Figure 1

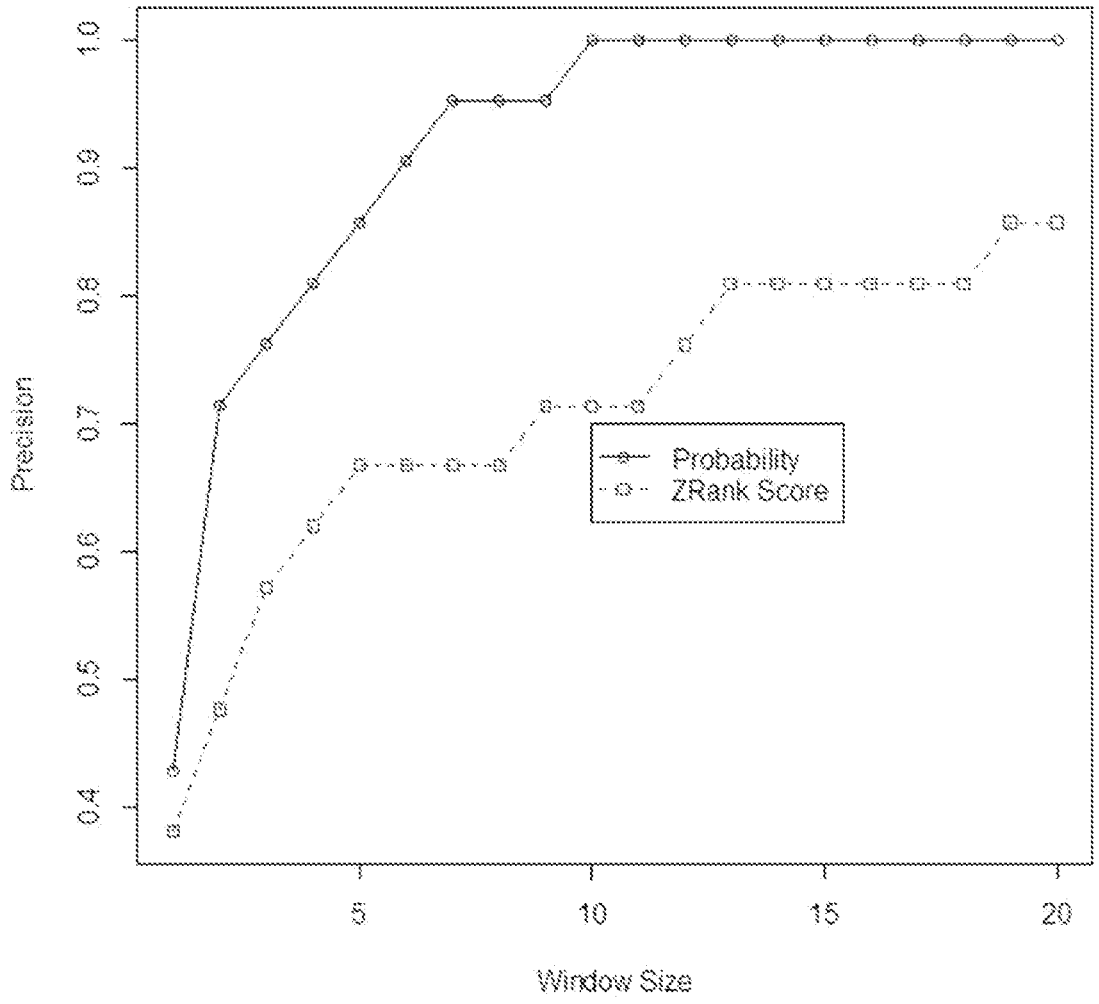

Precision
0.4
0.5
0.6
0.7
0.8
0.9
1.0
5
10
15
20
Window Size
Probability
ZRank Score

Figure 2

(A)

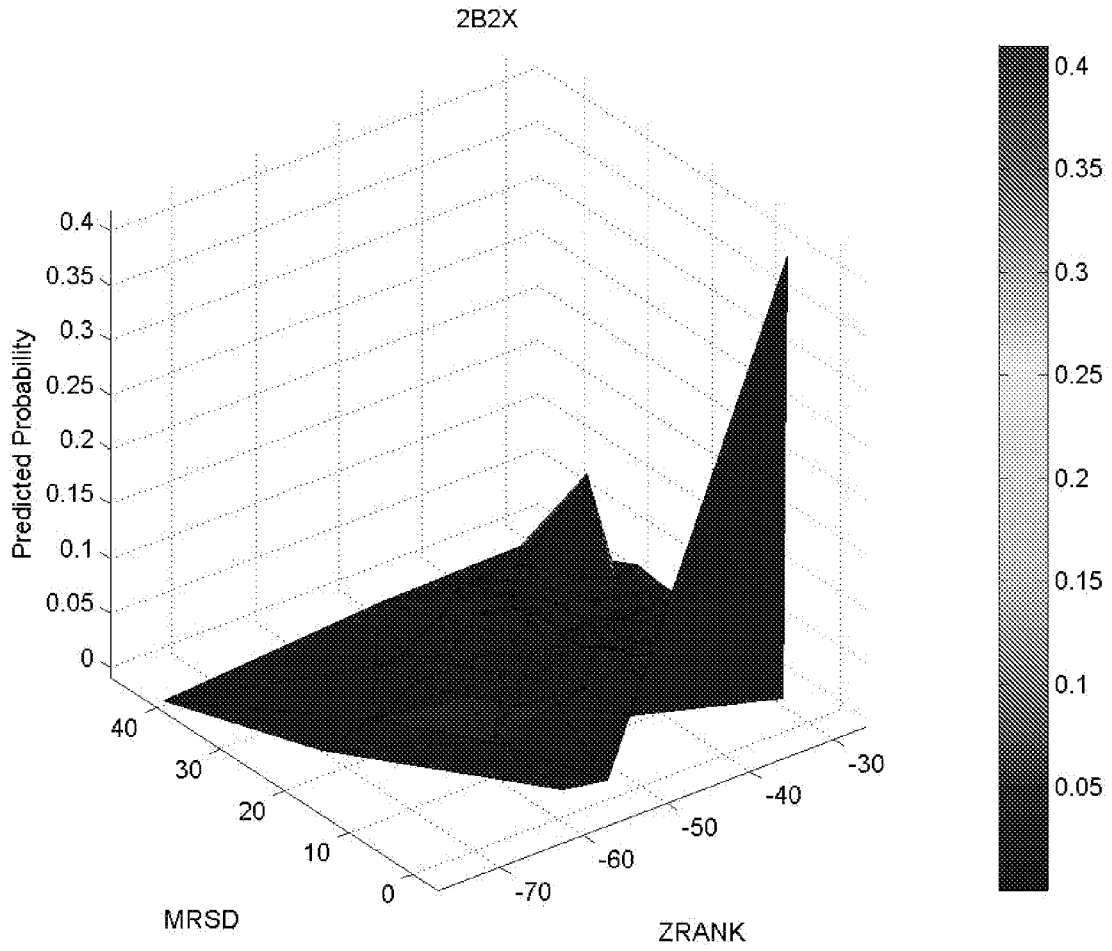

2B2X
Predicted Probability
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
40
30
20
10
0
MRSD
-30
-40
-50
-60
-70
ZRANK
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05

