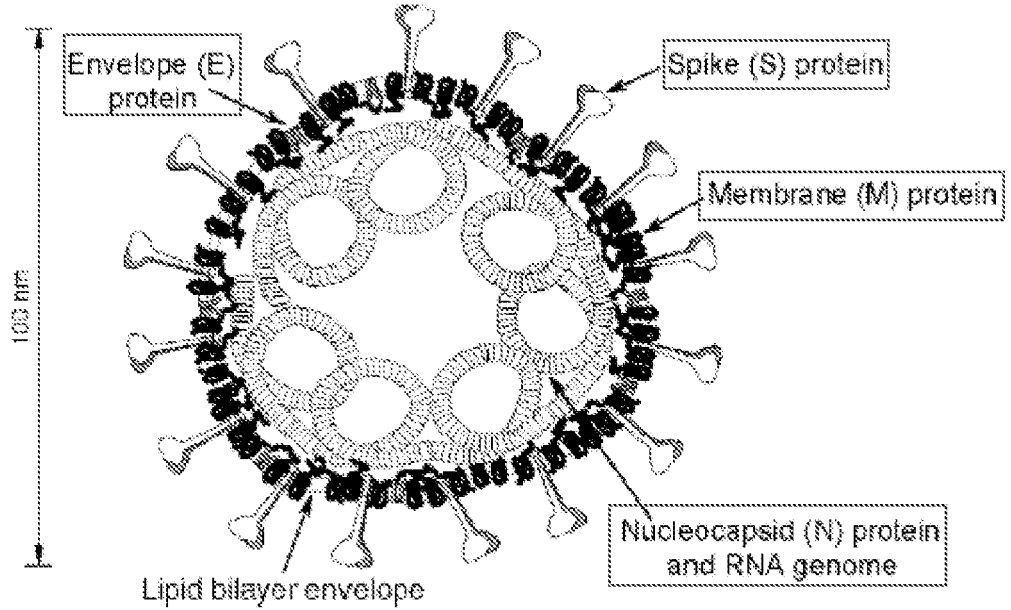
WO 2015/042373 PCT/US2014/056517

FIGURES

Figure 1

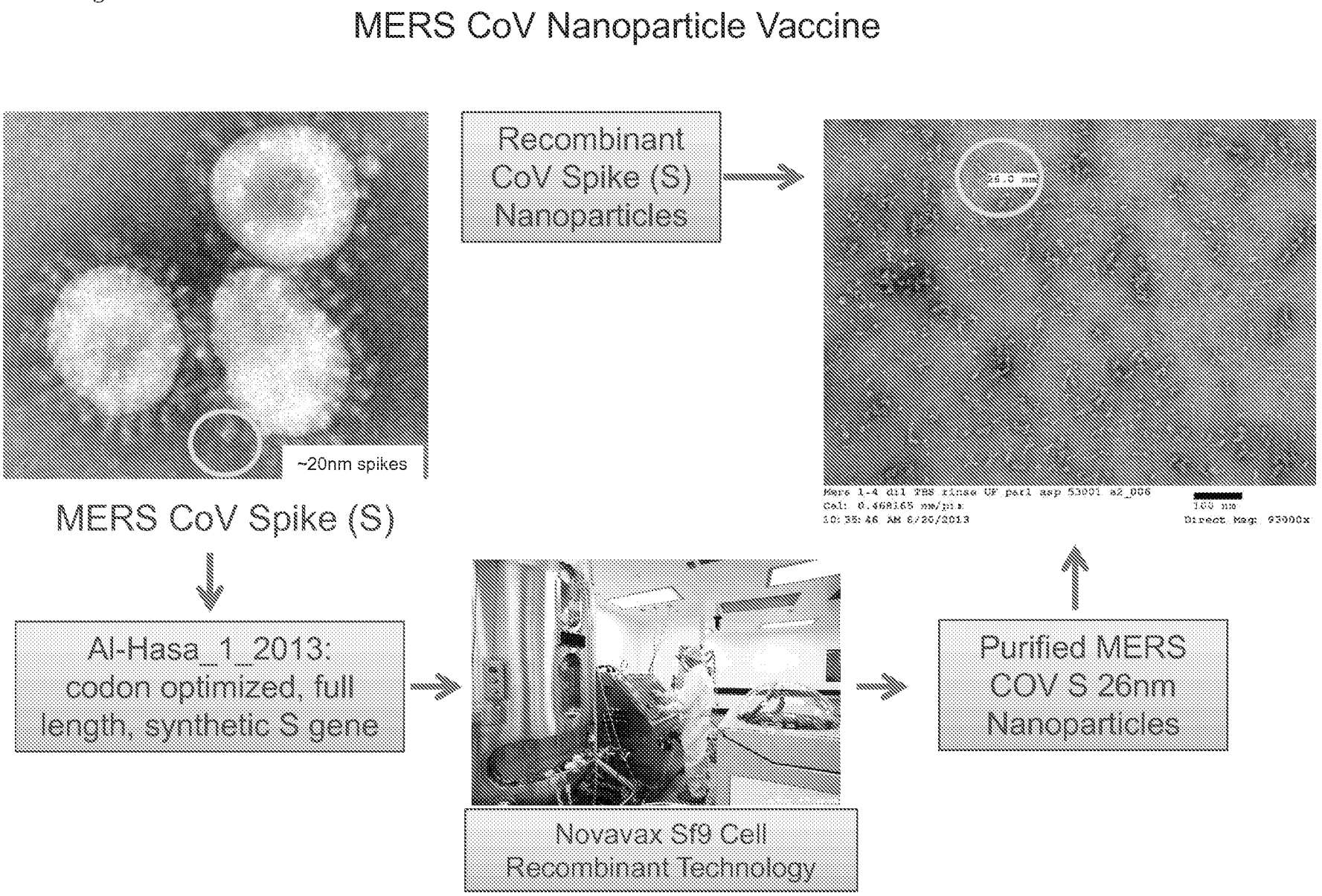
Coronavirus Structure



Masters, *Adv Virus Res* 2006

- Single strand RNA virus
- 30 kb genome with 14 ORFs
- Four structural proteins:
  - Spike (S)
  - Membrane (M)
  - Envelope (E)
  - Nucleocapsid (N)

Figure 2

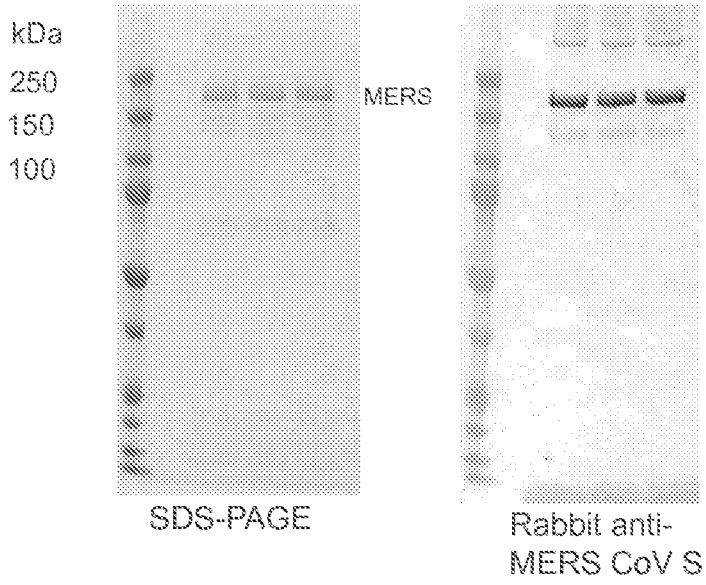

MERS CoV Nanoparticle Vaccine
~20nm spikes
MERS CoV Spike (S)
Recombinant CoV Spike (S) Nanoparticles
26.0 nm
Mers 1-4 dil PBS rinse UF pa1 asp 53001 a2_006
Col: 0.468165 nm/pix
10:35:46 AM 6/26/2013
100 nm
Direct Mag: 93000x
Al-Hasa_1_2013: codon optimized, full length, synthetic S gene
Novavax Sf9 Cell Recombinant Technology
Purified MERS COV S 26nm Nanoparticles

