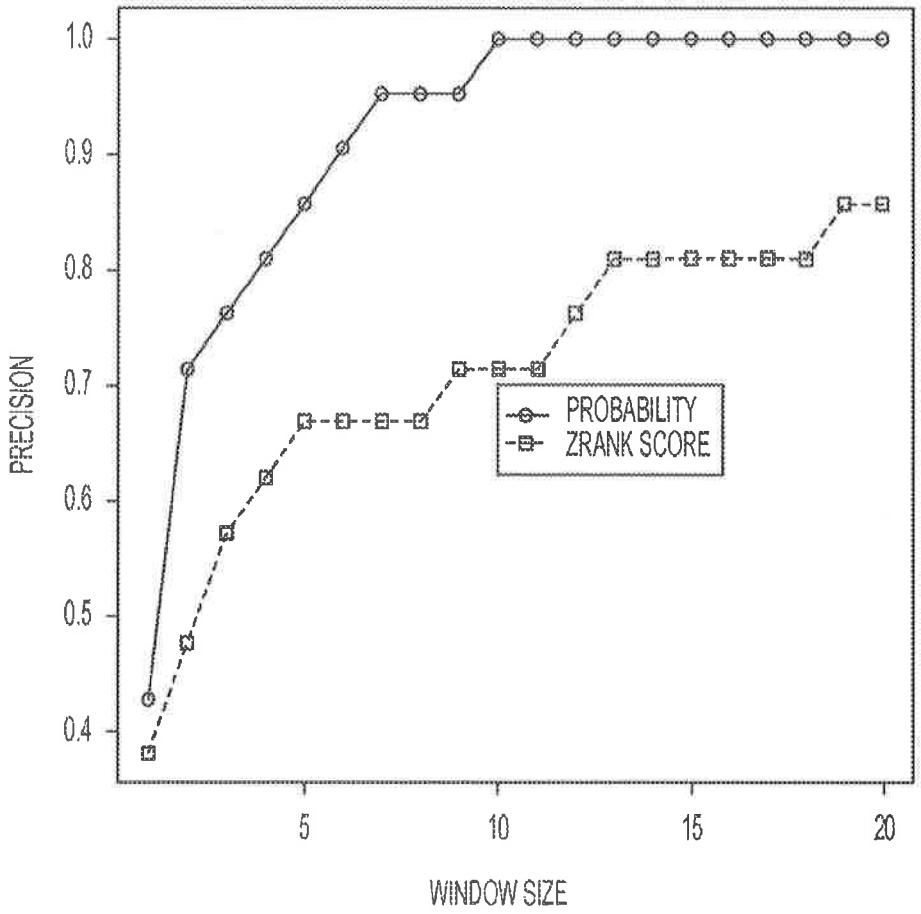

1.0
0.9
0.8
0.7
0.6
0.5
0.4
PRECISION
5
10
15
20
WINDOW SIZE
PROBABILITY
ZRANK SCORE

FIG. 1

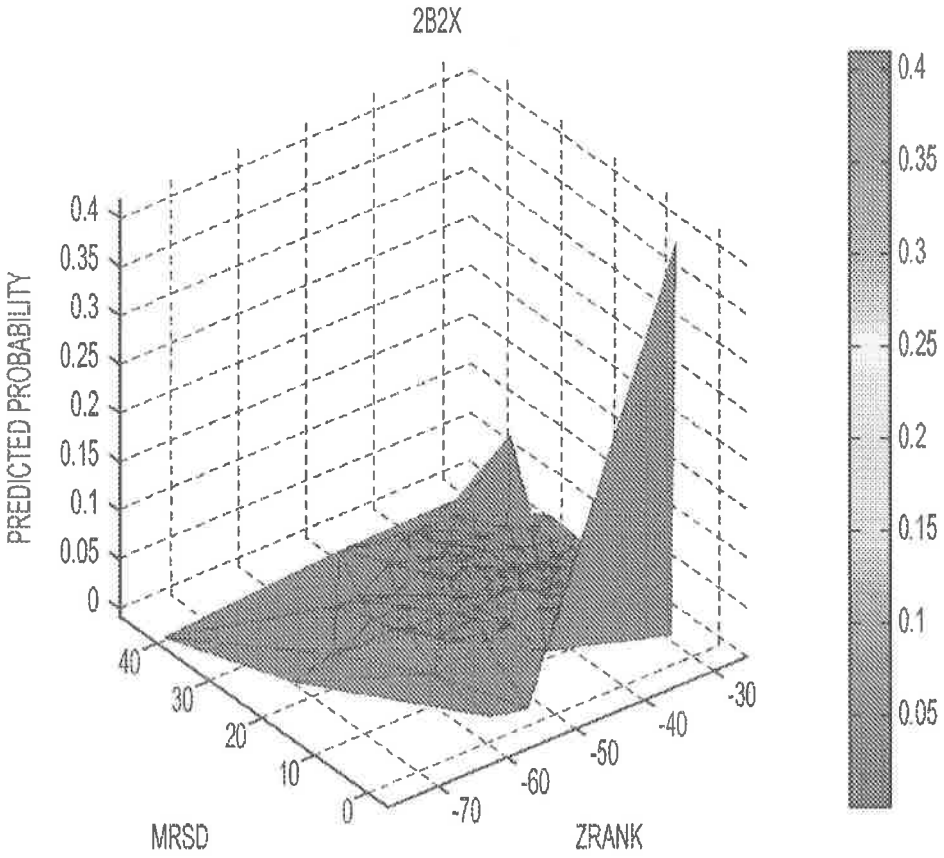

2B2X
PREDICTED PROBABILITY
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
40
30
20
10
0
MRSD
-70
-60
-50
-40
-30
ZRANK
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05

