

1	MEPLRLILLLEVT	ELSGAHNTT	VFQGVAGQSLQ	VSCPYDSMKH	WGRRKAWCRQL	GEKGPC	60
	+ PL LL+LLF	+ +	V Q VAGQ+L	V C Y	+K WC++	C	
6	LHPLLLLLLLFP	CGSQAQS--	KAQVLQSVAGQ	TLTVRCQYP	PTGSLYEKKG	WCKEASAL-VC	63
61	QRVVSTHNLWLL	SFLRRWNG	STAITDDTLG	GTLTITL	RNLQPHDAGLY	QCQSLHGSEADT	120
	R+V++ ++	W	I DD	G T+T+ +L+	D+G Y C+	S+	
64	IRLVTSSKPR	TMA----	WTSRFTIWDD	PDAGEFTV	MTDLREEDSG	HYWCRIYRPSDNSV	119
121	LKKVLEVLADP	132	<u>TREM-2 Human</u>				
	+ V ++ P						
120	SKSVRFYLVVSP	131	<u>NCTR2_HUMAN</u>				

FIG. 1A

Sequence ID: ICJ35715 Length: 230 Number of Matches: 1
Range 1: 6 to 110

Score	Expect	Method	Identities	Positives	Gaps	Frame
42.7 bits(99) 1e-090 Compositional matrix adjust. 34/107(32%) 49/107(45%) 4/107(3%)						
Features:						
TRM01	9	LLMMLFVSELRAATKLTTEEKYELNEGOTLDVKKCDYTLKKFASSQKAK----QIIRDGEMPKT				6
TRM02	6	LL+LFV+EL A T ++ QQ+L V C Y K +KAK Q+ Q +				
TRM01	67	LLLLFVTELSGANNTT--VFQVAGQSLQVSCPYOSKKNKNGRRKAWCQIGKNGCQQRV				6
TRM01	67	LACTERPSKNSHPVQVGRRIILEDYDHNGGLLAVRNVNLOVEDSGLYQC			113	
TRM02	64	++ + G + D G L + + NLO D+GLYQC			110	
TRM02	64	VSTNNLLSLFLRWNGCSTAITDQTLOGTLTITLNNLQPHDAGLYQC				

FIG. 2

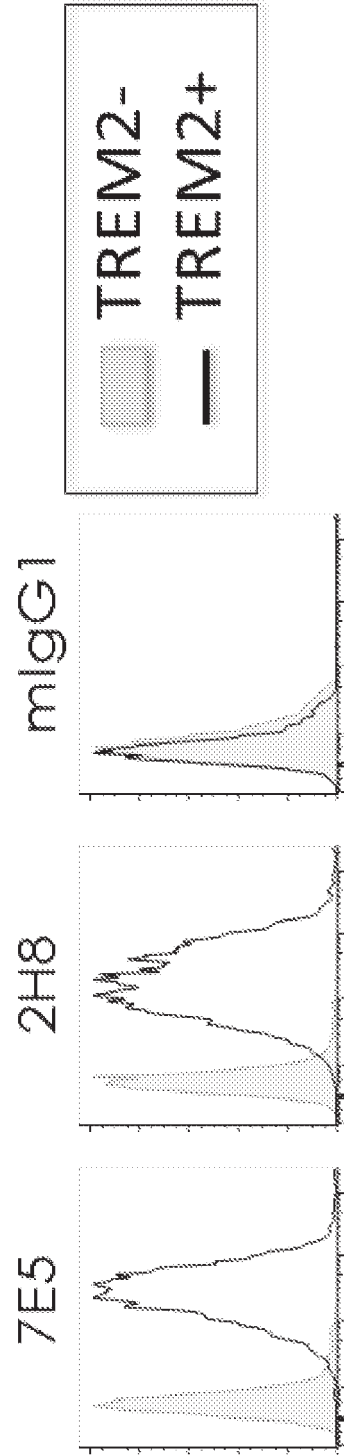


FIG. 3A

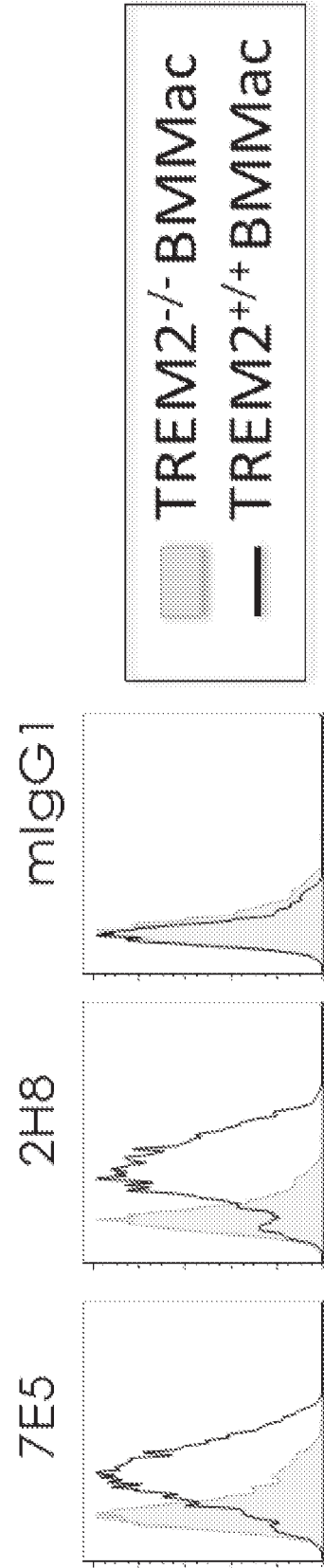


FIG. 3B

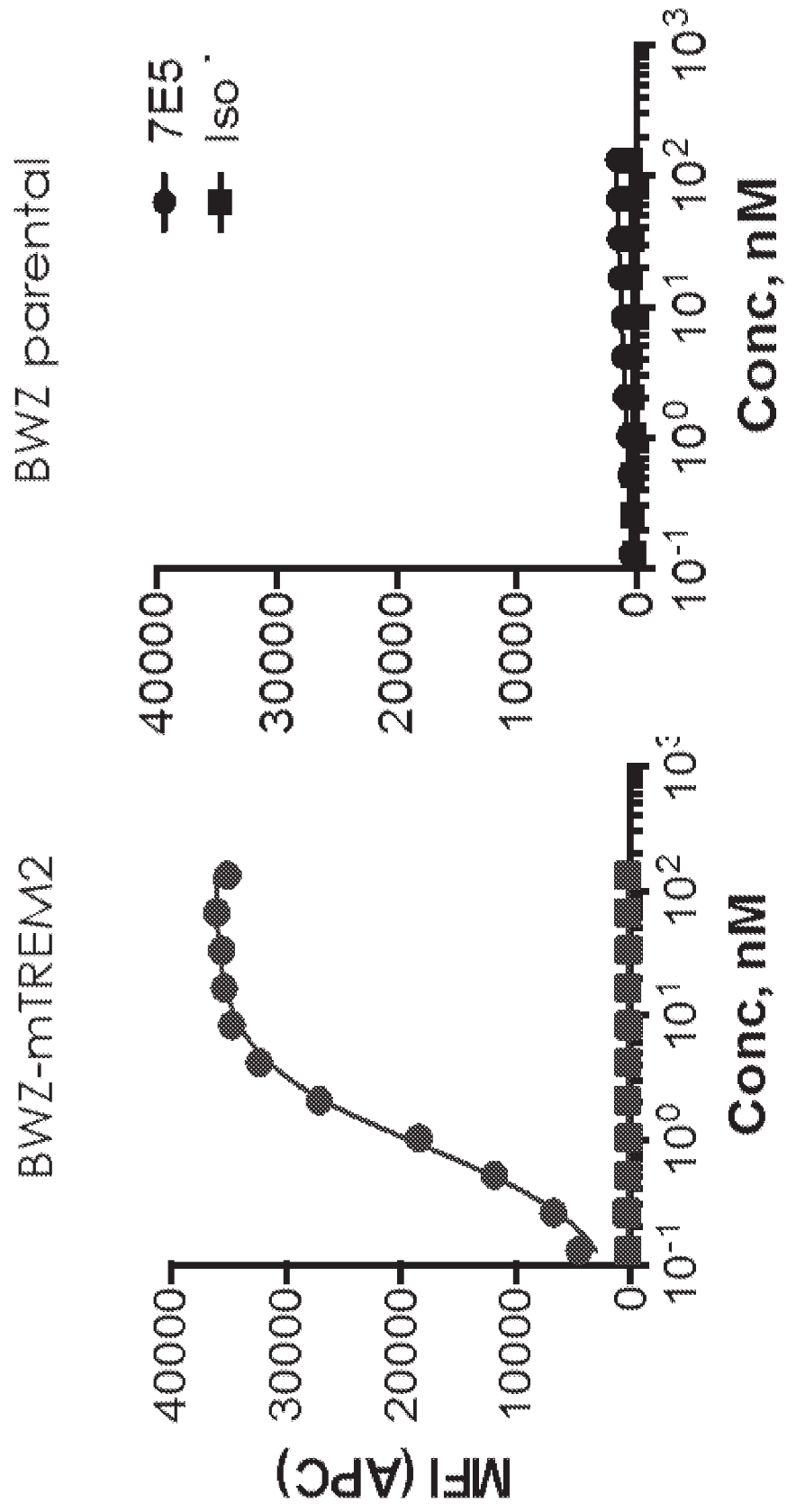
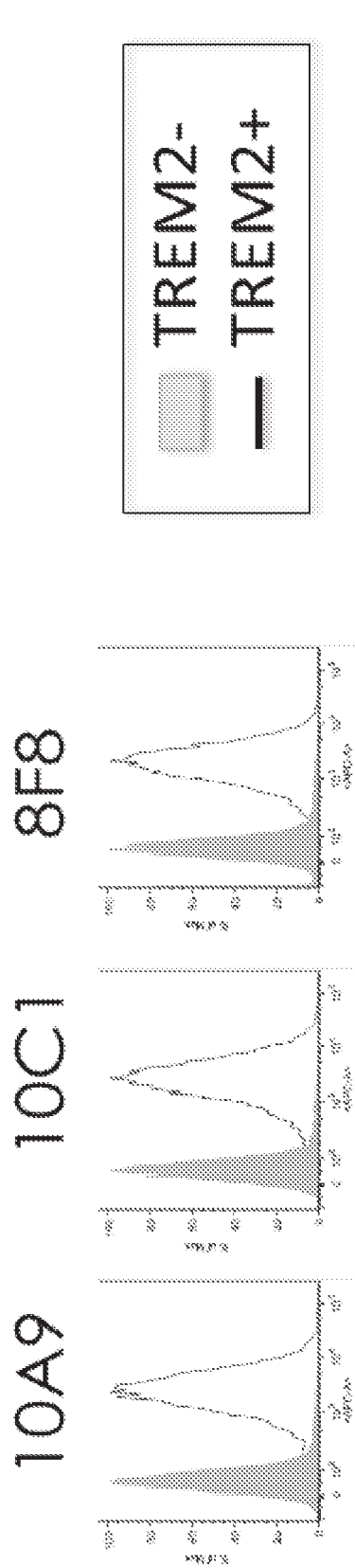
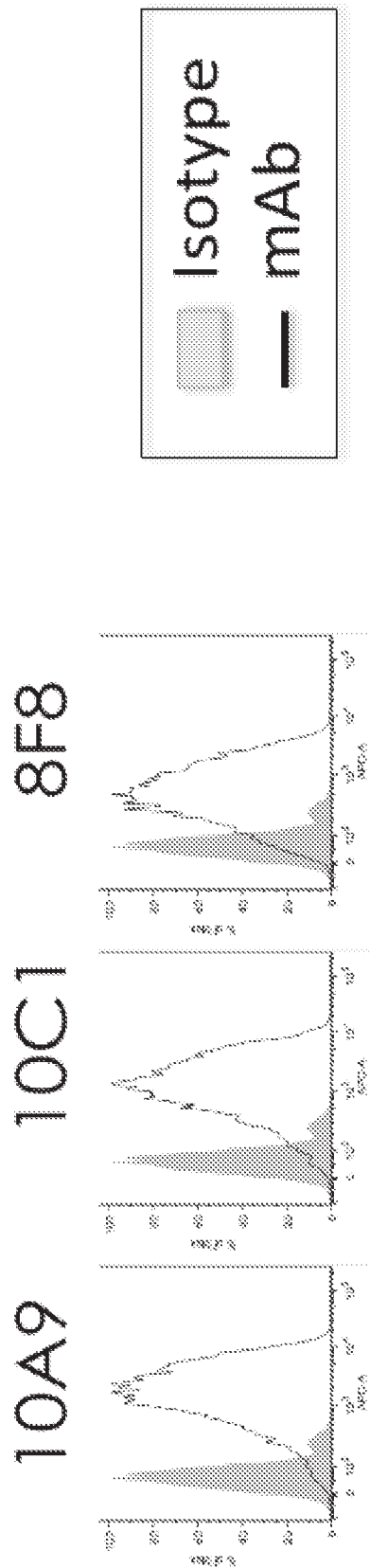


FIG. 3C



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

IGKV2-29*02 DIVMTQTPLSLSVTPGQPASISCKSSQSLIHS DGKTYLYWY LQKPGQSPQLLIYEVS NRFS

GVPDRFSGSGGTDFTLKISRVEAEDVGYYCMQSIQLPP

Joining region IMGT J00242|IGKJ2*01|YTFGGGTKLEIK

8

seq	10	20	30	40	50	60
AbM	10	20	30	40	50	60
	b b b	p b b	b b b	bi bi i	ii ibbi	i
T2-9F5.1	DVMTQTPLSLVP	SLGDAQASIS	RSSQSLVHSNGYTYLH	WY LQKPGQSPKLLIY	KVSNRFS	
	*	**	*	*	*	
2-29*02	DVMTQTPLSLSVTPGQPASIS	CKSSQSLIHS DGKTYLY	WY LQKPGQSPQLLIY	EVS NRFS		
h9F5-L1	DIVMTQTPLSLSVTPGQPASIS	CKSSQSLVHSNGYTYLH	WY LQKPGQSPQLLIY	KVSNRFS		
h9F5-L2	DVMTQTPLSLSVTPGQPASIS	CKSSQSLVHSNGYTYLH	WY LQKPGQSPQLLIY	KVSNRFS		

#

2

2

seq	70	80	90	100	110
AbM	70	80	90	100	110
	b b	b b b	ib bib	ibi iib	i b b b
T2-9F5.1	GVPDRFSGSGGTDFTLKISRVEAEDVGYYFC	SQSTRVPYIT	FGGGTKLEIK		
	*	*	*	*	
2-29*02	GVPDRFSGSGGTDFTLKISRVEAEDVGYYC	MQSIQLPP	FGGGTKLEIK		
h9F5-L1	GVPDRFSGSGGTDFTLKISRVEAEDVGYYC	SQSTRVPYIT	FGGGTKLEIK		
h9F5-L2	GVPDRFSGSGGTDFTLKISRVEAEDVGYYC	SQSTRVPYIT	FGGGTKLEIK		

L F

2

2

deamidation substitutions: Q/S/A/D

@ isoaspartate substitutions: Q/S/A

2

2

h9F5-L1 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) "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 isoaspartate (DG) formation).

