Figure 1

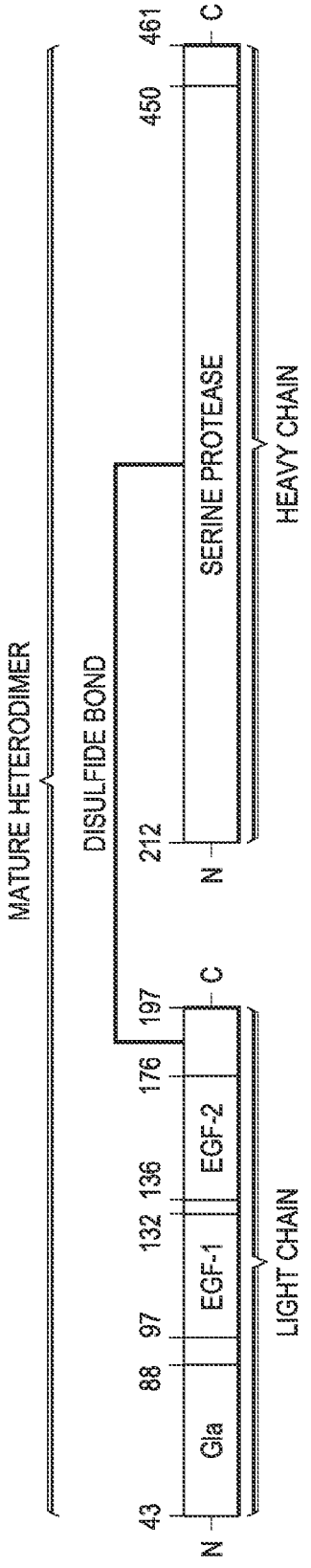

MATURE HETERODIMER
DISULFIDE BOND
N
43
Gla
88
97
EGF-1
132
136
EGF-2
176
197
C
LIGHT CHAIN
N
212
SERINE PROTEASE
450
461
C
HEAVY CHAIN

Figure 2

HEAVY CHAIN		HCDR1	HCDR2	HCDR3
C717 HEAVY CHAIN	46	ASGFTFGNHWMTWVRQAPGKGLEWVSGVSWNGSRTHYADSVK		GRFTISRDNSKNTLYLQMNSLRAEDTAVYYCALTGRSGWMRFPNWFDPWGQO
C7A23 HEAVY CHAIN	46	ASGFTFGNHWMTWVRQAPGKGLEWVSGVSWNGSRTHYADSVK		GRFTISRDNSKNTLYLQMNSLRAEDTAVYYCALTGRSGWMRFPNWFDPWGQO
T46J23 HEAVY CHAIN	46	ASGFTFGNHWMTWVRQAPGKGLEWVSGVSWNGSRTHYADSVK		GRFTISRDNSKNTLYLQMNSLRAEDTAVYYCALTGRSGWMRFPNWFDPWGQO
C22J13 HEAVY CHAIN	46	ASGFTFSSNYMSWVRQAPGKGLEWVAVISYDGSNKYYADSVK		GRFTISRDNSKNTLYLQMNSLRAEDTAMYYCALTGRSGWMRFPNWFDPWGQO
C25K23 HEAVY CHAIN	46	ASGFTFSSYWMSWVRQAPGKGLEWVSGVSWNGSRTHYADSVK		GRFTISRDNSKNTLYLQMNSLRAEDTAVYYCALTGRSGWMRFPNWFDPWGQO
C26B9 HEAVY CHAIN	46	ASGFTFSSYGMHWVRQAPGKGLEWVSVIYS-GGSTYYADSVK		GRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARMG-----RAFDIWGQO
03E7 HEAVY CHAIN	46	ASGFTFSSYSMNWVRQAPGKGLEWVSAISGSGGSTYYADSVK		GRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDRRV--RGIYDAFDMWGQO
T46P19 HEAVY CHAIN	46	ASGFTFSGYGMHWVRQAPGKGLEWVSGINWNGGSTGYADSVK		GRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARNRAT--RSGYYYFDSWGQO
R41C17 HEAVY CHAIN	46	ASGFTFSNYAMSWVRQSPGKGLEWVAVISYDGREKYYSDSVK		GRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDRG-----RTFDYWGQO
R41E3 HEAVY CHAIN	46	ASGFTFNNYAMTWVRQAPGKGLEWVSGVSWNGSRTHYADSVK		GRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARADSSSAGRWAGSLDYWGQO

Figure 2

LIGHT CHAIN		LCDR1	LCDR2	LCDR3
C717 LIGHT CHAIN	17	TISCTGSSSNIGAGYDVHWYQQLPGTAPKLLIYGNSNRPSGVPD		RFSGSKSGTSASLAISGLRSEDEAAYYCSSYVGSDL---VVFGGGTKI
C7A23 LIGHT CHAIN	17	TISCSGSSSNIGN-NYVSWYQQLPGTAPKLLIYRNNQRPSGVPD		RFSGSKSGTSASLAISGLRSEDEADYYCQSYDSDLSGPYVLFGGGTKI
T46J23 LIGHT CHAIN	16	TISCTGTSSNIGAGYDVHWYQQLPGTAPKLLIYDNNNRPSGVPD		RFSGSKSGTSASLAISGLRSEDEADYYCAAWDDSLNG--VVFGGGTKI
C22J13 LIGHT CHAIN	17	TISCSGSDSNIGS-NAVNWYQQLPGTAPKLLIYDNNKRPSGVPD		RFSGSKSGTSASLAISGLRSEDEADYYCSSYTSSNT---VVFGGGTKI
C25K23 LIGHT CHAIN	17	TISCTGSSSNIGAAYDVHWYQQLPGTAPKLLIYGNNKRPSGVPD		RFSGSKSGTSASLAISGLRSEDEADYYCQSYDSSLSG--SVFGGGTKI
C26B9 LIGHT CHAIN	17	TISCSGSSSNIRS-NTVNWYQQLPGTAPKLLIYGNSNRPSGVPD		RFSGSKSGTSASLAISGLRSEDEADYYCQSYDSSLSG-DVVFGGGTKI
03E7 LIGHT CHAIN	17	TISCTGSSSNIGAGFDVHWYQQLPGTAPKLLIYGNSNRPSGVPD		RFSGSKSGTSASLAISGLRSEDEADYYCATWQDTLTG--WMFGGGTKI
T46P19 LIGHT CHAIN	16	TISCTGSSSNIGAGYDVHWYQQLPGTAPKLLIYGNINRPSGVPD		RFSGSKSGTSASLAISGLRSEDEADYYCSSYTRSAT---LVFGGGTKI
R41C17 LIGHT CHAIN	16	TISCTGSSSNIGAGYVVHWYQQLPGTAPKLLIYRNNHRPSGVPD		RFSGSKSGTSASLAISGLRSEDEADYYCAAWDDSLNG--RVFGGGTKI
R41E3 LIGHT CHAIN	16	TISCSGSSSNIGN-NAVNWYQQLPGTAPKLLIYSNNQRPSGVPD		RFSGSKSGTSASLAISGLRSEDEADYYCSSYTSSST H--VVFGGGTKI