FIG. 2A

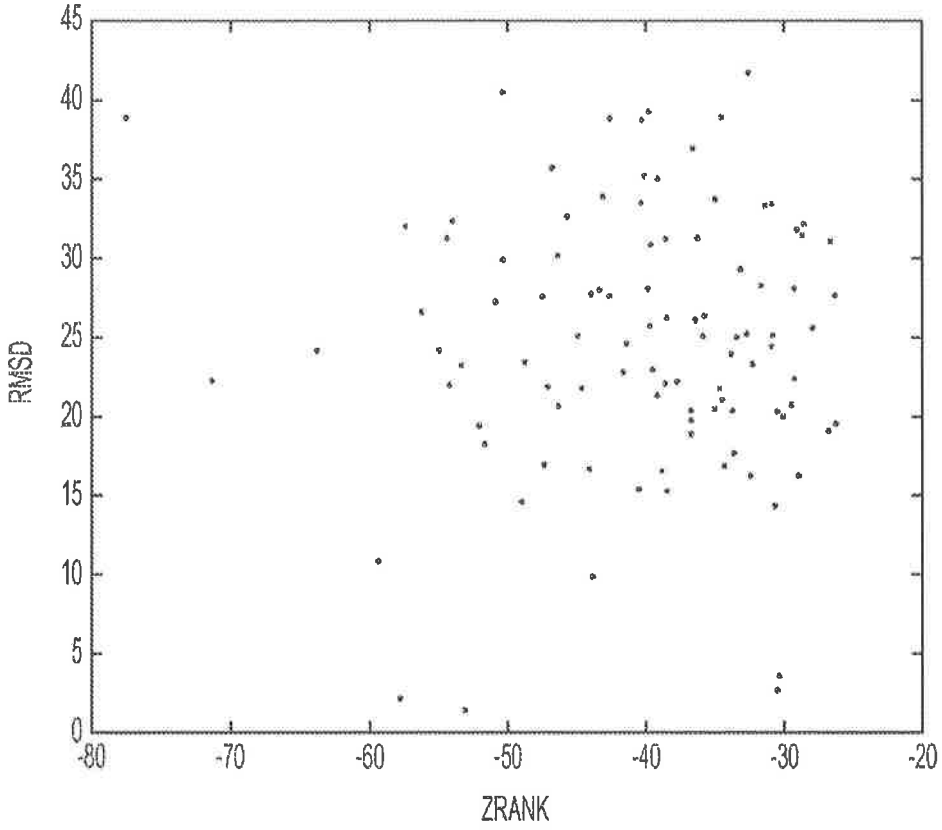


FIG. 2B

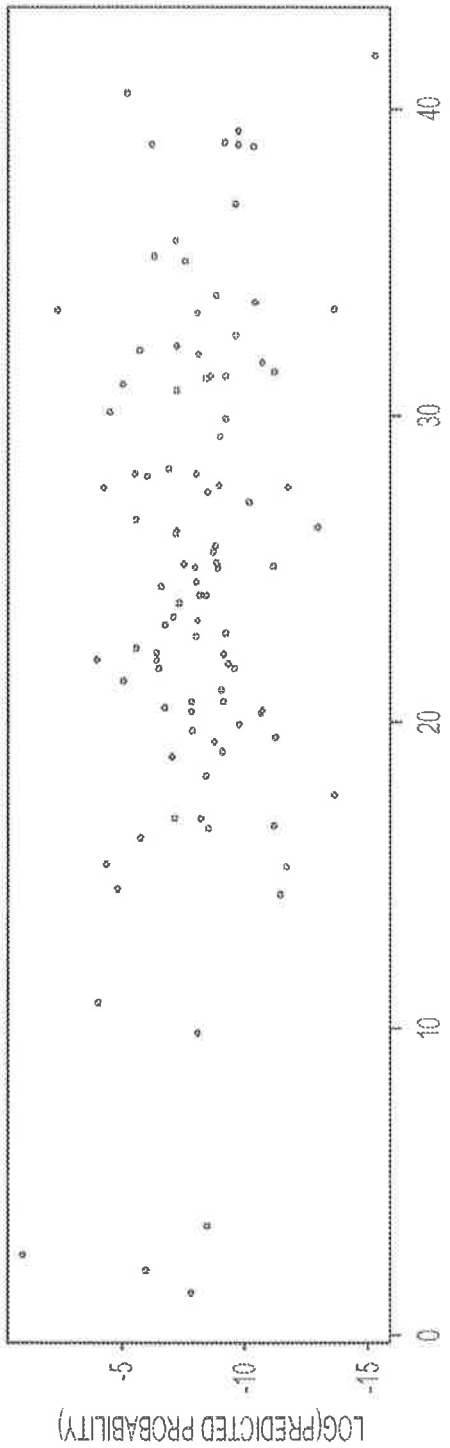
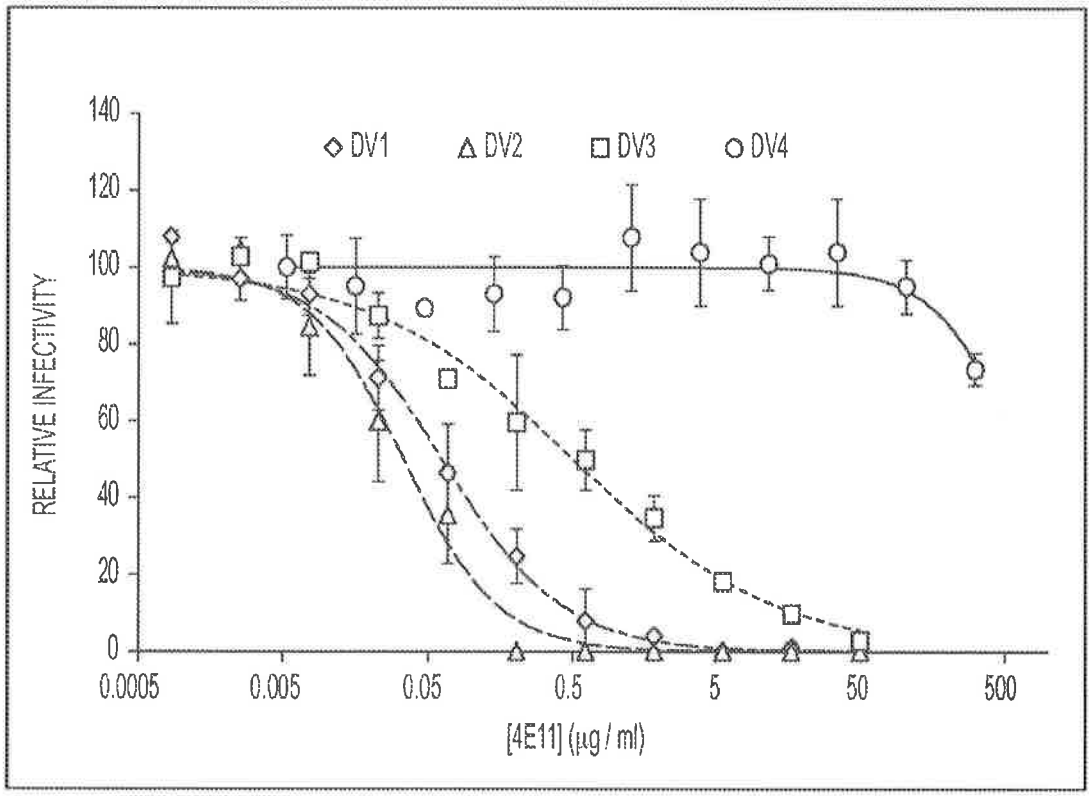


