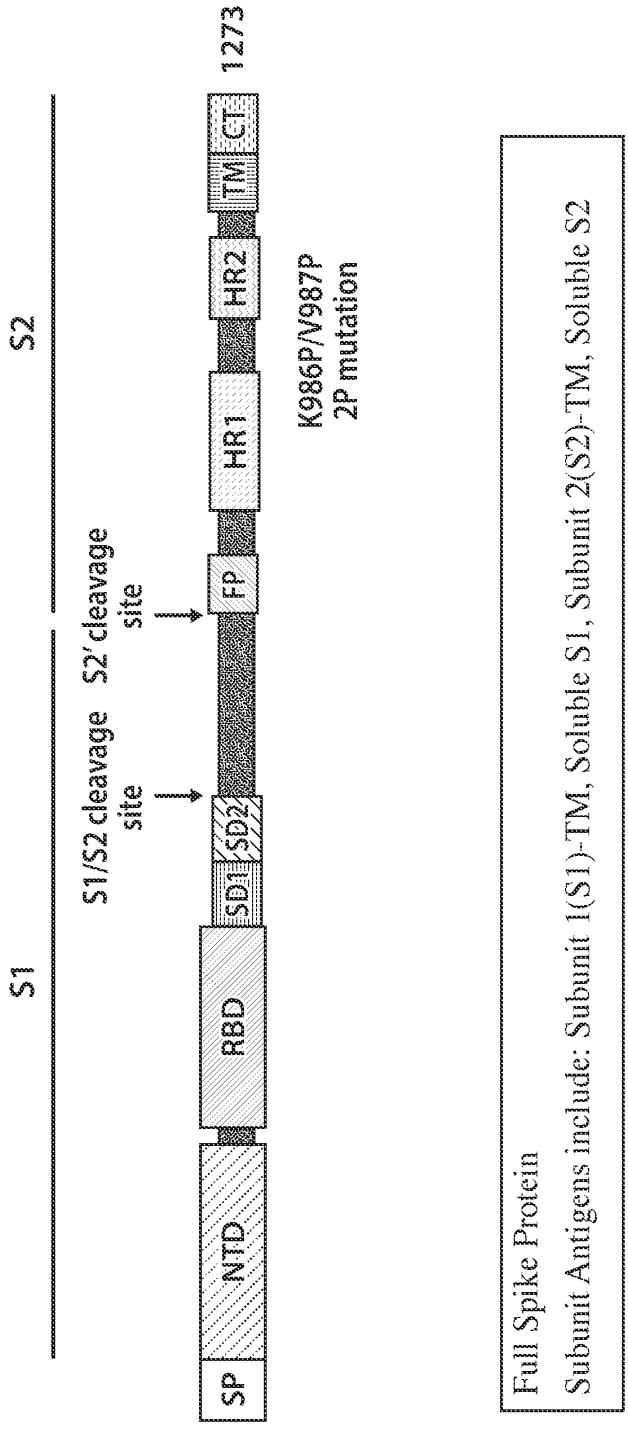

S1
S2
S1/S2 cleavage site
S2′ cleavage site
1
SP
NTD
RBD
SD1
SD2
FP
HR1
HR2
TM
CT
1273
K986P/V987P
2P mutation
Full Spike Protein
Subunit Antigens include: Subunit 1(S1)-TM, Soluble S1, Subunit 2(S2)-TM, Soluble S2