WO 2015/042373 PCT/US2014/056517

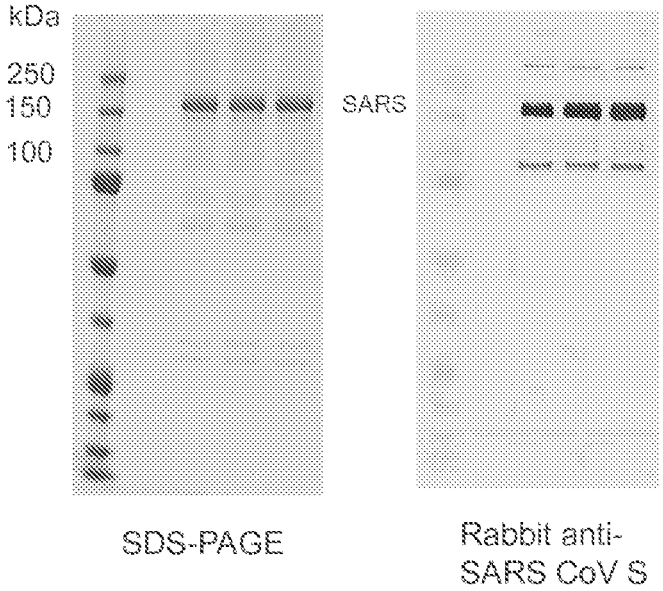
Figure 3

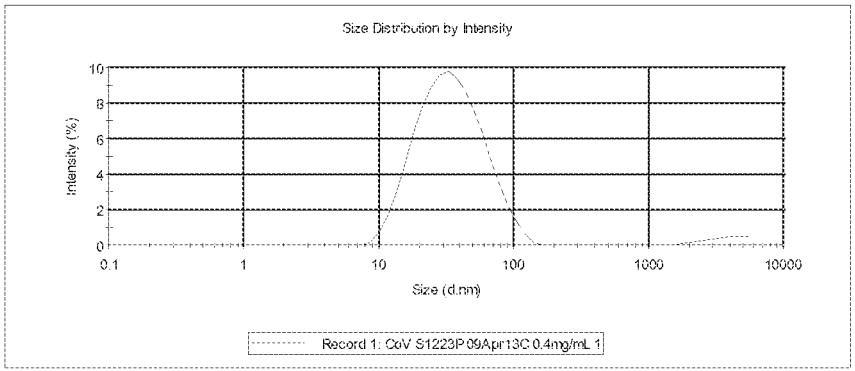
Purified MERS and SARS –CoV Nanoparticle Vaccines

MERS-CoV S



SARS-CoV S



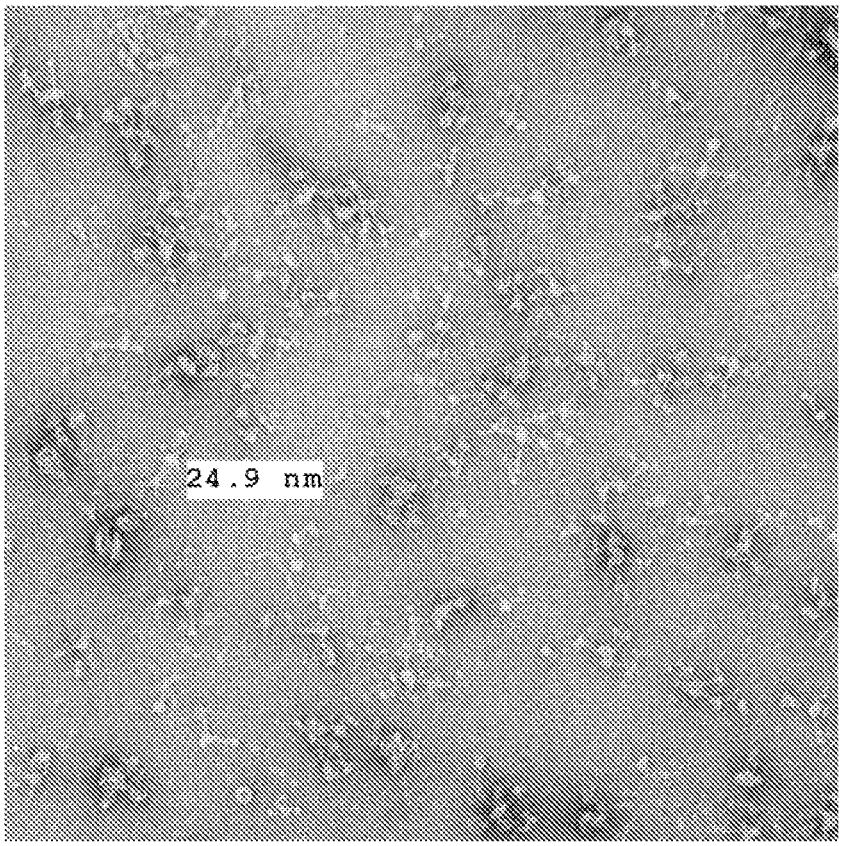


MERS CoV S nanoparticles

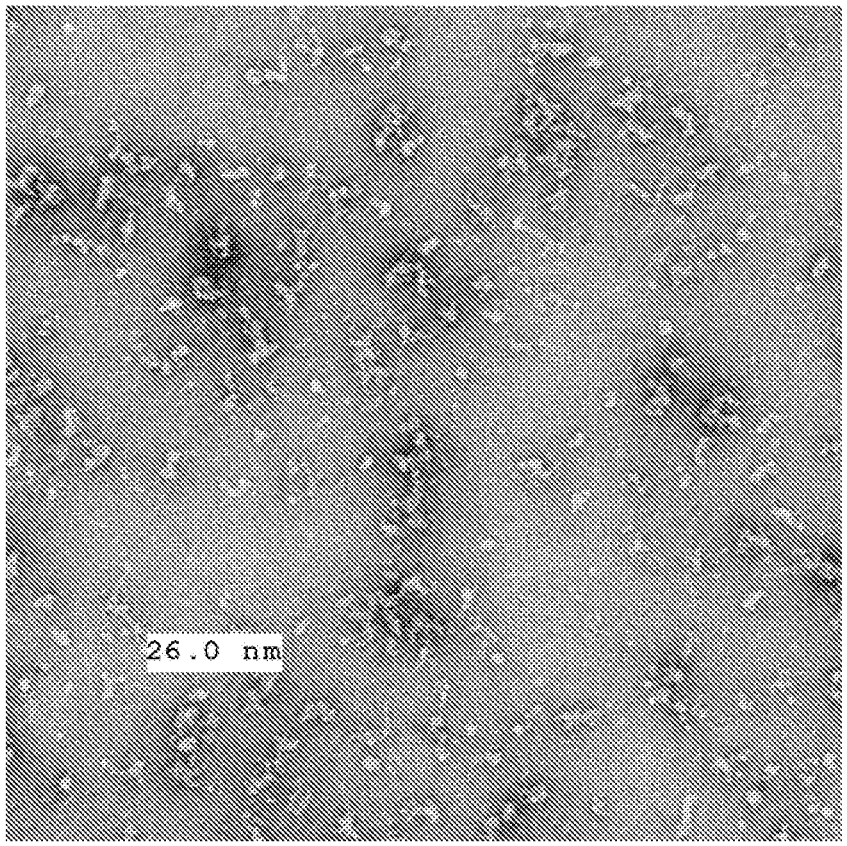
- Dynamic light scattering (DLS): 31nm
- Mean mass = 2,052 kDa
- Mean size = 4.5 S trimers/micelle
- EM particle = 26nM