Figure 3

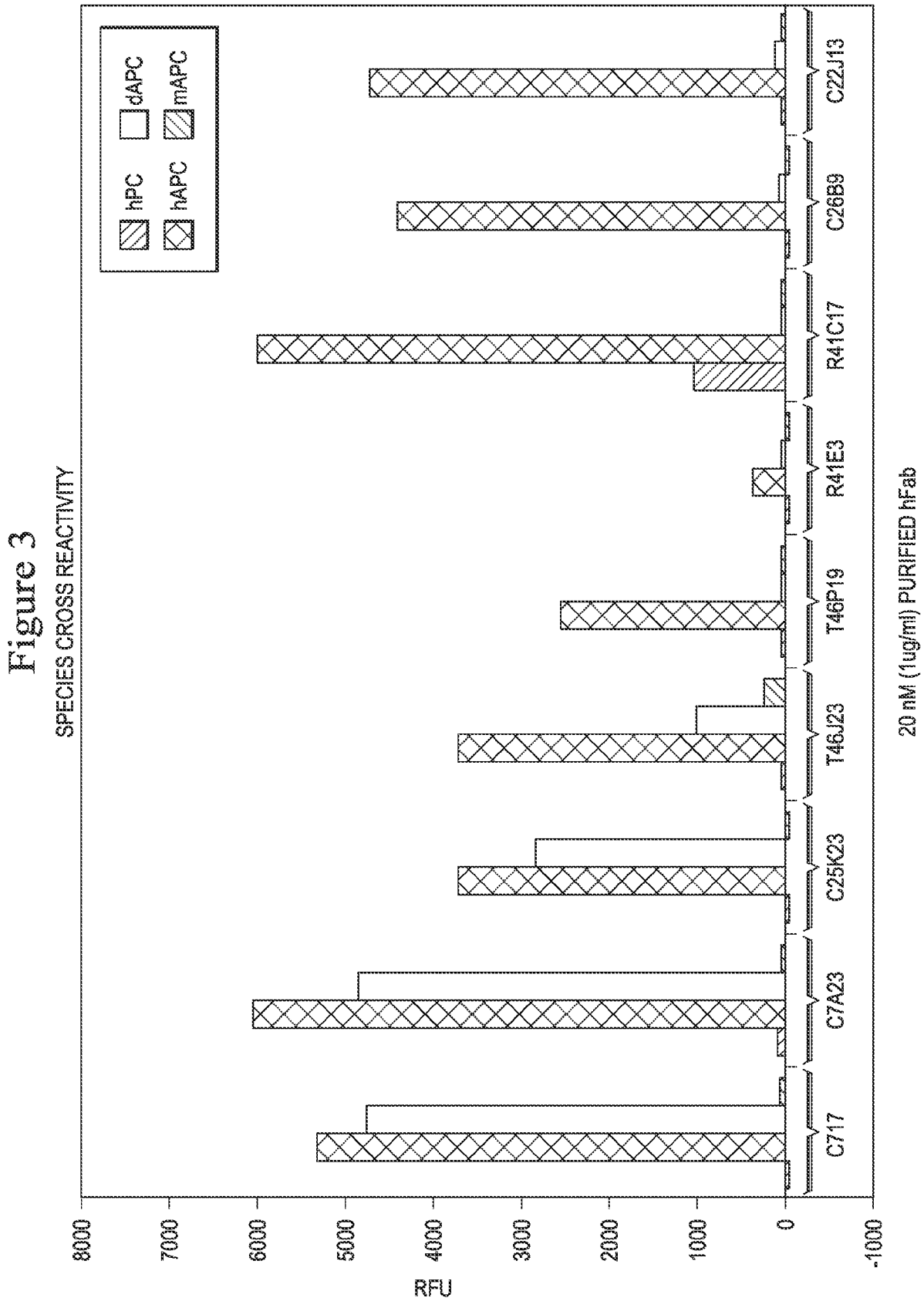

SPECIES CROSS REACTIVITY
hPC
dAPC
hAPC
mAPC
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
RFU
C717
C7A23
C25K23
T46J23
T46P19
R41E3
R41C17
C26B9
C22J13
20 nM (1ug/ml) PURIFIED hFab

Figure 4

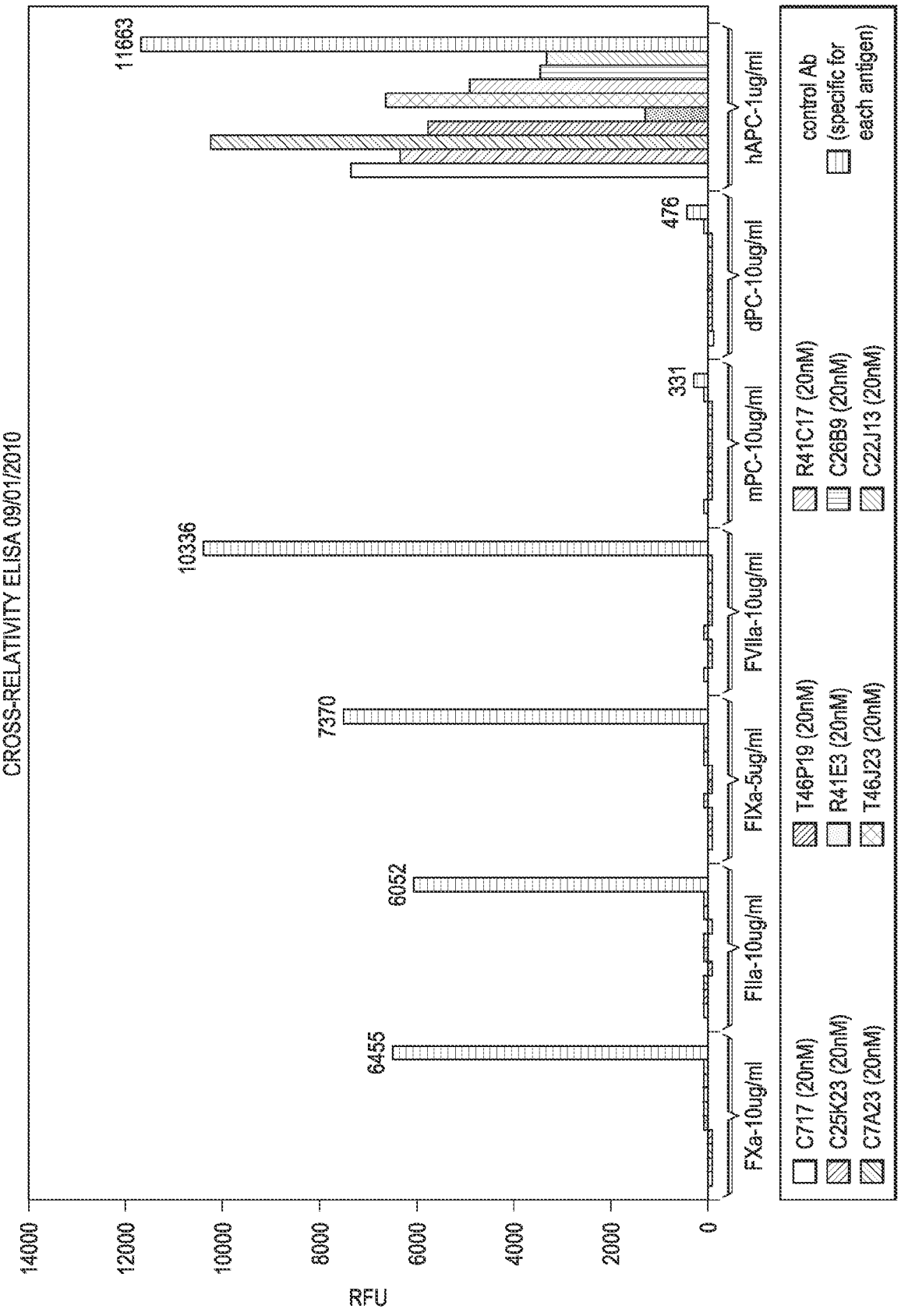

CROSS-RELATIVITY ELISA 09/01/2010
RFU
14000
12000
10000
8000
6000
4000
2000
0
6455
6052
7370
10336
331
476
11663
FXa-10ug/ml
FIIa-10ug/ml
FIXa-5ug/ml
FVIIa-10ug/ml
mPC-10ug/ml
dPC-10ug/ml
hAPC-1ug/ml
C717 (20nM)
C25K23 (20nM)
C7A23 (20nM)
T46P19 (20nM)
R41E3 (20nM)
T46J23 (20nM)
R41C17 (20nM)
C26B9 (20nM)
C22J13 (20nM)
control Ab
(specific for
each antigen)

