_143         ........................//...................D.//...........//......................//
BOT73_225         ........................//...................D.//...........//......................//
SAF65_103         ........................//...................D.//...........//......................//
SAF65_102         ........................//...................D.//...........//......................//
CNG70_46          ........................//...................D.//...........//......................//
CNG70_227         ........................//...................D.//...........//......................//
TAN65_kem         ........................//...................D.//...........//......................//
ETH72_16          ........................//...................D.//...........//......................//
ETH72_17          ........................//...................D.//...........//......................//
SOM77_1252        ........................//...................D.//...........//......................//
SOM77_1605        ........................//...................D.//...........//......................//
SOM77_ali         ........................//...................D.//...........//......................//
SUD47_jub         ........................//...................D.//...........//......................//
SUD47_rum         ........................//...................D.//...........//......................//
GER_hdlg          ........................//...................D.//...........//......................//
BSH74_nur         ......................I...//...................D.//...........//......................//
BSH74_shz         ......................I...//...................D.//...........//......................//
BSH74_sol         ......................I...//...................D.//...........//......................//
BSH75_banu        ......................I...//...................D.//...........//......................//
NEP73_175         ......................I...//...................D.//...........//......................//
UNK47_hig         ........................//...................D.//...........//......................//
IND53_mad         ........................//...................D.//...........//......................//
IND67_mah         ........................//...................D.//...........//............R....V...//
UNK46_hind        ........................//...................D.//...........//......................//
SUM70_222         ........................//...................D.//...........//......................//
SUM70_228         ........................//...................D.//...........//......................//
IND64_vel4        ........................//...................D.//...........//......................//
IND64_vel5        ........................//.....N.............D.//...........//......................//
IRN72_tbrz        ........................//...................D.//...........//......................//
AFG70_vlt4        ........................//...................D.//...........//......................//
YUG72_164         ........................//...................D.//...........//......................//
PAK69_lah         ........................//...................D.//...........//......................//
SYR72_119         ........................//...................D.//...........//......................//
KUW67_1629        ........................//...................D.//...........//......................//
UNK46_harv        ........................//...................D.//.......N...//......................//
CHN48_horn        ........................//...................D.//...........//......................//
JAP46_yam         ................S.......//...................D.//...........//......................//
JAP51_hrpr        ................S.......//...................D.//...........//......................//
JAP51_stwl        ................S.......//...................D.//...........//......................//
KOR47_lee         ........................//...................D.//...........//......................//
NIG69_001         MTRLSILLLLISLVYSTPYPQTQIS//DSPYDDLVTTITIKSLTAKAA//TSTTNDTDKVD//TSDIINTVSTSSGESTTDKTS//
GUI69_005         ........................//...................D.//...........//......................//
SLN68_258         ........................//...................D.//...........//......................//
BEN68_59          ........................//...................D.//...........//......................//
UNK52_but         ........................//...................D.//...........//......................//
BRZ66_39          ........................//...................D.//...........//..N...................//
BRZ66_gar         ........................//...................D.//...........//..N...................//
```

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```
                 230       240       250           290       300       310
                  |....|....|....|....|....|//|....|....|....|....|....|....|...*
BOT72_143         ................-----....//..A.............................*
BOT73_225         ................-----....//..A.............................*
SAF65_103         ................-----....//..A.............................*
SAF65_102         ................-----....//..A.............................*
CNG70_46          ................-----....//..A.............................*
CNG70_227         ................-----....//..A.............................*
TAN65_kem         ................-----....//..A.............................*
ETH72_16          ................-----....//..A.............................*
ETH72_17          ................-----....//..A.............................*
SOM77_1252        ....F...........-----....//..A.............................*
SOM77_1605        ....F...........-----....//..A.............................*
SOM77_ali         ....F...........-----....//..A.............................*
SUD47_jub         ................-----....//..A.............................*
SUD47_rum         ................-----....//..A.............................*
GER_hdlg          ................-----....//..A.............................*
BSH74_nur         ................-----....//..A.............................*
BSH74_shz         ................-----....//..A.............................*
BSH74_sol         ................-----....//..A.............................*
BSH75_banu        ................-----....//..A.............................*
NEP73_175         ................-----....//..A.............................*
UNK47_hig         ................-----....//..A.............................*
IND53_mad         ................-----....//..A.............................*
IND67_mah         ................-----....//..A.............................*
UNK46_hind        ................-----....//..A.............................*
SUM70_222         ................-----....//..A.............................*
SUM70_228         ................-----....//..A.............................*
IND64_vel4        ................-----....//..A.............................*
IND64_vel5        ................-----....//..A.............................*
IRN72_tbrz        ................-----....//..A.............................*
AFG70_vlt4        ................-----....//..A.............................*
YUG72_164         ................-----....//..A.............................*
PAK69_lah         ................-----....//..A.............................*
SYR72_119         ................-----....//..A.............................*
KUW67_1629        ................-----....//..A.............................*
UNK46_harv        ................-----....//..A.............................*
CHN48_horn        ................-----....//..A.............................*
JAP46_yam         ................-----....//..A.............................*
JAP51_hrpr        ................-----....//..A.............................*
JAP51_stwl        ................-----....//..A.............................*
KOR47_lee         ................-----....//..A.............................*
NIG69_001         VSTSSEIVTTKSTANDADLYDTHNDN//GIVALIILSAVAIFCITYYICNKRSRKYKTENKV*
GUI69_005         ....F...................//...............................*
SLN68_258         ....F...................//...............................*
BEN68_59          .......................//...............................*
UNK52_but         .......................//...............................*
BRZ66_39          .......................//...............................*
BRZ66_gar         .......................//.........................Q.....*
```

