

1	MEPLRLILLLEVTLELGAHNTTVFQGVAGQSLQVSCPYDSMKHHWGRRKAWCRQLGEKGPC	60
	+ PL LL+LLE + + V Q VAGQ+L V C Y +K WC++ C	
6	LHPLLLLLLLEFPGSQAQS-KAQVLQSVAGQTLTVRCQYPFTGSLYEKKGCWCKEASAL-VC	63
61	QRVVSTHNLWLLSFLRRWNGSTAITDDTLGGTLTITLRLNLQPHDAGLYQCQSLHGSEADT	120
	R+V++ ++ W I DD G T+T+ +L+ D+G Y C+ S+	
64	IRLVTSSKPRITMA-----WTSRFTIWDDPDAGFFTVMTDLREEDSGHYWCRIYRPSDNSV	119
121	LRKVLVEVLADP 132 <u>TREM-2</u> Human	
	+ V ++ P	
120	SKSVRFYLVVSP 131 NCTR2_HUMAN	

FIG. 1A

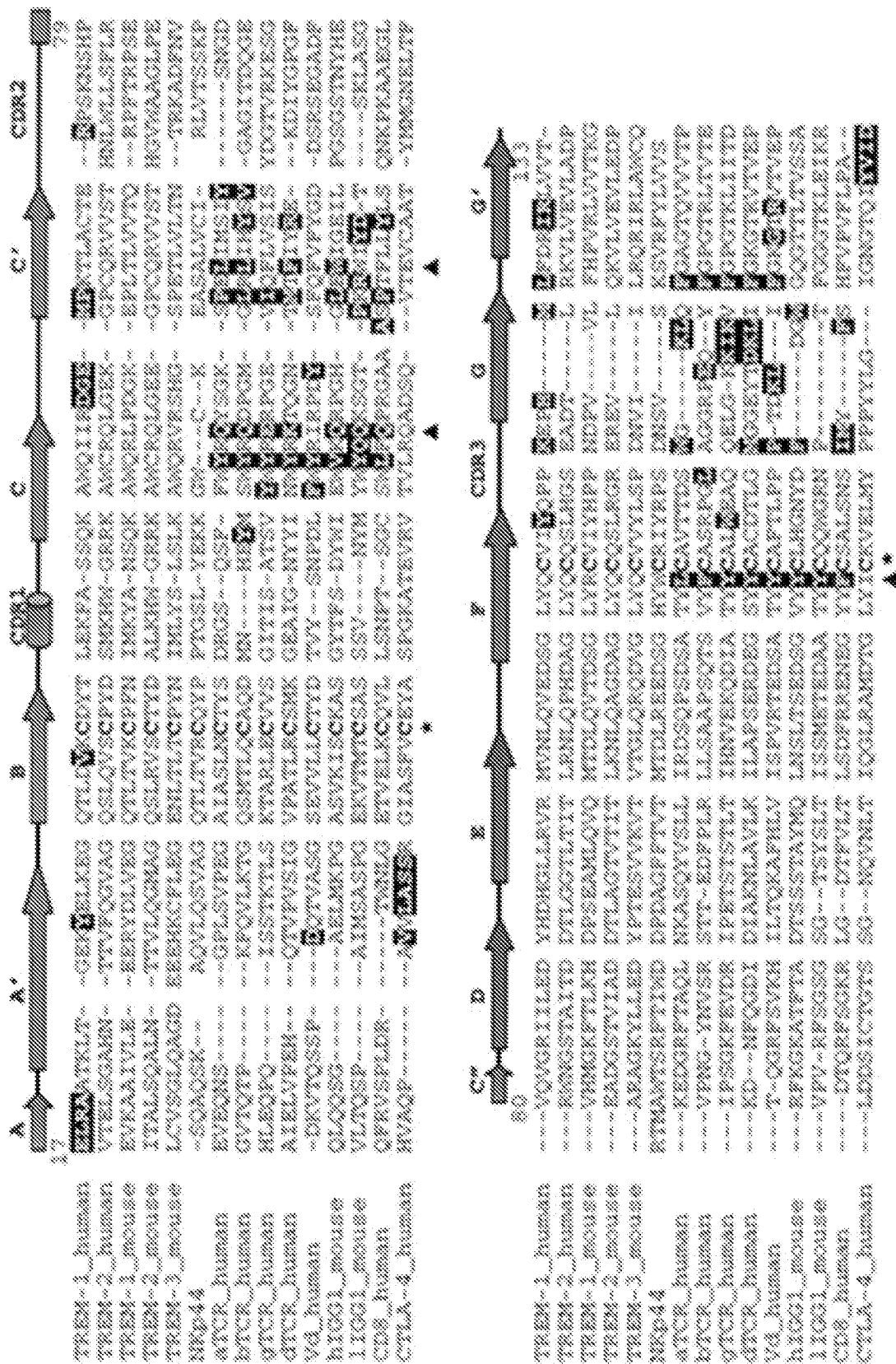


FIG. 1B

sp|Q9NZC2|TREM2_HUMAN Triggering receptor expressed on myeloid cells 2 OS=Homo sapiens GN=TREM2 PE=1 SV=1
Sequence ID: i0|35715 Length: 230 Number of Matches: 1
Range 1: 6 to 110

Score	Expect	Method	Identities	Positives	Gaps	Frame
42.7 bits(99)	1e-09(1)	Compositional matrix adjust.	34/107(32%)	49/107(45%)	4/107(3%)	
Features:						
TREM1	9	LLMMLFVSELRAATKLTTEKYTELKKEQTLQVWCQDTLTKFTASSQKAW---QIIRDCGEHPT	66			
TREM2	6	LL+LFFV+EL A + ++ CO+L V C Y K +KAW Q+ G +				
		LLILLFVTLSGANTT---VFQGVAGQSLOVSCFYDSKXKXKGRHAWCRQLGZKGCQGRV	63			
TREM1	67	LACTERPSKNSHPVQVGHIIILEDYNDHNGILKRVHVNLOVEDSGLYQC	113			
TREM2	64	++ + G + D G L + + NLO D+GLYQC				
		VSTNNLWLLSFLRRWNGSTATTDQTLGGTLITLNHNPDAAGLYQC	110			

FIG. 2

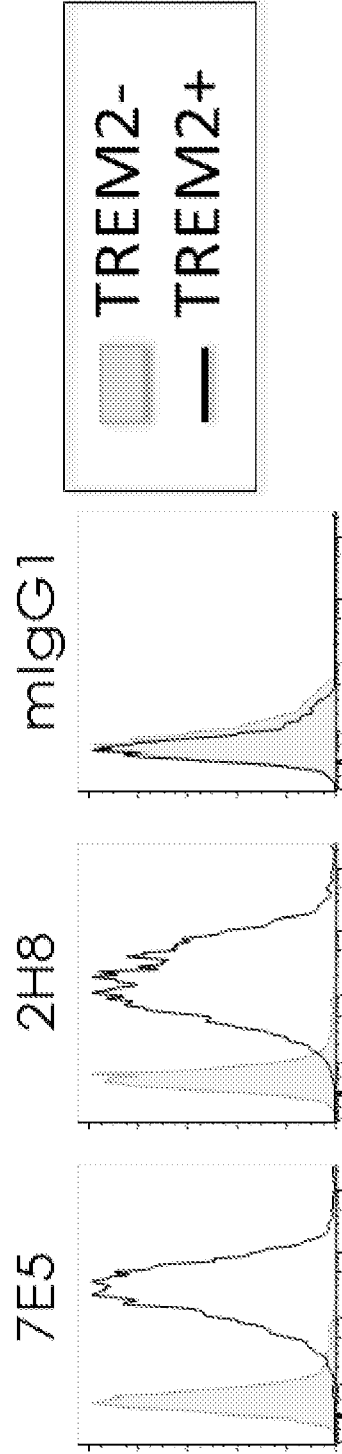


FIG. 3A

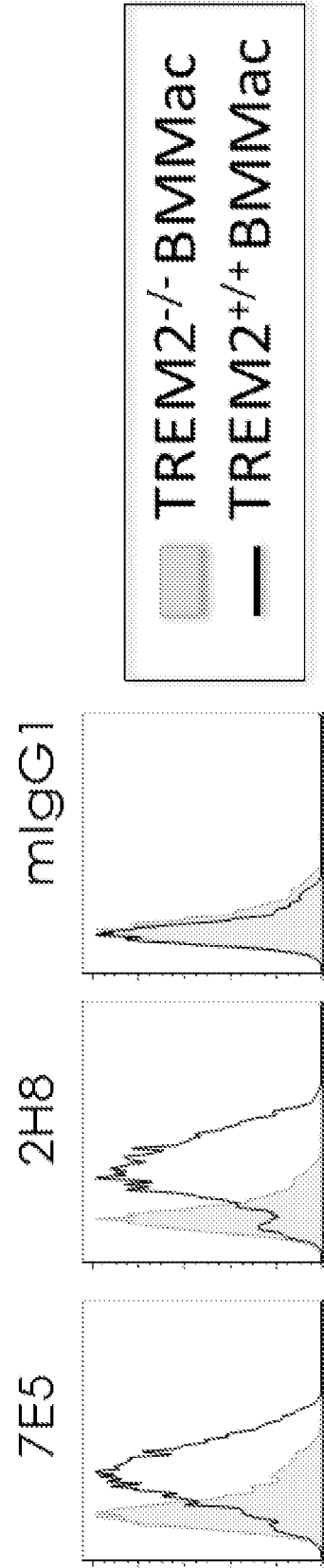


FIG. 3B

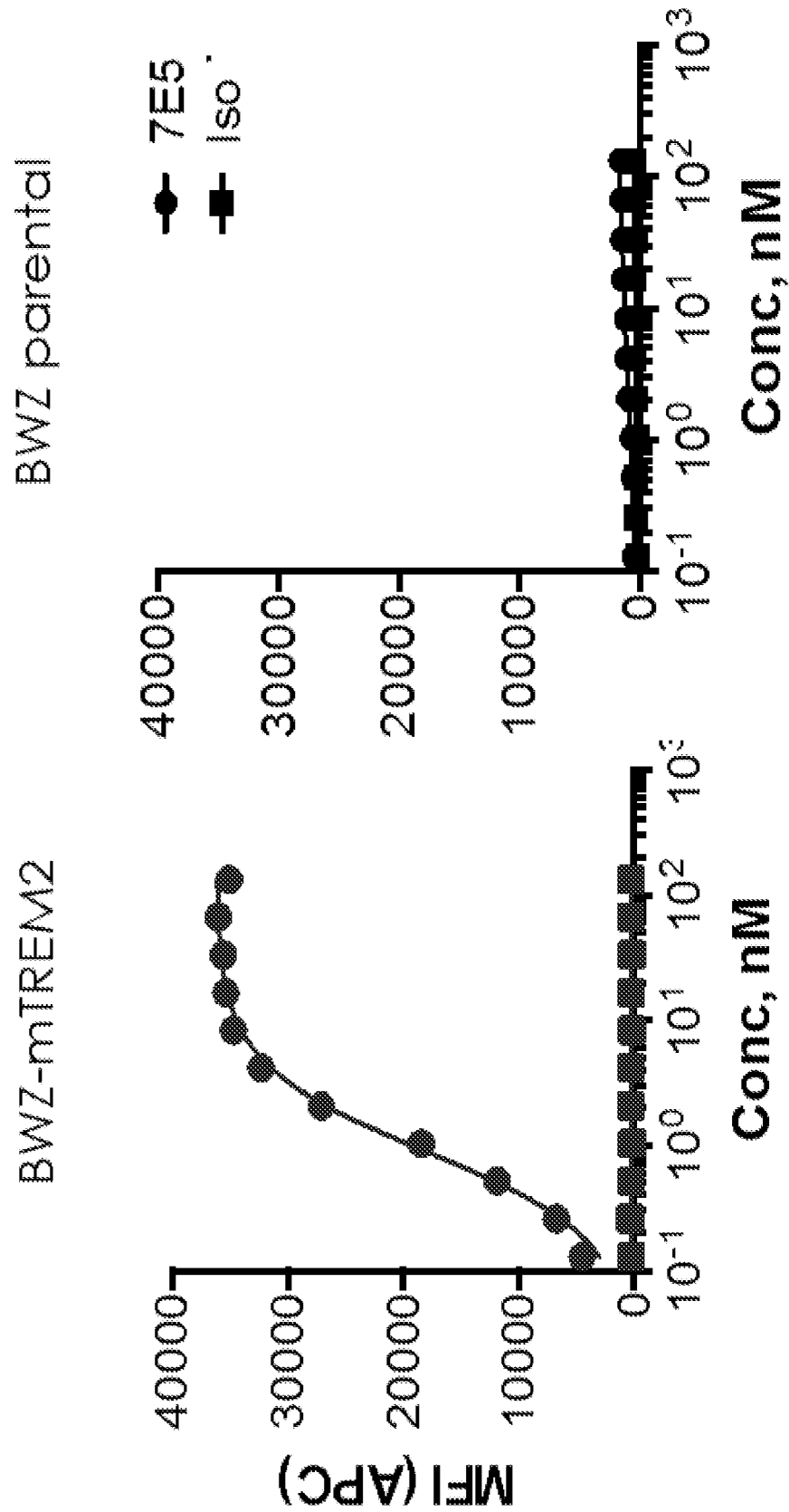


FIG. 3C

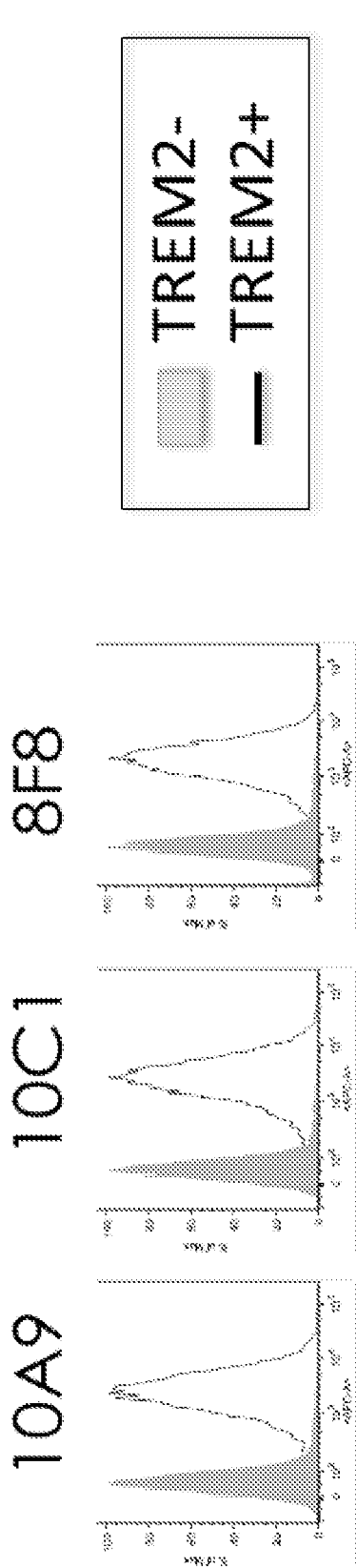


FIG. 4A

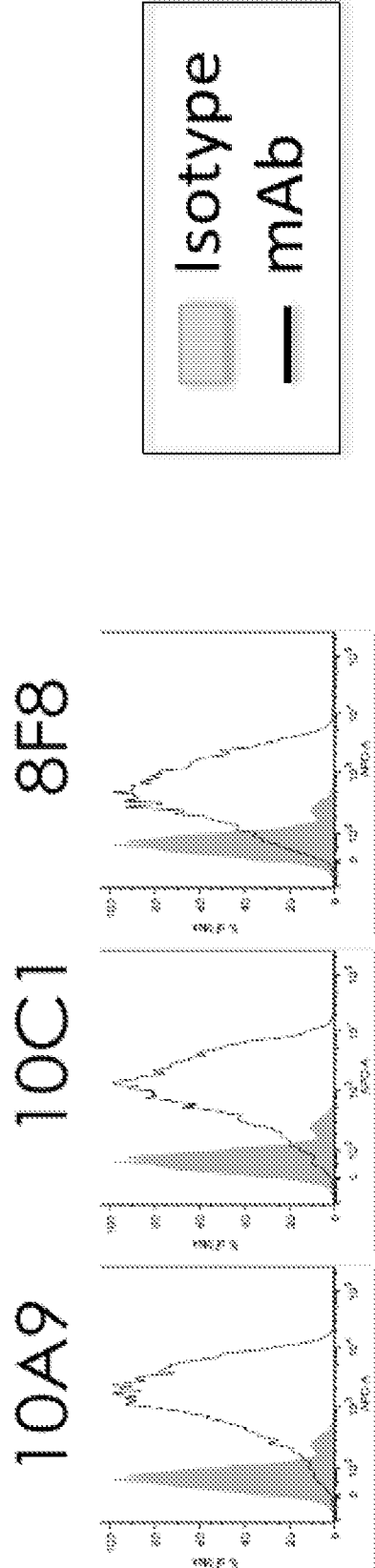


FIG. 4B

Potential humanized sequence based on IMGT IGKV2-29*02 acceptor framework (AbM CDR definition)

IGKV2-29*02 DIVMTQTPLSLSVTPGQPASISCKSSQSLHSDGKTYLYWLQKPGQSPQLLIYEVSNRFS

GVPDRFSGSGTDFTLKISRVEADVGYYCMQSIQLPP

Joining region IMGT J00242 | IGKJ2*01 | YTFGQGTKLEIK

seq 10 20 30 40 50 60
Abm 10 20 30abcde 40 50 60
b b b p p b b b b i i i i i
DVNMTQTPLSLPVSIGDQASISC RSSQSLVHNSGYTLH WYIQKPGSGPKLITY KVSNNRFS
T2-9F5.1

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2-29*02 D:\VMTQ\PLSLSVTPGQ\PASIC KSSQSLHSDGKTYLY WYLQKPGQSPQLLIY EVSNRFS

h9F5-L1 DIVMTQTPLSLSVTPGQPASISC RSSQSLVHSNGYTYLH WYLQKPGQSPQLLIY KVSNRFS

NGYTYLH WYLQKPGQSPQLLIY KVSNE

100

seq
AbM

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2-29*02 GVPDRFSGSGTDFTLKISRVEAEDVGVYYC MQSIQLPP FGQGTKLEIK

h9F5-L1 GVPDRFSGSGTDFTLKISRVEAEDGVYYC **SQSTRVPYT** FGQGTKEIK

VG VYYC

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	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	
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(1) CDR sequences noted in **bold**. CDR definitions are AbM from website www.bioinf.org.uk/abs/.
(2) Human germline and joining sequences from IMG® the international Immunogenetics® information system www.imgt.org (founder and director: Marie-Paule Lefranc, Montpellier, France).
(3) Residue numbering shown as sequential (seq) or according to Chothia from website www.bioinf.org.uk/abs/ (AbM).
(4) "b" notes buried sidechain; "p" notes partially buried; "i" notes sidechain at interface between VH and VL domains.
(5) Sequence differences between human and murine germlines noted by asterisk (*). (6) Potential additional mutations in frameworks are noted below sequence.
(7) Potential changes in CDR sequences noted below each CDR sequence. These may prevent asparagine (N) deamidation or isospartate (DG) formation).

FIG. 4C

Potential humanized sequence based on IMGT IGHV1-46*01 acceptor framework (AbM CDR definition)

IGHV1-46*01 QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYMHVWVROAPGGGLEWMIINPSGGSTS

YAKQFQGRVTMTTRDTSTSTVYMEISSLRSRSEDVAVYCAR

Joining region IMGT J00256|IGHJ4*01|YFDYWGQGLTVTVSS

		10	20	30	40	50	
seq		10	20	30	40	50	
AbM		10	20	30	40	50	a
		b b b	p b b b b	b b b	b i i i	ibb b	
T2-9F5.1		QVQLQQSGPELVKPGASLIKISKAS	GYAFSSSSMMN	WVKQRPQKGLEWIG	RIYPGDGDTN		
		* * *	z z	* * *	z		
1-46*01		QVQLVQSGAEVKKPGASVKVSCKAS	GYTFTSYMH	WVROAPGGGLEWIG	IINPSGGSTS		
h9F5-H1		QVQLVQSGAEVKKPGASVKVSCKAS	GYAFSSSSMMN	WVROAPGGGLEWIG	RIYPGDGDTN		
h9F5-H2		QVQLVQSGAEVKKPGASVKVSCKAS	GYAFSSSSMMN	WVROAPGGGLEWIG	RIYPGDGDTN		
h9F5-H3		QVQLVQSGAEVKKPGASVK:SKAS	GYAFSSSSMMN	WVROAPGGGLEWIG	RIYPGDGDTN		
		V	^		z	#	
		60	70	80	90	100	110 120
seq		60	70	80	abc	90	110 120
AbM		60	70	80	abc	90	110 120
		i b b b b	x b b b b	bibibb		i b b b	
T2-9F5.1		YNGEFRVRATLTADTSTTAYMQLSLTSDS	AVYFCAR	LLRNQPGESYAMDY	WGQGSLTVTVSS		
		*** ** z z z	** z *	*	z		
1-46*01		YAKQFQGRVTMTTRDTSTSTVYMEISSLRSRSEDVAVYCAR		LLRNQPGESYAMDY	WGQGSLTVTVSS		
h9F5-H1		YAKQFQGRVTMTTRDTSTSTVYMEISSLRSRSEDVAVYCAR		LLRNQPGESYAMDY	WGQGSLTVTVSS		
h9F5-H2		YAKQFQGRVTMTTRDTSTSTVYMEISSLRSRSEDVAVYCAR		LLRNQPGESYAMDY	WGQGSLTVTVSS		
h9F5-H3		YAKQFQGRVTMTTRDTSTSTVYMEISSLRSRSEDVAVYCAR		LLRNQPGESYAMDY	WGQGSLTVTVSS		
		N	F	#			

deamidation substitutions: Q/S/A
^ tryptophan oxidation substitutions: H/Y/F
@ isoaspartate substitutions: Q/S/A

h9F5-H1 is a "CDR-swap" with no changes to human framework. Subsequent sequences alter framework changes

shown in red (compared to sequence above it).

- (1) CDR sequences noted in bold. CDR definitions are AbM from website www.bioinf.org.uk/abs/.
(2) Human germline and joining sequences from IMGT® the international Immunogenetics® information system www.imgt.org (founder and director: Marie-Paule Lefranc, Montpellier, France).
(3) Residue numbering shown as sequential (seq) or according to Chothia from website www.bioinf.org.uk/abs/ (AbM).
(4) "p" notes buried sidechain; "p" notes partially buried; "l" notes sidechain at interface between VH and VL domains.
(5) Sequence differences between human and murine germlines noted by asterisk (*). (6) Potential additional mutations in frameworks are noted below sequence.
(7) Potential changes in CDR sequences noted below each CDR sequence. These may prevent asparagine (N) deamidation, tryptophan (W) oxidation, or isoaspartate (DG) formation.

FIG. 4D

Mutation	Binding Reactivity (% WT)			
	T21-9 Fab	T22 Fab	T45-10 Fab	9F5 MAb
K42A	2.0 (2)	0.0 (0)	70.1 (22)	130.8 (26)
G45A	46.1 (9)	9.7 (1)	128.8 (34)	145.0 (19)
R77A	170.0 (24)	138.7 (12)	15.4 (2)	123.8 (22)
H114A	29.1 (0)	8.0 (2)	70.6 (8)	114.5 (29)
E151A	238.0 (21)	148.7 (22)	96.8 (9)	4.8 (6)
D152A	191.8 (86)	140.9 (32)	98.3 (15)	2.7 (1)
H154A	250.8 (59)	138.0 (33)	82.6 (0)	3.0 (2)
E156A	162.0 (20)	154.7 (61)	103.8 (12)	17.7 (13)