Figure 5

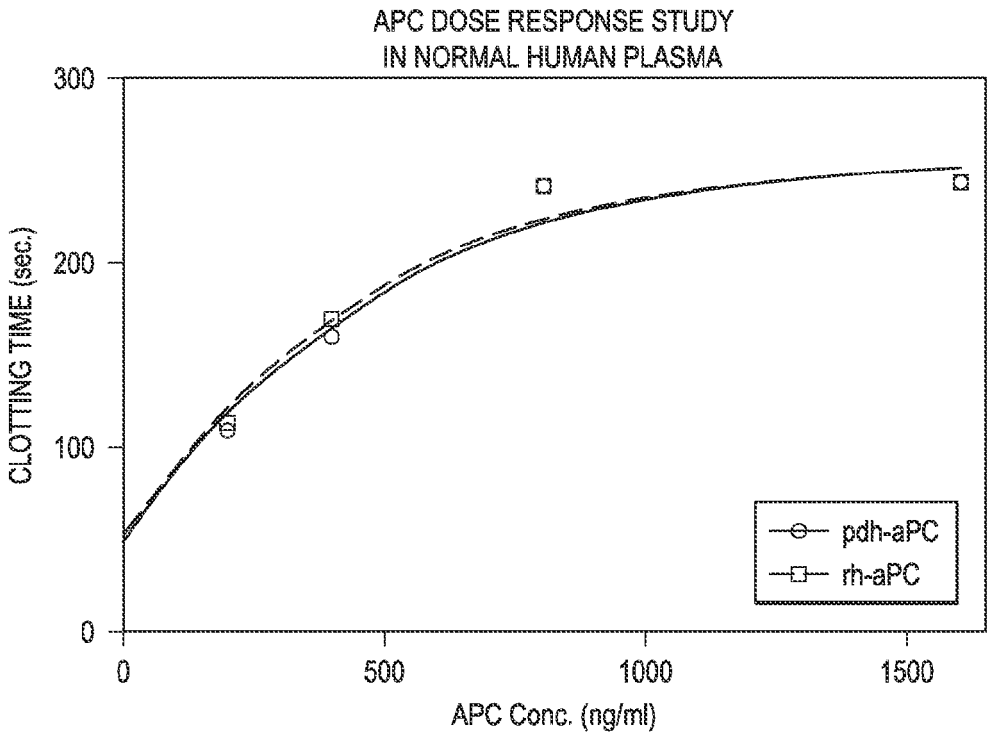


Figure 6

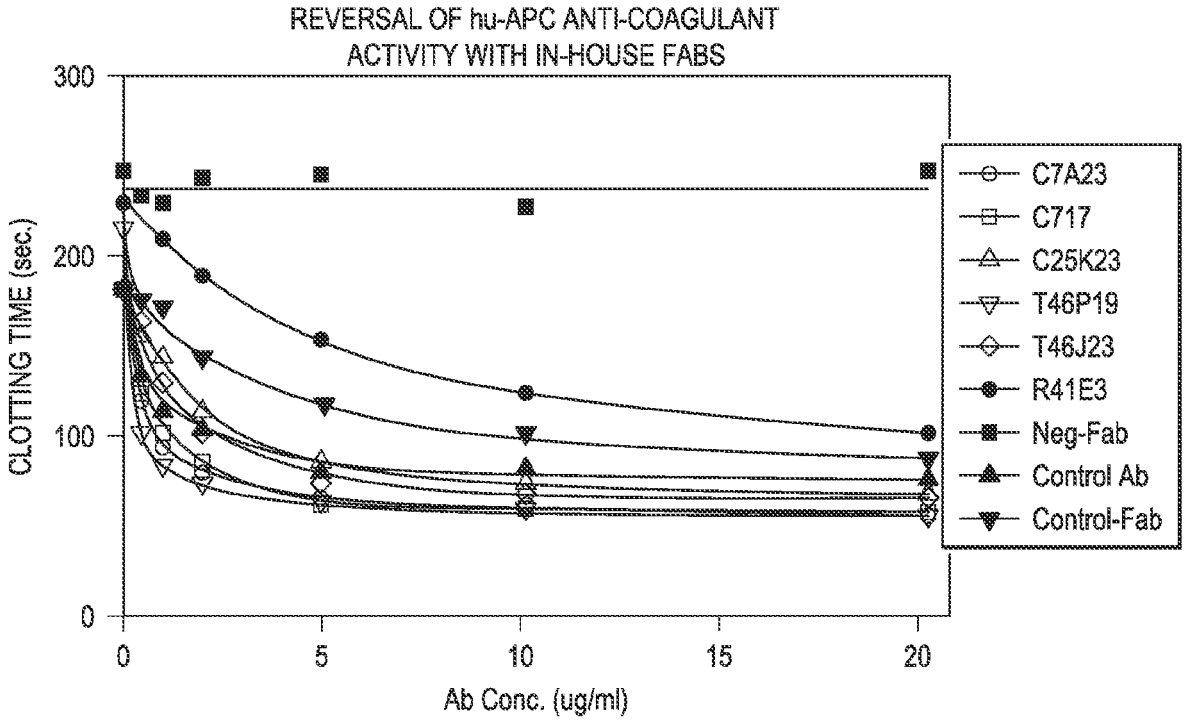


Figure 6

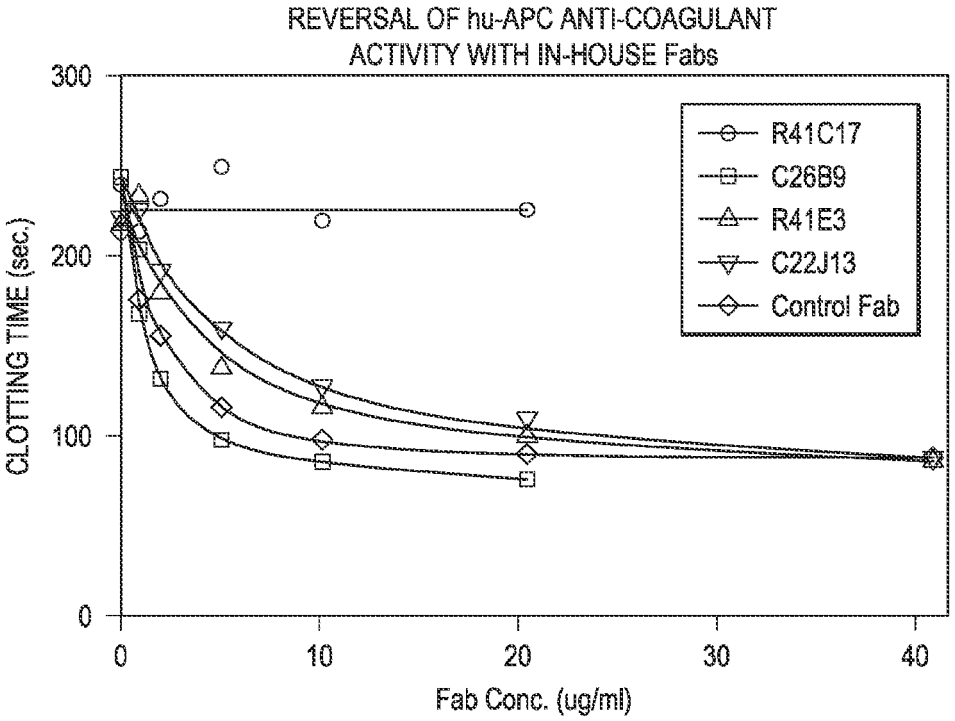


Figure 7

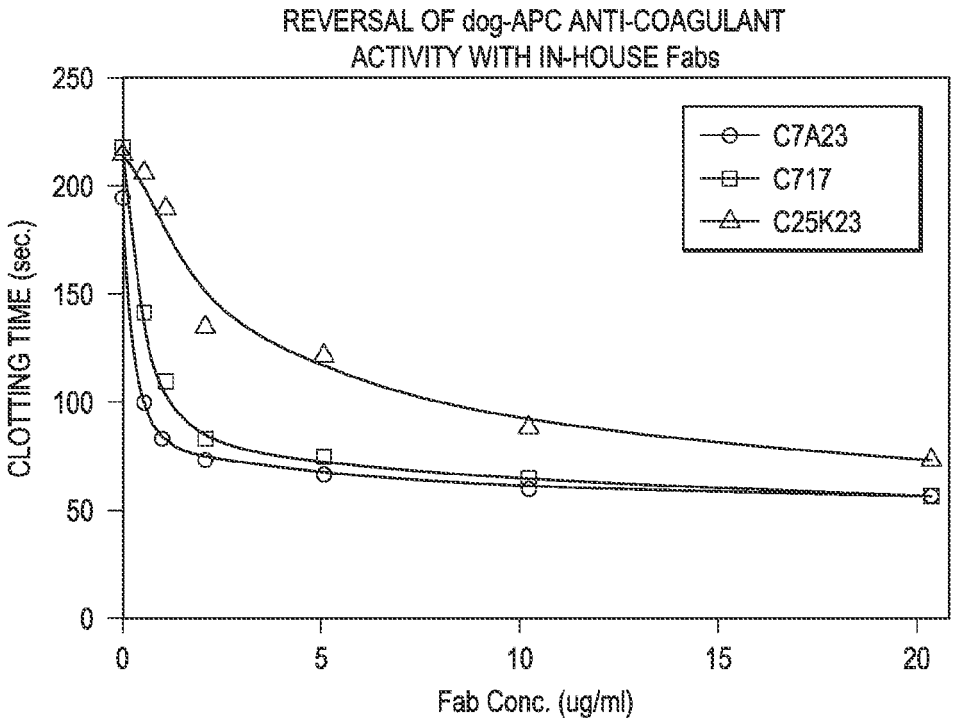
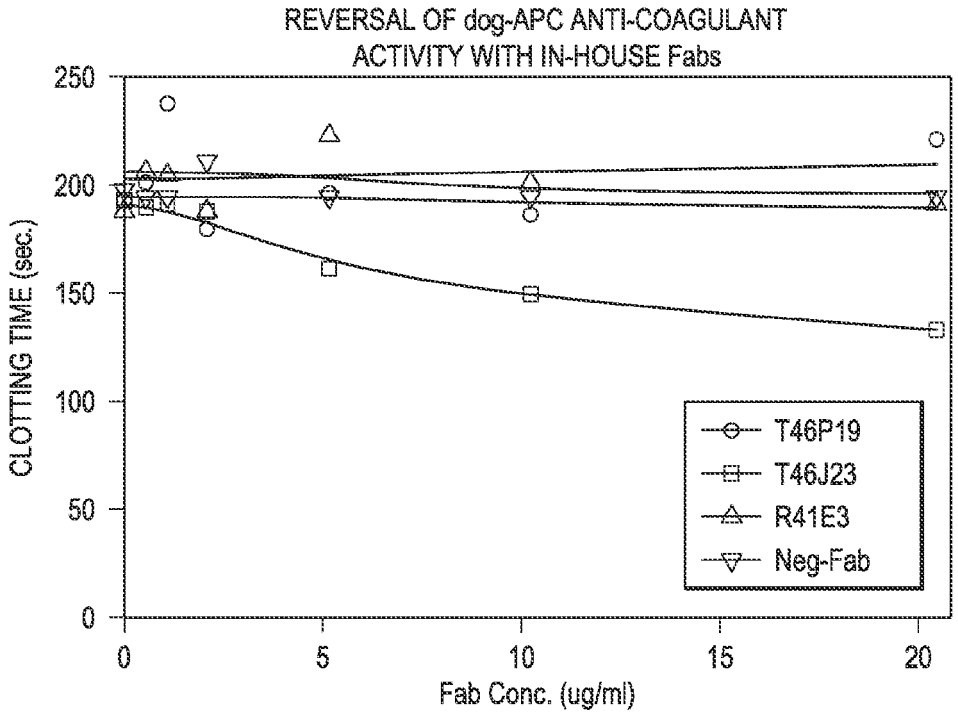


Figure 7



dog-APC (400 ng/ml)

Fab Conc. (ug/ml) (Fab:APC)	% INHIBITION					
	C7A23	C717	C25K23	T46P19	T46J23	R41E3
20.4 (60:1)	95.56	95.16	84.61	0.00	41.48	0.00
10.2 (30:1)	91.59	92.14	75.90	0.00	30.50	0.00
5.08 (15:1)	**88.11**	**48.35**	**55.77**	**0.00**	**21.12**	**0.00**
2.04 (6:1)	82.50	80.27	47.25	0.00	3.45	0.00
1.02 (3:1)	75.32	64.44	15.22	0.00	0.62	0.00
0.51 (1.5:1)	64.59	45.19	5.68	0.00	2.00	0.00
0	0.00	0.00	0.00	0.00	0.00	0.00

