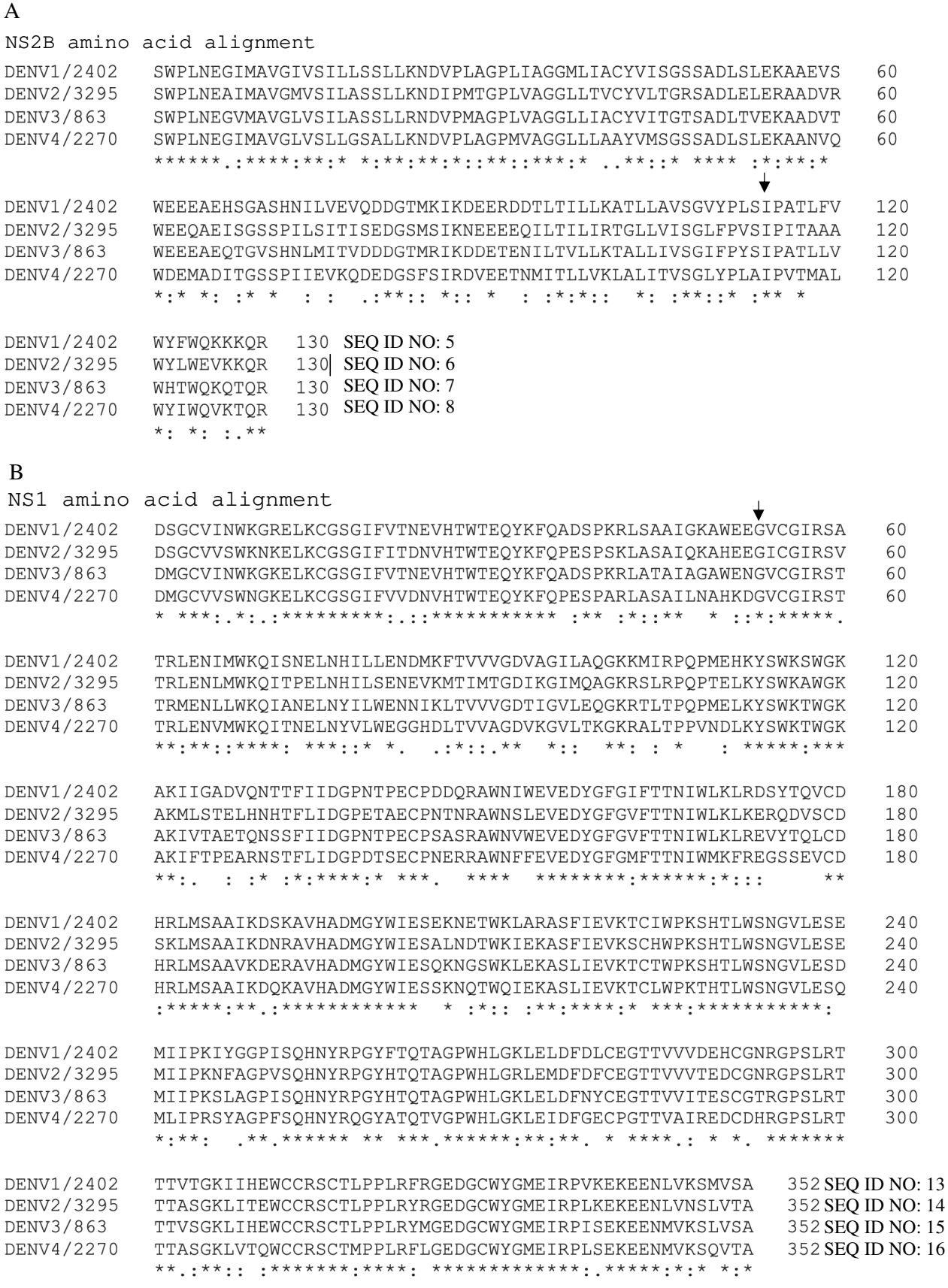
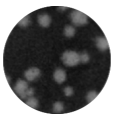
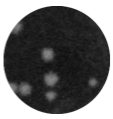
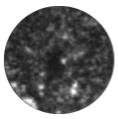
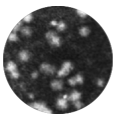
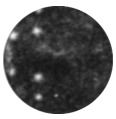
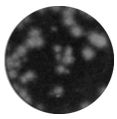
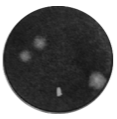
**FIG. 1**

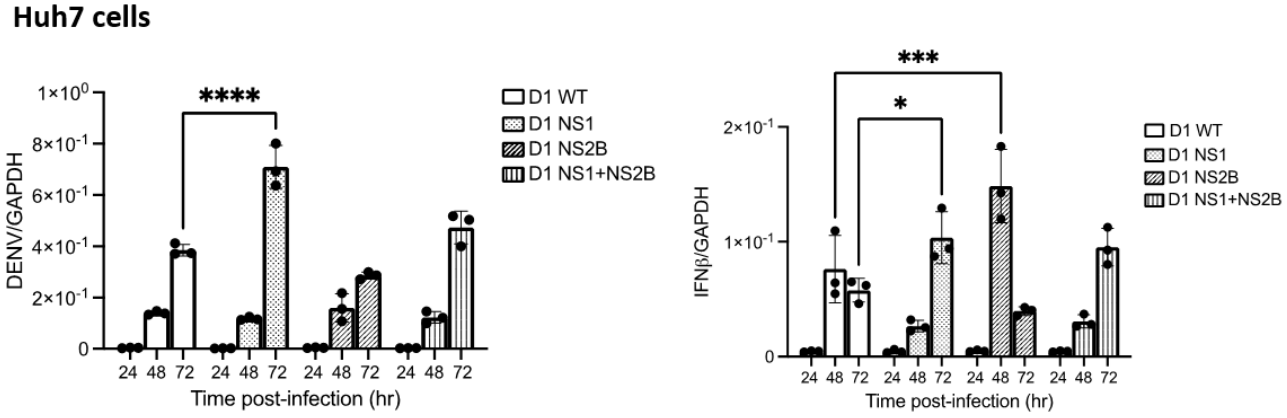

A
NS2B amino acid alignment
DENV1/2402 SWPLNEGIMAVGIVSILLSSLLKNDVPLAGPLIAGGMLIACYVISGSSADLSLEKAAEVS 60
DENV2/3295 SWPLNEAIMAVGMVSILASSLLKNDIPMTGPLVAGGLLTVCYVLTGRSADLELERAADVR 60
DENV3/863 SWPLNEGVMAVGLVSILASSLLRNDVPMAGPLVAGGLLIACYVITGTSADLTVEKAADVT 60
DENV4/2270 SWPLNEGIMAVGLVSLLGSALLKNDVPLAGPMVAGGLLLAAYVMSGSSADLSLEKAANVQ 60
DENV1/2402 WEEEAEHSGASHNILVEVQDDGTMKIKDEERDDTLTILLKATLLAVSGVYPLSIPATLFV 120
DENV2/3295 WEEQAEISGSSPILSITISEDGSMSIKNEEEEQILTILIRTGLLVISGLFPVSIPITAAA 120
DENV3/863 WEEEAEQTGVSHNLMITVDDDGTMRIKDDETENILTVLLKTALLIVSGIFPYSIPATLLV 120
DENV4/2270 WDEMADITGSSPIIEVKQDEDGSFSIRDVEETNMITLLVKLALITVSGLYPLAIPVTMAL 120
DENV1/2402 WYFWQKKKQR 130 SEQ ID NO: 5
DENV2/3295 WYLWEVKKQR 130 SEQ ID NO: 6
DENV3/863 WHTWQKQTQR 130 SEQ ID NO: 7
DENV4/2270 WYIWQVKTQR 130 SEQ ID NO: 8
B
NS1 amino acid alignment
DENV1/2402 DSGCVINWKGRELKCGSGIFVTNEVHTWTEQYKFQADSPKRLSAAIGKAWEEGVCGIRSA 60
DENV2/3295 DSGCVVSWKNKELKCGSGIFITDNVHTWTEQYKFQPESPSKLASAIQKAHEEGICGIRSV 60
DENV3/863 DMGCVINWKGKELKCGSGIFVTNEVHTWTEQYKFQADSPKRLATAIAGAWENGVCGIRST 60
DENV4/2270 DMGCVVSWNGKELKCGSGIFVVDNVHTWTEQYKFQPESPARLASAILNAHKDGVCGIRST 60
DENV1/2402 TRLENIMWKQISNELNHILLENDMKFTVVVGDVAGILAQGKKMIRPQPMEHKYSWKSWGK 120
DENV2/3295 TRLENLMWKQITPELNHILSENEVKMTIMTGDIKGIMQAGKRSLRPQPTELKYSWKAWGK 120
DENV3/863 TRMENLLWKQIANELNYILWENNIKLTVVVGDTIGVLEQGKRTLTPQPMELKYSWKTWGK 120
DENV4/2270 TRLENVMWKQITNELNYVLWEGGHDLTVVAGDVKGVLTKGKRALTPPVNDLKYSWKTWGK 120
DENV1/2402 AKIIGADVQNTTFIIDGPNTPECPDDQRAWNIWEVEDYGFGIFTTNIWLKLRDSYTQVCD 180
DENV2/3295 AKMLSTELHNHTFLIDGPETAECPNTNRAWNSLEVEDYGFGVFTTNIWLKLKERQDVSCD 180
DENV3/863 AKIVTAETQNSSFIIDGPNTPECPSASRAWNVWEVEDYGFGVFTTNIWLKLREVYTQLCD 180
DENV4/2270 AKIFTPEARNSTFLIDGPDTSECPNERRAWNFFEVEDYGFGMFTTNIWMKFREGSSEVCD 180
DENV1/2402 HRLMSAAIKDSKAVHADMGYWIESEKNETWKLARASFIEVKTCIWPKSHTLWSNGVLESE 240
DENV2/3295 SKLMSAAIKDNRAVHADMGYWIESALNDTWKIEKASFIEVKSCHWPKSHTLWSNGVLESE 240
DENV3/863 HRLMSAAVKDERAVHADMGYWIESQKNGSWKLEKASLIEVKTCTWPKSHTLWSNGVLESD 240
DENV4/2270 HRLMSAAIKDQKAVHADMGYWIESSKNQTWQIEKASLIEVKTCLWPKTHTLWSNGVLESQ 240
DENV1/2402 MIIPKIYGGPISQHNYRPGYFTQTAGPWHLGKLELDFDLCEGTTVVVDEHCGNRGPSLRT 300
DENV2/3295 MIIPKNFAGPVSQHNYRPGYHTQTAGPWHLGRLEMDFDFCEGTTVVVTEDCGNRGPSLRT 300
DENV3/863 MIIPKSLAGPISQHNYRPGYHTQTAGPWHLGKLELDFNYCEGTTVVITESCGTRGPSLRT 300
DENV4/2270 MLIPRSYAGPFSQHNYRQGYATQTVGPWHLGKLEIDFGECPGTTVAIREDCDHRGPSLRT 300
DENV1/2402 TTVTGKIIHEWCCRSCTLPPLRFRGEDGCWYGMEIRPVKEKEENLVKSMVSA 352 SEQ ID NO: 13
DENV2/3295 TTASGKLITEWCCRSCTLPPLRYRGEDGCWYGMEIRPLKEKEENLVNSLVTA 352 SEQ ID NO: 14
DENV3/863 TTVSGKLIHEWCCRSCTLPPLRYMGEDGCWYGMEIRPISEKEENMVKSLVSA 352 SEQ ID NO: 15
DENV4/2270 TTASGKLVTQWCCRSCTMPPLRFLGEDGCWYGMEIRPLSEKEENMVKSQVTA 352 SEQ ID NO: 16

