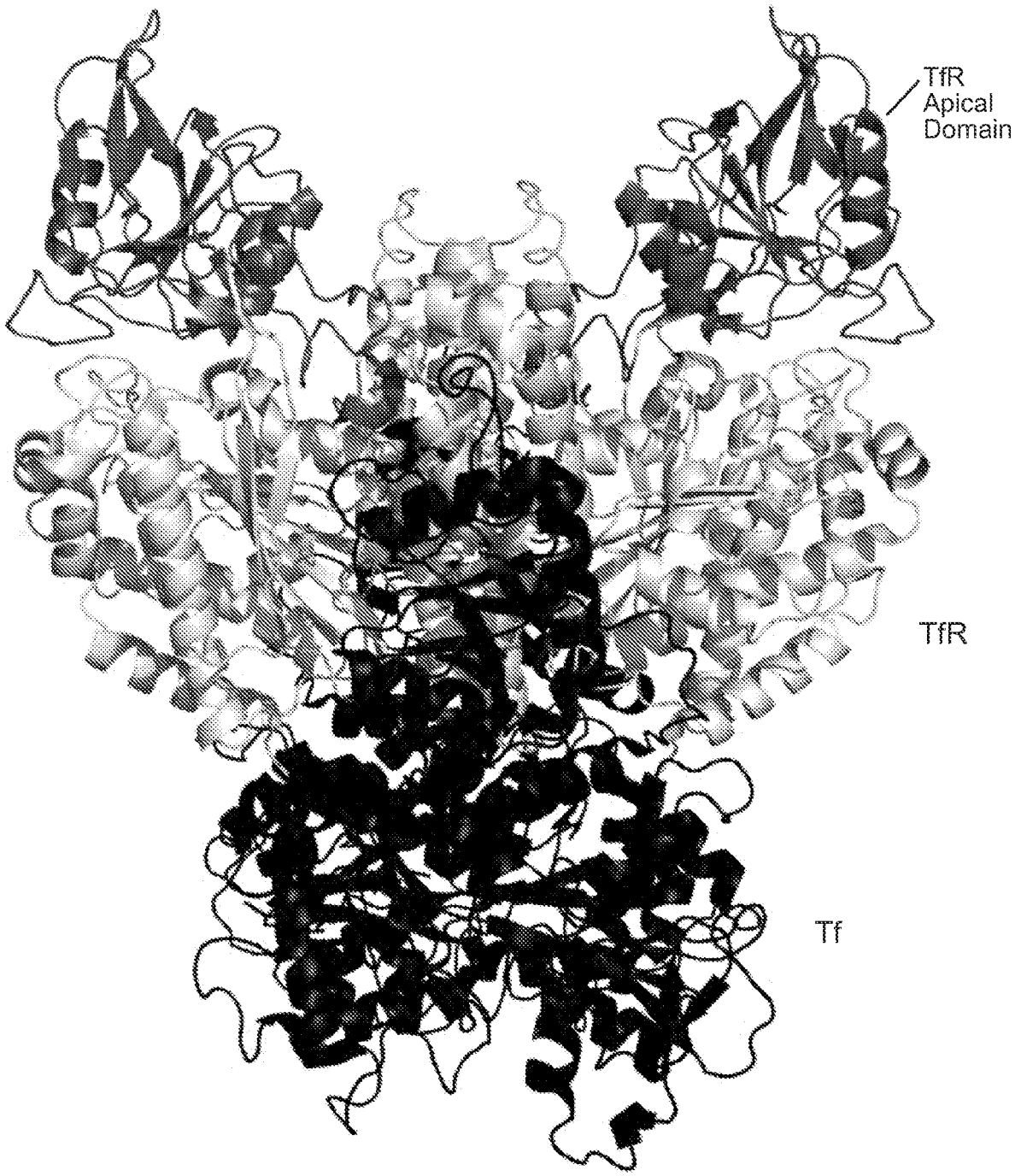


FIG. 1

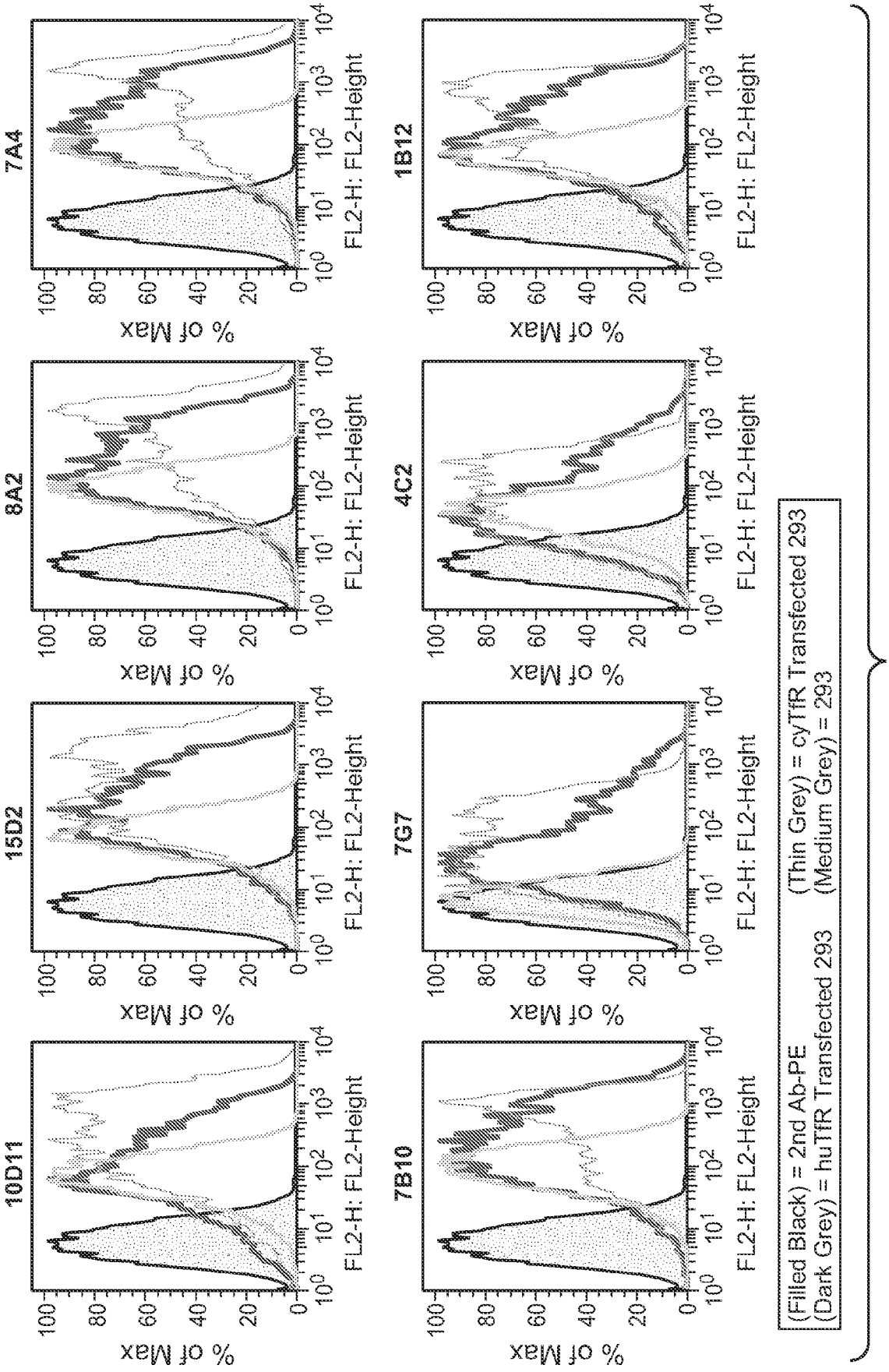

10D11
15D2
8A2
7A4
7B10
7G7
4C2
1B12
% of Max
FL2-H: FL2-Height
(Filled Black) = 2nd Ab-PE
(Dark Grey) = huTfR Transfected 293
(Thin Grey) = cyTfR Transfected 293
(Medium Grey) = 293

FIG. 2A

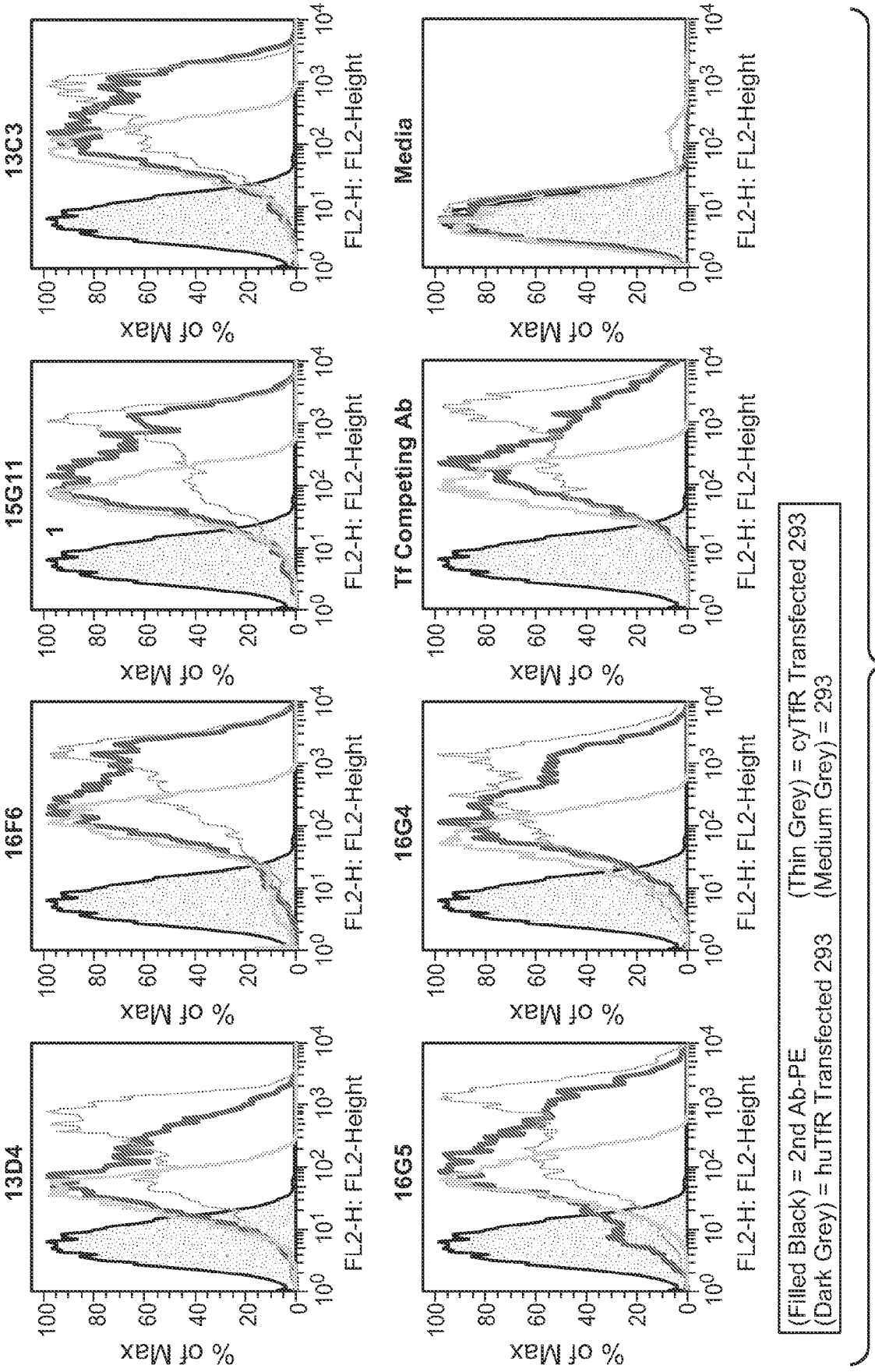

13C3
15G11
1
Media
16F6
Tf Competing Ab
13D4
16G4
16G5
% of Max
FL2-H: FL2-Height
(Filled Black) = 2nd Ab-PE
(Dark Grey) = huTfR Transfected 293
(Thin Grey) = cyTfR Transfected 293
(Medium Grey) = 293

FIG. 2B

Characterization of Human- and Cynomolgous Monkey-cross-reactive Anti-TfR Hybridomas that Don't Compete with Tf Binding to TfR

		Competes with Apical Domain Binder	huTfR ELISA Binding	Cyno TfR ELISA Binding	Biacore of Hybridoma or Chimeric IgG						
					huTfR			CynoTfR			Cy/hu KD Ratio
					Ka	Kd	KD	Ka	Kd	KD	
Class I	**7A4**	+++	+++	+++	2.11E+06	4.34E-04	2.06E-10	1.06E+06	6.63E-04	6.27E-10	3.04
	8A2	+++	+++	+++	1.22E+06	2.17E-04	1.79E-10	7.91E+05	7.15E-04	9.04E-10	5.06
	7A4 HC/8A2 LC	+++	+++	+++	3.01E+06	3.35E-04	1.12E-10	1.32E+06	1.22E-03	9.25E-10	8.29
	1502	+++	+++	+++							
	10D11	+++	+++	+++	1.66E+05	3.44E-04	2.08E-09	6.46E+04	5.81E-03	8.99E-08	43.32
	7B10	+++	+++	+++							
Class II	**15G11**	+++	+++	+++	8.90E+05	8.83E-04	9.92E-10	1.29E+06	3.35E-03	2.60E-09	2.62
	13C3	+++	+++	+++							
	16G5	+++	+++	+++							
	16G4	+++	+++	+++	4.77E+05	1.62E-03	3.40E-09	2.33E+05	5.23E-03	2.24E-08	6.59
Class III	**16F6**	+++	+++	+++	1.36E+05	2.81E-04	2.07E-09	1.23E+05	9.13E-04	7.45E-09	3.6
Class IV	**7G7**	-	+++	+++	1.33E+05	6.08E-03	4.57E-08	4.63E+04	1.21E-02	2.62E-07	5.73E
	4C2	-	+++	+++							
	1B12	-	+++	++	1.36E+05	2.76E-04	2.03E-09	1.34E+05	5.80E-03	4.34E-08	21.35
	13D4	-	+++	++	9.99E+04	9.49E-04	9.50E-09	7.06E+04	5.98E-04	8.47E-09	0.89

FIG. 2C

Light Chain Variable Region

CDR L1 - Contact
CDR L1 - Chothia
CDR L1 - Kabat

Kabat Number	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	27a	27b	27c	27d	28	29	30	31	32	33	34	35	36	37	38
7A4	D	I	V	L	T	Q	S	P	A	S	L	A	V	S	L	G	Q	R	A	T	I	S	C	R	A	S	E	S	V	D	D	Y	G	N	S	F	M	H	W	Y	Q	Q
8A2	D	I	V	L	T	Q	S	P	A	S	L	A	V	S	L	G	Q	R	A	T	I	S	C	R	A	S	E	S	V	D	S	Y	G	N	S	F	M	H	W	Y	Q	Q
15D2	D	I	V	L	T	Q	S	P	A	S	L	A	V	S	L	G	Q	R	A	T	I	S	C	R	A	S	E	S	V	D	S	Y	G	N	S	F	M	H	W	Y	Q	Q
10D11	D	I	V	L	T	Q	S	P	A	S	L	A	V	S	L	G	Q	R	A	T	I	S	C	R	A	S	E	S	V	D	S	Y	G	P	S	F	M	H	W	Y	Q	Q
7B10	D	I	V	L	T	Q	S	P	A	S	L	A	V	S	L	G	Q	R	A	T	I	S	C	R	A	S	E	S	V	D	D	Y	G	N	S	F	M	H	W	Y	Q	Q

CDR L2 - Contact
CDR L2 - Chothia
CDR L2 - Kabat

Kabat Number	39	40	41	42	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
7A4	K	P	G	Q	P	P	K	L	L	I	Y	R	A	S	N	L	E	S	G	I	P	A	R	F	S	G	S	G	S	R	T	D	F	T	L	T	I	N	P	V	E	A
8A2	K	P	G	Q	P	P	K	L	L	I	Y	R	A	S	N	L	E	S	G	I	P	A	R	F	S	G	S	G	S	R	T	D	F	T	L	T	I	N	P	V	E	A
15D2	K	P	G	Q	P	P	K	L	L	I	Y	R	A	S	N	L	E	S	G	I	P	A	R	F	S	G	S	G	S	R	T	D	F	T	L	T	I	N	P	V	E	A
10D11	K	P	G	Q	P	P	K	L	L	I	Y	R	A	S	N	L	E	S	G	I	P	A	R	F	S	G	S	G	S	R	T	D	F	T	L	T	I	N	P	V	E	A
7B10	K	P	G	Q	P	P	K	L	L	I	Y	R	A	S	N	L	E	S	G	I	P	A	R	F	S	G	S	G	S	R	T	D	F	T	L	T	I	N	P	V	E	A

CDR L3 - Contact
CDR L3 - Chothia
CDR L3 - Kabat

Kabat Number	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	
7A4	D	D	V	A	T	Y	Y	C	Q	Q	S	N	E	A	P	P	T	F	G	G	G	T	K	L	E	I	R	SEQ ID NO: 4
8A2	D	D	V	A	T	Y	Y	C	Q	Q	S	N	E	G	P	P	T	F	G	G	G	T	K	L	E	I	K	SEQ ID NO: 5
15D2	D	D	V	A	T	Y	Y	C	Q	Q	S	N	E	G	P	P	T	F	G	G	G	T	K	L	E	I	K	SEQ ID NO: 5
10D11	D	D	V	A	T	Y	Y	C	Q	H	S	N	E	D	P	P	T	F	G	G	G	T	R	L	E	I	K	SEQ ID NO: 6
7B10	D	D	V	A	T	Y	Y	C	Q	Q	S	N	E	A	P	P	T	F	G	G	G	T	K	L	E	I	R	SEQ ID NO: 4

FIG. 3A-1

Heavy Chain Variable Region

CDR H1 - Contact
CDR H1 - Chothia
CDR H1 - Kabat

Kabat Number	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
7A4	Q	V	Q	L	Q	Q	S	G	P	E	L	V	R	P	G	V	S	V	K	I	S	C	K	G	S	G	Y	T	F	T	D	Y	A	M	H	W	V	K	Q	S	H	A
8A2	Q	V	Q	L	Q	Q	S	G	P	E	L	V	R	P	G	V	S	V	K	I	S	C	K	G	S	G	Y	T	F	T	D	Y	G	M	H	W	V	K	Q	S	H	A
15D2	Q	V	Q	L	Q	Q	S	G	P	E	L	V	R	P	G	V	S	V	K	I	S	C	K	G	S	G	Y	T	V	T	D	Y	A	M	H	W	V	K	Q	S	H	A
10D11	Q	V	Q	L	Q	Q	S	G	P	E	L	V	R	P	G	V	A	V	K	I	S	C	K	G	S	G	Y	K	F	I	D	Y	G	M	H	W	V	K	Q	S	H	T
7B10	Q	V	Q	L	Q	Q	S	G	P	E	L	V	R	P	G	V	S	V	K	I	S	C	K	G	S	G	Y	T	F	T	D	Y	A	M	H	W	V	K	Q	S	H	A

CDR H2 - Contact
CDR H2 - Chothia
CDR H2 - Kabat

Kabat Number	43	44	45	46	47	48	49	50	51	52	52a	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	82a
7A4	K	S	L	E	W	I	G	G	I	S	T	Y	F	G	R	T	N	Y	N	Q	K	F	K	G	R	A	T	M	T	V	D	K	S	S	S	T	A	Y	M	E	L	A
8A2	K	S	L	E	W	I	G	V	I	S	P	Y	S	G	R	T	N	Y	N	Q	N	F	K	G	K	A	T	M	T	V	D	K	S	S	S	T	A	Y	L	E	L	A
15D2	K	S	L	E	W	I	G	V	I	S	F	Y	S	G	K	T	N	Y	N	Q	K	F	M	G	K	A	T	M	T	V	D	K	S	S	S	T	A	Y	M	E	L	A
10D11	K	S	L	Q	W	I	G	V	I	S	P	Y	S	G	K	T	N	Y	S	Q	K	F	K	G	K	A	T	M	T	V	D	K	S	S	S	T	A	Y	M	E	L	A
7B10	K	S	L	E	W	I	G	G	I	S	T	Y	F	G	R	T	N	Y	N	Q	K	F	K	G	R	A	T	M	T	V	D	K	S	S	S	T	A	Y	M	E	L	A

CDR H3 - Contact
CDR H3 - Chothia
CDR H3 - Kabat

Kabat Number	82b	82c	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	100a	100b	101	102	103	104	105	106	107	108	109	110	111	112	113	
7A4	R	L	T	S	E	D	S	A	L	Y	Y	C	A	R	G	L	S	G	N	Y	V	M	D	Y	W	G	Q	G	T	S	V	T	V	S	S	SEQ ID NO: 7
8A2	R	L	T	S	E	D	S	A	I	Y	Y	C	A	R	G	L	S	G	N	Y	V	V	D	Y	W	G	Q	G	T	S	V	T	V	S	S	SEQ ID NO: 8
15D2	R	L	T	S	E	D	S	A	I	Y	Y	C	A	R	G	L	S	G	N	Y	V	M	D	Y	W	G	Q	G	T	S	V	T	V	S	S	SEQ ID NO: 9
10D11	R	L	T	S	E	D	S	A	I	Y	Y	C	A	R	G	L	S	G	N	F	V	M	D	F	W	G	Q	G	T	S	V	T	V	S	S	SEQ ID NO: 10
7B10	R	L	T	S	E	D	S	A	L	Y	Y	C	A	R	G	L	S	G	N	Y	V	M	D	Y	W	G	Q	G	T	S	V	T	V	S	S	SEQ ID NO: 7

FIG. 3A-2

Light Chain Variable Region

CDR L1 - Contact
CDR L1 - Chothia
CDR L1 - Kabat

Kabat Number	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
15G11	D	I	Q	M	T	Q	S	P	A	S	L	S	V	S	V	G	E	T	V	T	I	T	C	R	A	S	D	N	L	Y	S	N	L	A	W	Y	Q	Q	K	Q	G	K
16G5	D	I	Q	L	T	Q	T	P	A	S	L	S	V	S	V	G	E	T	V	T	I	T	C	R	A	S	E	N	I	Y	S	N	L	A	W	Y	Q	Q	K	Q	G	K
13G3	D	I	Q	M	T	Q	S	P	A	S	L	S	V	S	V	G	E	T	V	T	I	T	C	R	A	S	D	N	I	Y	S	N	L	A	W	Y	Q	Q	K	Q	G	K
16G4	D	I	Q	M	T	Q	S	P	A	S	L	S	V	S	V	G	E	T	V	T	I	T	C	R	A	S	D	N	I	Y	S	N	L	A	W	Y	Q	Q	K	Q	G	K

CDR L2 - Contact
CDR L2 - Chothia
CDR L2 - Kabat

Kabat Number	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
15G11	S	P	Q	L	L	V	Y	D	A	T	N	L	A	D	G	V	P	S	R	F	S	G	S	G	S	G	T	Q	Y	S	L	K	I	N	S	L	Q	S	E	D	F	G
16G5	S	P	Q	L	L	V	Y	A	A	T	D	L	A	D	G	V	P	S	R	F	R	G	S	G	S	G	T	Q	Y	S	L	K	I	N	S	L	Q	S	E	D	F	G
13G3	S	P	Q	L	L	V	Y	A	A	T	N	L	A	D	G	V	P	S	R	F	S	G	S	G	S	G	T	Q	Y	S	L	K	I	N	S	L	Q	S	E	D	F	G
16G4	S	P	Q	L	L	V	Y	A	V	T	N	L	A	D	G	V	P	S	R	F	S	G	S	G	S	G	T	Q	Y	S	L	K	I	N	S	L	Q	S	E	D	F	G