Figure 8

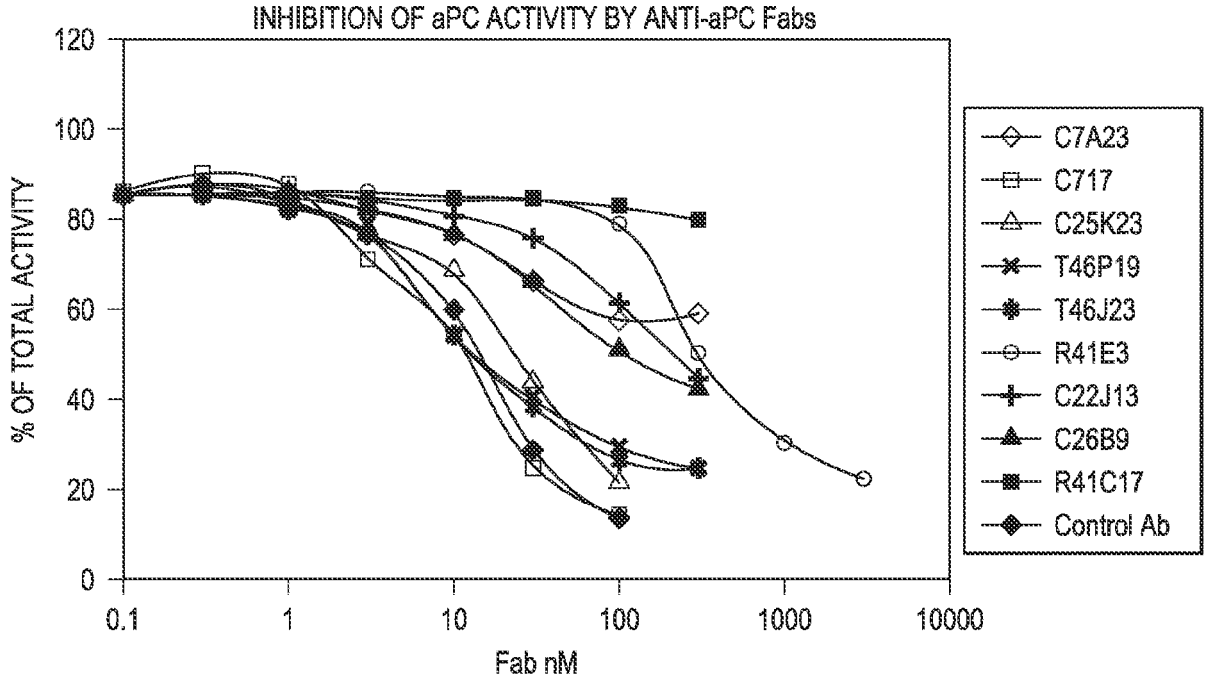


Figure 9

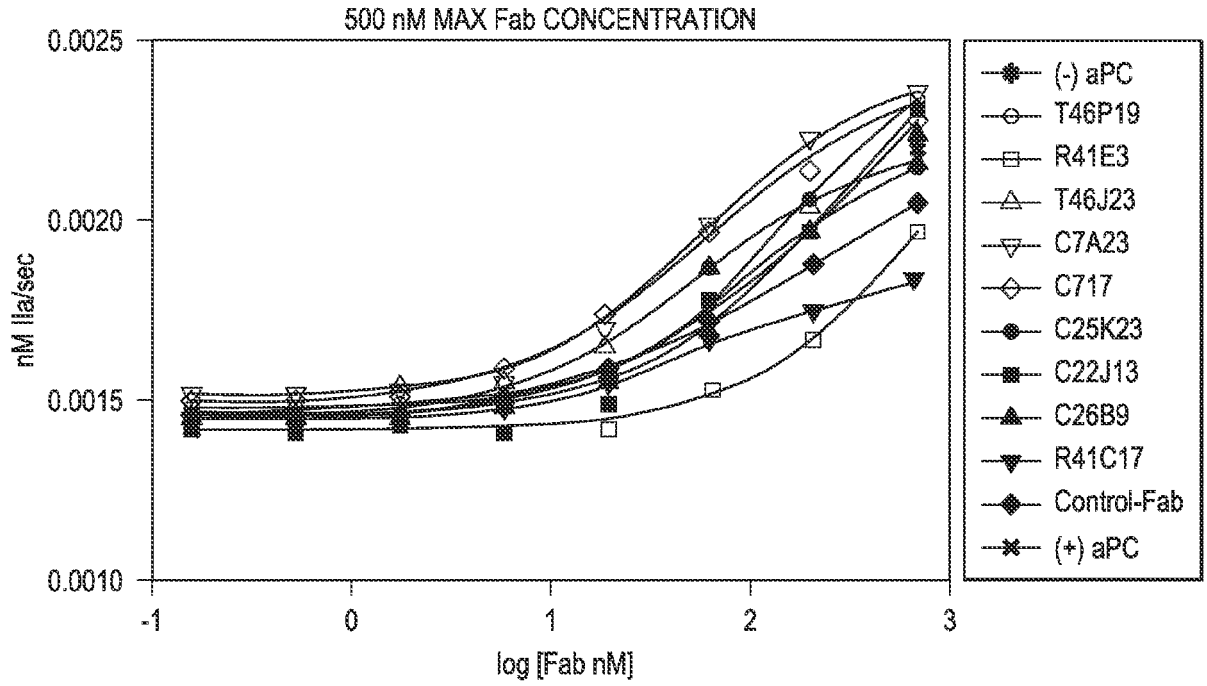


Figure 10

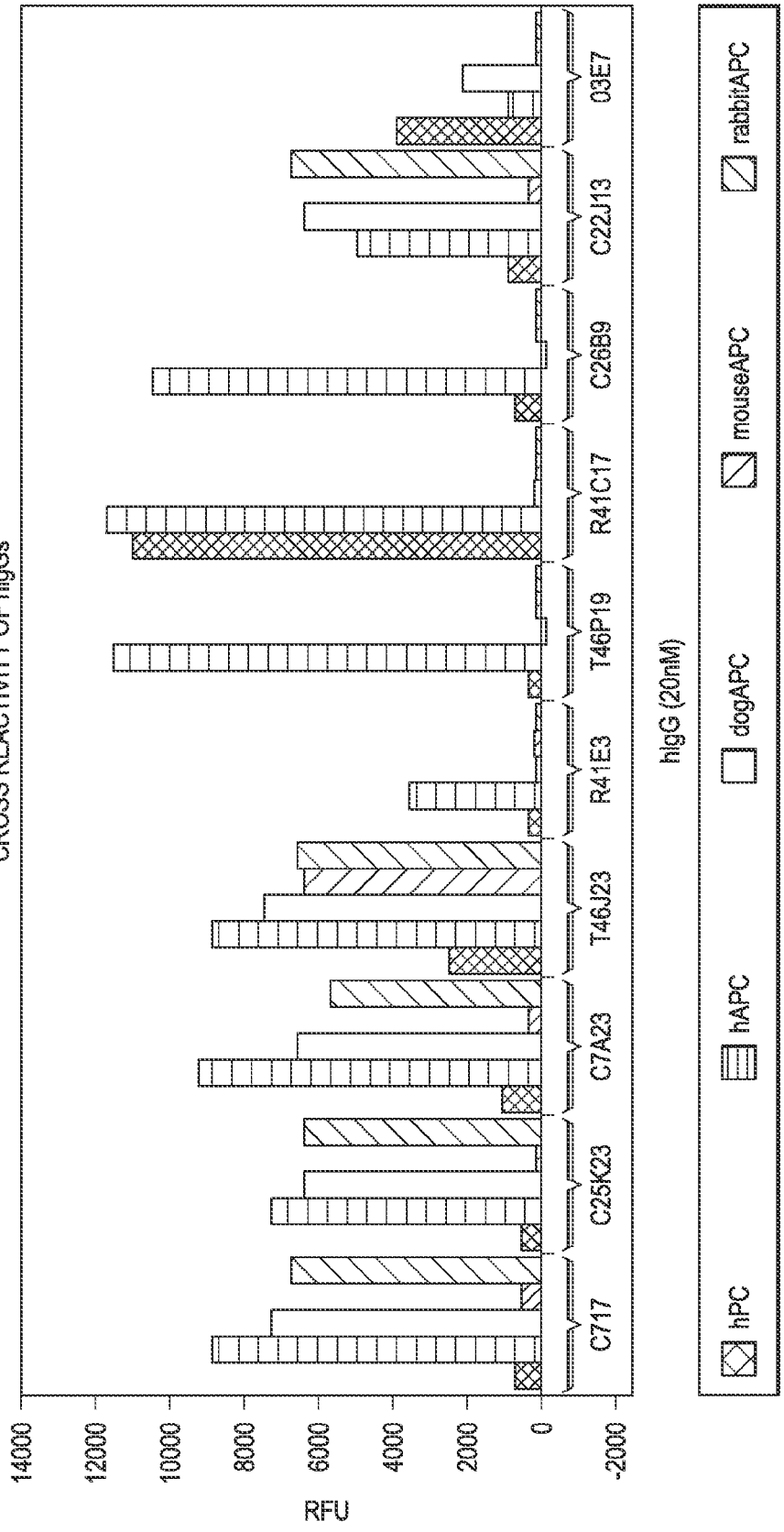
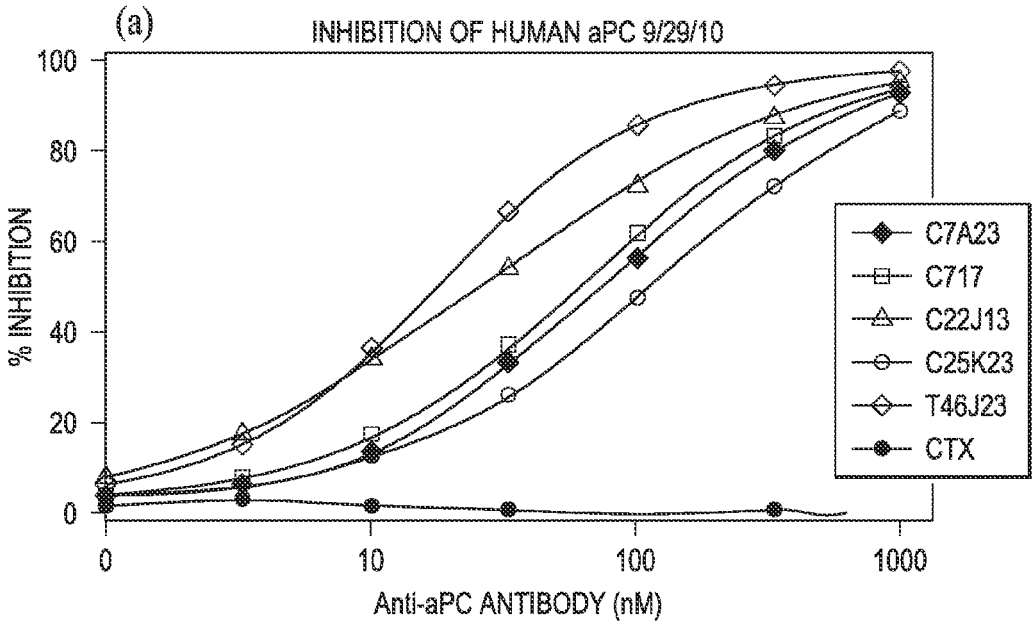