A

**FIG. 2**

| DENV1 | Parent strain (WT) | prM-29 | NS1-53 | NS2B-114 | NS1+NS2B | prM+NS1 | prM+NS2B |
|---|---|---|---|---|---|---|---|
| Plaque size |  |  |  |  |  |  |  |
| Passage 1 | - | 29V | 53D | NS2B-114I/T | NS1-53D, NS2B-114I/T | prM-29V NS1-53D | prM-29V NS2B-114T |
| Passage 2 | - | 29V | 53D | NS2B-114I/T | NS1-53D, NS2B-114I/T | prM-29V NS1-53D | prM-29V NS2B-114T |

B



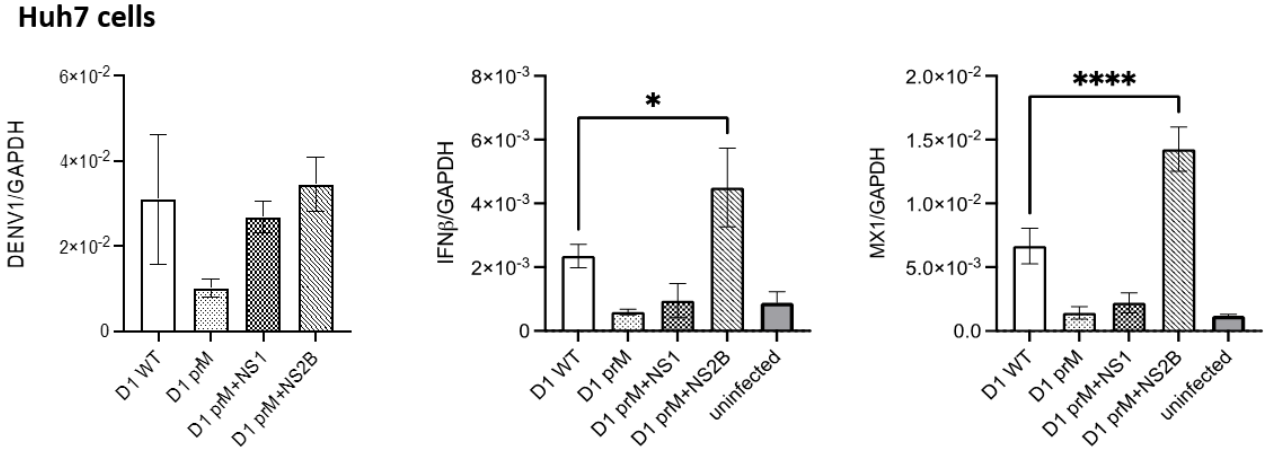
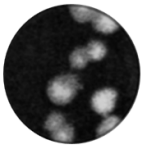
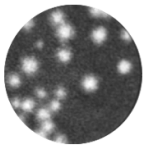
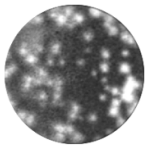
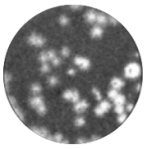



**FIG. 3**

A

| DENV2 | Parent strain (WT) | NS1-53 | NS2B-114 | NS1+NS2B |
|---|---|---|---|---|
| Plaque Size |  |  |  |  |
| Passage 1 | - | 53D | 114T | 53D, 114T |
| Passage 2 | - | 53G/D | 114T | 53D, 114T |
| Passage 4 | - | 53G | 114T | 53D, 114T |

B

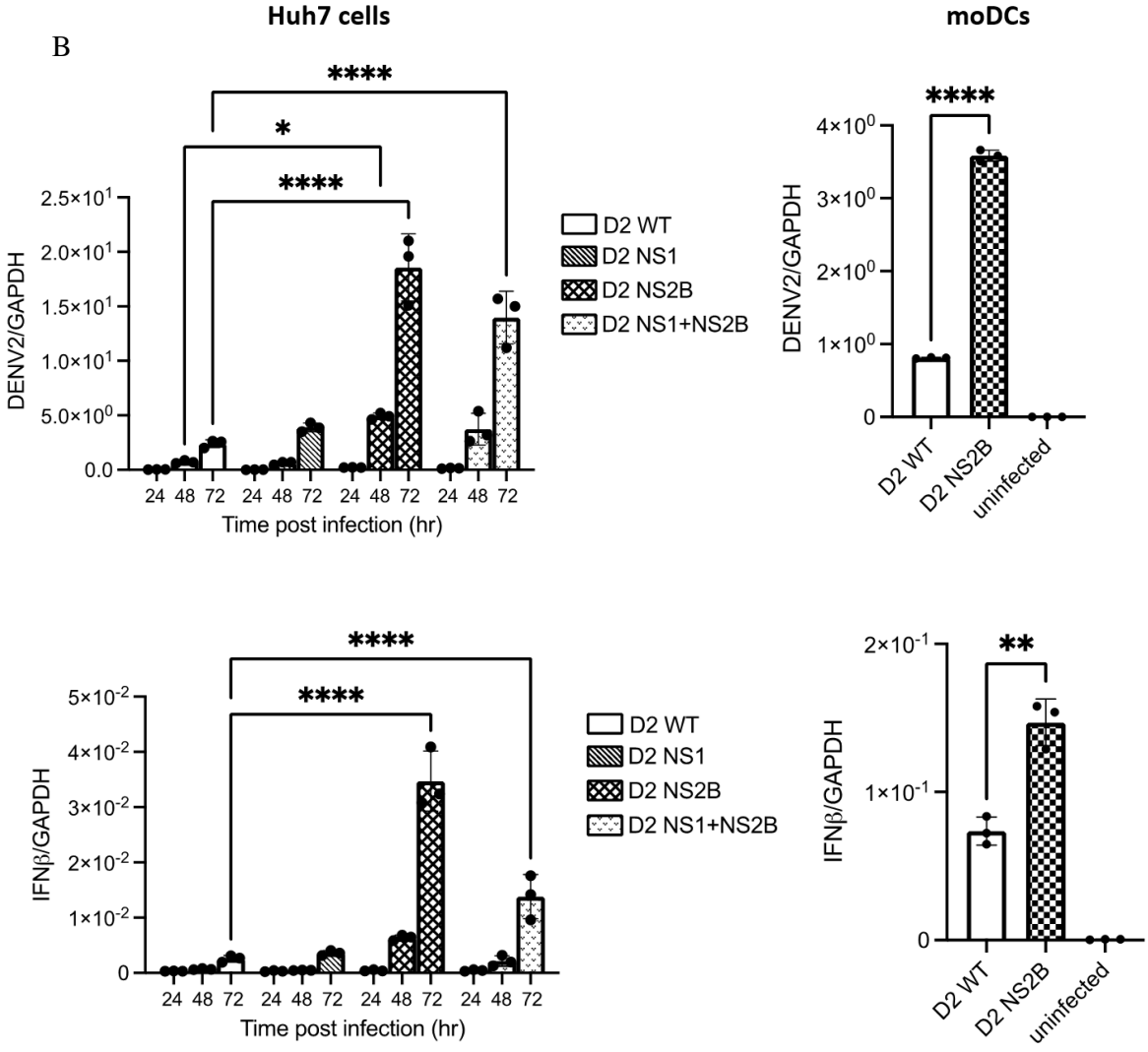
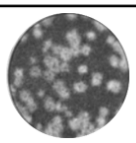
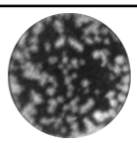
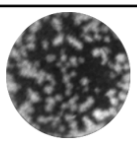
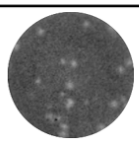
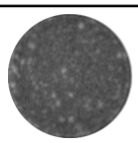
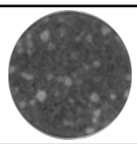


**FIG. 4**

A

| DENV3 | Parent strain (WT) | prM-29 | NS1-53 | NS2B-114 | NS1+NS2B | prM+NS2B |
|---|---|---|---|---|---|---|
| Plaque size |  |  |  |  |  |  |
| Passage1 | - | 29V | 53D | 114T | 53D, 114T | 29V, 114T |
| Passage 2 | - | 29V | 53G/D | 114T | 53D, 114T | 29V, 114T |
| Passage 4 | - | 29V | 53G/D | 114I/T | 53D, 114T | 29V, 114T |