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Supplementary Fig. S1b

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                         10 70       80 130      140 210       220       230 270      280 310      320     380
                  ....|....|//|....|....|//|....|....|//|....|....|....|....|//|....|....|//|....|....|//|....|....|//
BOT72_143         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
BOT73_225         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
SAF65_103         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
SAF65_102         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
CNG70_46          ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
CNG70_227         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
TAN65_kem         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
ETH72_16          ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
ETH72_17          ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
SOM77_1252        ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
SOM77_1605        ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
SOM77_ali         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
SUD47_jub         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
SUD47_rum         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
GER_hdlg          ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
BSH74_nur         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
BSH74_shz         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
BSH74_sol         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
BSH75_banu        ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
NEP73_175         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
UNK47_hig         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
IND53_mad         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
IND67_mah         ..........//....S......//..........//..Q.......T.....T....//.......T...//...........//....E......//
UNK46_hind        ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
SUM70_222         ..........//....S......//..........//..........T.....T....//.......T...//......V....//....E......//
SUM70_228         ..........//....S......//..........//..........T.....T....//.......T...//......V....//....E......//
IND64_vel4        ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
IND64_vel5        ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
IRN72_tbrz        ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
AFG70_vlt4        ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
YUG72_164         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
PAK69_lah         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
SYR72_119         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
KUW67_1629        ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
UNK46_harv        ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
CHN48_horn        ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
JAP46_yam         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
JAP51_hrpr        ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
JAP51_stwl        ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
KOR47_lee         ..........//....S......//..........//..........T.....T....//.......T...//...........//....E......//
NIG69_001         MLNRVQILMK//KLRSLPPIPMS//SISEINEWLSS//WARISSSLDQRHIKTIAVSVY//DIMTSTRNIIL//LISSDGARVIW//YEAFKTQSGAL//
GUI69_005         ..........//..........//..........//....................//...........//...........//...........//
SLN68_258         ..........//..........//..........//....................//...........//...........//...........//
BEN68_59          ..........//..........//..........//....................//...........//...........//...........//
UNK52_but         ..........//..........//......K....//..........T.........//.......T...//...........//...........//
BRZ66_39          ..........//..........//......K....//..........T.........//.......T...//...........//...........//
BRZ66_gar         ..........//..........//......K....//..........T.........//.......T...//...........//...........//
```

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```
                  410       420     540       550     620       630
                 //|....|....|....|//|....|....|//|....|....|....|....|.
BOT72_143        //................//..E........//....................*
BOT73_225        //................//..E........//....................*
SAF65_103        //................//..E........//....................*
SAF65_102        //................//..E........//....................*
CNG70_46         //................//..E........//....................*
CNG70_227        //................//..E........//....................*
TAN65_kem        //................//..E........//....................*
ETH72_16         //................//..E........//....................*
ETH72_17         //................//..E........//....................*
SOM77_1252       //................//..E........//....................*
SOM77_1605       //................//..E........//....................*
SOM77_ali        //................//..E........//....................*
SUD47_jub        //................//..E........//....................*
SUD47_rum        //................//..E........//....................*
GER_hdlg         //................//..E........//....................*
BSH74_nur        //................//..........//....................*
BSH74_shz        //................//..........//....................*
BSH74_sol        //................//..........//....................*
BSH75_banu       //................//..........//....................*
NEP73_175        //................//..........//....................*
UNK47_hig        //................//..E........//....................*
IND53_mad        //................//..E........//....................*
IND67_mah        //................//..E........//....................*
UNK46_hind       //................//..E........//....................*
SUM70_222        //................//..E........//....................*
SUM70_228        //................//..E........//....................*
IND64_vel4       //........E......//..E........//....................*
IND64_vel5       //........E......//..E........//....................*
IRN72_tbrz       //................//..E........//....................*
AFG70_vlt4       //................//..E........//....................*
YUG72_164        //................//..E........//....................*
PAK69_lah        //................//..E........//....................*
SYR72_119        //................//..E........//....................*
KUW67_1629       //................//..E........//....................*
UNK46_harv       //................//..E........//....................*
CHN48_horn       //................//..E........//....................*
JAP46_yam        //................//..E........//....................*
JAP51_hrpr       //................//..E........//....................*
JAP51_stwl       //................//..E........//....................*
KOR47_lee        //................//..E........//....................*
NIG69_001        //NRVSKNTGMGMYYPTN//IPKLKDCLLDS//ELYIRSSYKDINEVMSQMVKL*
GUI69_005        //................//..........//....................*
SLN68_258        //................//..........//....................*
BEN68_59         //................//..........//....................*
UNK52_but        //................//..........//....C...............*
BRZ66_39         //................//..........//....C...............*
BRZ66_gar        //................//..........//....C...............*
```

Supplementary Fig. S1. Amino acid alignment of 47 variola virus homologues of vaccinia virus IEV and EEV proteins. (a) Variola virus homologues of vaccinia virus A56 (haemagglutinin). (b) Variola virus homologues of vaccinia virus F12. //, Areas of complete homology that are deleted from the alignment; ·, identical amino acids; -, gaps within the coding region; *, open reading frame terminations.

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