FIG. 4E

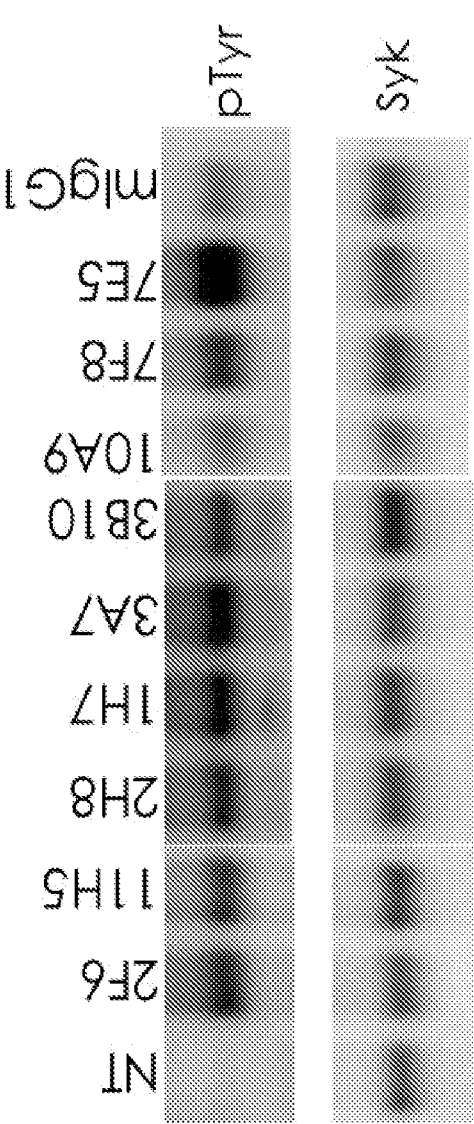


FIG. 5A

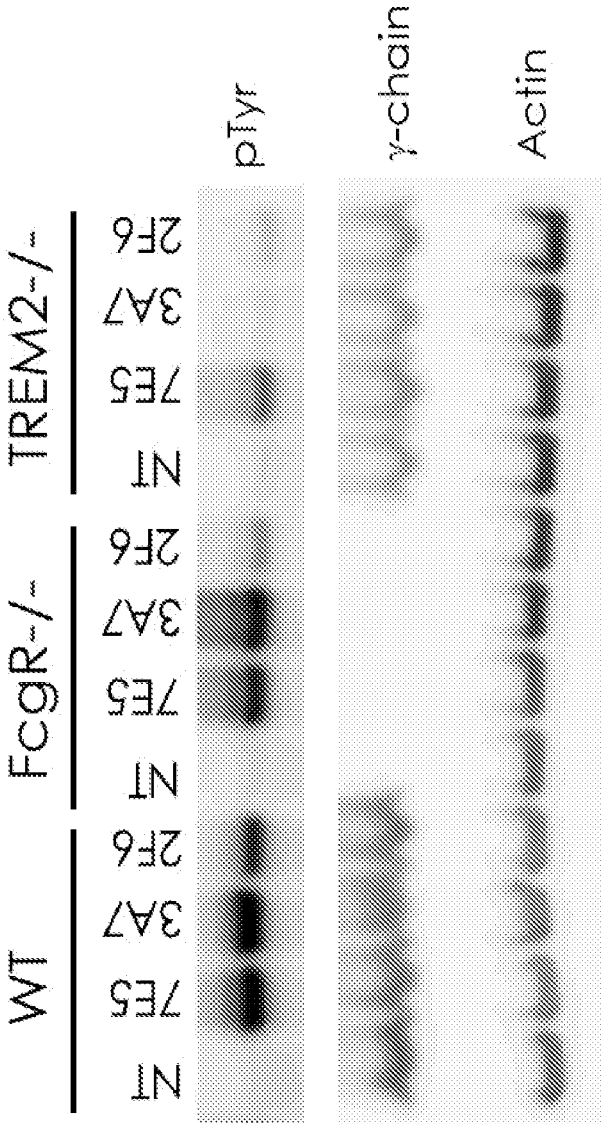


FIG. 5B

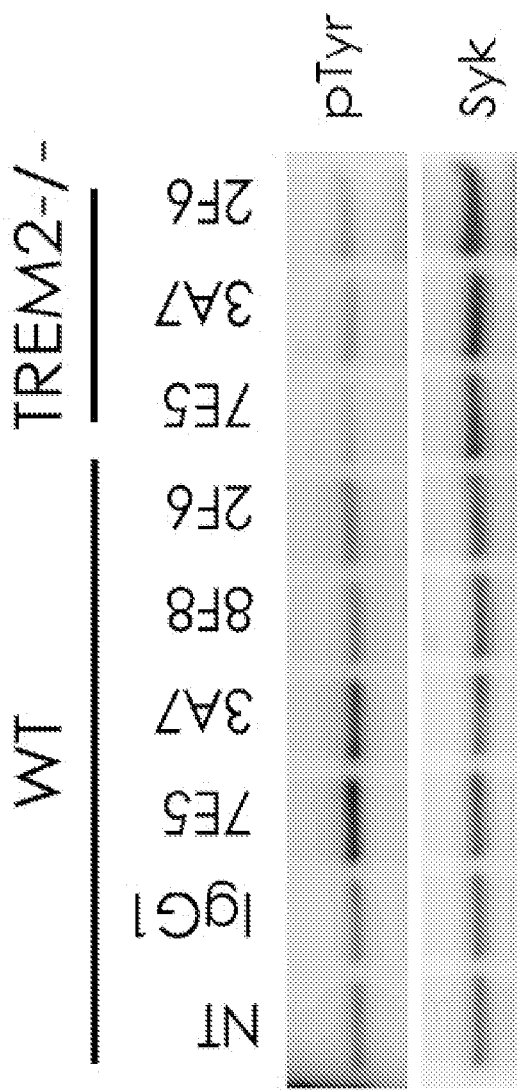


FIG. 6A

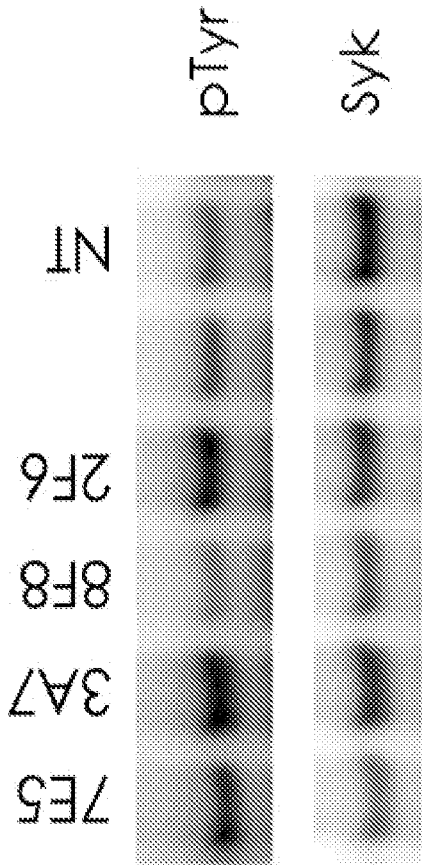


FIG. 6B

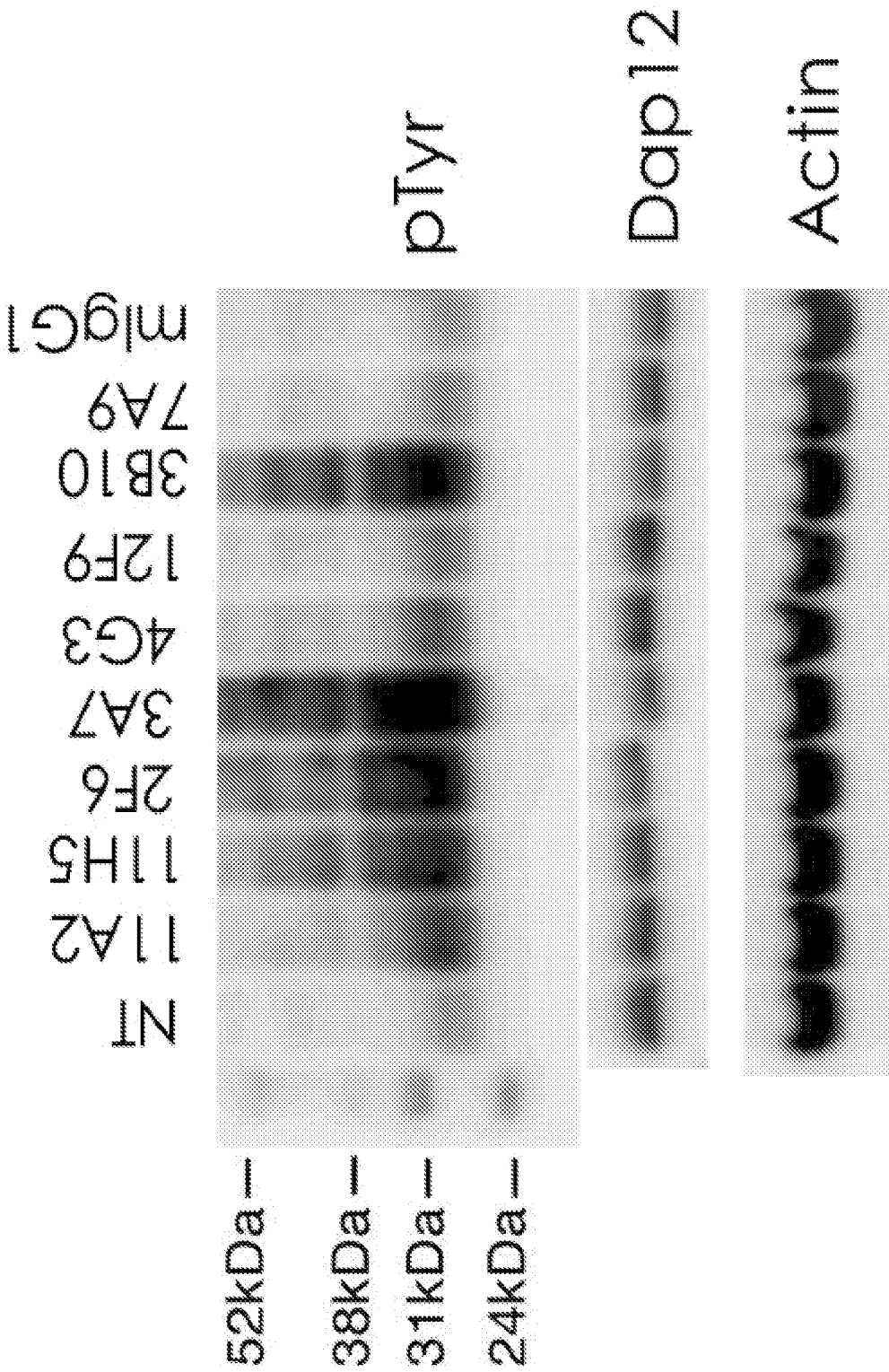


FIG. 7A

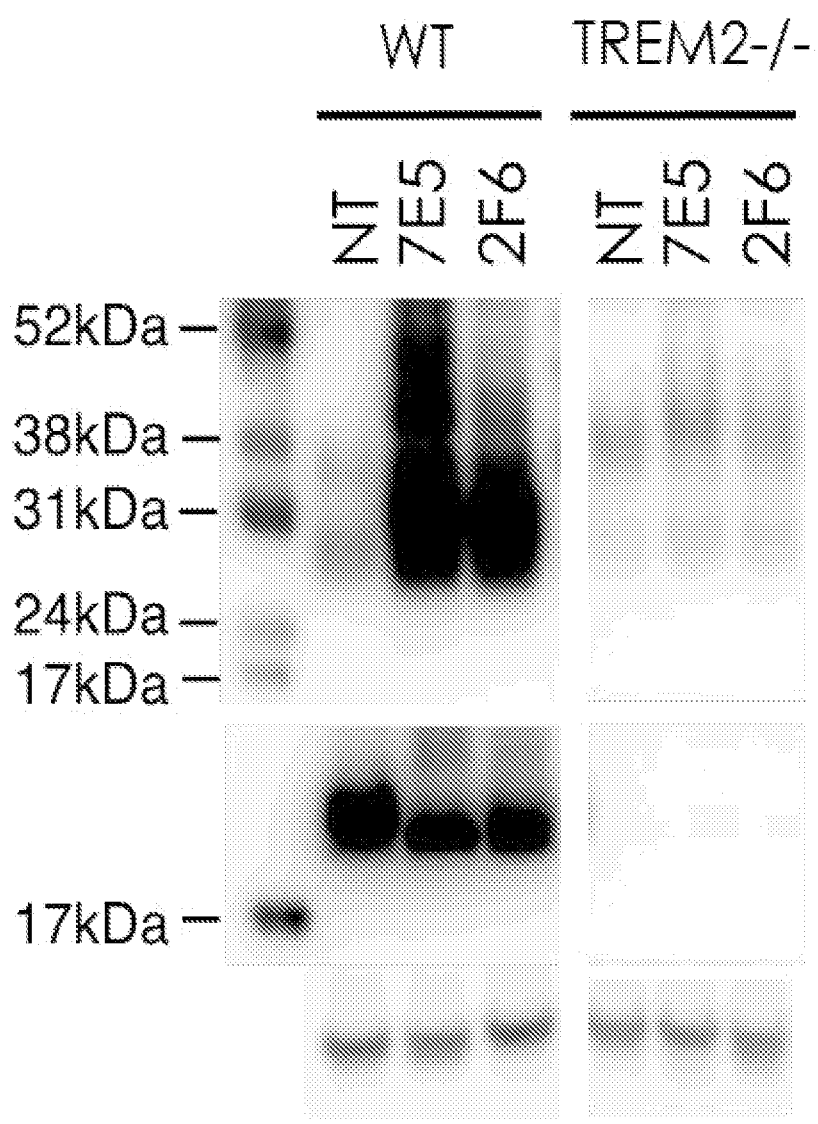


FIG. 7B

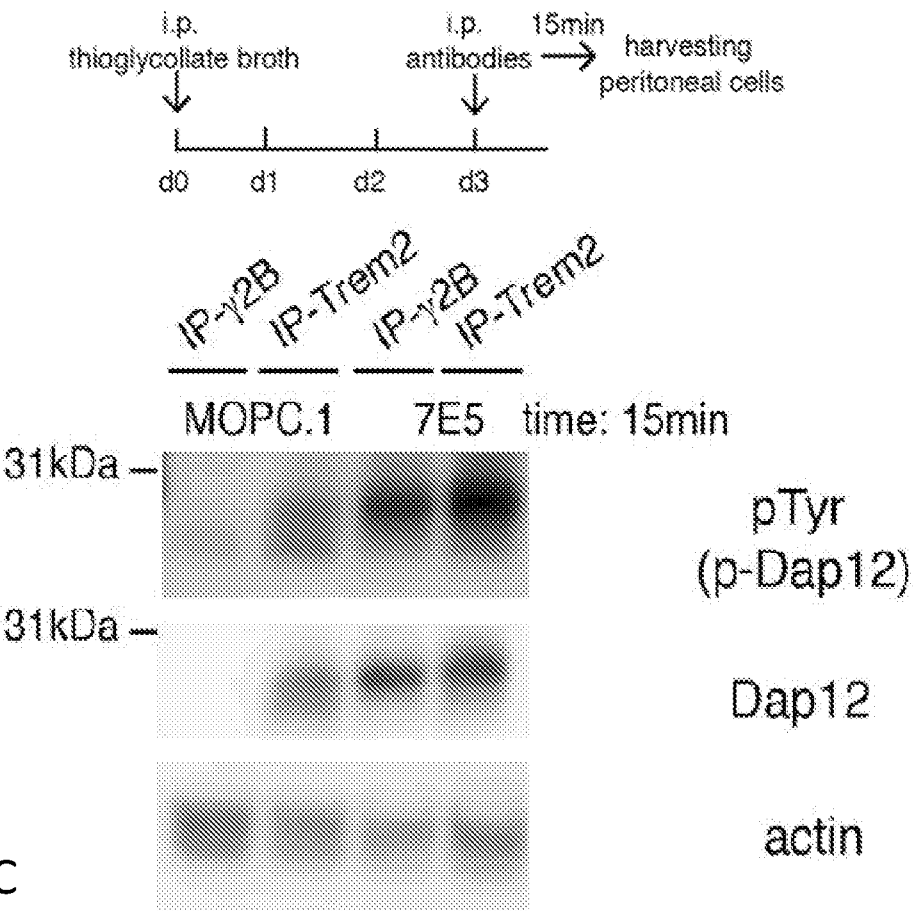


FIG. 7C

FC over IP-Trem2 of MOPC1-treated mouse

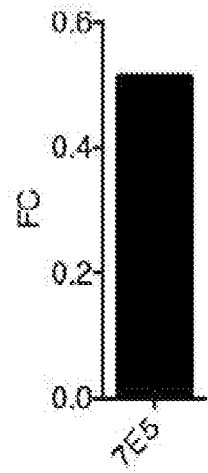


FIG. 7D

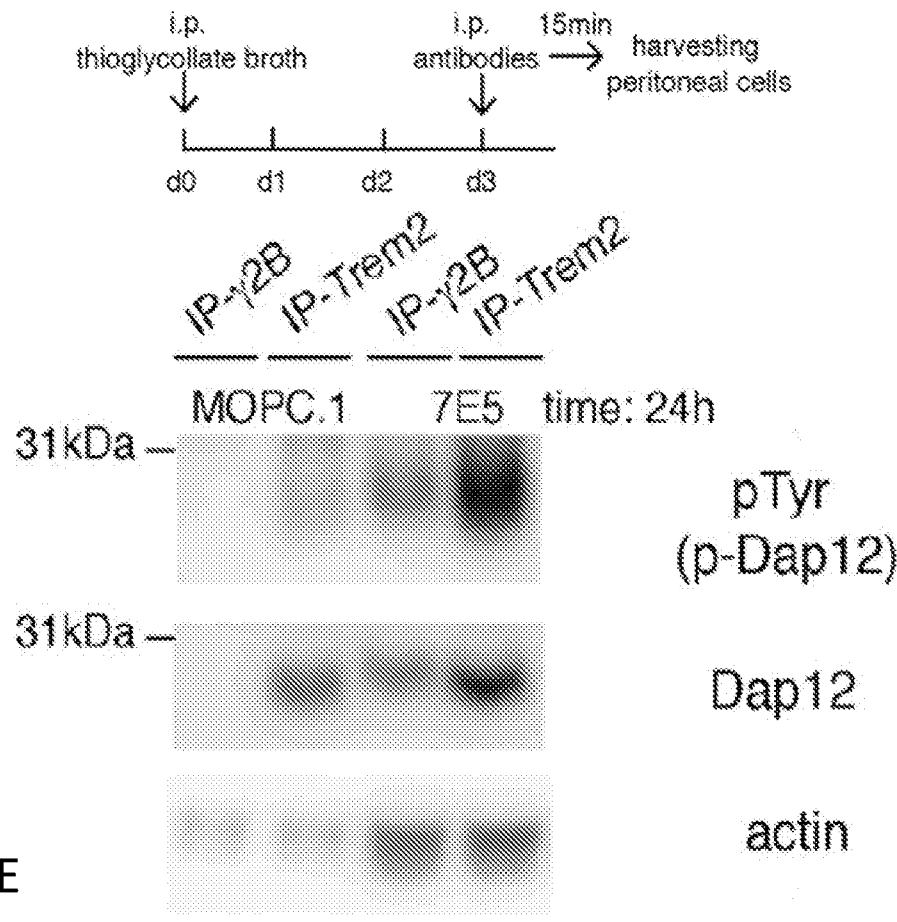


FIG. 7E

FC over IP-Trem2 of MOPC1-treated mouse

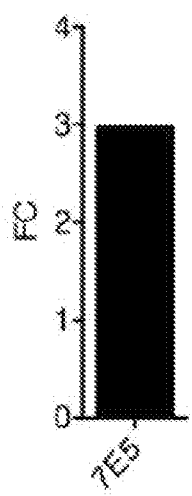


FIG. 7F

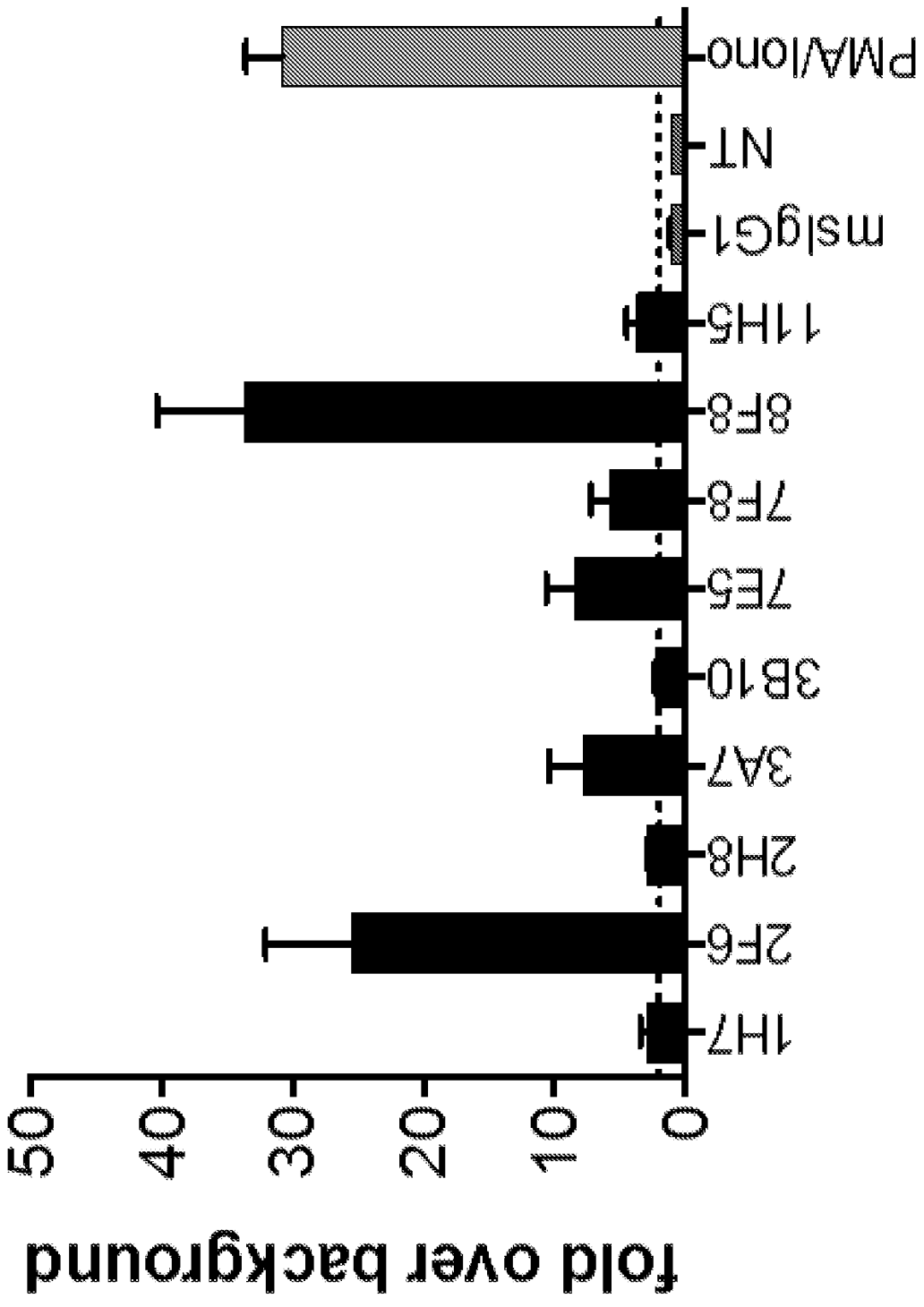


FIG. 8A

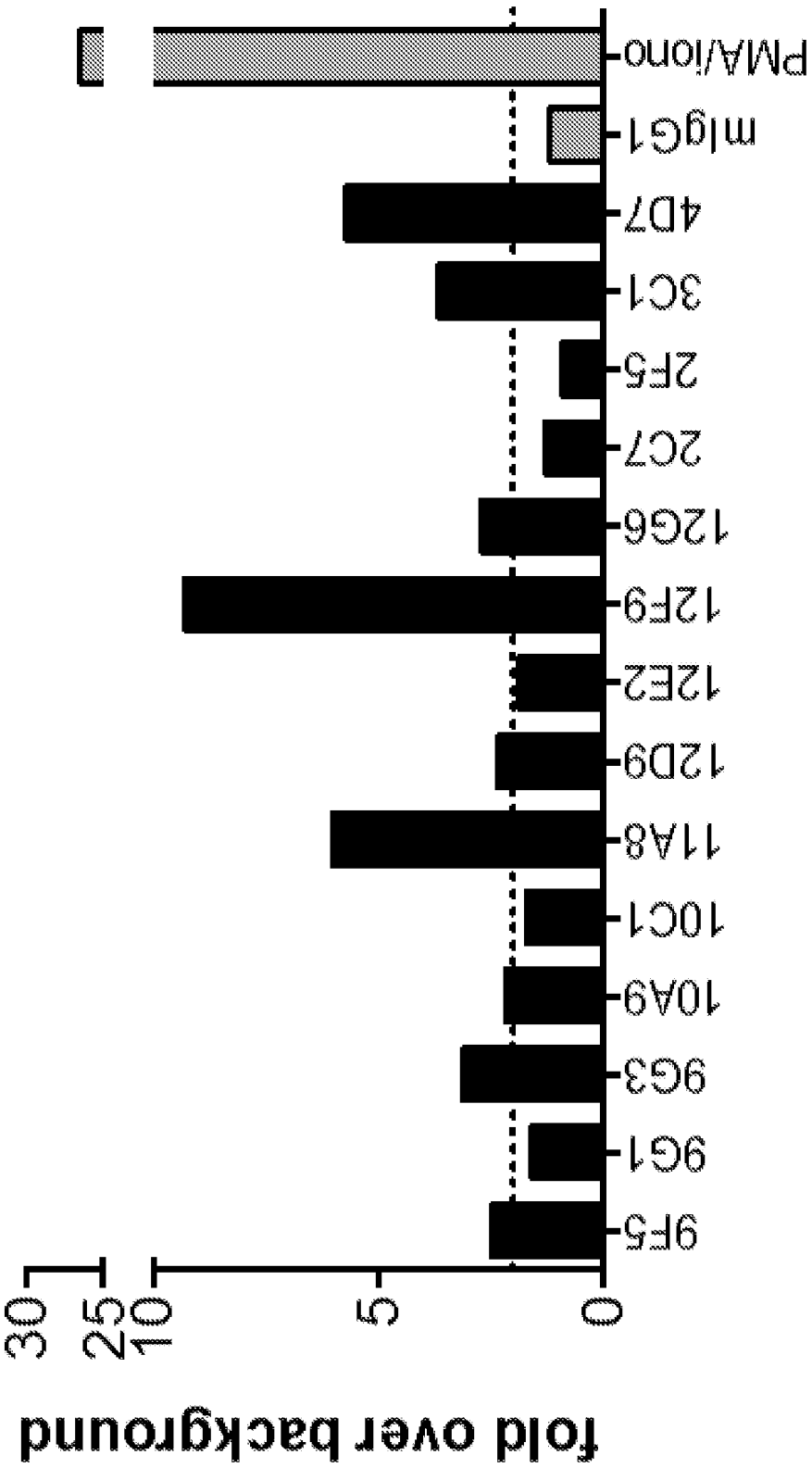


FIG. 8B

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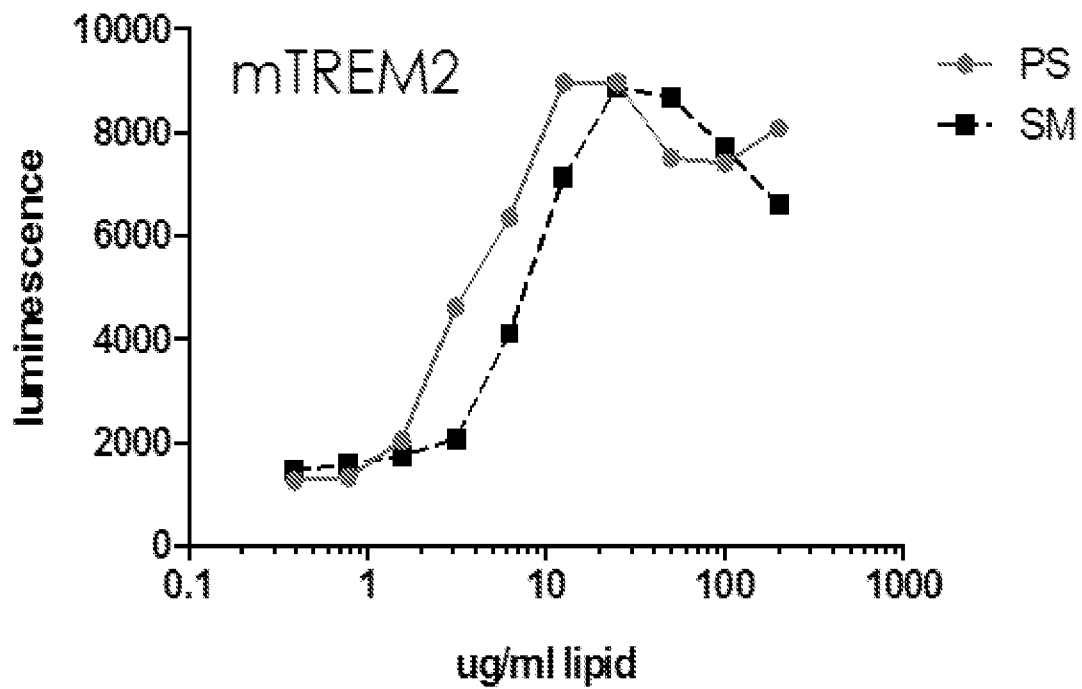


