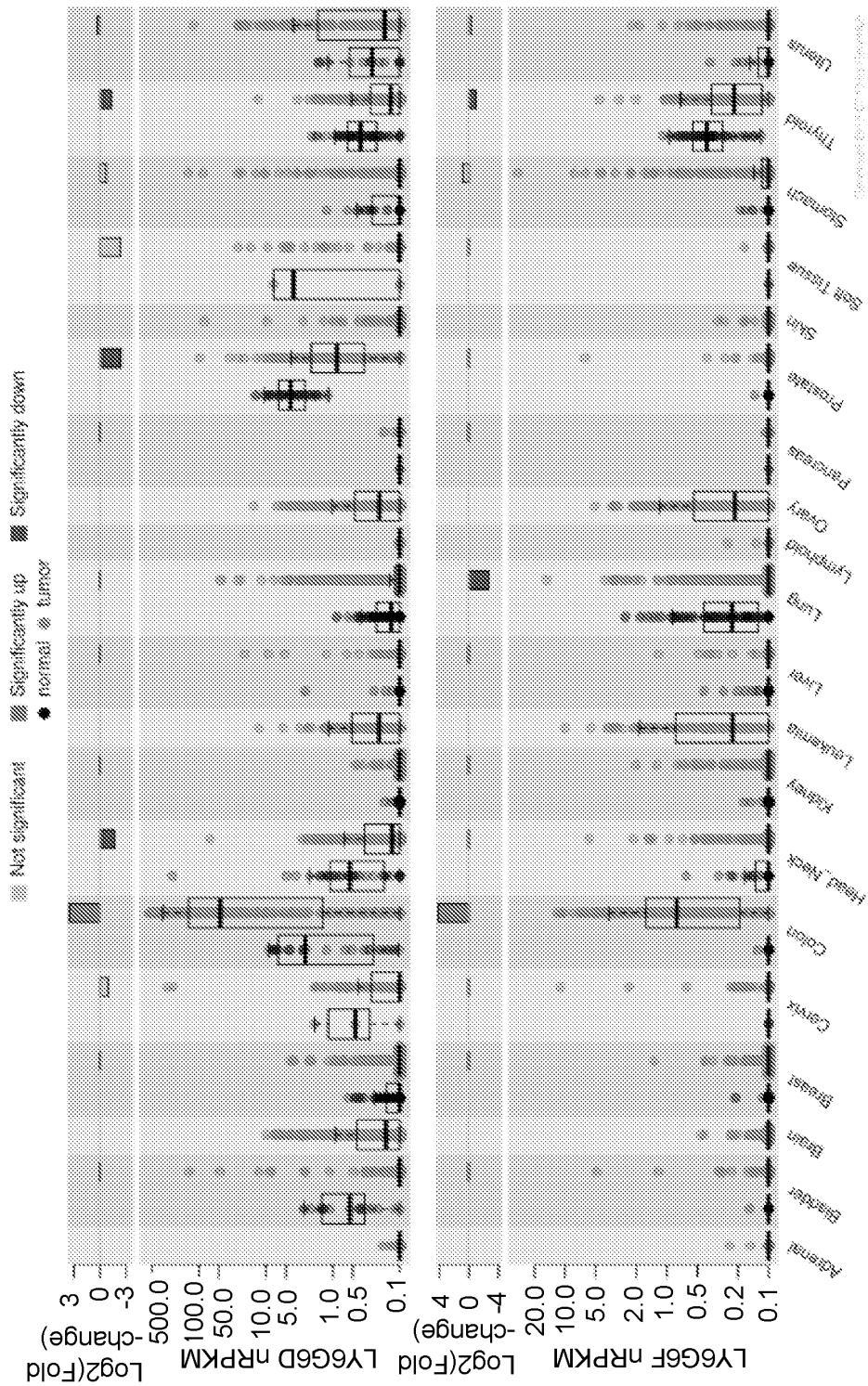


FIG. 1A



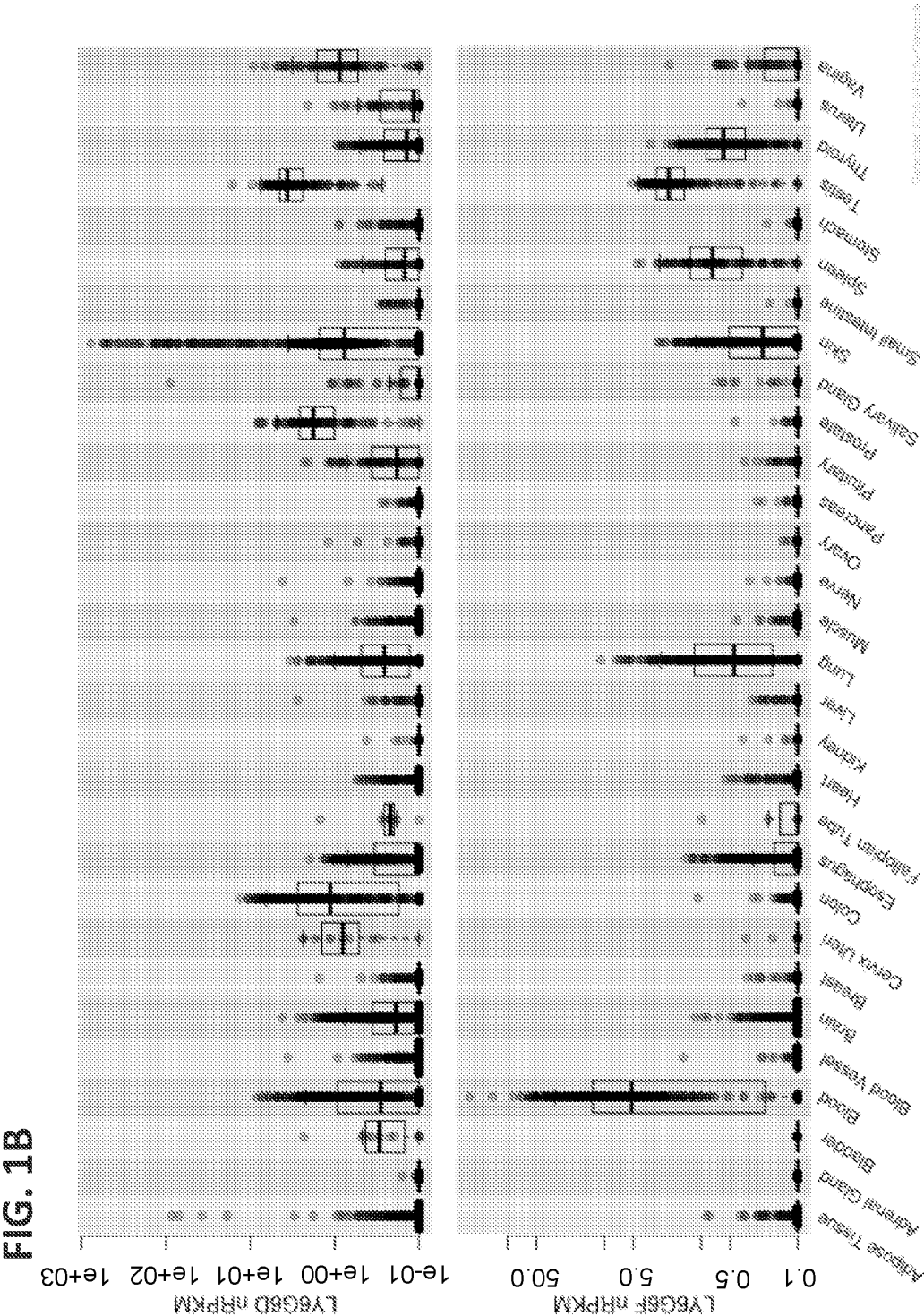


FIG. 1C

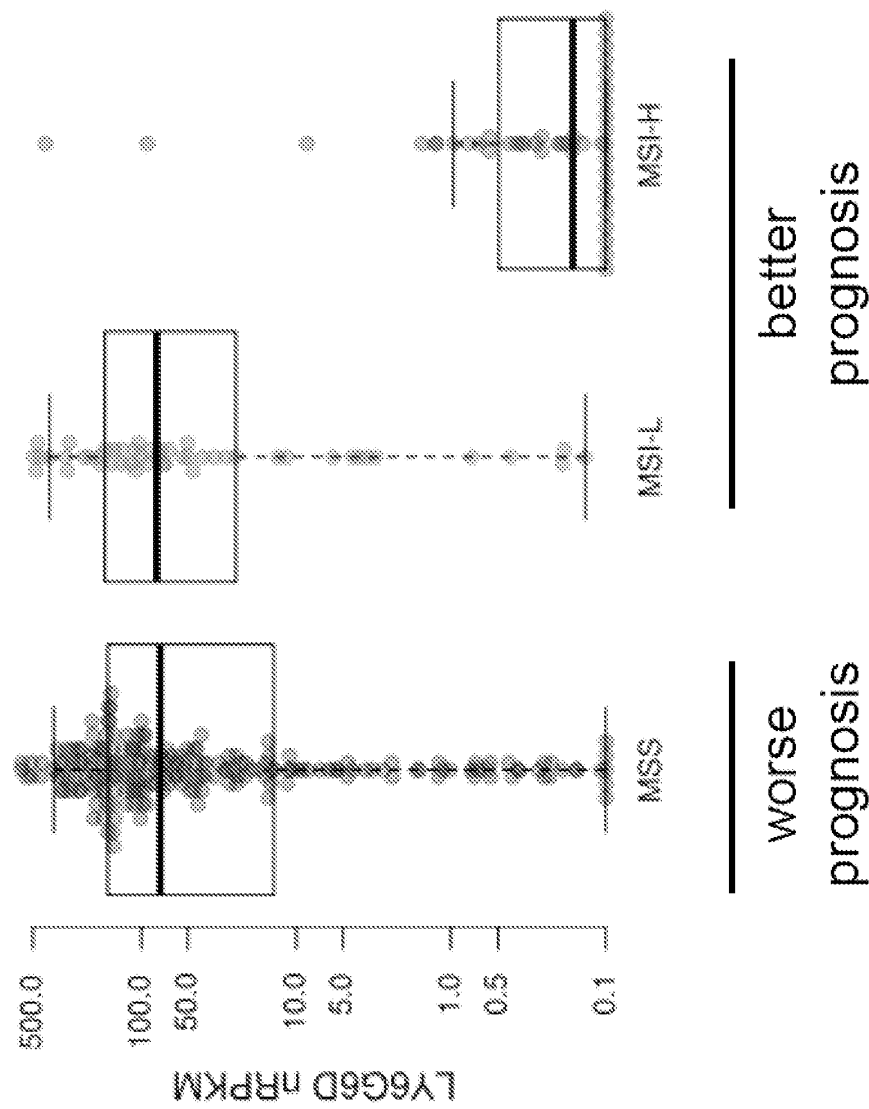




FIG. 2A

Normal colon



FIG. 2B

1+



FIG. 2C

2+

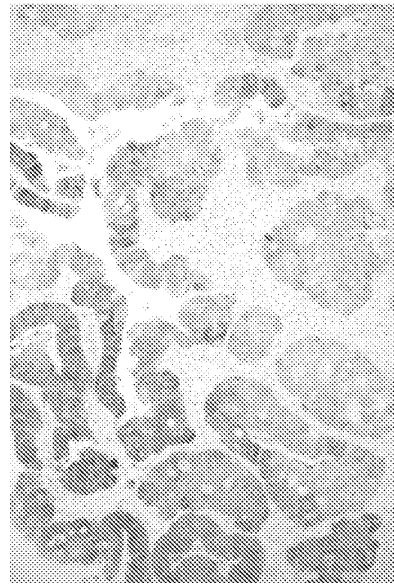


FIG. 2D

3+

FIG. 3A

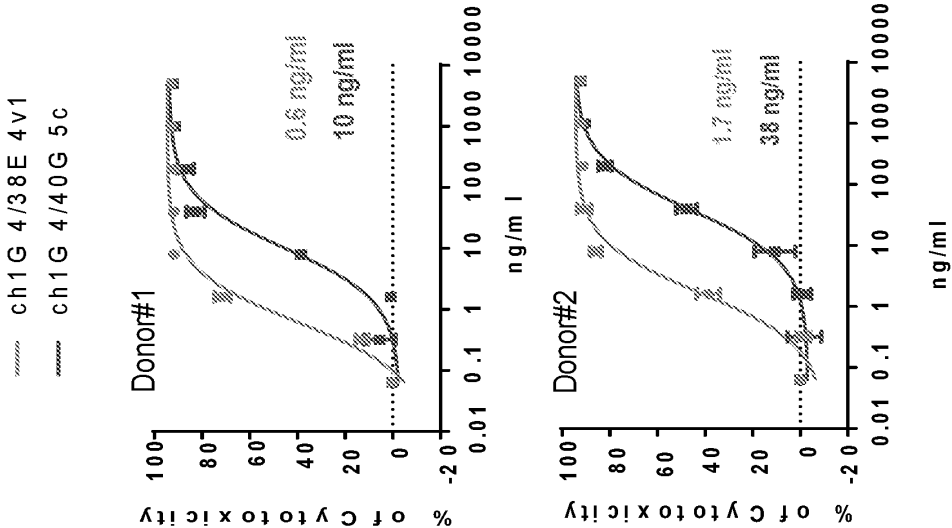
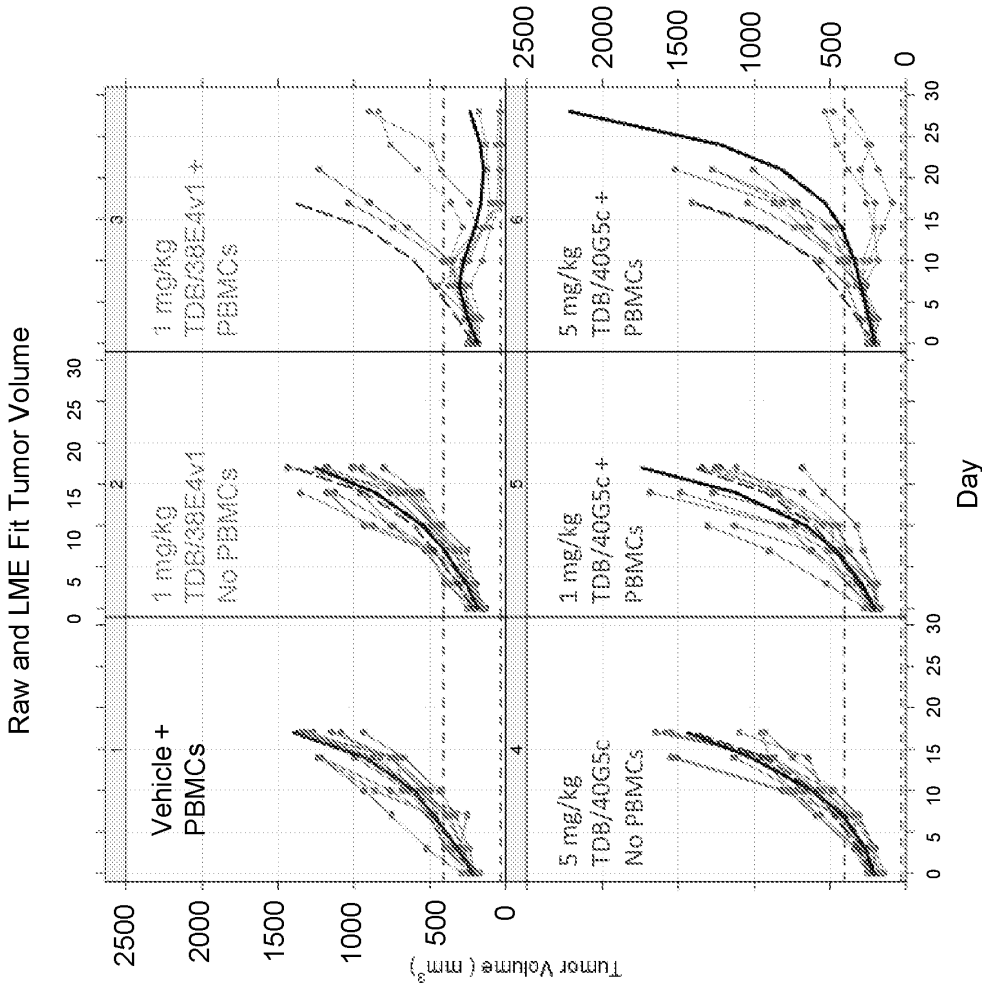


FIG. 3B



single dose IV; HT55 in NSG mice with human PBMCs

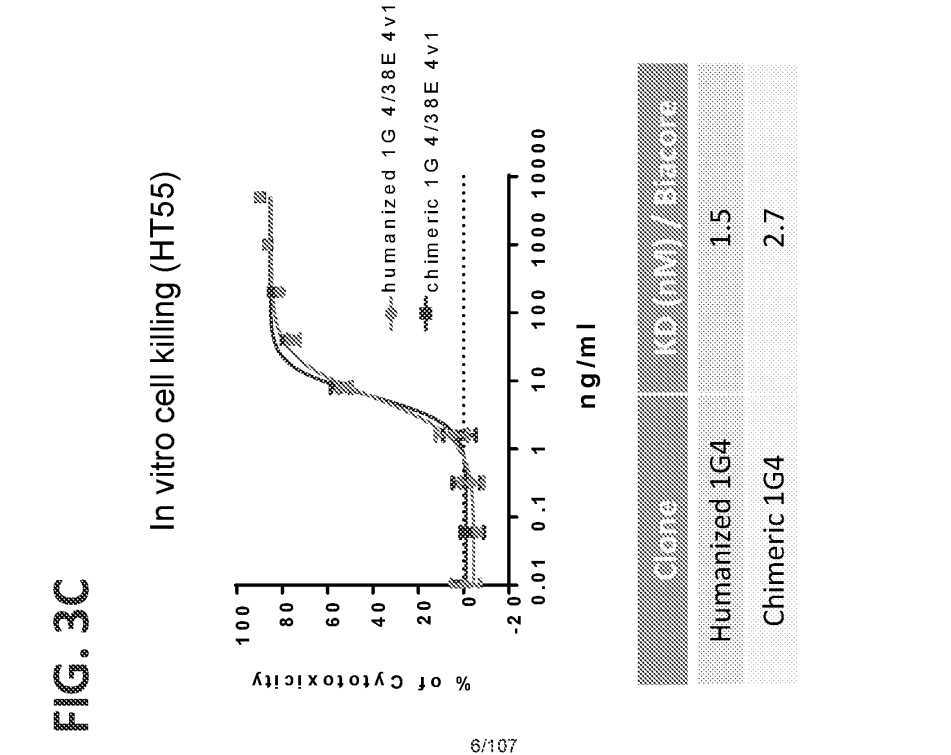
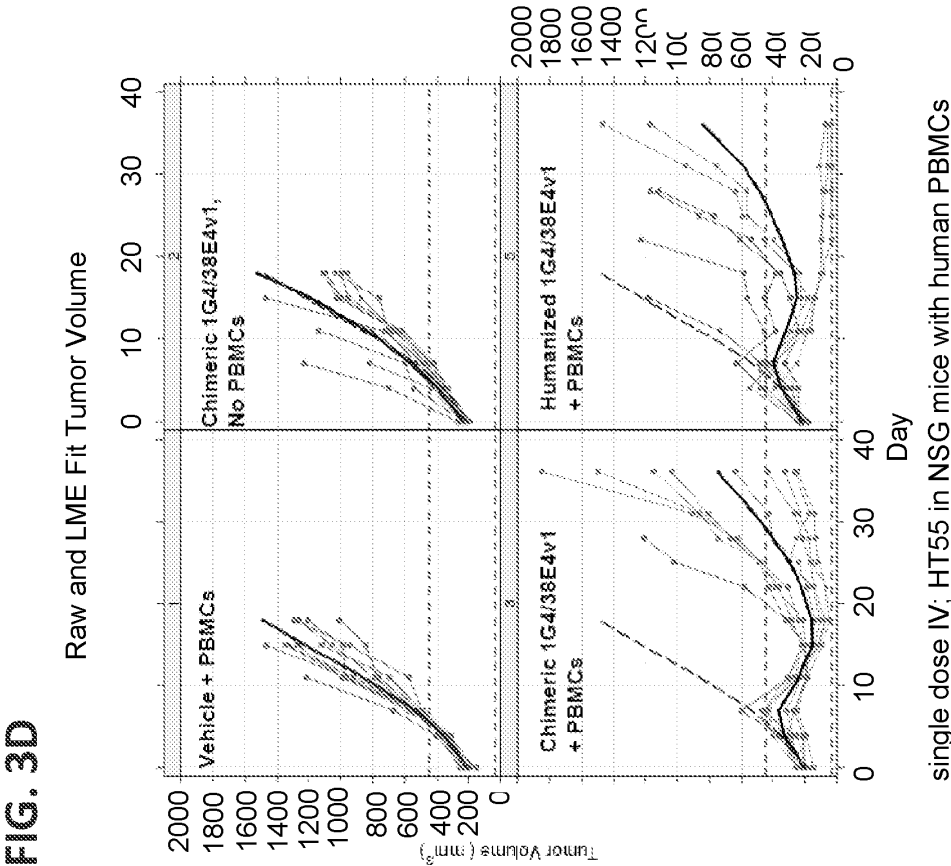


FIG. 4A

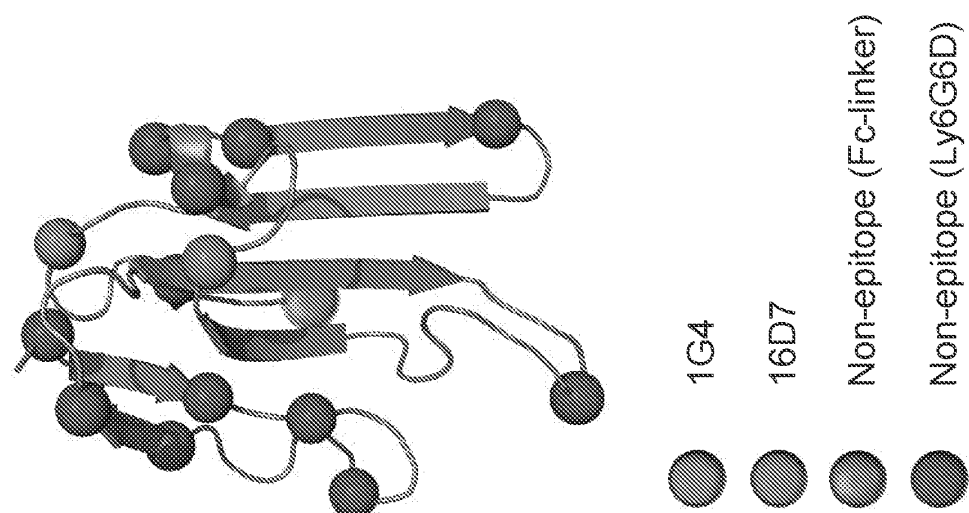


FIG. 4B

WT	M22S	G28S	G28N	S32N	A38N	G43N, G45S	P60A, P61S	A73N, H75S	V80S	V80N	T82N	D87N	G99N, L101S	A105S	S108N
% Glycosylated	0	1.72	11.5	0	8.17	41.2	7.32	98	94.5	91.6	97.9	5.98	99.4	30.1	85.9
3A4															
3H9															
7F2.C35a-HC															
11A11.C59-HC															
20F12.C35a-HC															
1D1															
chim16D7															
5D3															
5E4															
16D7.6															
3D3															
17F11															
2-6C9															
1F12															
14B6															
hu1G4 (prep 1)															
hu1G4 (prep 2)															
chim1G4															
4H7															
6E10															
20A12															
1C10															
1G11 {affinity ~-1G4}															
1F9 {-1G4}															
1A1															
16F7															
3E5 (*4F11)															
1D12															
1F1															
14E12															
9D6															
16G2															
10F7															

X=no binding detected w= significantly reduced binding

FIG. 4C

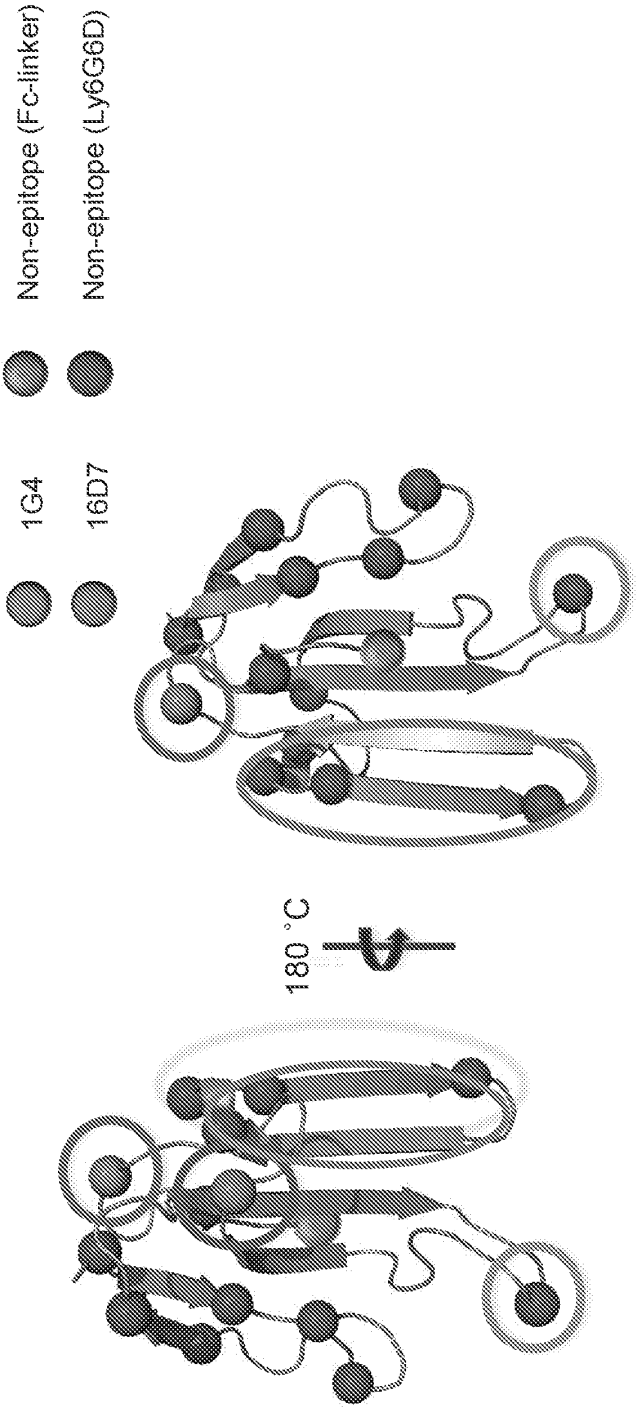
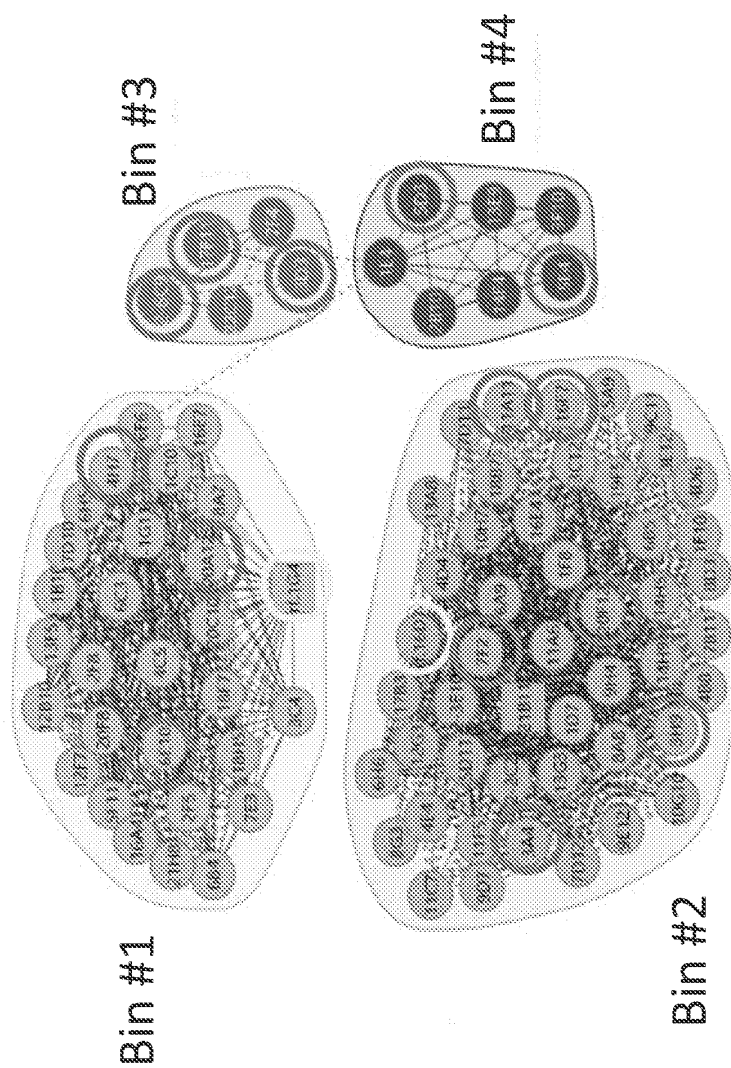


FIG. 4D



ਘਰ



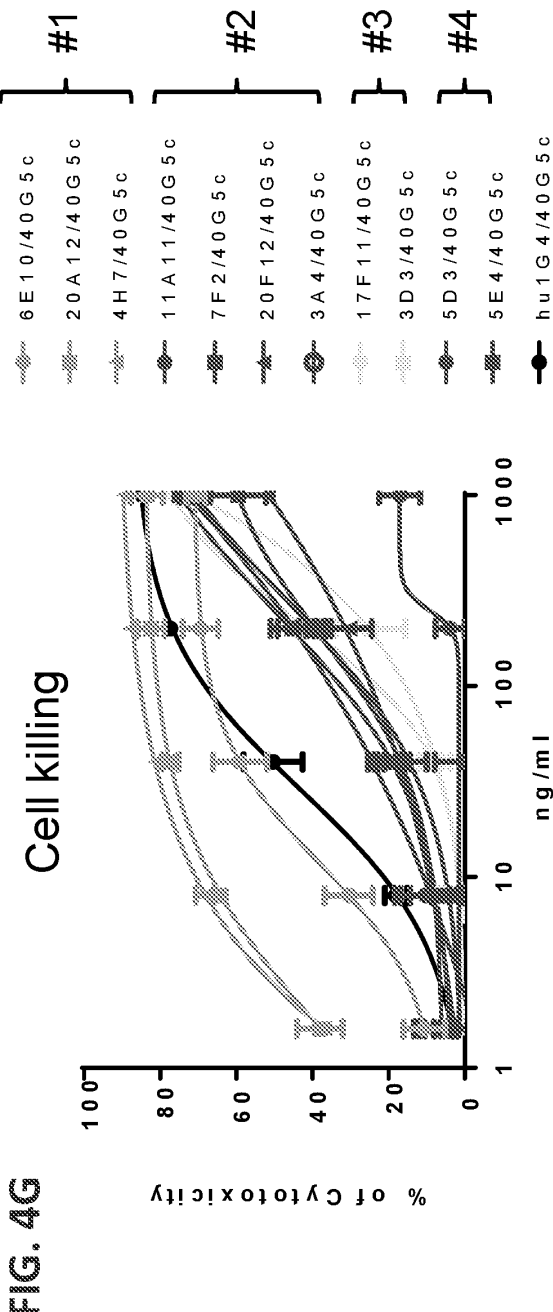
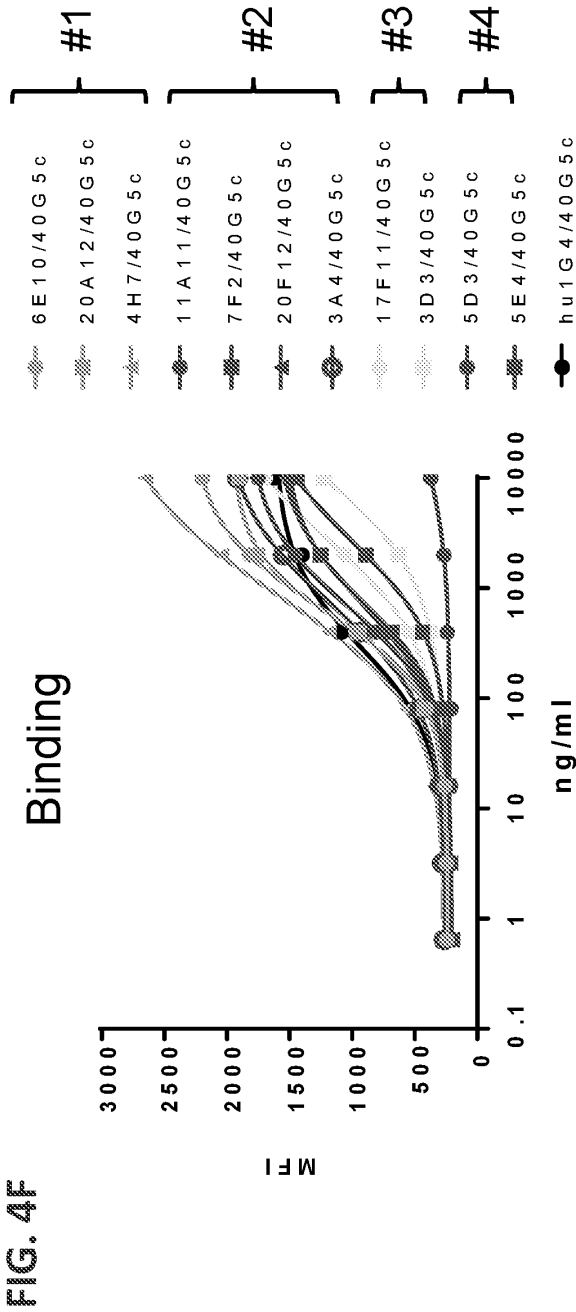


FIG. 4H

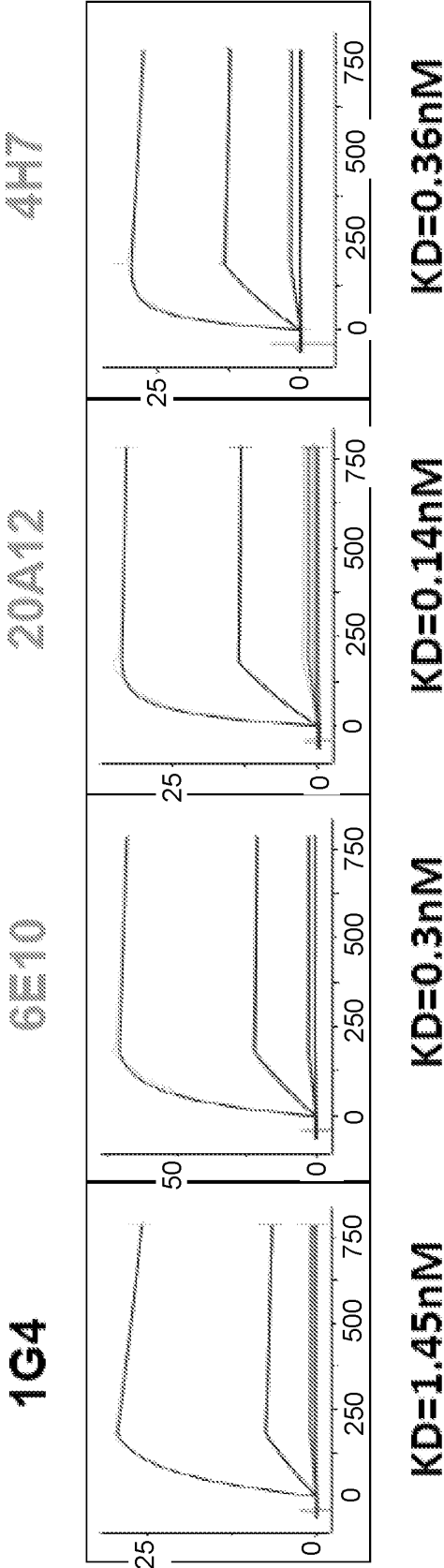


FIG. 5A

Heavy chain variable region

Kabat number 20A12.QNTv12	24	25	26	27	28	29	30	31	32	33	34	35	36	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	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																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																															
	CDR H1 - Contact										CDR H1 - Kabat																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																	

SEQ ID NO: 22

FIG. 5B

Light chain variable region

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	
20A12.QNTv12	D	I	Q	M	T	Q	S	P	S	T	L	S	A	S	V	G	D	R	V	T	I	T	C	Q	A	S
Kabat number																										
	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	
20A12.QNTv12	A	P	K	L	L	I	Y	D	A	S	K	L	P	S	G	V	P	S	R	F	S	G	S	G	T	
Kabat number																										
	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	
20A12.QNTv12	T	Y	C	Q	S	T	S	F	R	G	R	S	Y	Q	N	T	F	G	G	T	K	V	E	I	K	