CROSS REACTIVITY OF hIgGs
RFU
14000
12000
10000
8000
6000
4000
2000
0
-2000
C717
C25K23
C7A23
T46J23
R41E3
T46P19
R41C17
C26B9
C22J13
03E7
hIgG (20nM)
hPC
hAPC
dogAPC
mouseAPC
rabbitAPC

Figure 11


(a)
INHIBITION OF HUMAN aPC 9/29/10
% INHIBITION
100
80
60
40
20
0
0
10
100
1000
Anti-aPC ANTIBODY (nM)
C7A23
C717
C22J13
C25K23
T46J23
CTX

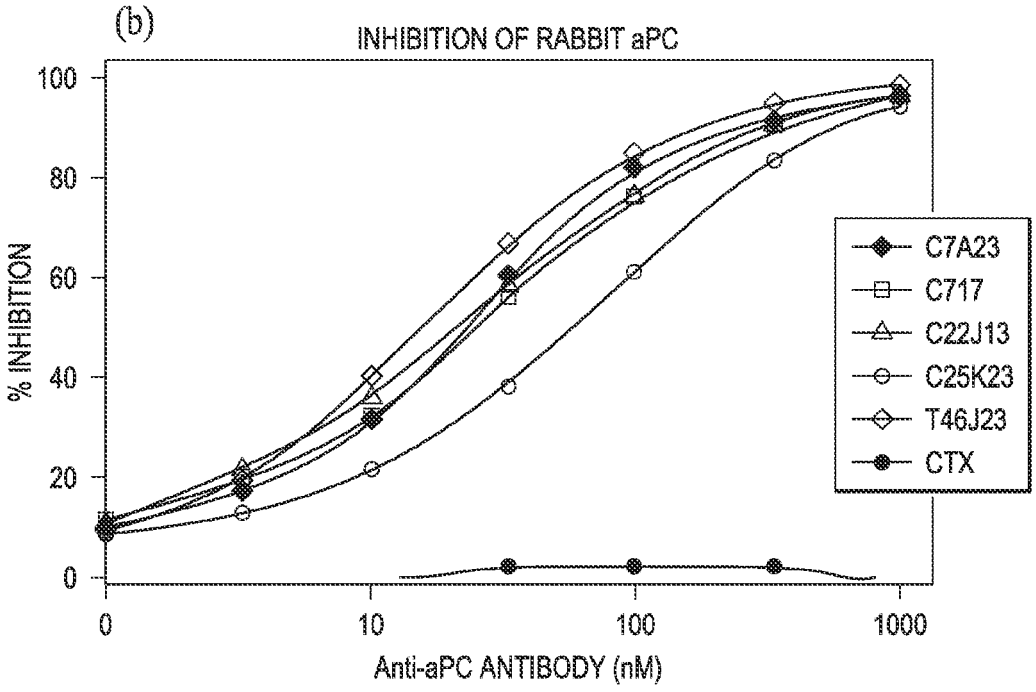
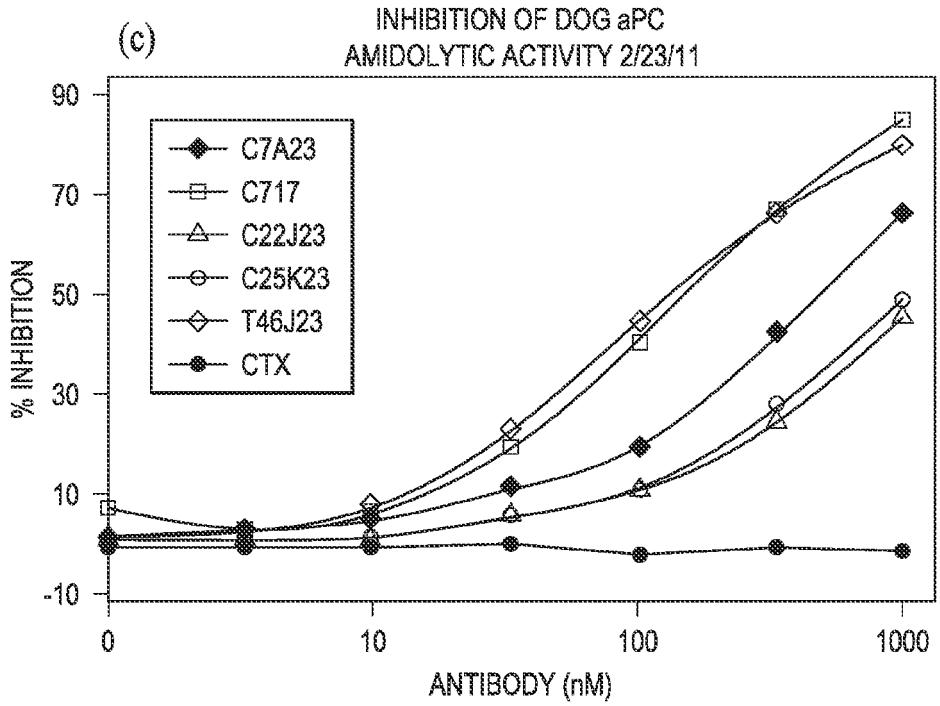

(b)
INHIBITION OF RABBIT aPC
% INHIBITION
100
80
60
40
20
0
0
10
100
1000
Anti-aPC ANTIBODY (nM)
C7A23
C717
C22J13
C25K23
T46J23
CTX

Figure 11


(c)
INHIBITION OF DOG aPC
AMIDOLYTIC ACTIVITY 2/23/11
% INHIBITION
ANTIBODY (nM)
C7A23
C717
C22J23
C25K23
T46J23
CTX
90
70
50
30
10
-10
0
10
100
1000