FIG. 8C

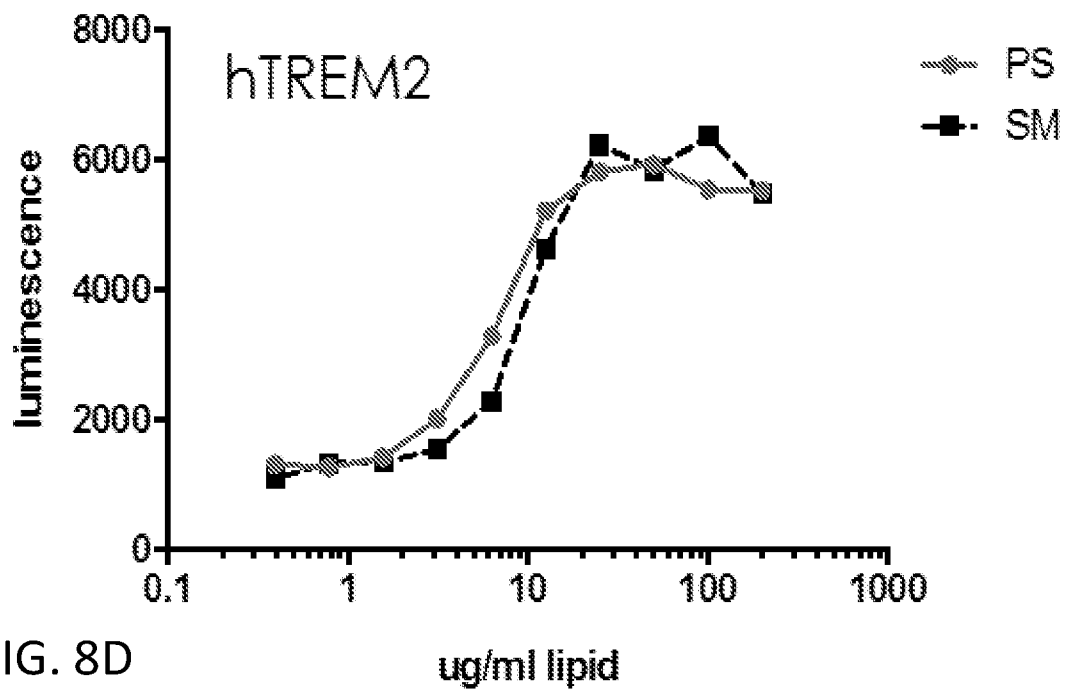


FIG. 8D

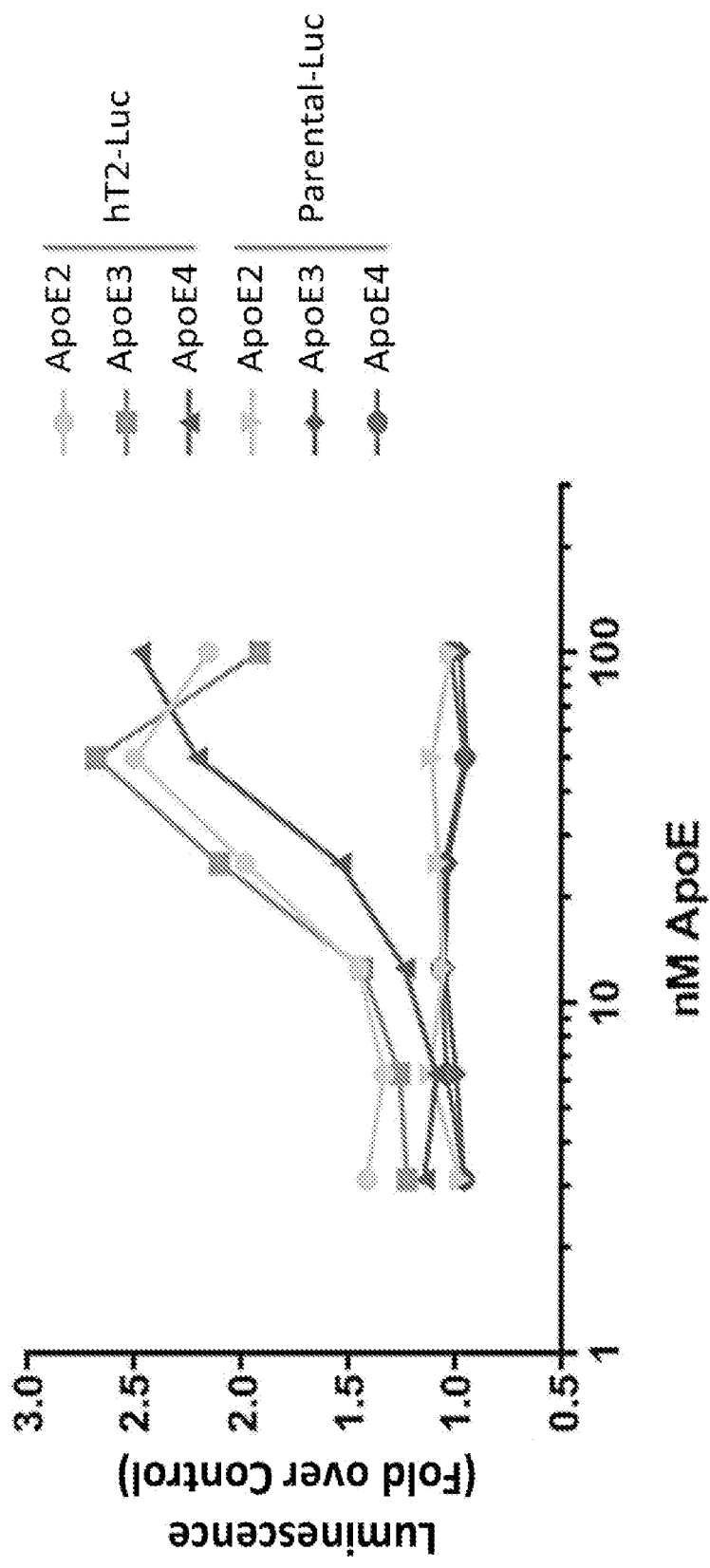


FIG. 8E

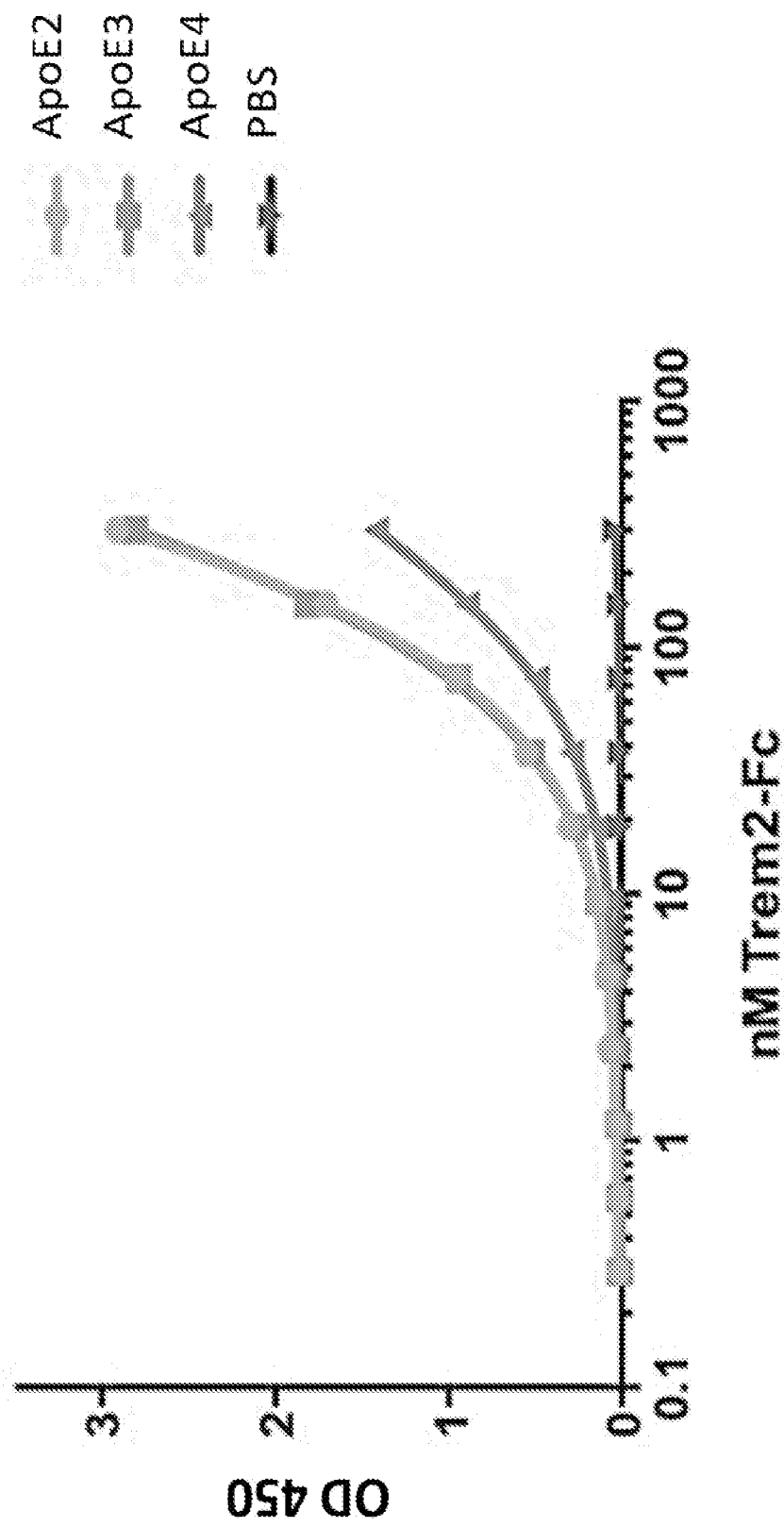


FIG. 8F

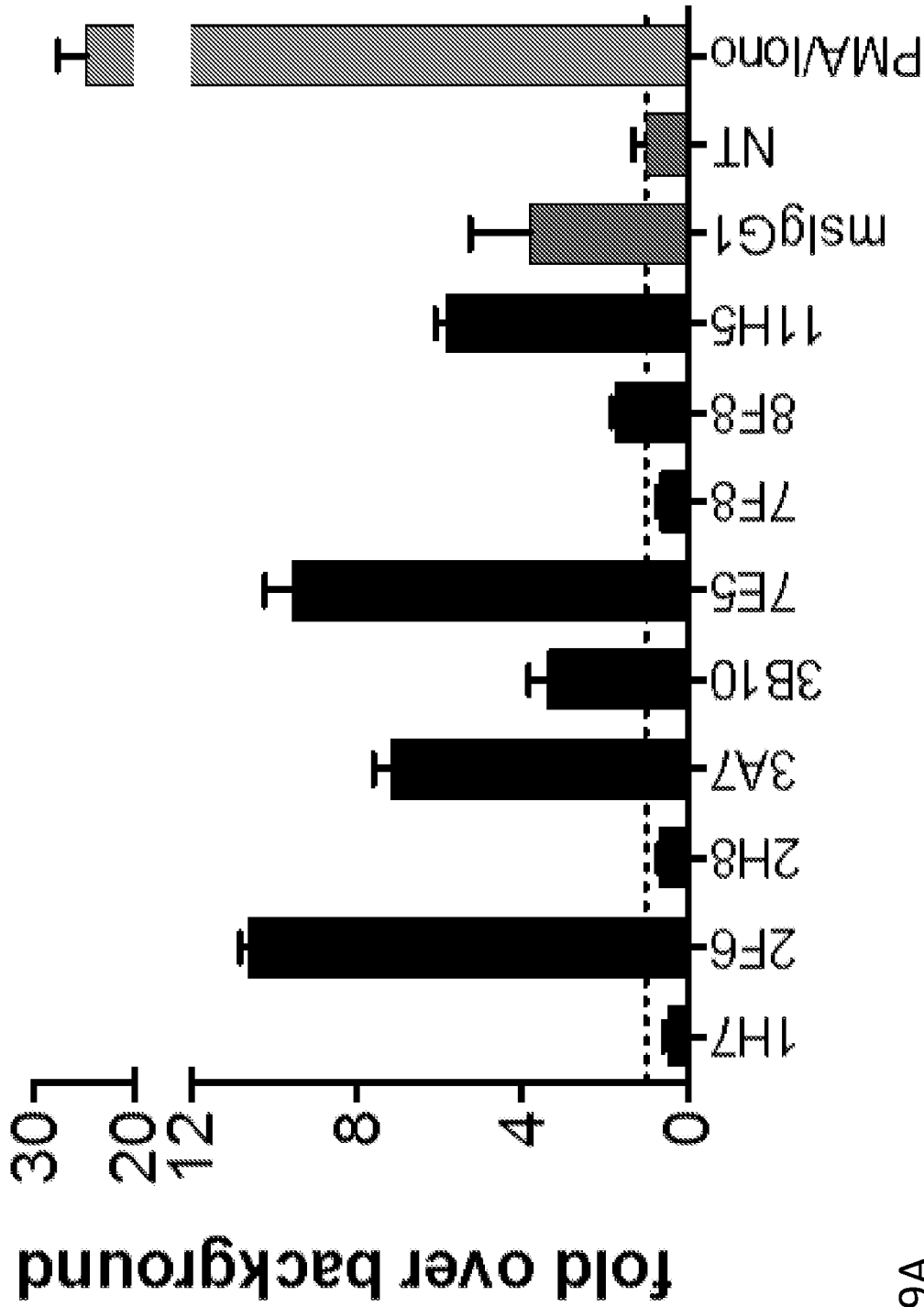


FIG. 9A

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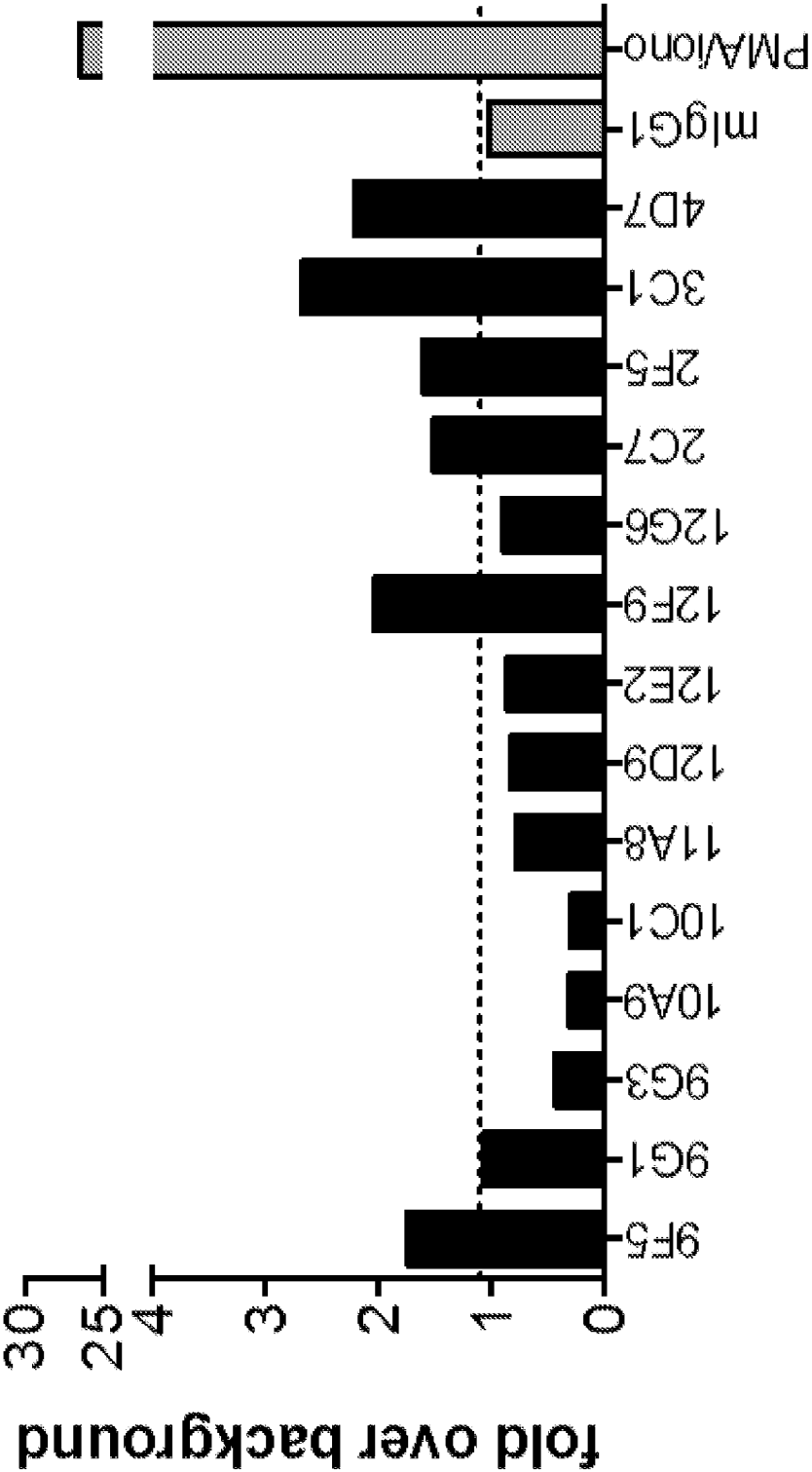


FIG. 9B

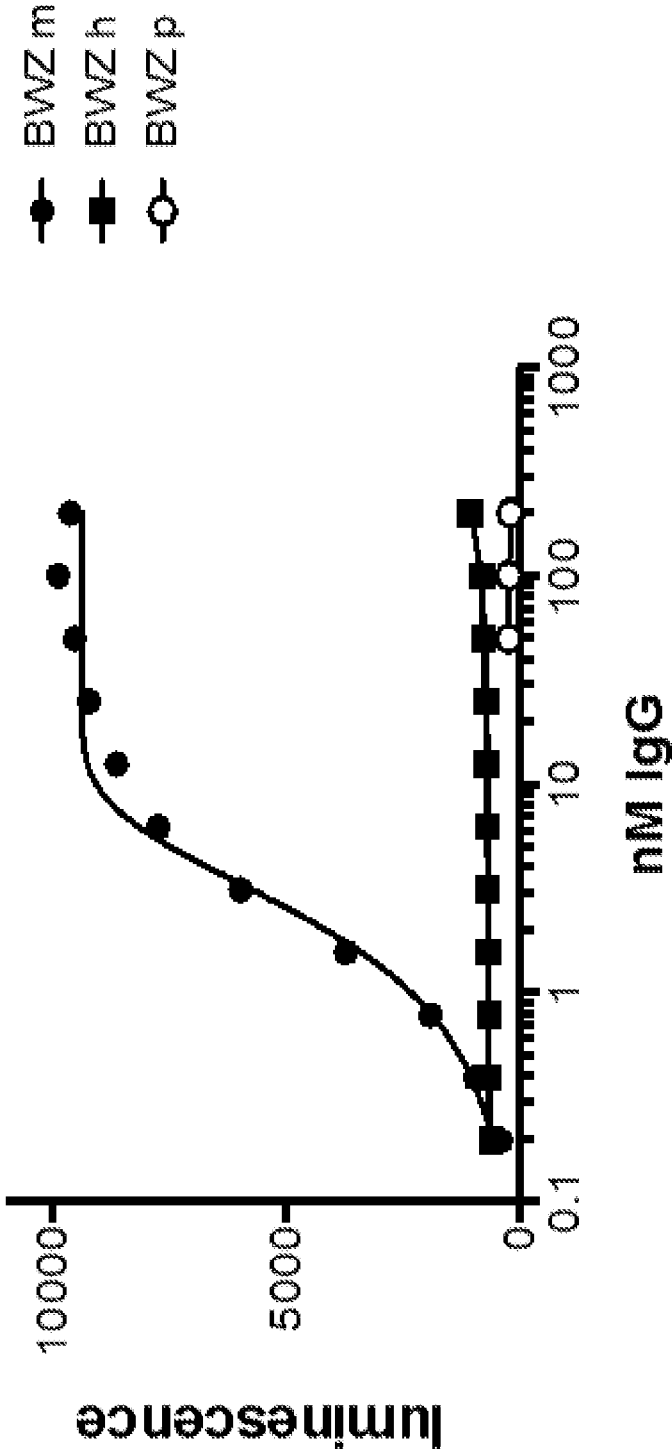


FIG. 9C

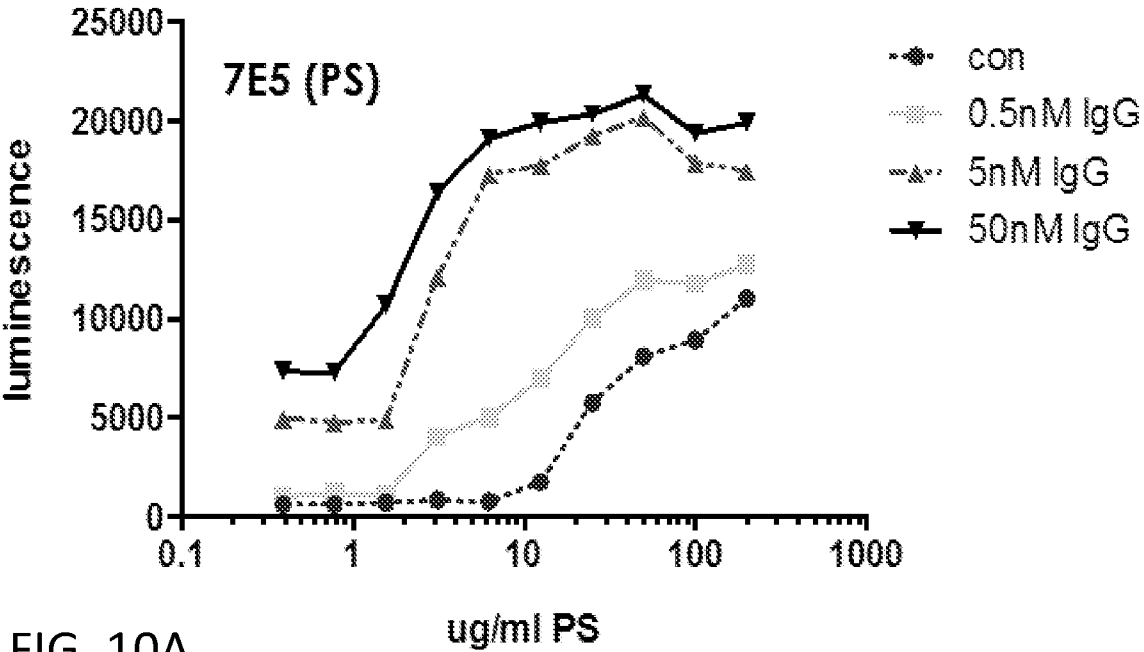


FIG. 10A

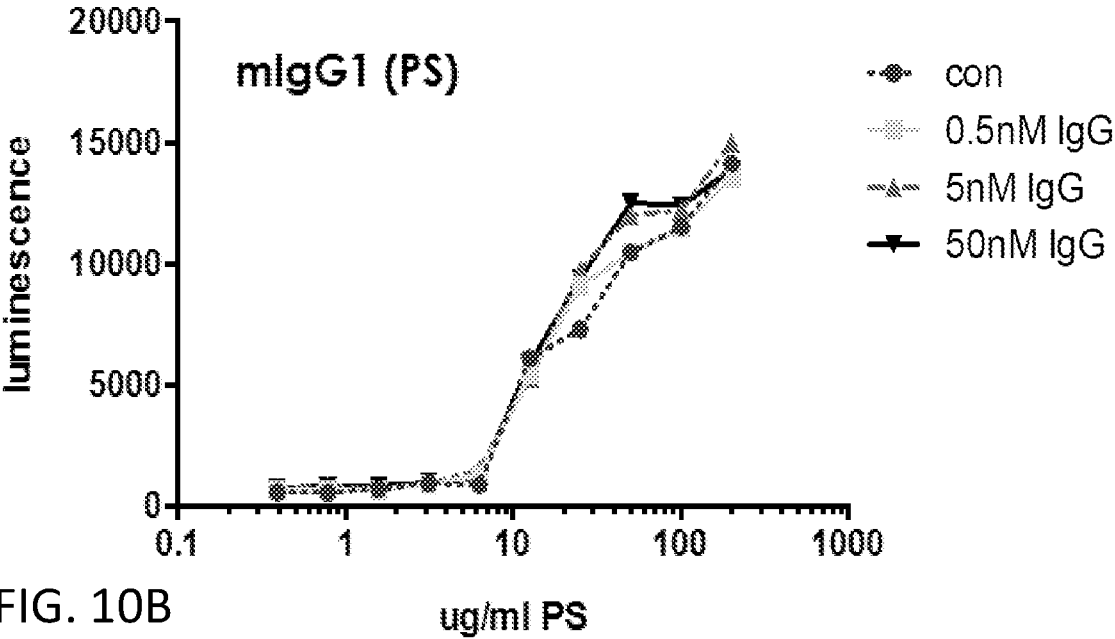


FIG. 10B

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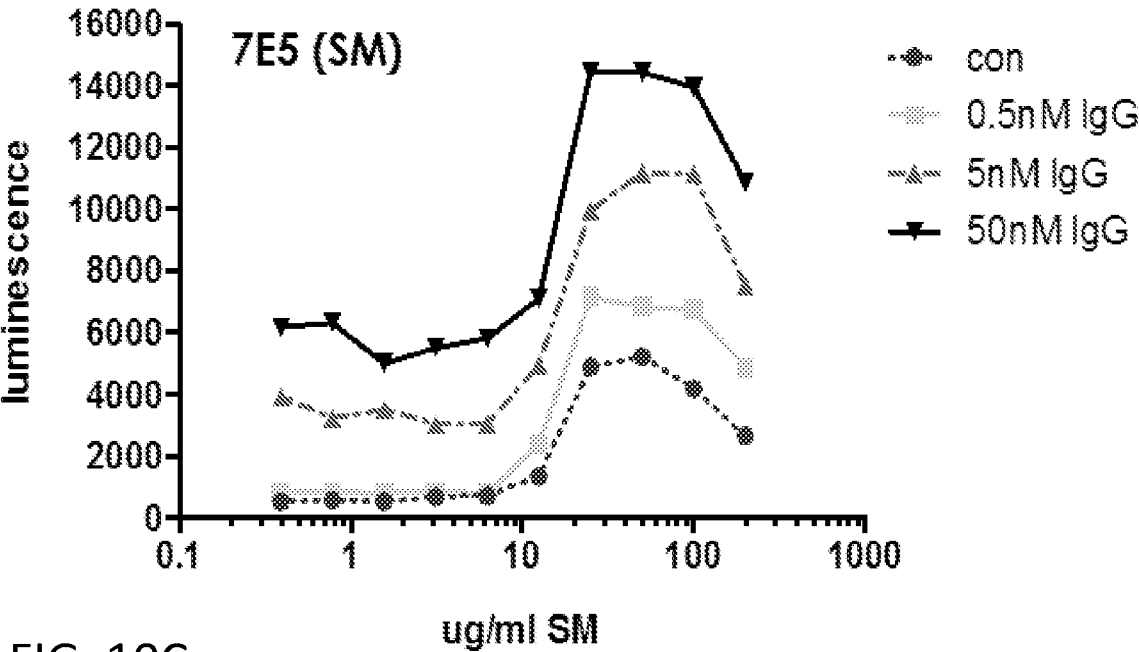


FIG. 10C

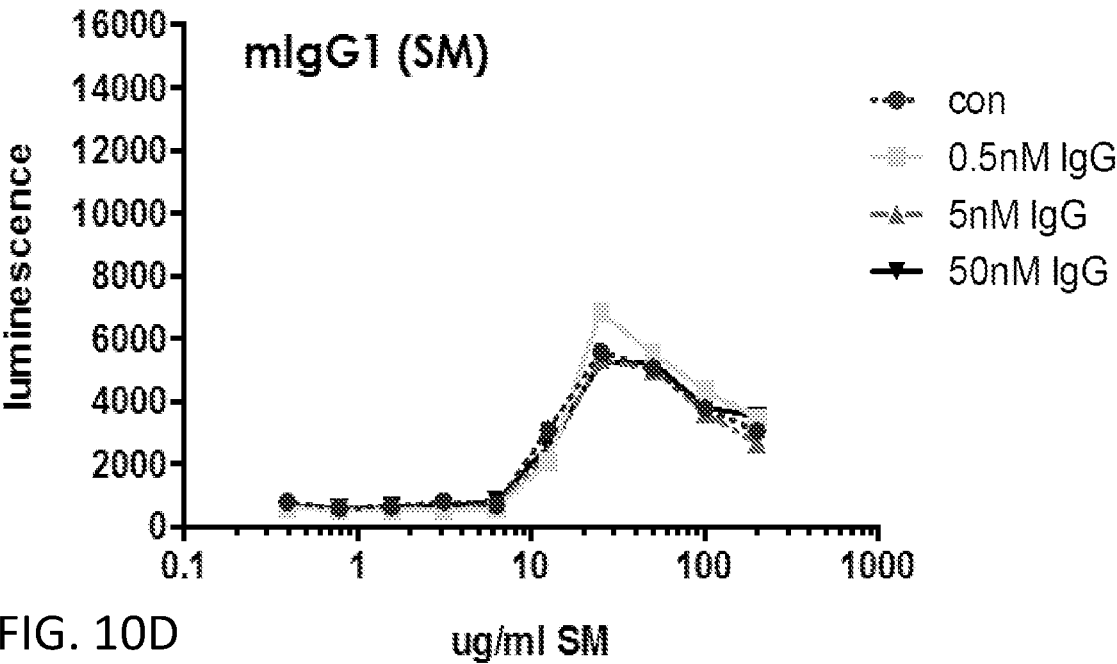


FIG. 10D

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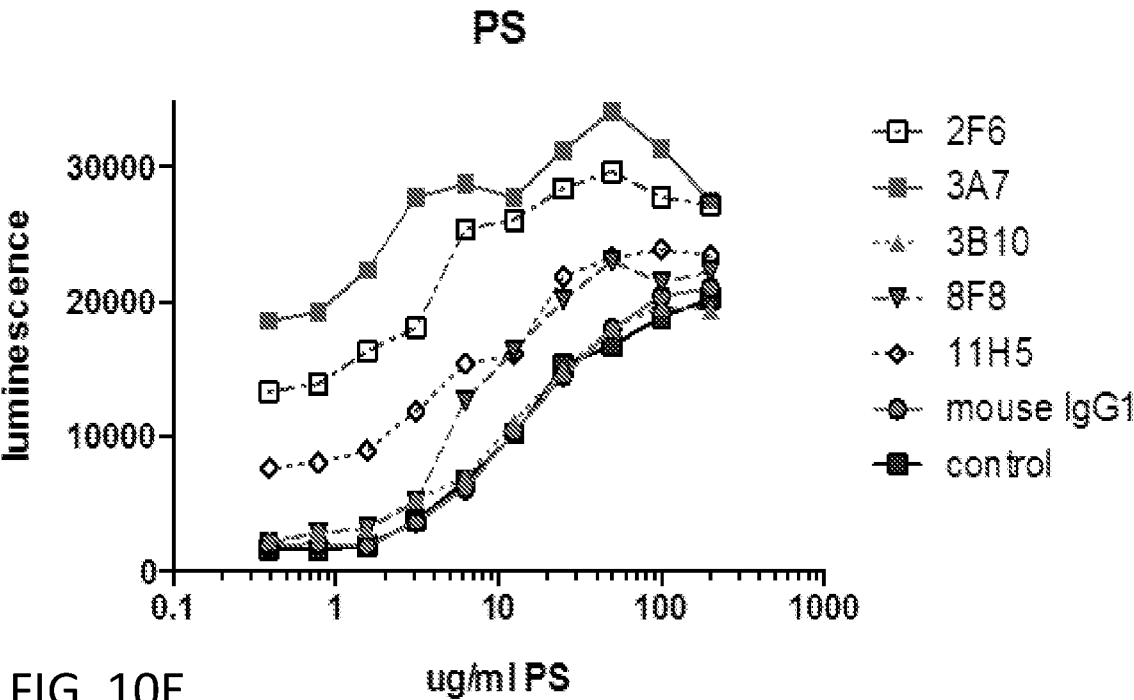


FIG. 10E

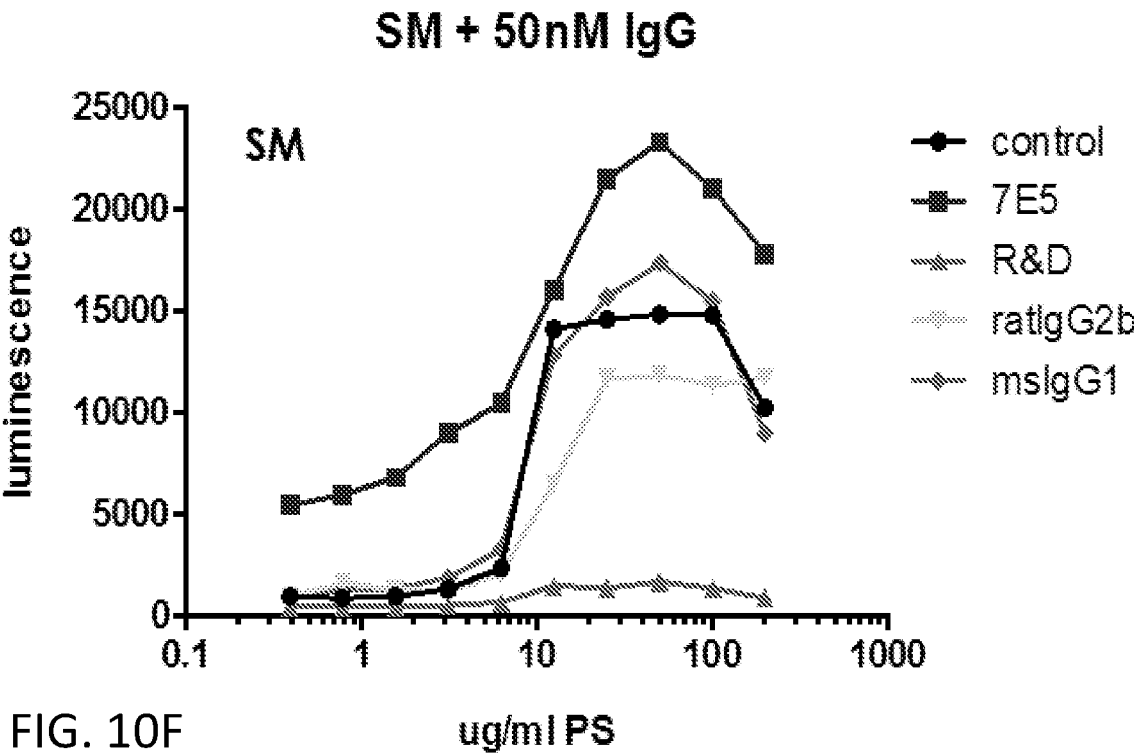


FIG. 10F

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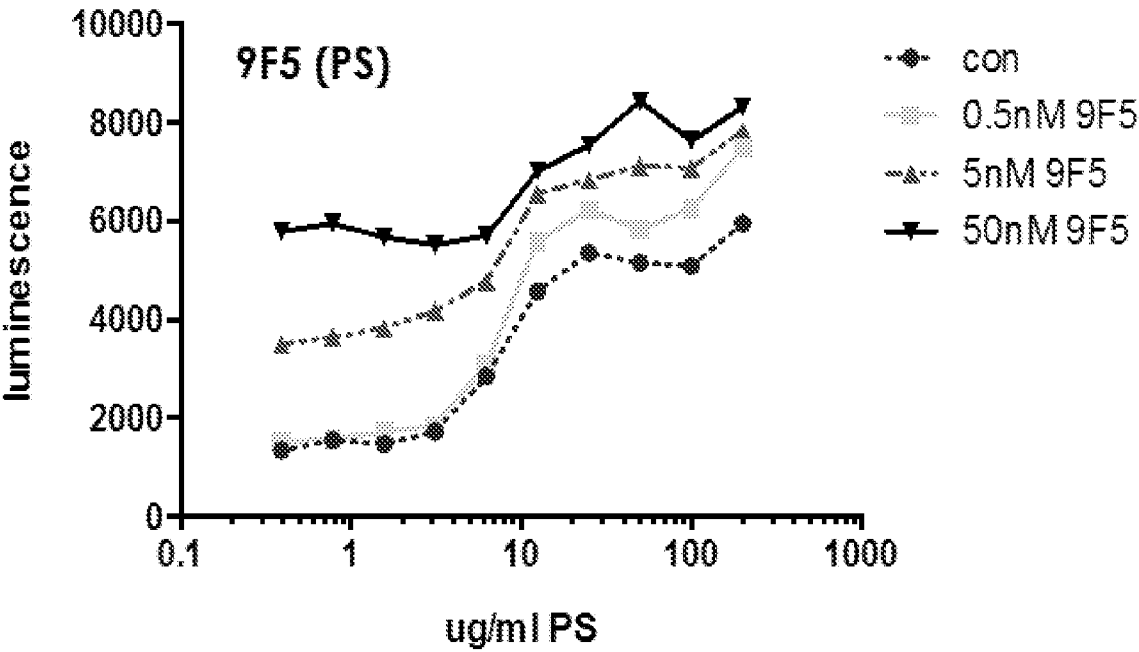


FIG. 11A

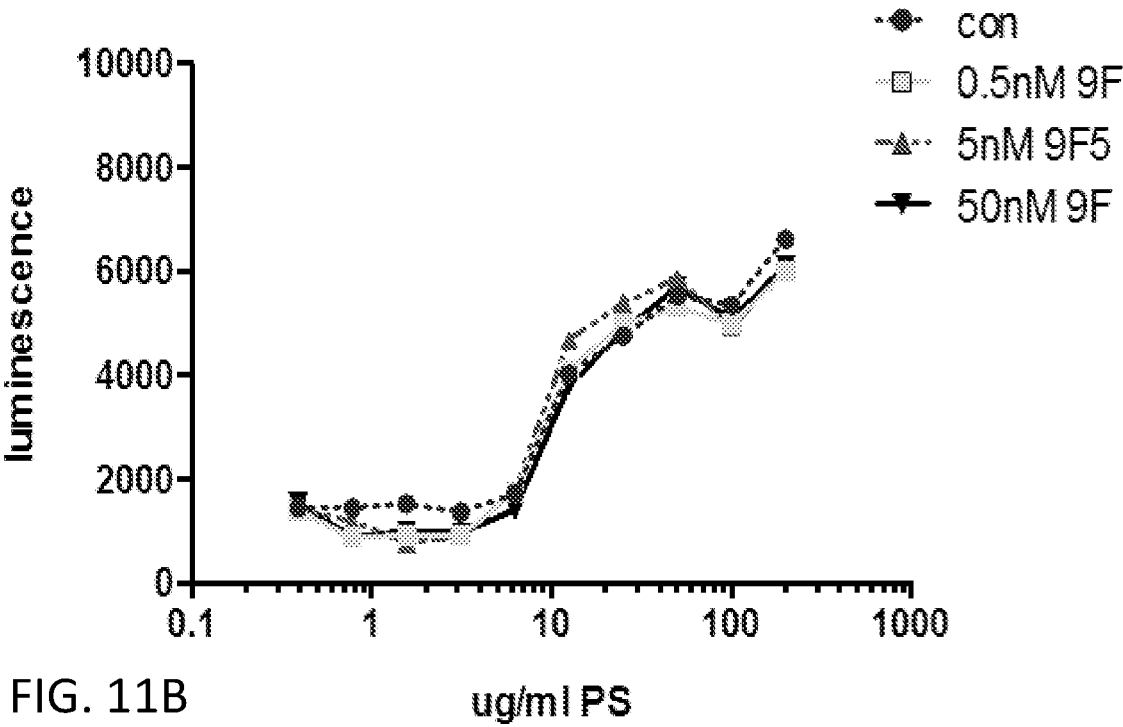


FIG. 11B

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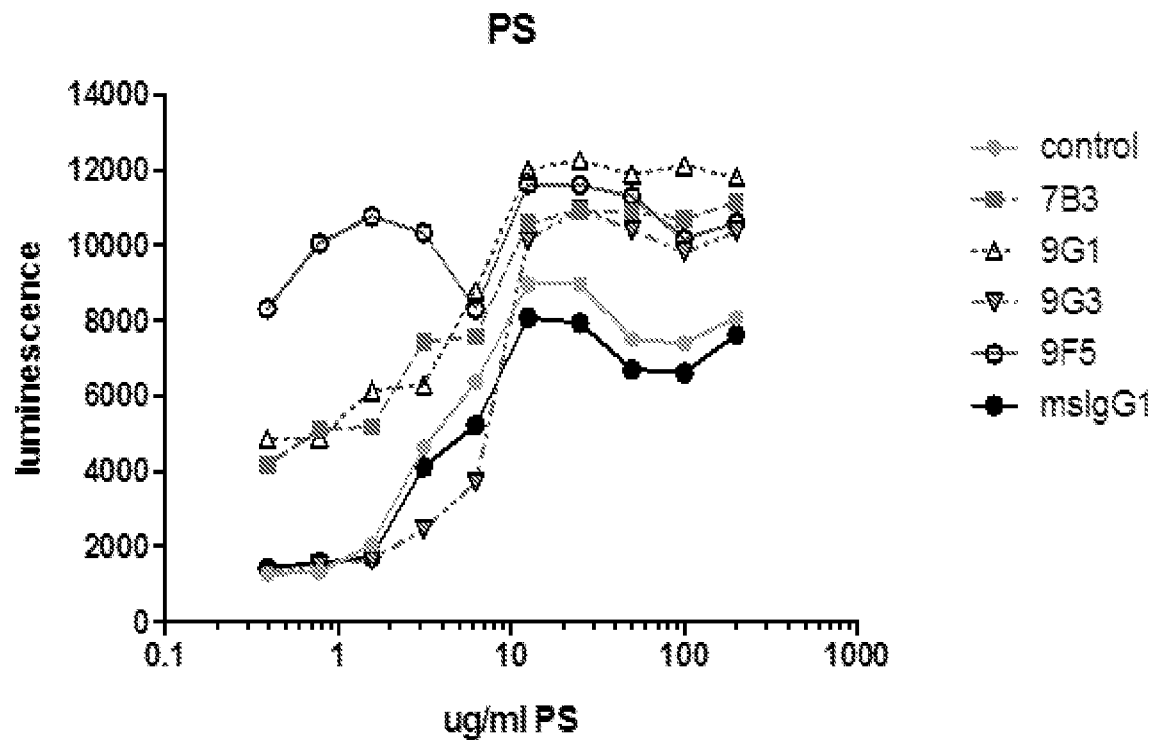