CDR L3 - Contact
CDR L3 - Chothia
CDR L3 - Kabat

Kabat Number	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	
15G11	T	Y	Y	C	Q	H	F	W	G	T	P	L	T	F	G	A	G	T	K	L	E	L	K	SEQ ID NO: 11
16G5	S	Y	Y	C	Q	H	F	W	G	T	P	L	T	F	G	A	G	T	K	L	E	L	I	SEQ ID NO: 12
13G3	S	Y	Y	C	Q	H	F	W	G	T	P	L	M	F	G	S	G	T	K	L	E	L	K	SEQ ID NO: 13
16G4	S	Y	Y	C	Q	H	F	W	G	T	P	L	T	F	G	A	G	T	K	L	E	L	K	SEQ ID NO: 14

FIG. 3B-1

Heavy Chain Variable Region

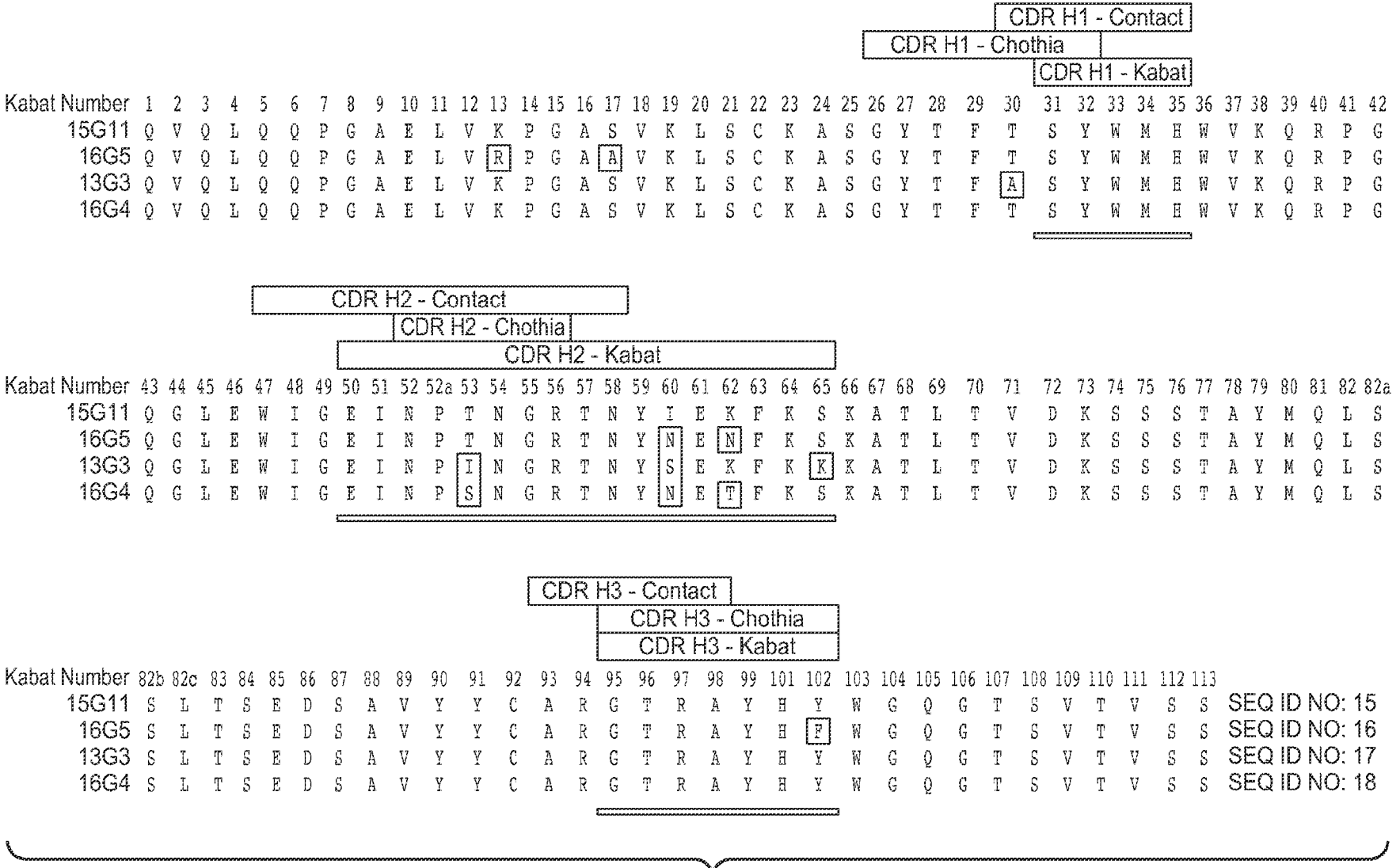


FIG. 3B-2

Light Chain Variable Region

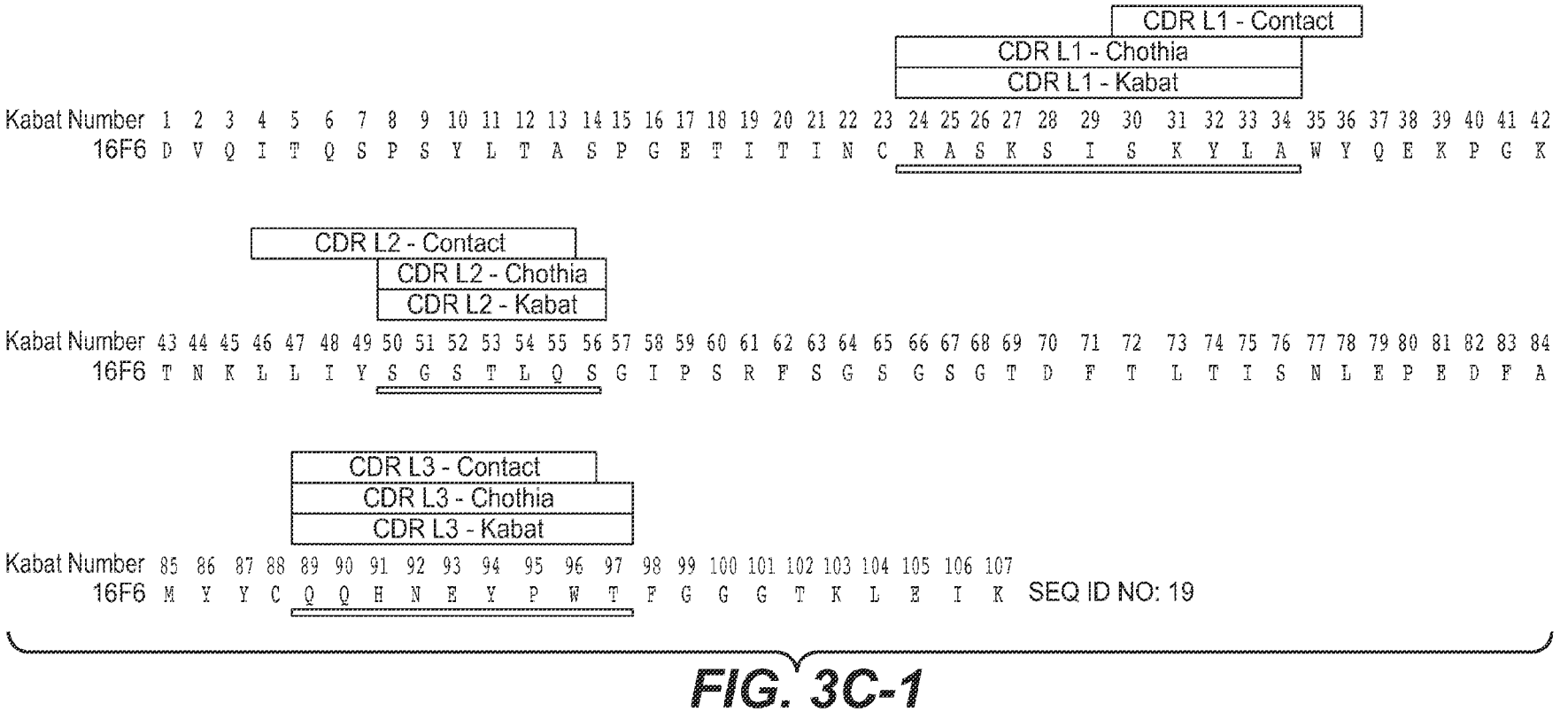


FIG. 3C-1

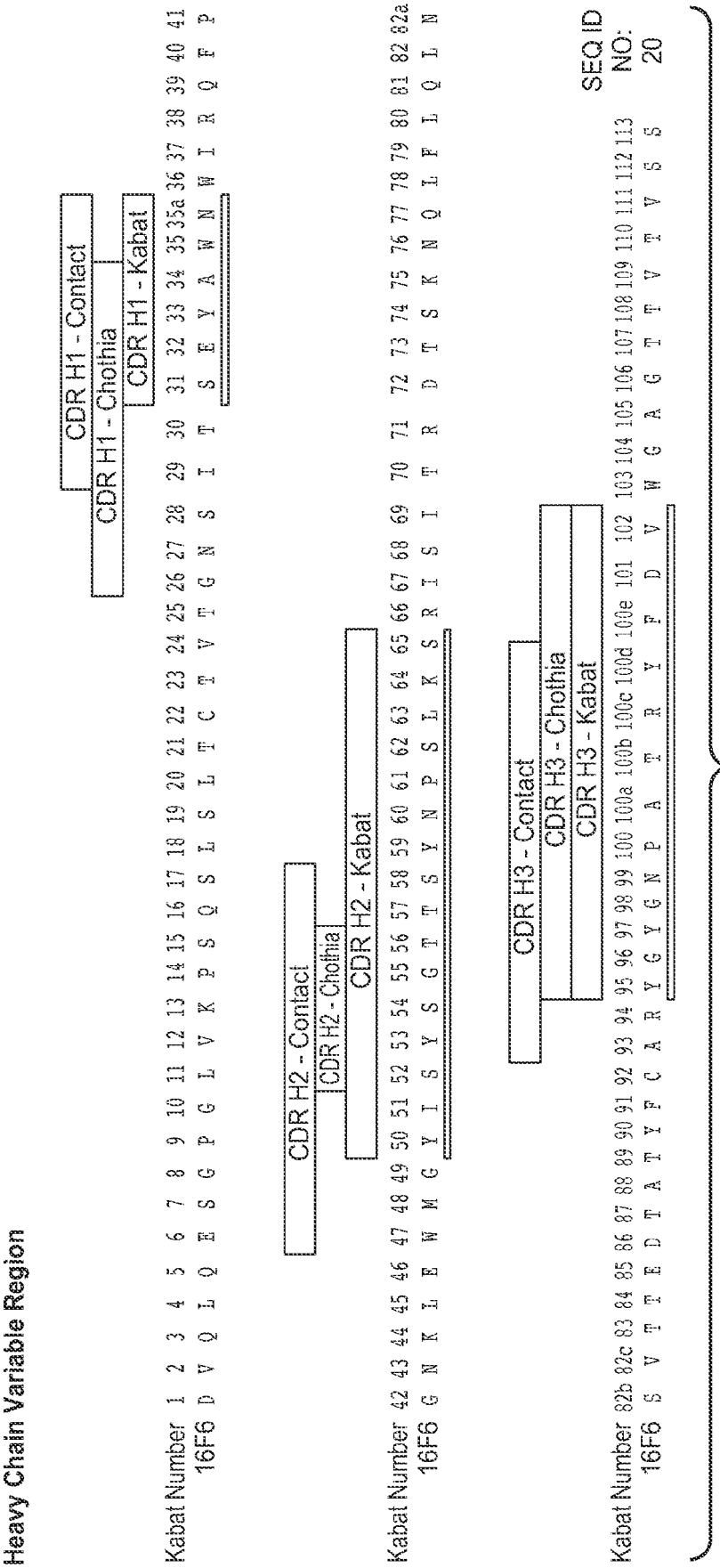

Heavy Chain Variable Region
CDR H1 - Contact
CDR H1 - Chothia
CDR H1 - Kabat
CDR H2 - Contact
CDR H2 - Chothia
CDR H2 - Kabat
CDR H3 - Contact
CDR H3 - Chothia
CDR H3 - Kabat
Kabat Number 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 35a 36 37 38 39 40 41
16F6 D V Q L Q E S G P G L V K P S Q S L S L T C T V T G N S I T S E Y A W N W I R Q F P
Kabat Number 42 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 82a
16F6 G N K L E W M G Y I S Y S G T T S Y N P S L K S R I S I T R D T S K N Q L F L Q L N
Kabat Number 82b 82c 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 100a 100b 100c 100d 100e 101 102 103 104 105 106 107 108 109 110 111 112 113
16F6 S V T T E D T A T Y F C A R Y G Y G N P A T R Y F D V W G A G T T V T V S S
SEQ ID NO: 20

FIG. 3C-2

Light Chain Variable Region

CDR L1 - Contact
CDR L1 - Chothia
CDR L1 - Kabat

Kabat Number	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	27a	27b	27c	27d	28	29	30	31	32	33	34	35	36	37	38
7G7	D	I	V	L	T	Q	S	P	A	S	L	A	V	S	L	G	Q	R	A	T	I	S	C	R	A	R	Q	S	V	S	T	S	S	Y	S	F	M	H	W	Y	R	Q
4C2	D	I	V	L	T	Q	S	P	A	S	L	A	V	S	L	G	Q	R	A	T	I	S	C	R	A	R	Q	S	V	S	T	S	S	Y	S	F	M	H	W	Y	Q	Q
1B12	Q	I	V	L	T	Q	S	P	A	I	M	S	A	S	L	G	G	R	V	T	M	T	C	T	T	S	S	S	.	.	.	V	P	S	S	Y	F	H	W	Y	Q	Q
13D4	D	I	Q	M	T	Q	T	T	S	S	L	S	A	S	L	G	D	R	V	T	I	N	C	R	A	G	Q	.	.	.	.	D	I	T	N	Y	L	N	W	F	Q	Q

CDR L2 - Contact
CDR L2 - Chothia
CDR L2 - Kabat

Kabat Number	39	40	41	41	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
7G7	K	A	G	Q	P	P	K	L	L	I	K	Y	A	S	I	Q	E	S	G	V	P	A	R	F	S	G	S	G	S	G	T	D	F	T	L	N	I	L	P	V	E	E
4C2	K	P	G	Q	P	P	K	L	L	I	K	Y	A	S	I	Q	E	S	G	V	P	A	R	F	S	G	S	G	S	G	T	D	F	T	L	N	I	L	P	V	E	E
1B12	K	P	G	S	S	P	K	L	W	I	Y	S	T	S	N	L	A	S	G	V	P	A	R	F	S	G	S	G	S	G	T	S	Y	S	L	T	I	S	S	M	E	A
13D4	K	P	D	G	T	V	K	L	L	I	Y	Y	T	S	R	L	H	S	G	V	P	S	R	F	S	G	S	G	S	G	T	D	Y	S	L	T	I	T	N	L	E	Q

CDR L3 - Contact
CDR L3 - Chothia
CDR L3 - Kabat

Kabat Number	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	
7G7	E	D	T	A	T	Y	Y	C	Q	H	T	W	E	I	P	F	T	F	G	S	G	T	K	L	E	I	K	SEQ ID NO: 21
4C2	E	D	T	A	T	Y	Y	C	Q	H	T	W	E	I	P	F	T	F	G	S	G	T	N	L	E	I	K	SEQ ID NO: 22
1B12	E	D	A	A	T	Y	Y	C	H	Q	Y	H	R	S	P	F	T	F	G	S	G	T	K	L	E	I	K	SEQ ID NO: 23
13D4	E	D	I	A	T	Y	F	C	Q	Q	A	N	T	L	P	Y	T	F	G	G	G	T	K	L	E	I	K	SEQ ID NO: 24

FIG. 3D-1

Heavy Chain Variable Region

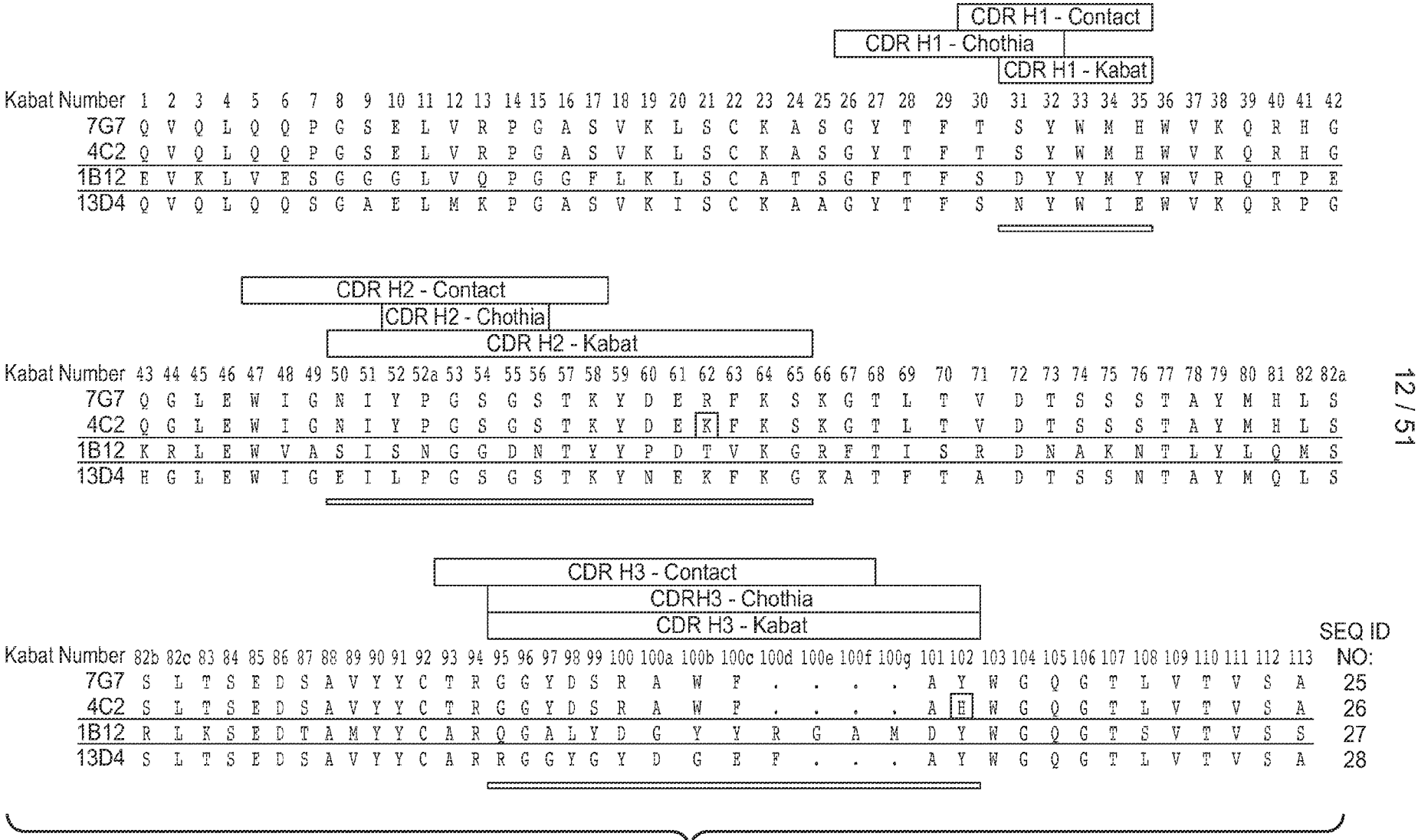
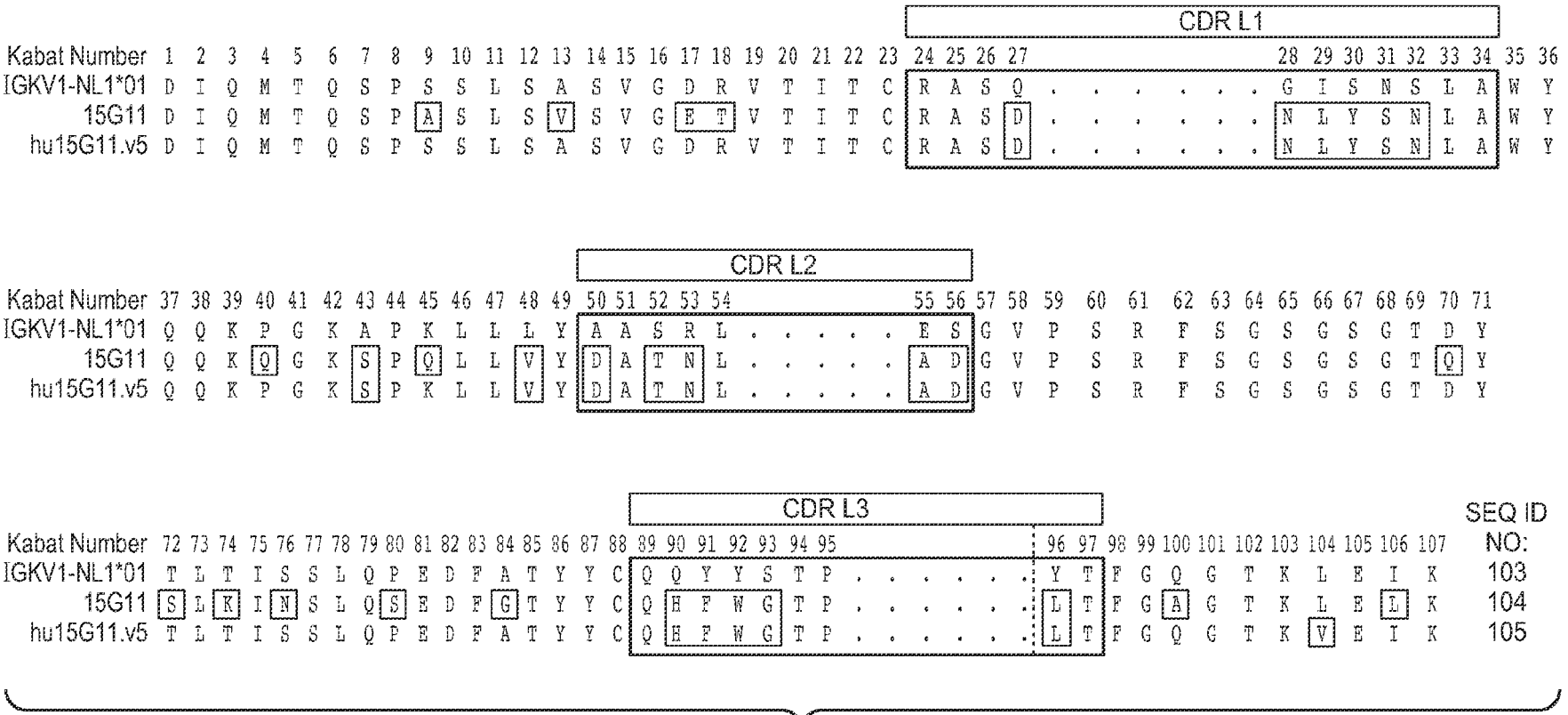