FIG. 1

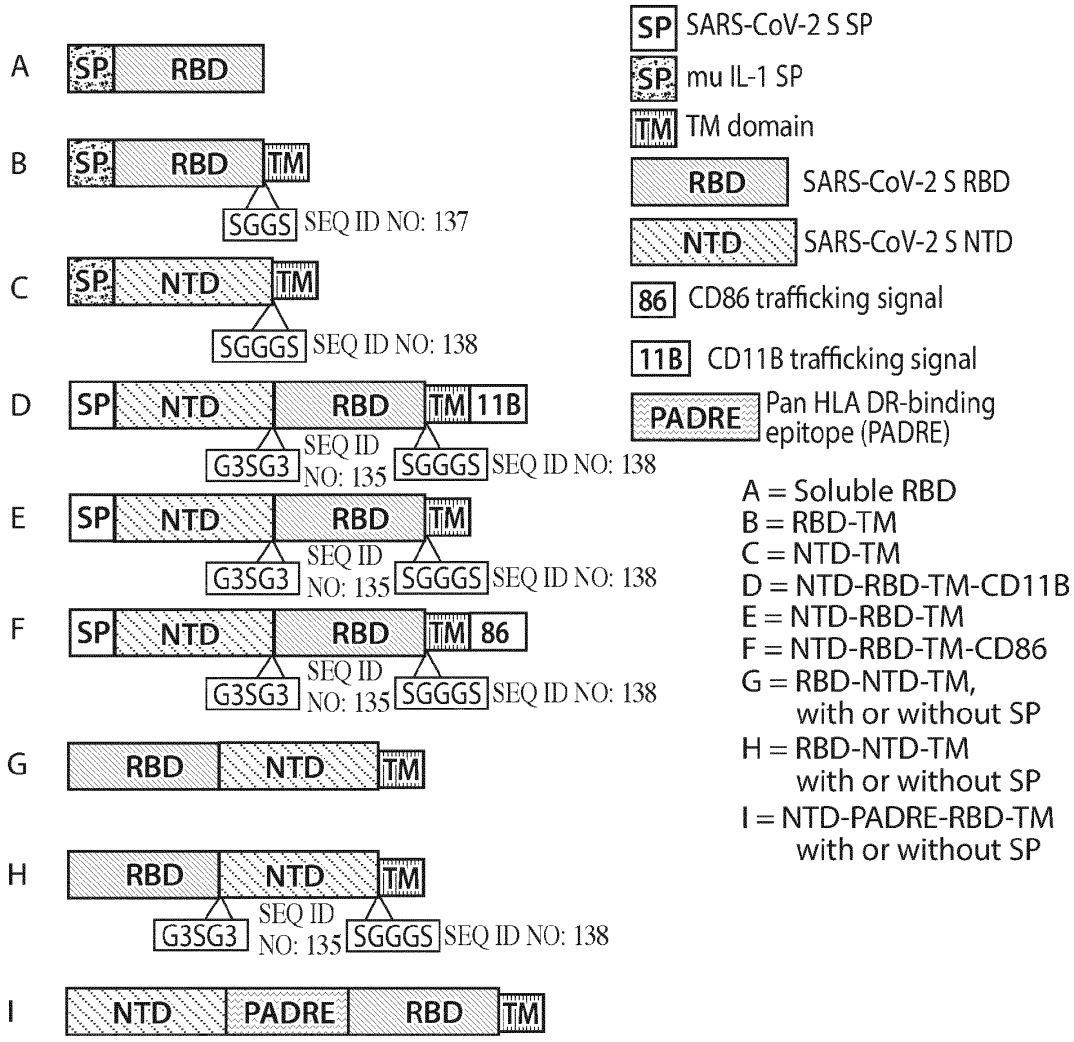

A
SP
RBD
B
SP
RBD
TM
SGGS
SEQ ID NO: 137
C
SP
NTD
TM
SGGGS
SEQ ID NO: 138
D
SP
NTD
RBD
TM
11B
G3SG3
SEQ ID NO: 135
SGGGS
SEQ ID NO: 138
E
SP
NTD
RBD
TM
G3SG3
SEQ ID NO: 135
SGGGS
SEQ ID NO: 138
F
SP
NTD
RBD
TM
86
G3SG3
SEQ ID NO: 135
SGGGS
SEQ ID NO: 138
G
RBD
NTD
TM
H
RBD
NTD
TM
G3SG3
SEQ ID NO: 135
SGGGS
SEQ ID NO: 138
I
NTD
PADRE
RBD
TM
SP SARS-CoV-2 S SP
SP mu IL-1 SP
TM TM domain
RBD SARS-CoV-2 S RBD
NTD SARS-CoV-2 S NTD
86 CD86 trafficking signal
11B CD11B trafficking signal
PADRE Pan HLA DR-binding epitope (PADRE)
A = Soluble RBD
B = RBD-TM
C = NTD-TM
D = NTD-RBD-TM-CD11B
E = NTD-RBD-TM
F = NTD-RBD-TM-CD86
G = RBD-NTD-TM, with or without SP
H = RBD-NTD-TM with or without SP
I = NTD-PADRE-RBD-TM with or without SP