FIG. 11C

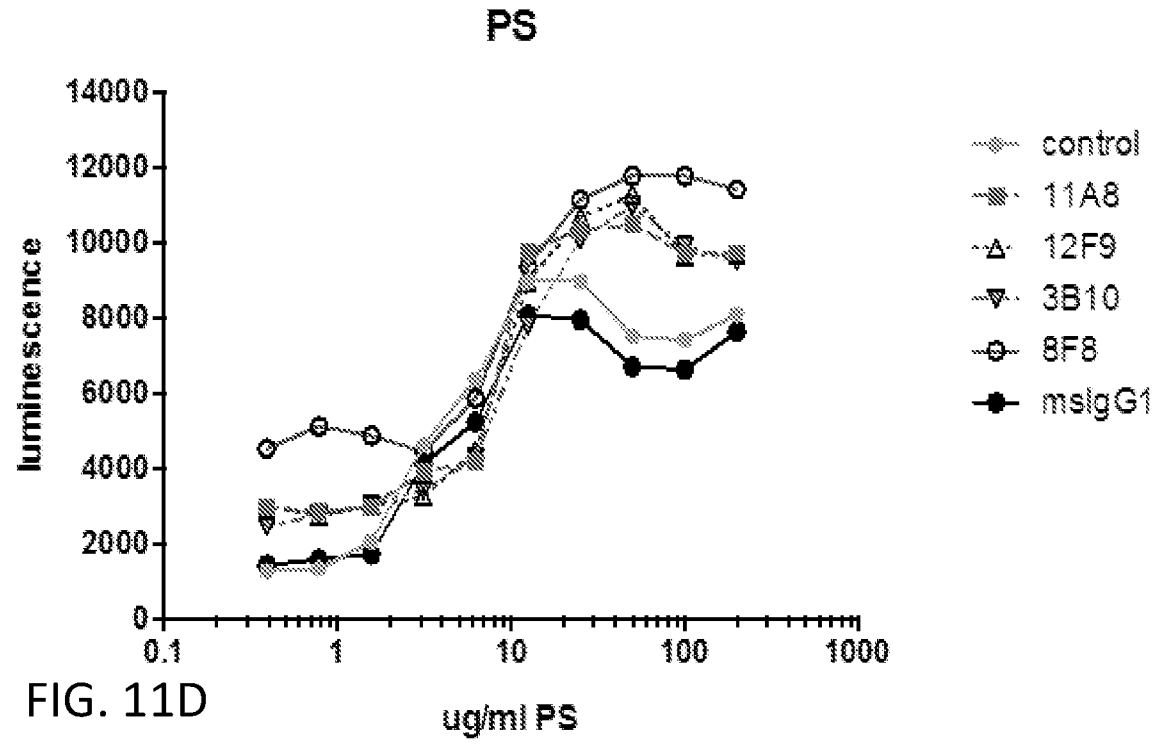


FIG. 11D

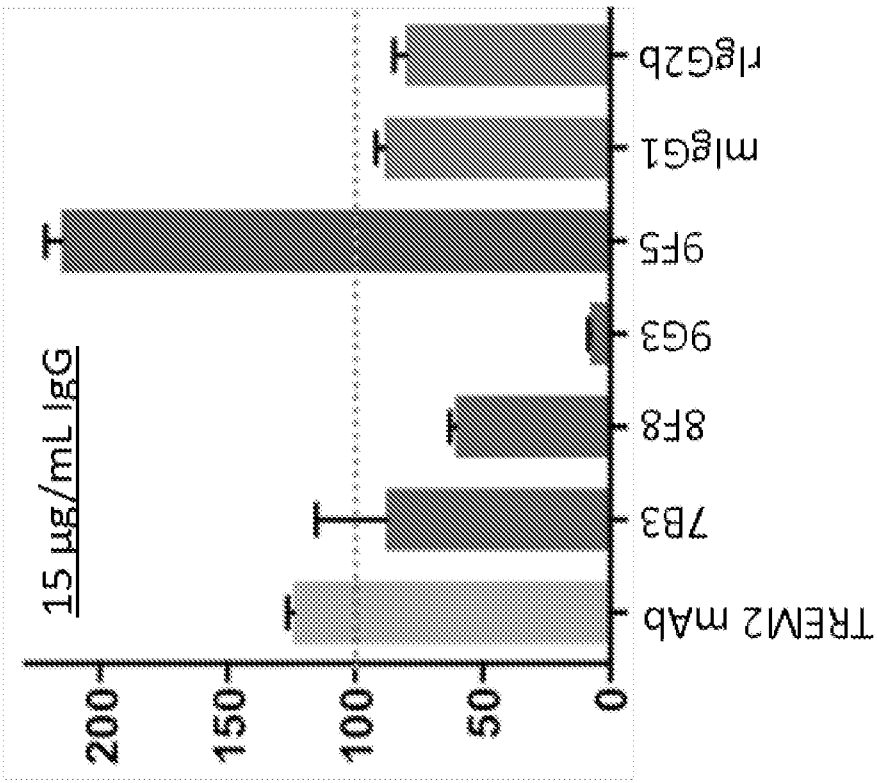


FIG. 11F

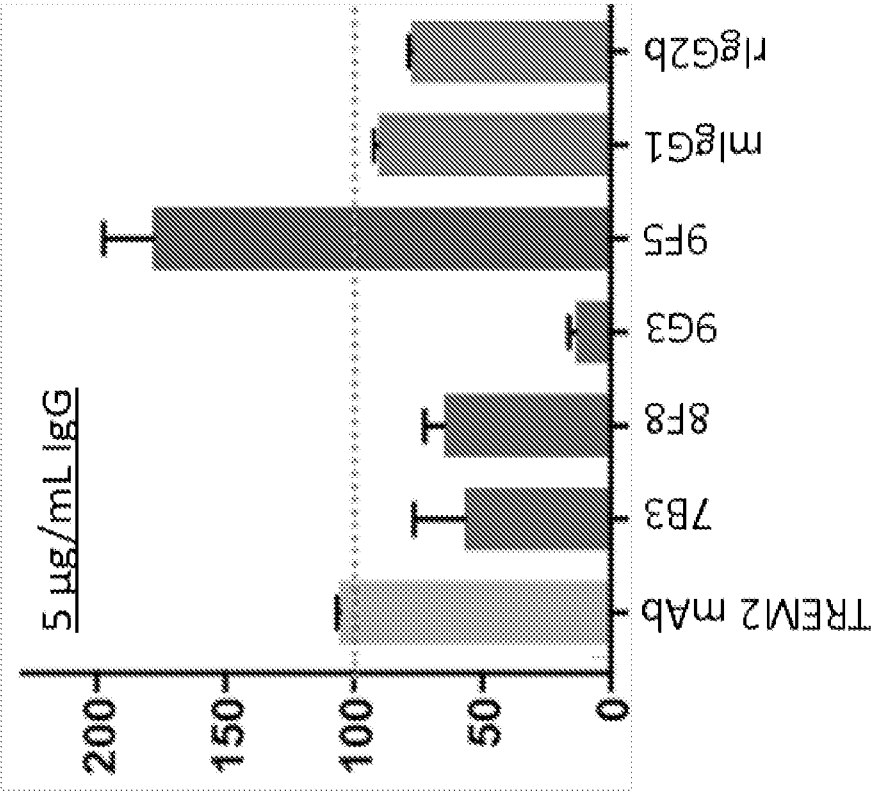


FIG. 11E

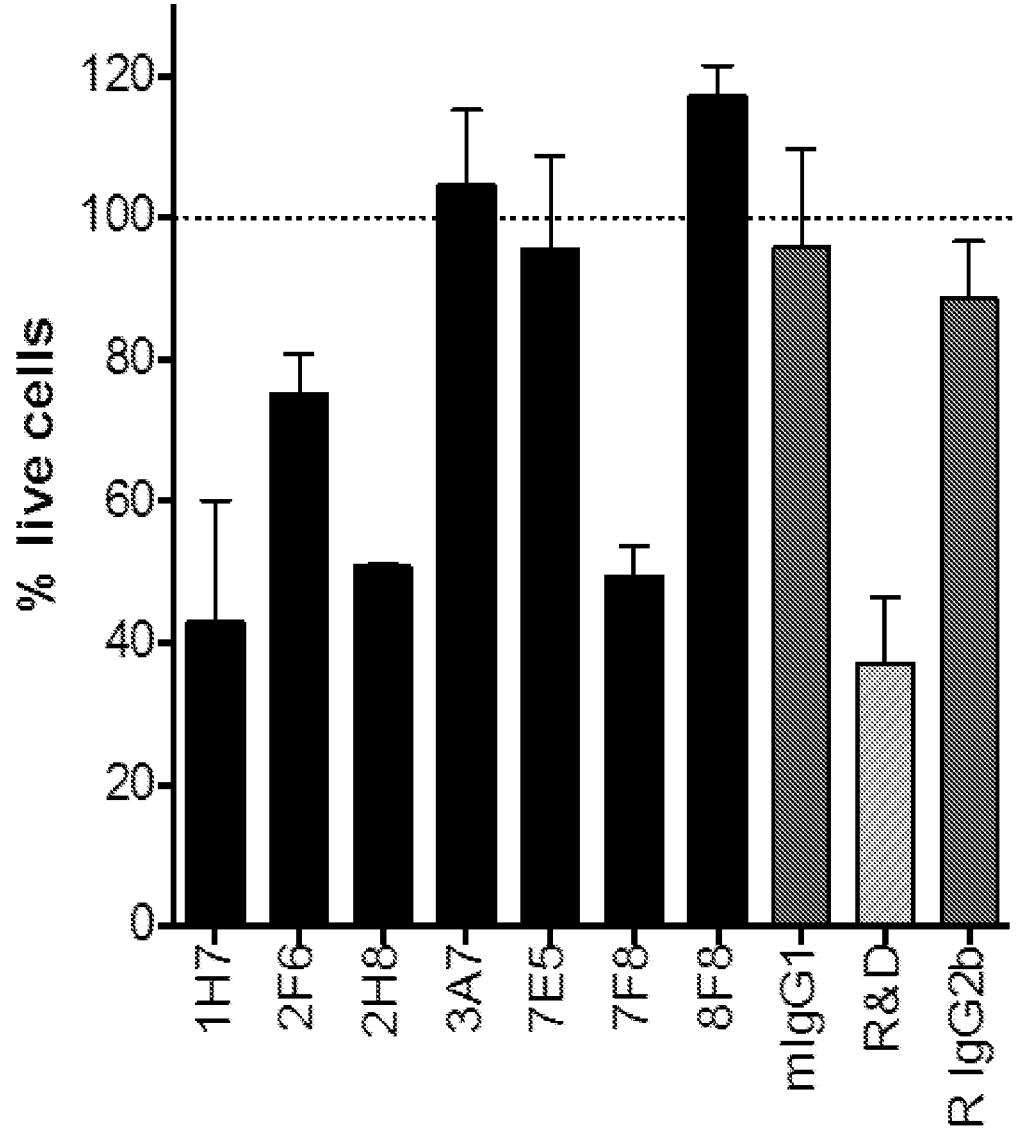
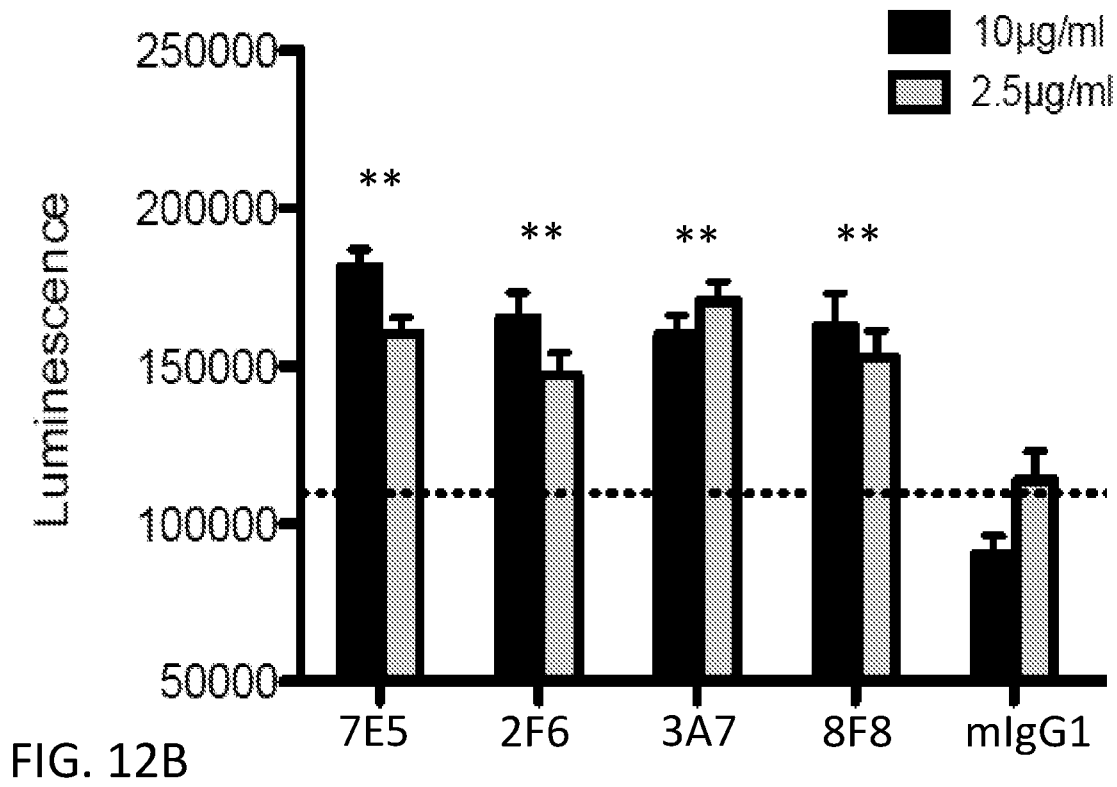
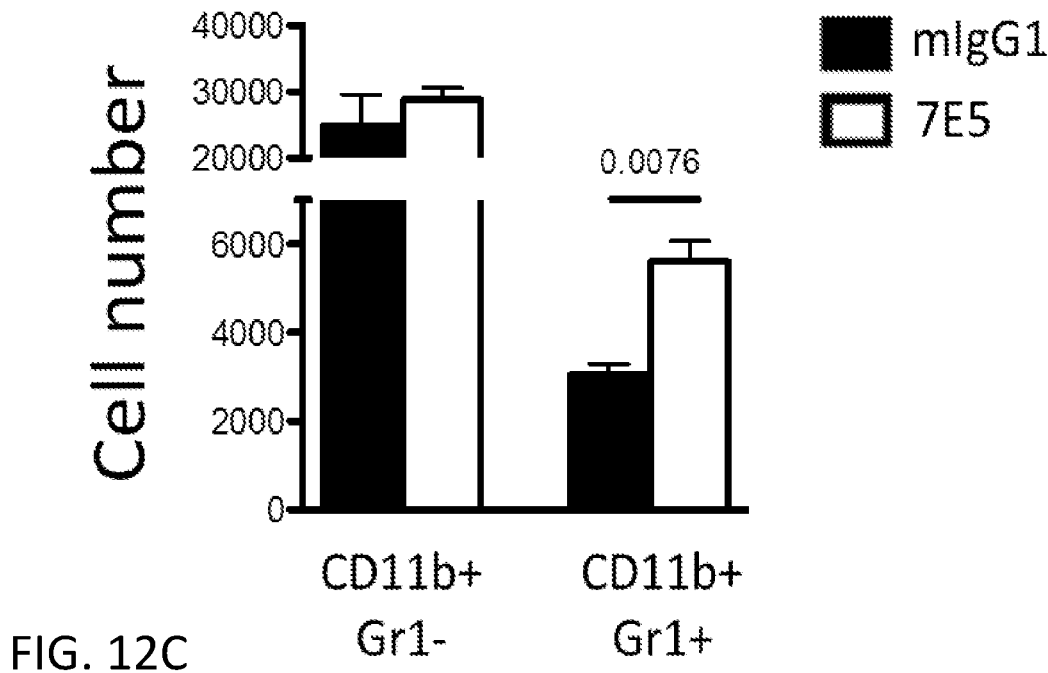


FIG. 12A



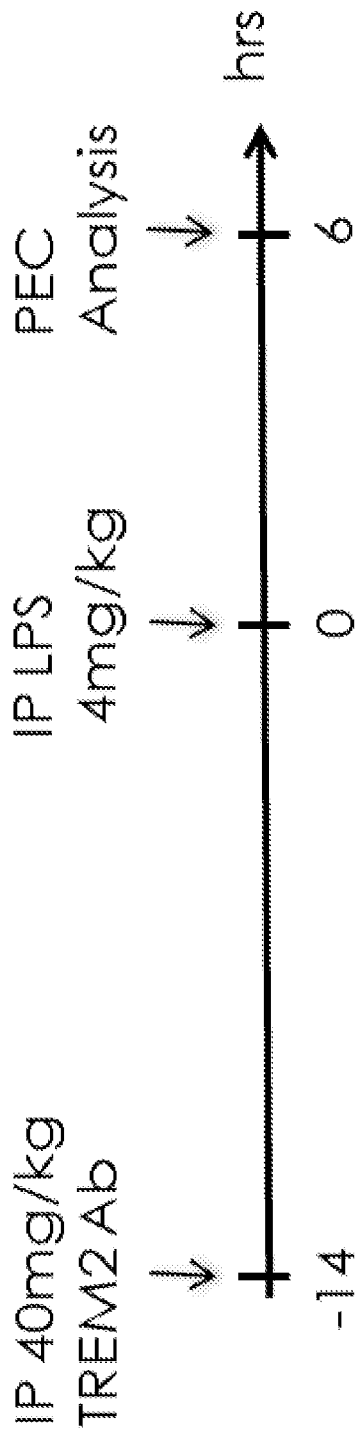


FIG. 13A

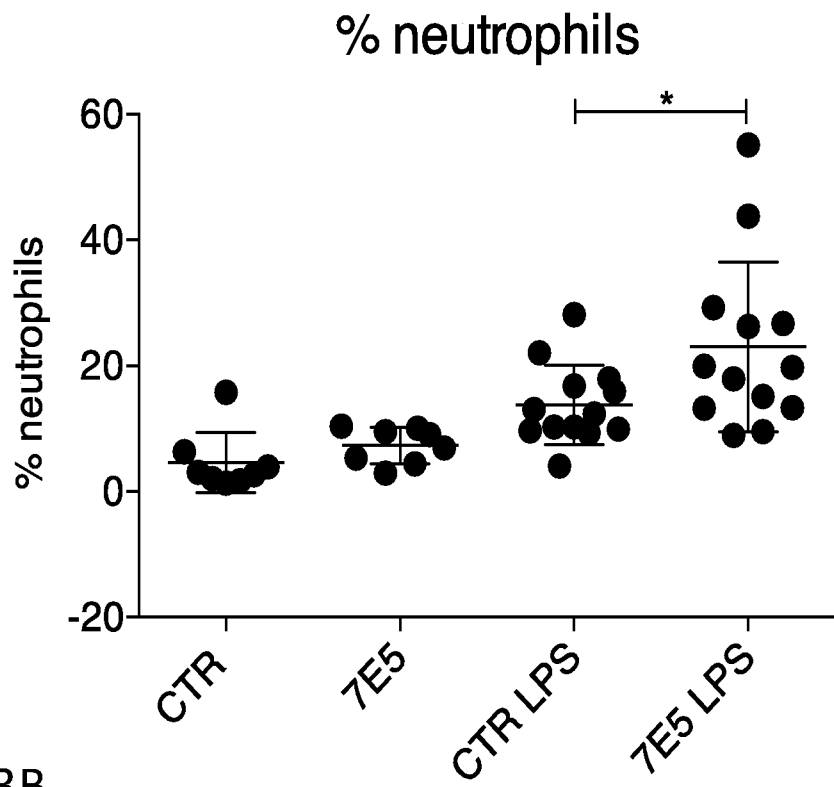


FIG. 13B

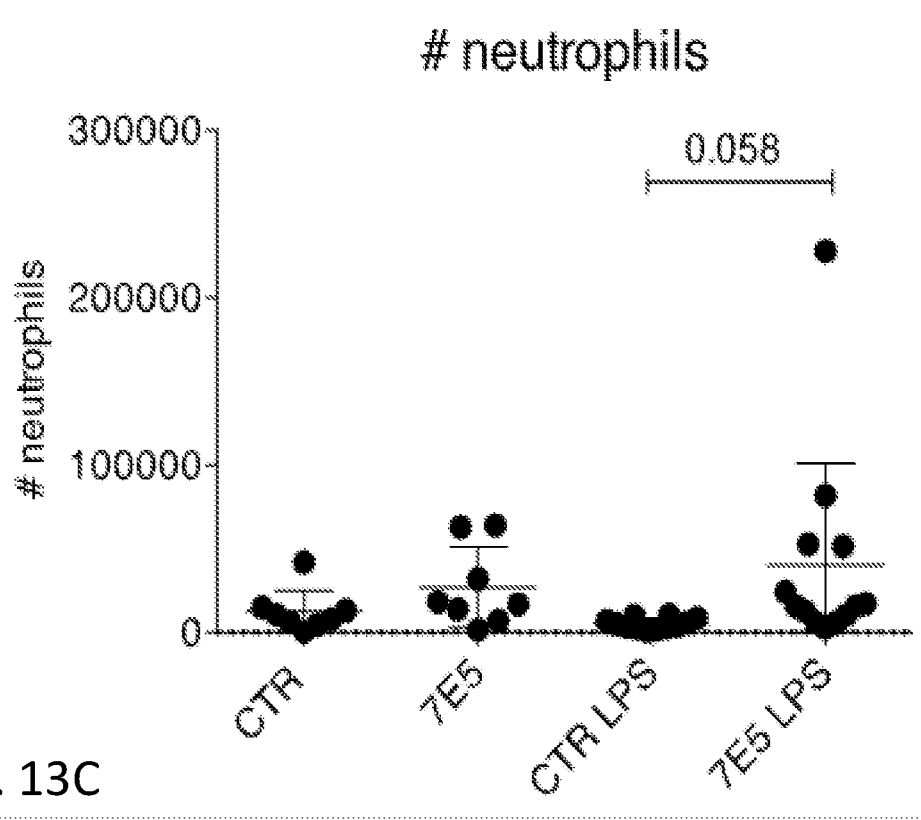


FIG. 13C

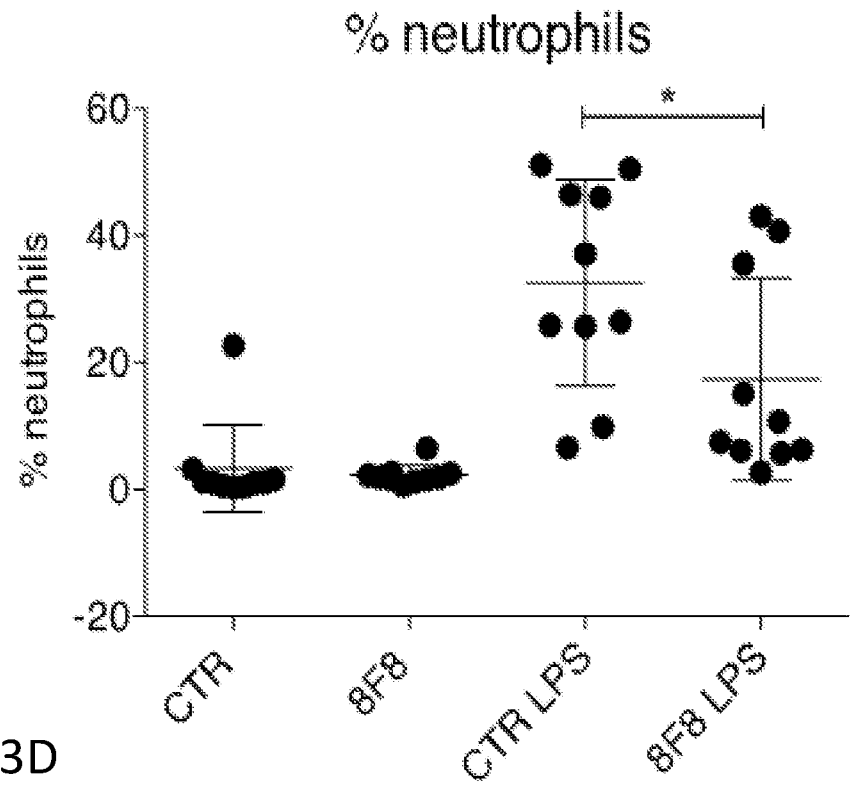


FIG. 13D

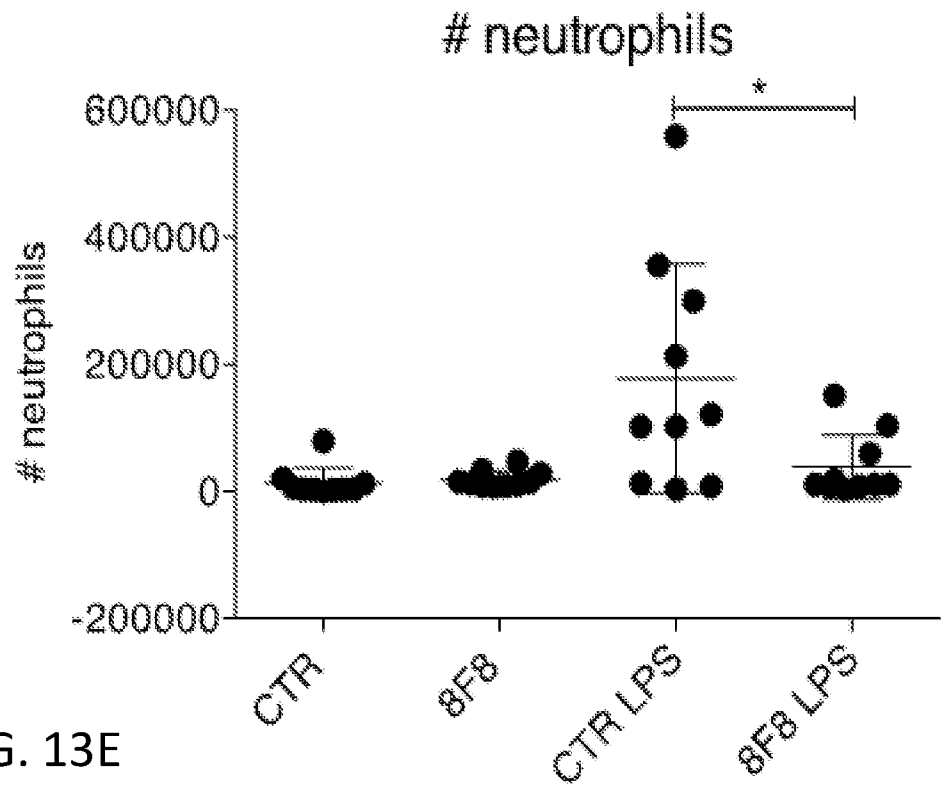


FIG. 13E

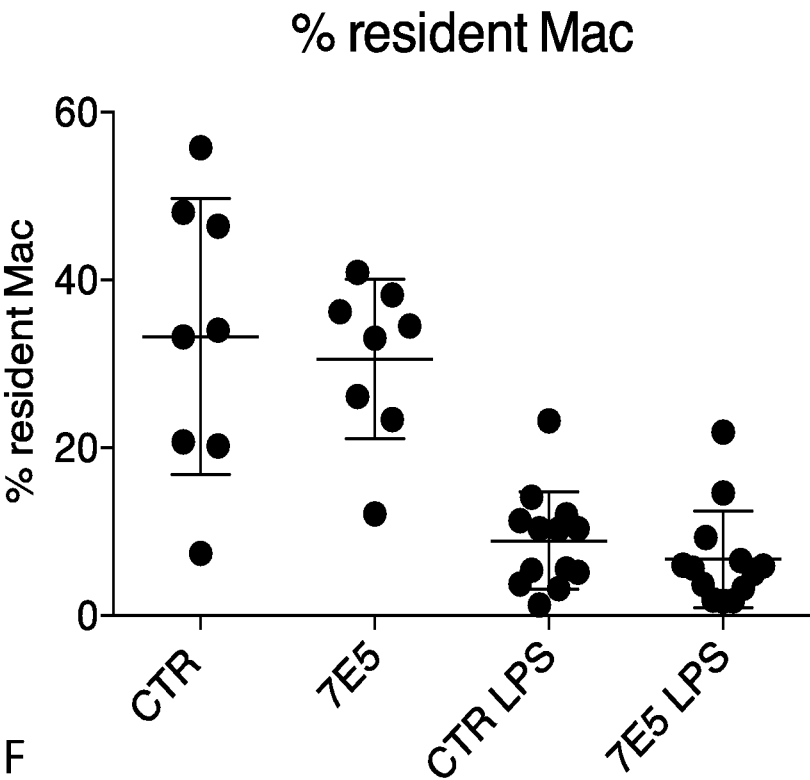


FIG. 13F

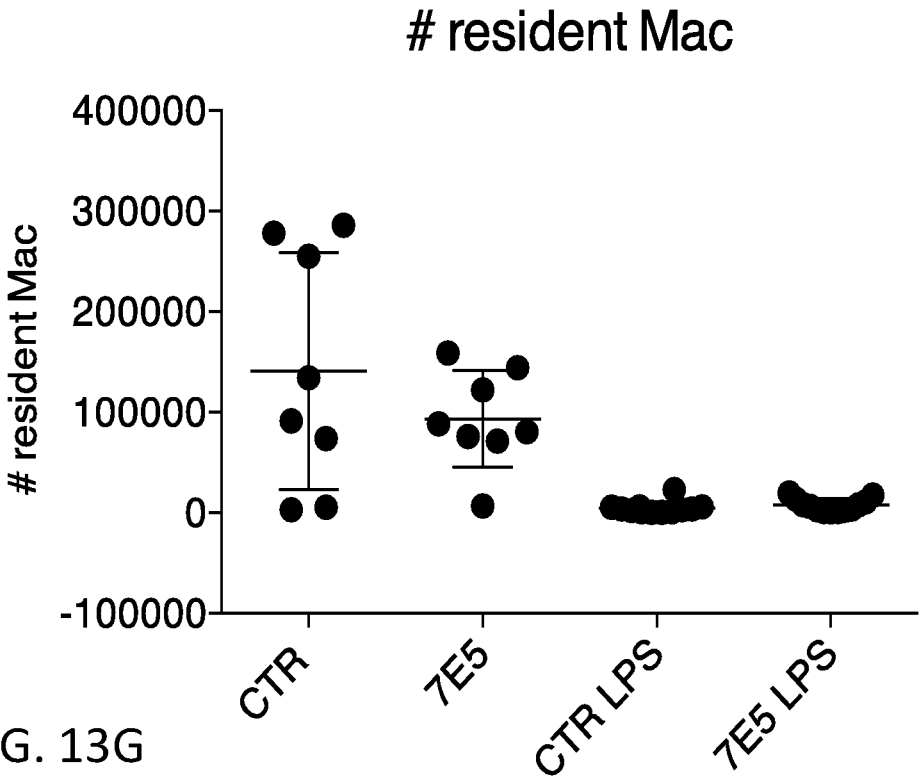


FIG. 13G

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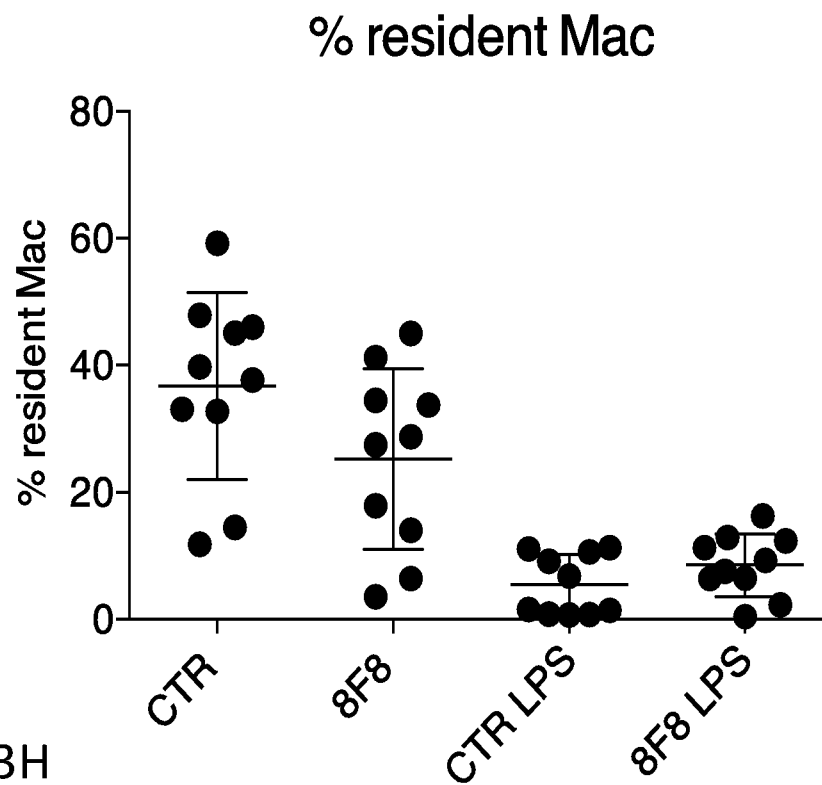


