

Fig. 1

MEVELVLLPLVSSQC~~V~~NLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFSN
 VTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIRGWIFGTTLDSKTQSLIVNN
 ATNVVIK~~V~~CEFCNDPFLGVYHKNNKSWMESEFRVYSSANNC~~T~~FEYVSQPFLMDLEG
 KQGNFKNLREFVFKNIDGYFKIYSKHTPINLVRDL~~P~~QGFSALEPLVDLPIGINITRFQTLAL
 HRSYLTPGDSSGWTAGAAAYVGYLQPR~~T~~FL~~L~~KYNENGTTTDAVDCALDPLSETKCTLK
 SFTVEKGIYQTSNFRVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNKRISNCVADYS
 VLYNSASFSTFKCYGVSP~~T~~KLNDLCFTNVYADSFVIRGDEV~~R~~QIAPGQTGKIADYN~~Y~~KLP
 DDFTGCVIAWNSNNLDSKVGGNYNLYRLFRKSNLKPFERDISTE~~I~~YQAGSTPCNGVEGF
 NCYFPLQSYGFQPTNGVGYQPYRVV~~V~~LSFELLHAPATVCGPKKSTNLVKNKCVNFNENG
 LTGTGVLTESNKKFLPFQ~~Q~~GRDIADTTDAVRDPQTLEILDITPCSF~~G~~GVSVITPGTNTSNQ
 VAVLYQDVNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNN~~S~~YEC~~D~~PIG
 AGICASYQTQ~~T~~NSP**RR**ARSVASQSIIAYTMSLGAENS~~V~~AYSNN~~S~~IAIPTNFTISVTTEILPVS
 MTKTSVDCTMYICGDSTEC~~S~~NLLQYGSFCTQLNRALTGIAVEQDKNTQEVFAQVKQIYK
 TPPIKDFGGNFSQILPDPSKPSKRSFIEDLLFNK~~V~~TLADAGFIKQYGDCLGDIAARDLICA
 QKFNGLT~~V~~LPPLTDEMIAQYTSALLAGTITSGWTFGAGAAALQIPFAMQMAYR~~F~~NGIGVT
 QNVLYENQKLIANQFNSAIGKIQDLSSTASALGKLQDVVNQNAQALNTLVKQLSSNFGA
 ISSVLNDILSR~~L~~DKVEAEVQIDRLITGR~~L~~QSLQTYVTQQLIRAAEIRASANLAATKMSECV
 LGQSKRVDFCGKGYHLMSPFQ~~S~~APHGVVFLHVTVYVPAQEKNFTTAPAICH~~D~~GKAHFPRE
 GV~~F~~VSN~~G~~THWFVTQRNFYEPQIITTDNTFVSGNCDVVIGIVNNTVYDPLQPELDSFKEEL
 DKYFKNHTSPDV~~D~~LDGDISGINASV~~V~~NIQKEIDRLNEVAKNLNESLIDLQELGKYEYIKWP
 WYIWLGFIAGLIAIVMTIMLCCMTSCC~~S~~CLKGCCSCGSCCKFDEDDSEPV~~L~~KGVKLHYT

Fig. 2

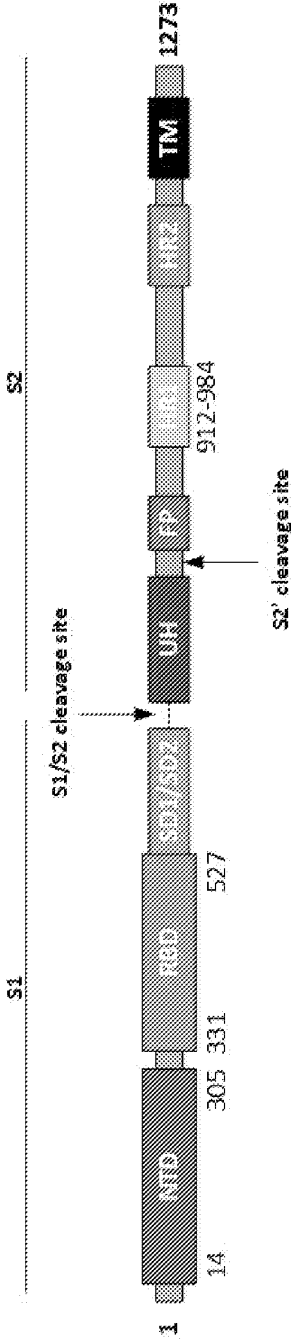


Fig. 3

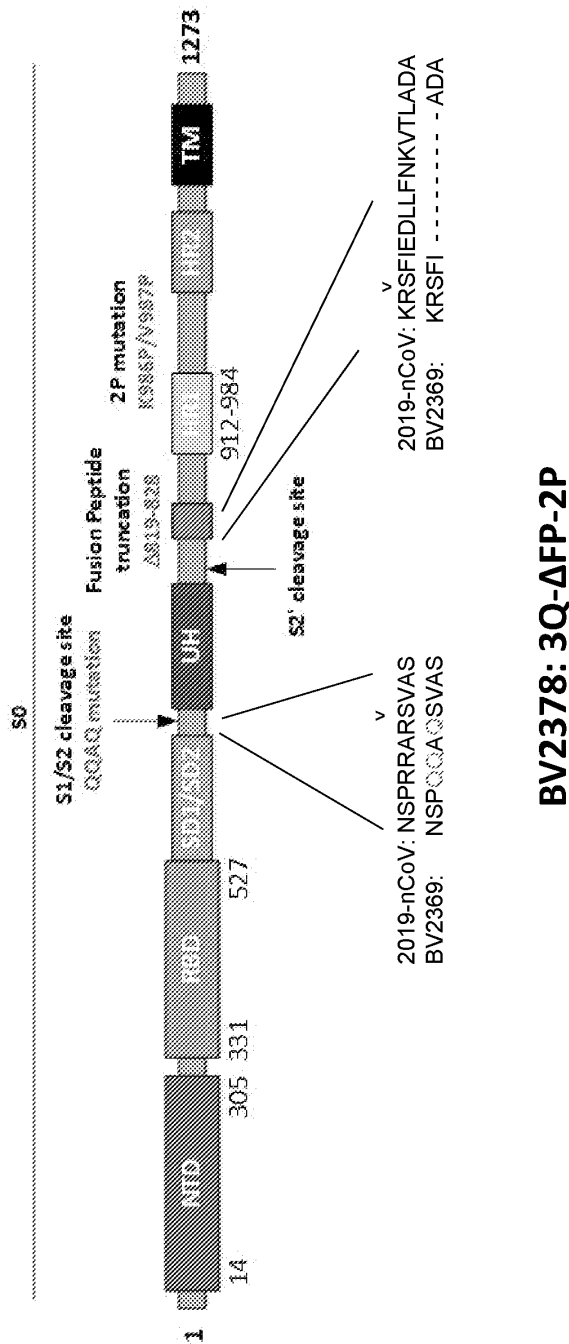


Fig. 4

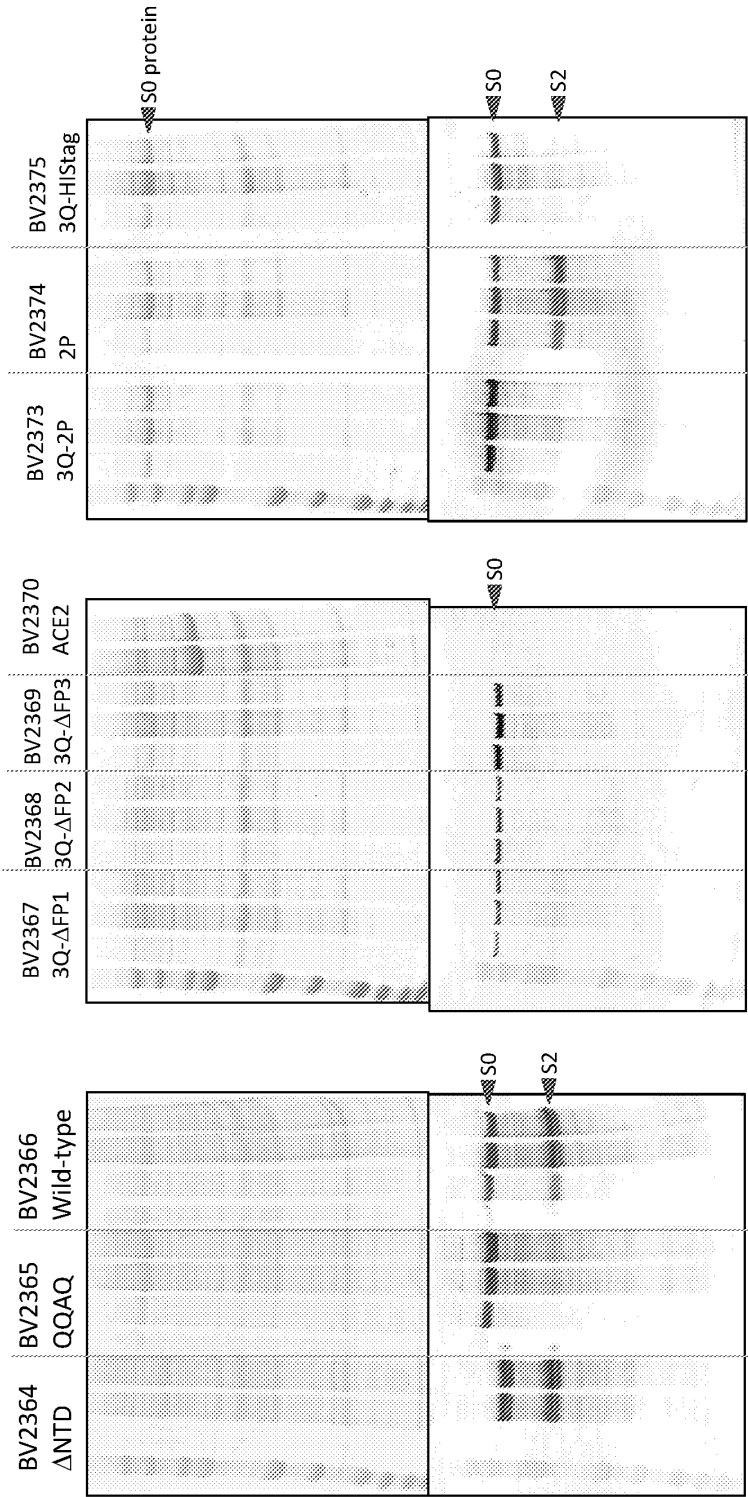
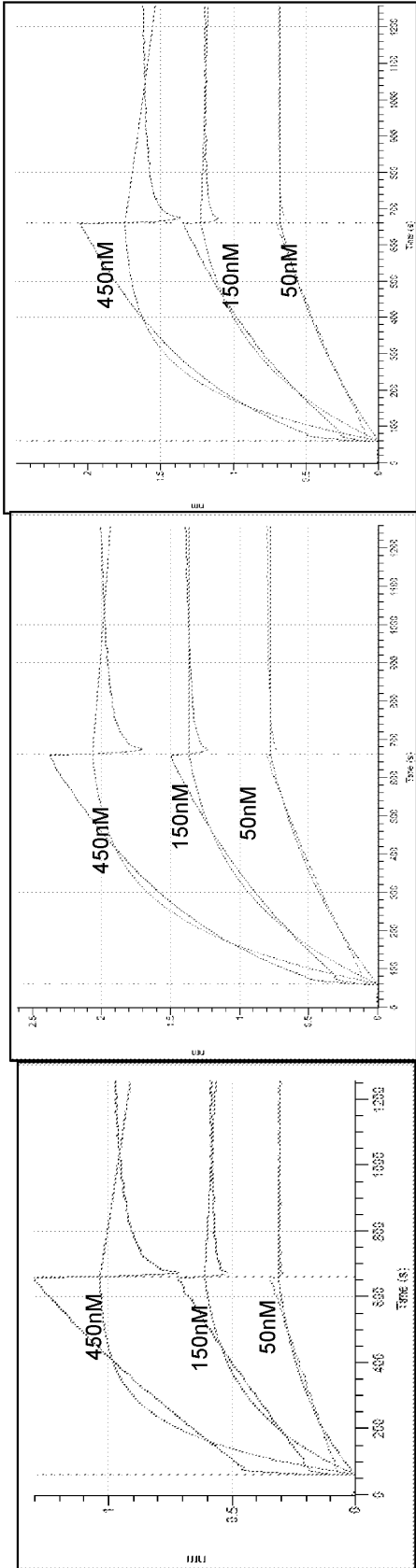


Fig. 5
BV2365: "QQAQ"
BV2373 : "3Q-2P"
BV2374: "2P"



BV2361 : "Full Length WT"
BV2365 : "QQAQ"
BV2369 : "3QΔFD"

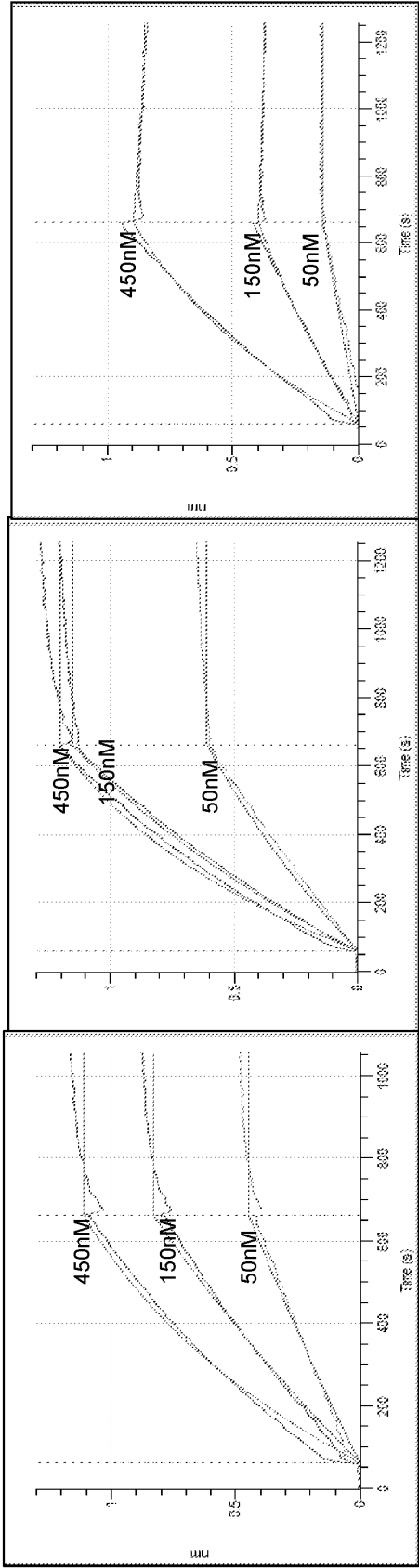


Fig. 6

Binding DPP4 receptor: MERS does not bind ACE2 receptor

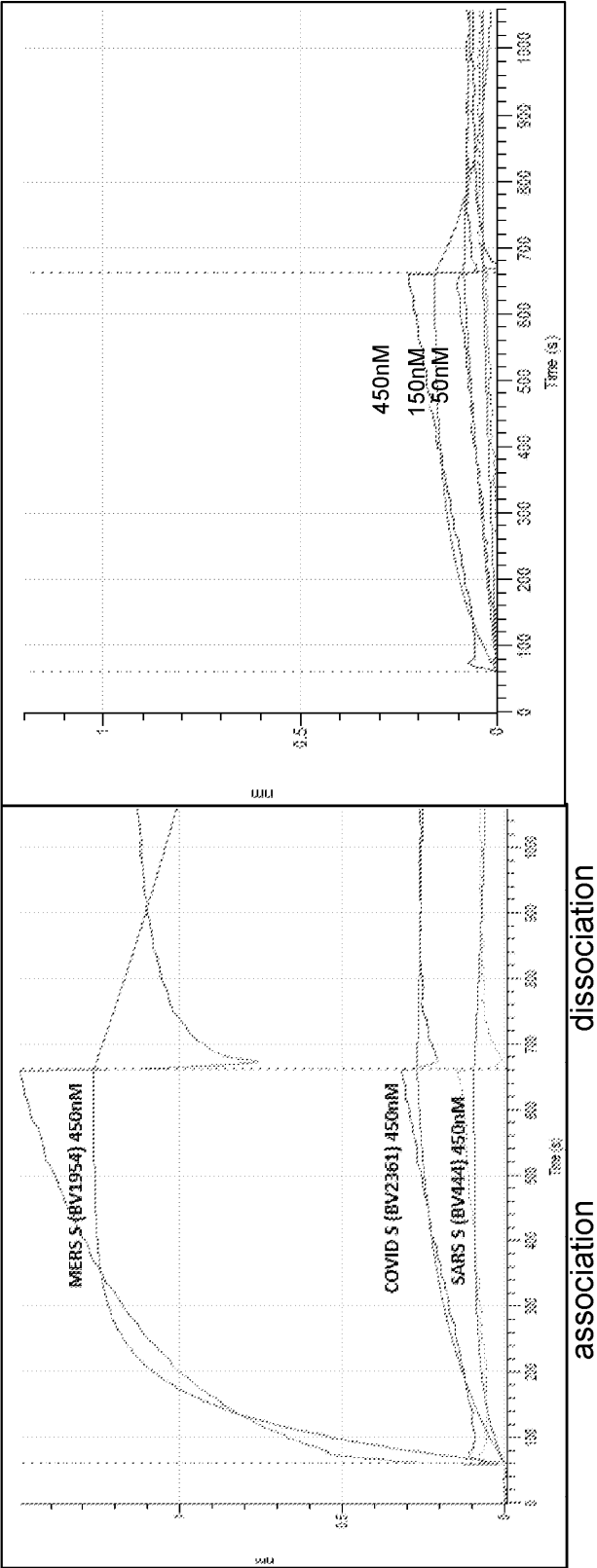


Fig. 7

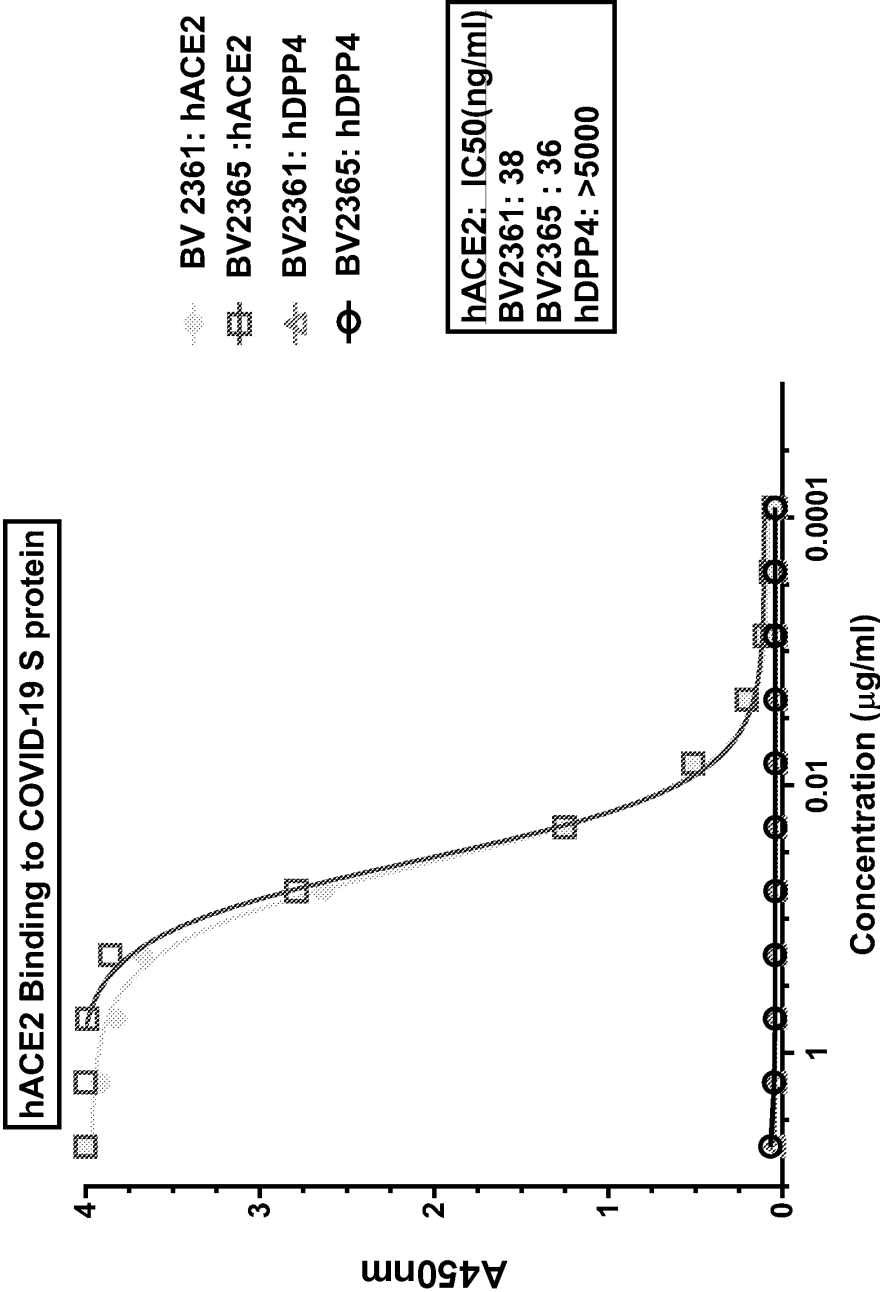
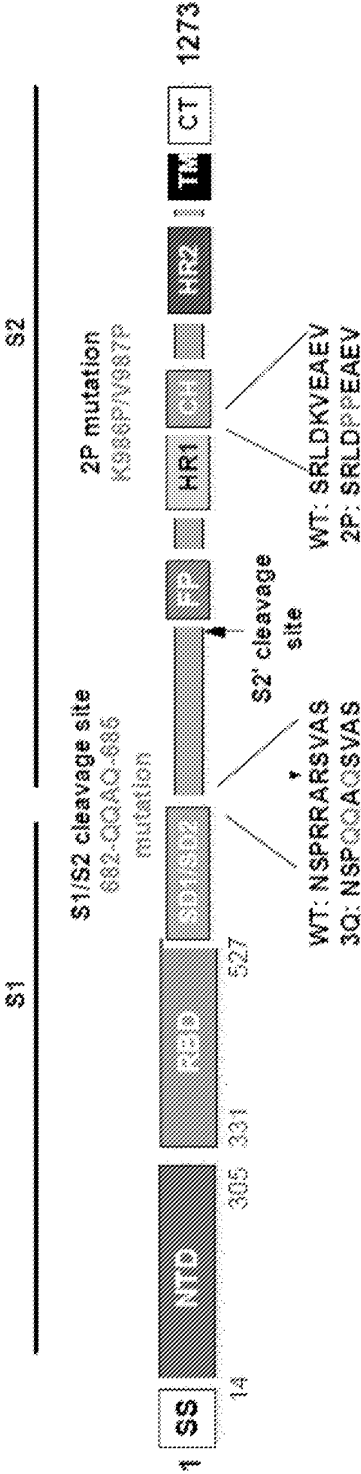


Fig. 8

BV2373



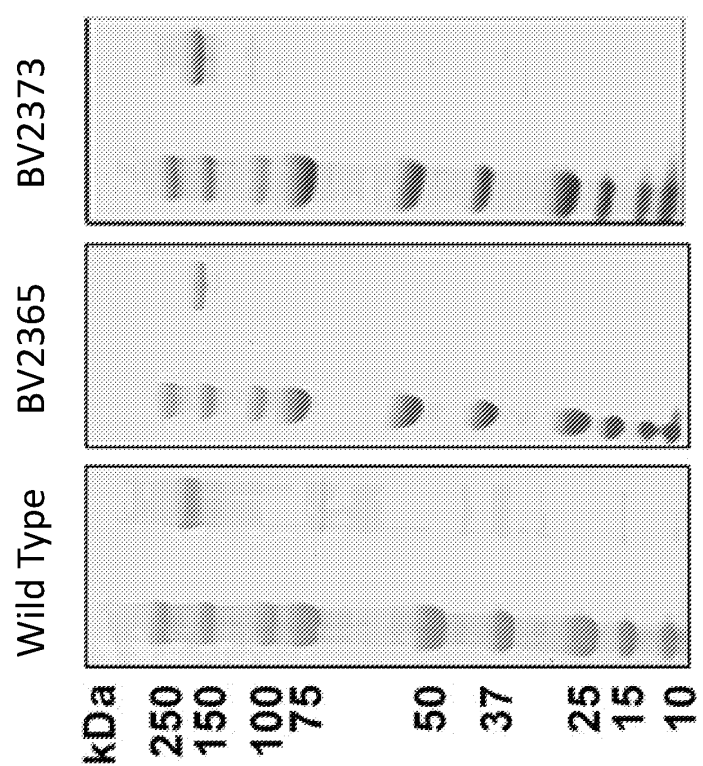
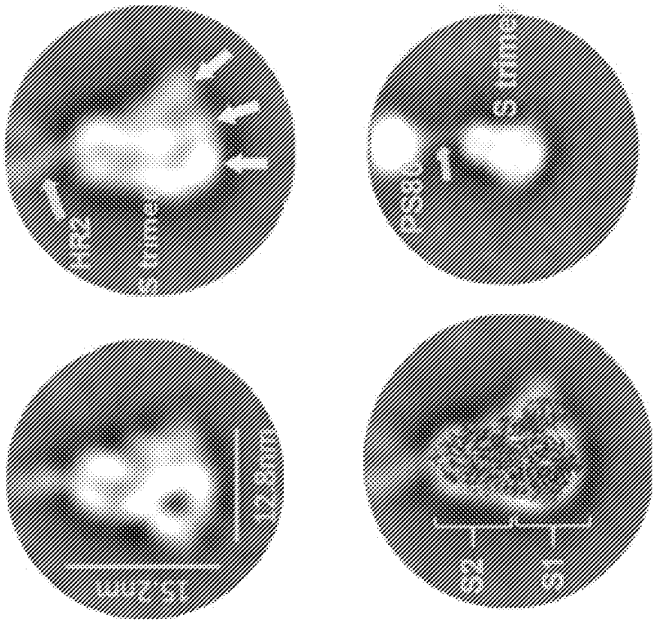