Figure 2

(B)

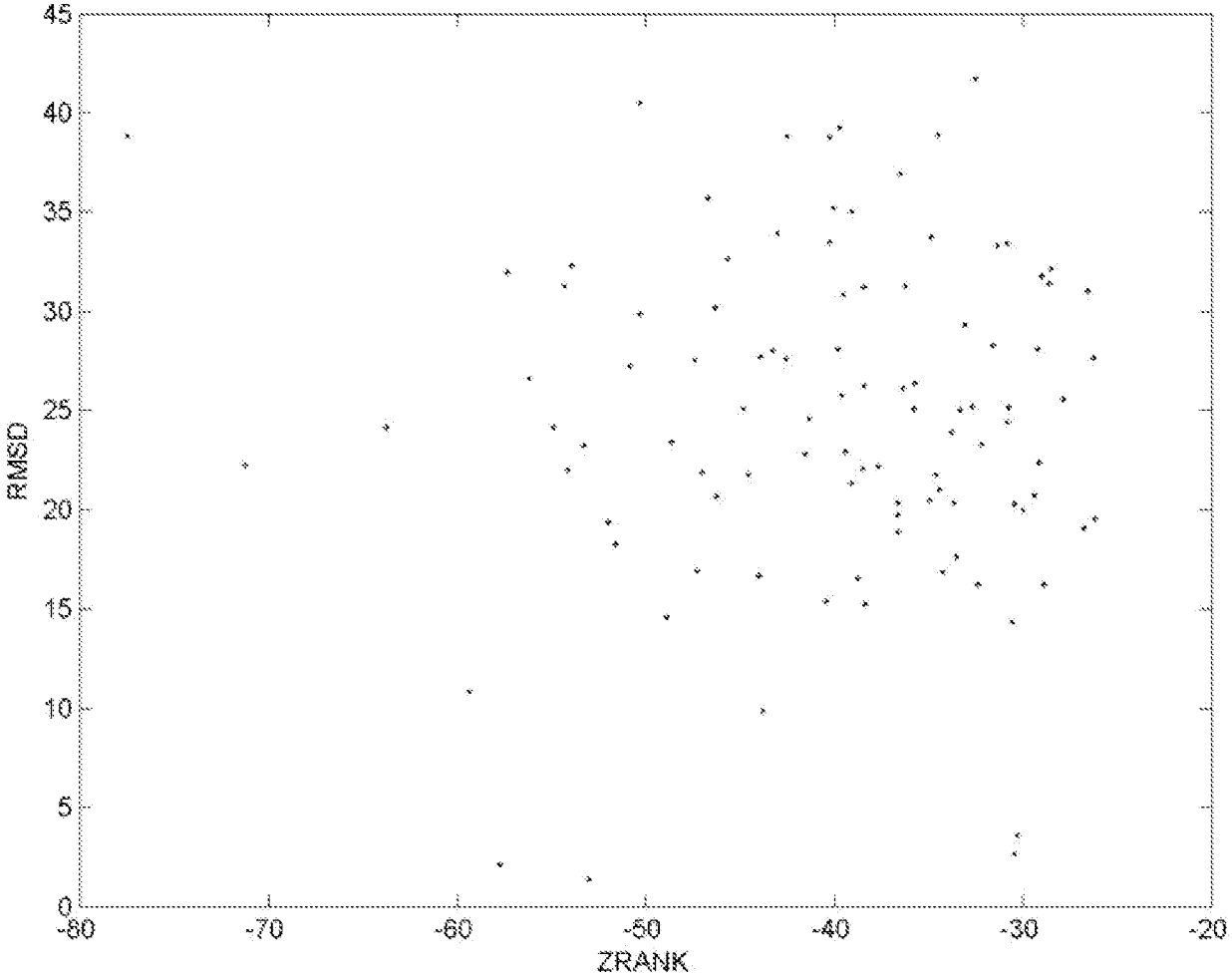


Figure 2

(C)