FIG. 13H

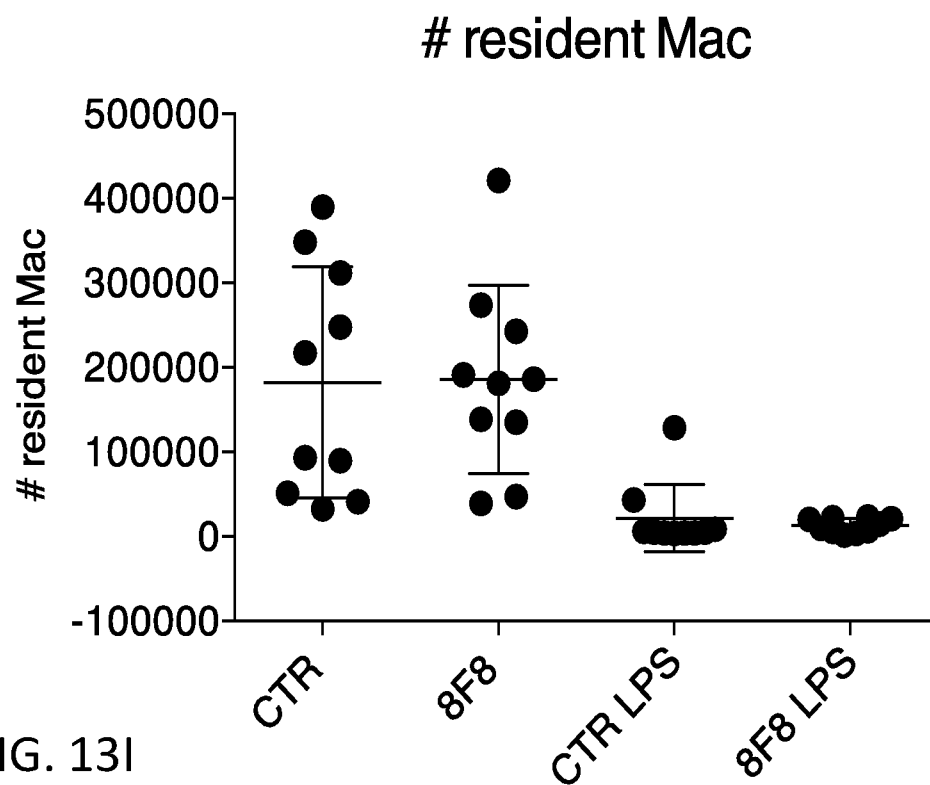


FIG. 13I

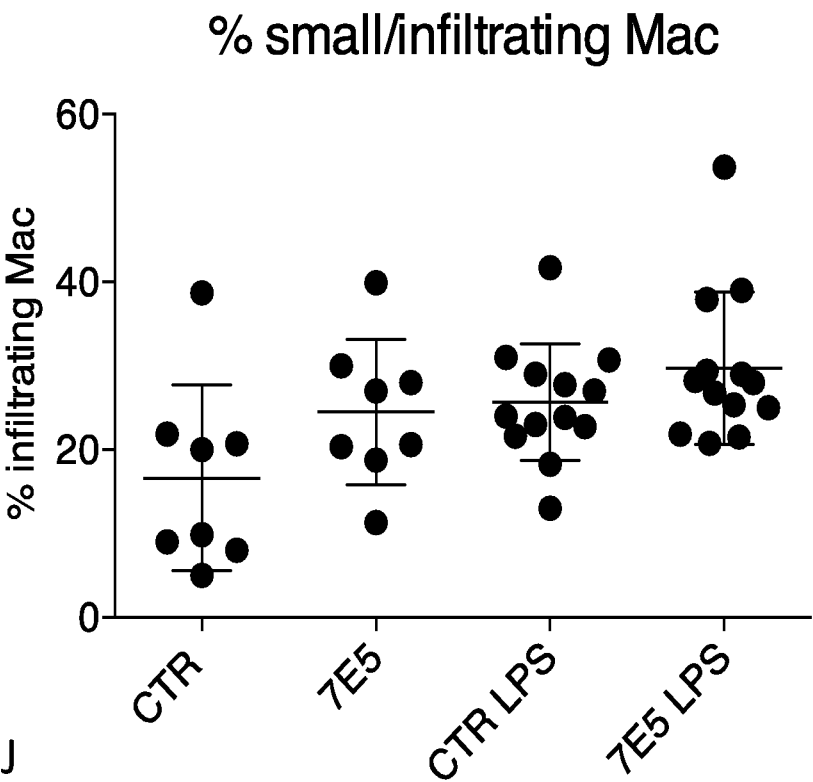


FIG. 13J

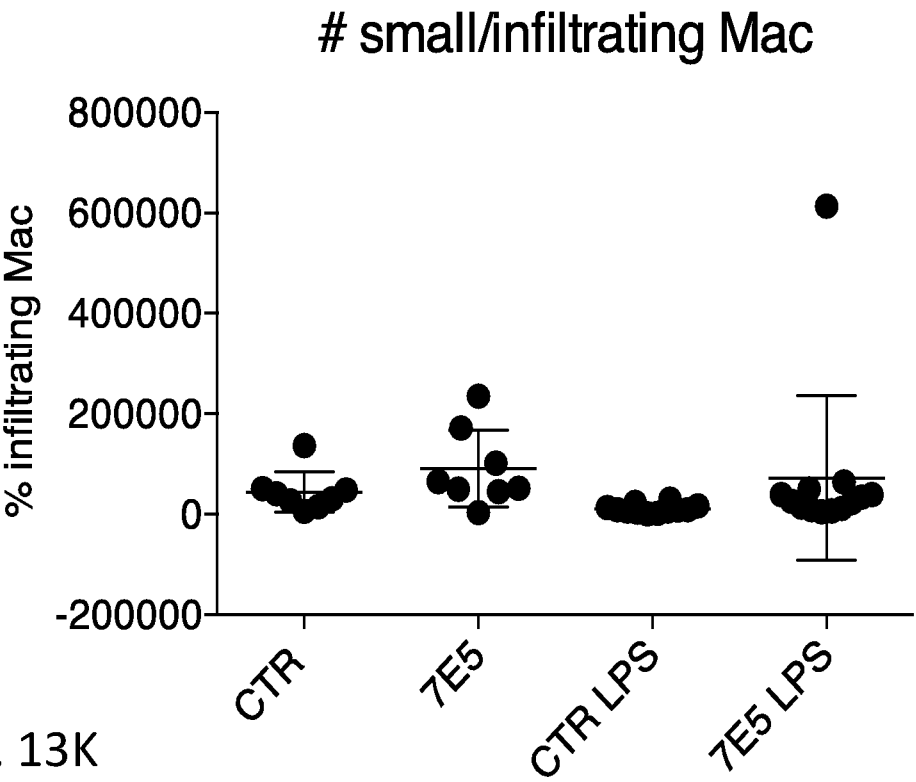


FIG. 13K

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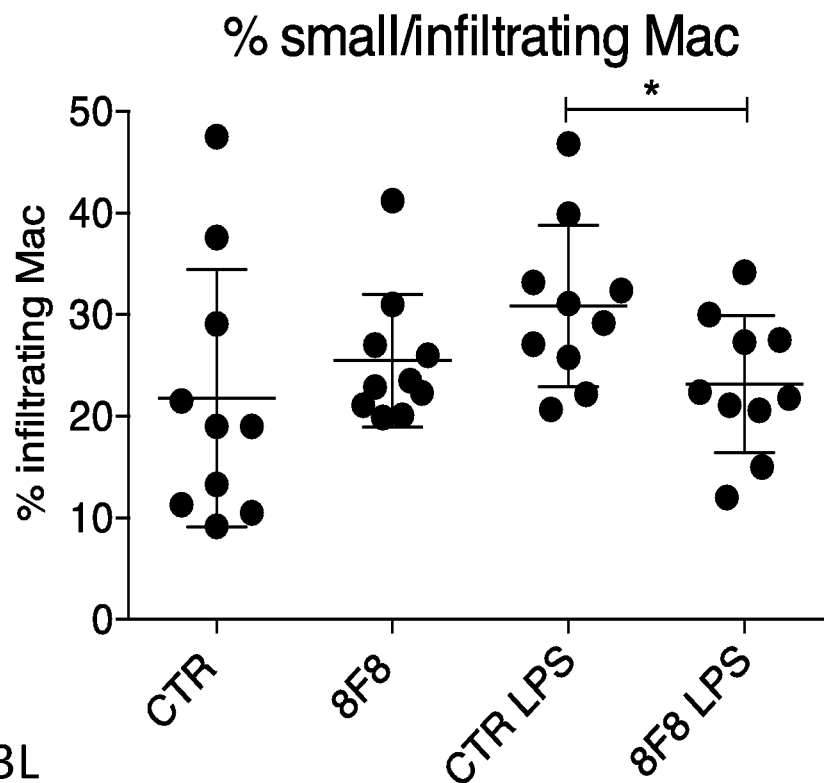


FIG. 13L

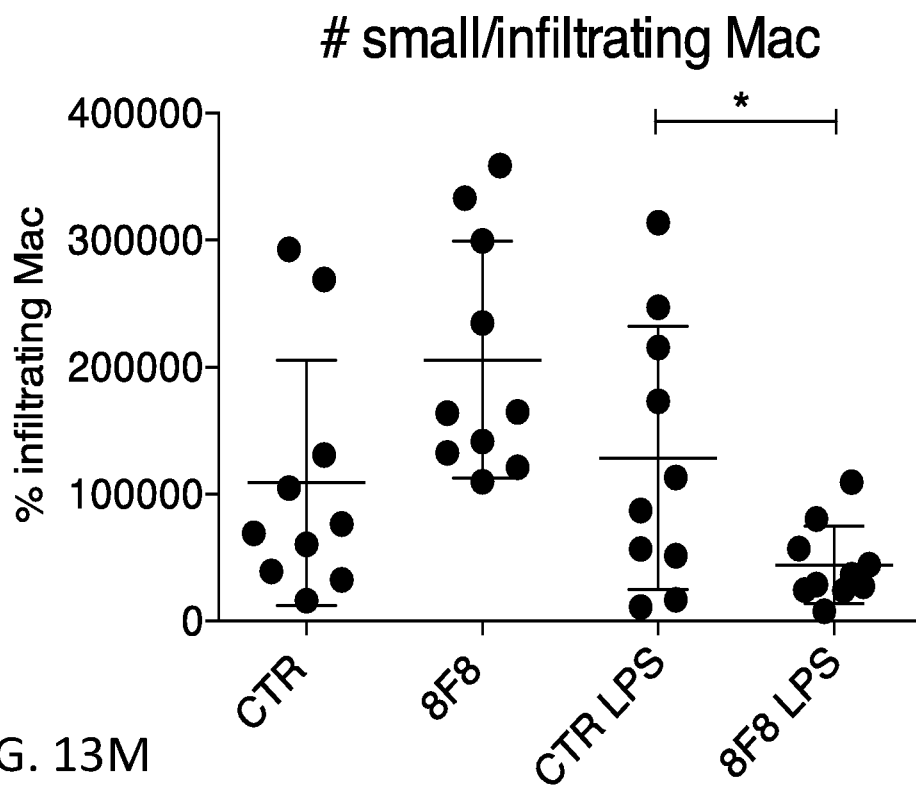


FIG. 13M

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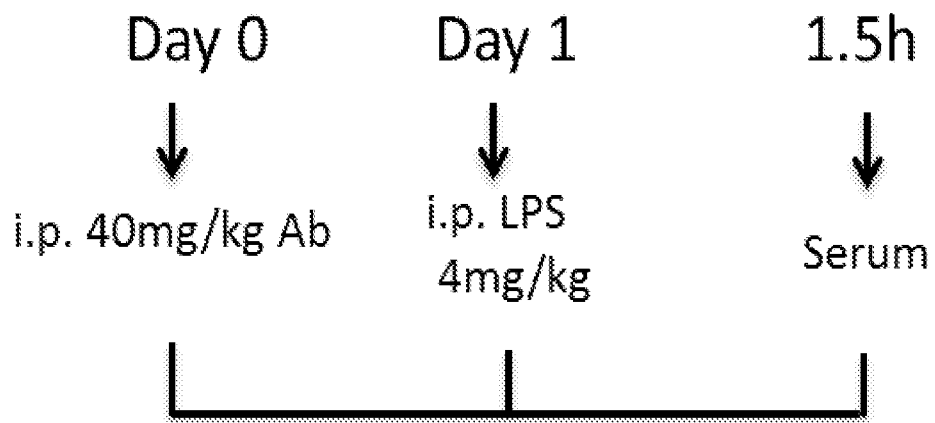


FIG. 13N

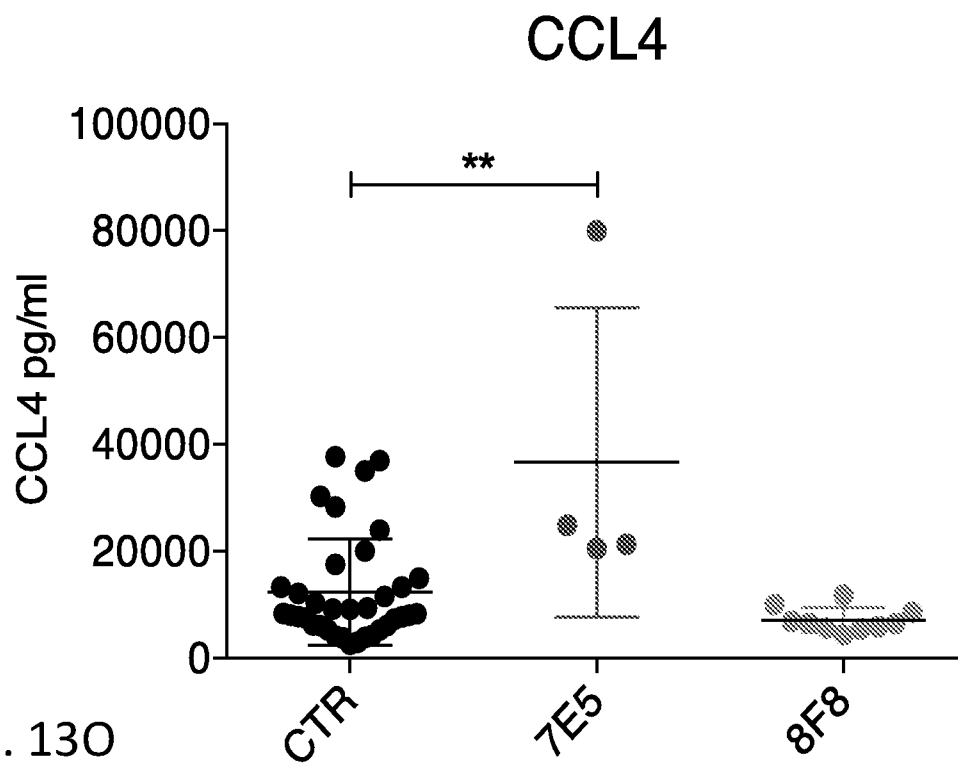
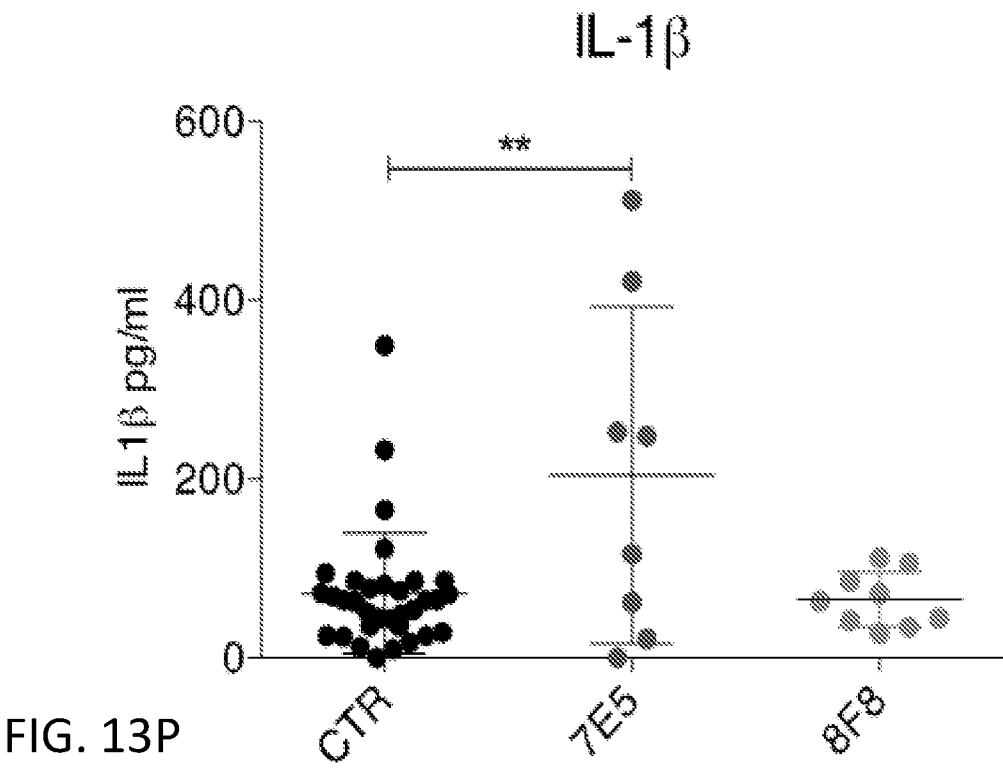
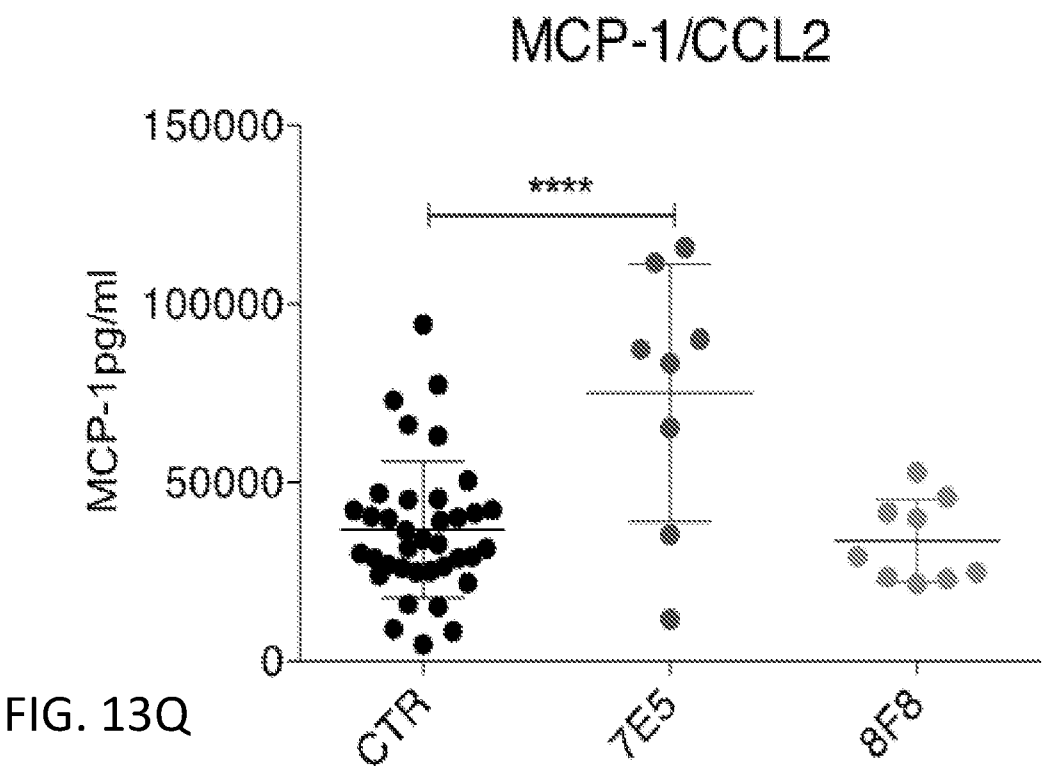


FIG. 13O



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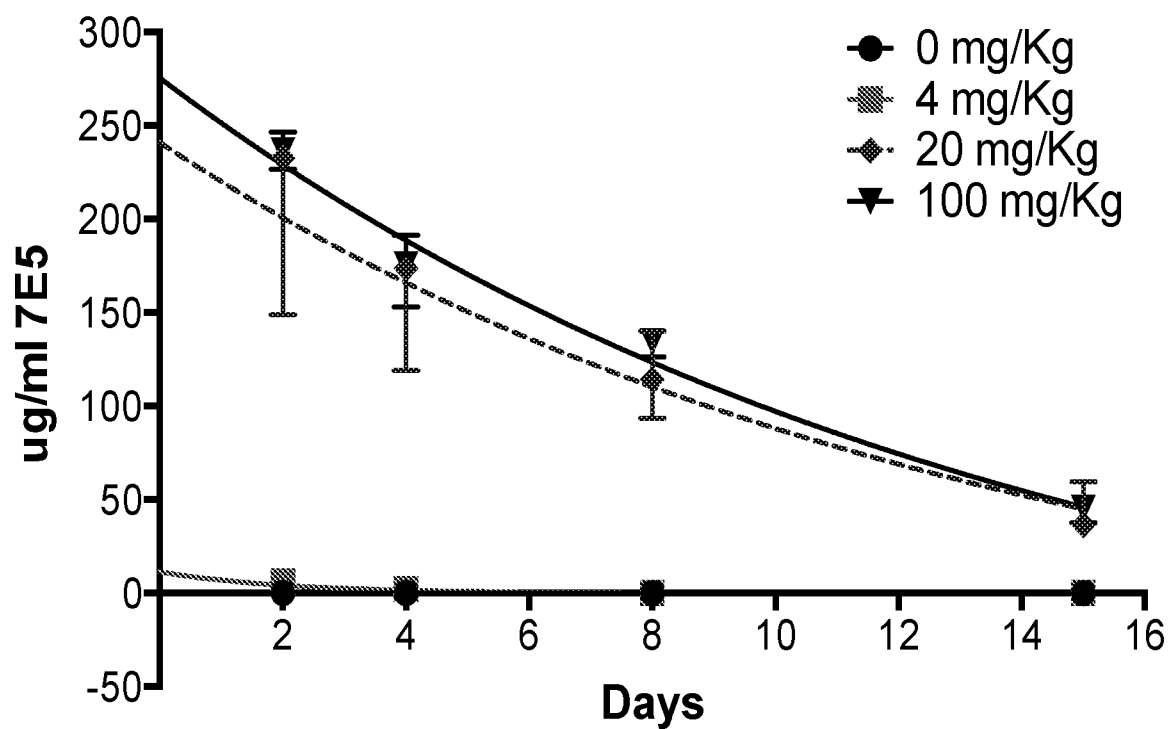


FIG. 14

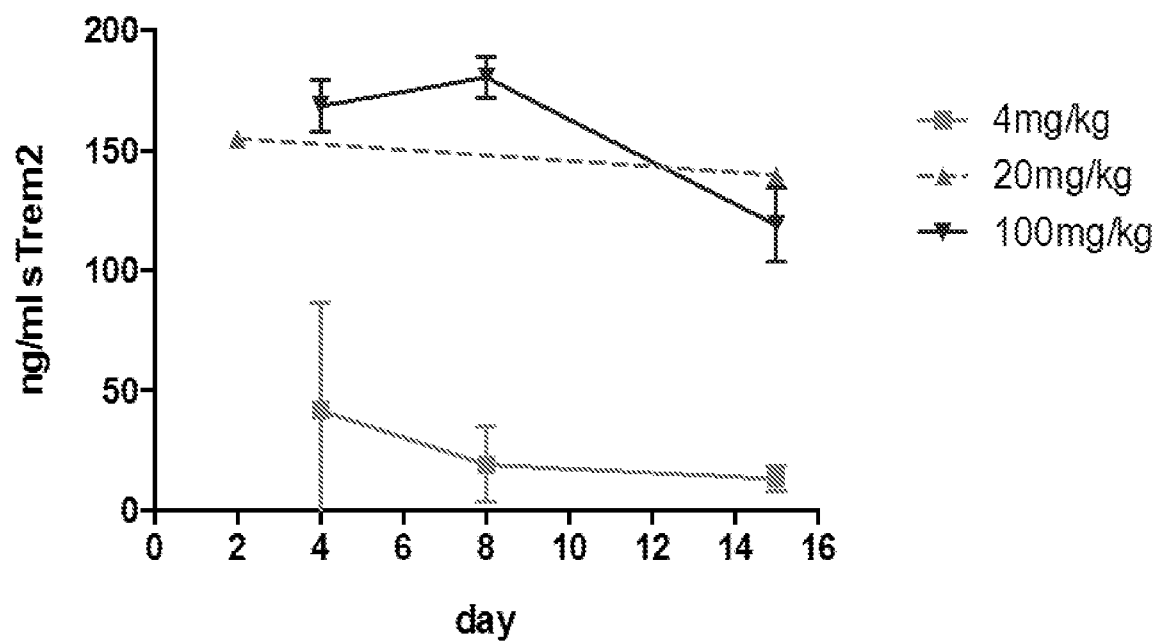
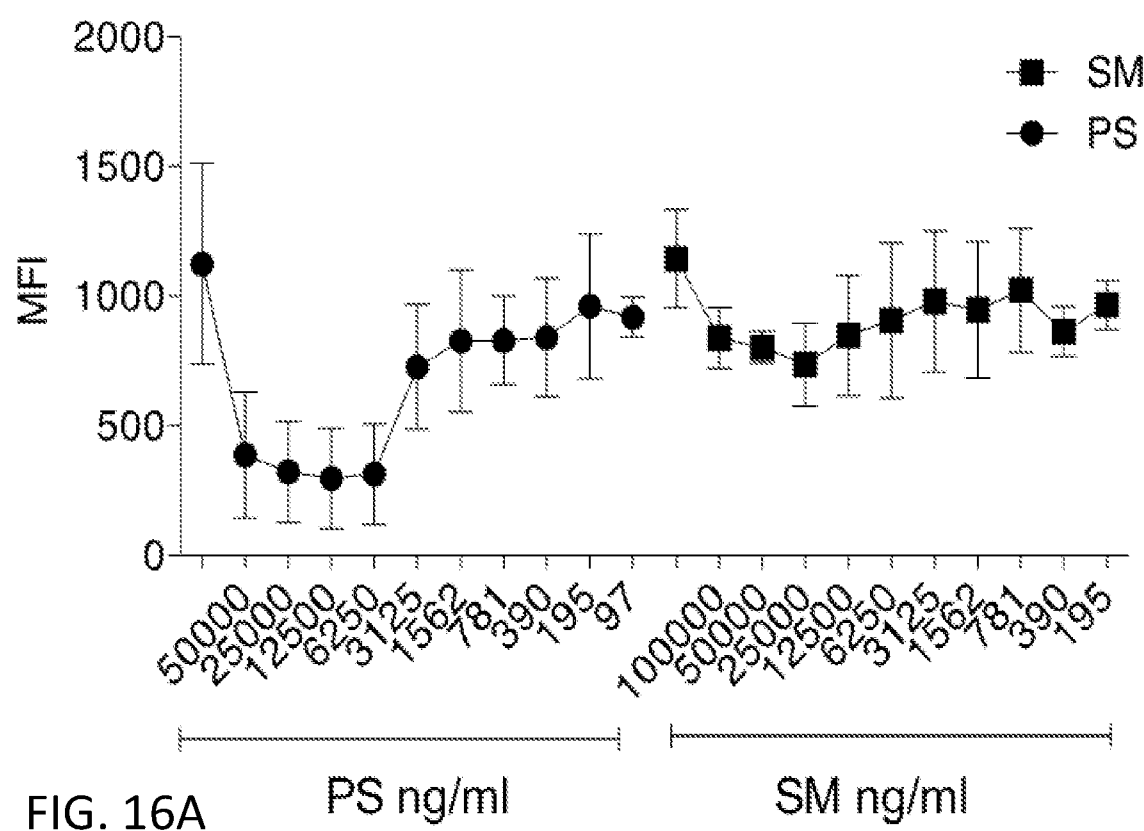
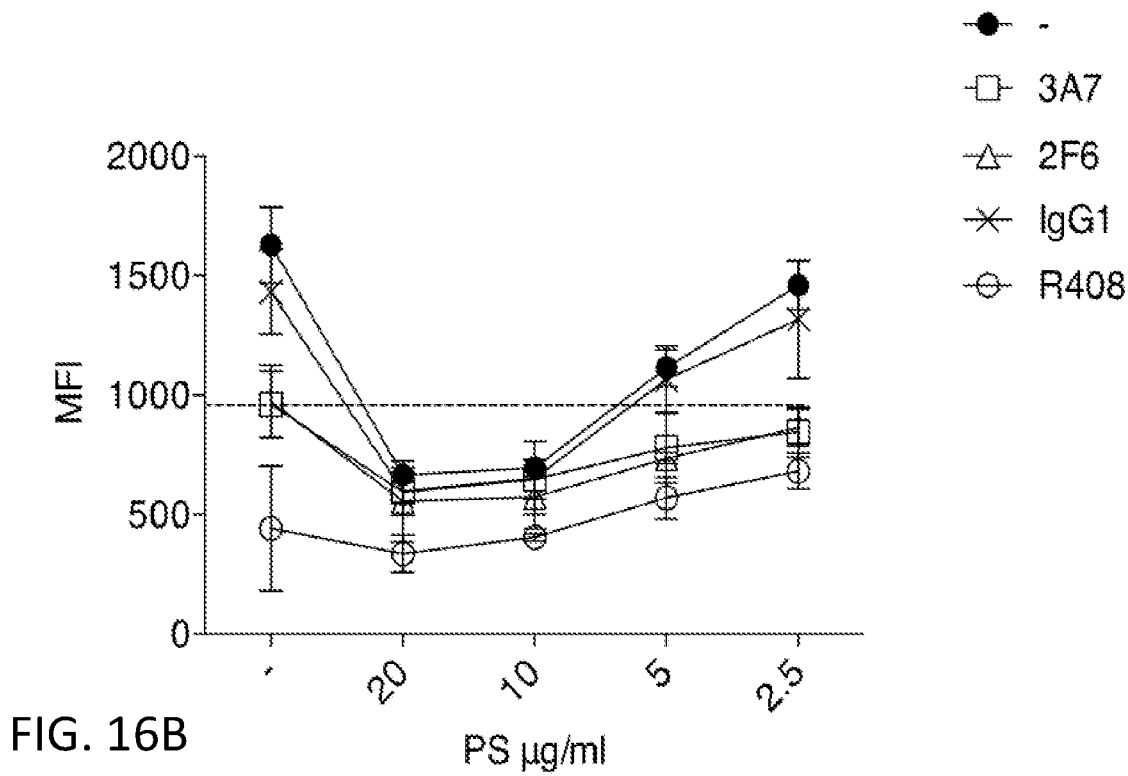