CDRL1-Contact

CDRL1-CH2

CDRL1-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

CDRL2-Contact

CDRL2-CH2

CDRL2-Kabat

26

27

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42

43

44

45

46

47

48

49

50

CDRL3-Contact

CDRL3-CH2

CDRL3-Kabat

51

52

53

54

55

56

57

58

59

60

61

62

63

64

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68

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71

72

73

74

75

SEQ ID NO: 23

SEQ ID NO: 23

Heavy chain variable region

SEQ ID NO: 10

FIG. 6B *10 complexes overlaid*

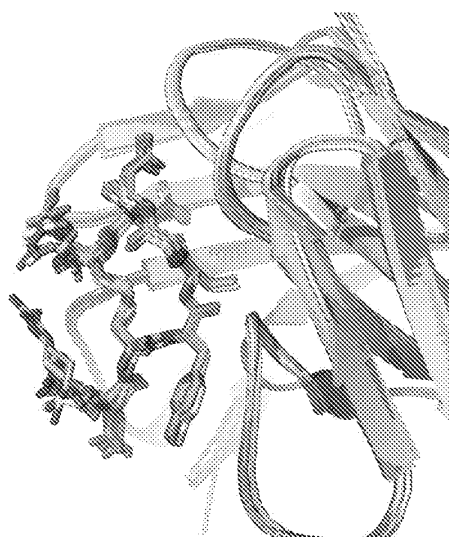


FIG. 6A

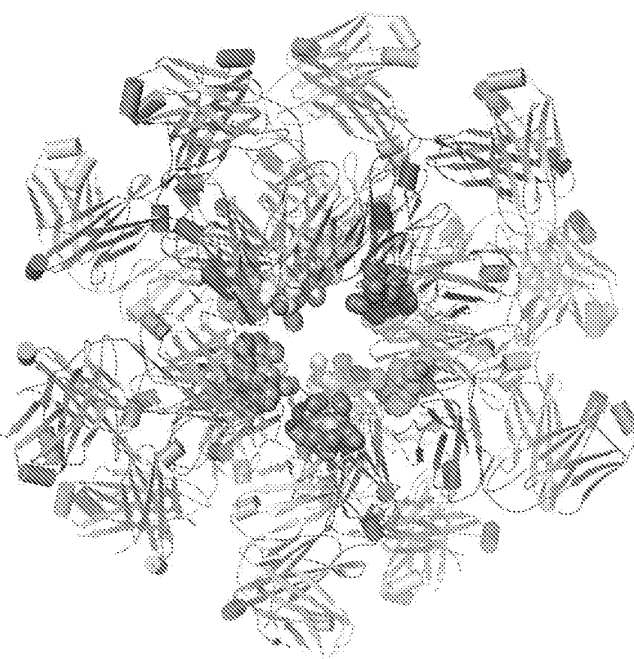


FIG. 6D

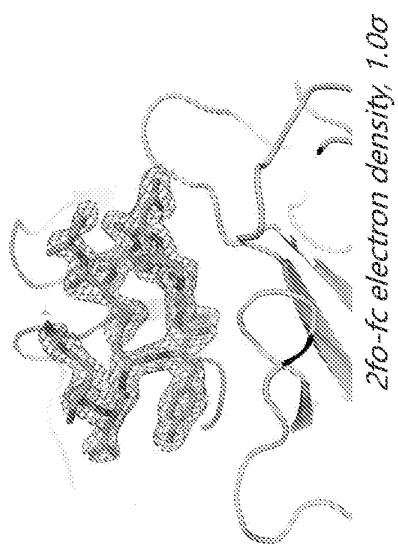


FIG. 6C



FIG. 6F

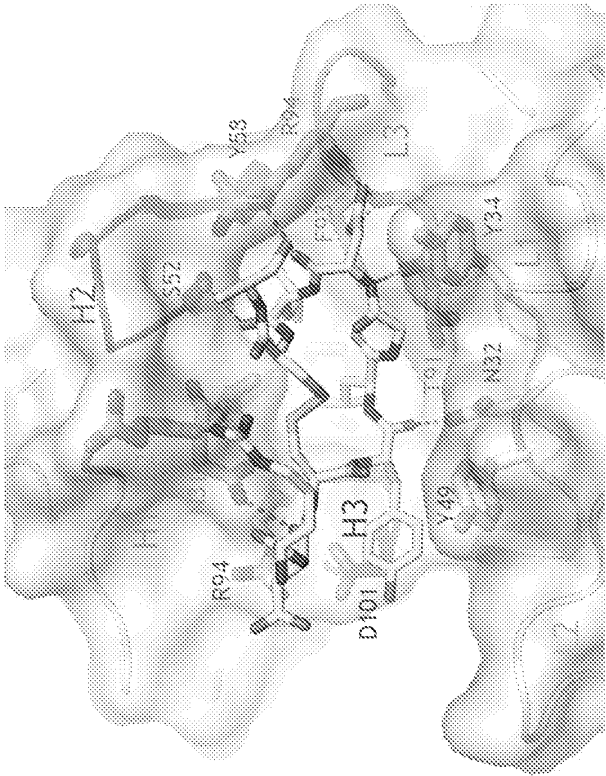


FIG. 6E

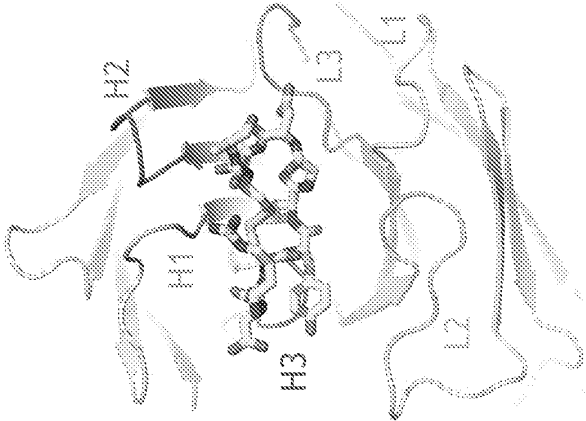


FIG. 7B

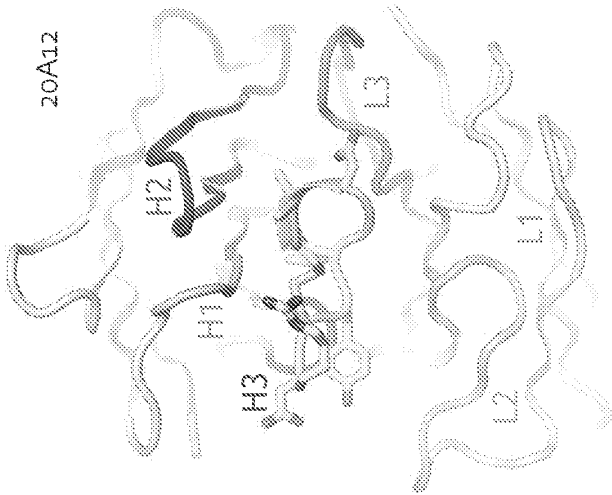
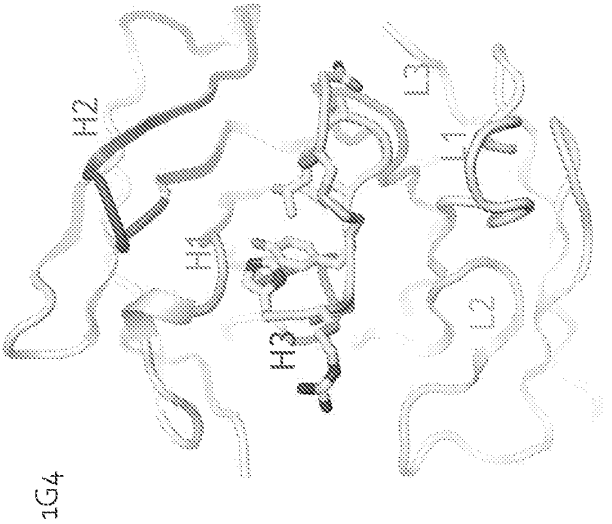


FIG. 7A



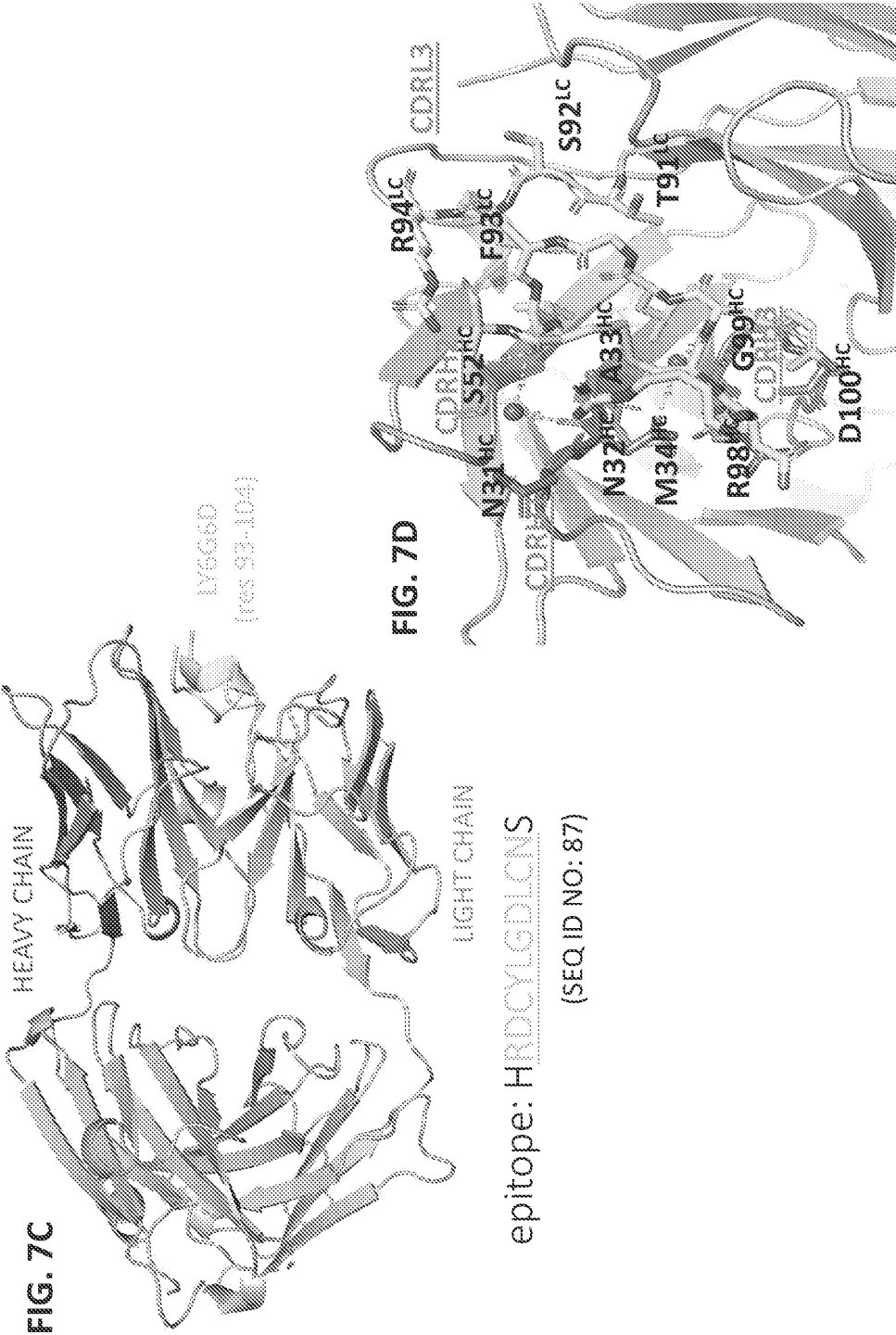




FIG. 7F

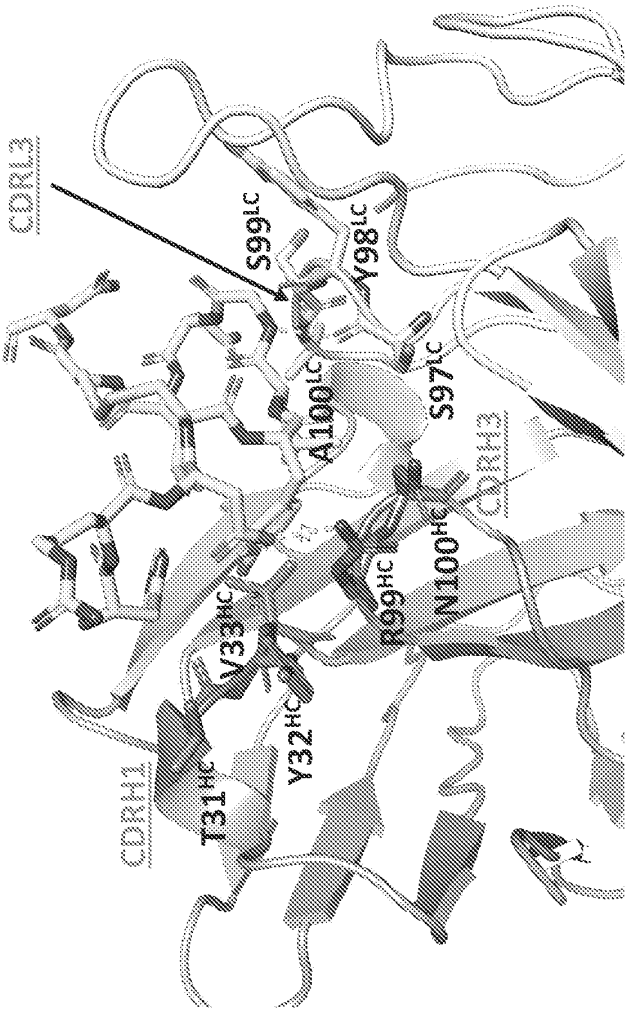


FIG. 8A

Humanized bispecific antibody produced in CHO (knob/hole, N297G)

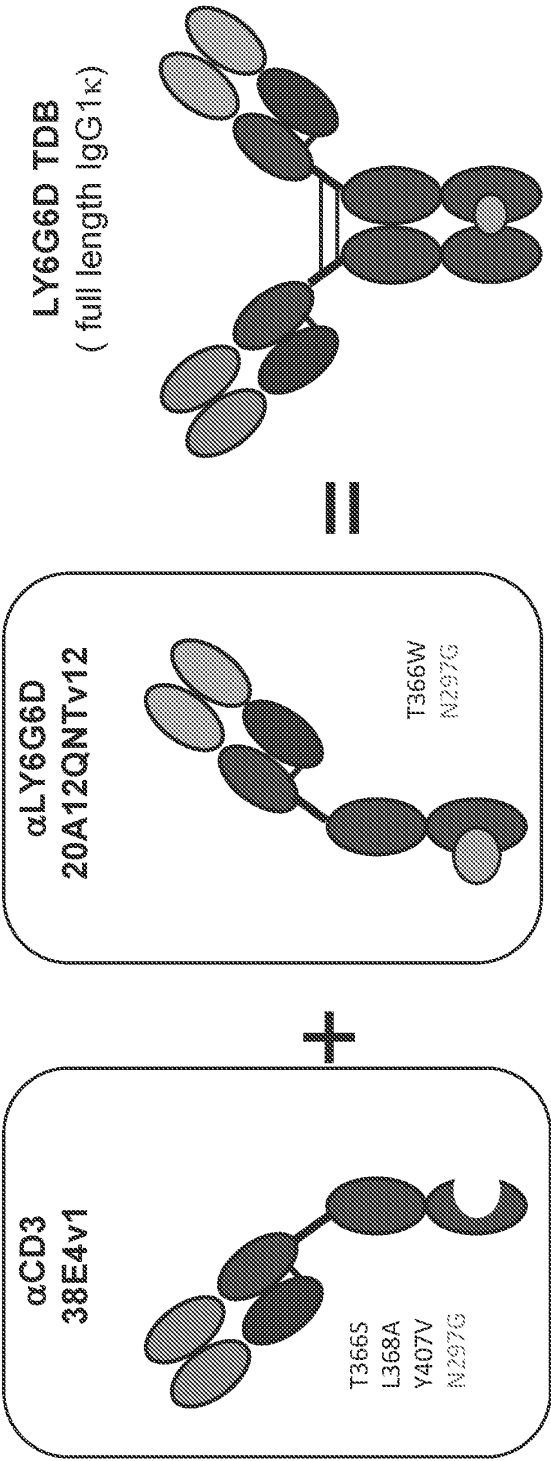
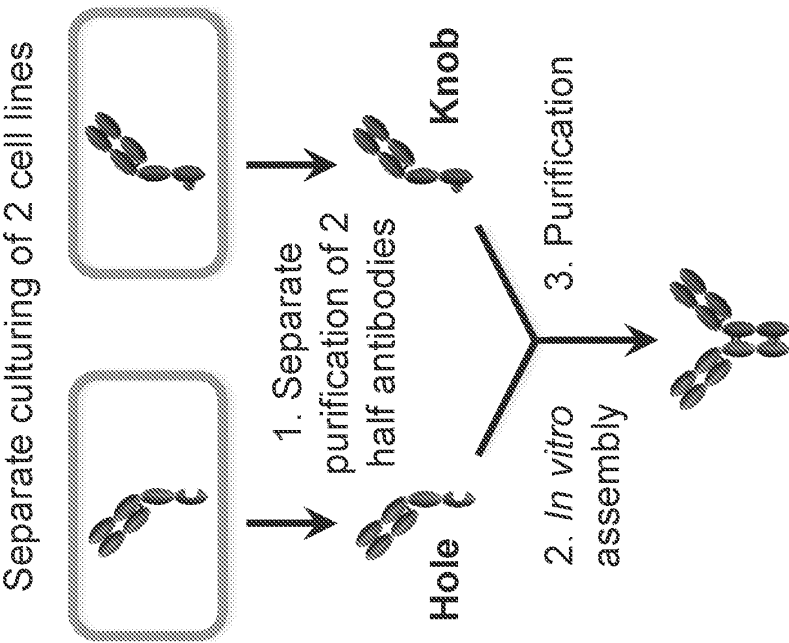


FIG. 8B 2-Cell Technology



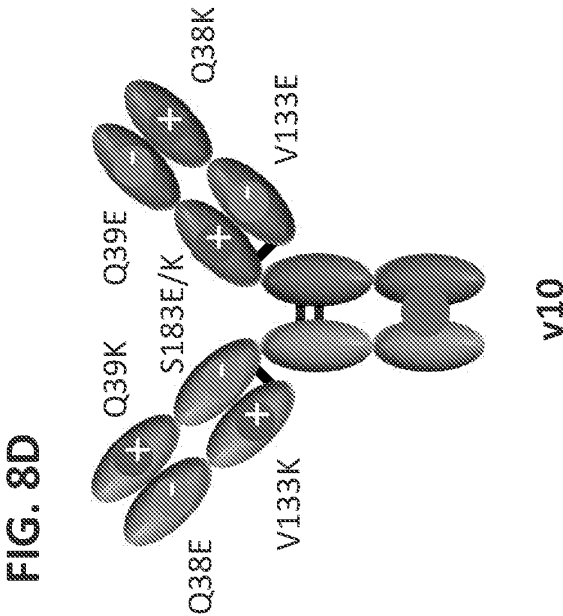
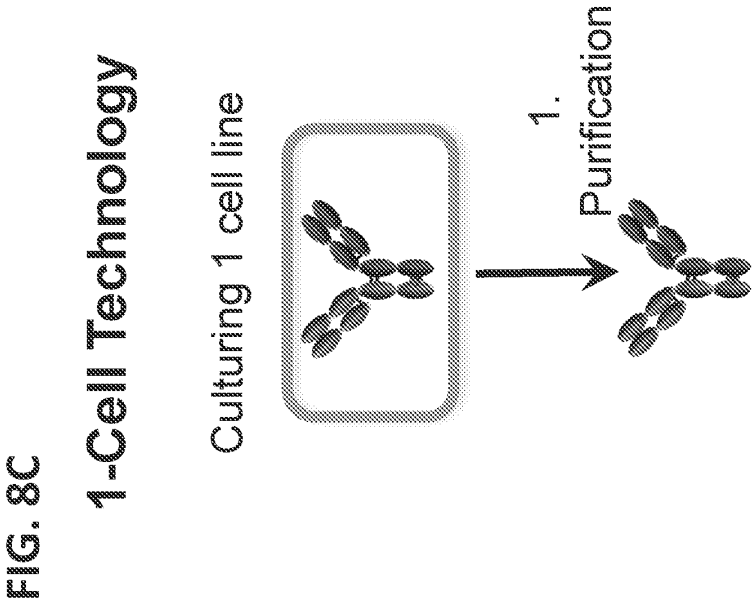


FIG. 8E

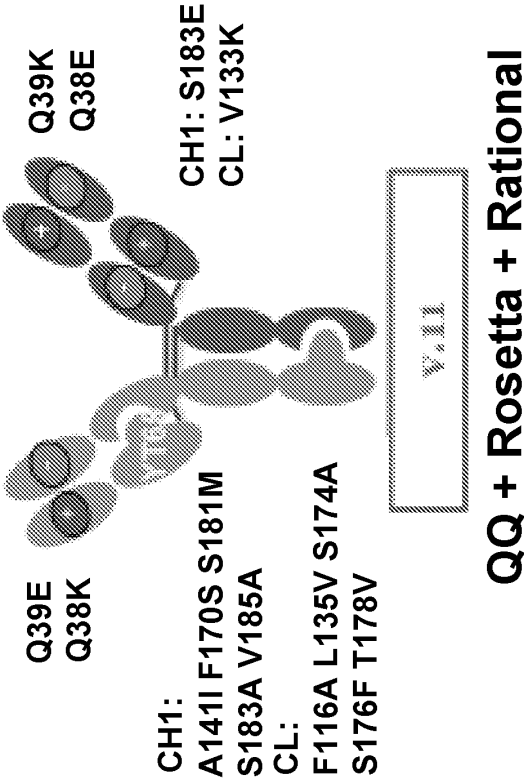


FIG. 9B

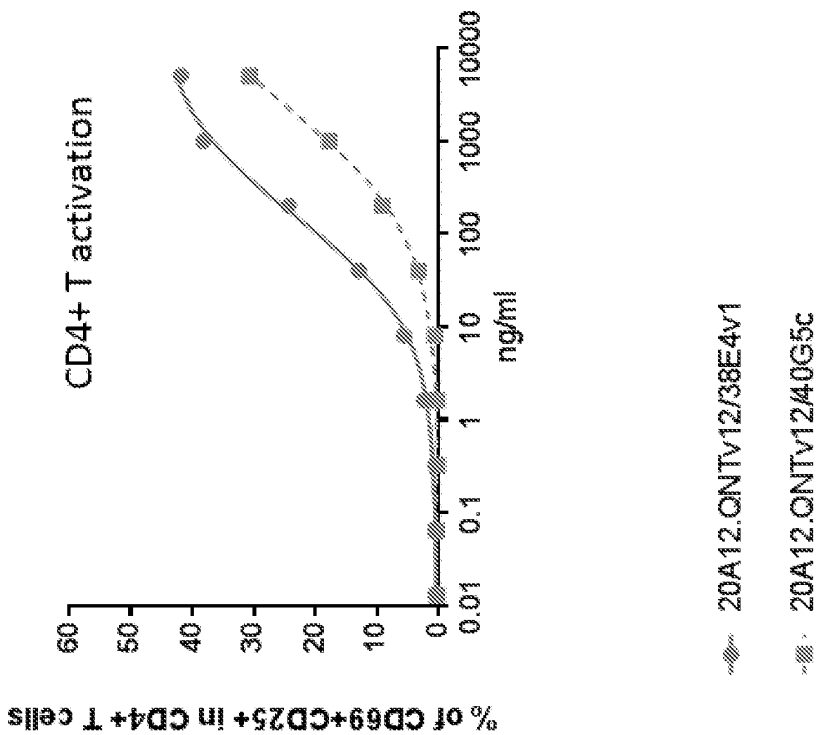


FIG. 9A

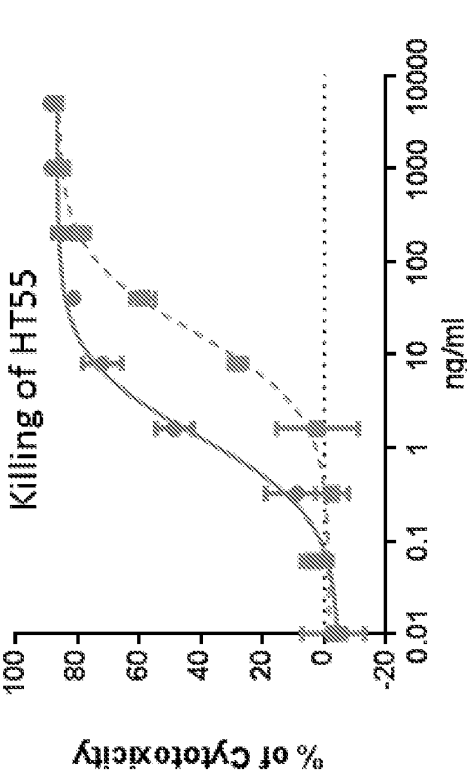


FIG. 9C

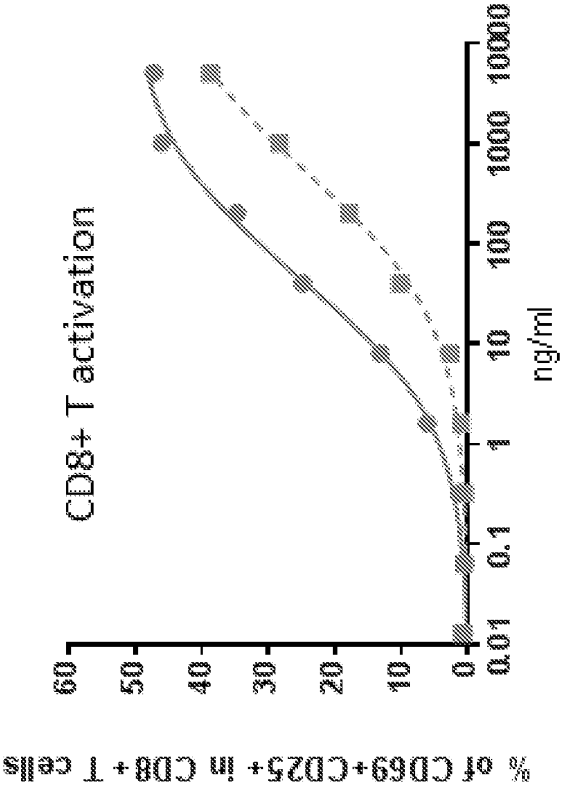


FIG. 10A

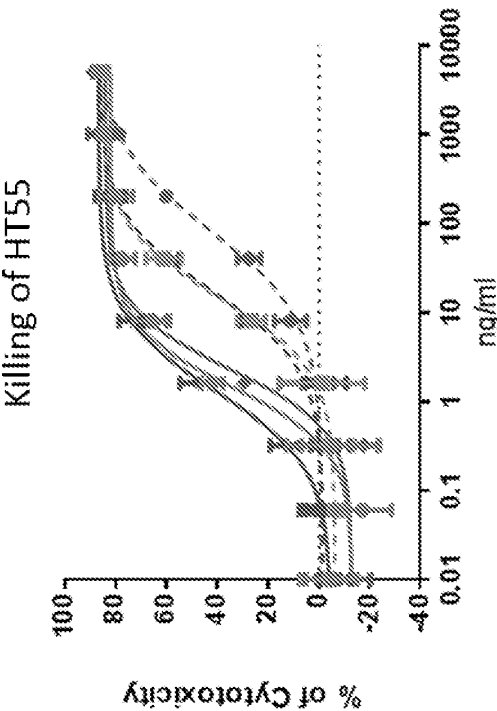


FIG. 10B

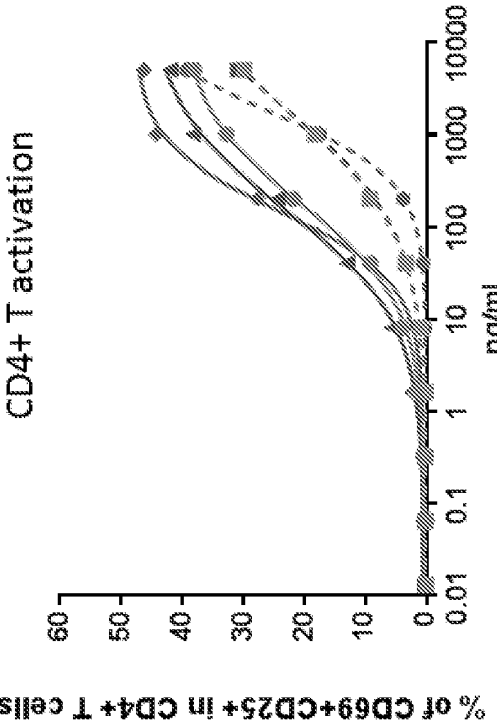
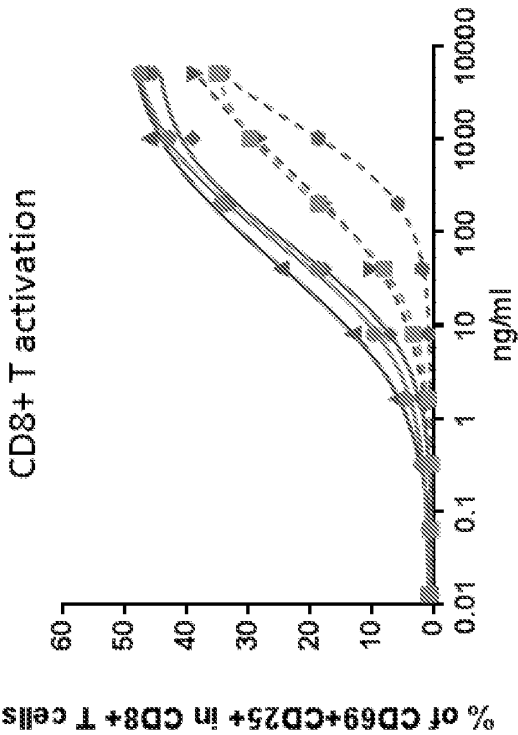


FIG. 10C



- 20A12.v1/38E4v1
- 20A12.v1/40G5c
- 20A12.QNTv12/38E4v1
- 20A12.QNTv12/40G5c
- 1G4/38E4v1
- 1G4/40G5c

FIG. 10D

Killing of HT55

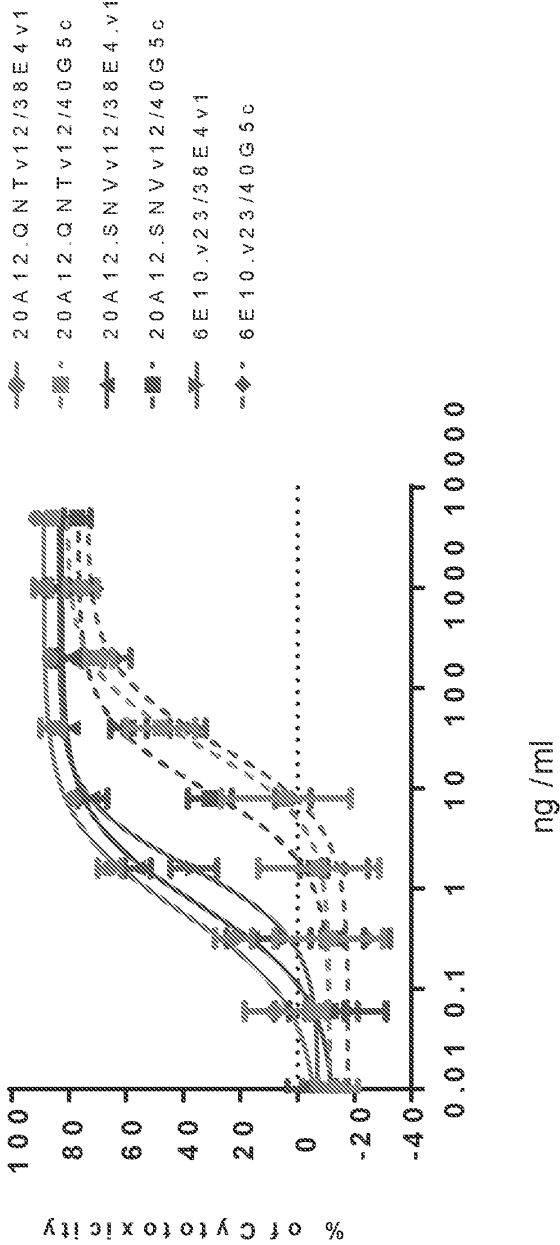


FIG. 11A

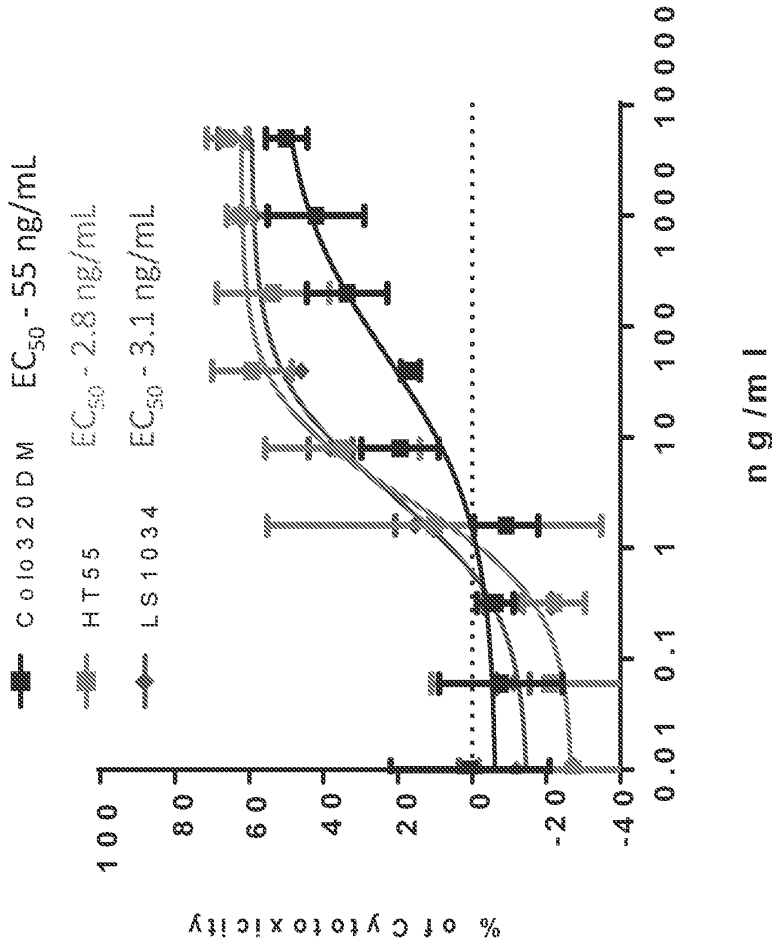
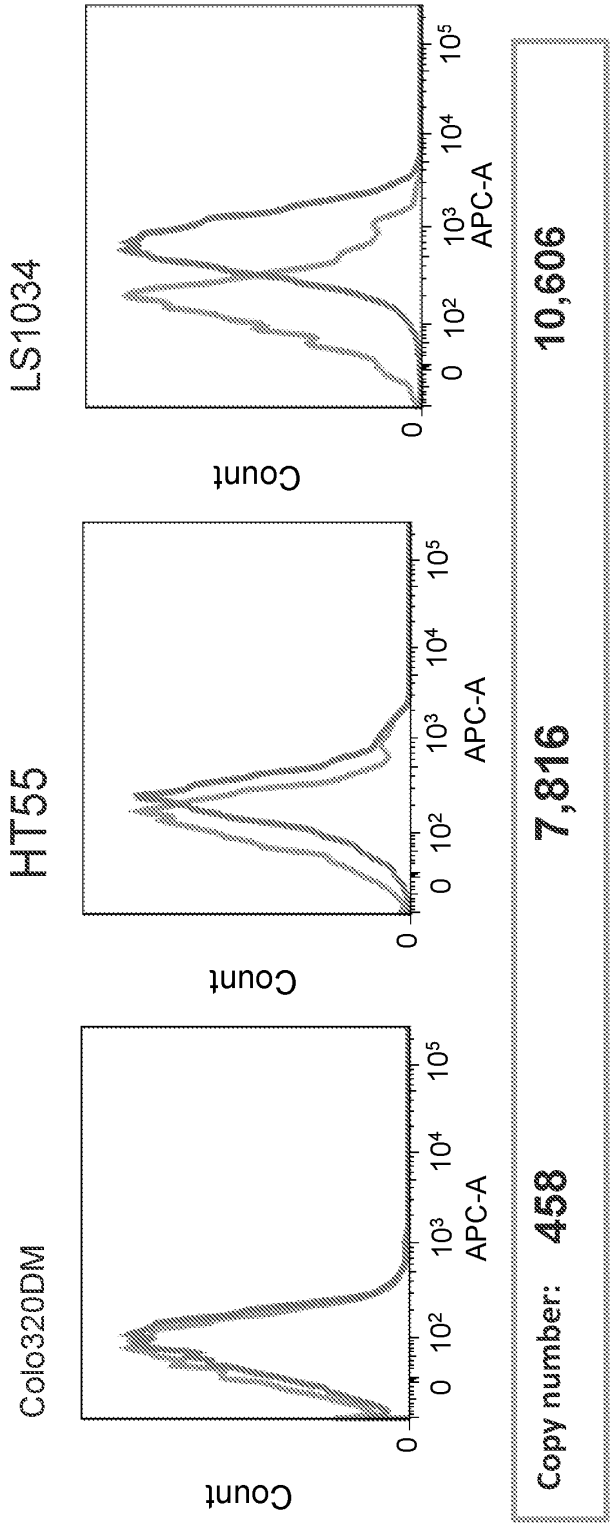