B

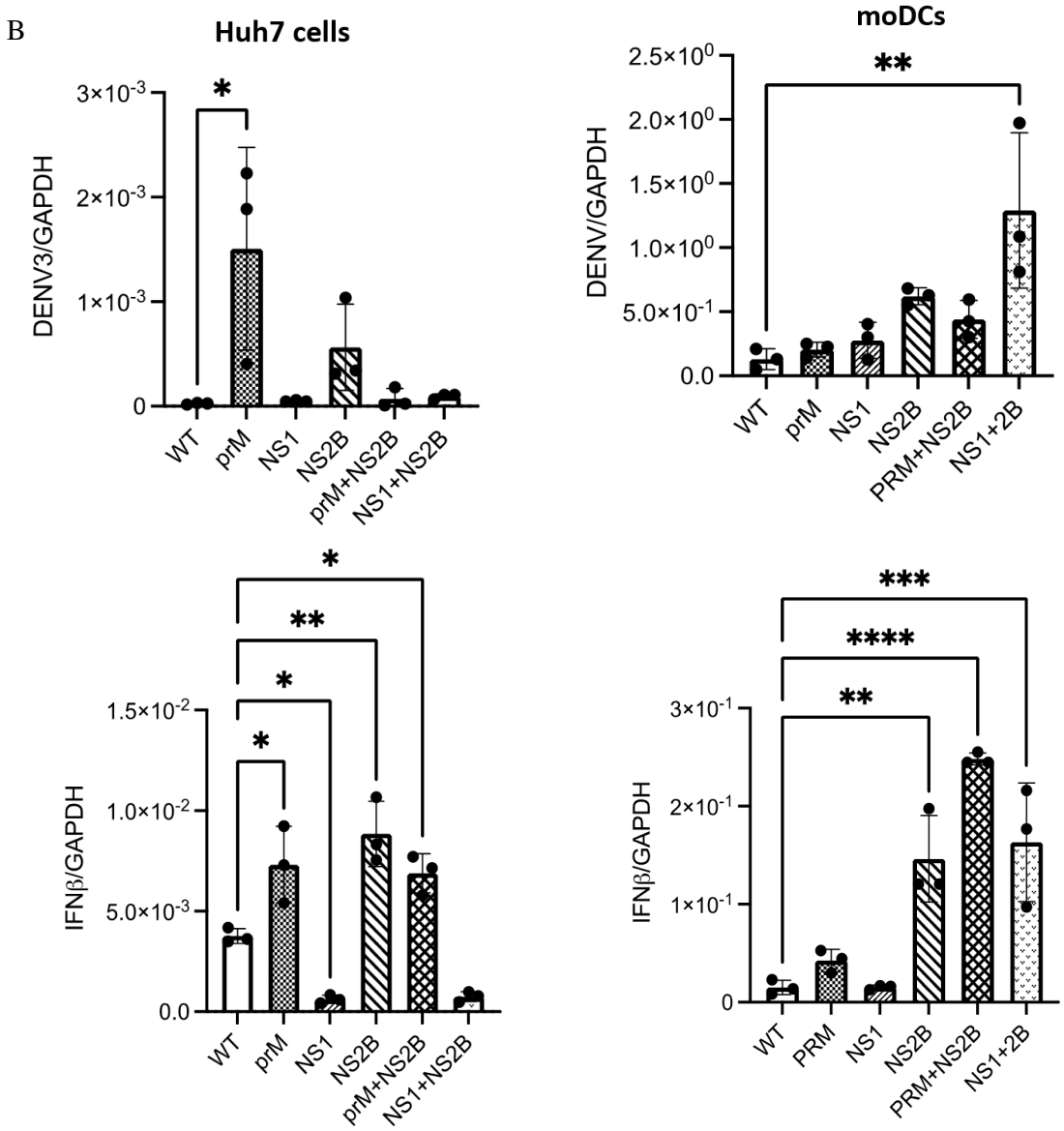
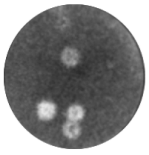
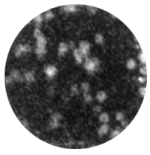
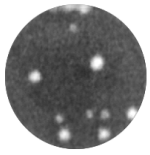
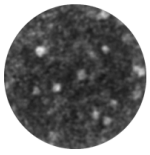


**Fig. 5**

A

| DENV4 | Parent strain (WT) | NS1-53 | NS2B-114 | NS1+NS2B |
|---|---|---|---|---|
| Plaque Size |  |  |  |  |
| Passage 1 | - | 53D | 114T | 53D, 114T |
| Passage 2 | - | 53D | 114T | 53D, 114T |

B

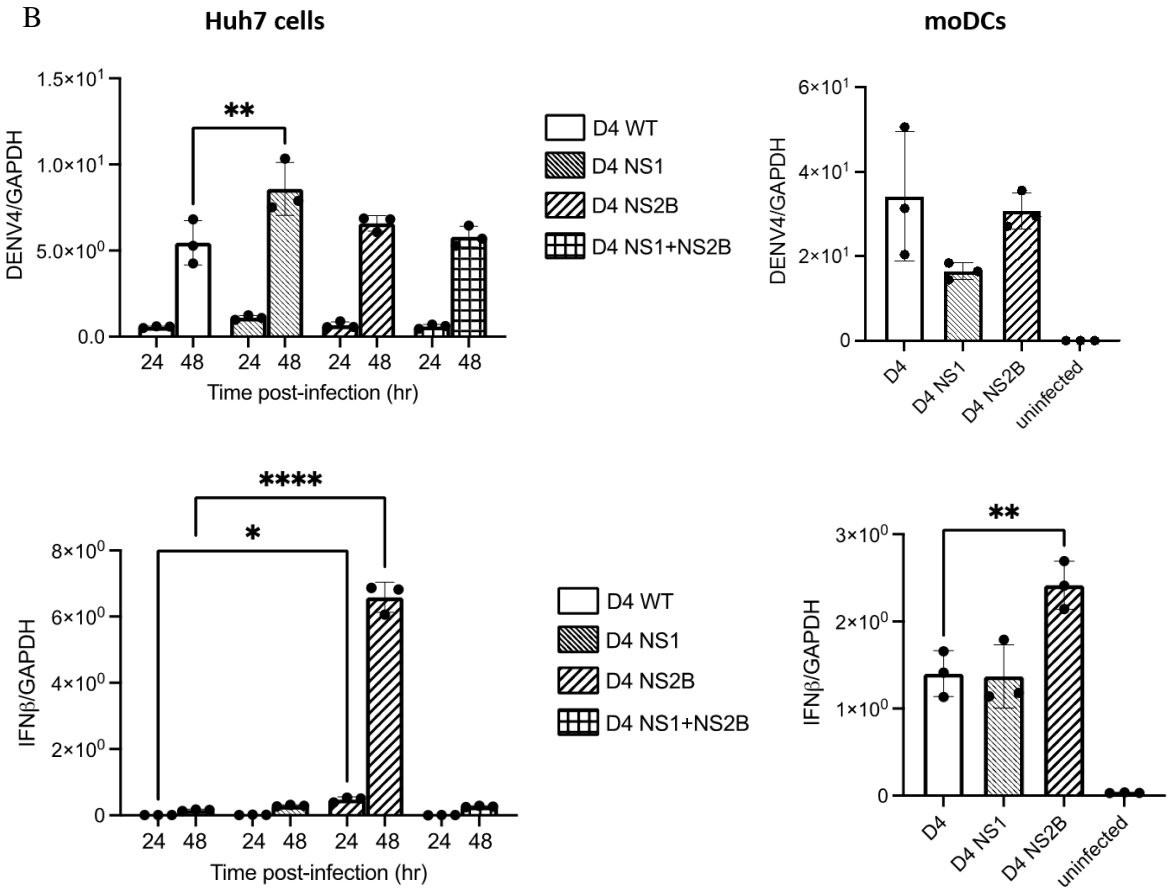
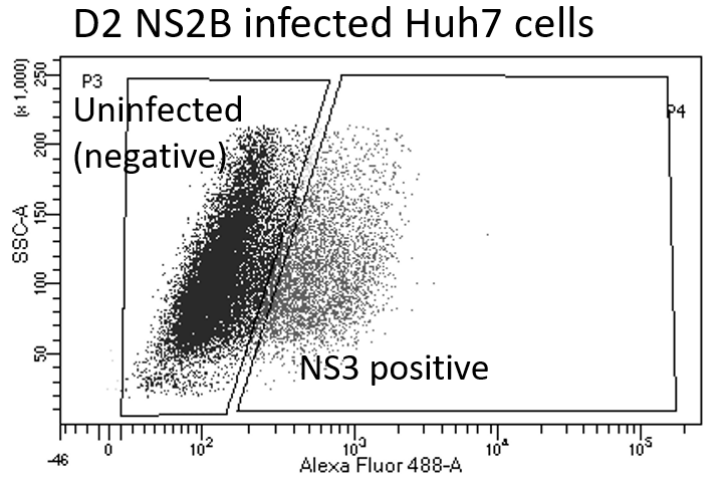


**Fig. 6**

A


D2 NS2B infected Huh7 cells
P3
Uninfected
(negative)
P4
NS3 positive
SSC-A
(x 1,000)
Alexa Fluor 488-A