FIG. 2

```
A ---------------------------------------------------------- 0
B ---------------------------------------------------------- 0
C mfvflvllplvssQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFS 60
D mfvflvllplvssQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFS 60
E mfvflvllplvssQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFS 60
F mfvflvllplvssQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFS 60

A ---------------------------------------------------------- 0
B ---------------------------------------------------------- 0
C NVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIV 120
D NVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIV 120
E NVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIV 120
F NVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIV 120

A ---------------------------------------------------------- 0
B ---------------------------------------------------------- 0
C NNATNVVIKVCEFQFCNDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLE 180
D NNATNVVIKVCEFQFCNDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLE 180
E NNATNVVIKVCEFQFCNDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLE 180
F NNATNVVIKVCEFQFCNDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLE 180

A ---------------------------------------------------------- 0
B ---------------------------------------------------------- 0
C GKQGNFKNLREFVFKNIDGYFKIYSKHTPINLVRDLPQGFSALEPLVDLPIGINITRFQT 240
D GKQGNFKNLREFVFKNIDGYFKIYSKHTPINLVRDLPQGFSALEPLVDLPIGINITRFQT 240
E GKQGNFKNLREFVFKNIDGYFKIYSKHTPINLVRDLPQGFSALEPLVDLPIGINITRFQT 240
F GKQGNFKNLREFVFKNIDGYFKIYSKHTPINLVRDLPQGFSALEPLVDLPIGINITRFQT 240

A ------------------------------------------mysmqlascvtltlvll 17
B ------------------------------------------mysmqlascvtltlvll 17
C LLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDSgggsILAIY 300
D LLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDgggsqgg--- 300
E LLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDgggsqgg--- 300
F LLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDgggsqgg--- 300

A vnsQPNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSASFSTFKCYGVSPT 77
B vnsQPNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSASFSTFKCYGVSPT 77
C STVASSLVLLVSLGAISF---------------------------------------- 318
D ----PNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSASFSTFKCYGVSPT 353
E ----PNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSASFSTFKCYGVSPT 353
F ----PNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSASFSTFKCYGVSPT 353

A KLNDLCFTNVYADSFVIRGDEVRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKV 137
B KLNDLCFTNVYADSFVIRGDEVRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKV 137
C ---------------------------------------------------------- 318
D KLNDLCFTNVYADSFVIRGDEVRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKV 413
E KLNDLCFTNVYADSFVIRGDEVRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKV 413
F KLNDLCFTNVYADSFVIRGDEVRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKV 413
```

FIG. 3

A **GGNYNYLYRLFRKSNLKPFERDISTEIYQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGY** 197
B **GGNYNYLYRLFRKSNLKPFERDISTEIYQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGY** 197
C ---------- 318
D **GGNYNYLYRLFRKSNLKPFERDISTEIYQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGY** 473
E **GGNYNYLYRLFRKSNLKPFERDISTEIYQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGY** 473
F **GGNYNYLYRLFRKSNLKPFERDISTEIYQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGY** 473

A **QPYRVVVLSFELLHAPATVCGPK**---------- 220
B **QPYRVVVLSFELLHAPATVCGPK***sgggs**ILAIYSTVASSLVLLVSLGAISF*---------- 248
C ---------- 318
D **QPYRVVVLSFELLHAPATVCGPK**sgggs*ILAIYSTVASSLVLLVSLGAISFkrqykdmms* 533
E *QPYRVVVLSFELLHAPATVCGPK*sgggs*ILAIYSTVASSLVLLVSLGAISF*---------- 524
F **QPYRVVVLSFELLHAPATVCGPK**sgggs*ILAIYSTVASSLVLLVSLGAISF***kkkkrprns** 533

A ---------- 220 SEQ ID NO: 62
B ---------- 248 SEQ ID NO: 77
C ---------- 318 SEQ ID NO: 47
D egg-ppqaepq---------- 543 SEQ ID NO: 98
E ---------- 524 SEQ ID NO: 92
F **ykcgtntmereeseqtkkrekihipersdeaqrvfkssktsscdksdtcf** 583 SEQ ID NO: 95

Lowercase – signal peptide
UPPERCASE – NTD
UPPERCASE – RBD
lowercase – linker
UPPERCASE – TM domain
lowercase – CD86
lowercase – CD11B

FIG. 3 (continued)