Fig. 10



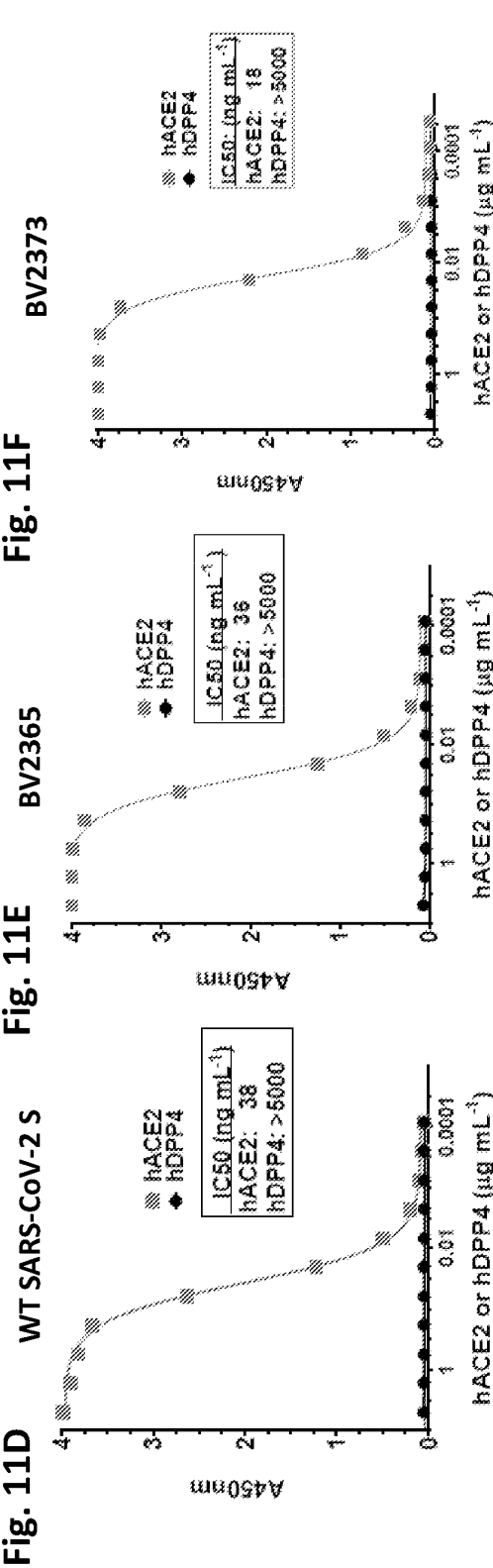
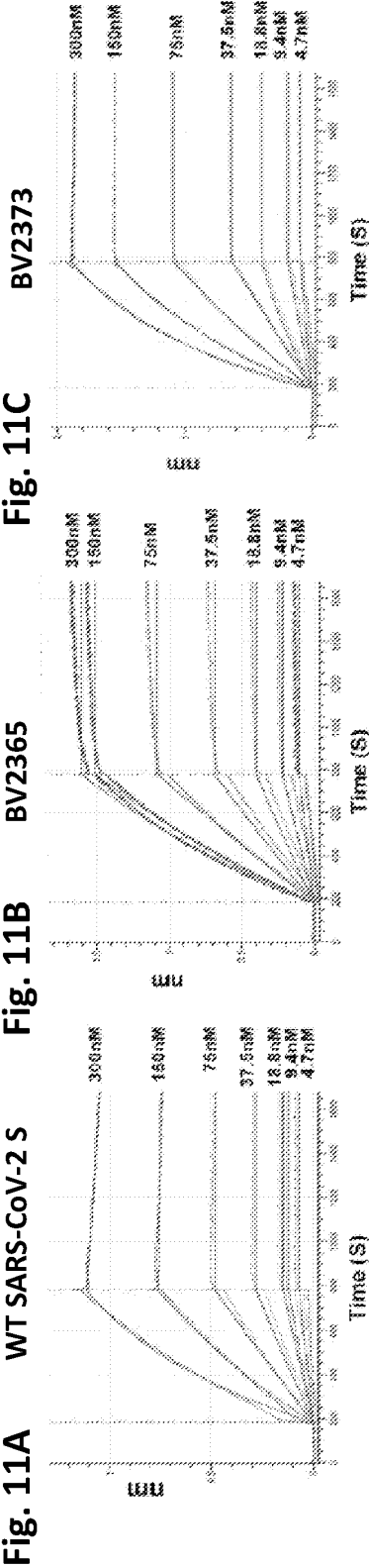


Fig. 12A

BV2373 Binding to hACE2 under stress conditions

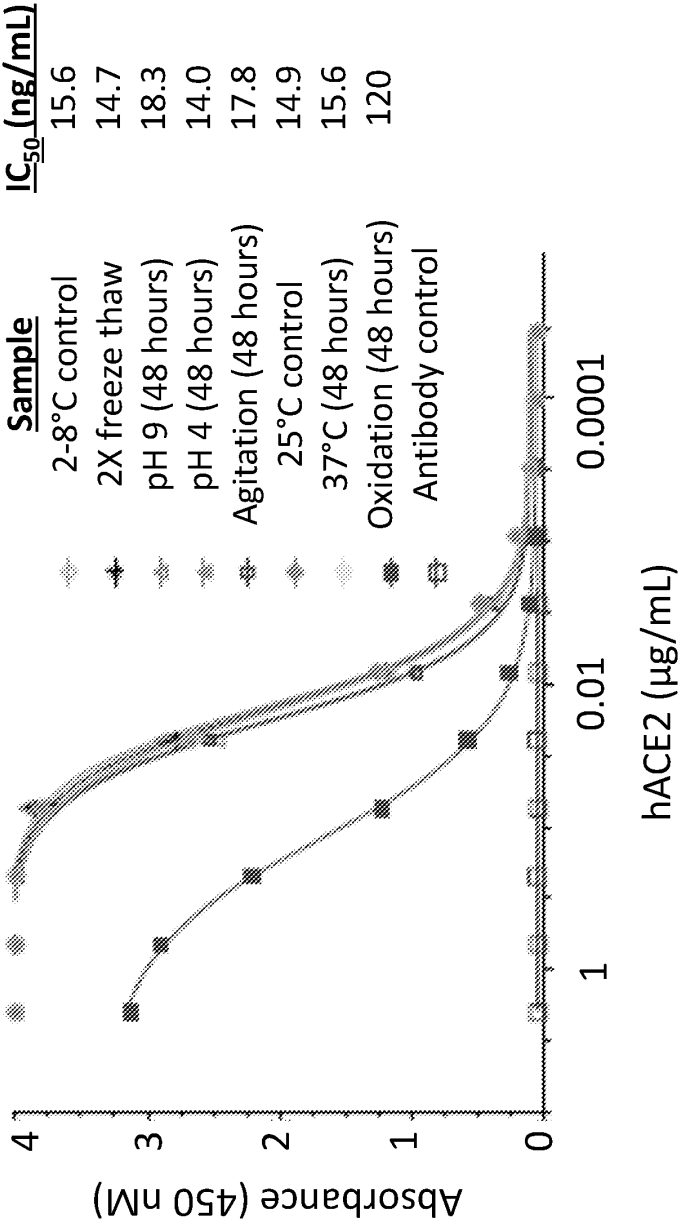


Fig. 12B

BV2365 Binding to hACE2 under stress conditions

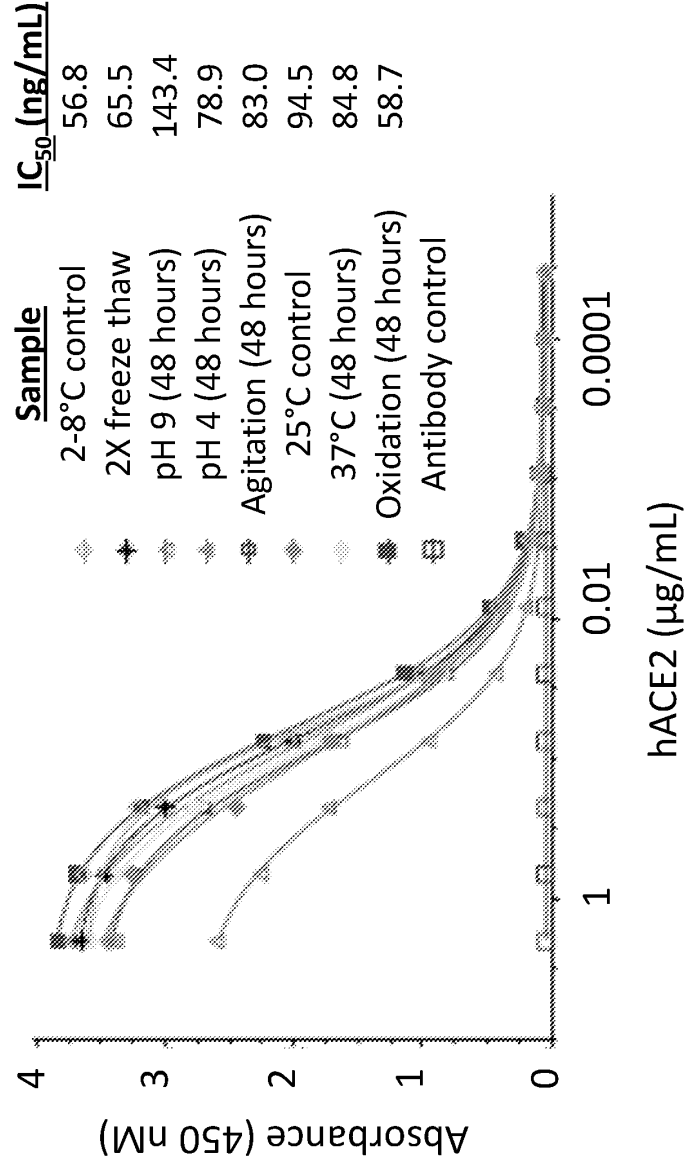


Fig. 13A

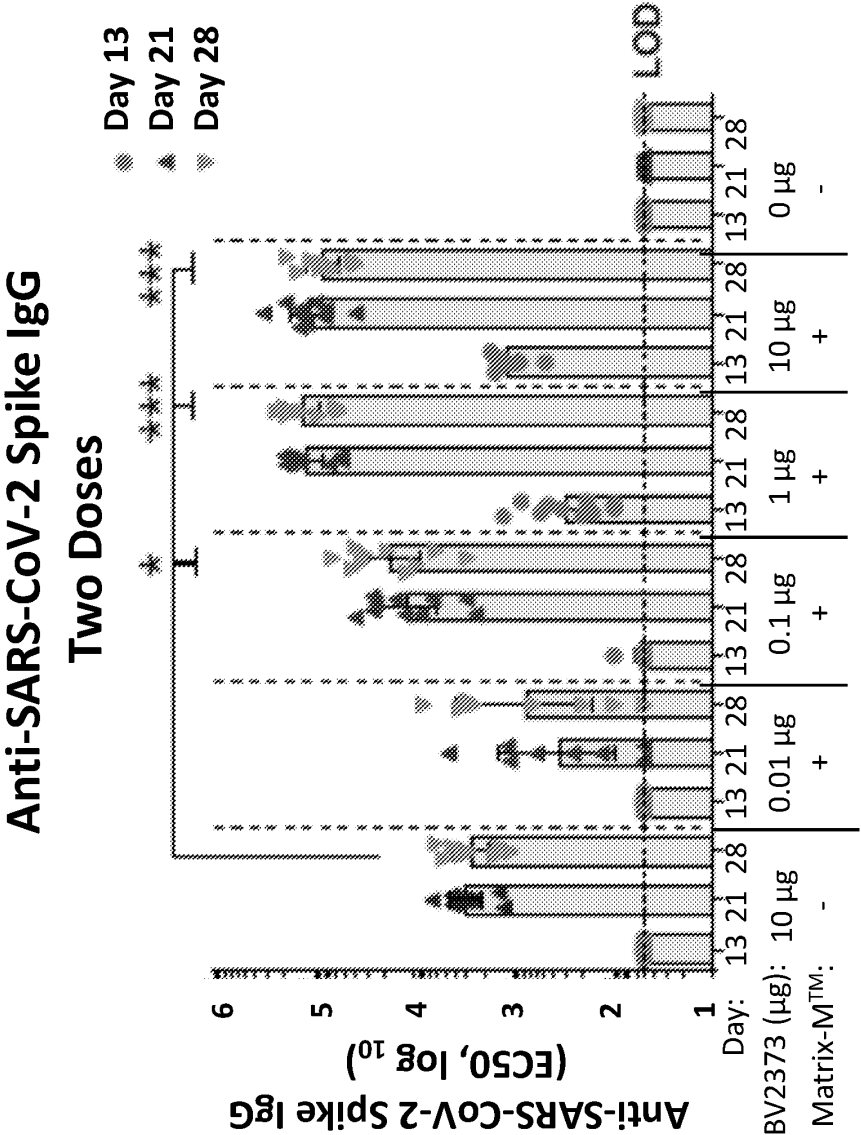


Fig. 13B

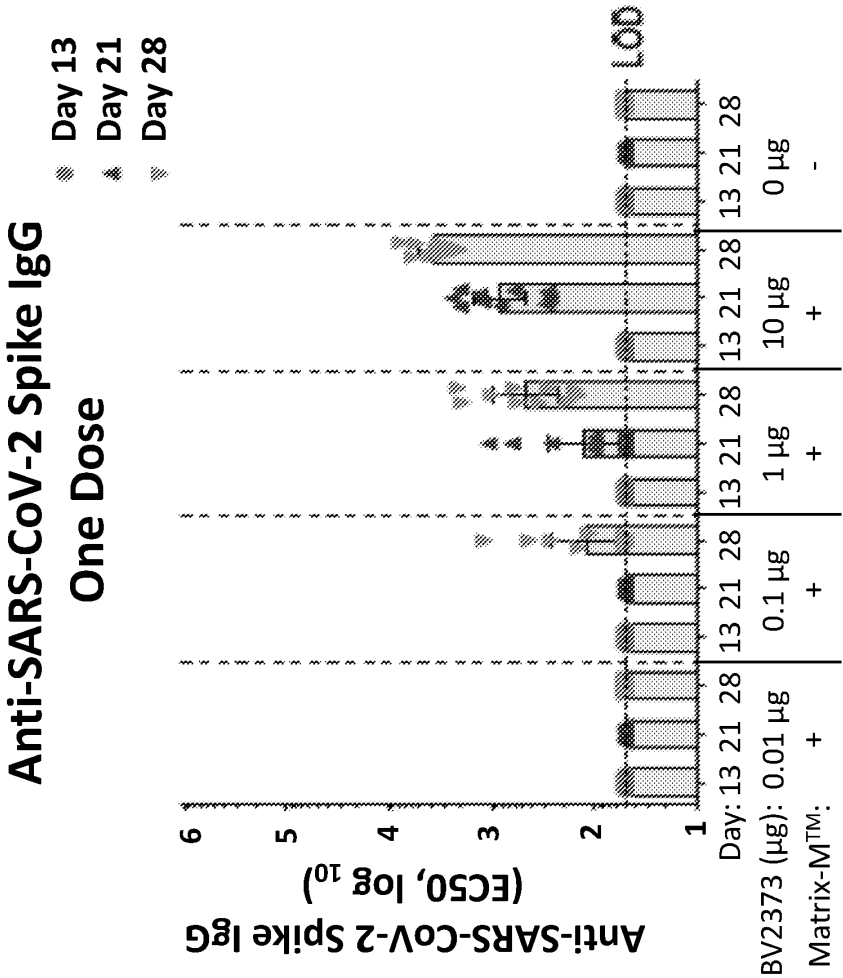


Fig. 14

hACE2 Receptor Blocking Antibody

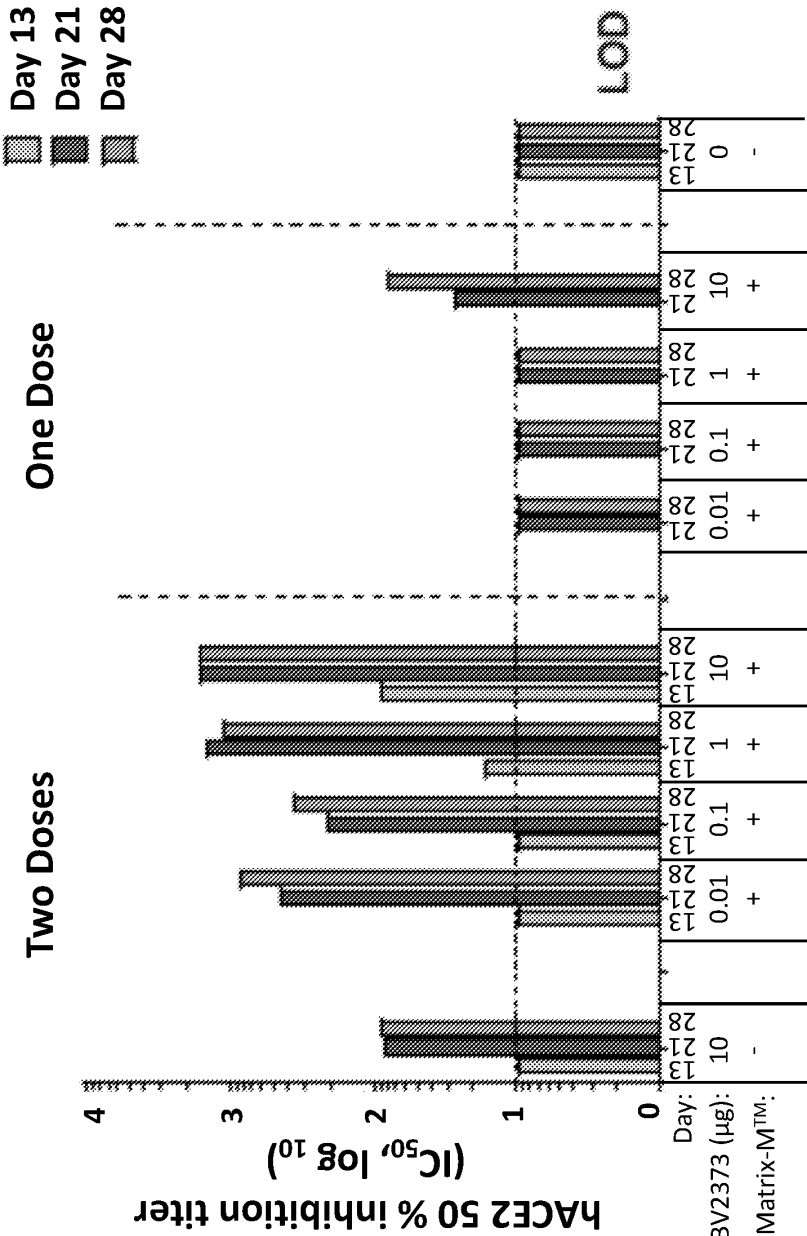


Fig. 15

SARS-CoV-2 Neutralizing Antibody
(21 days post immunization)

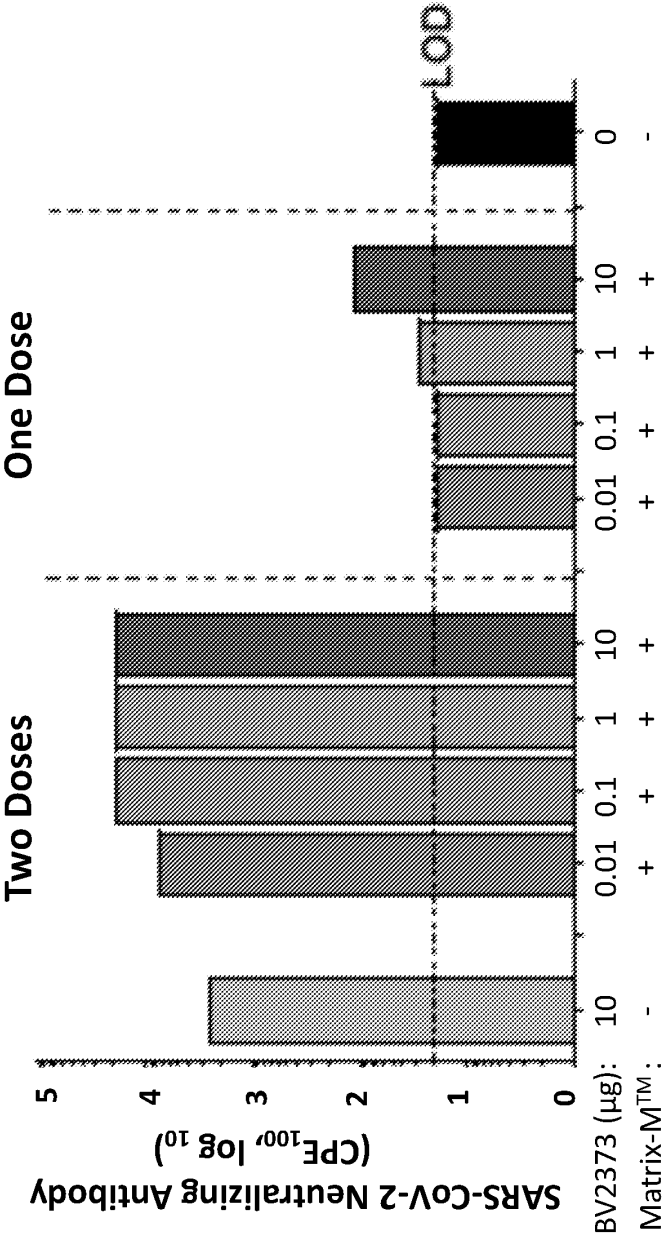


Fig. 16

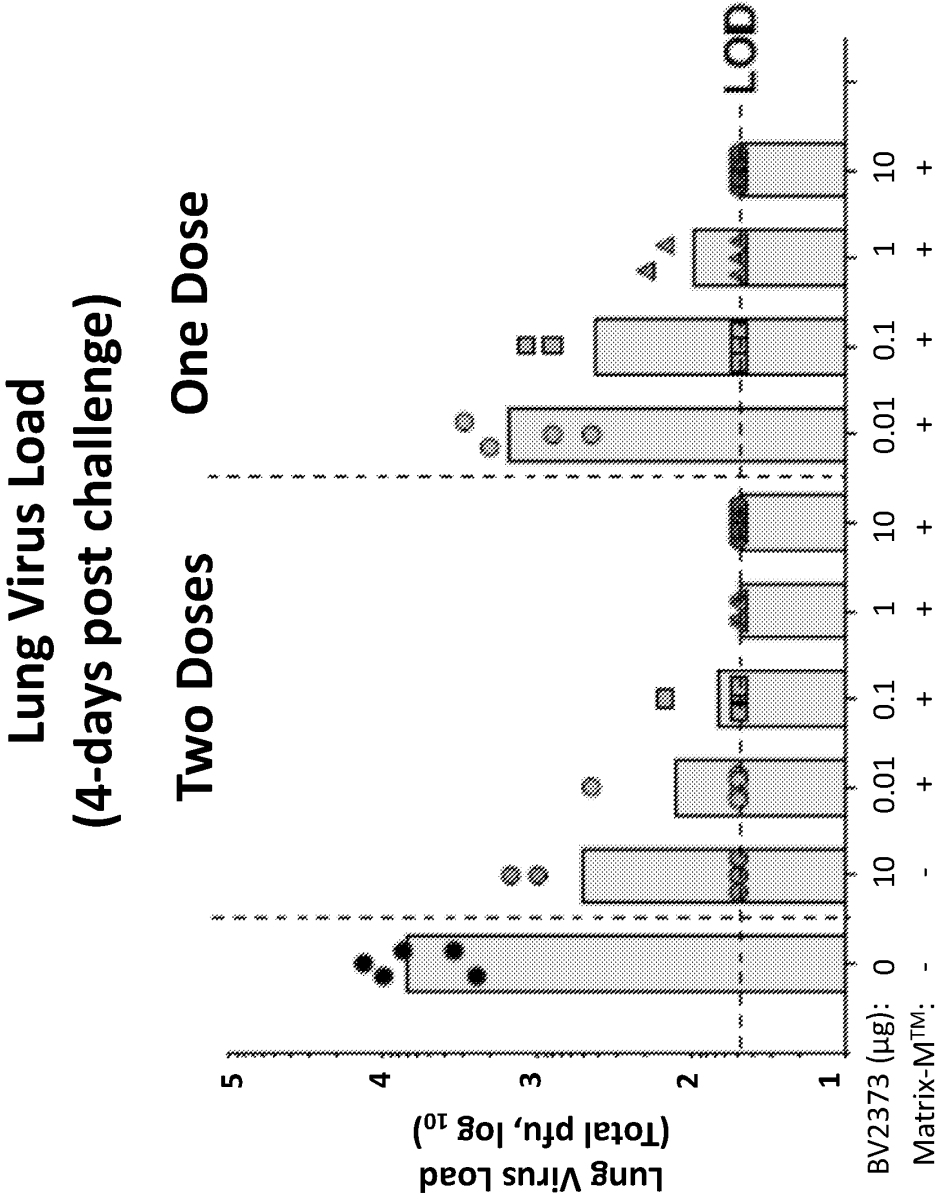


Fig. 17A

% Weight Change (One Dose)