FIG. 3D-2

Humanization of 15G11 to Generate hu15G11.v5

Light Chain, Kappa: Mouse Antibody Aligned to Human Germlines



SEQ ID NO:
103
104
105

FIG. 4A-1

Humanization of 15G11 to Generate Hu15G11.v5

Heavy Chain: Mouse Antibody Aligned to Human Germlines

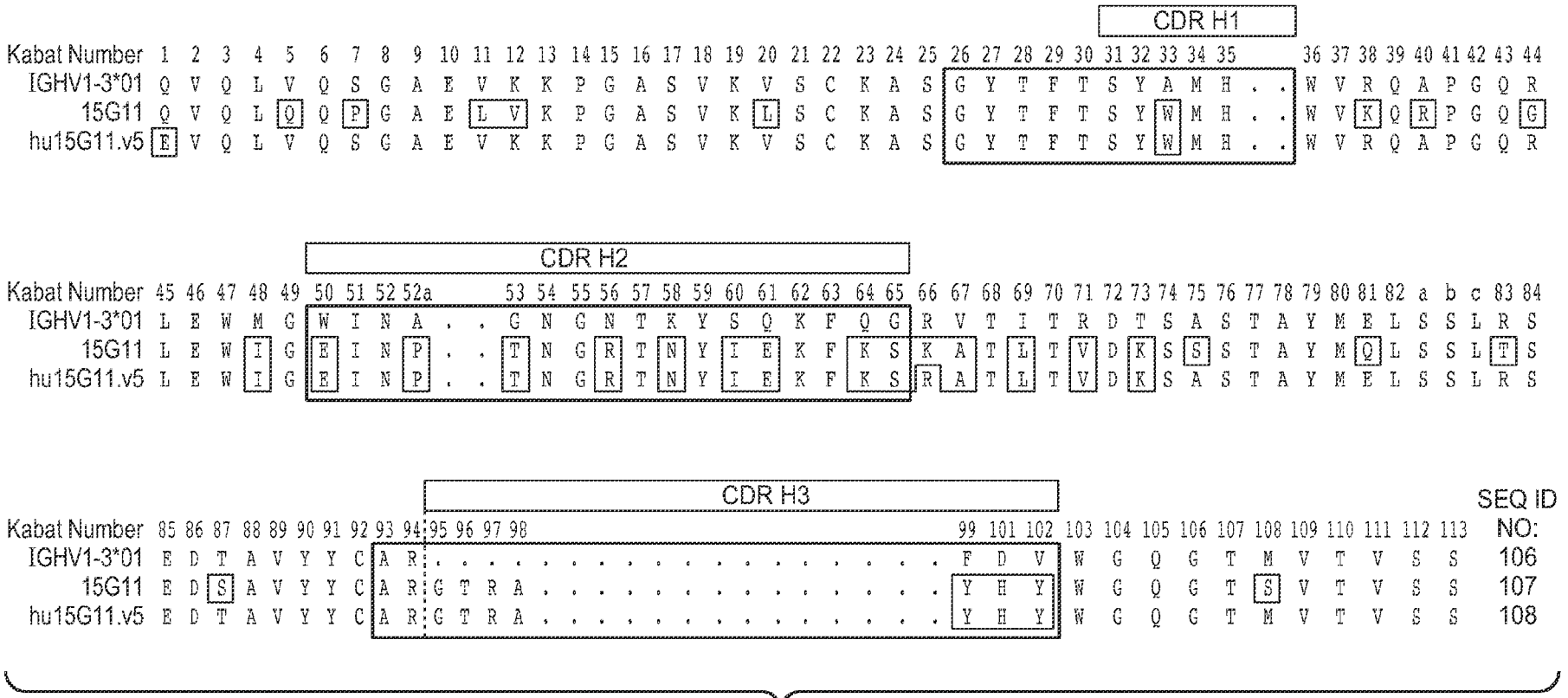


FIG. 4A-2

Humanization of 7A4/8A2 to Generate hu7A4.v15

Light Chain, Kappa: Mouse Antibody Aligned to Human Germlines

CDR L1: Kabat 24–34

Kabat Number	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	a	b	c	d	e	f	28	29	30	31	32	33	34	35	36
IGKV4-1*01	D	I	V	M	T	Q	S	P	D	S	L	A	V	S	L	G	E	R	A	T	I	N	C	K	S	S	Q	S	V	L	Y	S	S	N	N	K	N	Y	L	A	W	Y
8A2/7A4	D	I	V	L	T	Q	S	P	A	S	L	A	V	S	L	G	Q	R	A	T	I	S	C	R	A	S	E	S	V	D	S	.	.	Y	G	N	S	F	M	H	W	Y
hu7A4.v15	D	I	V	M	T	Q	S	P	D	S	L	A	V	S	L	G	E	R	A	T	I	N	C	R	A	S	E	S	V	D	S	.	.	Y	G	N	S	F	M	H	W	Y

CDR L2: Kabat 50–56

Kabat Number	37	38	39	40	41	42	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
IGKV4-1*01	Q	Q	K	P	G	Q	P	P	K	L	L	I	Y	W	A	S	T	R	.	.	.	.	.	E	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F
8A2/7A4	Q	Q	K	P	G	Q	P	P	K	L	L	I	Y	R	A	S	N	L	.	.	.	.	.	E	S	G	I	P	A	R	F	S	G	S	G	S	R	T	D	F
hu7A4.v15	Q	Q	K	P	G	Q	P	P	K	L	L	I	Y	R	A	S	N	L	.	.	.	.	.	E	S	G	V	P	D	R	F	S	G	S	G	S	R	T	D	F

CDR L3: Kabat 89–97

Kabat Number	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95							96	97	98	99	100	101	102	103	104	105	106	107	SEQ ID NO:
IGKV4-1*01	T	L	T	I	S	S	L	Q	A	E	D	V	A	V	Y	Y	C	Q	Q	Y	Y	S	T	P	.	.	.	.	.	.	Y	T	F	G	Q	G	T	K	L	E	I	K	109
8A2/7A4	T	L	T	I	N	P	V	E	A	D	D	V	A	T	Y	Y	C	Q	Q	S	N	E	G	P	.	.	.	.	.	.	P	T	F	G	G	G	T	K	L	E	I	K	110
hu7A4.v15	T	L	T	I	S	S	L	Q	A	E	D	V	A	V	Y	Y	C	Q	Q	S	N	E	A	P	.	.	.	.	.	.	P	T	F	G	Q	G	T	K	L	E	I	K	111

FIG. 4B-1

Humanization of 7A4/8A2 to Generate hu7A4.v15

Heavy Chain: Mouse Antibody Aligned to Human Germlines

CDR H1

Kabat Number	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	43	44
IGHV4-2*02	Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	G	A	S	V	K	V	S	C	K	A	S	G	Y	T	F	T	G	Y	Y	M	H	.	.	W	V	R	Q	A	P	G	Q	G
8A2/7A4	Q	V	Q	L	Q	Q	S	G	P	E	L	V	R	P	G	V	S	V	K	I	S	C	K	G	S	G	Y	T	F	T	D	Y	A	M	H	.	.	W	V	K	Q	S	H	A	K	S
hu7A4.v15	E	V	Q	L	V	Q	S	G	A	E	V	K	K	P	G	A	S	V	K	V	S	C	K	G	S	G	Y	T	F	T	D	Y	A	M	H	.	.	W	V	R	Q	A	P	G	Q	G

CDR H2

Kabat Number	45	46	47	48	49	50	51	52	a			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	a	b	c	83	84
IGHV4-2*02	L	E	W	M	G	W	I	N	P	.	.	N	S	G	G	T	N	Y	A	Q	K	F	Q	G	R	V	T	M	T	R	D	T	S	I	S	T	A	Y	M	E	L	S	R	L	R	S
8A2/7A4	L	E	W	I	G	G	I	S	T	.	.	Y	F	G	R	T	N	Y	N	Q	K	F	K	G	R	A	T	M	T	V	D	K	S	S	S	T	A	Y	M	E	L	A	R	L	T	S
hu7A4.v15	L	E	W	M	G	G	I	S	T	.	.	Y	F	G	R	T	N	Y	N	Q	K	F	K	G	R	V	T	M	T	V	D	T	S	I	S	T	A	Y	M	E	L	S	R	L	R	S

CDR H3

Kabat Number	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	A		B	101	102	103	104	105	106	107	108	109	110	111	112	113	SEQ ID NO:
IGHV4-2*02	D	D	T	A	V	Y	Y	C	A	R	.	.	.	.	.	.	.	. . . .	M	D	V	W	G	Q	G	T	T	V	T	V	S	S	112
8A2/7A4	E	D	S	A	L	Y	Y	C	A	R	G	L	S	G	N	Y	V	. . . .	M	D	Y	W	G	Q	G	T	S	V	T	V	S	S	113
hu7A4.v15	D	D	T	A	V	Y	Y	C	A	R	G	L	S	G	N	Y	V	. . . .	M	D	Y	W	G	Q	G	T	T	V	T	V	S	S	114

FIG. 4B-2

Humanization of 7G7 to Generate hu7G7.v1

Light Chain, Kappa: Mouse Antibody Aligned to K4H1

CDR L1

Kabat Number	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	a	b	c	d	e	f	28	29	30	31	32	33	34	35	36
K4H1	D	I	V	M	T	Q	S	P	D	S	L	A	V	S	L	G	E	R	A	T	I	N	C	K	S	S	Q	S	V	L	Y	S	S	N	N	K	N	Y	L	A	W	Y
7G7	D	I	V	L	T	Q	S	P	A	S	L	A	V	S	L	G	Q	R	A	T	I	S	C	R	A	R	Q	S	V	S	T	.	.	S	S	Y	S	F	M	H	W	Y
hu7G7.v1	D	I	V	M	T	Q	S	P	D	S	L	A	V	S	L	G	E	R	A	T	I	N	C	R	A	R	Q	S	V	S	T	.	.	S	S	Y	S	F	M	H	W	Y

CDR L2

Kabat Number	37	38	39	40	41	42	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
K4H1	Q	Q	K	P	G	Q	P	P	K	L	L	I	Y	W	A	S	T	R	.	.	.	.	.	E	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F
7G7	R	Q	K	A	G	Q	P	P	K	L	L	I	K	Y	A	S	I	Q	.	.	.	.	.	E	S	G	V	P	A	R	F	S	G	S	G	S	G	T	D	F
hu7G7.v1	Q	Q	K	P	G	Q	P	P	K	L	L	I	K	Y	A	S	I	Q	.	.	.	.	.	E	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F

CDR L3

Kabat Number	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95								96	97	98	99	100	101	102	103	104	105	106	107	SEQ ID NO:
K4H1	T	L	T	I	S	S	L	Q	A	E	D	V	A	V	Y	Y	C	Q	Q	Y	Y	S	T	P	.	.	.	.	.	.	.	F	T	F	G	Q	G	T	K	V	E	I	K	115
7G7	T	L	N	I	L	P	V	E	E	E	D	T	A	T	Y	Y	C	Q	H	T	W	E	I	P	.	.	.	.	.	.	.	F	T	F	G	S	G	T	K	L	E	I	K	116
hu7G7.v1	T	L	T	I	S	S	L	Q	A	E	D	V	A	V	Y	Y	C	Q	H	T	W	E	I	P	.	.	.	.	.	.	.	F	T	F	G	Q	G	T	K	V	E	I	K	117

FIG. 4C-1

Humanization of 7G7 to Generate hu7G7.v1

Heavy Chain: Mouse Antibody Aligned to K4H1

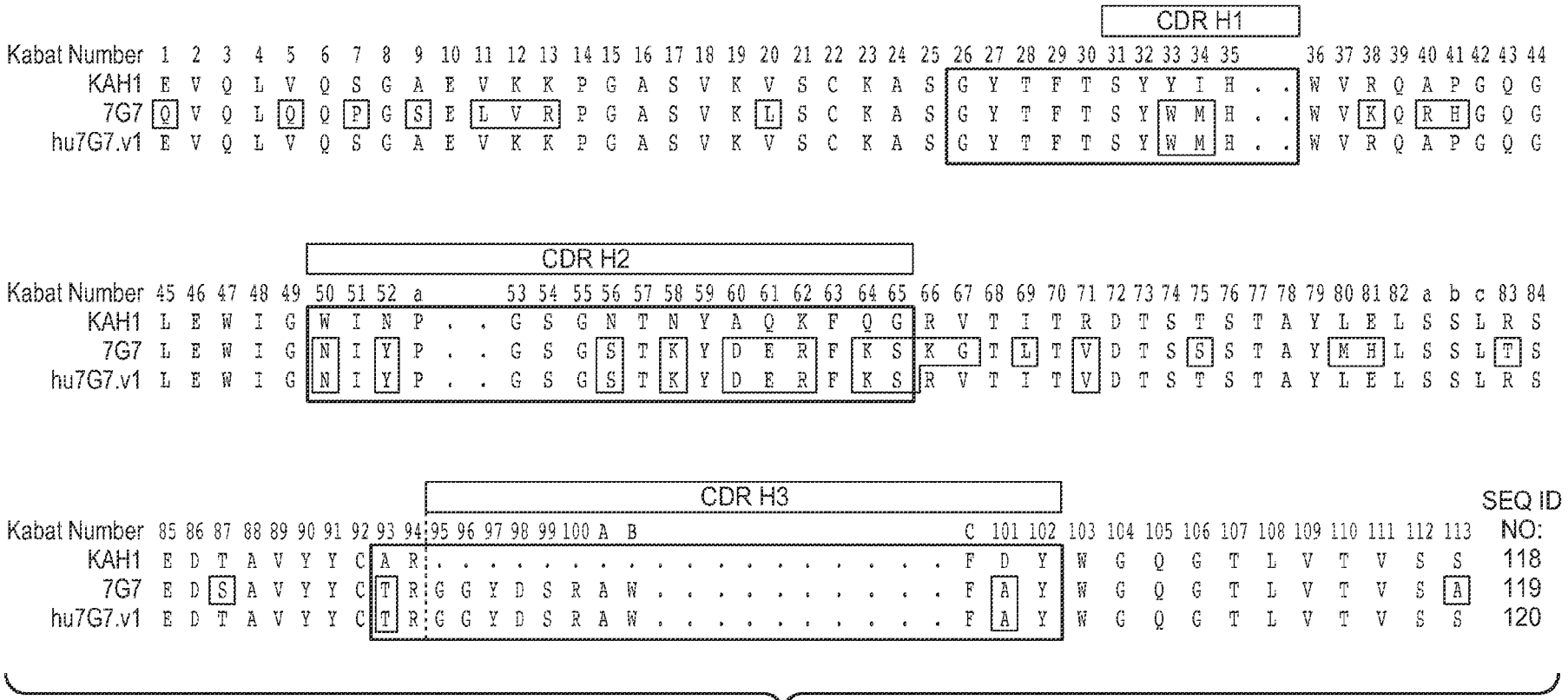


FIG. 4C-2

Humanization of 16F6 to Generate hu16F6.v4

Light Chain, Kappa: Mouse Antibody Aligned to Human Germlines

CDR L1 (Kabat 24–34)

Kabat Number	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
IGKV4-9*01	D	I	Q	L	T	Q	S	P	S	F	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
16F6	D	V	Q	I	T	Q	S	P	S	Y	L	T	A	S	P	G	E	T	I	T	I	N	C	R	A	S	K	. . . .	S	I	S	K	Y	L	A	W	Y
hu16F6.v4	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	K	. . . .	S	I	S	K	Y	L	A	W	Y

CDR L2 (Kabat 50–56)

Kabat Number	37	38	39	40	41	42	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
IGKV4-9*01	Q	Q	K	P	G	K	A	P	K	L	L	I	Y	A	A	S	T	L	. . . . . .	Q	S	G	V	P	S	R	F	S	G	S	G	S	G	T	E	F
16F6	Q	E	K	P	G	K	T	N	K	L	L	I	Y	S	G	S	T	L	. . . . . .	Q	S	G	I	P	S	R	F	S	G	S	G	S	G	T	D	F
hu16F6.v4	Q	Q	K	P	G	K	T	N	K	L	L	L	Y	S	G	S	T	L	. . . . . .	Q	S	G	V	P	S	R	F	S	G	S	G	S	G	T	D	Y

CDR L3 (Kabat 89–97)

Kabat Number	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95		96	97	98	99	100	101	102	103	104	105	106	107	SEQ ID NO:
IGKV4-9*01	T	L	T	I	S	S	L	Q	P	E	D	F	A	T	Y	Y	C	Q	Q	L	N	S	Y	P	. . . .	W	T	F	G	Q	G	T	K	V	E	I	K	121
16F6	T	L	T	I	S	N	L	E	P	E	D	F	A	M	Y	Y	C	Q	Q	H	N	E	Y	P	. . . .	W	T	F	G	G	G	T	K	L	E	I	K	122
hu16F6.v4	T	L	T	I	S	S	L	Q	P	E	D	F	A	T	Y	Y	C	Q	Q	H	N	E	Y	P	. . . .	W	T	F	G	Q	G	T	K	V	E	I	K	123

FIG. 4D-1

Humanization of 16F6 to Generate hu16F6.v4

Heavy Chain: Mouse Antibody Aligned to Human Germlines

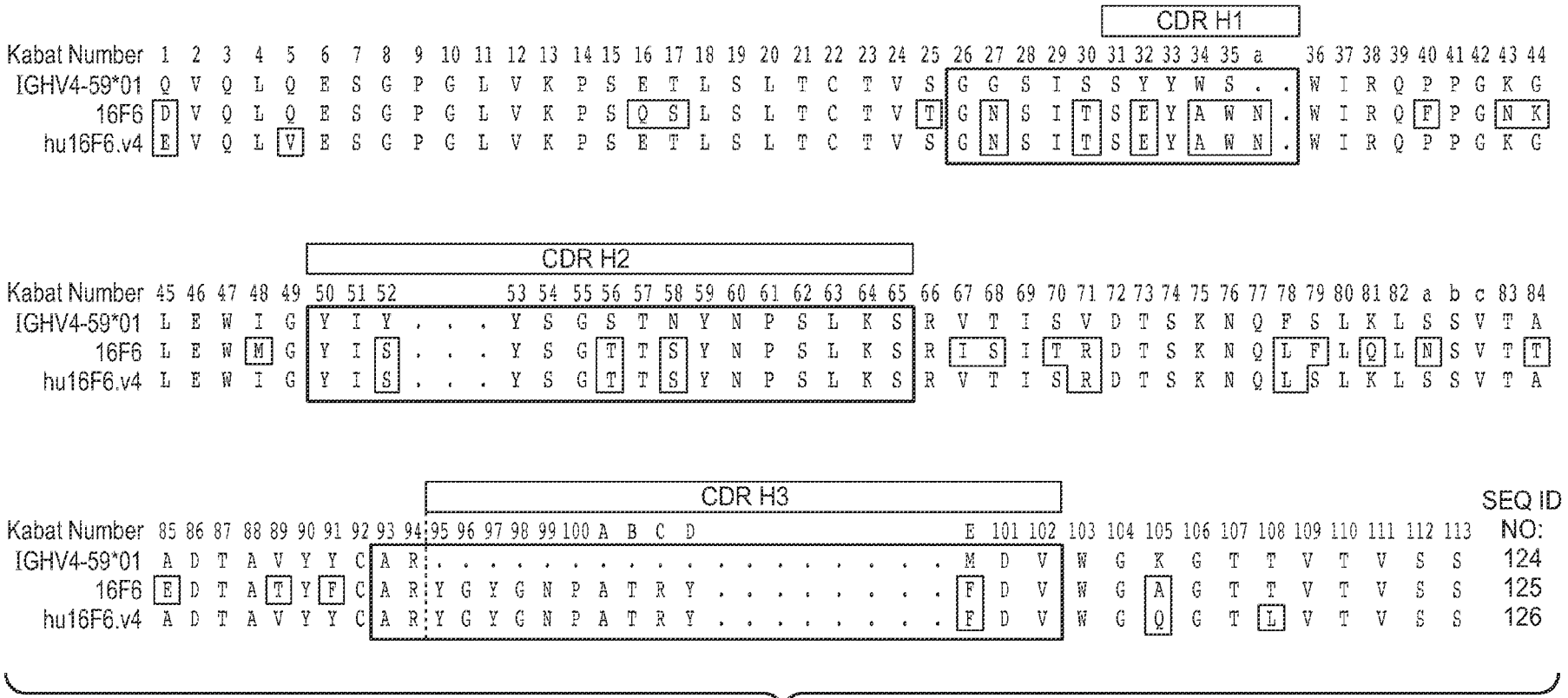


FIG. 4D-2

FIG. 4E-1

FIG. 4E-2

FIG. 4E

FIG. 4E-1

15G11, 7A4 and 16F6 Humanization Variants

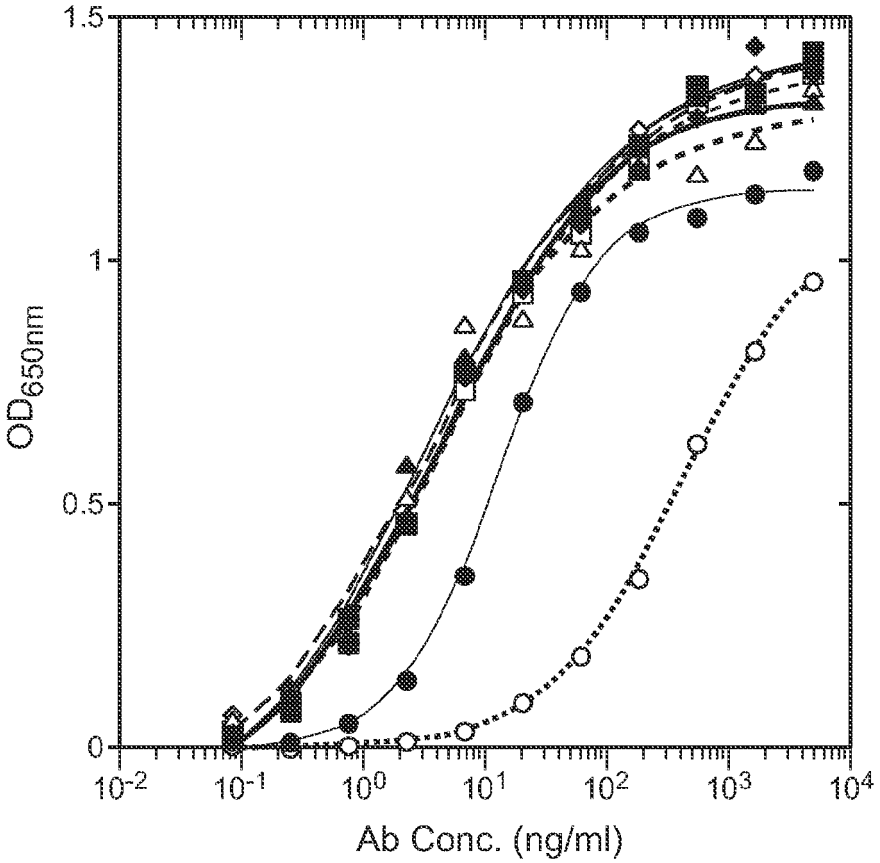
	LC		HC					huTfR			CynoTfR			Cy/hu Ratio
	43	48	48	67	69	71	73	Ka	Kd	KD	Ka	Kd	KD	
mu15G11	S	V	I	A	L	V	K	8.900E+05	8.825E-04	9.916E-10	1.288E+06	3.349E-03	2.600E-09	2.6
hu15G11.v1	A	L	M	V	I	R	T	6.240E+05	3.194E-03	5.119E-09	8.571E+05	8.670E-03	1.012E-08	2.0
hu15G11.v2	A	L	M	V	I	V	T	3.520E+05	3.290E-03	9.347E-09	4.554E+05	8.021E-03	1.761E-08	1.9
hu15G11.v3	S	V	M	V	I	R	T	5.703E+05	2.347E-03	4.115E-09	8.044E+05	4.292E-03	5.336E-09	1.3
hu15G11.v4	S	V	M	V	I	V	T	4.773E+05	1.855E-03	3.886E-09	5.732E+05	4.033E-03	7.036E-09	1.8
hu15G11.v5	S	V	I	A	L	V	K	6.46E+05	0.00215	3.33E-09	5.43E+05	0.00641	1.18E-08	3.5

	LC		HC				huTfR			CynoTfR			Cy/hu Ratio
	27d	58	68	94	24	71	Ka	Kd	KD	Ka	Kd	KD	
ch 7A4	D	I	R	A	G	V	2.11E+06	4.34E-04	2.06E-10	1.06E+06	6.63E-04	6.27E-10	3.04
ch7A4/8A2	S	I	R	G	G	V	3.007E+06	3.353E-04	1.115E-10	1.315E+06	1.216E-03	9.247E-10	8.3
hu7A4.v1	S	V	G	G	A	R	1.41E+06	3.94E-04	2.79E-10	9.15E+05	1.53E-03	1.67E-09	6.0
hu7A4.v2	S	V	G	G	G	R	1.60E+06	3.71E-04	2.32E-10	9.62E+05	1.17E-03	1.22E-09	5.3
hu7A4.v3	S	V	G	G	A	V	6.24E+05	3.39E-04	5.43E-10	3.22E+05	9.34E-04	2.90E-09	5.3
hu7A4.v4	S	V	G	G	G	V	4.82E+05	2.95E-04	6.12E-10	2.52E+05	9.66E-04	3.83E-09	6.3
hu7A4.v5	S	I	G	G	A	R	1.748E+06	6.363 E-04	3.640E-10	1.461E+06	1.757E-03	1.203E-09	3.3
hu7A4.v6	S	I	G	G	G	R	2.845E+06	7.396 E-04	2.600E-10	1.780E+06	1.883E-03	1.058E-09	4.1

hu7A4.v7	S	I	G	G	A	V	1.113E+06	5.735E-04	5.153E-10	2.428E+06	2.855E-03	1.176E-09	2.3
hu7A4.v8	S	I	G	G	G	V	8.326E+05	1.077E-03	1.294E-09	2.768E+05	3.411E-03	1.232E-08	9.5
hu7A4.v9	S	V	R	G	A	R	1.930E+06	2.304E-04	1.194E-10	1.280E+06	5.477E-04	4.279E-10	3.6
hu7A4.v10	S	V	R	G	G	R	1.684E+06	2.407E-04	1.429E-10	1.115E+06	5.632E-04	5.051E-10	3.5
hu7A4.v11	S	V	R	G	A	V	1.487E+06	2.323E-04	1.562E-10	8.049E+05	7.588E-04	9.427E-10	6.0
hu7A4.v12	S	V	R	G	G	V	9.159E+05	1.833E-04	2.001E-10	4.587E+05	9.580E-04	2.089E-09	10.4
hu7A4.v13	S	V	G	A	G	V	4.51E+05	6.14E-04	1.36E-09	2.13E+05	2.42E-03	1.14E-08	8.3
hu7A4.v14	S	I	G	A	G	V	6.14E+05	7.33E-04	1.19E-09	2.30E+05	3.61E-03	1.57E-08	13.2
hu7A4.v15	S	V	R	A	G	V	6.73E+05	3.77E-04	5.61E-10	2.90E+05	2.26E-03	7.80E-09	13.9