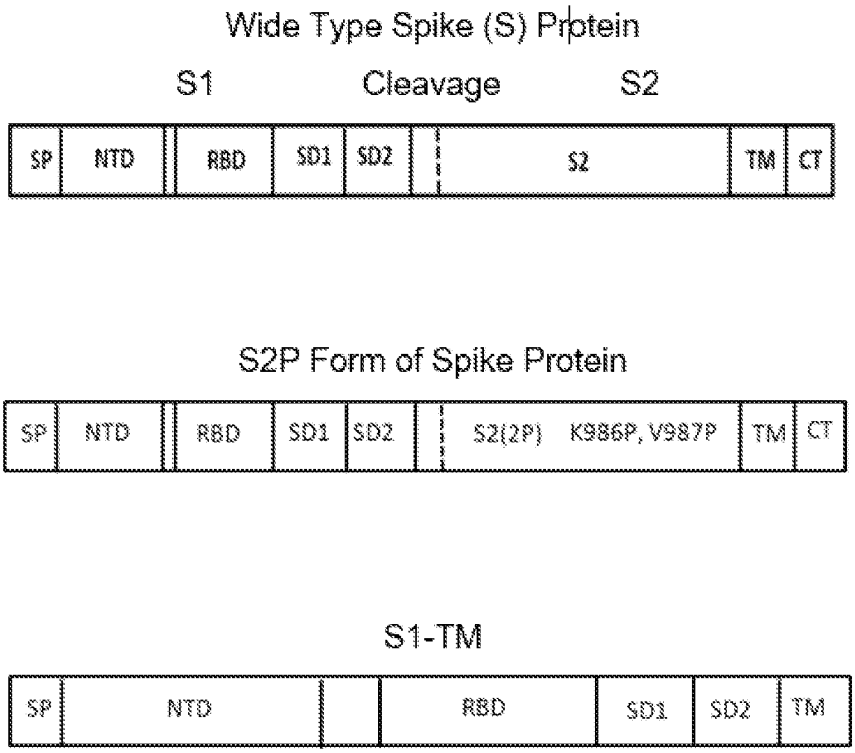

Wide Type Spike (S) Protein
S1
Cleavage
S2
SP
NTD
RBD
SD1
SD2
S2
TM
CT
S2P Form of Spike Protein
SP
NTD
RBD
SD1
SD2
S2(2P)
K986P, V987P
TM
CT
S1-TM
SP
NTD
RBD
SD1
SD2
TM

FIG. 4

```
G mfvflvllplvssQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFS 60
H mfvflvllplvssQCVNLTTRTQLPPAYTNSFTRGVYYPDKVCRSSVLHSTQDLFLPFFS 60
I mfvflvllplvssQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFS 60
J mfvflvllplvssQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFS 60
K mfvflvllplvssQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFS 60
L mfvflvllplvssQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFS 60
  ************************************** *****************

G NVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIV 120
H NVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIV 120
I NVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIV 120
J NVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIV 120
K NVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIV 120
L NVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIV 120
  ************************************************************

G NNATNVVIKVCEFQFCNDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLE 180
H NNATNVVIKVCEFQFCNDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLE 180
I NNATNVVIKVCEFQFCNDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLE 180
J NNATNVVIKVCEFQFCNDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLE 180
K NNATNVVIKVCEFQFCNDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLE 180
L NNATNVVIKVCEFQFCNDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLE 180
  ************************************************************

G GKQGNFKNLREFVFKNIDGYFKIYSKHTPINLVRDLPQGFSALEPLVDLPIGINITRFQT 240
H GKQGNFKNLREFVFKNIDGYFKIYSKHTPINLVRDLPQGFSALEPLVDLPIGINITRFQT 240
I GKQGNFKNLREFVFKNIDGYFKIYSKHTPINLVRDLPQGFSALEPLVDLPIGINITRFQT 240
J GKQGNFKNLREFVFKNIDGYFKIYSKHTPINLVRDLPQGFSALEPLVDLPIGINITRFQT 240
K GKQGNFKNLREFVFKNIDGYFKIYSKHTPINLVRDLPQGFSALEPLVDLPIGINITRFQT 240
L GKQGNFKNLREFVFKNIDGYFKIYSKHTPINLVRDLPQGFSALEPLVDLPIGINITRFQT 240
  ************************************************************

G LLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDCALDPLSETK 300
H LLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDCALDPLSETK 300
I LLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDCALDPLSETK 300
J LLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDCALDPLSETK 300
K LLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDCALDPLSETK 300
L LLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDCALDPLSETK 300
  ************************************************************

G CTLKSFTVgsgggsgggsgggsgggsggQPTESIVRFPNITNLCPFGEVFNATRFASVYA 360
H CTLKSFTVgsgggsgggsgggsgggsggQPTESIVRFPNITNLCPFGEVFNATRFASVYA 360
I CTLKSFTVEKGIYQ--------TSNFRVQPTESIVRFPNITNLCPFGEVFNATRFASVYA 352
J CTLKSFTVEKGIYQ--------TSNFRVQPTESIVRFPNITNLCPFGEVFNATRFASVYA 352
K CTLKSFTVEKGIYQ--------TSNFRVQPTESIVRFPNITNLCPFGEVFNATRFASVYA 352
L CTLKSFTVEKGIYQ--------TSNFRVQPTESIVRFPNITNLCPFGEVFNATRFASVYA 352
  ******** .*  .         ..   ********************************
```