2

FIG. 4C

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

IGHV1-46*01 QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYMHVWVRQAPGGGLEWMIINPSGGSTS

YAKQFQGRVTMTTRDTSTSTVYMELSLSRSEDATVYYCAR

Joining region IMGT J00256|IGHJ4*01|YFDYWGQGLTVTVSS

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 b i i	i i b b b		
T2-9F5.1	QVQLVQSGPELVKPGASLKISCKAS	GYAFSSSWMN	WVKQRPCKGLEWIG	RIYPGDGDTN		
	*	*	*	*	*	*
1-46*01	QVQLVQSGAEVKKPGASVKVSCKAS	GYTFTSYMH	WVRQAPGGGLEW%G	IINPSGGSTS		
h9F5-H1	QVQLVQSGAEVKKPGASVKVSCKAS	GYAFSSSWMN	WVRQAPGGGLEW%G	RIYPGDGDTN		
h9F5-H2	QVQLVQSGAEVKKPGASVKVSCKAS	GYAFSSSWMN	WVRQAPGGGLEW%G	RIYPGDGDTN		
h9F5-H3	QVQLVQSGAEVKKPGASVK:SKAS	GYAFSSSWMN	WVRQAPGGGLEWIG	RIYPGDGDTN		
		V	^	⋄	#	
seq	60	70	80	90	100	110
AbM	60	70	80	abc	90	110
	i b b b b x	b b b b b	b i b b b			i b b b
T2-9F5.1	YNGEFRVRAITLTADTSTTAYMQLSLTSDSAVYFCAR	LLRNQPGESYAMDY	WGQGASVTVSS			
	***	**	*	*	*	*
1-46*01	YAKQFQGRVT%T%DTSTSTVYMELSLSRSEDATVYYCAR					
h9F5-H1	YAKQFQGRVTMTTRDTSTSTVYMELSLSRSEDATVYYCAR	LLRNQPGESYAMDY	WGQGLTVTVSS			
h9F5-H2	YAKQFQGRVTMT%DTSTSTVYMELSLSRSEDATVYYCAR	LLRNQPGESYAMDY	WGQGLTVTVSS			
h9F5-H3	YAKQFQGR%T% ADT STSTAYMELSLSRSEDATVYYCAR	LLRNQPGESYAMDY	WGQG&LTVTVSS			
	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

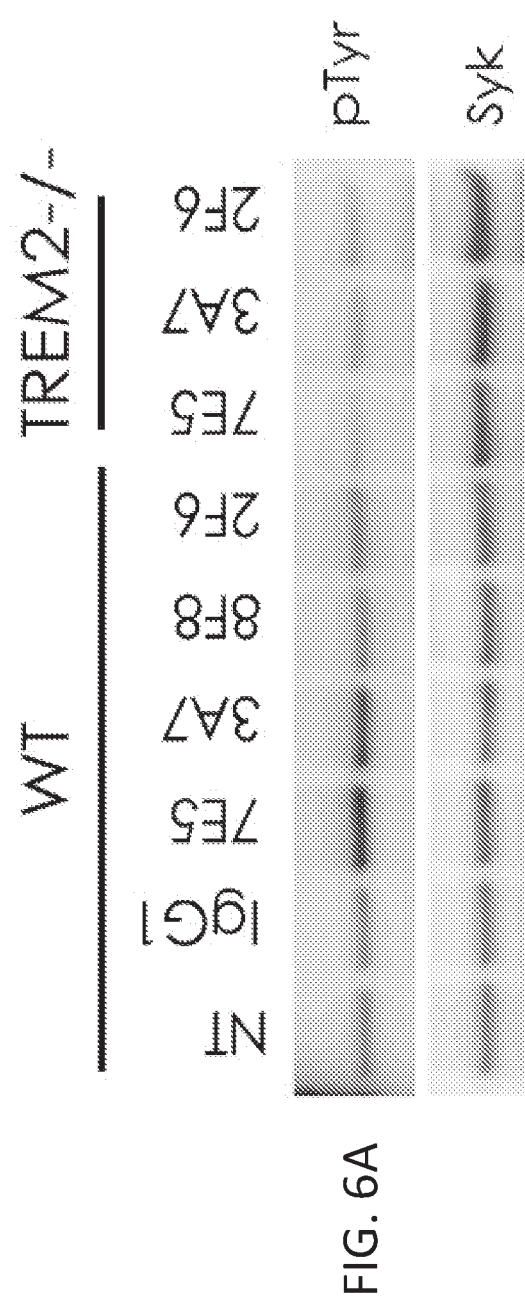
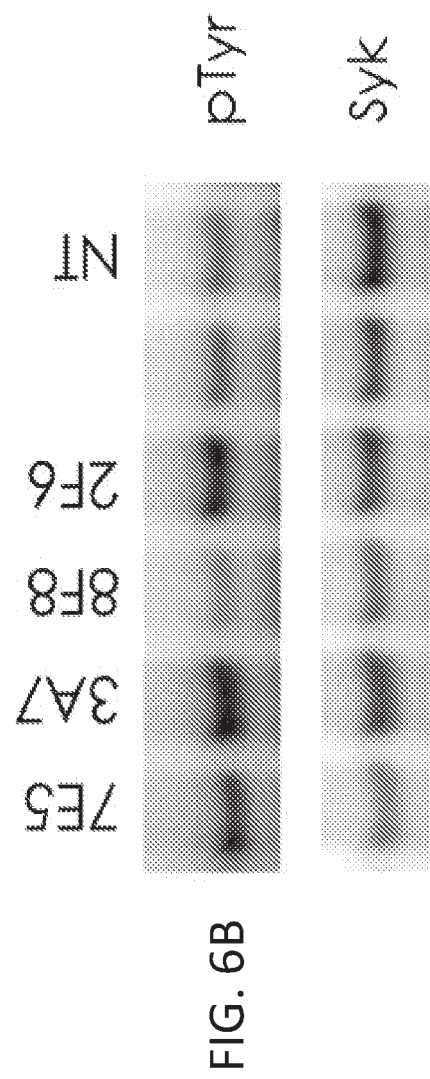
shown in red (compared to sequence above it).