	LC		HC		huTfR			CynoTfR			Cy/hu Ratio
	43	44	71	78	Ka	Kd	KD	Ka	Kd	KD	
mu16F6	T	N	R	L	1.36E+05	2.81E-04	2.07E-09	1.23E+05	9.13E-04	7.45E-09	3.6
hu16F6.v1	A	P	V	F	4.10E+04	7.67E-04	1.87E-08	4.64E+04	0.009242	1.99E-07	10.7
hu16F6.v2	A	P	R	L	4.62E+04	1.97E-04	4.25E-09	4.38E+04	0.002981	6.81E-08	16.0
hu16F6.v3	T	N	V	F	7.86E+04	3.23E-04	4.11E-09	7.26E+04	0.002503	3.45E-08	8.4
hu16F6.v4	T	N	R	L	8.99E+04	7.94E-05	8.84E-10	8.30E+04	9.13E-04	1.10E-08	12.5

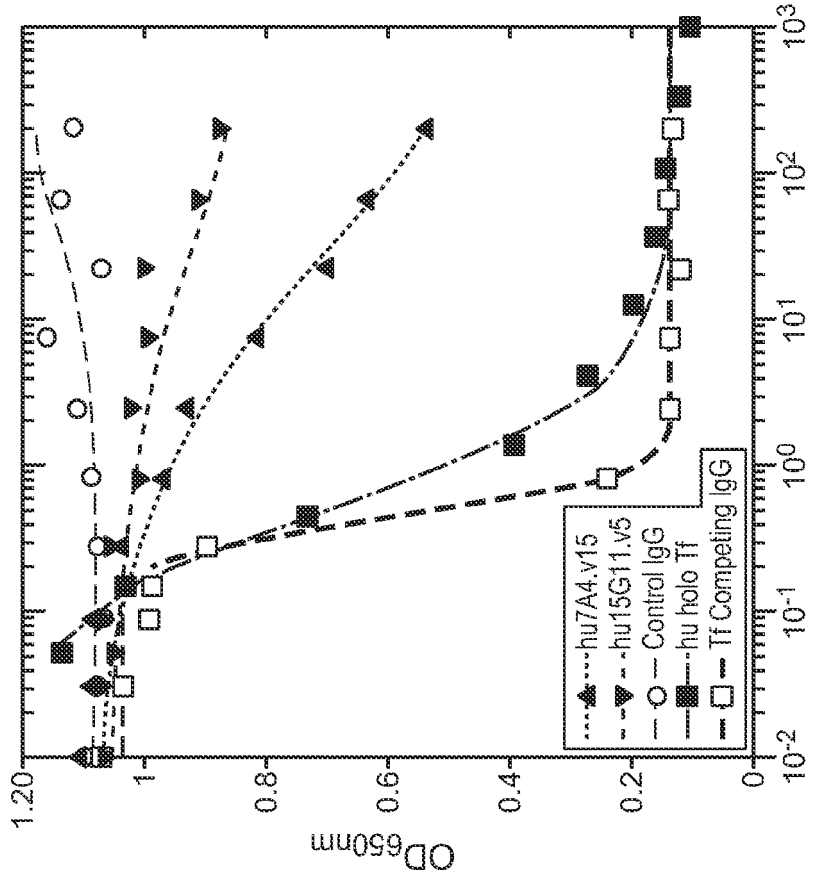
FIG. 4E-2



Antibody binding in the (open, dashed line) presence or (filled, solid line) absence of 6.3 μM holo-Tf

hu7A4.v15 - Square
hu15G11.v5 - Diamond
hu7G7.v1 - Triangle
Tf Competing Antibody - Circle

FIG. 5


OD650nm
Ab Conc. (ug/ml)
hu7A4.v15
hu15G11.v5
Control IgG
hu holo Tf
Tf Competing IgG

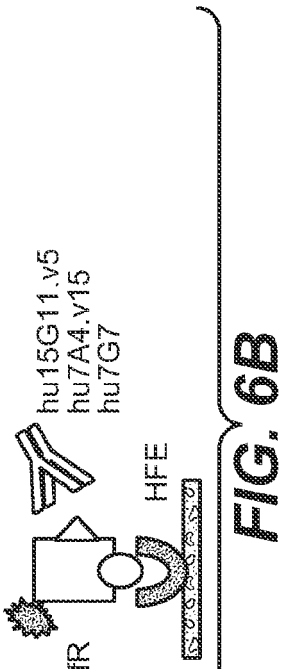
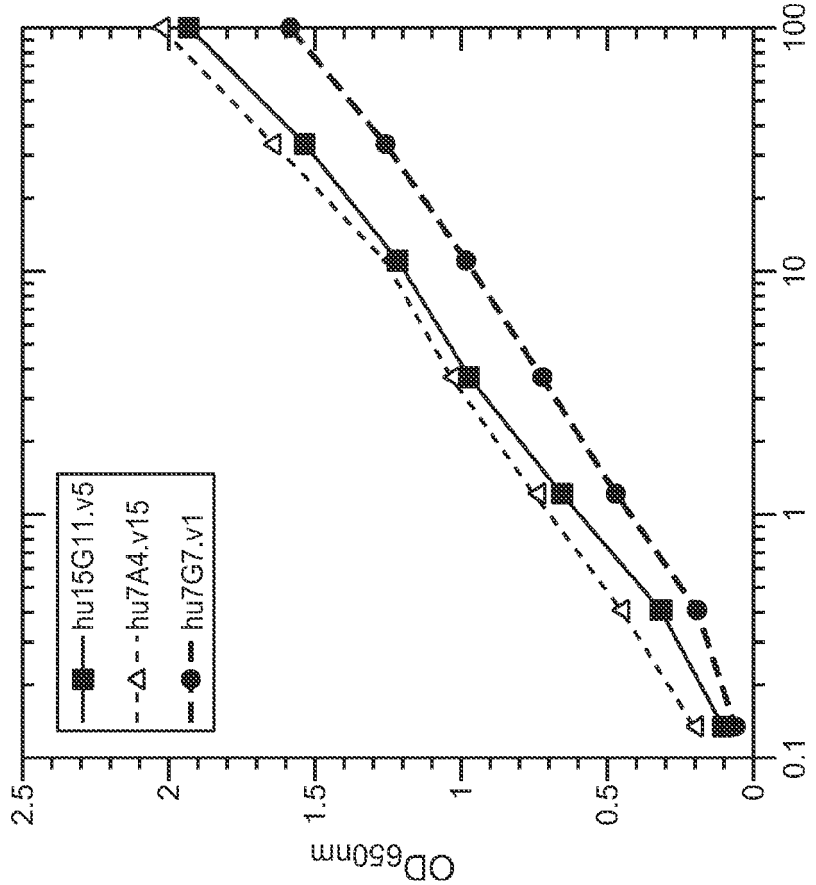

hu15G11.v5
hu7A4.v15
hu7G7
huTfR
HFE

FIG. 6B


OD650nm
Ab Conc. (ug/ml)
hu15G11.v5
hu7A4.v15
hu7G7.v1


hu15G11.v5
hu7A4.v15
hu7G7
huTfR
HFE

FIG. 6A

	15G11 Variant IgG	ELIZA (EC50) Using IgG huTfR (ng/ml)	ELIZA (EC50) Using IgG CynoTfR (ng/ml)	Biacore (SCK) 1:1 fit (IgG) huTfR (nM)	Biacore (SCK) 1:1 fit (IgG) CynoTfR (nM)	Biacore Steady State (IgG) huTfR (nM)	Biacore Steady State (IgG) CynoTfR (nM)	Biacore (Fab) huTfR (nM)	Biacore (Fab) CynoTfR (nM)
	15G11.v5	16± 1	20± 2	3.3	12			4.7	16
CDR-H3	T96A	274	3378	173		433			
	V99A	16.1	21.8						
	H101A	14.2	21.6						
	V102A	15.7	22.3						
CDR-L3	Q89A	30	506	125	268	212	591		
	H90A	13	24						
	F91A	45.8	953.3	167 ± 69		228 ± 152		383	
	W92A	11.8	44.1	31	32	123	327	280	370
	G93A	14.5	50.8	40	61	150	412	245	1300
	T94A	16.8	29.3						
	P95A	10.6	40.6	29	57	94	258	170	886
	L96A	9.9	18						
	T97A	13.4	15.7						

CDR L3									SEQ ID
89	90	91	92	93	94	95	96	97	NO:
Q	H	F	W	G	T	P	L	T	128

CDR H3								SEQ ID
95	96	97	98	99	101	102		NO:
G	T	R	A	Y	H	Y		129

FIG. 7A

	7A4 Variant IgG	ELIZA (EC50) Using IgG huTfR (ng/ml)	ELIZA (EC50) Using IgG CynoTfR (ng/ml)	Biacore (SCK) 1:1 fit (IgG) huTfR (nM)	Biacore (SCK) 1:1 fit (IgG) CynoTfR (nM)	Biacore Steady State (IgG) huTfR (nM)	Biacore Steady State (IgG) CynoTfR (nM)	Biacore (Fab) huTfR (nM)	Biacore (Fab) CynoTfR (nM)
	7A4.v15	14.8	14.2	0.58	7.8			0.4	4.3
CDR-H3	G95A	13.5	41.8						
	L96A	15.5	28.7						
	S97A								
	G98A	19.4	24.7						
	N99A	17	82.2	11	22	19	77		
	Y100A	15.9	24						
	V100aA								
	M100bA	16.1	16.9						
	D101A	17.3	18.5						
	Y102A	12.6	17.8						
CDR-L3	Q89A	10.9	13.8						
	Q90A	9.3	181	16	570	41	329	130	760
	S91A	11.3	16.3						
	N92A	8.7	13.7						
	E93A	12.2	17.6						
	P95A	9.7	15.9						
	P96A	10	16.2						
	T97A	12	22.6						

CDR L3									SEQ ID
89	90	91	92	93	94	95	96	97	NO:
Q	Q	S	N	E	A	P	P	T	130

CDR H3											SEQ ID
95	96	97	98	99	100	100a	100b	101	102		NO:
G	L	S	G	N	Y	V	M	D	Y		131

FIG. 7B

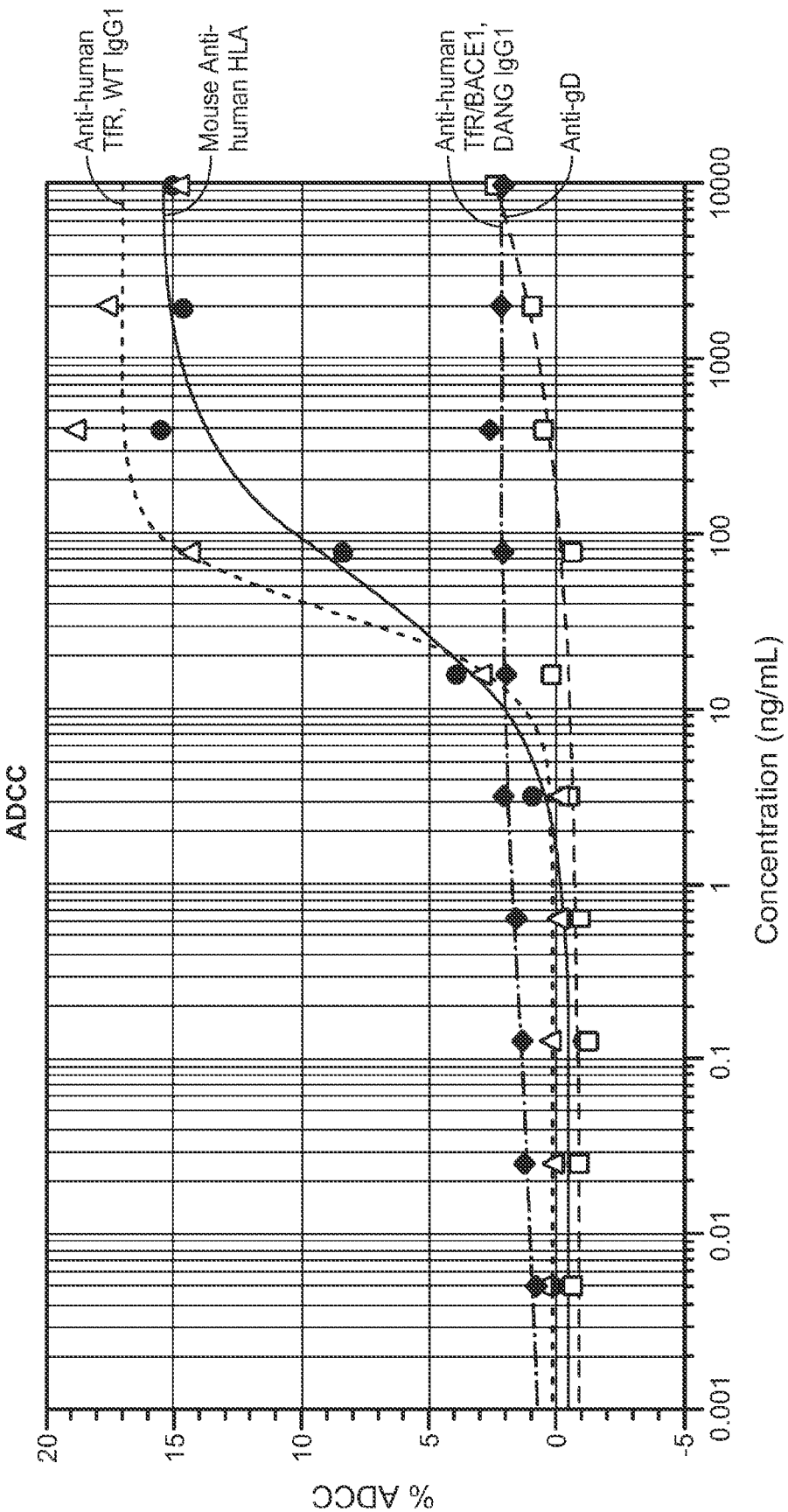

ADCC
% ADCC
20
15
10
5
0
-5
0.001
0.01
0.1
1
10
100
1000
10000
Concentration (ng/mL)
Anti-human TfR, WT IgG1
Mouse Anti-human HLA
Anti-human TfR/BACE1, DANG IgG1
Anti-gD

FIG. 8A

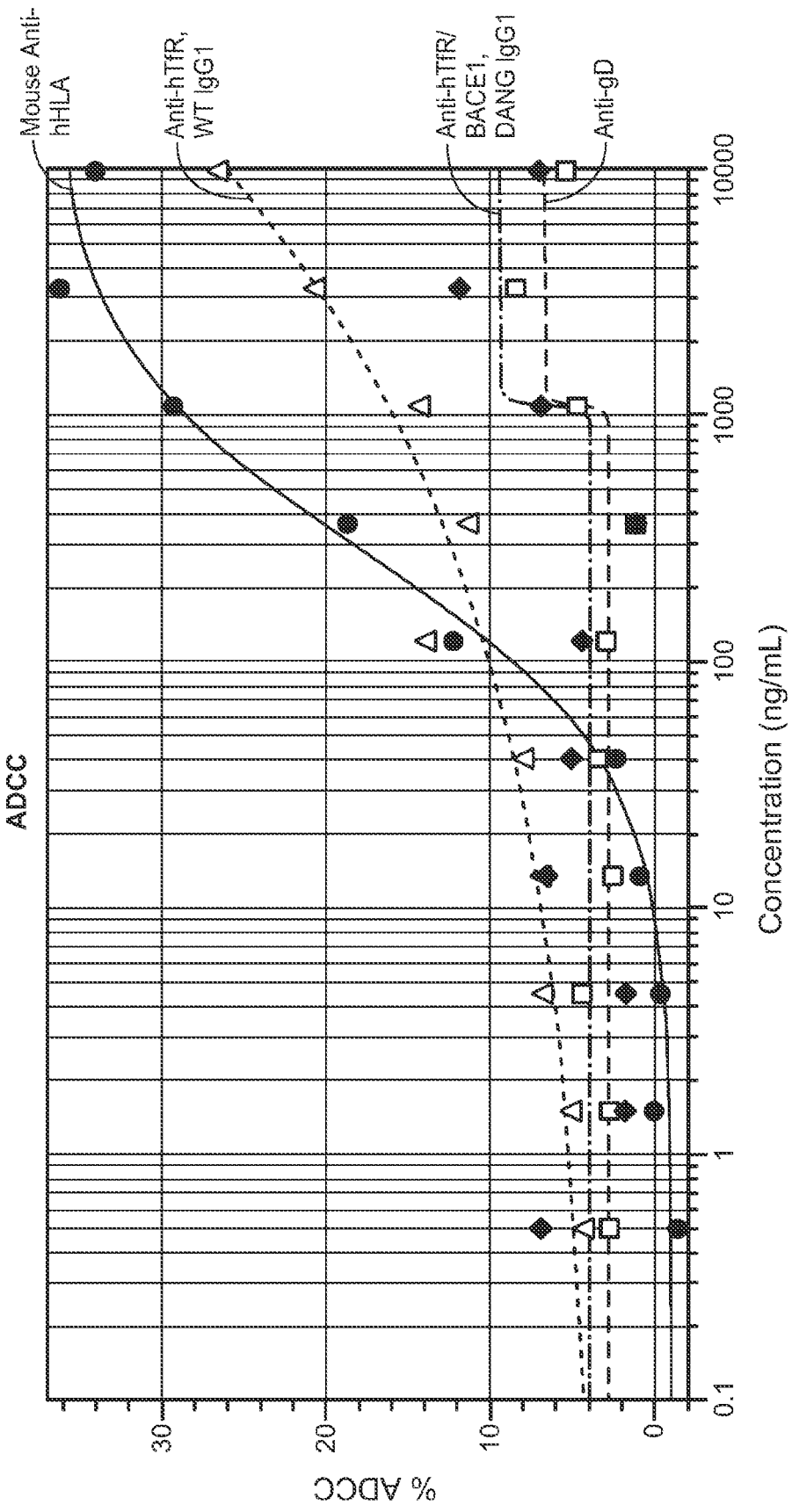

Mouse Anti-hHLA
Anti-hTfR, WT IgG1
Anti-hTfR/ BACE1, DANG IgG1
Anti-gD
ADCC
% ADCC
Concentration (ng/mL)
0
10
20
30
0.1
1
10
100
1000
10000

FIG. 8B

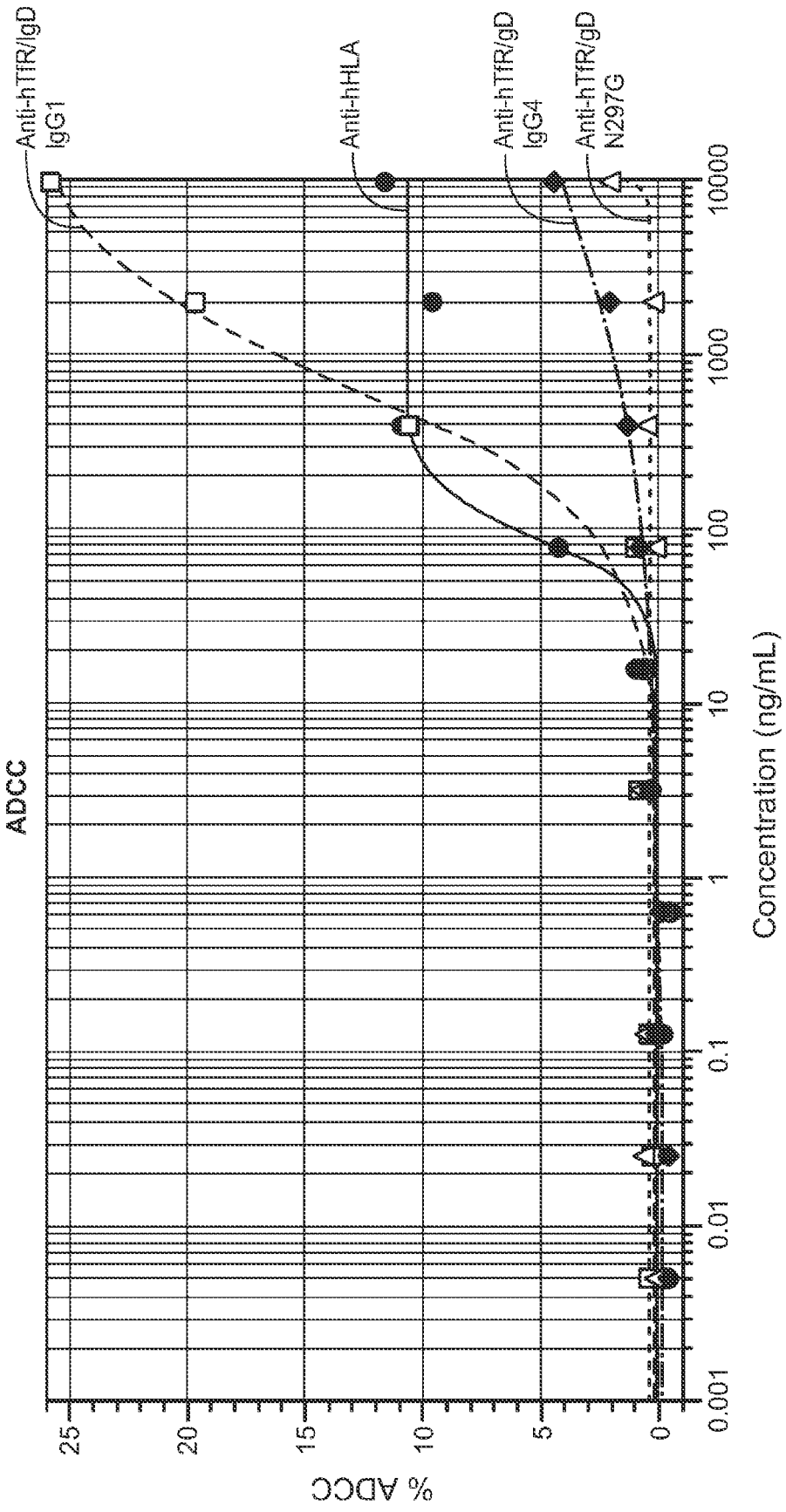

Anti-hTfR/IgD IgG1
Anti-hHLA
Anti-hTfR/gD IgG4
Anti-hTfR/gD N297G
ADCC
% ADCC
0
5
10
15
20
25
0.001
0.01
0.1
1
10
100
1000
10000
Concentration (ng/mL)

