

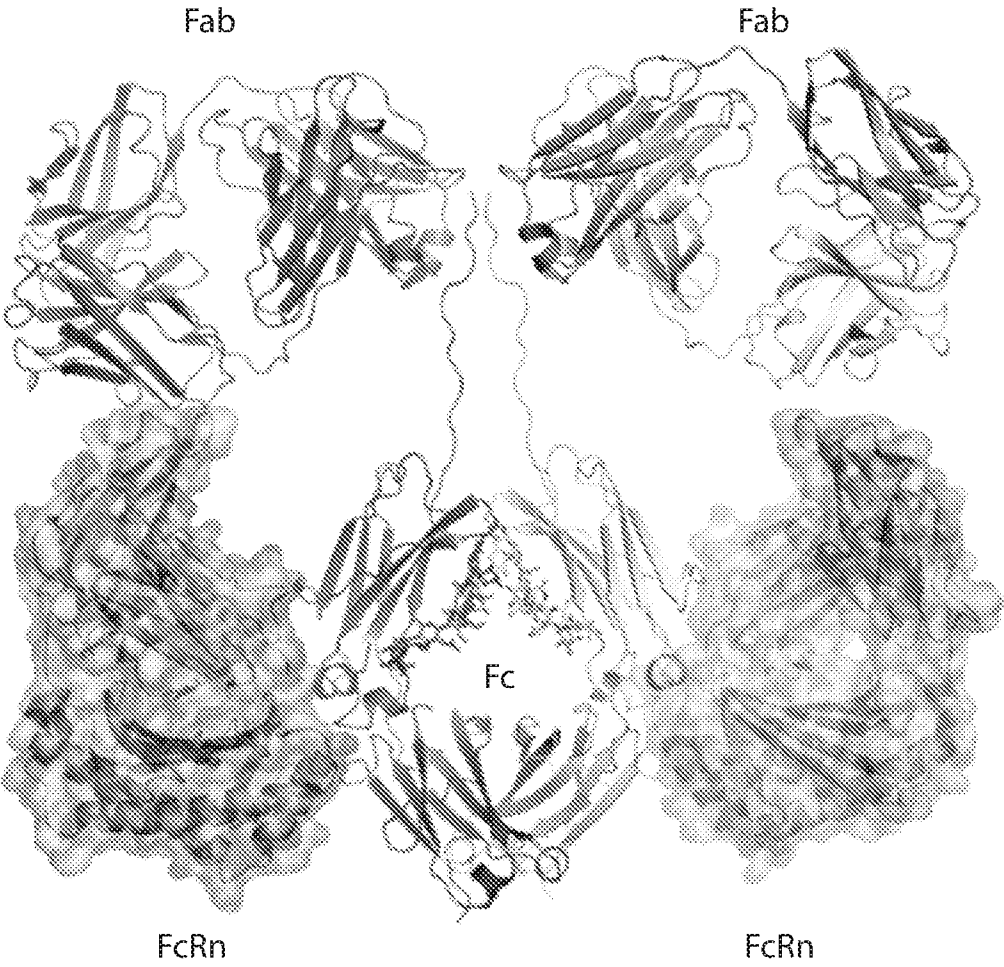


FIG. 1

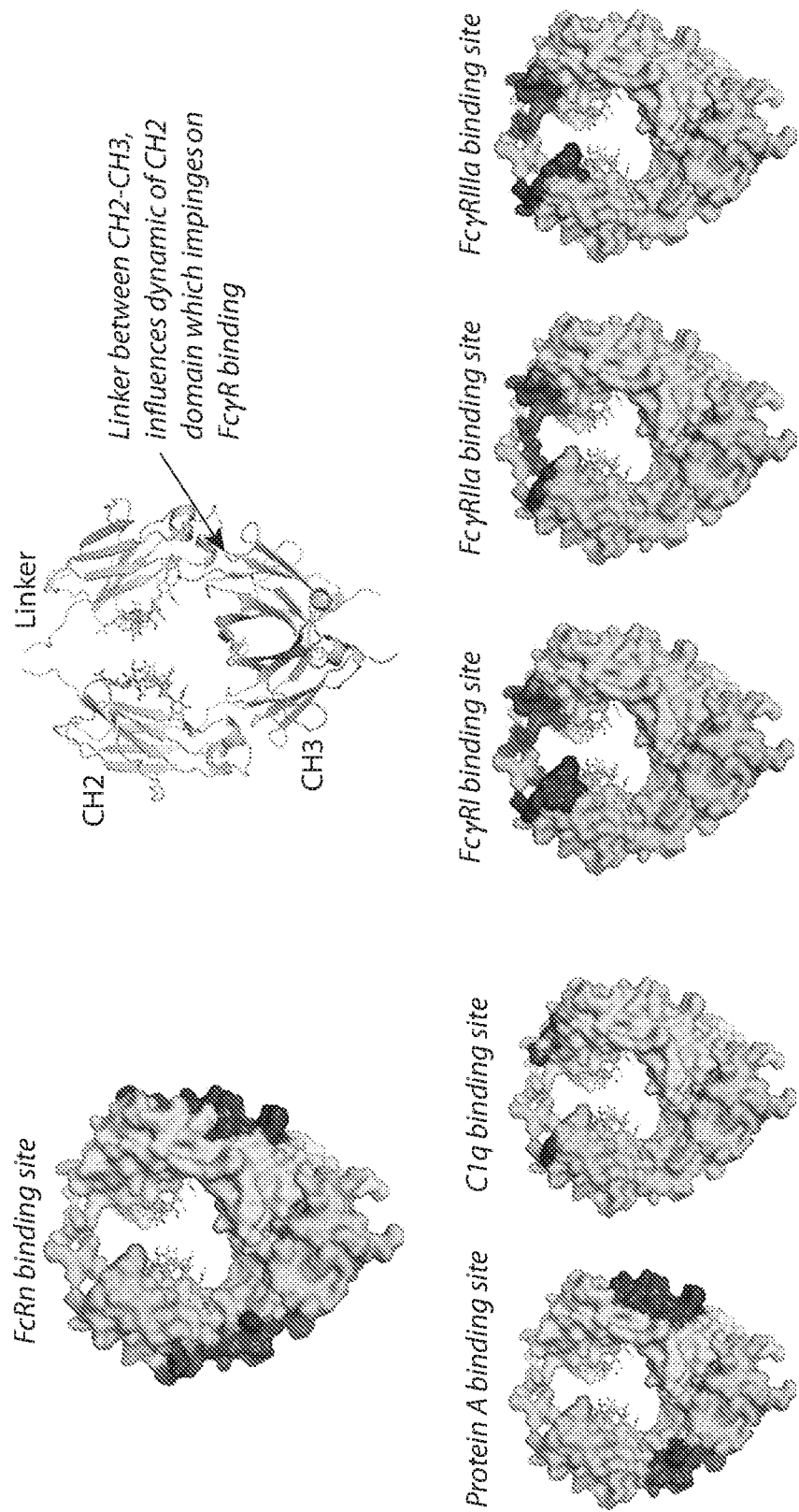


FIG. 2

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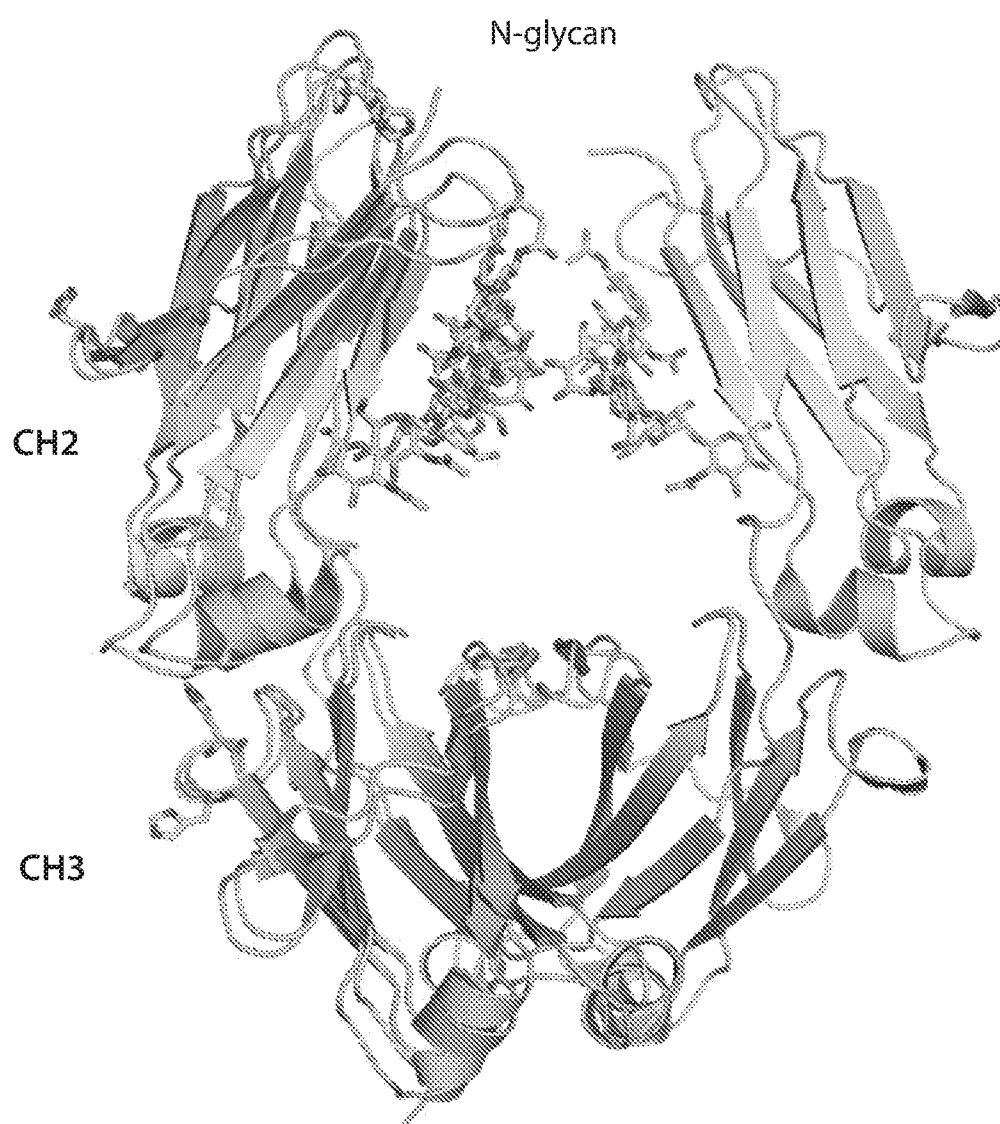
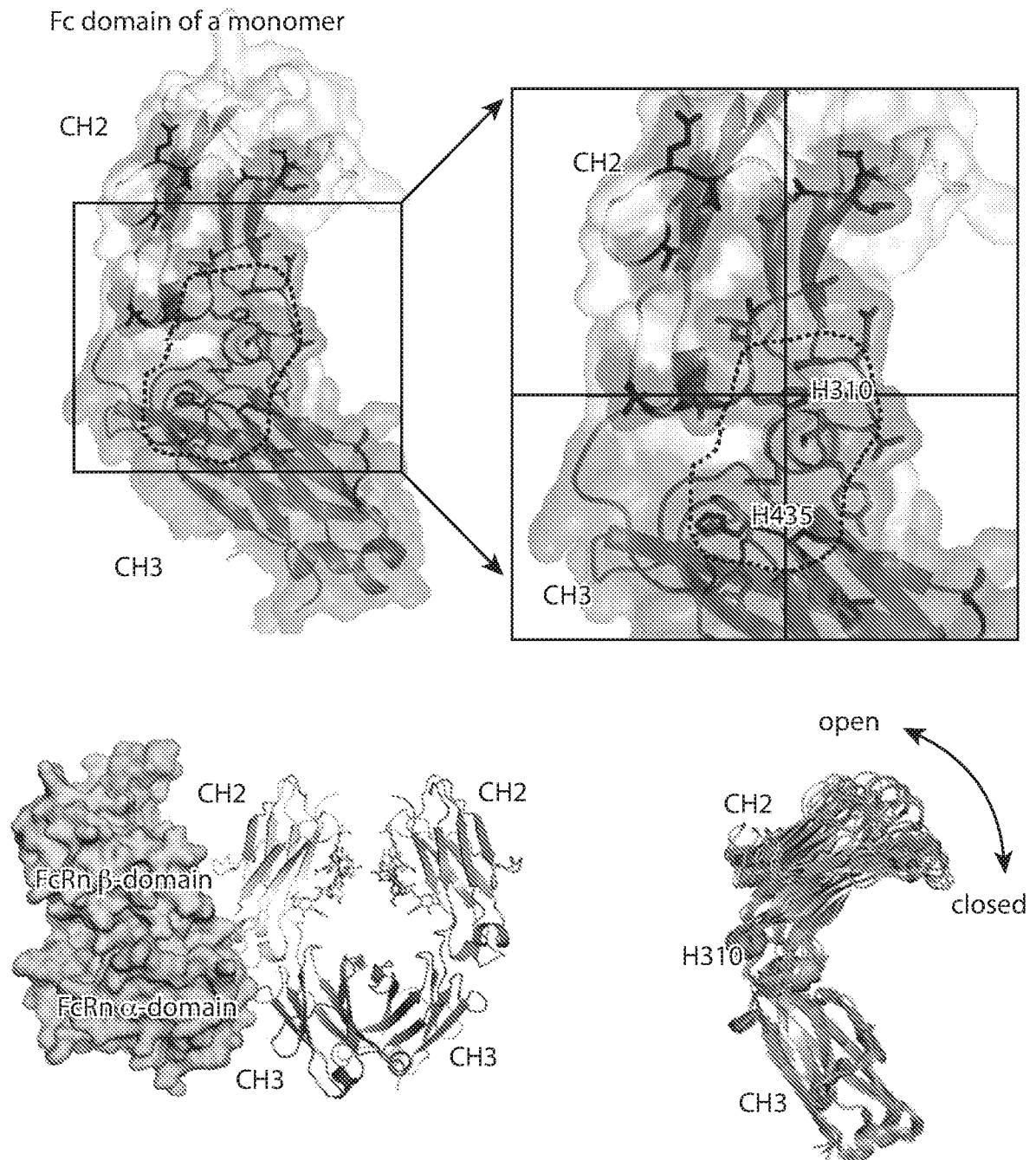
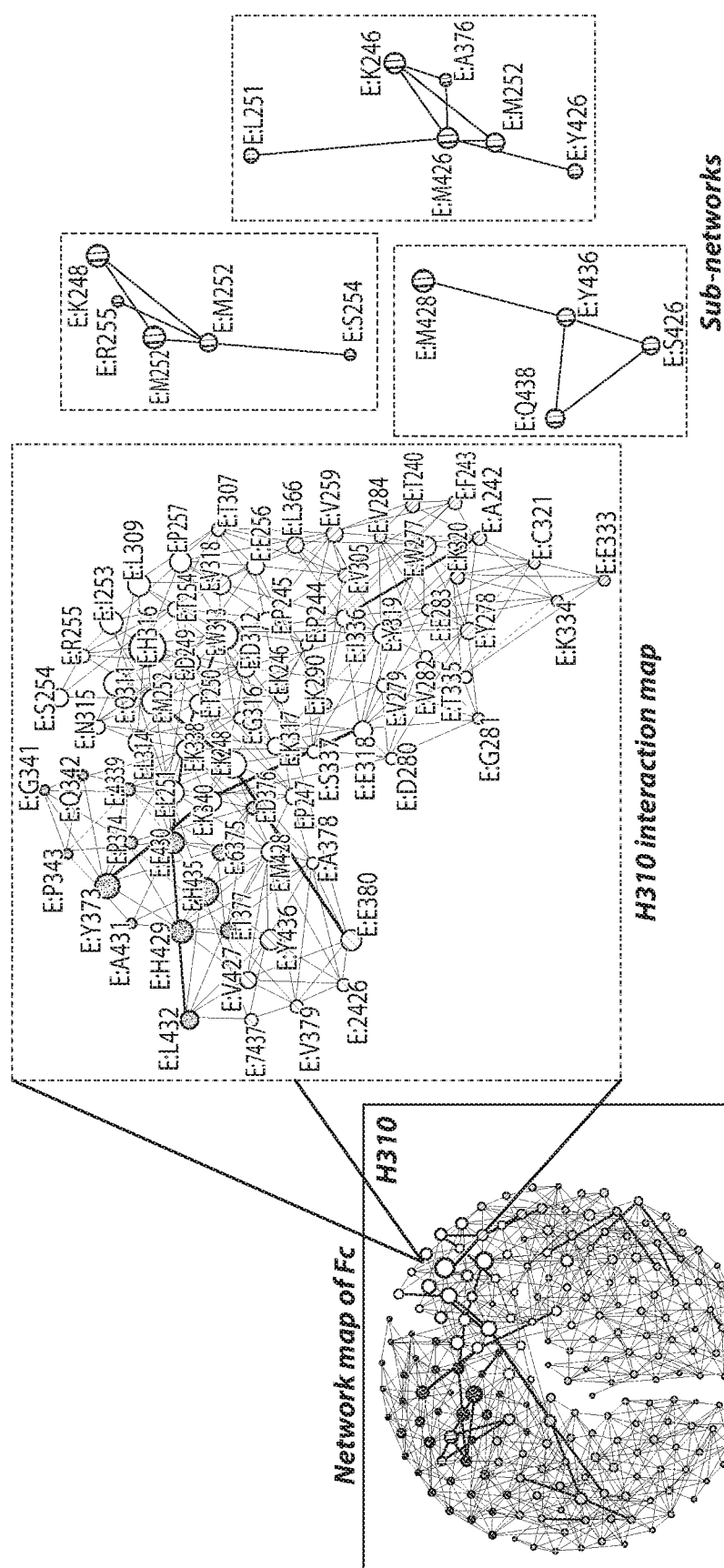


