

FIG. 1A

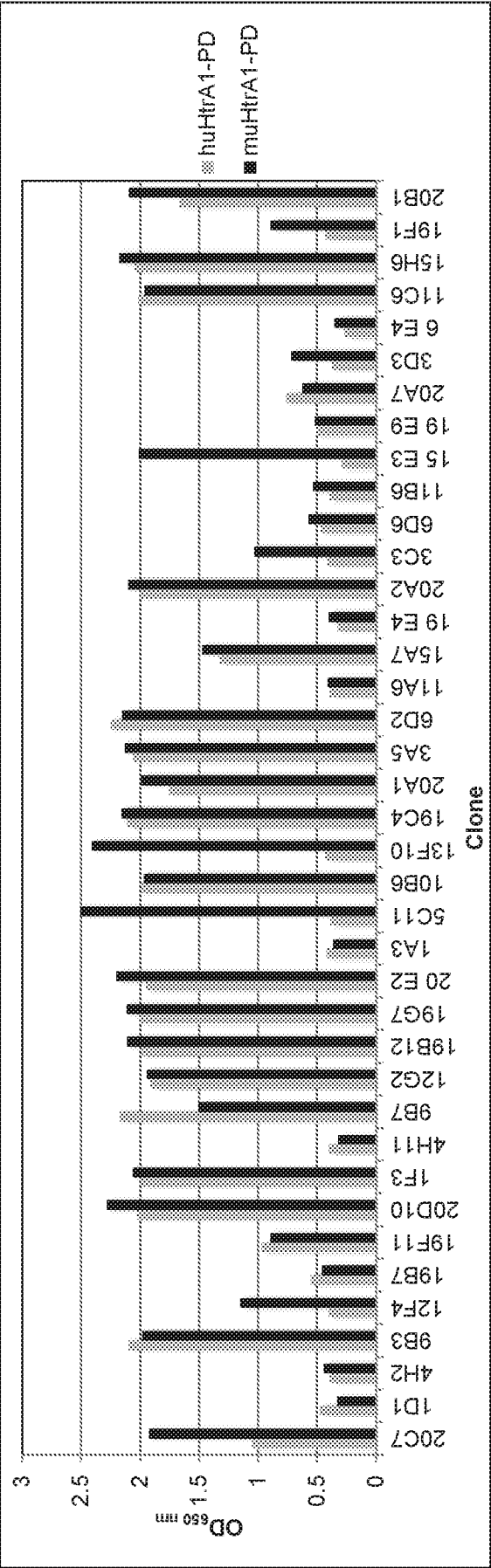


FIG. 1B

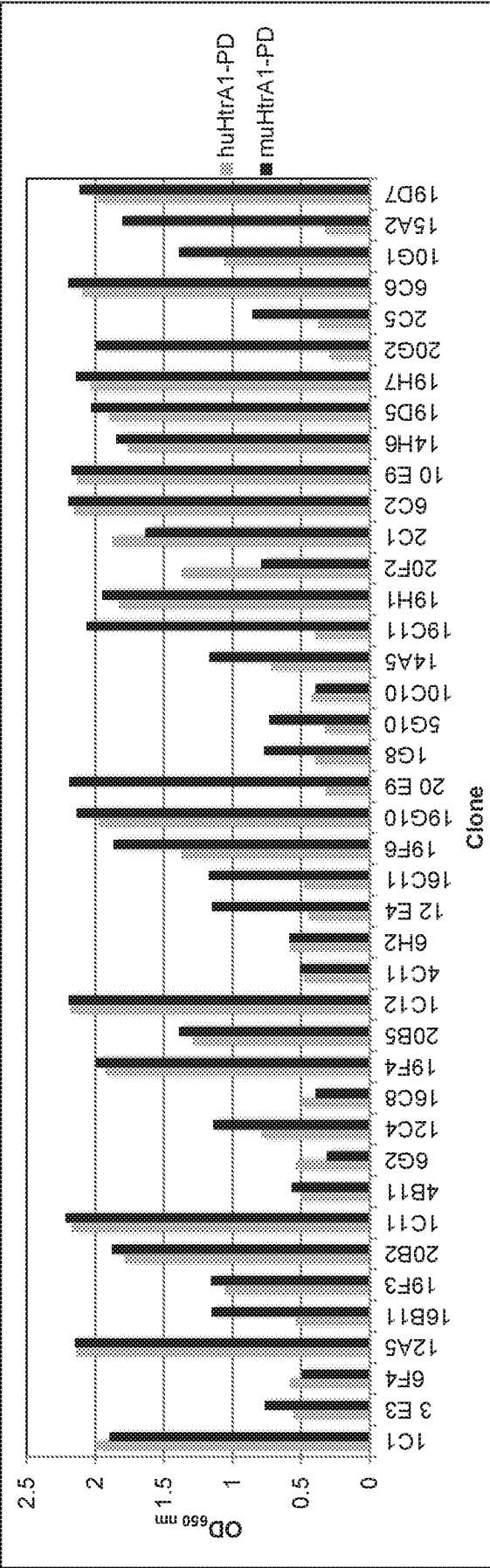


FIG. 2A

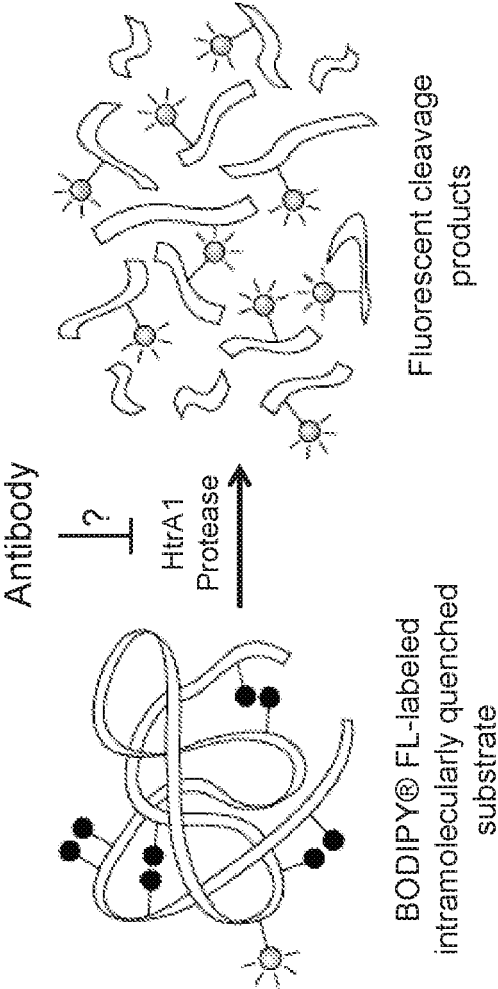


FIG. 2C

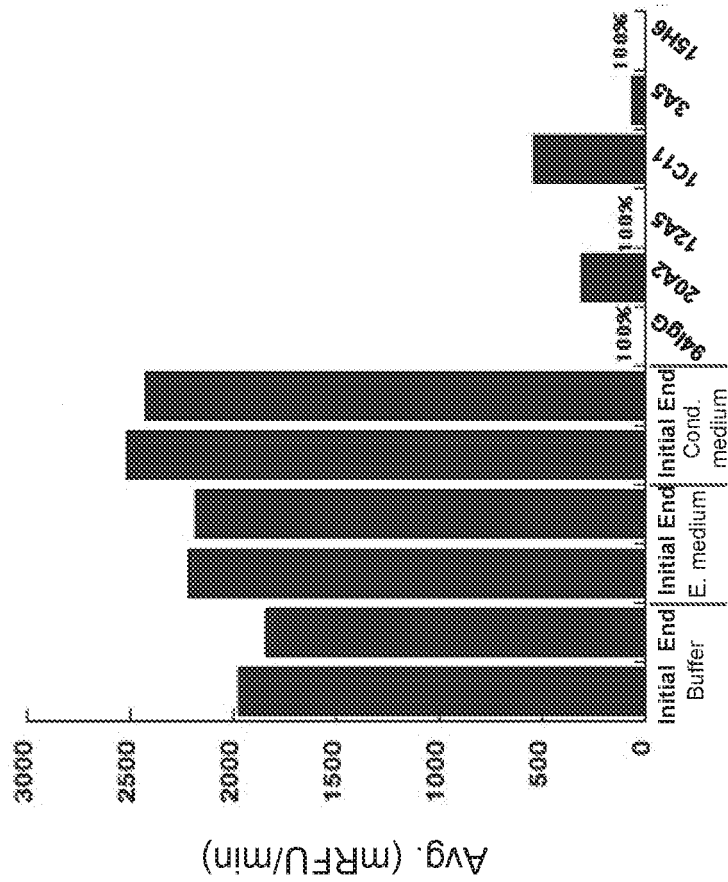


FIG. 2B

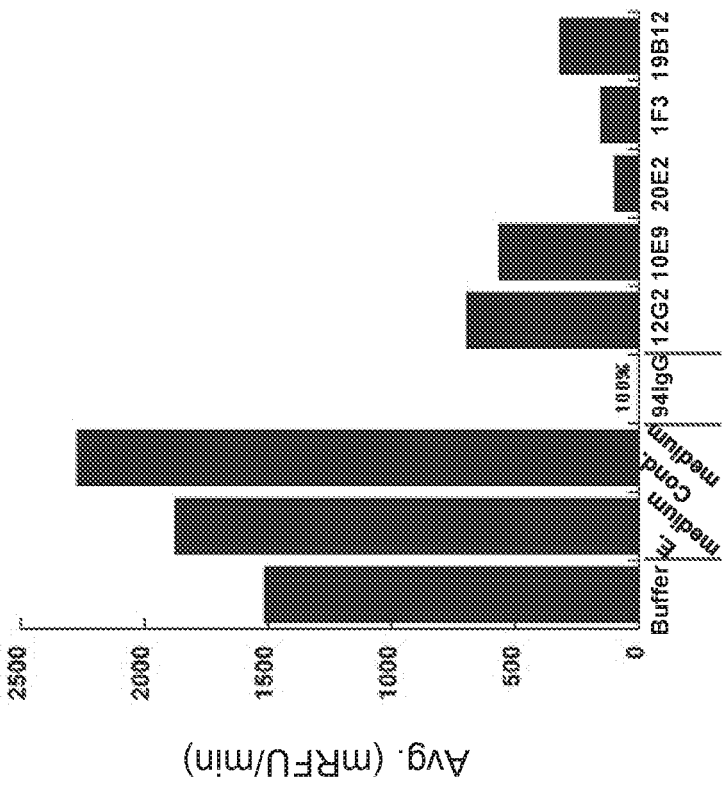
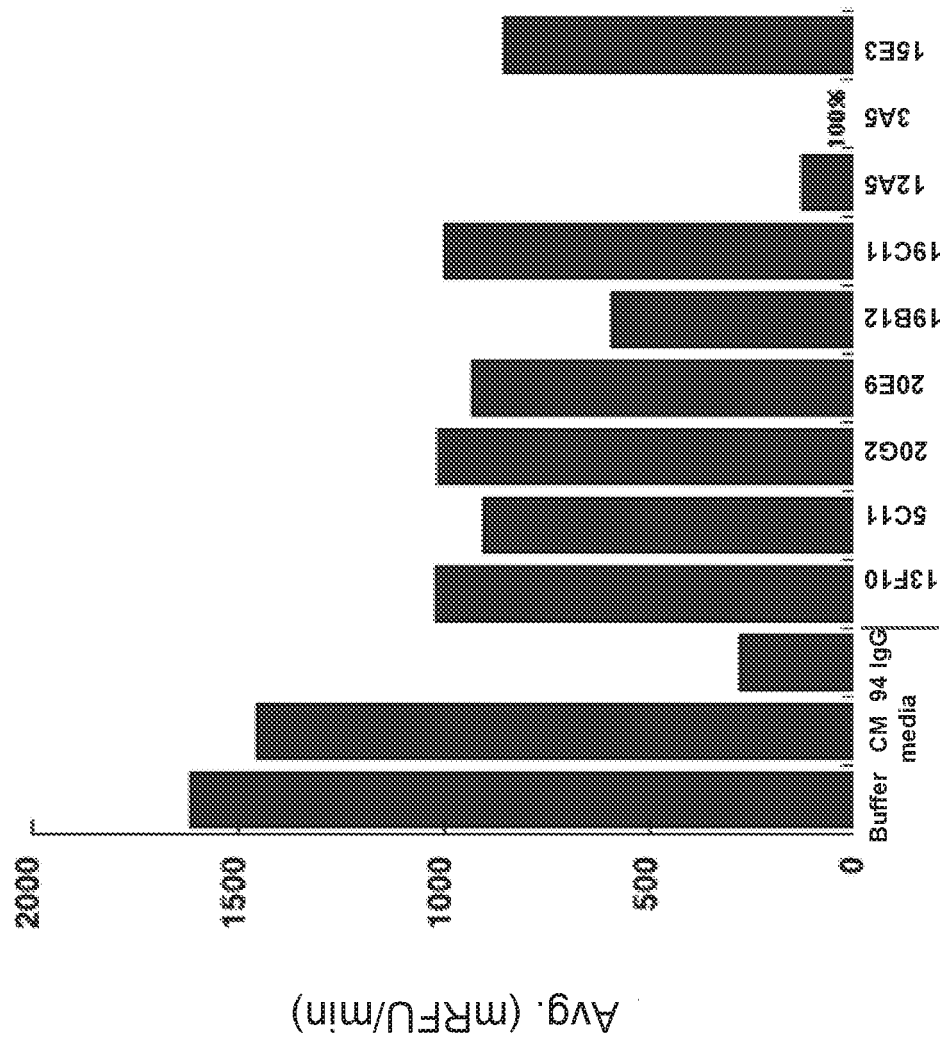