B

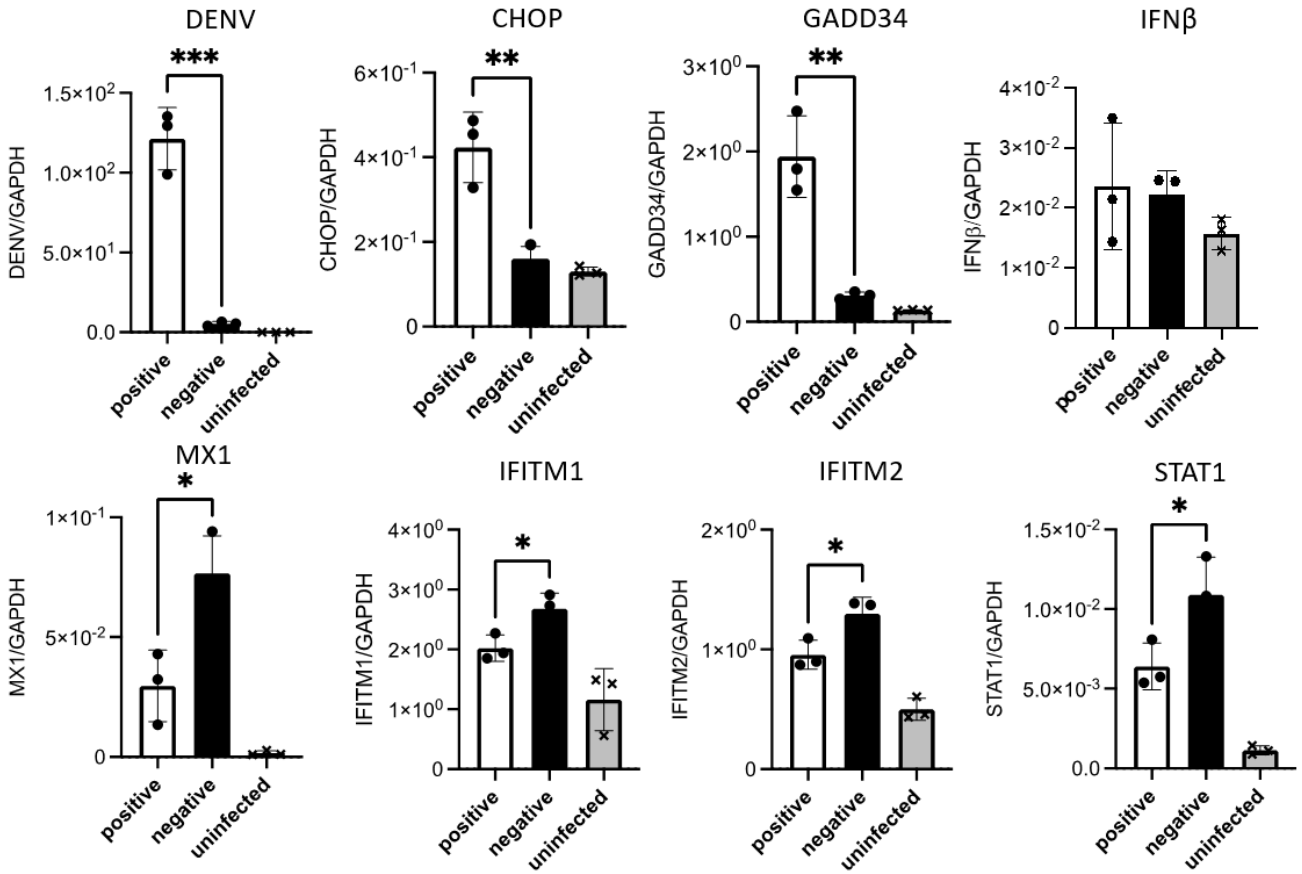

DENV
DENV/GAPDH
CHOP
CHOP/GAPDH
GADD34
GADD34/GAPDH
IFNβ
IFNβ/GAPDH
MX1
MX1/GAPDH
IFITM1
IFITM1/GAPDH
IFITM2
IFITM2/GAPDH
STAT1
STAT1/GAPDH
positive
negative
uninfected

**FIG. 7**

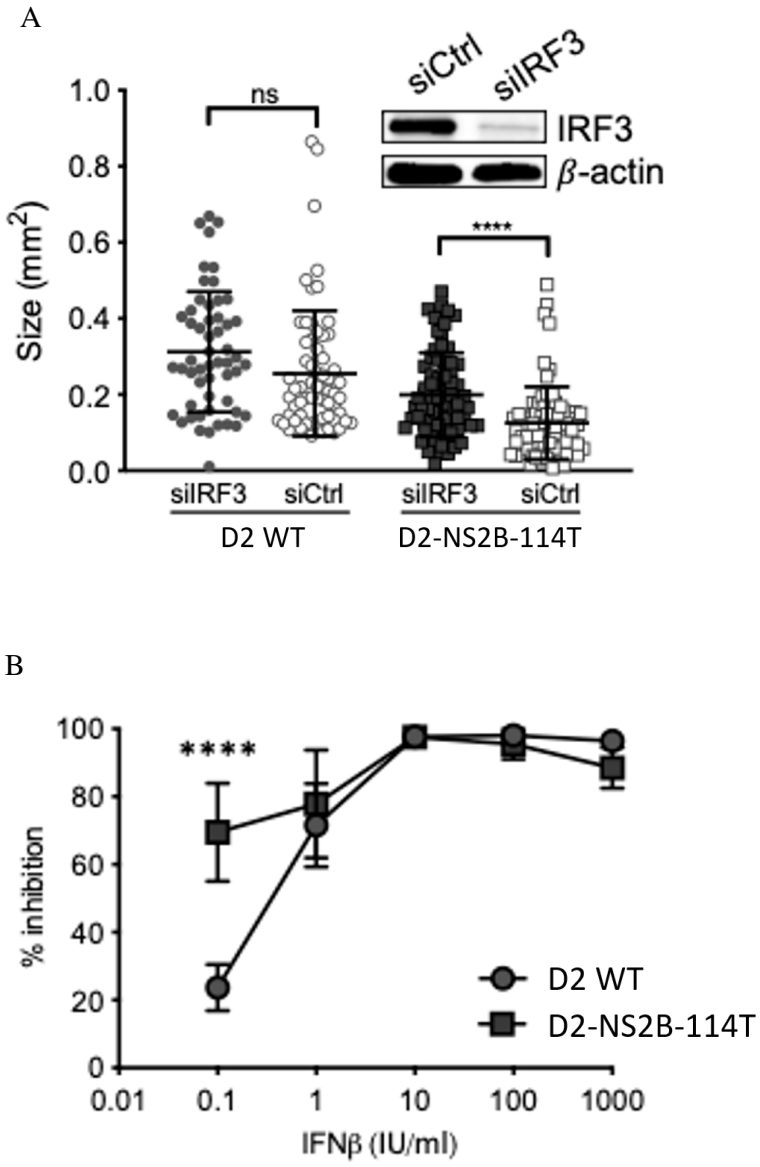
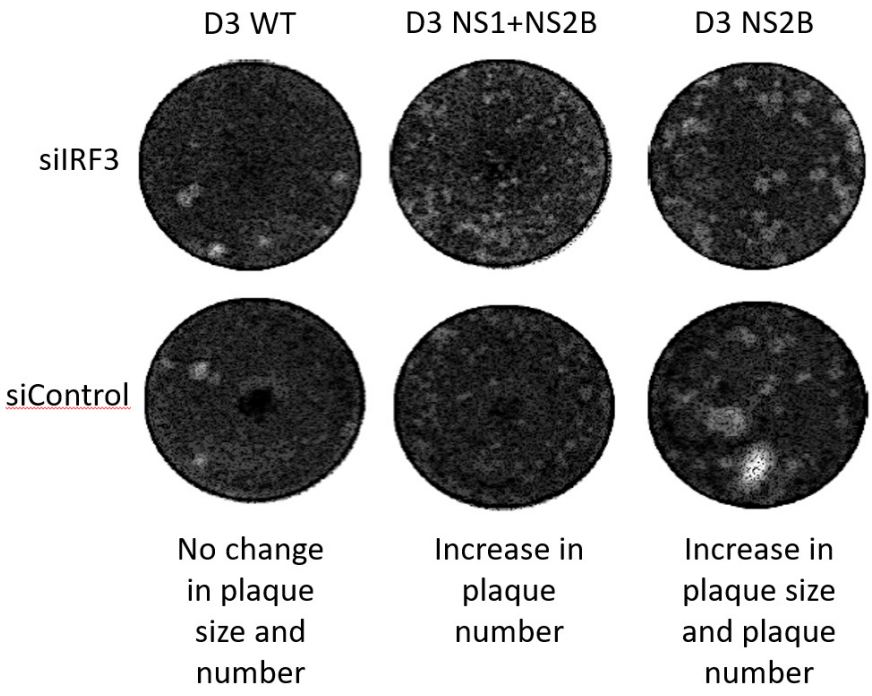

A
siCtrl
siIRF3
IRF3
β-actin
ns
****
Size (mm2)
1.0
0.8
0.6
0.4
0.2
0.0
siIRF3
siCtrl
siIRF3
siCtrl
D2 WT
D2-NS2B-114T
B
****
% inhibition
100
80
60
40
20
0
0.01
0.1
1
10
100
1000
IFNβ (IU/ml)
D2 WT
D2-NS2B-114T

**FIG. 8**


D3 WT
D3 NS1+NS2B
D3 NS2B
siIRF3
siControl
No change in plaque size and number
Increase in plaque number
Increase in plaque size and plaque number