FIG. 2C



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

FIG. 3

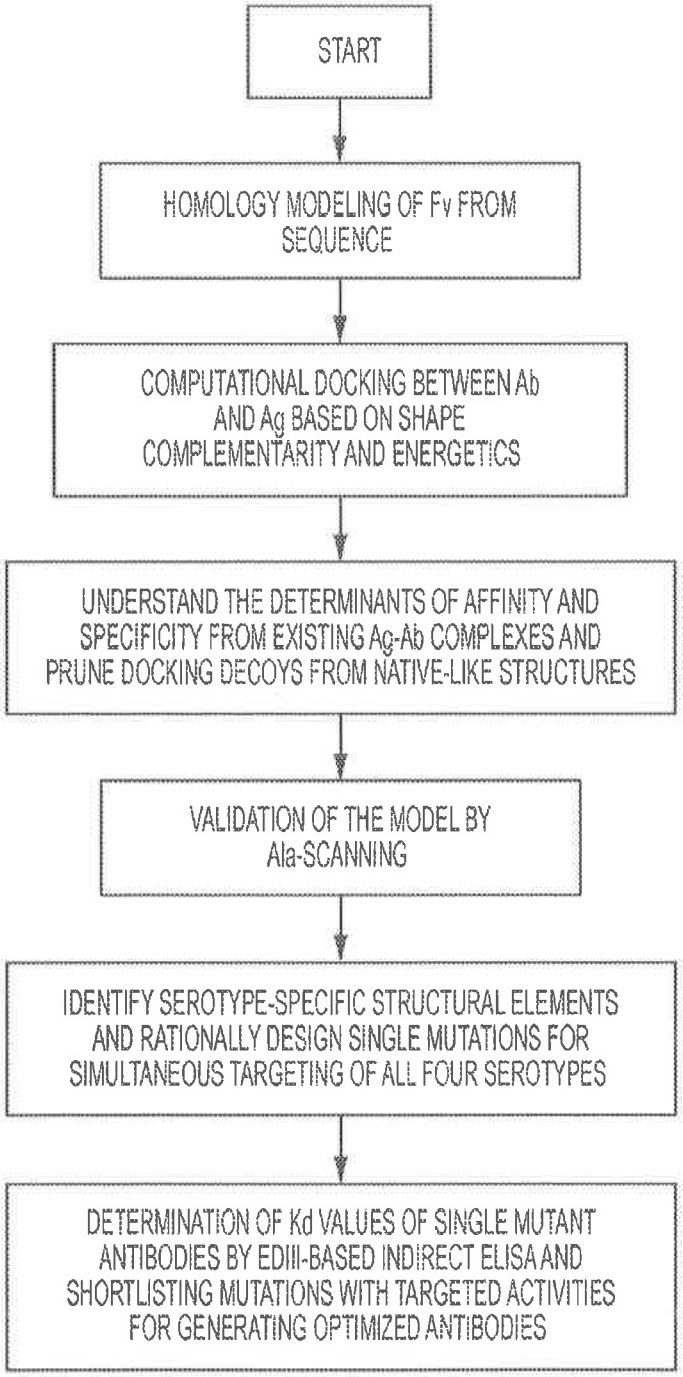

START
HOMOLOGY MODELING OF Fv FROM SEQUENCE
COMPUTATIONAL DOCKING BETWEEN Ab AND Ag BASED ON SHAPE COMPLEMENTARITY AND ENERGETICS
UNDERSTAND THE DETERMINANTS OF AFFINITY AND SPECIFICITY FROM EXISTING Ag-Ab COMPLEXES AND PRUNE DOCKING DECOYS FROM NATIVE-LIKE STRUCTURES
VALIDATION OF THE MODEL BY Ala-SCANNING
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