FIG. 3A



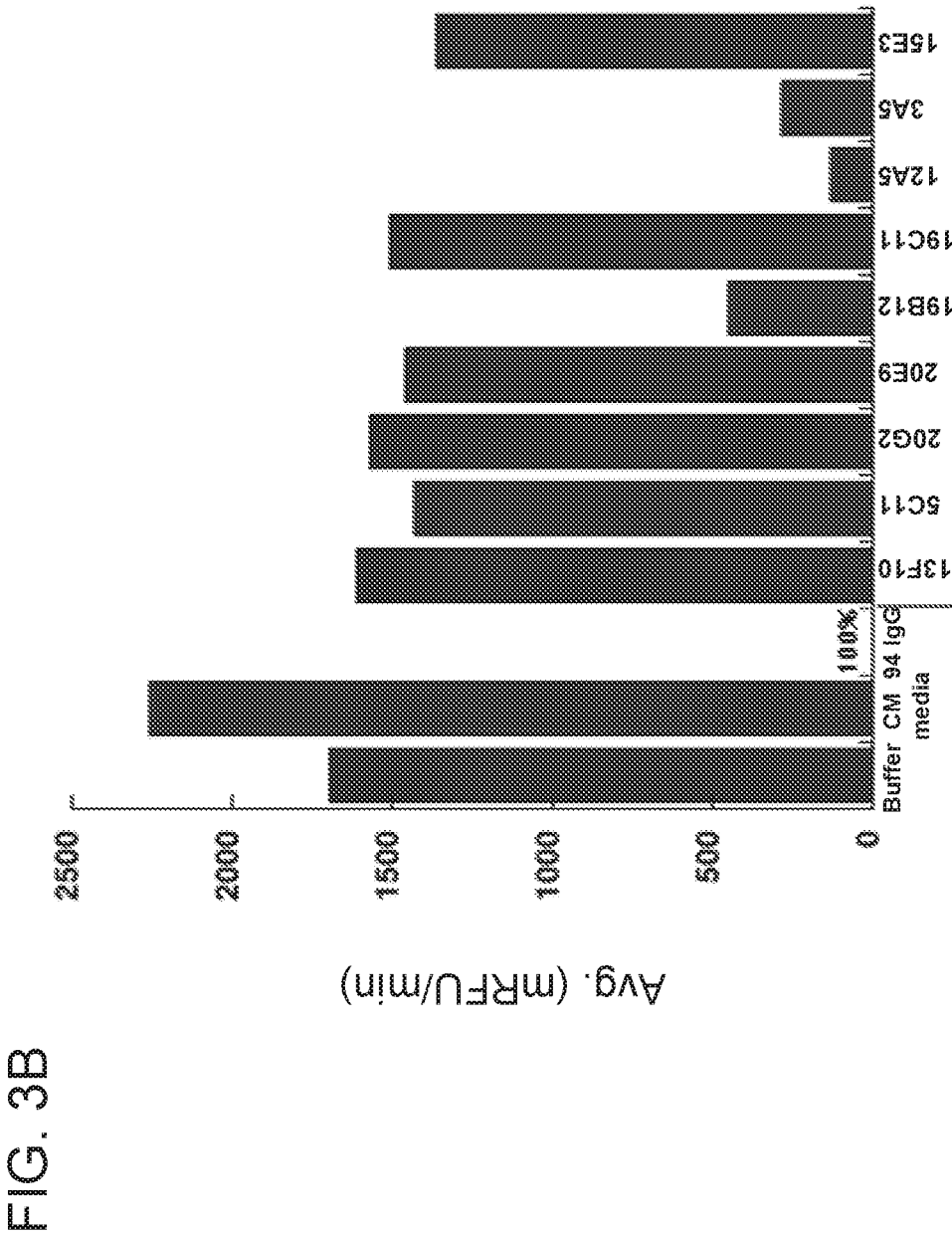


FIG. 4A

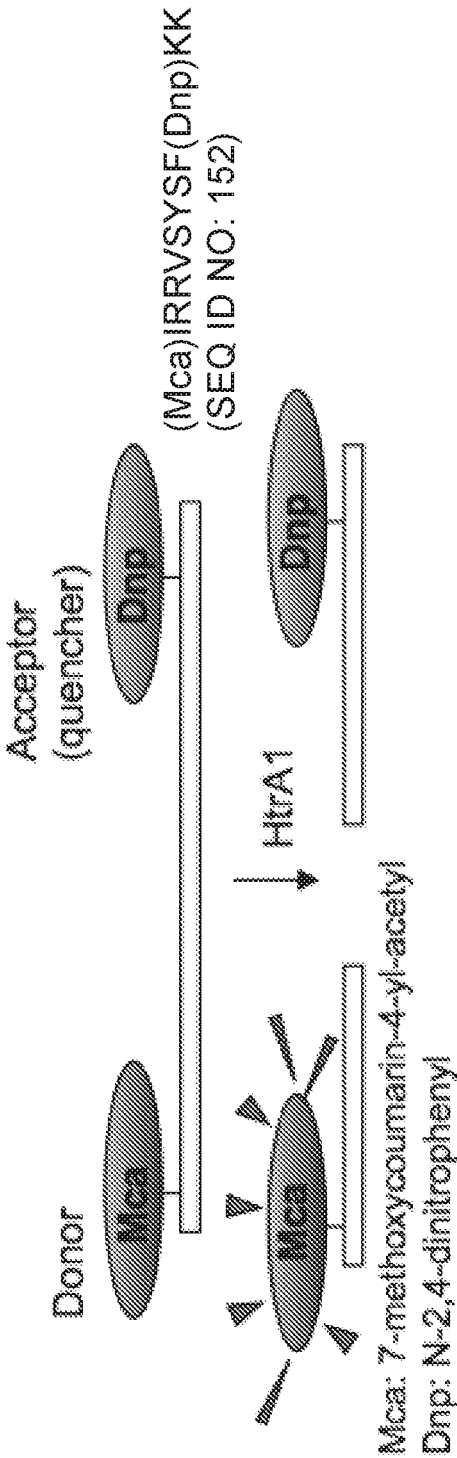


FIG. 4C

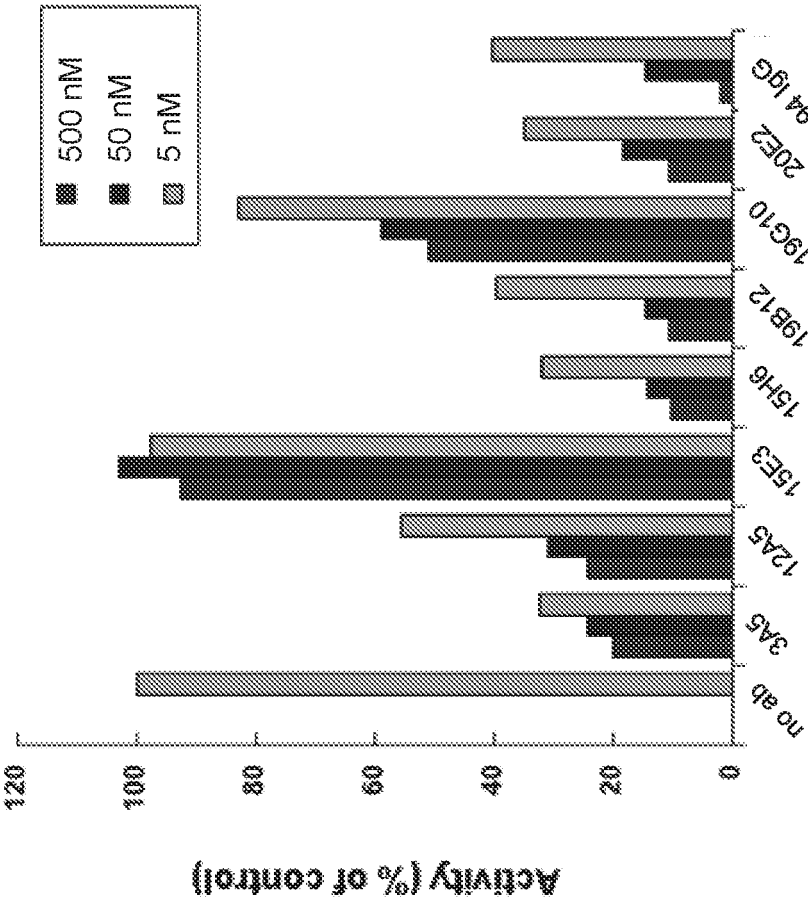


FIG. 4B

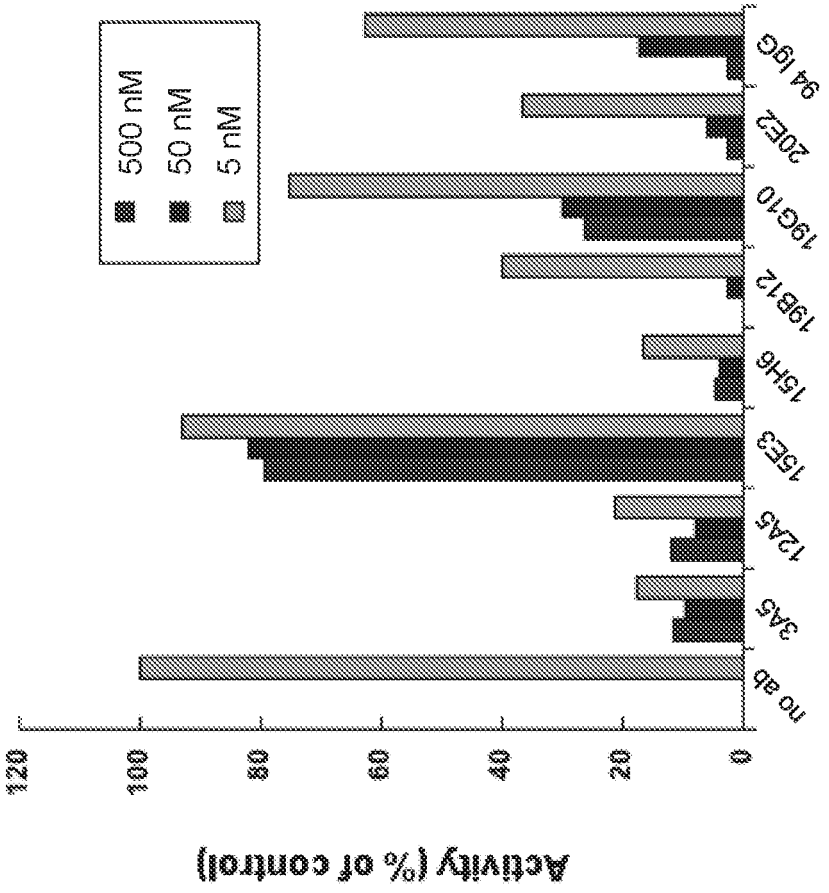


FIG. 5A

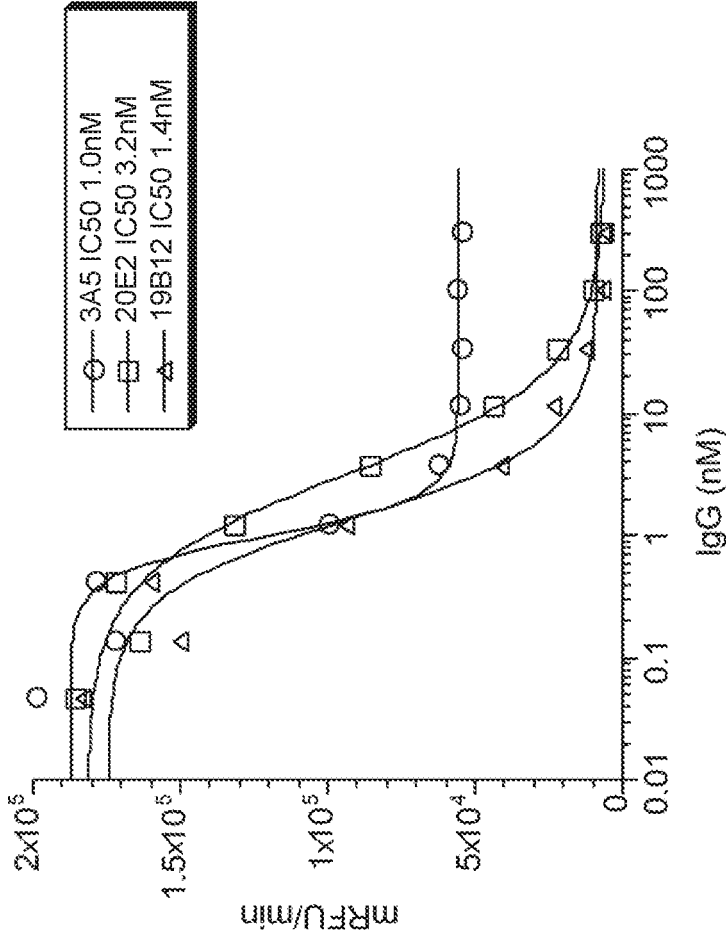


FIG. 5B

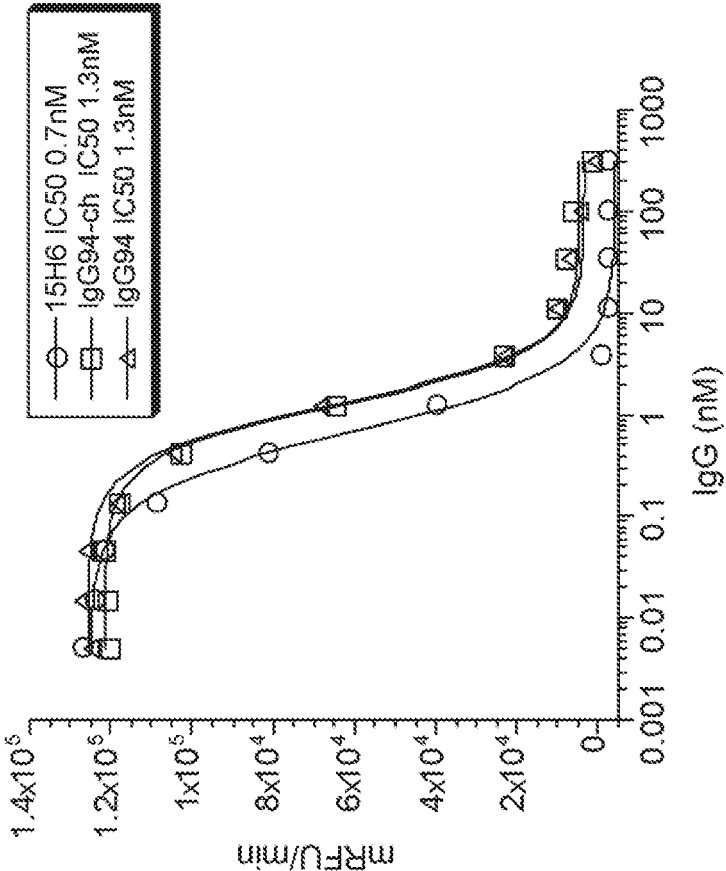


FIG. 5C

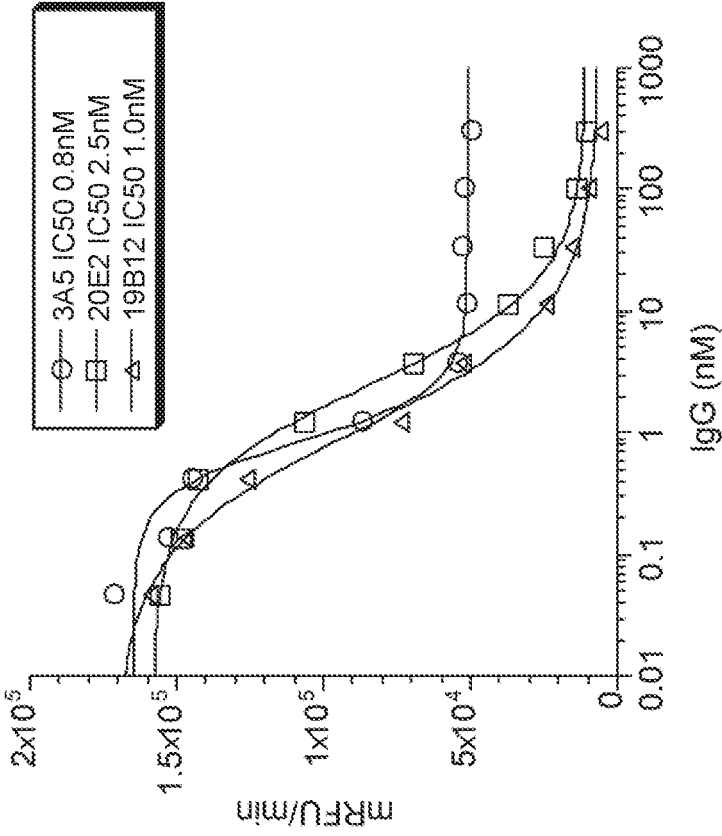
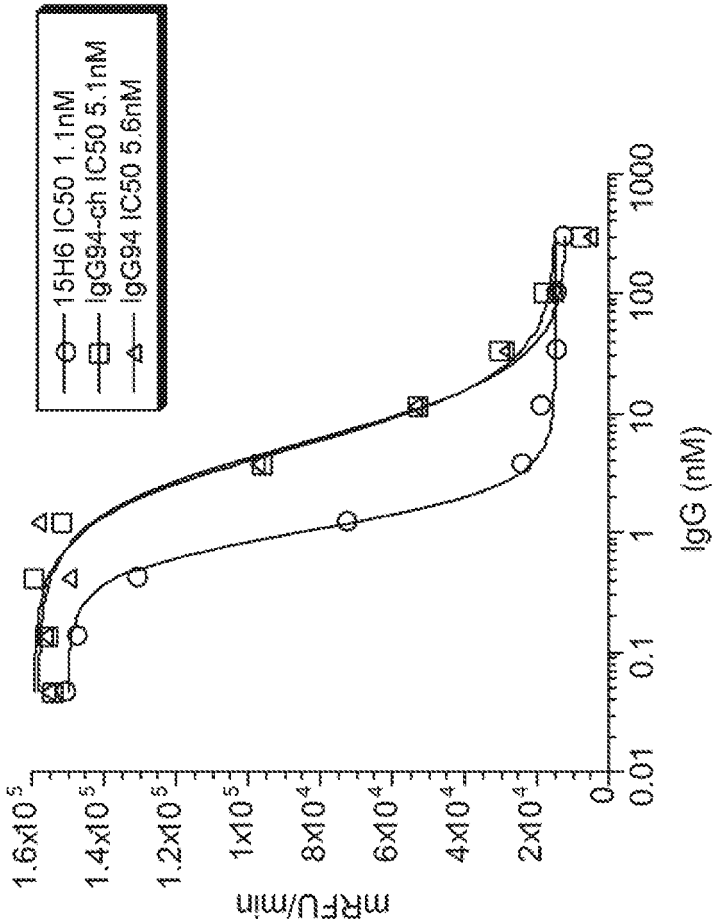


FIG. 5D



6A
G
L

1	E	V	K	L	V	E	S	G	G	T	T	Y	V	S	D	T	I	K	G	R	F	T	I	S	R	D	N	A	K	N	T	L	Y	L	Q	M	S	T	I	K	S	E	D	T	A	I	V	F	C	A	R	Q	N	100																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																						
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FIG. 7A

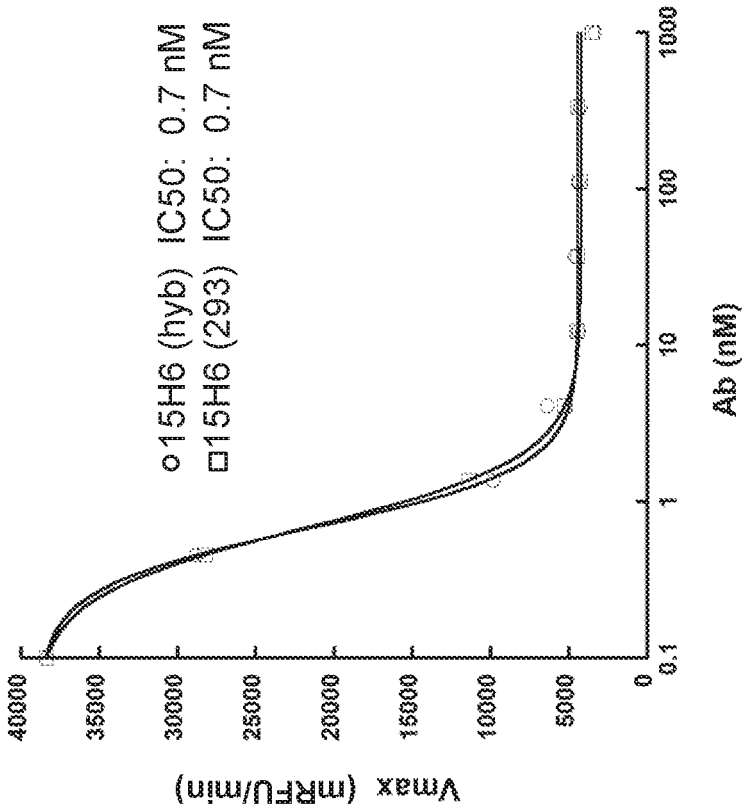


FIG. 7B

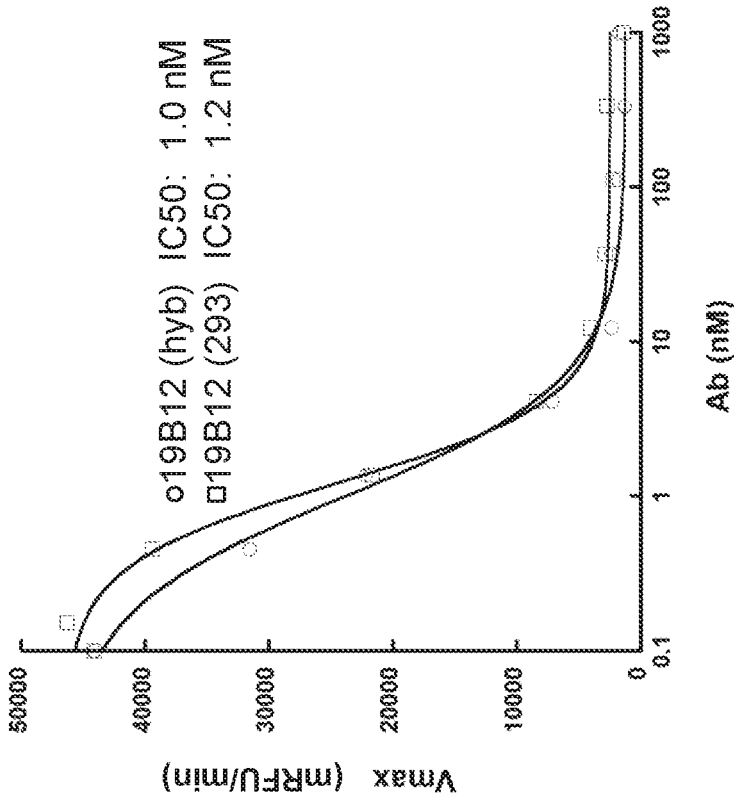


FIG. 8A

Kabat number	HVR-L1 - Contact																															
	HVR-L1 - Kabat																															
	HVR-L2 - Contact																															
	HVR-L2 - Kabat																															
	HVR-L3 - Contact																															
	HVR-L3 - Kabat																															
	HVR-L4 - Contact																															
	HVR-L4 - Kabat																															
	HVR-L5 - Contact																															
	HVR-L5 - Kabat																															