Figure 4

Electron Microscopy: MERS and SARS CoV S Nanoparticles



SARS CoV Spike (S)



MERS CoV Spike (S)

Figure 5

MERS-CoV Mouse Immunogenicity

Study Design

Group	Purified S Antigen	Dose (µg)	Alum Adjuvant (120µg)	Matrix M1 Adjuvant (5µg)	N/Group	Immunization (days)	Blood Draw (days)
1	MERS-CoV	10.0	-	-	10	0, 14	0, 21, 45
2		3.0	-	-	10	0, 14	0, 21, 45
3		1.0	-	-	10	0, 14	0, 21, 45
4		3.0	+	-	10	0, 14	0, 21, 45
5		1.0	+	-	10	0, 14	0, 21, 45
6		3.0	-	+	10	0, 14	0, 21, 45
7		1.0	-	+	10	0, 14	0, 21, 45
8	SARS-CoV	3.0	-	-	10	0, 14	0, 21, 45
9		3.0	+	-	10	0, 14	0, 21, 45
10		3.0		+	10	0, 14	0, 21, 45

Time Line

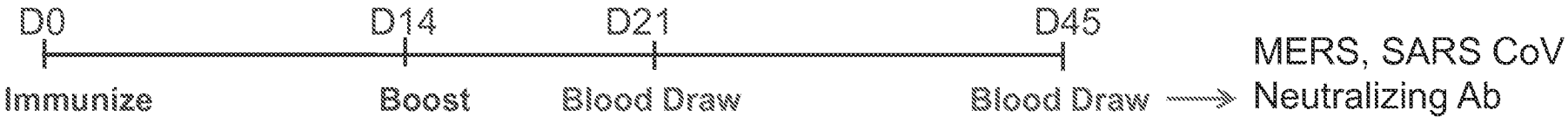


Figure 6

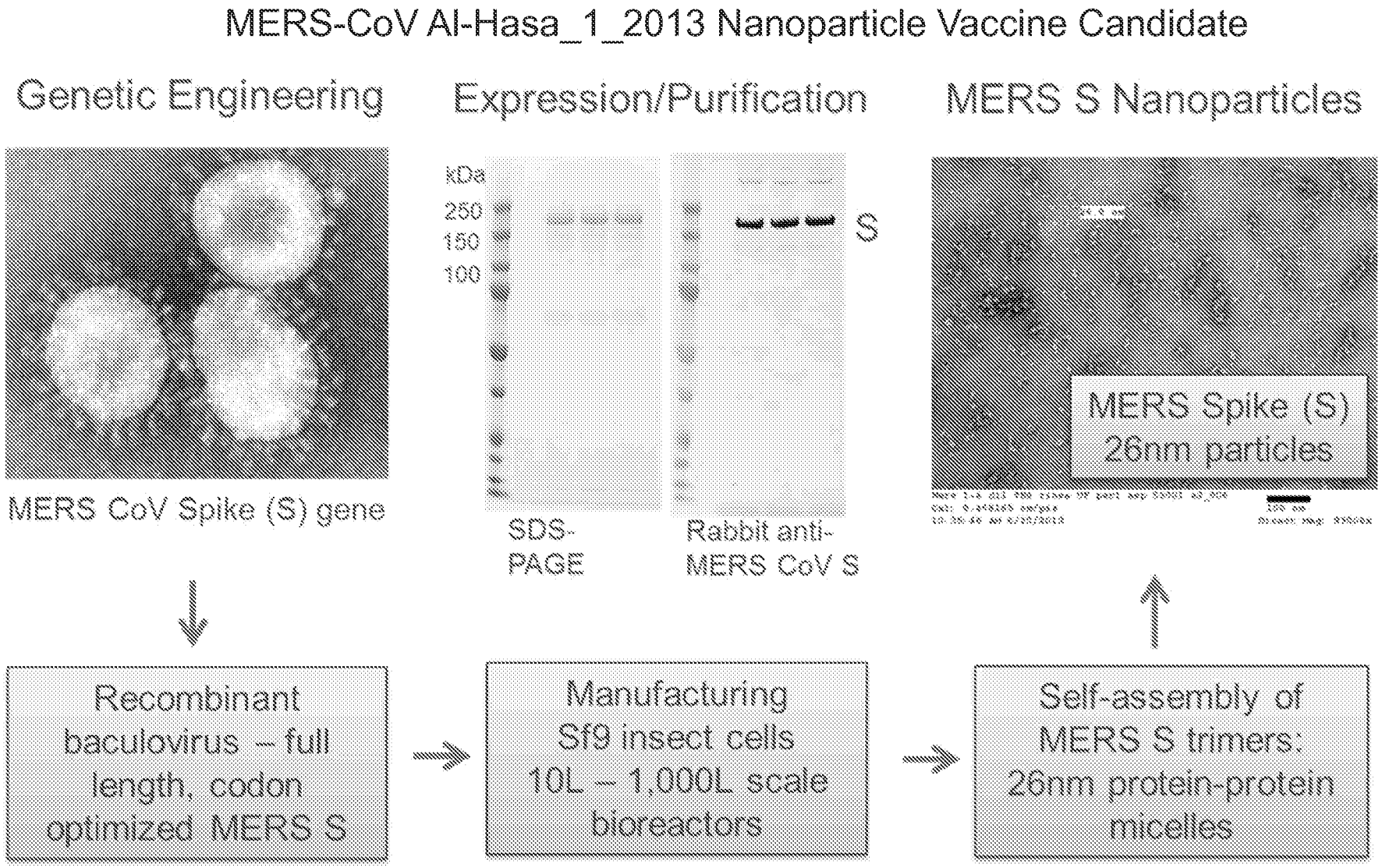

MERS-CoV Al-Hasa_1_2013 Nanoparticle Vaccine Candidate
Genetic Engineering
Expression/Purification
MERS S Nanoparticles
MERS CoV Spike (S) gene
kDa
250
150
100
S
SDS-PAGE
Rabbit anti-MERS CoV S
MERS Spike (S) 26nm particles
Recombinant baculovirus – full length, codon optimized MERS S
Manufacturing Sf9 insect cells 10L – 1,000L scale bioreactors
Self-assembly of MERS S trimers: 26nm protein-protein micelles