- (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



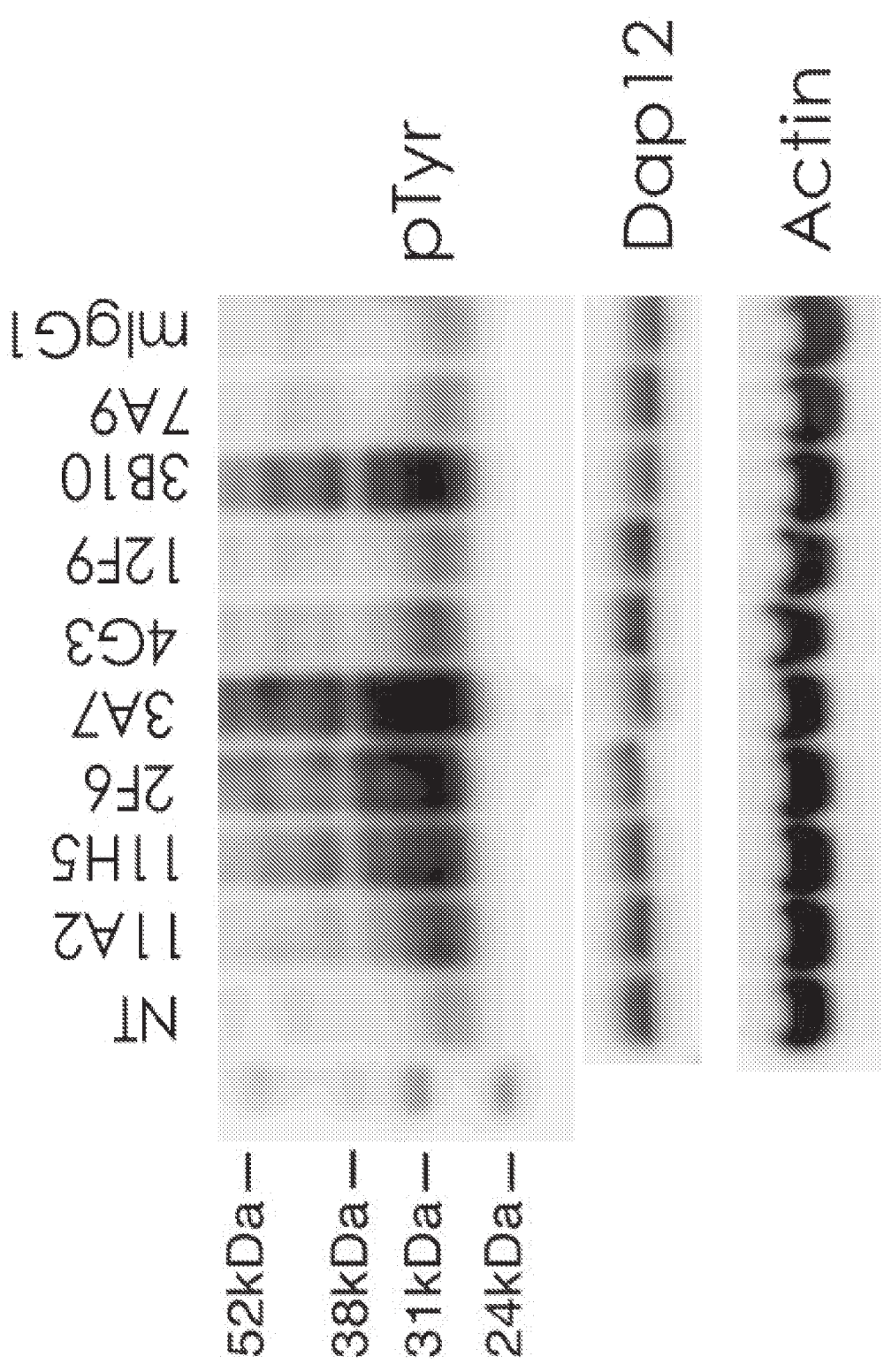


FIG. 7A

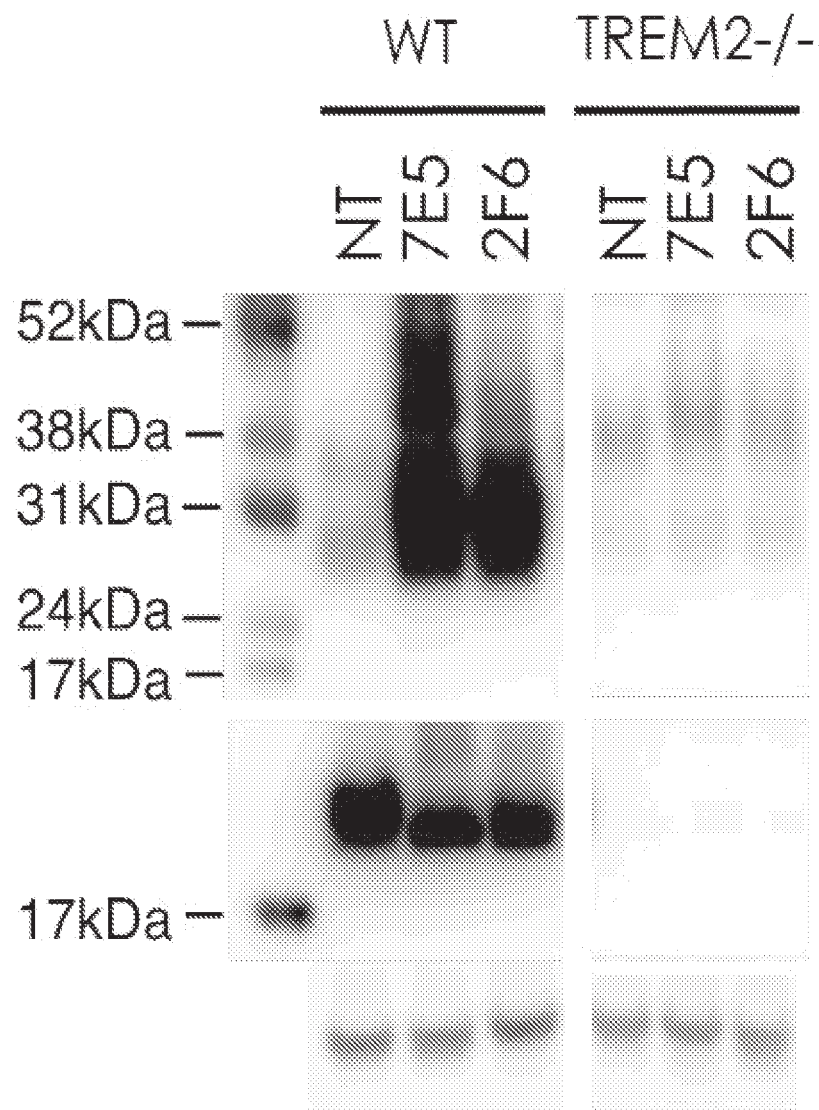


FIG. 7B

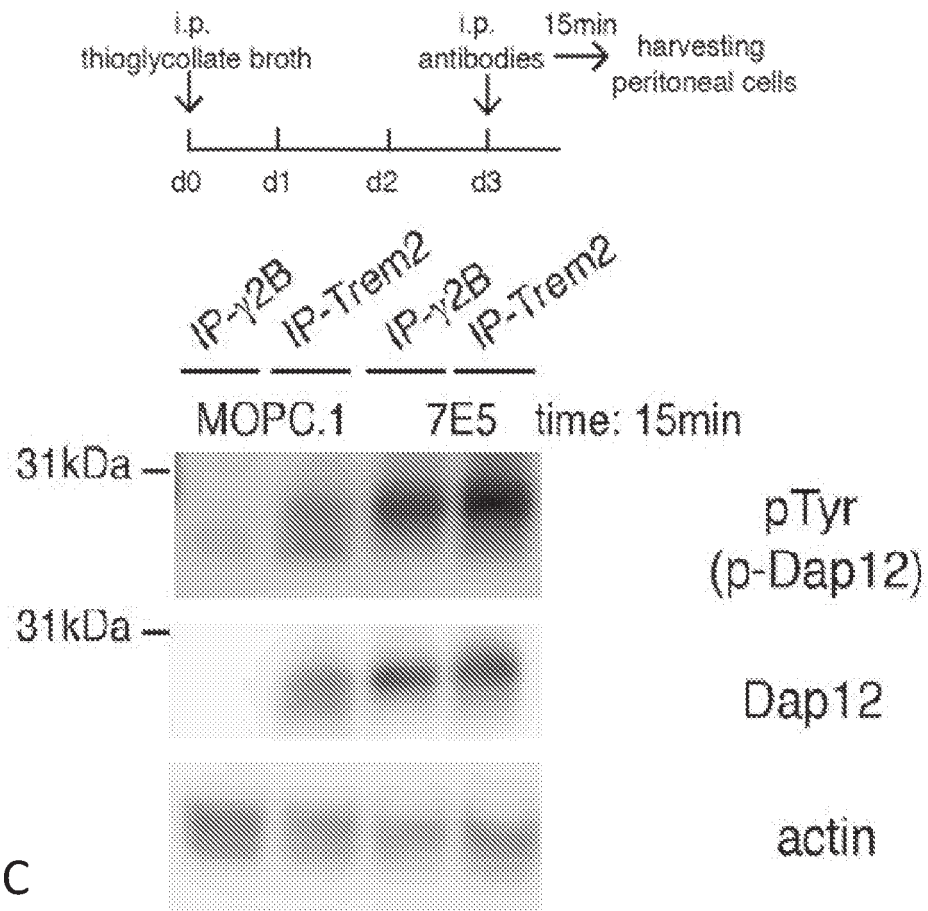


FIG. 7C

FC over IP-Trem2 of
MOPC1-treated mouse

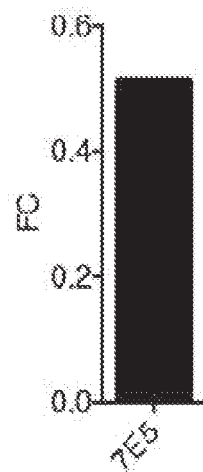


FIG. 7D