Human Consensus K1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	
m15H6	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q	G	I	S	S	Y	L	A	W	Y	Q	Q	K	P	G	K	
h15H6.v1	Q	I	V	L	S	Q	S	P	A	I	L	S	A	S	P	G	E	K	V	T	M	T	T	C	R	A	S	.	S	S	V	N	F	I	H	W	Y	Q	Q	K	P	G	K
h15H6.v2	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	.	S	S	V	N	F	I	H	W	Y	Q	Q	K	P	G	K	
h15H6.v2.APEG (h15H6.v3)	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	.	S	S	V	N	F	I	H	W	Y	Q	Q	K	P	G	K	

Human Consensus K1	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84		
m15H6	A	P	K	L	L	I	Y	A	A	S	S	L	Q	S	G	V	P	S	R	F	S	G	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P	E	D	F	A
h15H6.v1	S	P	K	P	W	I	S	A	T	S	N	L	A	S	G	V	P	P	R	F	S	G	S	G	S	G	S	G	T	S	Y	S	L	T	I	S	R	V	E	A	E	D	A	
h15H6.v2	A	P	K	P	W	I	S	A	T	S	N	L	A	S	G	V	P	S	R	F	S	G	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P	E	D	F	A
h15H6.v2.APEG (h15H6.v3)	A	P	K	P	L	I	S	A	T	S	N	L	A	S	G	V	P	S	R	F	S	G	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P	E	D	F	A

Human Consensus K1	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107
m15H6	T	Y	Y	C	Q	Q	Y	Y	S	Y	P	F	T	F	G	Q	G	T	K	V	E	I	K
h15H6.v1	T	Y	Y	C	Q	Q	W	S	S	N	P	W	T	F	G	Q	G	T	K	L	E	I	K
h15H6.v2	T	Y	Y	C	Q	Q	W	S	S	N	P	W	T	F	G	Q	G	T	K	V	E	I	K
h15H6.v2.APEG (h15H6.v3)	T	Y	Y	C	Q	Q	W	S	S	A	P	W	T	F	G	Q	G	T	K	V	E	I	K

Human Consensus K1	(SEQ ID NO: 71)
m15H6	(SEQ ID NO: 23)
h15H6.v1	(SEQ ID NO: 72)
h15H6.v2	(SEQ ID NO: 73)
h15H6.v2.APEG (h15H6.v3)	(SEQ ID NO: 74)

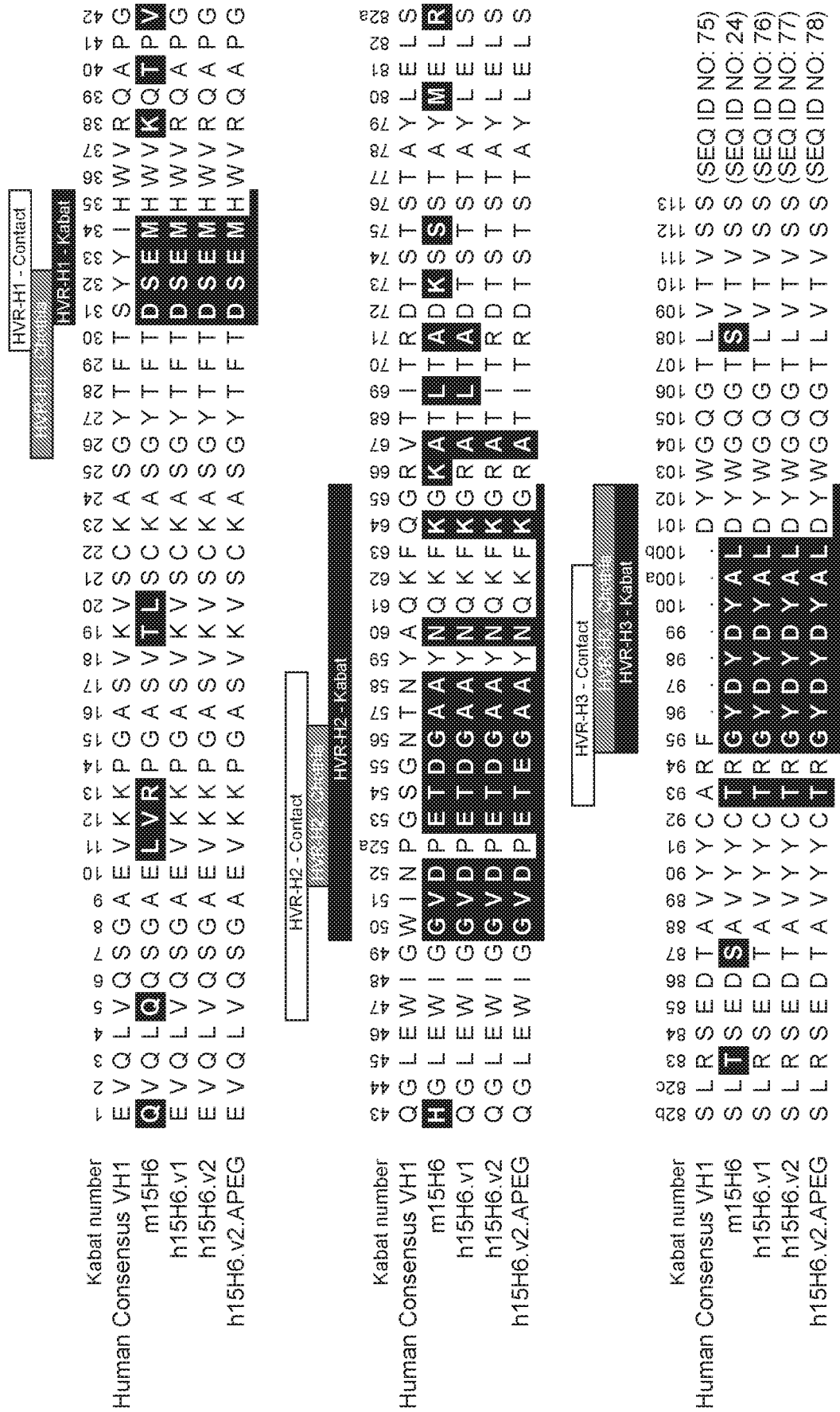


FIG. 9A

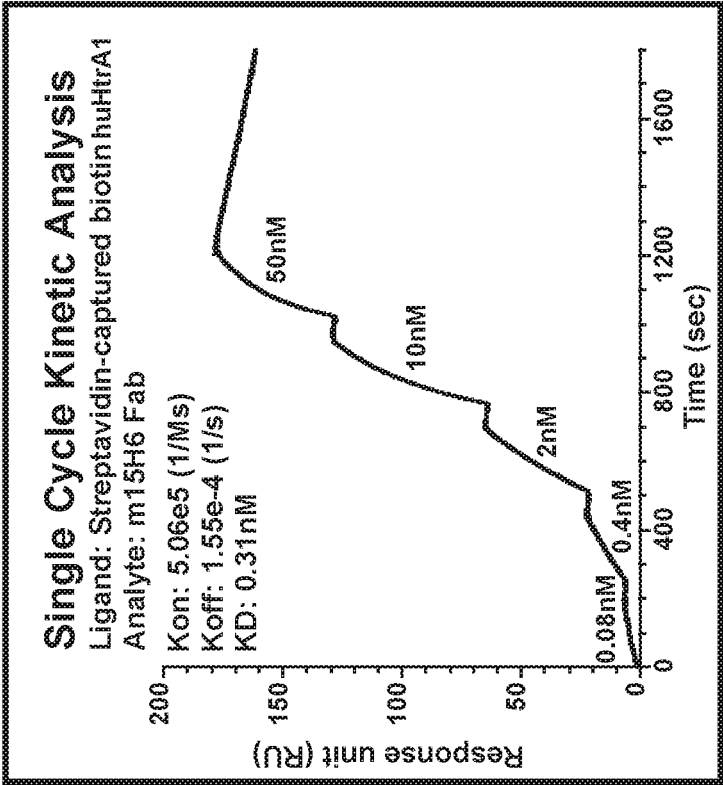


FIG. 9B

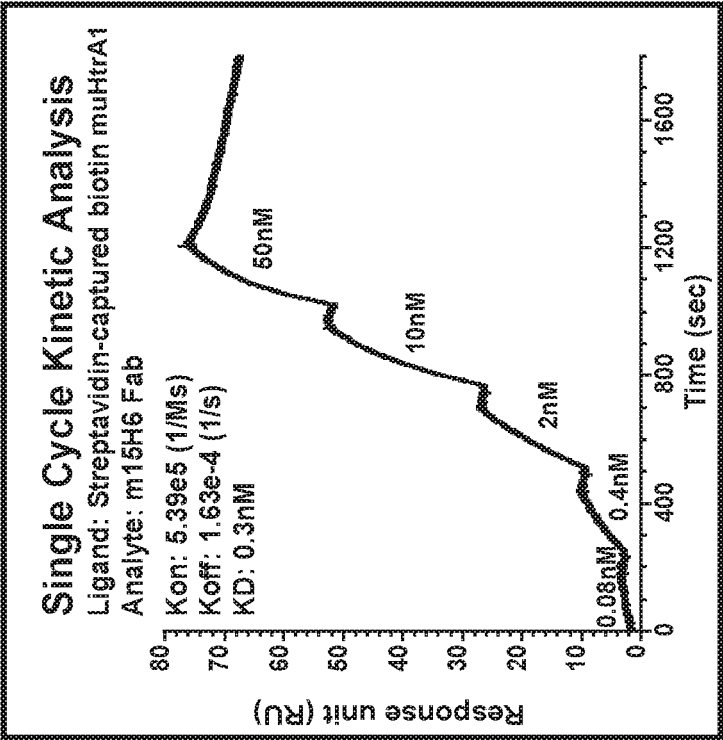


FIG. 9D

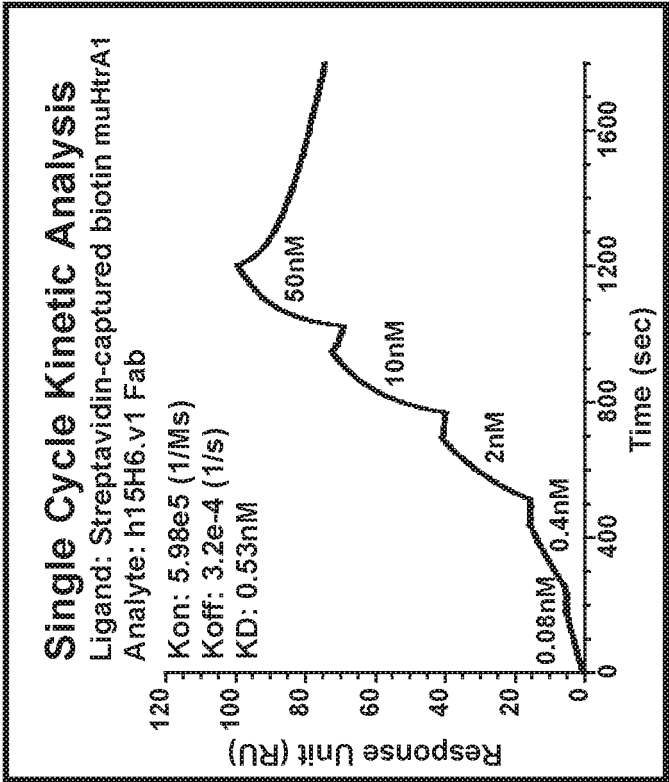


FIG. 9C

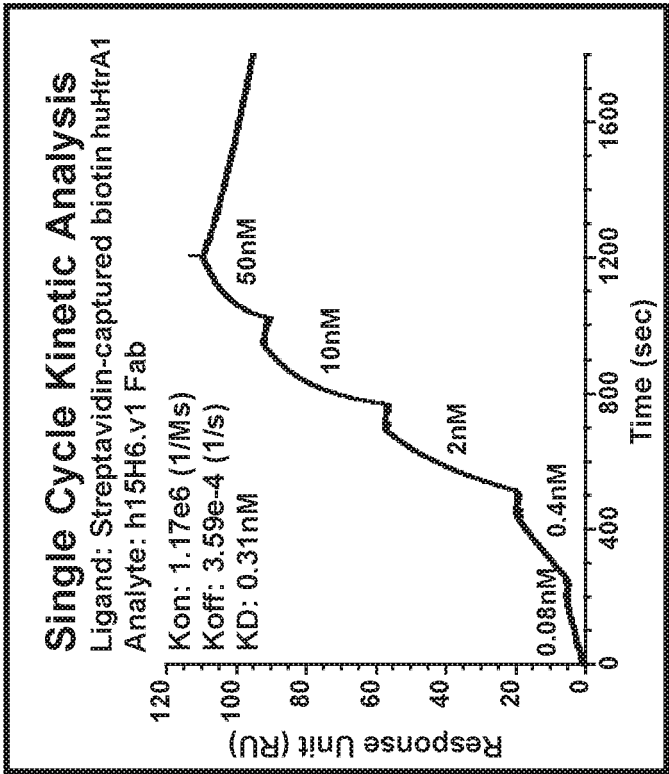


FIG. 10A

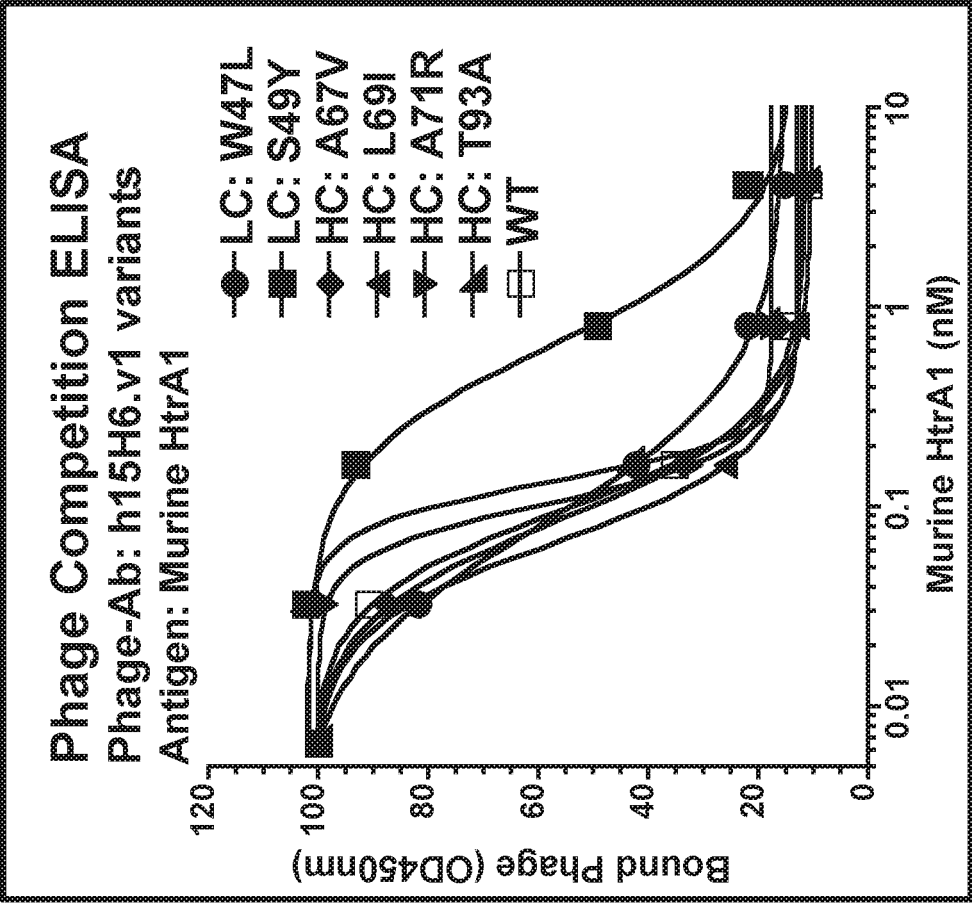
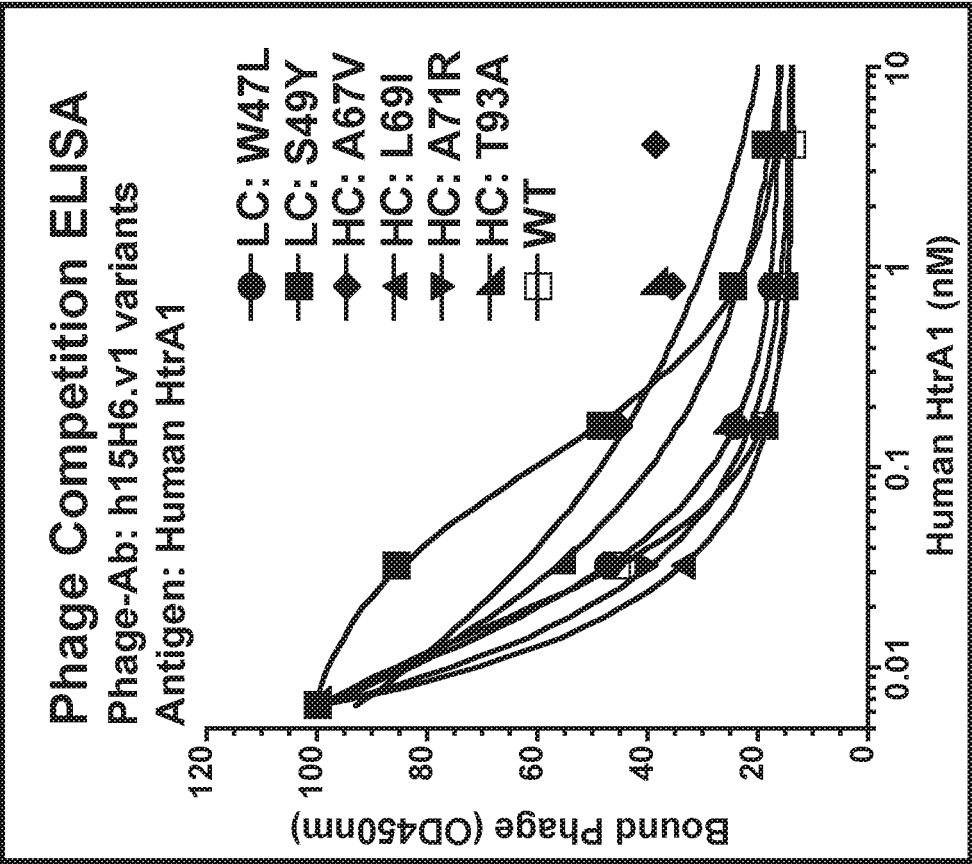