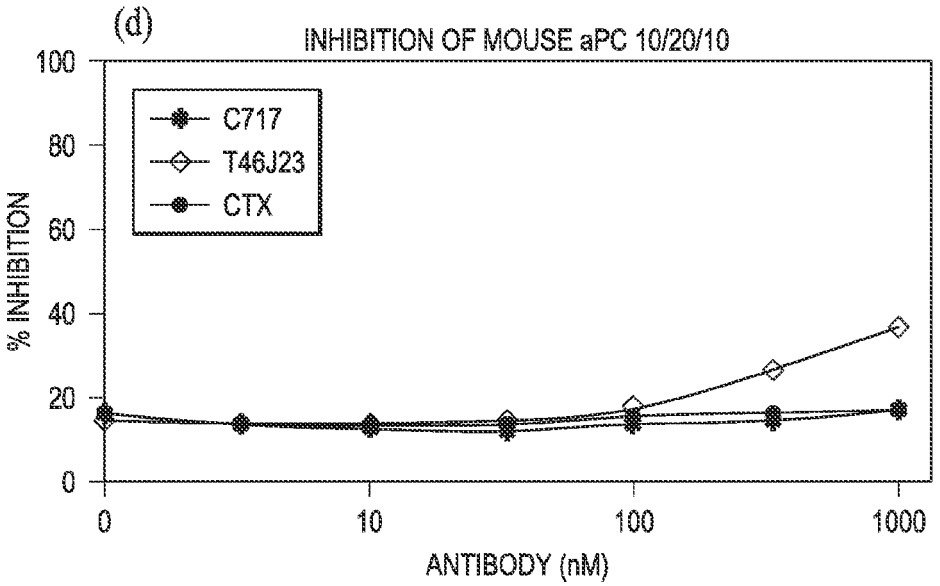

(d)
INHIBITION OF MOUSE aPC 10/20/10
% INHIBITION
ANTIBODY (nM)
C717
T46J23
CTX
100
80
60
40
20
0
0
10
100
1000

Figure 12

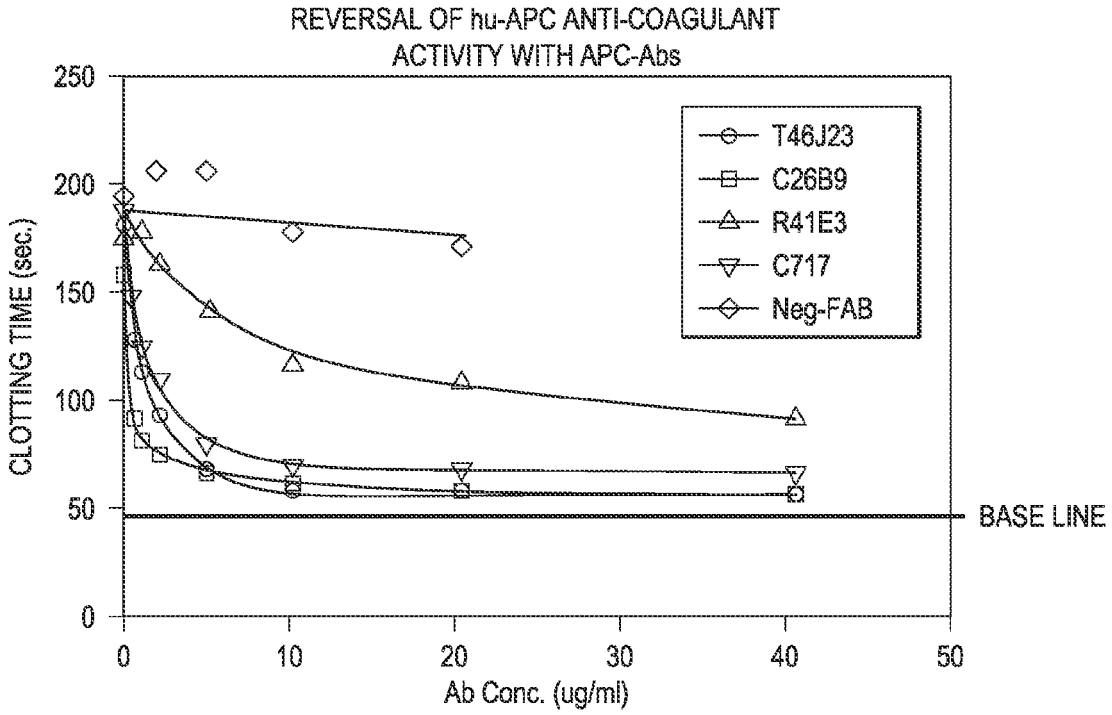

REVERSAL OF hu-APC ANTI-COAGULANT ACTIVITY WITH APC-Abs
CLOTTING TIME (sec.)
250
200
150
100
50
0
0
10
20
30
40
50
Ab Conc. (ug/ml)
T46J23
C26B9
R41E3
C717
Neg-FAB
BASE LINE

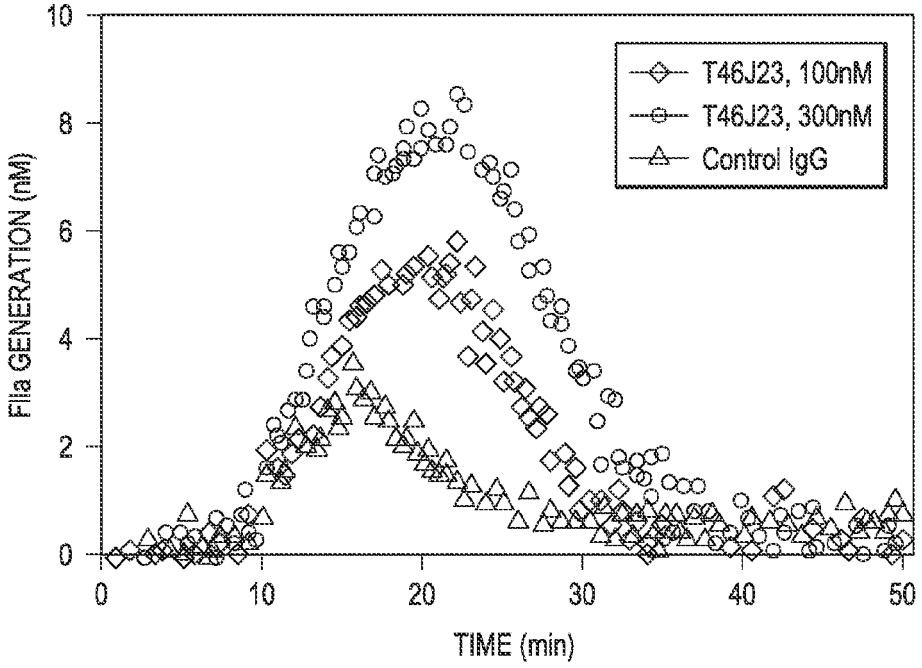
Figure 12

hu-APC (400 ng/ml)

Fab Conc. (ug/ml) (Ab:APC)	CLOTTING TIME					% INHIBITION					
	T46J23	C26B9	R41E3	C717	Neg-IgG	T46J23	C26B9	R41E3	C717	Neg-IgG
163.2 (163:1)			75					80.02		
81.6 (81:1)			80.8					75.43		
40.8 (40:1)	53	56	91.5	62.6		98.45	96.64	66.98	92.89	
20.4 (20:1)	57.9	58.2	109.2	67.4	170.5	94.67	94.53	53.00	89.33	16.07
10.2 (10:1)	59.1	62.0	117	73.2	177.8	93.74	90.89	46.84	85.04	10.88
5.08 (5:1)	68.8	66.3	142.4	79.6	205.5	86.24	86.77	26.78	80.30	-8.82
2.04 (2:1)	93.3	73.5	165.1	109	204.9	67.31	79.87	8.85	58.52	-8.39
1.02 (1:1)	114.1	81.5	177.5	124.8	169.8	51.24	72.20	-0.95	46.81	16.57
0.51 (0.5:1)	129.0	91.5	174.4	147.1	158.1	39.72	62.61	1.50	30.30	24.89
0	180.4	156.8	176.3	188	193.1	0.00	0.00	0.00	0.00	0.00
50% FACT	51.0	52.5	49.7	53.0	52.5					

* R41E3 IS LESS POTENT THAN OTHER IgGs IN INHIBITING THE hu-APC IN APTT ASSAY

Figure 13


T46J23, 100nM
T46J23, 300nM
Control IgG
FIIa GENERATION (nM)
TIME (min)
0
2
4
6
8
10
0
10
20
30
40
50