FIG. 11B



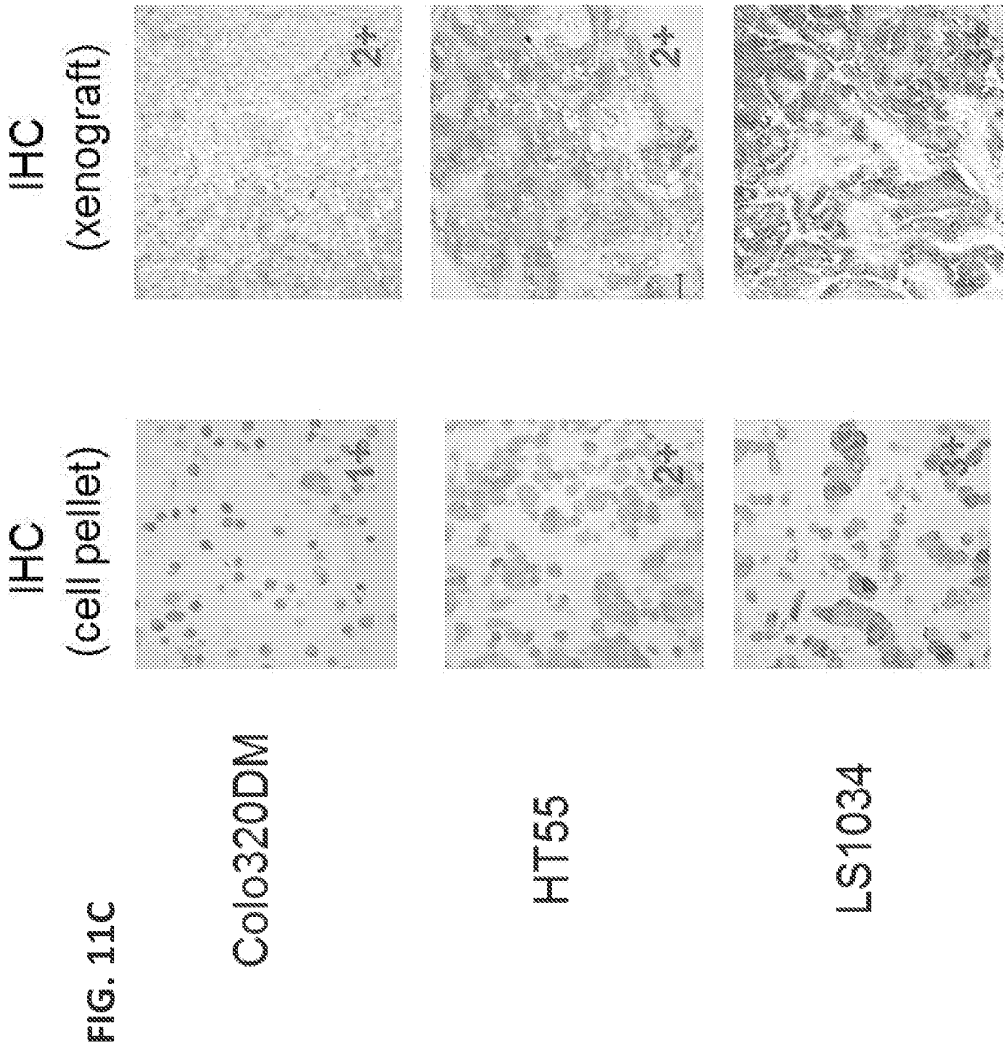


FIG. 11D

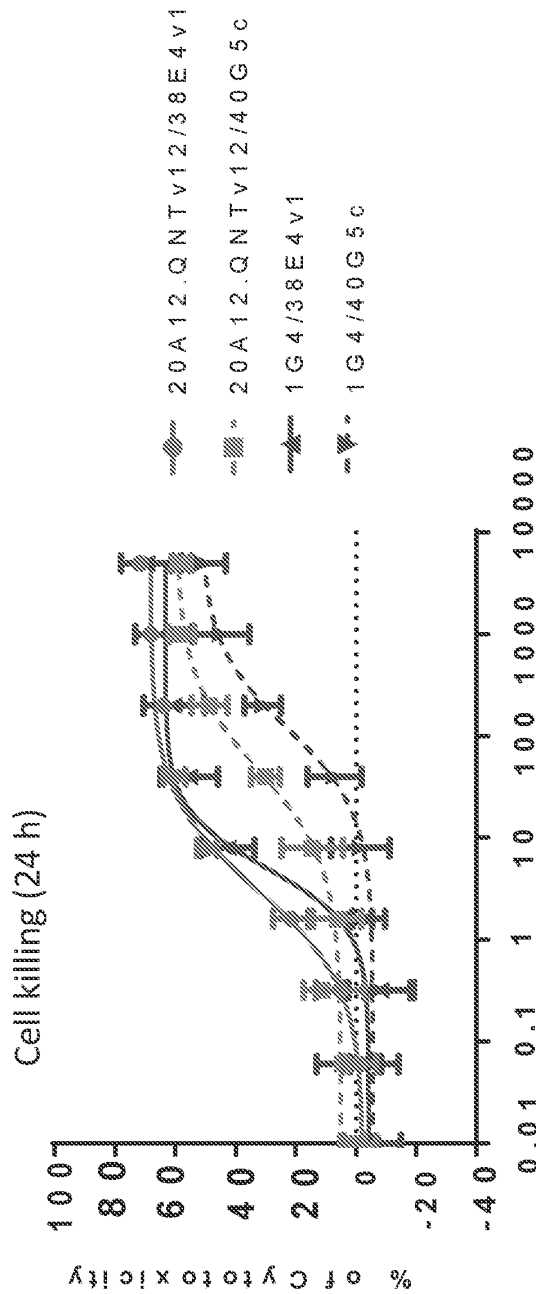


FIG. 11E

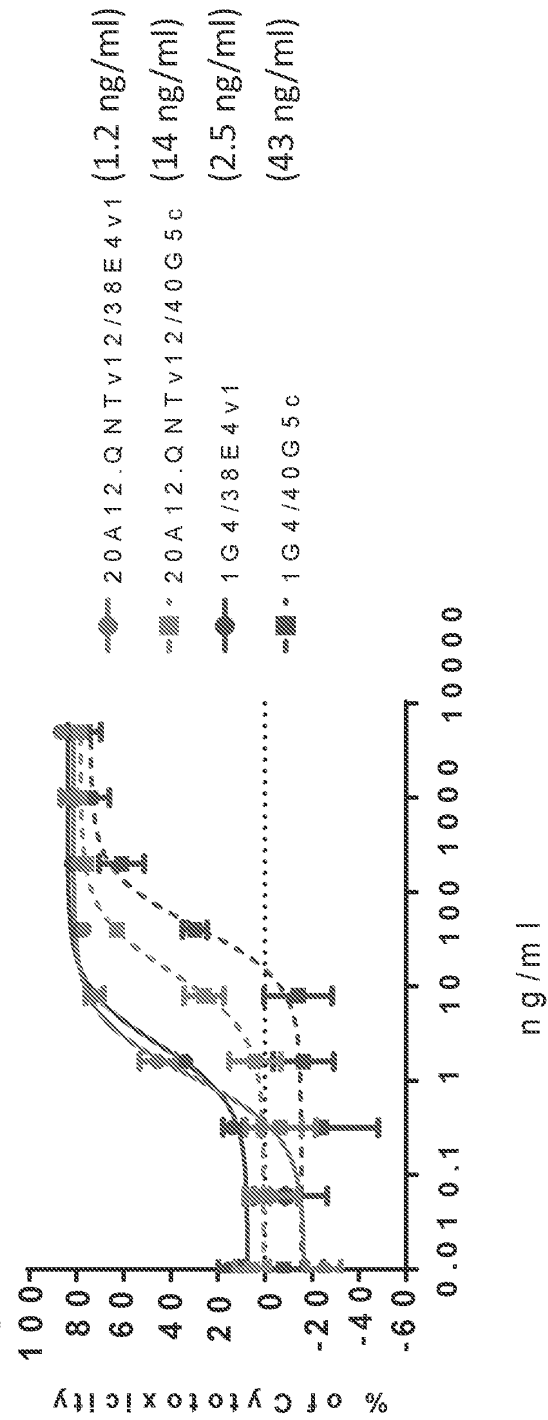


FIG. 11F

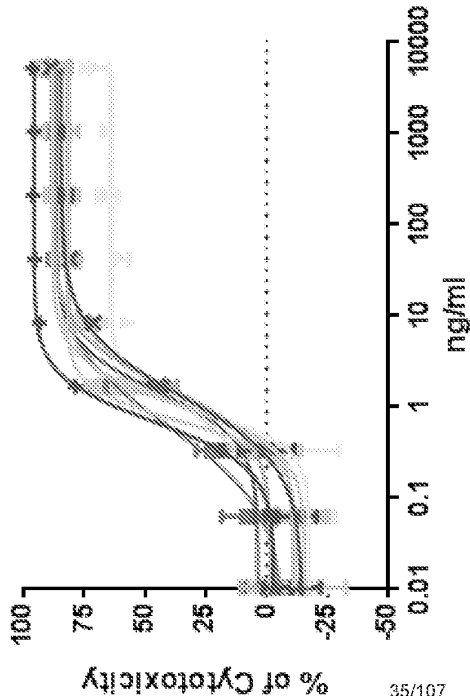


FIG. 11G

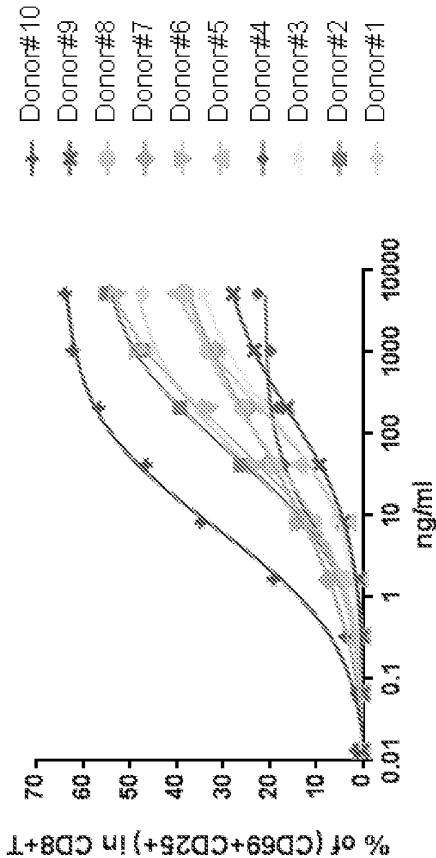
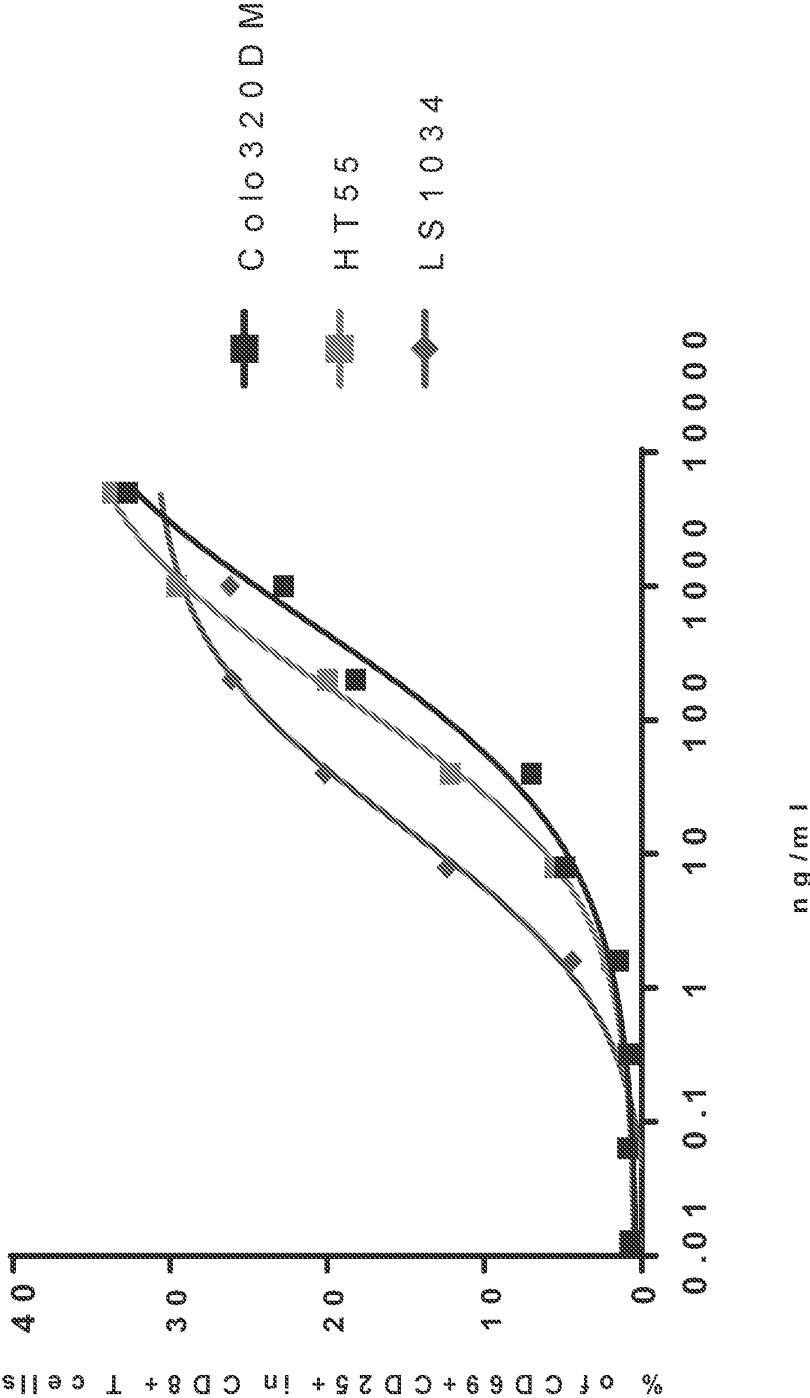
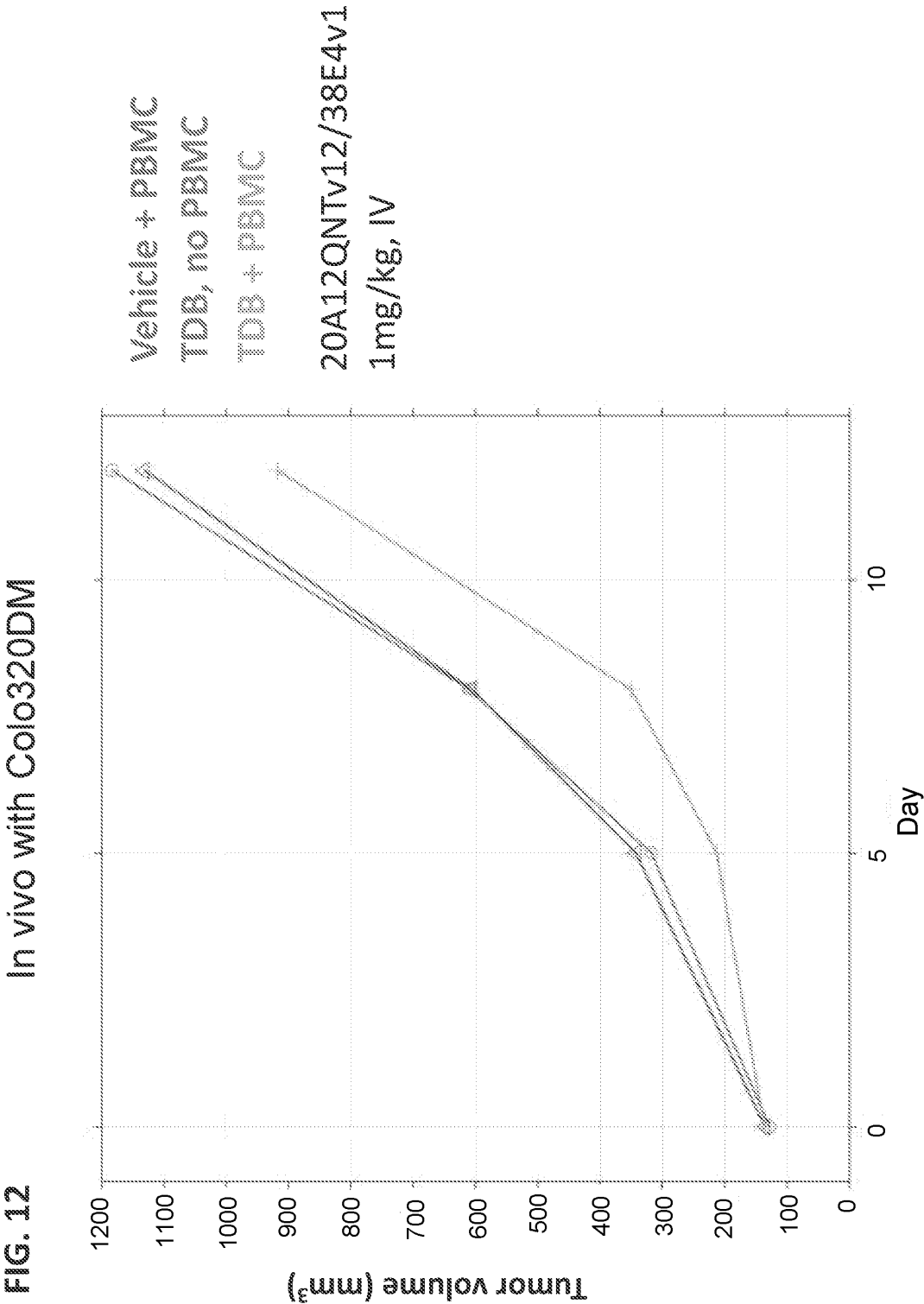


FIG. 11H

EC50 (ng/ml)	Donor#1	Donor#2	Donor#3	Donor#4	Donor#5	Donor#6	Donor#7	Donor#8	Donor#9	Donor#10	Average	SD
Cell killing	1.322	0.5913	0.7991	1.420	0.6606	0.9859	1.687	1.017	1.260	0.6592	1.04	0.37
CD8+T activation	44.96	55.95	146.9	6.832	214.3	98.29	72.78	56.73	167.9	6.697	87.1	69.3

FIG. 11
CD8+T activation





37/107

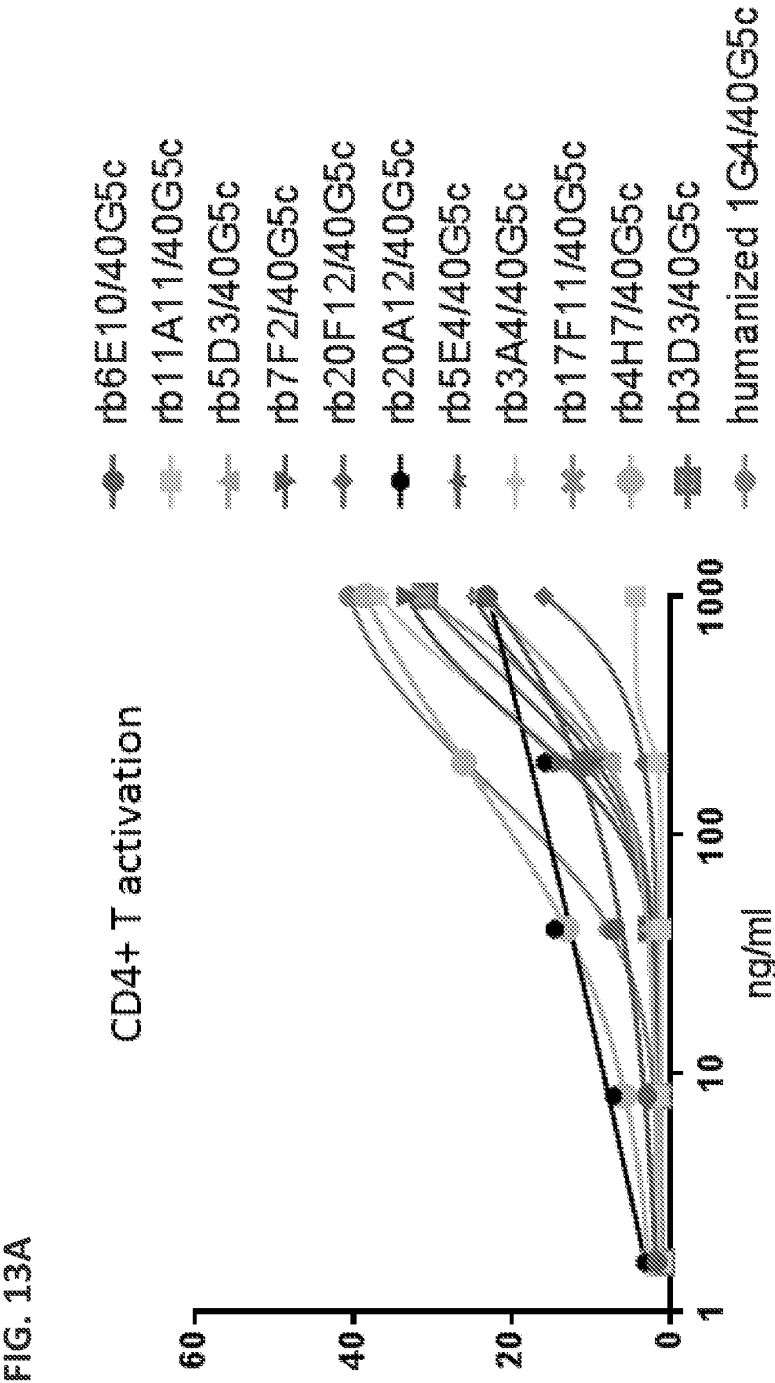


FIG. 13B

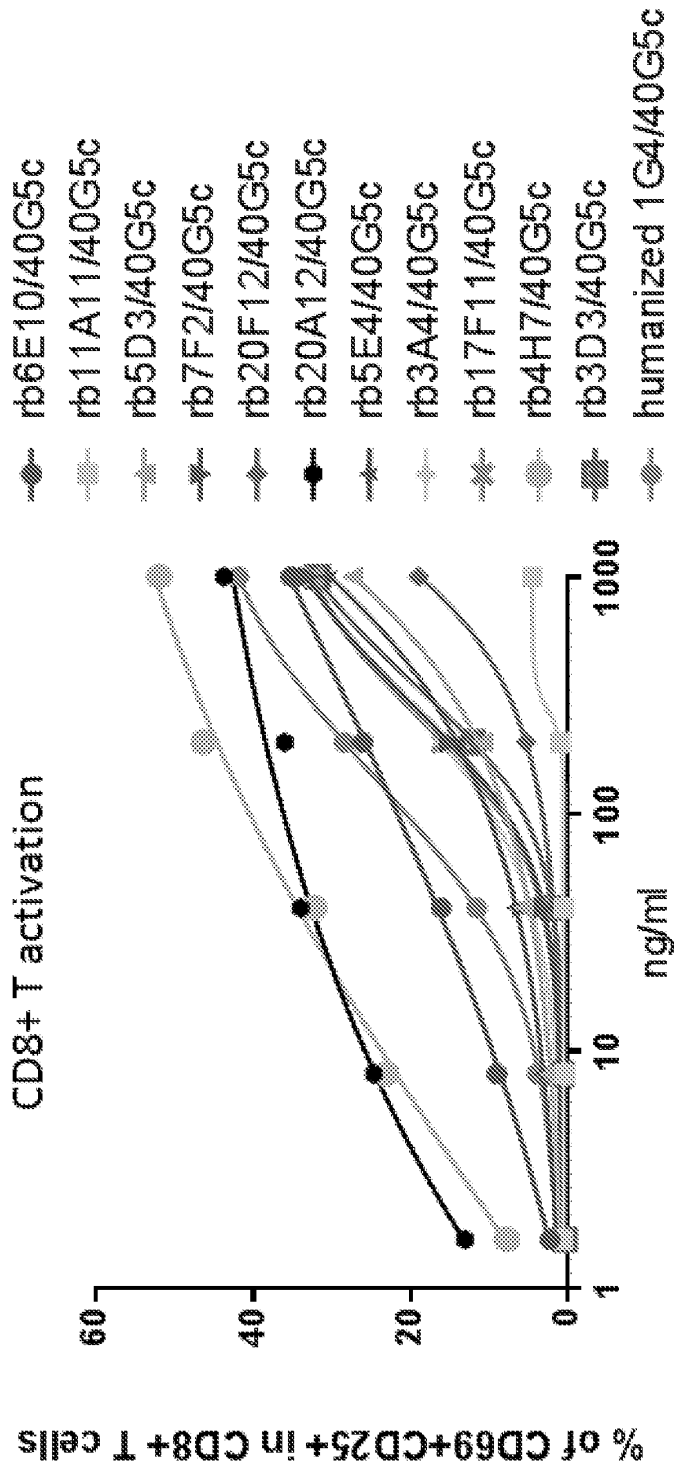
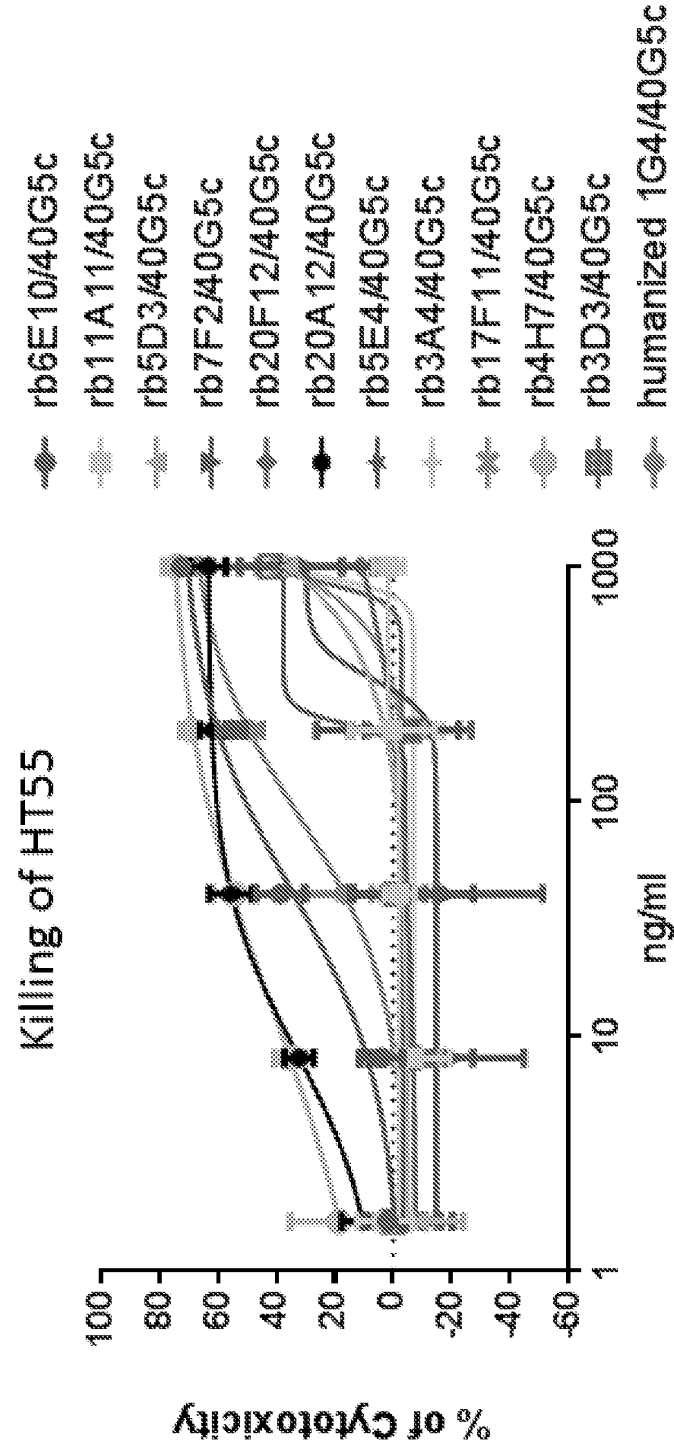