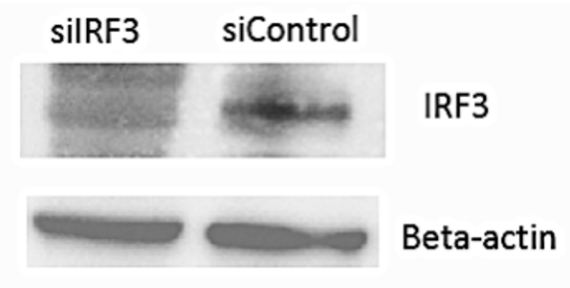

siIRF3
siControl
IRF3
Beta-actin

**Fig. 9**

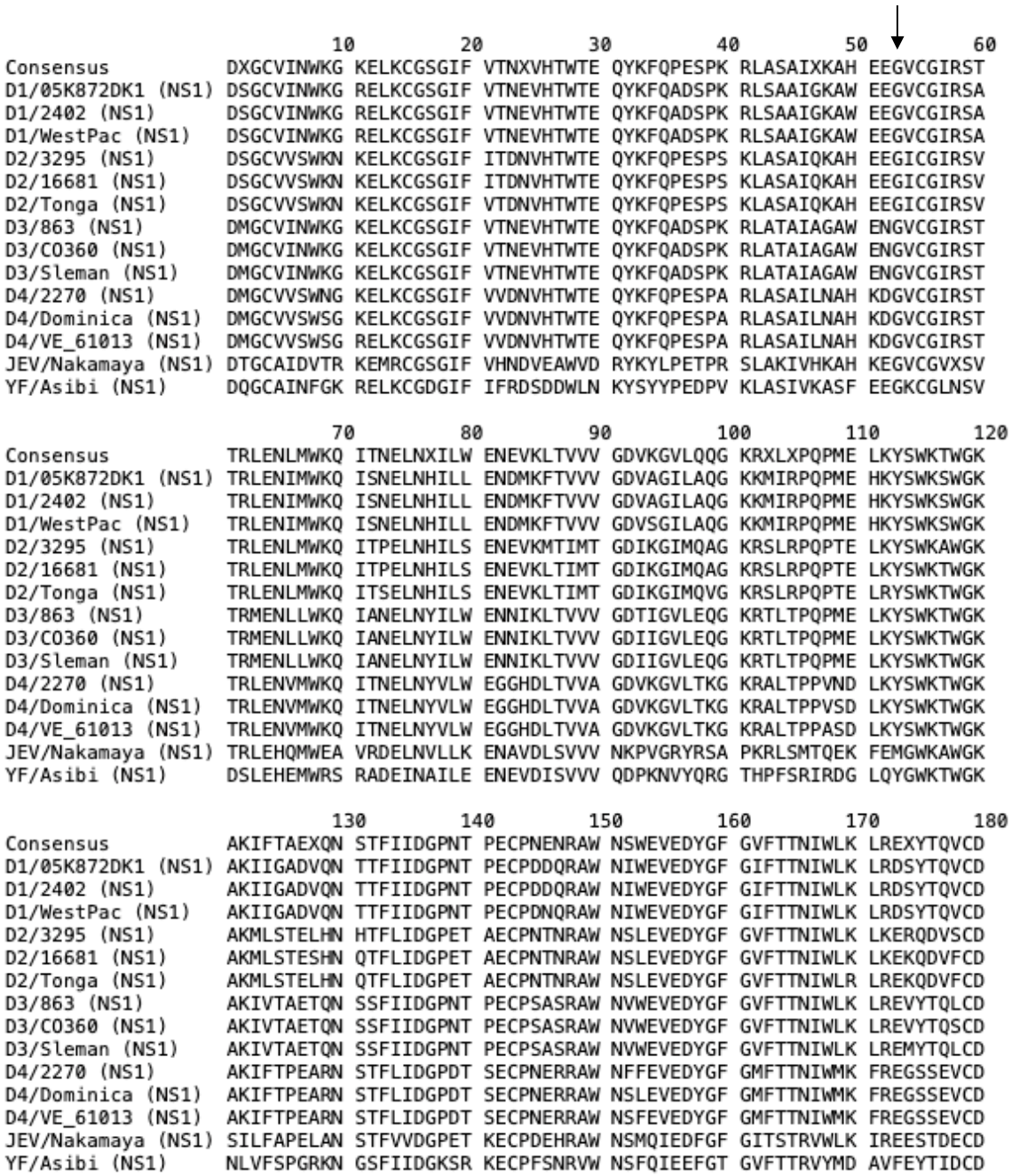

10 20 30 40 50 60
Consensus DXGCVINWKG KELKCGSGIF VTNXVHTWTE QYKFQPESPK RLASAIXKAH EEGVCGIRST
D1/05K872DK1 (NS1) DSGCVINWKG RELKCGSGIF VTNEVHTWTE QYKFQADSPK RLSAAIGKAW EEGVCGIRSA
D1/2402 (NS1) DSGCVINWKG RELKCGSGIF VTNEVHTWTE QYKFQADSPK RLSAAIGKAW EEGVCGIRSA
D1/WestPac (NS1) DSGCVINWKG RELKCGSGIF VTNEVHTWTE QYKFQADSPK RLSAAIGKAW EEGVCGIRSA
D2/3295 (NS1) DSGCVVSWKN KELKCGSGIF ITDNVHTWTE QYKFQPESPS KLASAIQKAH EEGICGIRSV
D2/16681 (NS1) DSGCVVSWKN KELKCGSGIF ITDNVHTWTE QYKFQPESPS KLASAIQKAH EEGICGIRSV
D2/Tonga (NS1) DSGCVVSWKN KELKCGSGIF VTDNVHTWTE QYKFQPESPS KLASAIQKAH EEGICGIRSV
D3/863 (NS1) DMGCVINWKG KELKCGSGIF VTNEVHTWTE QYKFQADSPK RLATAIAGAW ENGVCGIRST
D3/CO360 (NS1) DMGCVINWKG KELKCGSGIF VTNEVHTWTE QYKFQADSPK RLATAIAGAW ENGVCGIRST
D3/Sleman (NS1) DMGCVINWKG KELKCGSGIF VTNEVHTWTE QYKFQADSPK RLATAIAGAW ENGVCGIRST
D4/2270 (NS1) DMGCVVSWNG KELKCGSGIF VVDNVHTWTE QYKFQPESPA RLASAILNAH KDGVCGIRST
D4/Dominica (NS1) DMGCVVSWSG KELKCGSGIF VVDNVHTWTE QYKFQPESPA RLASAILNAH KDGVCGIRST
D4/VE_61013 (NS1) DMGCVVSWSG RELKCGSGIF VVDNVHTWTE QYKFQPESPA RLASAILNAH KDGVCGIRST
JEV/Nakamaya (NS1) DTGCAIDVTR KEMRCGSGIF VHNDVEAWVD RYKYLPETPR SLAKIVHKAH KEGVCGVXSV
YF/Asibi (NS1) DQGCAINFGK RELKCGDGIF IFRDSDDWLN KYSYYPEDPV KLASIVKASF EEGKCGLNSV
70 80 90 100 110 120
Consensus TRLENLMWKQ ITNELNXILW ENEVKLTVVV GDVKGVLQQG KRXLXPQPME LKYSWKTWGK
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D1/2402 (NS1) TRLENIMWKQ ISNELNHILL ENDMKFTVVV GDVAGILAQG KKMIRPQPME HKYSWKSWGK
D1/WestPac (NS1) TRLENIMWKQ ISNELNHILL ENDMKFTVVV GDVSGILAQG KKMIRPQPME HKYSWKSWGK
D2/3295 (NS1) TRLENLMWKQ ITPELNHILS ENEVKMTIMT GDIKGIMQAG KRSLRPQPTE LKYSWKAWGK
D2/16681 (NS1) TRLENLMWKQ ITPELNHILS ENEVKLTIMT GDIKGIMQAG KRSLRPQPTE LKYSWKTWGK
D2/Tonga (NS1) TRLENLMWKQ ITSELNHILS ENEVKLTIMT GDIKGIMQVG KRSLRPQPTE LRYSWKTWGK
D3/863 (NS1) TRMENLLWKQ IANELNYILW ENNIKLTVVV GDTIGVLEQG KRTLTPQPME LKYSWKTWGK
D3/CO360 (NS1) TRMENLLWKQ IANELNYILW ENNIKLTVVV GDIIGVLEQG KRTLTPQPME LKYSWKTWGK
D3/Sleman (NS1) TRMENLLWKQ IANELNYILW ENNIKLTVVV GDIIGVLEQG KRTLTPQPME LKYSWKTWGK
D4/2270 (NS1) TRLENVMWKQ ITNELNYVLW EGGHDLTVVA GDVKGVLTKG KRALTPPVND LKYSWKTWGK
D4/Dominica (NS1) TRLENVMWKQ ITNELNYVLW EGGHDLTVVA GDVKGVLTKG KRALTPPVSD LKYSWKTWGK
D4/VE_61013 (NS1) TRLENVMWKQ ITNELNYVLW EGGHDLTVVA GDVKGVLTKG KRALTPPASD LKYSWKTWGK
JEV/Nakamaya (NS1) TRLEHQMWEA VRDELNVLLK ENAVDLSVVV NKPVGRYRSA PKRLSMTQEK FEMGWKAWGK
YF/Asibi (NS1) DSLEHEMWRS RADEINAILE ENEVDISVVV QDPKNVYQRG THPFSRIRDG LQYGWKTWGK
130 140 150 160 170 180
Consensus AKIFTAEXQN STFIIDGPNT PECPNENRAW NSWEVEDYGF GVFTTNIWLK LREXYTQVCD
D1/05K872DK1 (NS1) AKIIGADVQN TTFIIDGPNT PECPDDQRAW NIWEVEDYGF GIFTTNIWLK LRDSYTQVCD
D1/2402 (NS1) AKIIGADVQN TTFIIDGPNT PECPDDQRAW NIWEVEDYGF GIFTTNIWLK LRDSYTQVCD
D1/WestPac (NS1) AKIIGADVQN TTFIIDGPNT PECPDNQRAW NIWEVEDYGF GIFTTNIWLK LRDSYTQVCD
D2/3295 (NS1) AKMLSTELHN HTFLIDGPET AECPNTNRAW NSLEVEDYGF GVFTTNIWLK LKERQDVSCD
D2/16681 (NS1) AKMLSTESHN QTFLIDGPET AECPNTNRAW NSLEVEDYGF GVFTTNIWLK LKEKQDVFCD
D2/Tonga (NS1) AKMLSTELHN QTFLIDGPET AECPNTNRAW NSLEVEDYGF GVFTTNIWLR LREKQDVFCD
D3/863 (NS1) AKIVTAETQN SSFIIDGPNT PECPSASRAW NVWEVEDYGF GVFTTNIWLK LREVYTQLCD
D3/CO360 (NS1) AKIVTAETQN SSFIIDGPNT PECPSASRAW NVWEVEDYGF GVFTTNIWLK LREVYTQSCD
D3/Sleman (NS1) AKIVTAETQN SSFIIDGPNT PECPSASRAW NVWEVEDYGF GVFTTNIWLK LREMYTQLCD
D4/2270 (NS1) AKIFTPEARN STFLIDGPDT SECPNERRAW NFFEVEDYGF GMFTTNIWMK FREGSSEVCD
D4/Dominica (NS1) AKIFTPEARN STFLIDGPDT SECPNERRAW NSLEVEDYGF GMFTTNIWMK FREGSSEVCD
D4/VE_61013 (NS1) AKIFTPEARN STFLIDGPDT SECPNERRAW NSFEVEDYGF GMFTTNIWMK FREGSSEVCD
JEV/Nakamaya (NS1) SILFAPELAN STFVVDGPET KECPDEHRAW NSMQIEDFGF GITSTRVWLK IREESTDECD
YF/Asibi (NS1) NLVFSPGRKN GSFIIDGKSR KECPFSNRVW NSFQIEEFGT GVFTTRVYMD AVFEYTIDCD