FIG. 9A

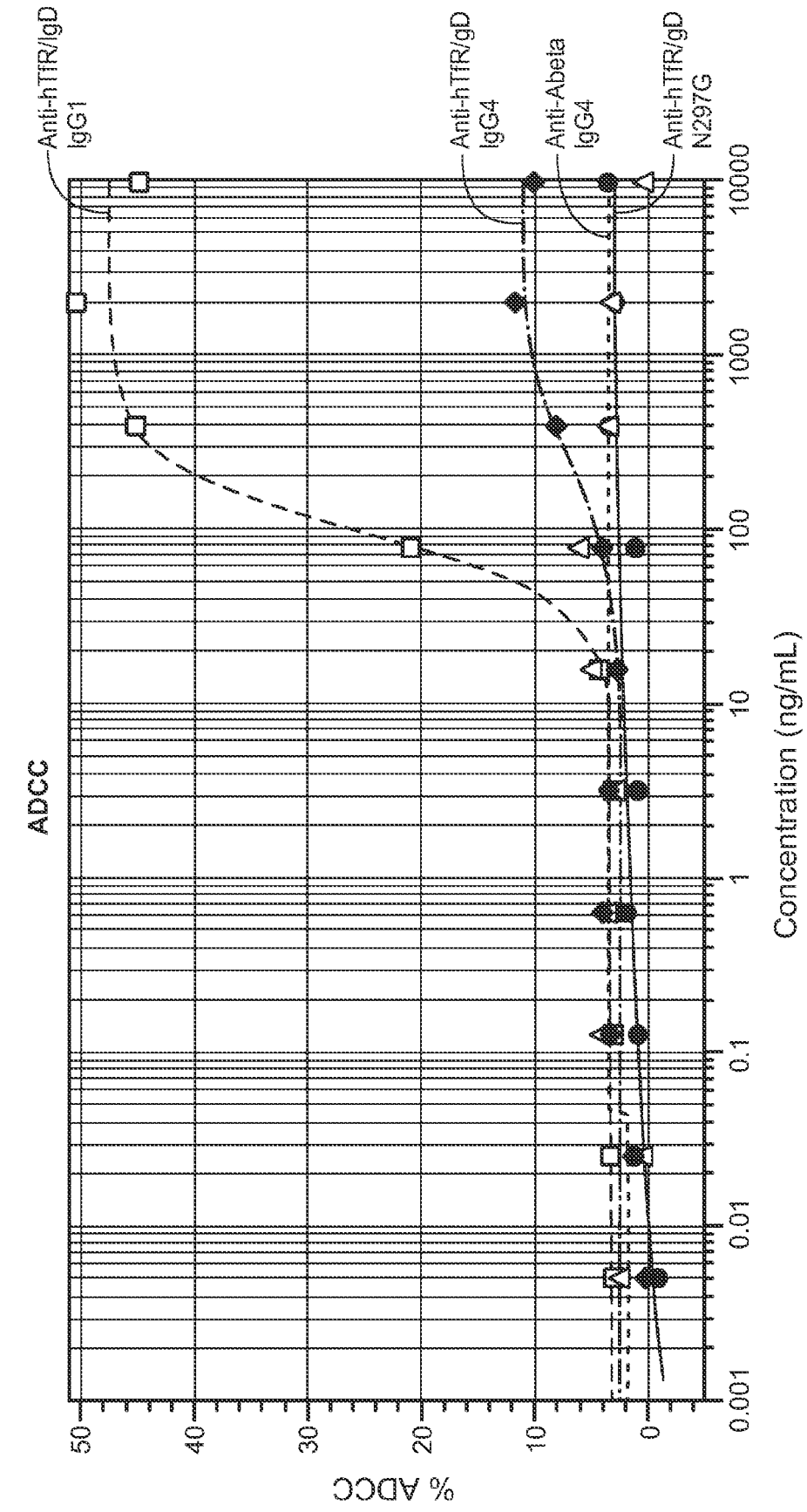

Anti-hTfR/IgD IgG1
Anti-hTfR/gD IgG4
Anti-Abeta IgG4
Anti-hTfR/gD N297G
ADCC
% ADCC
Concentration (ng/mL)
0.001
0.01
0.1
1
10
100
1000
10000
0
10
20
30
40
50

FIG. 9B

Grp	N	Tx	Isotype	Dose (mg/kg)	TfR Variant	Biacore huTfR (nM, Fab)	Biacore CynoTfR (nM, Fab)
1	5	Anti-gD	hIgG1	30			
2	5	Anti-TfR[1]/BACE1	hIgG1 DANG	30	hu15G11.v5	6 ± 2	19 ± 9
3	5	Anti-TfR[2]/BACE1	hIgG1 DANG	30	hu15G11.LC92A	230 ± 140	440 ± 160

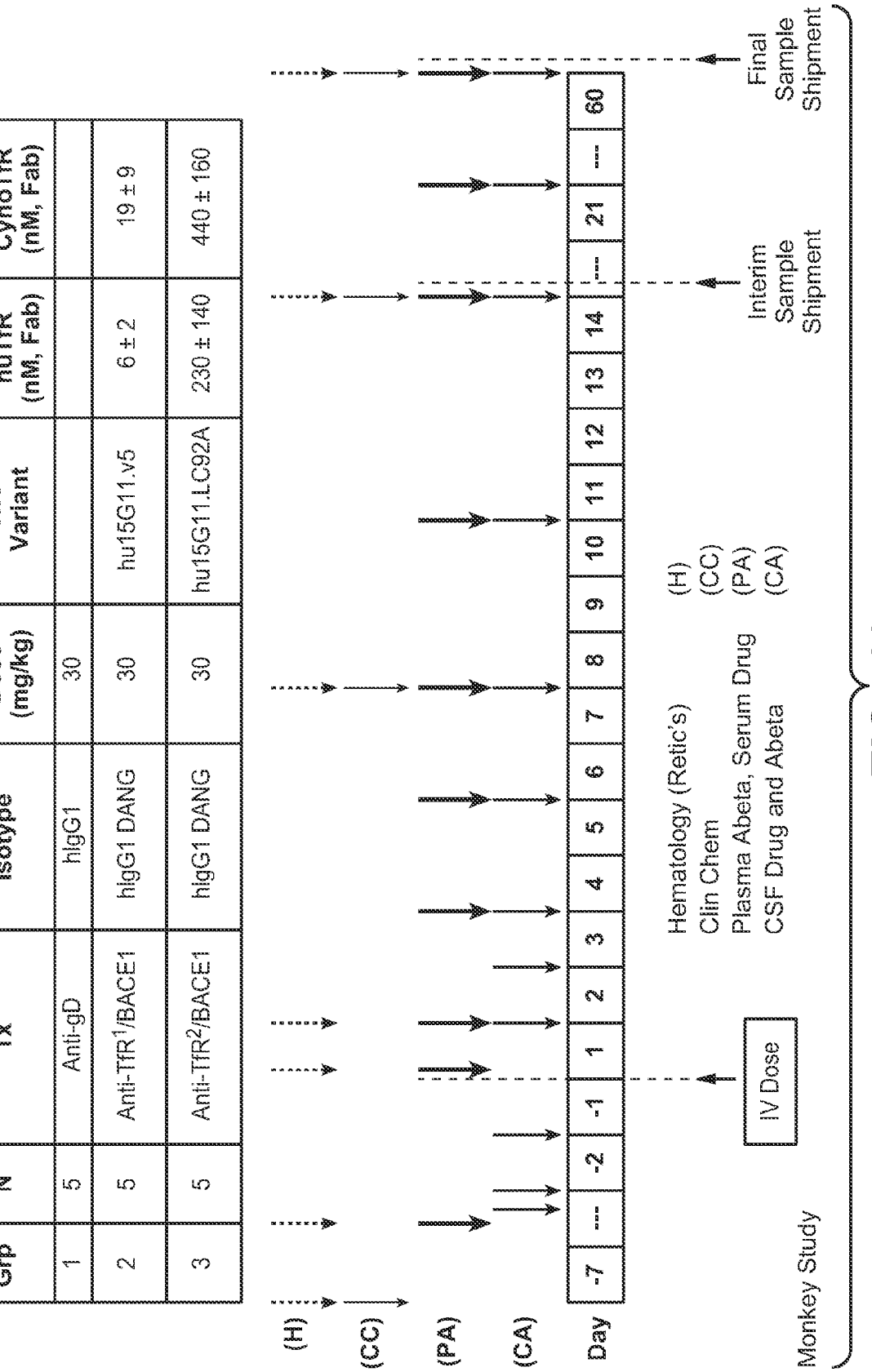


FIG. 10

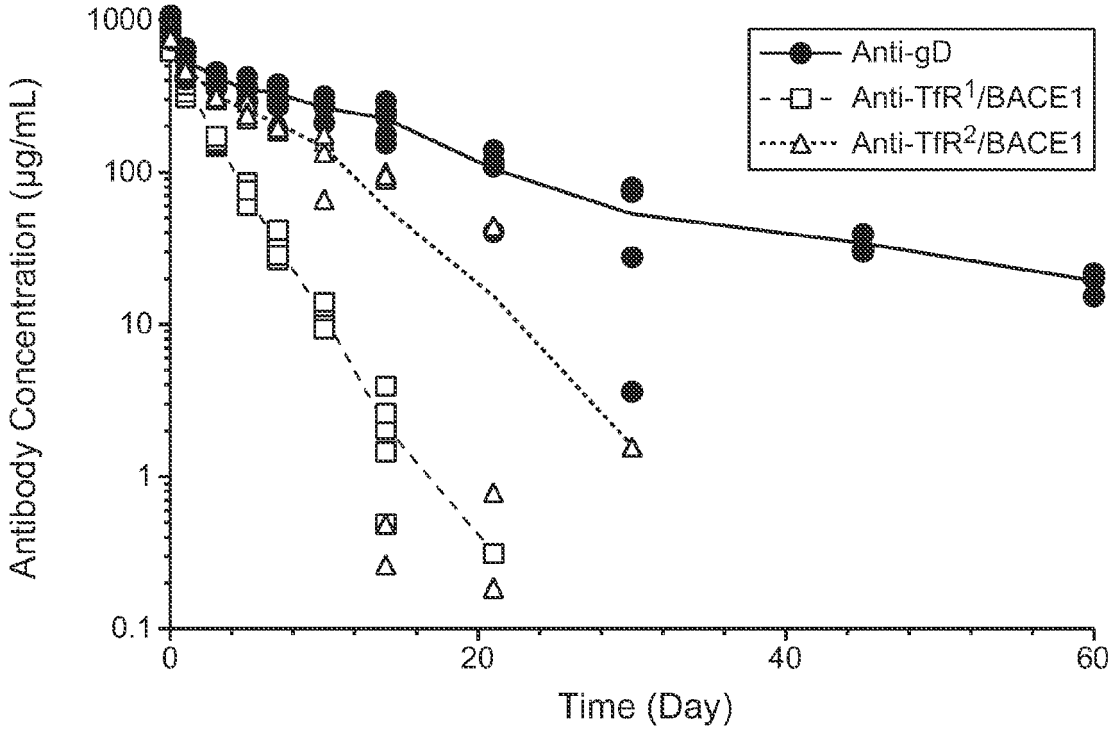


FIG. 11A

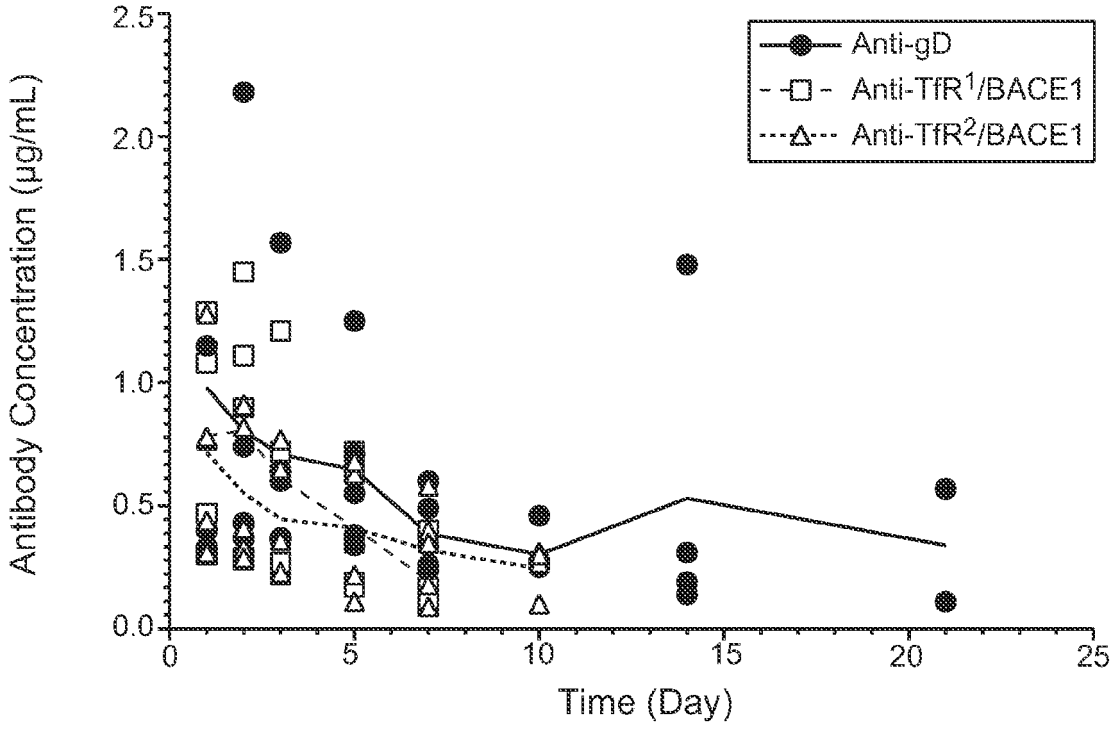


FIG. 11B

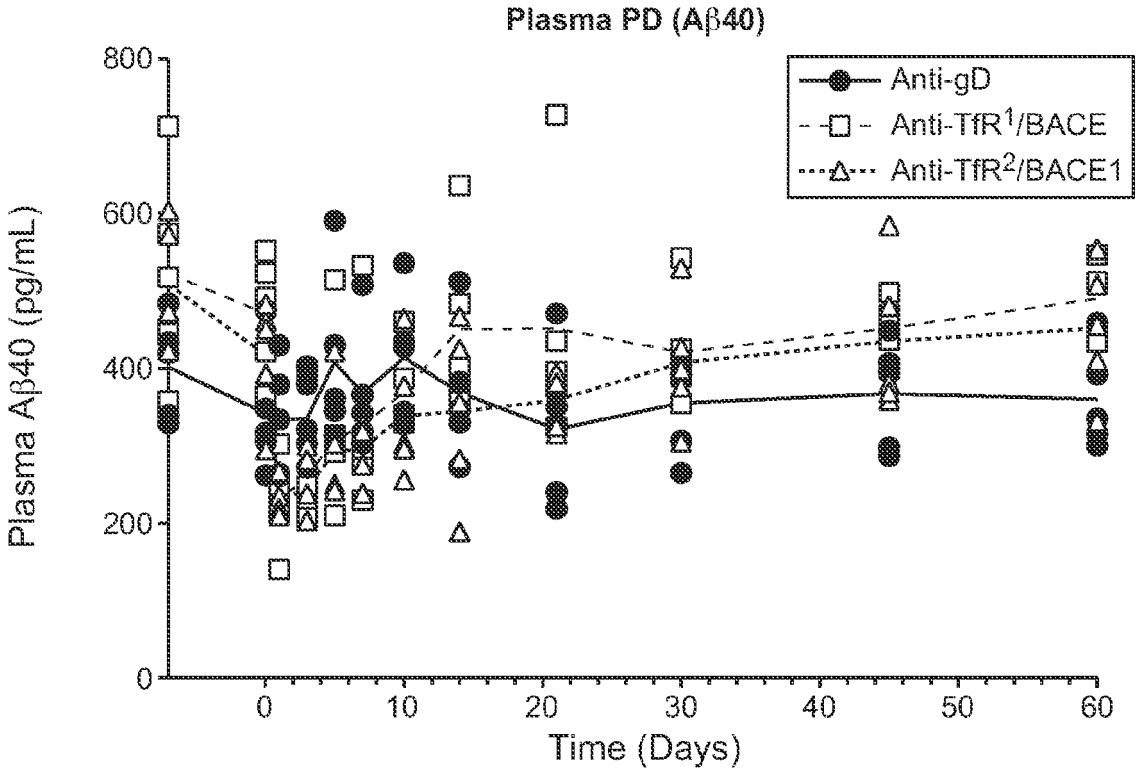


FIG. 12A

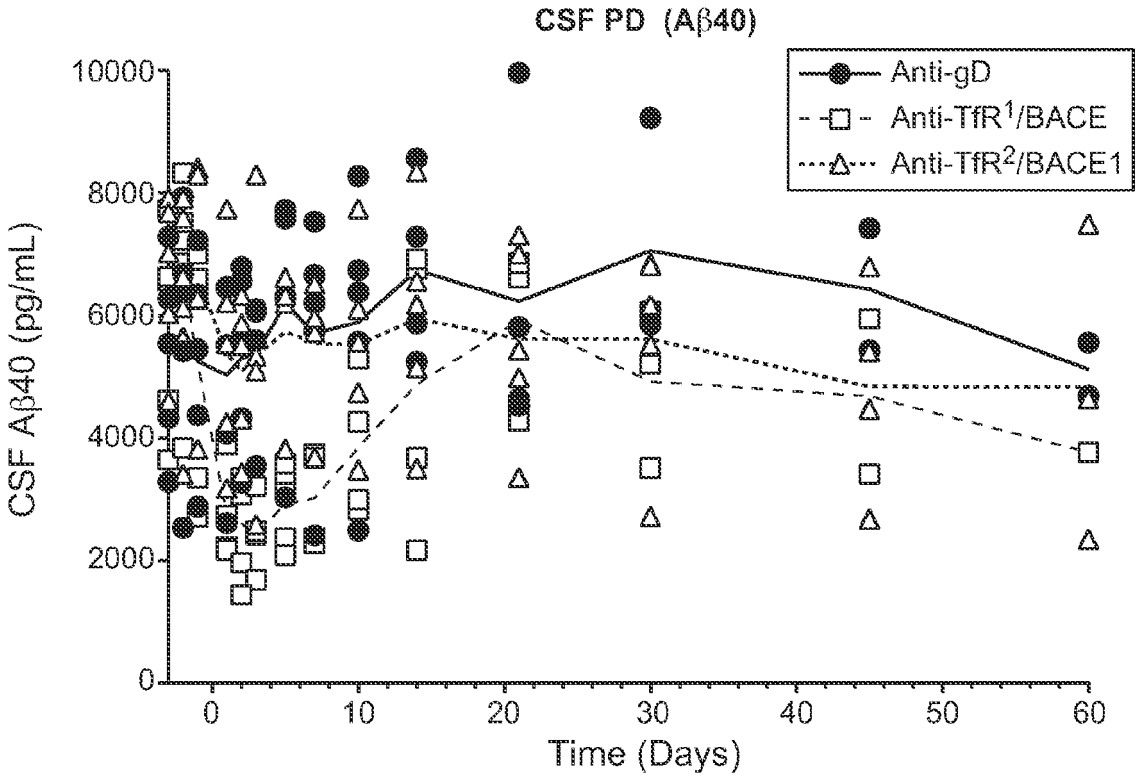


FIG. 12B

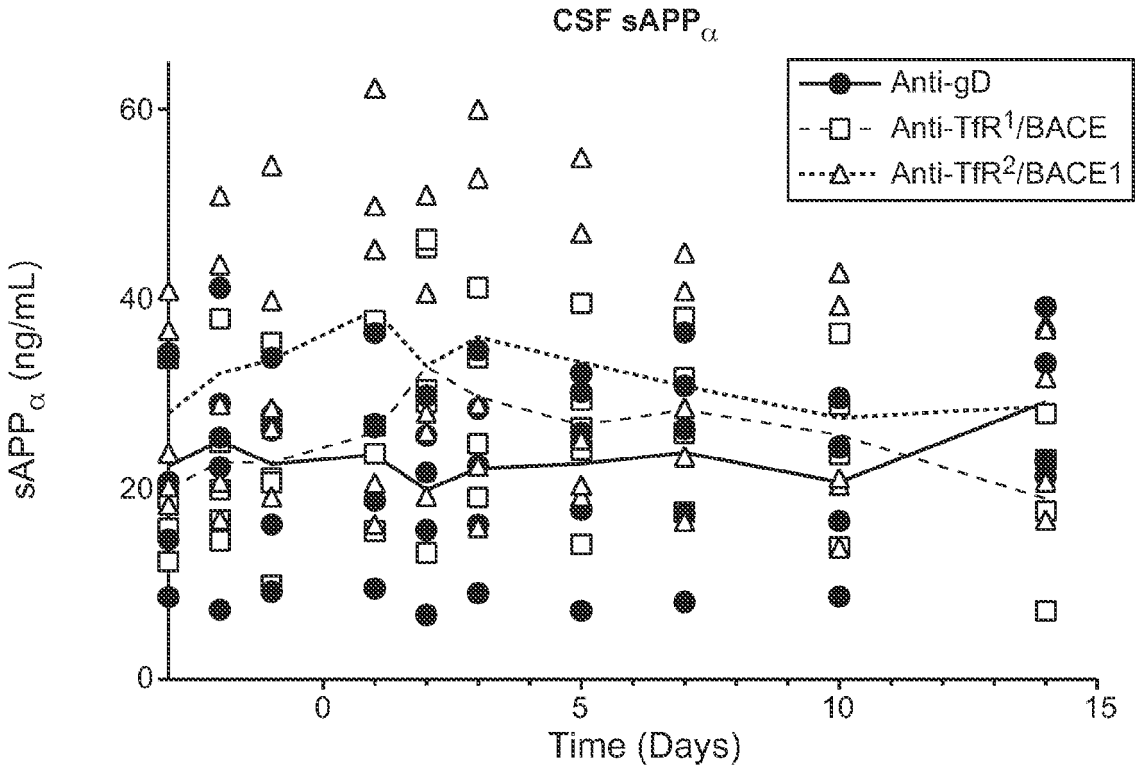


FIG. 12C

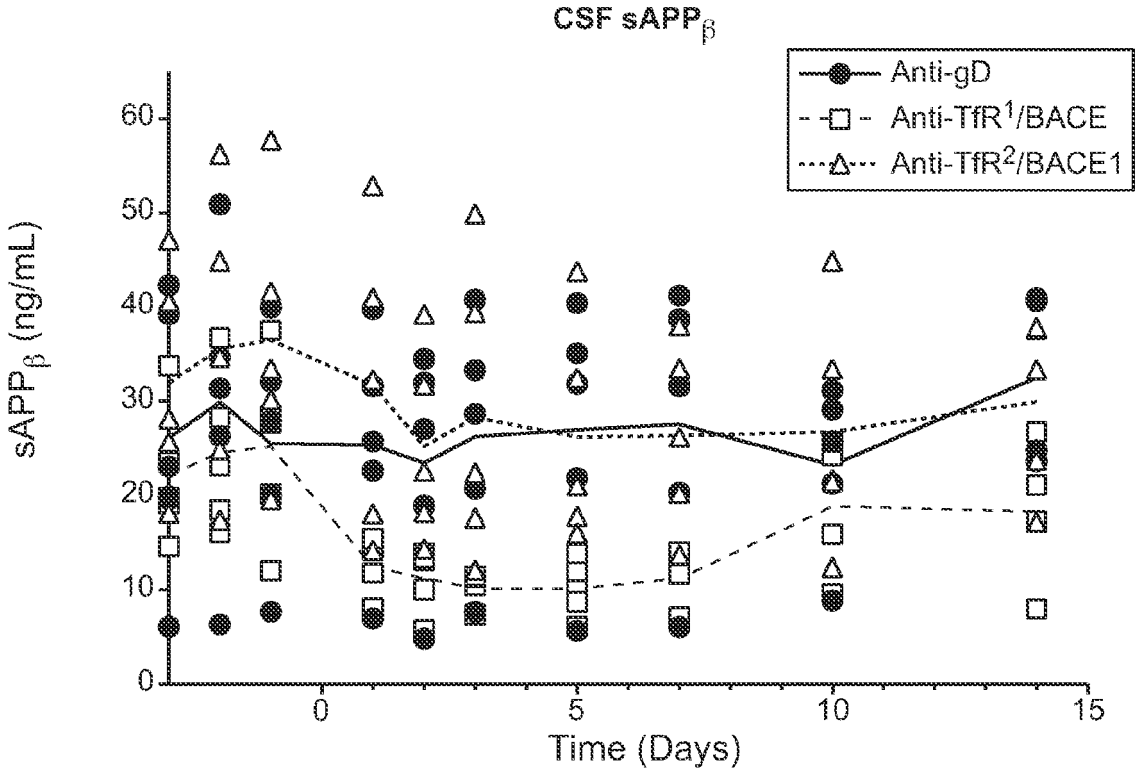


FIG. 12D

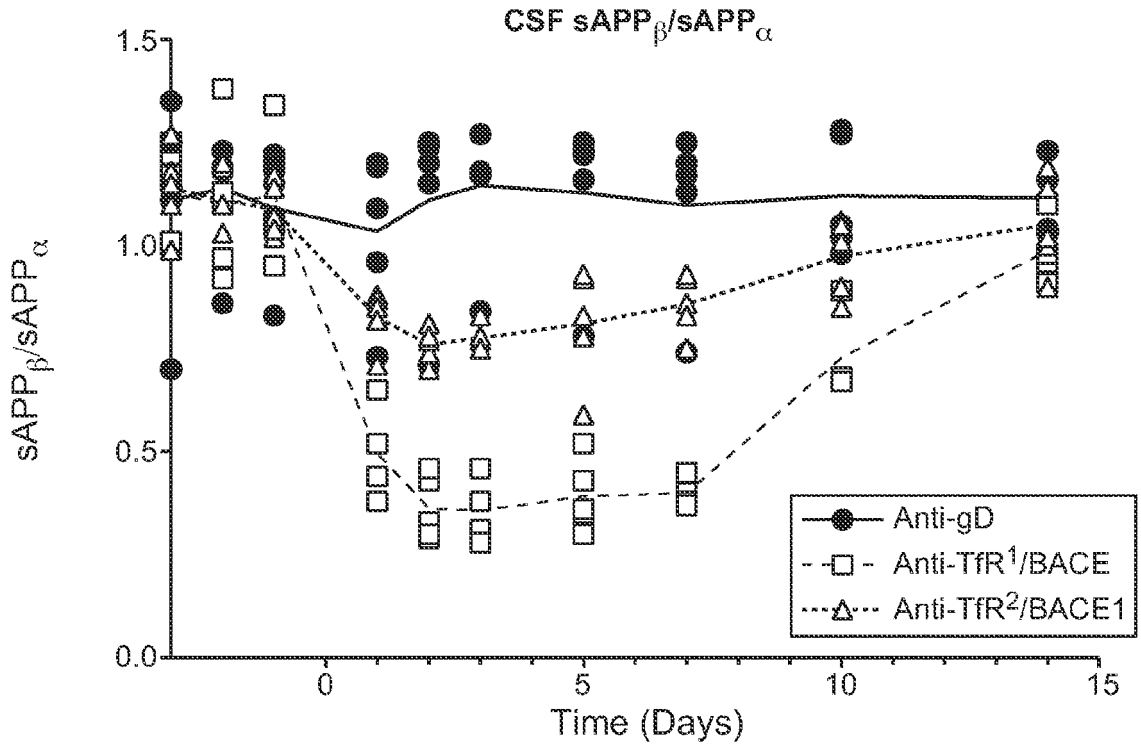

CSF sAPPβ/sAPPα
sAPPβ/sAPPα
1.5
1.0
0.5
0.0
0
5
10
15
Time (Days)
Anti-gD
Anti-TfR1/BACE
Anti-TfR2/BACE1