FIG. 13C



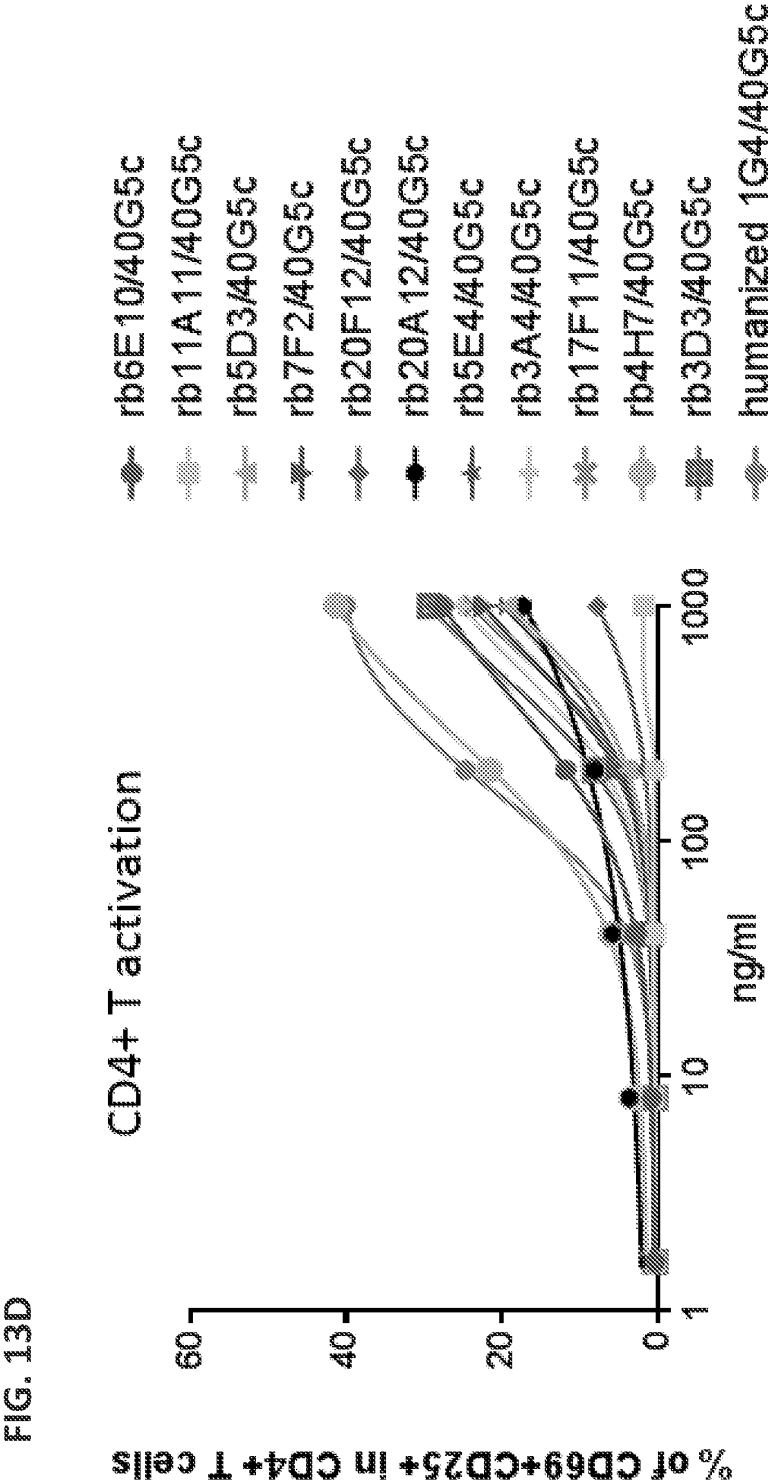


FIG. 13E

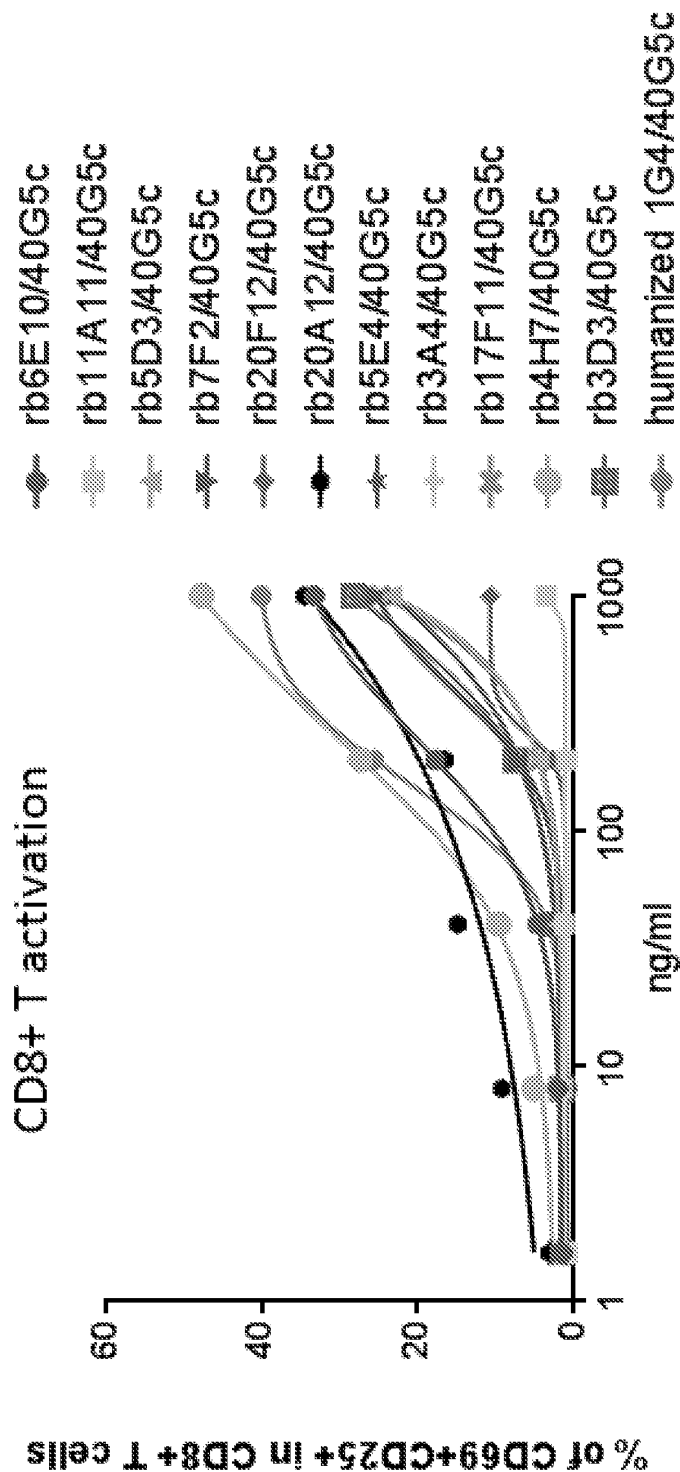


FIG. 14A

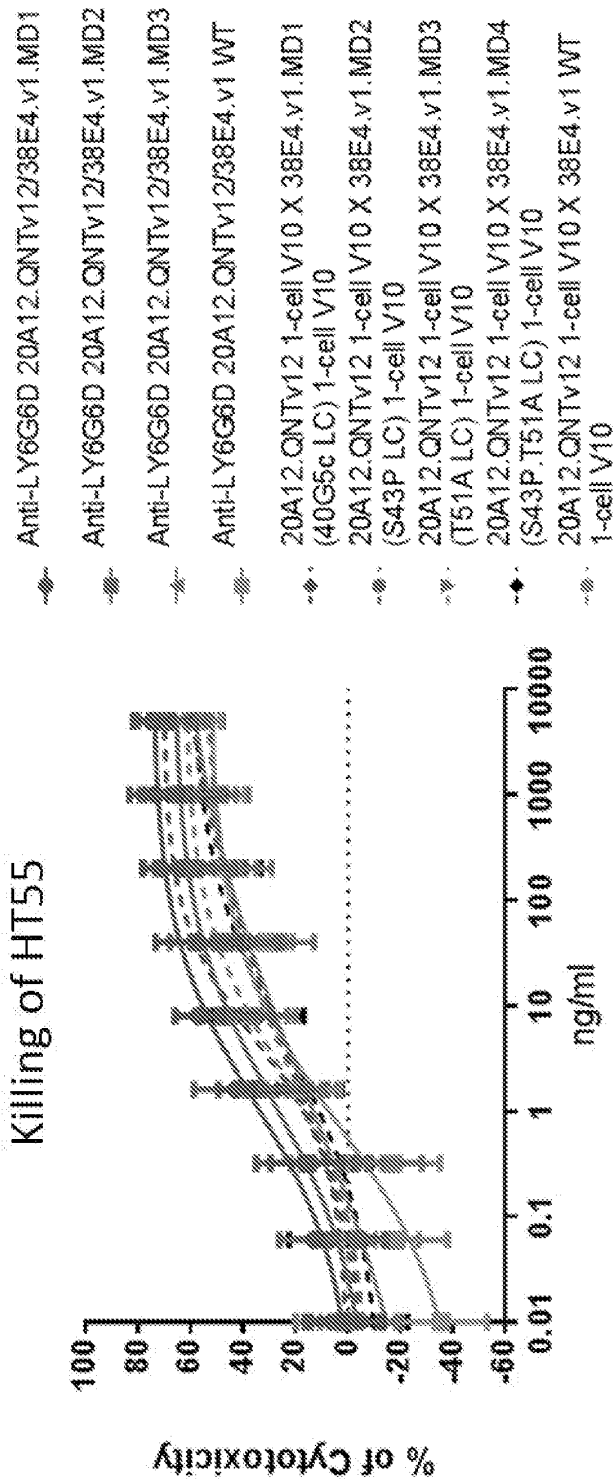


FIG. 14B

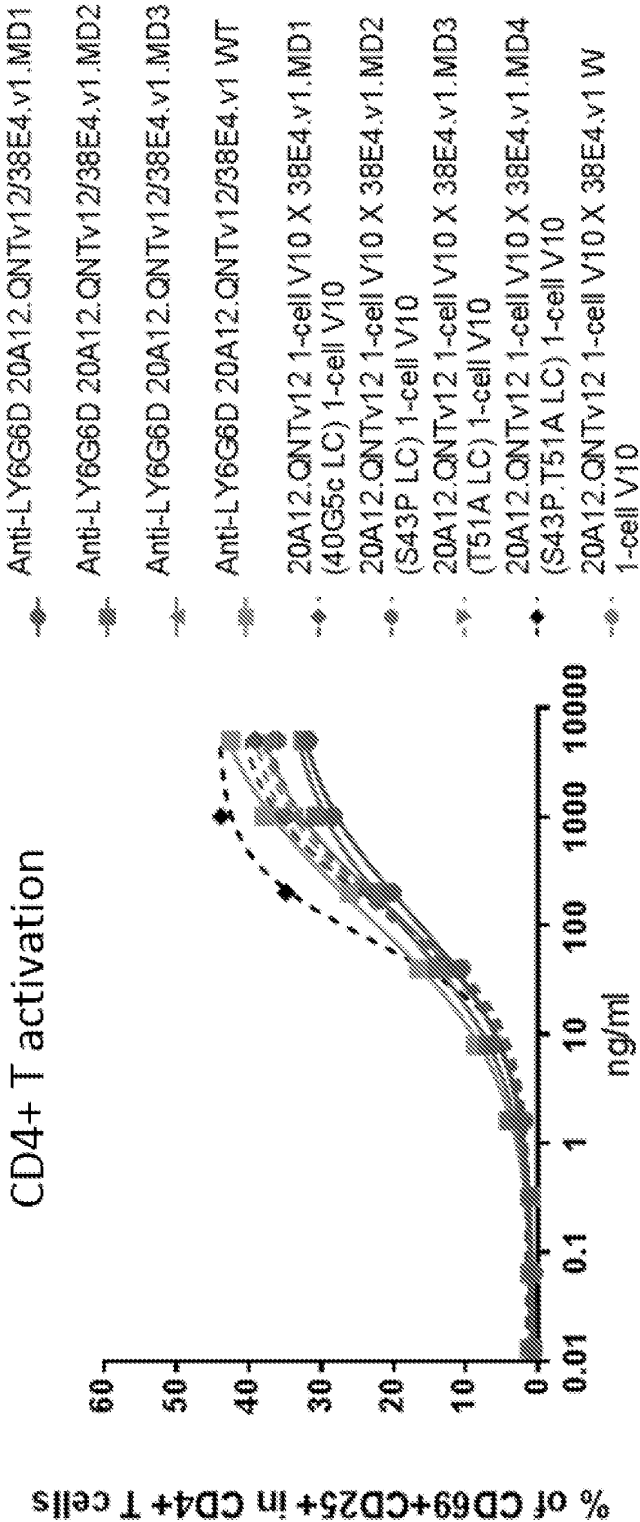


FIG. 14C

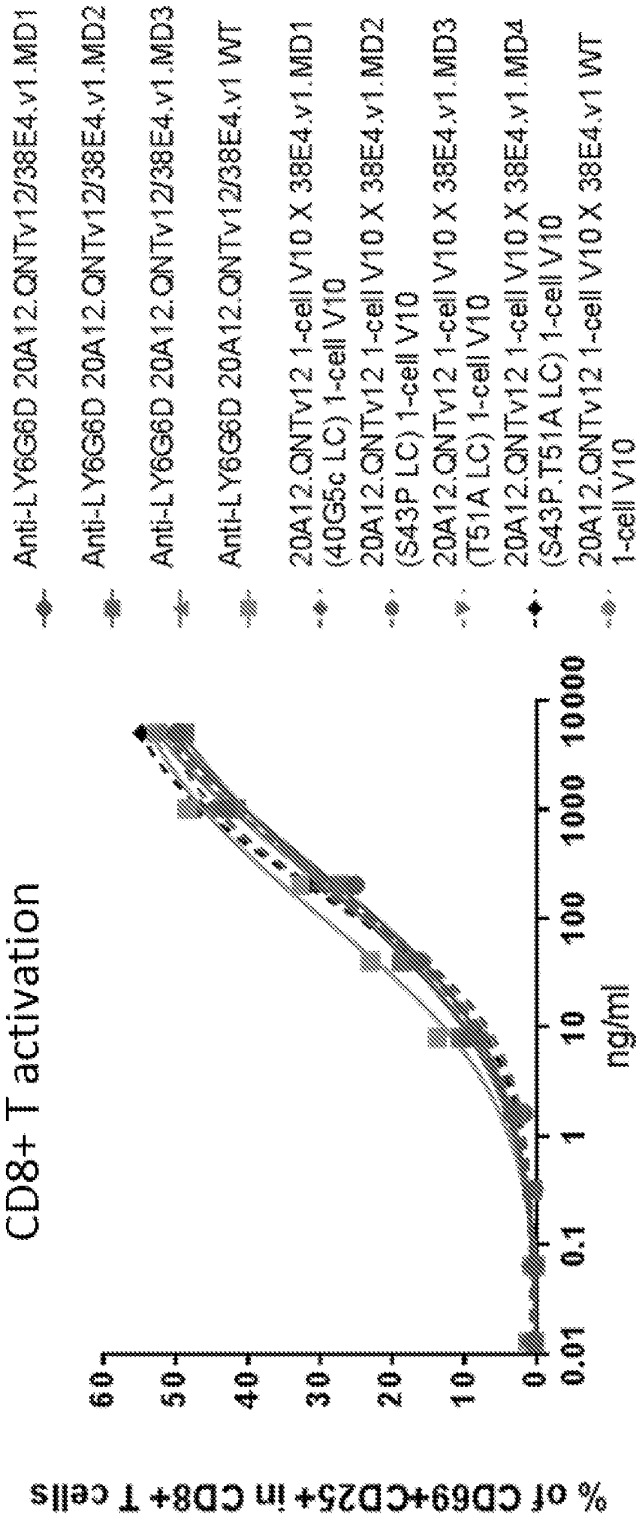


FIG. 15A

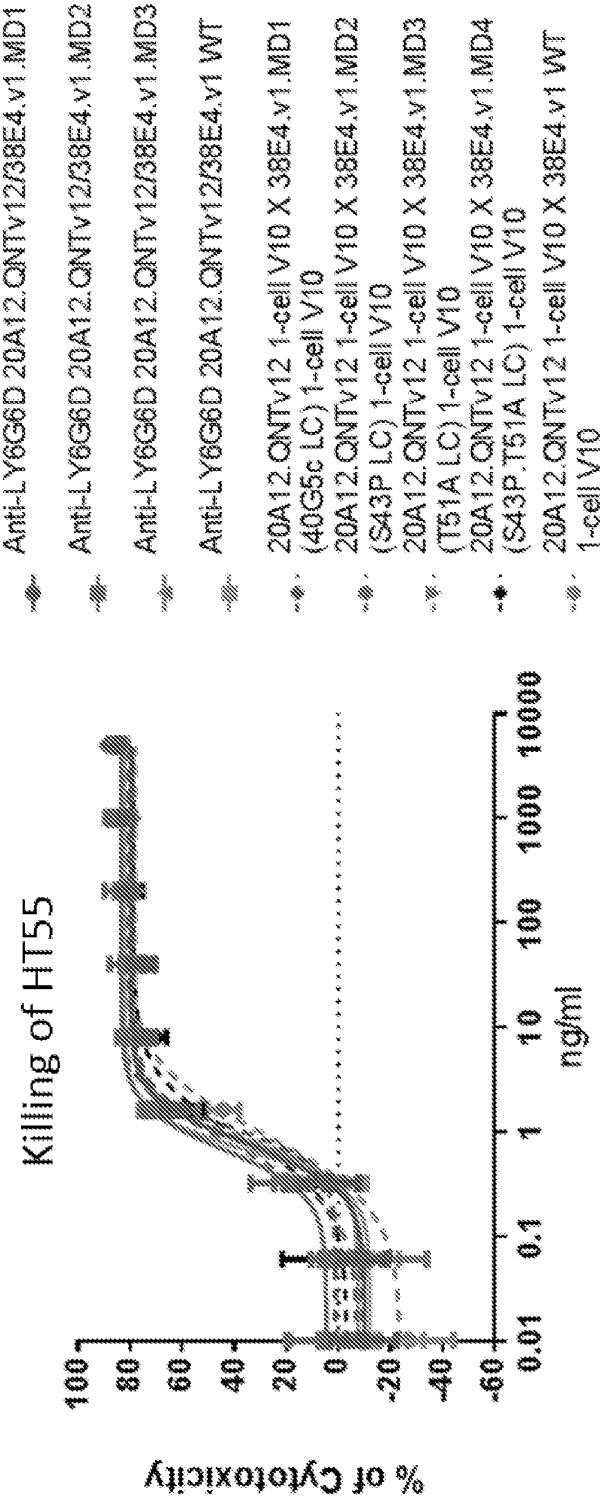


FIG. 15B

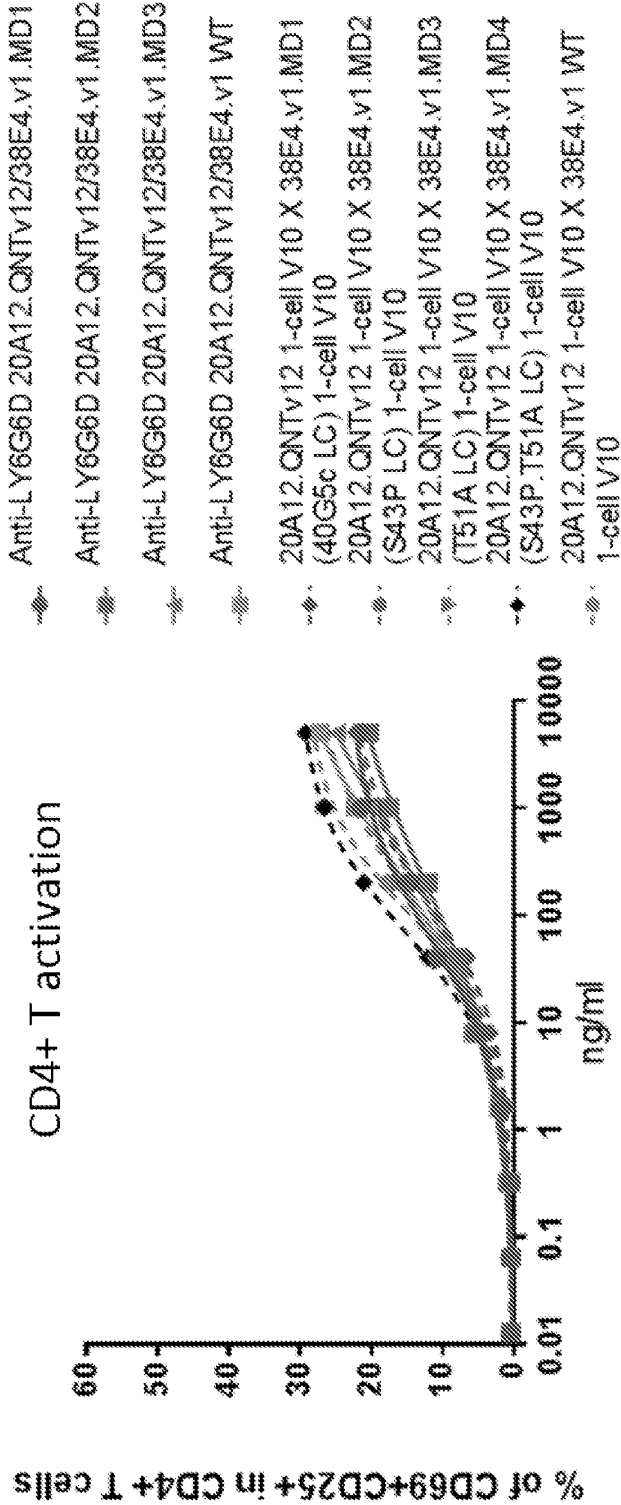
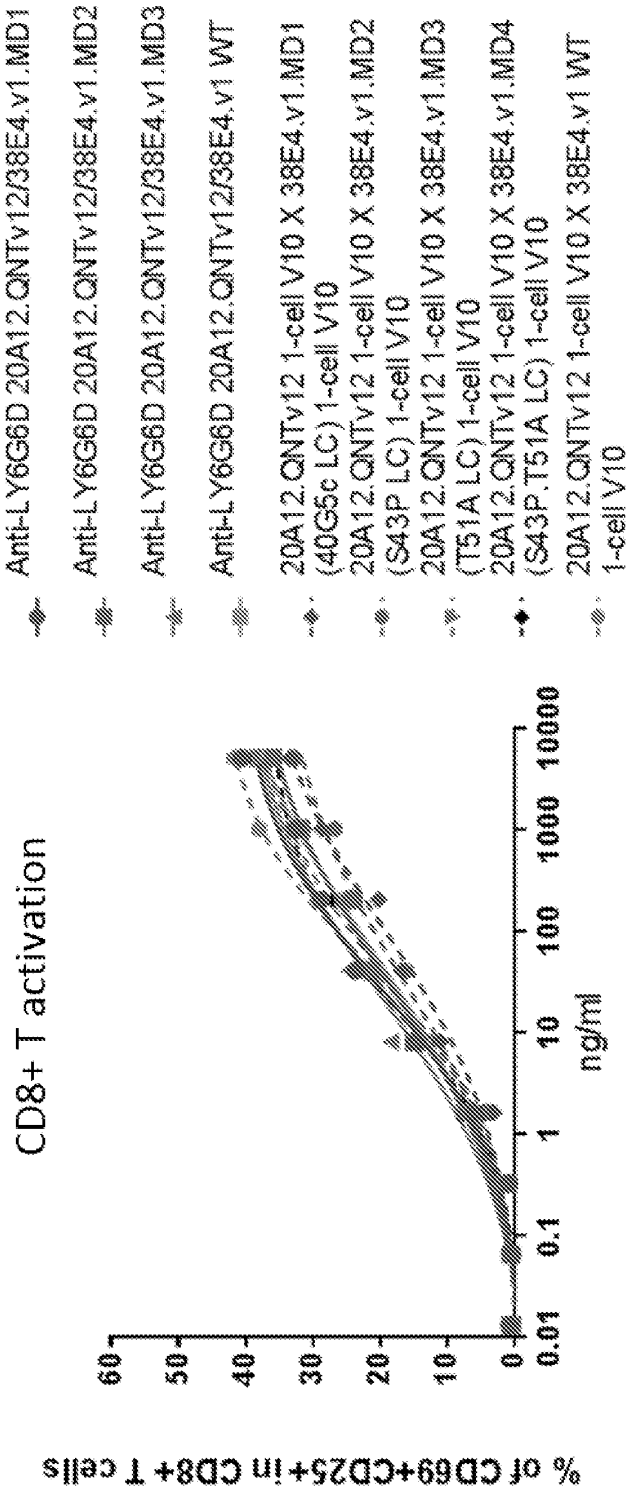


FIG. 15C



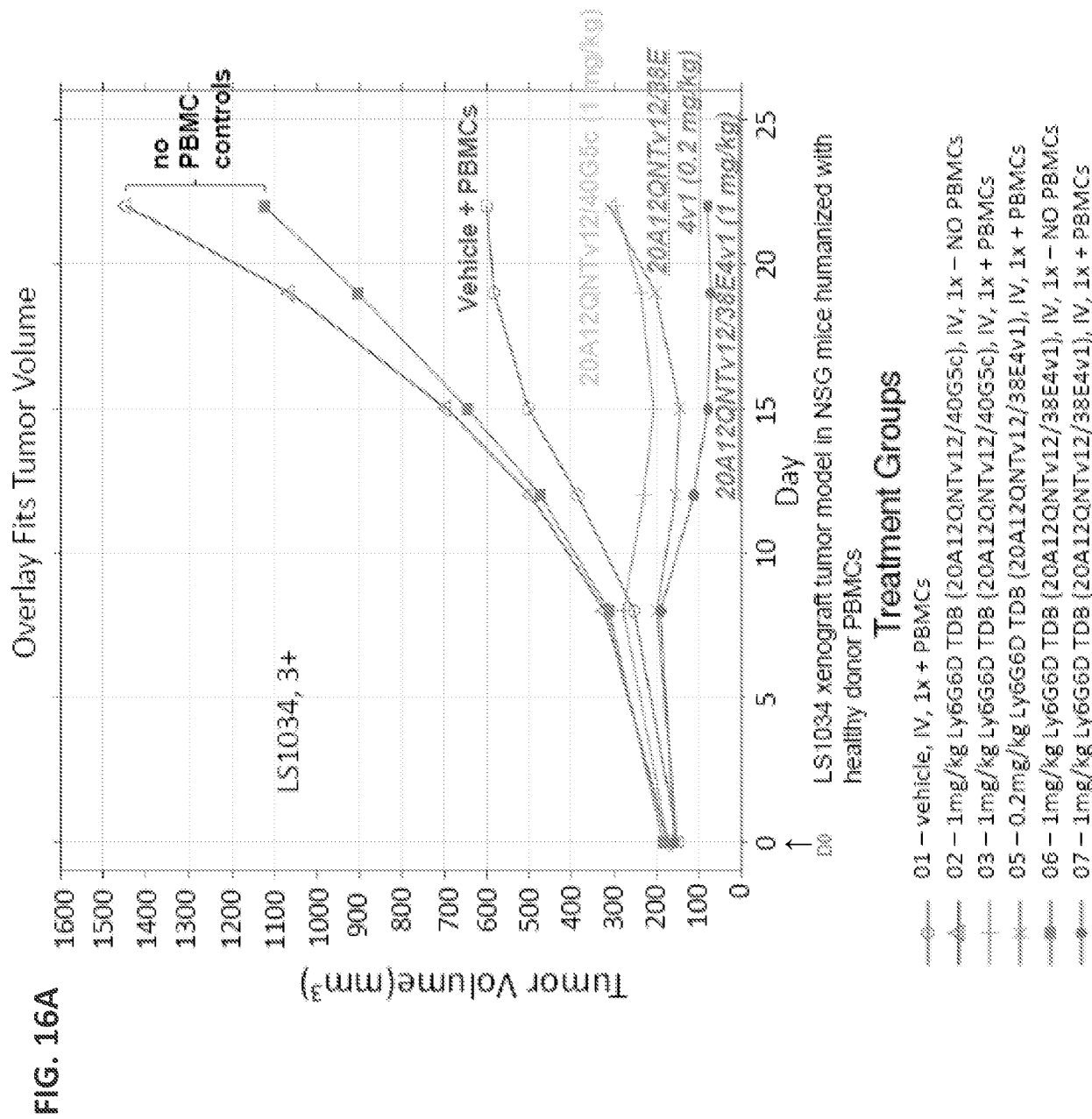


FIG. 16B

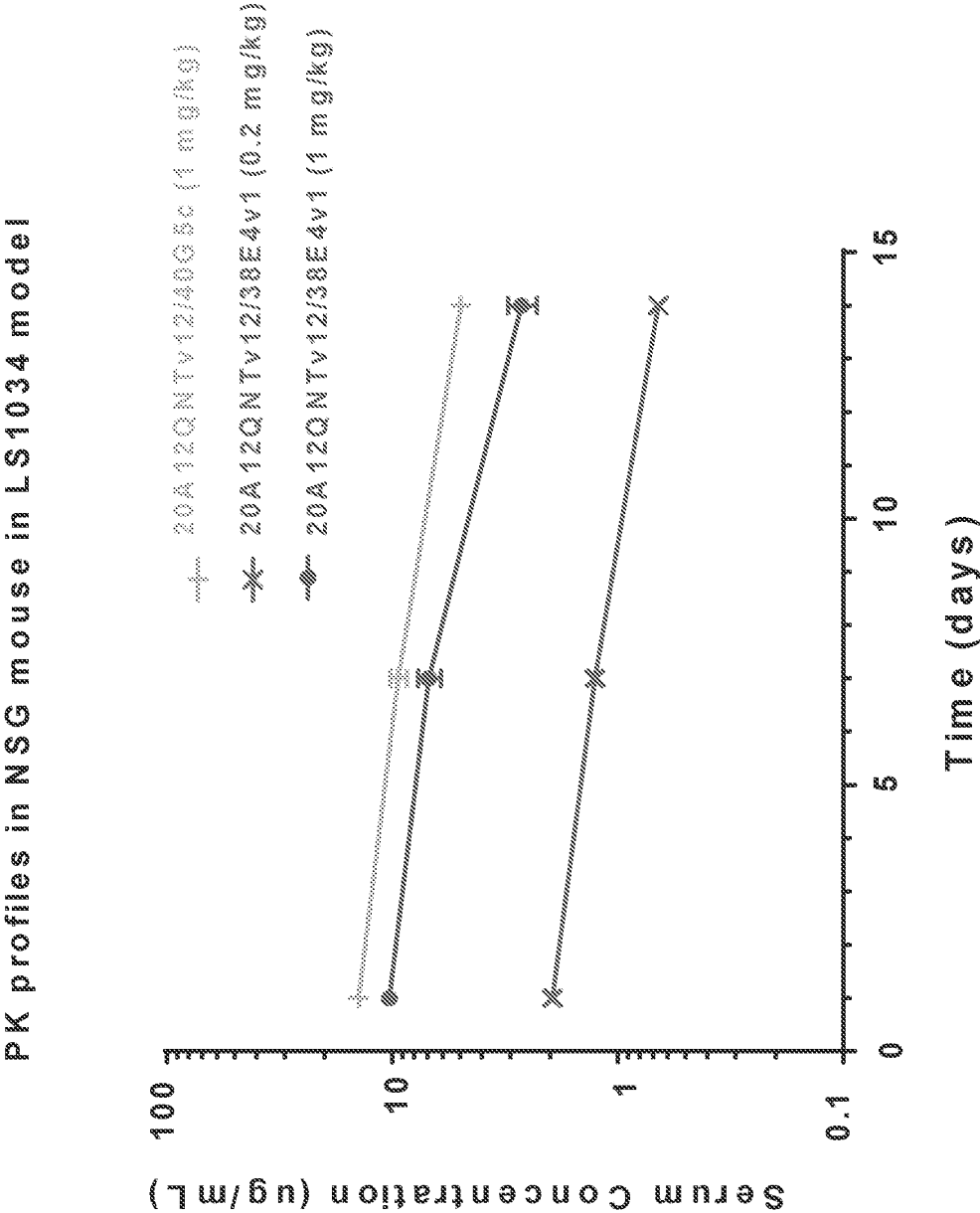
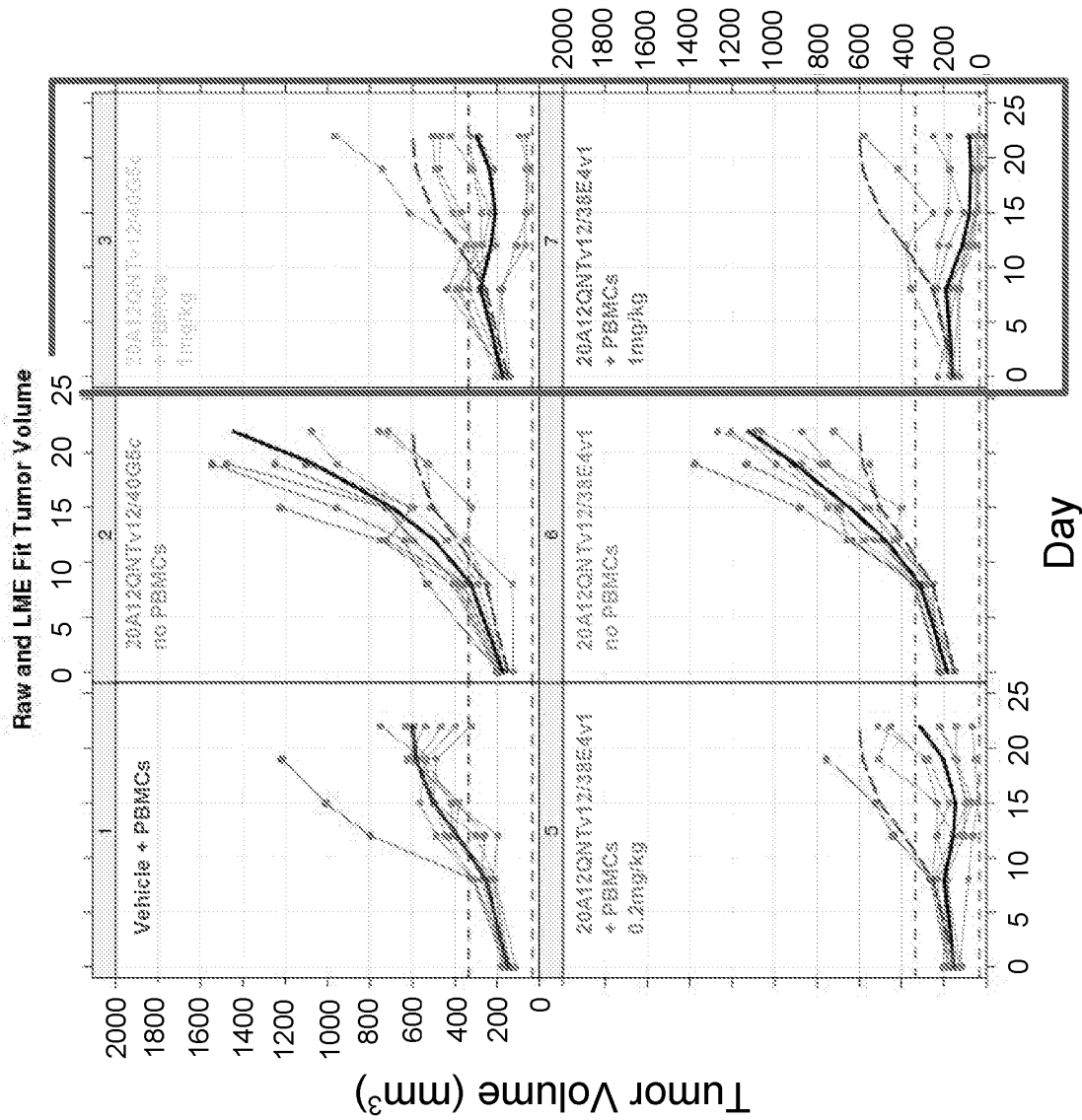


FIG. 16C



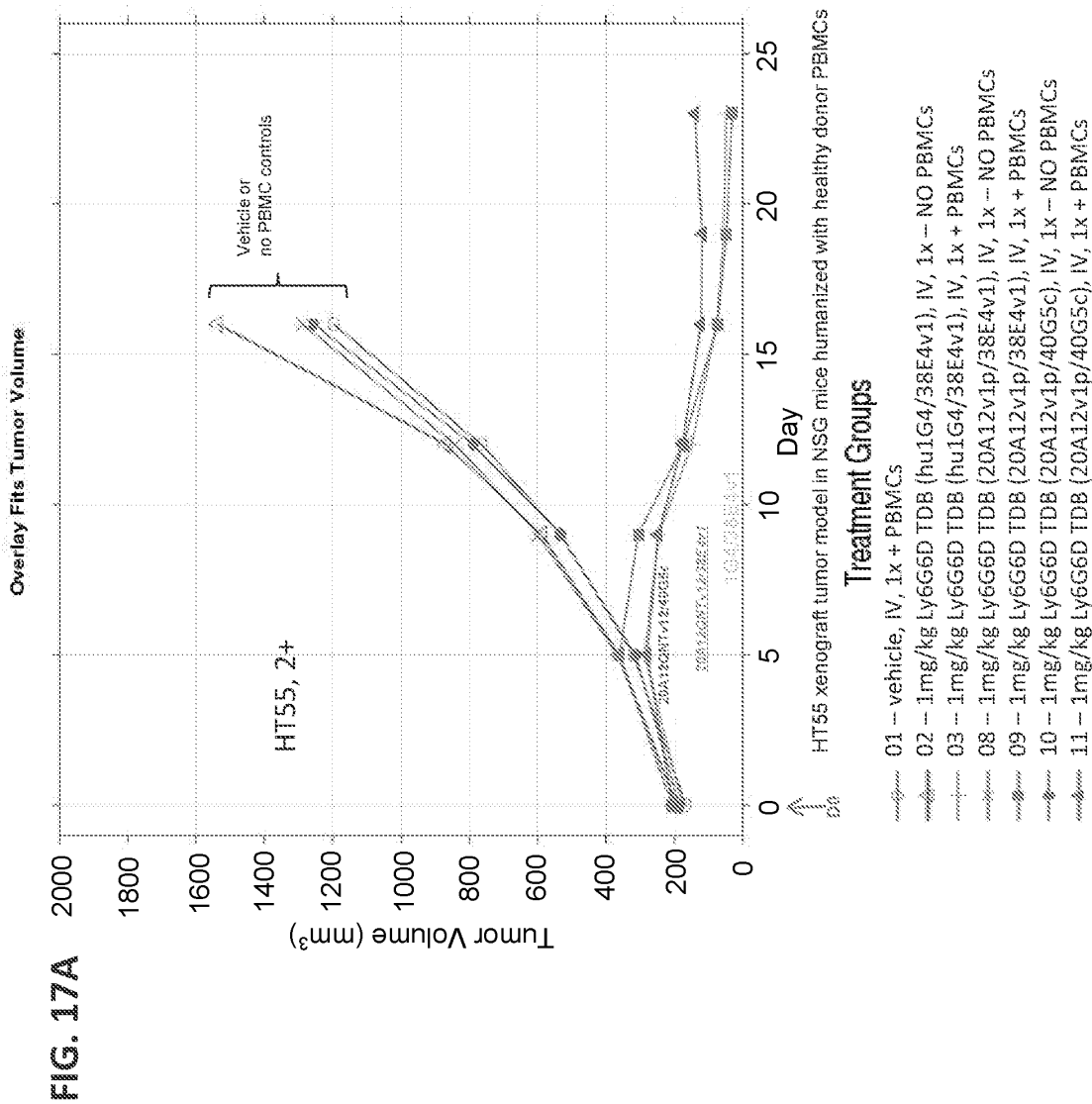


FIG. 17B

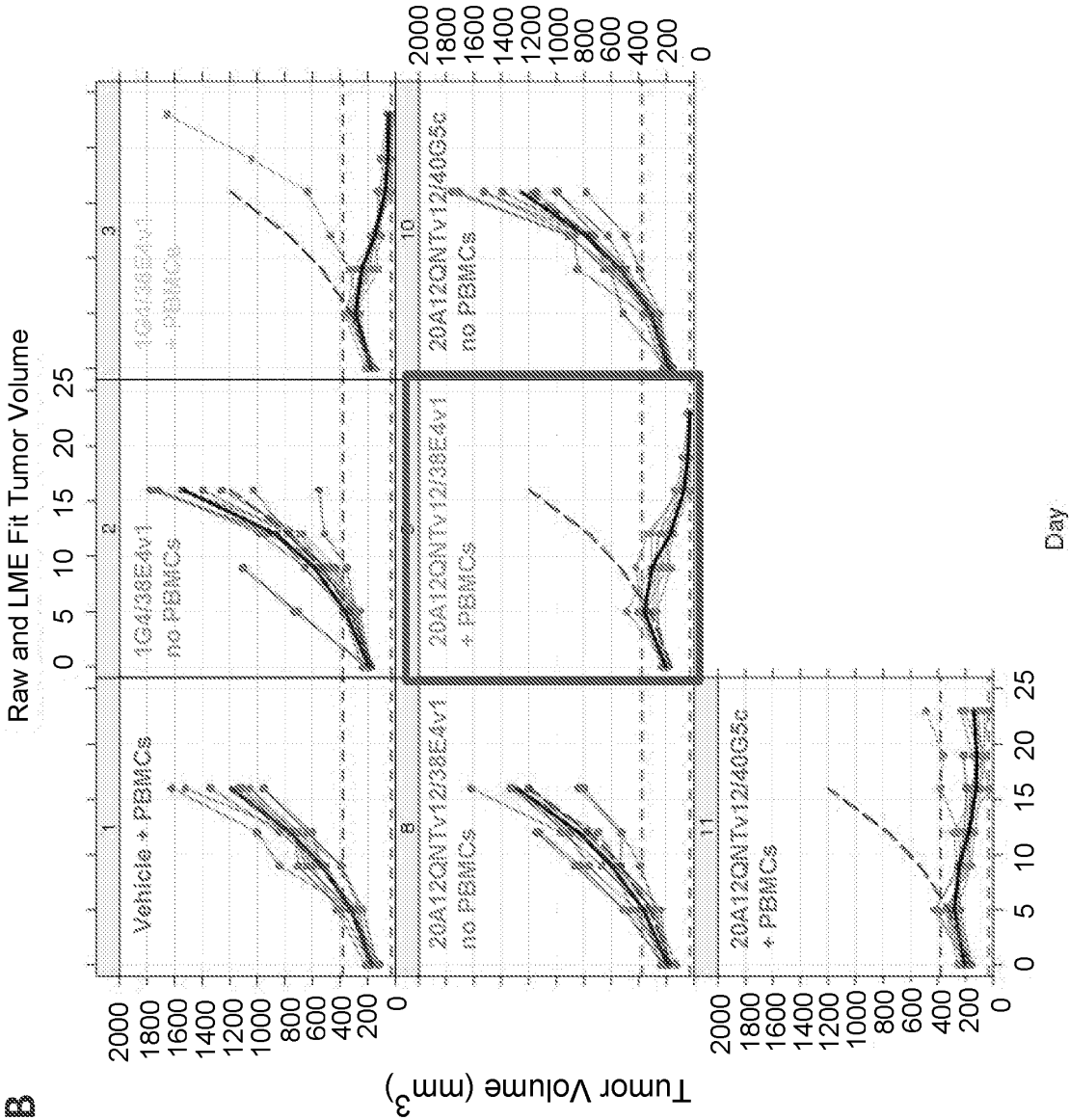


FIG. 17C

PK of LY6G6D TDBs in HT55 mouse model

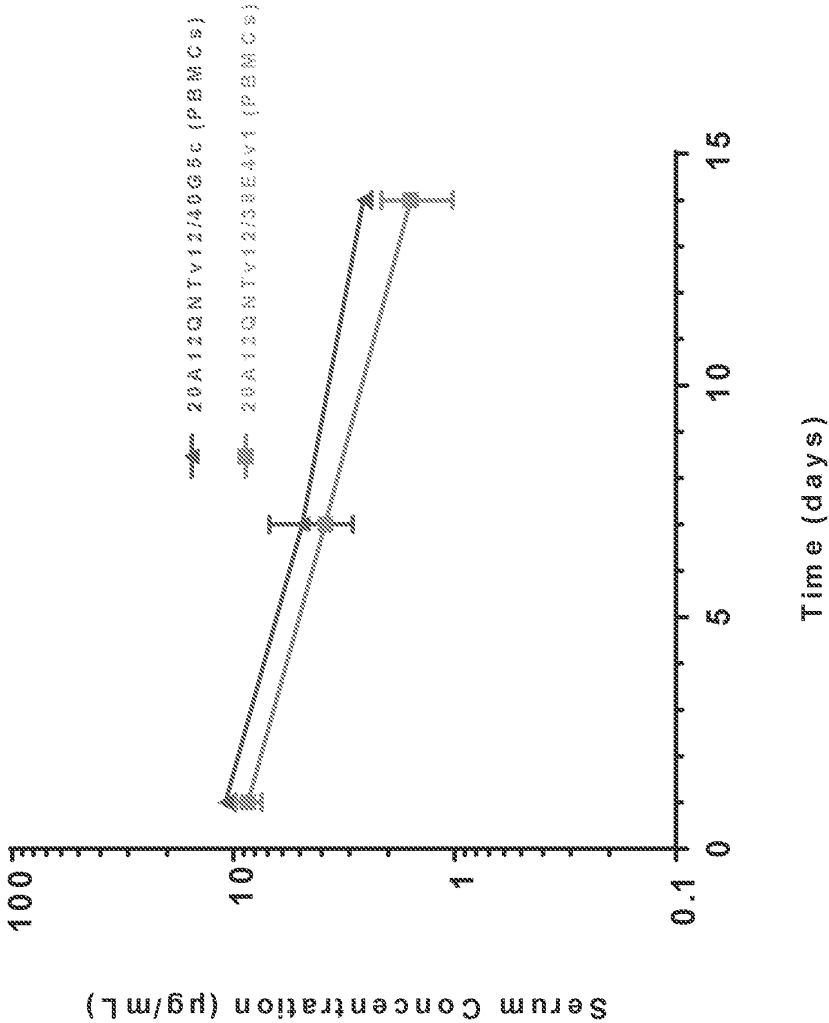
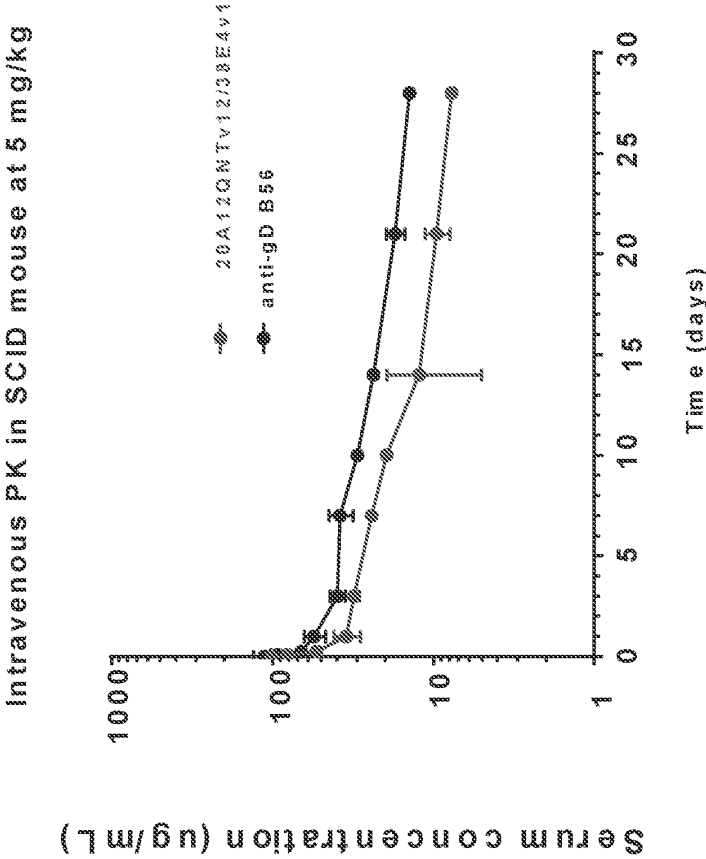
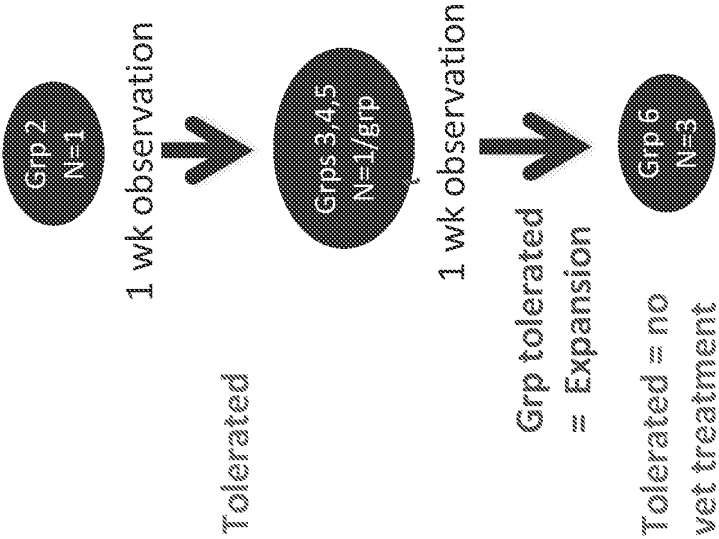