FIG. 4

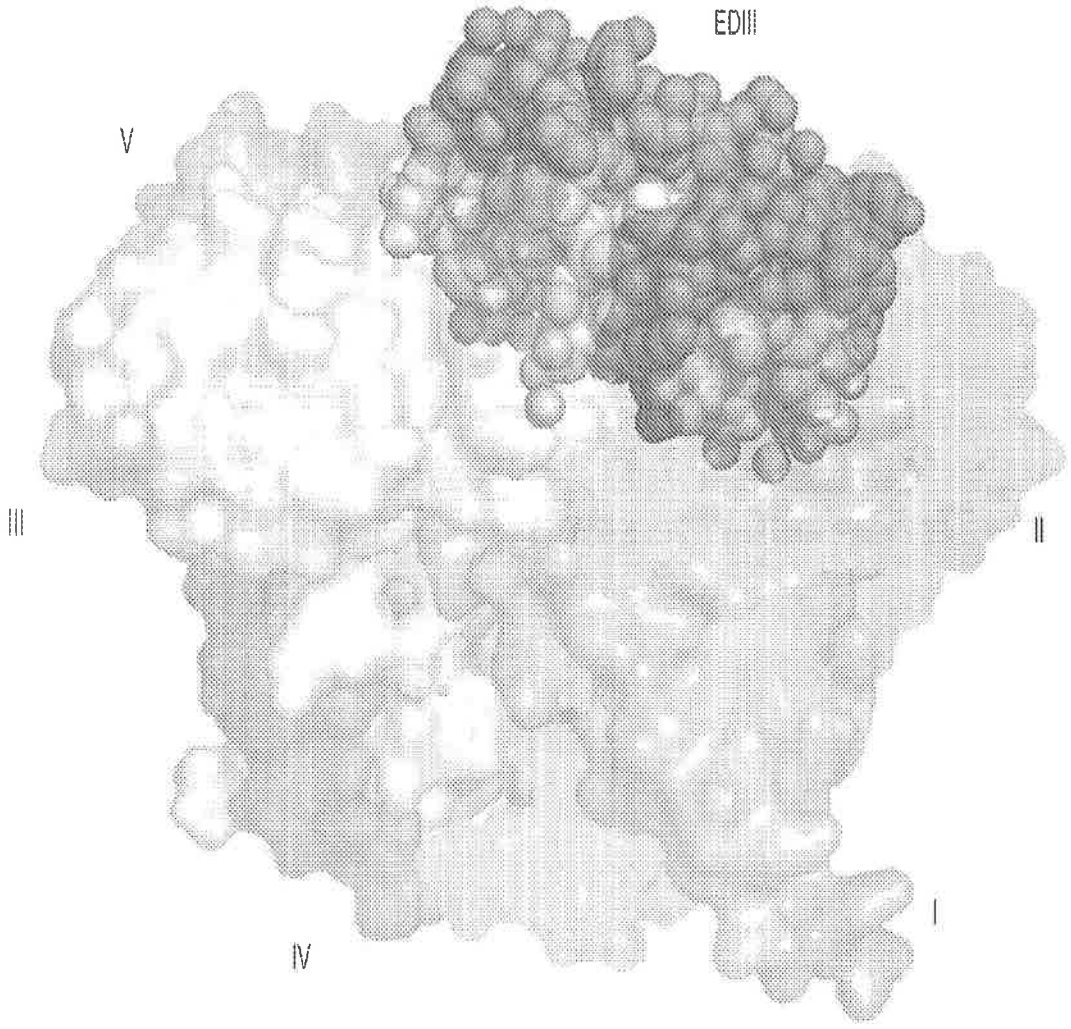


FIG. 5

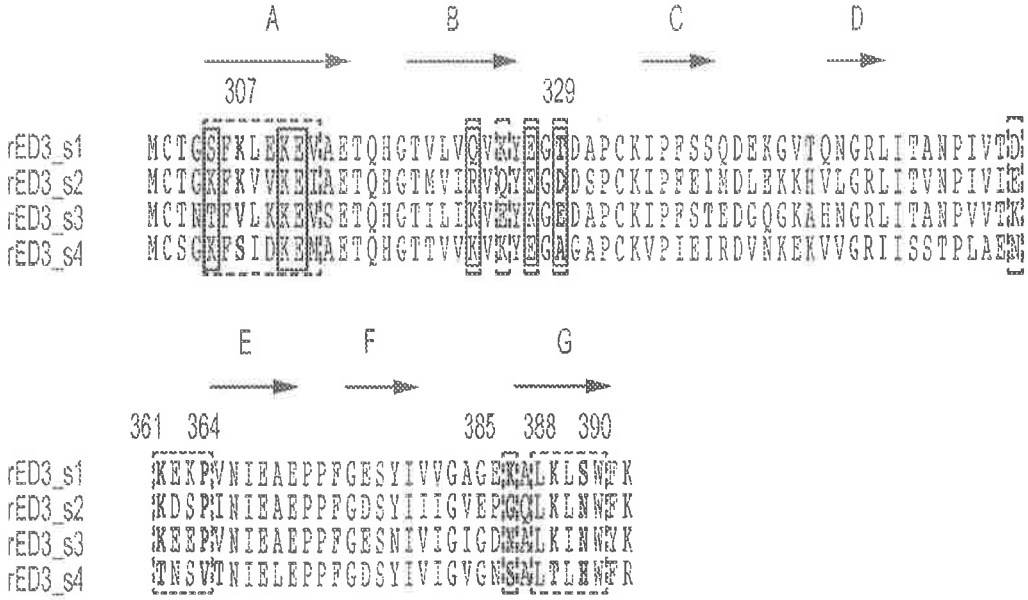

A
B
C
D
307
329
rED3_s1
rED3_s2
rED3_s3
rED3_s4
E
F
G
361 364
385 388 390
rED3_s1
rED3_s2
rED3_s3
rED3_s4