FIG. 10B



h15H6.v2 HVR-L3: W91 variants

FIG. 11A

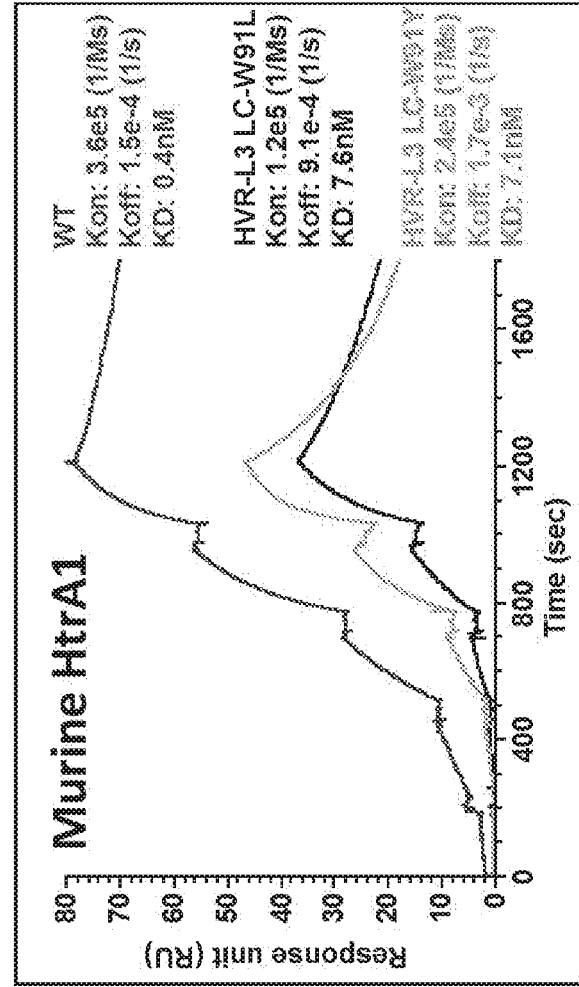
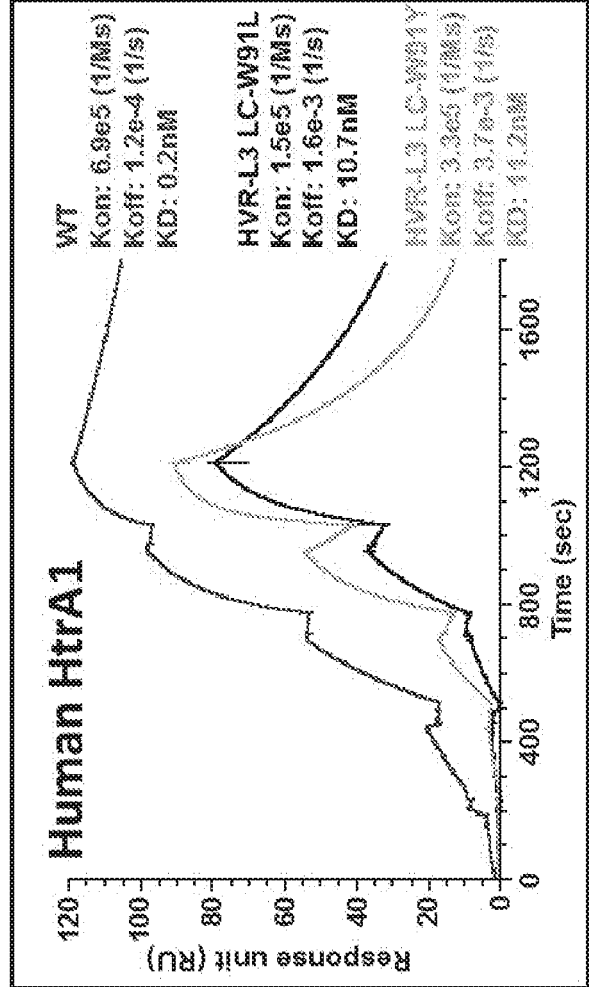


FIG. 11B



h15H6.v2 HVR-L3: N94 P95 variants

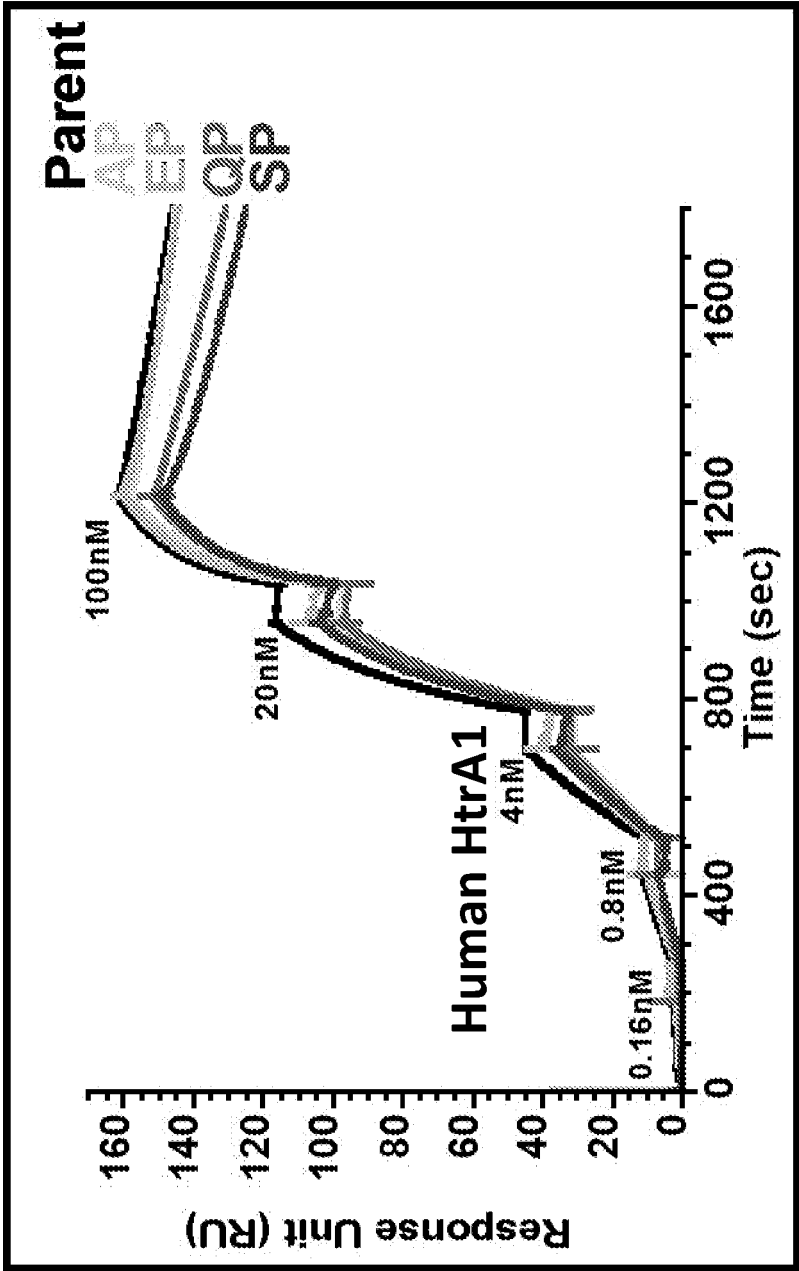


FIG. 12A

xHtrA1 h15H6.v2 NP Variants (Fab)	Human HtrA1		
	Kon ($10^5 \text{M}^{-1} \text{s}^{-1}$)	Koff (10^{-4}s^{-1})	KD (nM)
Parent	6.3	1.6	0.25
AP	4.5	1.4	0.31
EP	5.2	1.7	0.33
QP	5.6	2.9	0.52
SP	4.8	2.5	0.52

FIG. 12B

h15H6.v2 HVR-H2: D55 G56 variants

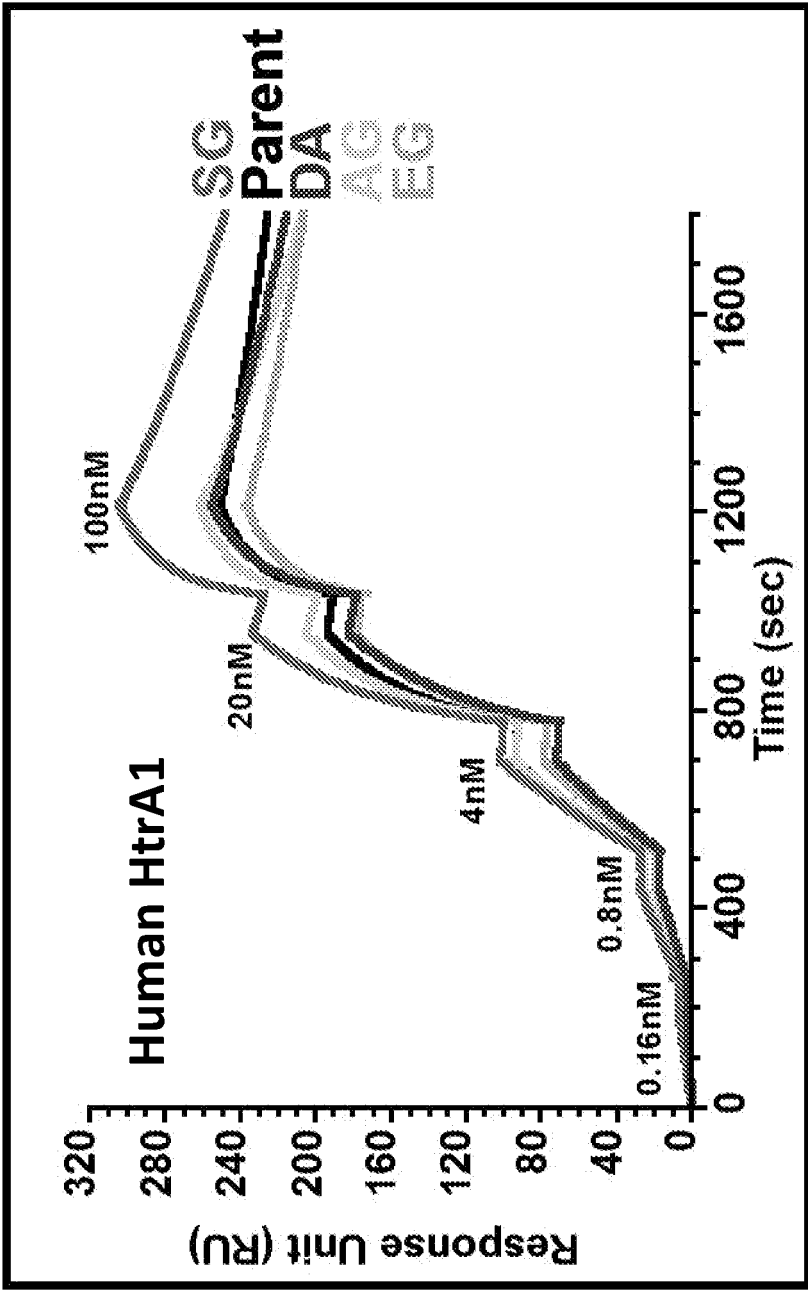


FIG. 13A

xHtrA1 h15H6.v2 DG Variants (Fab)	Human HtrA1		
	Kon ($10^5 \text{M}^{-1} \text{s}^{-1}$)	Koff (10^{-4}s^{-1})	KD (nM)
Parent	4.3	1.4	0.33
AG	4.6	3.5	0.76
EG	3.8	2.1	0.55
SG	4.1	3.2	0.78
DA	3.2	2.7	0.84

FIG. 13B

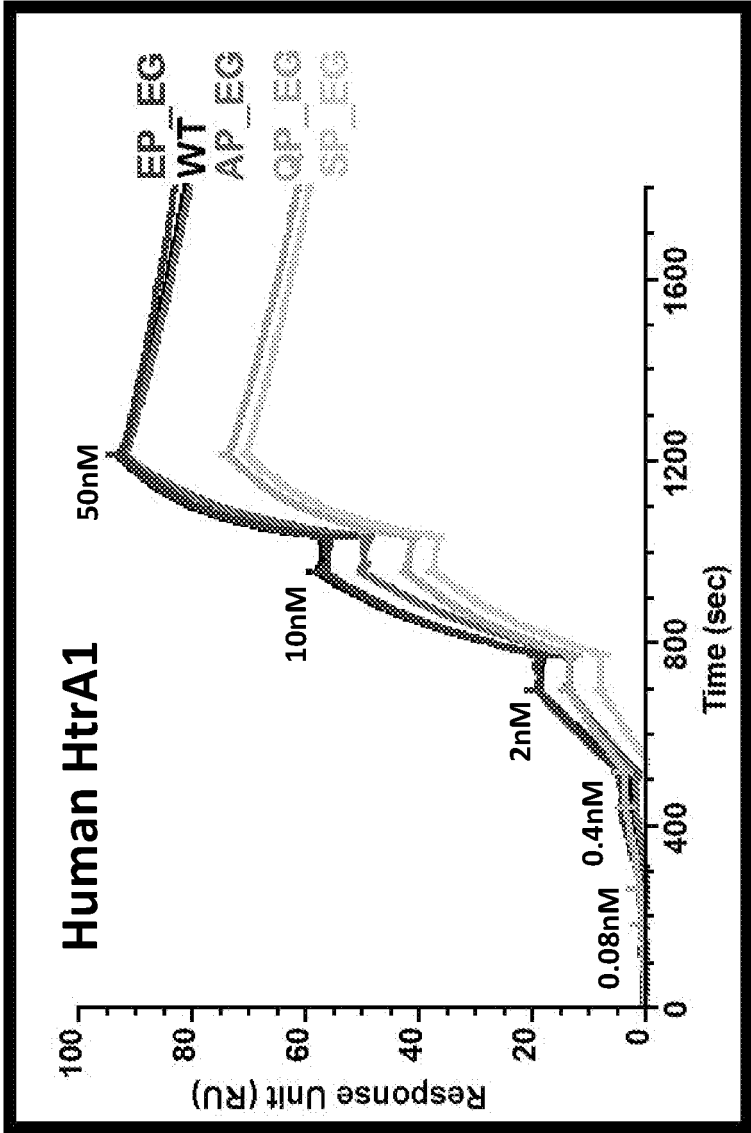


FIG. 14A

xHtrA1 h15H6.v2 variants (Fab)	Human HtrA1-PD (N=2)		
	Kon ($10^5 \text{M}^{-1} \text{s}^{-1}$)	Koff (10^{-4}s^{-1})	KD (nM)
NP_DG (WT)	4.9 ± 0.6	2.1 ± 0.2	0.4 ± 0.1
AP_EG	3.5 ± 0.1	2.1 ± 0.1	0.6 ± 0.1
EP_EG	4.5 ± 0.1	1.8 ± 0.1	0.4 ± 0.1
QP_EG	3.8 ± 0.1	2.9 ± 0.2	0.8 ± 0.1
SP_EG	3.5 ± 0.1	2.9 ± 0.1	0.8 ± 0.1

FIG. 14B

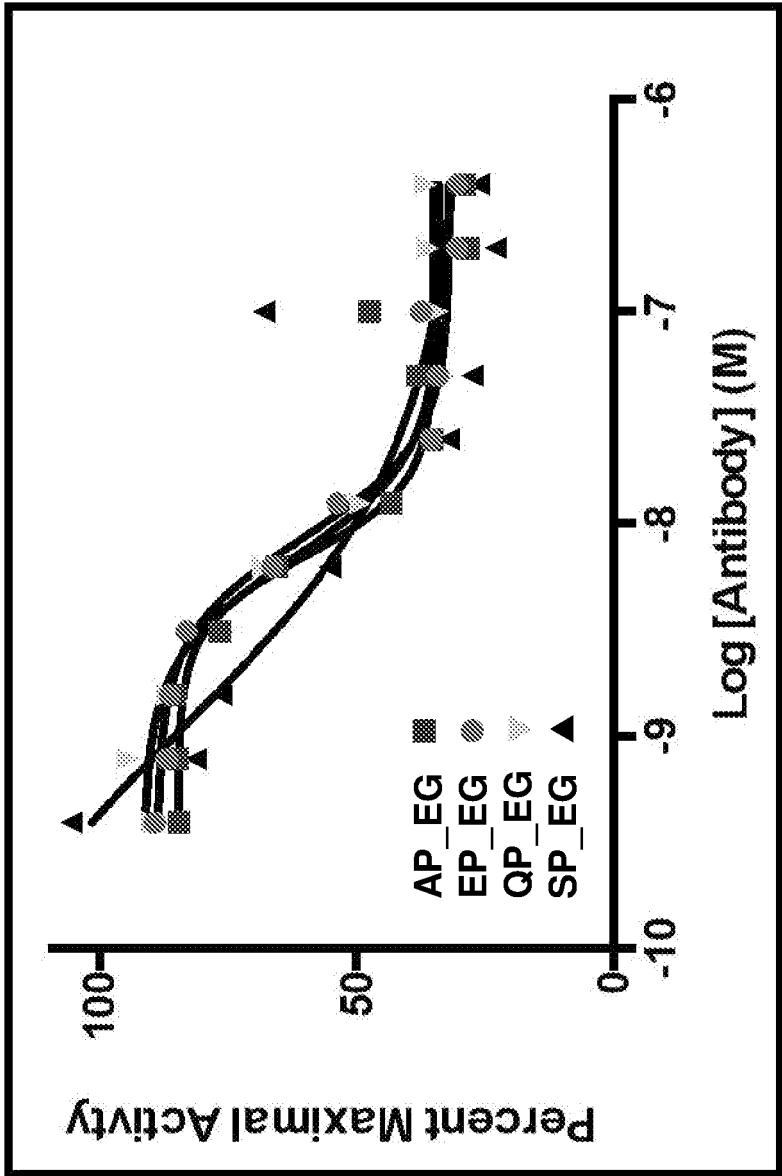


FIG. 14C

FIG. 14D

Clones	FRET IC50 (nM)
h15H6.v2 FL	5.9 ± 1.2
h15H6.v2 Fab	8.1 ± 0.6
AP_EG Fab	8.9 ± 2.6
EP_EG Fab	9.4 ± 1.3
QP_EG Fab	7.6 ± 0.7
SP_EG Fab	7.5 ± 3.1