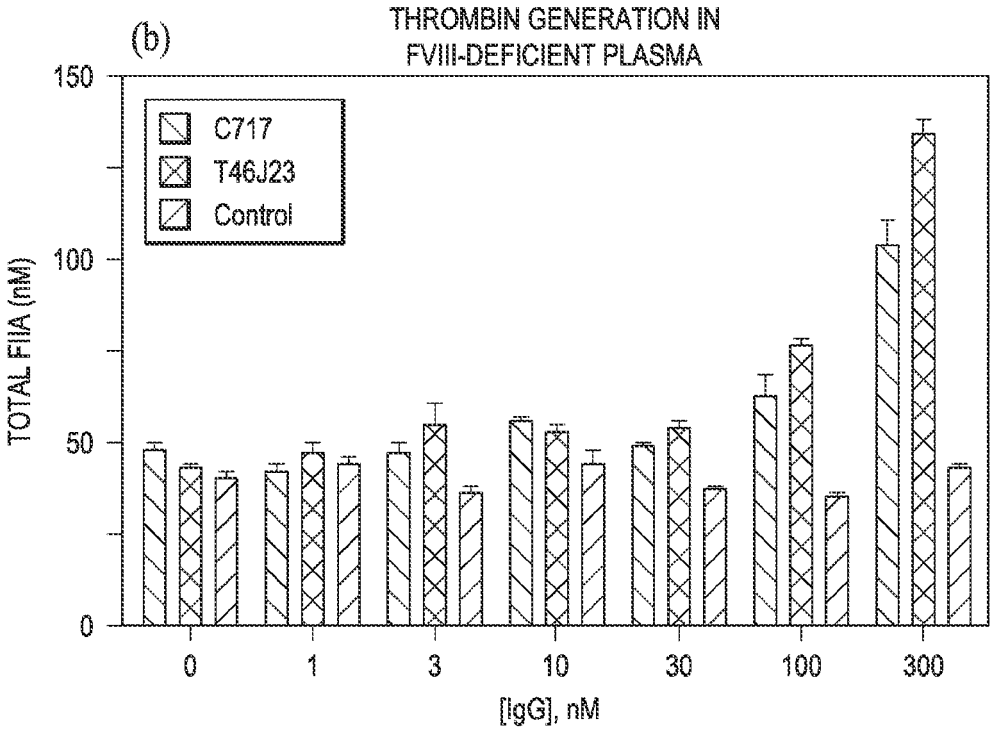
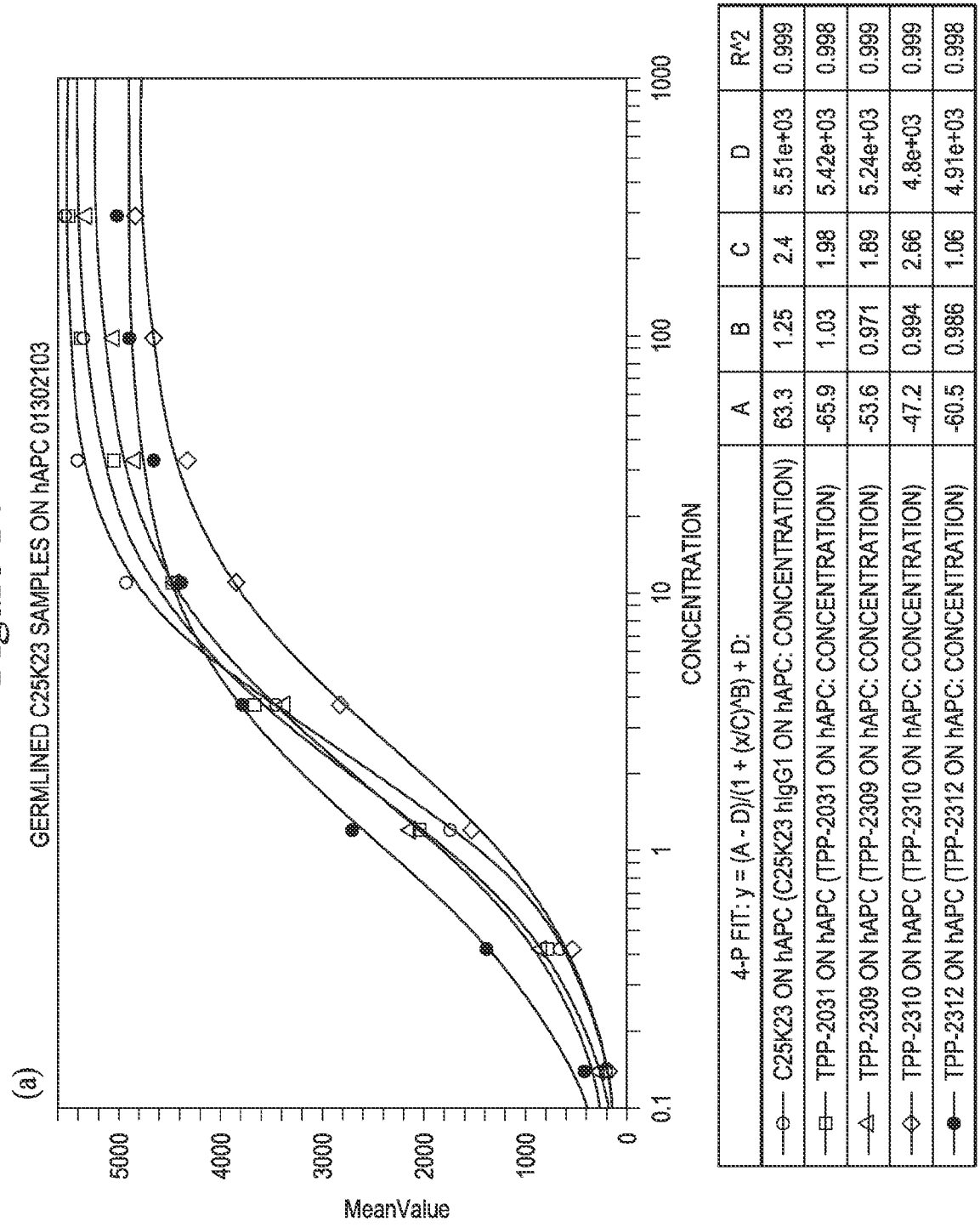
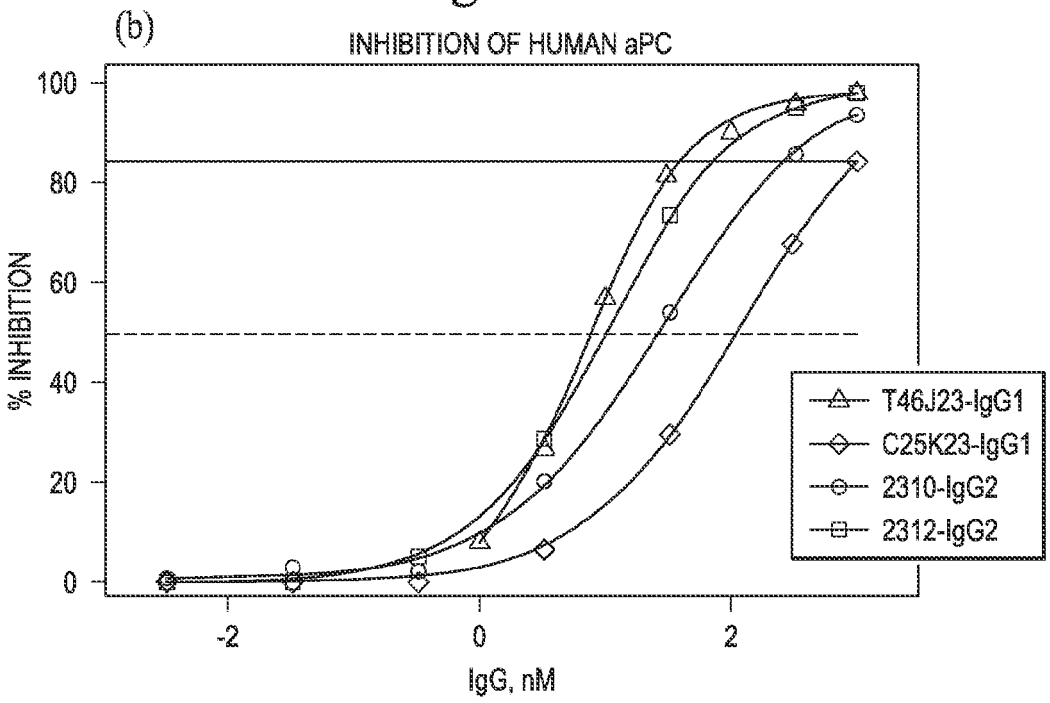

(b)
THROMBIN GENERATION IN
FVIII-DEFICIENT PLASMA
C717
T46J23
Control
TOTAL FIIA (nM)
[IgG], nM
0
50
100
150
0
1
3
10
30
100
300

Figure 14



4-P FIT: y = (A - D)/(1 + (x/C)^B) + D:	A	B	C	D	R^2
C25K23 ON hAPC (C25K23 hIgG1 ON hAPC: CONCENTRATION)	63.3	1.25	2.4	5.51e+03	0.999
TPP-2031 ON hAPC (TPP-2031 ON hAPC: CONCENTRATION)	-65.9	1.03	1.98	5.42e+03	0.998
TPP-2309 ON hAPC (TPP-2309 ON hAPC: CONCENTRATION)	-53.6	0.971	1.89	5.24e+03	0.999
TPP-2310 ON hAPC (TPP-2310 ON hAPC: CONCENTRATION)	-47.2	0.994	2.66	4.8e+03	0.999
TPP-2312 ON hAPC (TPP-2312 ON hAPC: CONCENTRATION)	-60.5	0.986	1.06	4.91e+03	0.998

Figure 14


(b)
INHIBITION OF HUMAN aPC
% INHIBITION
100
80
60
40
20
0
-2
0
2
IgG, nM
T46J23-IgG1
C25K23-IgG1
2310-IgG2
2312-IgG2

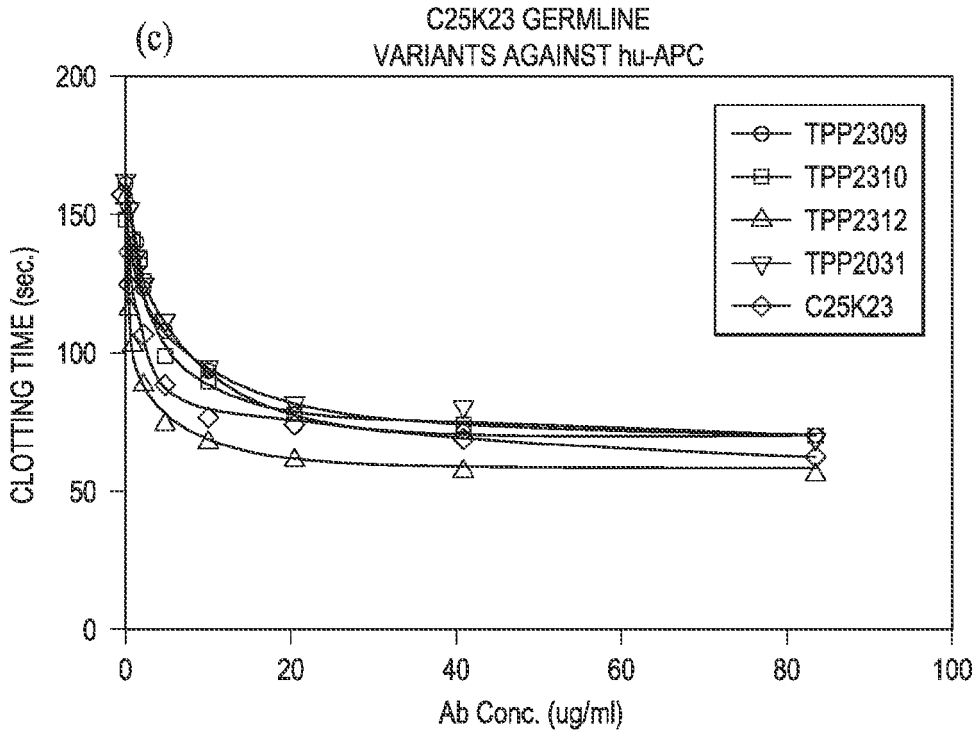

(c)
C25K23 GERMLINE
VARIANTS AGAINST hu-APC
CLOTTING TIME (sec.)
200
150
100
50
0
0
20
40
60
80
100
Ab Conc. (ug/ml)
TPP2309
TPP2310
TPP2312
TPP2031
C25K23