FIG. 3

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Each node represents an amino acids
Amino acids colored based on the network community they belong

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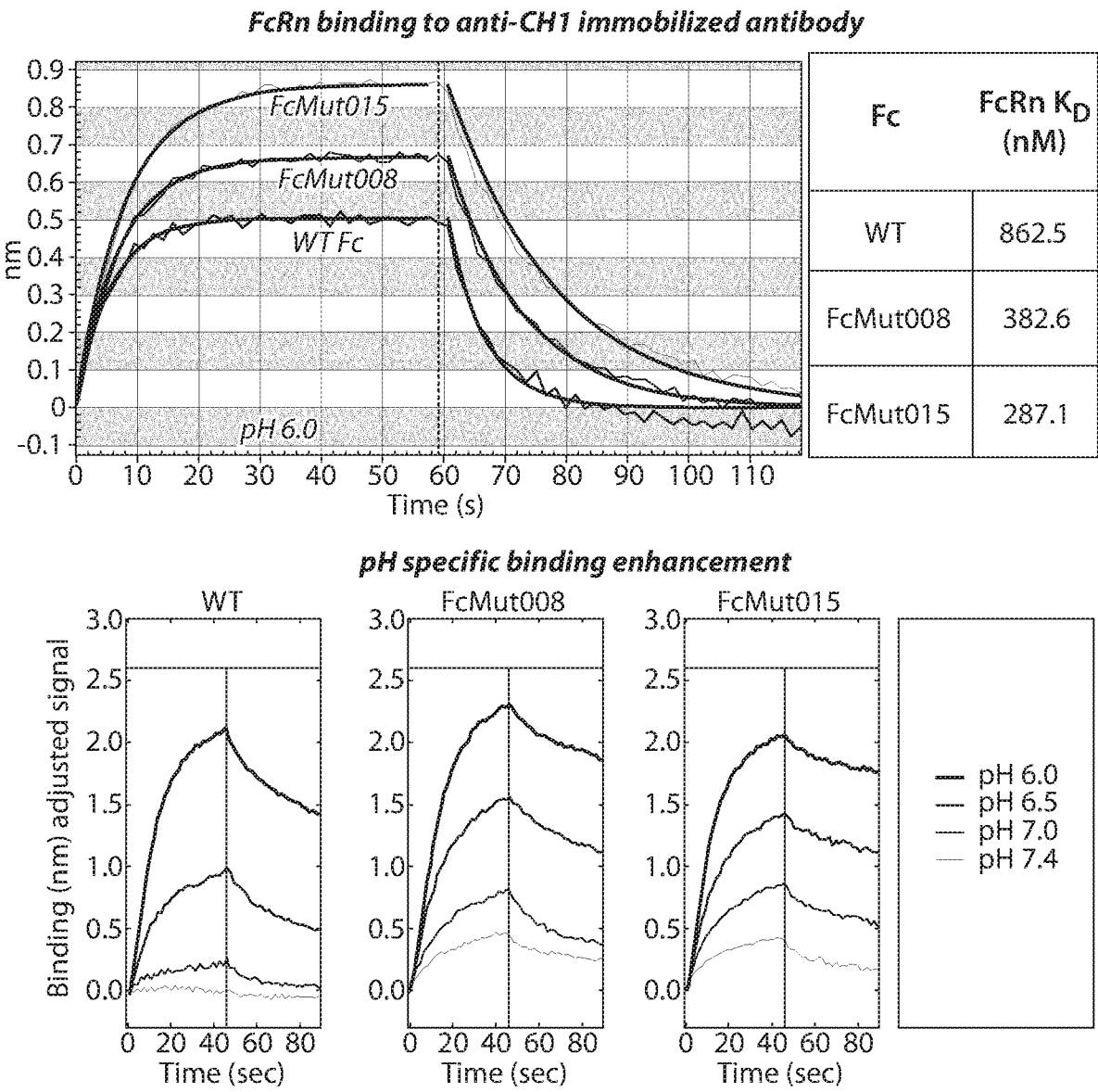