FIG. 15B

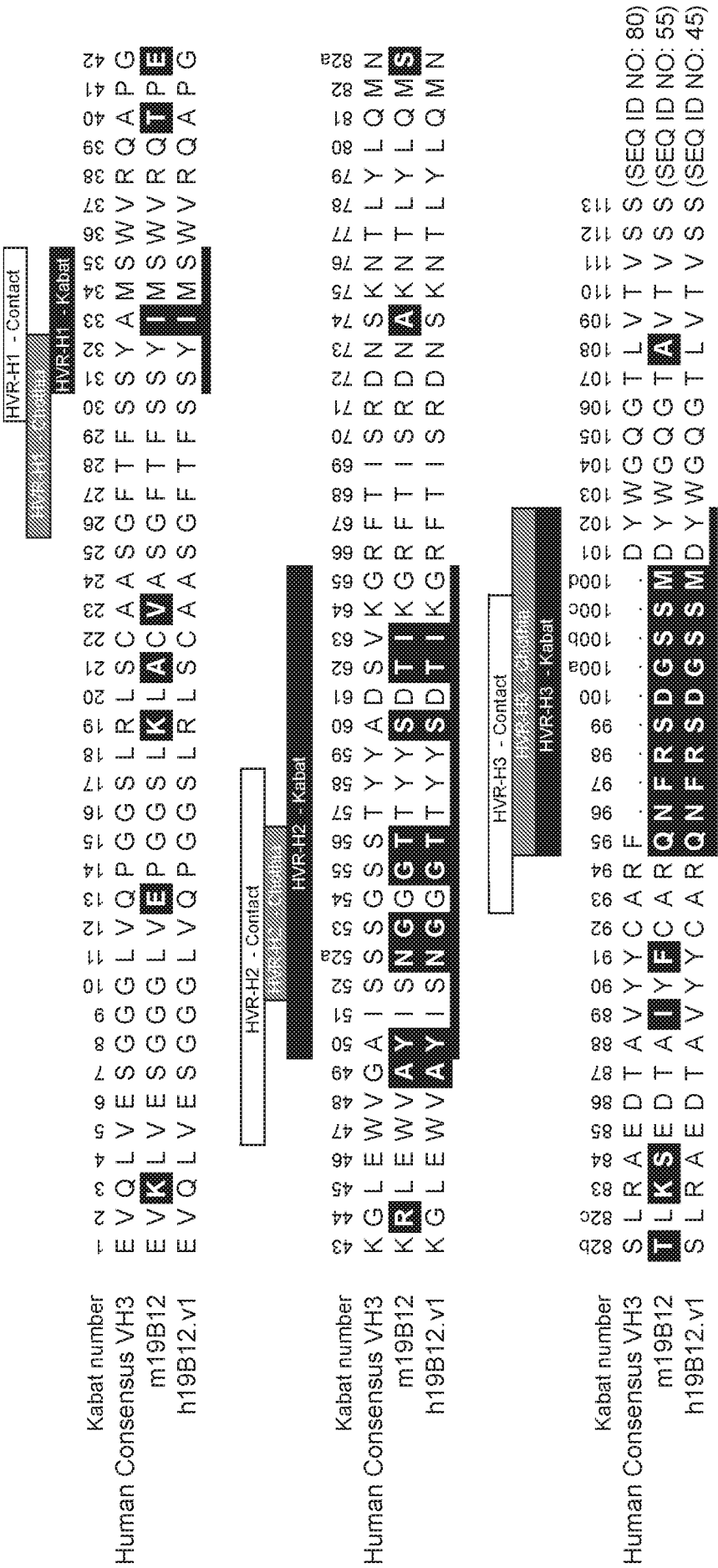


FIG. 16A

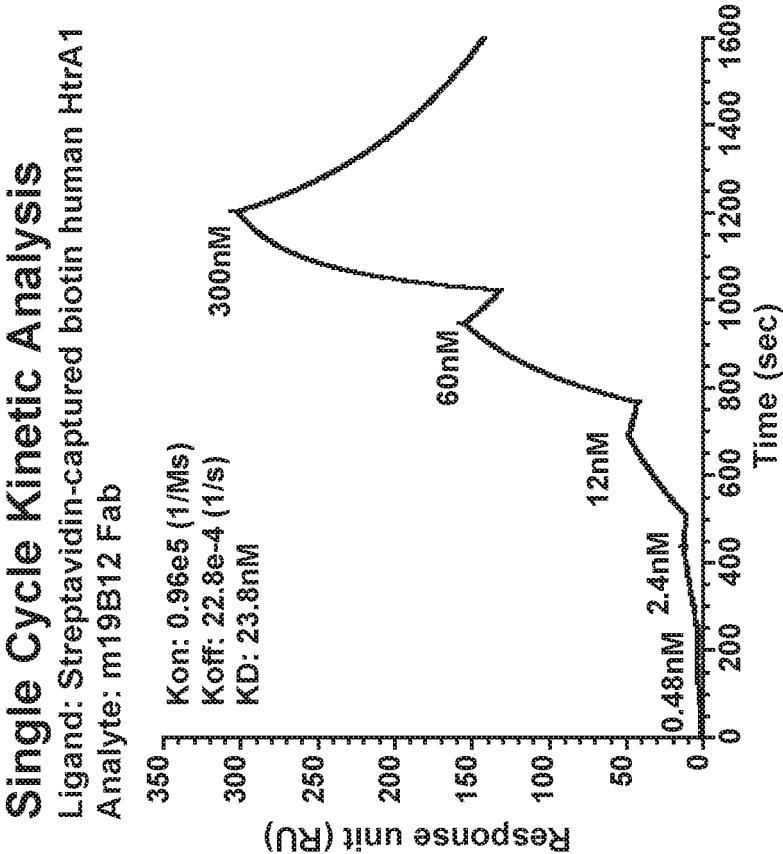


FIG. 16B

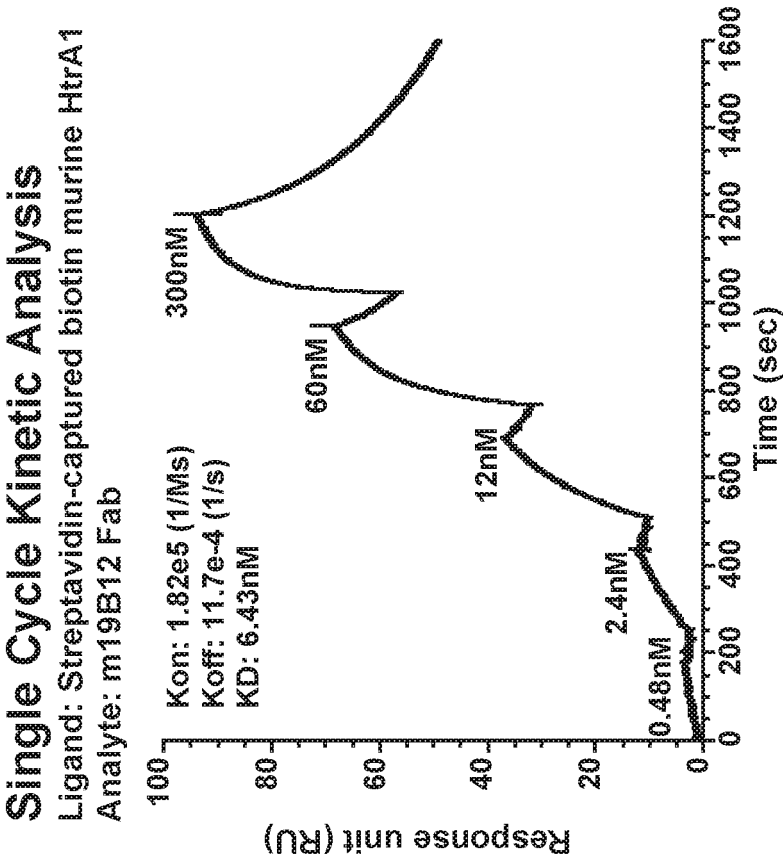


FIG. 16C

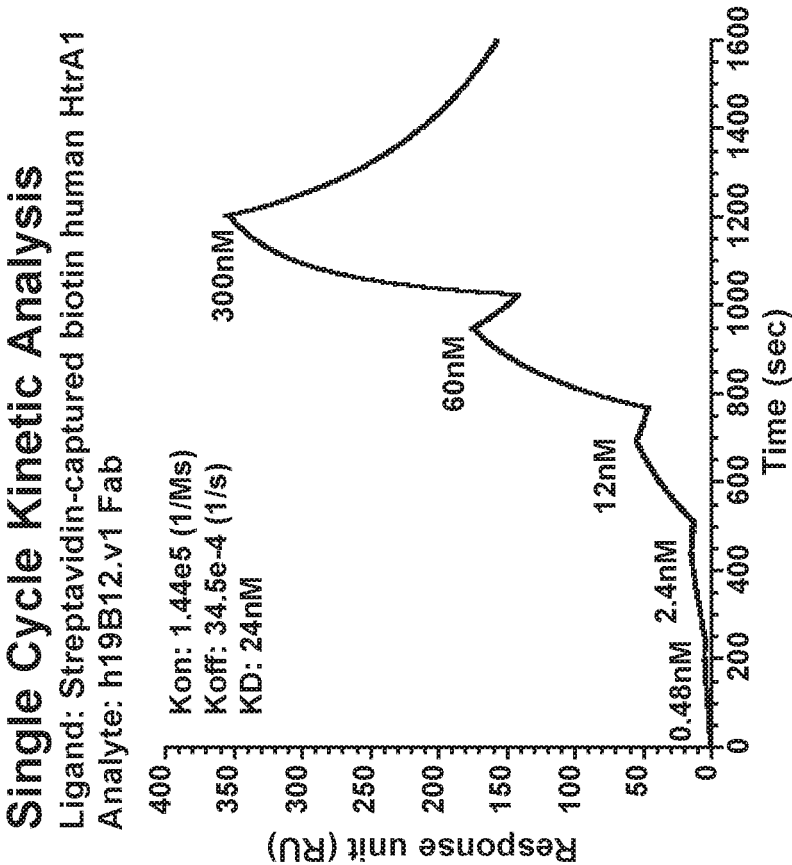


FIG. 16D

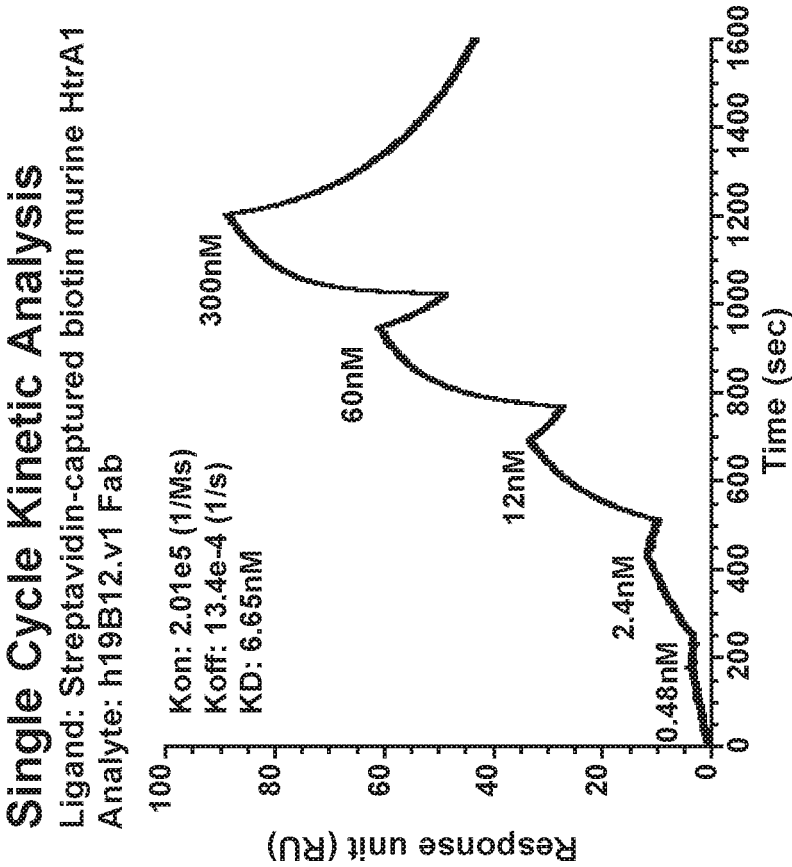


FIG. 17

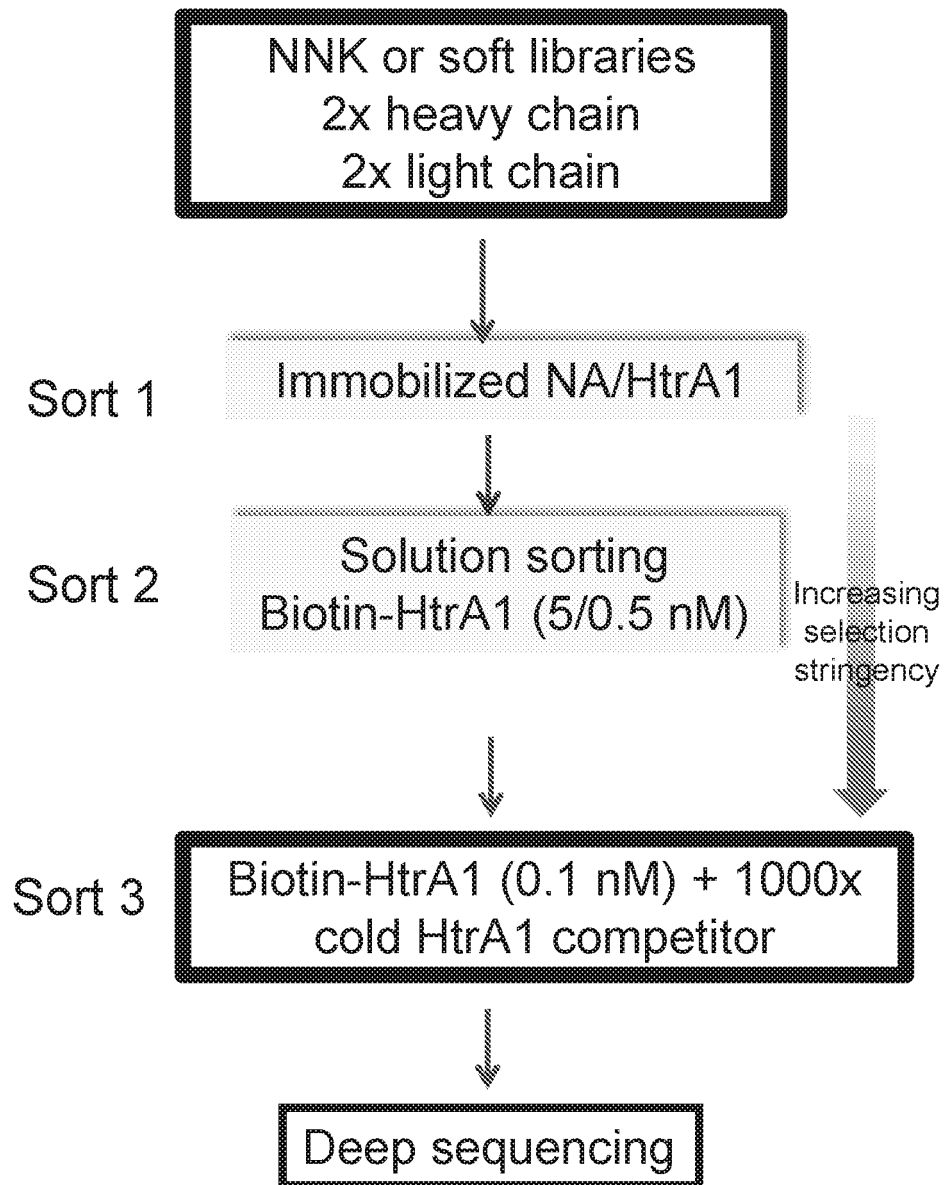


FIG. 18A

LC NNK library heatmap

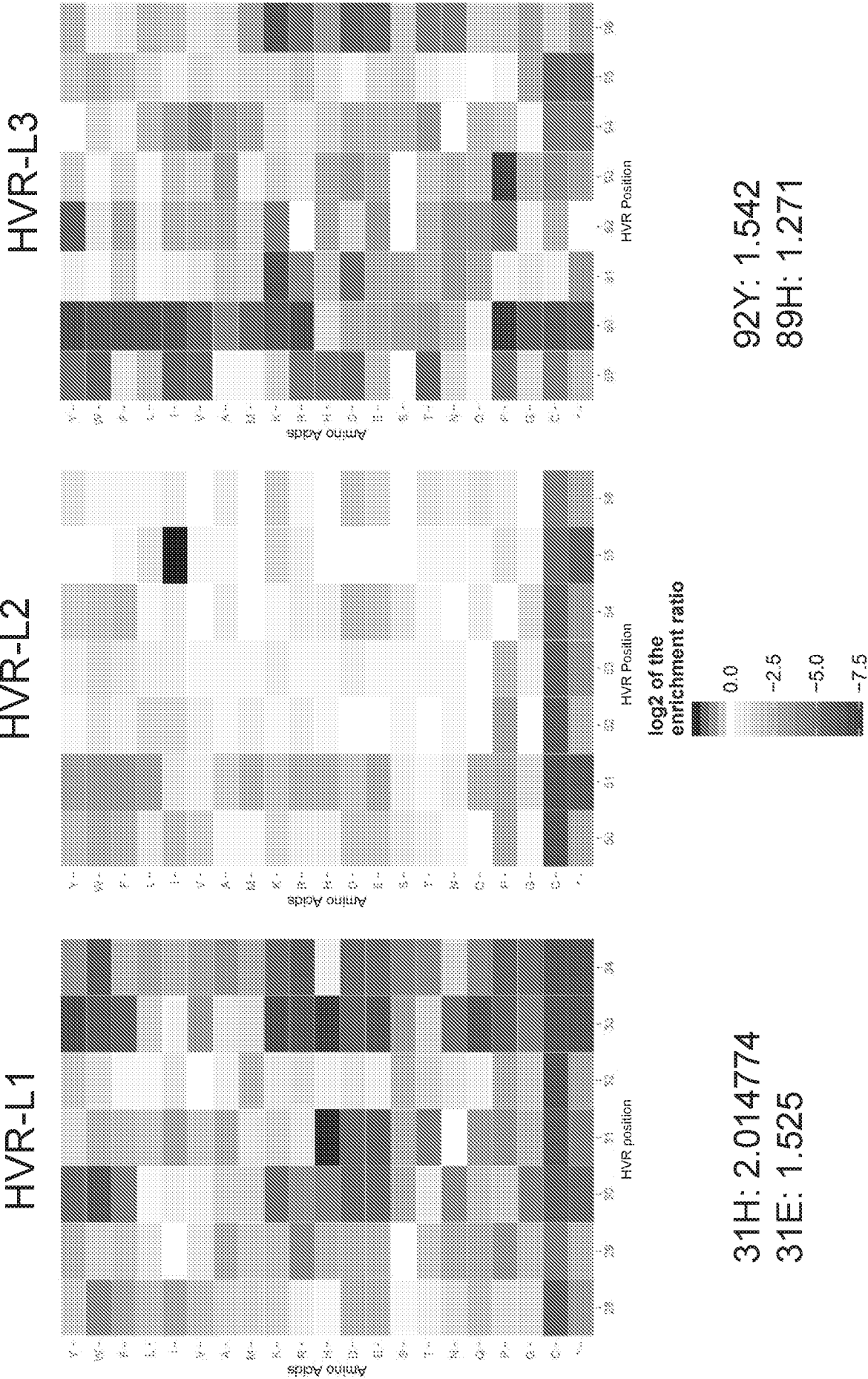


FIG. 18B

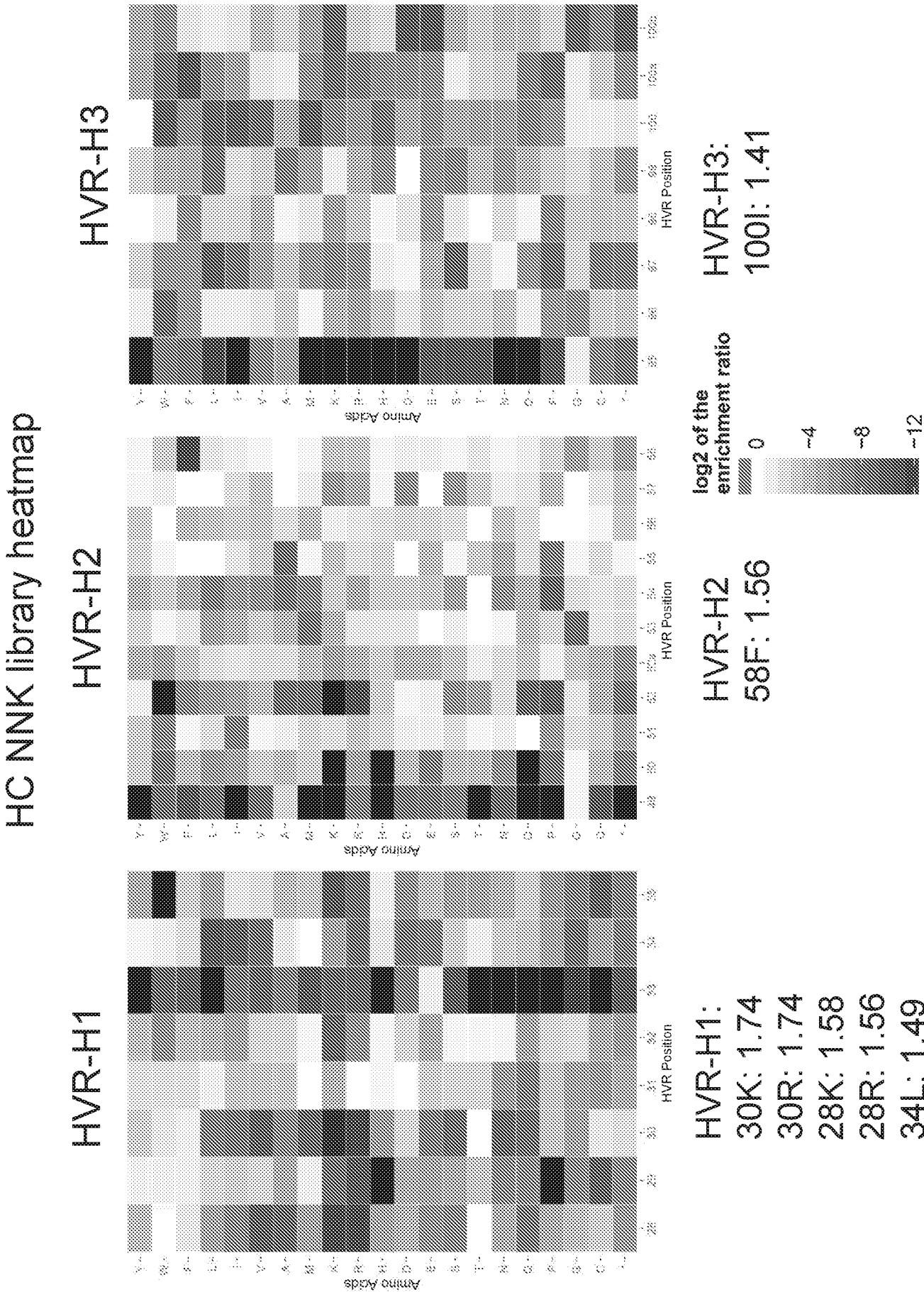


FIG. 19

HC	NNK	soft
30K	x	x
30R	x	
28K	x	x
28R	x	
34L	x	
53A		x
58F	x	x
100I	x	
100aP		x

LC	NNK	soft	NNK epistasis
29R		x	
31H	x		
31E	x	x	
53H		x	
53E		x	
89H	x		
92Y	x		
92K		x	
93I		x	
92K_32V			x

FIG. 20

Sample	k_{on} (1/Ms)	k_{off} (1/s)	KD (M)
LC3.HC3	8.01E+05	4.93E-05	6.16E-11
LC3.HC1	8.85E+05	7.95E-05	8.98E-11
APEG.LC37.HC13	4.31E+05	4.09E-05	9.50E-11
APEG.LC3.HC1	4.28E+05	4.55E-05	1.06E-10
h15H6.v4 (APEG.LC3.HC3)	3.09E+05	3.29E-05	1.06E-10
APEG.LC3.HC2	3.50E+05	4.08E-05	1.17E-10
APEG.LC347.HC13	3.71E+05	4.88E-05	1.31E-10
APEG.LC7.HC1	2.00E+05	2.75E-05	1.37E-10
APEG.LC37.HC23	4.38E+05	6.41E-05	1.46E-10
APEG.LC347.HC23	3.97E+05	6.47E-05	1.63E-10
h15H6.v2	7.22E+05	1.58E-04	2.19E-10
APEG.LC7.HC2	2.13E+05	6.60E-05	3.09E-10
APEG.LC7.HC3	2.39E+05	7.93E-05	3.32E-10
h15H6.v3 (h15H6.v2.APEG)	3.15E+05	1.72E-04	5.46E-10

FIG. 21A

Light chain variable region

Kabat number	HVR-L1 - Contact	HVR-L1 - Chothia	HVR-L1 - Kabat
h15H6.v2	DIQMTQSPSSLSASVGD	DIQMTQSPSSLSASVGD	DIQMTQSPSSLSASVGD
h15H6.v2.APEG	DIQMTQSPSSLSASVGD	DIQMTQSPSSLSASVGD	DIQMTQSPSSLSASVGD
APEG.LC3.HC1	DIQMTQSPSSLSASVGD	DIQMTQSPSSLSASVGD	DIQMTQSPSSLSASVGD
APEG.LC3.HC3	DIQMTQSPSSLSASVGD	DIQMTQSPSSLSASVGD	DIQMTQSPSSLSASVGD
APEG.LC37.HC13	DIQMTQSPSSLSASVGD	DIQMTQSPSSLSASVGD	DIQMTQSPSSLSASVGD
APEG.LC37.HC23	DIQMTQSPSSLSASVGD	DIQMTQSPSSLSASVGD	DIQMTQSPSSLSASVGD
APEG.LC347.HC13	DIQMTQSPSSLSASVGD	DIQMTQSPSSLSASVGD	DIQMTQSPSSLSASVGD
APEG.LC347.HC23	DIQMTQSPSSLSASVGD	DIQMTQSPSSLSASVGD	DIQMTQSPSSLSASVGD

Kabat number	HVR-L2 - Contact	HVR-L2 - Chothia	HVR-L2 - Kabat
h15H6.v2	APKPLISATSNLASGV	APKPLISATSNLASGV	APKPLISATSNLASGV
h15H6.v2.APEG	APKPLISATSNLASGV	APKPLISATSNLASGV	APKPLISATSNLASGV
APEG.LC3.HC1	APKPLISATSNLASGV	APKPLISATSNLASGV	APKPLISATSNLASGV
APEG.LC3.HC3	APKPLISATSNLASGV	APKPLISATSNLASGV	APKPLISATSNLASGV
APEG.LC37.HC13	APKPLISATSNLASGV	APKPLISATSNLASGV	APKPLISATSNLASGV
APEG.LC37.HC23	APKPLISATSNLASGV	APKPLISATSNLASGV	APKPLISATSNLASGV
APEG.LC347.HC13	APKPLISATSNLASGV	APKPLISATSNLASGV	APKPLISATSNLASGV
APEG.LC347.HC23	APKPLISATSNLASGV	APKPLISATSNLASGV	APKPLISATSNLASGV

Kabat number	HVR-L3 - Contact	HVR-L3 - Chothia	HVR-L3 - Kabat
h15H6.v2	TYCQWSSNP	TYCQWSSNP	TYCQWSSNP
h15H6.v2.APEG	TYCQWSSNP	TYCQWSSNP	TYCQWSSNP
APEG.LC3.HC1	TYCQWSSNP	TYCQWSSNP	TYCQWSSNP
APEG.LC3.HC3	TYCQWSSNP	TYCQWSSNP	TYCQWSSNP
APEG.LC37.HC13	TYCQWSSNP	TYCQWSSNP	TYCQWSSNP
APEG.LC37.HC23	TYCQWSSNP	TYCQWSSNP	TYCQWSSNP
APEG.LC347.HC13	TYCQWSSNP	TYCQWSSNP	TYCQWSSNP
APEG.LC347.HC23	TYCQWSSNP	TYCQWSSNP	TYCQWSSNP

(SEQ ID NO: 73)
(SEQ ID NO: 74)
(SEQ ID NO: 22)
(SEQ ID NO: 22)
(SEQ ID NO: 105)
(SEQ ID NO: 105)
(SEQ ID NO: 108)
(SEQ ID NO: 108)

Heavy chain variable region

Kabat number	h15H6.v2	h15H6.v2.APEG	APEG.LC3.HC1	APEG.LC3.HC3	APEGLC37.HC13	APEGLC37.HC23	APEGLC347.HC13	APEGLC347.HC23																											
1	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
2	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
3	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
4	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