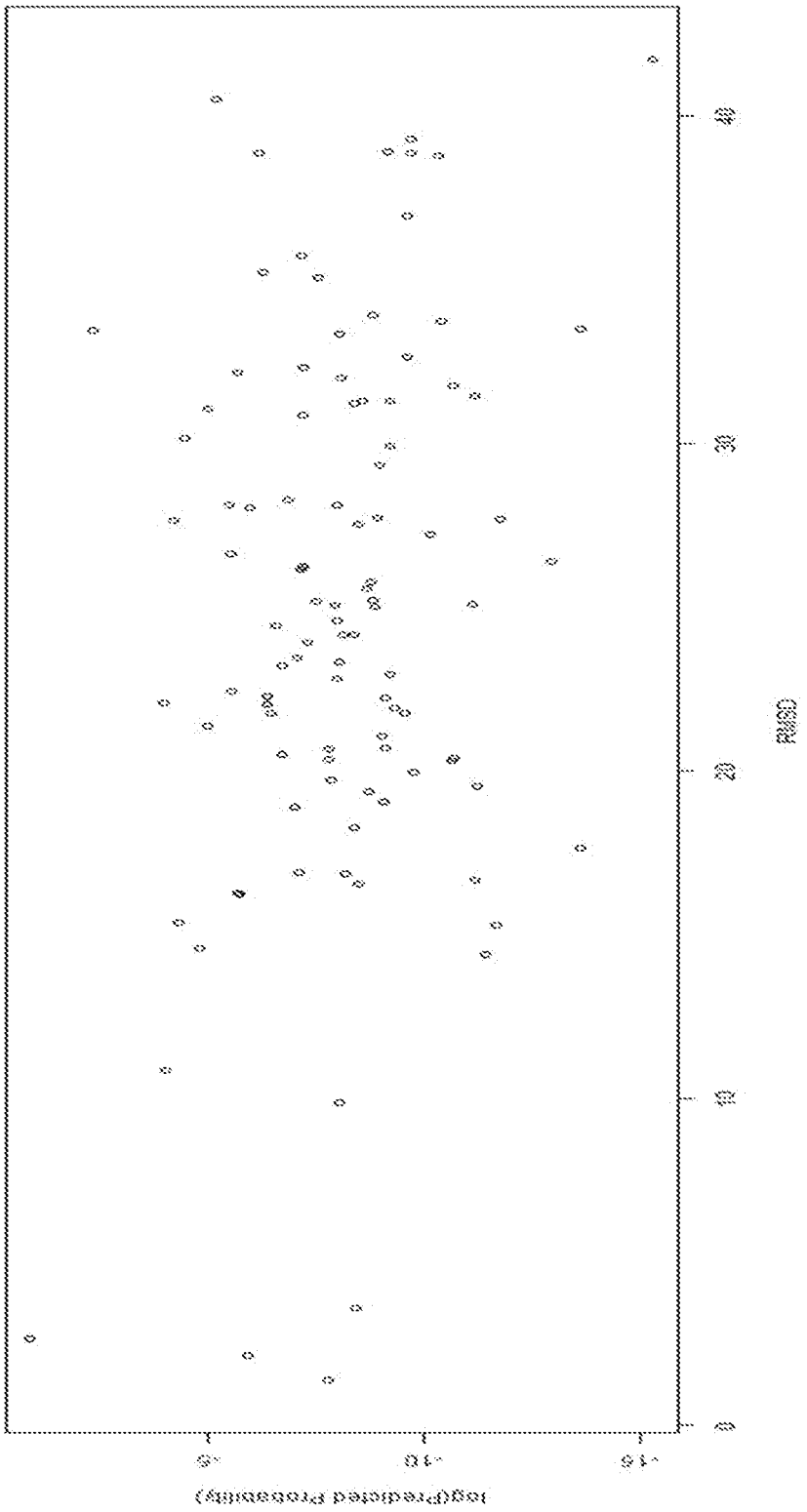
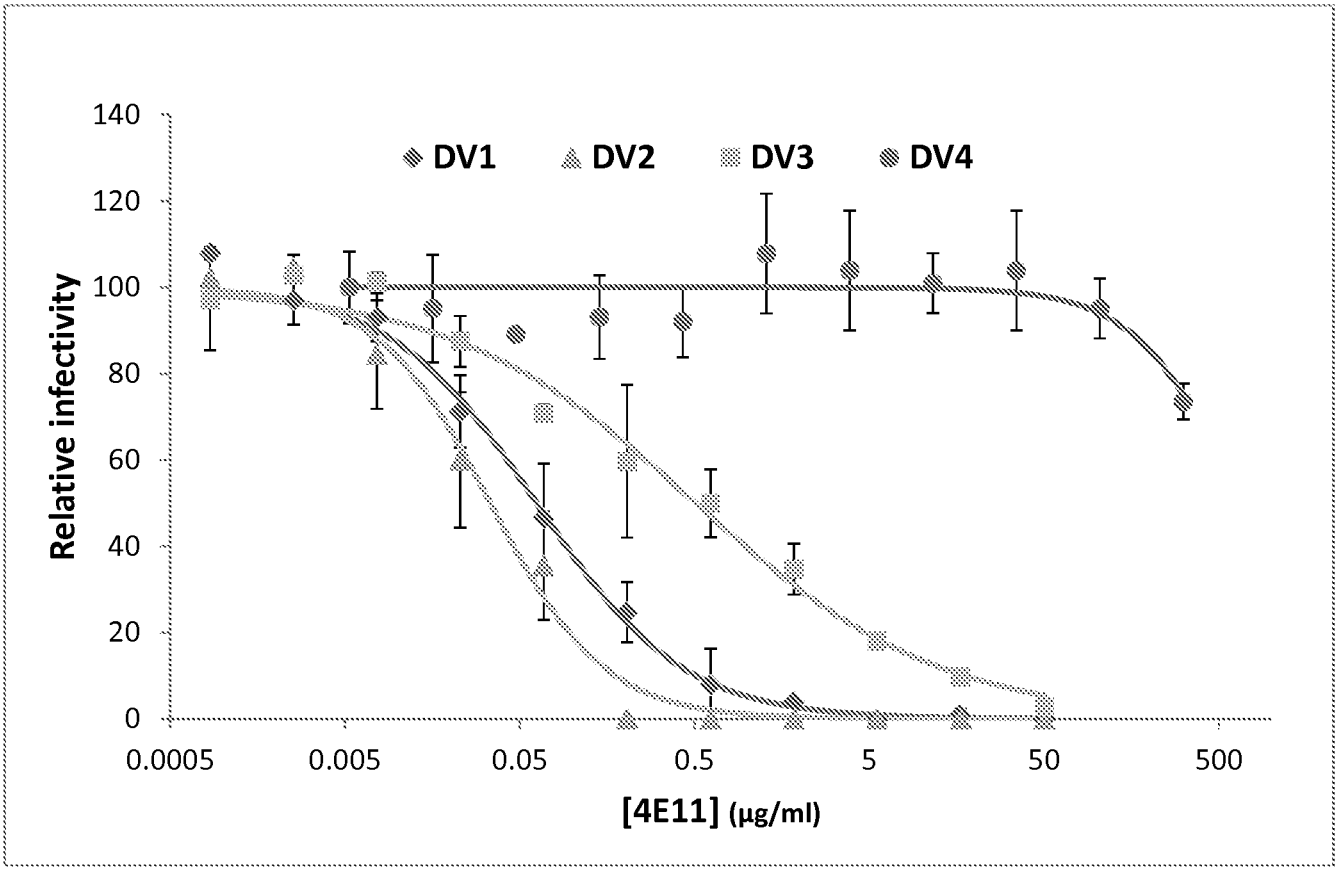