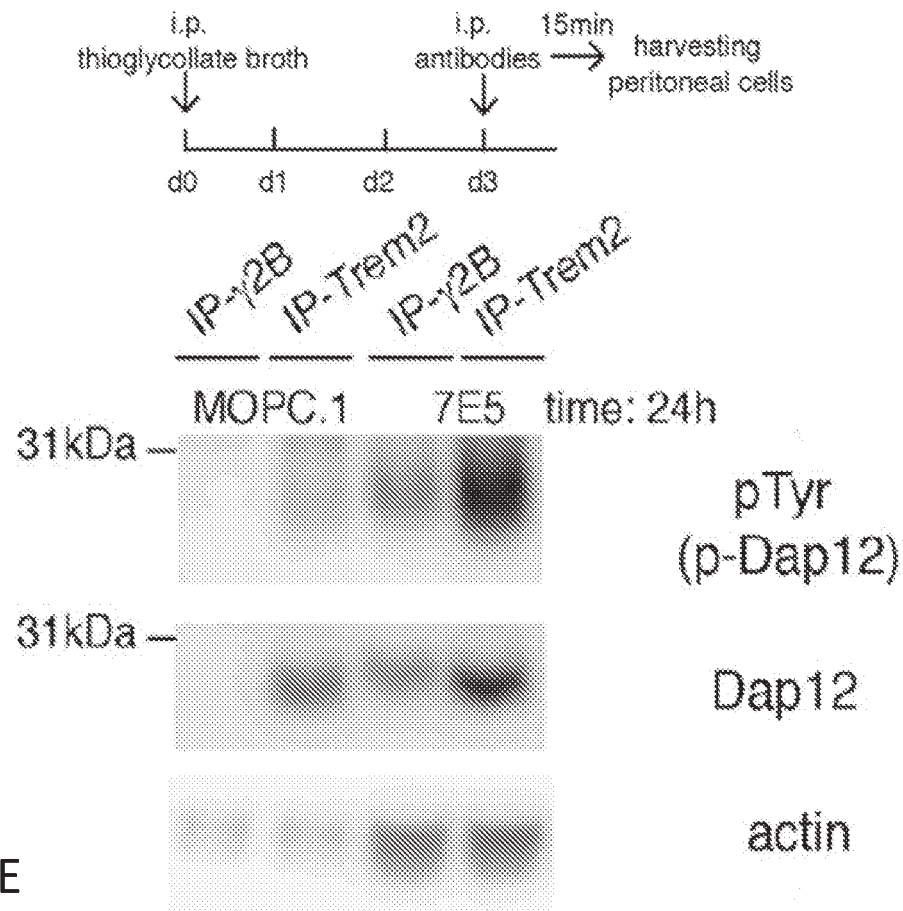


FIG. 7E

FC over IP-Trem2 of
MOPC1-treated mouse

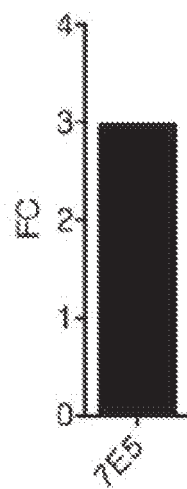


FIG. 7F

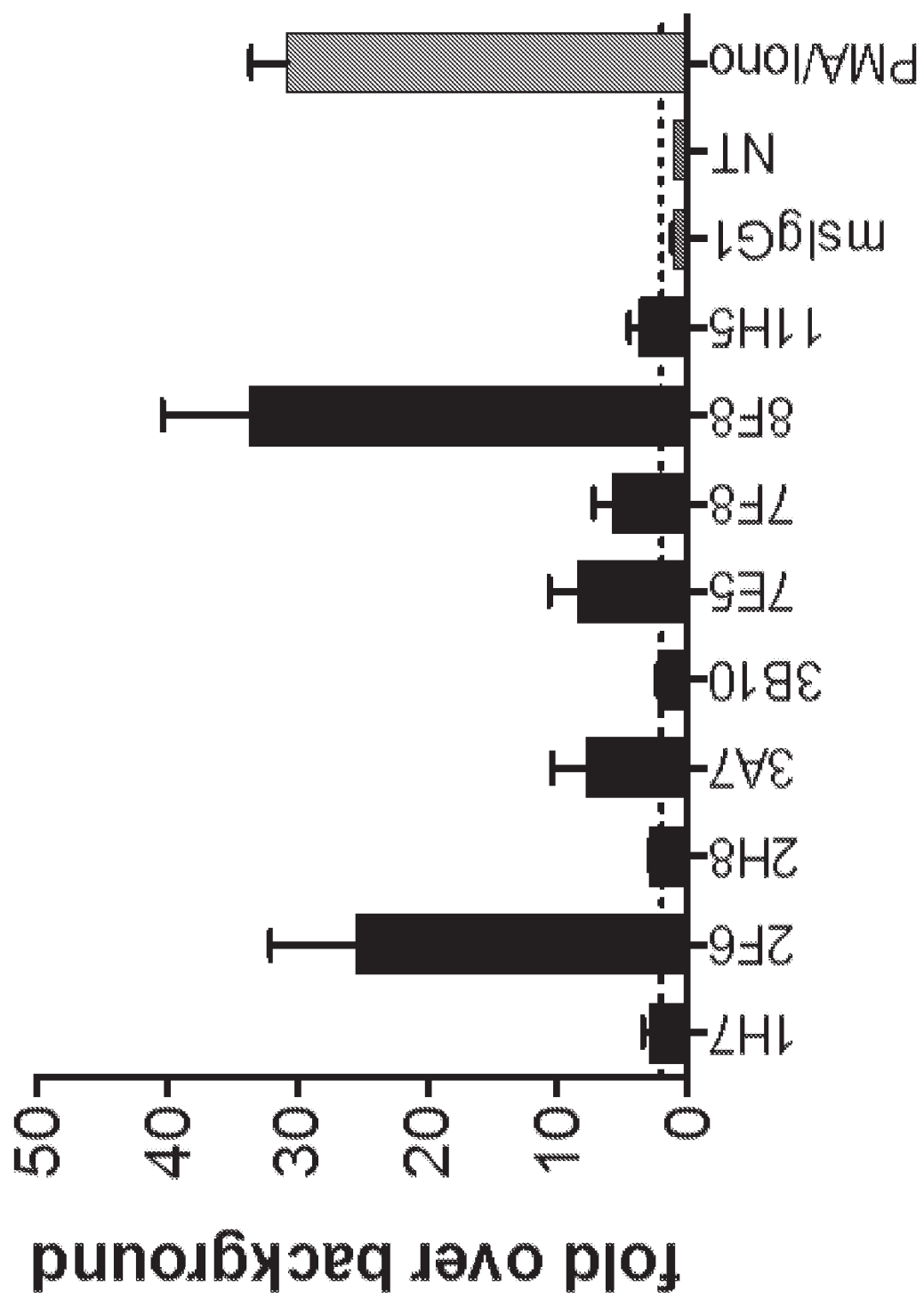


FIG. 8A

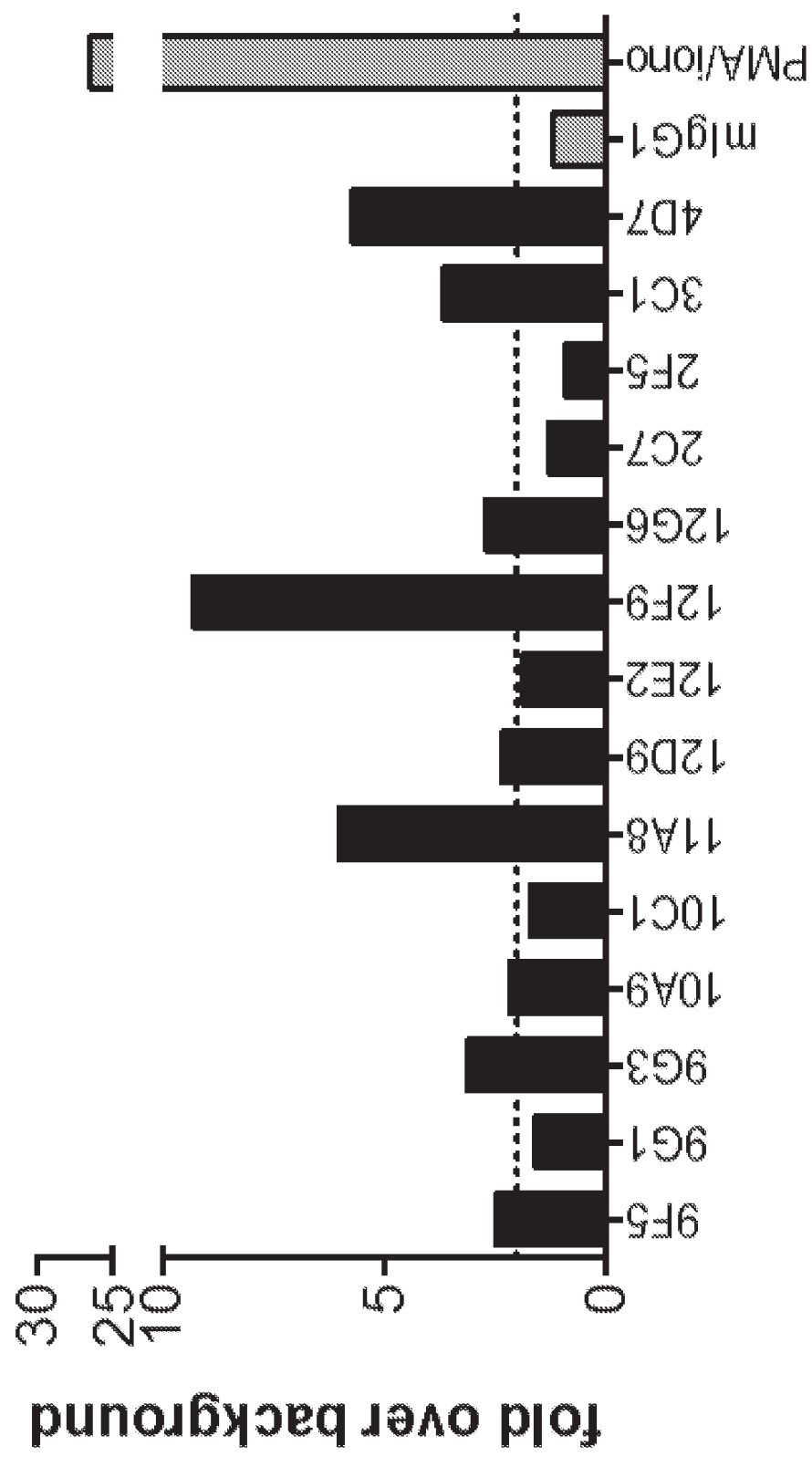


FIG. 8B

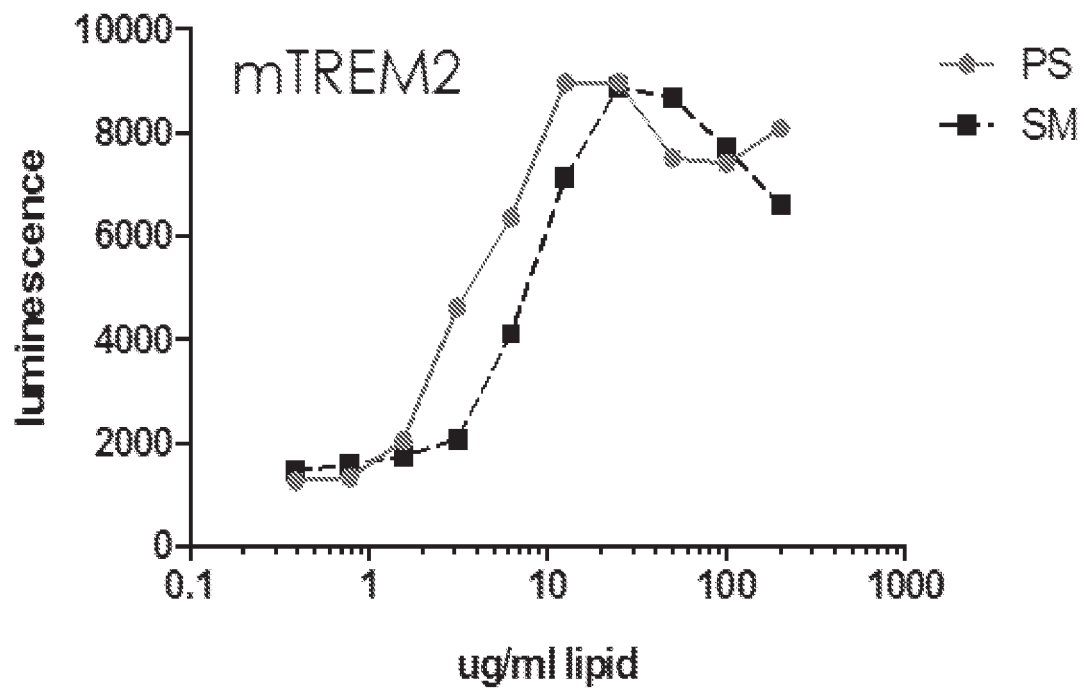


FIG. 8C

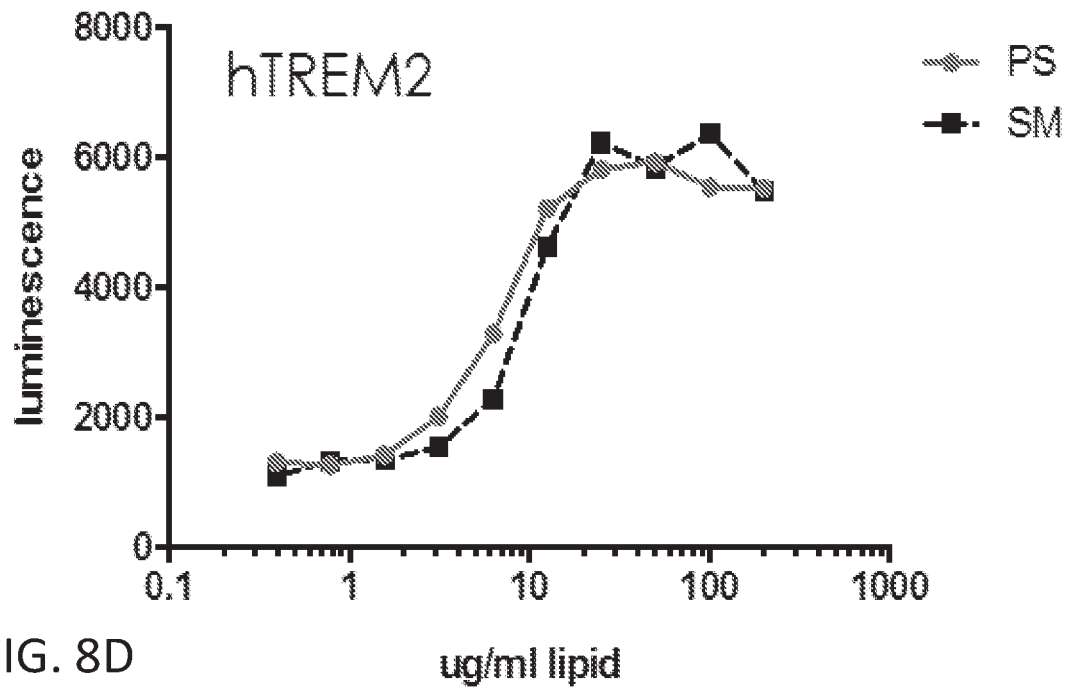


FIG. 8D