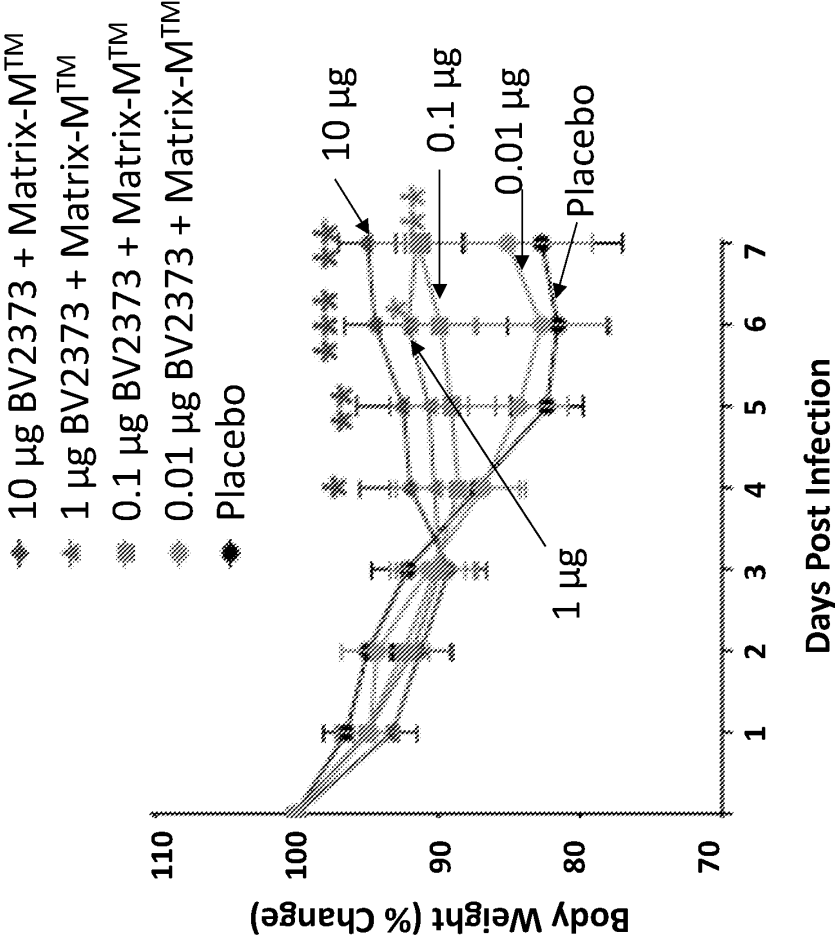


Fig. 17B

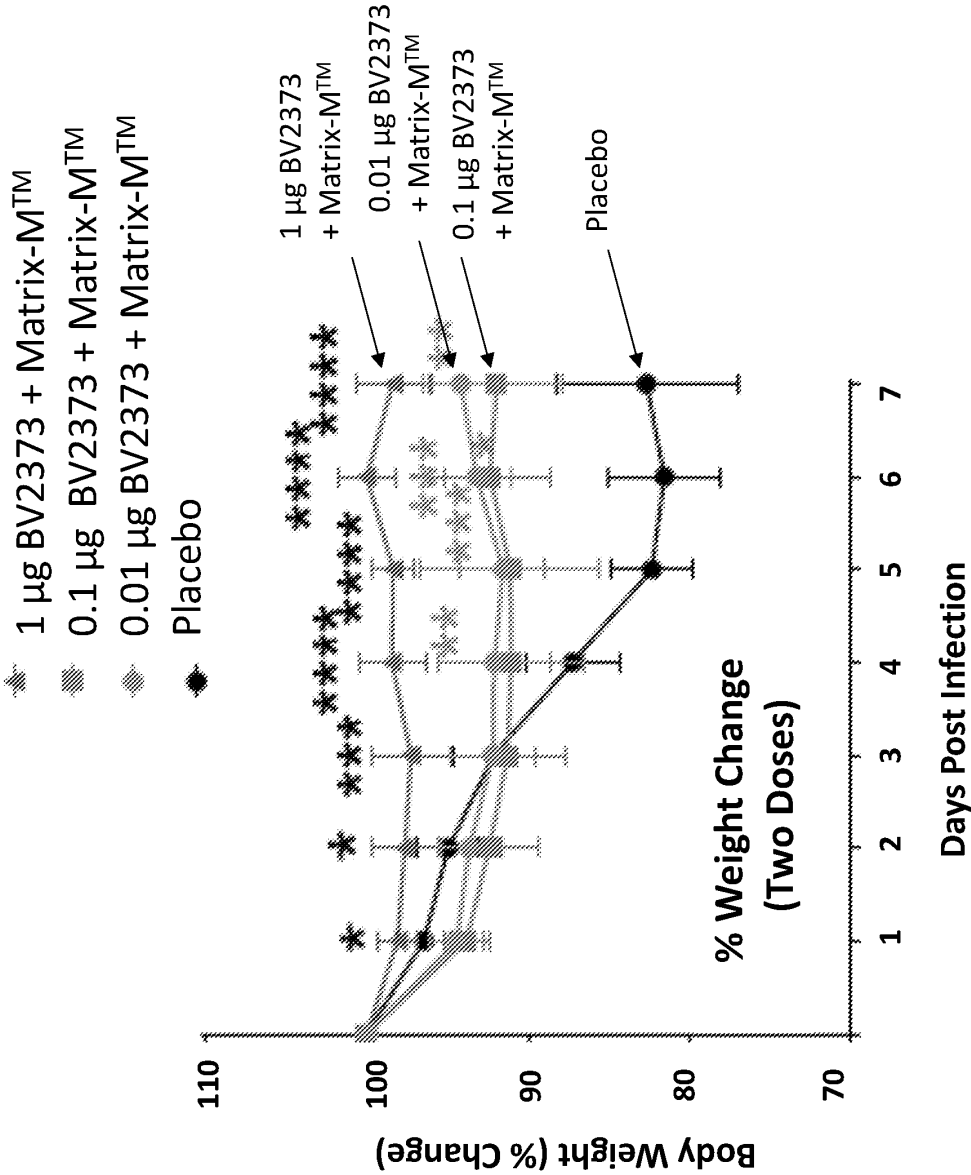


Fig. 17C

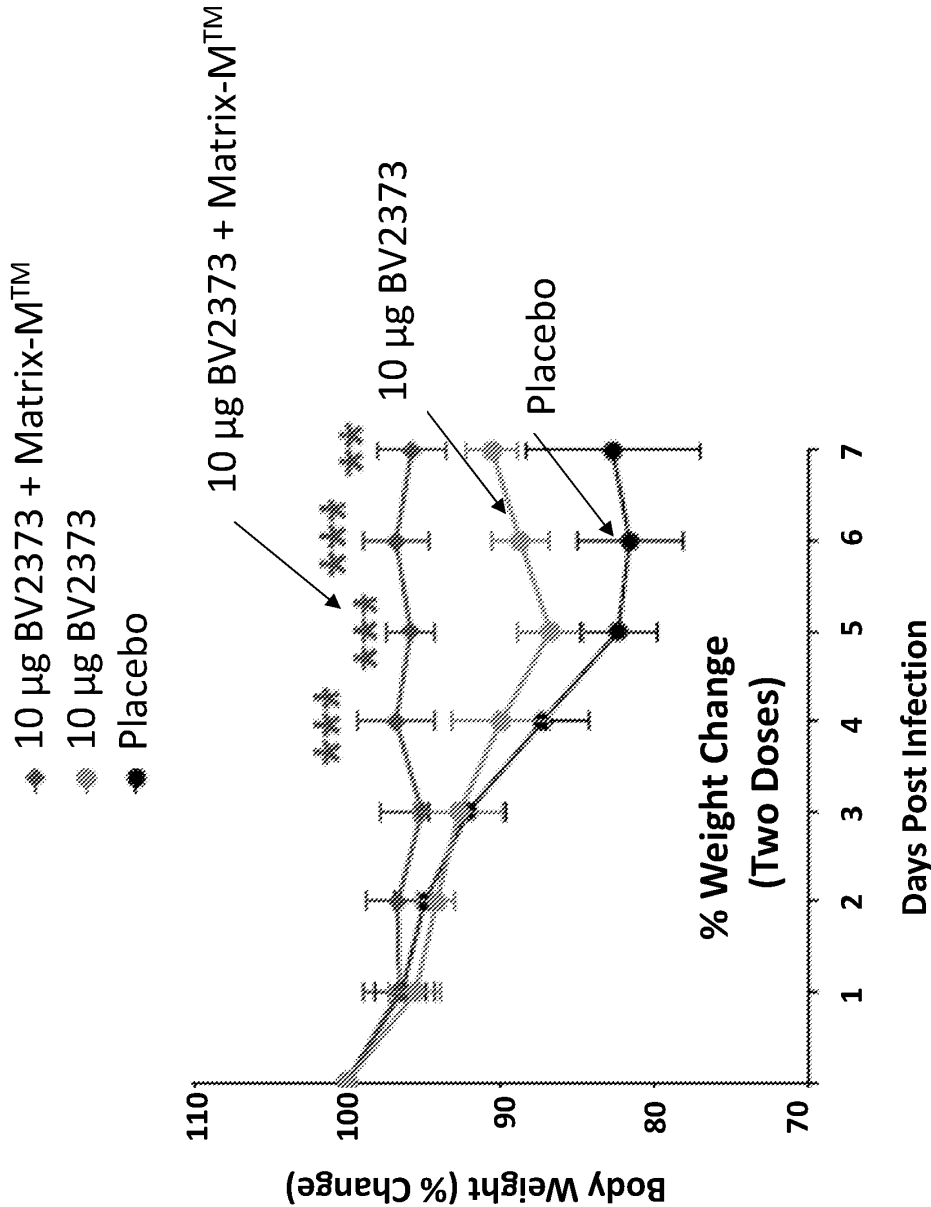


Fig. 18A

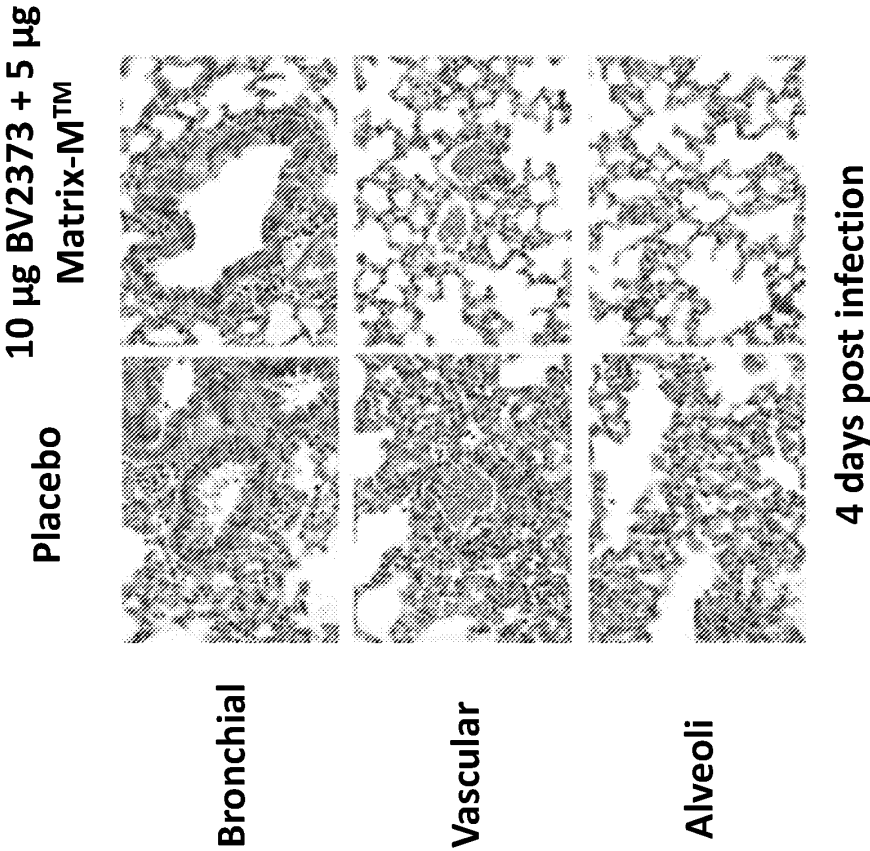


Fig. 18B

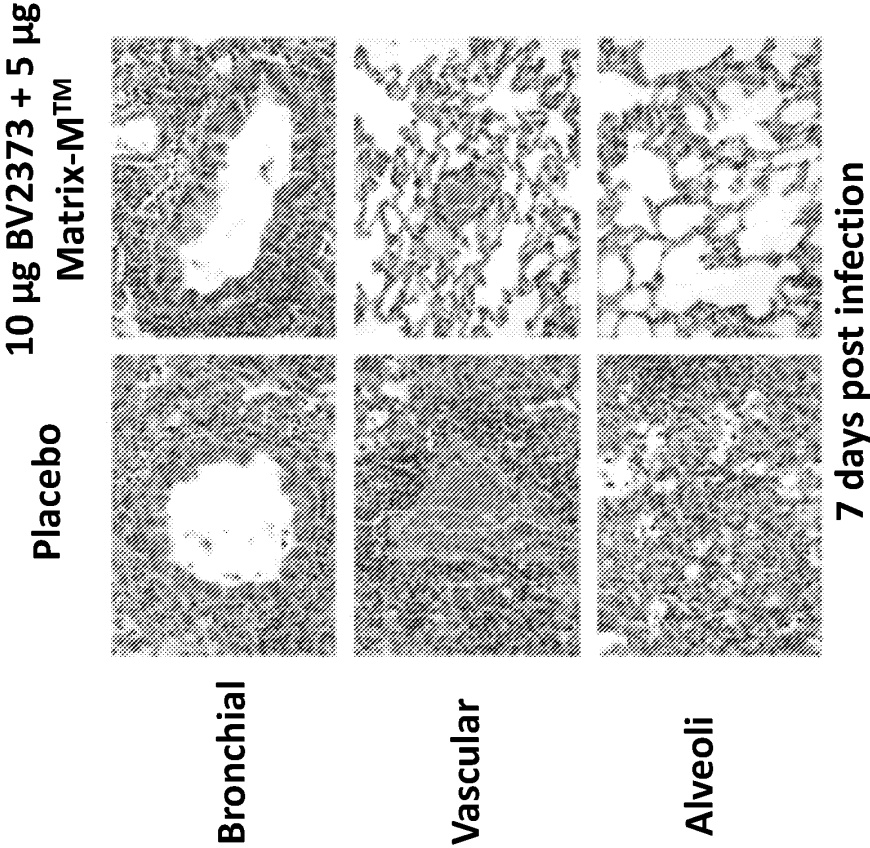


Fig. 19

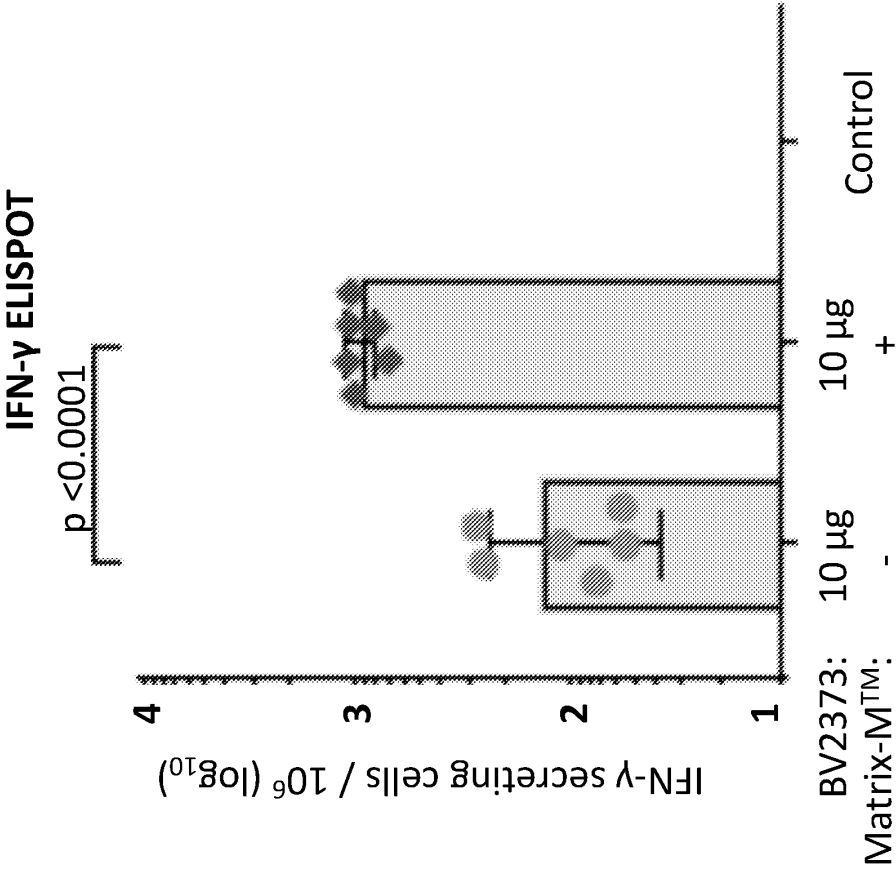


Fig. 20A

IFN- γ ⁺ CD4⁺ T cells

p < 0.0001

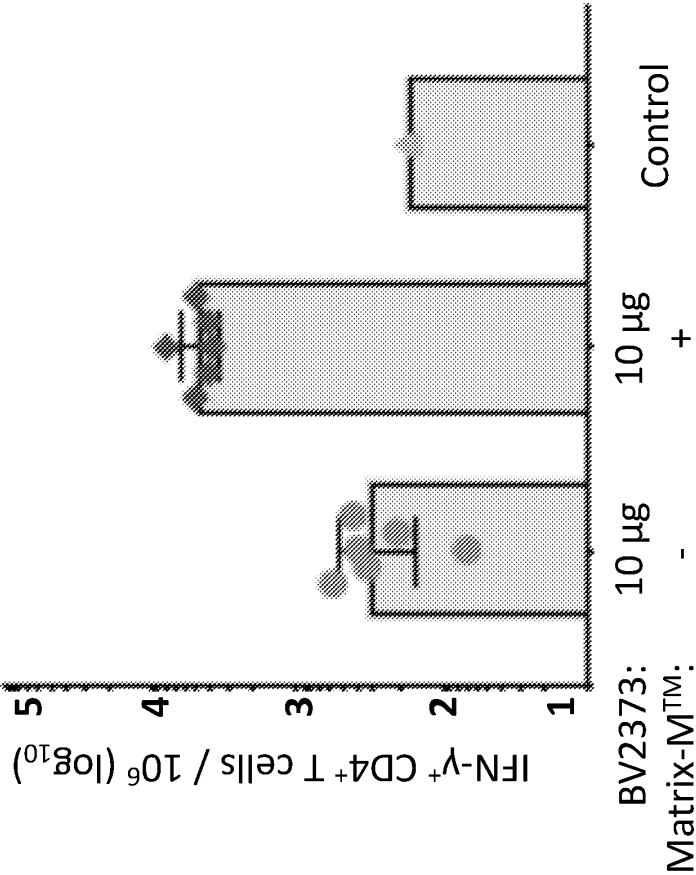


Fig. 20B

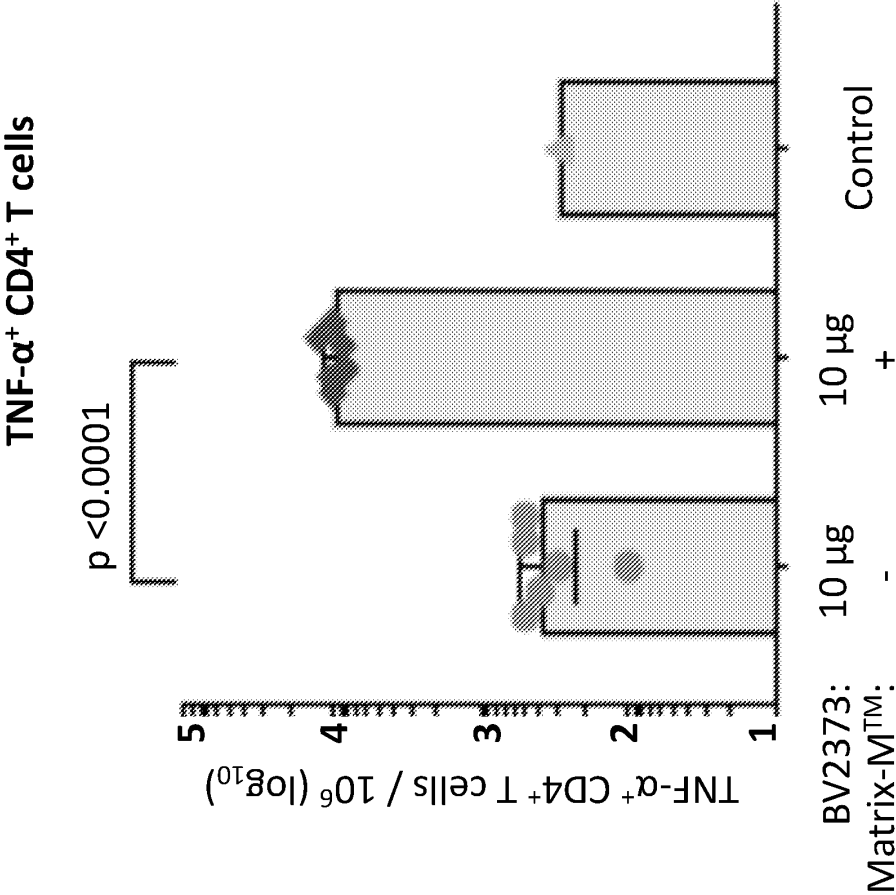


Fig. 20C

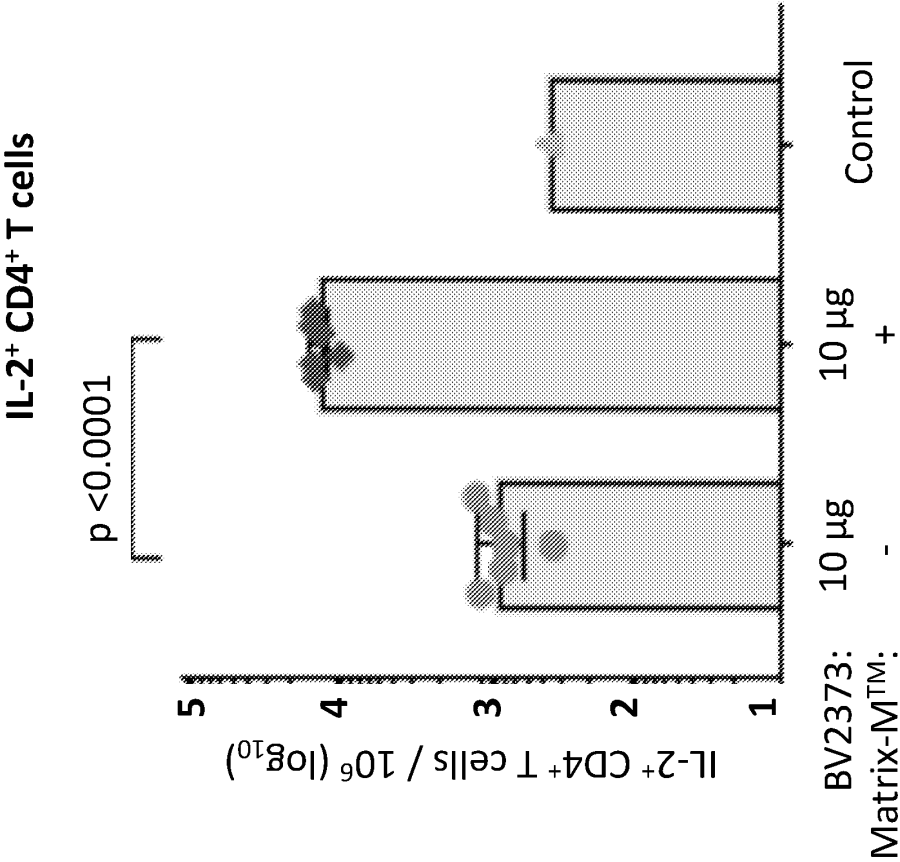


Fig. 20D

Two Cytokine⁺ CD4⁺ T cells

p < 0.0001

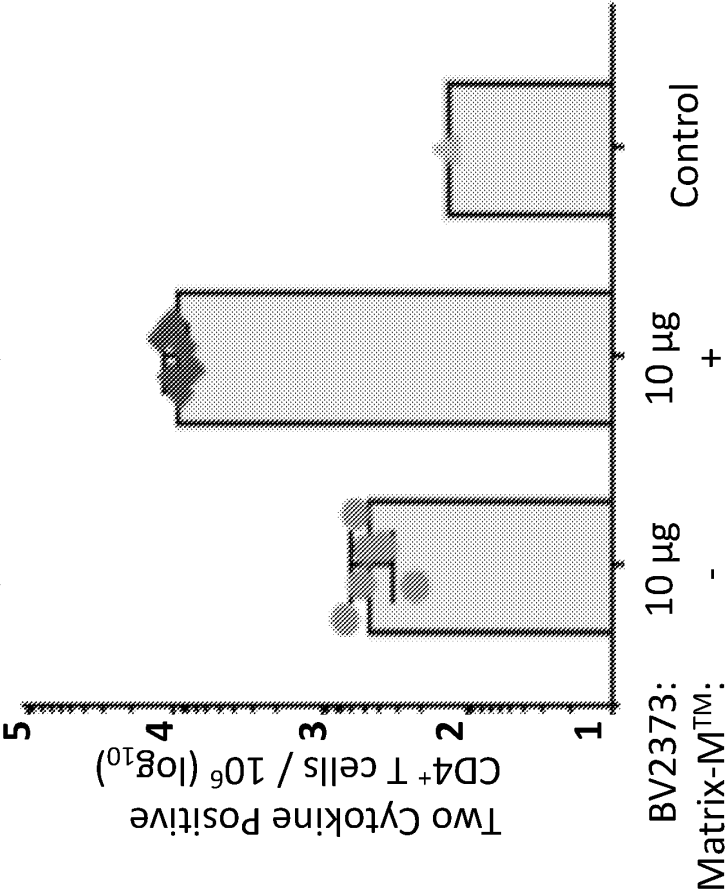


Fig. 20E

IFN- γ^+ , TNF- α^+ , IL-2 $^+$ CD4 $^+$ T cells

p = 0.0004

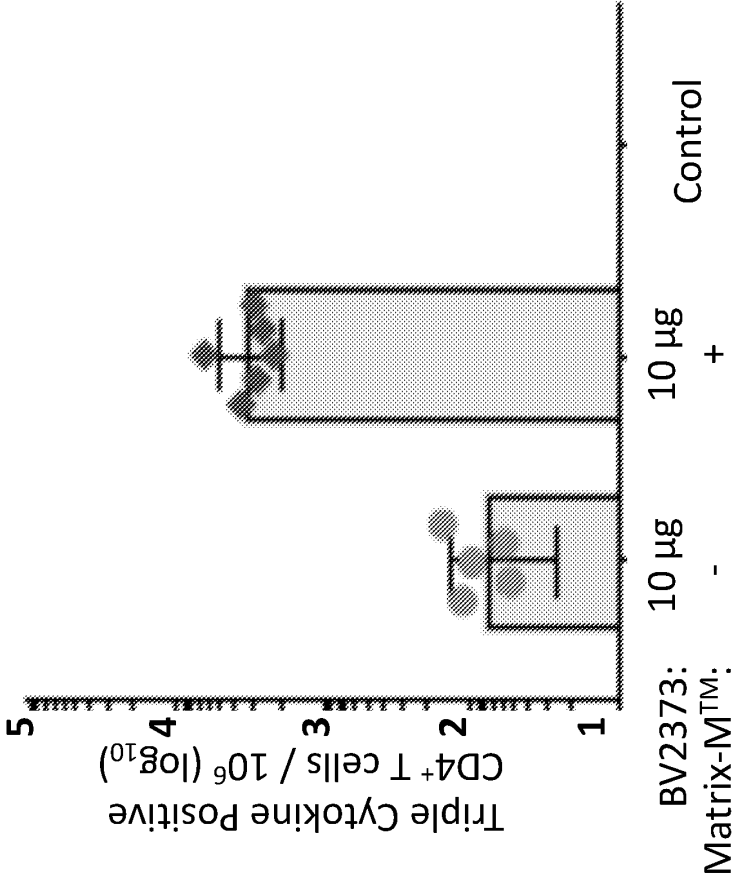


Fig. 21A

IFN- γ ⁺ CD8⁺ T cells