Figure 3



EDIII-DV1 K_D (nM)	EDIII-DV2 K_D (nM)	EDIII-DV3 K_D (nM)	EDIII-DV4 K_D (nM)
0.328	5.20	21.8	40,793

Figure 4

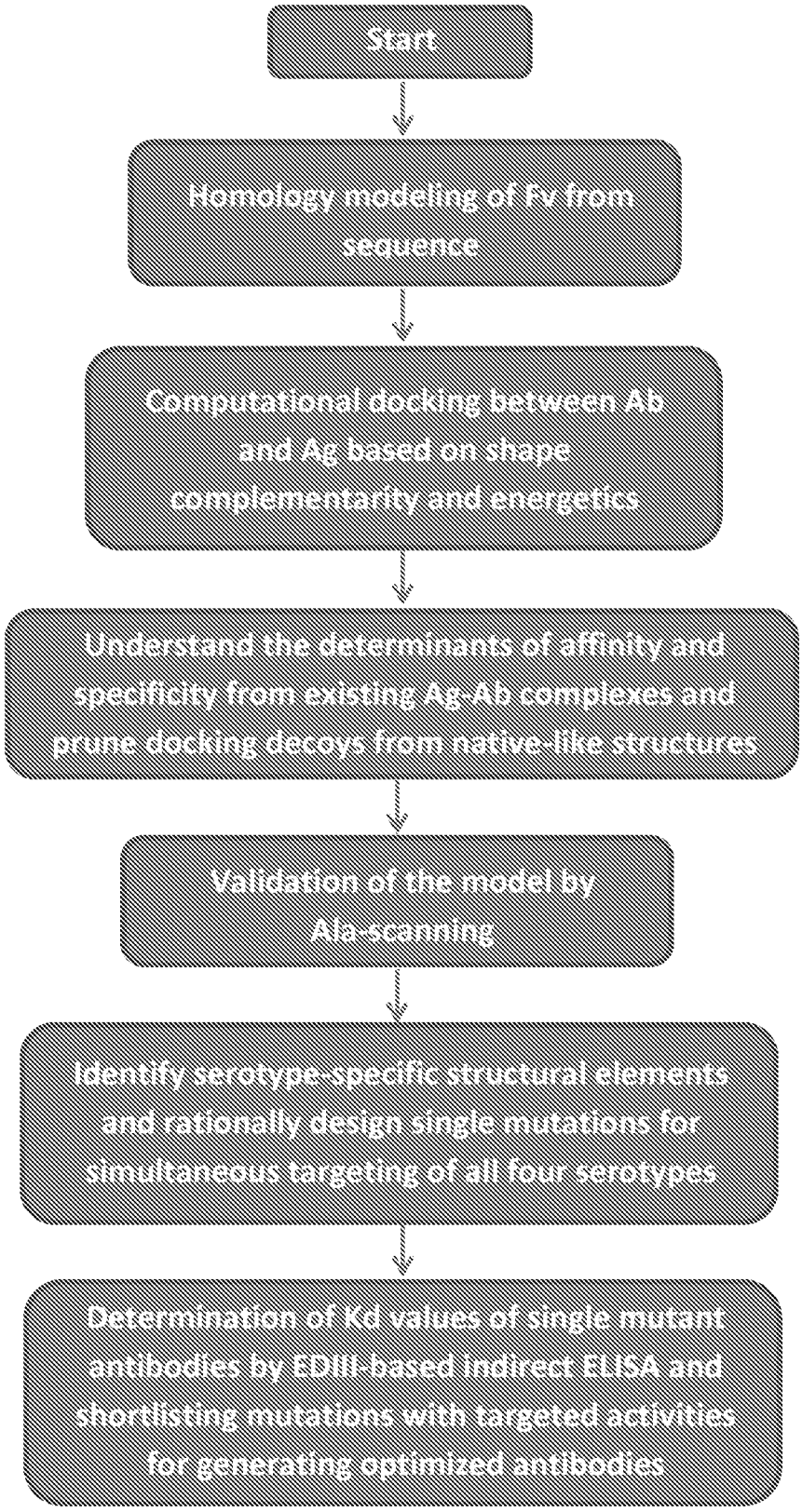

Start
Homology modeling of Fv from sequence
Computational docking between Ab and Ag based on shape complementarity and energetics
Understand the determinants of affinity and specificity from existing Ag-Ab complexes and prune docking decoys from native-like structures
Validation of the model by Ala-scanning
Identify serotype-specific structural elements and rationally design single mutations for simultaneous targeting of all four serotypes
Determination of Kd values of single mutant antibodies by EDIII-based Indirect ELISA and shortlisting mutations with targeted activities for generating optimized antibodies