FIG. 6A

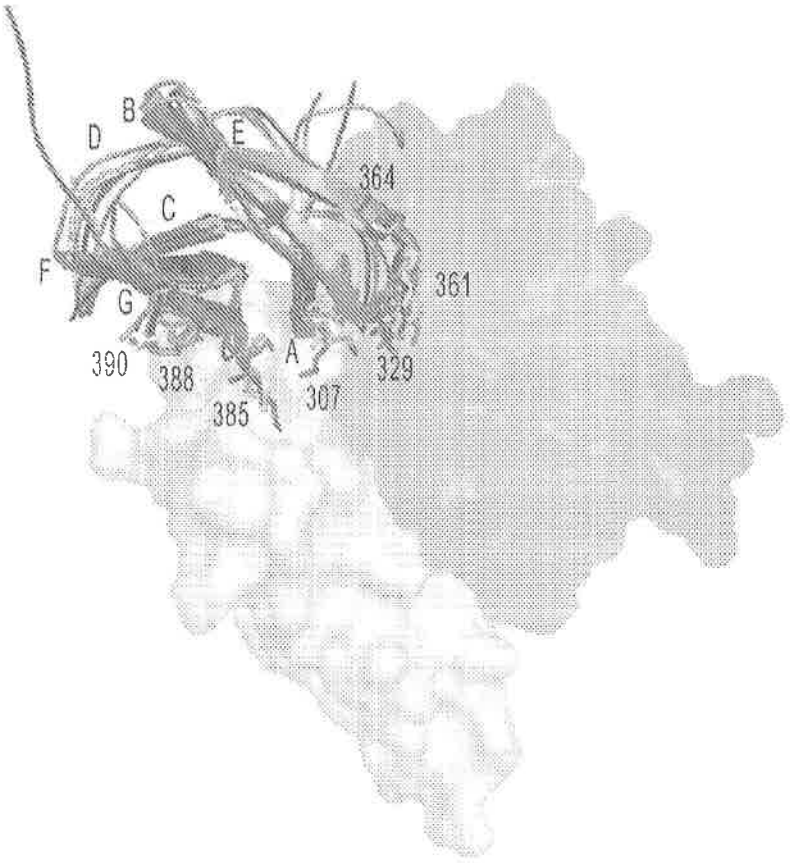

B
D
E
364
C
F
361
G
390
388
A
329
385
307

FIG. 6B

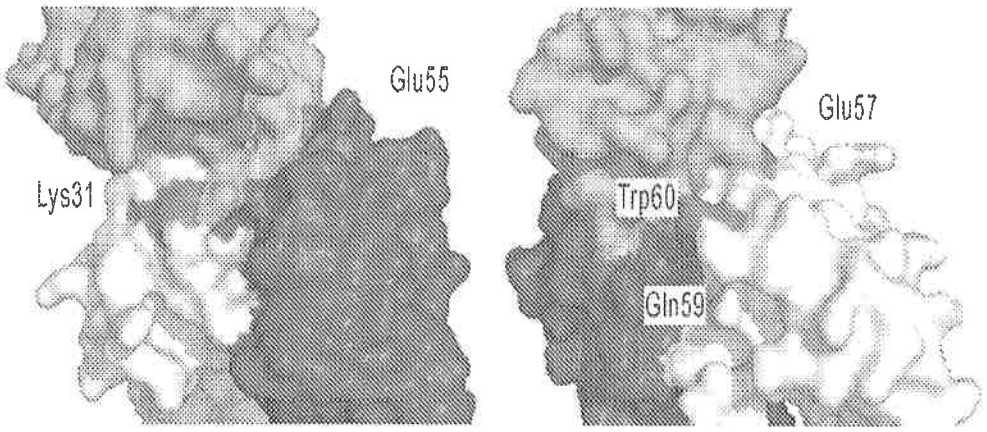


FIG. 7

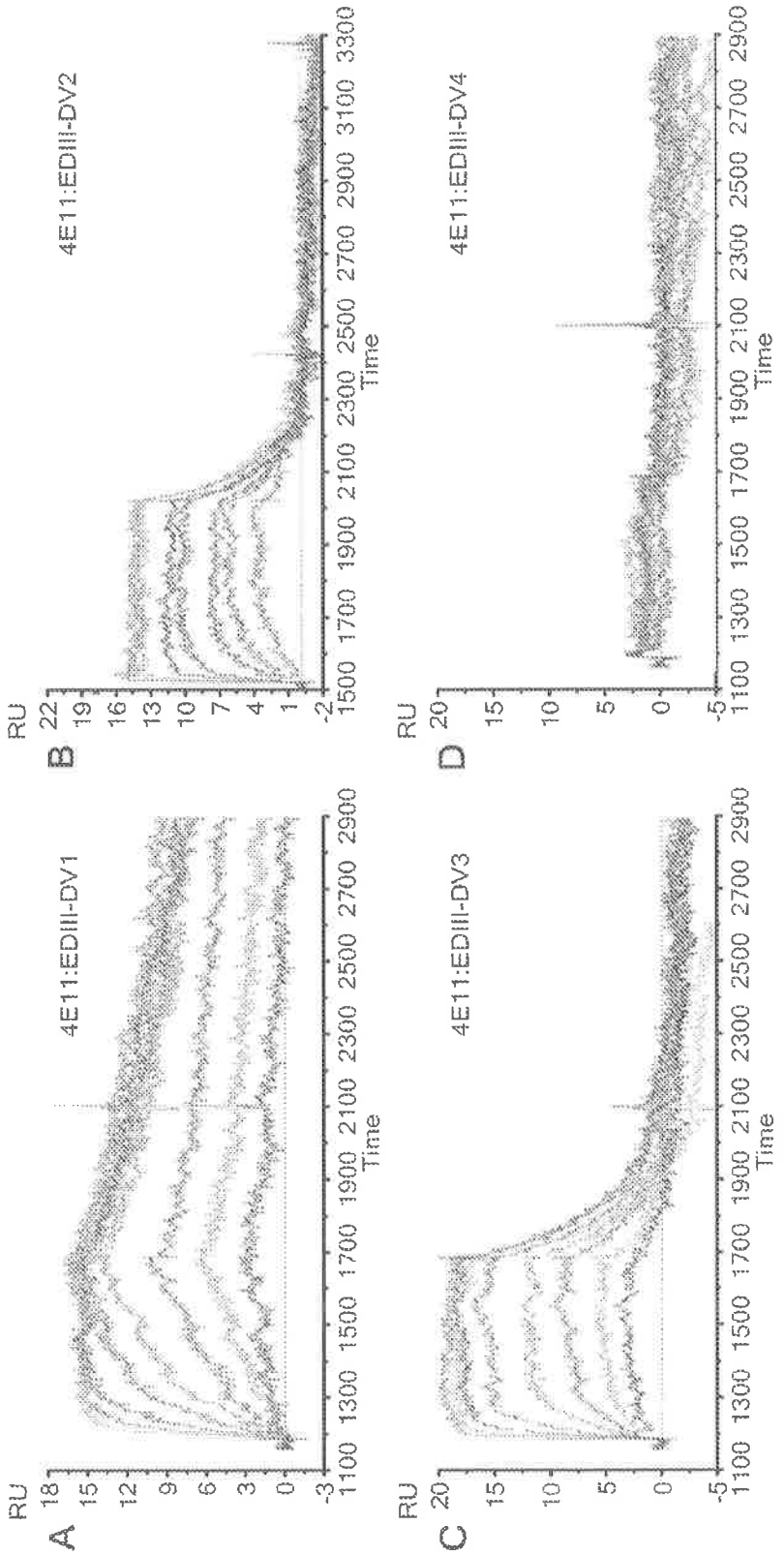

A
4E11:EDIII-DV1
RU
Time
B
4E11:EDIII-DV2
RU
Time
C
4E11:EDIII-DV3
RU
Time
D
4E11:EDIII-DV4
RU
Time