FIG. 6

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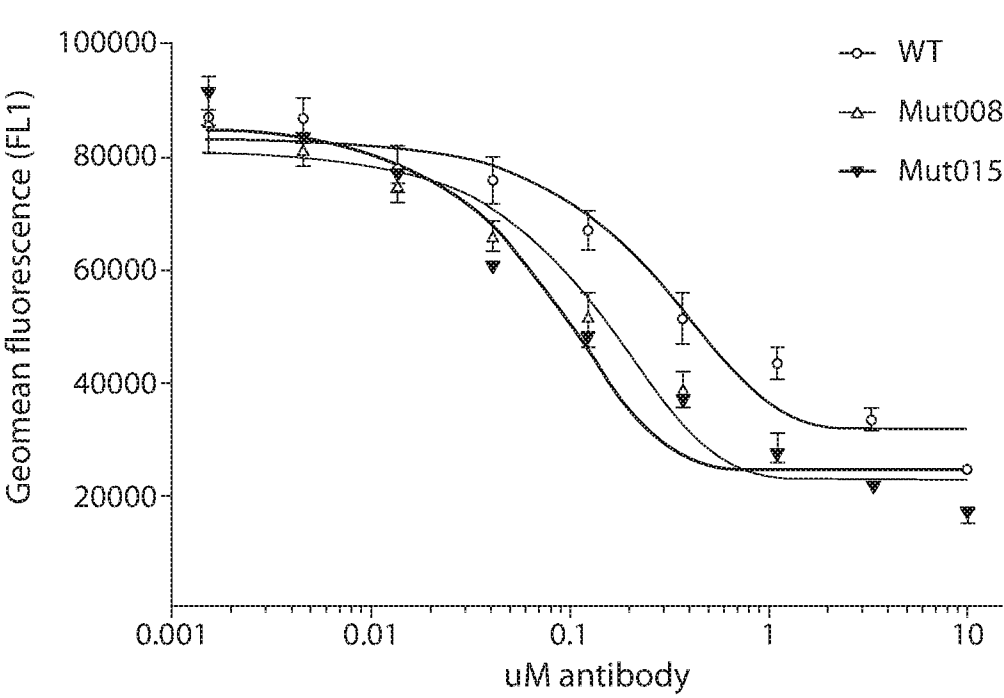


FIG. 7

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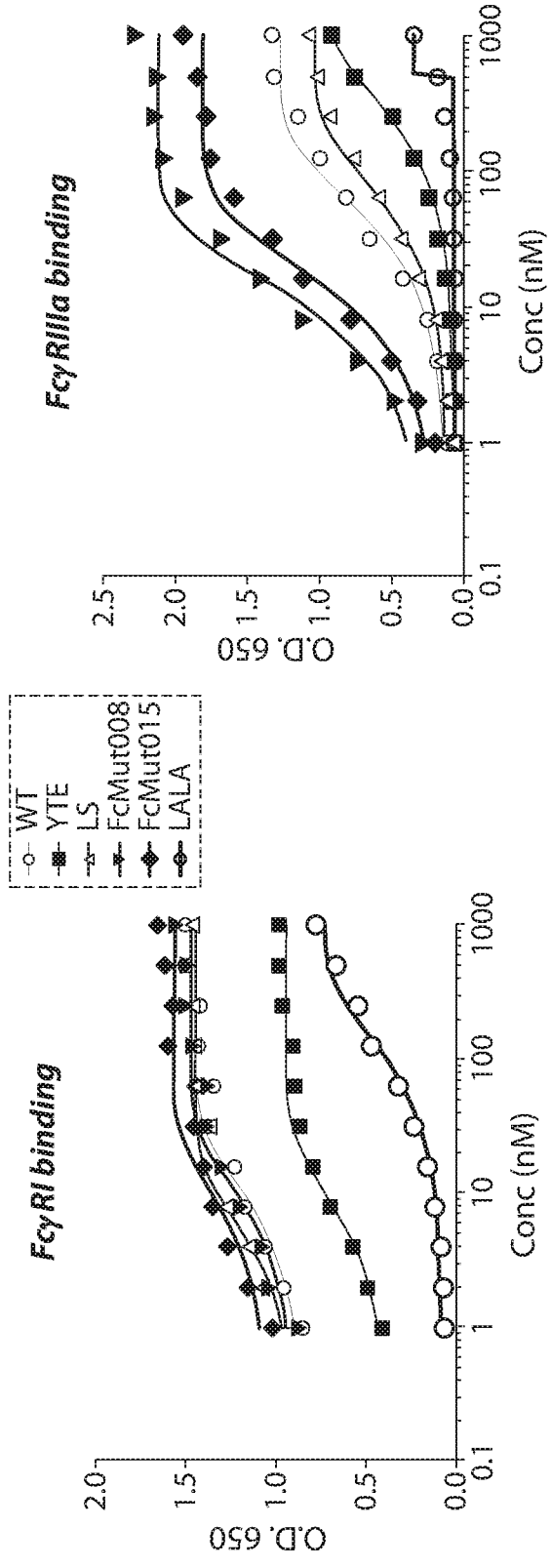