Figure 5

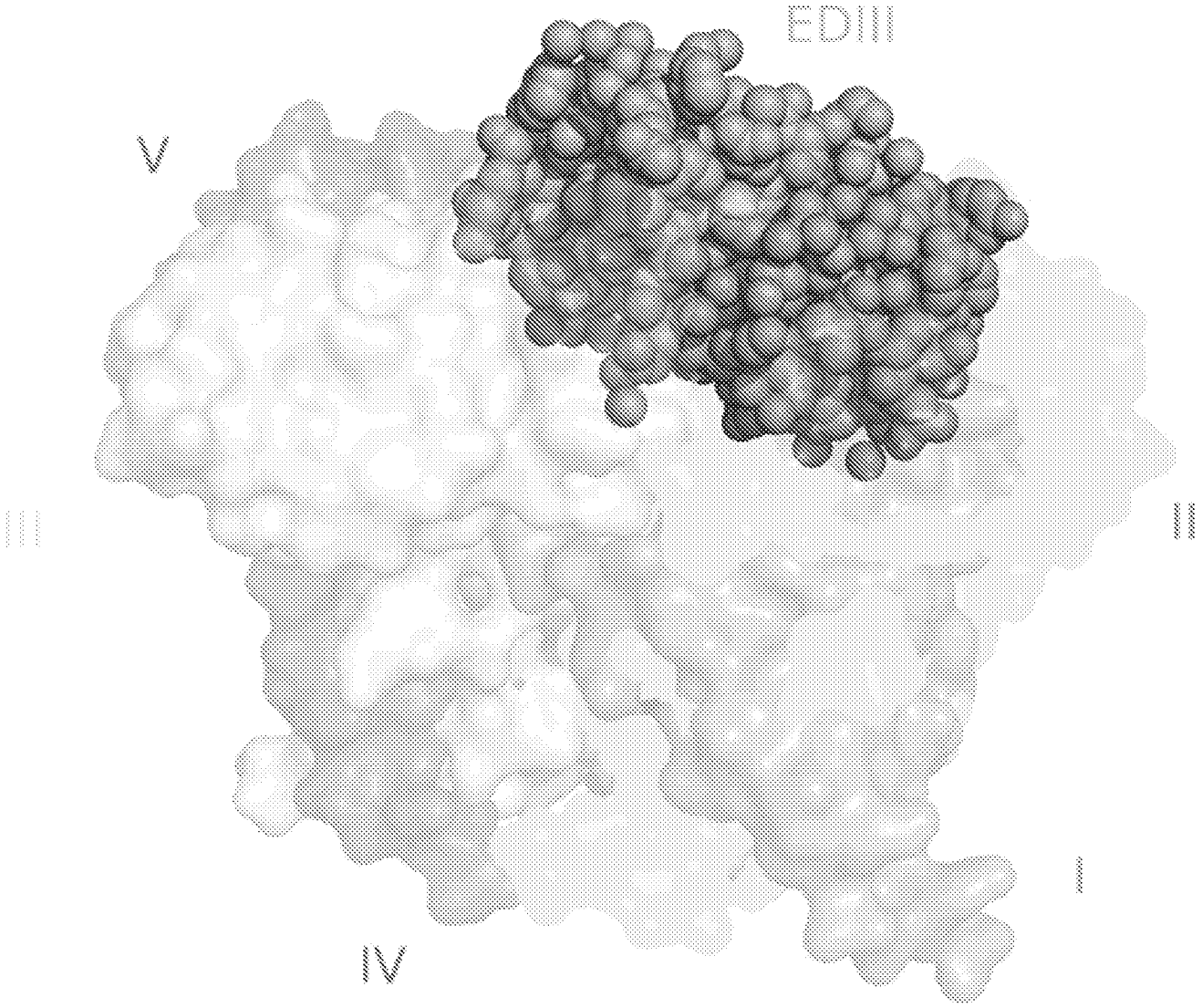


Figure 6

(A)

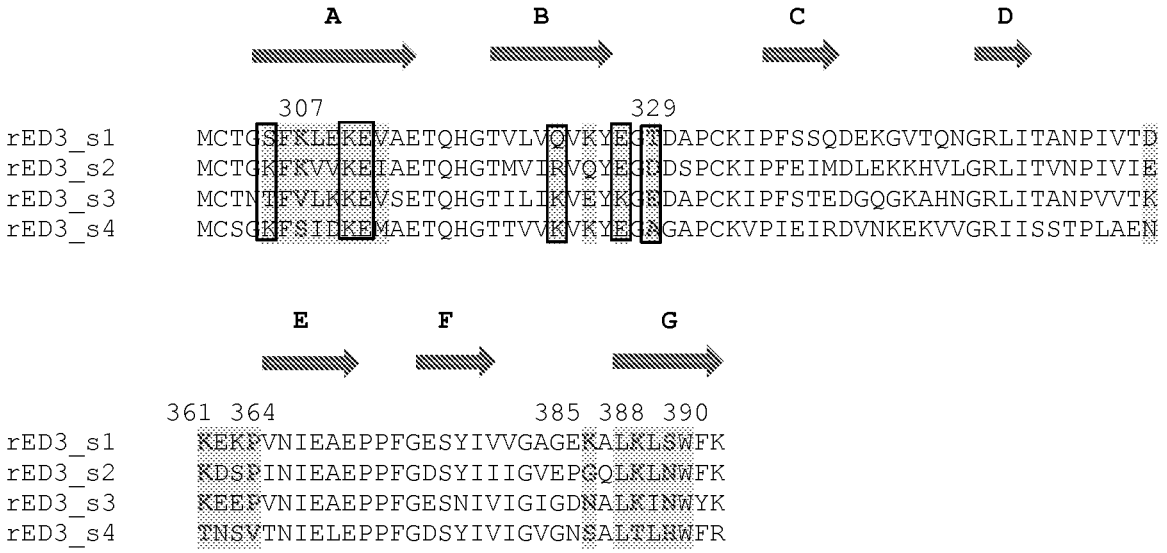

A
B
C
D
307
329
rED3_s1 MCTGSFKLEKEVAETQHGTVLVQVKYEGTDAPCKIPFSSQDEKGVTQNGRLITANPIVTD
rED3_s2 MCTGKFKVVKEIAETQHGTMVIRVQYEGDSPCKIPFEIMDLEKKHVLGRLITVNPIVIE
rED3_s3 MCTNTFVLKKEVSETQHGTILIKVEYKGEDAPCKIPFSTEDGQGKAHNGRLITANPVVTK
rED3_s4 MCSGKFSIKKEMAETQHGTTVVKVKYEGNGAPCKVPIEIRDVNKEKVVGRIISSTPLAEN
E
F
G
361 364
385 388 390
rED3_s1 KEKPVNIEAEPPFGESYIVVGAGEKALKLSWFK
rED3_s2 KDSPINIEAEPPFGDSYIIIGVEPGQLKLNWFK
rED3_s3 KEEPVNIEAEPPFGESNIVIGIGDNALKINWYK
rED3_s4 TNSVTNIELEPPFGDSYIVIGVGNSALTLNWFR

Figure 6

(B)