FIG. 5

```
G WNRKRISNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAP 420
H WNRKRISNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAP 420
I WNRKRISNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAP 412
J WNRKRISNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAP 412
K WNRKRISNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAP 412
L WNRKRISNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAP 412
  ************************************************************

G GQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDISTEI 480
H GQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDISTEI 480
I GQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDISTEI 472
J GQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDISTEI 472
K GQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDISTEI 472
L GQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDISTEI 472
  ************************************************************

G YQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVVVLSFELLHAPATVCGPKKSTN 540
H YQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVVVLSFELLHAPATVCGPKKSTN 540
I YQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVVVLSFELLHAPATVCGPKKST- 531
J YQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVVVLSFELLHAPATVCGPKKSTN 532
K YQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVVVLSFELLHAPATVCGPKKSTN 532
L YQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVVVLSFELLHAPATVCGPKKSTN 532
************************************************************

G LVKNKCVNFNFNGLTGTGVLTESNKKFLPFQQFGRDIADTTDAVRDPQTLEILDITPCSF 600
H LVKNKCVNFNFNGLTGTGVLTESNKKFLPFCQFGRDIADTTDAVRDPQTLEILDITPCSF 600
I ------------------------------------------------------------ 531
J LVKNKCVNFNFNGLTGTGVLTESNKKFLPFQQFGRDIADTTDAVRDPQTLEILDITPCSF 592
K LVKNKCVNFNFNGLTGTGVLTESNKKFLPFQQFGRDIADTTDAVRDPQTLEILDITPCSF 592
L LVKNKCVNFNFNGLTGTGVLTESNKKFLPFQQFGRDIADTTDAVRDPQTLEILDITPCSF 592

G GG---------------------------------------------------------- 602
H GG---------------------------------------------------------- 602
I ------------------------------------------------------------ 531
J GG---------------------------------------------------------- 594
K GGVSVITPGTNTSNQVAVLYQDVNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIG 652
L GGVSVITPGTNTSNQVAVLYQDVNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIG 652

G ----------------------------sgggsILAIYSTVASSLVLLVSLGAISF 630  SEQ ID NO: 26
H ----------------------------sgggsILAIYSTVASSLVLLVSLGAISF 630  SEQ ID NO: 29
I ----------------------------sgggsILAIYSTVASSLVLLVSLGAISF 559  SEQ ID NO: 20
J ----------------------------sgggsILAIYSTVASSLVLLVSLGAISF 622  SEQ ID NO: 23
K AEHVNNSYECDIPIGAGICASYQTQTNS---------------------------- 680  SEQ ID NO: 5
L AEHVNNSYECDIPIGAGICASYQTQTNsgggsILAIYSTVASSLVLLVSLGAISF 707  SEQ ID NO: 17
                                *
```

Lowercase – signal peptide
UPPERCASE – NTD
UPPERCASE – RBD
lowercase – linker
UPPERCASE – TM domain

G = S1-594-PolyG-TM
H = S1-594-PolyG-DS-TM
I = S1-531-TM
J = S1-594-TM
K = Soluble S1 Subunit
L = S1-666-TM

FIG. 5 (continued)