FIG. 18



Group	C _{max} (ug/mL)	AUC ₀₋₂₄ (day*ug/mL)	CL (mL/day/kg)	t _{1/2} (days)
20A12QNTv.12/38E4.v1 TDB	102	497	7.67	13.9
anti-gD 586	113	782	4.53	15.7

FIG. 19



Dosed Group	Dose (mg/kg)	No. of animals
1	0	2
2	1	1
3	2	1
4	4	1
5	8	1
6	15	2

Note, N=2 instead of 3 in group 6 due to material limitation

FIG. 20A

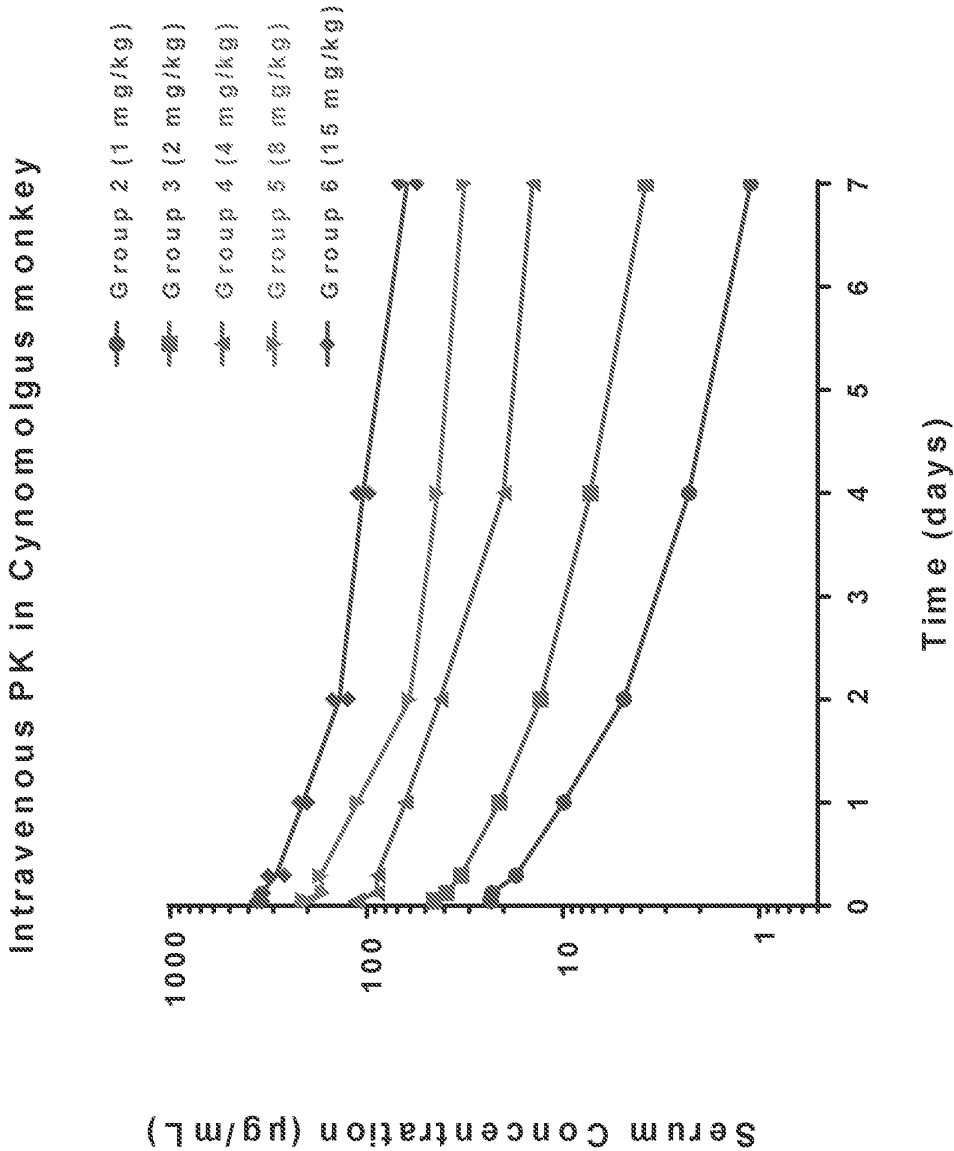
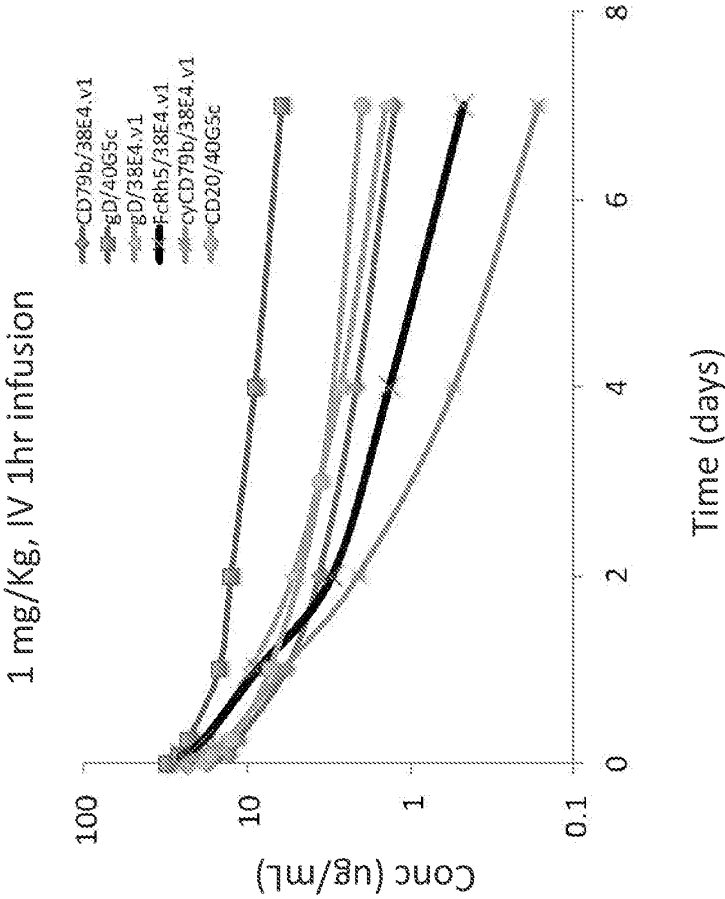


FIG. 20B



TDB	CL (mL/kg/d)
gD/40G5c	6.0
gD/38E4.v1	19.7
CD20/40G5c	22.3
FcRh5/38E4.v1	33.6
CD79b/38E4.v1	28.5
cyCD79b/38E4.v1	50
HER2/40G5c*	13.4
<u>20A12.QNTv.12/38E4v1</u> <u>[1 mg/kg]*</u>	<u>25.9</u>
<u>20A12.QNTv.12/38E4v1</u> <u>[15 mg/kg]*</u>	<u>11.7</u>

* Data not shown in the graph

FIG. 21

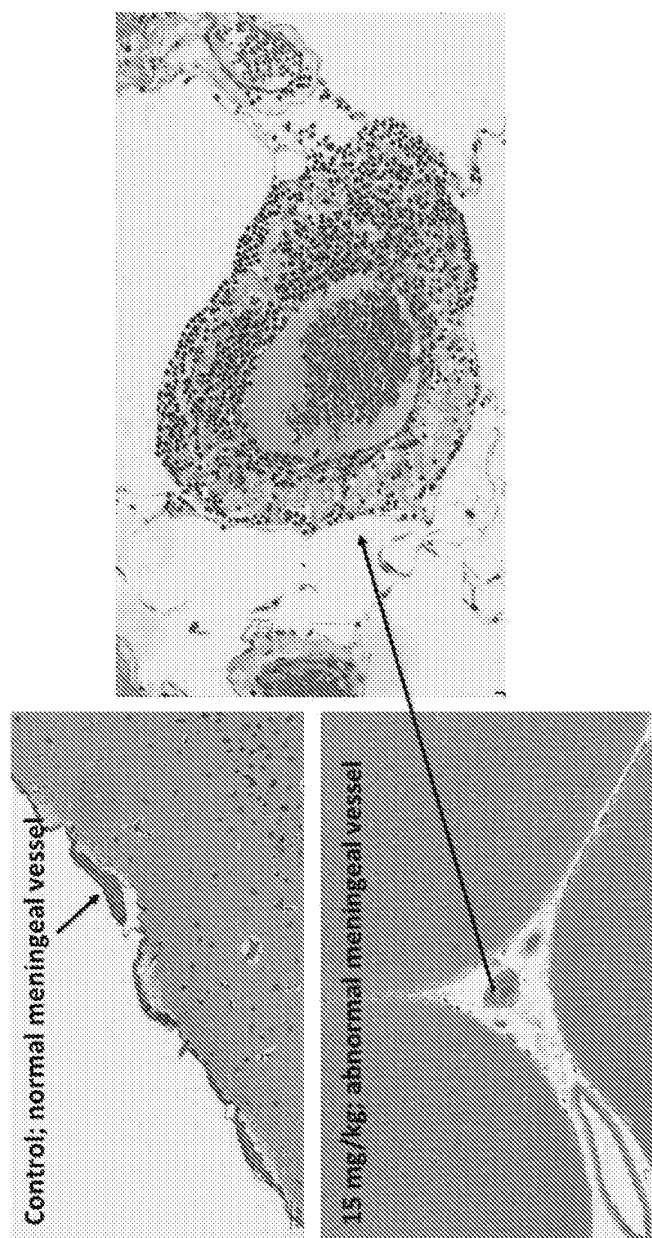
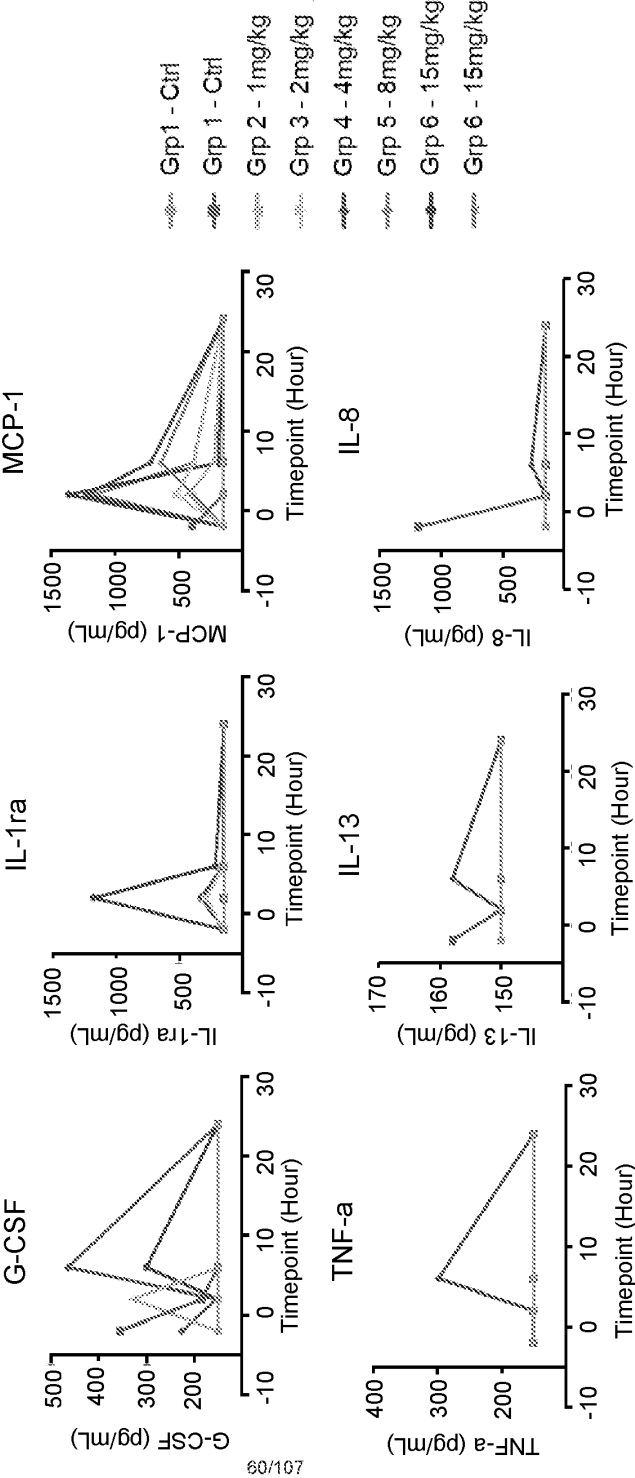


FIG. 22A



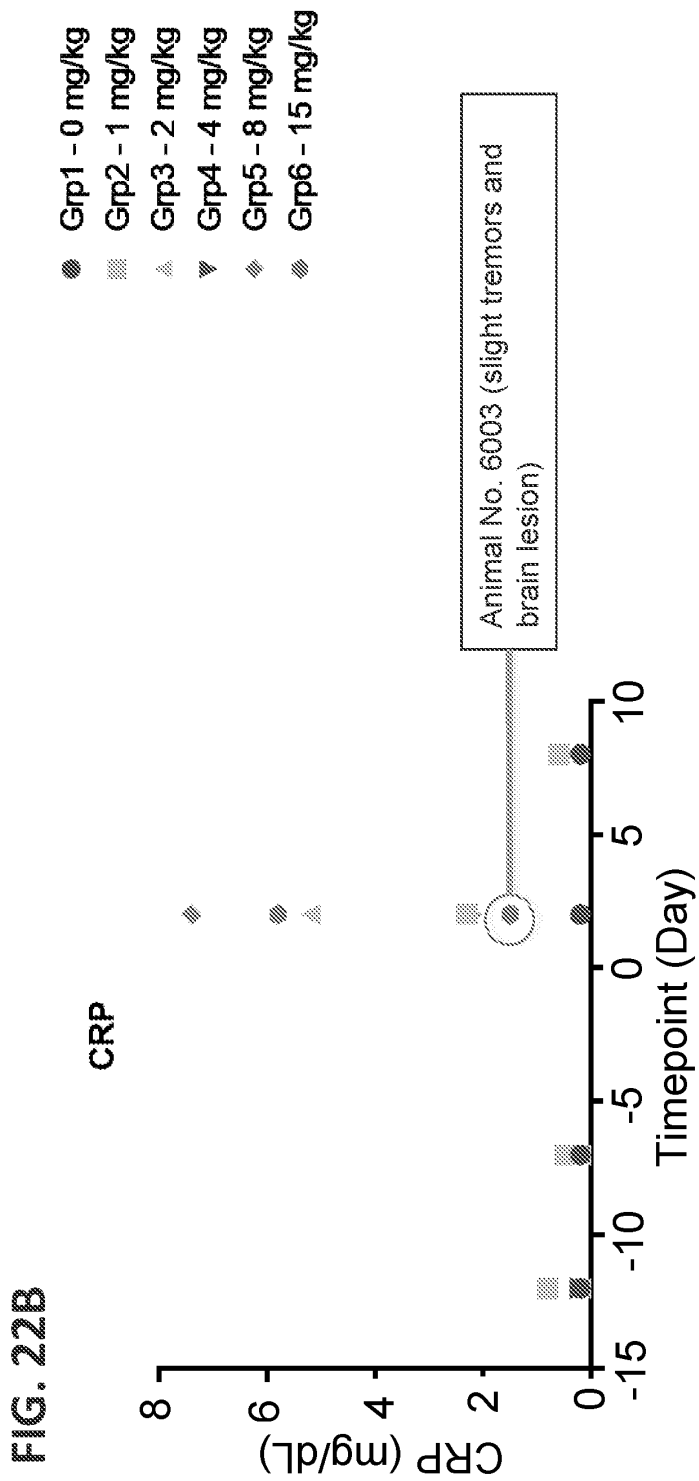


FIG. 23A

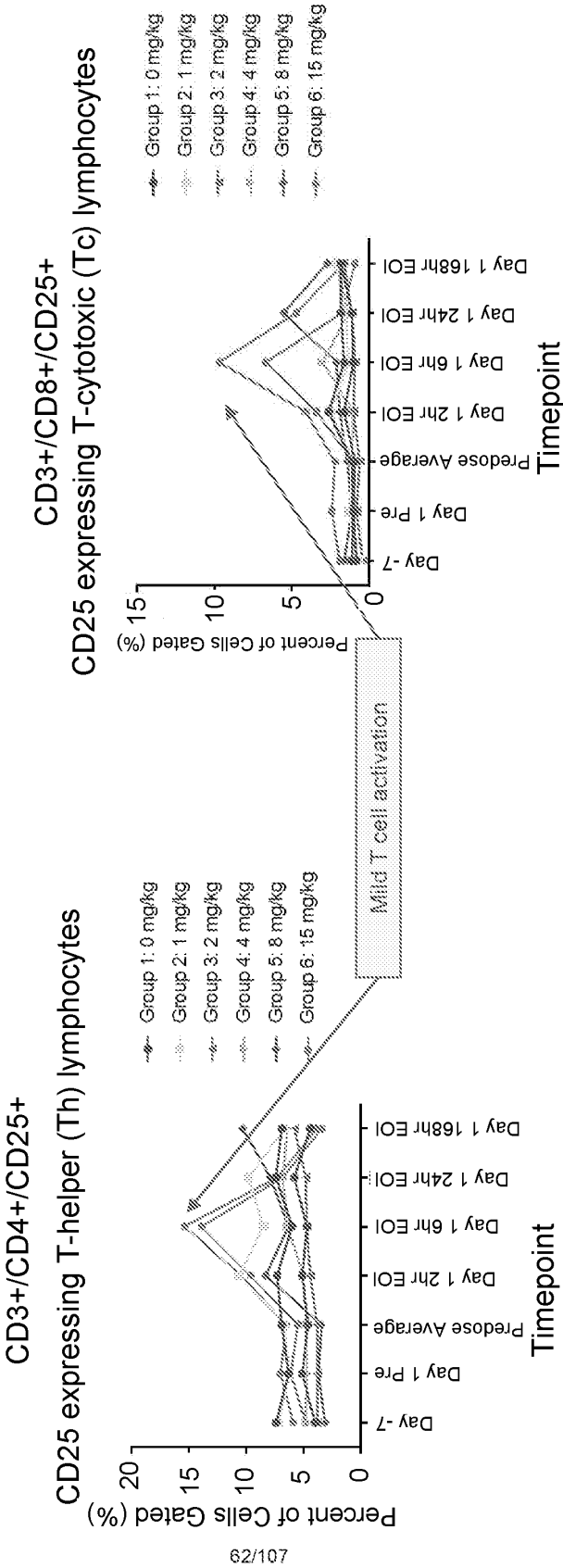


FIG. 23B

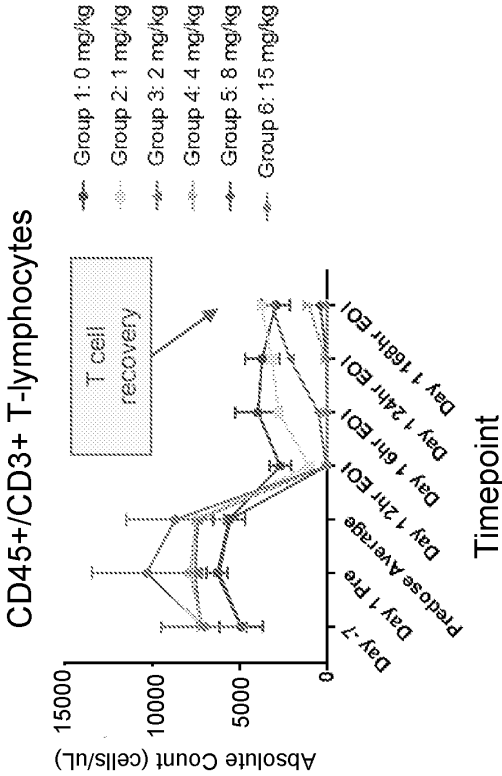


FIG. 23C

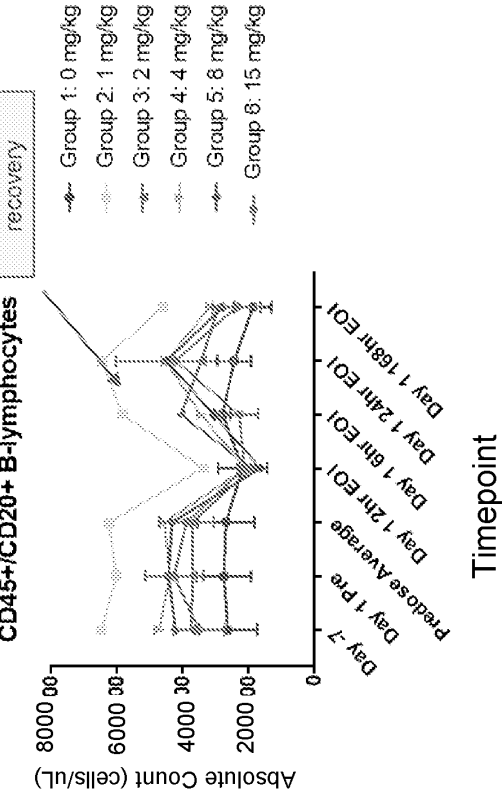


FIG. 23D

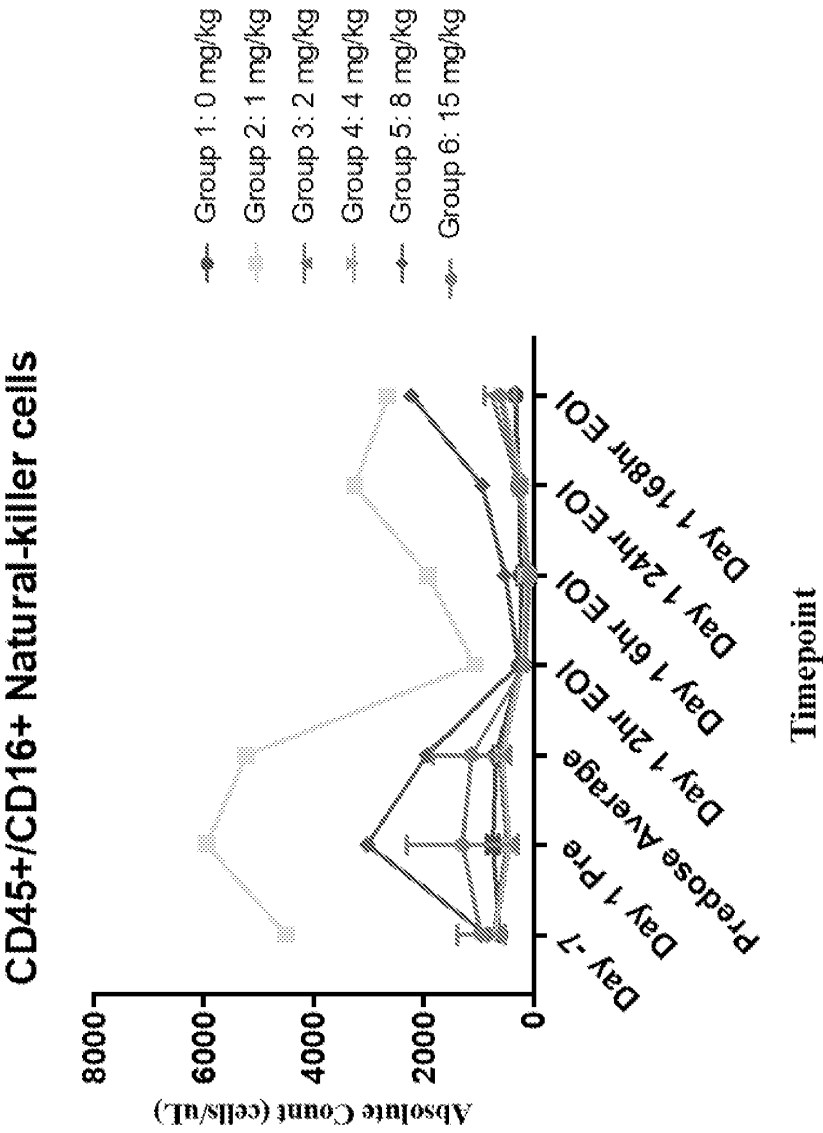


FIG. 24A

human

cyno

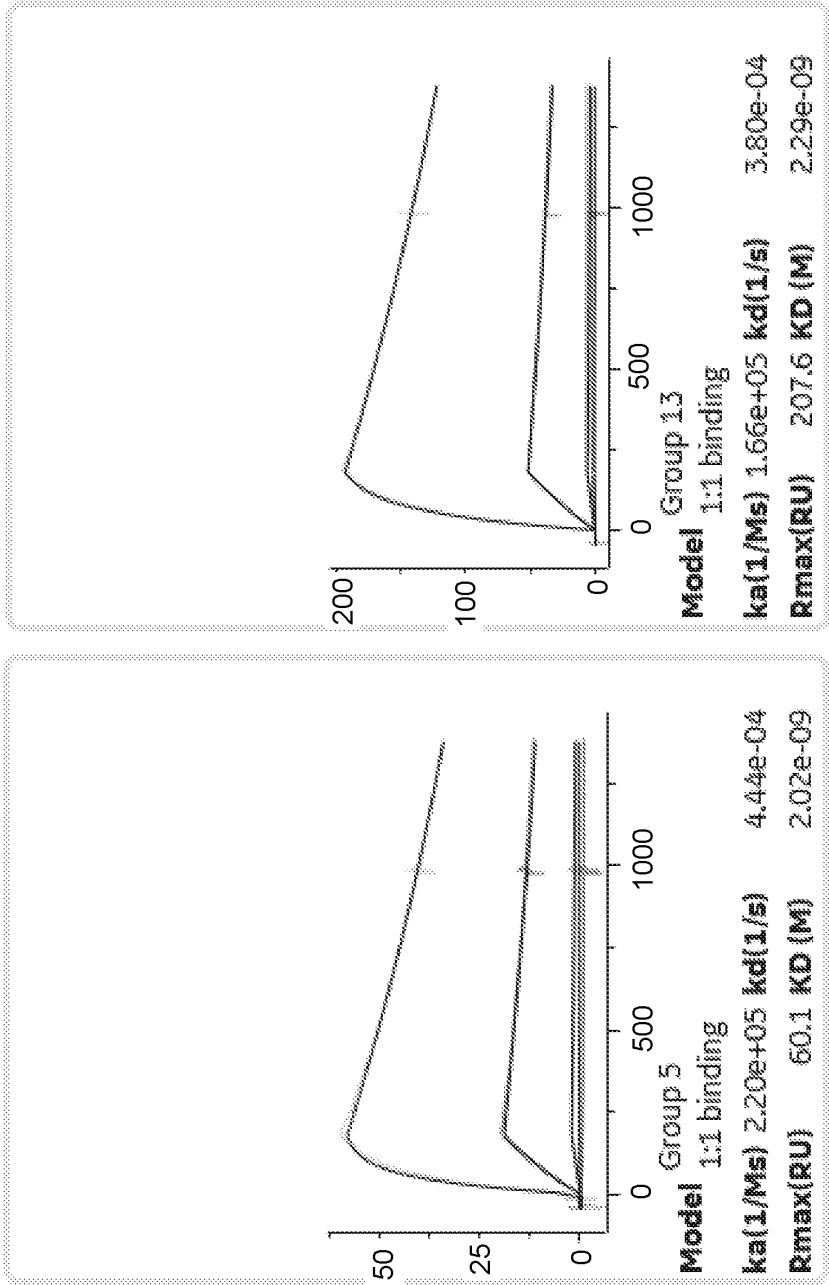
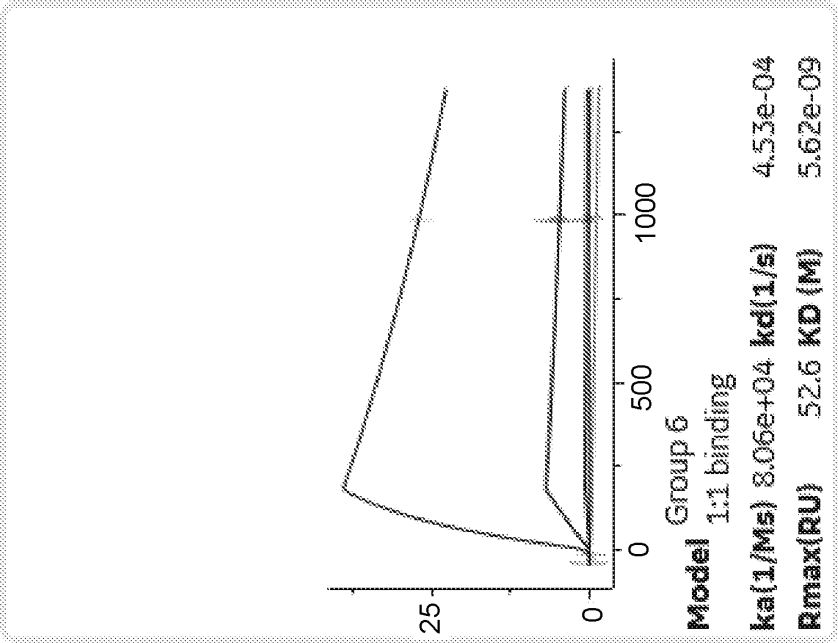


FIG. 24B

human



cyno

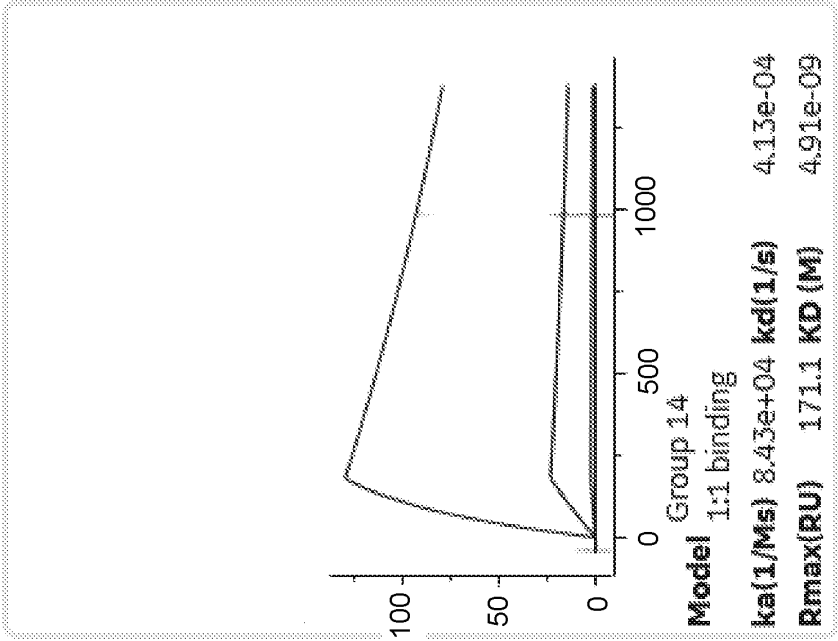


FIG. 24C

human

cyno

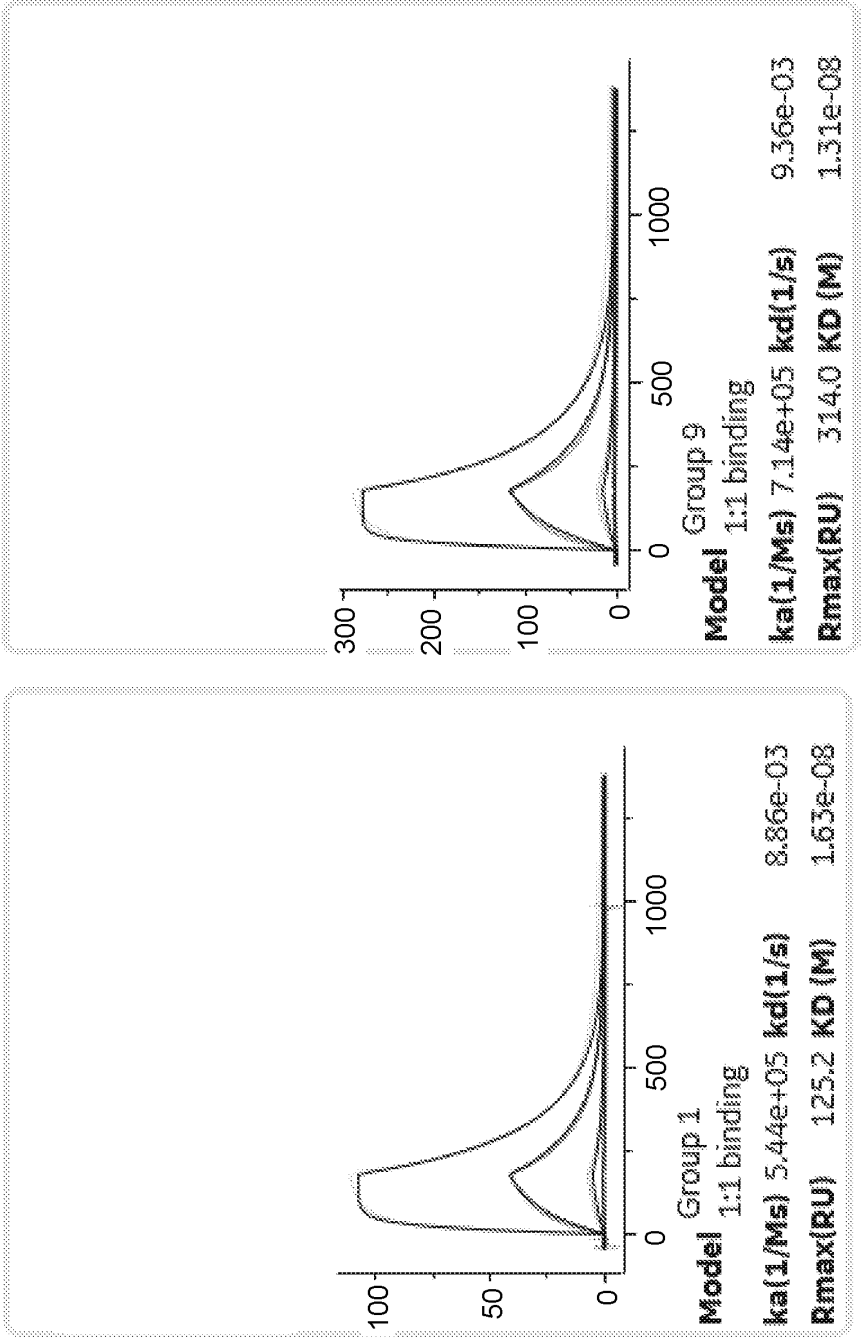


FIG. 24D

human cyno

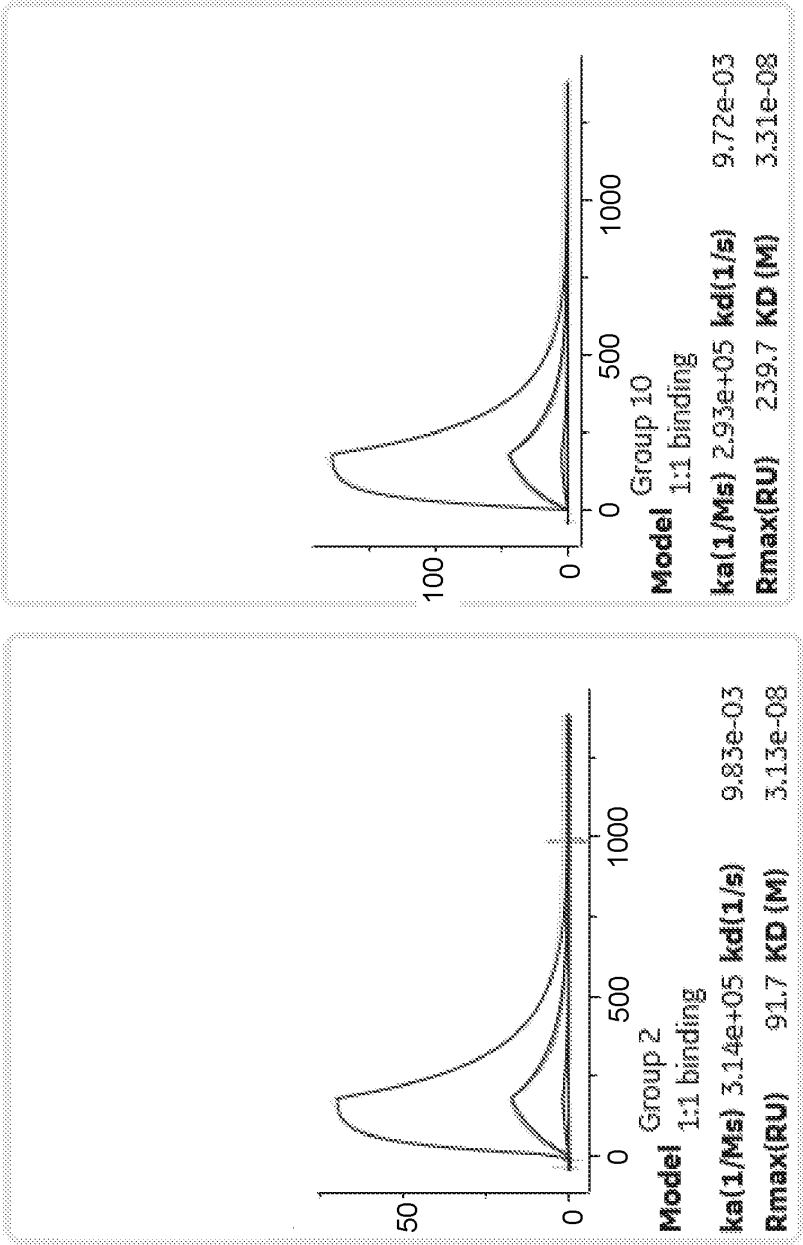
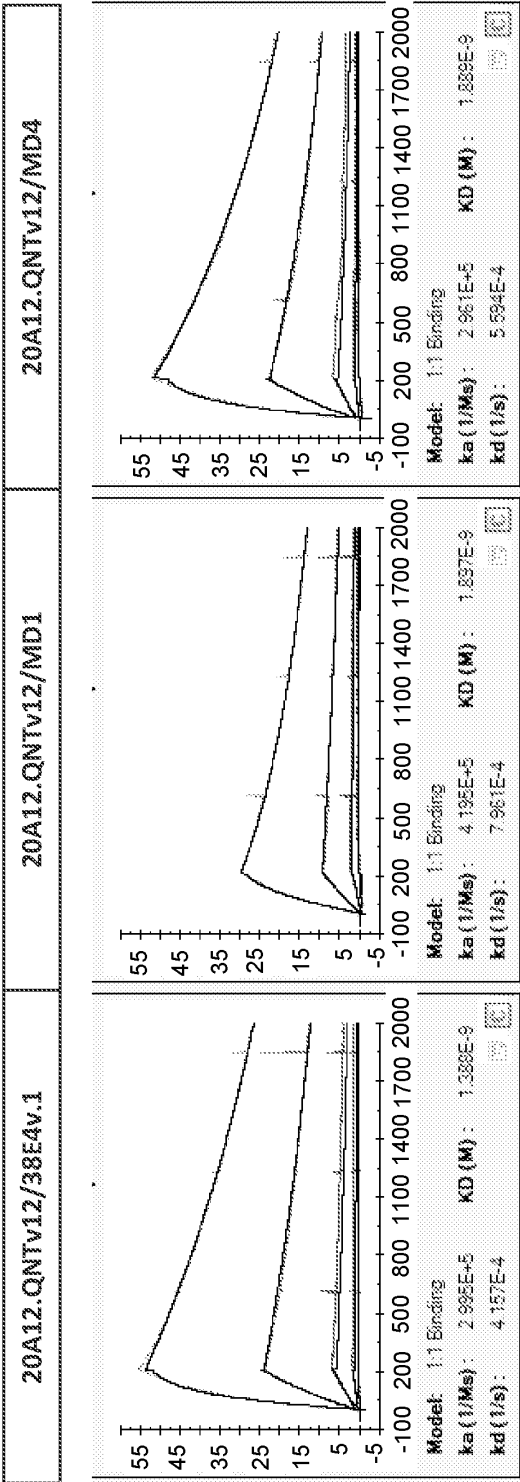