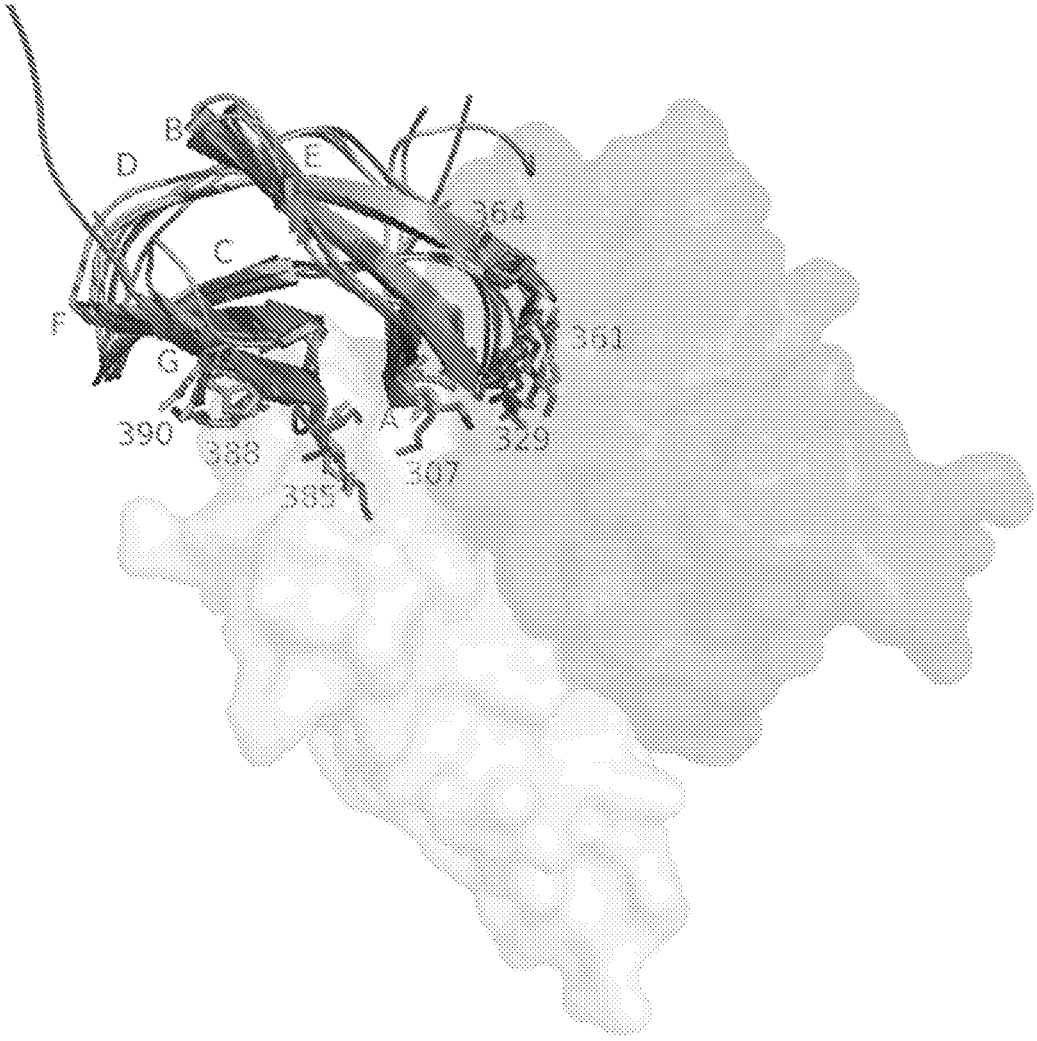


Figure 7

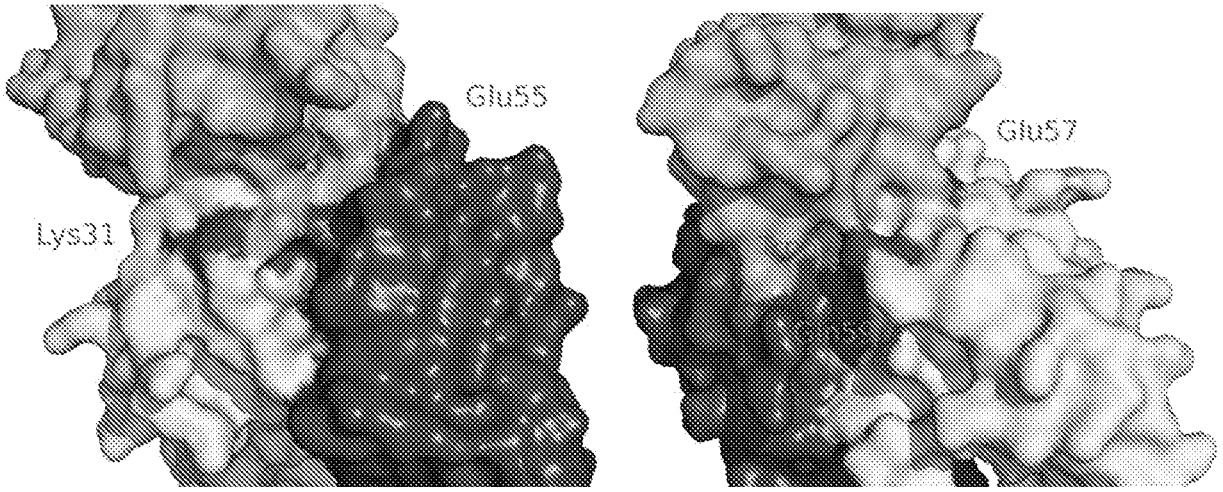


Figure 8

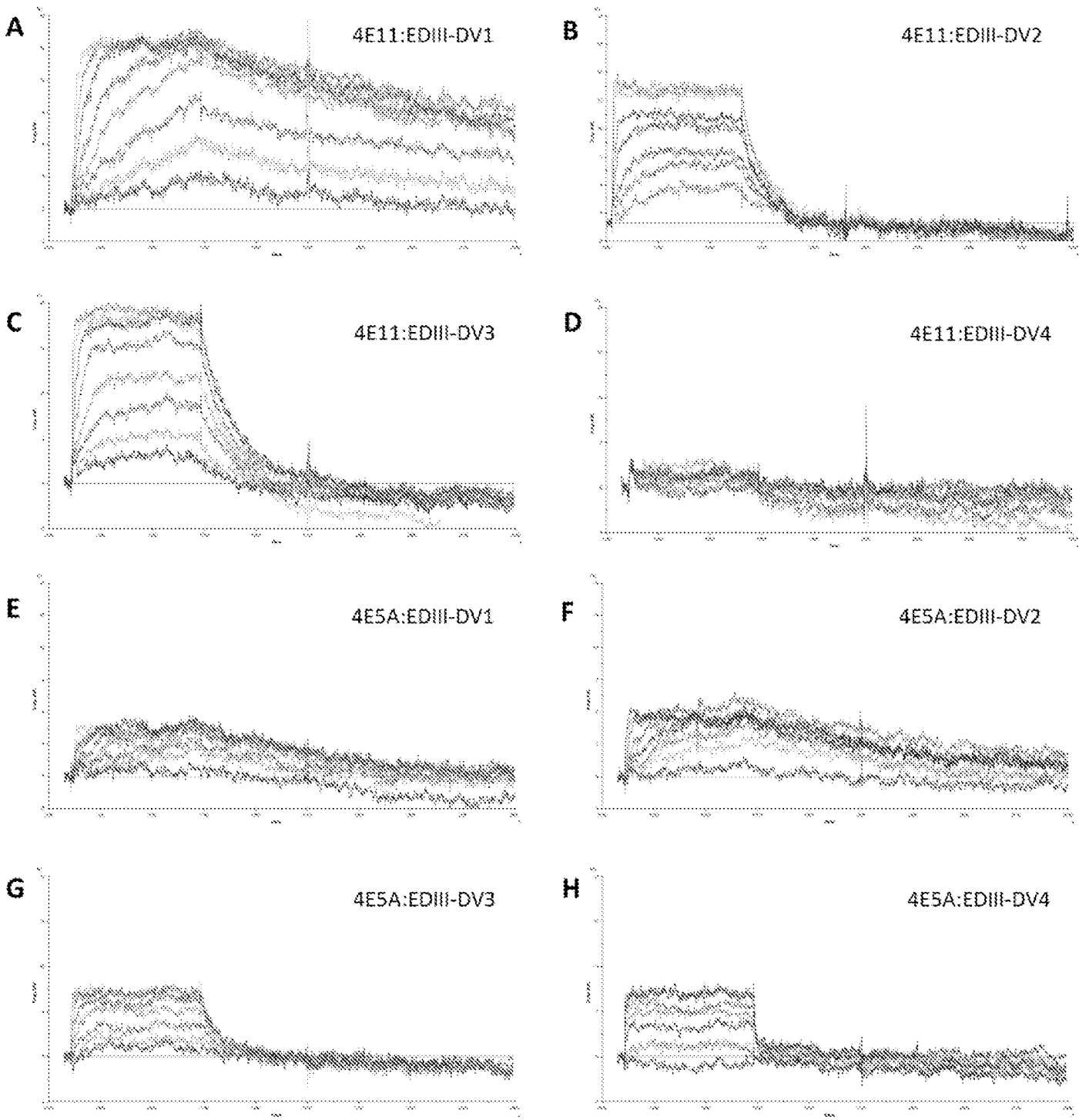
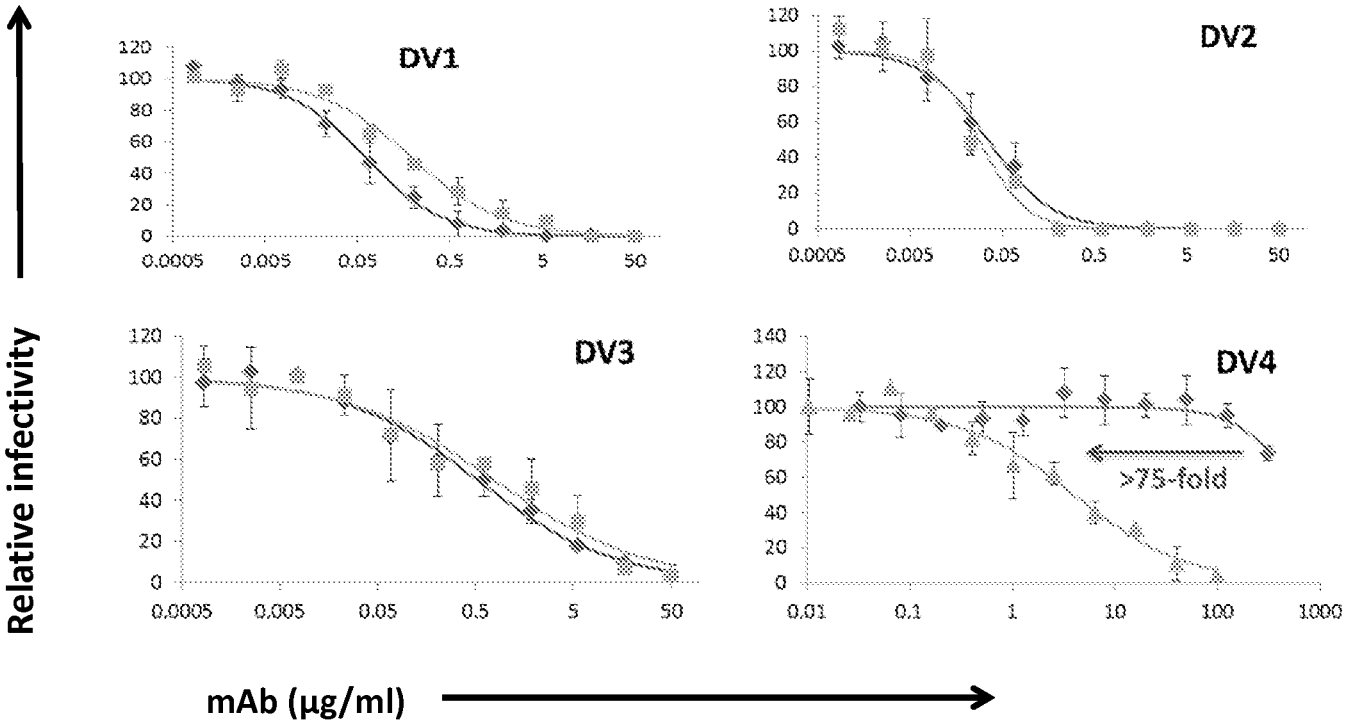

A
4E11:EDIII-DV1
B
4E11:EDIII-DV2
C
4E11:EDIII-DV3
D
4E11:EDIII-DV4
E
4E5A:EDIII-DV1
F
4E5A:EDIII-DV2
G
4E5A:EDIII-DV3
H
4E5A:EDIII-DV4

Figure 9



mAb	DV1 EC50 (µg/ml)	DV2 EC50 (µg/ml)	DV3 EC50 (µg/ml)	DV4 EC50 (µg/ml)
4e11 WT	0.062	0.034	0.52	>300
4e11-5A	0.19	0.028	0.77	4.0