Figure 7

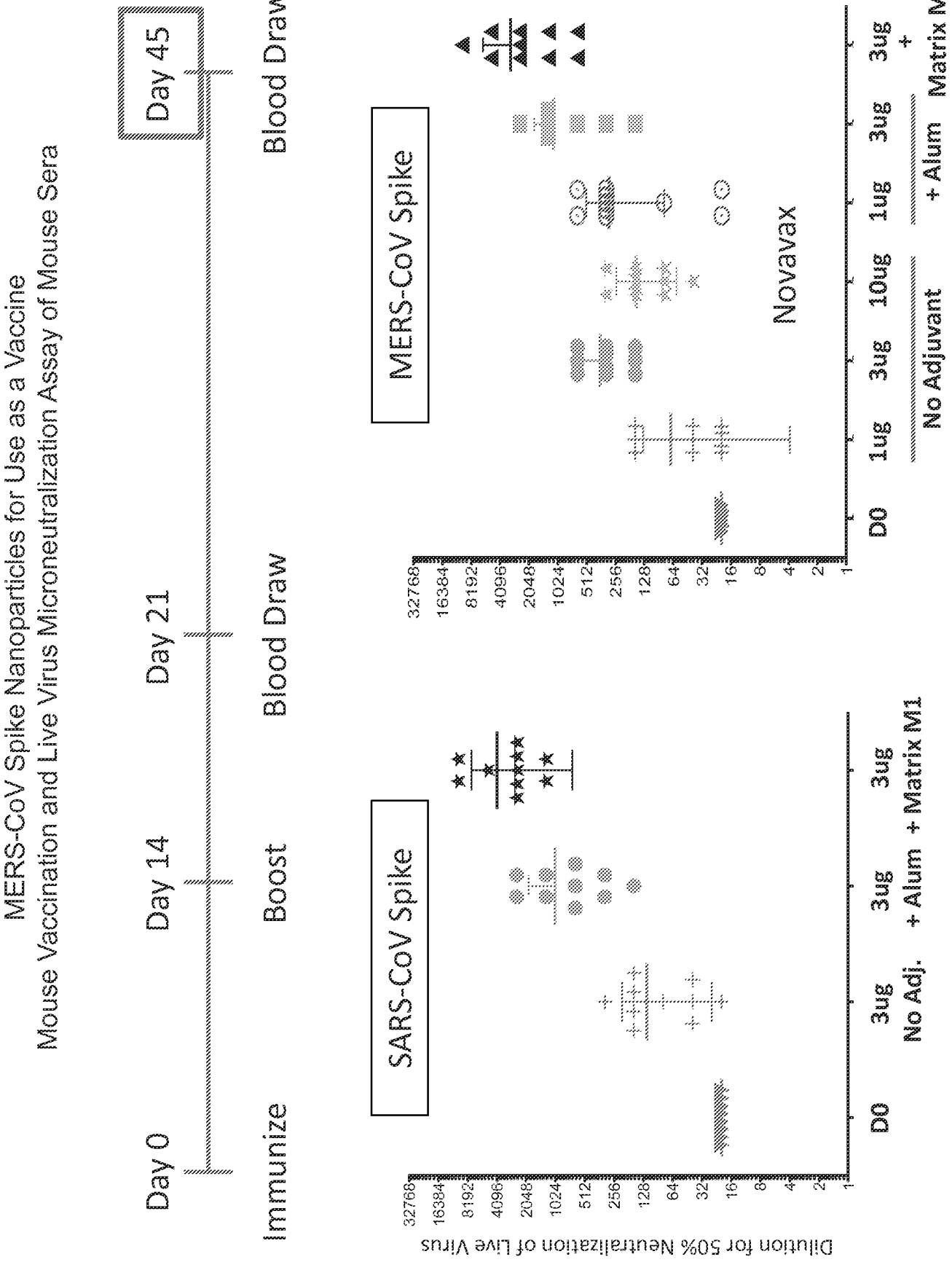

MERS-CoV Spike Nanoparticles for Use as a Vaccine
Mouse Vaccination and Live Virus Microneutralization Assay of Mouse Sera
Day 0
Day 14
Day 21
Day 45
Immunize
Boost
Blood Draw
Blood Draw
SARS-CoV Spike
MERS-CoV Spike
Dilution for 50% Neutralization of Live Virus
32768
16384
8192
4096
2048
1024
512
256
128
64
32
16
8
4
2
1
D0
3ug
3ug
3ug
No Adj.
+ Alum
+ Matrix M1
D0
1ug
3ug
10ug
1ug
3ug
3ug
No Adjuvant
+ Alum
+ Matrix M1
Novavax

Figure 8A: Codon Optimized sequence for MERS Al Hasa 1 spike protein (nucleotide sequence)

ATGATCCACTCCGTGTTCCTGTTGATGTTCCTGTTGACTCCTACCGAAAGCTACGTTGAT
GTTGGTCCAGATTCCGTGAAGAGCGCCTGCATCGAGGTGGATATCCAGCAAACATTCTTC
GACAAGACCTGGCCGAGGCCCATCGATGTCTCCAAGGCTGACGGTATCATCTACCCTCAG
GGCAGAACTTACTCTAACATCACTATCACATACCAAGGCCTGTTCCCATACCAGGGTGAC
CACGGCGATATGTACGTCTACAGCGCTGGACACGCTACCGGAACCACTCCTCAGAAGCTC
TTCGTTGCCAACTACTCACAGGACGTGAAGCAATTCGCTAACGGATTCGTGGTCCGTATC
GGTGCTGCCGCTAACAGCACCGGTACTGTGATCATCTCTCCCAGCACTTCAGCCACAATC
CGCAAGATCTACCCTGCTTTCATGCTGGGTTCCTCTGTGGGCAACTTCTCCGATGGAAAG
ATGGGCAGGTTCTTCAACCACACTCTCGTCCTGCTCCCTGACGGCTGCGGAACATTGCTG
AGGGCCTTCTACTGTATCTTGGAGCCTAGATCTGGCAACCACTGCCCAGCTGGAAACAGC
TACACCTCATTCGCCACCTACCACACTCCAGCTACAGACTGTAGCGATGGTAACTACAAC
CGTAACGCTTCGTTGAACTCCTTCAAGGAATACTTCAACCTGCGCAACTGCACATTCATG
TACACCTACAACATCACTGAGGACGAAATCCTGGAGTGGTTCGGAATCACACAGACCGCC
CAAGGTGTTCACCTCTTCAGCTCACGTTACGTGGATTTGTACGGTGGCAACATGTTCCAG
TTCGCTACTCTCCCAGTCTACGACACAATCAAGTACTACTCCATCATCCCGCACTCTATC
CGTAGCATCCAATCAGACCGCAAGGCCTGGGCCGCTTTCTACGTCTACAAGCTGCAGCCT
CTCACCTTCCTCTTGGATTTCTCCGTTGACGGCTACATCCGTCGCGCTATCGATTGCGGA
TTCAACGACTTGTCTCAGCTGCACTGTTCGTACGAATCCTTCGACGTCGAGTCGGGAGTT
TACTCCGTGTCGTCCTTCGAGGCCAAGCCCTCGGGTTCCGTTGTGGAGCAAGCTGAGGGT
GTGGAGTGCGACTTCTCTCCTCTGCTCAGCGGTACTCCCCCTCAGGTCTACAACTTCAAG
CGTCTGGTTTTCACCAACTGCAACTACAACCTCACTAAGTTGCTGTCTTTGTTCAGCGTG
AACGACTTCACCTGCTCACAGATCTCGCCCGCCGCTATCGCTAGCAACTGTTACTCTAGC
CTGATCCTCGATTACTTCTCATACCCACTGTCCATGAAGTCTGACCTCAGCGTCTCATCG
GCCGGCCCGATCTCCCAATTCAACTACAAGCAGTCTTTCAGCAACCCTACCTGCTTGATC
CTGGCTACTGTGCCACACAACCTGACAACCATCACAAAGCCGCTCAAGTACTCTTACATC
AACAAGTGCTCAAGGCTCTTGTCGGACGATAGAACCGAAGTCCCACAACTGGTGAACGCT
AACCAGTACTCCCCTTGCGTCTCTATCGTTCCAAGCACCGTCTGGGAAGACGGCGATTAC
TACCGCAAGCAGCTCTCCCCCTTGGAGGGAGGTGGCTGGTTGGTGGCCTCAGGATCGACA
GTCGCTATGACCGAGCAGCTGCAAATGGGTTTCGGCATCACTGTGCAGTACGGTACTGAT
ACAAACTCCGTCTGCCCTAAGCTGGAATTCGCCAACGACACAAAGATCGCTTCTCAGCTG
GGTAACTGCGTGGAGTACTCCCTCTACGGCGTGTCTGGACGCGGTGTCTTCCAAAACTGT
ACTGCCGTCGGTGTTCGTCAGCAACGCTTCGTCTACGACGCTTACCAGAACCTCGTTGGT
TACTACTCCGACGATGGCAACTACTACTGCTTGAGGGCTTGTGTGTCCGTGCCCGTGTCC
GTGATCTACGACAAGGAAACCAAGACTCACGCCACCCTGTTCGGTAGCGTGGCTTGCGAG
CACATCTCCTCTACTATGTCACAATACTCCAGGTCTACAAGATCGATGCTCAAGAGGAGA
GACTCCACATACGGACCATTGCAGACCCCAGTGGGATGCGTCCTCGGTTTGGTGAACAGC
TCACTGTTCGTGGAAGATTGCAAGCTGCCCCTCGGCCAGTCCCTGTGTGCTCTCCCGGAC
ACCCCCTCTACATTGACCCCGCGTTCAGTTCGCTCGGTGCCCGGAGAGATGAGACTGGCT
TCCATCGCTTTCAACCACCCAATCCAGGTGGACCAATTGAACTCGTCCTACTTCAAGCTG
AGCATCCCGACAAACTTCTCATTCGGTGTCACCCAGGAGTACATCCAAACTACAATCCAG
AAGGTCACCGTTGACTGCAAGCAGTACGTGTGTAACGGCTTCCAAAAGTGCGAACAGCTG
CTCAGGGAGTACGGACAATTCTGTTCTAAGATCAACCAGGCCTTGCACGGTGCTAACCTG
CGTCAAGACGATTCTGTGCGCAACCTGTTCGCCAGCGTCAAGTCTAGCCAGTCATCGCCT
ATCATCCCAGGATTCGGTGGTGACTTCAACCTCACCTTGCTGGAACCTGTCAGCATCTCA
ACTGGTTCGAGGTCCGCCAGATCTGCTATCGAGGATCTCTTGTTCGACAAGGTGACCATC
GCTGACCCCGGCTACATGCAAGGATACGACGATTGCATGCAGCAAGGCCCTGCCAGCGCT
AGAGATCTGATCTGTGCCCAGTACGTTGCTGGATACAAGGTGTTGCCACCGCTGATGGAC
GTGAACATGGAAGCCGCTTACACCTCCTCCCTGCTGGGTTCCATCGCTGGCGTCGGATGG