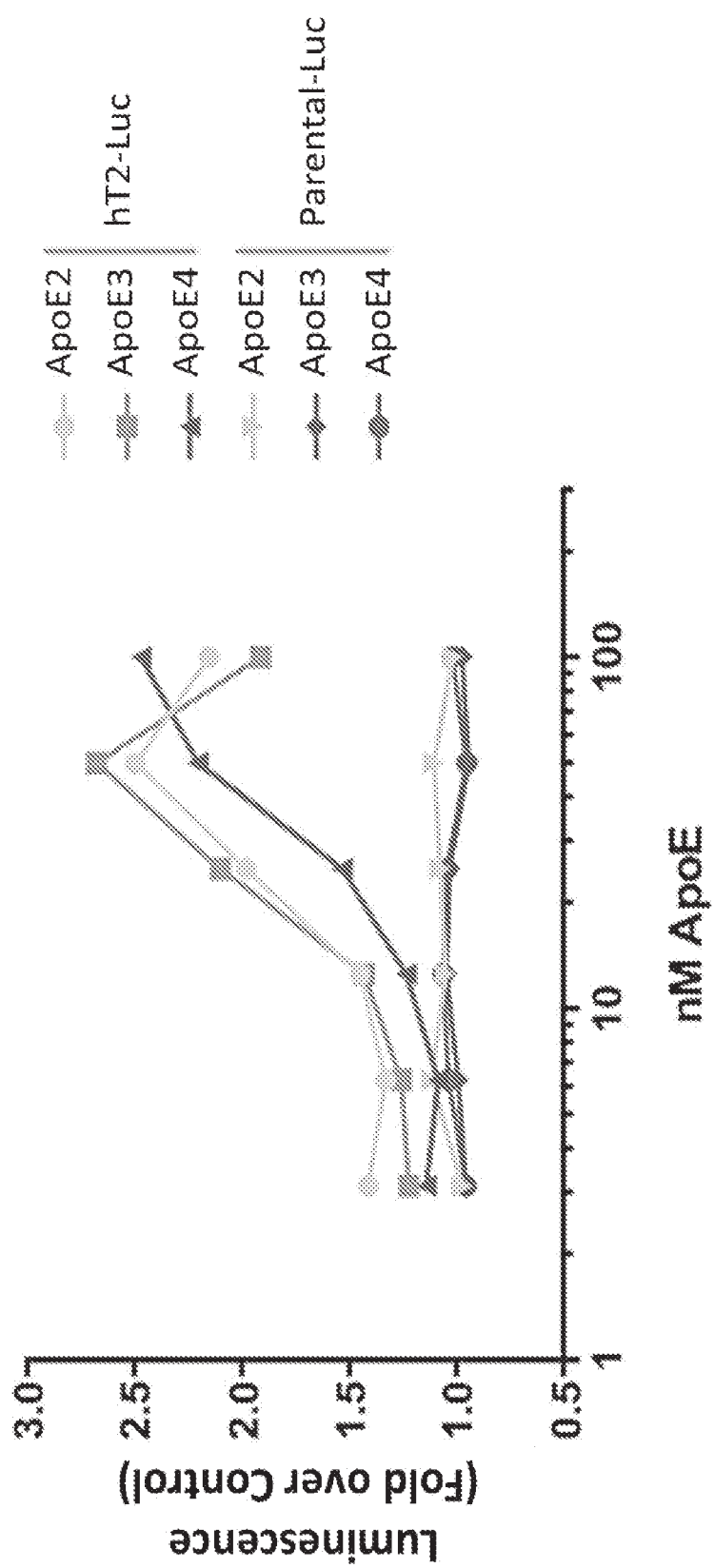


FIG. 8E

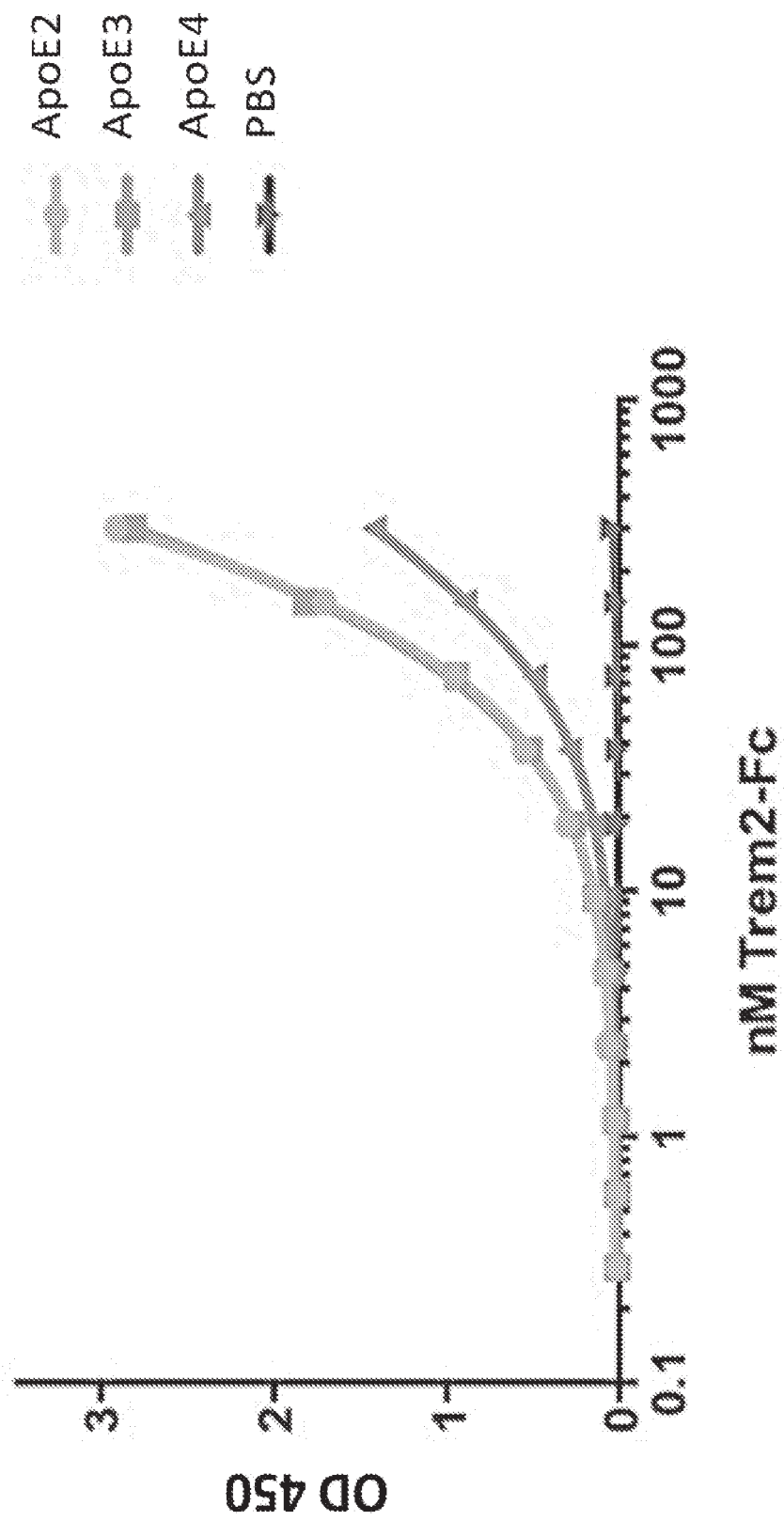


FIG. 8F

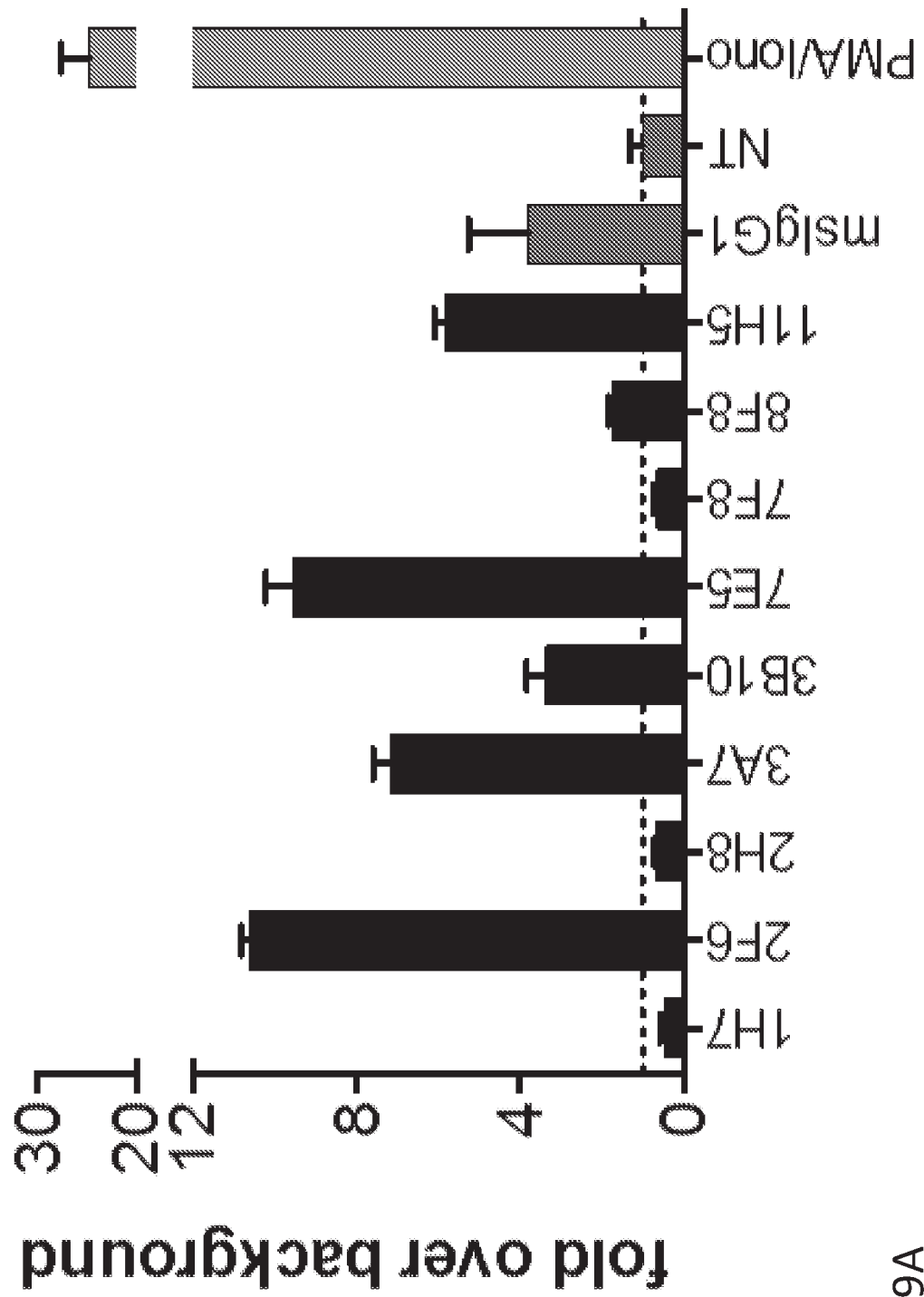


FIG. 9A

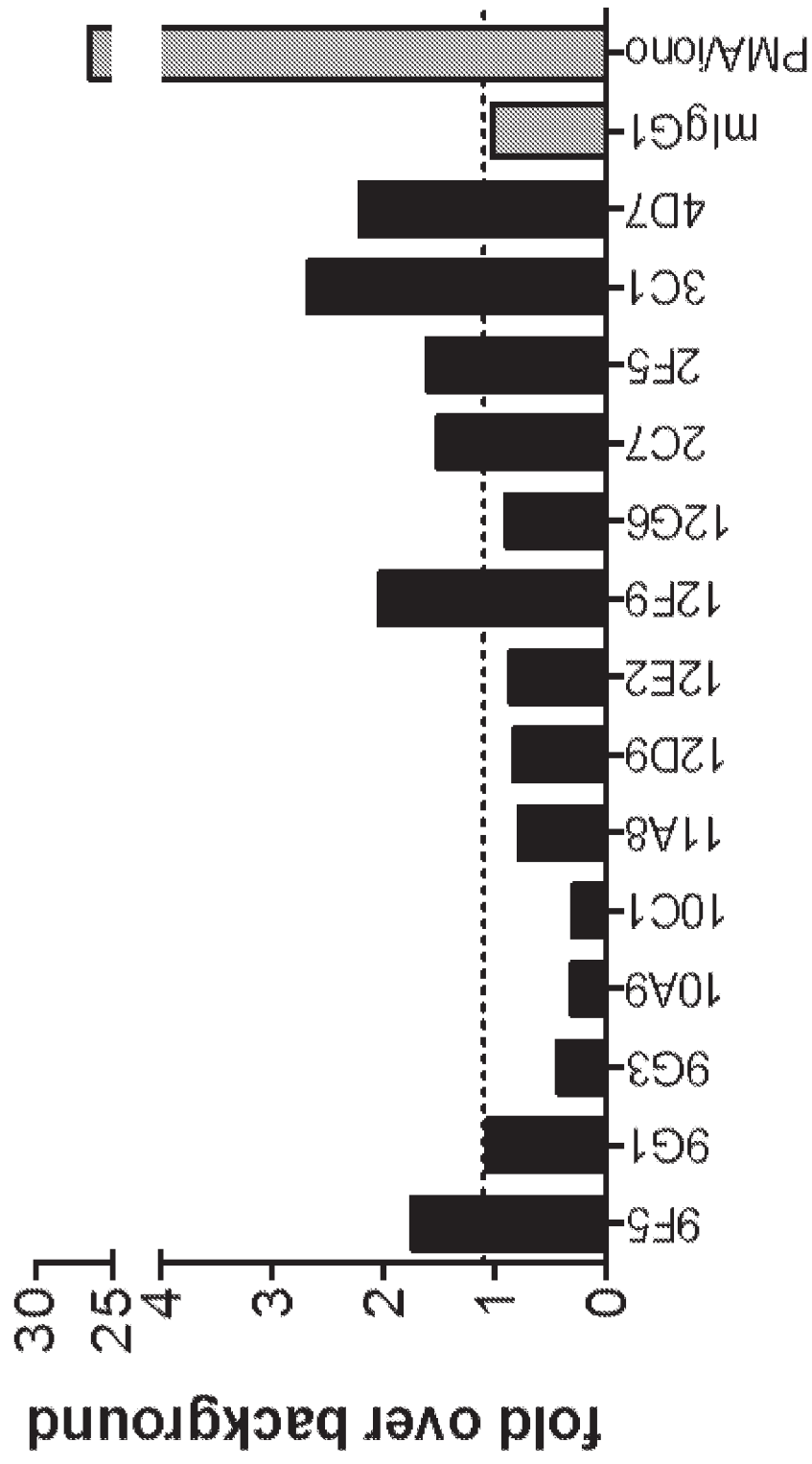


FIG. 9B

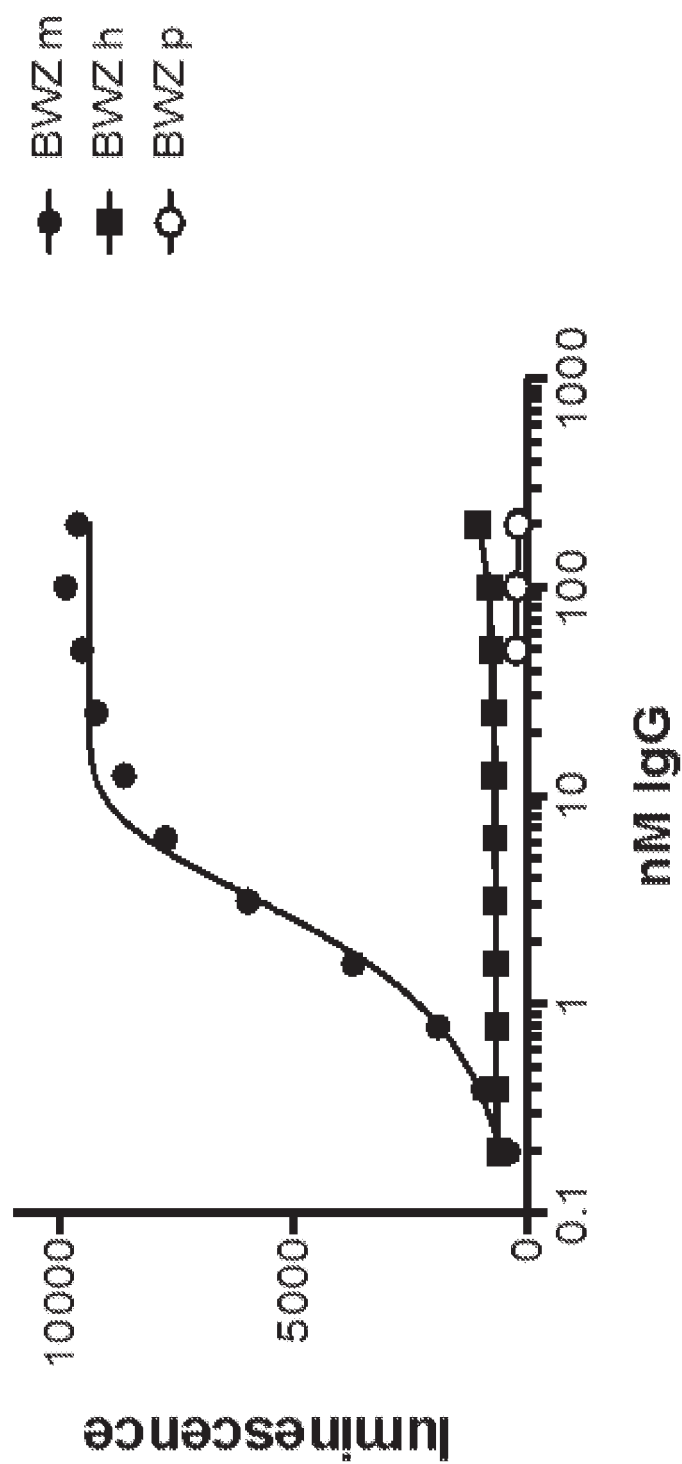


FIG. 9C

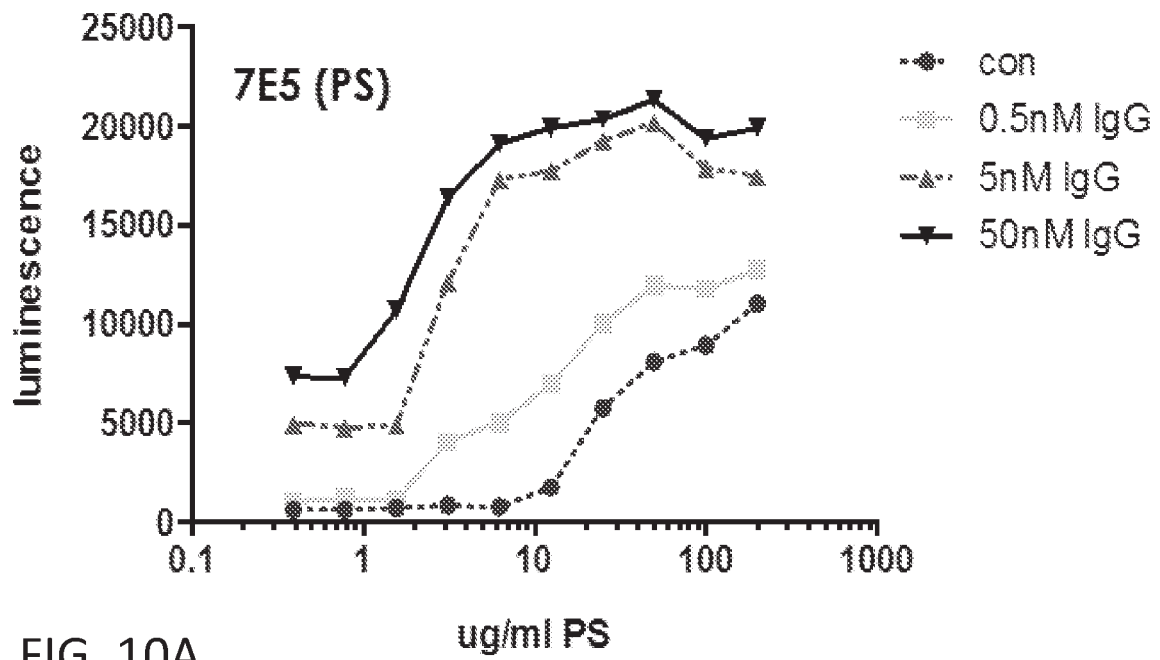


FIG. 10A