FIG. 25



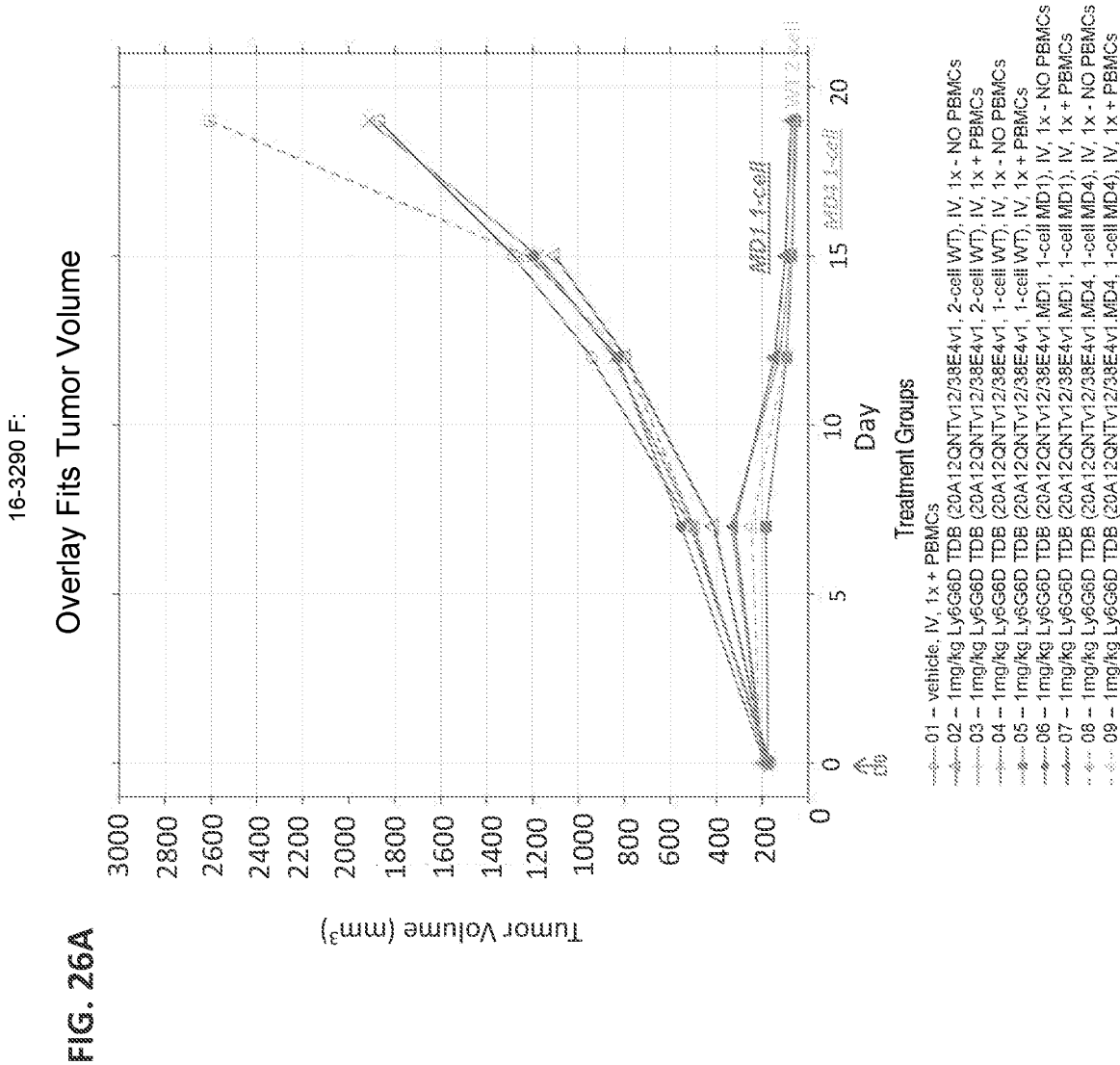


FIG. 26B

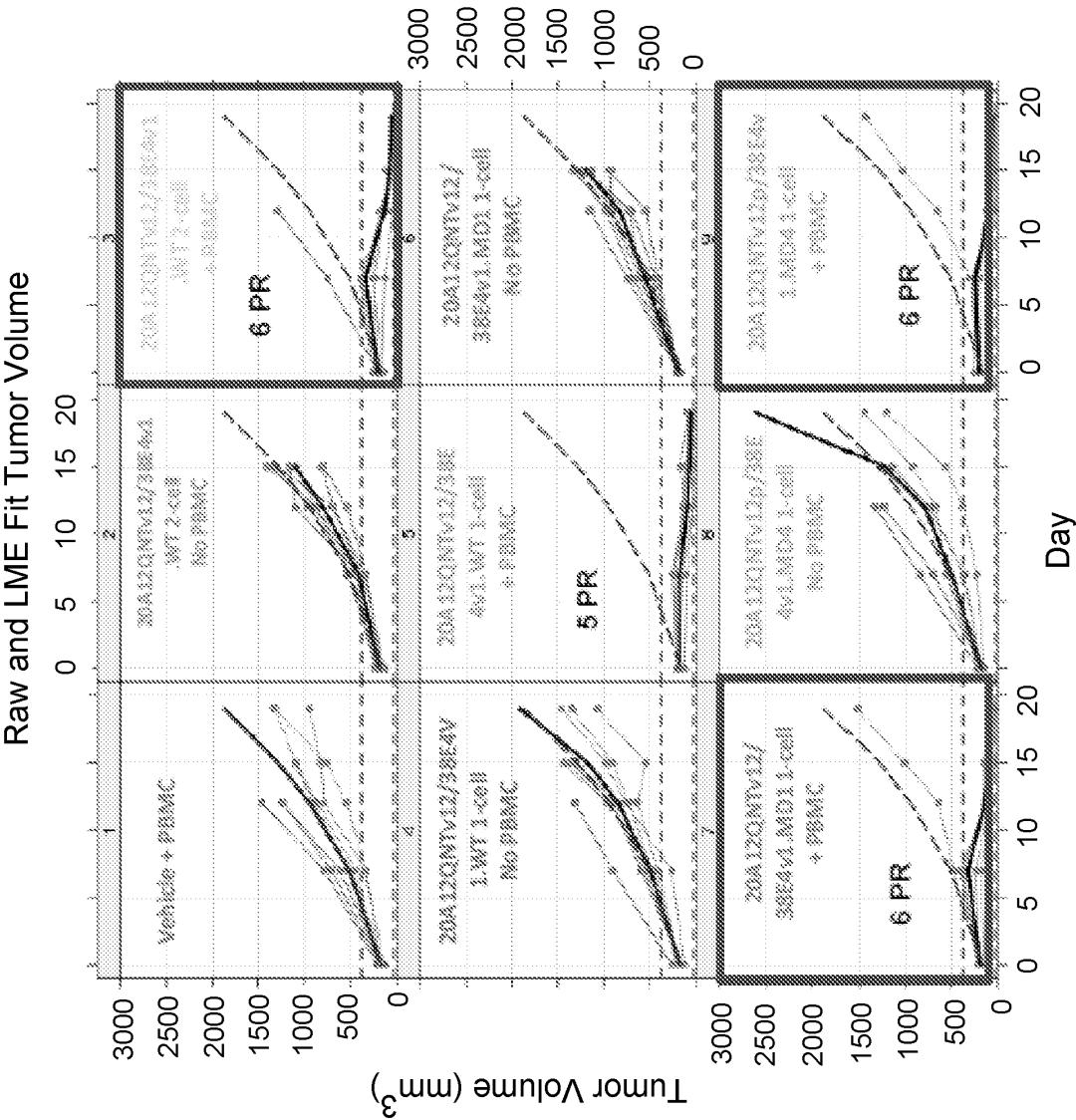
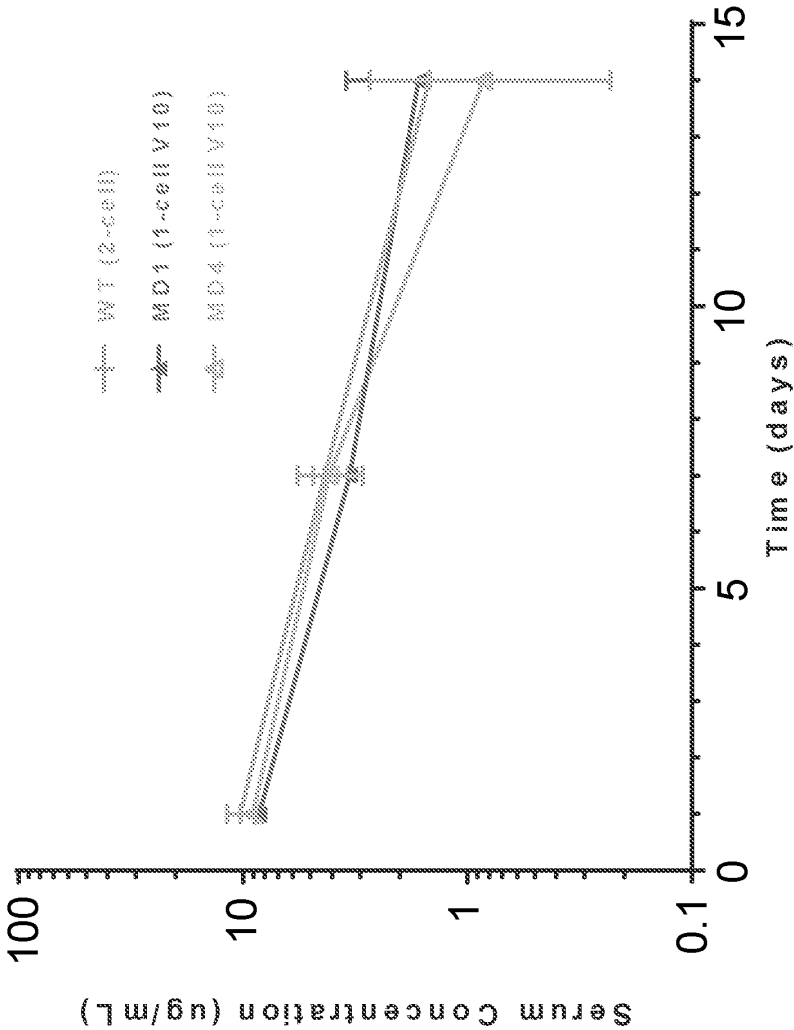


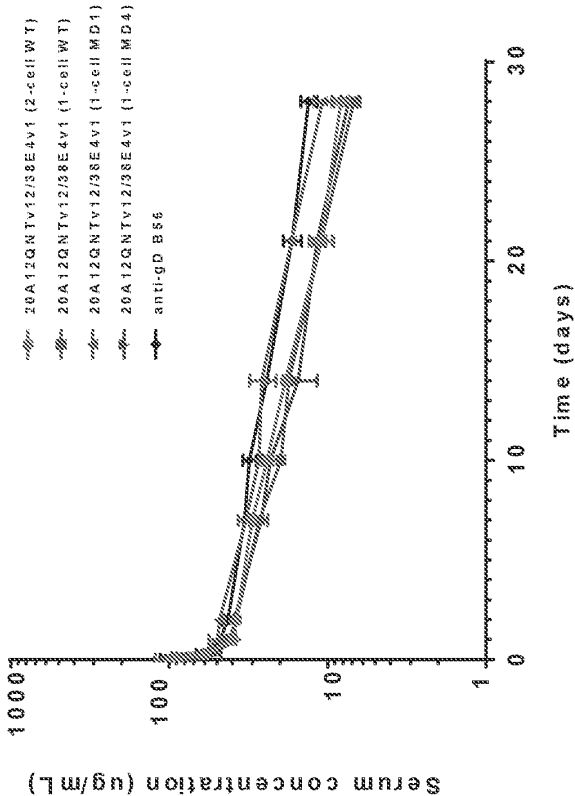
FIG. 27

PK profiles in NSG mouse in HT55 model



IVPK of LY6G6D TDBs in SCID mouse @ 5 mg/kg

FIG. 28



Group#	Group	C _{max} (ug/ml)	AUC _{0-∞} (ug/ml·day)	Cl (ml/day/kg)	V _d (ml/kg)	t _{1/2} (days)
1	20A12.QNTv12-38E4.v1 (2-cell WT)	99.2	603	6.73	110	11.8
2	20A12.QNTv12-38E4.v1 (1-cell WT)	105	569	7.35	111	11.2
3	20A12.QNTv12-38E4.v1 (1-cell MD1)	107	760	5.23	92.0	12.5
4	20A12.QNTv12-38E4.v1 (1-cell MD4)	95.0	566	7.23	116	11.8
5	Anti-gD B56	103	756	4.81	102	14.9

FIG. 29A

Light chain variable region

		CDR L1 - Contact	
		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 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		
38E4v1	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 L L N S R T R K N Y L A W Y		
38E4v1.MD1	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 L L N S R T R K N Y L A W Y		
38E4v1.MD4	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 L L N S R T R K N Y L A W Y		
40G5c	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 L L N S R T R K N Y L A W Y		
		CDR L2 - Contact	
		CDR L2 - 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 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		
38E4v1	Q Q K P G Q S P K L L I Y W T S T R K S G V P D R F S G S G T D F T L T I S S L		
38E4v1.MD1	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 T D F T L T I S S L		
38E4v1.MD4	Q Q K P G Q P P K L L I Y W A S T R K S G V P D R F S G S G T D F T L T I S S L		
40G5c	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 T D F T L T I S S L		
		CDR L3 - Contact	
		CDR L3 - 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 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		
38E4v1	Q A E D V A V Y Y C K Q S F I L - R T F G Q G T K V E I K		
38E4v1.MD1	Q A E D V A V Y Y C T Q S F I L - R T F G Q G T K V E I K		
38E4v1.MD4	Q A E D V A V Y Y C K Q S F I L - R T F G Q G T K V E I K		
40G5c	Q A E D V A V Y Y C T Q S F I L - R T F G Q G T K V E I K		
		SEQ ID NO: 93	
		SEQ ID NO: 53	
		SEQ ID NO: 94	
		SEQ ID NO: 53	

FIG. 29B

Heavy chain variable region

		CDR H1 - Contact	
		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	22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45	
38E4v1	E 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 F T F T S Y Y I H W V R Q A P G	46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69	
38E4v1MD1	E 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 F T F T S Y Y I H W V R Q A P G	70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93	
38E4v1MD4	E 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 F T F T S Y Y I H W V R Q A P G	94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117	
40G5c	E 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 N Y Y I H W V R Q A P G	118 119 120 121 122 123 124 125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141	
		CDR H2 - Contact	
		CDR H2 - Kabat	
Kabat number	142 143 144 145 146 147 148 149 150 151 152 153 154 155 156 157 158 159 160 161 162 163 164	165 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 182 183 184 185 186 187	
38E4v1	Q G L E W I G W I Y P E N D N T K Y N E K F K D R V T I T A D T S T S T A Y L E L S	188 189 190 191 192 193 194 195 196 197 198 199 200 201 202 203 204 205 206 207 208 209 210 211	
38E4v1MD1	Q G L E W I G W I Y P E N D N T K Y N E K F K D R V T I T A D T S T S T A Y L E L S	212 213 214 215 216 217 218 219 220 221 222 223 224 225 226 227 228 229 230 231 232 233 234	
38E4v1MD4	Q G L E W I G W I Y P E N D N T K Y N E K F K D R V T I T A D T S T S T A Y L E L S	235 236 237 238 239 240 241 242 243 244 245 246 247 248 249 250 251 252 253 254 255 256 257	
40G5c	Q G L E W I G W I Y P G D G N T K Y N E K F K G R A T L T A D T S T S T A Y L E L S	258 259 260 261 262 263 264 265 266 267 268 269 270 271 272 273 274 275 276 277 278 279 280	
		CDR H3 - Contact	
		CDR H3 - Kabat	
Kabat number	281 282 283 284 285 286 287 288 289 290 291 292 293 294 295 296 297 298 299 300 301 302 303	304 305 306 307 308 309 310 311 312 313 314 315 316 317 318 319 320 321 322 323 324 325 326	
38E4v1	S L R S E D T A V Y Y C A R D G Y S R Y Y F D Y W G Q G T L V T V S S	327 328 329 330 331 332 333 334 335 336 337 338 339 340 341 342 343 344 345 346 347 348 349	
38E4v1MD1	S L R S E D T A V Y Y C A R D G Y S R Y Y F D Y W G Q G T L V T V S S	350 351 352 353 354 355 356 357 358 359 360 361 362 363 364 365 366 367 368 369 370 371 372	
38E4v1MD4	S L R S E D T A V Y Y C A R D G Y S R Y Y F D Y W G Q G T L V T V S S	373 374 375 376 377 378 379 380 381 382 383 384 385 386 387 388 389 390 391 392 393 394 395	
40G5c	S L R S E D T A V Y Y C A R D S Y S N Y Y F D Y W G Q G T L V T V S S	396 397 398 399 400 401 402 403 404 405 406 407 408 409 410 411 412 413 414 415 416 417 418	

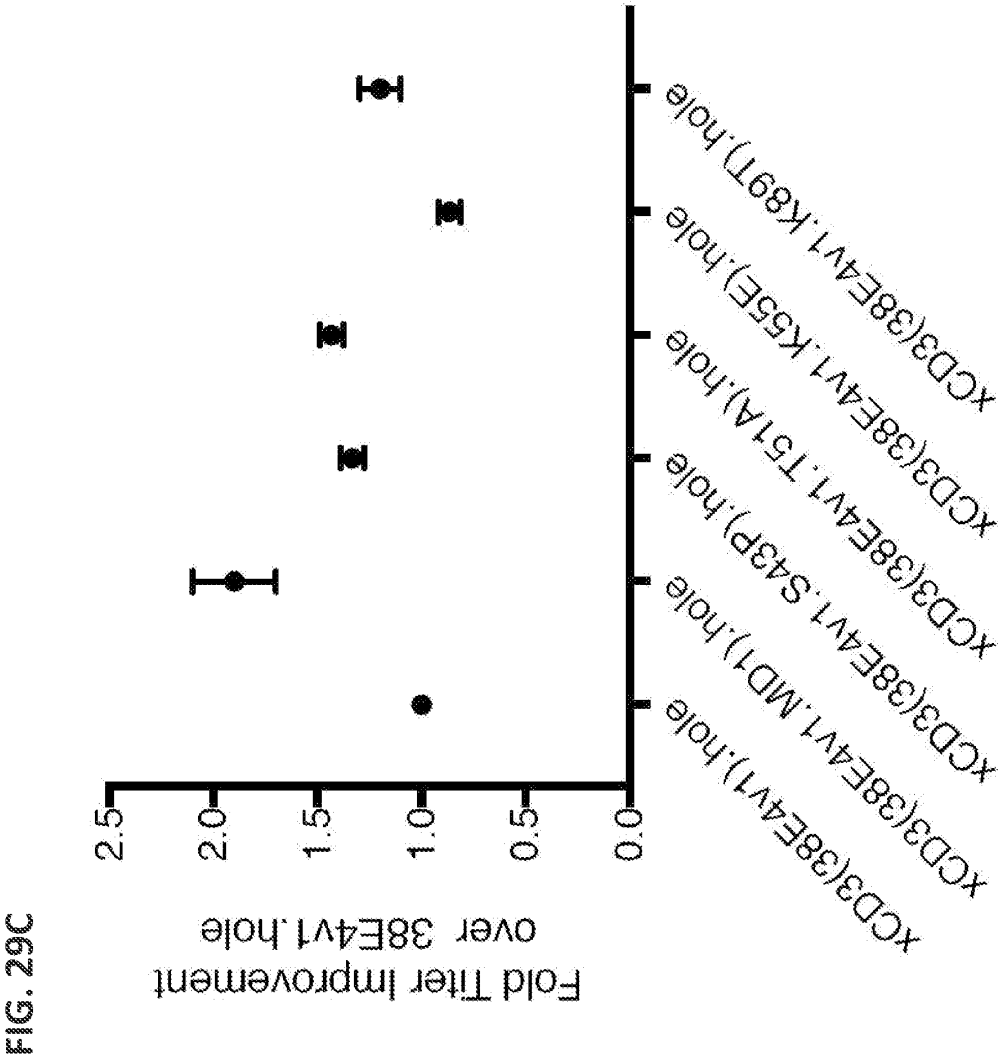
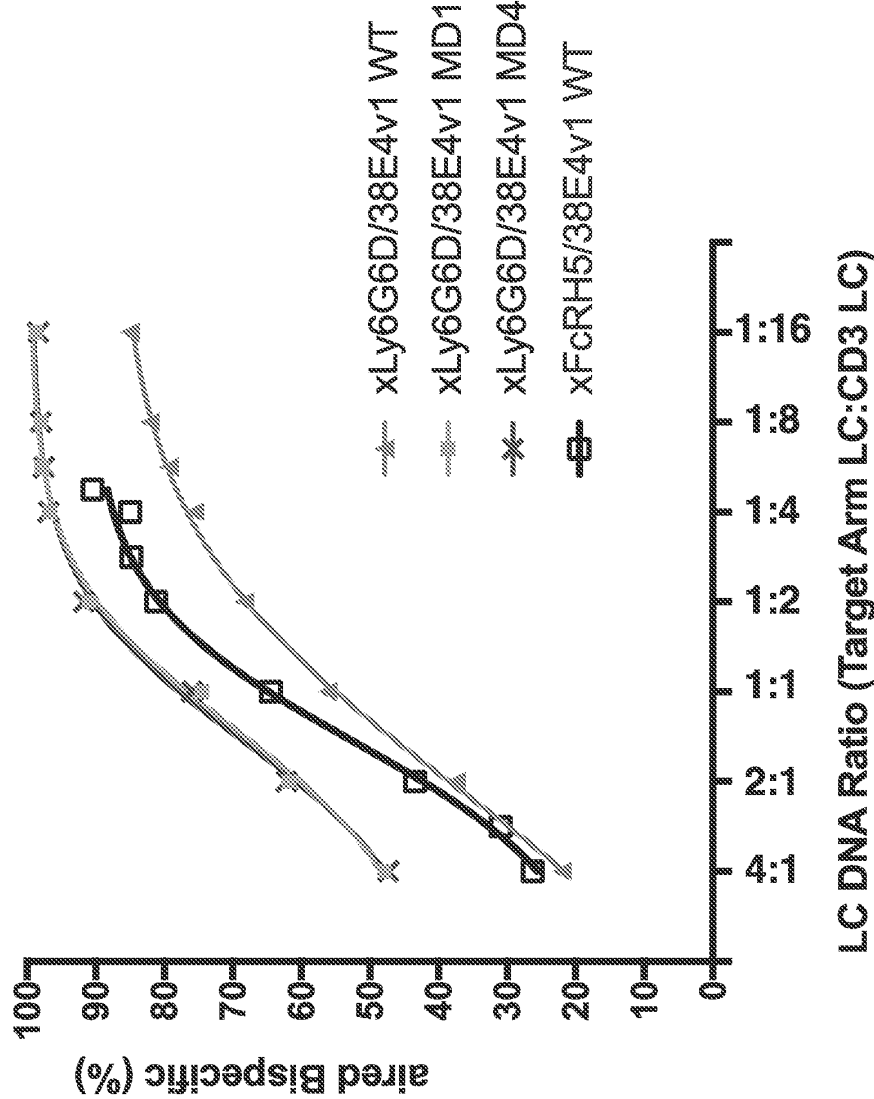


FIG. 29D



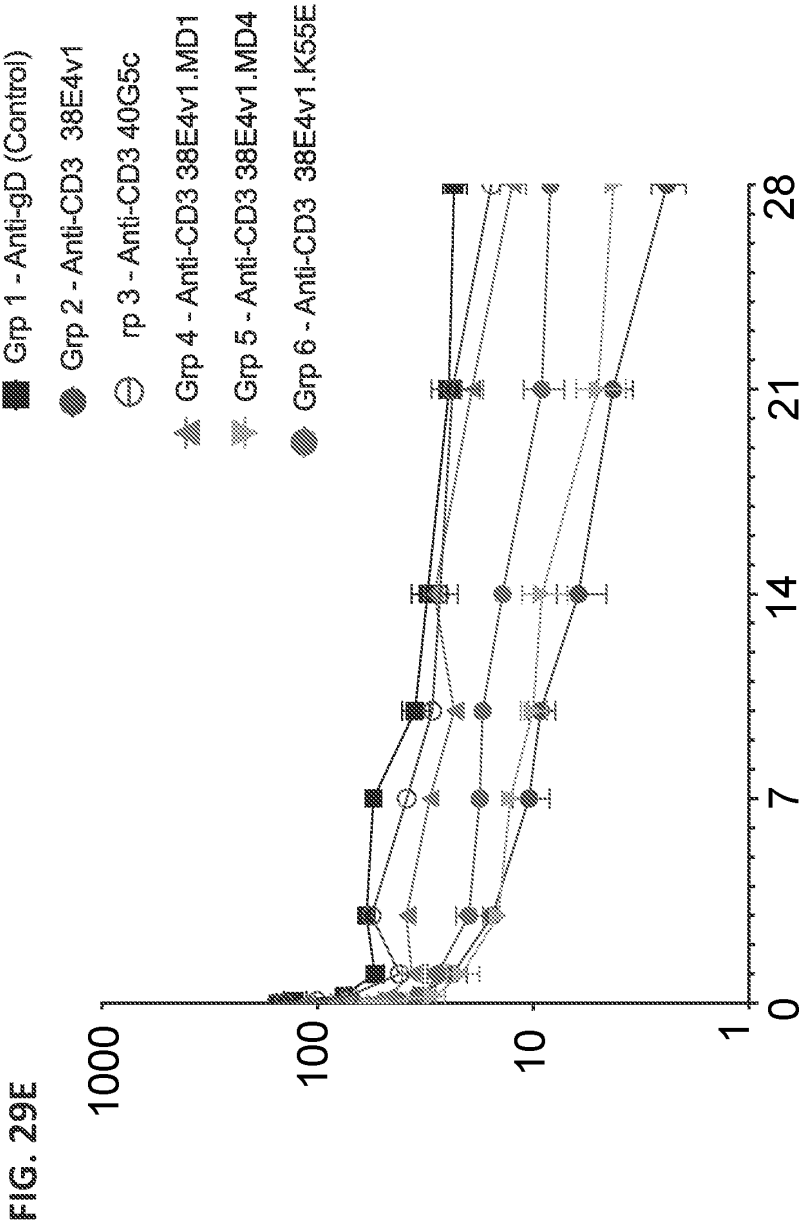


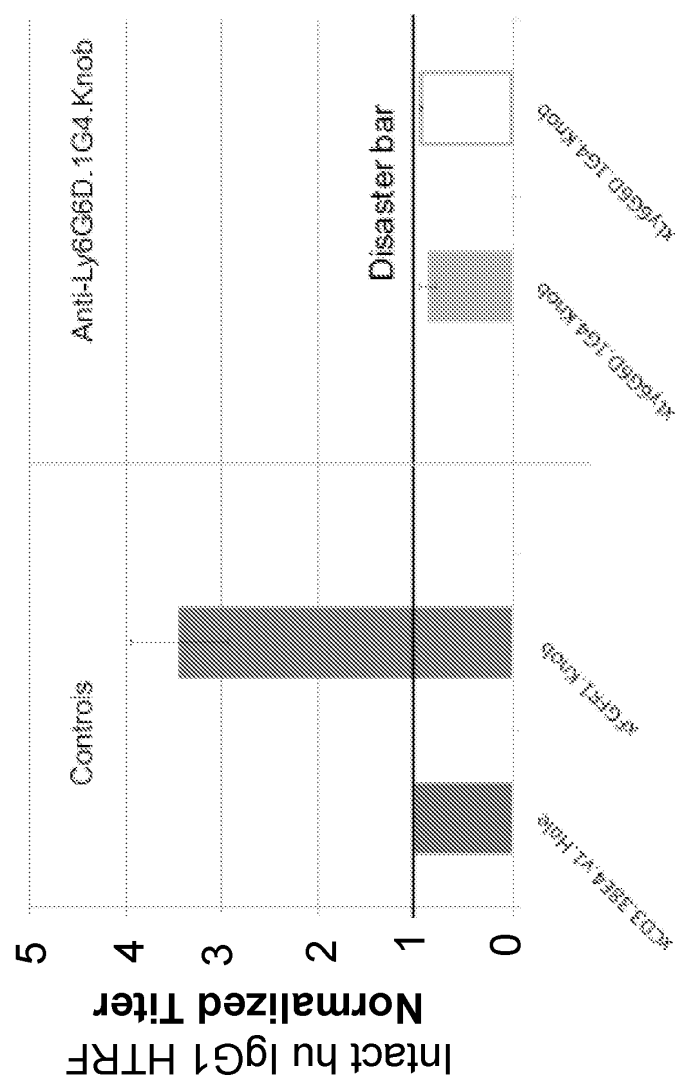
FIG. 29f

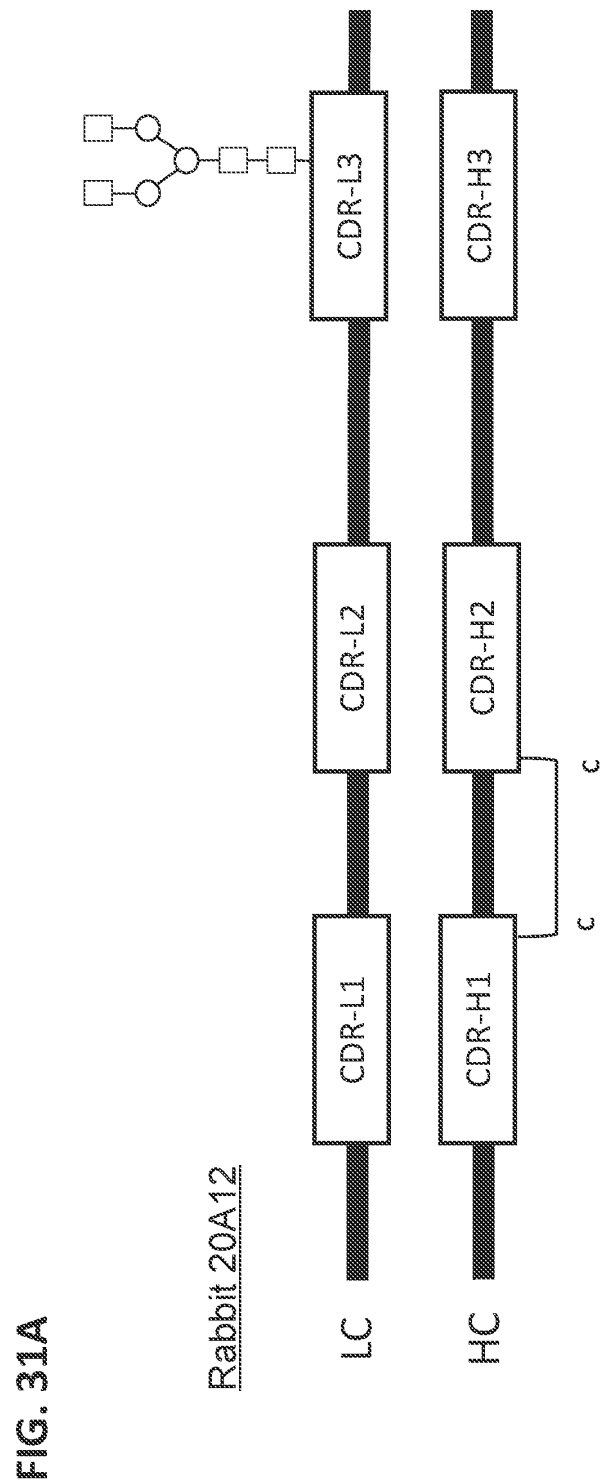
Kabat number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136	137	138	139	140	141	142	143	144	145	146	147	148	149	150	151	152	153	154	155	156	157	158	159	160	161	162	163	164	165	166	167	168	169	170	171	172	173	174	175	176	177	178	179	180	181	182	183	184	185	186	187	188	189	190	191	192	193	194	195	196	197	198	199	200	201	202	203	204	205	206	207	208	209	210	211	212	213	214	215	216	217	218	219	220	221	222	223	224	225	226	227	228	229	230	231	232	233	234	235	236	237	238	239	240	241	242	243	244	245	246	247	248	249	250	251	252	253	254	255	256	257	258	259	260	261	262	263	264	265	266	267	268	269	270	271	272	273	274	275	276	277	278	279	280	281	282	283	284	285	286	287	288	289	290	291	292	293	294	295	296	297	298	299	300	301	302	303	304	305	306	307	308	309	310	311	312	313	314	315	316	317	318	319	320	321	322	323	324	325	326	327	328	329	330	331	332	333	334	335	336	337	338	339	340	341	342	343	344	345	346	347	348	349	350	351	352	353	354	355	356	357	358	359	360	361	362	363	364	365	366	367	368	369	370	371	372	373	374	375	376	377	378	379	380	381	382	383	384	385	386	387	388	389	390	391	392	393	394	395	396	397	398	399	400	401	402	403	404	405	406	407	408	409	410	411	412	413	414	415	416	417	418	419	420	421	422	423	424	425	426	427	428	429	430	431	432	433	434	435	436	437	438	439	440	441	442	443	444	445	446	447	448	449	450	451	452	453	454	455	456	457	458	459	460	461	462	463	464	465	466	467	468	469	470	471	472	473	474	475	476	477	478	479	480	481	482	483	484	485	486	487	488	489	490	491	492	493	494	495	496	497	498	499	500	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525	526	527	528	529	530	531	532	533	534	535	536	537	538	539	540	541	542	543	544	545	546	547	548	549	550	551	552	553	554	555	556	557	558	559	560	561	562	563	564	565	566	567	568	569	570	571	572	573	574	575	576	577	578	579	580	581	582	583	584	585	586	587	588	589	590	591	592	593	594	595	596	597	598	599	600	601	602	603	604	605	606	607	608	609	610	611	612	613	614	615	616	617	618	619	620	621	622	623	624	625	626	627	628	629	630	631	632	633	634	635	636	637	638	639	640	641	642	643	644	645	646	647	648	649	650	651	652	653	654	655	656	657	658	659	660	661	662	663	664	665	666	667	668	669	670	671	672	673	674	675	676	677	678	679	680	681	682	683	684	685	686	687	688	689	690	691	692	693	694	695	696	697	698	699	700	701	702	703	704	705	706	707	708	709	710	711	712	713	714	715	716	717	718	719	720	721	722	723	724	725	726	727	728	729	730	731	732	733	734	735	736	737	738	739	740	741	742	743	744	745	746	747	748	749	750	751	752	753	754	755	756	757	758	759	760	761	762	763	764	765	766	767	768	769	770	771	772	773	774	775	776	777	778	779	780	781	782	783	784	785	786	787	788	789	790	791	792	793	794	795	796	797	798	799	800	801	802	803	804	805	806	807	808	809	810	811	812	813	814	815	816	817	818	819	820	821	822	823	824	825	826	827	828	829	830	831	832	833	834	835	836	837	838	839	840	841	842	843	844	845	846	847	848	849	850	851	852	853	854	855	856	857	858	859	860	861	862	863	864	865	866	867	868	869	870	871	872	873	874	875	876	877	878	879	880	881	882	883	884	885	886	887	888	889	890	891	892	893	894	895	896	897	898	899	900	901	902	903	904	905	906	907	908	909	910	911	912	913	914	915	916	917	918	919	920	921	922	923	924	925	926	927	928	929	930	931	932	933	934	935	936	937	938	939	940	941	942	943	944	945	946	947	948	949	950	951	952	953	954	955	956	957	958	959	960	961	962	963	964	965	966	967	968	969	970	971	972	973	974	975	976	977	978	979	980	981	982	983	984	985	986	987	988	989	990	991	992	993	994	995	996	997	998	999	1000	1001	1002	1003	1004	1005	1006	1007	1008	1009	1010	1011	1012	1013	1014	1015	1016	1017	1018	1019	1020	1021	1022	1023	1024	1025	1026	1027	1028	1029	1030	1031	1032	1033	1034	1035	1036	1037	1038	1039	1040	1041	1042	1043	1044	1045	1046	1047	1048	1049	1050	1051	1052	1053	1054	1055	1056	1057	1058	1059	1060	1061	1062	1063	1064	1065	1066	1067	1068	1069	1070	1071	1072	1073	1074	1075	1076	1077	1078	1079	1080	1081	1082	1083	1084	1085	1086	1087	1088	1089	1090	1091	1092	1093	1094	1095	1096	1097	1098	1099	1100	1101	1102	1103	1104	1105	1106	1107	1108	1109	1110	1111	1112	1113	1114	1115	1116	1117	1118	1119	1120	1121	1122	1123	1124	1125	1126	1127	1128	1129	1130	1131	1132	1133	1134	1135	1136	1137	1138	1139	1140	1141	1142	1143	1144	1145	1146	1147	1148	1149	1150	1151	1152	1153	1154	1155	1156	1157	1158	1159	1160	1161	1162	1163	1164	1165	1166	1167	1168	1169	1170	1171	1172	1173	1174	1175	1176	1177	1178	1179	1180	1181	1182	1183	1184	1185	1186	1187	1188	1189	1190	1191	1192	1193	1194	1195	1196	1197	1198	1199	1200	1201	1202	1203	1204	1205	1206	1207	1208	1209	1210	1211	1212	1213	1214	1215	1216	1217	1218	1219	1220	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FIG. 29G