Figure 8B: Codon Optimized sequence for MERS Al Hasa 1 spike protein

ACTGCTGGTCTCAGCTCATTCGCCGCTATCCCCTTCGCCCAAAGCATCTTCTACCGTTTG
AACGGTGTCGGCATCACTCAGCAAGTTTTGTCAGAGAACCAGAAGCTGATCGCTAACAAG
TTCAACCAAGCCCTGGGCGCTATGCAGACCGGATTCACCACTACAAACGAAGCCTTCCGT
AAGGTGCAAGACGCTGTCAACAACAACGCCCAGGCTCTCTCCAAGTTGGCCTCCGAGCTG
TCTAACACCTTCGGCGCCATCTCTGCTAGCATCGGAGATATCATCCAGCGTCTGGACGTG
CTCGAGCAGGATGCTCAAATCGACAGGCTGATCAACGGCAGATTGACCACTCTGAACGCC
TTCGTCGCTCAGCAACTCGTTAGATCAGAATCGGCTGCTCTGTCCGCTCAGCTCGCTAAG
GACAAGGTGAACGAGTGCGTGAAGGCCCAAAGCAAGCGTTCAGGTTTCTGTGGACAGGGC
ACCCACATCGTGTCTTTCGTCGTGAACGCTCCCAACGGTCTGTACTTCATGCACGTCGGC
TACTACCCTTCAAACCACATCGAGGTGGTCTCGGCCTACGGTCTCTGCGATGCCGCTAAC
CCGACTAACTGTATCGCTCCCGTGAACGGCTACTTCATCAAGACCAACAACACTCGCATC
GTGGACGAATGGTCCTACACCGGCTCGTCCTTCTACGCCCCTGAGCCAATCACTTCACTG
AACACAAAGTACGTCGCTCCCCACGTTACTTACCAGAACATCTCGACAAACTTGCCCCCT
CCATTGCTGGGTAACTCAACCGGCATCGACTTCCAAGATGAACTGGACGAGTTCTTCAAG
AACGTGTCCACATCTATCCCTAACTTCGGCTCCCTGACCCAGATCAACACAACCCTCTTG
GATCTCACTTACGAAATGTTGTCCCTGCAGCAAGTTGTGAAGGCCCTGAACGAATCTTAC
ATCGATCTCAAGGAGTTGGGAAACTACACCTACTACAACAAGTGGCCATGGTACATCTGG
CTCGGATTCATCGCTGGTTTGGTGGCCCTCGCTTTGTGCGTCTTCTTCATCCTGTGCTGT
ACCGGCTGCGGAACTAACTGTATGGGCAAGCTGAAGTGCAACCGTTGCTGTGATCGCTAC
GAGGAATACGACCTGGAGCCCCACAAGGTGCACGTCCACTAA

Figure 9: Codon Optimized sequence for MERS Al Hasa 1 spike protein (amino acid sequence)

```
>MERS_AlHasa1
   1 mihsvfllmf lltptesyvd vgpdsvksac ievdiqqtff dktwprpidv skadgiiypq
  61 grtysnitit yqglfpyqgd hgdmyvysag hatgttpqkl fvanysqdvk qfangfvvri
 121 gaaanstgtv iispstsati rkiypafmlg ssvgnfsdgk mgrffnhtlv llpdgcgtll
 181 rafycilepr sgnhcpagns ytsfatyhtp atdcsdgnyn rnaslnsfke yfnlrnctfm
 241 ytynitedei lewfgitqta qgvhlfssry vdlyggnmfq fatlpvydti kyysiiphsi
 301 rsiqsdrkaw aafyvyklqp ltflldfsvd gyirraidcg fndlsqlhcs yesfdvesgv
 361 ysvssfeakp sgsvveqaeg vecdfsplls gtppqvynfk rlvftncnyn ltkllslfsv
 421 ndftcsqisp aaiasncyss lildyfsypl smksdlsvss agpisqfnyk qsfsnptcli
 481 latvphnltt itkplkysyi nkcsrllsdd rtevpqlvna nqyspcvsiv pstvwedgdy
 541 yrkqlspleg ggwlvasgst vamteqlqmg fgitvqygtd tnsvcpklef andtkiasql
 601 gncveyslyg vsgrgvfqnc tavgvrqqrf vydayqnlvg yysddgnyyc lracvsvpvs
 661 viydketkth atlfgsvace hisstmsqys rstrsmlkrr dstygplqtp vgcvlglvns
 721 slfvedcklp lgqslcalpd tpstltprsv rsvpgemrla siafnhpiqv dqlnssyfkl
 781 siptnfsfgv tqeyiqttiq kvtvdckqyv cngfqkceql lreygqfcsk inqalhganl
 841 rqddsvrnlf asvkssqssp iipgfggdfn ltllepvsis tgsrsarsai edllfdkvti
 901 adpgymqgyd dcmqqgpasa rdlicaqyva gykvlpplmd vnmeaaytss llgsiagvgw
 961 taglssfaai pfaqsifyrl ngvgitqqvl senqkliank fnqalgamqt gfttttneafr
1021 kvqdavnnna qalsklasel sntfgaisas igdiiqrldv leqdaqidrl ingrlttlna
1081 fvaqqlvrse saalsaqlak dkvnecvkaq skrsgfcgqg thivsfvvna pnglyfmhvg
1141 yypsnhievv saygicdaan ptnciapvng yfiktnntri vdewsytgss fyapepitsl
1201 ntkyvaphvt yqnistnlpp pllgnstgid fqdeldeffk nvstsipnfg sltqinttll
1261 dltyemlslq qvvkalnesy idlkelgnyt yynkwpwyiw lgfiaglval alcvffilcc
1321 tgcgtncmgk lkcnrccdry eeydlephkv hvh
```