FIG. 15



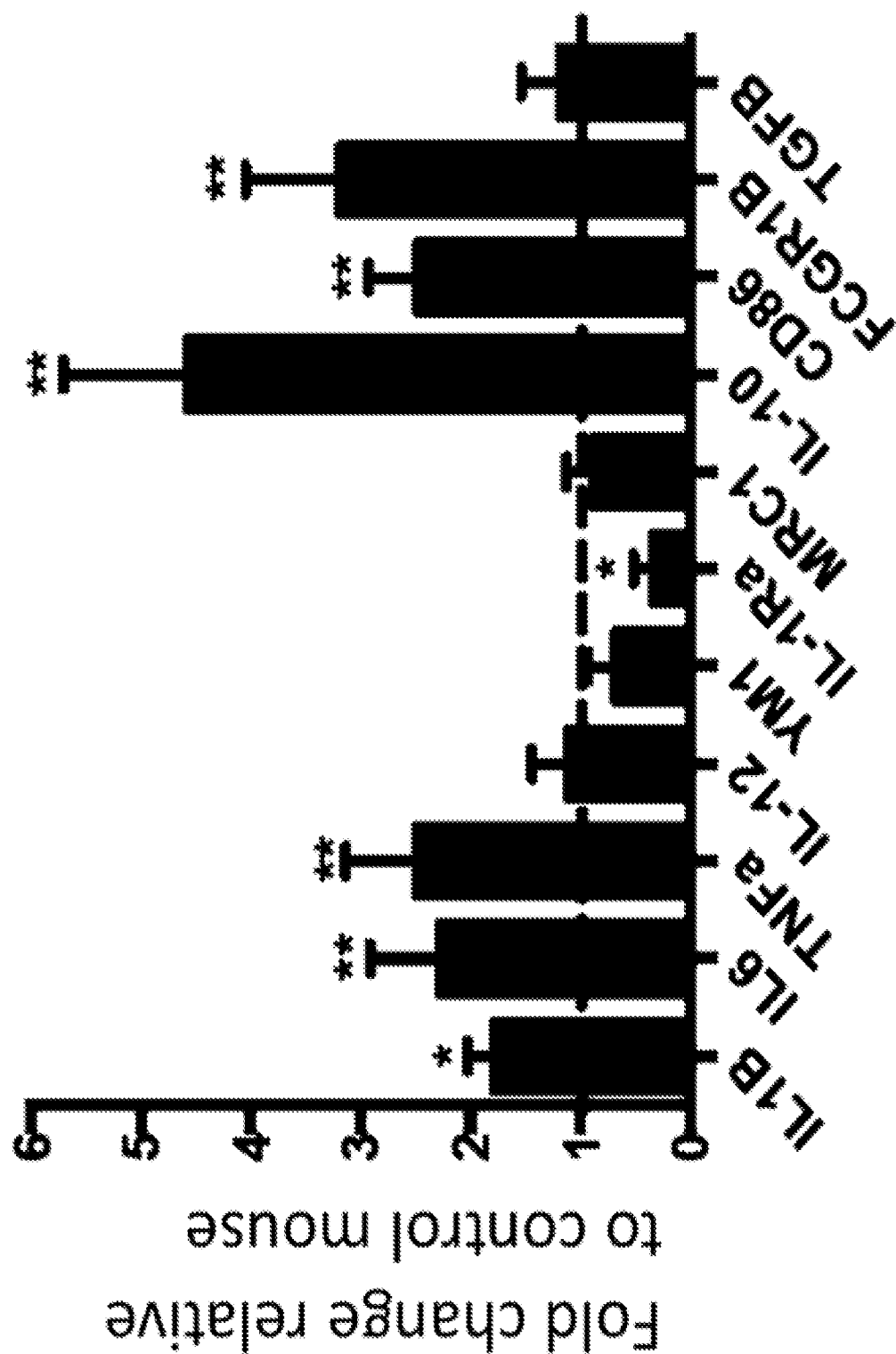


FIG. 17A

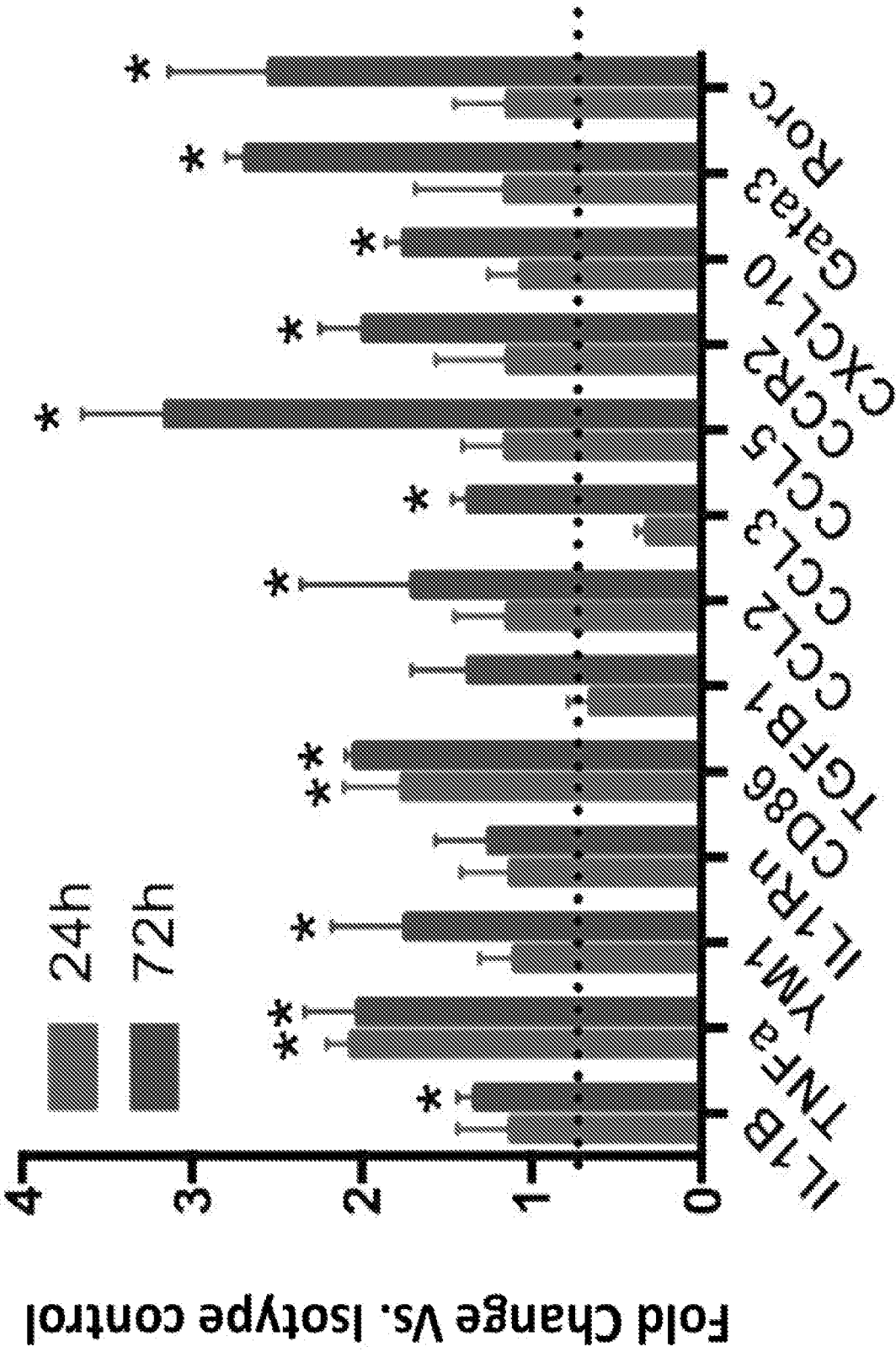


FIG. 17B

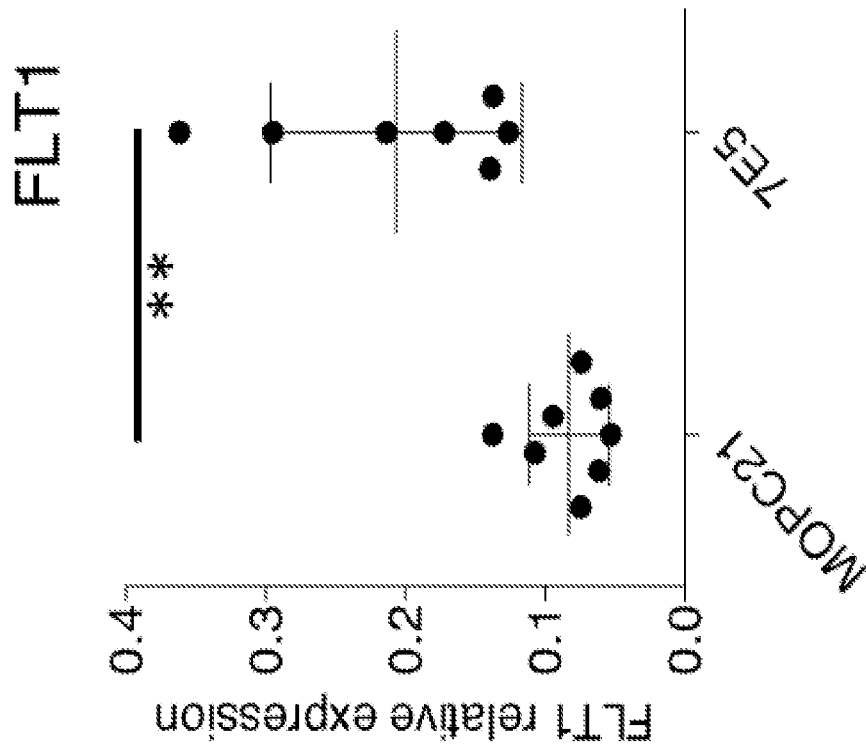


FIG. 17C

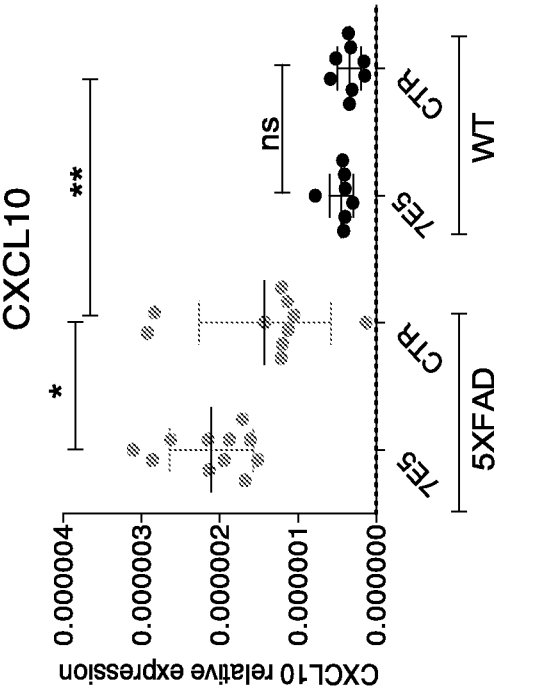


FIG. 17E

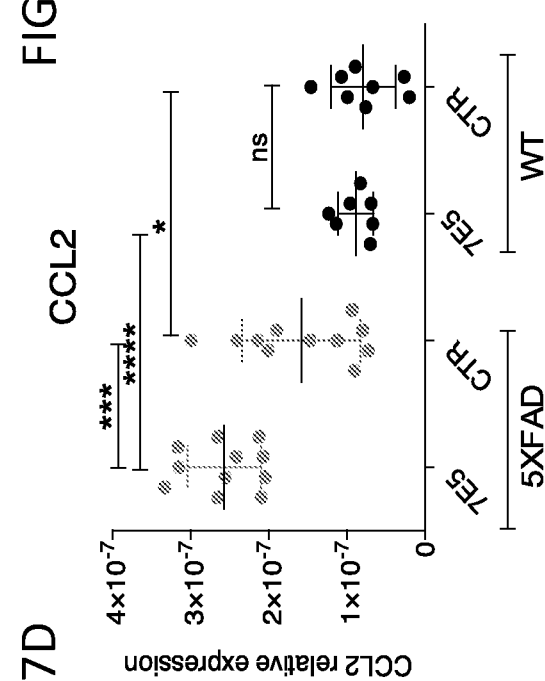
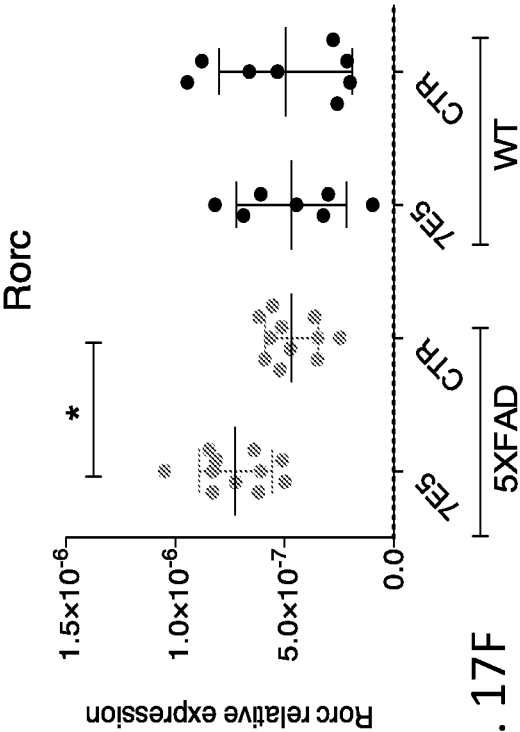


FIG. 17F

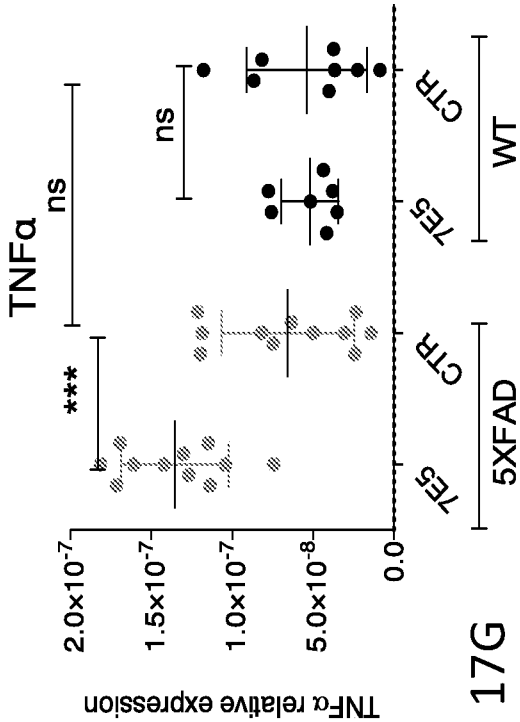


FIG. 17G

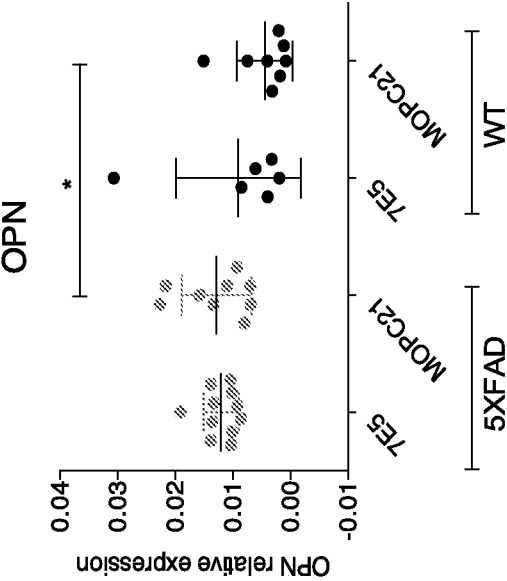


FIG. 17I

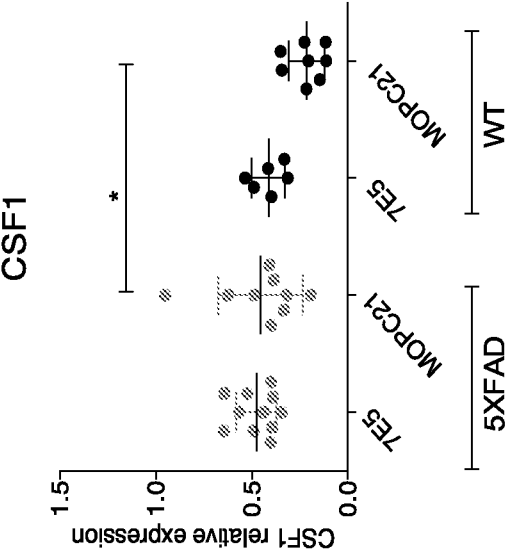


FIG. 17H

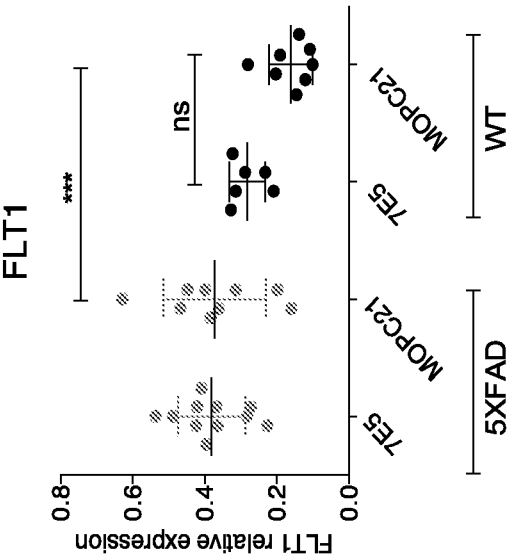


FIG. 17K

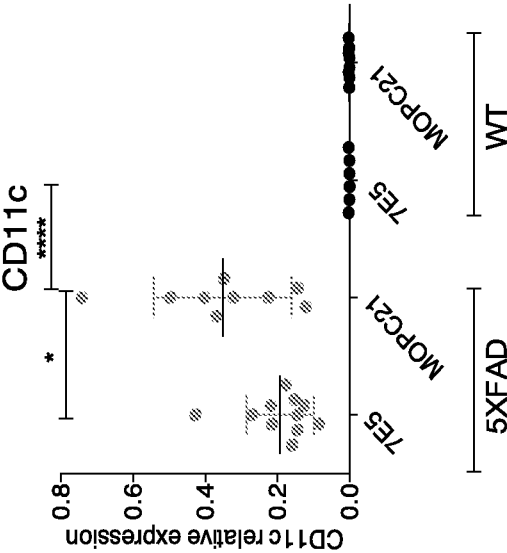


FIG. 17J

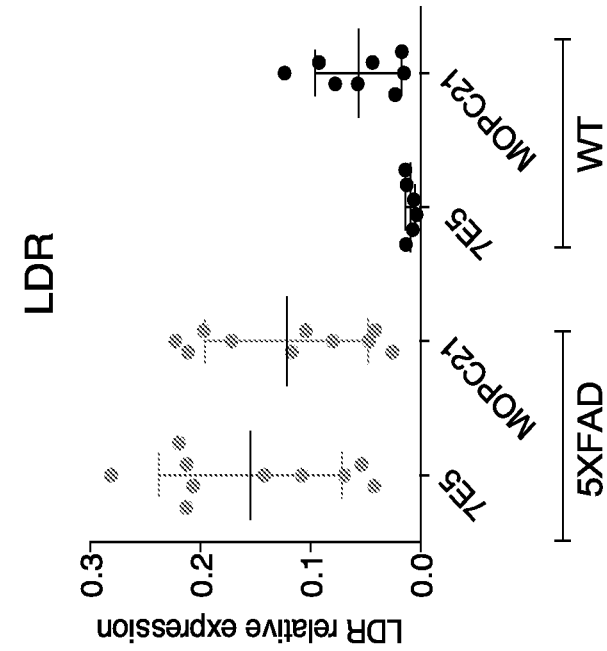


FIG. 17M

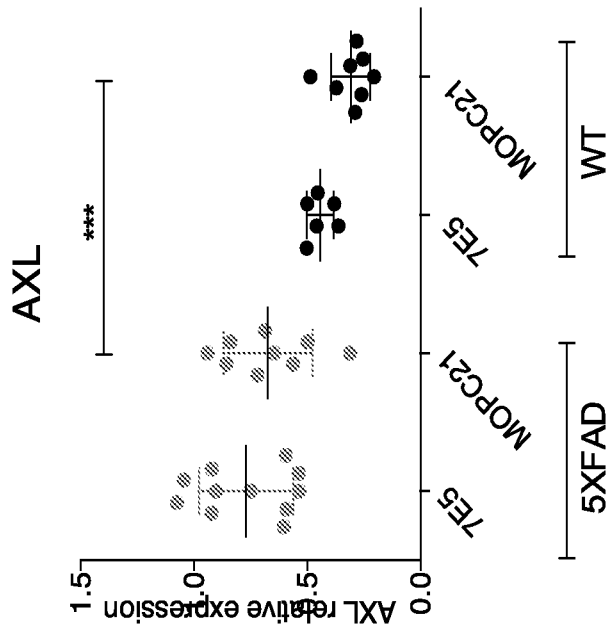
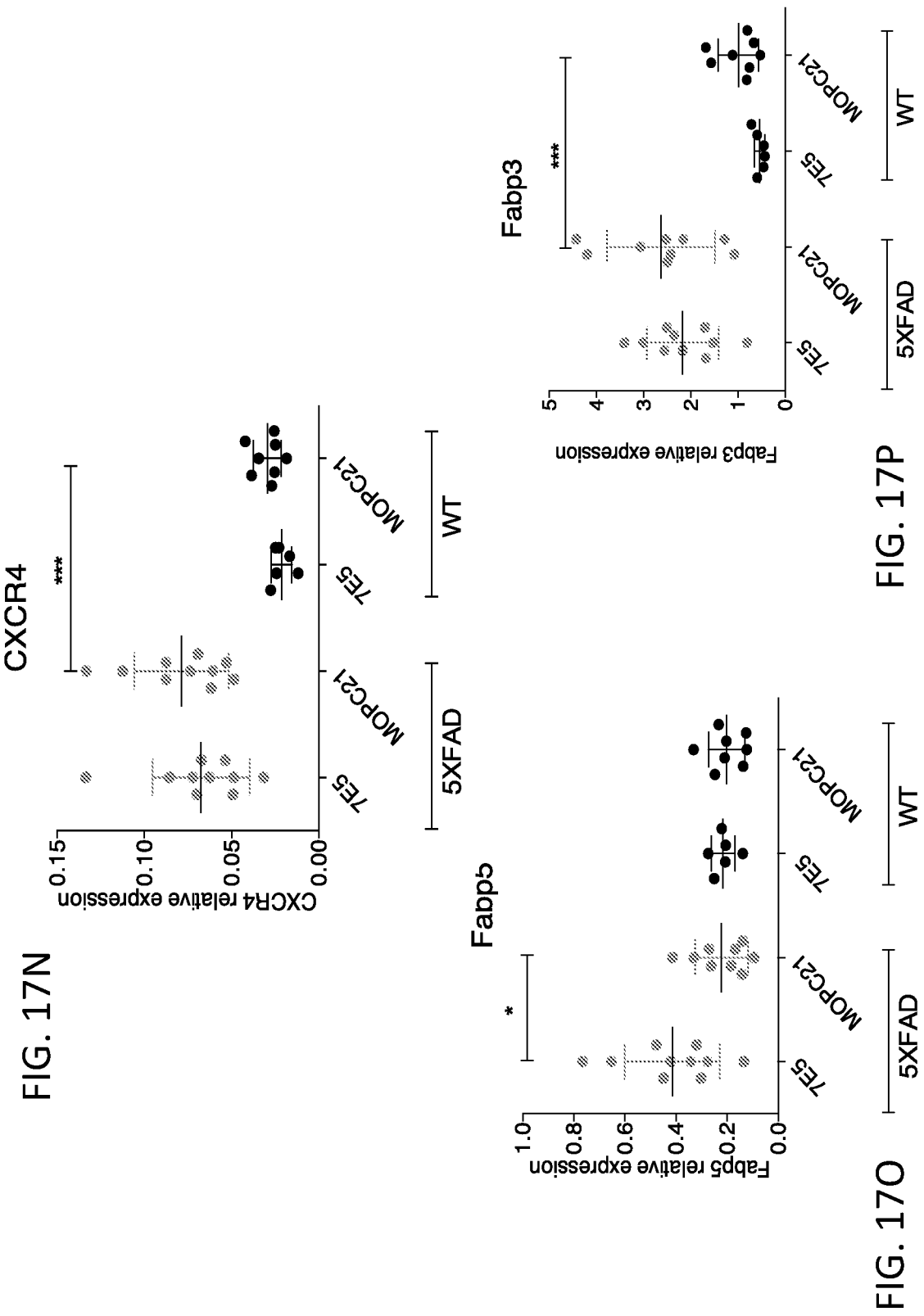