**Fig. 9 (Cont'd)**

```
                          190        200        210        220        230        240
Consensus          HRLMSAAIKD XKAVHADMGY WIES-EKNXT WKJEKASFIE VKTCTWPKSH TLWSNGVLES
D1/05K872DK1 (NS1) HRLMSAAIKD SKAVHADMGY WIES-EKNET WKLARASFIE VKTCIWPKSH TLWSNGVPES
D1/2402 (NS1)      HRLMSAAIKD SKAVHADMGY WIES-EKNET WKLARASFIE VKTCIWPKSH TLWSNGVLES
D1/WestPac (NS1)   HRLMSAAIKD SKAVHADMGY WIES-EKNET WKLARASFIE VKTCIWPKSH TLWSNGVLES
D2/3295 (NS1)      SKLMSAAIKD NRAVHADMGY WIES-ALNDT WKIEKASFIE VKSCHWPKSH TLWSNGVLES
D2/16681 (NS1)     SKLMSAAIKD NRAVHADMGY WIES-ALNDT WKIEKASFIE VKNCHWPKSH TLWSNGVLES
D2/Tonga (NS1)     SKLMSAAIKD NRAVHADMGY WIES-ALNDT WKIEKASFIE VKSCHWPKSH TLWSNGVLES
D3/863 (NS1)       HRLMSAAVKD ERAVHADMGY WIES-QKNGS WKLEKASLIE VKTCTWPKSH TLWSNGVLES
D3/CO360 (NS1)     HRLMSAAIKD ERAVHADMGY WIES-QKNGS WKLEKASFIE VKTCTWPKSH TLWSNGVLES
D3/Sleman (NS1)    HRLMSAAVKD ERAVHADMGY WIES-QKNGS WKLEKASLIE VKTCTWPKSH TLWSNGVLES
D4/2270 (NS1)      HRLMSAAIKD QKAVHADMGY WIES-SKNQT WQIEKASLIE VKTCLWPKTH TLWSNGVLES
D4/Dominica (NS1)  HRLMSAAIKD QKAVHADMGY WIES-SKNQT WQIEKASLIE VKTCLWPKTH TLWSNGVLES
D4/VE_61013 (NS1)  HRLMSAAIKD QKAVHADMGY WIES-SKNQT WQIERASLIE VKTCLWPKTH TLWSNGVLES
JEV/Nakamaya (NS1) GAIIGTAVKG HVAVHSDLSY WIES-RYNDT WKLERAVFGE VKSCTWPETH TLWGDGVEES
YF/Asibi (NS1)     GSILGAAVNG KKSAHGSPTF WMGSHEVNGT WMIHTLEALD YKECEWPLTH TI-GTSVEES

                          250        260        270        280        290        300
Consensus          EMIIPKSYAG PISQHNYRPG YHTQTAGPWH LGKLELDFDY CEGTTVVITE DCGNRGPSLR
D1/05K872DK1 (NS1) EMIIPKIYGG PISQHNYRPG YFTQTAGPWH LGKLELDFDL CEGTTVVVDE HCGNRGPSLR
D1/2402 (NS1)      EMIIPKIYGG PISQHNYRPG YFTQTAGPWH LGKLELDFDL CEGTTVVVDE HCGNRGPSLR
D1/WestPac (NS1)   EMIIPKIYGG PISQHNYRPG YFTQTAGPWH LGKLELDFDL CEGTTVVVDE HCGNRGPSLR
D2/3295 (NS1)      EMIIPKNFAG PVSQHNYRPG YHTQTAGPWH LGRLEMDFDF CEGTTVVVTE DCGNRGPSLR
D2/16681 (NS1)     EMIIPKNLAG PVSQHNYRPG YHTQITGPWH LGKLEMDFDF CDGTTVVVTE DCGNRGPSLR
D2/Tonga (NS1)     EMVIPKNFAG PVSQHNNRPG YYTQTAGPWH LGKLEMDFDF CEGTTVVVTE DCGNRGPSLR
D3/863 (NS1)       DMIIPKSLAG PISQHNYRPG YHTQTAGPWH LGKLELDFNY CEGTTVVITE SCGTRGPSLR
D3/CO360 (NS1)     DMIIPKSLAG PISQHNHRPG YHTQTAGPWH LGKLELDFNY CEGTTVVITE NCGTRGPSLR
D3/Sleman (NS1)    DMIIPKSLAG PISQHNYRPG YHTQTAGPWH LGKLELDFNY CEGTTVVITE NCGTRGPSLR
D4/2270 (NS1)      QMLIPRSYAG PFSQHNYRQG YATQTVGPWH LGKLEIDFGE CPGTTVAIRE DCDHRGPSLR
D4/Dominica (NS1)  QMLIPKSYAG PFSQHNYRQG YATQTVGPWH LGKLEIDFGE CPGTTVTIQE DCDHRGPSLR
D4/VE_61013 (NS1)  QMLIPKSYAG PFSQHNYRQG YATQTVGPWH LGKLEIDFGE CPGTTVTIQE NCDHRGPSLR
JEV/Nakamaya (NS1) ELIIPHTIAG PKSKHNRREG YKTQNQGPWD ENGIVLDFDY CPGTKVTITE DCGKRGPSVR
YF/Asibi (NS1)     EMFMPRSIGG PVSSHNHIPG YKVQTNGPWM QVPLEVKREA CPGTSVIIDG NCDGRGKSTR

                          310        320        330        340        350
Consensus          TTTXSGKLIT EWCCRSCTLP PLRFRGEDGC WYGMEIRPLK EKEENLVKSL VTA-----SEQ ID NO: 57
D1/05K872DK1 (NS1) TTTVTGKIIH EWCCRSCTLP PLRFRGEDGC WYGMEIRPVK EKEENLVKSM VSA-----SEQ ID NO: 78
D1/2402 (NS1)      TTTVTGKIIH EWCCRSCTLP PLRFRGEDGC WYGMEIRPVK EKEENLVKSM VSA-----SEQ ID NO: 13
D1/WestPac (NS1)   TTTVTGKTIH EWCCRSCTLP PLRFKGEDGC WYGMEIRPVK EKEENLVKSM VSA-----SEQ ID NO: 79
D2/3295 (NS1)      TTTASGKLIT EWCCRSCTLP PLRYRGEDGC WYGMEIRPLK EKEENLVNSL VTA-----SEQ ID NO: 14
D2/16681 (NS1)     TTTASGKLIT EWCCRSCTLP PLRYRGEDGC WYGMEIRPLK EKEENLVNSL VTA-----SEQ ID NO: 80
D2/Tonga (NS1)     TTTASGKLIT EWCCRSCTLP PLRYRGEDGC WYGMEIRPLK EKEENLVSSL VTA-----SEQ ID NO: 81
D3/863 (NS1)       TTTVSGKLIH EWCCRSCTLP PLRYMGEDGC WYGMEIRPIS EKEENMVKSL VSA-----SEQ ID NO: 15
D3/CO360 (NS1)     TTTVSGKLIH EWCCRSCTLP PLRYMGEDGC WYGMEIRPIN EKEENMVKSL VSA-----SEQ ID NO: 82
D3/Sleman (NS1)    TTTVSGKLIH EWCCRSCTLP PLRYMGEDGC WYGMEIRPIN EKEENMVKSL VSA-----SEQ ID NO: 83
D4/2270 (NS1)      TTTASGKLVT QWCCRSCTMP PLRFLGEDGC WYGMEIRPLS EKEENMVKSQ VTA-----SEQ ID NO: 16
D4/Dominica (NS1)  TTTASGKLVT QWCCRSCTMP PLRFLGEDGC WYGMEIRPLS EKEENMVKSQ VTA-----SEQ ID NO: 84
D4/VE_61013 (NS1)  TTTASGKLVT QWCCRSCTMP PLRFLGEDGC WYGMEIRPLS EKEENMVKSQ VTA-----SEQ ID NO: 85
JEV/Nakamaya (NS1) TTTDSGKLIT DWCCRSCSLP PLRFRTENGC WYGMEIRPVR HDETTLVRSQ VDA-----SEQ ID NO: 86
YF/Asibi (NS1)     STTDSGKIIP EWCCRSCTMP PVSFHGSDGC WYPMEIRPRK THESHLVRSW VTA-----SEQ ID NO: 87
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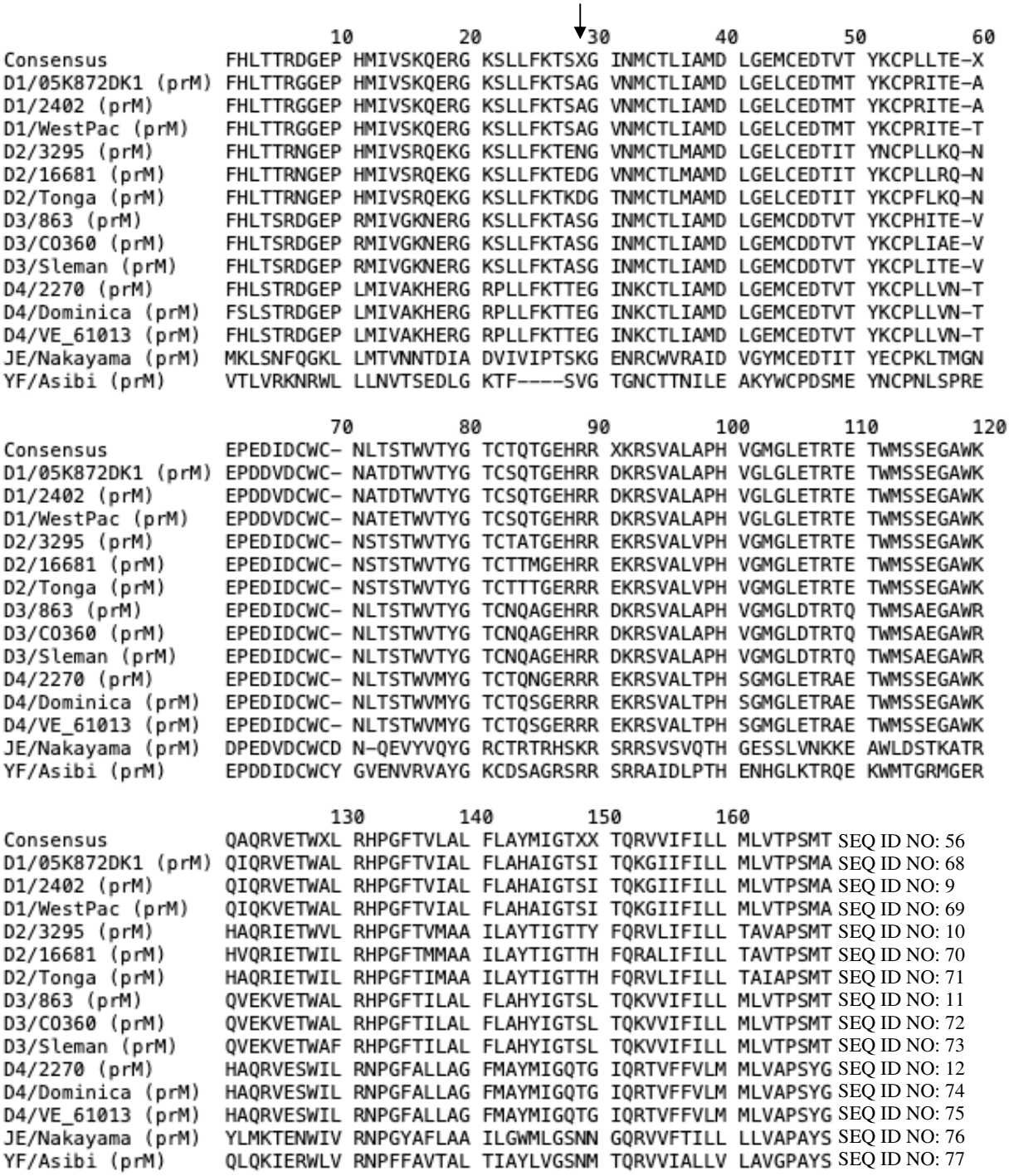
**Fig. 10**