FIG. 8

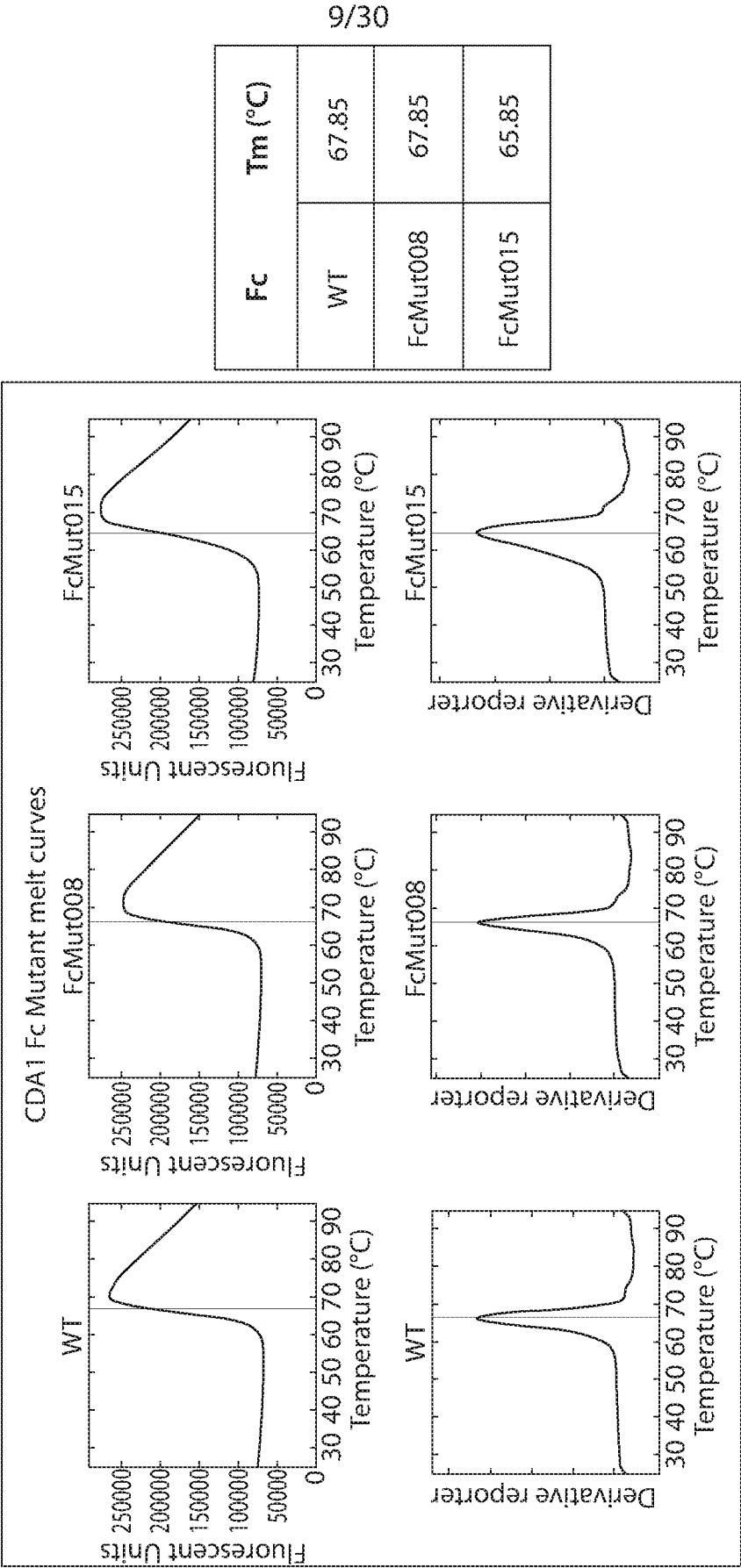


FIG.9

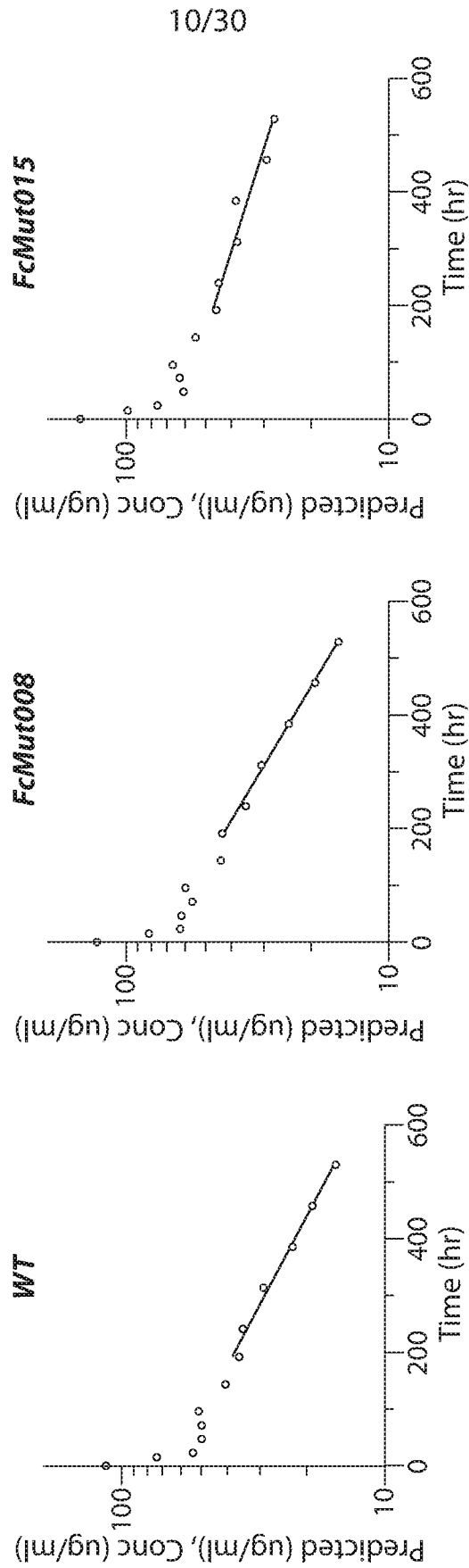


FIG. 10

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Name	Mutation	k_d (fold decrease*)	k_{on} (fold increase*)	k_{off} (fold decrease*)
FcMut229	T256D_H285D_T307R_Q311V_A378V	14.0	3.7	3.7
FcMut213	H285D_T307Q_A378V	13.2	3.8	3.3
FcMut215	T307Q_Q311V_A378V	12.4	3.4	3.7
FcMut228	T256D_N286D_T307R_Q311V_A378V	12.4	3.2	4.0
FcMut227	T256D_H285D_N286D_T307R_A378V	11.6	3.6	3.2
FcMut183	T256D_Q311V_A378V	11.0	3.2	3.2
FcMut223	T256D_H285D_A378V	10.3	3.7	2.7
FcMut216	H285D_Q311V_A378V	9.6	3.4	2.8
FcMut186	T256D_T307R_Q311V_A378V	9.5	2.9	3.1
FcMut197	H285N_T307Q_N315D	9.1	2.9	3.0
FcMut171	T256D_N286D_T307R_Q311V	8.5	2.5	3.1
FcMut219	T256D_N315D_A378V	7.9	2.8	2.8
FcMut045	T256D_T307R_Q311V	5.9	2.3	2.6
WT	NONE	1.0	1.0	1.0
YTE (<i>Medimmune</i>)	M252Y_S254T_T256E	8.5	2.3	3.6
LS (<i>Xencor</i>)	M428L_N434S	9.2	2.6	3.6

FIG. 11A

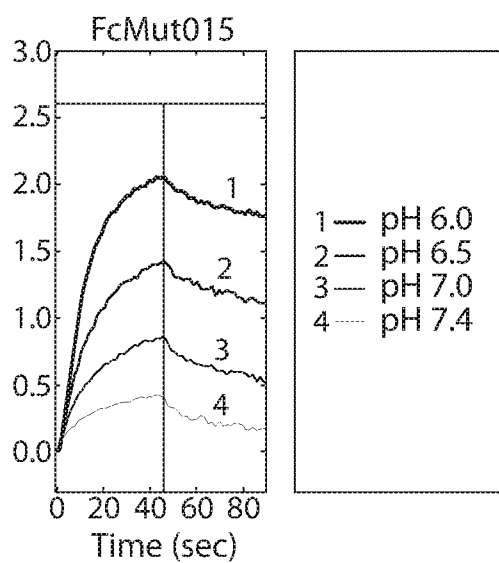


FIG. 11B

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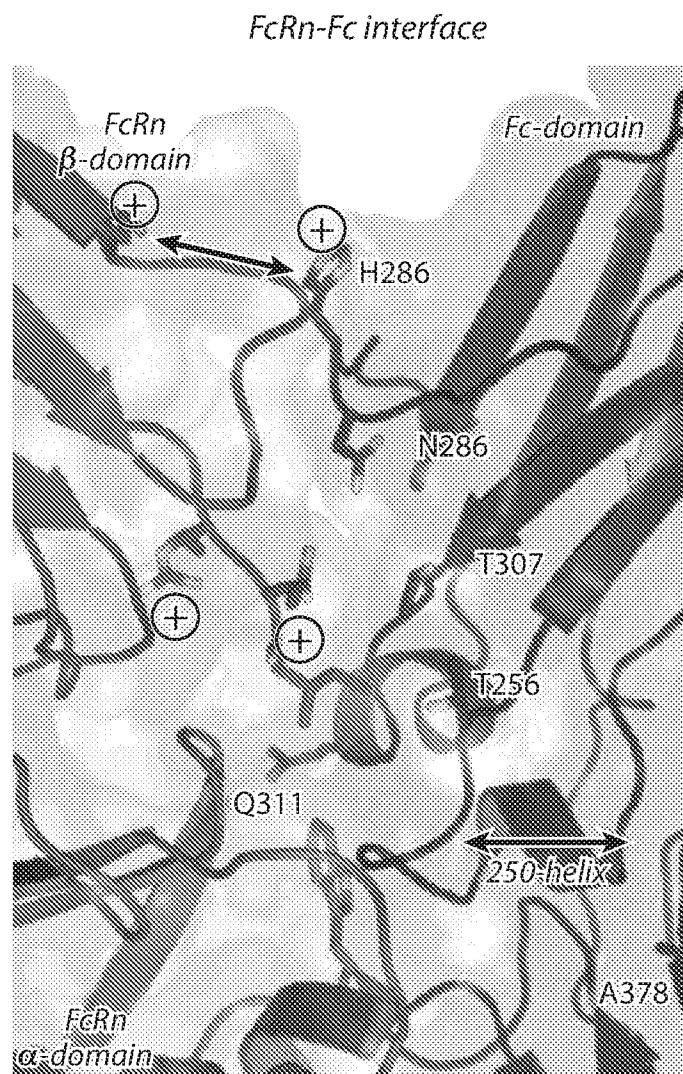


FIG. 11C

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Mutant	TM (sypro Orange)	SEC elution time (min)	Expi293 Expression (µg/mL)	SDS-PAGE	Protein A
WT	68.9	8.5	>80	✓	++
YTE	61.7	8.5	>80	✓	++
LS	68.0	8.5	>80	✓	++
FcMut045	64.8	8.5	>80	✓	++
FcMut171	64.8	8.5	>80	✓	++
FcMut183	64.0	8.5	>80	✓	++
FcMut186	63.7	8.5	>80	✓	++
FcMut197	68.4	8.5	>80	✓	++
FcMut213	70.2	8.5	>80	✓	++
FcMut215	69.2	8.5	>80	✓	++
FcMut216	65.8	8.5	>80	✓	++
FcMut219	66.7	8.5	>80	✓	++
FcMut223	64.3	8.4	>80	✓	++
FcMut227	66.6	8.4	>80	✓	++
FcMut228	66.7	8.5	>80	✓	++
FcMut229	64.6	8.5	>80	✓	++

FIG. 12

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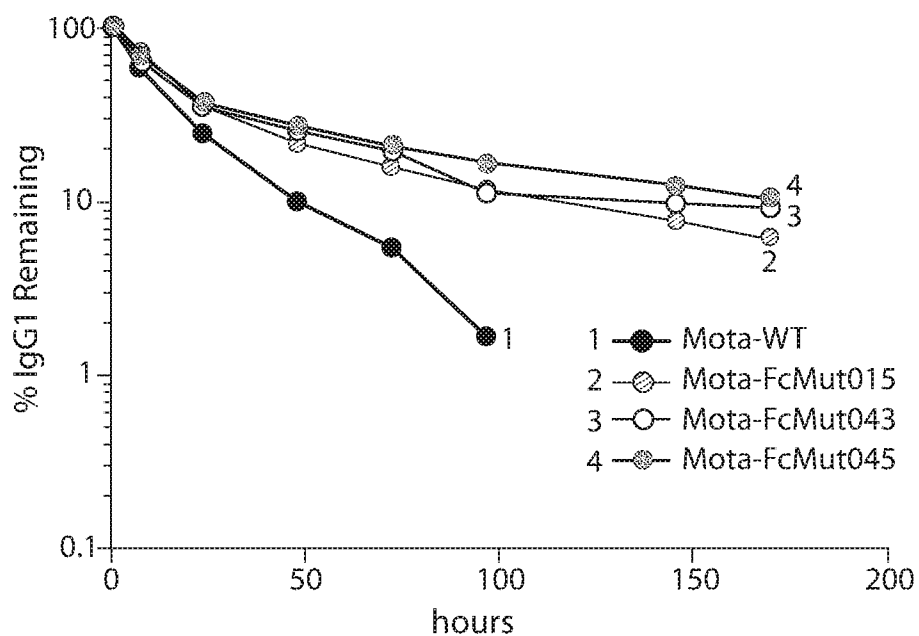


FIG. 13A

Group	Half-life (hr)	Fold increase	C _{max} (μg/ml)	AUC _{inf} (hr*μg/ml)	Clearance (ml/hr/kg)
WT	32		24.4	514.71	3.89
FcMut015	123	3.9	24.7	1168.46	1.71
FcMut045	166	5.2	23.9	1540.65	1.30

FIG. 13B

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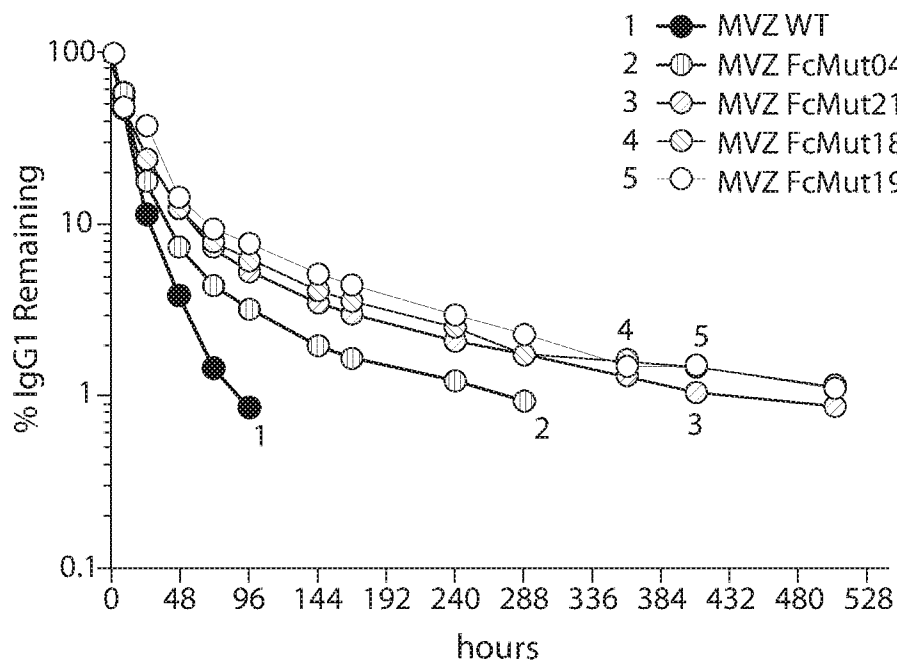