FIG. 8A-D

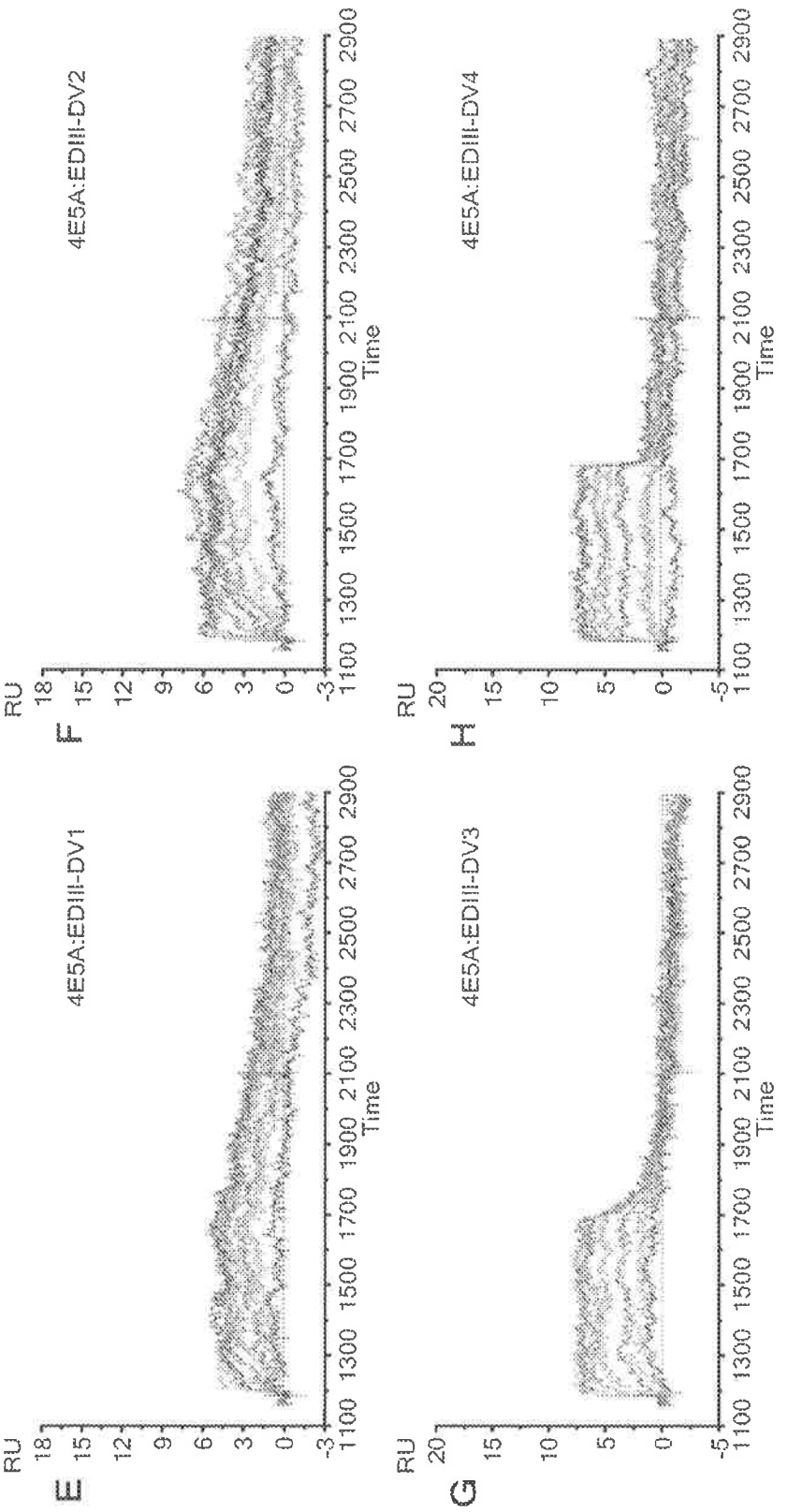
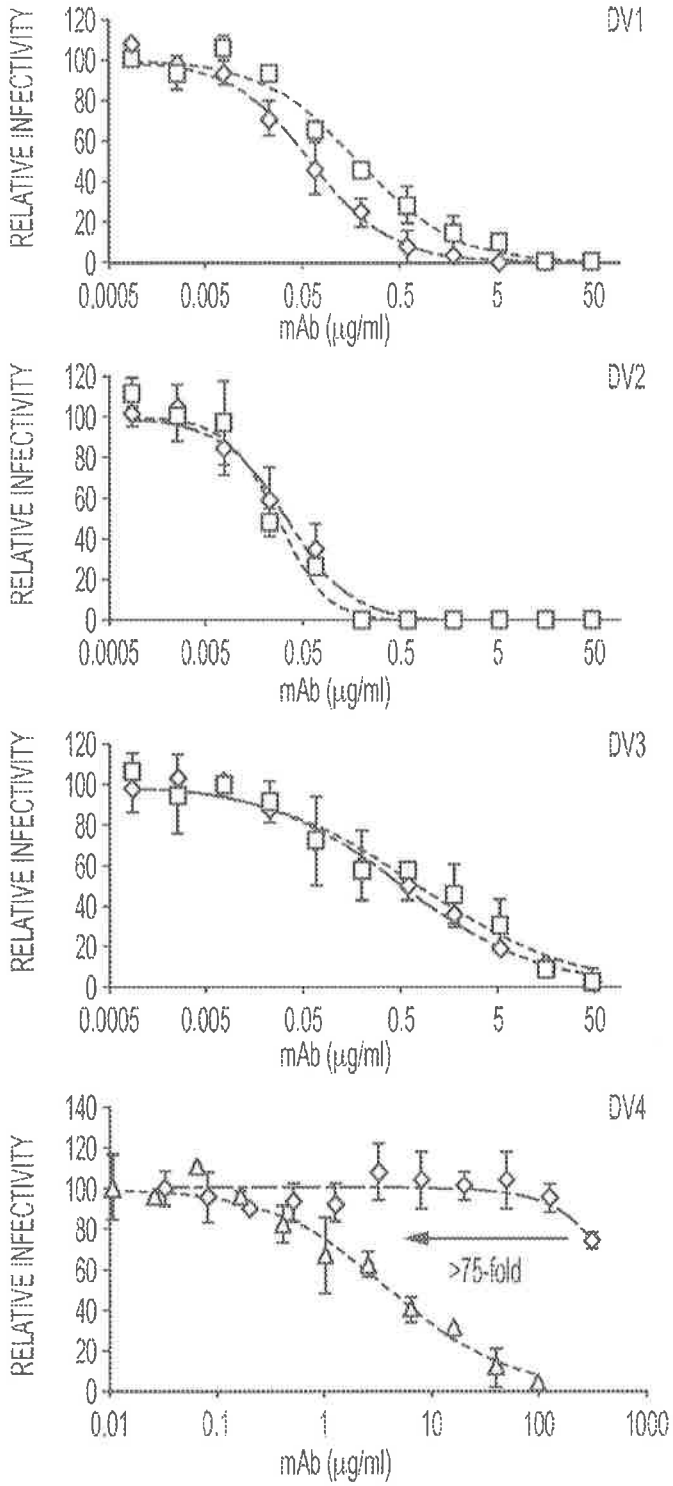