p < 0.0001

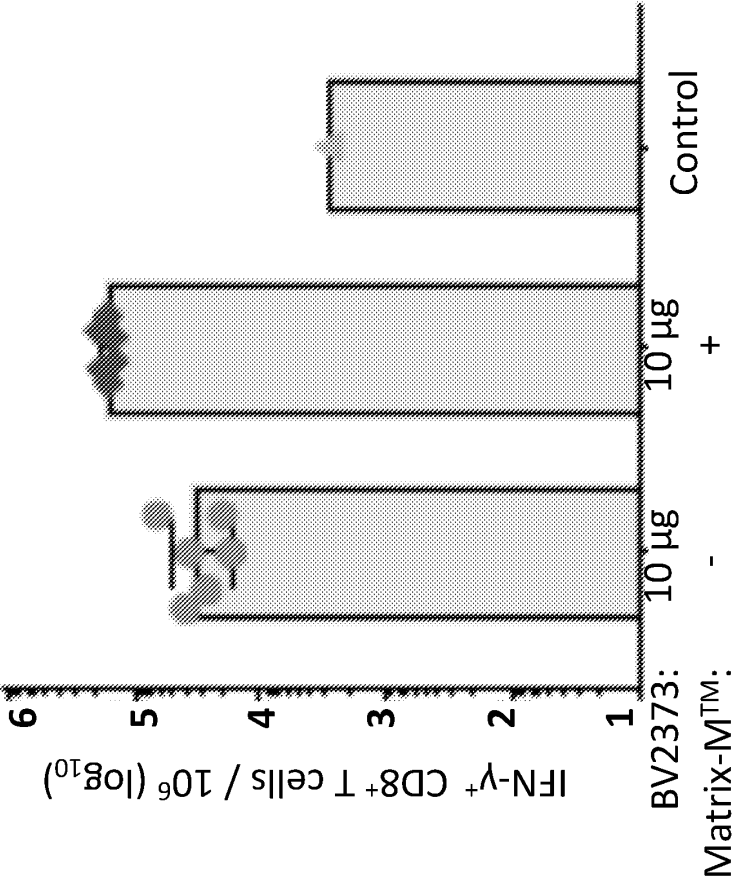


Fig. 21B

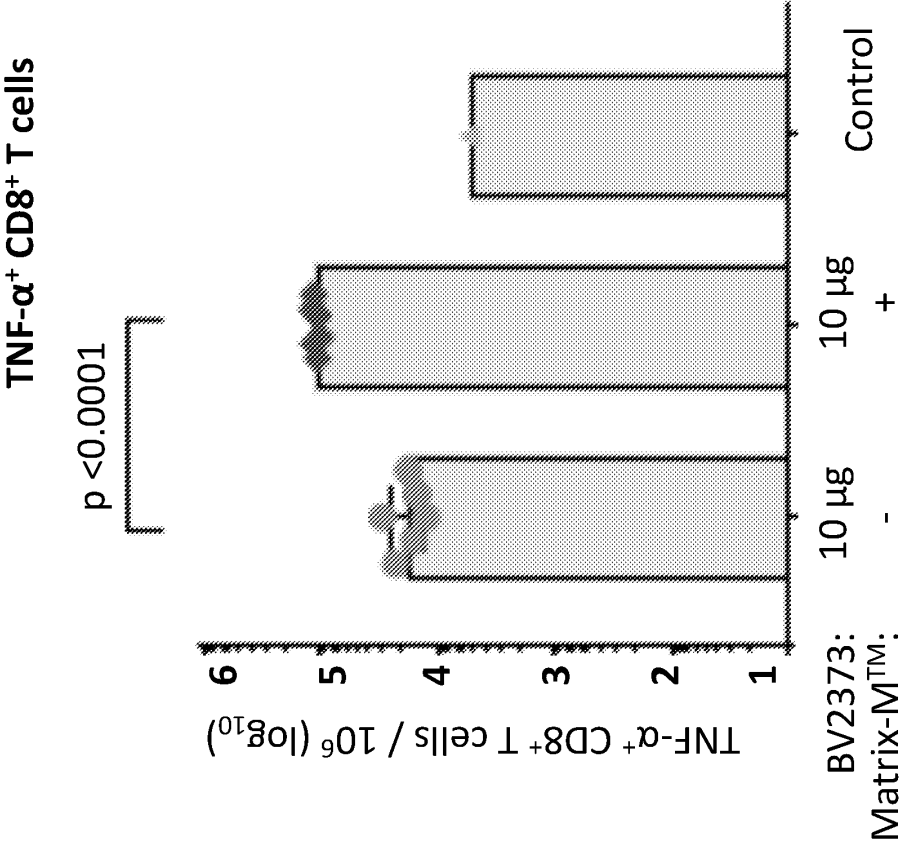


Fig. 21C

IL-2⁺ CD8⁺ T cells

p < 0.0001

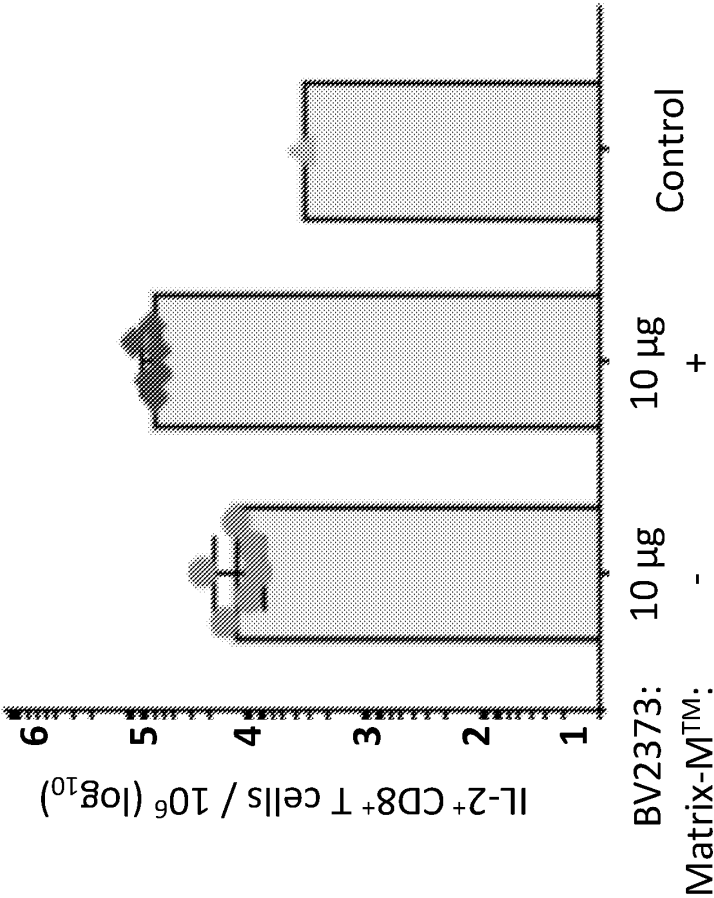


Fig. 21D

Two Cytokine⁺ CD8⁺ T cells

p < 0.0001

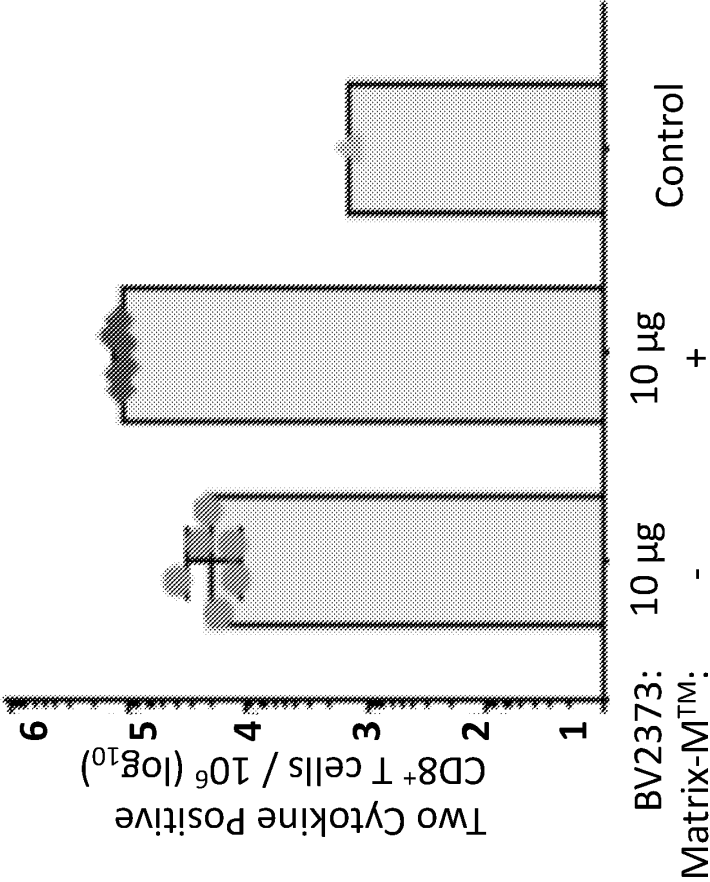


Fig. 21E

IFN- γ^+ , TNF- α^+ , IL-2 $^+$ CD8 $^+$ T cells

p < 0.0001

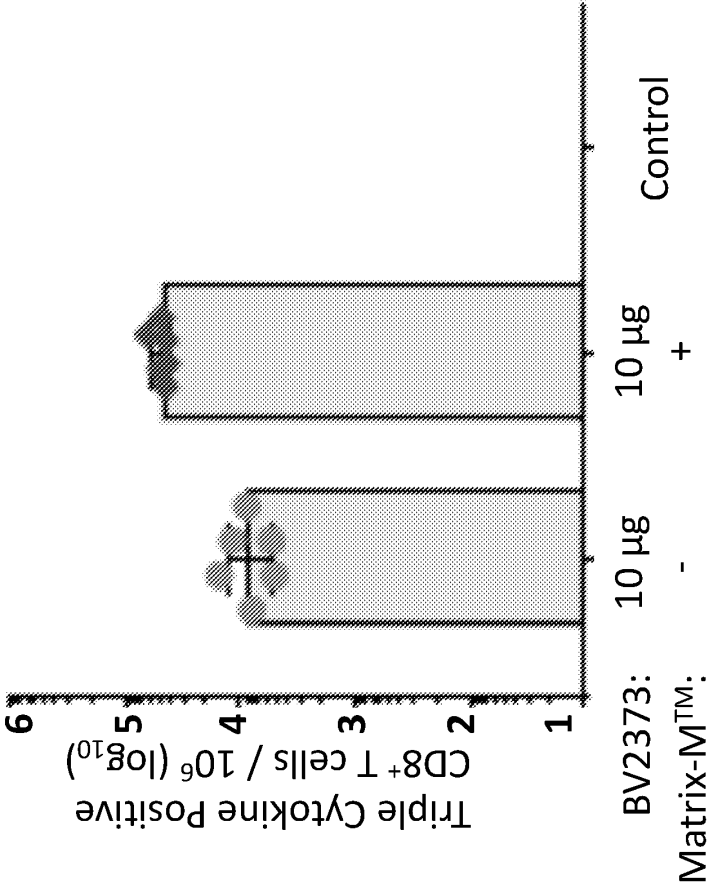


Fig. 22

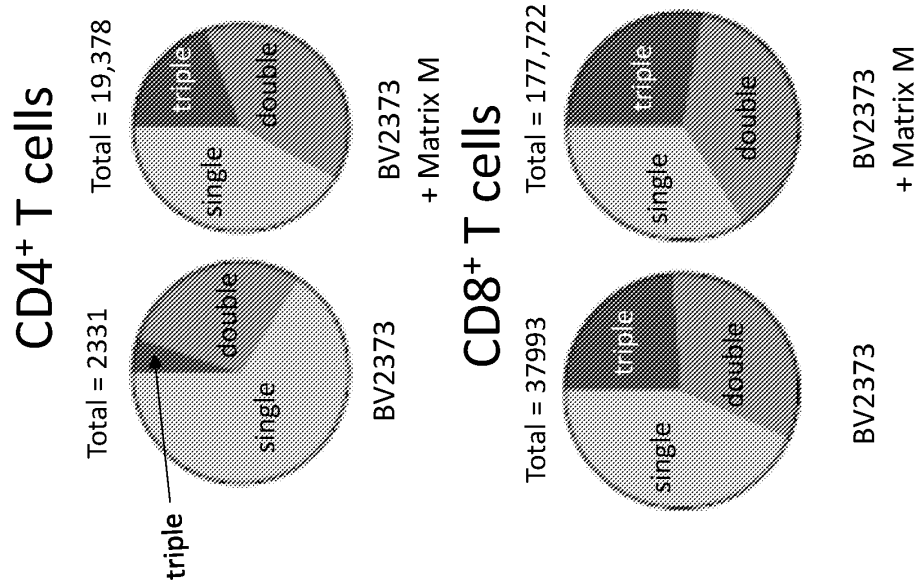


Fig. 23A

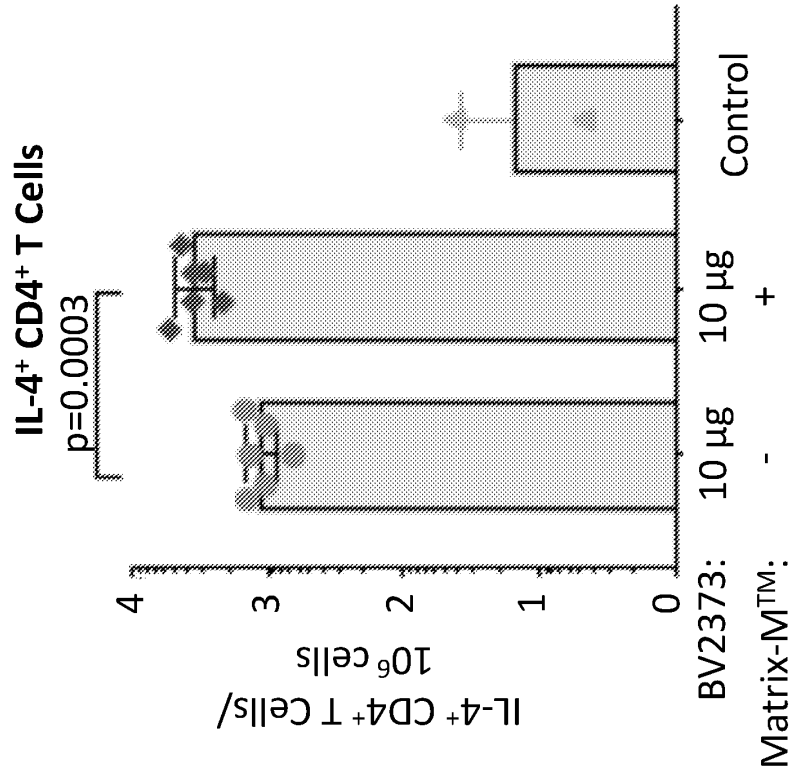


Fig. 23B

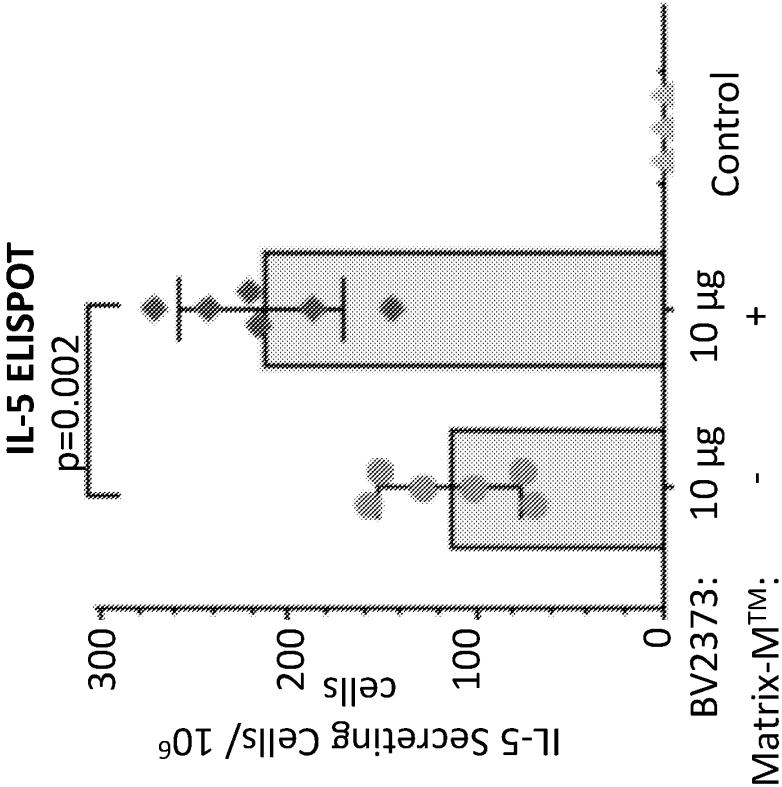


Fig. 23C

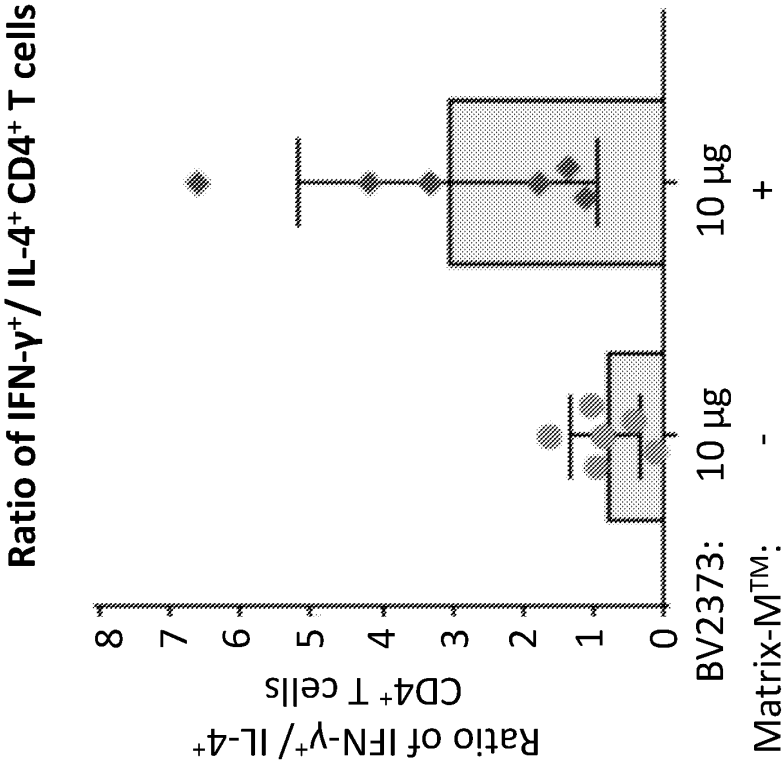


Fig. 24A

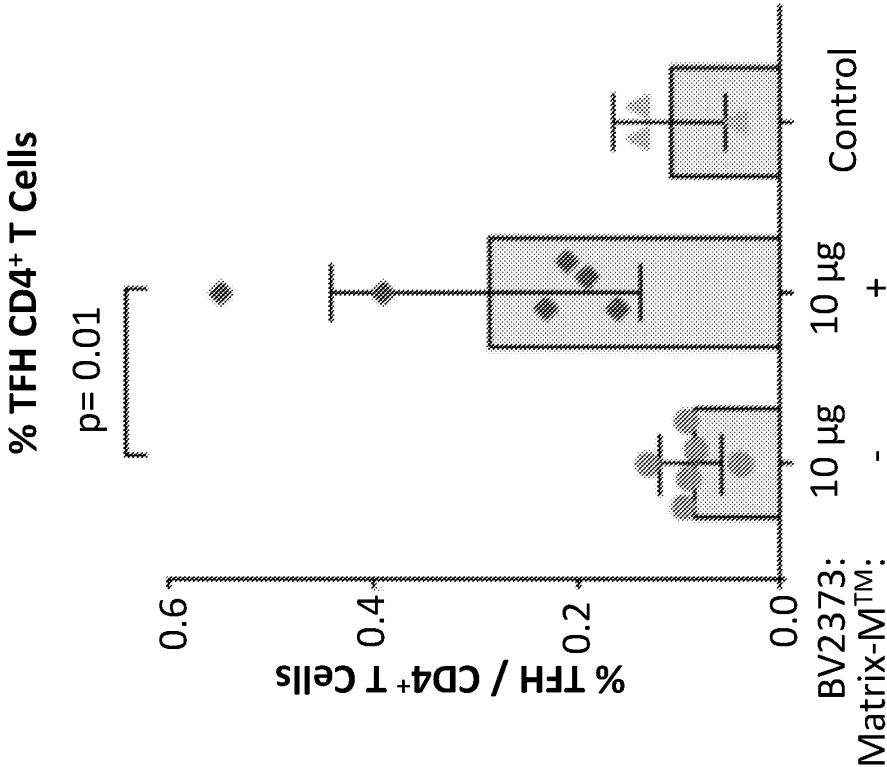


Fig. 24B

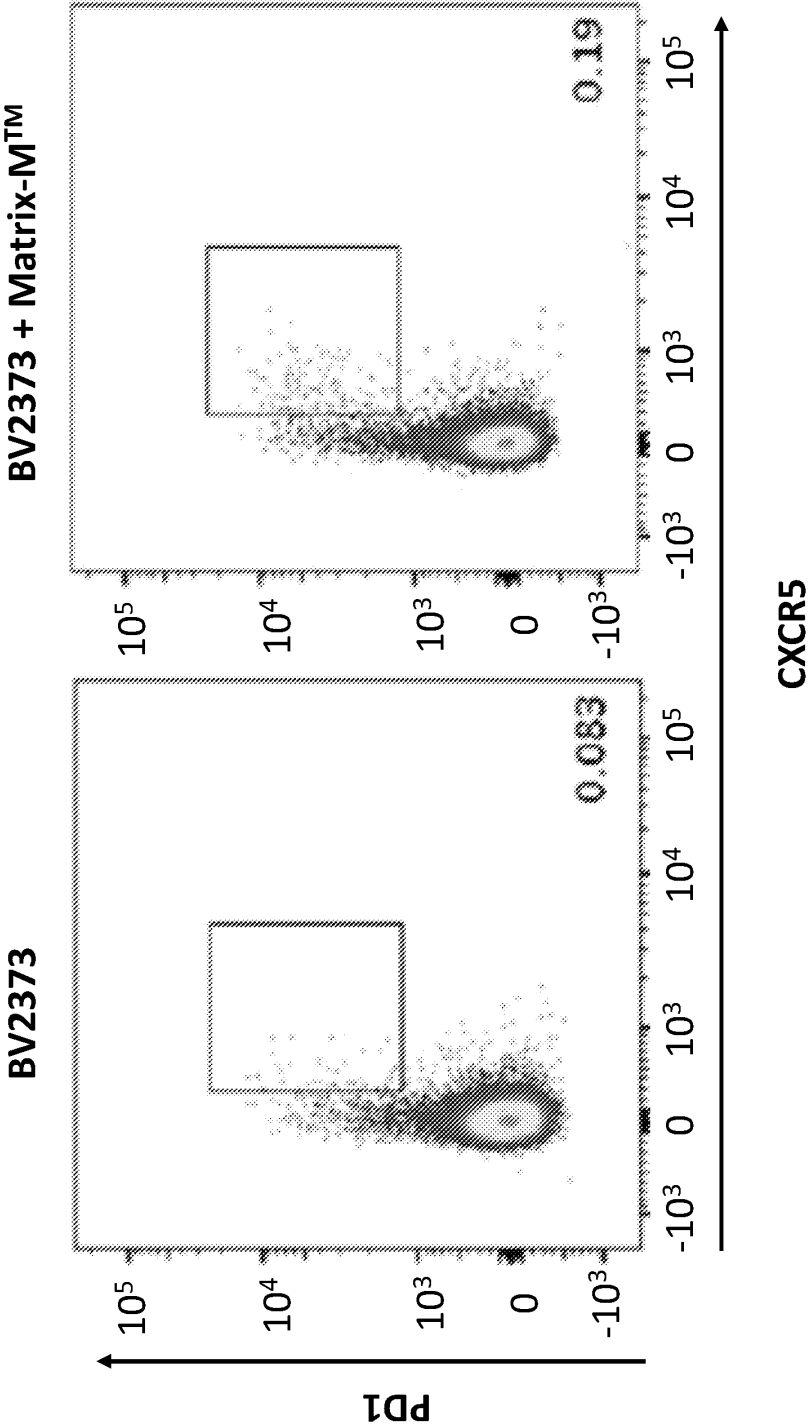


Fig. 25A