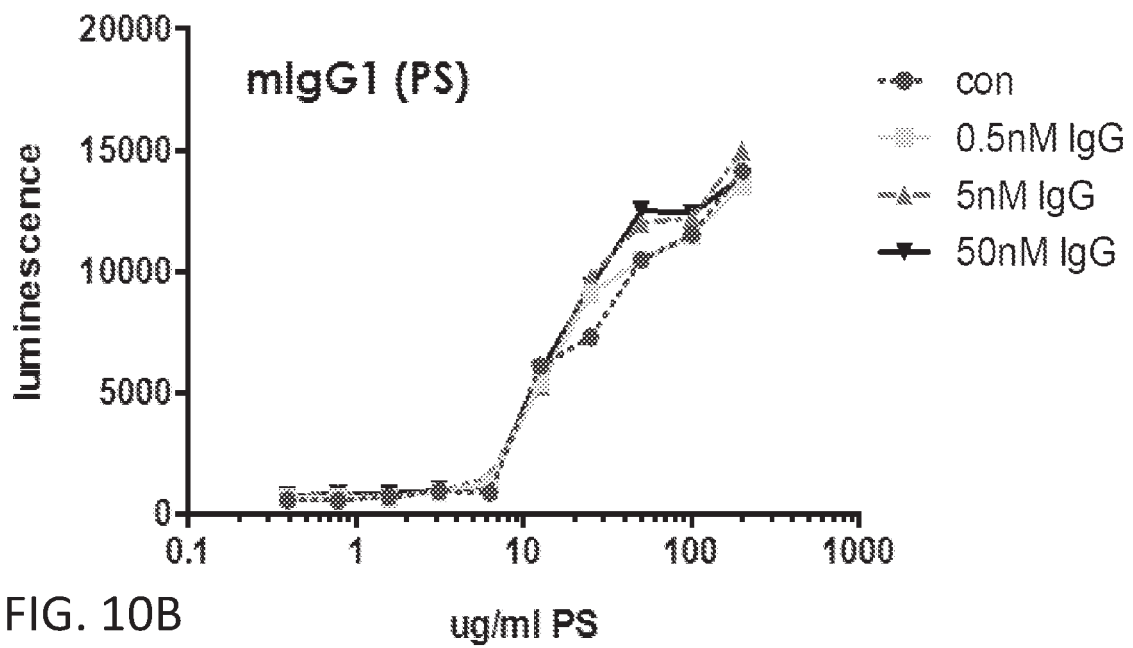


FIG. 10B

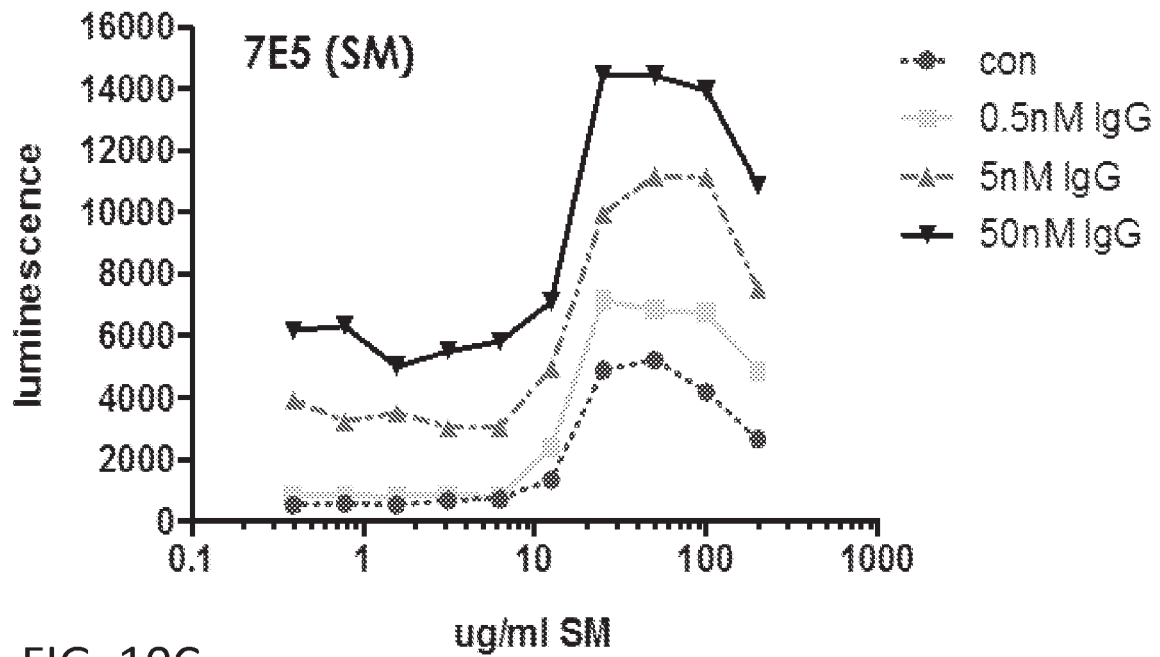


FIG. 10C

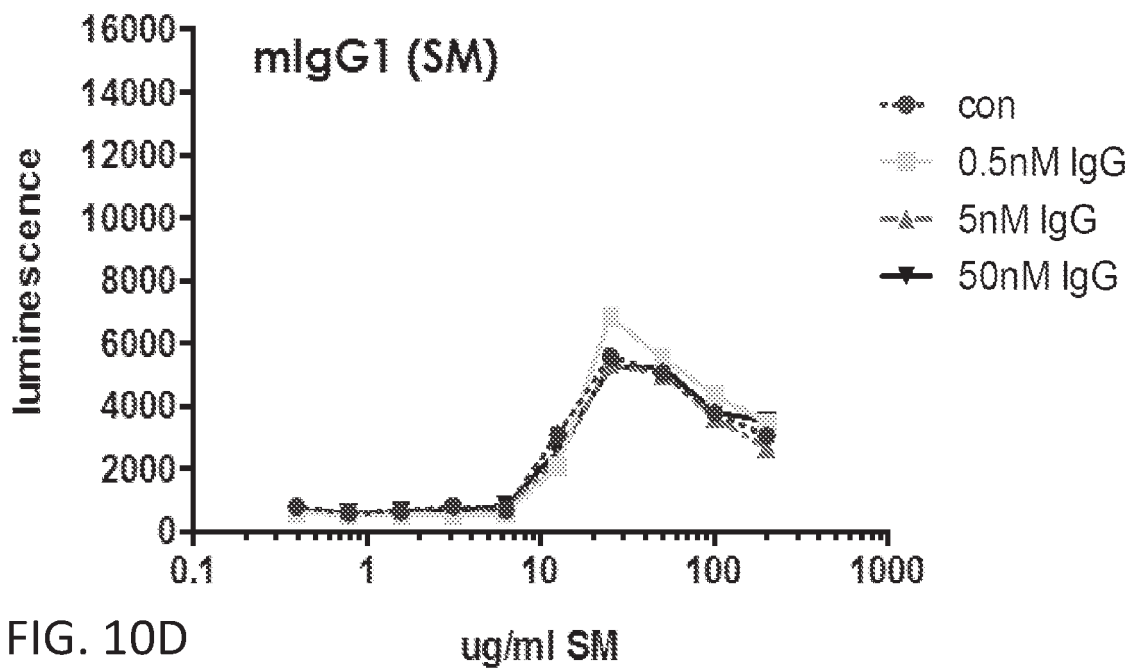


FIG. 10D

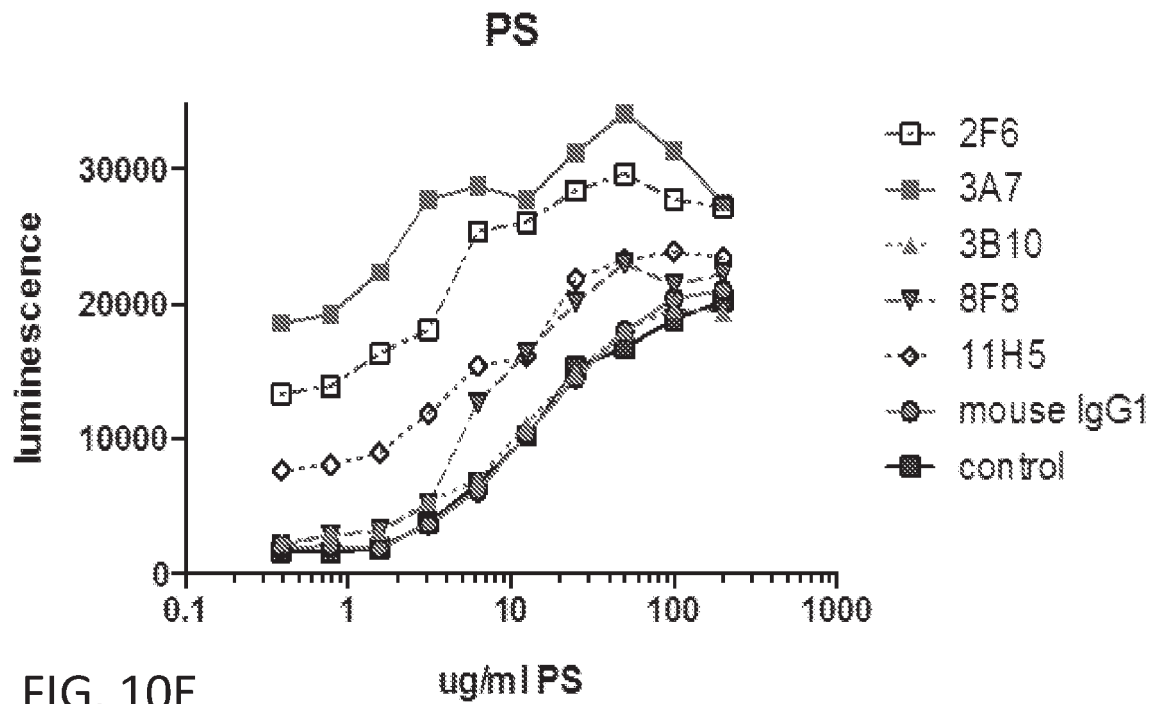


FIG. 10E

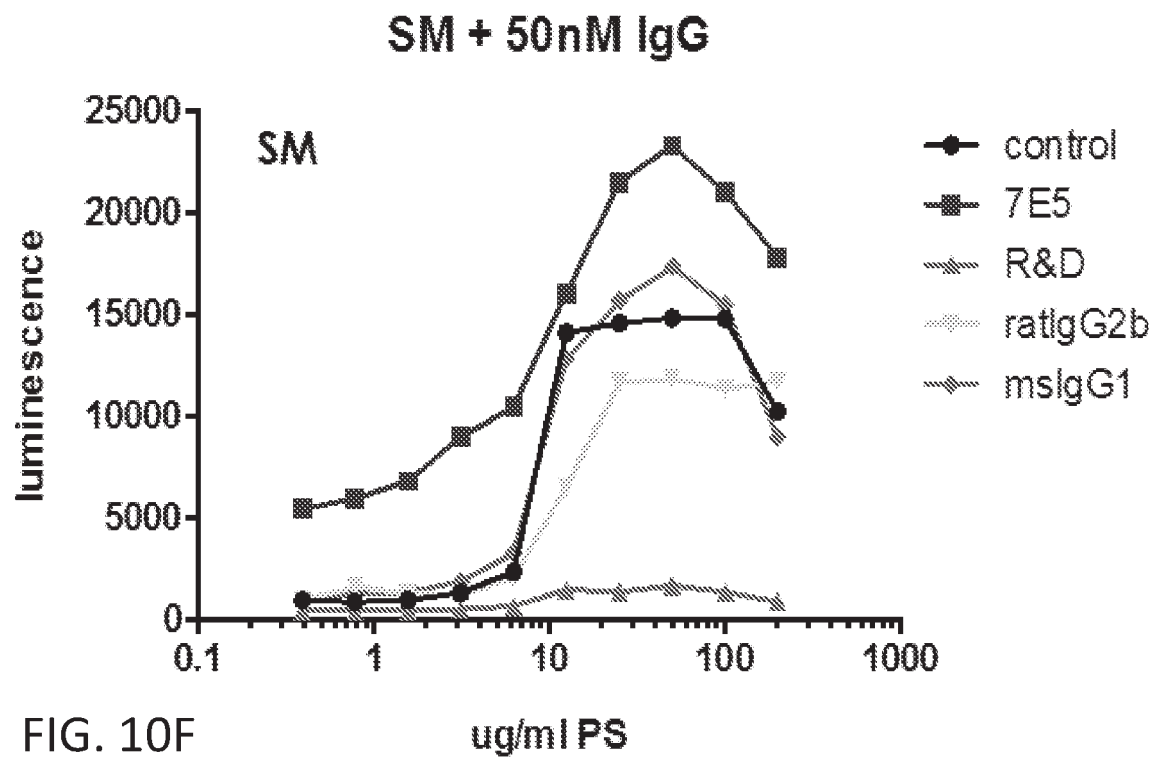


FIG. 10F

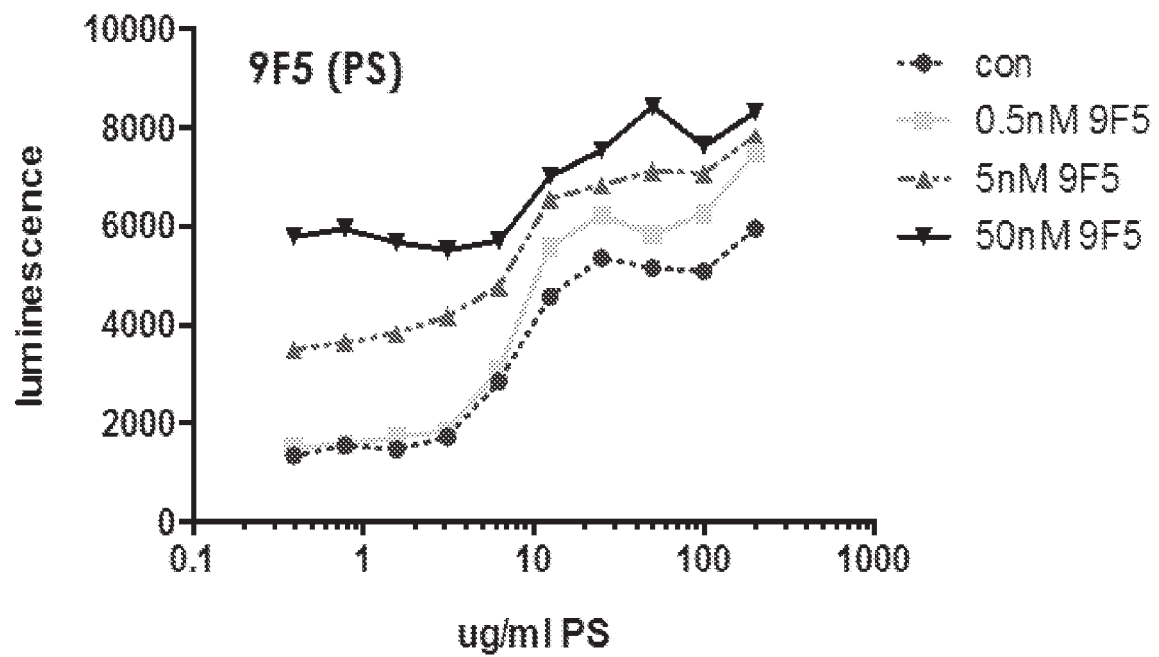


FIG. 11A

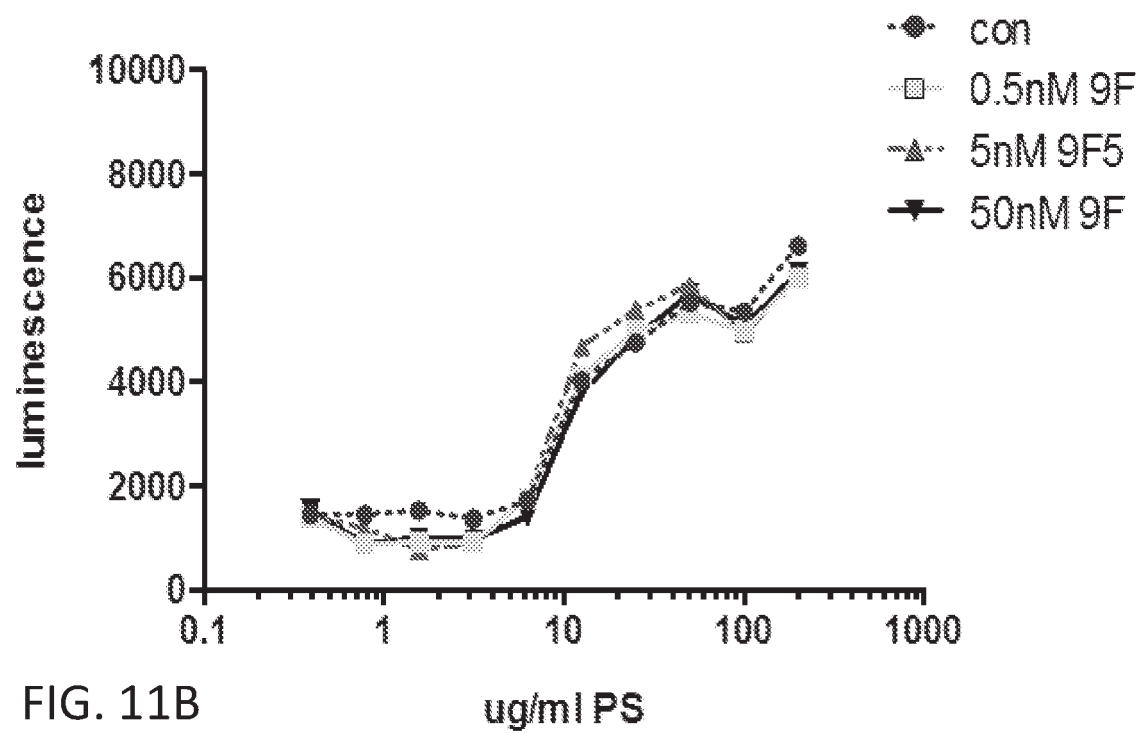