Figure 15

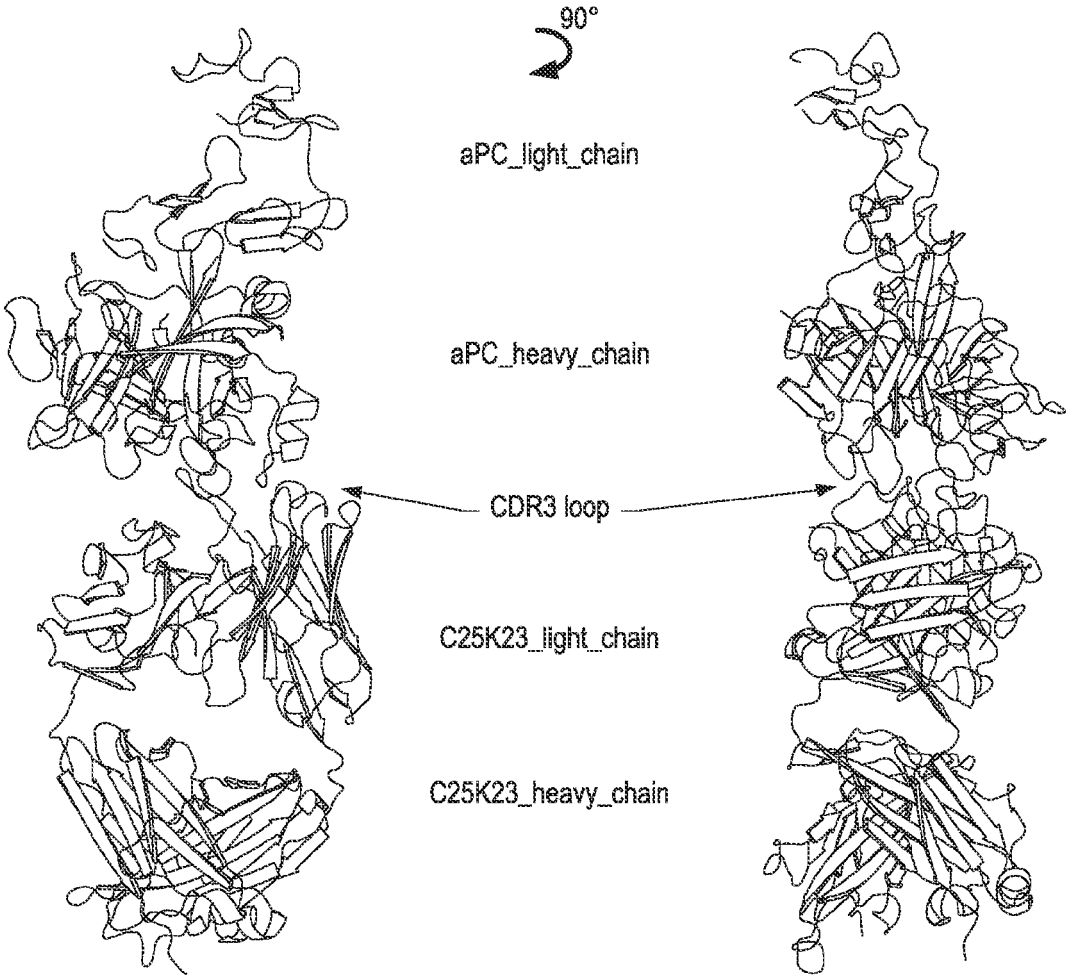

90°
aPC_light_chain
aPC_heavy_chain
CDR3 loop
C25K23_light_chain
C25K23_heavy_chain

Figure 16

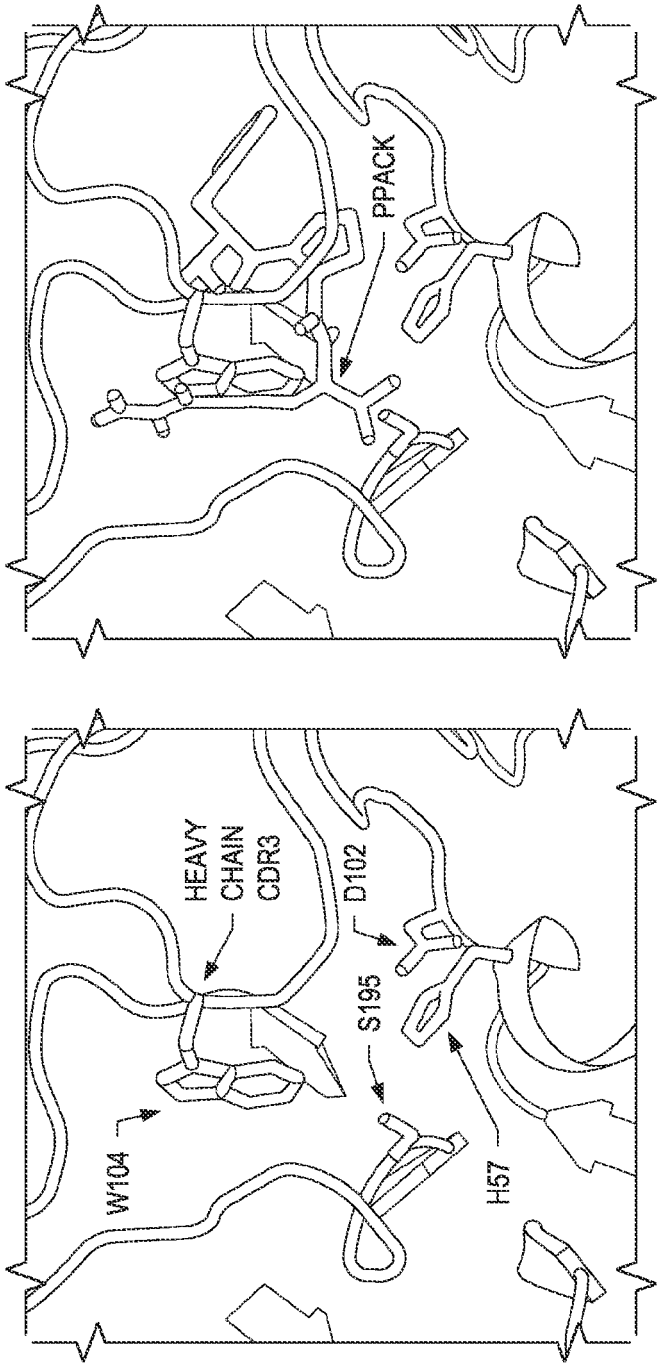
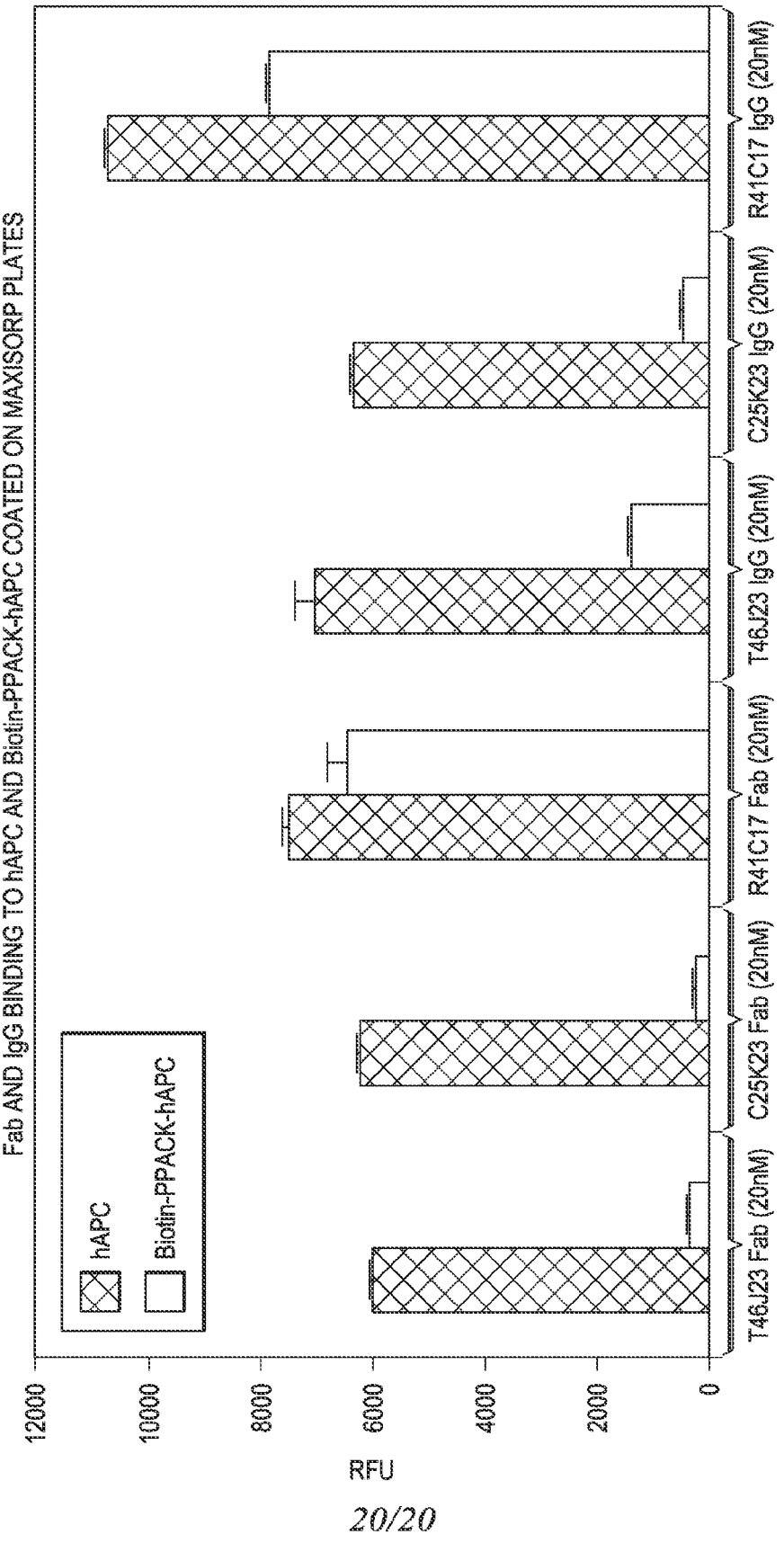


Figure 17


Fab AND IgG BINDING TO hAPC AND Biotin-PPACK-hAPC COATED ON MAXISORP PLATES
hAPC
Biotin-PPACK-hAPC
RFU
12000
10000
8000
6000
4000
2000
0
T46J23 Fab (20nM)
C25K23 Fab (20nM)
R41C17 Fab (20nM)
T46J23 IgG (20nM)
C25K23 IgG (20nM)
R41C17 IgG (20nM)