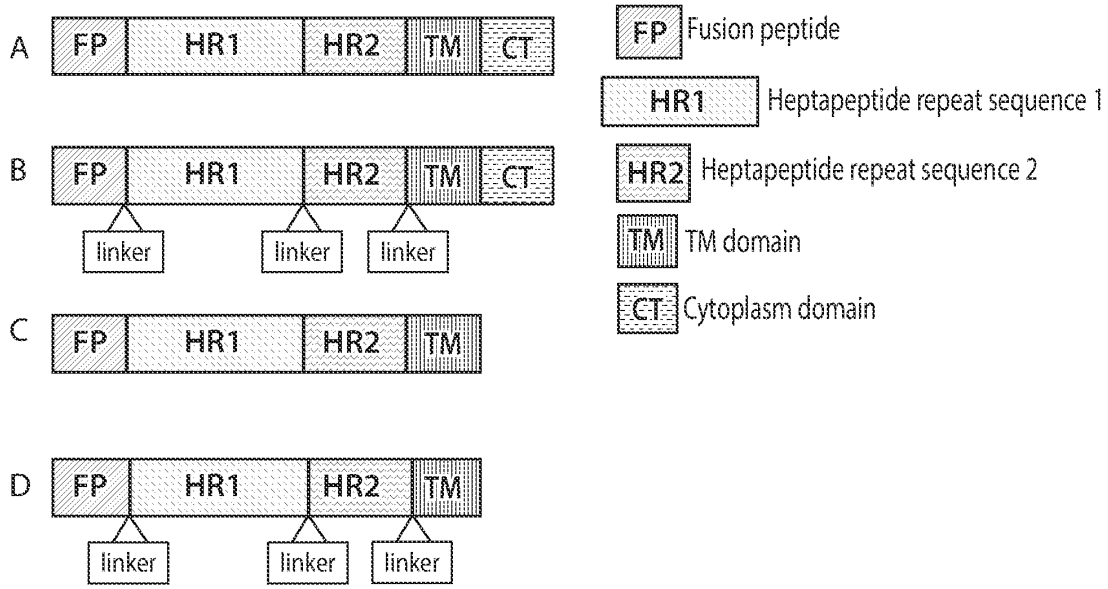

A
FP
HR1
HR2
TM
CT
B
FP
HR1
HR2
TM
CT
linker
linker
linker
C
FP
HR1
HR2
TM
D
FP
HR1
HR2
TM
linker
linker
linker
FP Fusion peptide
HR1 Heptapeptide repeat sequence 1
HR2 Heptapeptide repeat sequence 2
TM TM domain
CT Cytoplasm domain

FIG. 6

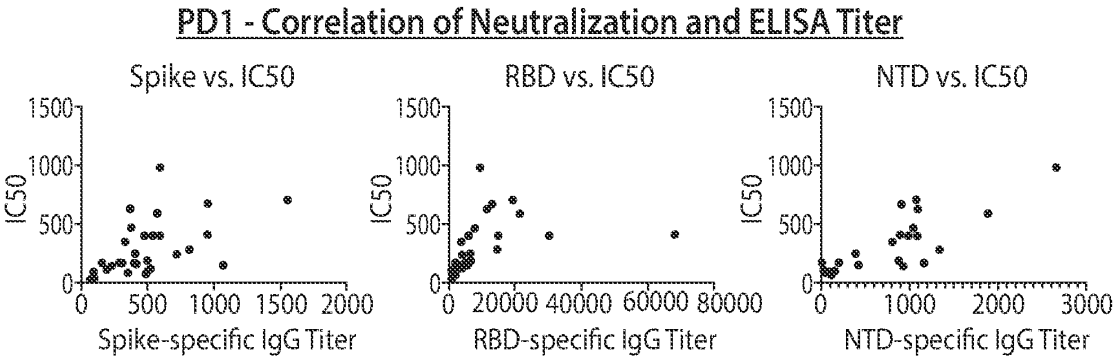

PD1 - Correlation of Neutralization and ELISA Titer
Spike vs. IC50
RBD vs. IC50
NTD vs. IC50
IC50
1500
1000
500
0
0 500 1000 1500 2000
Spike-specific IgG Titer
0 20000 40000 60000 80000
RBD-specific IgG Titer
0 1000 2000 3000
NTD-specific IgG Titer