FIG. 14A

Group	Half-life (hr)	Fold increase	C _{max} (μg/ml)	AUC _{inf} (hr*μg/ml)	Clearance (ml/hr/kg)
WT	19		101.5	1343.13	3.72
FcMut045	135	7.0	112.3	2374.28	2.11
FcMut183	192	9.9	95.4	3216.24	1.55
FcMut197	165	8.6	81.7	3074.29	1.63
FcMut213	182	9.4	107.2	3408.52	1.47

FIG. 14B

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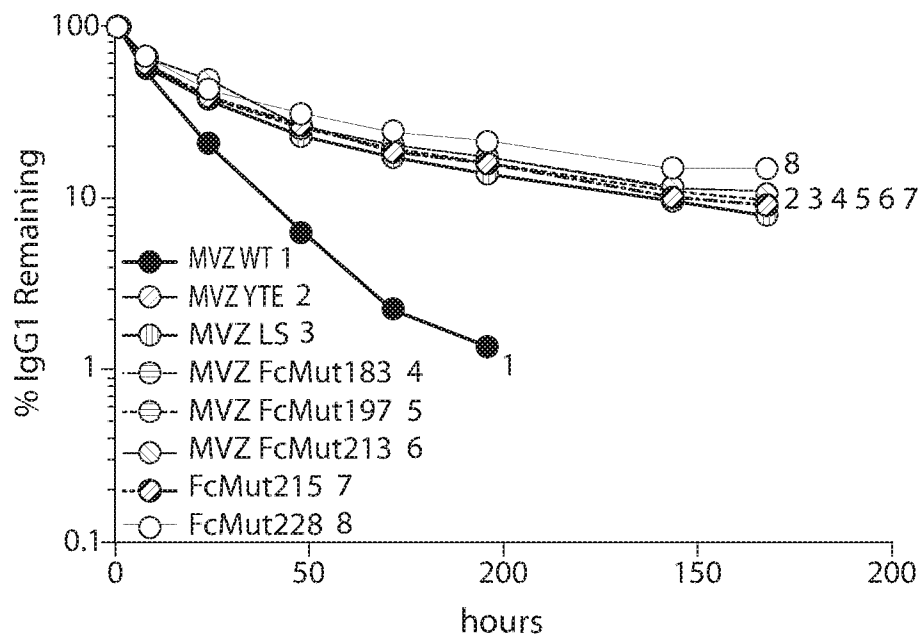


FIG. 14C

Group	Half-life (hr)	Fold increase	C _{max} (µg/ml)	AUC _{inf} (hr*µg/ml)	Clearance (ml/hr/kg)
WT	22		29.3	513.87	3.89
YTE	86	3.9	26.3	1302.33	1.54
LS	87	4.0	30.6	1482.35	1.35
FcMut183	90	4.1	24.9	1384.34	1.44
FcMut197	94	4.3	22.0	1191.66	1.68
FcMut213	96	4.4	21.4	1286.27	1.55
FcMut215	87	4.0	27.3	1395.92	1.43
FcMut228	123	5.6	20.1	1509.50	1.32

FIG. 14D

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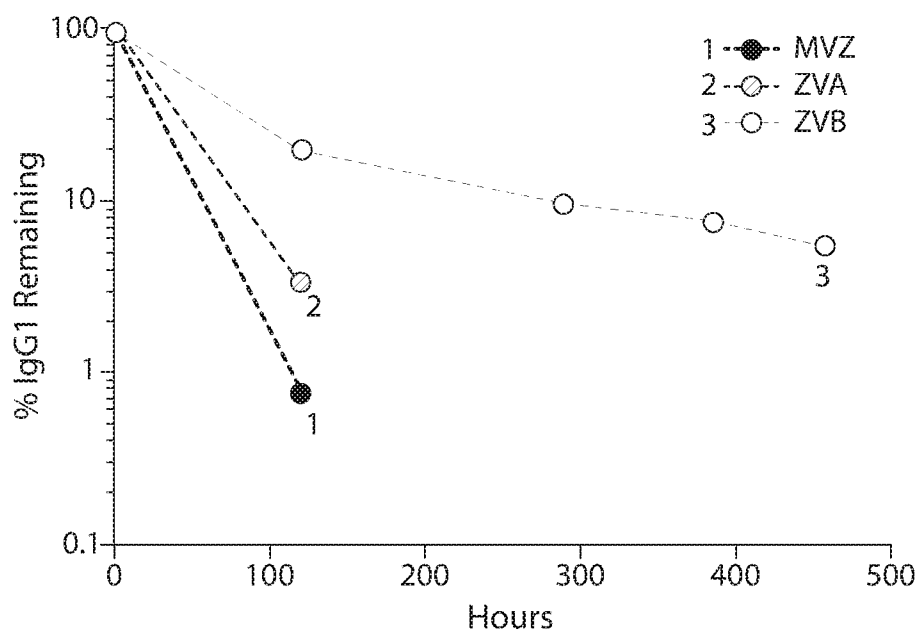


FIG. 15

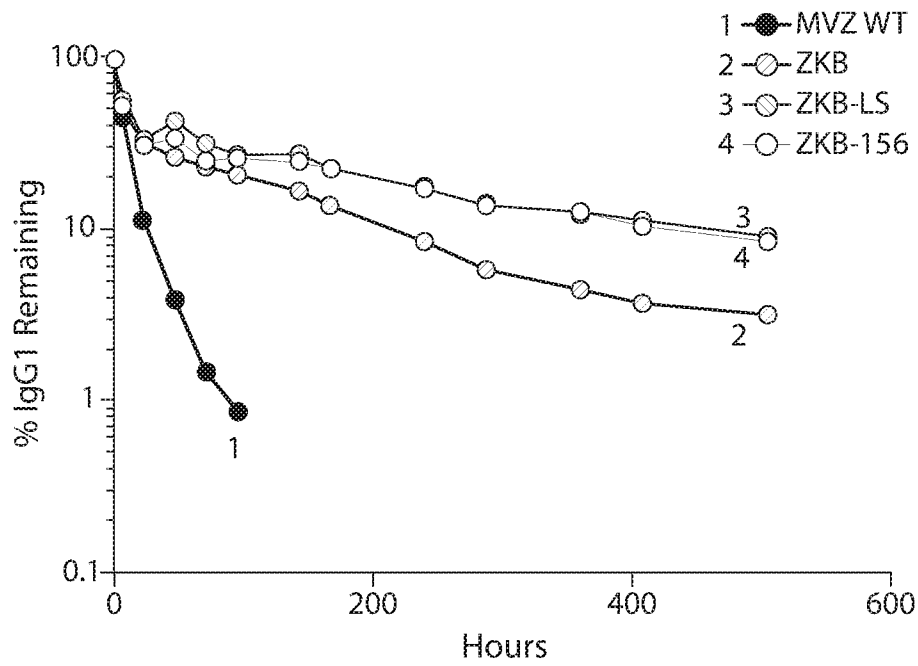


FIG. 16

Mutant	FcγRI (ELISA)	FcγRIIA (octet)	FcγRIIB (octet)	FcγRIIA (ELISA)	C1q (ELISA)
WT	++	++	++	++	++
YTE	+	+	+	+	++
LS	++	++	++	++	++
FcMut045	++	++	++	++	++
FcMut171	+	++	++	++	++
FcMut183	++	++	+++	+++	++
FcMut186	+++	+++	+++	+++	++
FcMut197	++	++	++	+++	+
FcMut213	++	+++	+++	++	++
FcMut215	++	+++	+++	+++	++
FcMut216	++	+++	+++	++	++
FcMut219	++	+++	+++	+++	++
FcMut223	+	+++	+++	++	++
FcMut227	+	+++	+++	++	+
FcMut228	+	+	++	++	++
FcMut229	++	+++	+++	++	++

FIG. 17A

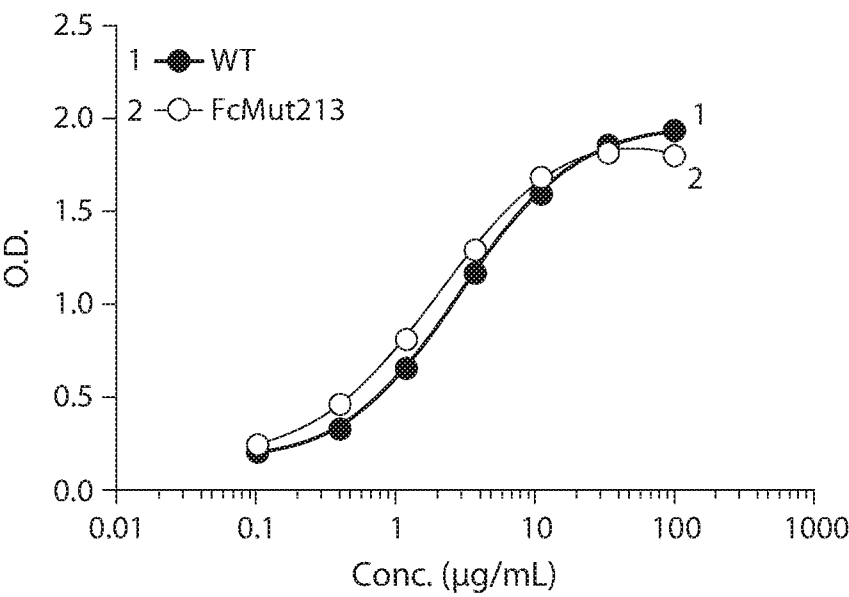


FIG. 17B

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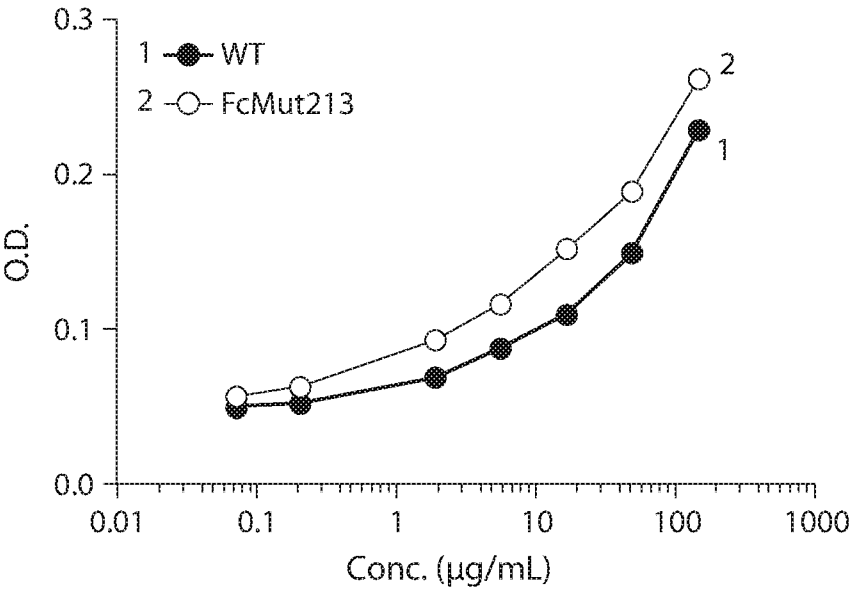