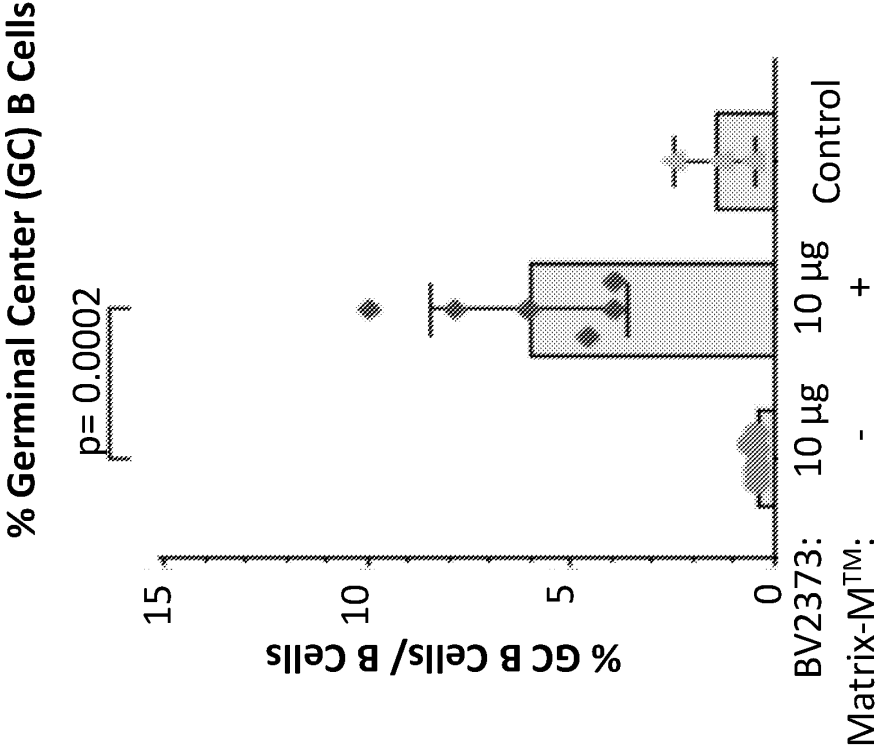


Fig. 25B

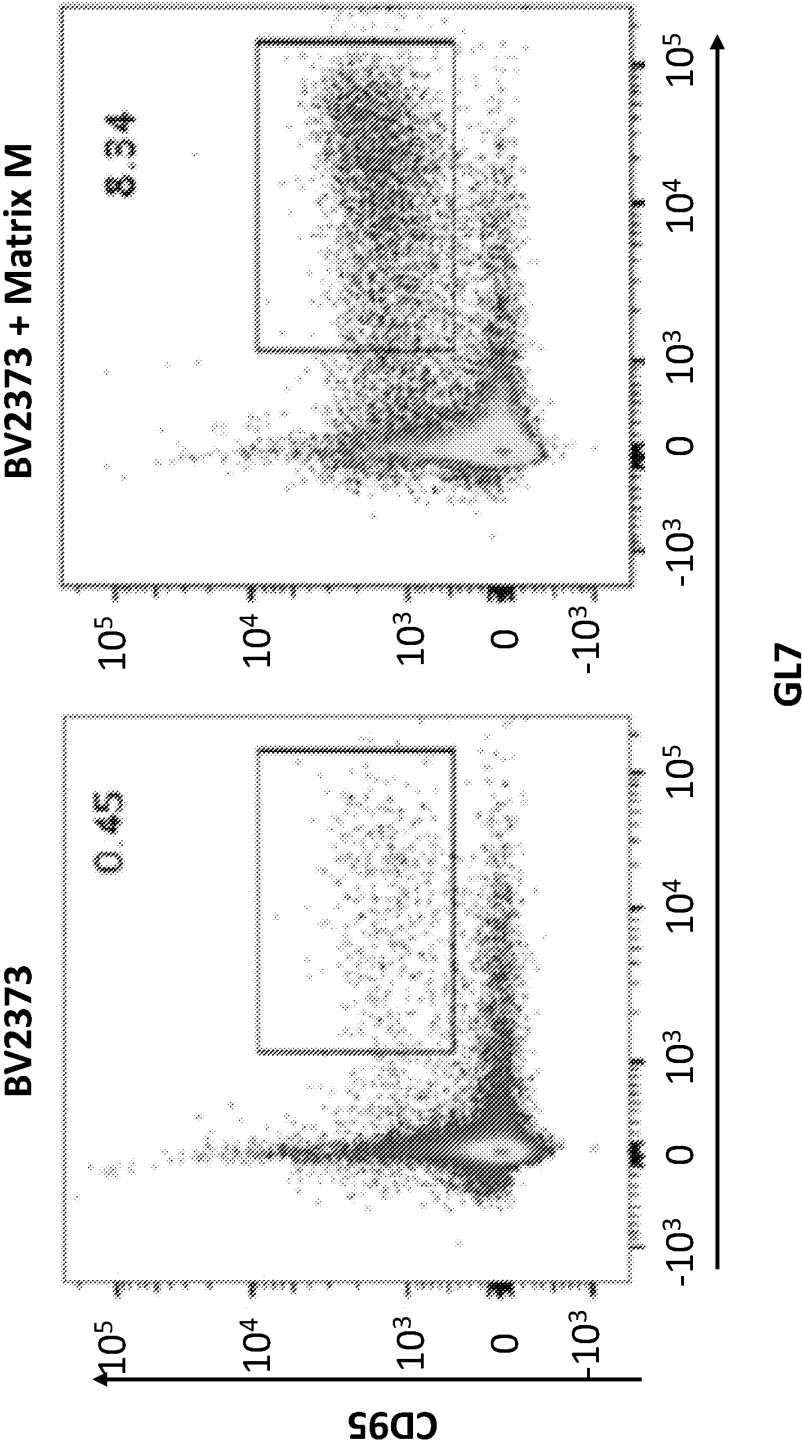


Fig. 26A

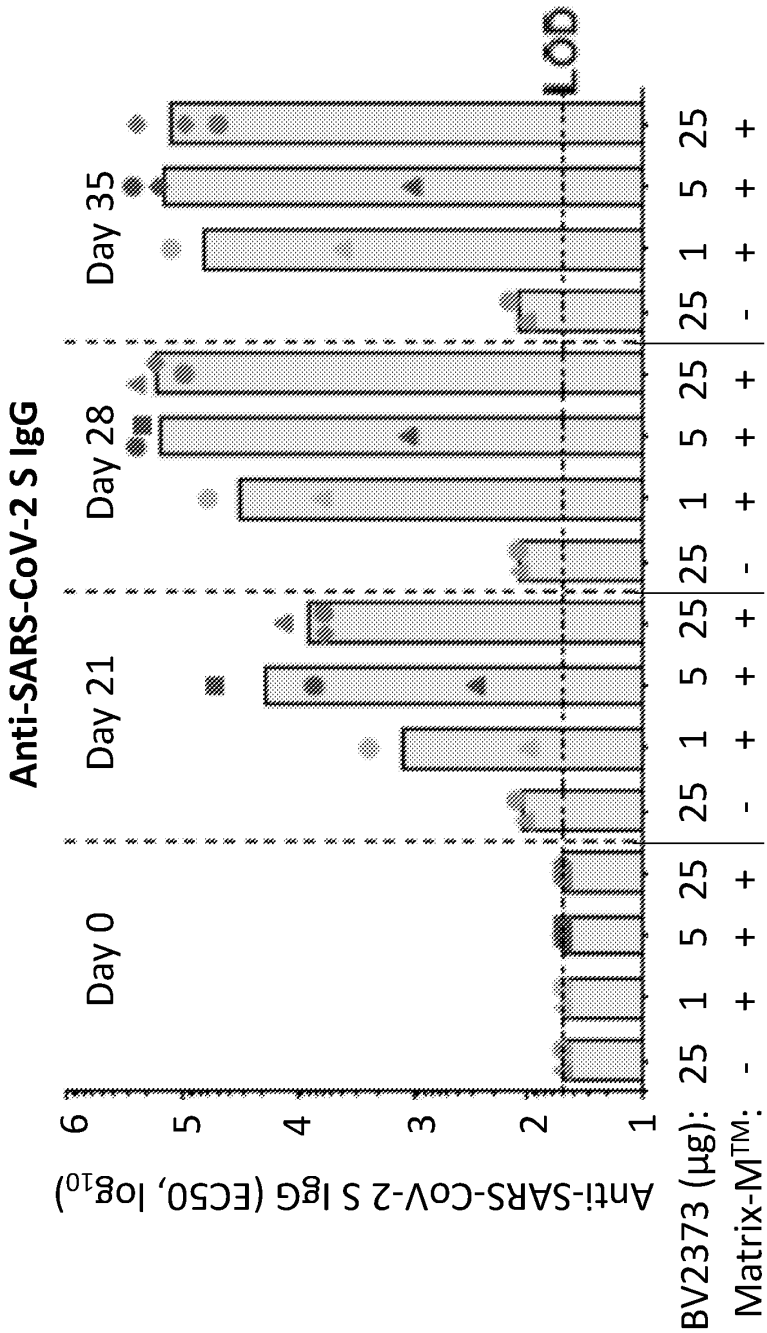


Fig. 26B

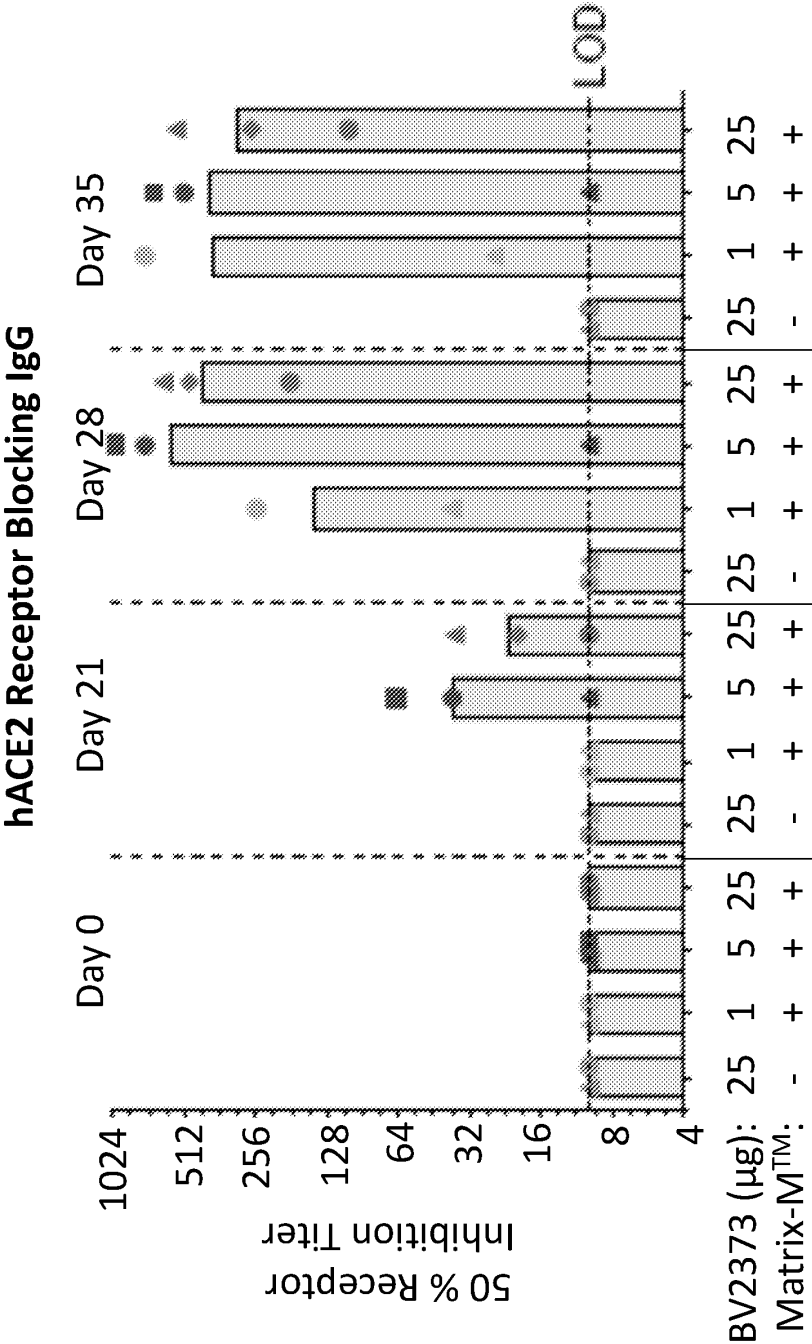


Fig. 26C

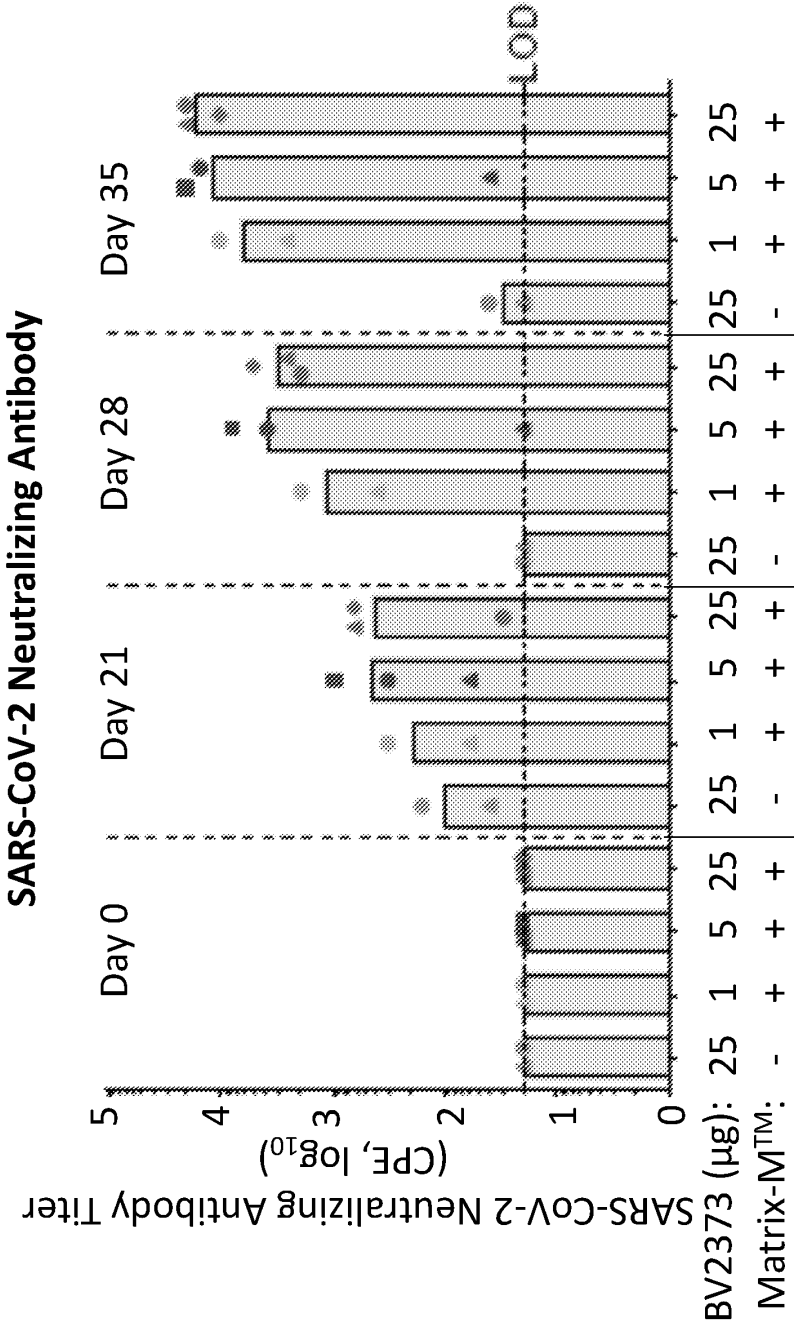


Fig. 27

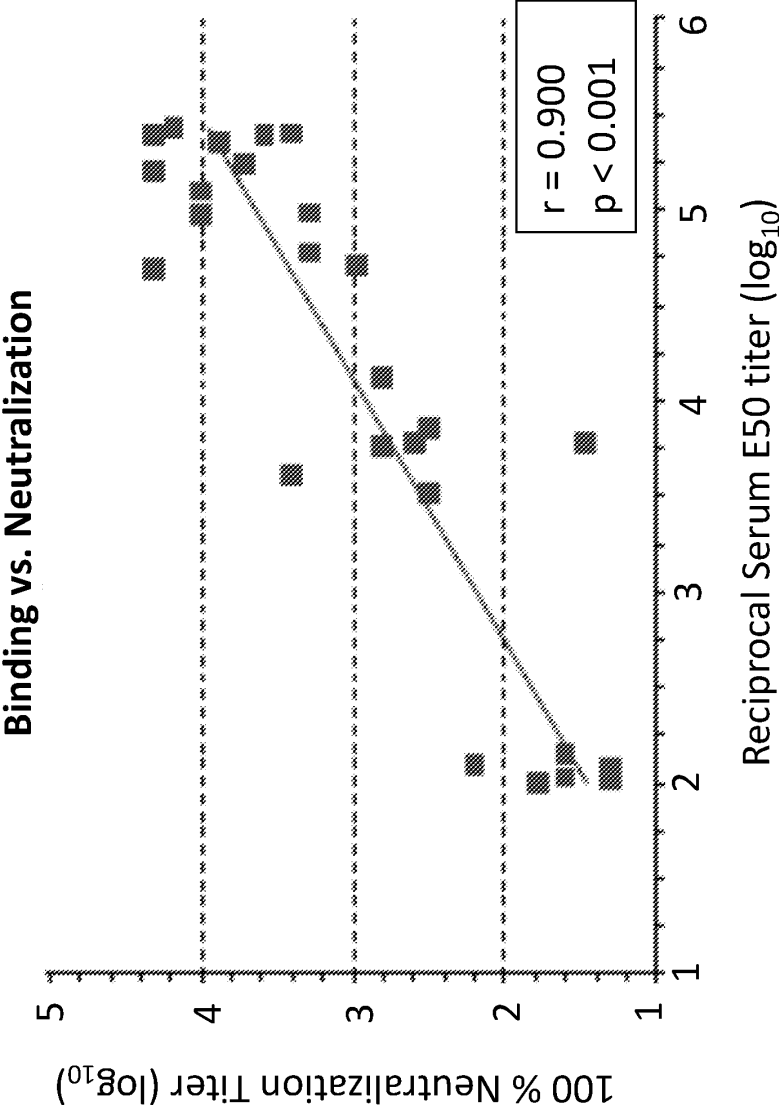


Fig. 28

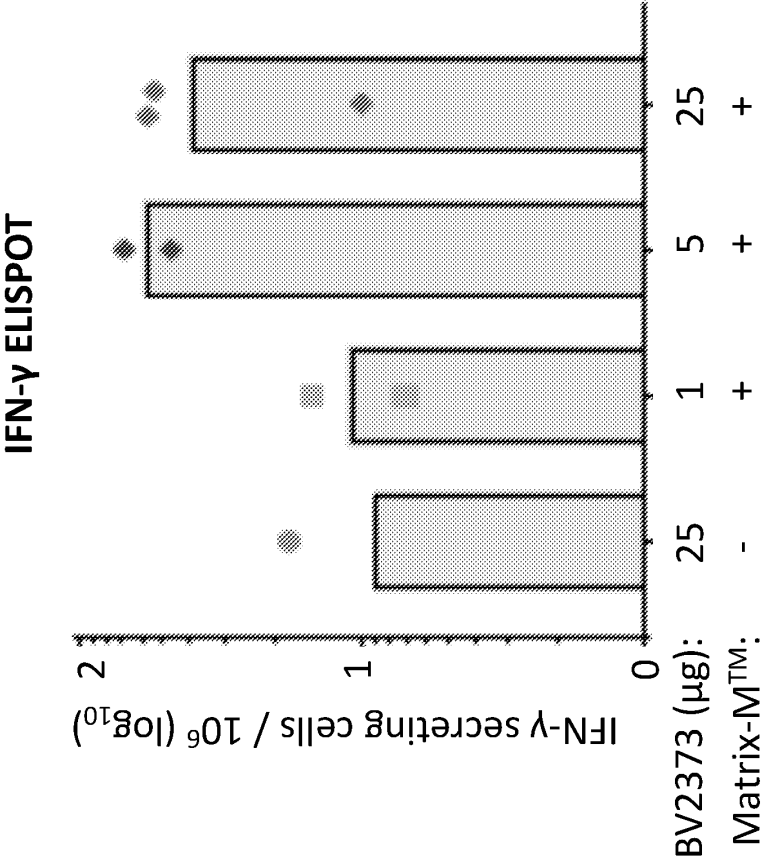


Fig. 29A

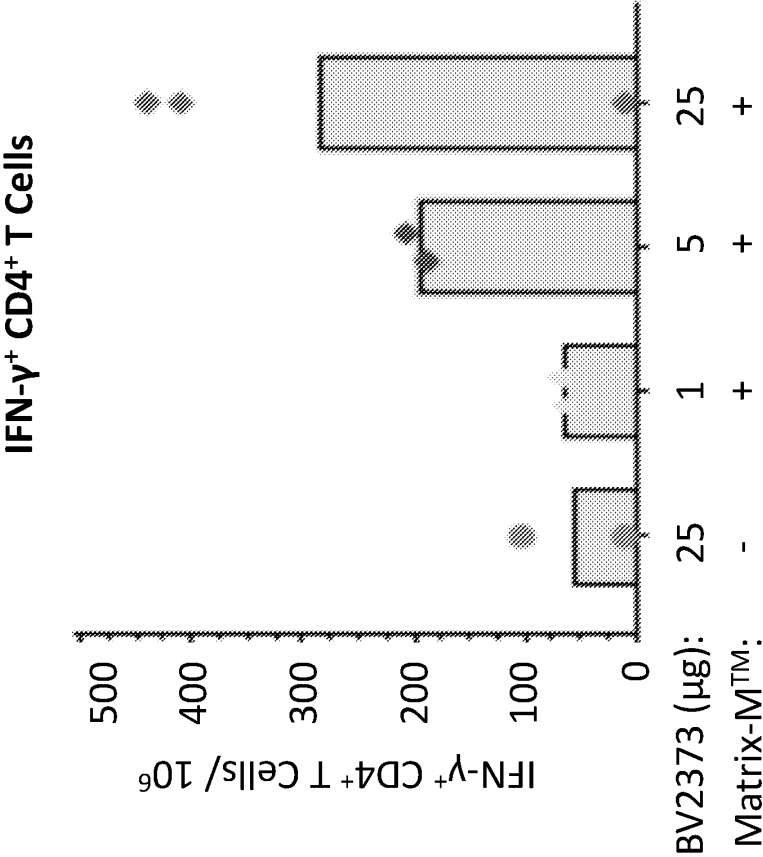


Fig. 29B

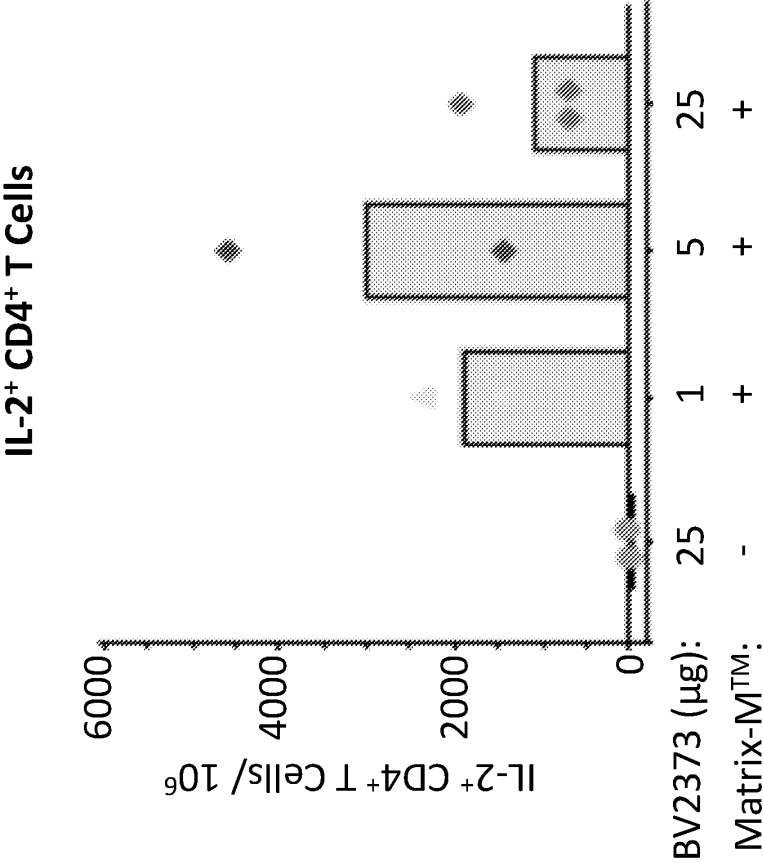


Fig. 29C

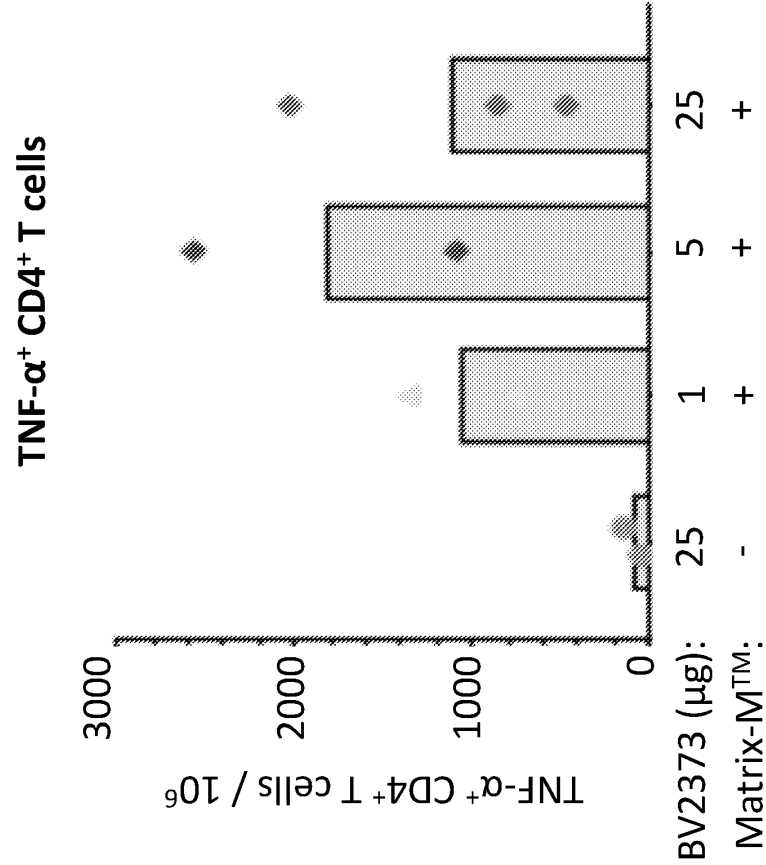


Fig. 29D

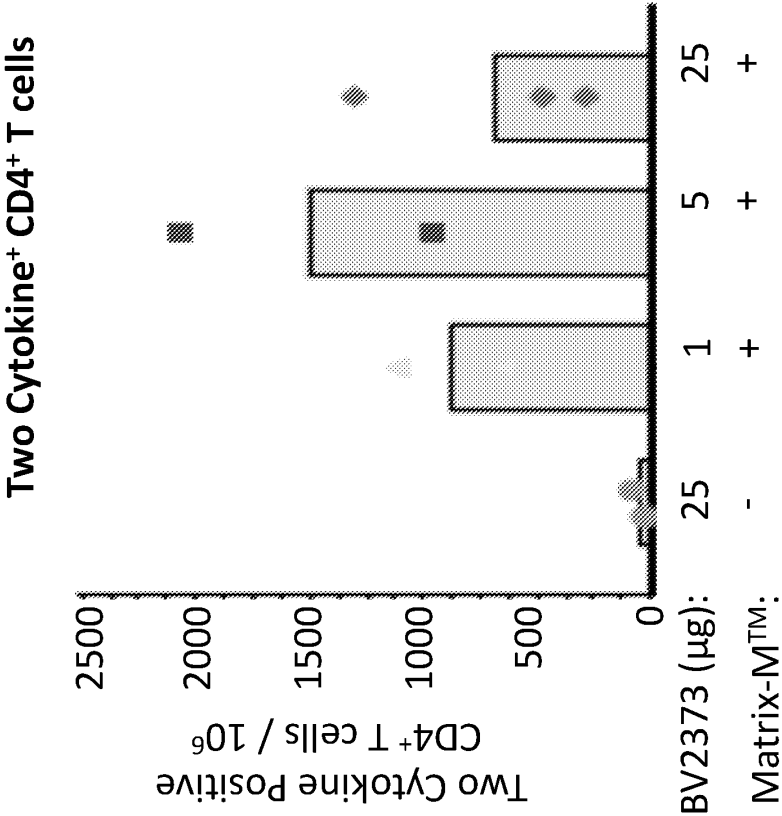


Fig. 29E

IFN- γ^+ , TNF- α^+ , IL-2 $^+$ CD4 $^+$ T cells

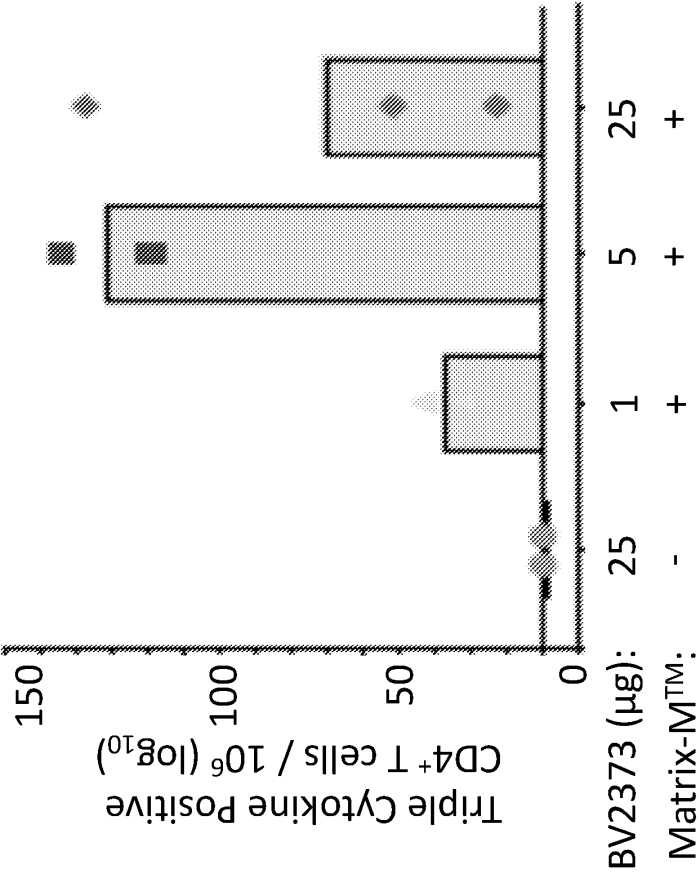


Fig. 30

BV2384: CoV-2019/GSAS/K986P/V987P (SEQ ID NO: 109)