5	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
6	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
7	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
8	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
9	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
10	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
11	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
12	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
13	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
14	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
15	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
16	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
17	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
18	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
19	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
20	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
21	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
22	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
23	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
24	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
25	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
26	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
27	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
28	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
29	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
30	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
31	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
32	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
33	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
34	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
35	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
36	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
37	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
38	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
39	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
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41	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G
42	E	V	Q	L	V	Q	S	G	A	E	V	K	V	S	C	K	A	S	G	Y	T	F	T	D	S	E	M	H	W	V	R	Q	A	P	G

Kabat number	h15H6.v2	h15H6.v2.APEG	APEG.LC3.HC1	APEG.LC3.HC3	APEGLC37.HC13	APEGLC37.HC23	APEGLC347.HC13	APEGLC347.HC23																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																		
43	Q	G	L	E	W	I	G	G	V	D	P	E	T	E	G	A	A	Y	N	Q	K	F	K	G	R	A	T	I	T	R	R	D	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S	T	S

FIG. 22A

Affinity Matured Variant	Protein Conc. (μ M)	Protein Conc. (mg/mL)	IC50 Values (nM)					Maximal Inhibition (%)
			N of 1	N of 2	N of 3	Average (nM)	StDev (nM)	
h15H6.v2.APEG (h15H6.v3)	23.25	1.1	0.501	0.421	0.448	0.457	0.04	78.36
APEG.LC3.HC1	7.40	0.35	0.437	0.404	0.482	0.441	0.04	92.72
APEG.LC3.HC2	6.13	0.29	0.422	0.386	0.432	0.413	0.02	90.64
APEG.LC3.HC3 (h15H6.v4)	7.19	0.34	0.402	0.358	0.399	0.386	0.02	93.57
APEG.LC7.HC1	6.34	0.3	0.415	0.582	0.506	0.501	0.08	92.64
APEG.LC7.HC2	6.34	0.3	0.419	0.559	0.447	0.475	0.07	87.82
APEG.LC7.HC3	6.55	0.31	0.377	0.539	0.456	0.457	0.08	93.71
APEG.LC37.HC13	6.13	0.29	0.539	0.633	0.612	0.595	0.05	87.02
APEG.LC37.HC23	5.07	0.24	0.556	0.441	0.522	0.506	0.06	94.69
APEG.LC347.HC13	5.49	0.26	0.584	0.544	0.578	0.569	0.02	95.03
APEG.LC347.HC23	6.55	0.31	0.594	0.517	0.561	0.557	0.04	94.97
h15H6.v2	6.13	0.29	0.394	0.414	0.374	0.394	0.02	82.44
LC3.HC1	5.07	0.24	0.442	0.492	0.424	0.453	0.04	92.09
LC3.HC3	5.28	0.25	0.448	0.460	0.356	0.421	0.06	96.34