FIG. 17C

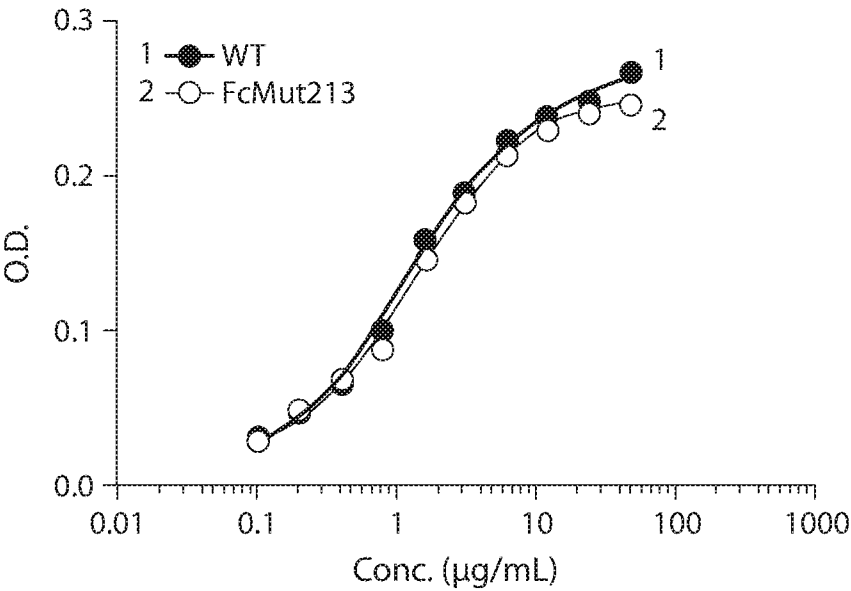


FIG. 17D

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Antibody	Mutations	CDC EC50 (ug/mL)*	C1q binding
RTX WT	None	0.715	0.87
RTX YTE	M252Y_S254T_T256E	> 20	1.05
RTX LS	M428L_N434S	0.352	1.05
RTX FcMut045	T256D_T307R_Q311V	0.353	0.87
RTX FcMut183	T256D_Q311V_A378V	0.103	1.36
RTX FcMut186	T256D_T307R_Q311V_A378V	0.158	0.51
RTX FcMut197	H285N_T307Q_N315D	2.543	0.49
RTX FcMut213	H285D_T307Q_A378V	0.267	1.09
RTX FcMut215	T307Q_Q311V_A378V	0.141	1.03
RTX FcMut222	T256D_T307Q_Q311V	0.577	0.94
RTX FcMut224	T256D_H285D_T307R_Q311V	0.576	0.82
RTX FcMut226	T256D_H285D_N286D_T307ER_Q311V	0.745	0.79
RTX FcMut227	T256D_H285D_N286D_T307R_A378V	0.228	0.99
RTX FcMut228	T256D_N286D_T307R_Q311V_A378V	0.220	0.89
RTX FcMut229	T256D_H286D_T307R_Q311V_A378V	0.140	1.29
RTX LALA	L234A_L235A	> 20	NA
RTX FcMut037	L235V_G236A	> 20	NA

FIG. 18

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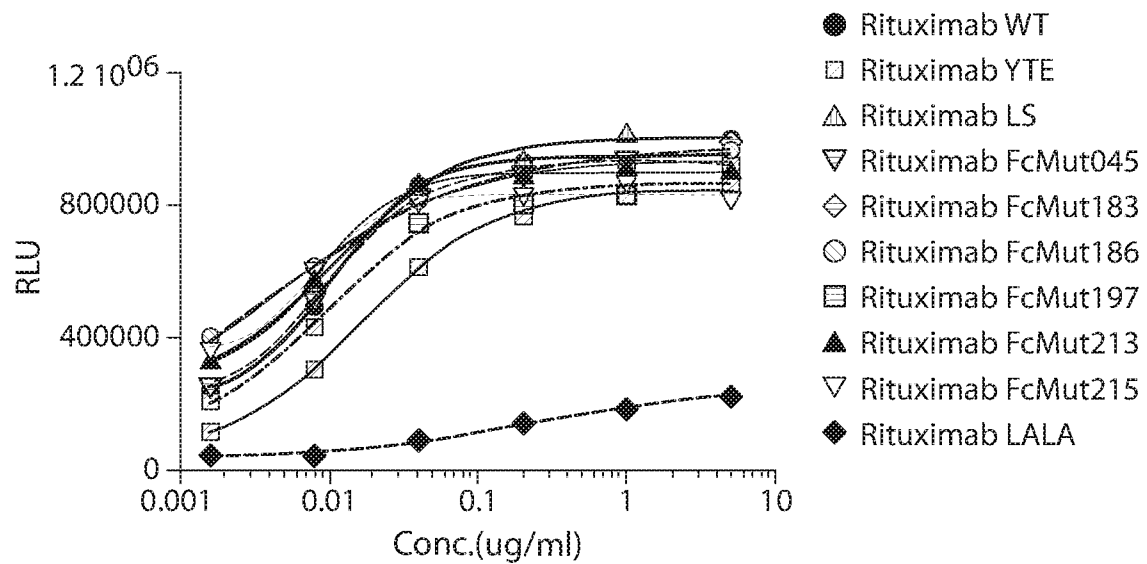


FIG. 19A

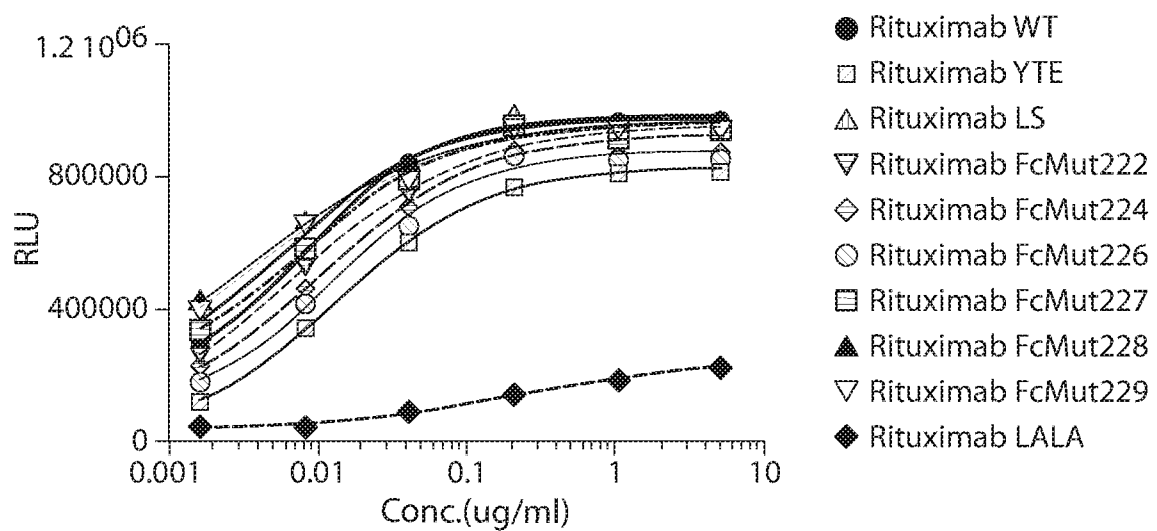


FIG. 19B

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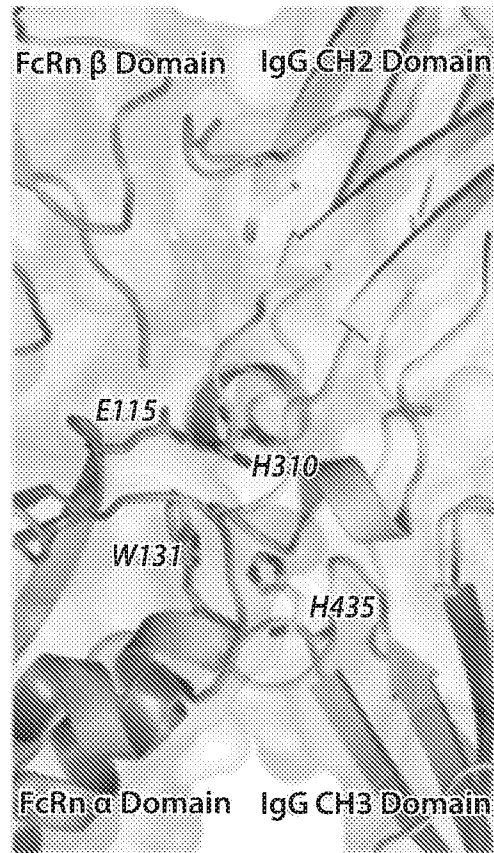


FIG. 20A

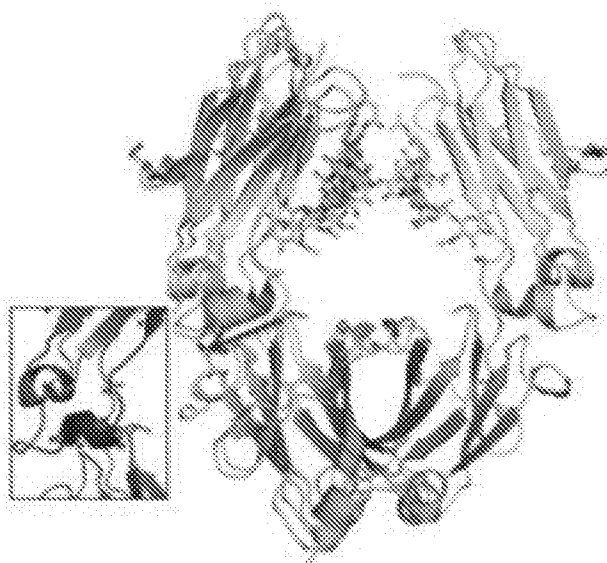


FIG. 20B

Set	Amino acids
Contact Residues	L251, I253, R255, P257, H285, N286, K288, T307, V308, L309, Q311, L314, H310, H433, N434, H435, Y436
Peripheral Residues	M252, T256, T307, L309, Q311 H433, N434, Y436, N286, K288
Non-contact residues	A287, V308, N315, L314, L432, H429, E430, A431
Residues with potential to modulate 250-helix dynamics	P244, P245, T250, L251, P247 E380, M428, A378, D376, P257, V308, A287, L306, H427