Isoelectric Pt (pI) 5.89

Signal
peptide

MFVFLVLLPLVSSQCVNLTTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFSNVTFHAIHVSGT
NGTKREFDNPVLPFNDGVYFASTEKSNIRGWIFGTTLDSKTQSLLVNNATNVVIKVCEFFQFCNDPFLGVYYH
KNKSWMESEFRVYSSANNCTFEYVSQPFLLMDLEGKQGNFKNLREFVEKNIDGYFKIYSKHTPINLVRDL PQG
FSALEPLVDLPIGINITRFQTLALHRSYLPGDSSSGWTAGAAAYVGYLQPRTFLLKYNENGTITDAVDCAL
DPLSETKCTLKSFVEKGIYQTSNFRVQPTESIVRFPNITNLCPPFGEVFNATRFASVYAWNKRKRSNCVADYS
VLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVQRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSN
NLDSKVGGNYNLYRLFRKSNLKPFERDISTEIIYQAGSTPCNGVEGNCYFPLQSYGFQPTNGVGYPYRVVV
LSFELLHAPATVCGPKKSTNLVKNKCVNFNENGLTGTGVLTESNKKFLPFQQFGRDIADTTDAVRDPQTLEIL
DITPCSFGGVSVITPGTNTSNQVAVLYQDVNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNN
SYECDIPIGAGICASYQTQTNSP**GSAS**SVASQSI IAYTMSLGAENSVAYSNNSLAIPTNFTISVTTEILPVSM
TKTSVDCMTMYICGDSTECSNLLLLQYGSFCTQLNRALTGIAVEQDKNTQEVFAQVKQIYKTPPIKDFGGNFSQ
ILPDPSKPSKRSFIEDLLFNKVTLADAGFIKQYGDCLGDIARDLICAQKFNGLTVLPPLLTDEMIAQYTSAL
LAGTITSGWTFGAGAAALQIPFAMQMAYRFNGIGVTQNVL YENQKLIANQFNSAIGKIQDSSLSTASALGKLQD
VVNQNAQALNTLVKQLSSNFGAISSVLNDILSRLD**PP**PEAEVQIDRLITGRQLSLQTYVTQQLIRAAEIRASAN
LAATKMSECVLGQSKRVDFCGKGHYHMSFPQSA PHGVFLHVTYVPAQEKNTTAPAI CHDGKAHFPREGVFV
SNGTHWFTQRNFYEPQIITTDNTFVSGNCDVIGIVNNTVYDPLQPELDSFELDKYFKNHTSPDVDLGDIS
GINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEQYIKWPWYIWLGFIAGLIAIVMVTIMLCMTSCCSC
LKGCCSCGSCCKFDEDDSEPV LKGVKLHYT

Fig. 31

BV2373 (SEQ ID NO: 86)

CoV-2019/QQAQ/K986P/V987P

Inactive furin
cleavage site

Signal
peptide

MEVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFSNVTFHAIHVS
NGTKREFDNPVLPFNDGVYFASTEKSNIRGWIFGTTLDSKTQSLLI VNNATNVIVKVEFQFCNDPFLGVYH
KNKSWMESEFRVYSSANNCTFEYVSQPFMLDLEGGKQGNFKNLREFVEKNIDGYFKIYSKHTPINLVRDL
PQG FSALEPLVDLPIGINITRFQTLALHRSYLT PGDSSSGWTAGAAAYVGYLQPRTFLLKYNENGTTITDA
VDCA LDPLSETKCTLKSFTEKGIYQTSNFRVQPTESIVRFPNITNLCPEGEVFNATREFASVYAWNKRK
ISNCVADY SVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRLAPGQTGKIADYNYKL
PDDFTGCVIAWNS NNLDKVGGNYNLYRLFRKSNLKPFERDISTEIIYQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVV
VLSFELLHAPATVCGPKKSTNLVKNKCVNFNFNGLTGTGVLTESNKKFLPFQQFGRIADTTDAVRDPQTLEI
LDITPCSFGGVSVITPGTNTSNQVAVLYQDVNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGA
EHVN NSYECDIPIGAGICASYQTQTNSP**QQAQ**SVASQSI IAYTMSLGAENSVAYSNNISAIPTNFTISVTTEILPVS
MTKTSVDC TMYICGDSTEC SNLLLYG SFTQLNRALTGIAVEQDKNTQEVFAQVKQIYKTPPIKDFGGFNFS
QILPDPSKPSKRSFIEDLLFNKVTLADAGFIKQYGDCLGDI AARDLICAQKFNGLTVLPPLLTDEMIAQY
TSA LLAGTITSGWTFGAGAAIQIPFAMQMAYRFGNGIGVTQNVLYENQKLIANQFNSAIGKIQDSLSSTASALGKLQ
DVVNQNAQALNTLVKQLSSNFGAISVLNDILSRLD**PP**EAQVQIDRLITGRLQSLQTYVTQQLIRAAEIRASA
NLAATKMSECVLGQSKRVDFCGKGYHLMSFPQSA PHGVFLHVTYVPAQEKNTTAPAI CHDGKAHFPREGVF
VSNGTWVFTQRNFYEPQIIITDNTFVSGNCDVVGIVNNTVYDPLQPELDSFKEELDKYFKNHTSPD
VDLGD ISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYQIKWPWYIWLGFIAGLIAIVMVTIMLCMTSCC
SCLKGCCSCGSCCKFEDEDDSEPV LKGVKLHYT

Fig. 32

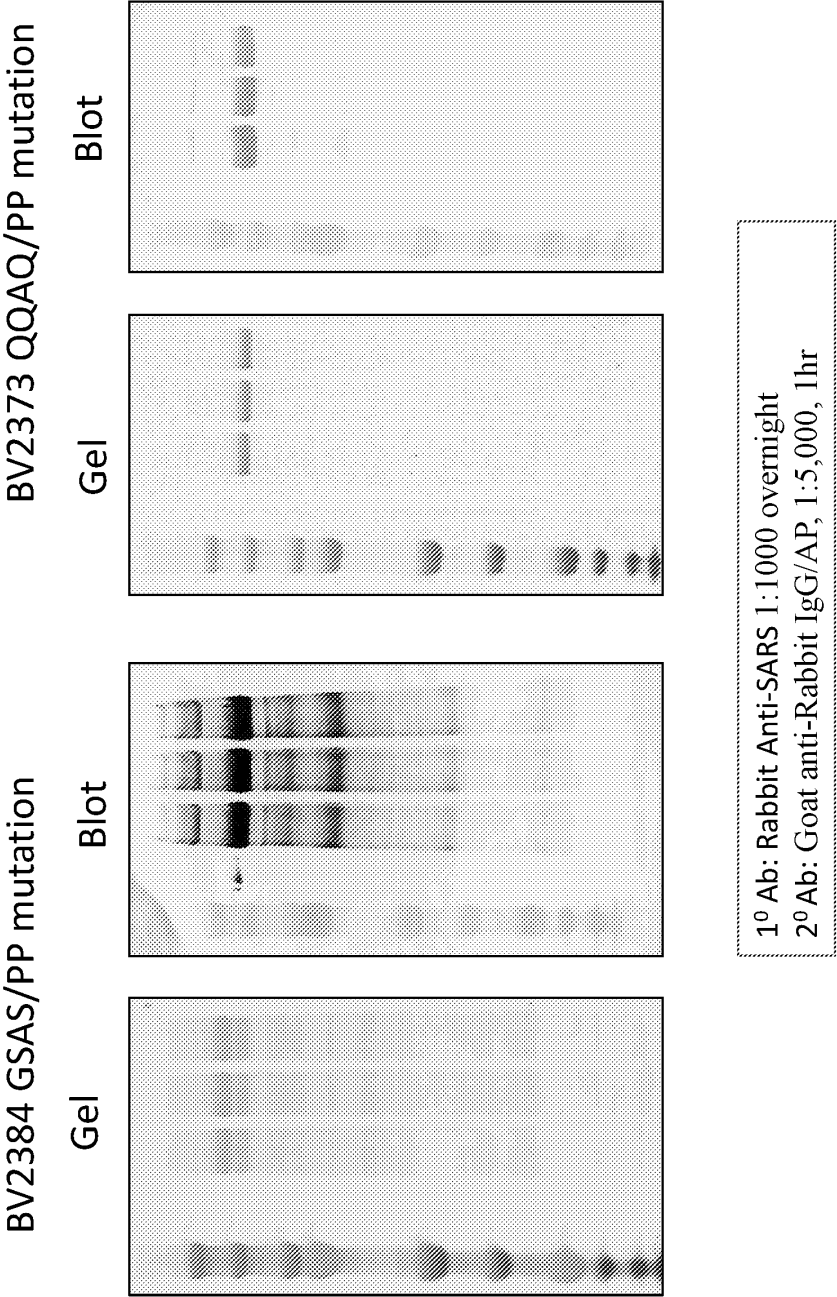
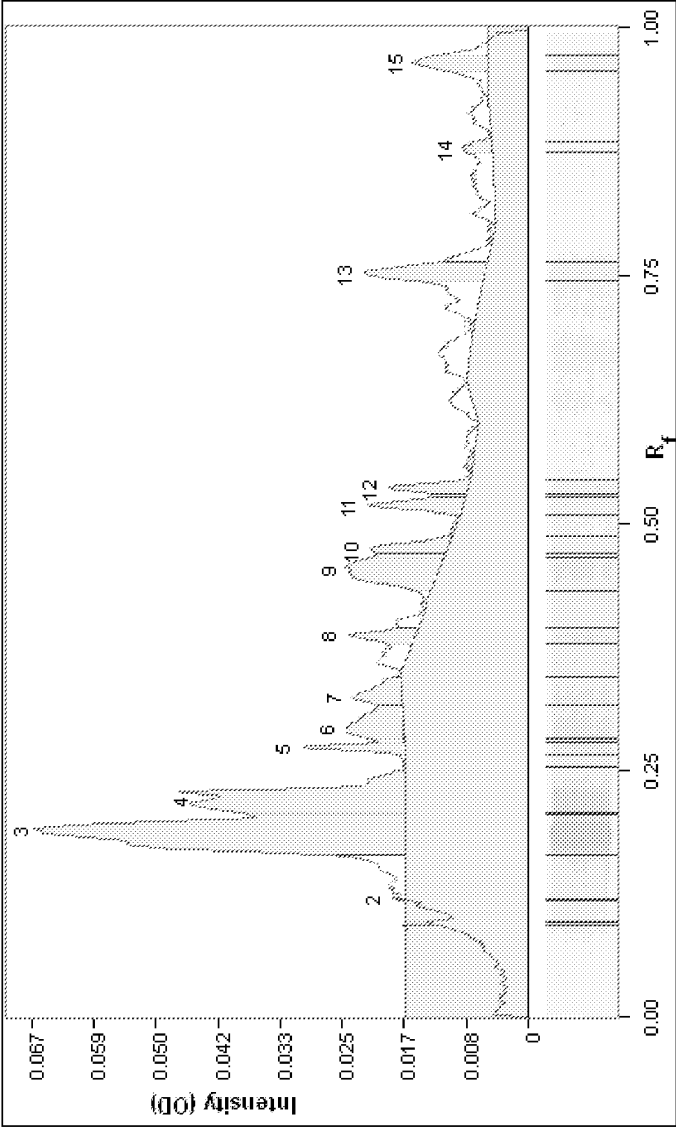


Fig. 33

Densitometry



Protein concentration:

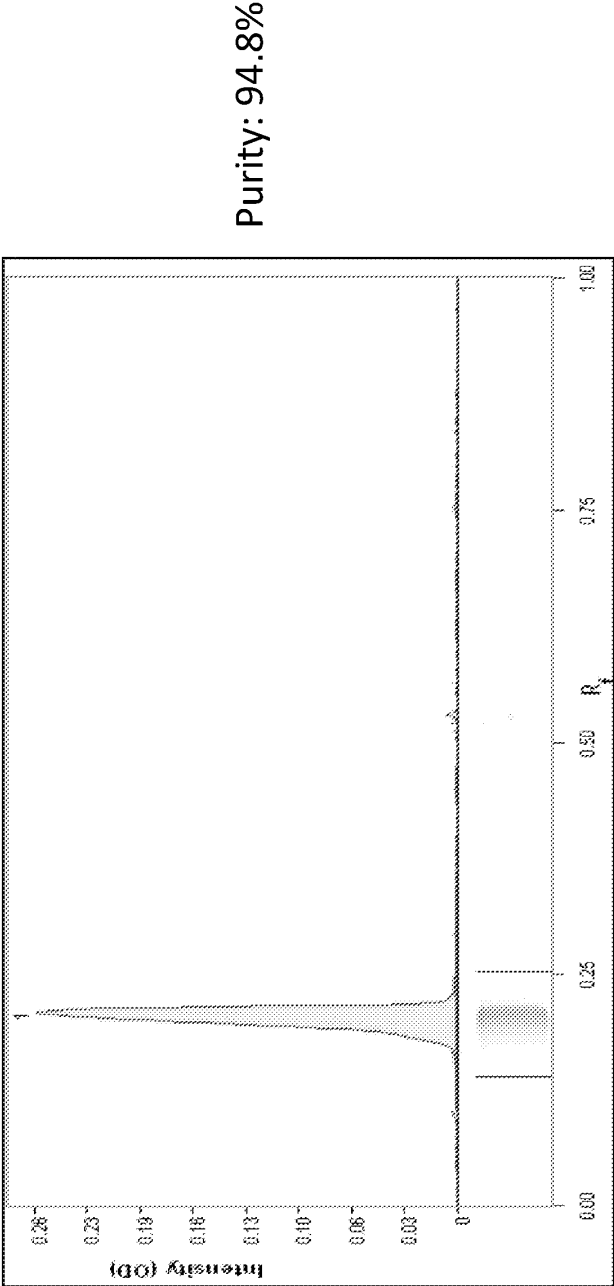
$A_{280}(0.9226) - A_{340}(0.187) = 0.7356 / 1.067 = 0.6894 \text{ mg/mL}$

Total Volume: $19.0\text{mL} \times 0.6894 \text{ mg/mL} = 13.098 \text{ mg}$

Yield: $13.098\text{mg} / 4.8 \text{ liter} = 2.728 \text{ mg/L}$

Fig. 34

Densitometry



Protein concentration:

A280(0.8368) - A340(0.0248) = 0.8142 / 1.067 = 0.761 mg/mL

Total Volume: 42.47mL X 0.761 mg/mL = 42.32 mg

Yield: 42.32mg/5 liter = 6.4 mg/L

Fig. 35A

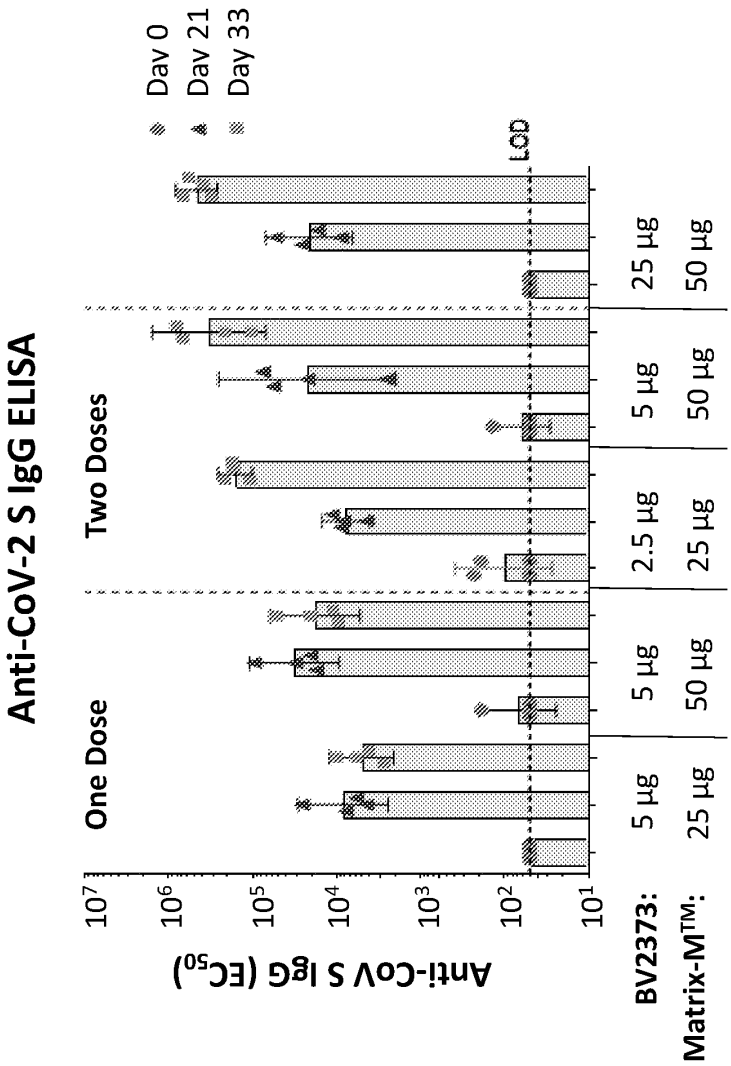


Fig. 35B

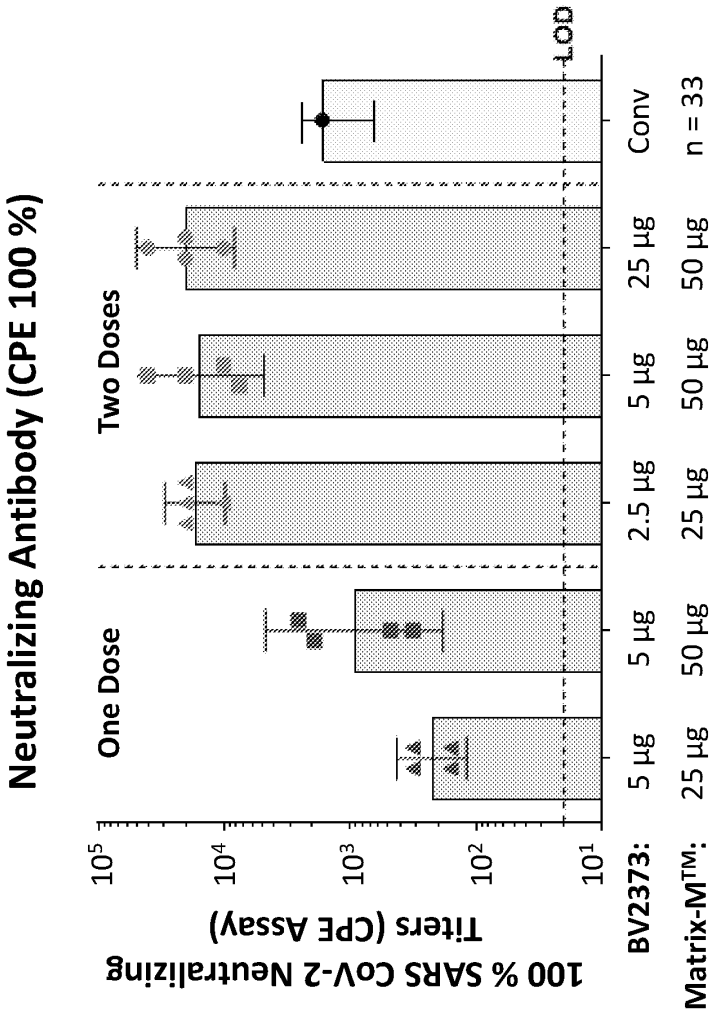


Fig. 36A

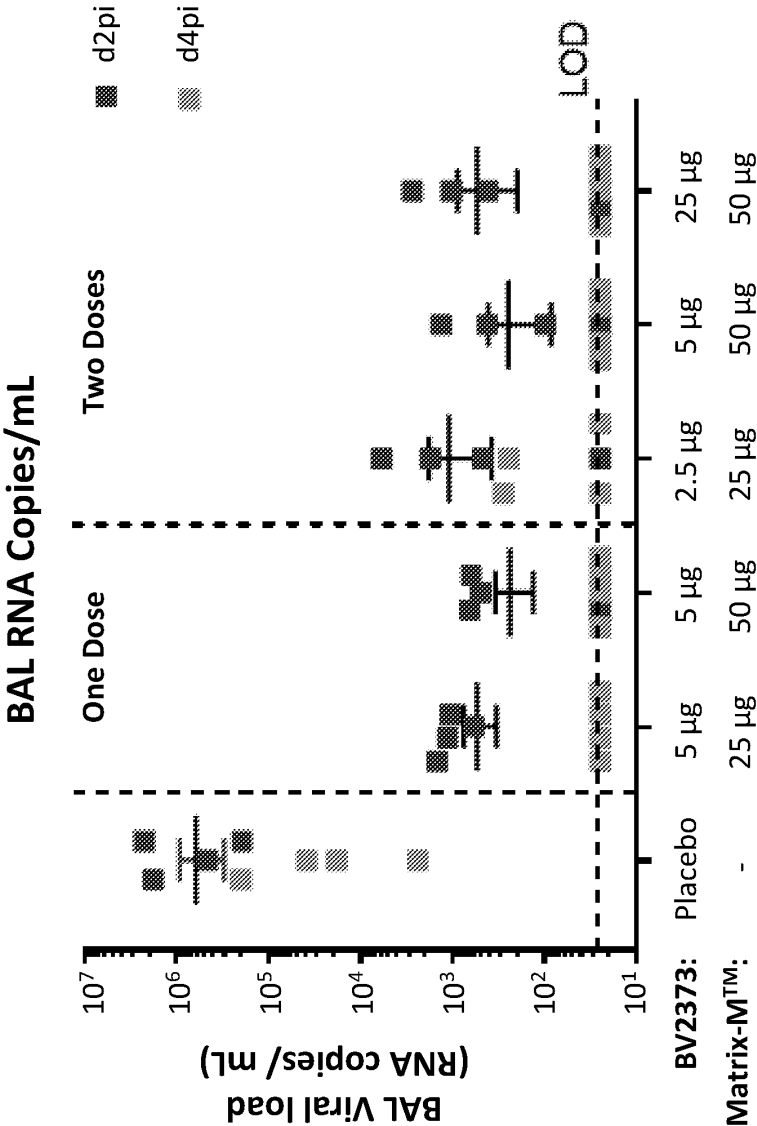


Fig. 36B

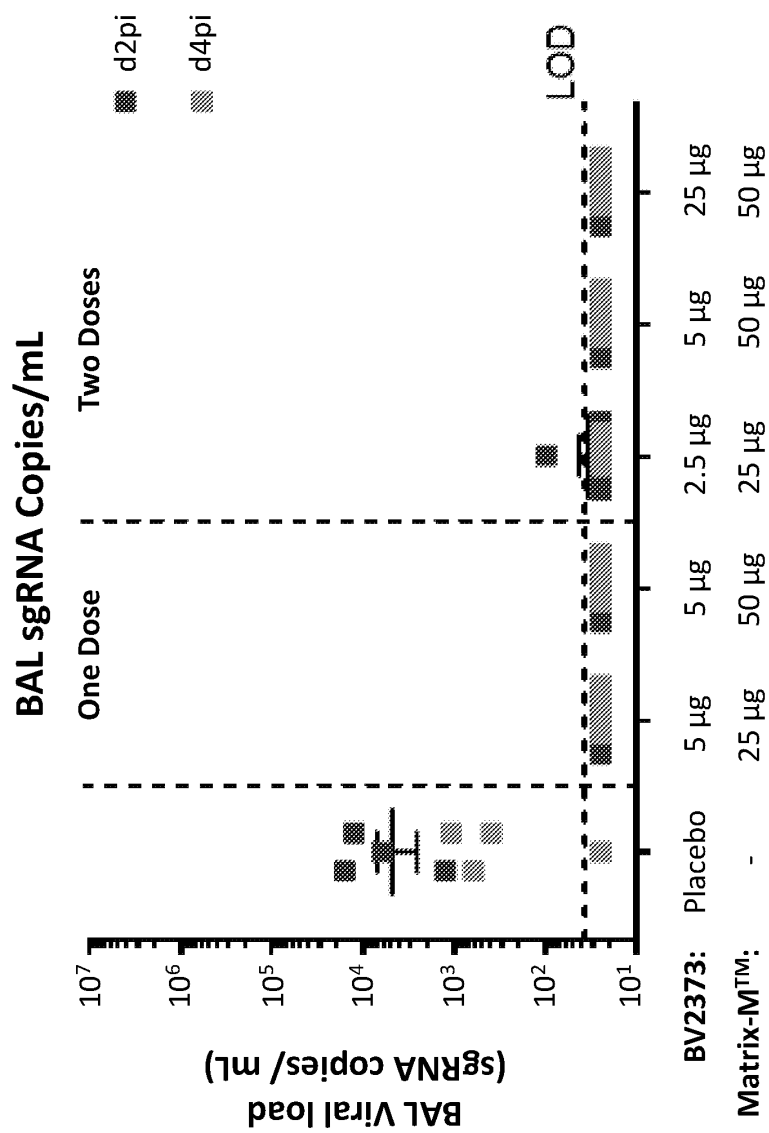


Fig. 37A

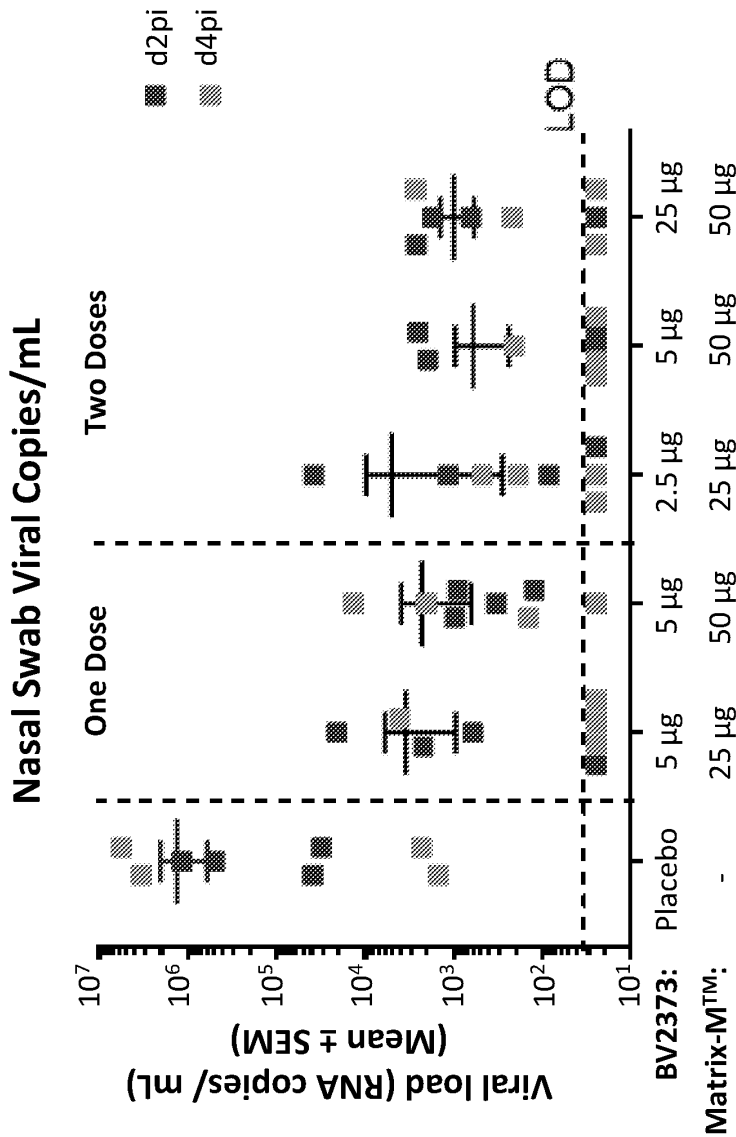


Fig. 37B

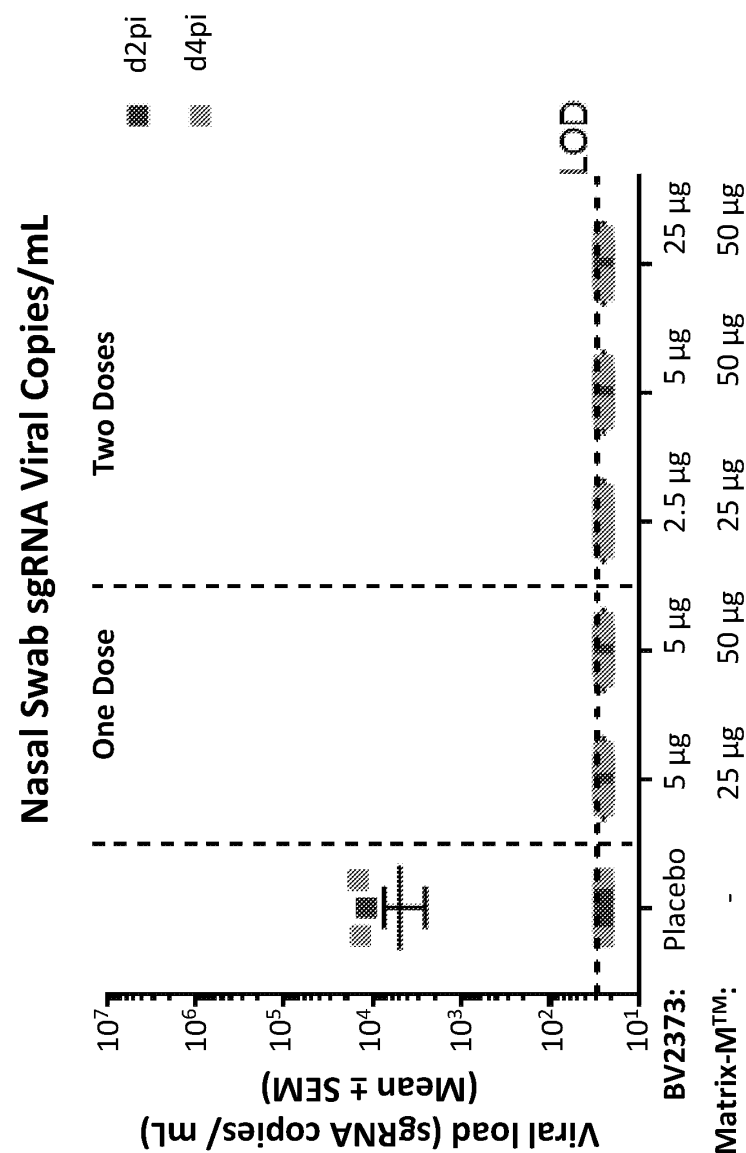


Fig. 38A

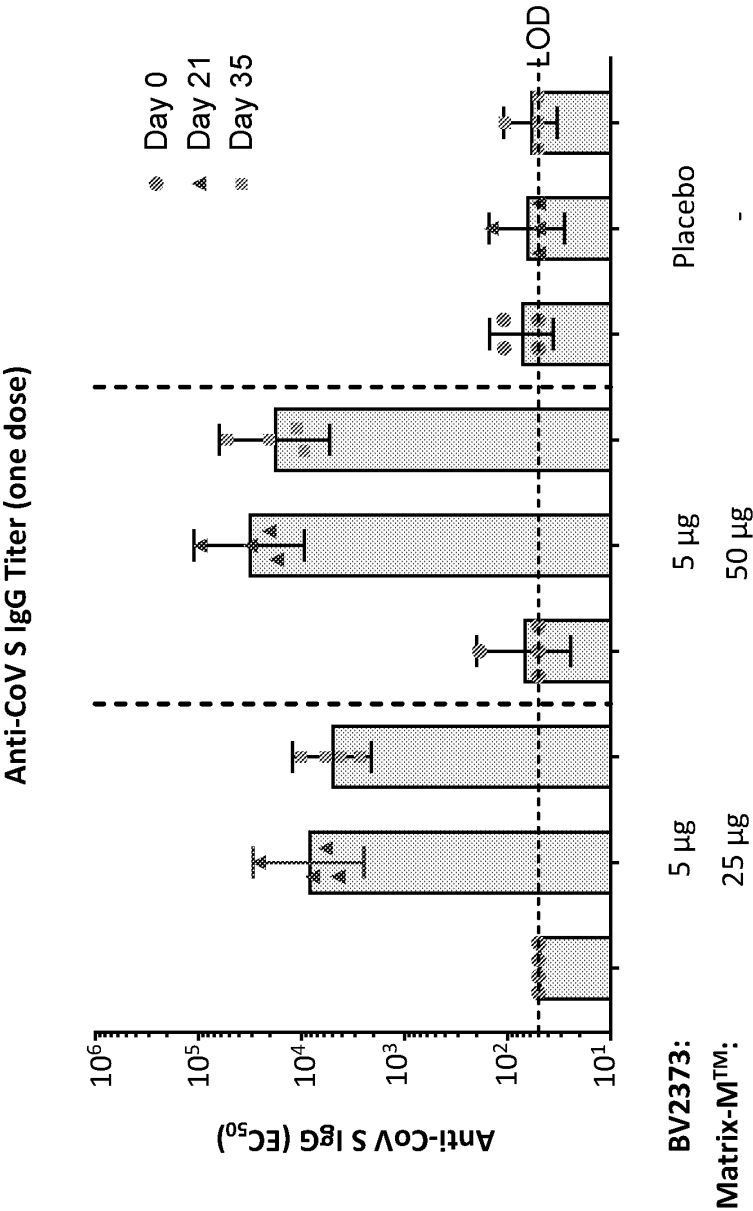


Fig. 38B

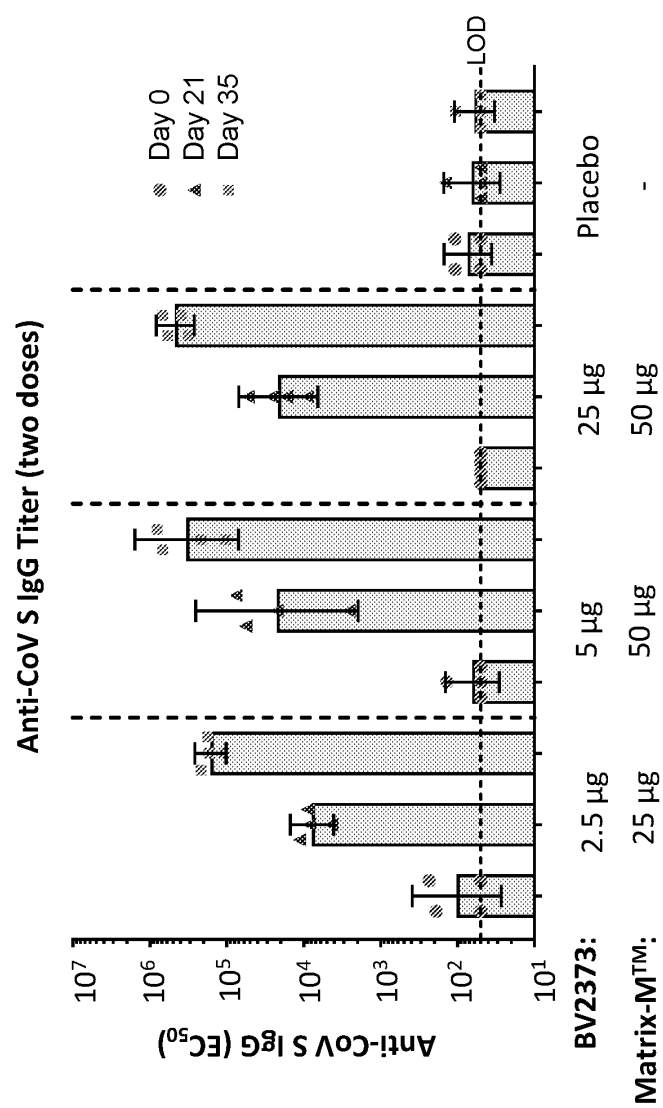


Fig. 38C

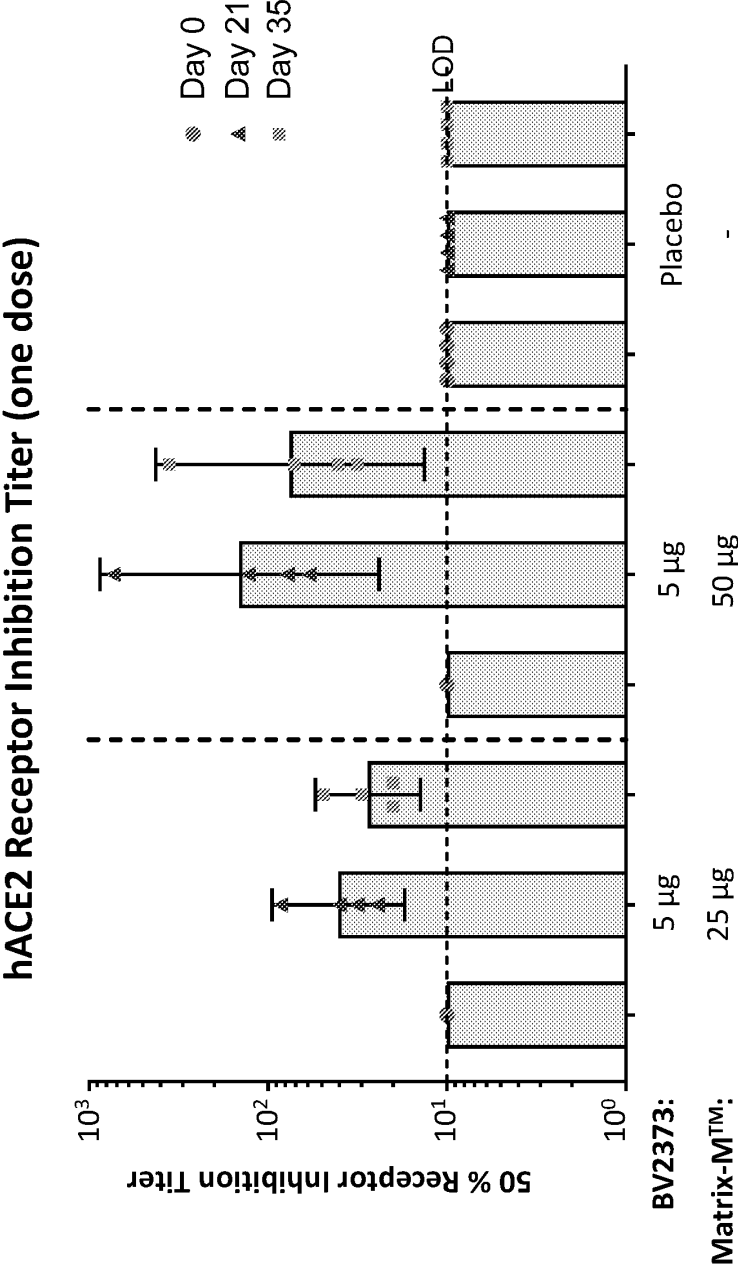


Fig. 38D

hACE2 Receptor Inhibition Titer (two doses)

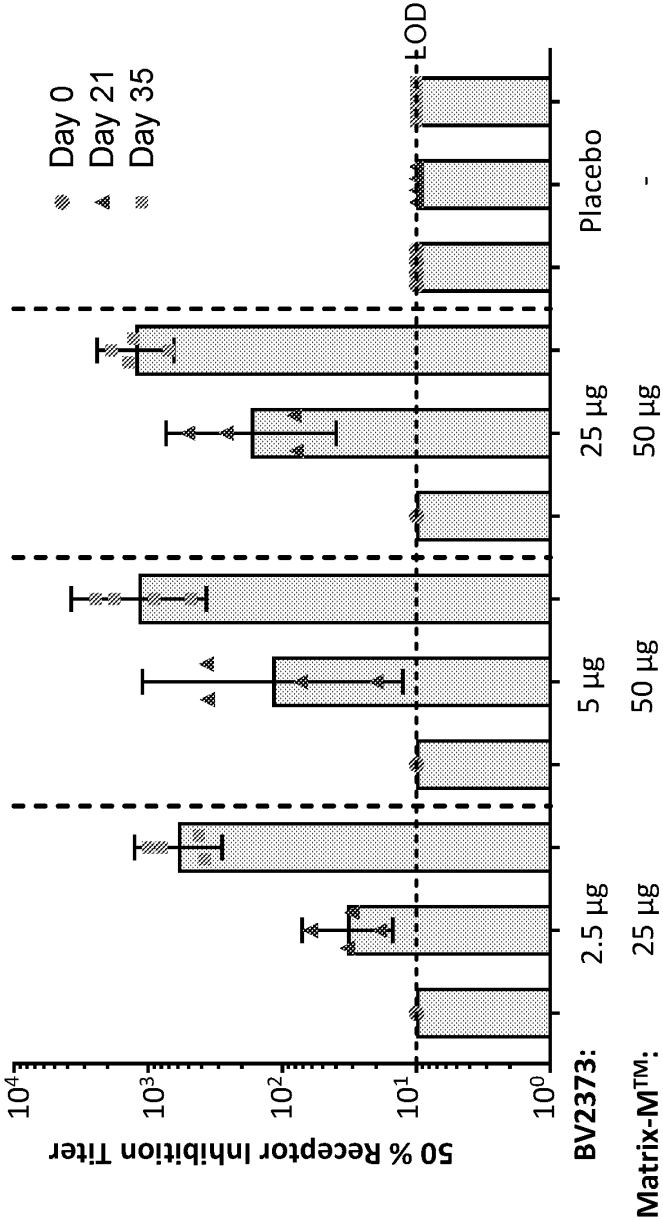


Fig. 38E
Correlation of Anti-S IgG Titer and hACE2 Receptor Inhibition
in macaques

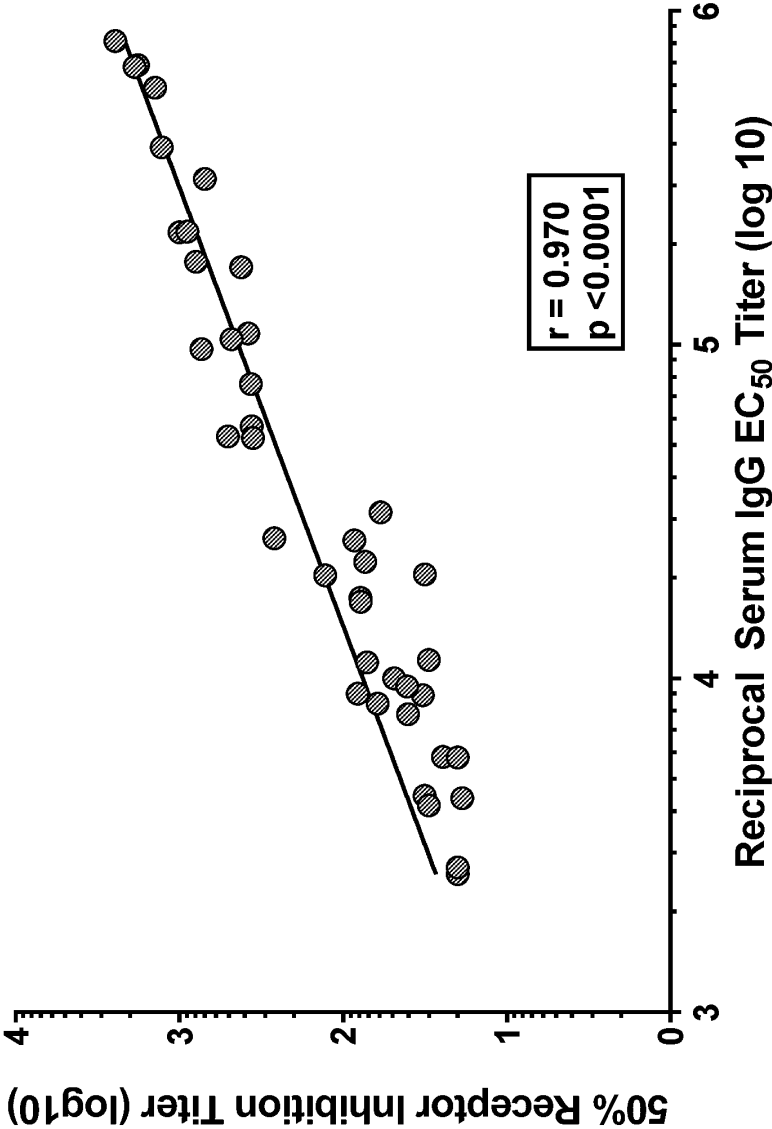


Fig. 39

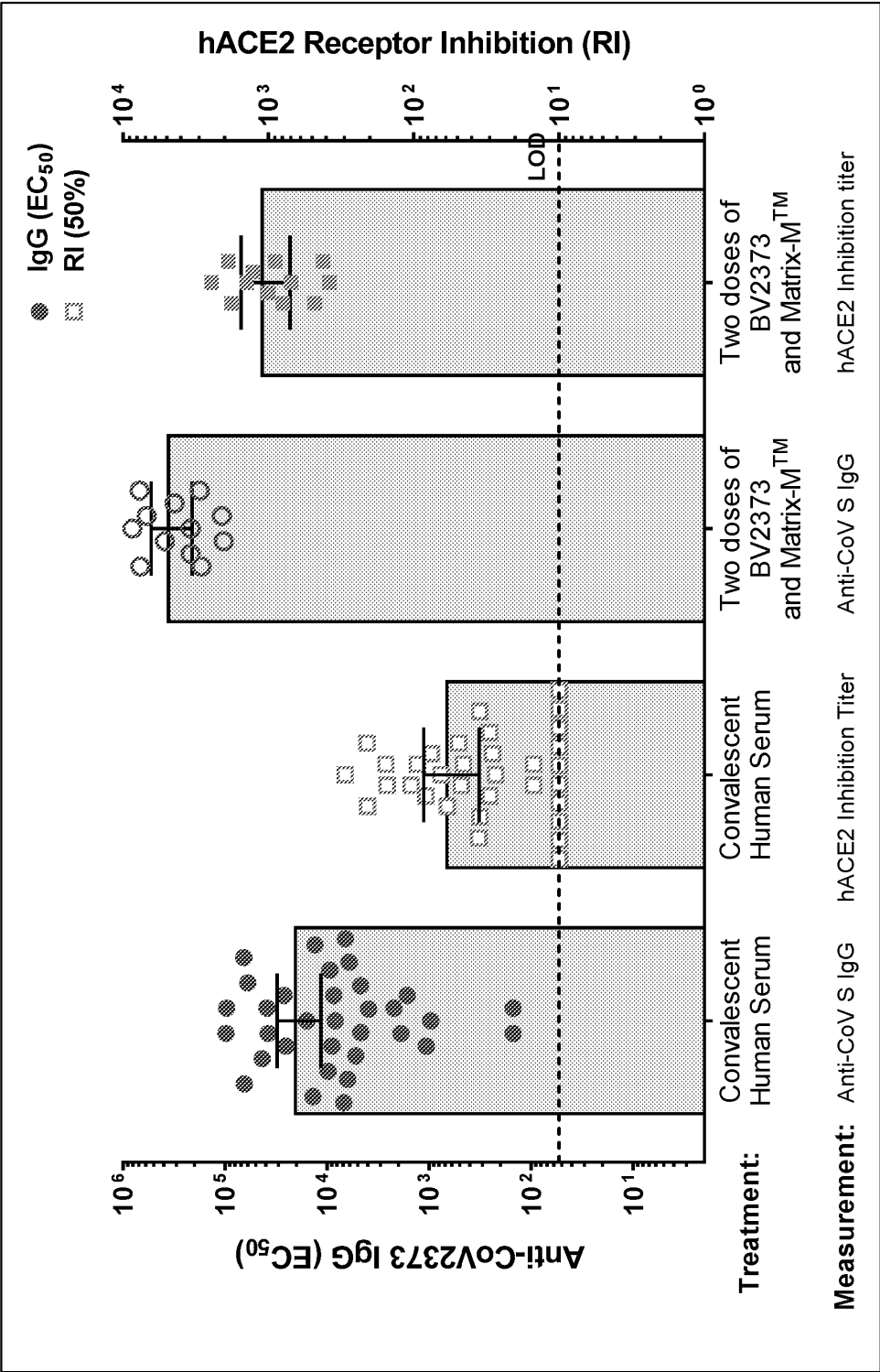


Fig. 40A

SARS-CoV-2 Neutralizing Titers by CPE (100% neutralization)

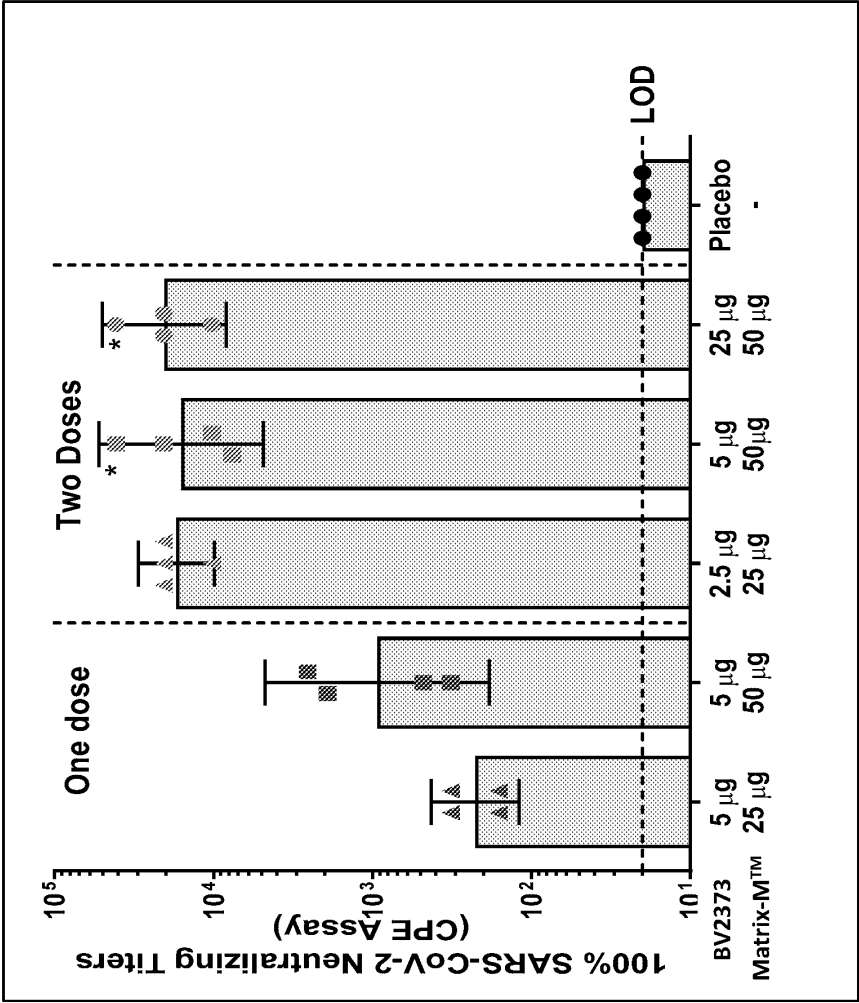


Fig. 40B
SARS-CoV-2 Neutralizing Titers by PRNT (EC90 titers)