FIG. 17L



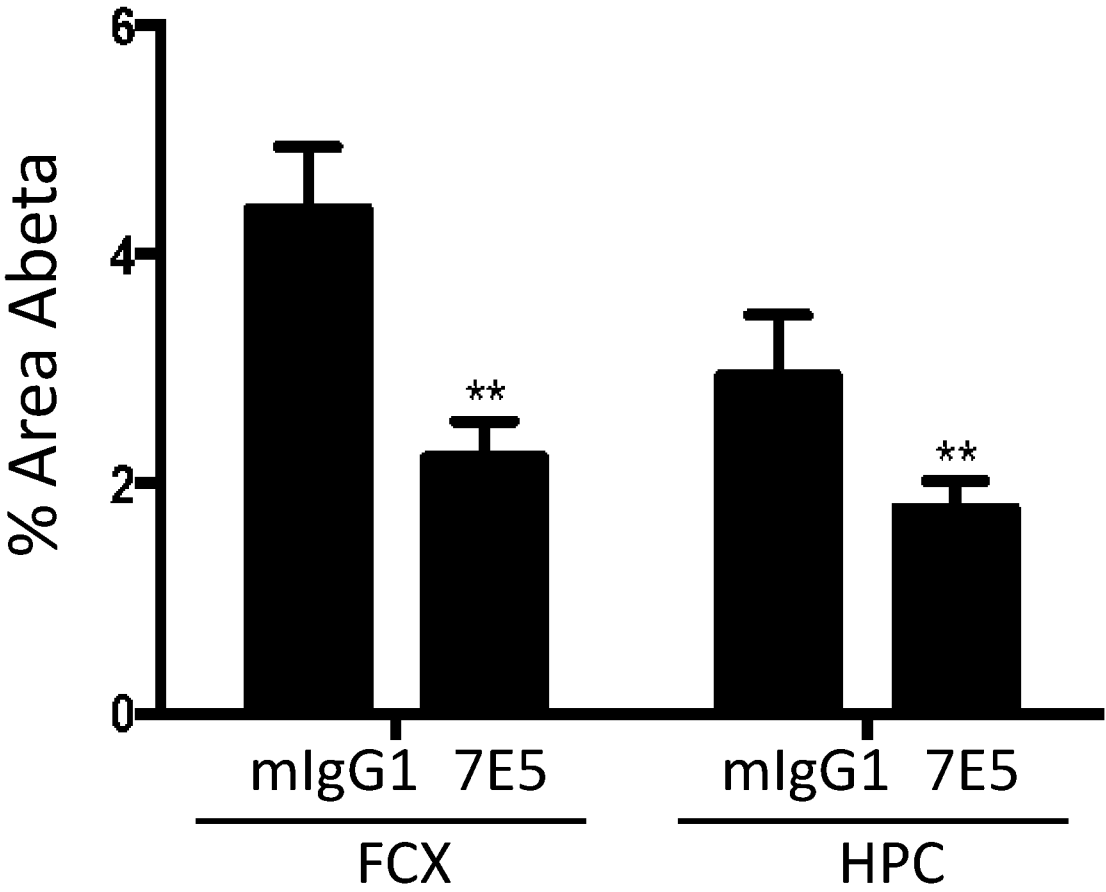


FIG. 17Q

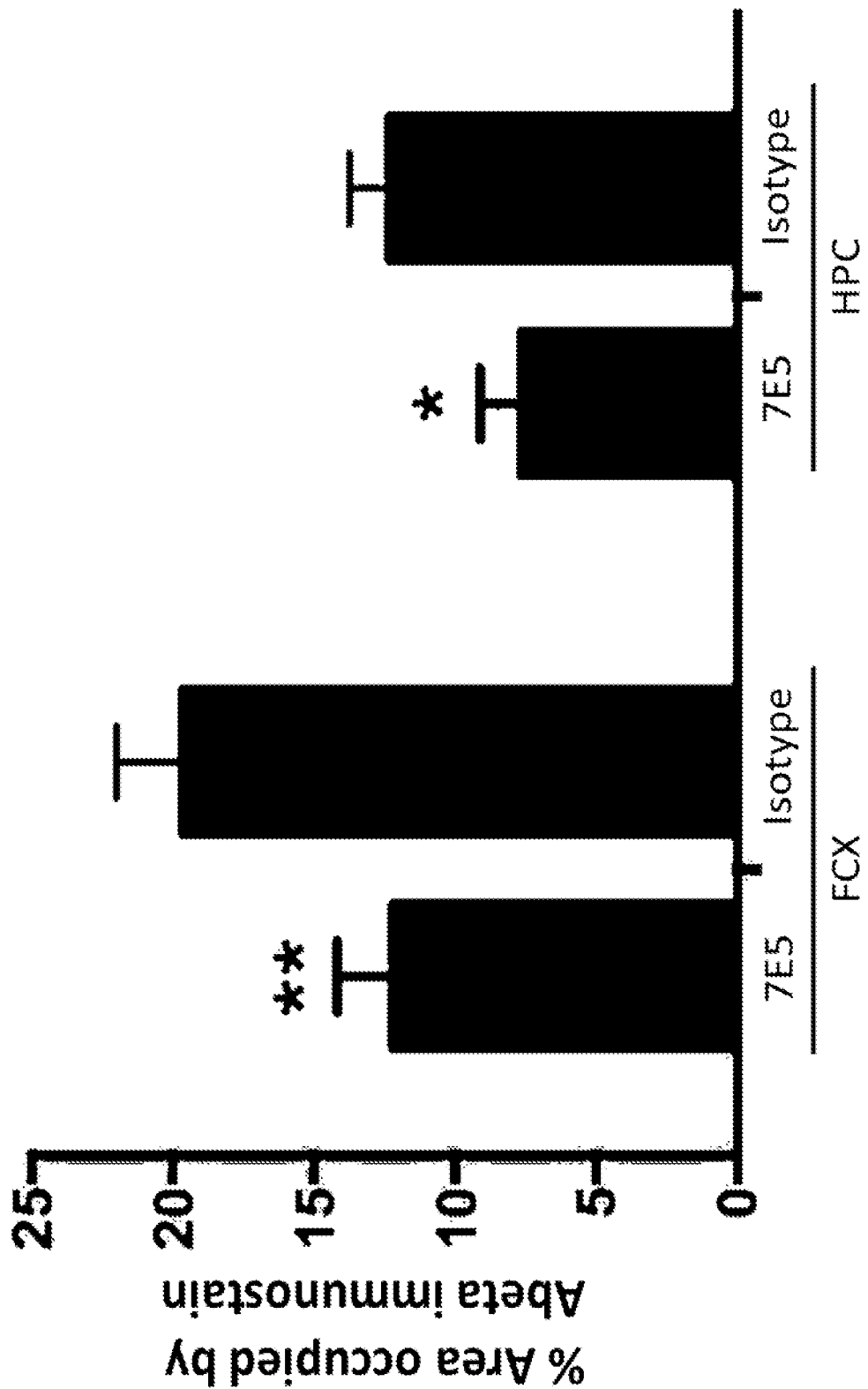


FIG. 17R

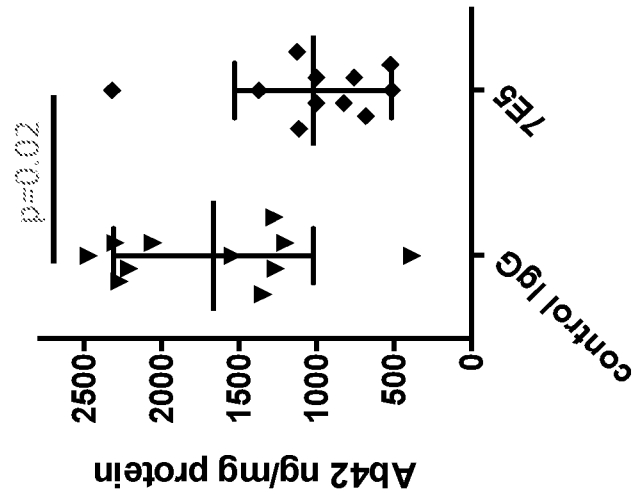


FIG. 17U

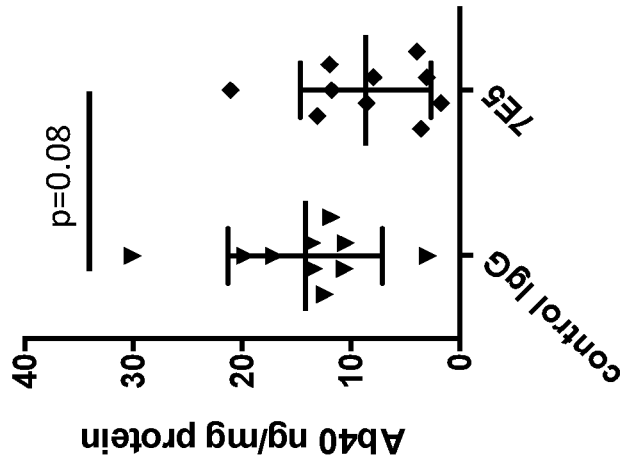


FIG. 17T

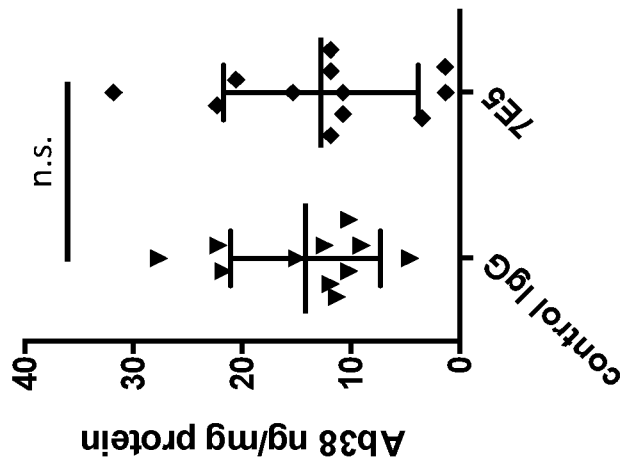


FIG. 17S

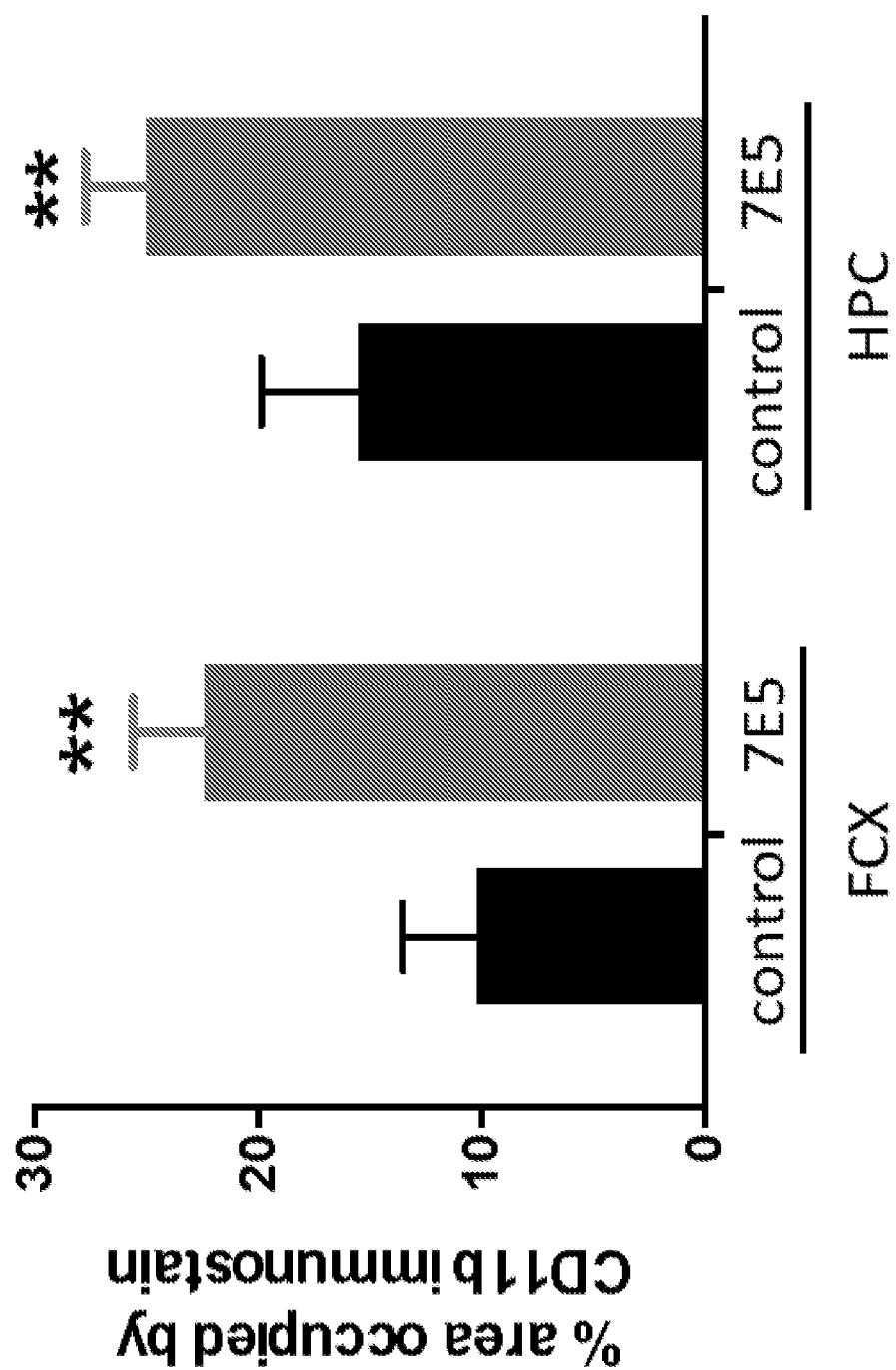


FIG. 17V

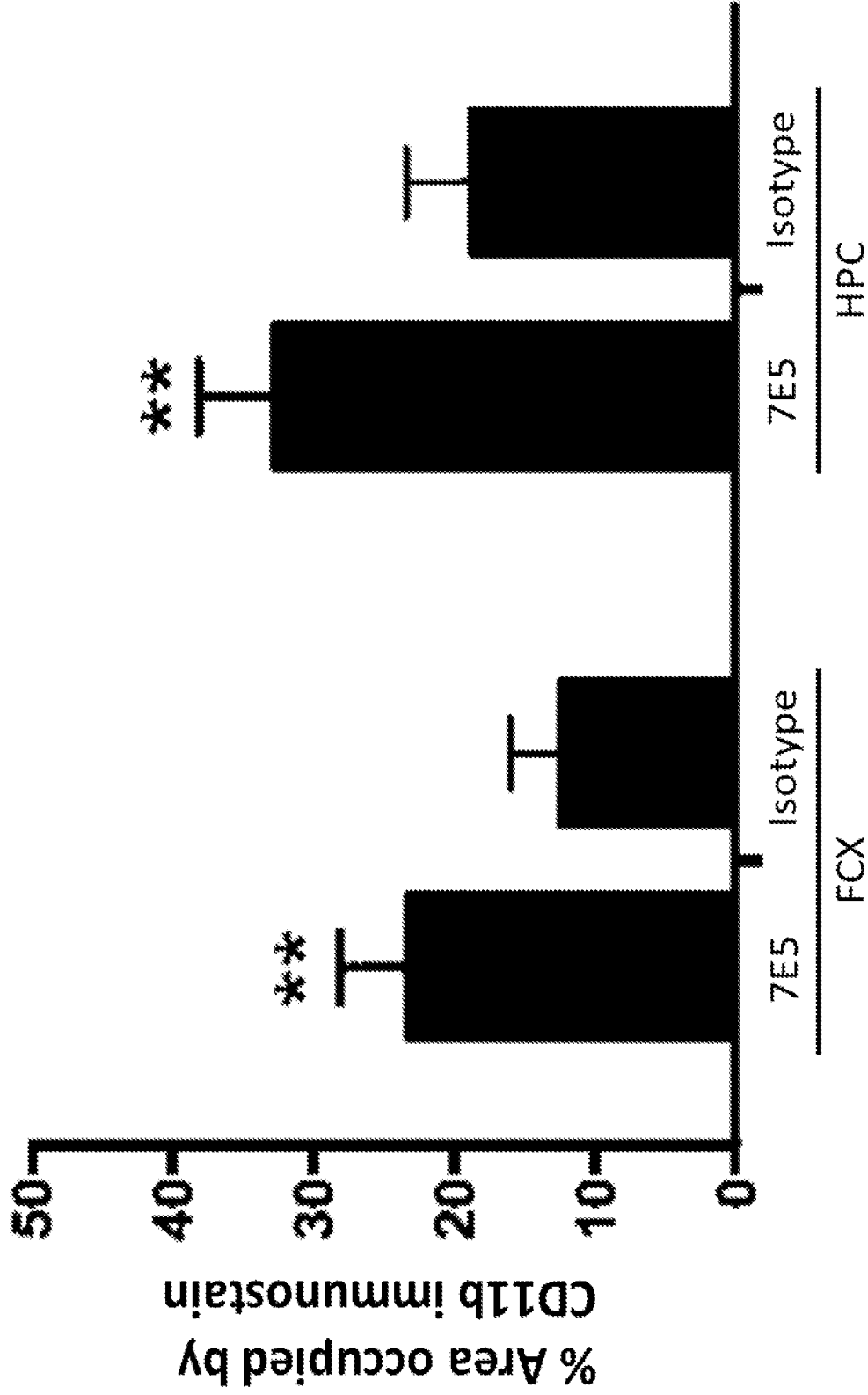


FIG. 17W

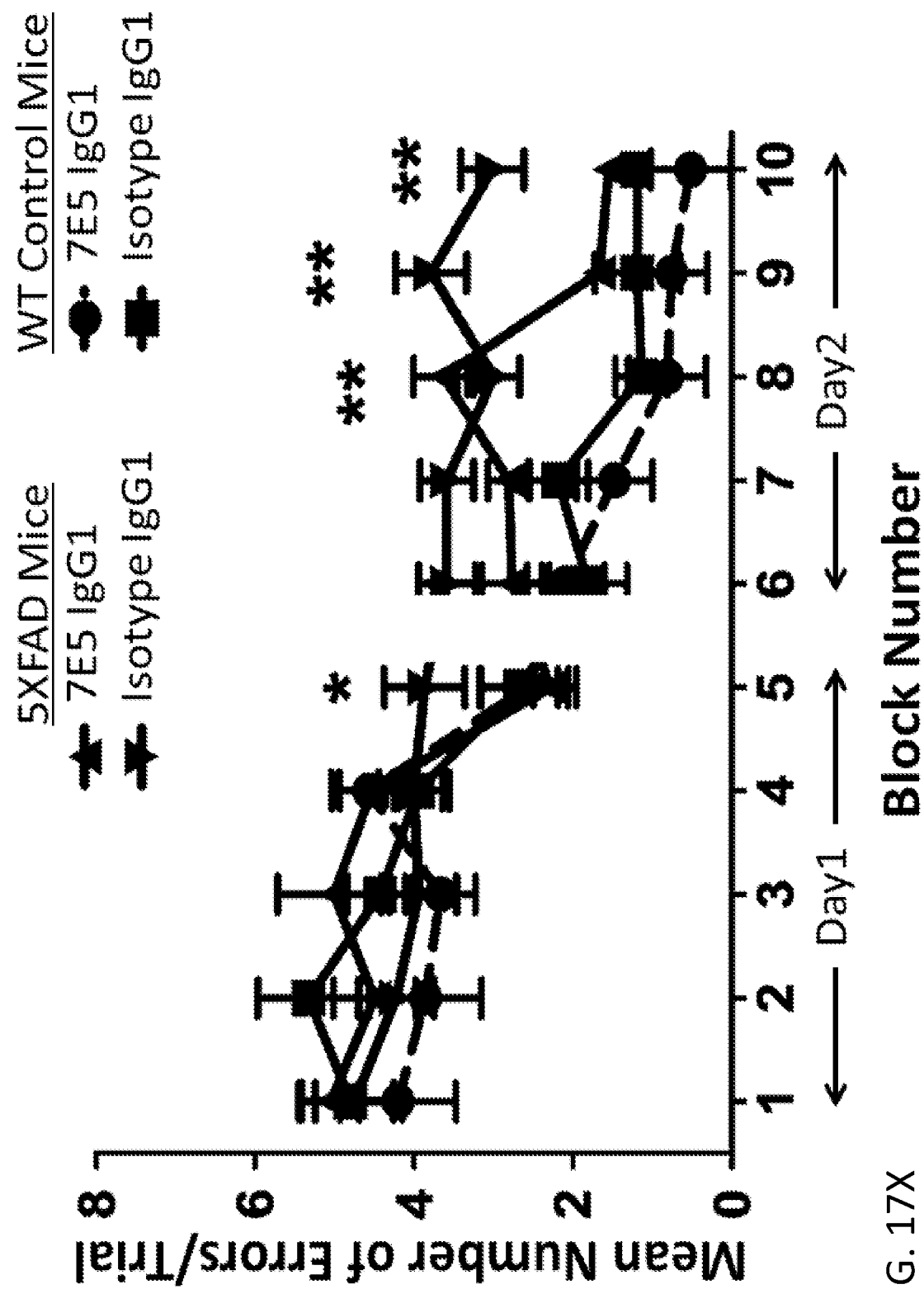


FIG. 17X

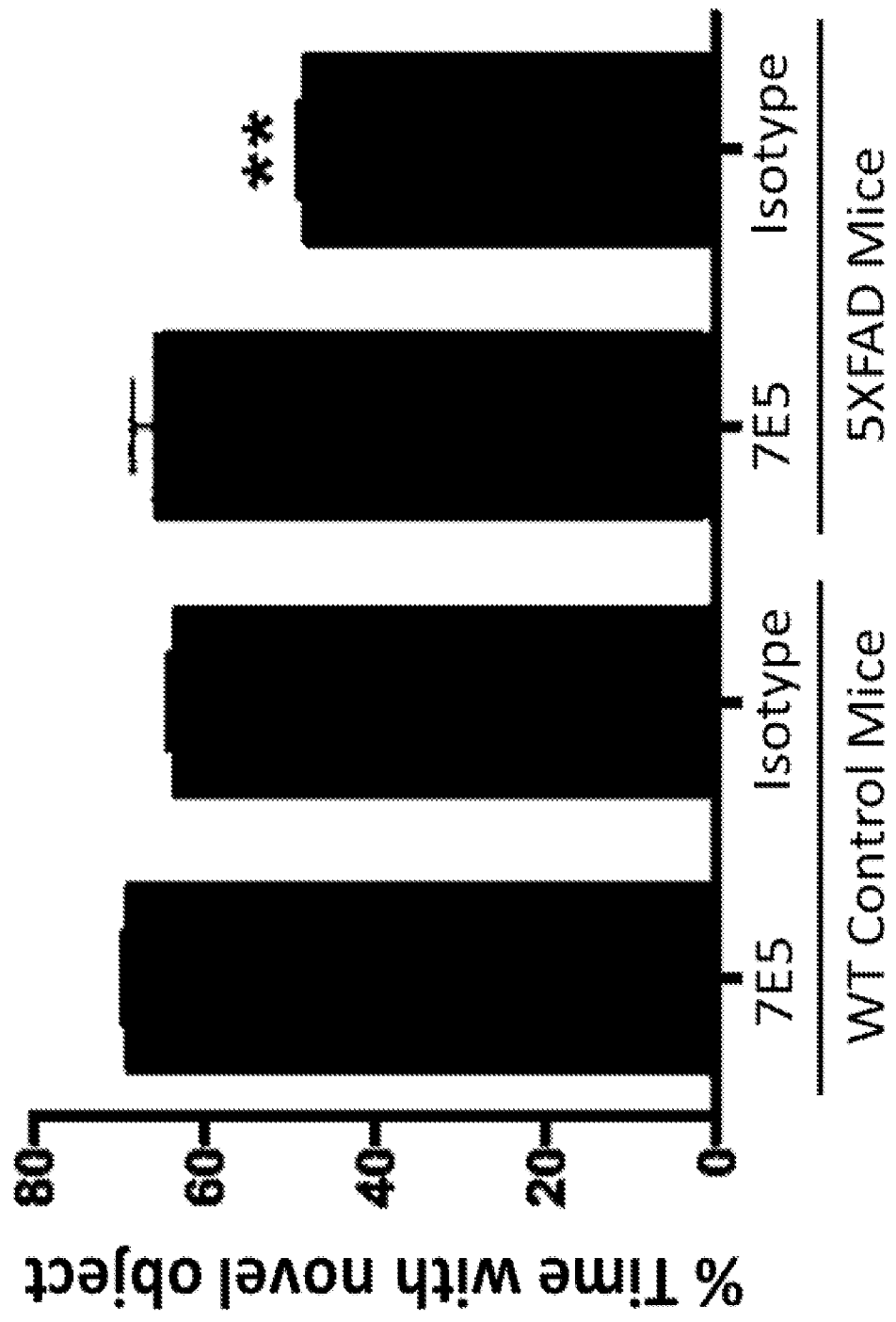


FIG. 17Y

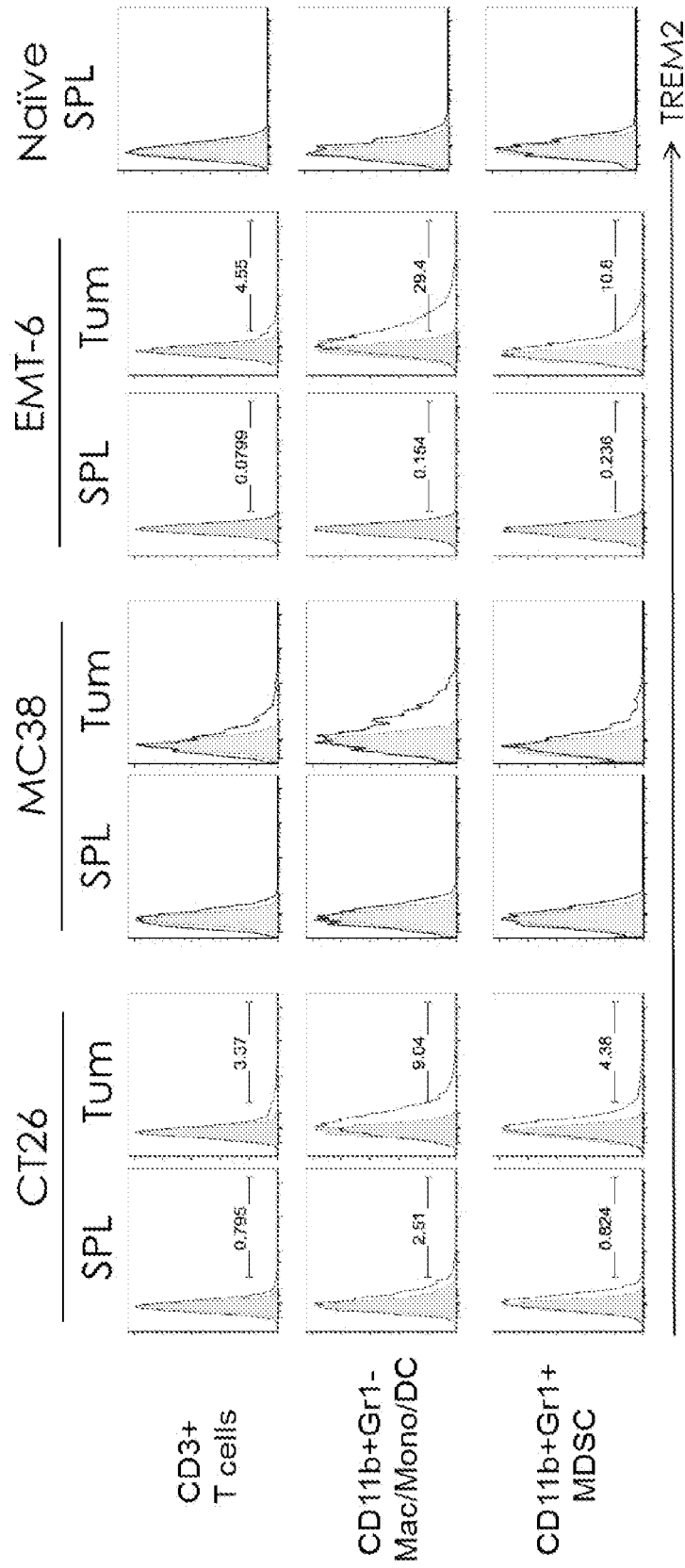


FIG. 18

FIG. 19A

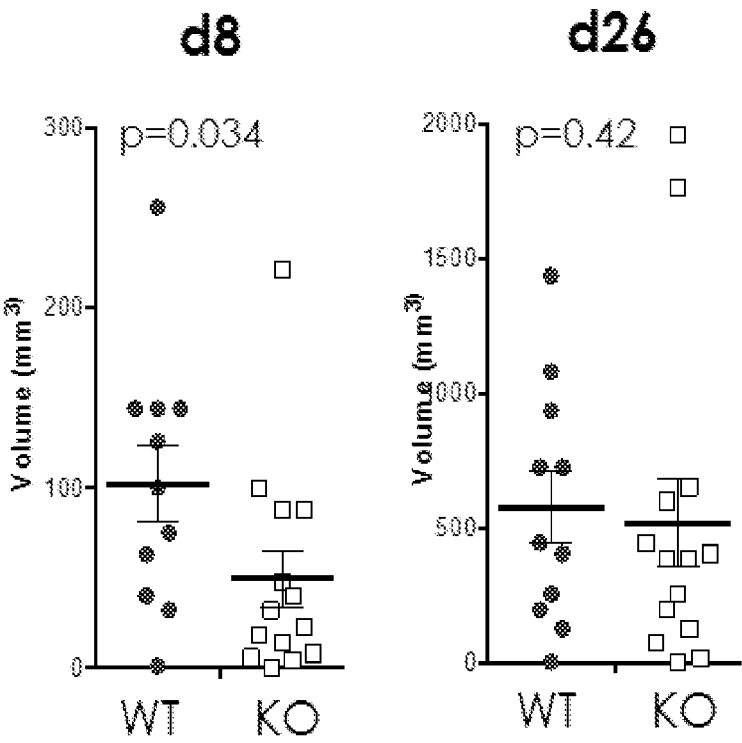
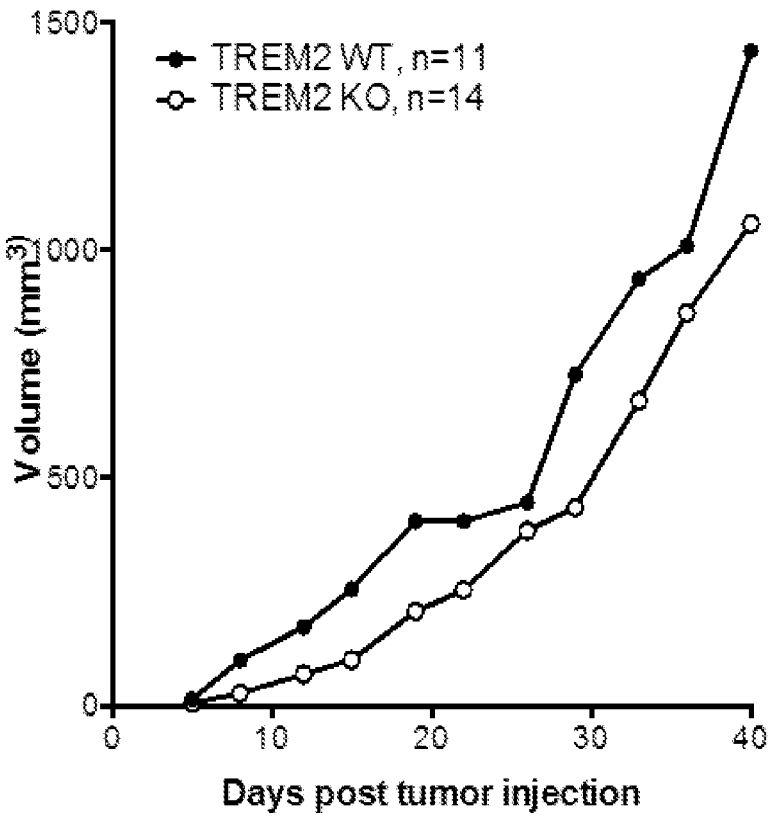