FIG. 21A

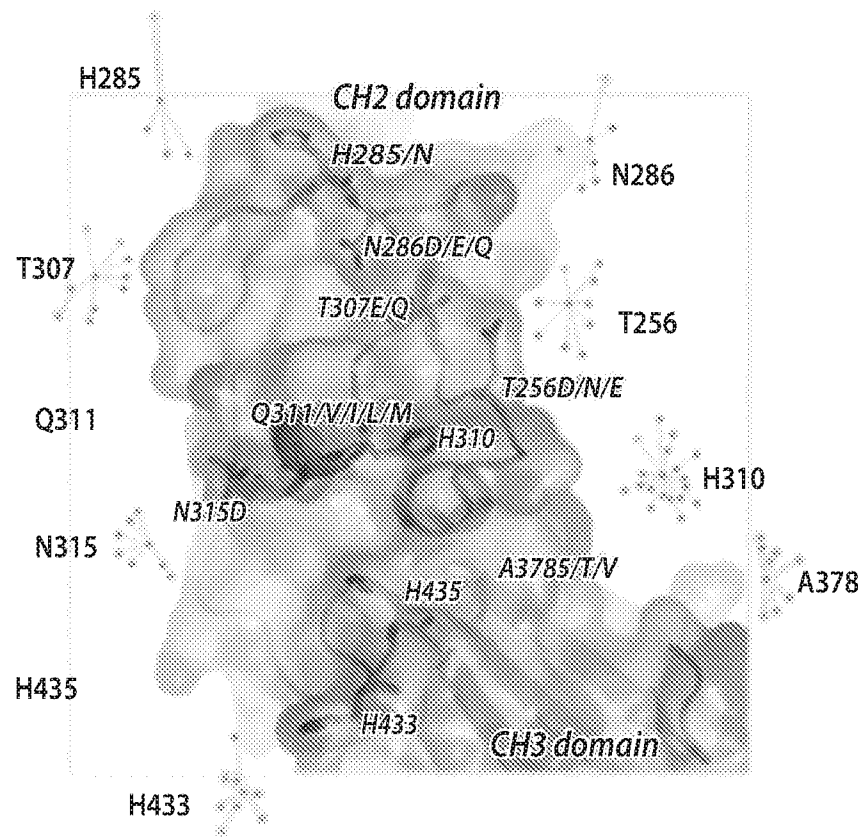


FIG. 21B

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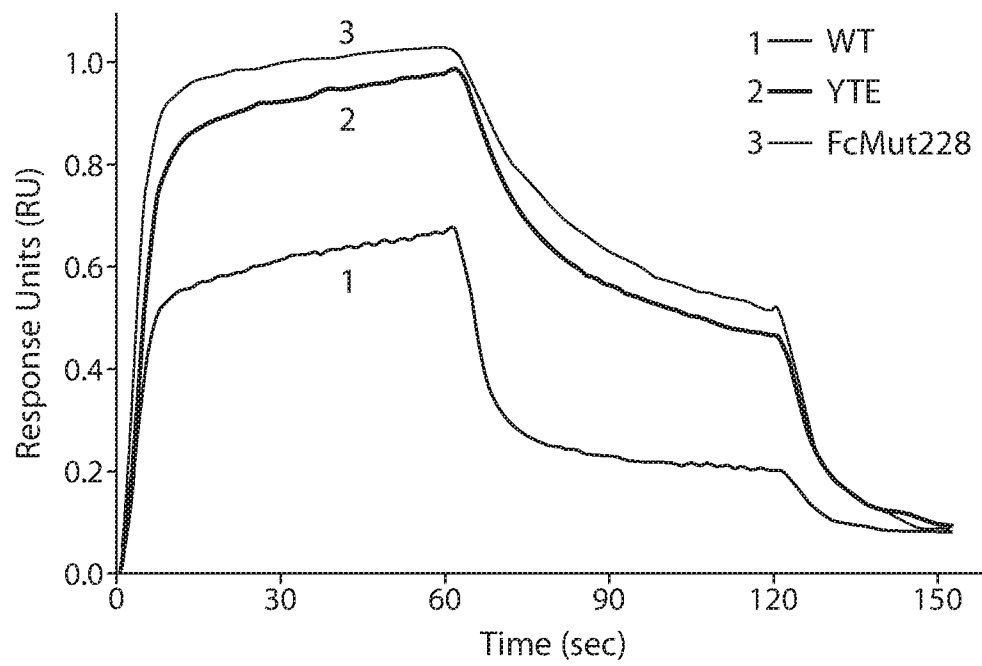


FIG. 22

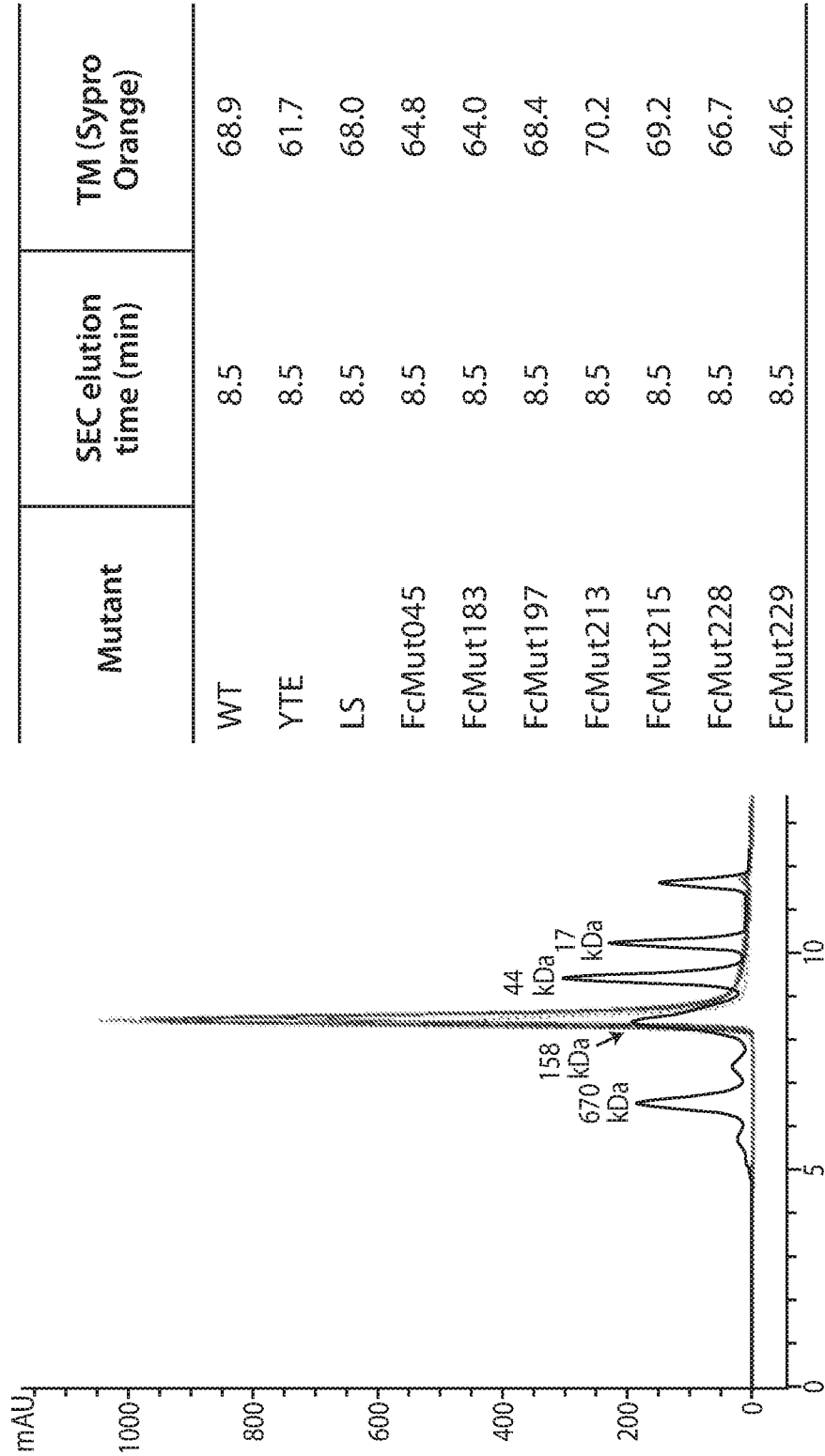


FIG. 23

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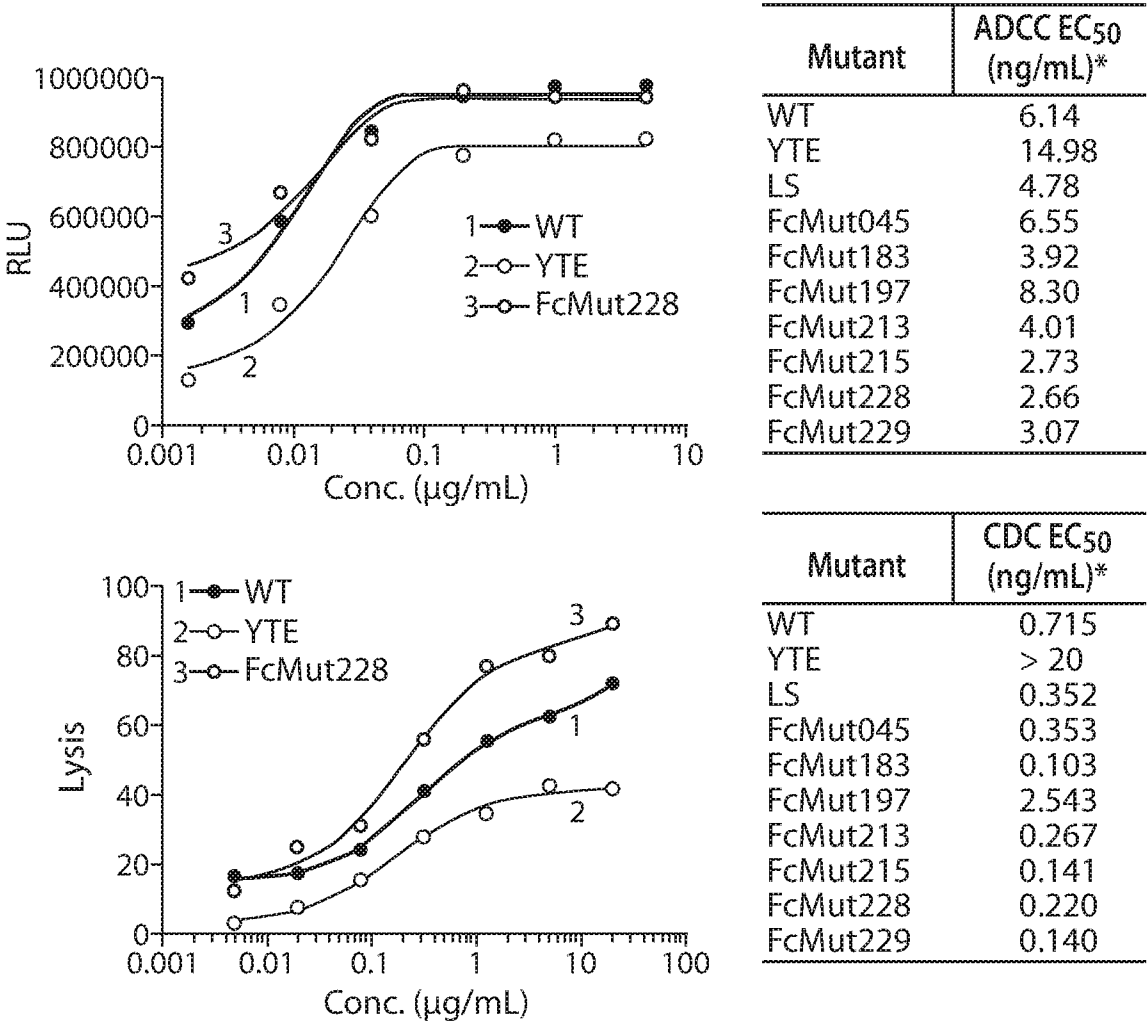