Figure 10

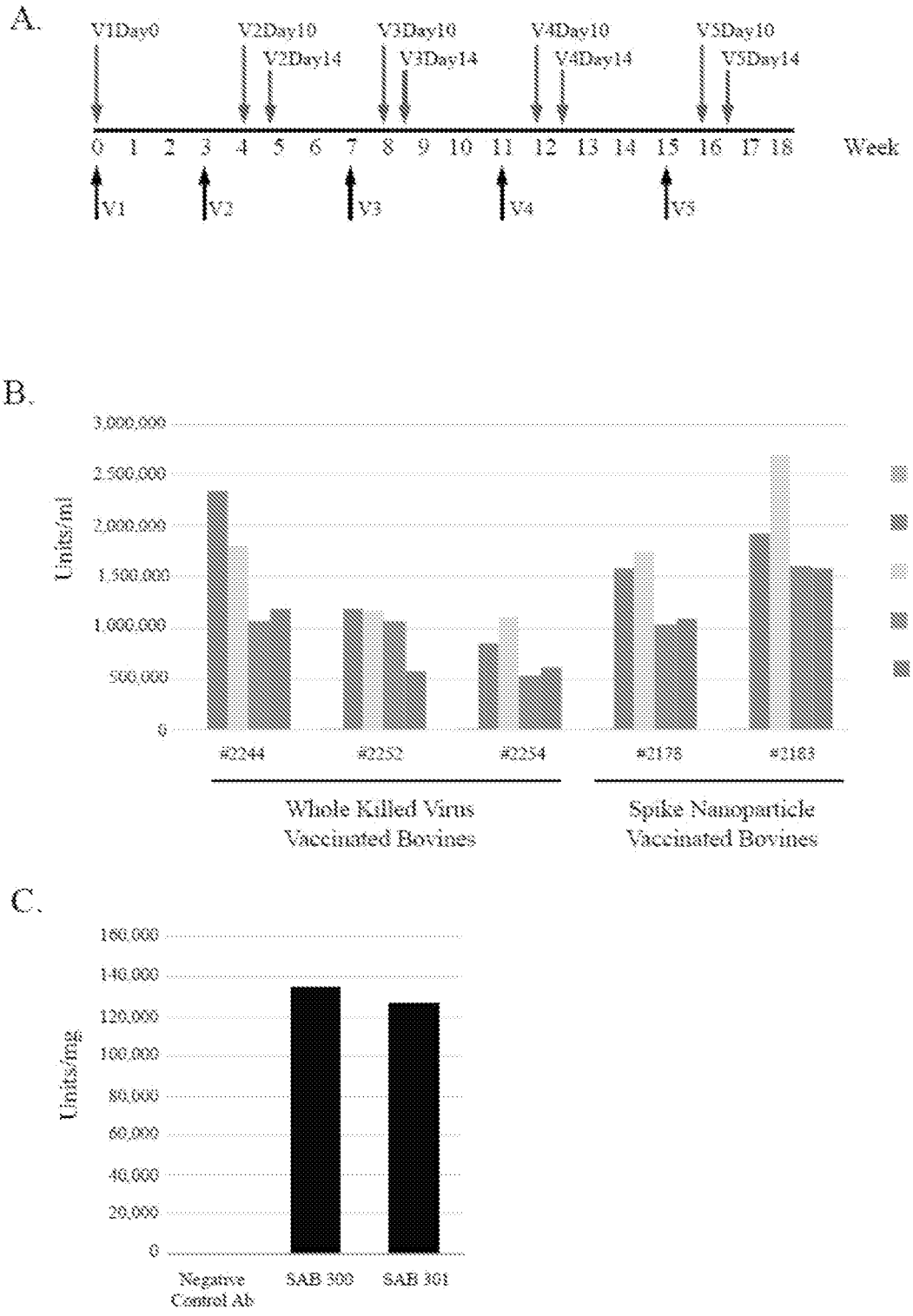

A.
V1Day0
V2Day10
V2Day14
V3Day10
V3Day14
V4Day10
V4Day14
V5Day10
V5Day14
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
Week
V1
V2
V3
V4
V5
B.
3,000,000
2,500,000
2,000,000
1,500,000
1,000,000
500,000
0
Units/ml
Pre-V1
V2D10
V3D10
V4D10
V5D10
#2244
#2252
#2254
#2178
#2183
Whole Killed Virus Vaccinated Bovines
Spike Nanoparticle Vaccinated Bovines
C.
160,000
140,000
120,000
100,000
80,000
60,000
40,000
20,000
0
Units/mg
Negative Control Ab
SAB 300
SAB 301

Figure 11

A.

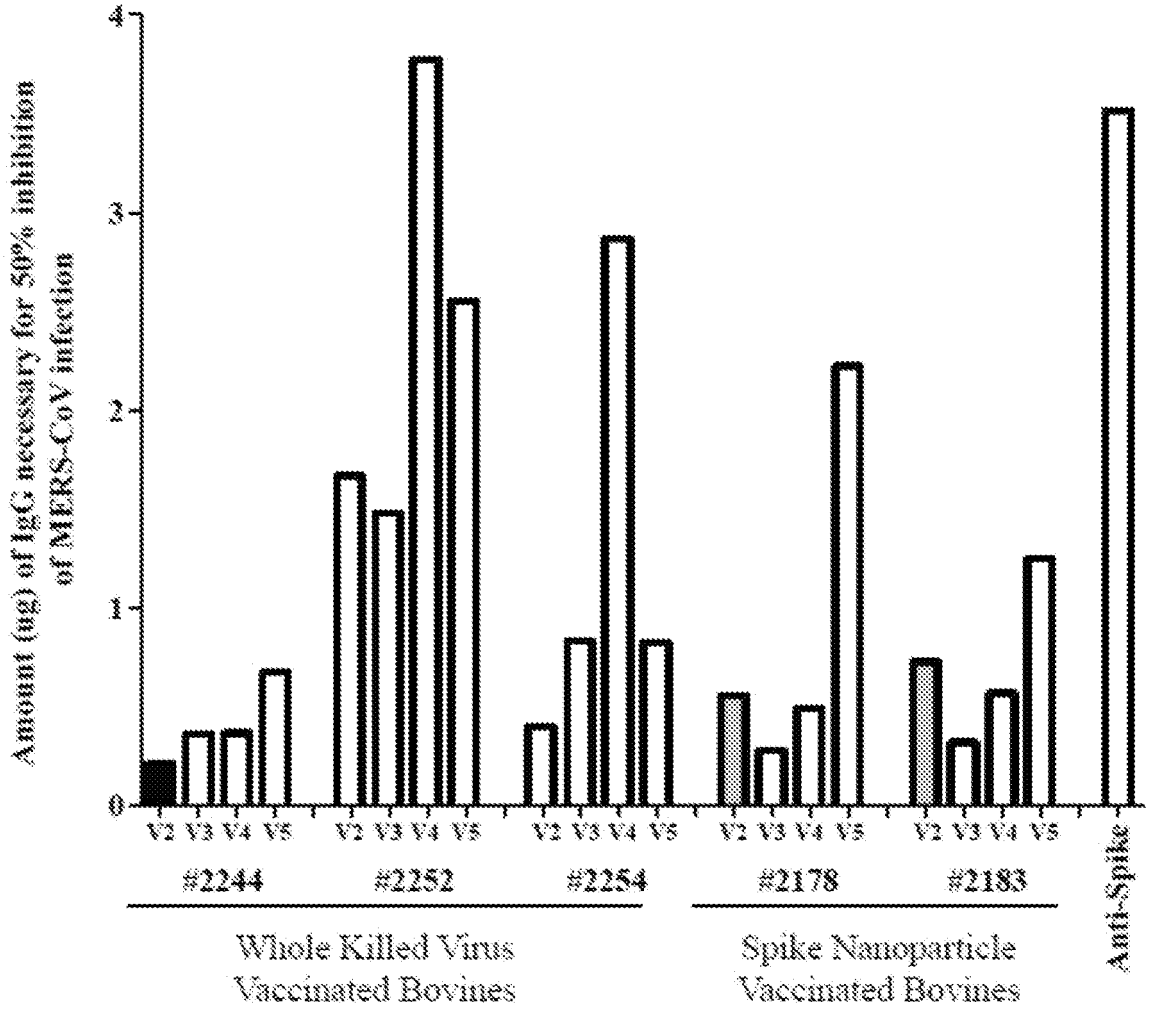

Amount (ug) of IgG necessary for 50% inhibition of MERS-CoV infection
0
1
2
3
4
V2 V3 V4 V5
#2244
#2252
#2254
#2178
#2183
Anti-Spike
Whole Killed Virus Vaccinated Bovines
Spike Nanoparticle Vaccinated Bovines