FIG. 11B

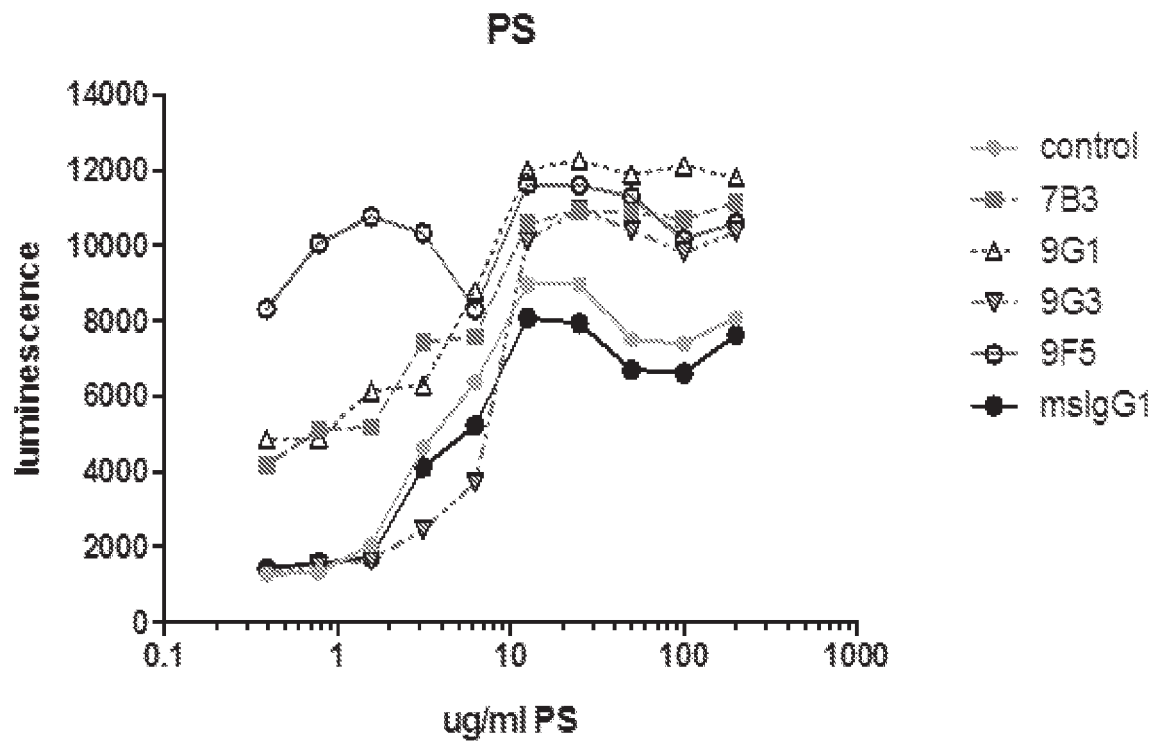


FIG. 11C

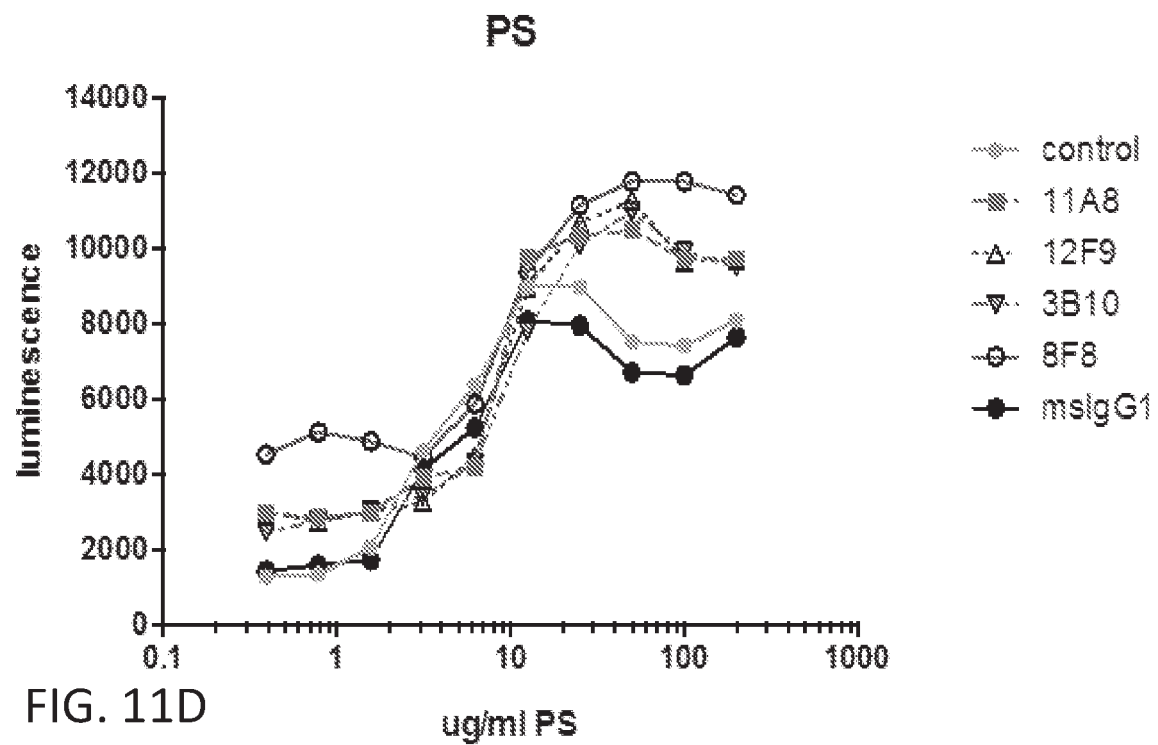


FIG. 11D

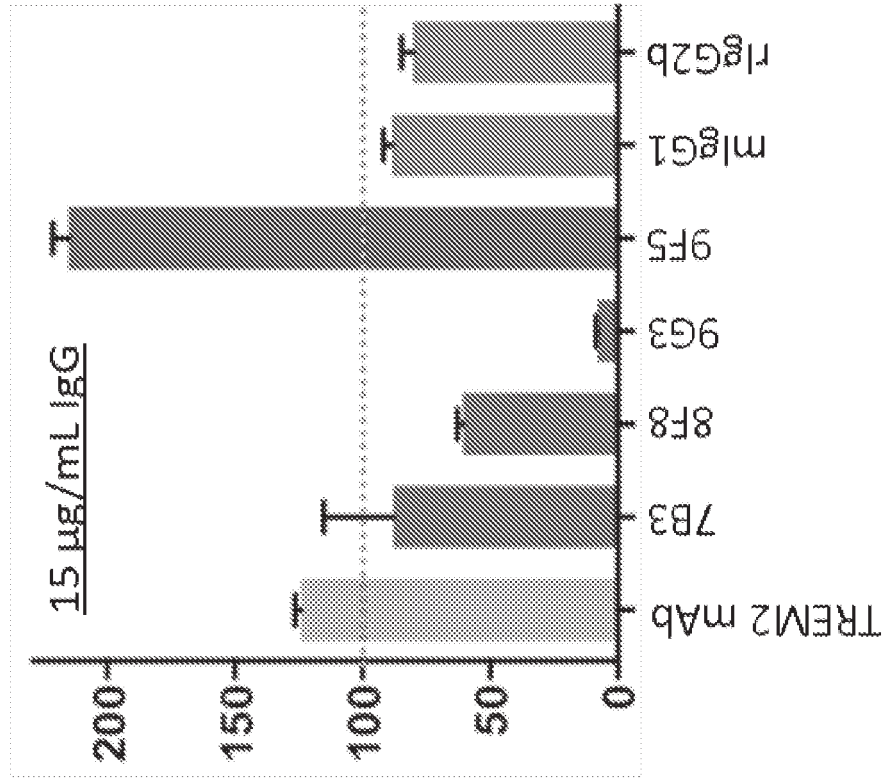


FIG. 11F

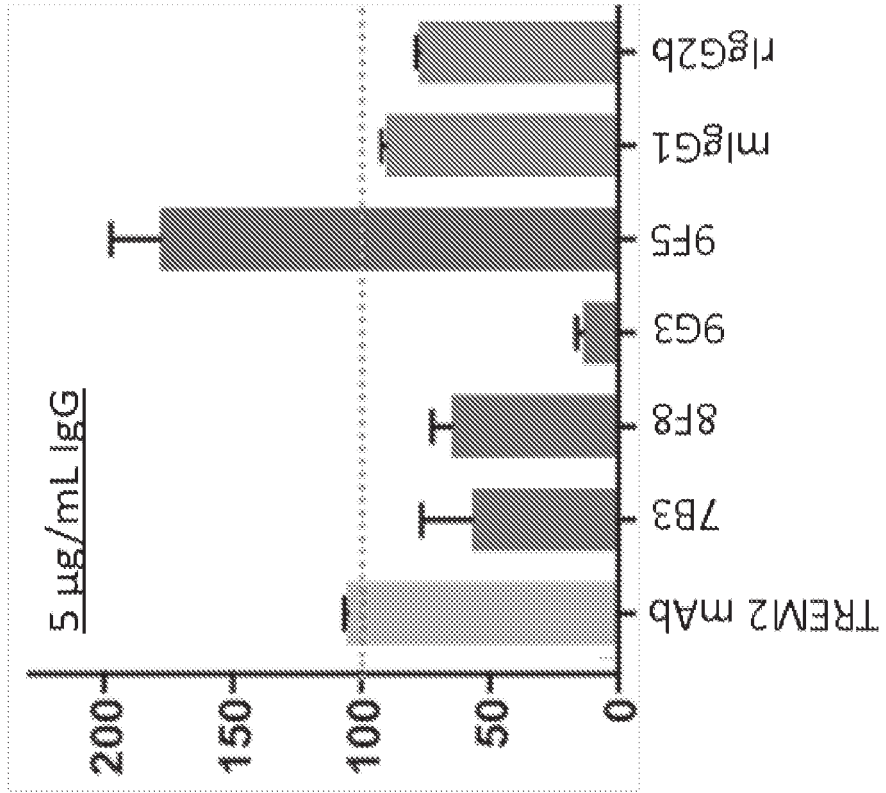


FIG. 11E

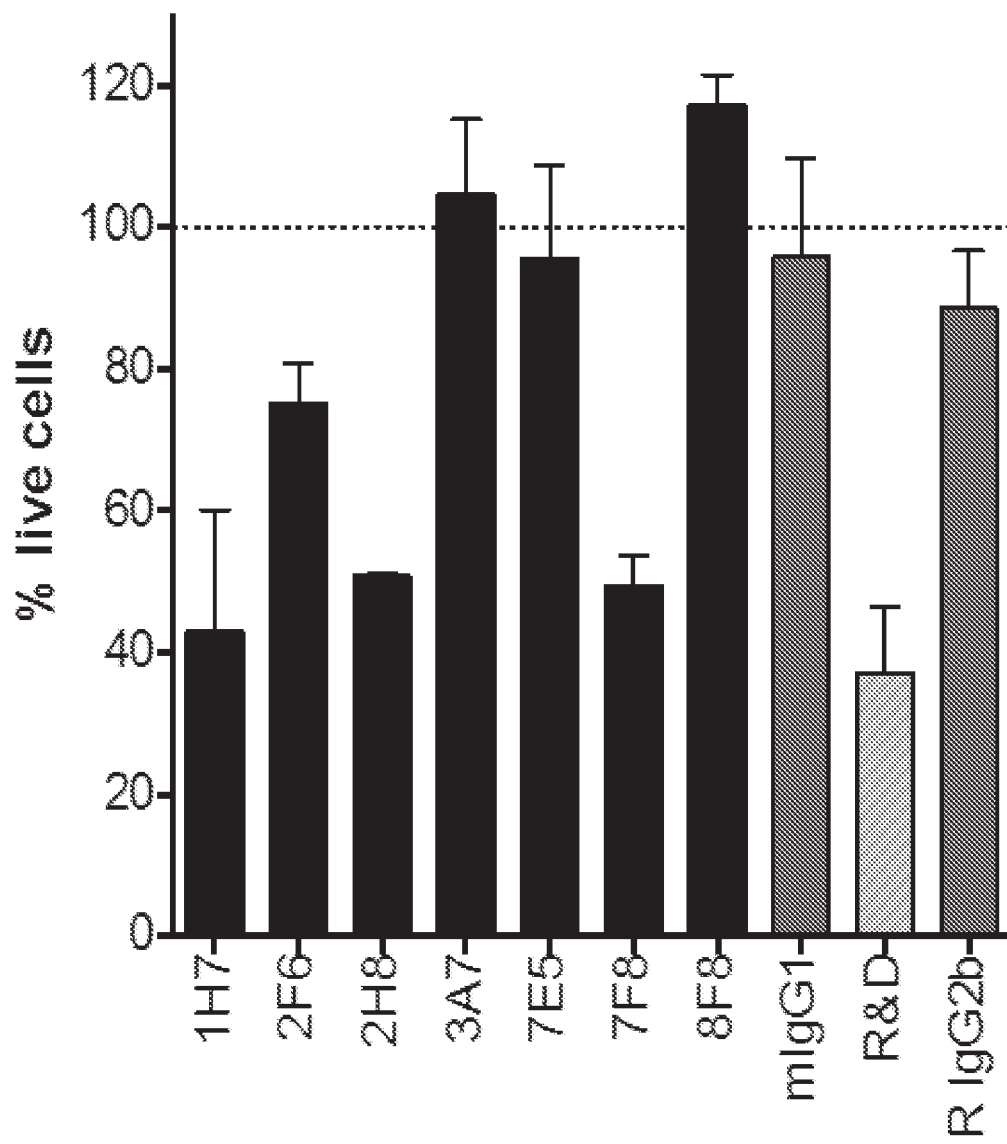


FIG. 12A

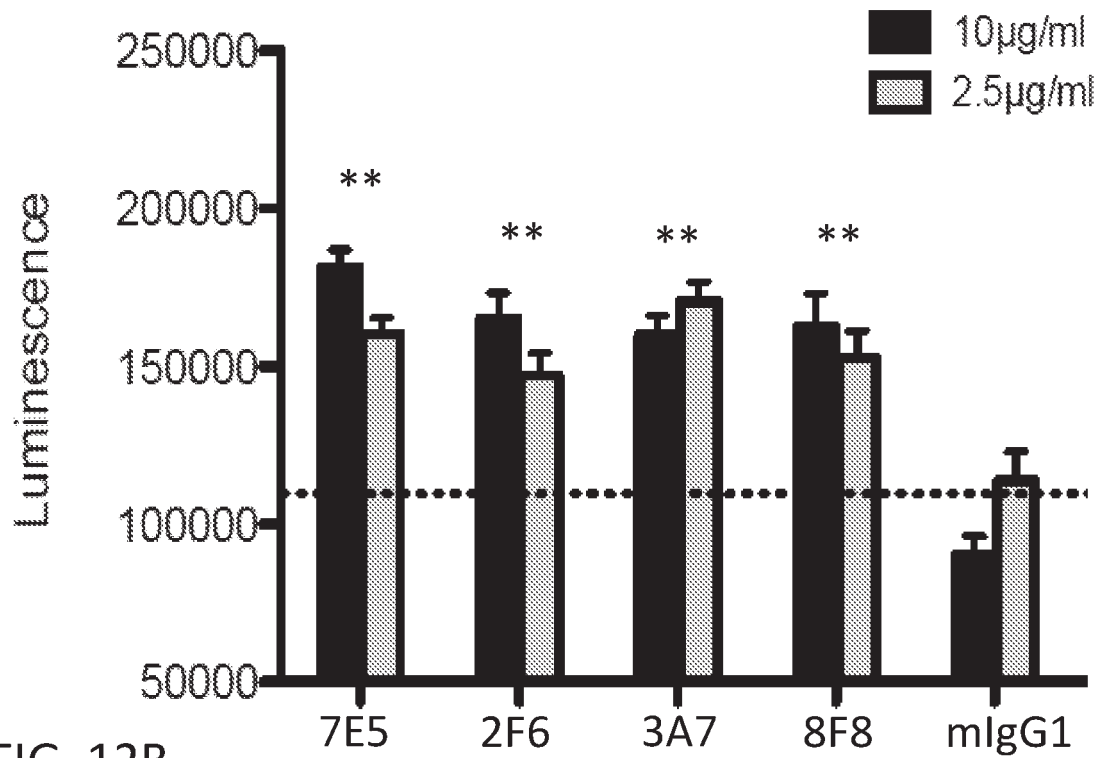