FIG. 24

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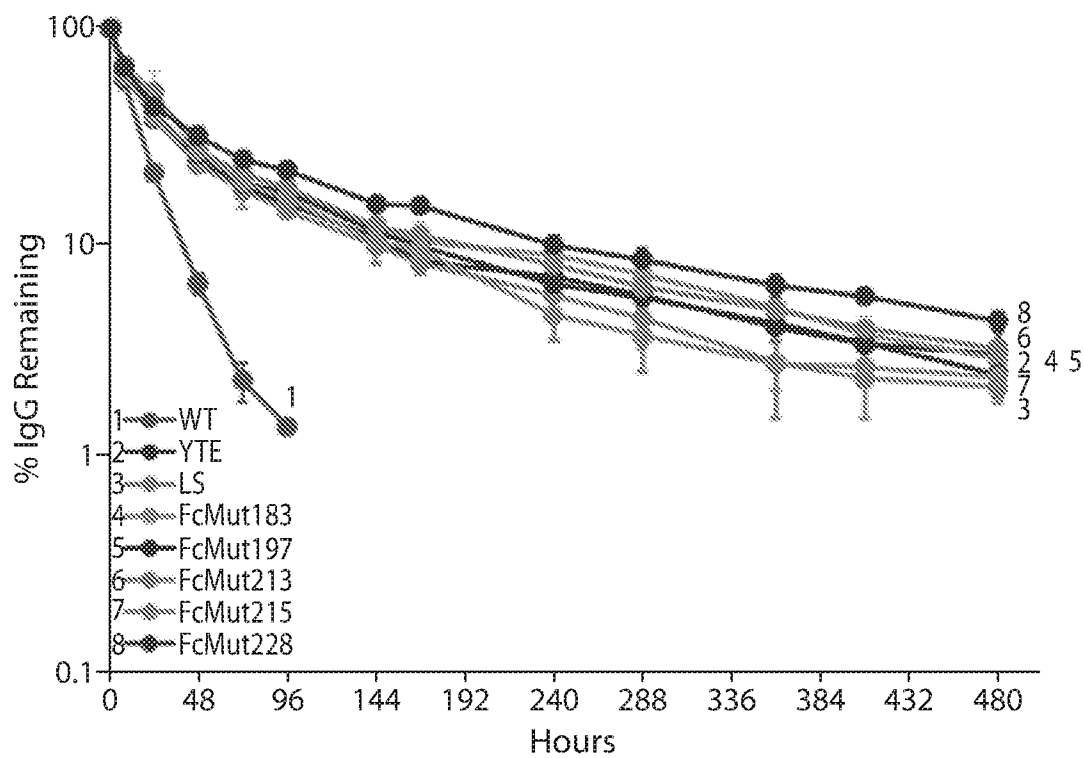


FIG. 25A

Group	Half-life (hr)	Fold increase	C _{max} (μg/ml)	AUC _{inf} (hr*μg/ml)	Clearance (ml/hr/kg)
WT	22		29.3	513.87	3.89
YTE	193	8.8	26.3	1682.46	1.19
LS	167	7.6	30.6	1731.27	1.16
FcMut183	145	6.6	24.9	1689.29	1.18
FcMut197	170	7.8	22.0	1385.48	1.44
FCMut213	184	8.4	21.4	1546.14	1.29
FcMut215	220	10.1	27.3	1587.99	1.26
FcMut228	207	9.5	20.1	1741.26	1.15

FIG. 25B

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Fab	Fc	Mutations	EC ₅₀ (ug/mL)
Motavizumab	WT	None	8.50
Motavizumab	YTE	M252Y_S254T_T256E	10.09
Motavizumab	LS	M428L_N434S	14.49
Motavizumab	FcMut045	T256D_T307R_Q311V	7.73
Motavizumab	FcMut183	T256D_Q311V_A378V	7.41
Motavizumab	FcMut197	H285N_T307Q_N315D	12.32
Motavizumab	FcMut213	H285D_T307Q_A378V	10.54
Motavizumab	FcMut215	T307Q_Q311V_A378V	7.80
Motavizumab	FcMut228	T256D_N286D_T307R_Q311V_A378V	10.45

FIG. 26

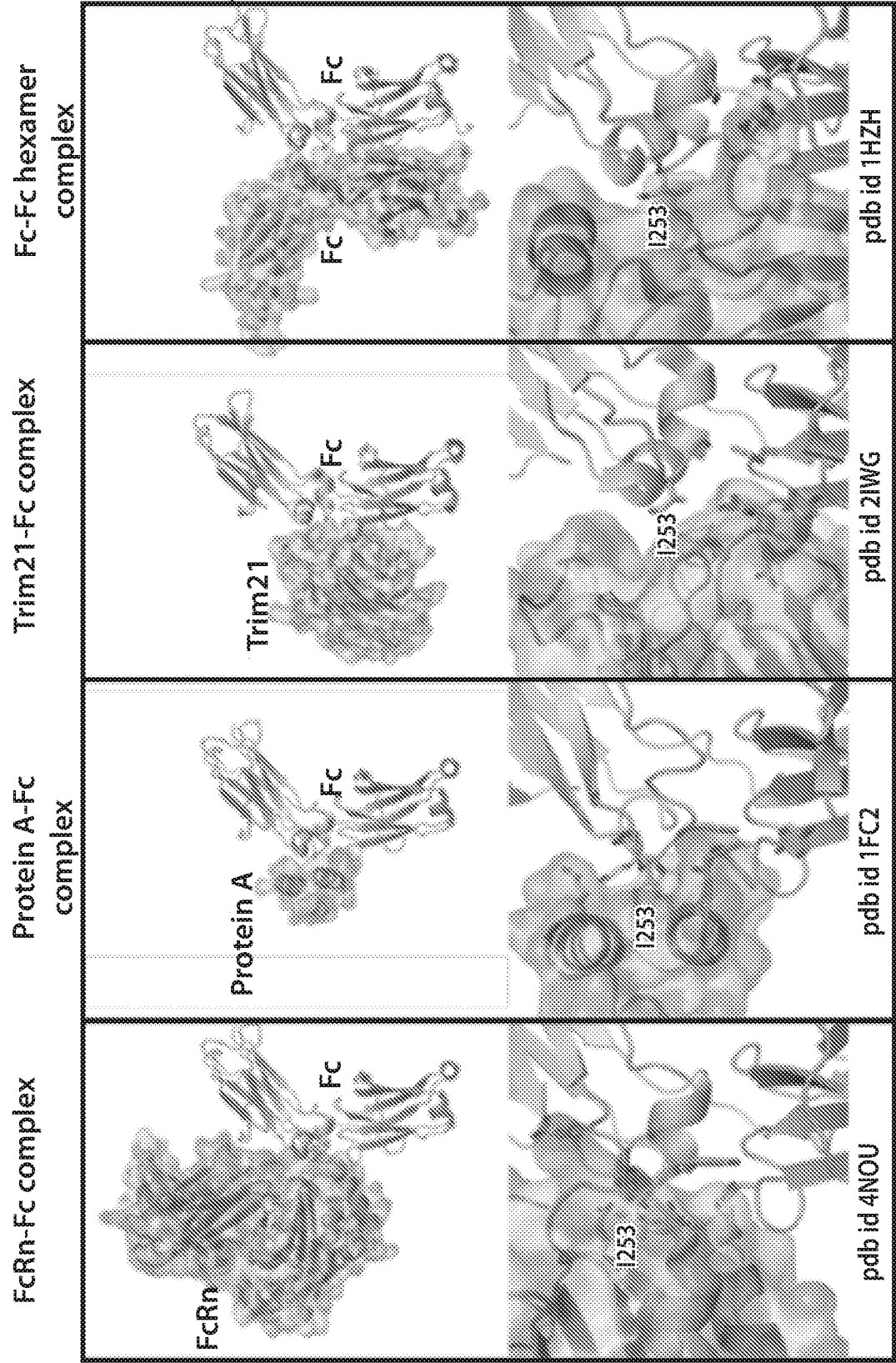


FIG. 27A

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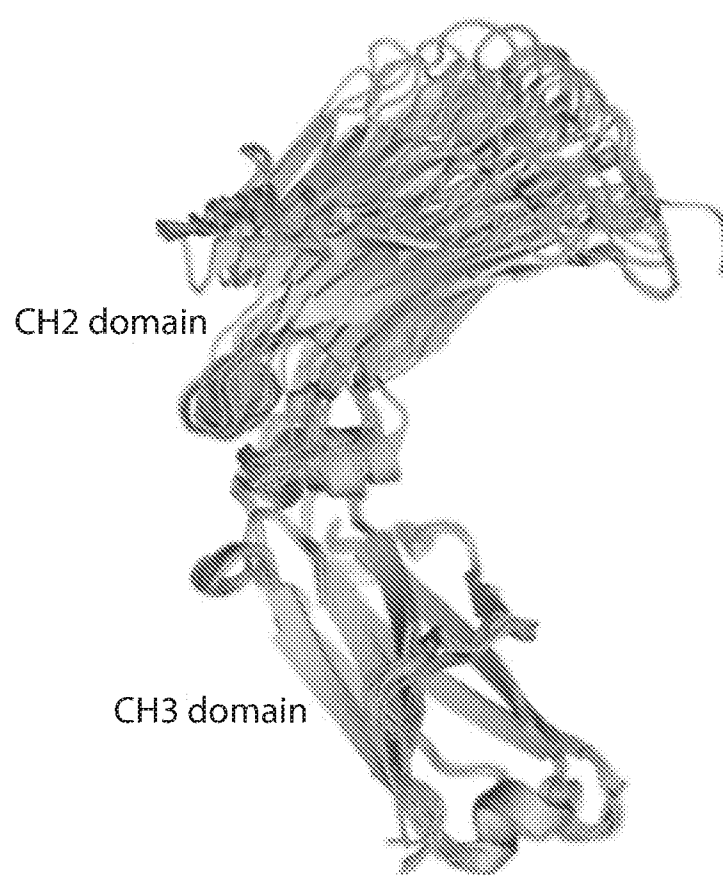


FIG. 27B