E
4E5A:EDIII-DV1
F
4E5A:EDIII-DV2
G
4E5A:EDIII-DV3
H
4E5A:EDIII-DV4
RU
Time
1100 1300 1500 1700 1900 2100 2300 2500 2700 2900

FIG. 8E-H



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

FIG. 9

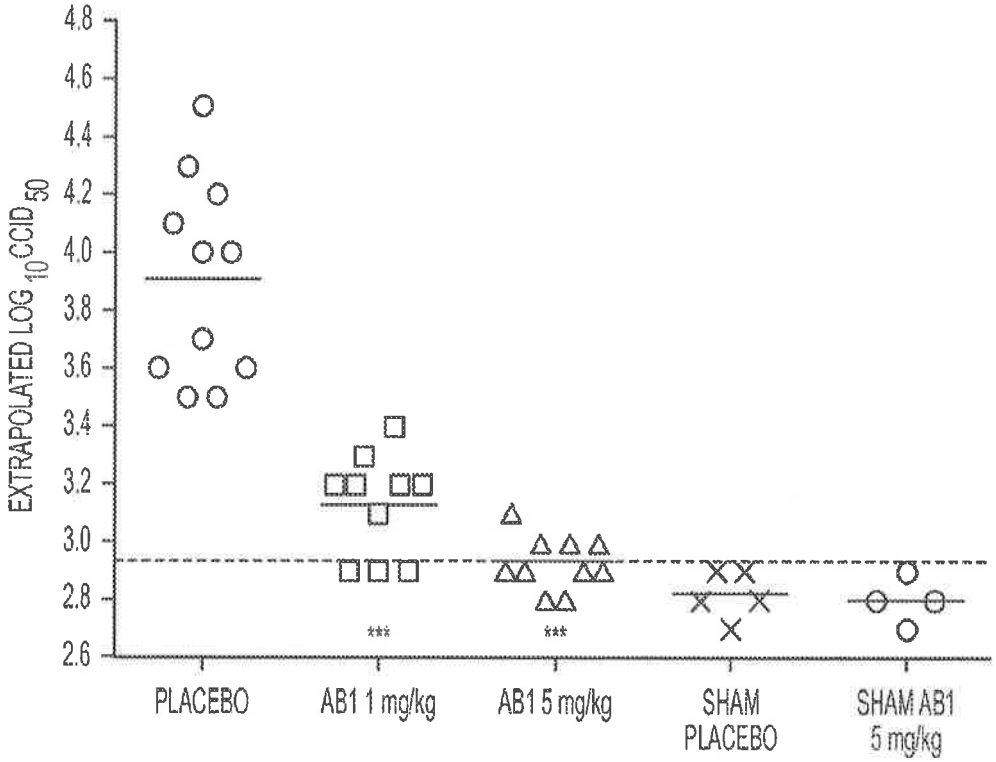

EXTRAPOLATED LOG 10 CCID 50
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
***
***
PLACEBO
AB1 1 mg/kg
AB1 5 mg/kg
SHAM PLACEBO
SHAM AB1 5 mg/kg

FIG. 10

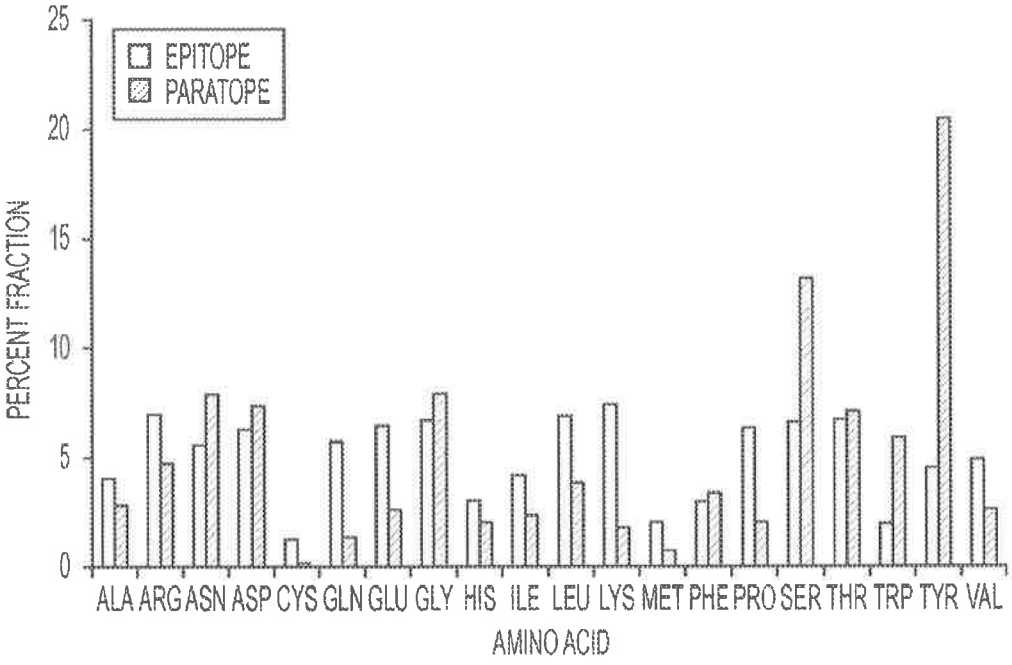

EPITOPE
PARATOPE
PERCENT FRACTION
25
20
15
10
5
0
ALA ARG ASN ASP CYS GLN GLU GLY HIS ILE LEU LYS MET PHE PRO SER THR TRP TYR VAL
AMINO ACID