FIG. 12E

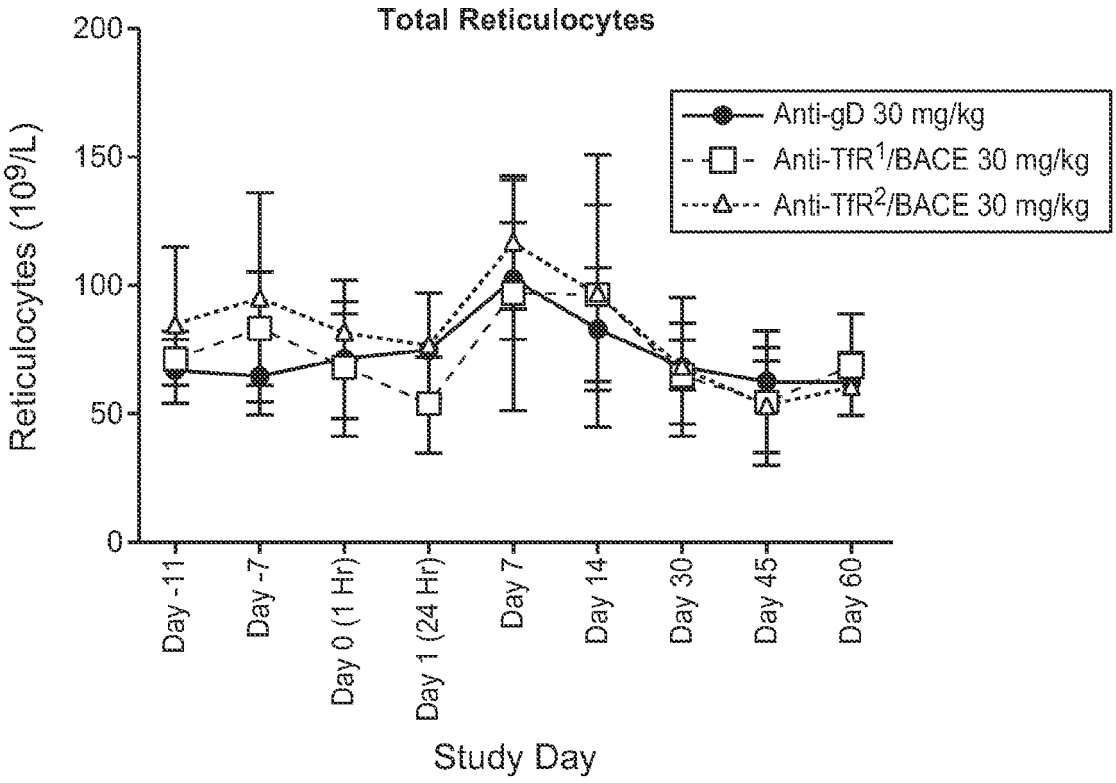


FIG. 13A

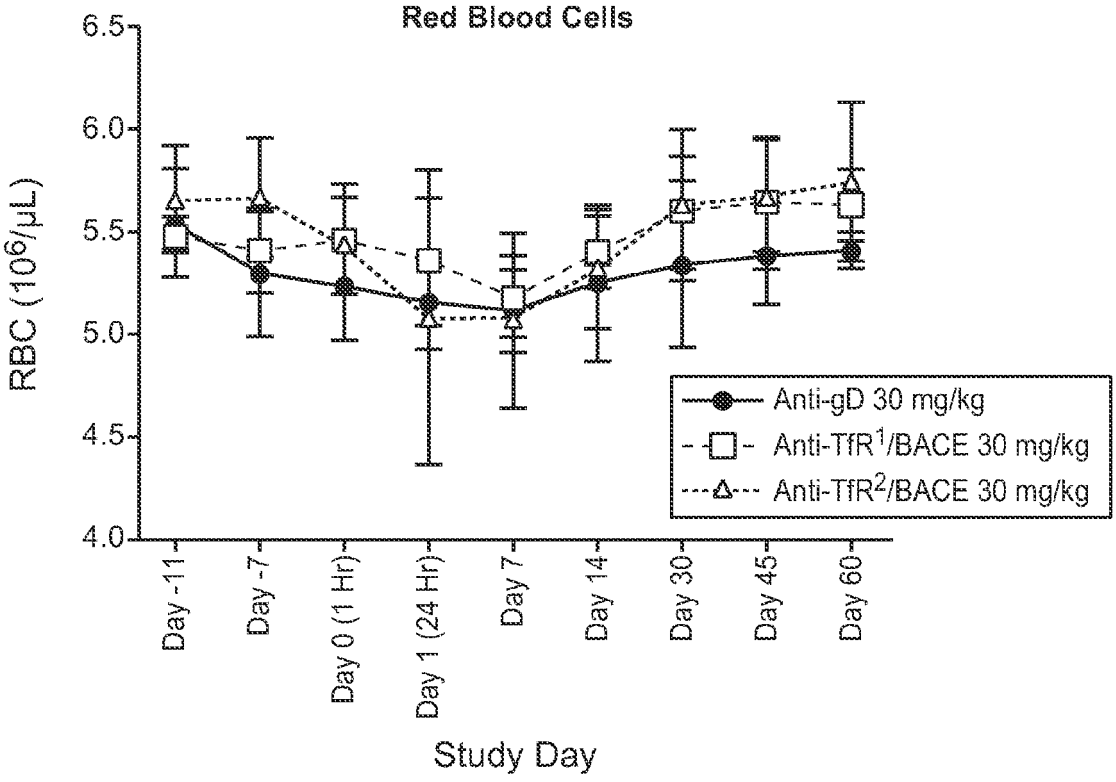


FIG. 13B

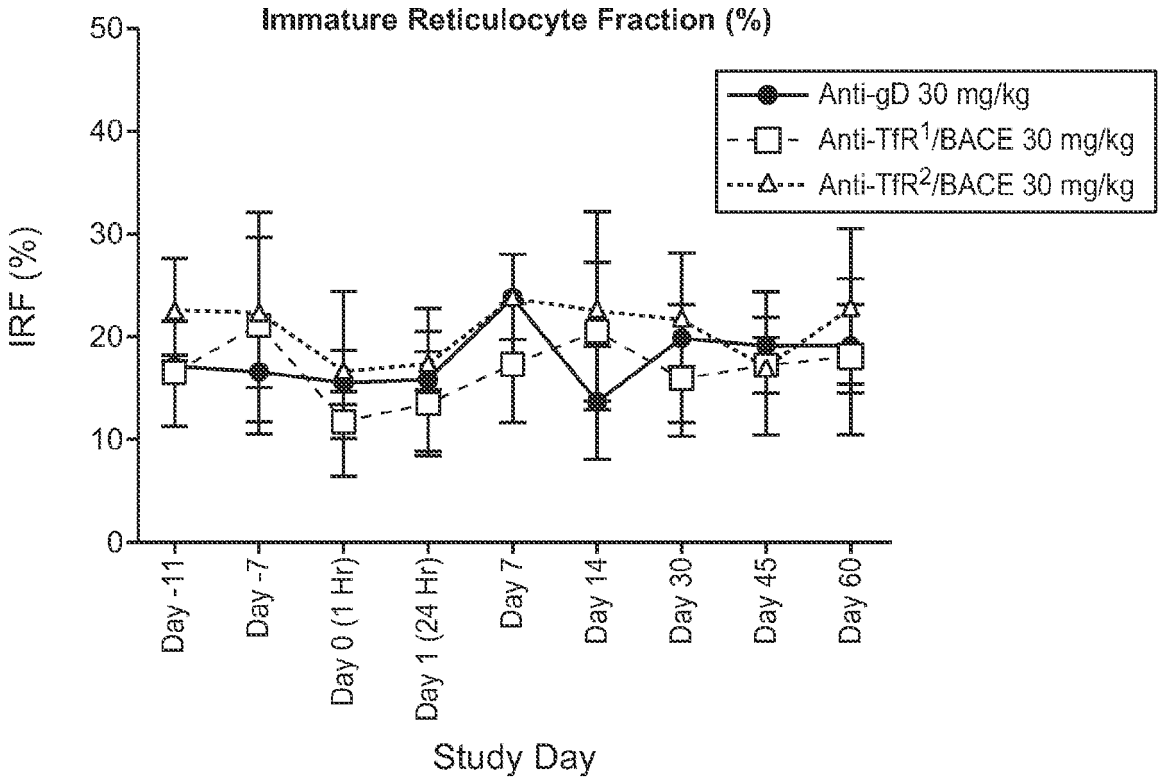


FIG. 13C

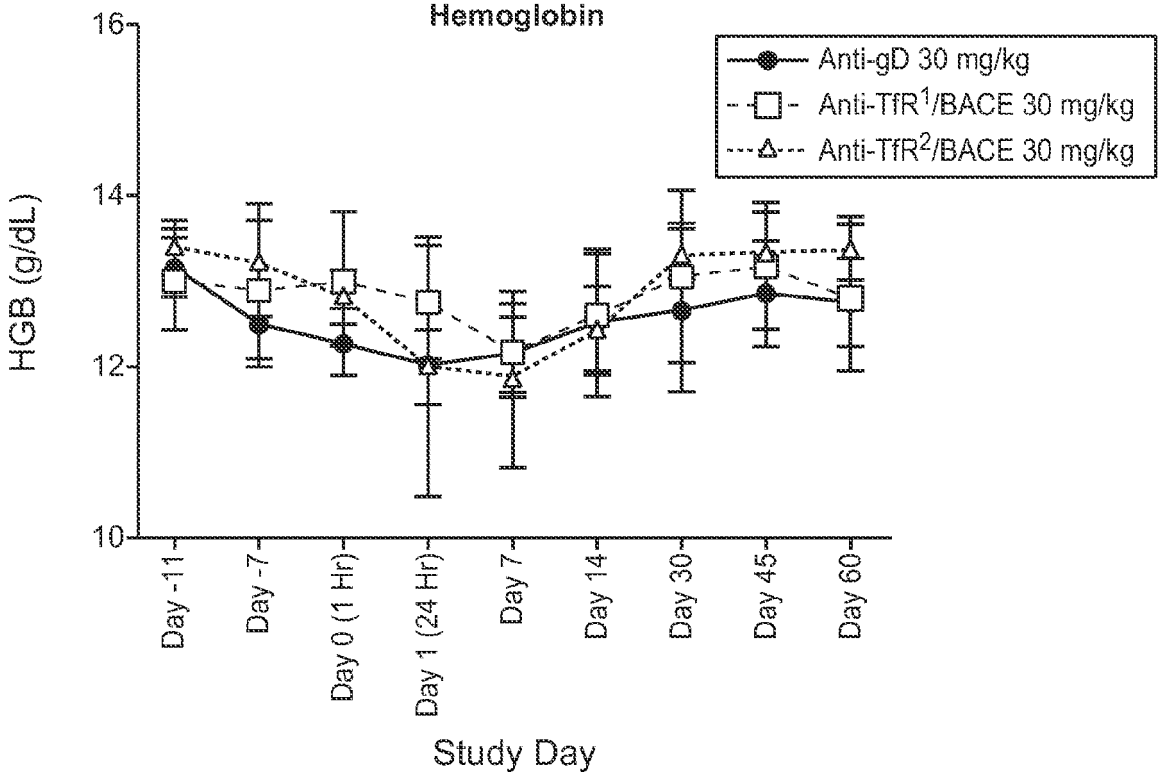


FIG. 13D

Grp	N	Tx	Isotype	Dose (mg/kg)	TfR Variant	Biacore huTfR (nM, Fab)	Biacore CynoTfR (nM, Fab)
1	5	Anti-gD	hIgG1	30			
2	5	Anti-TfR[1]/BACE1	hIgG1 DANG	30	hu15G11.v5	6 ± 2	19 ± 9
3	5	Anti-TfR[2]/BACE1	hIgG1 DANG	30	hu15G11.LC92A	230 ± 140	440 ± 160
4	5	Anti-BACE1	hIgG1	30	N/A	-	-