```
                          10         20         30         40         50
Consensus                 SWPLNEGIMA VGLVSILASS LLKNDVP-MA GPLVAGGLLI ACYVISGSSA
D1/05K872DK1 (NS2B)       SWPLNEGIMA VGIVSILLSS LLKNDVP-LA GPLIAGGMLI ACYVISGSSA
D1/2402 (NS2B)            SWPLNEGIMA VGIVSILLSS LLKNDVP-LA GPLIAGGMLI ACYVISGSSA
D1/WestPac (NS2B)         SWPLNEGIMA VGIVSILLSS LLKNDVP-LA GPLIAGGMLI ACYVISGSSA
D2/3295 (NS2B)            SWPLNEAIMA VGMVSILASS LLKNDIP-MT GPLVAGGLLT VCYVLTGRSA
D2/16681 (NS2B)           SWPLNEAIMA VGMVSILASS LLKNDIP-MT GPLVAGGLLT VCYVLTGRSA
D2/Tonga (NS2B)           SWPLNEAIMA VGMVSILASS LLKNDIP-MT GPLVAGGLLT VCYVLTGRSA
D3/863 (NS2B)             SWPLNEGVMA VGLVSILASS LLRNDVP-MA GPLVAGGLLI ACYVITGTSA
D3/CO360 (NS2B)           SWPLNEGVMA VGLVSILASS LLRNDVP-MA GPLVAGGLLI ACYVITGTSA
D3/Sleman (NS2B)          SWPLNEGVMA VGLVSILASS LLRNDVP-MA GPLVAGGLLI ACYVITGTSA
D4/2270 (NS2B)            SWPLNEGIMA VGLVSLLGSA LLKNDVP-LA GPMVAGGLLL AAYVMSGSSA
D4/Dominca (NS2B)         SWPLNEGIMA VGLVSLLGSA LLKNDVP-LA GPMVAGGLLL AAYVMSGSSA
D4/VE_61013 (NS2B)        SWPLNEGIMA VGLVSLLGSA LLKNDVP-LA GPMVAGGLLL AAYVMSGSSV
JE/Nakayama (NS2B)        GWPATEFLSA VGLMFAIVGG LAELDIESMS IPFMLAGLMA VSYVVSGKAT
YF/Asibi (NS2B)           SIPVNEALAA AGLVGVLA-G LAFQEMENFL GPIAVGGILM MLVSVAGRVD

                          60         70         80         90         100
Consensus                 DLSLEKAADV SWEEEAEIXG SSXXLXVTVD XDGXMSIKDE EEENTLTILL
D1/05K872DK1 (NS2B)       DLSLEKAAEV SWEEEAEHSG ASHNILVEVQ DDGTMKIKDE ERDDTLTILL
D1/2402 (NS2B)            DLSLEKAAEV SWEEEAEHSG ASHNILVEVQ DDGTMKIKDE ERDDTLTILL
D1/WestPac (NS2B)         DLSLEKAAEV SWEEEAEHSG ASHNILVEVQ DDGTMKIKDE ERDDTLTILL
D2/3295 (NS2B)            DLELERAADV RWEEQAEISG SSPILSITIS EDGSMSIKNE EEEQILTILI
D2/16681 (NS2B)           DLELERAADV KWEDQAEISG SSPILSITIS EDGSMSIKNE EEEQTLTILI
D2/Tonga (NS2B)           DLELERATDV KWDDQAEISG SSPILSITIS EDGSMSIKNE EEEQTLTILI
D3/863 (NS2B)             DLTVEKAADV TWEEEAEQTG VSHNLMITVD DDGTMRIKDD ETENILTVLL
D3/CO360 (NS2B)           DLTVEKAADV TWEEEAEQTG VSHNLMITVD DDGTMRIKDD ETENILTVLL
D3/Sleman (NS2B)          DLTVEKAADV TWEEEAEQTG VSHNLMITVD DDGTMRIKDD ETENILTVLL
D4/2270 (NS2B)            DLSLEKAANV QWDEMADITG SSPIIEVKQD EDGSFSIRDV EETNMITLLV
D4/Dominca (NS2B)         DLSLEKAANV QWDEMADITG SSPIIEVKQD EDGSFSIRDV EETNMITLLV
D4/VE_61013 (NS2B)        DLSLEKAANV QWDEMADITG SSPIIEVKQD EDGSFSIRDV EETNMITLLV
JE/Nakayama (NS2B)        DMWLERAADI SWEMDAAITG SSRRLDVKLD DDGDFHLIDD PGVPWKVWVL
YF/Asibi (NS2B)           GLELKKLGEV SWEEEAEISG SSARYDVALS EQGEFKLLSE EKVPWDQVVM