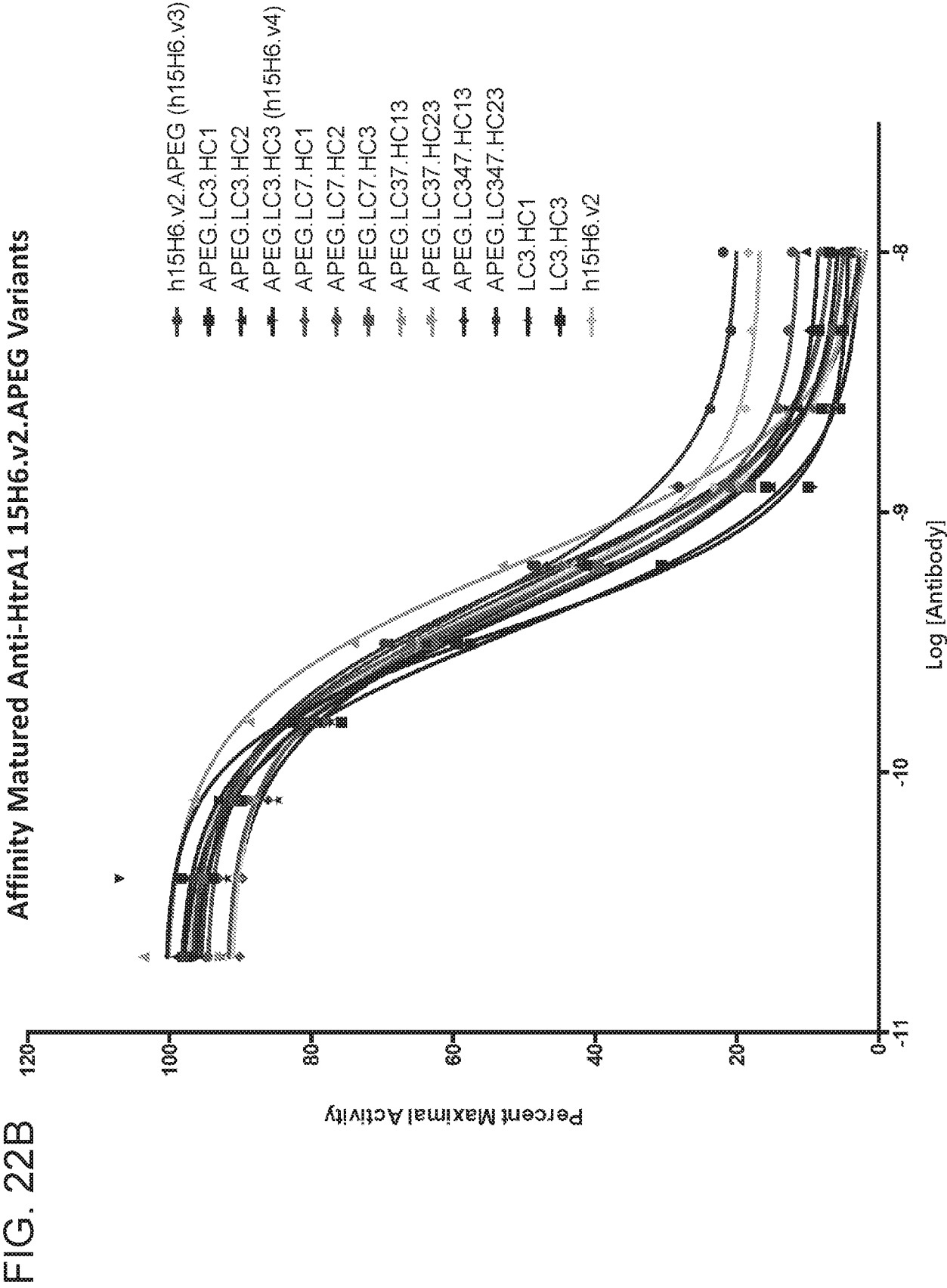


FIG. 23A

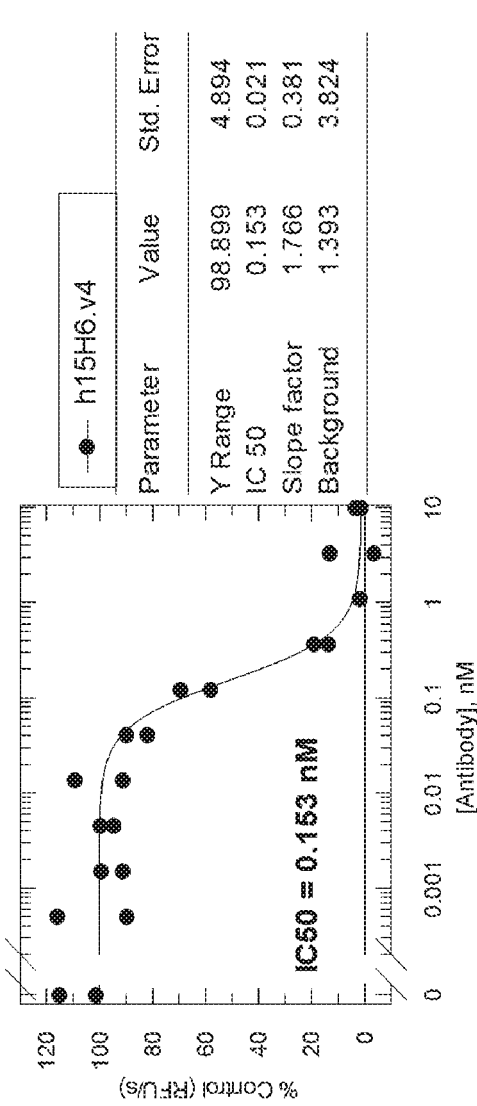
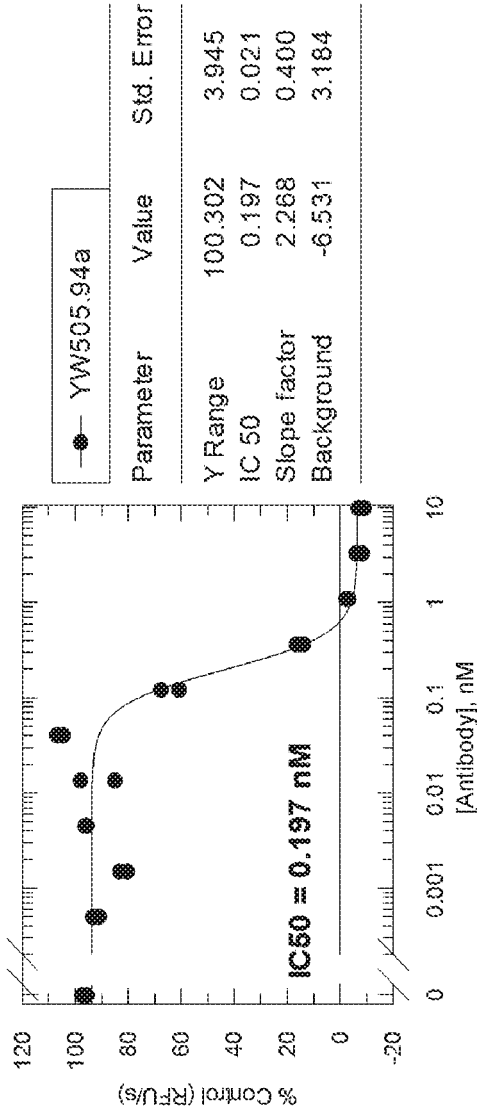
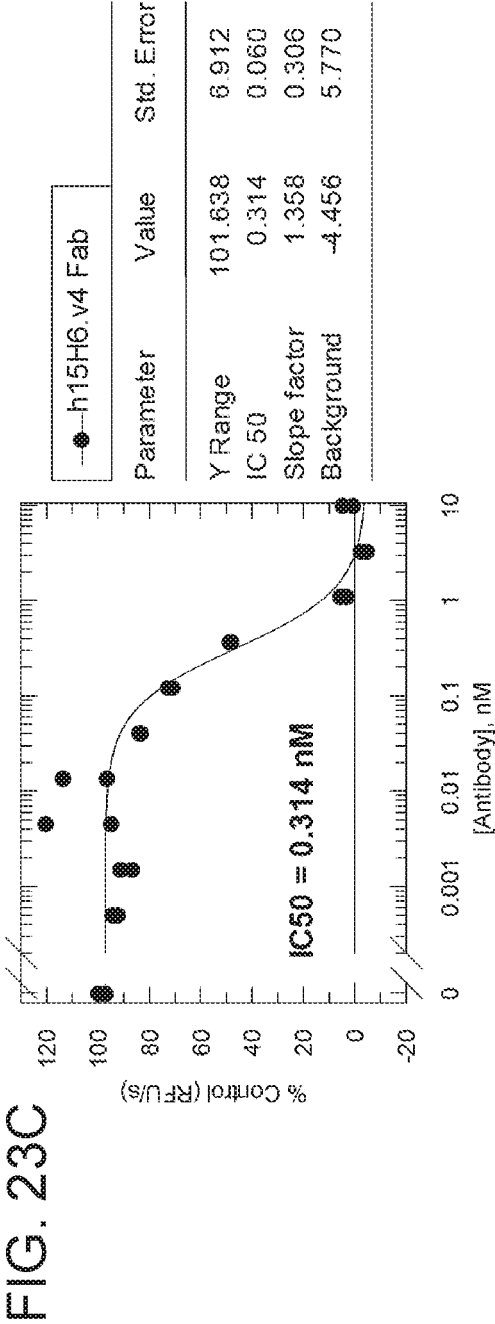
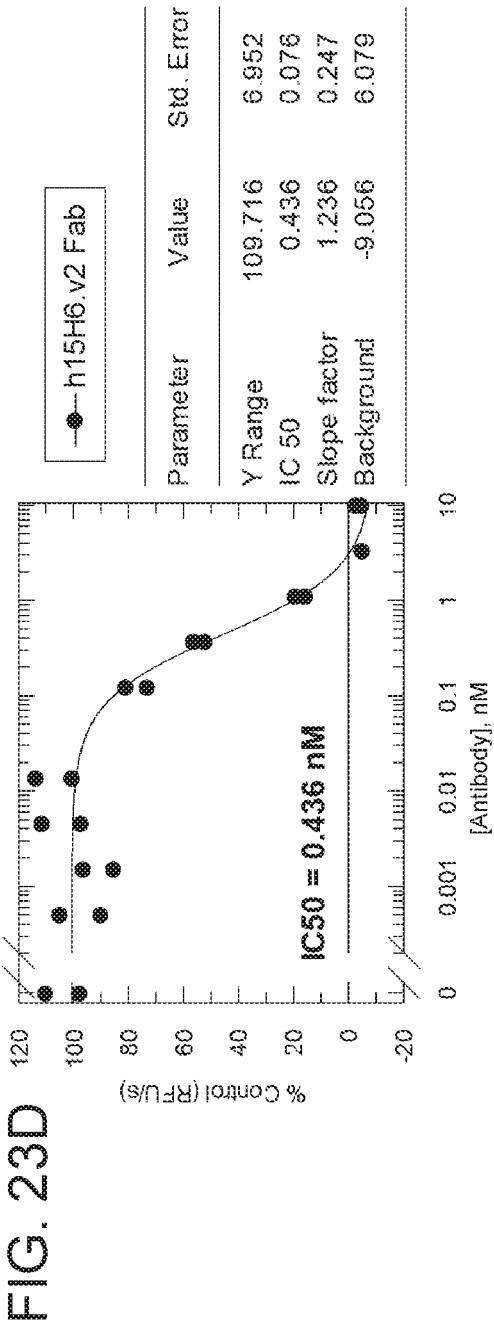
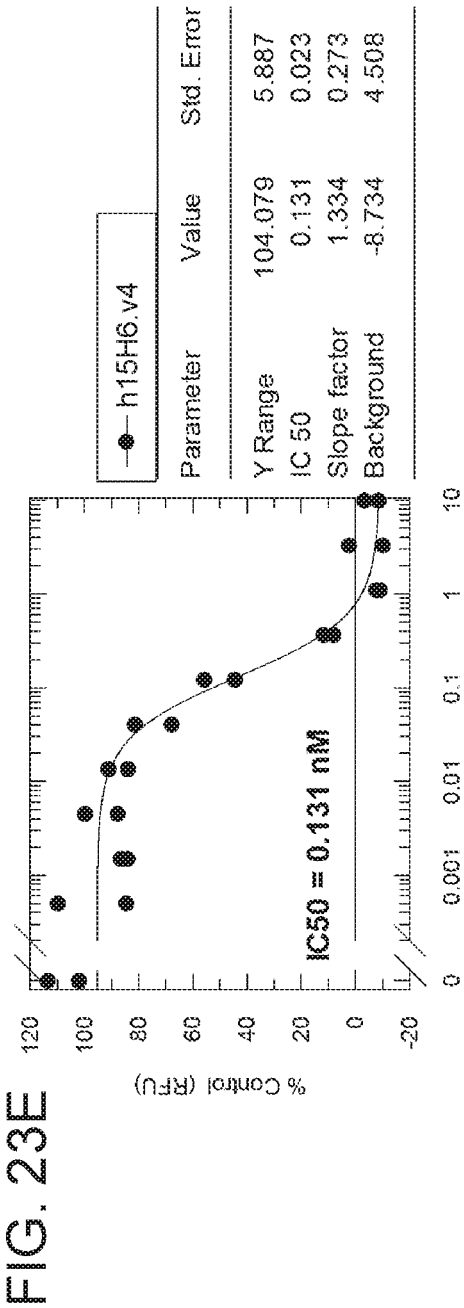
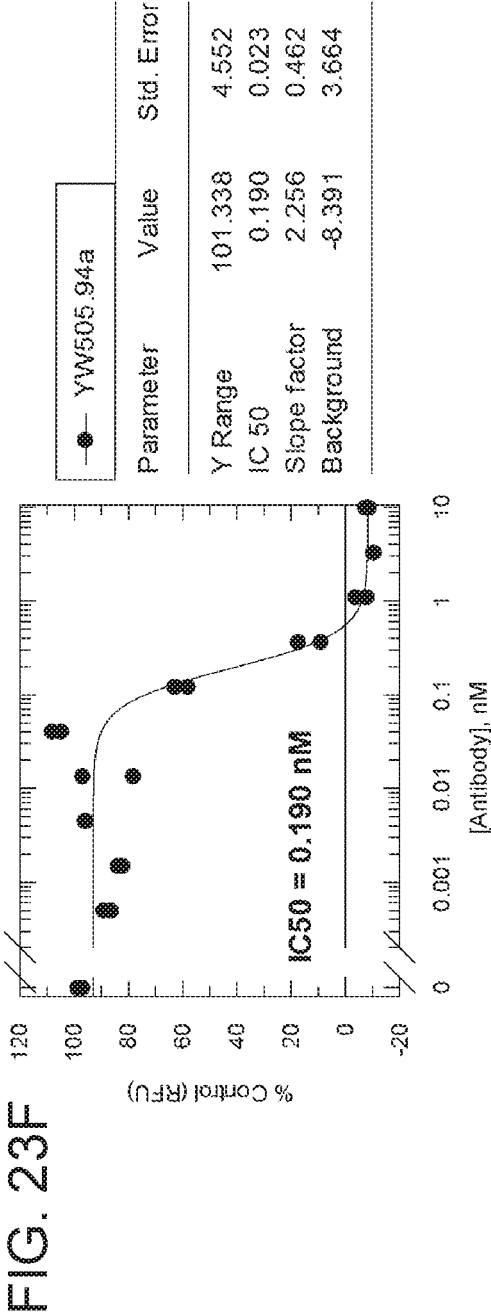


FIG. 23B







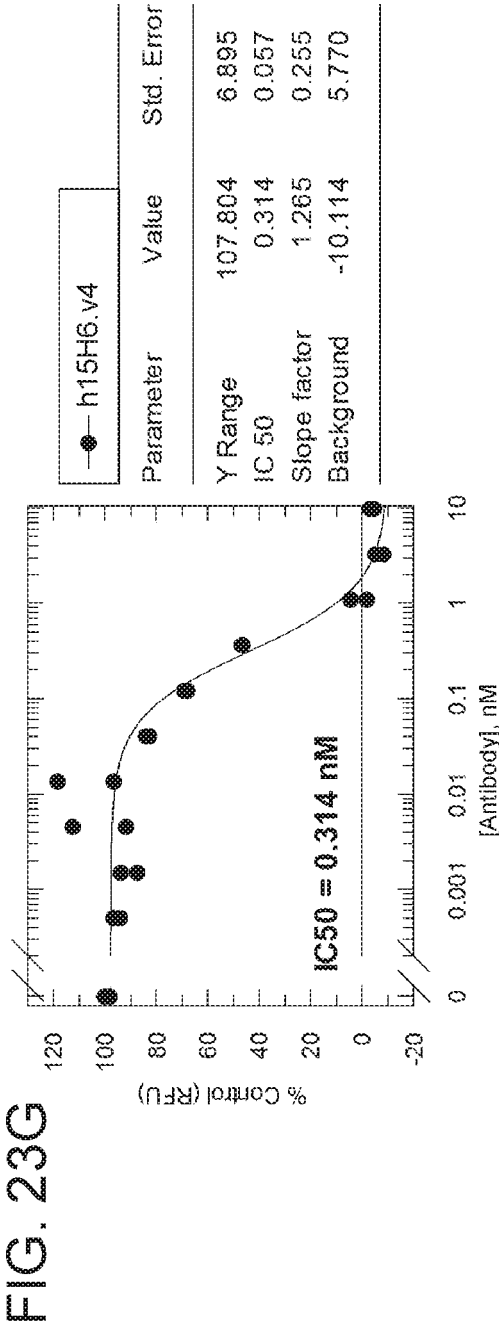
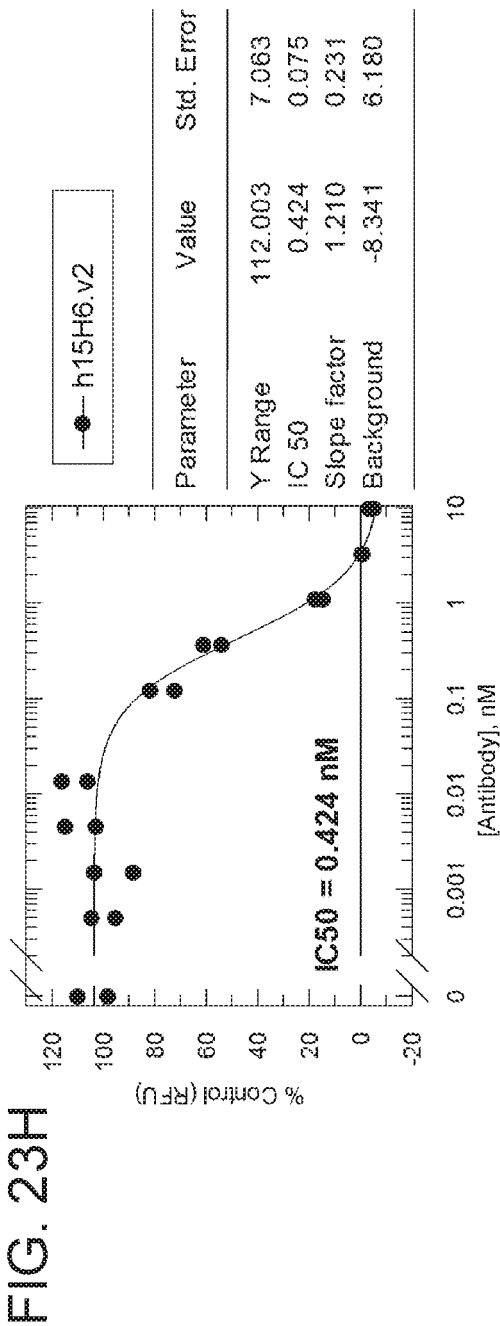


FIG. 24A

Antibody	analysis	I		II		III		IC50 mean	StDev	CV%
		IC50 (nM)	slope	IC50 (nM)	slope	IC50 (nM)	slope			
h15H6.v4										
mAb	RFU/s	0.153	1.77	0.133	1.36	0.077	1.56	0.121	0.039	33%
YW505.94a										
mAb	RFU/s	0.197	2.27	0.063	1.23	0.111	1.42	0.124	0.068	55%
h15H6.v4										
Fab	RFU/s	0.314	1.36	0.316	1.63	0.233	1.63	0.288	0.047	16%
h15H6.v2										
Fab	RFU/s	0.436	1.24	0.271	1.19	0.304	1.74	0.337	0.087	26%

40/50

FIG. 24B

Antibody	analysis	I		II		III		IC90 mean	StDev	CV%
		IC90 (nM)	slope	IC90 (nM)	slope	IC90 (nM)	slope			
h15H6.v4										
mAb	RFU/s	0.529433591	1.77	0.66911466	1.360.314908687	1.56	1.56	0.504	0.178	35%
YW505.94a										
mAb	RFU/s	0.518605807	2.270.375965044	1.230.521584583	1.42	1.42	0.472	0.083	0.083	18%
h15H6.v4										
Fab	RFU/s	1.579714309	1.361.216499501	1.630.896975898	1.63	1.63	1.231	0.342	0.342	28%
h15H6.v2										
Fab	RFU/s	2.564701939	1.241.717329984	1.191.074703885	1.74	1.74	1.786	0.747	0.747	42%

FIG. 25A

IC50's from 4-parameter fits:									
Antibody	analysis	IV		V		VI		StDev	CV%
		IC50 (nM)	slope	IC50 (nM)	slope	IC50 (nM)	slope		
	RFU/s	0.102	1.49	0.172	1.56	0.208	1.28	0.054	34%
h15H6.v4 Fab	RFU	0.066	0.765	0.149	0.912	0.194	1.3	0.065	48%

FIG. 25B

IC90's calculated from the IC50's and slopes of the above fits:

Antibody	analysis	IV		V		VI		StDev	CV%
		IC90 (nM)	slope	IC90 (nM)	slope	IC90 (nM)	slope		
	RFU/s	0.446	1.49	0.703	1.56	1.158	1.28	0.360	47%
h15H6.v4 Fab	RFU	1.167	0.765	1.658	0.912	1.052	1.3	0.322	25%