Figure 10

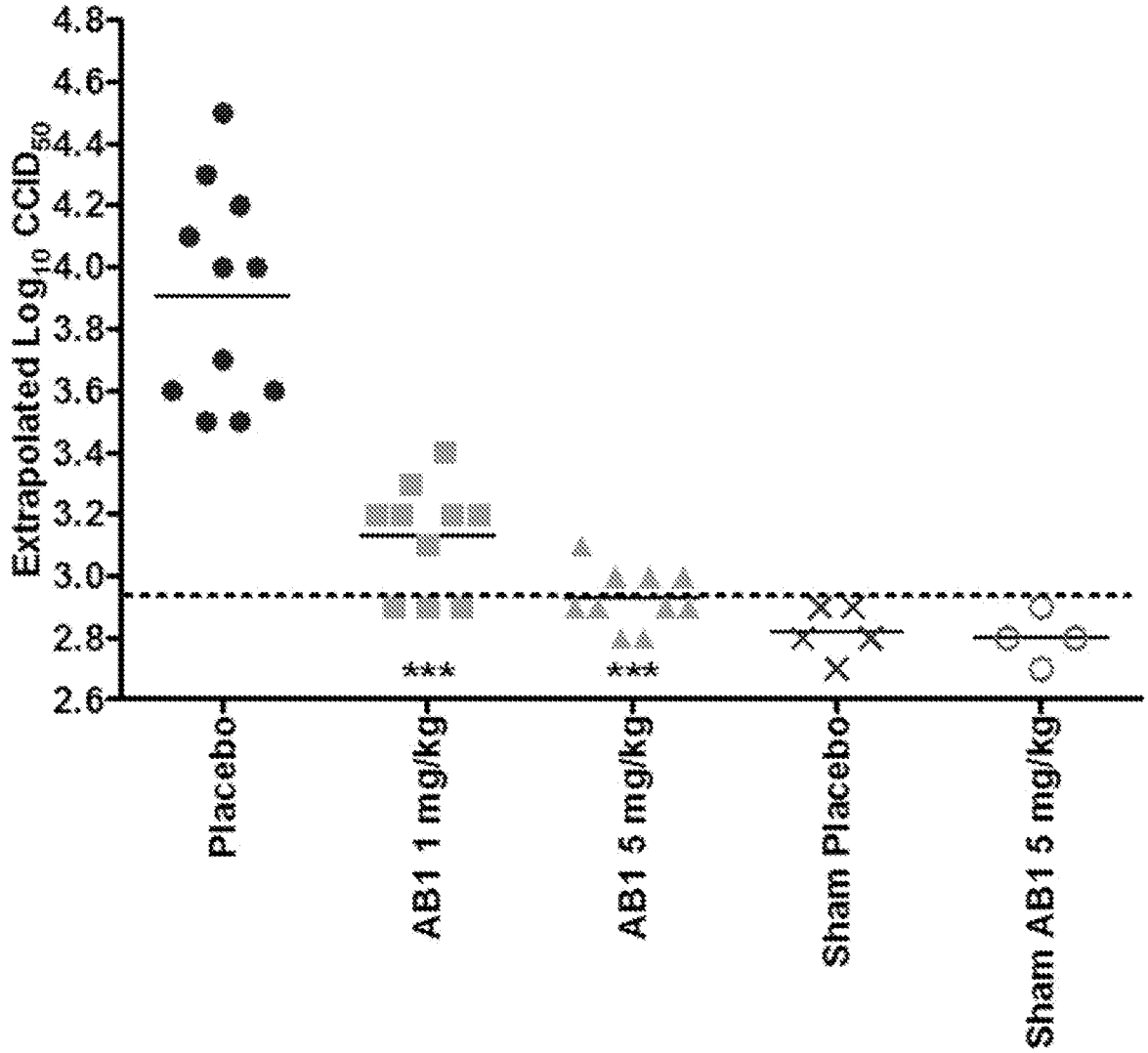
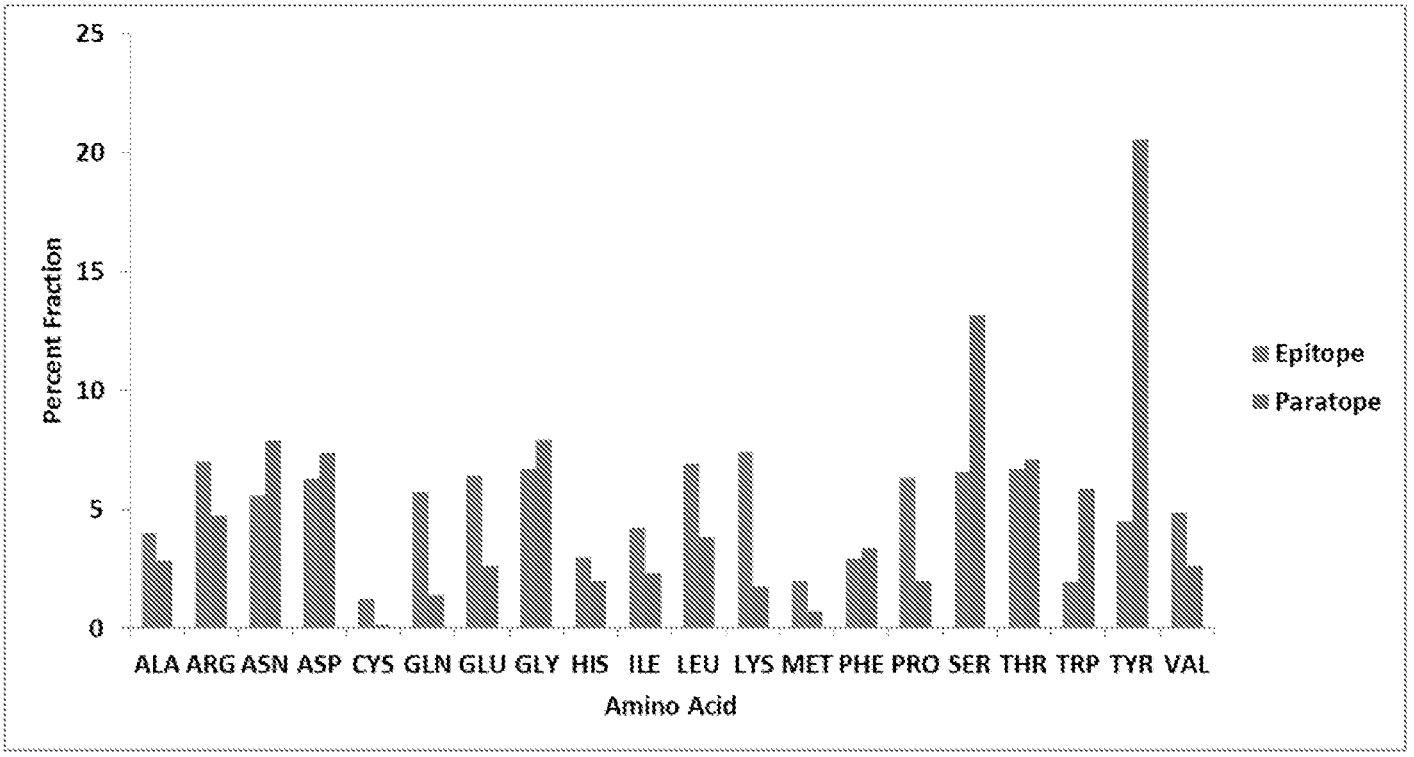

Extrapolated Log10 CCID50
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
***
***
Placebo
AB1 1 mg/kg
AB1 5 mg/kg
Sham Placebo
Sham AB1 5 mg/kg

Figure 11


25
20
15
10
5
0
Percent Fraction
ALA ARG ASN ASP CYS GLN GLU GLY HIS ILE LEU LYS MET PHE PRO SER THR TRP TYR VAL
Amino Acid
Epitope
Paratope