Figure 11

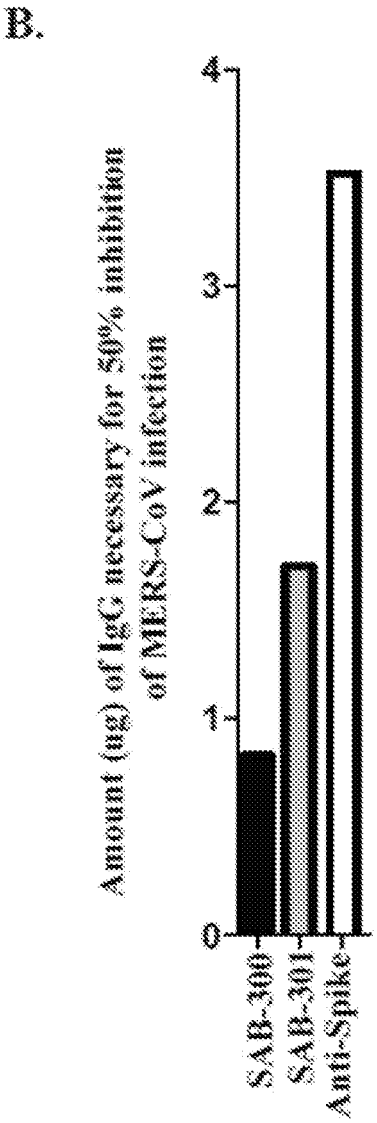
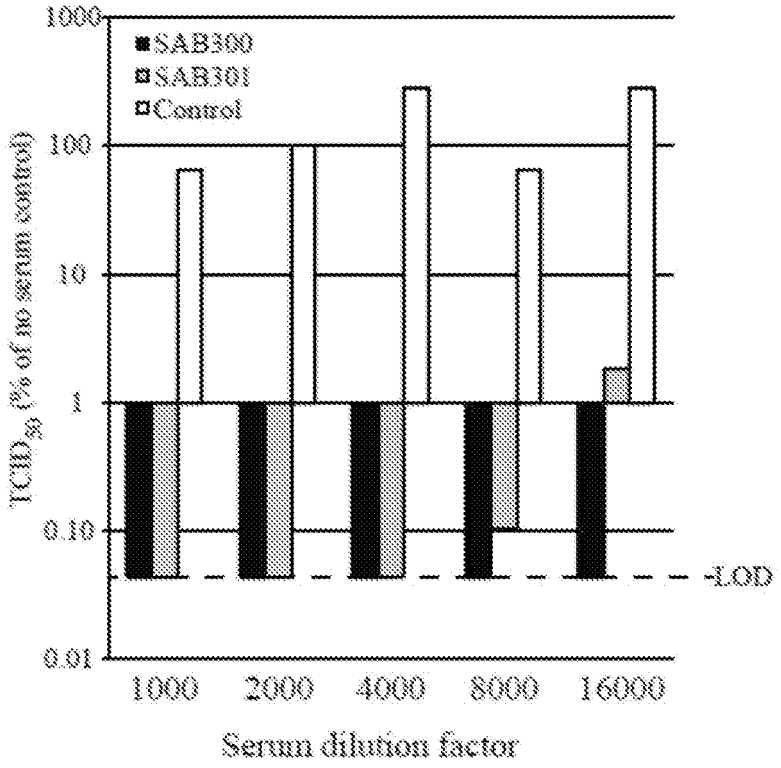

B.
Amount (ug) of IgG necessary for 50% inhibition of MERS-CoV infection
0
1
2
3
4
SAB-300
SAB-301
Anti-Spike

Figure 12

A.


1000
100
10
1
0.10
0.01
SAB300
SAB301
Control
TCID50 (% of no serum control)
-LOD
1000
2000
4000
8000
16000
Serum dilution factor

B.

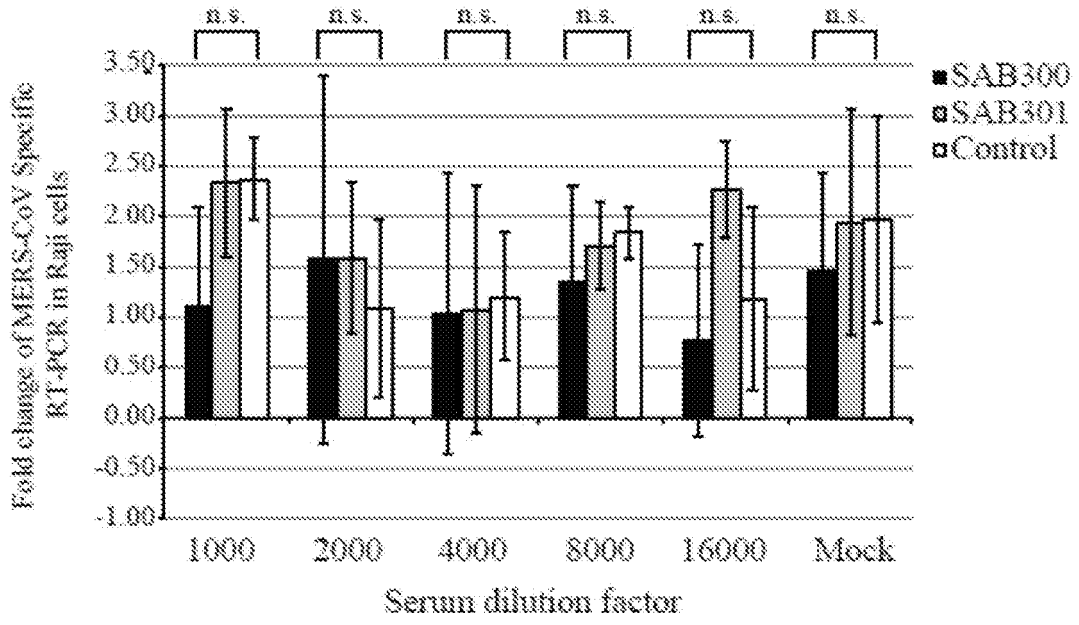
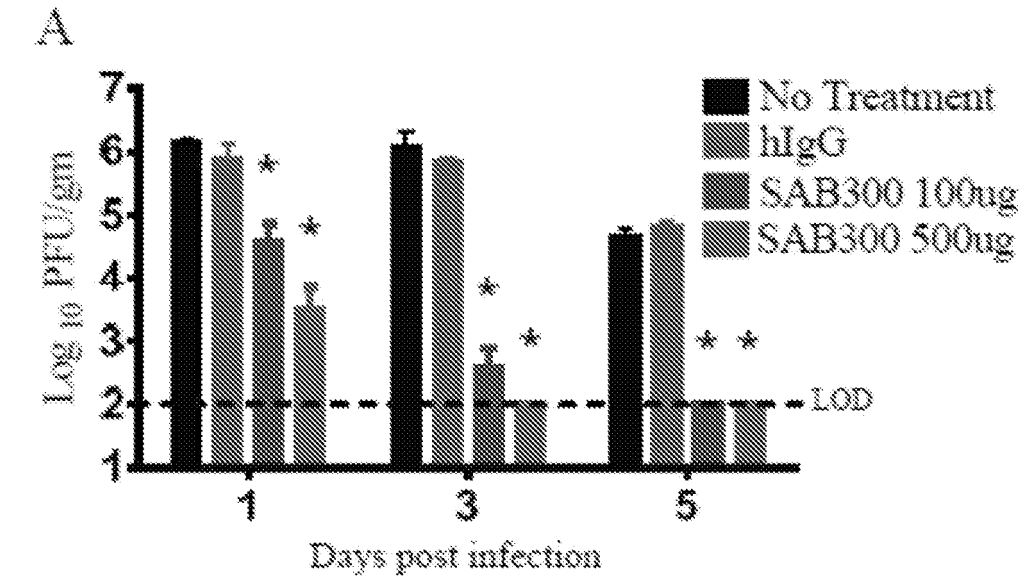

n.s.
n.s.
n.s.
n.s.
n.s.
n.s.
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
-0.50
-1.00
Fold change of MERS-CoV Specific RT-PCR in Raji cells
SAB300
SAB301
Control
1000
2000
4000
8000
16000
Mock
Serum dilution factor