FIG. 7

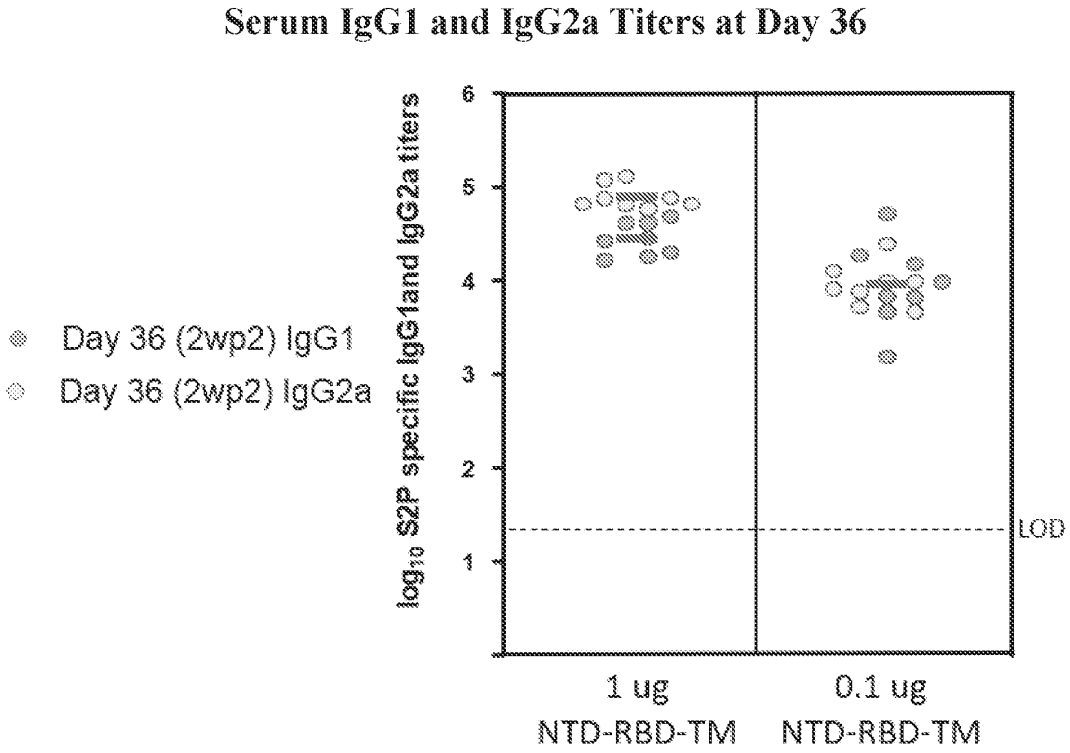

Serum IgG1 and IgG2a Titers at Day 36
Day 36 (2wp2) IgG1
Day 36 (2wp2) IgG2a
log10 S2P specific IgG1and IgG2a titers
6
5
4
3
2
1
LOD
1 ug
NTD-RBD-TM
0.1 ug
NTD-RBD-TM

FIG. 8A

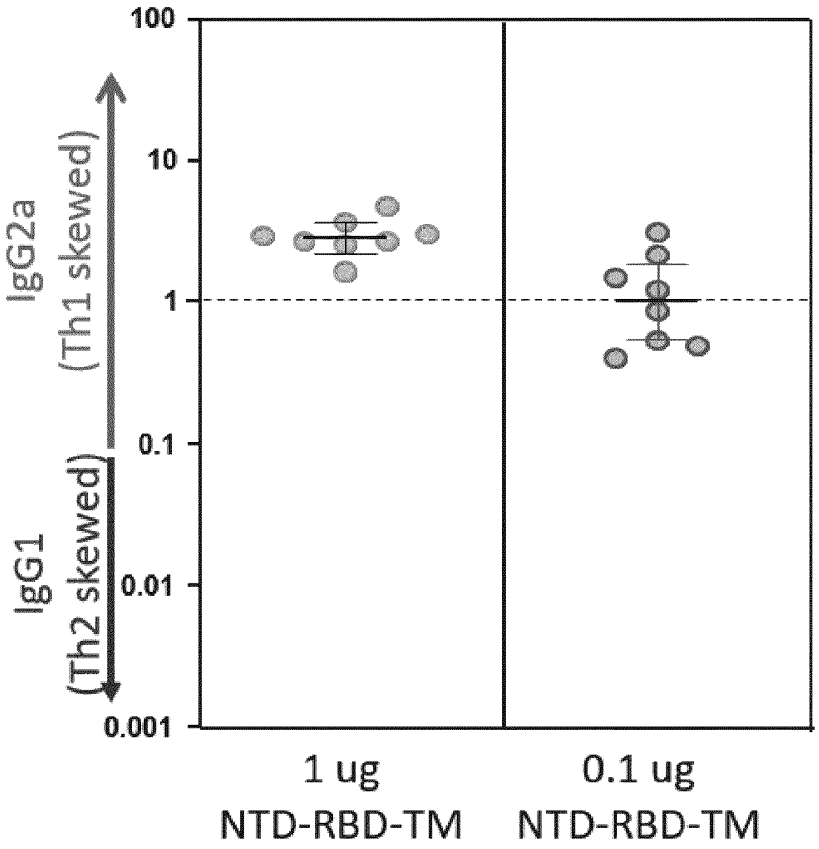

SARS-CoV-2 IgG2a/IgG1ratio PD2 Day 36
100
10
1
0.1
0.01
0.001
IgG2a
(Th1 skewed)
IgG1
(Th2 skewed)
1 ug
NTD-RBD-TM
0.1 ug
NTD-RBD-TM