FIG. 26A

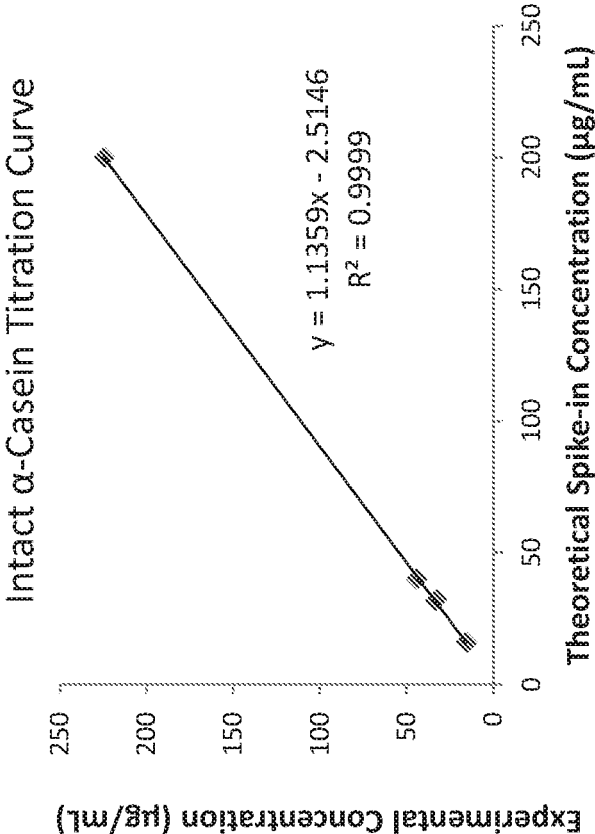


FIG. 26B

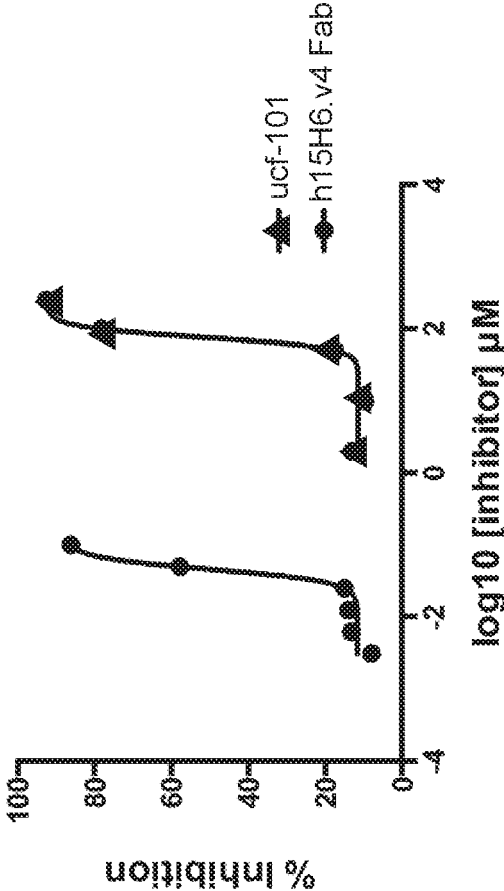


FIG. 27A

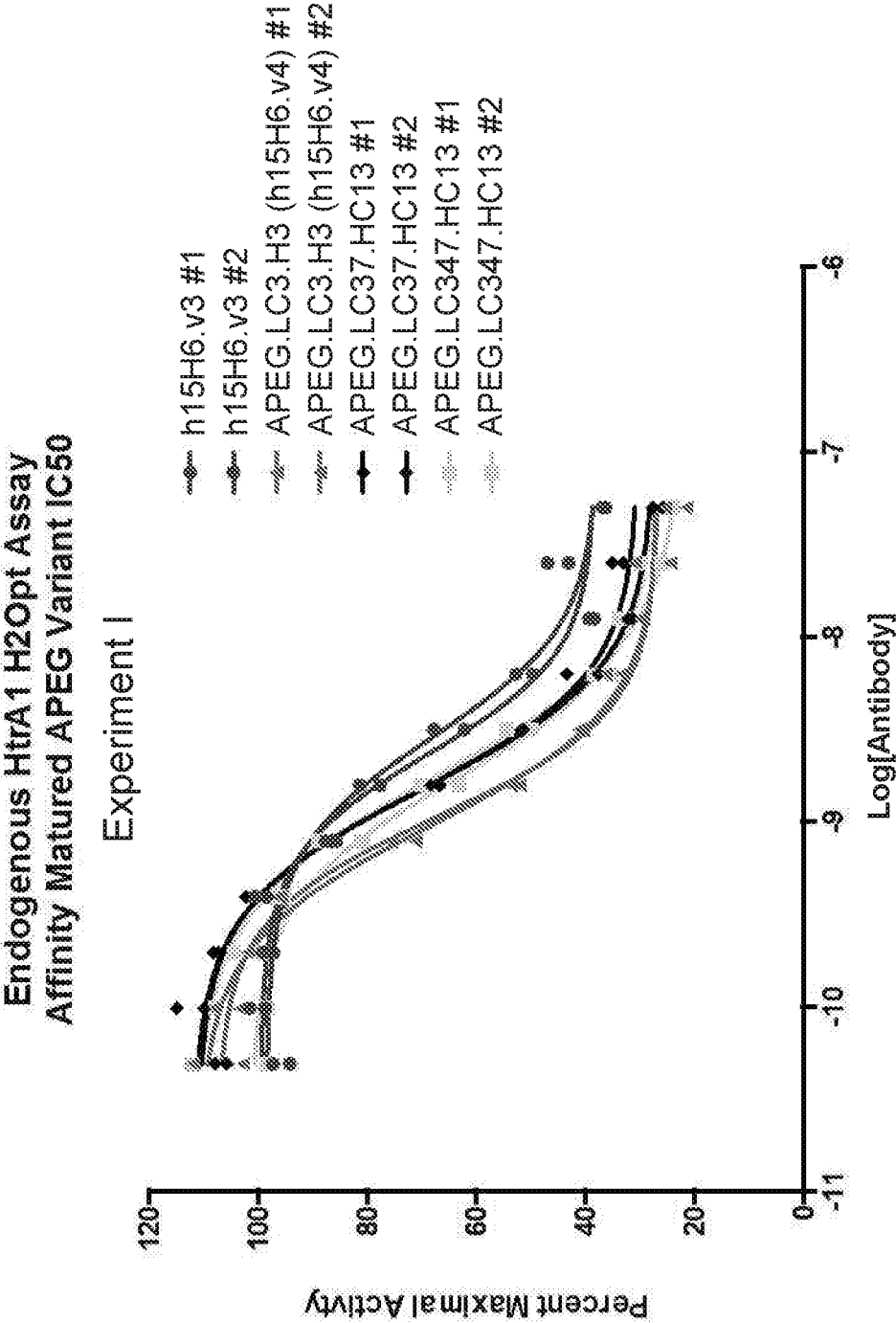


FIG. 27B

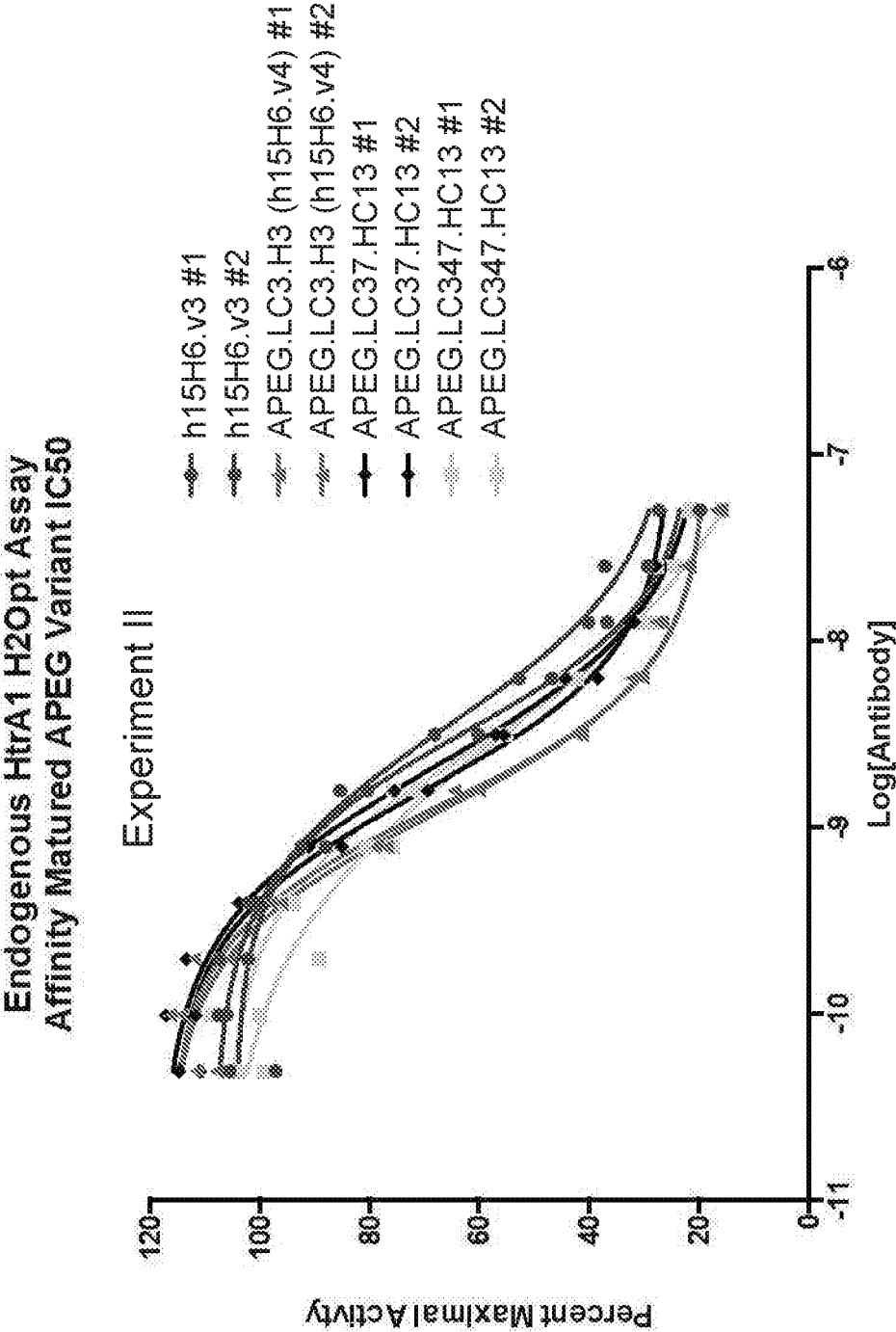


FIG. 27C

Anti-HtrA1 Affinity Matured Variants
Endogenous HtrA1 Activity Assay IC50

Affinity Matured Variant	IC50					Maximal Inhibition (%)		
	Expt. I	Expt. II	Average (nM)	StDev (nM)	Expt. I	Expt. II	Average (%)	StDev (%)
h15H6.v2.APEG (h15H6.v3)	2.571	3.33	2.9505	0.54	76.41	63.39	69.9	9.21
APEG.LC3.HC3 (h15H6.v4)	1.004	1.246	1.125	0.17	83.49	76.67	80.08	4.82
APEG.LC37.HC13	1.4815	1.822	1.65175	0.24	76.5	73.27	74.885	2.28
APEG.LC347.HC3	1.7225	2.8415	2.282	0.79	81.26	75.79	78.525	3.87

FIG. 28

Sample	k_{on} (1/Ms)	k_{off} (1/s)	KD (M)	IC50 FRET (nM)	StDev	IC90 FRET (nM)	StDev	Max inhibition
h15H6.v2	7.22E+05	1.58E-04	2.19E-10	0.44	0.08	1.87	0.66	91
h15H6.v3	3.15E+05	1.72E-04	5.46E-10	0.41	0.12	2.77	2.07	77
h15H6.v3 cyno	4.05E+05	2.30E-04	5.67E-10	n.d.	n.d.	n.d.	n.d.	n.d.
h15H6.v4	3.09E+05	3.29E-05	1.06E-10	0.30	0.10	1.19	0.04	100
YW505.94a.28	1.69E+06	5.74E-03	3.40E-9	0.52	0.03	2.73	0.93	100

FIG. 29A

Human HtrA1

mqjpraallp|lllllaapasaQLSRAGRSAPLAAGCPDRCEPARCPPQPEHCEGGRARDACGCCE
 VCGAPEGAAACGLQEGPCGEGLCQCVVPFGVPASATVRRRAQAAGLCVCASSEPVCGSDA
 NTYANLCQLRAASRRSERLHRPPVIVLQRGACGQGEDPNSLRHKYNFIADVVEKIAP
AVVHIELRKLPEFSKREVPVASGSGFIVSEDLIVTNAHVVTNKHVRVKVELKNGATYE
AKIKDVDEKADIALIKIDHQGLPVLILGRSSELRPGFEVVAIGSPFSLQNTVTTIGIVSTI
QRGKELGLRNSDMDYIOTDAIINYGNSSGGLVNL DGEVIGINTLKVTAGISFAIPSDKI
KKFLETESHDRQAKGKAVTKKKYIGIRMMSLTSSKAKELKDRHRDFPDVLSGAYHIEVIPD
 TPAEAGGLKENDVIISINGQSVVSANDVSDVIKRESTLNMVVRRGNEDIMITVPIEIDP (SEQ ID NO:121)

FIG. 29B

Murine HtrA1

mqslrtllsl|lllllaapsla|PSGTGRSAPAAATVCPEHCDPTRCAPPTDCEGGRVDRDACGCCVC
 GALEGAACGLQEGPCGEGLCQCVVPFGVPASATVRRRAQAAGLCVCASSEPVCGSDAKT
 YTNLCQLRAASRRSEKLRQPPVIVLQRGACGQGEDPNSLRHKYNFIADVVEKIAPAV
VHIELYRKLPEFSKREVPVASGSGFIVSEDLIVTNAHVVTNKNRVKVELKNGATYEAKI
KDVDEKADIALIKIDHQGLPVLILGRSSELRPGFEVVAIGSPFSLQNTVTTIGIVSTIQR
GGKELGLRNSDMDYIOTDAIINYGNSSGGLVNL DGEVIGINTLKVTAGISFAIPSDKIKK
FLTESHDRQAKGKAVTKKKYIGIRMMSLTSSKAKELKDRHRDFPDVLSGAYHIEVIPDT
 PAEAGGLKENDVIISINGQSVVTANDVSDVIKKENTLNMVVRRGNEDIVITVPIEIDP (SEQ ID NO:155)

FIG. 30

VL Domain

WT DIQVTQSPSSLSASVGDRTITCITSTIDIDDMNYQKPKVPKLLISGNTLRPGVPSRFSGSGTFTLTISSLQP
 TM DIQVTQSPSSLSASVGDRTITCITSTIDIESDMNYQKPKVPKLLISGNTLRPGVPSRFSGSGTFTLTISSLQP
 TM.D92E DIQVTQSPSSLSASVGDRTITCITSTIDIESDMNYQKPKVPKLLISGNTLRPGVPSRFSGSGTFTLTISSLQP
 S1ESD DIQVTQSPSSLSASVGDRTITCITSTISIESDMNYQKPKVPKLLISGNTLRPGVPSRFSGSGTFTLTISSLQP
 S1ESD.N103S DIQVTQSPSSLSASVGDRTITCITSTISIESDMNYQKPKVPKLLISGNTLRPGVPSRFSGSGTFTLTISSLQP

WT EDVATYYCLOSDELPTTFGQGTKEIK (SEQ ID NO: 120)
 TM EDVATYYCLOSDELPTTFGQGTKEIK (SEQ ID NO: 133)
 TM.D92E EDVATYYCLOSDELPTTFGQGTKEIK (SEQ ID NO: 134)
 S1ESD EDVATYYCLOSDELPTTFGQGTKEIK (SEQ ID NO: 135)
 S1ESD.N103S EDVATYYCLOSDELPTTFGQGTKEIK (SEQ ID NO: 135)

VH Domain

WT EVQLVQSGPELKKPGASVYVSCKASGYTFITNYGMNWVQAPOQGLEWMGWINTYTGETTYADDFKGRFVFSLDTSVSTAY
 TM EVQLVQSGPELKKPGASVYVSCKASGYTFITNYGMNWVQAPOQGLEWMGWINTYTGETTYADDFKGRFVFSLDTSVSTAY
 TM.D92E EVQLVQSGPELKKPGASVYVSCKASGYTFITNYGMNWVQAPOQGLEWMGWINTYTGETTYADDFKGRFVFSLDTSVSTAY
 S1ESD EVQLVQSGPELKKPGASVYVSCKASGYTFITNYGMNWVQAPOQGLEWMGWINTYTGETTYADDFKGRFVFSLDTSVSTAY
 S1ESD.N103S EVQLVQSGPELKKPGASVYVSCKASGYTFITNYGMNWVQAPOQGLEWMGWINTYTGETTYADDFKGRFVFSLDTSVSTAY

WT LQISSIKAEQTAVYYCEREQGVNHWGQGLVTVS (SEQ ID NO: 119)
 TM LQISSIKAEQTAVYYCEREQGVNHWGQGLVTVS (SEQ ID NO: 131)
 TM.D92E LQISSIKAEQTAVYYCEREQGVNHWGQGLVTVS (SEQ ID NO: 131)
 S1ESD LQISSIKAEQTAVYYCEREQGVNHWGQGLVTVS (SEQ ID NO: 131)
 S1ESD.N103S LQISSIKAEQTAVYYCEREQGVNHWGQGLVTVS (SEQ ID NO: 132)

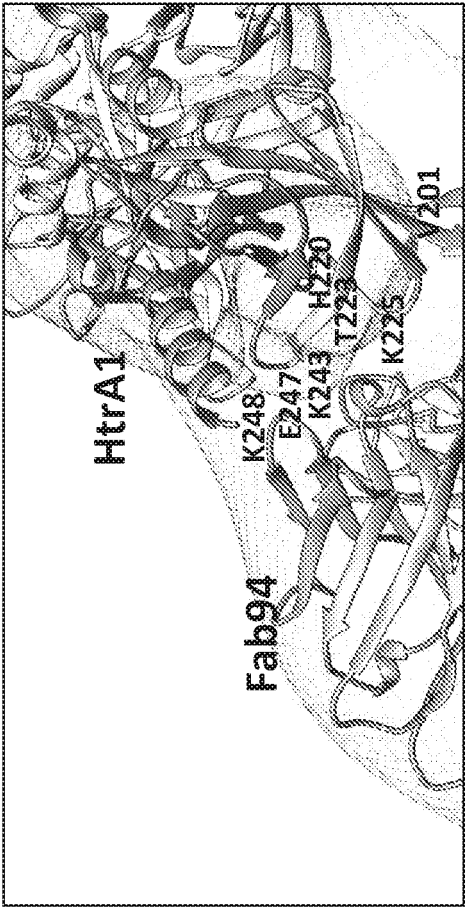


FIG. 31A



FIG. 31B

FIG. 32A

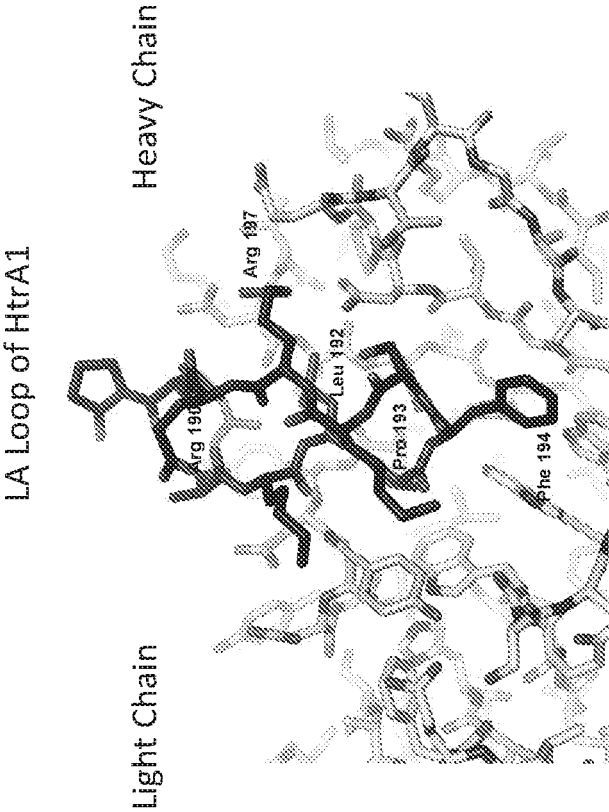


FIG. 32B