Figure 13


A
Log 10 PFU/gm
7
6
5
4
3
2
1
No Treatment
hIgG
SAB300 100ug
SAB300 500ug
LOD
1
3
5
Days post infection

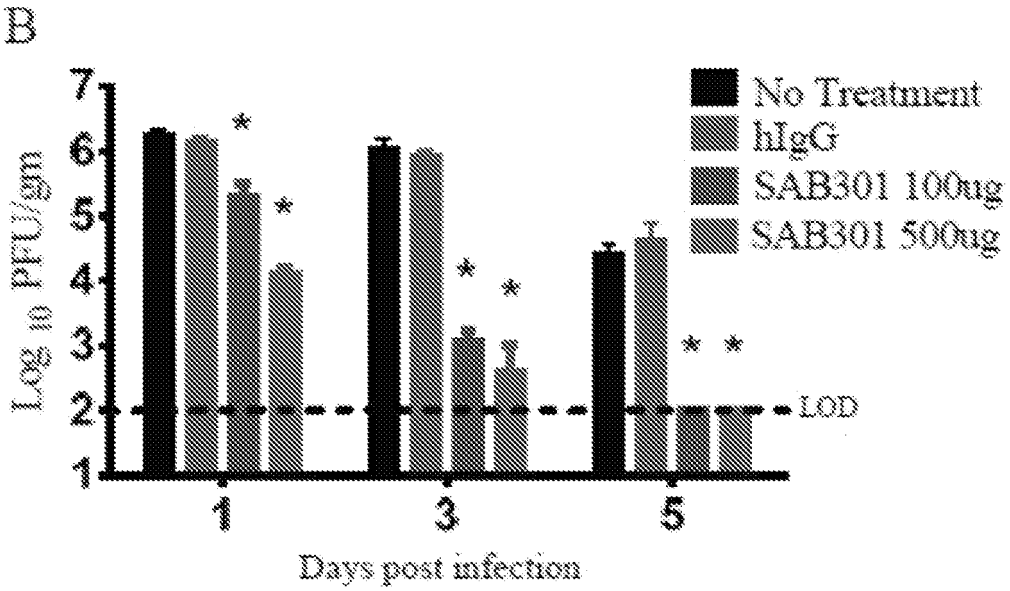
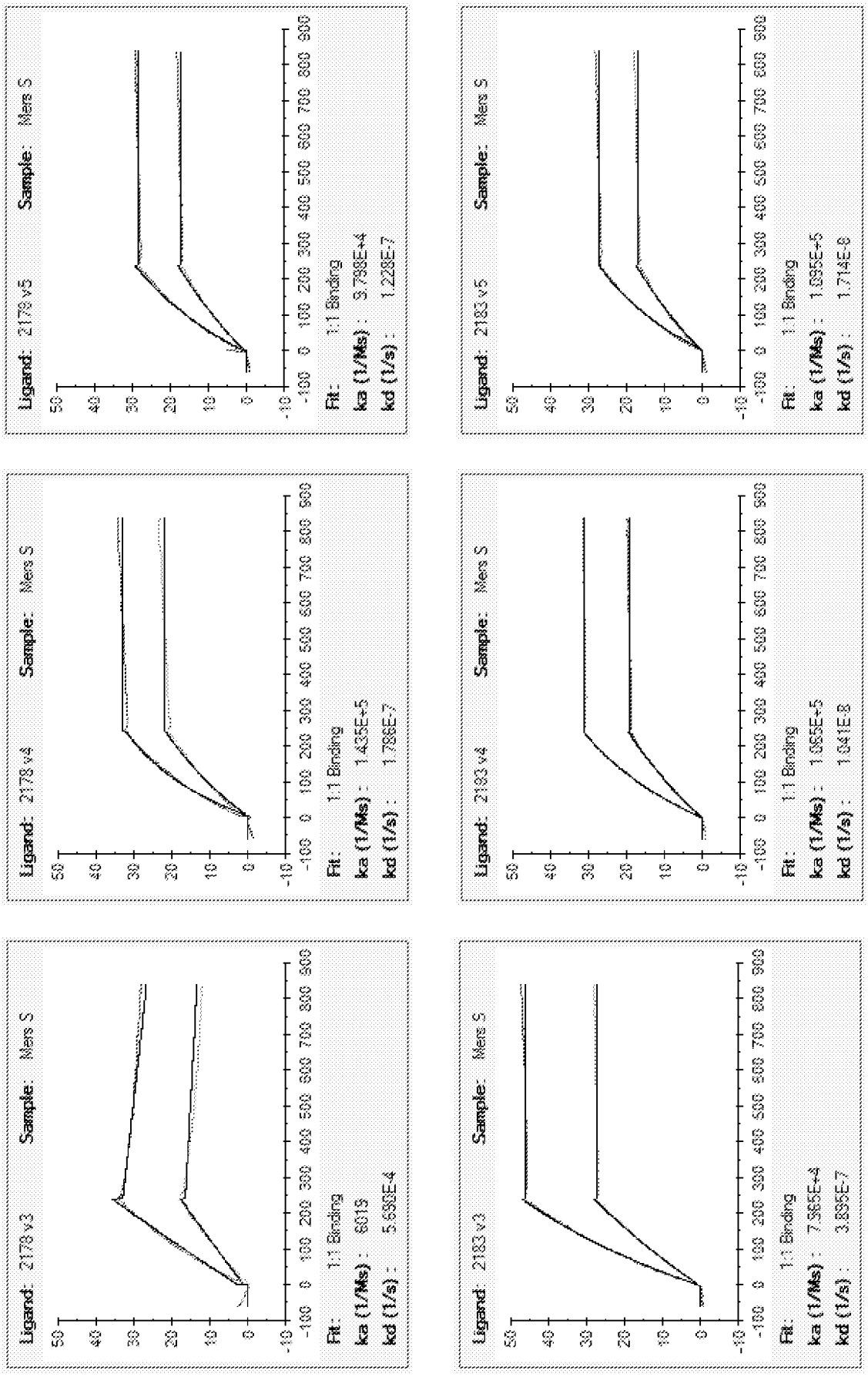

B
Log 10 PFU/gm
7
6
5
4
3
2
1
No Treatment
hIgG
SAB301 100ug
SAB301 500ug
LOD
1
3
5
Days post infection

Figure 14


Ligand: 2178 v3
Sample: Mers S
Fit: 1:1 Binding
ka (1/Ms) : 6013
kd (1/s) : 5.693E-4
Ligand: 2178 v4
Sample: Mers S
Fit: 1:1 Binding
ka (1/Ms) : 1.435E+5
kd (1/s) : 1.788E-7
Ligand: 2178 v5
Sample: Mers S
Fit: 1:1 Binding
ka (1/Ms) : 3.738E+4
kd (1/s) : 1.228E-7
Ligand: 2183 v3
Sample: Mers S
Fit: 1:1 Binding
ka (1/Ms) : 7.365E+4
kd (1/s) : 3.835E-7
Ligand: 2183 v4
Sample: Mers S
Fit: 1:1 Binding
ka (1/Ms) : 1.055E+5
kd (1/s) : 1.041E-8
Ligand: 2183 v5
Sample: Mers S
Fit: 1:1 Binding
ka (1/Ms) : 1.695E+5
kd (1/s) : 1.714E-8