FIG. 8B

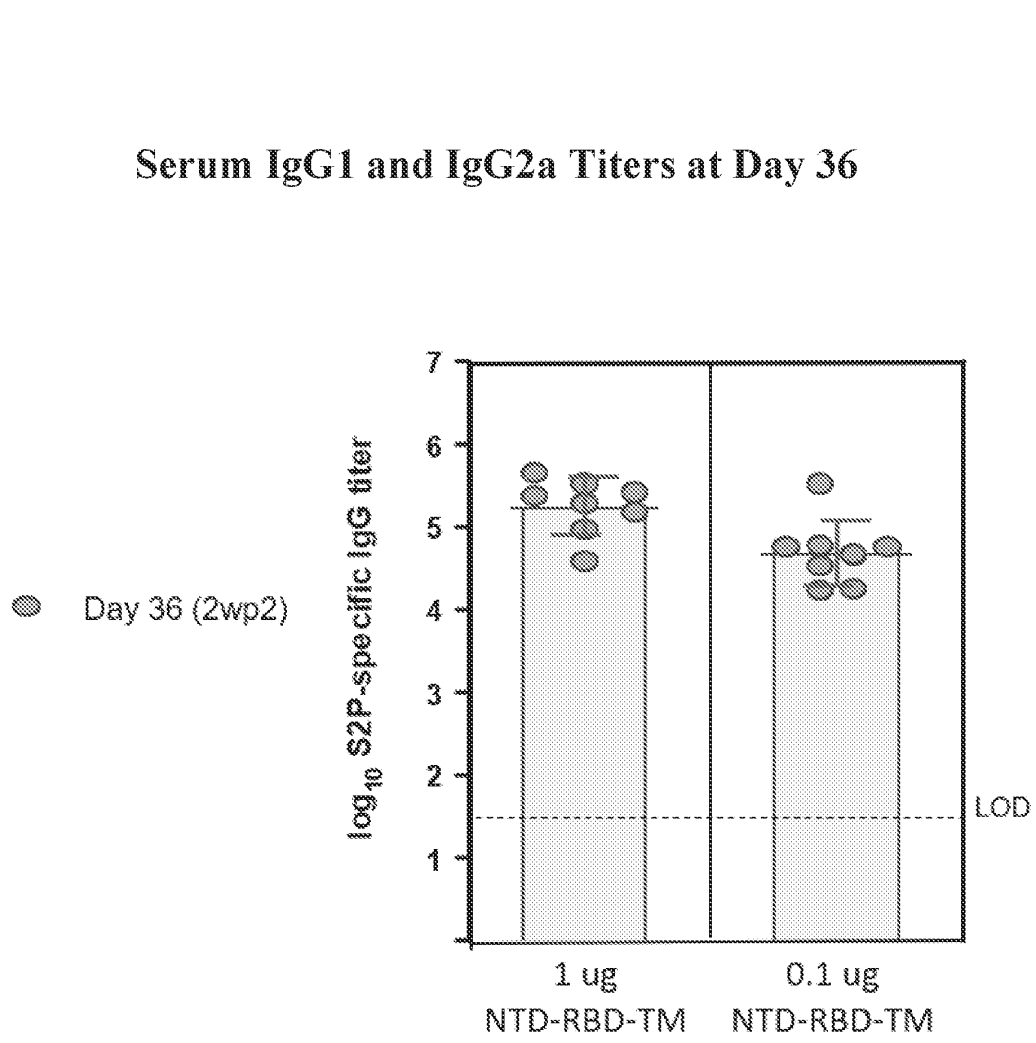

Serum IgG1 and IgG2a Titers at Day 36
Day 36 (2wp2)
log10 S2P-specific IgG titer
7
6
5
4
3
2
1
LOD
1 ug
NTD-RBD-TM
0.1 ug
NTD-RBD-TM

FIG. 8C