FIG. 19B



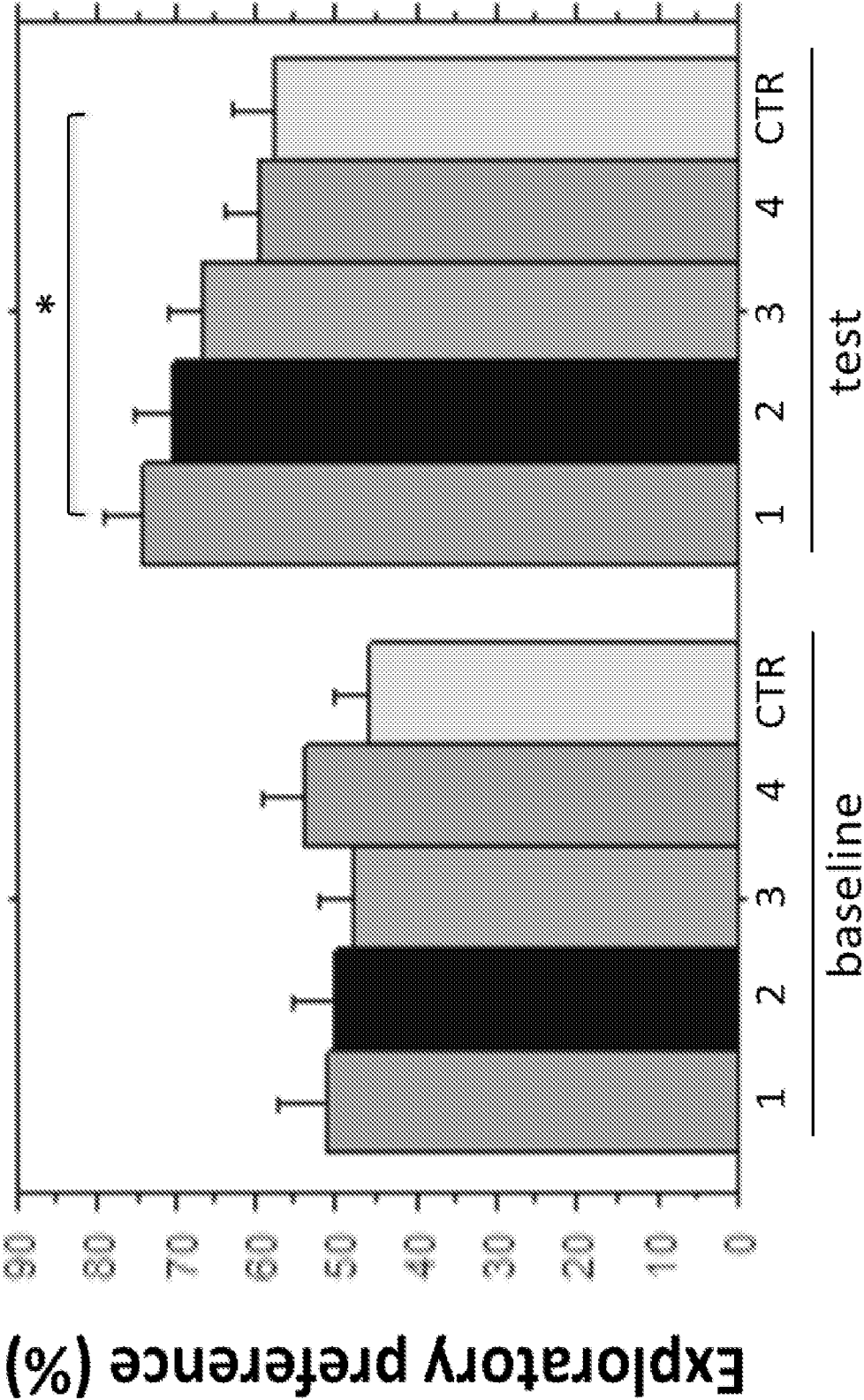


FIG. 20

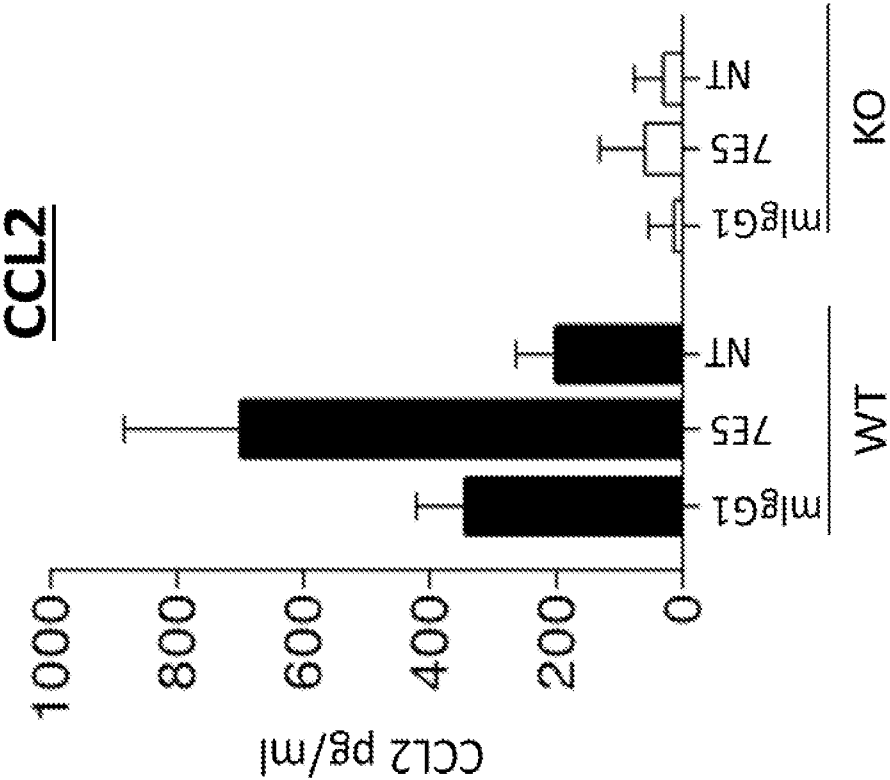


FIG. 21B

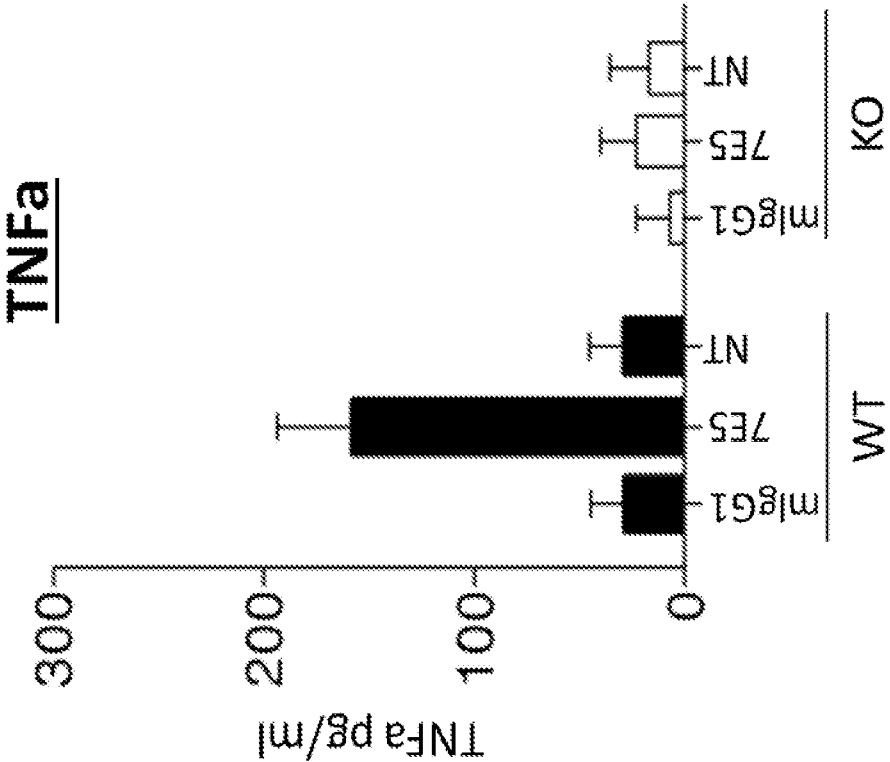


FIG. 21A

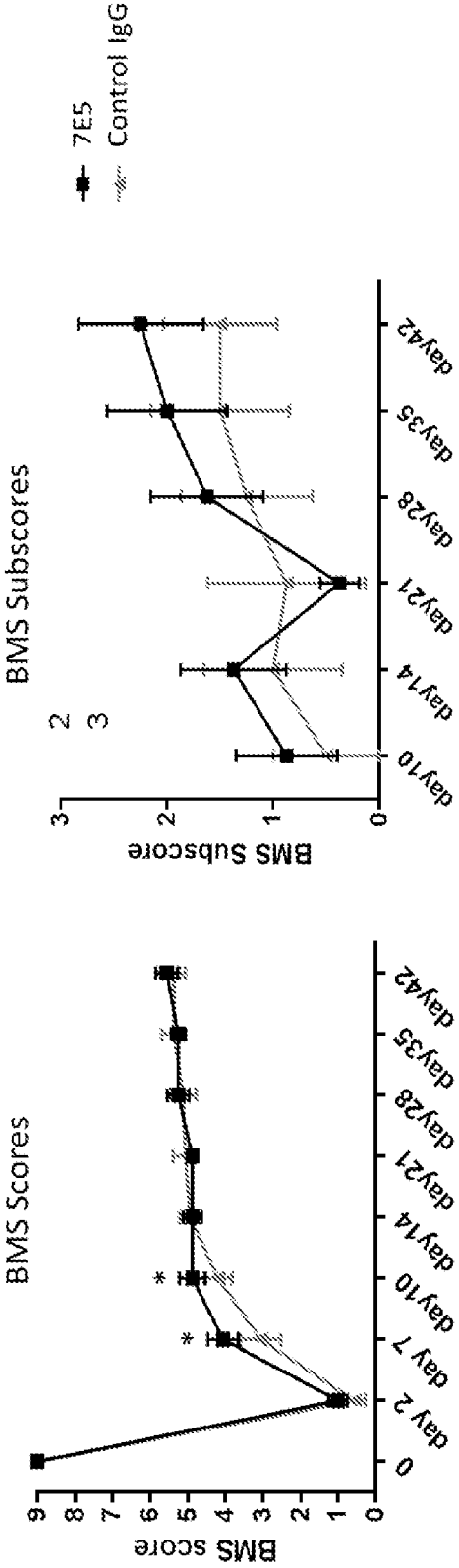


FIG. 22A

FIG. 22B

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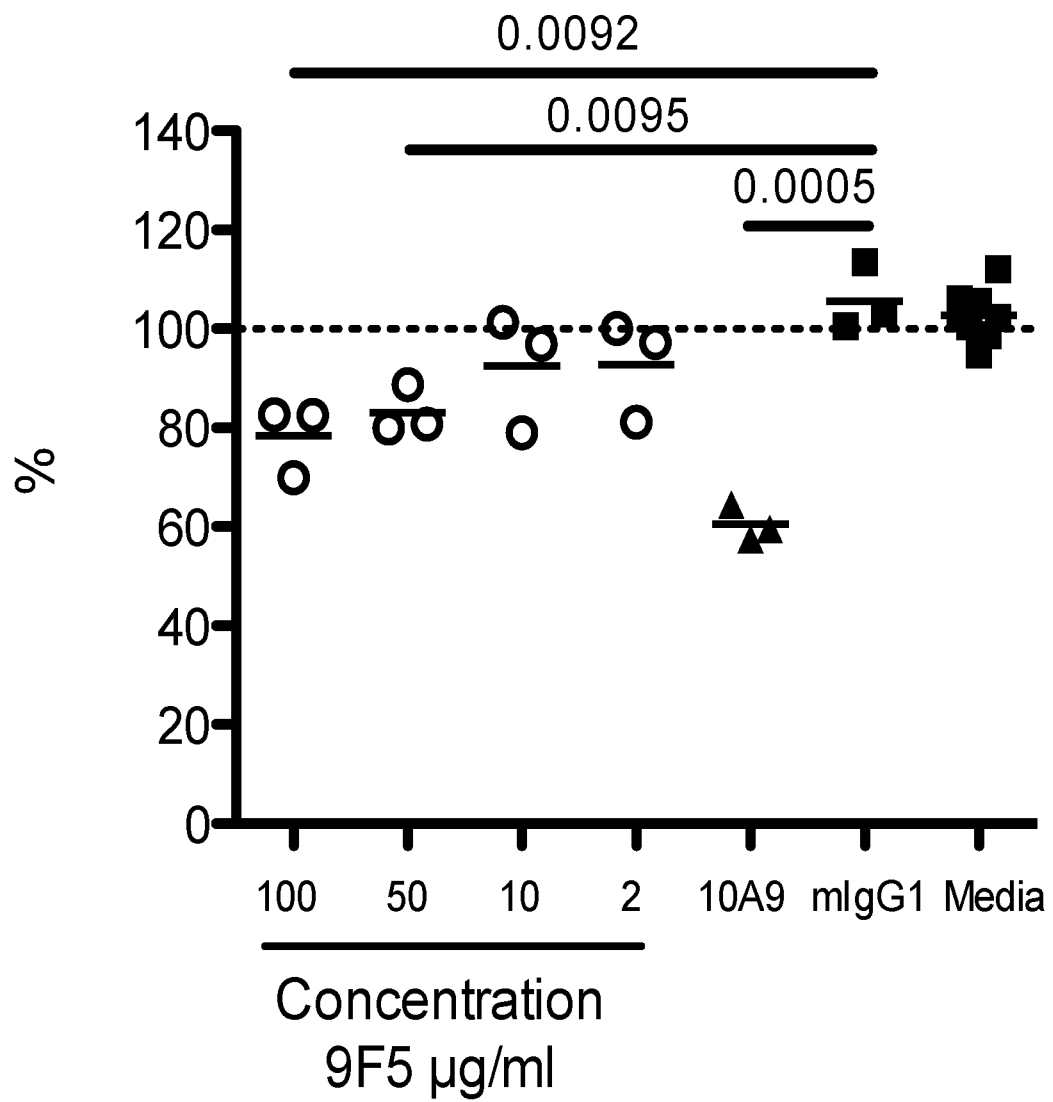


FIG. 23

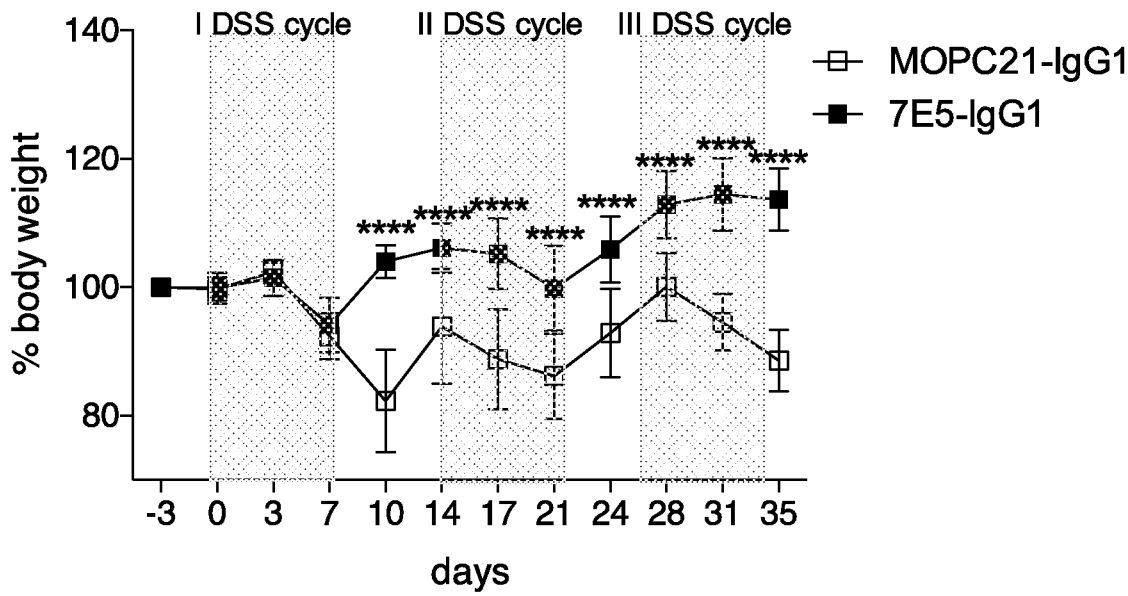


FIG. 24A

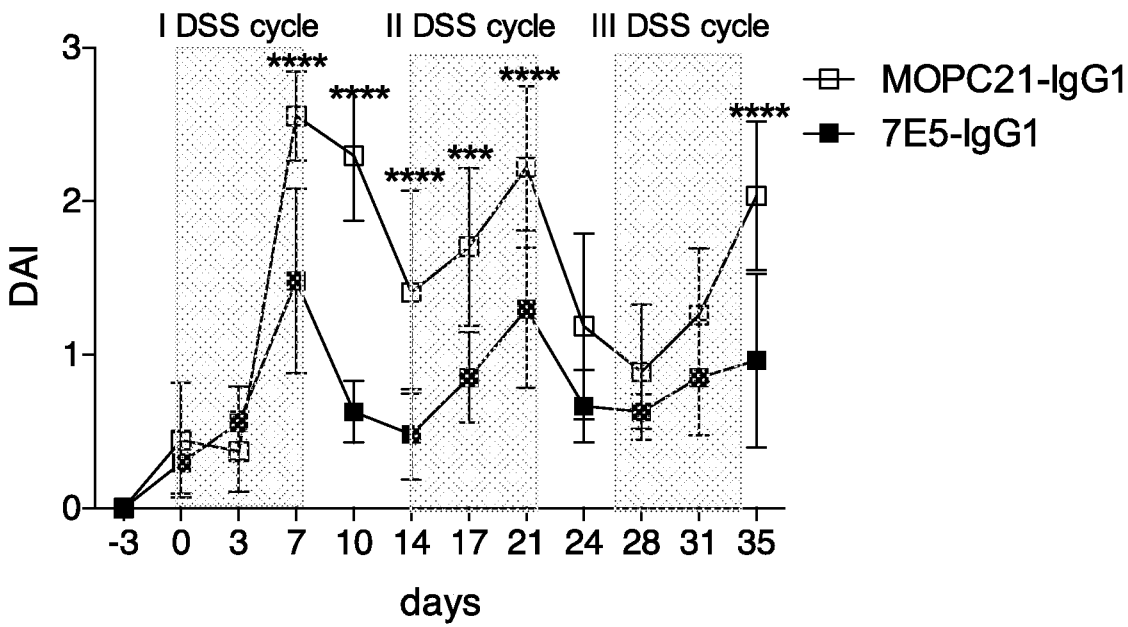


FIG. 24B

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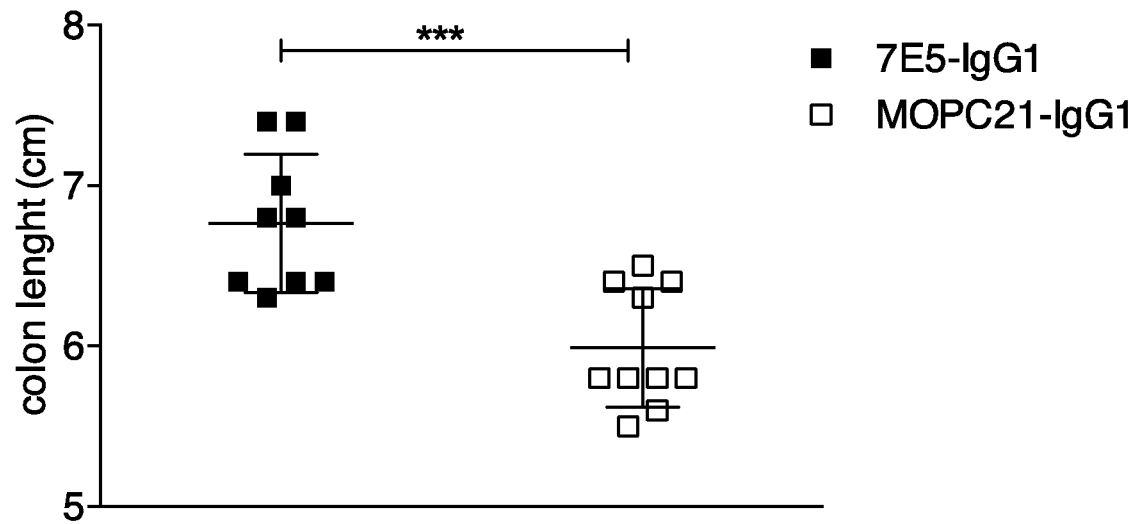


FIG. 24C

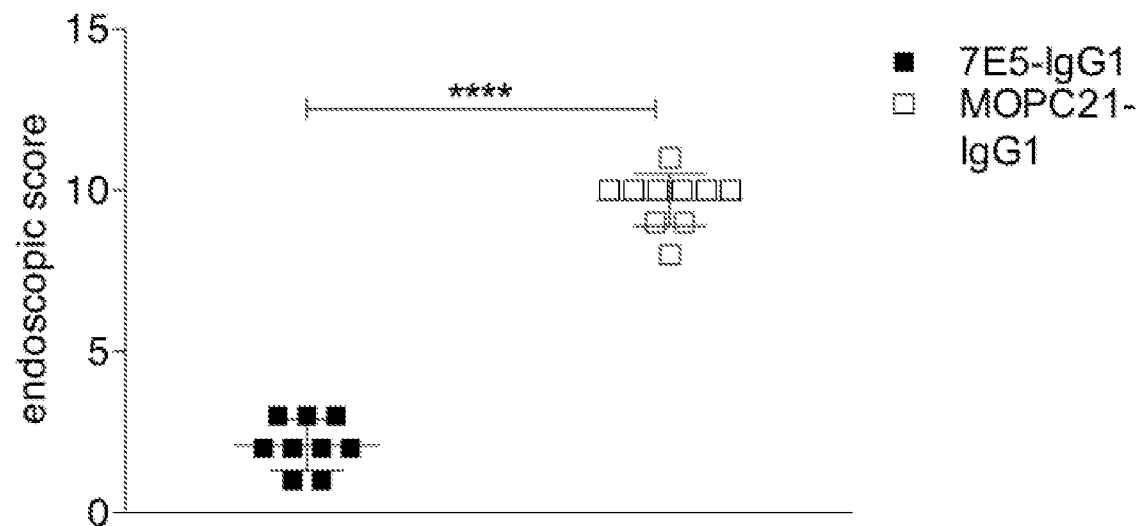


FIG. 24D

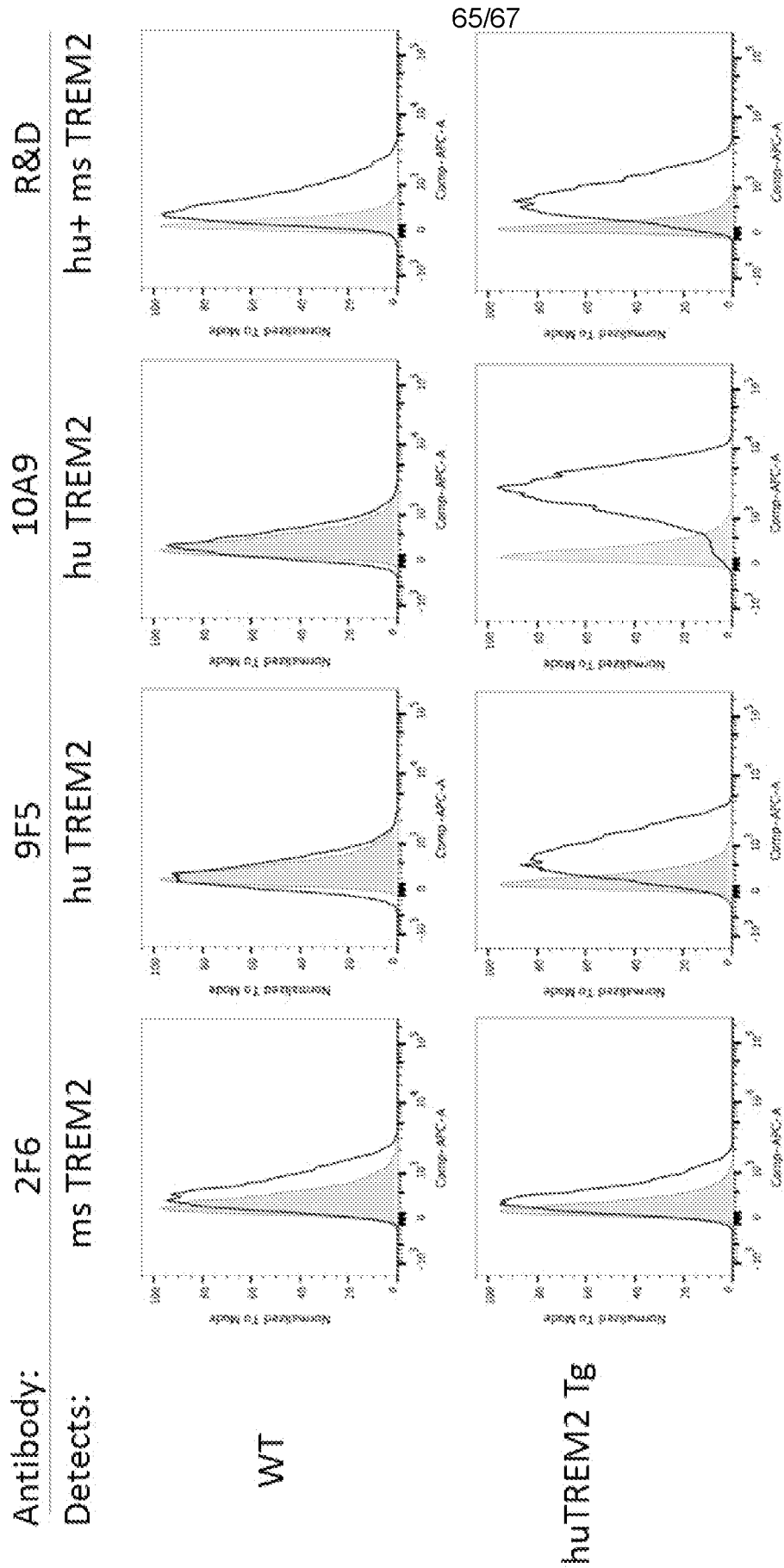


FIG. 25A

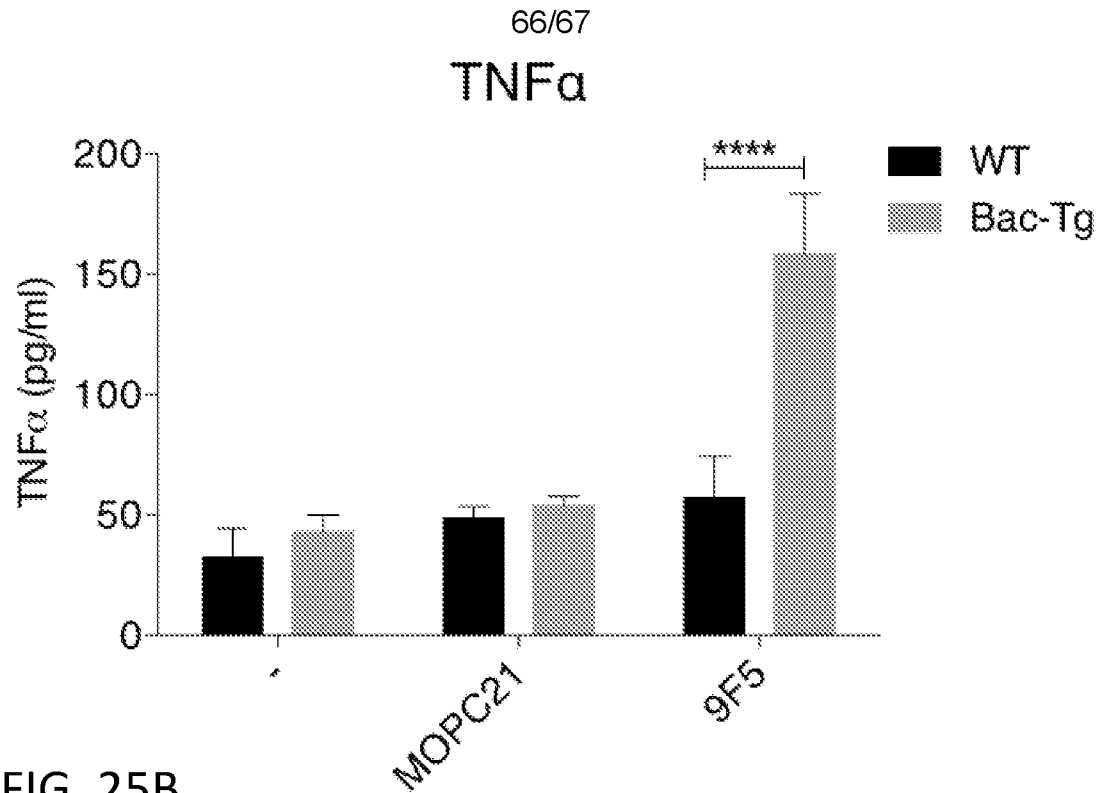


FIG. 25B

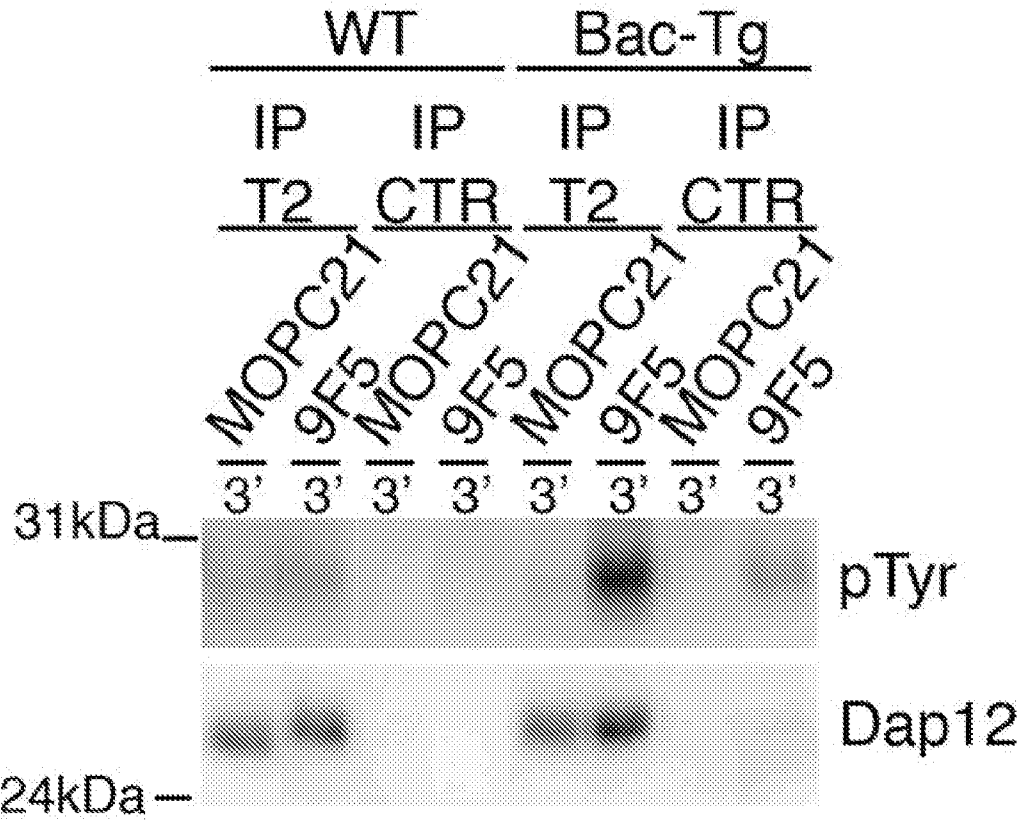


FIG. 25C

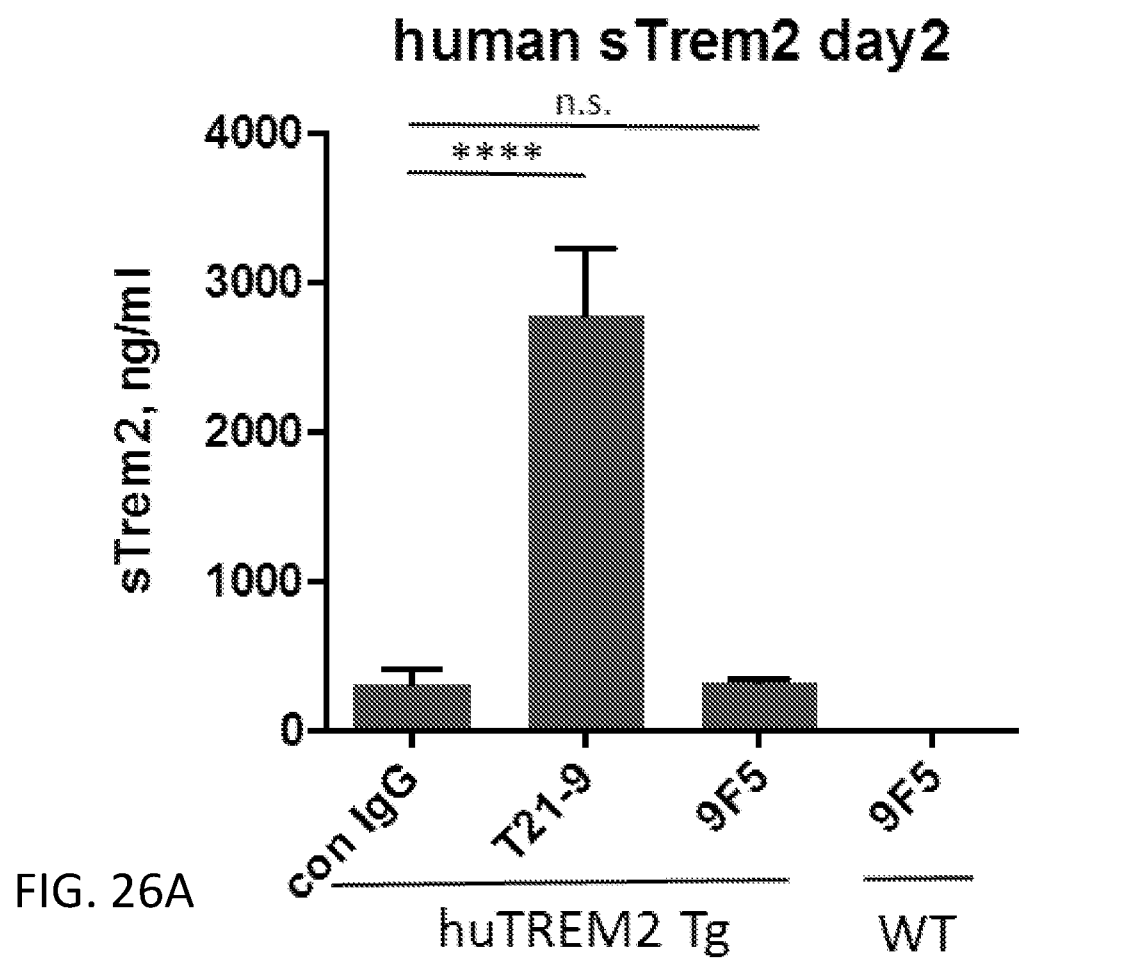


FIG. 26A

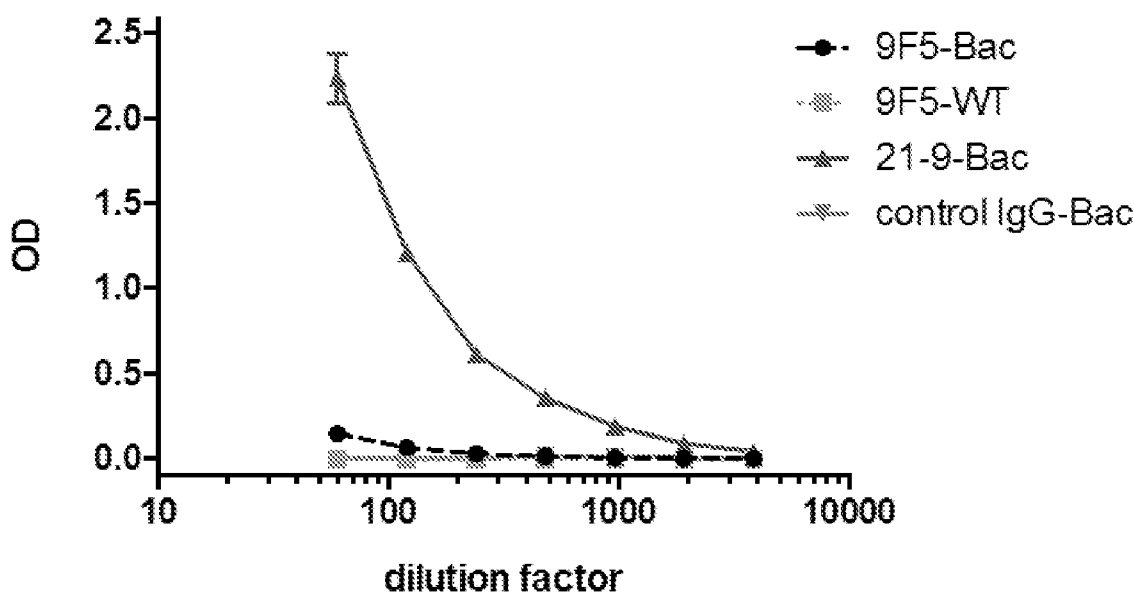


FIG. 26B