FIG. 11

mAb	EDIII-DV1		EDIII-DV2		EDIII-DV3		EDIII-DV4	
	K_D (nM)	REL AFFINITY	K_D (nM)	REL AFFINITY	K_D (nM)	REL AFFINITY	K_D (nM)	REL AFFINITY
4E5A	0.368		<0.3		24.2		126.2	
VH_A25_del	1.27	0.29	<0.3		19.8	1.22	235.6	0.54
VH_S26_del	<0.3	>1.23	<0.3		5.47	4.42	14.2	8.89
VH_G27_del	<0.3	>1.23	<0.3		9.05	2.67	26.4	4.78
VH_G27A	<0.3	>1.23	<0.3		20.6	1.17	43.2	2.92
VH_G27P	4.58	0.08	<0.3		33.1	0.73	1971	0.06
VH_Y106R	<0.3	>1.23	<0.3		33.4	0.72	271.7	0.46
VL_E97R	0.361	1.02	<0.3		25.2	0.96	116.1	1.09
VL_E97K	0.371	0.99	<0.3		24.6	0.98	103.7	1.22
VL_E97Q	0.449	0.82	<0.3		23.3	1.04	114.5	1.10

FIG. 12

LIGAND	ANALYTE	ka (1/Ms)	kd (1/s)	KD (M)	Chi2	Rmax (RU)
4E5A	DV1	2.52E+06	5.46E-04	2.17E-10	0.409	24.6
4E5-del-25	DV1	9.33E+05	1.33E-03	1.43E-09	0.282	32.4
4E5-del26	DV1	2.07E+06	2.44E-04	1.18E-10	1.12	27.8
4E5-del27	DV1	1.52E+06	4.71E-04	3.10E-10	0.644	36.1
4E5-G27A	DV1	1.04E+06	8.38E-05	8.05E-11	0.382	30.6
4E5-G27P	DV1	3.05E+06	8.41E-03	2.76E-09	0.804	25.2

LIGAND	ANALYTE	ka (1/Ms)	kd (1/s)	KD (M)	Chi2	Rmax (RU)
V2-4E5A	DV2	3.77E+06	4.88E-04	1.29E-10	0.345	25.4
4E5-del-25	DV2	2.74E+06	1.82E-04	6.64E-11	0.292	34.1
4E5-del26	DV2	3.51E+06	3.63E-04	1.04E-10	0.463	35.1
4E5-del27	DV2	2.09E+06	5.63E-04	2.69E-10	0.468	36.0
4E5-G27A	DV2	2.08E+06	4.19E-04	2.02E-10	0.601	35.8
4E5-G27P	DV2	1.99E+06	5.27E-04	2.65E-10	0.268	32.8

FIG. 13A

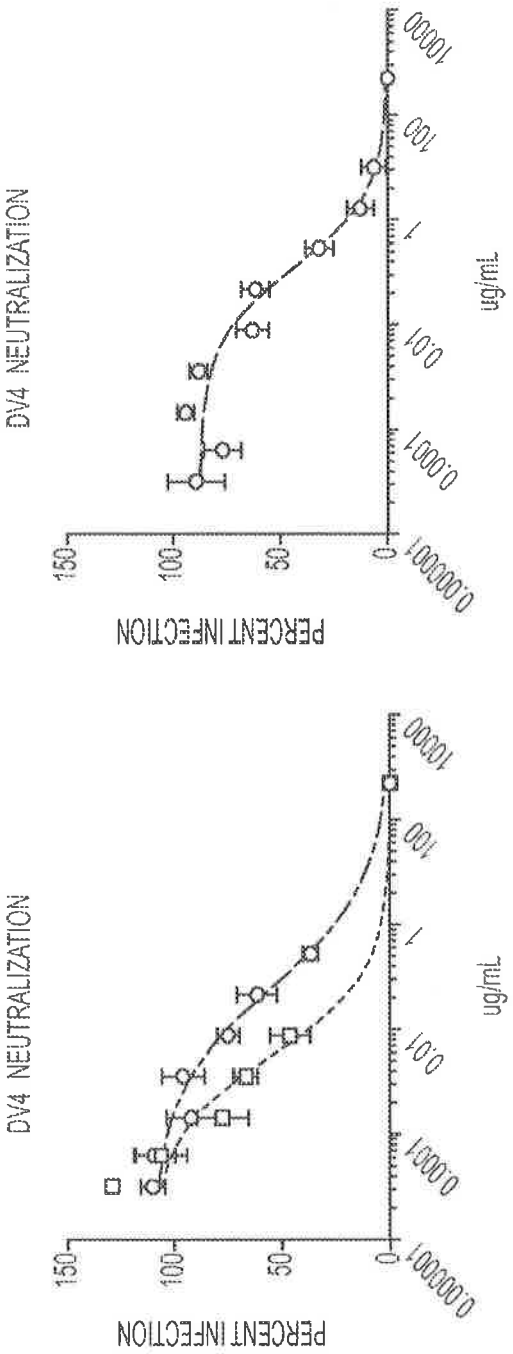
LIGAND	ANALYTE	ka (1/Ms)	kd (1/s)	KD (M)	Chi2	Rmax (RU)
4E5A	DV3	1.12E+07	3.04E-02	2.72E-09	0.452	25.0
4E5-del-25	DV3	4.98E+06	2.69E-02	5.40E-09	0.8	37.0
4E5.del26	DV3	2.13E+07	5.54E-02	2.60E-09	0.589	33.0
4E5.del27	DV3	2.02E+07	4.83E-02	2.39E-09	0.504	25.3
4E5-G27A	DV3	2.33E+09	7.54E+00	3.24E-09	1.2	28.2
4E5-G27P	DV3	2.95E+06	1.33E-02	4.52E-09	1.9	28.9

LIGAND	ANALYTE	ka (1/Ms)	kd (1/s)	KD (M)	Chi2	Rmax (RU)
V2-4E5A	DV4	5.03E+06	6.32E-02	1.26E-08	1.69	16.7
4E5-del-25	DV4	4.99E+06	1.30E-01	2.59E-08	0.45	4.6
4E5.del26	DV4	6.69E+08	4.37E+00	6.54E-09	1.19	42.4
4E5.del27	DV4	2.34E+06	1.88E-02	8.04E-09	2.27	26.5
4E5-G27A	DV4	1.83E+06	4.06E-02	2.21E-08	1.32	31.0
4E5-G27P	DV4	NO BINDING				

FIG. 13B

scFv	EDIII-DV4 (YSD)	
	K_D (nM)	REL AFFINITY
4E5A	650	
VH_S26_del	66	9.8
VH_G27_del	128	5.1
VH_G27A	185	3.8
VH_G27P	53312	0.01

FIG. 14



mAb	IC-50 (ng/ml)
4E5A (-○-)	61.8
VH_S26_del (-□-)	3.2
4G2 (-○-)	117.2

FIG. 15