Kabat number		CDR H1 - Contact		CDR H3 - Kabat			
38E4v1	EVQLVQSGAEVKKPGASVKVSCKASGFTFTSYIHWVRRKAPG	38E4v1	EVQLVQSGAEVKKPGASVKVSCKASGFTFTSYIHWVRRKAPG	38E4v1	EVQLVQSGAEVKKPGASVKVSCKASGFTFTSYIHWVRRKAPG	38E4v1	EVQLVQSGAEVKKPGASVKVSCKASGFTFTSYIHWVRRKAPG
38E4v1MD1	EVQLVQSGAEVKKPGASVKVSCKASGFTFTSYIHWVRRKAPG	38E4v1MD1	EVQLVQSGAEVKKPGASVKVSCKASGFTFTSYIHWVRRKAPG	38E4v1MD1	EVQLVQSGAEVKKPGASVKVSCKASGFTFTSYIHWVRRKAPG	38E4v1MD1	EVQLVQSGAEVKKPGASVKVSCKASGFTFTSYIHWVRRKAPG
38E4v1MD4	EVQLVQSGAEVKKPGASVKVSCKASGFTFTSYIHWVRRKAPG	38E4v1MD4	EVQLVQSGAEVKKPGASVKVSCKASGFTFTSYIHWVRRKAPG	38E4v1MD4	EVQLVQSGAEVKKPGASVKVSCKASGFTFTSYIHWVRRKAPG	38E4v1MD4	EVQLVQSGAEVKKPGASVKVSCKASGFTFTSYIHWVRRKAPG
40G5c	EVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYIHWVRRKAPG	40G5c	EVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYIHWVRRKAPG	40G5c	EVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYIHWVRRKAPG	40G5c	EVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYIHWVRRKAPG
Kabat number		CDR H2 - Contact		CDR H2 - Kabat			
38E4v1	QGLEWIGWIYPENDNTKYNKFKDRVTITADTSTSTAYLELS	38E4v1	QGLEWIGWIYPENDNTKYNKFKDRVTITADTSTSTAYLELS	38E4v1	QGLEWIGWIYPENDNTKYNKFKDRVTITADTSTSTAYLELS	38E4v1	QGLEWIGWIYPENDNTKYNKFKDRVTITADTSTSTAYLELS
38E4v1MD1	QGLEWIGWIYPENDNTKYNKFKDRVTITADTSTSTAYLELS	38E4v1MD1	QGLEWIGWIYPENDNTKYNKFKDRVTITADTSTSTAYLELS	38E4v1MD1	QGLEWIGWIYPENDNTKYNKFKDRVTITADTSTSTAYLELS	38E4v1MD1	QGLEWIGWIYPENDNTKYNKFKDRVTITADTSTSTAYLELS
38E4v1MD4	QGLEWIGWIYPENDNTKYNKFKDRVTITADTSTSTAYLELS	38E4v1MD4	QGLEWIGWIYPENDNTKYNKFKDRVTITADTSTSTAYLELS	38E4v1MD4	QGLEWIGWIYPENDNTKYNKFKDRVTITADTSTSTAYLELS	38E4v1MD4	QGLEWIGWIYPENDNTKYNKFKDRVTITADTSTSTAYLELS
40G5c	QGLEWIGWIYPGNGNTKYNKFKGRATL	40G5c	QGLEWIGWIYPGNGNTKYNKFKGRATL	40G5c	QGLEWIGWIYPGNGNTKYNKFKGRATL	40G5c	QGLEWIGWIYPGNGNTKYNKFKGRATL
Kabat number		CDR H3 - Contact		CDR H3 - Kabat			
38E4v1	SLRSEDTAVYVCARDGYSRYYFDYWGQGT	38E4v1	SLRSEDTAVYVCARDGYSRYYFDYWGQGT	38E4v1	SLRSEDTAVYVCARDGYSRYYFDYWGQGT	38E4v1	SLRSEDTAVYVCARDGYSRYYFDYWGQGT
38E4v1MD1	SLRSEDTAVYVCARDGYSRYYFDYWGQGT	38E4v1MD1	SLRSEDTAVYVCARDGYSRYYFDYWGQGT	38E4v1MD1	SLRSEDTAVYVCARDGYSRYYFDYWGQGT	38E4v1MD1	SLRSEDTAVYVCARDGYSRYYFDYWGQGT
38E4v1MD4	SLRSEDTAVYVCARDGYSRYYFDYWGQGT	38E4v1MD4	SLRSEDTAVYVCARDGYSRYYFDYWGQGT	38E4v1MD4	SLRSEDTAVYVCARDGYSRYYFDYWGQGT	38E4v1MD4	SLRSEDTAVYVCARDGYSRYYFDYWGQGT
40G5c	SLRSEDTAVYVCARDGYSNYYFDYWGQGT	40G5c	SLRSEDTAVYVCARDGYSNYYFDYWGQGT	40G5c	SLRSEDTAVYVCARDGYSNYYFDYWGQGT	40G5c	SLRSEDTAVYVCARDGYSNYYFDYWGQGT

0306





313

Heavy Chain Frameworks

V.3-23

75.5%

Vernier

7.3-30

74.5%

8. Vernier

Light Chain Frameworks



85.3%

July 2014

93-1717

8.5%

Index

77.2%

0.000000

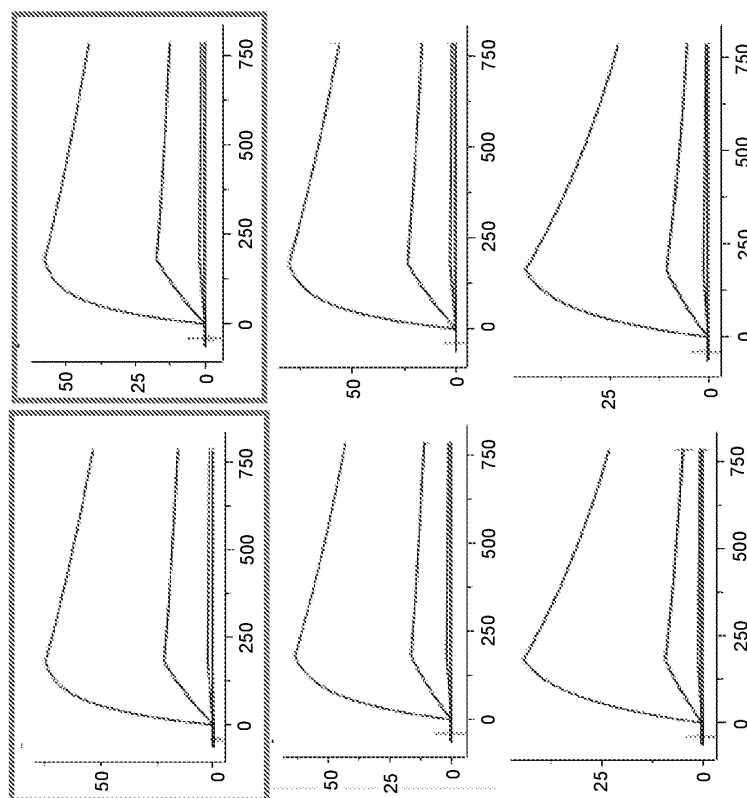


FIG. 31C

ID	Human VL germline	Verrier positions	Partial charge: Non-human Verrier	Human identity: Low	Partial charge: All human Verrier	Human identity: High	Prevalence in repertoire
1	HIGKV1D-39*01	1	3.8	85.3%	3.8	86.3%	13.3%
2	HIGKV1-39*01	1	3.8	85.3%	3.8	86.3%	12.7%
3	HIGKV1-5*01	1	3.8	85.3%	3.8	86.3%	4.7%
4	HIGKV1-5*02	1	3.8	85.3%	3.8	86.3%	4.7%
5	HIGKV1D-33*01	1	3.8	85.3%	3.8	86.3%	3.1%
6	HIGKV1-33*01	1	3.8	85.3%	3.8	86.3%	1.6%
7	HIGKV1-5*03	1	3.8	84.2%	3.8	85.3%	4.7%
8	HIGKV1-9*01	2	3.8	83.2%	3.8	85.3%	2.2%
9	HIGKV1-27*01	1	3.8	83.2%	3.8	84.2%	1.8%
10	HIGKV1-8*01	1	5.8	83.2%	5.8	84.2%	0.7%
11	HIGKV1-12*01	1	3.8	82.1%	3.8	83.2%	1.7%
12	HIGKV1-12*02	1	3.8	82.1%	3.8	83.2%	1.7%
13	HIGKV1D-12*01	1	3.8	82.1%	3.8	83.2%	1.6%
14	HIGKV1D-12*02	1	3.8	82.1%	3.8	83.2%	1.6%
15	HIGKV1-18*01	3	3.8	82.1%	3.8	85.3%	1.3%
16	HIGKV1-18*02	3	3.8	82.1%	3.8	85.3%	1.3%
17	HIGKV1-6*01	1	4.8	82.1%	4.8	83.2%	0.9%
18	HIGKV1-6*02	1	4.8	82.1%	4.8	83.2%	0.9%
19	HIGKV3-11*01	3	2.0	81.1%	2.0	84.2%	8.0%
20	HIGKV1-17*01	2	3.8	81.1%	4.8	83.2%	1.1%
21	HIGKV1-17*02	2	3.8	81.1%	4.8	83.2%	1.1%
22	HIGKV1-17*03	3	3.8	81.1%	4.8	84.2%	1.1%
23	HIGKV3-11*02	4	2.0	80.0%	3.0	84.2%	8.0%
24	HIGKV3-15*01	2	2.9	78.9%	2.9	81.1%	6.3%
25	HIGKV3-20*01	3	2.0	78.1%	2.0	81.3%	21.8%
26	HIGKV4-1*01	0	0.8	77.2%	0.8	77.2%	4.9%
27	HIGKV2D-29*01	0	1.8	76.0%	1.8	76.0%	2.0%
28	HIGKV2D-28*01	1	0.9	75.0%	0.9	76.0%	2.5%
29	HIGKV2-28*01	1	0.9	75.0%	0.9	76.0%	2.0%
30	HIGKV3D-29*02	1	1.8	75.0%	1.8	76.0%	2.0%
31	HIGKV2-24*01	1	2.8	75.0%	2.8	76.0%	0.9%
32	HIGKV2-30*01	4	2.8	73.0%	3.9	77.0%	2.0%
33	HIGKV2-30*02	4	2.8	73.0%	3.8	77.0%	2.0%

FIG. 31D

ID	Human	VH germline	Vernier positions	Partial charge: Non-human Vernier	Human identity: Low	Partial charge: All human Vernier	Human identity: High	Prevalence in repertoire
1	hIGHV3-23*01		9	-0.2	75.5%	0.8	82.7%	7.6%
2	hIGHV3-23*04		9	-0.2	75.5%	0.8	82.7%	7.6%
3	hIGHV3-23*02		9	-0.2	74.5%	0.8	81.6%	7.6%
4	hIGHV3-30*01		8	0.8	74.5%	1.8	80.6%	6.5%
5	hIGHV3-30*04		8	0.8	74.5%	1.8	80.6%	6.6%
6	hIGHV3-30*07		8	0.8	74.5%	1.8	80.6%	6.6%
7	hIGHV3-30*09		8	0.8	74.5%	1.8	80.6%	6.6%
8	hIGHV3-30*11		8	0.8	74.5%	1.8	80.6%	6.6%
9	hIGHV3-30*14		8	0.8	74.5%	1.8	80.6%	6.6%
10	hIGHV3-30*15		8	0.8	74.5%	1.8	80.6%	6.6%
11	hIGHV3-30*16		8	0.8	74.5%	1.8	80.6%	6.6%
12	hIGHV3-30*17		8	0.8	74.5%	1.8	80.6%	6.6%
13	hIGHV3-48*01		9	-0.2	74.5%	0.8	81.6%	2.4%
14	hIGHV3-48*02		9	-1.2	74.5%	-0.2	81.6%	2.4%
15	hIGHV3-48*03		9	-0.2	74.5%	0.8	81.6%	2.4%
16	hIGHV3-30*3*01		8	0.8	74.5%	1.8	80.6%	2.1%
17	hIGHV3-64*01		10	-0.2	74.5%	0.8	82.7%	0.7%
18	hIGHV3-64*02		10	-1.1	74.5%	-0.1	82.7%	0.7%
19	hIGHV3-23*03		9	-0.2	73.5%	0.8	80.6%	7.6%
20	hIGHV3-30*03		8	0.8	73.5%	1.8	79.6%	6.6%
21	hIGHV3-30*05		8	1.8	73.5%	2.8	79.6%	6.6%
22	hIGHV3-30*06		8	0.8	73.5%	1.8	79.6%	6.6%
23	hIGHV3-30*08		8	0.8	73.5%	1.8	79.6%	6.6%
24	hIGHV3-30*10		8	0.8	73.5%	1.8	79.6%	6.6%
25	hIGHV3-30*12		8	0.8	73.5%	1.8	79.6%	6.6%
26	hIGHV3-30*13		8	1.8	73.5%	2.8	79.6%	6.6%
27	hIGHV3-30*19		8	0.8	73.5%	1.8	79.6%	6.6%
28	hIGHV3-7*01		8	-0.2	73.5%	0.8	79.6%	3.5%
29	hIGHV3-33*02		8	-0.2	73.5%	0.8	79.6%	2.8%
30	hIGHV3-33*05		8	0.8	73.5%	1.8	79.6%	2.8%
31	hIGHV3-21*01		9	0.8	73.5%	1.8	80.6%	2.4%
32	hIGHV3-21*02		9	0.8	73.5%	1.8	80.6%	2.4%
33	hIGHV3-11*01		10	0.8	73.5%	1.8	81.6%	2.1%

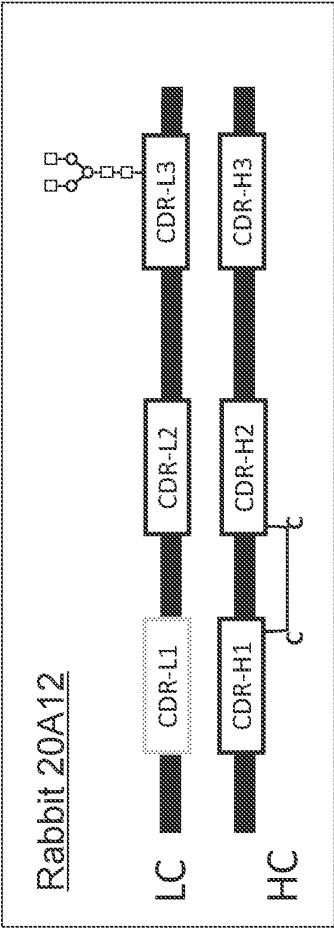


FIG. 32A

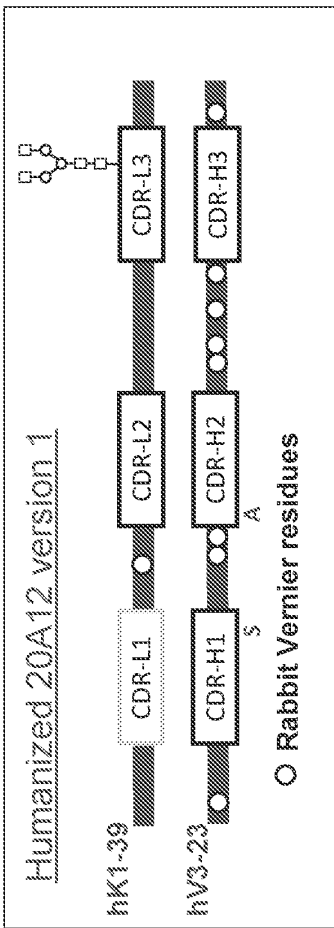


FIG. 32B

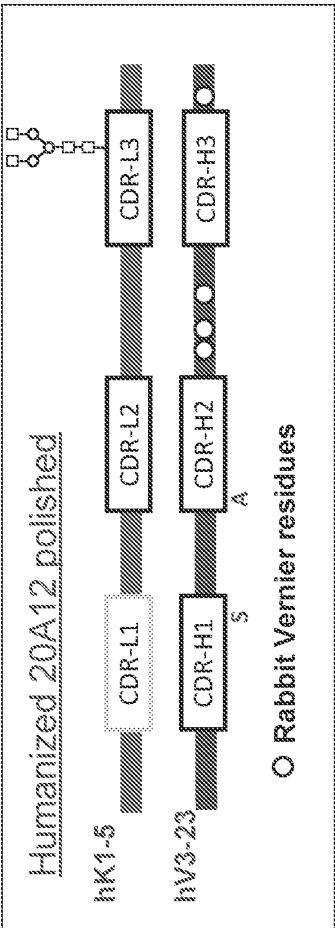


FIG. 32C

FIG. 32D

	Rab/humanized Variant	KD (nM)
rb.20A12		0.122
rb.20A12.5A		0.705
L1H1	All rabbit Vernier	2.447
L1H2	H: Q2V	1.585
L1H3	H: I48V	0.963
L1H4	H: A49S	1.377
L1H5	H: K71R	1.824
L1H6	H: S73N	2.241
L1H7	H: V78L	3.262
L1H8	H: F91Y	1.749
L1H9	H: P105R	2.014
L1H10	H: all human Vernier	2.792
L2H1	L: P43A	2.456
L2H10	All human Vernier	2.450

FIG. 33A

ID	Human VL germline	Vernier positions	Partial charge: Non-human Vernier	Human identity: Low	Partial charge: All human Vernier	Human identity: High	Prevalence in repertoire
1	hIGKV3-20*01	4	0.5	78.4%	-0.5	82.5%	21.8%
2	hIGKV1-5*01	4	2.3	78.4%	1.3	82.5%	4.7%
3	hIGKV1-5*02	4	2.3	78.4%	1.3	82.5%	4.7%
4	hIGKV1-5*03	4	2.3	78.4%	1.3	82.5%	4.7%
5	hIGKV1-9*01	3	2.4	78.4%	1.4	81.4%	2.2%
6	hIGKV1-27*01	4	2.3	78.4%	1.3	82.5%	1.8%
7	hIGKV4-1*01	4	-0.6	78.2%	-1.6	82.2%	4.9%
8	hIGKVID-39*01	4	2.3	77.3%	1.3	81.4%	13.3%
9	hIGKV1-39*01	4	2.3	77.3%	1.3	81.4%	12.7%
10	hIGKV3-15*01	5	1.4	77.3%	0.4	82.5%	6.3%
11	hIGKV1-12*01	4	2.3	77.3%	1.3	81.4%	1.7%
12	hIGKV1-12*02	4	2.3	77.3%	1.3	81.4%	1.7%
13	hIGKVID-12*01	4	2.3	77.3%	1.3	81.4%	1.6%
14	hIGKVID-12*02	4	2.3	77.3%	1.3	81.4%	1.6%
15	hIGKV1-16*01	4	2.3	77.3%	1.3	81.4%	1.3%
16	hIGKV1-16*02	4	2.3	77.3%	1.3	81.4%	1.3%
17	hIGKV1-17*03	4	2.4	77.3%	2.4	81.4%	1.1%
18	hIGKV1-8*01	4	4.3	77.3%	3.3	81.4%	0.7%
19	hIGKV3-11*01	4	0.4	76.3%	-0.6	80.4%	8.0%
20	hIGKV1-6*01	4	3.3	76.3%	2.3	80.4%	0.9%
21	hIGKV1-6*02	4	3.3	76.3%	2.3	80.4%	0.9%
22	hIGKV3-11*02	5	0.4	75.3%	0.4	80.4%	8.0%
23	hIGKVID-33*01	4	2.3	75.3%	1.3	79.4%	3.1%
24	hIGKV1-33*01	4	2.3	75.3%	1.3	79.4%	1.6%
25	hIGKV1-17*01	5	2.4	75.3%	2.4	80.4%	1.1%
26	hIGKV1-17*02	5	2.4	75.3%	2.4	80.4%	1.1%
27	hIGKV2D-28*01	4	-0.6	74.0%	-1.6	78.0%	2.5%
28	hIGKV2-28*01	4	-0.6	74.0%	-1.6	78.0%	2.0%
29	hIGKV2-30*01	4	1.4	74.0%	1.4	78.0%	2.0%
30	hIGKV2-30*02	4	1.4	74.0%	1.4	78.0%	2.0%

FIG. 33B

ID	Human VH germline	Vernier positions	Partial charge: Non-human Vernier	Human Identity: Low	Partial charge: human Vernier	Human Identity: High	Prevalence in repertoire
1	hIGHV3-53*01	10	1.6	74.5%	2.6	82.7%	1.1%
2	hIGHV3-53*02	10	1.6	74.5%	2.6	82.7%	1.1%
3	hIGHV3-53*03	10	1.6	74.5%	2.6	82.7%	1.1%
4	hIGHV3-53*04	10	3.3	74.5%	4.3	82.7%	1.1%
5	hIGHV3-66*01	10	1.6	74.5%	2.6	82.7%	0.8%
6	hIGHV3-66*02	10	1.6	74.5%	2.6	82.7%	0.8%
7	hIGHV3-66*04	10	1.6	74.5%	2.6	82.7%	0.8%
8	hIGHV4-4*01	8	2.5	73.7%	3.5	79.8%	1.7%
9	hIGHV4-4*02	8	2.5	73.7%	3.5	79.8%	1.7%
10	hIGHV3-48*01	10	1.6	73.5%	2.6	81.6%	2.4%
11	hIGHV3-48*02	10	0.6	73.5%	1.6	81.6%	2.4%
12	hIGHV3-66*03	10	1.6	73.5%	2.6	81.6%	0.8%
13	hIGHV4-59*03	9	1.6	73.2%	1.6	80.4%	3.3%
14	hIGHV4-59*06	9	1.6	73.2%	1.6	80.4%	3.3%
15	hIGHV1-69*02	10	1.7	72.4%	2.7	80.6%	7.7%
16	hIGHV1-69*04	10	1.7	72.4%	2.7	80.6%	7.7%
17	hIGHV1-69*09	10	1.7	72.4%	2.7	80.6%	7.7%
18	hIGHV1-69*10	10	1.7	72.4%	2.7	80.6%	7.7%
19	hIGHV3-23*03	10	1.6	72.4%	2.6	80.6%	7.6%
20	hIGHV5-51*01	10	2.6	72.4%	3.6	80.6%	6.0%
21	hIGHV5-51*03	10	2.6	72.4%	3.6	80.6%	6.0%
22	hIGHV5-51*04	10	2.6	72.4%	3.6	80.6%	6.0%
23	hIGHV4-59*01	9	1.6	72.4%	1.6	79.6%	3.3%
24	hIGHV4-59*02	9	1.6	72.4%	1.6	79.6%	3.3%
25	hIGHV4-59*07	9	1.6	72.4%	1.6	79.6%	3.3%
26	hIGHV3-21*01	10	2.6	72.4%	3.6	80.6%	2.4%
27	hIGHV3-21*02	10	2.6	72.4%	3.6	80.6%	2.4%
28	hIGHV3-48*03	10	1.6	72.4%	2.6	80.6%	2.4%
29	hIGHV4-4*08	9	1.6	72.4%	1.6	79.6%	1.7%
30	hIGHV4-59*04	10	1.6	72.2%	1.6	80.4%	3.3%

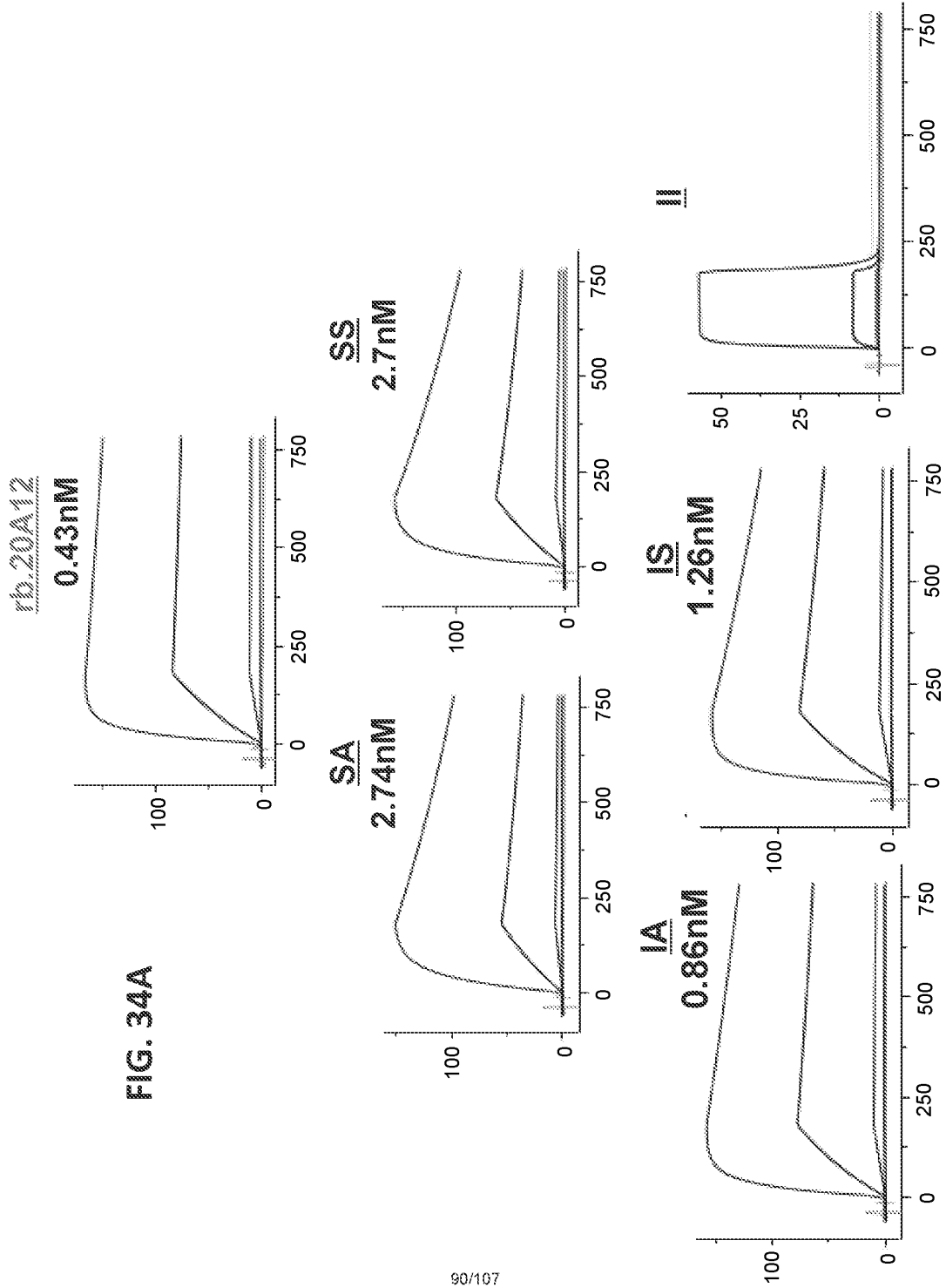
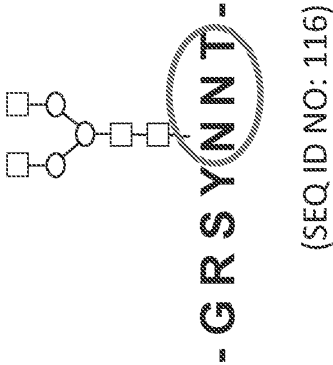


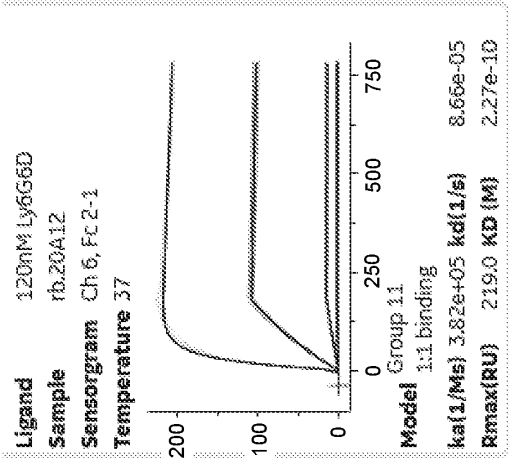
FIG. 34B



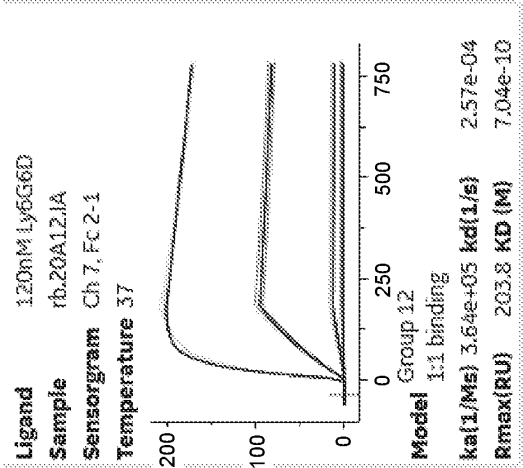
Mutation	KD (nM)
Parental NNT	0.43
QNT	0.28
QNV	0.22
SNT	0.25
SNA	0.27
ANT	0.26
NNA	0.26
NNV	0.22
GNT	0.34
SNV	0.23

FIG. 34C

Rabbit 20A12



Rabbit 20A12.1A



Hu.20A12.QNTv12

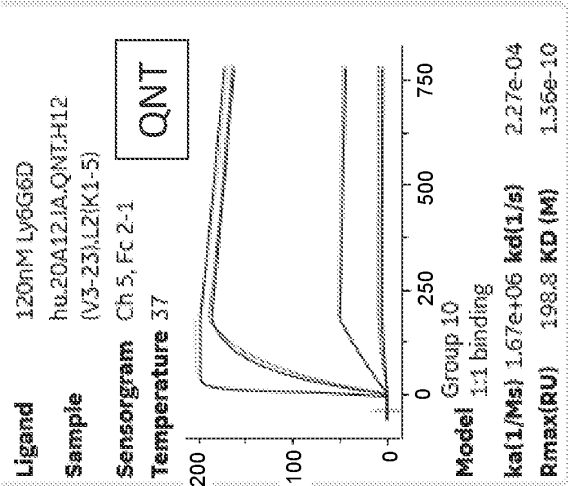
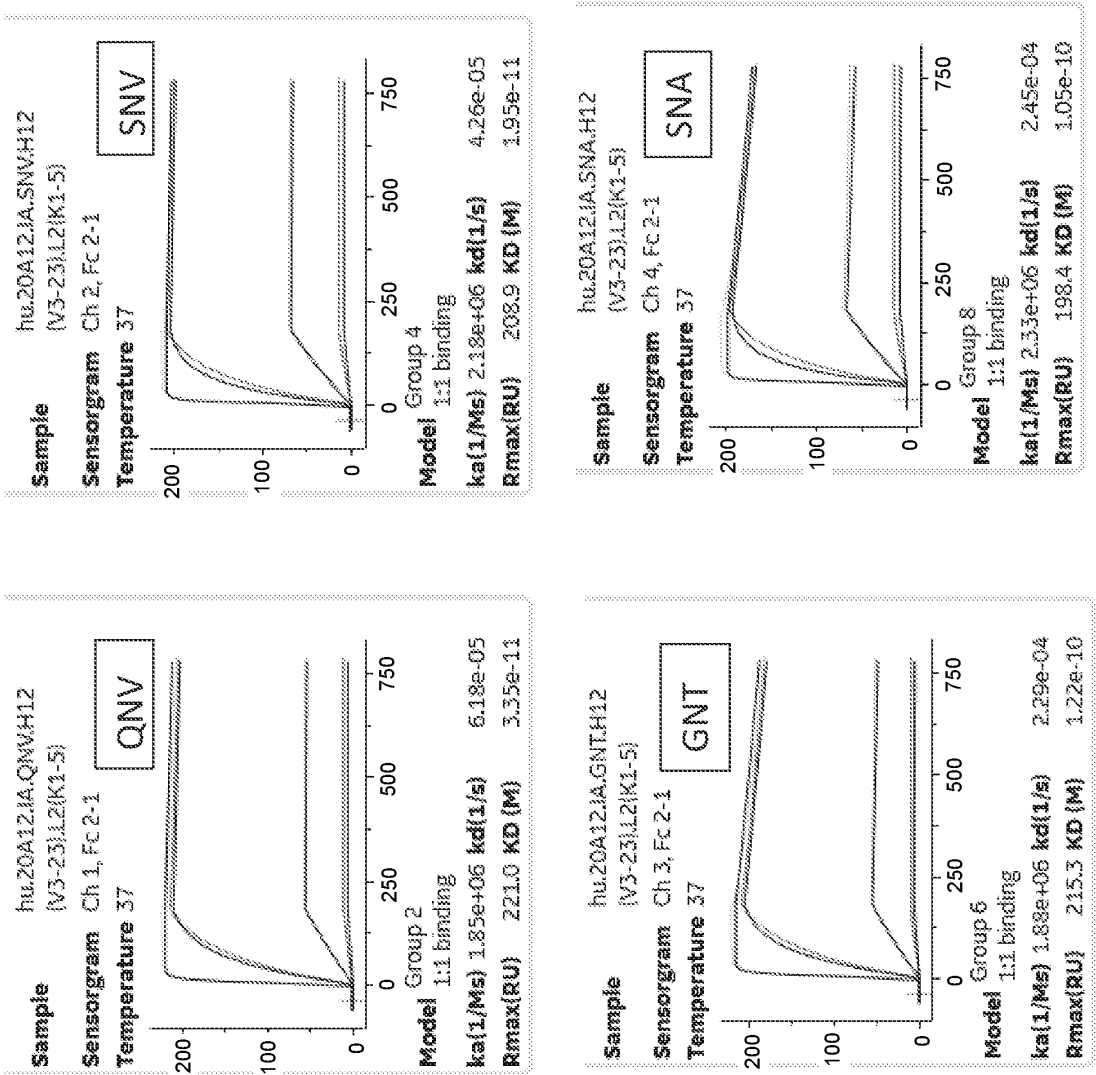