                          110   ↓    120        130
Consensus                 KTALLVVSGL XPLSIPATLA VWYXWQKKTQ R SEQ ID NO: 55
D1/05K872DK1 (NS2B)       KATLLAVSGV YPLSIPATLF VWYFWQKKKQ R SEQ ID NO: 58
D1/2402 (NS2B)            KATLLAVSGV YPLSIPATLF VWYFWQKKKQ R SEQ ID NO: 5
D1/WestPac (NS2B)         KATLLAISGV YPMSIPATLF VWYFWQKKKQ R SEQ ID NO: 59
D2/3295 (NS2B)            RTGLLVISGL FPVSIPITAA AWYLWEVKKQ R SEQ ID NO: 6
D2/16681 (NS2B)           RTGLLVISGL FPVSIPITAA AWYLWEVKKQ R SEQ ID NO: 60
D2/Tonga (NS2B)           RTGLLVISGL FPVSIPITAA AWYLWEVKKQ R SEQ ID NO: 61
D3/863 (NS2B)             KTALLIVSGI FPYSIPATLL VWHTWQKQTQ R SEQ ID NO: 7
D3/CO360 (NS2B)           KTALLIVSGI FPYSIPATLL VWHTWQKQTQ R SEQ ID NO: 62
D3/Sleman (NS2B)          KTALLIVSGI FPYSIPATLL VWHTWQKQTQ R SEQ ID NO: 63
D4/2270 (NS2B)            KLALITVSGL YPLAIPVTMA LWYIWQVKTQ R SEQ ID NO: 8
D4/Dominca (NS2B)         KLALITVSGL YPLAIPVTMT LWYMWQVKTQ R SEQ ID NO: 64
D4/VE_61013 (NS2B)        KLALITVSGL YPLAIPITMT LWYMWQVKTQ R SEQ ID NO: 65
JE/Nakayama (NS2B)        RMSCIGLAAL TPWAIVPAAF GYWLTLKTTK R SEQ ID NO: 66
YF/Asibi (NS2B)           TSLALVGAAI HPFALLLVLA GWLFHVRGAR R SEQ ID NO: 67
```

**Fig. 11**



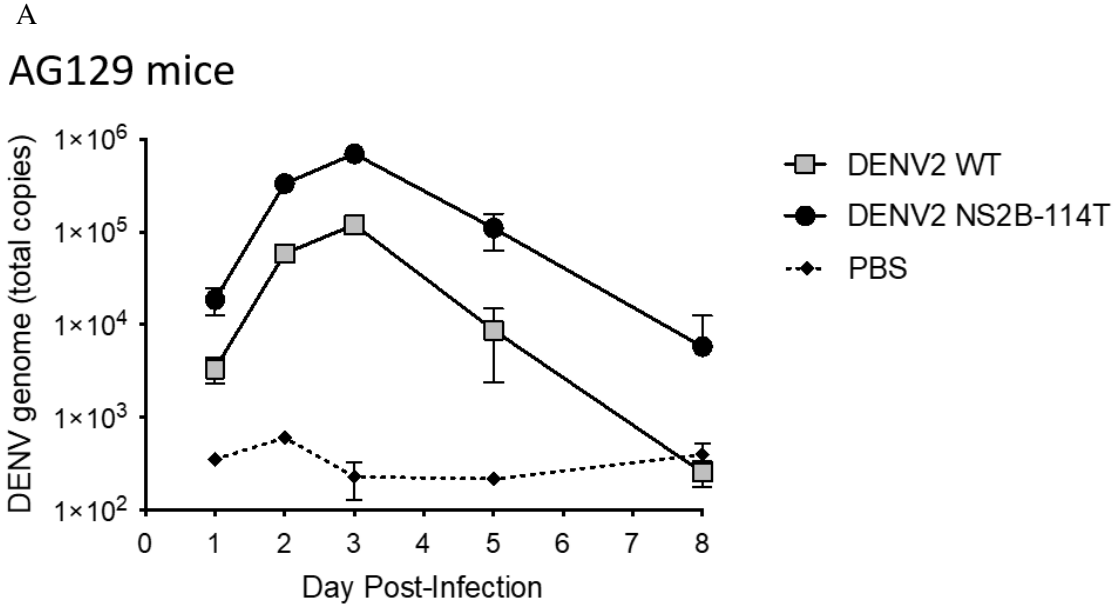
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                          10         20         30         40         50         60
Consensus                 FHLTTRDGEP HMIVSKQERG KSLLFKTSXG INMCTLIAMD LGEMCEDTVT YKCPLLTE-X
D1/05K872DK1 (prM)        FHLTTRGGEP HMIVSKQERG KSLLFKTSAG VNMCTLIAMD LGELCEDTMT YKCPRITE-A
D1/2402 (prM)             FHLTTRGGEP HMIVSKQERG KSLLFKTSAG VNMCTLIAMD LGELCEDTMT YKCPRITE-A
D1/WestPac (prM)          FHLTTRGGEP HMIVSKQERG KSLLFKTSAG VNMCTLIAMD LGELCEDTMT YKCPRITE-T
D2/3295 (prM)             FHLTTRNGEP HMIVSRQEKG KSLLFKTENG VNMCTLMAMD LGELCEDTIT YNCPLLKQ-N
D2/16681 (prM)            FHLTTRNGEP HMIVSRQEKG KSLLFKTEDG VNMCTLMAMD LGELCEDTIT YKCPLLRQ-N
D2/Tonga (prM)            FHLTTRNGEP HMIVSRQEKG KSLLFKTKDG TNMCTLMAMD LGELCEDTIT YKCPFLKQ-N
D3/863 (prM)              FHLTSRDGEP RMIVGKNERG KSLLFKTASG INMCTLIAMD LGEMCDDTVT YKCPHITE-V
D3/CO360 (prM)            FHLTSRDGEP RMIVGKNERG KSLLFKTASG INMCTLIAMD LGEMCDDTVT YKCPLIAE-V
D3/Sleman (prM)           FHLTSRDGEP RMIVGKNERG KSLLFKTASG INMCTLIAMD LGEMCDDTVT YKCPLITE-V
D4/2270 (prM)             FHLSTRDGEP LMIVAKHERG RPLLFKTTEG INKCTLIAMD LGEMCEDTVT YKCPLLVN-T
D4/Dominica (prM)         FSLSTRDGEP LMIVAKHERG RPLLFKTTEG INKCTLIAMD LGEMCEDTVT YKCPLLVN-T
D4/VE_61013 (prM)         FHLSTRDGEP LMIVAKHERG RPLLFKTTEG INKCTLIAMD LGEMCEDTVT YKCPLLVN-T
JE/Nakayama (prM)         MKLSNFQGKL LMTVNNTDIA DVIVIPTSKG ENRCWVRAID VGYMCEDTIT YECPKLTMGN
YF/Asibi (prM)            VTLVRKNRWL LLNVTSEDLG KTF----SVG TGNCTTNILE AKYWCPDSME YNCPNLSPRE

                          70         80         90         100        110        120
Consensus                 EPEDIDCWC- NLTSTWVTYG TCTQTGEHRR XKRSVALAPH VGMGLETRTE TWMSSEGAWK
D1/05K872DK1 (prM)        EPDDVDCWC- NATDTWVTYG TCSQTGEHRR DKRSVALAPH VGLGLETRTE TWMSSEGAWK
D1/2402 (prM)             EPDDVDCWC- NATDTWVTYG TCSQTGEHRR DKRSVALAPH VGLGLETRTE TWMSSEGAWK
D1/WestPac (prM)          EPDDVDCWC- NATETWVTYG TCSQTGEHRR DKRSVALAPH VGLGLETRTE TWMSSEGAWK
D2/3295 (prM)             EPEDIDCWC- NSTSTWVTYG TCTATGEHRR EKRSVALVPH VGMGLETRTE TWMSSEGAWK
D2/16681 (prM)            EPEDIDCWC- NSTSTWVTYG TCTTMGEHRR EKRSVALVPH VGMGLETRTE TWMSSEGAWK
D2/Tonga (prM)            EPEDIDCWC- NSTSTWVTYG TCTTTGERRR EKRSVALVPH VGMGLETRTE TWMSSEGAWK
D3/863 (prM)              EPEDIDCWC- NLTSTWVTYG TCNQAGEHRR DKRSVALAPH VGMGLDTRTQ TWMSAEGAWR
D3/CO360 (prM)            EPEDIDCWC- NLTSTWVTYG TCNQAGEHRR DKRSVALAPH VGMGLDTRTQ TWMSAEGAWR
D3/Sleman (prM)           EPEDIDCWC- NLTSTWVTYG TCNQAGEHRR DKRSVALAPH VGMGLDTRTQ TWMSAEGAWR
D4/2270 (prM)             EPEDIDCWC- NLTSTWVMYG TCTQNGERRR EKRSVALTPH SGMGLETRAE TWMSSEGAWK
D4/Dominica (prM)         EPEDIDCWC- NLTSTWVMYG TCTQSGERRR EKRSVALTPH SGMGLETRAE TWMSSEGAWK
D4/VE_61013 (prM)         EPEDIDCWC- NLTSTWVMYG TCTQSGERRR EKRSVALTPH SGMGLETRAE TWMSSEGAWK
JE/Nakayama (prM)         DPEDVDCWCD N-QEVYVQYG RCTRTRHSKR SRRSVSVQTH GESSLVNKKE AWLDSTKATR
YF/Asibi (prM)            EPDDIDCWCY GVENVRVAYG KCDSAGRSRR SRRAIDLPTH ENHGLKTRQE KWMTGRMGER

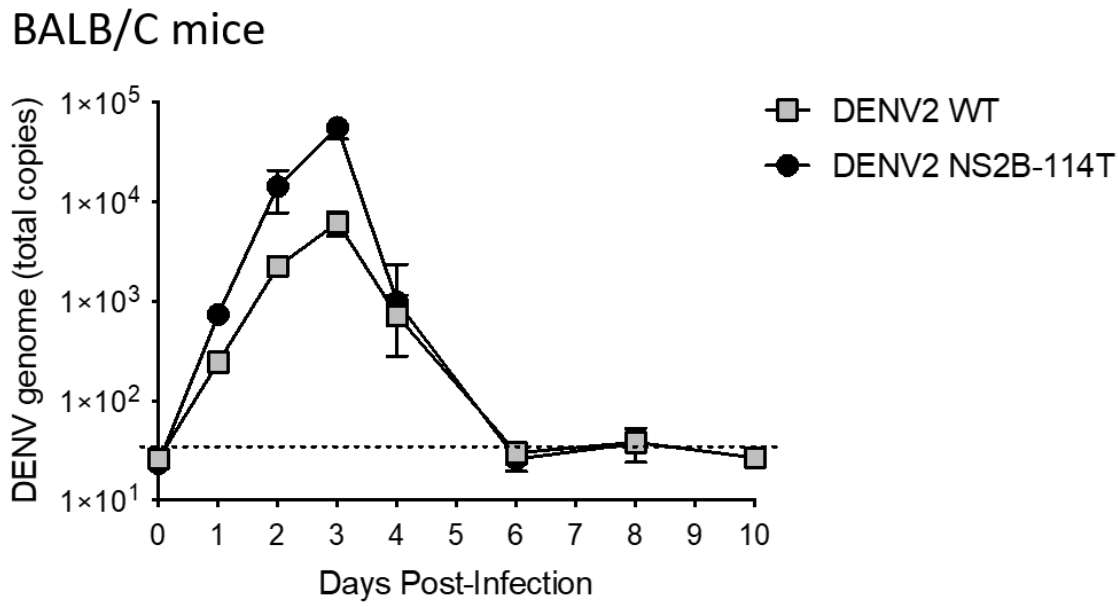
                          130        140        150        160
Consensus                 QAQRVETWXL RHPGFTVLAL FLAYMIGTXX TQRVVIFILL MLVTPSMT SEQ ID NO: 56
D1/05K872DK1 (prM)        QIQRVETWAL RHPGFTVIAL FLAHAIGTSI TQKGIIFILL MLVTPSMA SEQ ID NO: 68
D1/2402 (prM)             QIQRVETWAL RHPGFTVIAL FLAHAIGTSI TQKGIIFILL MLVTPSMA SEQ ID NO: 9
D1/WestPac (prM)          QIQKVETWAL RHPGFTVIAL FLAHAIGTSI TQKGIIFILL MLVTPSMA SEQ ID NO: 69
D2/3295 (prM)             HAQRIETWVL RHPGFTVMAA ILAYTIGTTY FQRVLIFILL TAVAPSMT SEQ ID NO: 10
D2/16681 (prM)            HVQRIETWIL RHPGFTMMAA ILAYTIGTTH FQRALIFILL TAVTPSMT SEQ ID NO: 70
D2/Tonga (prM)            HAQRIETWIL RHPGFTIMAA ILAYTIGTTH FQRVLIFILL TAIAPSMT SEQ ID NO: 71
D3/863 (prM)              QVEKVETWAL RHPGFTILAL FLAHYIGTSL TQKVVIFILL MLVTPSMT SEQ ID NO: 11
D3/CO360 (prM)            QVEKVETWAL RHPGFTILAL FLAHYIGTSL TQKVVIFILL MLVTPSMT SEQ ID NO: 72
D3/Sleman (prM)           QVEKVETWAF RHPGFTILAL FLAHYIGTSL TQKVVIFILL MLVTPSMT SEQ ID NO: 73
D4/2270 (prM)             HAQRVESWIL RNPGFALLAG FMAYMIGQTG IQRTVFFVLM MLVAPSYG SEQ ID NO: 12
D4/Dominica (prM)         HAQRVESWIL RNPGFALLAG FMAYMIGQTG IQRTVFFVLM MLVAPSYG SEQ ID NO: 74
D4/VE_61013 (prM)         HAQRVESWIL RNPGFALLAG FMAYMIGQTG IQRTVFFVLM MLVAPSYG SEQ ID NO: 75
JE/Nakayama (prM)         YLMKTENWIV RNPGYAFLAA ILGWMLGSNN GQRVVFTILL LLVAPAYS SEQ ID NO: 76
YF/Asibi (prM)            QLQKIERWLV RNPFFAVTAL TIAYLVGSNM TQRVVIALLV LAVGPAYS SEQ ID NO: 77
```

**Fig. 12**

A


AG129 mice
DENV genome (total copies)
1×10^6
1×10^5
1×10^4
1×10^3
1×10^2
0 1 2 3 4 5 6 7 8
Day Post-Infection
DENV2 WT
DENV2 NS2B-114T
PBS

B


BALB/C mice
DENV genome (total copies)
1×10^5
1×10^4
1×10^3
1×10^2
1×10^1
0 1 2 3 4 5 6 7 8 9 10
Days Post-Infection
DENV2 WT
DENV2 NS2B-114T