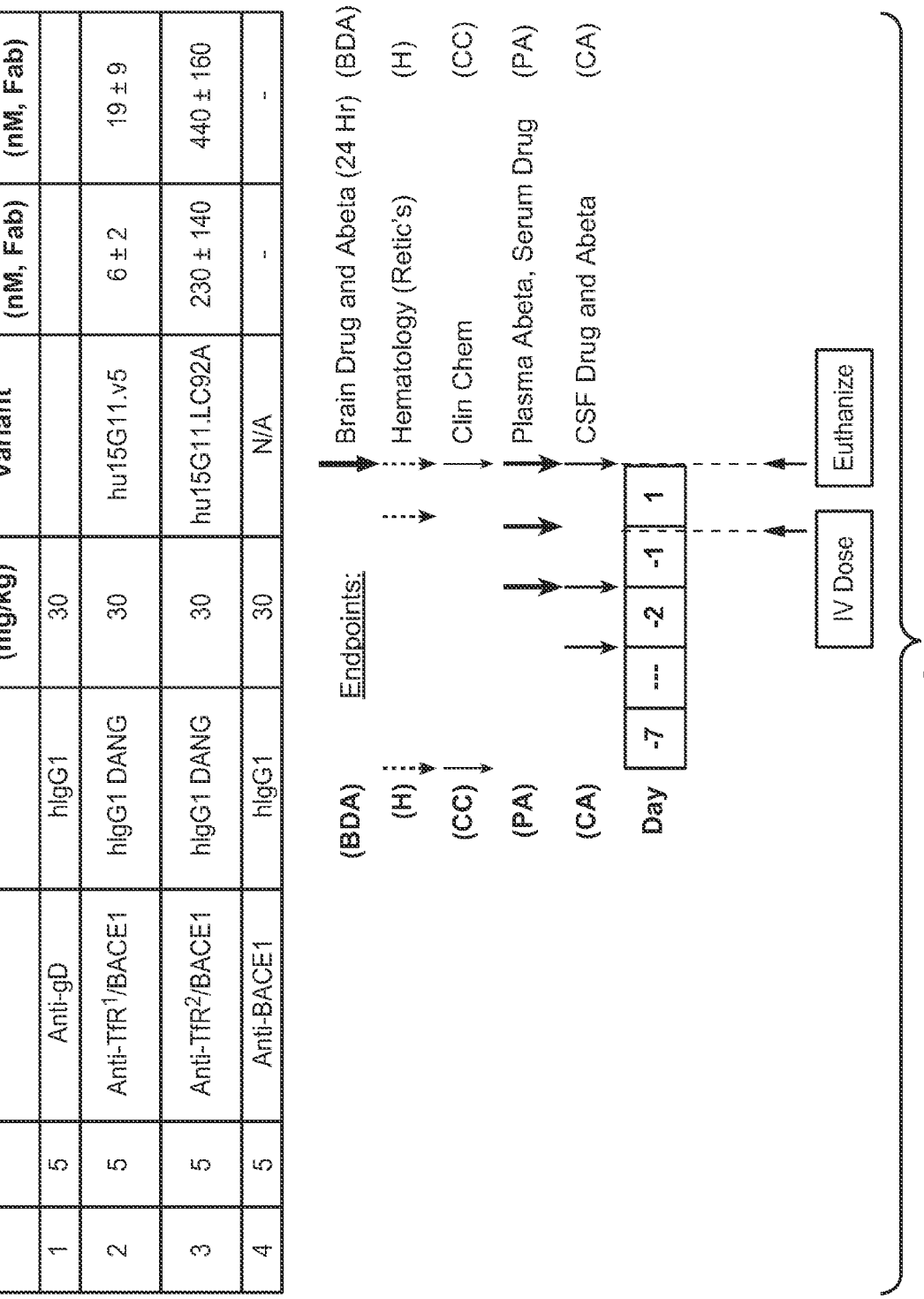


FIG. 14

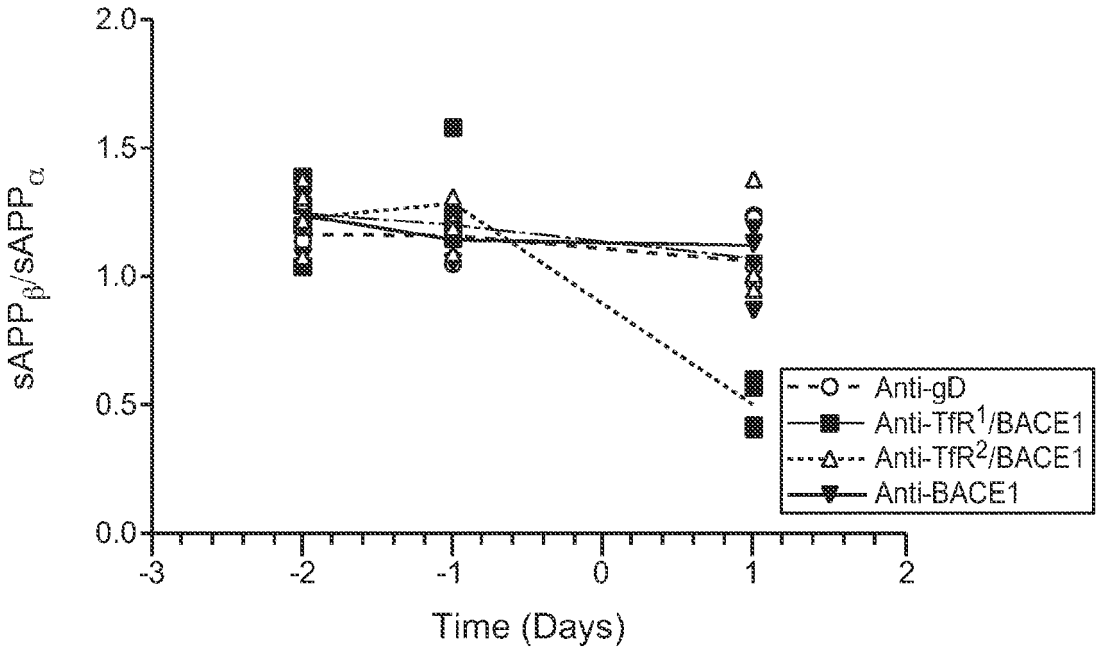


FIG. 15A

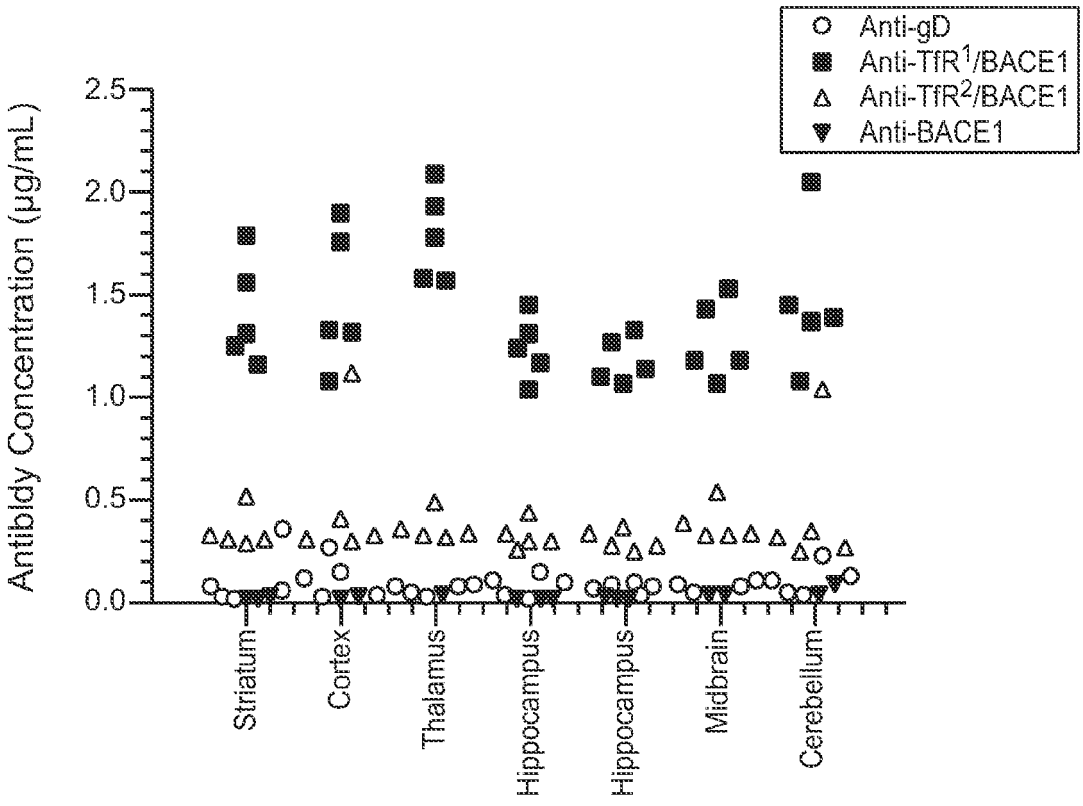


FIG. 15B

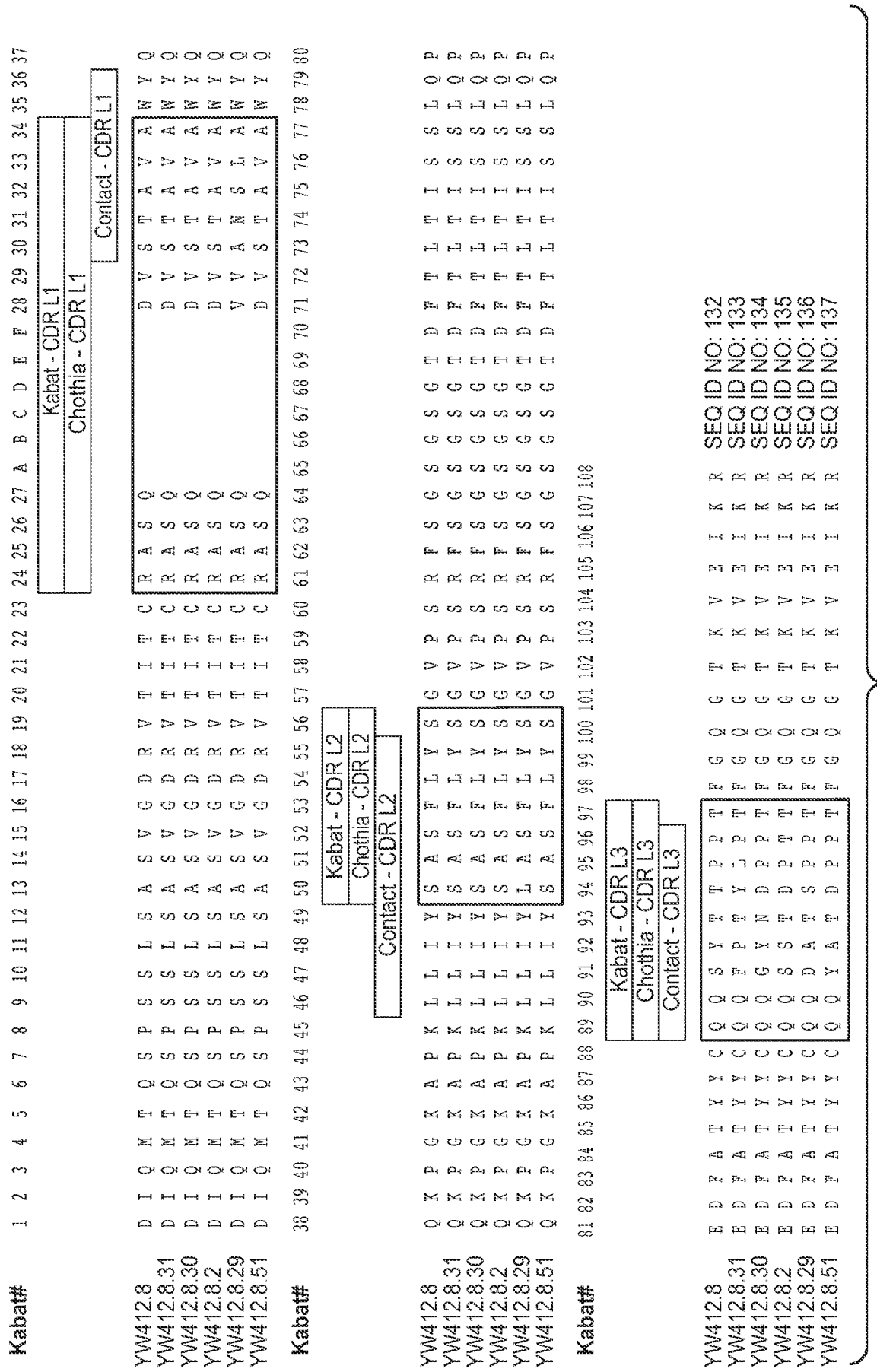

Kabat - CDR L1
Chothia - CDR L1
Contact - CDR L1
Kabat - CDR L2
Chothia - CDR L2
Contact - CDR L2
Kabat - CDR L3
Chothia - CDR L3
Contact - CDR L3
SEQ ID NO: 132
SEQ ID NO: 133
SEQ ID NO: 134
SEQ ID NO: 135
SEQ ID NO: 136
SEQ ID NO: 137

FIG. 16A

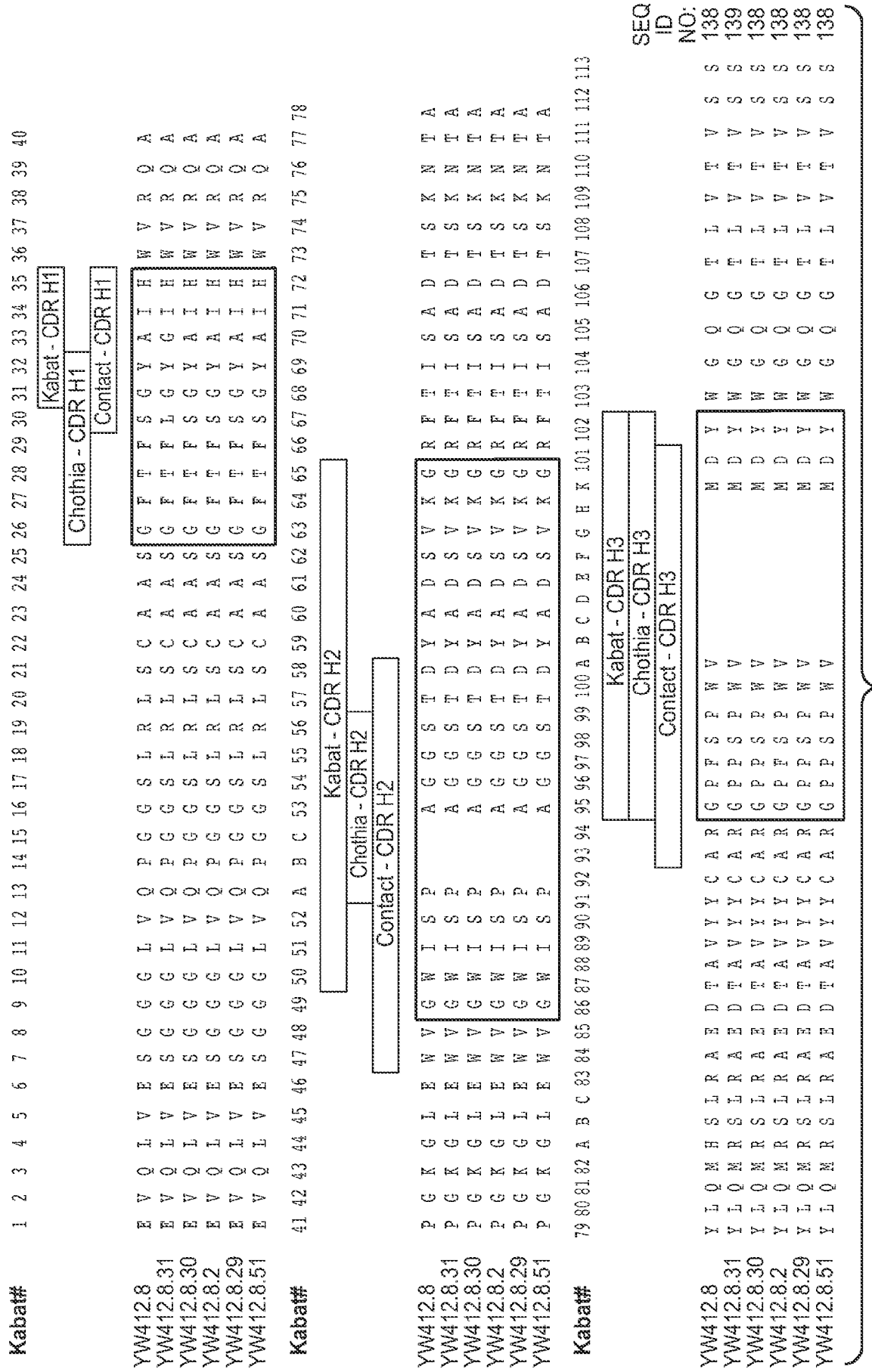

Kabat#
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40
Kabat - CDR H1
Chothia - CDR H1
Contact - CDR H1
YW412.8 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S G Y A I H W V R Q A
YW412.8.31 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F L G Y G I H W V R Q A
YW412.8.30 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S G Y A I H W V R Q A
YW412.8.2 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S G Y A I H W V R Q A
YW412.8.29 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S G Y A I H W V R Q A
YW412.8.51 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S G Y A I H W V R Q A
Kabat#
41 42 43 44 45 46 47 48 49 50 51 52 A B C 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
Kabat - CDR H2
Chothia - CDR H2
Contact - CDR H2
YW412.8 P G K G L E W V G W I S P A G G S T D Y A D S V K G R F T I S A D T S K N T A
YW412.8.31 P G K G L E W V G W I S P A G G S T D Y A D S V K G R F T I S A D T S K N T A
YW412.8.30 P G K G L E W V G W I S P A G G S T D Y A D S V K G R F T I S A D T S K N T A
YW412.8.2 P G K G L E W V G W I S P A G G S T D Y A D S V K G R F T I S A D T S K N T A
YW412.8.29 P G K G L E W V G W I S P A G G S T D Y A D S V K G R F T I S A D T S K N T A
YW412.8.51 P G K G L E W V G W I S P A G G S T D Y A D S V K G R F T I S A D T S K N T A
Kabat#
79 80 81 82 A B C 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 A B C D E F G H K 101 102 103 104 105 106 107 108 109 110 111 112 113
Kabat - CDR H3
Chothia - CDR H3
Contact - CDR H3
SEQ ID NO:
YW412.8 Y L Q M H S L R A E D T A V Y Y C A R G P F S P W V M D Y W G Q G T L V T V S S 138
YW412.8.31 Y L Q M R S L R A E D T A V Y Y C A R G P P S P W V M D Y W G Q G T L V T V S S 139
YW412.8.30 Y L Q M R S L R A E D T A V Y Y C A R G P P S P W V M D Y W G Q G T L V T V S S 138
YW412.8.2 Y L Q M R S L R A E D T A V Y Y C A R G P F T S P W V M D Y W G Q G T L V T V S S 138
YW412.8.29 Y L Q M R S L R A E D T A V Y Y C A R G P P S P W V M D Y W G Q G T L V T V S S 138
YW412.8.51 Y L Q M R S L R A E D T A V Y Y C A R G P P S P W V M D Y W G Q G T L V T V S S 138

FIG. 16B

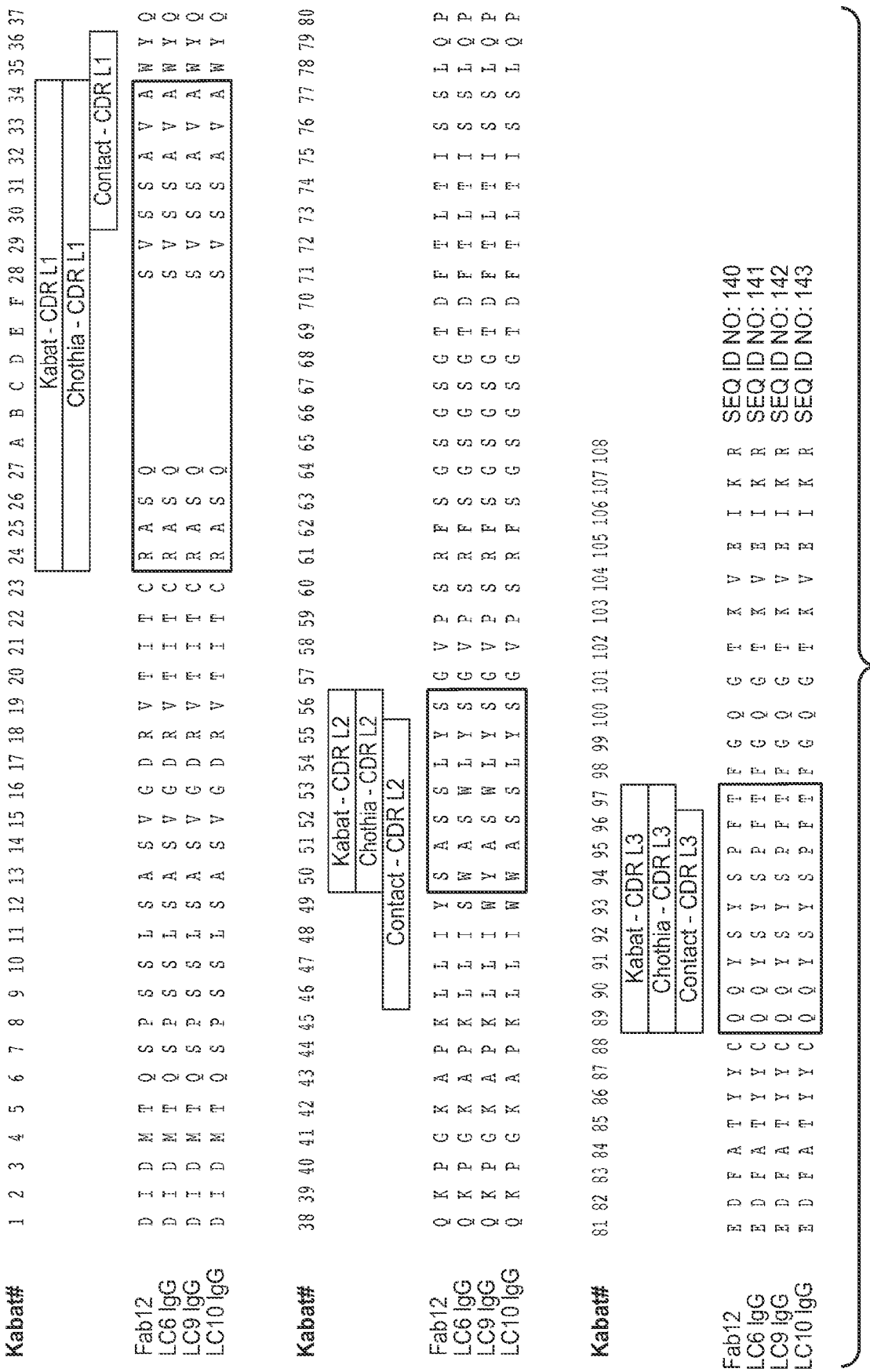

Kabat#
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 A B C D E F 28 29 30 31 32 33 34 35 36 37
Kabat - CDR L1
Chothia - CDR L1
Contact - CDR L1
Fab12 D I D M T Q S P S S L S A S V G D R V T I T C R A S Q S V S S A V A W Y Q
LC6 IgG D I D M T Q S P S S L S A S V G D R V T I T C R A S Q S V S S A V A W Y Q
LC9 IgG D I D M T Q S P S S L S A S V G D R V T I T C R A S Q S V S S A V A W Y Q
LC10 IgG D I D M T Q S P S S L S A S V G D R V T I T C R A S Q S V S S A V A W Y Q
Kabat#
38 39 40 41 42 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
Kabat - CDR L2
Chothia - CDR L2
Contact - CDR L2
Fab12 Q K P G K A P K L L I Y S A S S L Y S G V P S R F S G S G S G T D F T L T I S S L Q P
LC6 IgG Q K P G K A P K L L I S W A S W L Y S G V P S R F S G S G S G T D F T L T I S S L Q P
LC9 IgG Q K P G K A P K L L I W Y A S W L Y S G V P S R F S G S G S G T D F T L T I S S L Q P
LC10 IgG Q K P G K A P K L L I W W A S S L Y S G V P S R F S G S G S G T D F T L T I S S L Q P
Kabat#
81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108
Kabat - CDR L3
Chothia - CDR L3
Contact - CDR L3
Fab12 E D F A T Y Y Y C Q Q Y S Y S P F T F G Q G T K V E I K R SEQ ID NO: 140
LC6 IgG E D F A T Y Y Y C Q Q Y S Y S P F T F G Q G T K V E I K R SEQ ID NO: 141
LC9 IgG E D F A T Y Y Y C Q Q Y S Y S P F T F G Q G T K V E I K R SEQ ID NO: 142
LC10 IgG E D F A T Y Y Y C Q Q Y S Y S P F T F G Q G T K V E I K R SEQ ID NO: 143

FIG. 17A

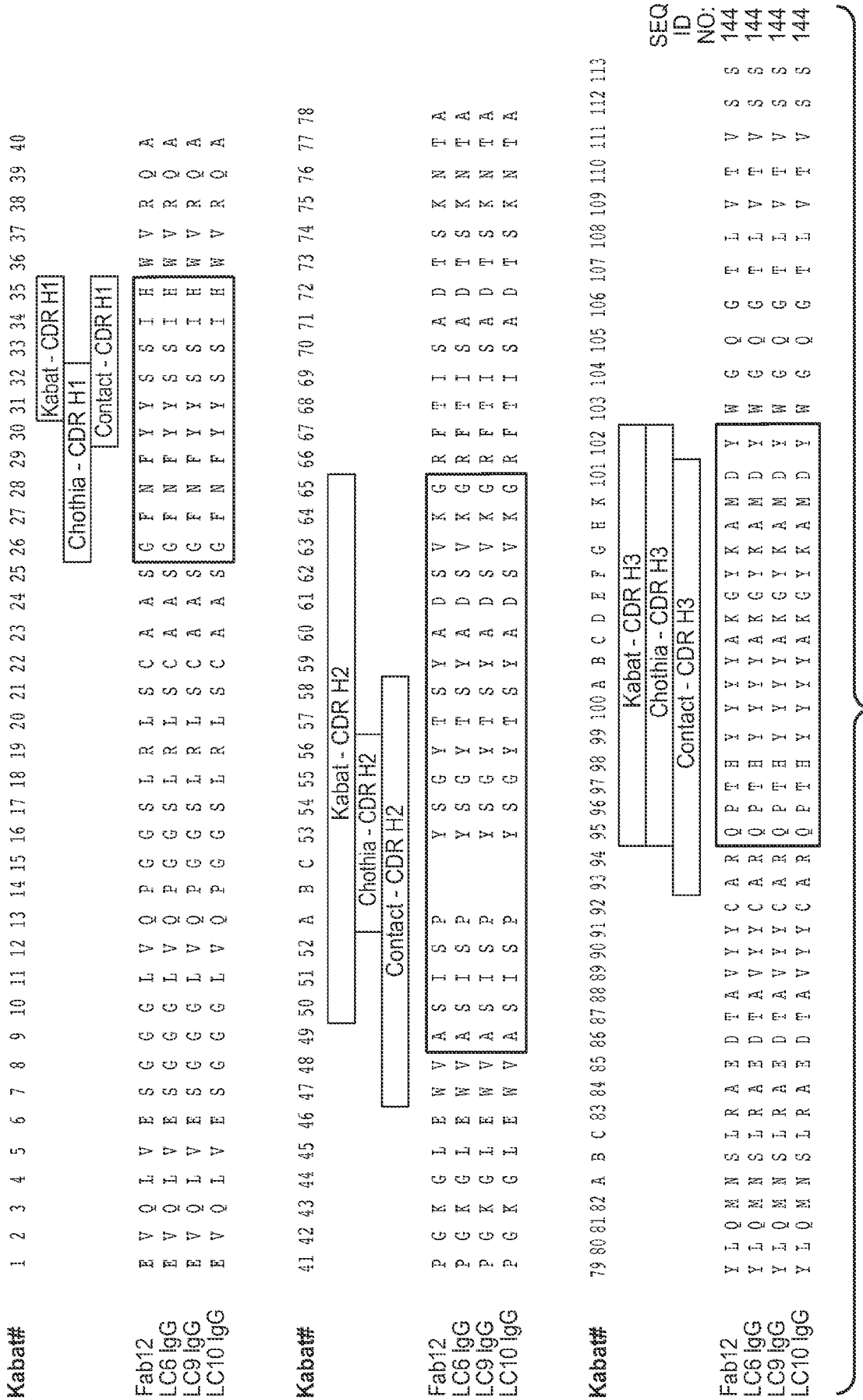

Kabat#
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40
Kabat - CDR H1
Chothia - CDR H1
Contact - CDR H1
Fab12 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F N F Y Y S S I H W V R Q A
LC6 IgG E V Q L V E S G G G L V Q P G G S L R L S C A A S G F N F Y Y S S I H W V R Q A
LC9 IgG E V Q L V E S G G G L V Q P G G S L R L S C A A S G F N F Y Y S S I H W V R Q A
LC10 IgG E V Q L V E S G G G L V Q P G G S L R L S C A A S G F N F Y Y S S I H W V R Q A
Kabat#
41 42 43 44 45 46 47 48 49 50 51 52 A B C 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
Kabat - CDR H2
Chothia - CDR H2
Contact - CDR H2
Fab12 P G K G L E W V A S I S P Y S G G Y T S Y A D S V K G R F T I S A D T S K N T A
LC6 IgG P G K G L E W V A S I S P Y S G G Y T S Y A D S V K G R F T I S A D T S K N T A
LC9 IgG P G K G L E W V A S I S P Y S G G Y T S Y A D S V K G R F T I S A D T S K N T A
LC10 IgG P G K G L E W V A S I S P Y S G G Y T S Y A D S V K G R F T I S A D T S K N T A
Kabat#
79 80 81 82 A B C 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 A B C D E F G H K 101 102 103 104 105 106 107 108 109 110 111 112 113
Kabat - CDR H3
Chothia - CDR H3
Contact - CDR H3
Fab12 Y L Q M N S L R A E D T A V Y Y C A R Q P T H Y Y Y Y A K G Y K A M D Y W G Q G T L V T V S S
LC6 IgG Y L Q M N S L R A E D T A V Y Y C A R Q P T H Y Y Y Y A K G Y K A M D Y W G Q G T L V T V S S
LC9 IgG Y L Q M N S L R A E D T A V Y Y C A R Q P T H Y Y Y Y A K G Y K A M D Y W G Q G T L V T V S S
LC10 IgG Y L Q M N S L R A E D T A V Y Y C A R Q P T H Y Y Y Y A K G Y K A M D Y W G Q G T L V T V S S
SEQ ID NO: 144
144
144
144

FIG. 17B

```
  1  EVQLVESGGG LVQPGGSLRL SCAASGFTFS SYGMSWVRQA PGKGLELVAS
 51  INSNGGSTYY PDSVKGRFTI SRDNAKNSLY LQMNSLRAED TAVYYCASGD
101  YWGQGTTVTV SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT
151  VSWNSGALTS GVHTFPAVLQ SSGLYSLSSV VTVPSSSLGT KTYTCNVDHK
201  PSNTKVDKRV ESKYGPPCPP CPAPEFLGGP SVFLFPPKPK DTLMISRTPE
251  VTCVVVDVSQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS TYRVVSVLTV
301  LHQDWLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM
351  TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL DSDGSFFLYS
401  RLTVDKSRWQ EGNVFSCSVM HEALHNHYTQ KSLSLSLG  (SEQ 10 NO: 145)
```

FIG. 18A

```
  1  DIVMTQSPLS LPVTPGEPAS ISCRSSQSLV YSNGDTYLHW YLQKPGQSPQ
 51  LLIYKVSNRF SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYCSQSTHVP
101  WTFGQGTKVE IKRTVAAPSV FIFPPSDEQL KSGTASVVCL LNNFYPREAK
151  VQWKVDNALQ SGNSQESVTE QDSKDSTYSL SSTLTLSKAD YEKHKVYACE
201  VTHQGLSSPV TKSFNRGEC  (SEQ 10 NO: 146)
```