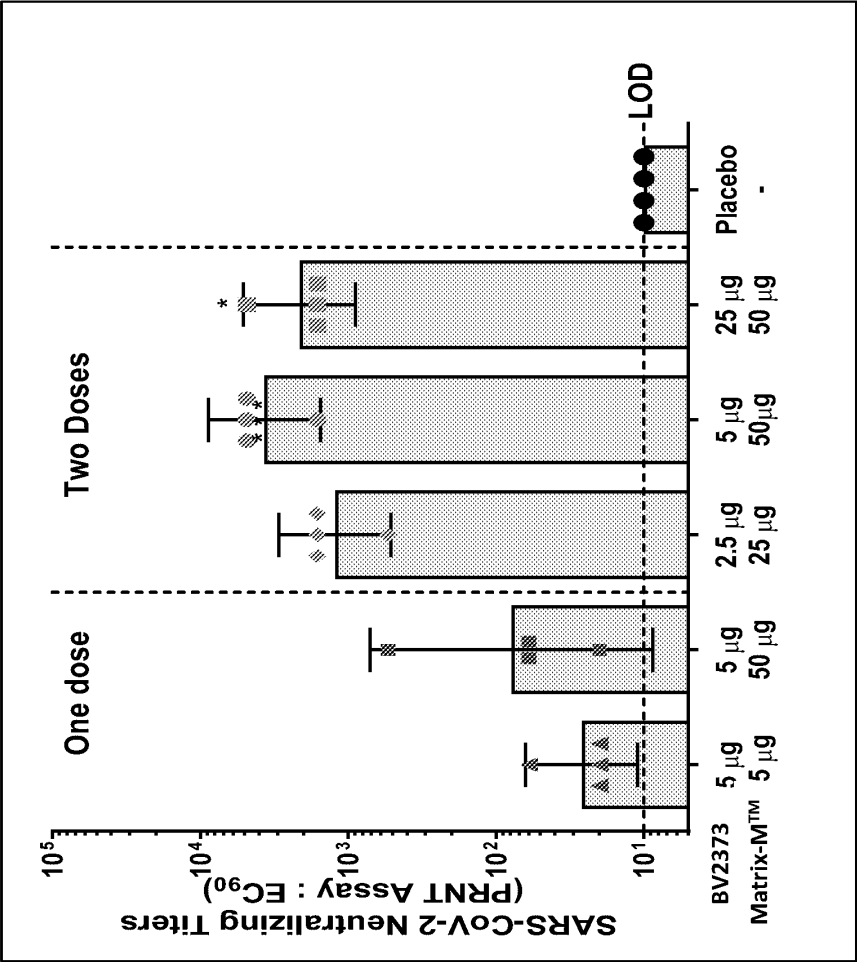


Fig. 42A

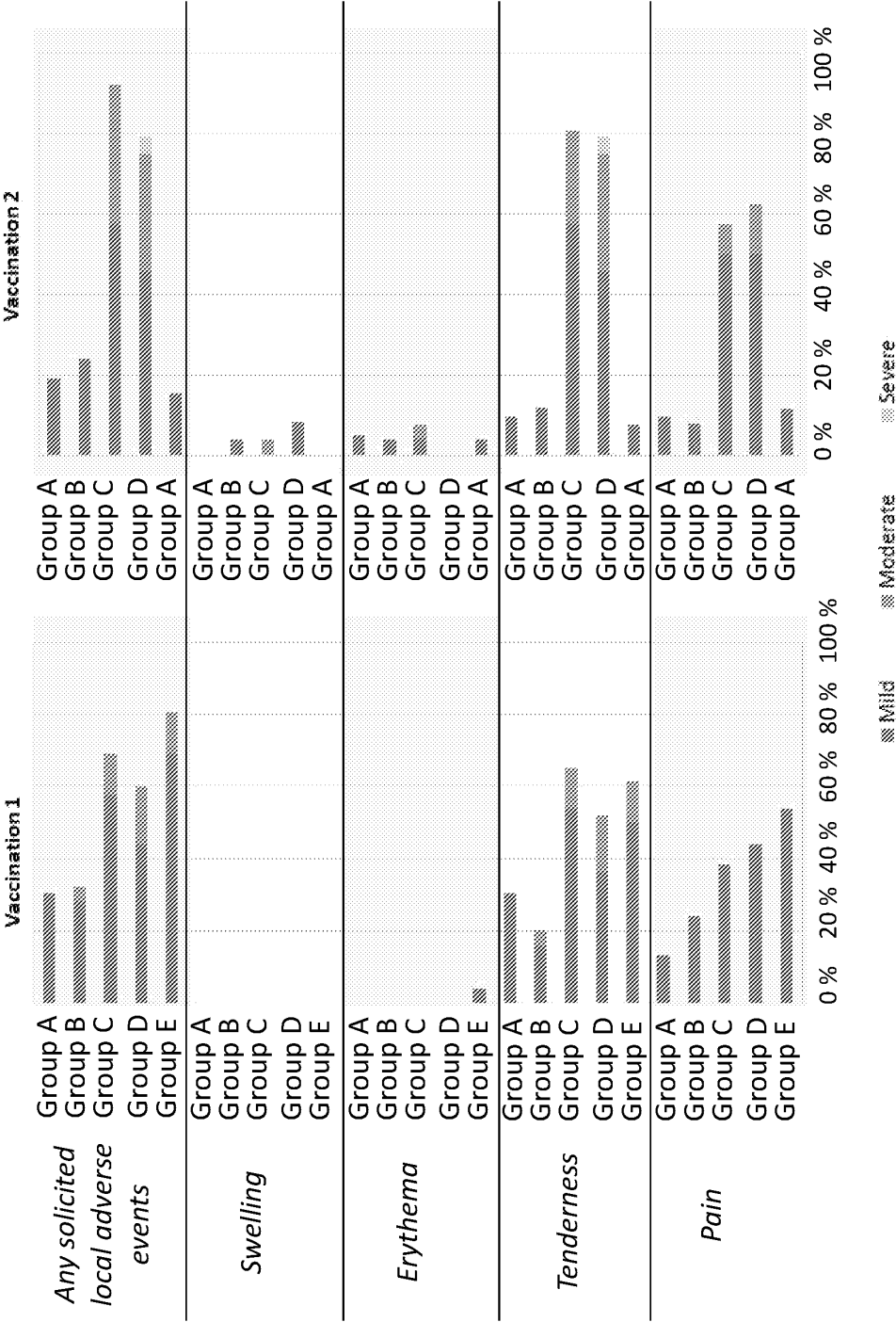


Fig. 43A

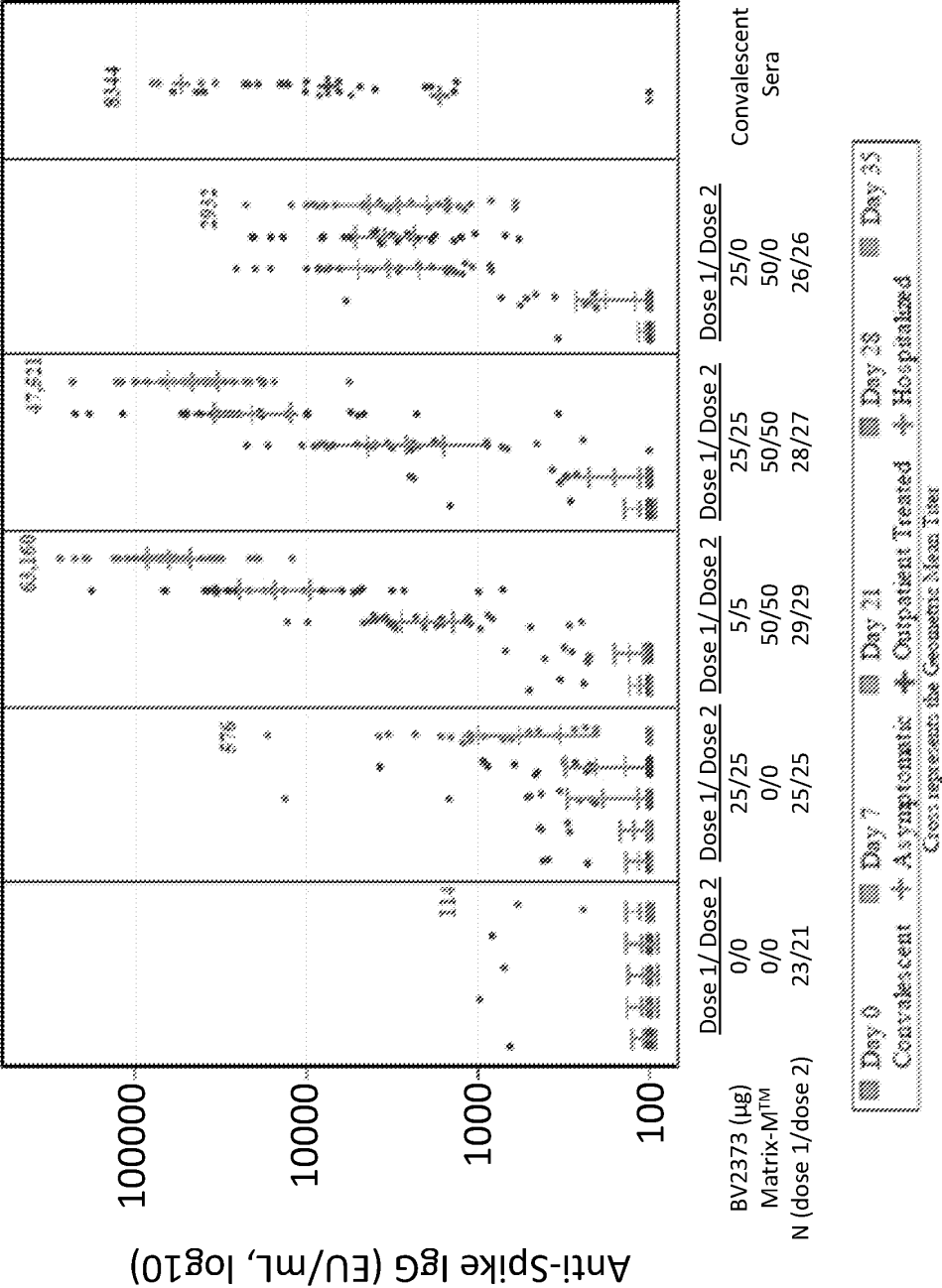


Fig. 43B

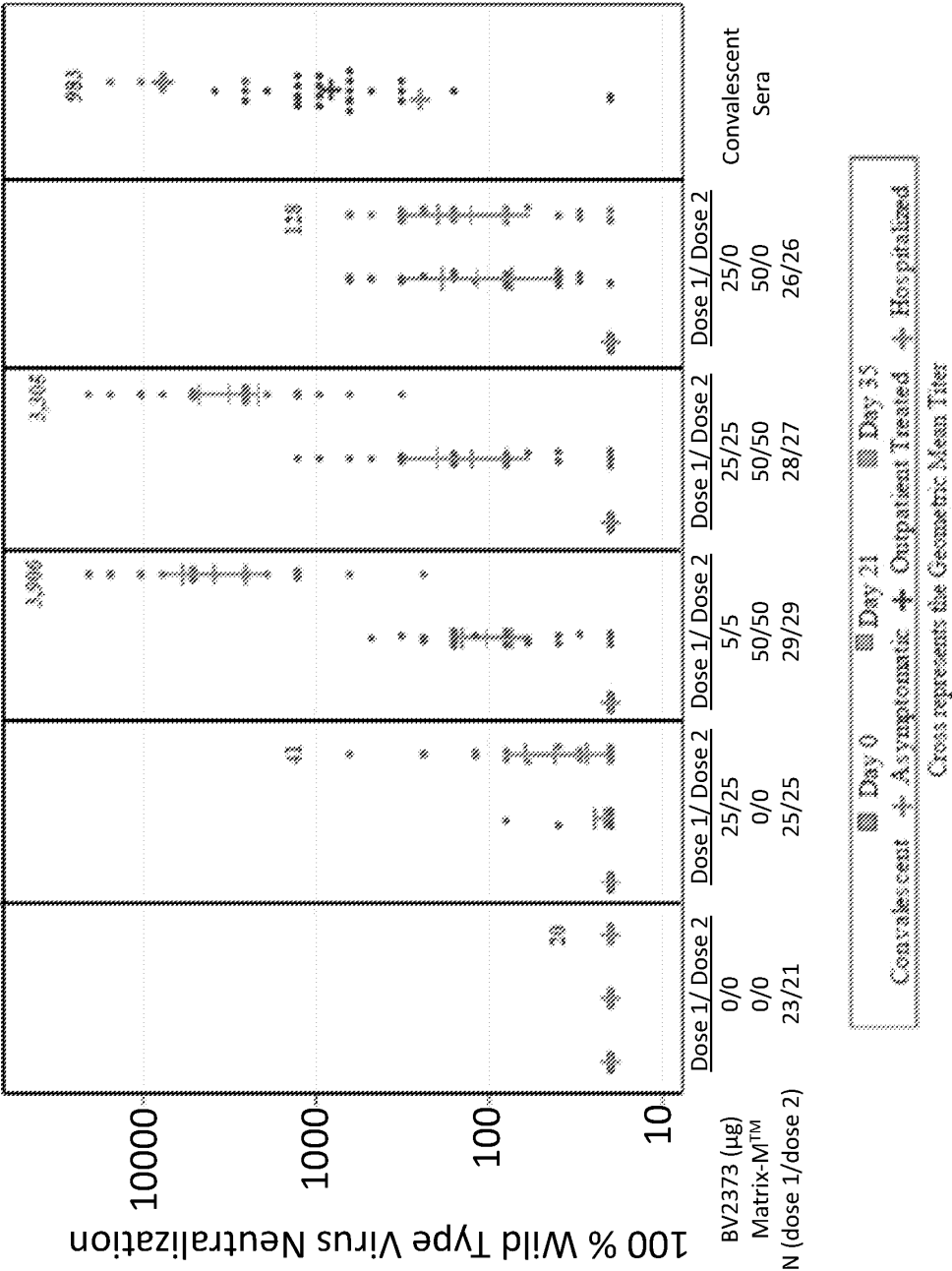


Fig. 44A

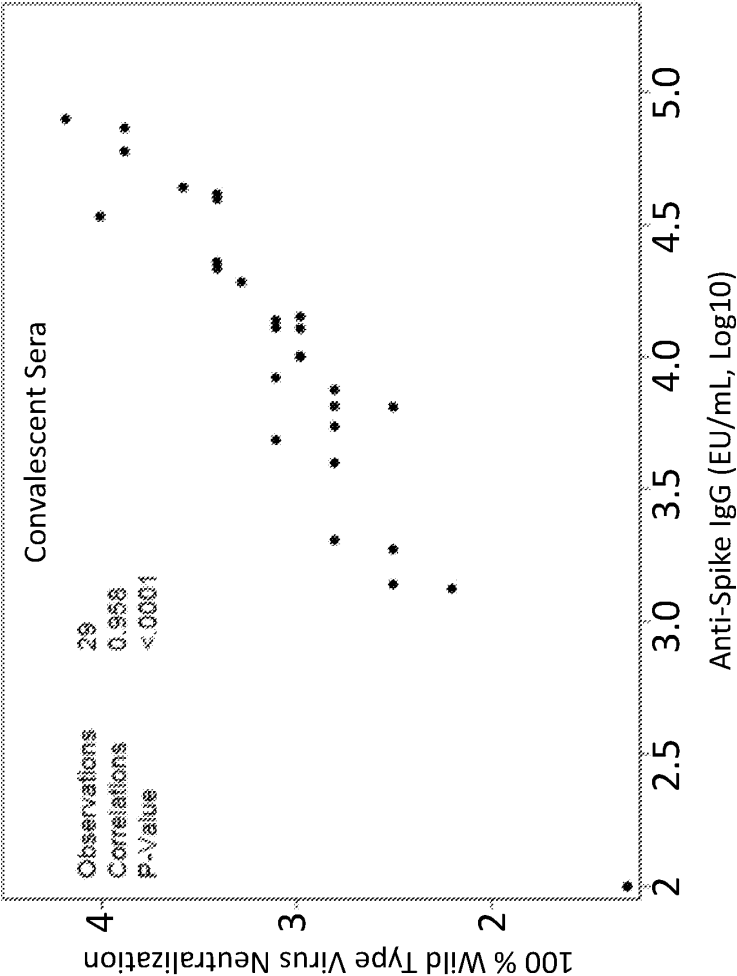


Fig. 44B

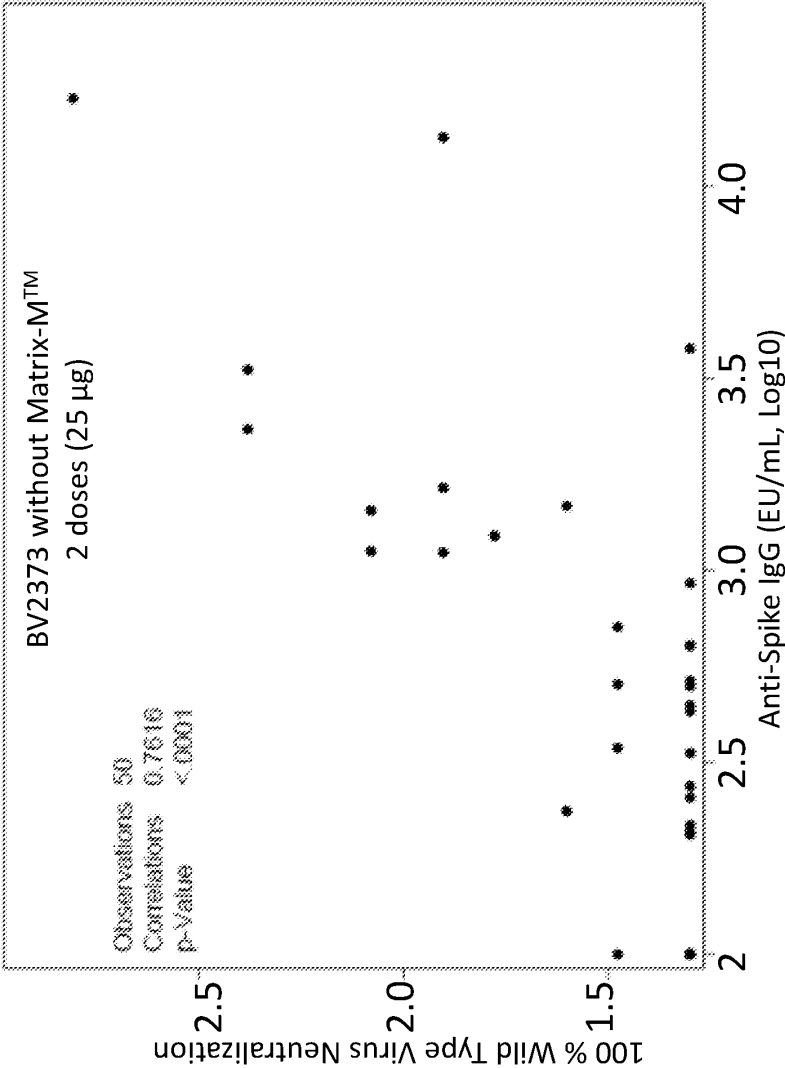


Fig. 44C

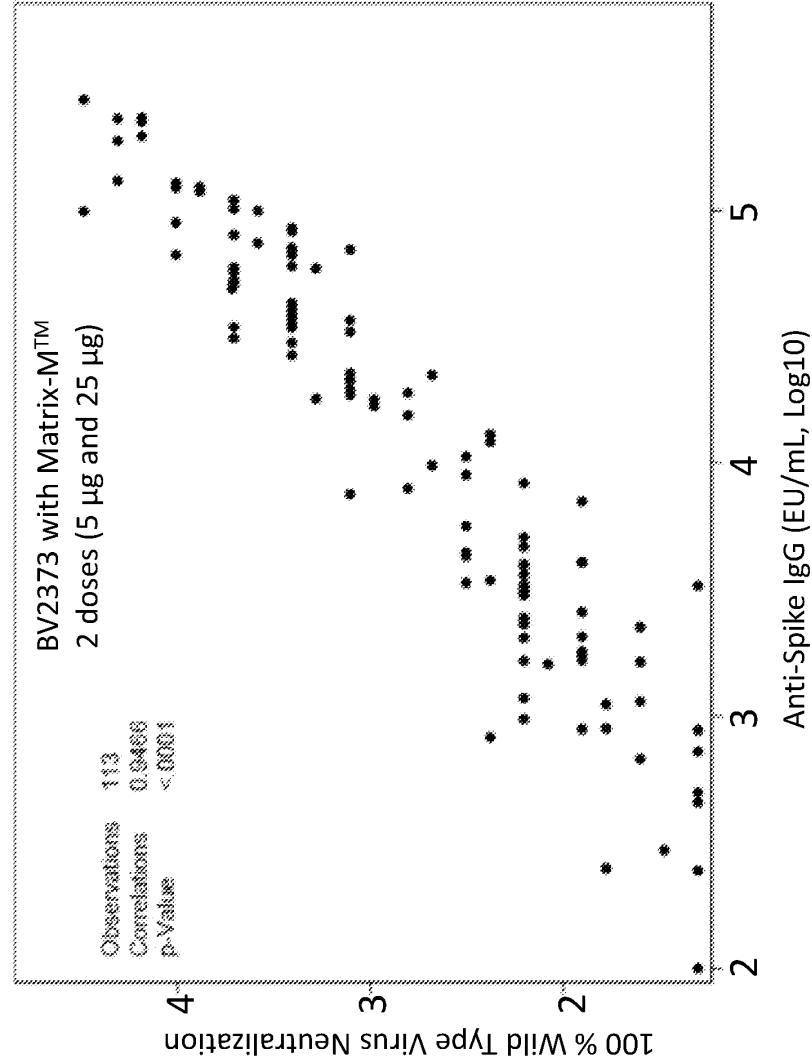


Fig. 45A

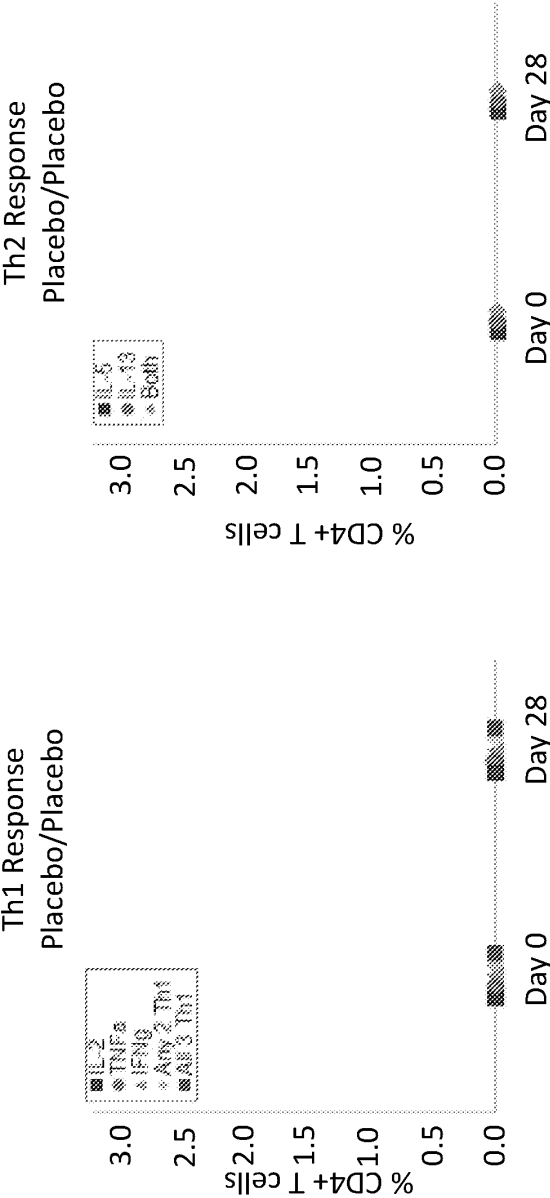


Fig. 45B

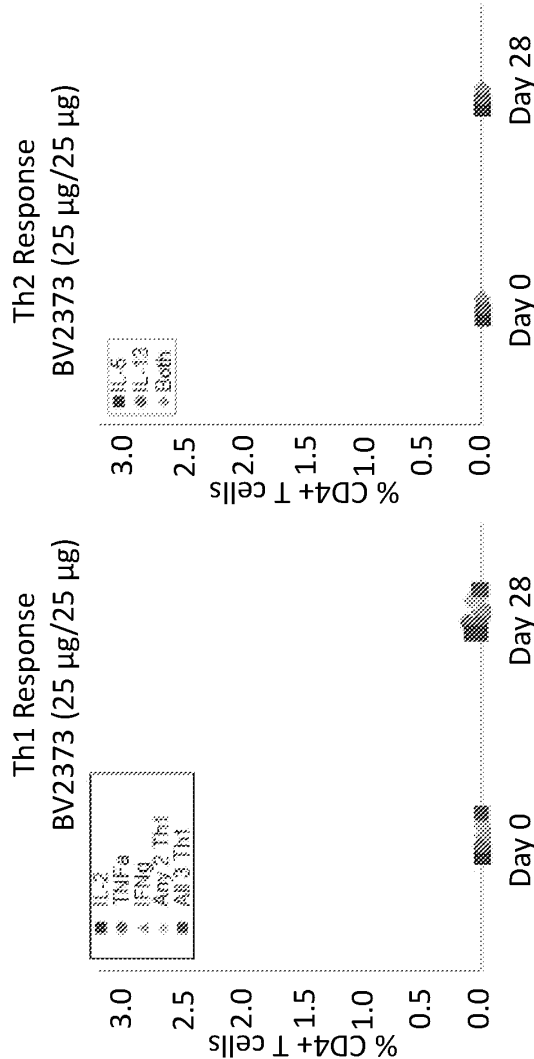


Fig. 45C

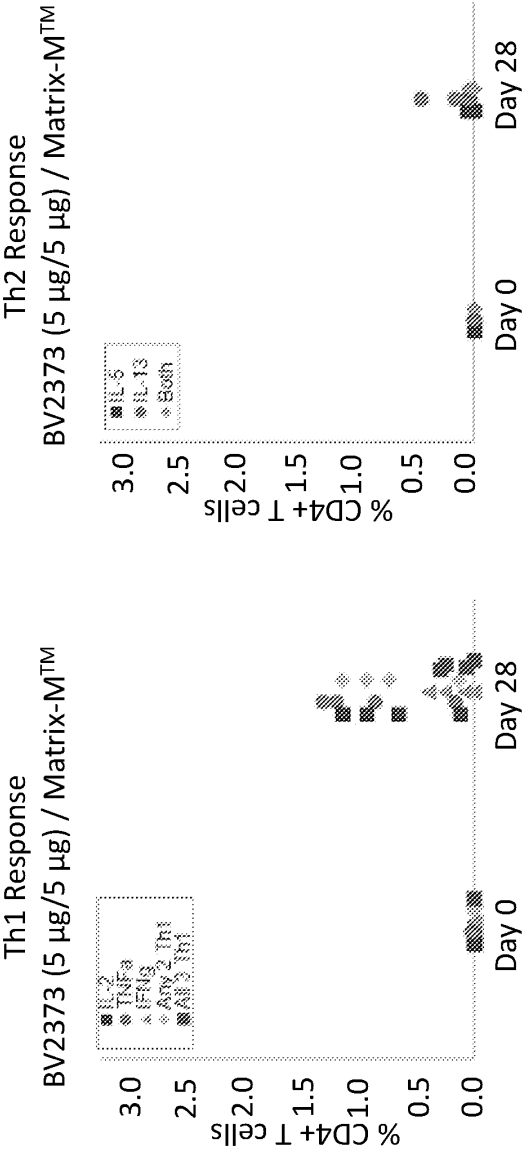


Fig. 45D

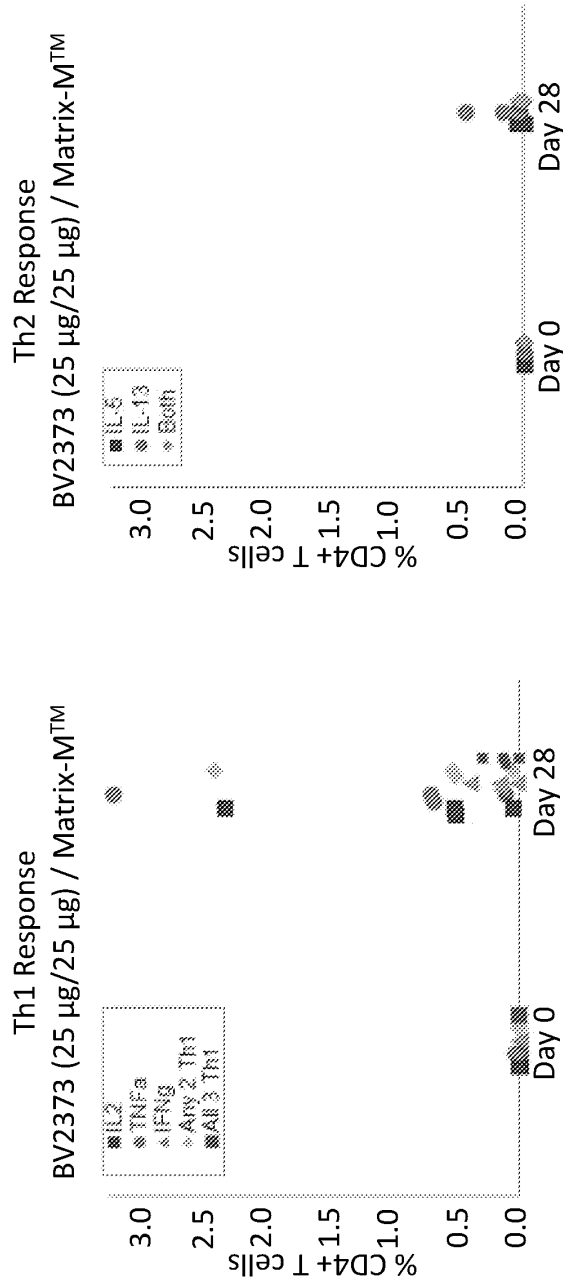


Fig. 46A

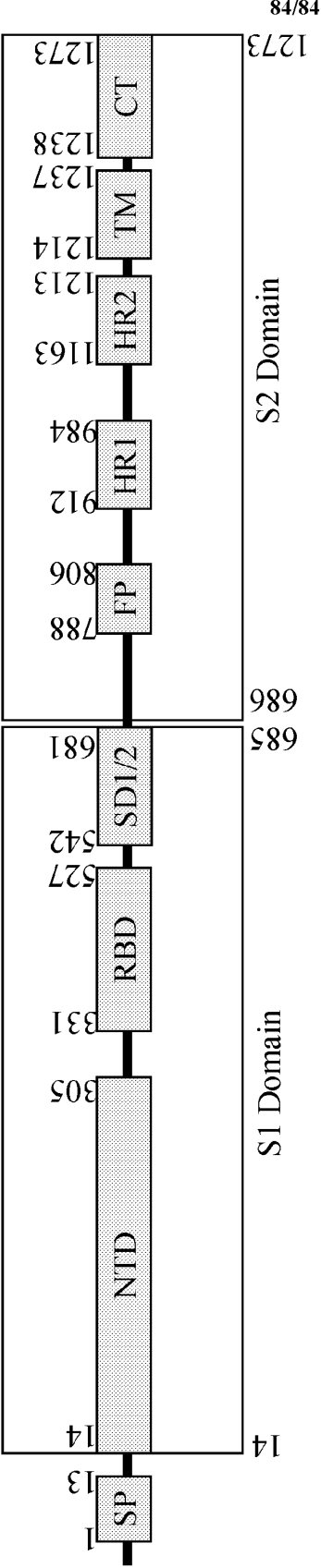


Fig. 46B