FIG. 34D



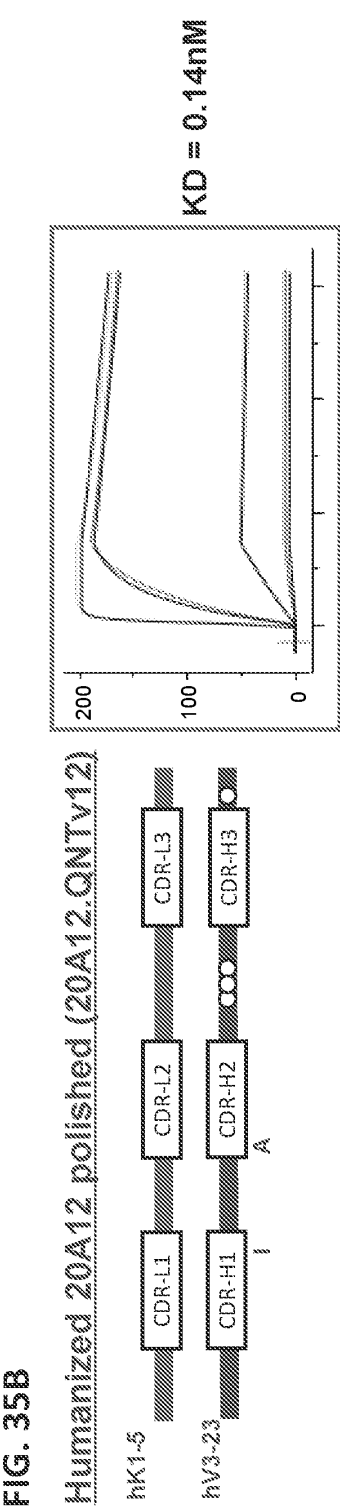
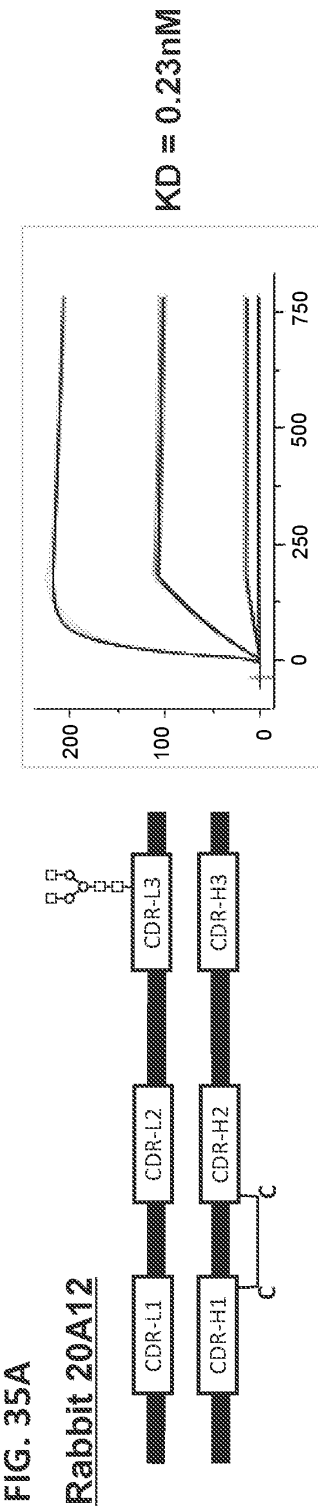
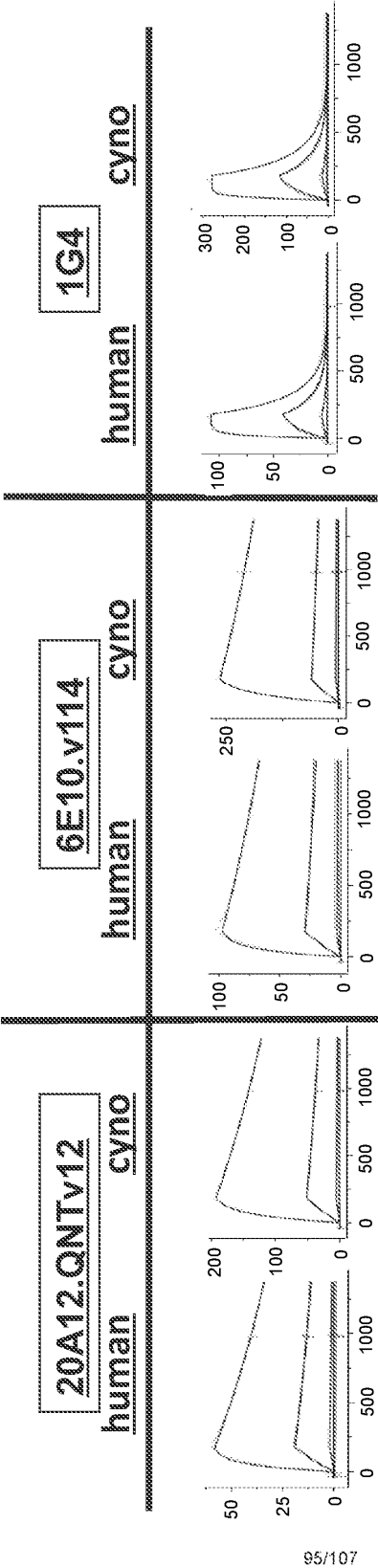


FIG. 36



Anti-Ly6G6D/CD3 TDB	human Ly6G6D	cyno Ly6G6D
	KD (nM)	KD (nM)
20A12.QNTv12/38E4v1	2.02	2.29
6E10.H11L4/38E4v1	1.58	1.87
1G4/38E4v1	16.30	13.12

FIG. 37

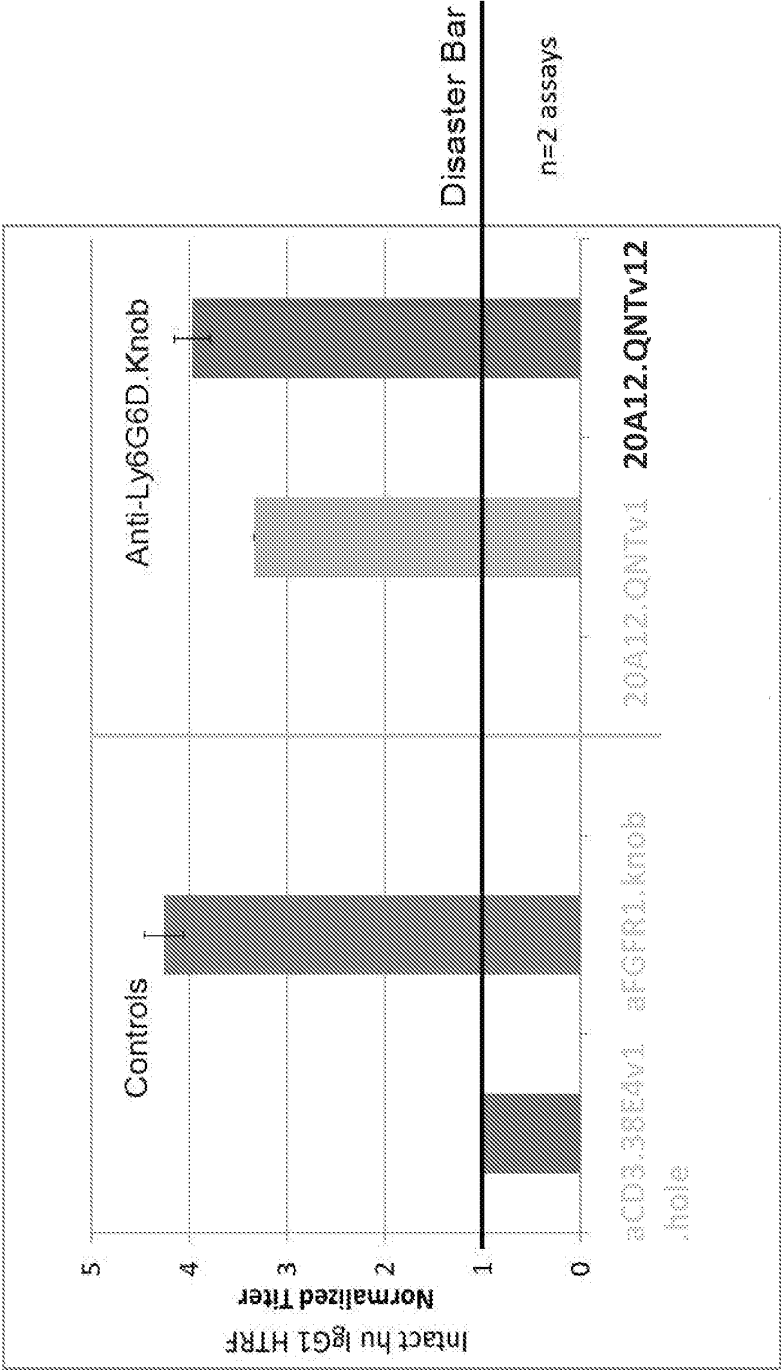


FIG. 38

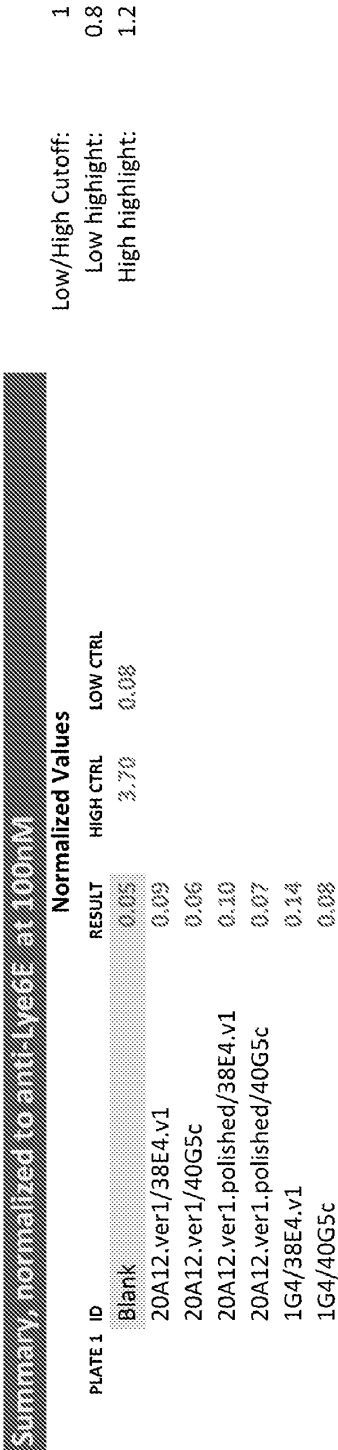


FIG. 39

	20A12.QNTv12/38E4v1	20A12.QNTv12/40G5c
SEC	Monomer loss (0.3%) is acceptable at t=2-wk	Monomer loss (0.4%) is acceptable at t=2-wk
Charge Variants	Main Peak loss (7.3%) is acceptable at t=2-wk	Main Peak loss (8.8%) is acceptable at t=2-wk
Reduced mass	no change upon stress	no change upon stress
Thermo Stress	20A12.QNTv12	20A12.QNTv12
	38E4v1	40G5c
AAPH Oxidation Stress	- D(50)A - N(55)T - D(55)G - D(101)Y - N(31)N - N(55)T - D(28)P	- N(55)T - D(54)G - N(31)Y - D(55)S - N(55)Y - D(101)Y - D(50)A - N(31)Y - N(27a)S
	- M(34) - W(52) - M(53)	- M(34) - W(52) - M(53) - W(50) - W(50)

No apparent issues.

Caution -- risk of delays, additional resource requirements and/or compromises on delivery method, shelf-life, etc...

High probability of delays, additional resource requirements and/or compromises on delivery method, shelf-life, etc.

FIG. 40A

Light chain, Kappa: Humanized antibody aligned to hu.20A12.K1-39.V3-23

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					
	K1-39	D	I	Q	M	T	Q	S	P	S	L	S	A	S	V	G	D	R	V	T	I	T	C	Q	A	S	E		S	I	T	R	Y	L	N	W	Y				
	K1-5	D	I	Q	M	T	Q	S	P	S	L	S	A	S	V	G	D	R	V	T	I	T	C	Q	A	S	E		S	I	T	R	Y	L	N	W	Y				
	K4-1	D	I	Q	M	T	Q	S	P	S	L	S	A	S	V	G	D	R	V	T	I	T	C	Q	A	S	E		S	I	T	R	Y	L	N	W	Y				
CDR L1																																									
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						
	K1-39	Q	Q	K	P	G	K	P	P	K	L	I	Y	D	A	S	K	L																							
	K1-5	Q	Q	K	P	G	K	P	P	K	L	I	Y	D	A	S	K	L																							
	K4-1	Q	Q	K	P	G	K	P	P	K	L	I	Y	D	A	S	K	L																							
CDR L2																																									
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					
	K1-39	T	L	T	I	S	S	L	O	P	E	F	A	T	Y	Y	C	Q	S	T	S	F	R	G	R	S	Y	N		N	T	F	G	G	G	T	K	V	E	I	K
	K1-5	T	L	T	I	S	S	L	O	P	E	F	A	T	Y	Y	C	Q	S	T	S	F	R	G	R	S	Y	N		N	T	F	G	G	G	T	K	V	E	I	K
	K4-1	T	L	T	I	S	S	L	O	P	E	F	A	T	Y	Y	C	Q	S	T	S	F	R	G	R	S	Y	N		N	T	F	G	G	G	T	K	V	E	I	K
CDR L3																																									

* Fv-CDR interactions: Padlan M.J. Immune (1994) 31:159; Padlan and Winter J.M.S. (1992) 224:307
* Vh-VL interactions: Padlan M.J. Immune (1994) 31:169

FIG. 40C

Light chain: kappa: Humanized antibody aligned to human germlines

Label 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	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	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136	137	138	139	140	141	142	143	144	145	146	147	148	149	150	151	152	153	154	155	156	157	158	159	160	161	162	163	164	165	166	167	168	169	170	171	172	173	174	175	176	177	178	179	180	181	182	183	184	185	186	187	188	189	190	191	192	193	194	195	196	197	198	199	200	201	202	203	204	205	206	207	208	209	210	211	212	213	214	215	216	217	218	219	220	221	222	223	224	225	226	227	228	229	230	231	232	233	234	235	236	237	238	239	240	241	242	243	244	245	246	247	248	249	250	251	252	253	254	255	256	257	258	259	260	261	262	263	264	265	266	267	268	269	270	271	272	273	274	275	276	277	278	279	280	281	282	283	284	285	286	287	288	289	290	291	292	293	294	295	296	297	298	299	300	301	302	303	304	305	306	307	308	309	310	311	312	313	314	315	316	317	318	319	320	321	322	323	324	325	326	327	328	329	330	331	332	333	334	335	336	337	338	339	340	341	342	343	344	345	346	347	348	349	350	351	352	353	354	355	356	357	358	359	360	361	362	363	364	365	366	367	368	369	370	371	372	373	374	375	376	377	378	379	380	381	382	383	384	385	386	387	388	389	390	391	392	393	394	395	396	397	398	399	400	401	402	403	404	405	406	407	408	409	410	411	412	413	414	415	416	417	418	419	420	421	422	423	424	425	426	427	428	429	430	431	432	433	434	435	436	437	438	439	440	441	442	443	444	445	446	447	448	449	450	451	452	453	454	455	456	457	458	459	460	461	462	463	464	465	466	467	468	469	470	471	472	473	474	475	476	477	478	479	480	481	482	483	484	485	486	487	488	489	490	491	492	493	494	495	496	497	498	499	500	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525	526	527	528	529	530	531	532	533	534	535	536	537	538	539	540	541	542	543	544	545	546	547	548	549	550	551	552	553	554	555	556	557	558	559	560	561	562	563	564	565	566	567	568	569	570	571	572	573	574	575	576	577	578	579	580	581	582	583	584	585	586	587	588	589	590	591	592	593	594	595	596	597	598	599	600	601	602	603	604	605	606	607	608	609	610	611	612	613	614	615	616	617	618	619	620	621	622	623	624	625	626	627	628	629	630	631	632	633	634	635	636	637	638	639	640	641	642	643	644	645	646	647	648	649	650	651	652	653	654	655	656	657	658	659	660	661	662	663	664	665	666	667	668	669	670	671	672	673	674	675	676	677	678	679	680	681	682	683	684	685	686	687	688	689	690	691	692	693	694	695	696	697	698	699	700	701	702	703	704	705	706	707	708	709	710	711	712	713	714	715	716	717	718	719	720	721	722	723	724	725	726	727	728	729	730	731	732	733	734	735	736	737	738	739	740	741	742	743	744	745	746	747	748	749	750	751	752	753	754	755	756	757	758	759	760	761	762	763	764	765	766	767	768	769	770	771	772	773	774	775	776	777	778	779	780	781	782	783	784	785	786	787	788	789	790	791	792	793	794	795	796	797	798	799	800	801	802	803	804	805	806	807	808	809	810	811	812	813	814	815	816	817	818	819	820	821	822	823	824	825	826	827	828	829	830	831	832	833	834	835	836	837	838	839	840	841	842	843	844	845	846	847	848	849	850	851	852	853	854	855	856	857	858	859	860	861	862	863	864	865	866	867	868	869	870	871	872	873	874	875	876	877	878	879	880	881	882	883	884	885	886	887	888	889	890	891	892	893	894	895	896	897	898	899	900	901	902	903	904	905	906	907	908	909	910	911	912	913	914	915	916	917	918	919	920	921	922	923	924	925	926	927	928	929	930	931	932	933	934	935	936	937	938	939	940	941	942	943	944	945	946	947	948	949	950	951	952	953	954	955	956	957	958	959	960	961	962	963	964	965	966	967	968	969	970	971	972	973	974	975	976	977	978	979	980	981	982	983	984	985	986	987	988	989	990	991	992	993	994	995	996	997	998	999	1000	1001	1002	1003	1004	1005	1006	1007	1008	1009	1010	1011	1012	1013	1014	1015	1016	1017	1018	1019	1020	1021	1022	1023	1024	1025	1026	1027	1028	1029	1030	1031	1032	1033	1034	1035	1036	1037	1038	1039	1040	1041	1042	1043	1044	1045	1046	1047	1048	1049	1050	1051	1052	1053	1054	1055	1056	1057	1058	1059	1060	1061	1062	1063	1064	1065	1066	1067	1068	1069	1070	1071	1072	1073	1074	1075	1076	1077	1078	1079	1080	1081	1082	1083	1084	1085	1086	1087	1088	1089	1090	1091	1092	1093	1094	1095	1096	1097	1098	1099	1100	1101	1102	1103	1104	1105	1106	1107	1108	1109	1110	1111	1112	1113	1114	1115	1116	1117	1118	1119	1120	1121	1122	1123	1124	1125	1126	1127	1128	1129	1130	1131	1132	1133	1134	1135	1136	1137	1138	1139	1140	1141	1142	1143	1144	1145	1146	1147	1148	1149	1150	1151	1152	1153	1154	1155	1156	1157	1158	1159	1160	1161	1162	1163	1164	1165	1166	1167	1168	1169	1170	1171	1172	1173	1174	1175	1176	1177	1178	1179	1180	1181	1182	1183	1184	1185	1186	1187	1188	1189	1190	1191	1192	1193	1194	1195	1196	1197	1198	1199	1200	1201	1202	1203	1204	1205	1206	1207	1208	1209	1210	1211	1212	1213	1214	1215	1216	1217	1218	1219	1220	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FIG. 41

SEC	Low Con His-Acetate, pH 5.5. Monomer loss (-0.1%) is acceptable at t=2-wk
Reduced mass	Masses are as expected with no change upon stress
Peptide mapping	Thermal Stress Platform Test Data (Low Con His-Acetate, pH 5.5) - N(30)N - D(95a)A - N(32)S - D(94)G and D(58)Y in CDR-H2 is unstable, 30.2% increase in isomerization (17.0% in t=0 and 47.2% in t=2-wk) *unable to determine site of isomerization Thermal Stress PBS Test Data (PBS, pH 7.4) - 0.3% increase in N(30)N deamidation (2.9% in t=0 and 3.2% in t=2-wk) - 0.5% increase in D(95a)A isomerization (1.5% in t=0 and 2.0% in t=2-wk) - -0.4% decrease in N(32)S deamidation (3.3% in t=0 and 2.9% in t=2-wk) - 18.0% increase in D(54)G and D(58)Y isomerization (16.9% in t=0 and 34.9% in t=2-wk) *unable to determine site of isomerization

FIG. 42

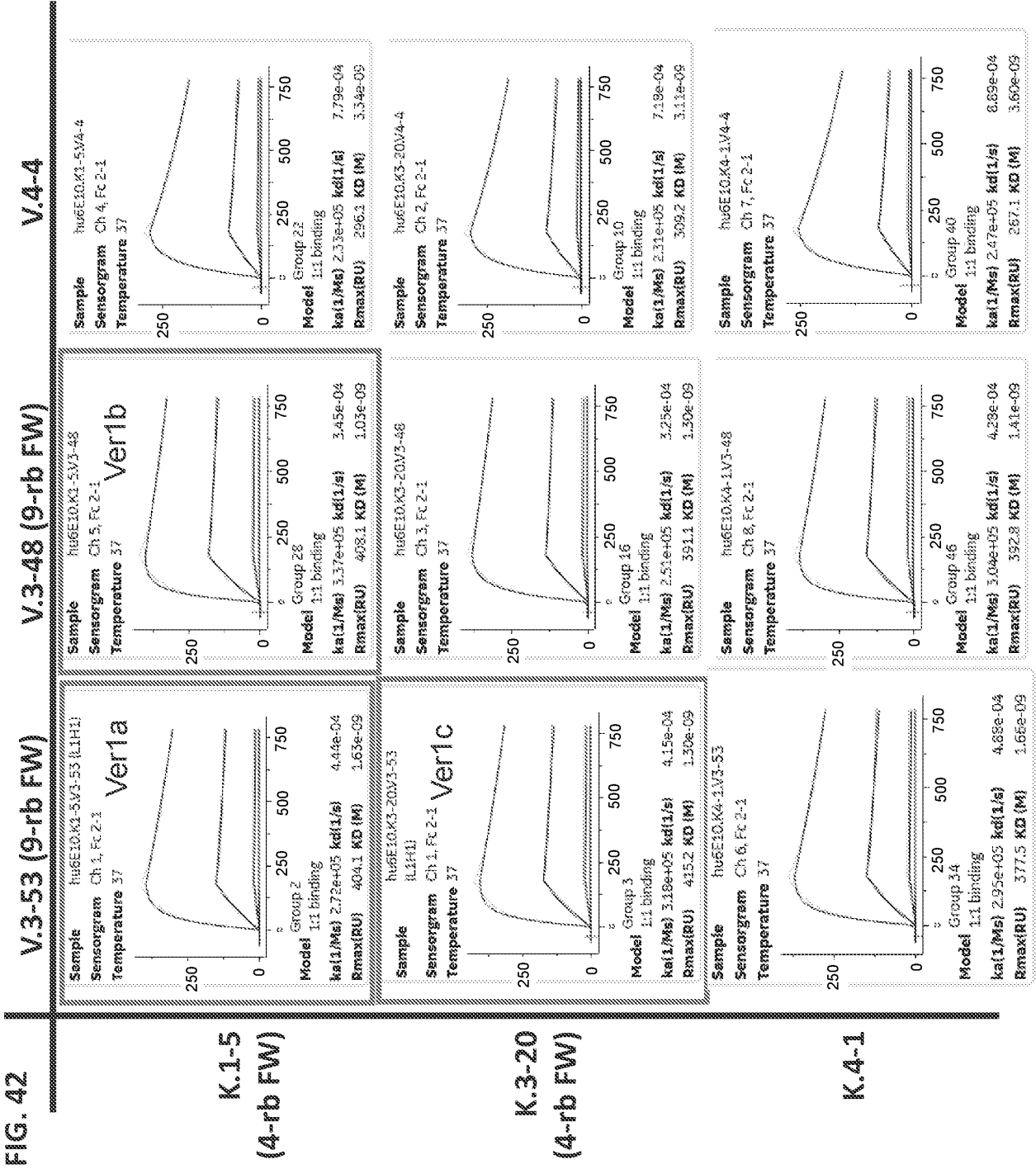


FIG. 43A

Light chain, Kappa: Humanized antibody aligned to hu.6E10.K3-20

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			
hu.6E10.K3-20	E	A	V	L	T	Q	S	P	Q	T	L	S	L	S	P	Q	E	R	A	T	L	S	C	Q	S	S	E	S	V	W	H	N	N	W	L	A	W	F
hu.6E10.K1-5	Q	A	L	T	Q	S	P	Q	T	L	S	L	S	P	Q	E	R	A	T	L	S	C	Q	S	S	E	S	V	W	H	N	N	W	L	A	W	F	
hu.6E10.K4-1	Q	A	V	L	T	Q	S	P	Q	T	L	S	L	S	P	Q	E	R	A	T	L	S	C	Q	S	S	E	S	V	W	H	N	N	W	L	A	W	F

CPR13

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
hu.6E10.K3-20	Q	Q	K	P	G	Q	R	P	R	L	L	I	Y	G	A	S	T	L	A	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F
hu.6E10.K1-5	Q	Q	K	P	G	Q	R	P	R	L	L	I	Y	G	A	S	T	L	A	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F
hu.6E10.K4-1	Q	Q	K	P	G	Q	R	P	R	L	L	I	Y	G	A	S	T	L	A	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F

CPR13

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	
hu.6E10.K3-20	T	L	T	I	S	R	L	E	P	E	D	F	A	V	Y	Y	C	A	G	G	Y	S	S	S	D	A	H	V	F	G	G	T	K	V	E	I	K
hu.6E10.K1-5	T	L	T	I	S	R	L	E	P	E	D	F	A	V	Y	Y	C	A	G	G	Y	S	S	S	D	A	H	V	F	G	G	T	K	V	E	I	K
hu.6E10.K4-1	T	L	T	I	S	R	L	E	P	E	D	F	A	V	Y	Y	C	A	G	G	Y	S	S	S	D	A	H	V	F	G	G	T	K	V	E	I	K

CPR13

SEQ ID NO.132

SEQ ID NO.133

SEQ ID NO.134

Heavy chain, Humanized antibody aligned to hu.6E10.V3-53

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					
hu.6E10.V3-53	E	Q	L	V	E	S	G	G	L	I	Q	P	G	S	L	R	L	S	C	A	V	S	G	L	S	L	S	T	N	S	I	N	W	V	R	Q	A	P	G	K	G
hu.6E10.V4-4	E	Q	L	V	E	S	G	G	L	I	Q	P	G	S	L	R	L	S	C	A	V	S	G	L	S	L	S	T	N	S	I	N	W	V	R	Q	A	P	G	K	G
hu.6E10.V3-49	E	Q	L	V	E	S	G	G	L	I	Q	P	G	S	L	R	L	S	C	A	V	S	G	L	S	L	S	T	N	S	I	N	W	V	R	Q	A	P	G	K	G

CDS-H1

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	72	73	74	75	76	77	78	79	80	81	82	83	84
hu.6E10.V3-53	L	E	W	I	G	Y	I	Y	H	G	Q	I	A	D	Y	A	S	W	A	K	G	R	F	T	I	S	K	D	S	S	K	N	T	V	Y	L	O	M	N	S	L	R	A					
hu.6E10.V4-4	L	E	W	I	G	Y	I	Y	H	G	Q	I	A	D	Y	A	S	W	A	K	G	R	F	T	I	S	K	D	S	S	K	N	T	V	Y	L	O	M	N	S	L	R	A					
hu.6E10.V3-49	L	E	W	I	G	Y	I	Y	H	G	Q	I	A	D	Y	A	S	W	A	K	G	R	F	T	I	S	K	D	S	S	K	N	T	V	Y	L	O	M	N	S	L	R	A					

CDS-H2

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	108	109	110	111	112	113		
hu.6E10.V3-53	E	D	T	A	V	Y	F	C	A	S	G	A	G	Y	S	L	F	T	L	W	S	P	O	T	L	V	T	V	S	S	SEQ ID NO: 135
hu.6E10.V4-4	E	D	T	A	V	Y	F	C	A	S	G	A	G	Y	S	L	F	T	L	W	S	P	O	T	L	V	T	V	S	S	SEQ ID NO: 136
hu.6E10.V3-49	E	D	T	A	V	Y	F	C	A	S	G	A	G	Y	S	L	F	T	L	W	S	P	O	T	L	V	T	V	S	S	SEQ ID NO: 137

CDS-H3

• FW-CDR interactions: Padiam Mol. Biomed. (1993) 31:165; Fokke and Winder, JMB (1992) 224:487
 • VH-VL interactions: Padiam Mol. Biomed. (1994) 31:163

Light chain, kappa: Not significantly aligned to human genes

[illegible]

FIG. 43D

Light chain, Kappa: Rabbit antibody aligned to human germlines

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	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	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136	137	138	139	140	141	142	143	144	145	146	147	148	149	150	151	152	153	154	155	156	157	158	159	160	161	162	163	164	165	166	167	168	169	170	171	172	173	174	175	176	177	178	179	180	181	182	183	184	185	186	187	188	189	190	191	192	193	194	195	196	197	198	199	200	201	202	203	204	205	206	207	208	209	210	211	212	213	214	215	216	217	218	219	220	221	222	223	224	225	226	227	228	229	230	231	232	233	234	235	236	237	238	239	240	241	242	243	244	245	246	247	248	249	250	251	252	253	254	255	256	257	258	259	260	261	262	263	264	265	266	267	268	269	270	271	272	273	274	275	276	277	278	279	280	281	282	283	284	285	286	287	288	289	290	291	292	293	294	295	296	297	298	299	300	301	302	303	304	305	306	307	308	309	310	311	312	313	314	315	316	317	318	319	320	321	322	323	324	325	326	327	328	329	330	331	332	333	334	335	336	337	338	339	340	341	342	343	344	345	346	347	348	349	350	351	352	353	354	355	356	357	358	359	360	361	362	363	364	365	366	367	368	369	370	371	372	373	374	375	376	377	378	379	380	381	382	383	384	385	386	387	388	389	390	391	392	393	394	395	396	397	398	399	400	401	402	403	404	405	406	407	408	409	410	411	412	413	414	415	416	417	418	419	420	421	422	423	424	425	426	427	428	429	430	431	432	433	434	435	436	437	438	439	440	441	442	443	444	445	446	447	448	449	450	451	452	453	454	455	456	457	458	459	460	461	462	463	464	465	466	467	468	469	470	471	472	473	474	475	476	477	478	479	480	481	482	483	484	485	486	487	488	489	490	491	492	493	494	495	496	497	498	499	500	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525	526	527	528	529	530	531	532	533	534	535	536	537	538	539	540	541	542	543	544	545	546	547	548	549	550	551	552	553	554	555	556	557	558	559	560	561	562	563	564	565	566	567	568	569	570	571	572	573	574	575	576	577	578	579	580	581	582	583	584	585	586	587	588	589	590	591	592	593	594	595	596	597	598	599	600	601	602	603	604	605	606	607	608	609	610	611	612	613	614	615	616	617	618	619	620	621	622	623	624	625	626	627	628	629	630	631	632	633	634	635	636	637	638	639	640	641	642	643	644	645	646	647	648	649	650	651	652	653	654	655	656	657	658	659	660	661	662	663	664	665	666	667	668	669	670	671	672	673	674	675	676	677	678	679	680	681	682	683	684	685	686	687	688	689	690	691	692	693	694	695	696	697	698	699	700	701	702	703	704	705	706	707	708	709	710	711	712	713	714	715	716	717	718	719	720	721	722	723	724	725	726	727	728	729	730	731	732	733	734	735	736	737	738	739	740	741	742	743	744	745	746	747	748	749	750	751	752	753	754	755	756	757	758	759	760	761	762	763	764	765	766	767	768	769	770	771	772	773	774	775	776	777	778	779	780	781	782	783	784	785	786	787	788	789	790	791	792	793	794	795	796	797	798	799	800	801	802	803	804	805	806	807	808	809	810	811	812	813	814	815	816	817	818	819	820	821	822	823	824	825	826	827	828	829	830	831	832	833	834	835	836	837	838	839	840	841	842	843	844	845	846	847	848	849	850	851	852	853	854	855	856	857	858	859	860	861	862	863	864	865	866	867	868	869	870	871	872	873	874	875	876	877	878	879	880	881	882	883	884	885	886	887	888	889	890	891	892	893	894	895	896	897	898	899	900	901	902	903	904	905	906	907	908	909	910	911	912	913	914	915	916	917	918	919	920	921	922	923	924	925	926	927	928	929	930	931	932	933	934	935	936	937	938	939	940	941	942	943	944	945	946	947	948	949	950	951	952	953	954	955	956	957	958	959	960	961	962	963	964	965	966	967	968	969	970	971	972	973	974	975	976	977	978	979	980	981	982	983	984	985	986	987	988	989	990	991	992	993	994	995	996	997	998	999	1000	1001	1002	1003	1004	1005	1006	1007	1008	1009	1010	1011	1012	1013	1014	1015	1016	1017	1018	1019	1020	1021	1022	1023	1024	1025	1026	1027	1028	1029	1030	1031	1032	1033	1034	1035	1036	1037	1038	1039	1040	1041	1042	1043	1044	1045	1046	1047	1048	1049	1050	1051	1052	1053	1054	1055	1056	1057	1058	1059	1060	1061	1062	1063	1064	1065	1066	1067	1068	1069	1070	1071	1072	1073	1074	1075	1076	1077	1078	1079	1080	1081	1082	1083	1084	1085	1086	1087	1088	1089	1090	1091	1092	1093	1094	1095	1096	1097	1098	1099	1100	1101	1102	1103	1104	1105	1106	1107	1108	1109	1110	1111	1112	1113	1114	1115	1116	1117	1118	1119	1120	1121	1122	1123	1124	1125	1126	1127	1128	1129	1130	1131	1132	1133	1134	1135	1136	1137	1138	1139	1140	1141	1142	1143	1144	1145	1146	1147	1148	1149	1150	1151	1152	1153	1154	1155	1156	1157	1158	1159	1160	1161	1162	1163	1164	1165	1166	1167	1168	1169	1170	1171	1172	1173	1174	1175	1176	1177	1178	1179	1180	1181	1182	1183	1184	1185	1186	1187	1188	1189	1190	1191	1192	1193	1194	1195	1196	1197	1198	1199	1200	1201	1202	1203	1204	1205	1206	1207	1208	1209	1210	1211	1212	1213	1214	1215	1216	1217	1218	1219	1220	1221	1222	1223	1224	1225	1226	1227	1228	1229	1230	1231	1232	1233	1234	1235	1236	1237	1238	1239	1240	1241	1242	1243	1244	1245	1246	1247	1248	1249	1250	1251	1252	1253	1254	1255	1256	1257	1258	1259	1260	1261	1262	1263	1264	1265	1266	1267	1268	1269	1270	1271	1272	1273	1274	1275	1276	1277	1278	1279	1280	1281	1282	1283	1284	1285	1286	1287	1288	1289	1290	1291	1292	1293	1294	1295	1296	1297	1298	1299	1300	1301	1302	1303	1304	1305	1306	1307	1308	1309	1310	1311	1312	1313	1314	1315	1316	1317	1318	1319	1320	1321	1322	1323	1324	1325	1326	1327	1328	1329	1330	1331	1332	1333	1334	1335	1336	1337	1338	1339	1340	1341	1342	1343	1344	1345	1346	1347	1348	1349	1350	1351	1352	1353	1354	1355	1356	1357	1358	1359	1360	1361	1362	1363	1364	1365	1366	1367	1368	1369	1370	1371	1372	1373	1374	1375	1376	1377	1378	1379	1380	1381	1382	1383	1384	1385	1386	1387	1388	1389	1390	1391	1392	1393	1394	1395	1396	1397	1398	1399	1400	1401	1402	1403	1404	1405	1406	1407	1408	1409	1410	1411	1412	1413	1414	1415	1416	1417	1418	1419	1420	1421	1422	1423	1424	1425	1426	1427	1428	1429	1430	1431	1432	1433	1434	1435	1436	1437	1438	1439	1440	1441	1442	1443	1444	1445	1446	1447	1448	1449	1450	1451	1452	1453	1454	1455	1456	1457	1458	1459	1460	1461	1462	1463	1464	1465	1466	1467	1468	1469	1470	1471	1472	1473	1474	1475	1476
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