FIG. 18B

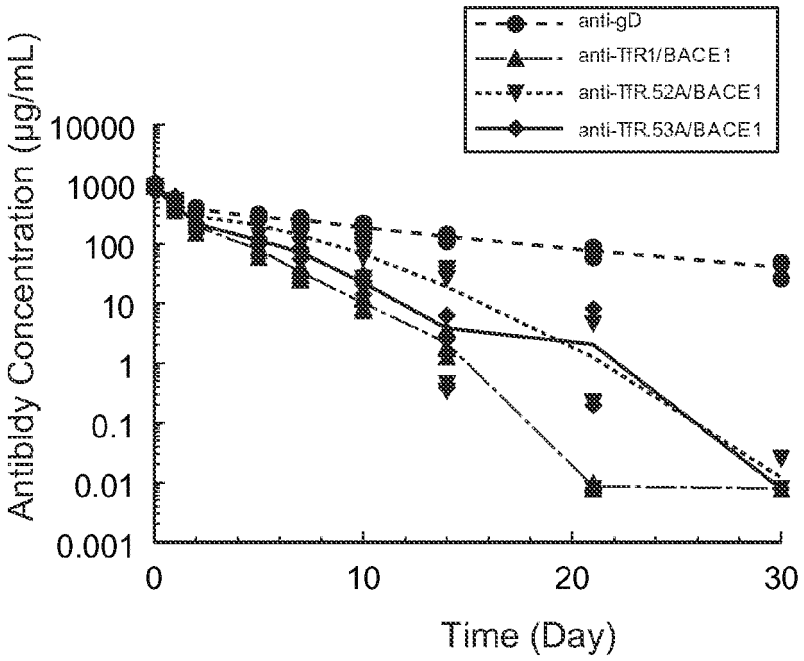

anti-gD
anti-TfR1/BACE1
anti-TfR.52A/BACE1
anti-TfR.53A/BACE1
Antibidy Concentration (µg/mL)
10000
1000
100
10
1
0.1
0.01
0.001
0
10
20
30
Time (Day)

FIG. 19

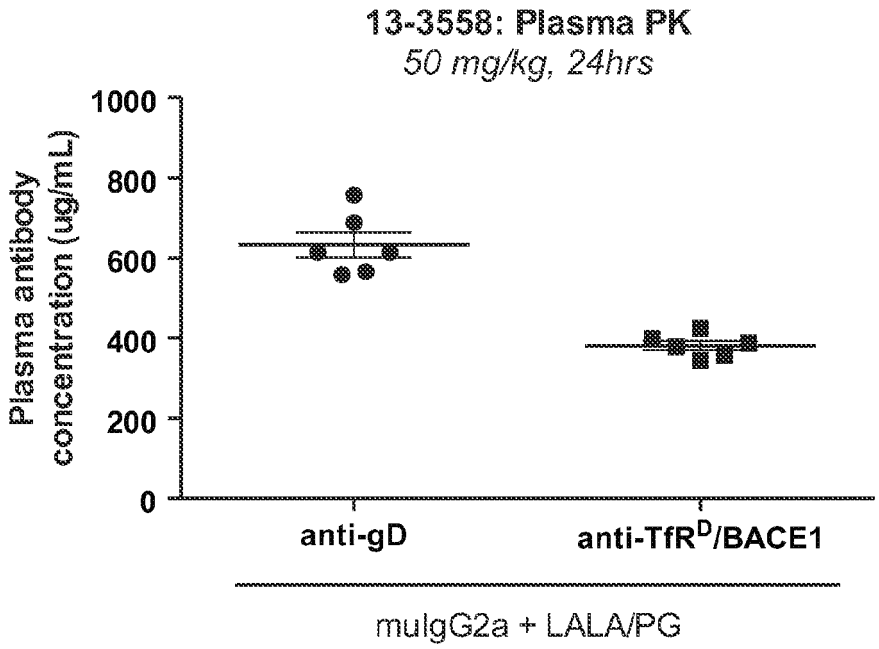

13-3558: Plasma PK
50 mg/kg, 24hrs
Plasma antibody concentration (ug/mL)
1000
800
600
400
200
0
anti-gD
anti-TfR^D/BACE1
muIgG2a + LALA/PG

FIG. 20

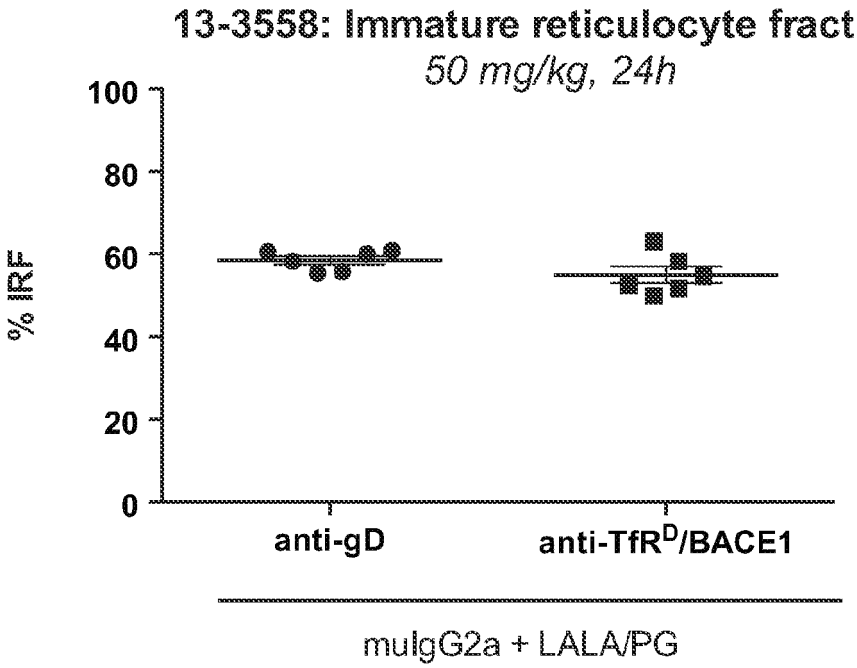


FIG. 21A

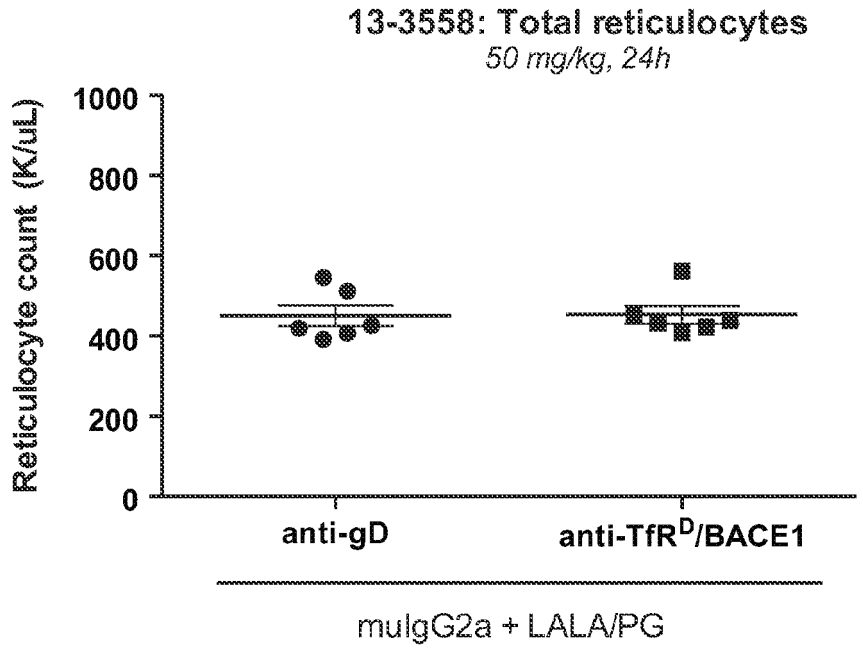


FIG. 21B

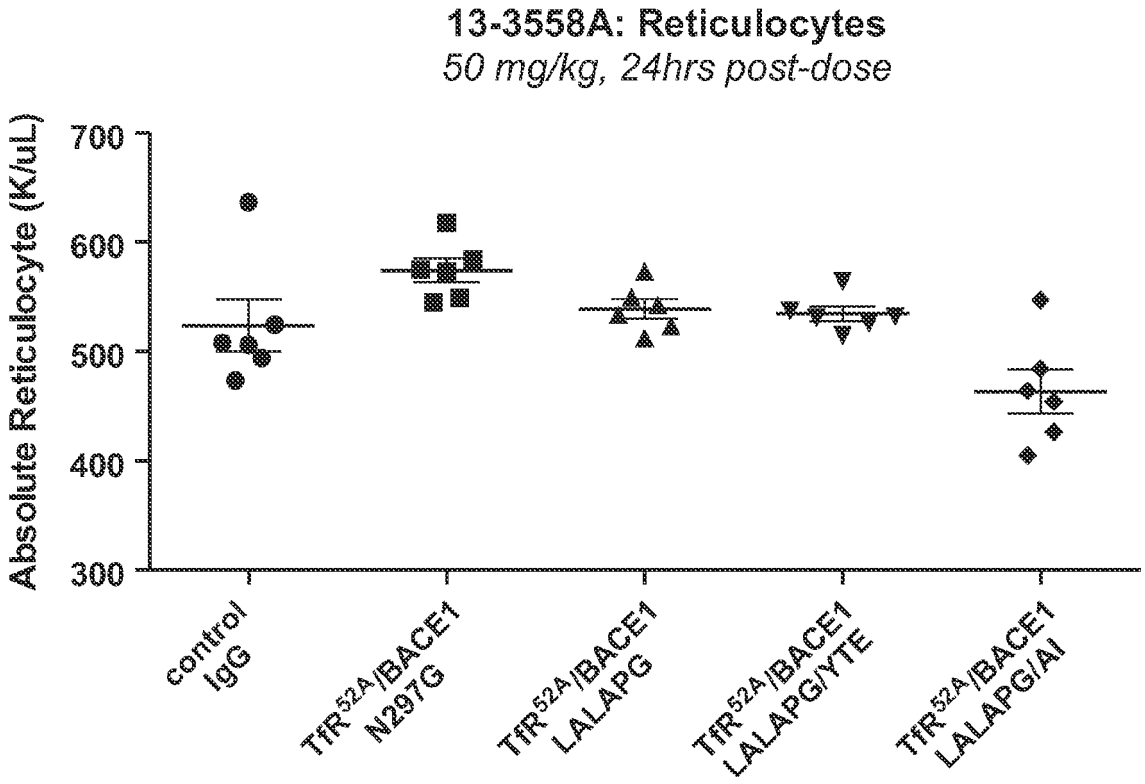

13-3558A: Reticulocytes
50 mg/kg, 24hrs post-dose
Absolute Reticulocyte (K/uL)
700
600
500
400
300
control IgG
TfR52A/BACE1 N297G
TfR52A/BACE1 LALAPG
TfR52A/BACE1 LALAPG/YTE
TfR52A/BACE1 LALAPG/AI

FIG. 22

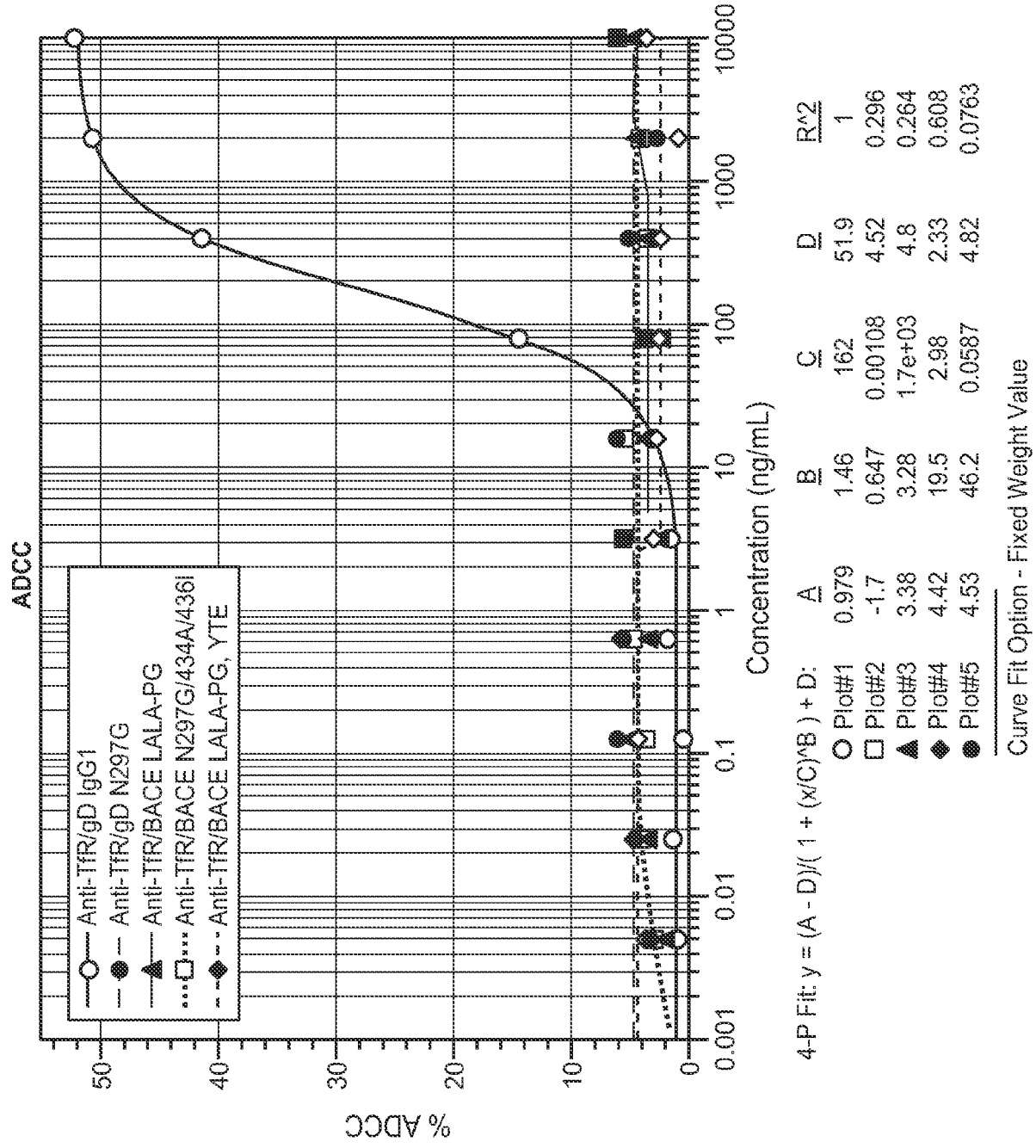

ADCC
Anti-TfR/gD IgG1
Anti-TfR/gD N297G
Anti-TfR/BACE LALA-PG
Anti-TfR/BACE N297G/434A/436I
Anti-TfR/BACE LALA-PG, YTE
% ADCC
Concentration (ng/mL)
0.001
0.01
0.1
1
10
100
1000
10000
0
10
20
30
40
50
4-P Fit: y = (A - D)/(1 + (x/C)^B) + D:
A B C D R^2
Plot#1 0.979 1.46 162 51.9 1
Plot#2 -1.7 0.647 0.00108 4.52 0.296
Plot#3 3.38 3.28 1.7e+03 4.8 0.264
Plot#4 4.42 19.5 2.98 2.33 0.608
Plot#5 4.53 46.2 0.0587 4.82 0.0763
Curve Fit Option - Fixed Weight Value

FIG. 23

Light Chain Variable Region

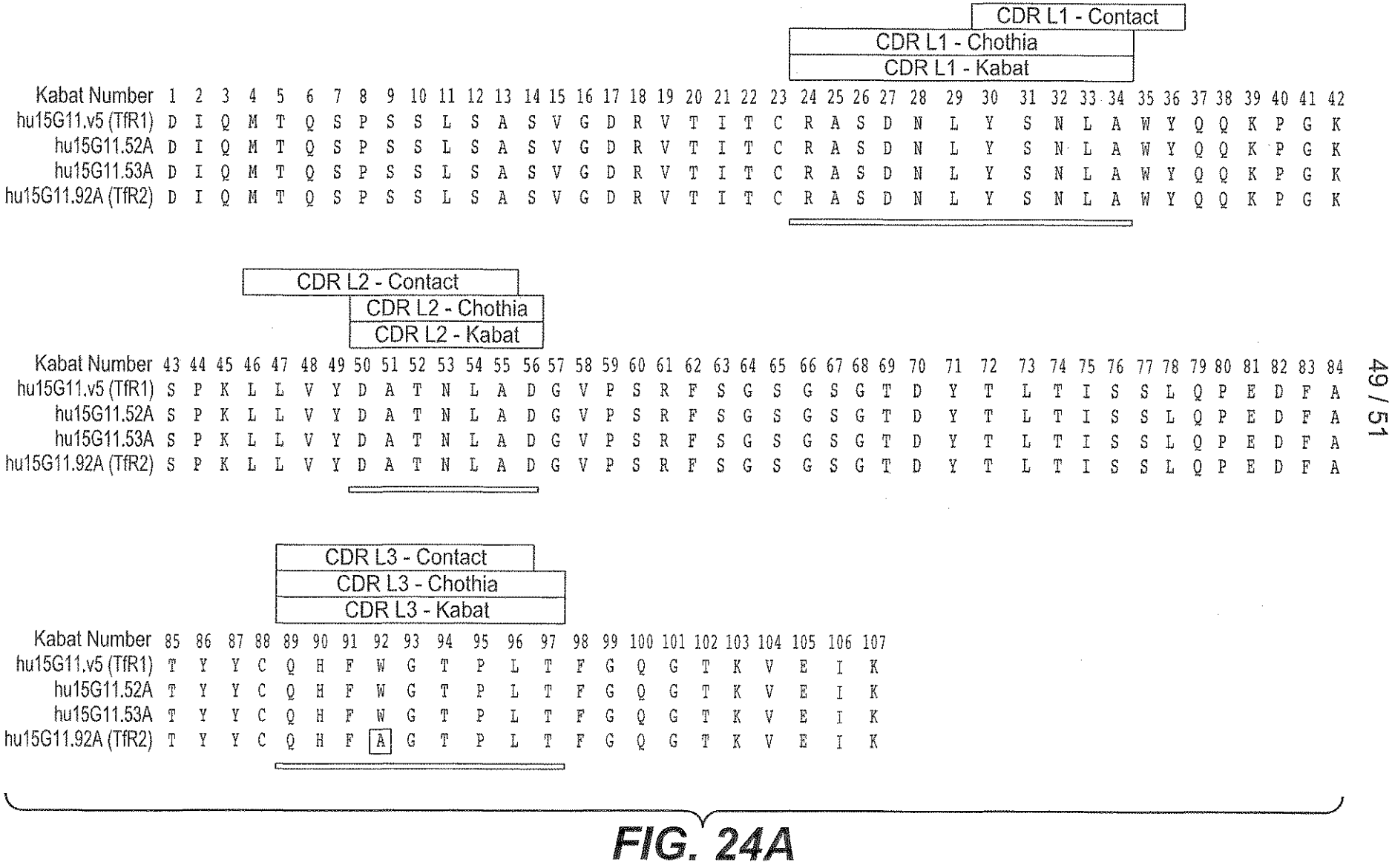


FIG. 24A

Heavy Chain Variable Region

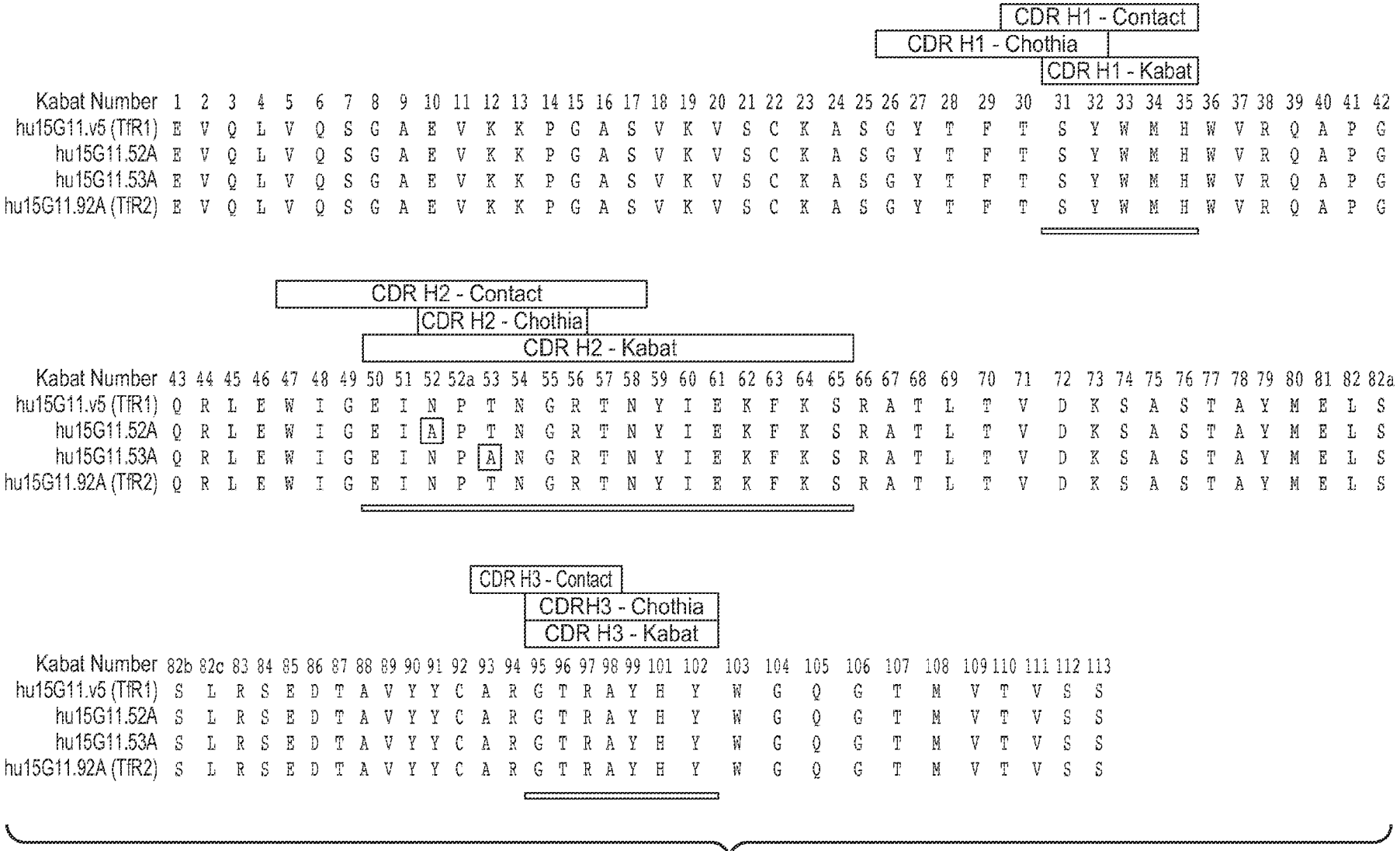


FIG. 24B

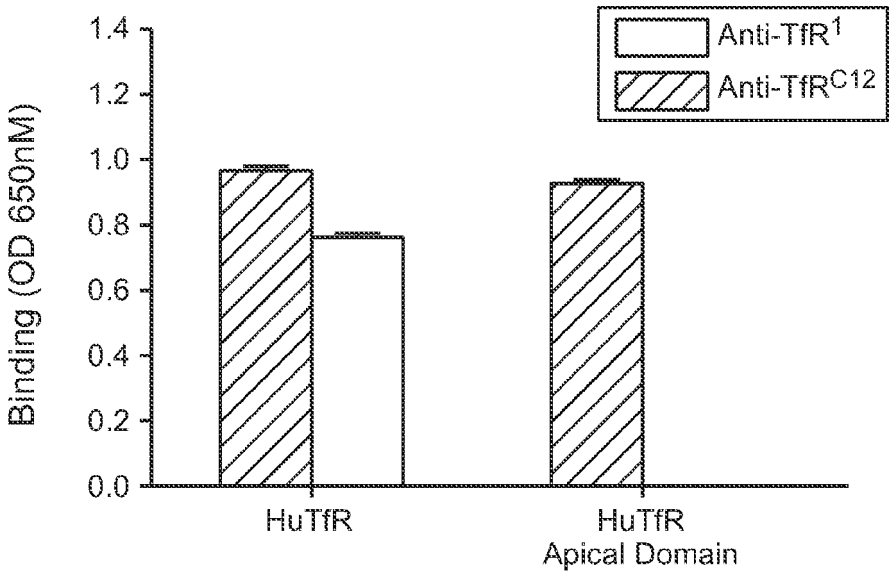

Binding (OD 650nM)
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
Anti-TfR1
Anti-TfRC12
HuTfR
HuTfR
Apical Domain

FIG. 25