FIG. 12B

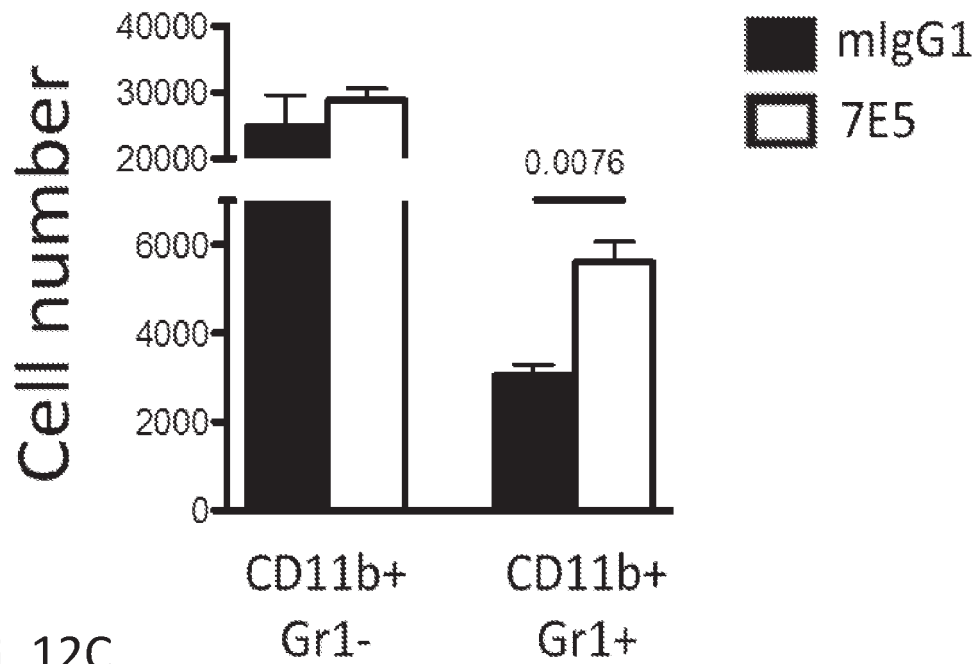


FIG. 12C

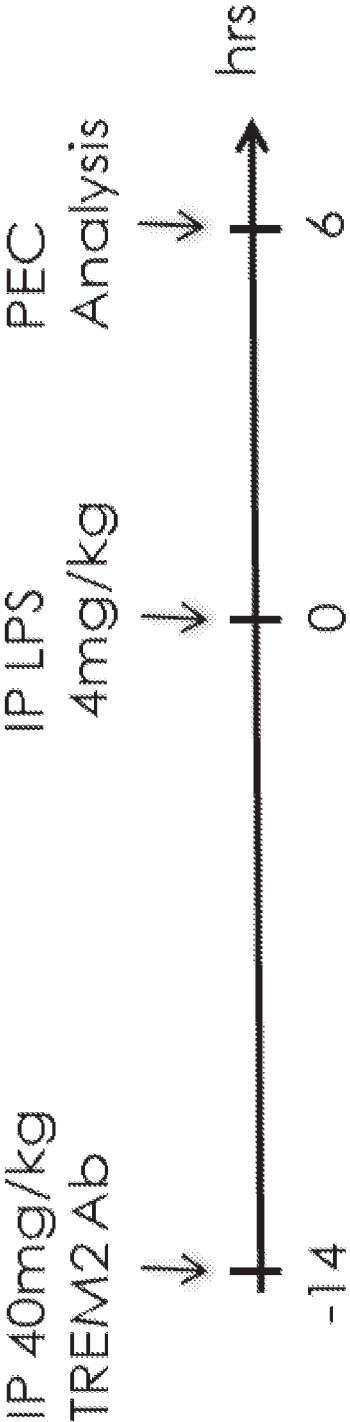


FIG. 13A

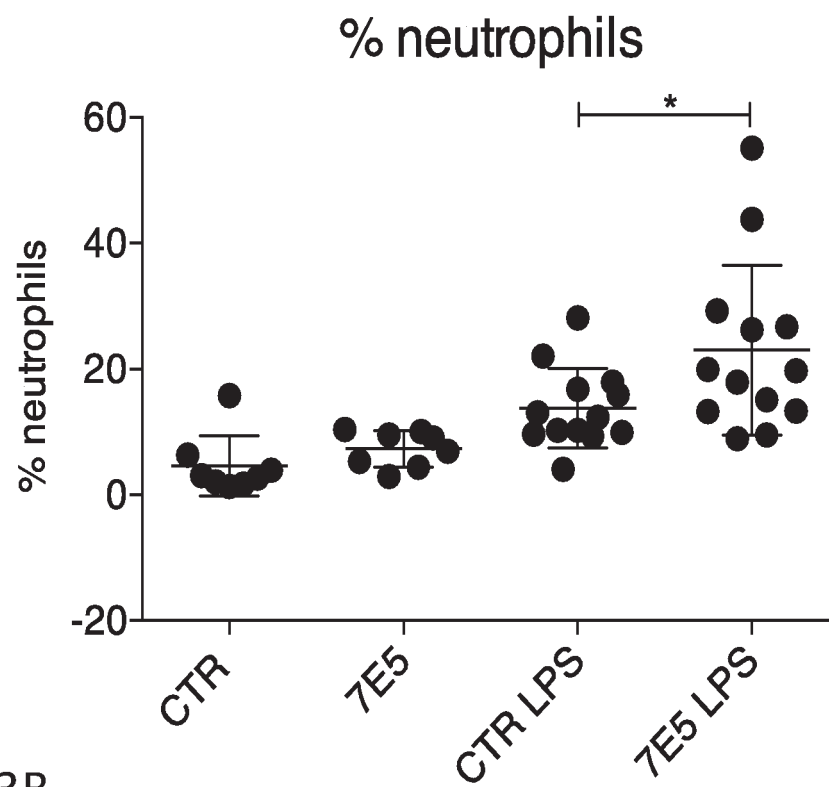


FIG. 13B

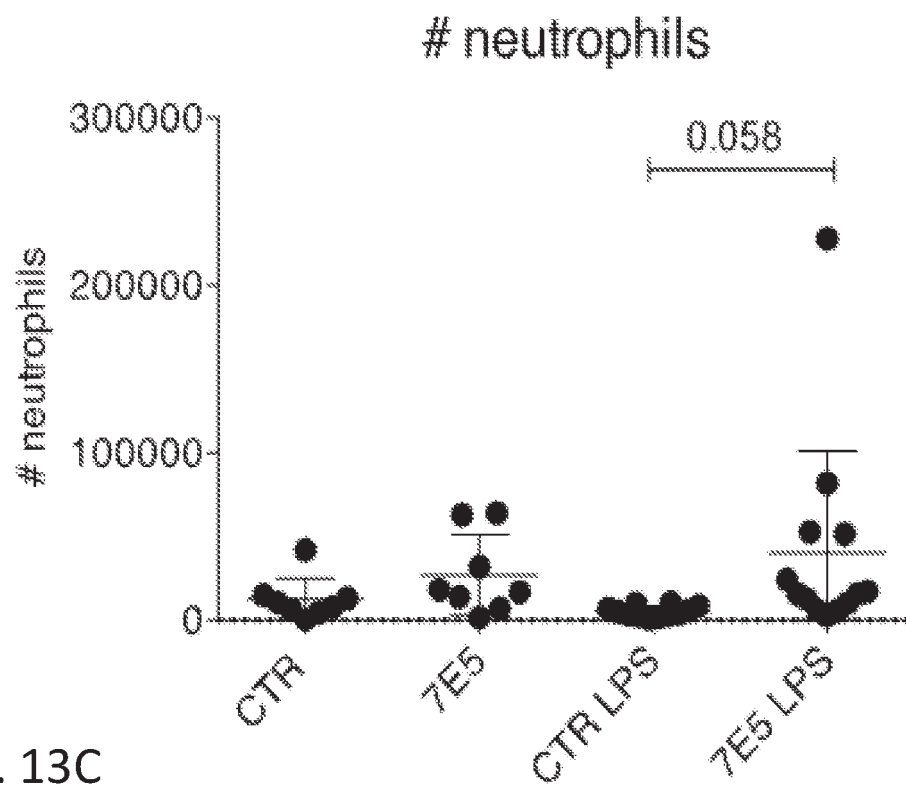


FIG. 13C

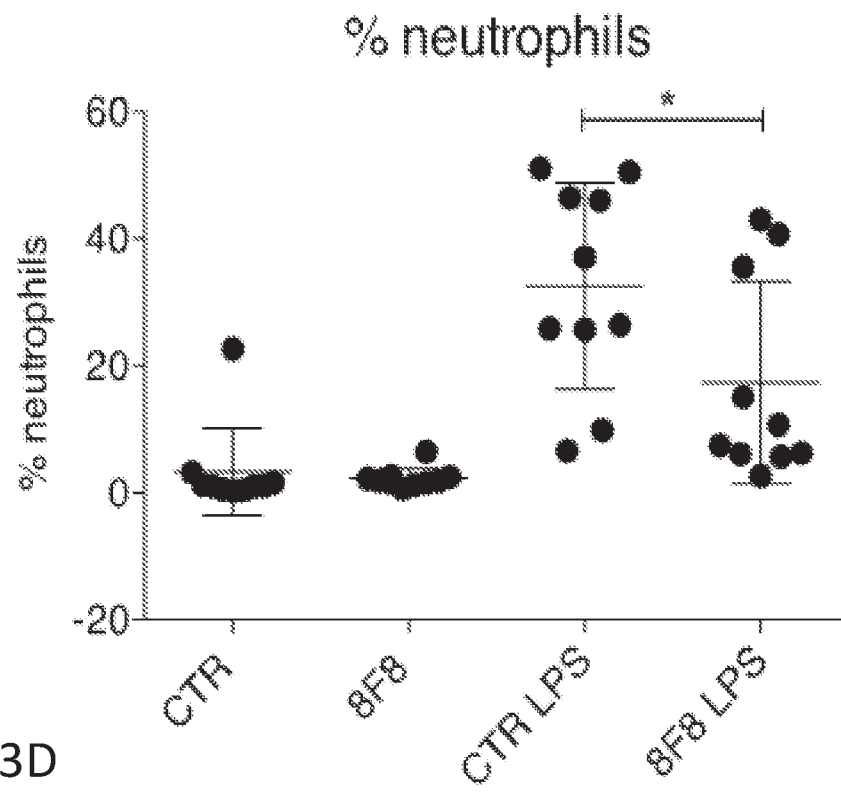


FIG. 13D

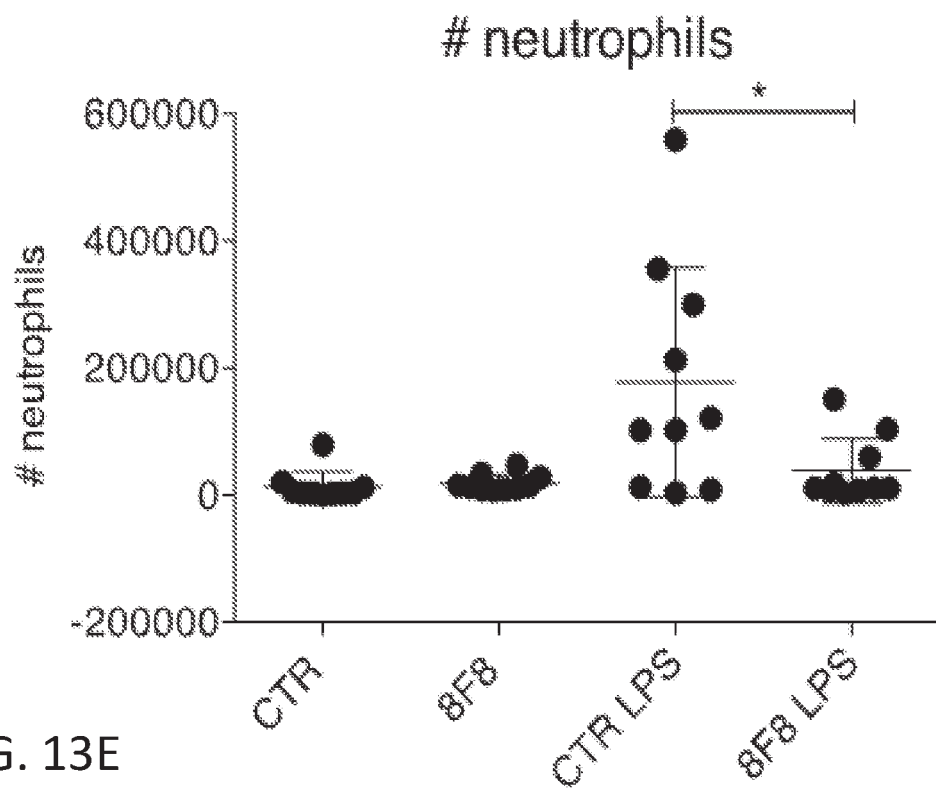


FIG. 13E

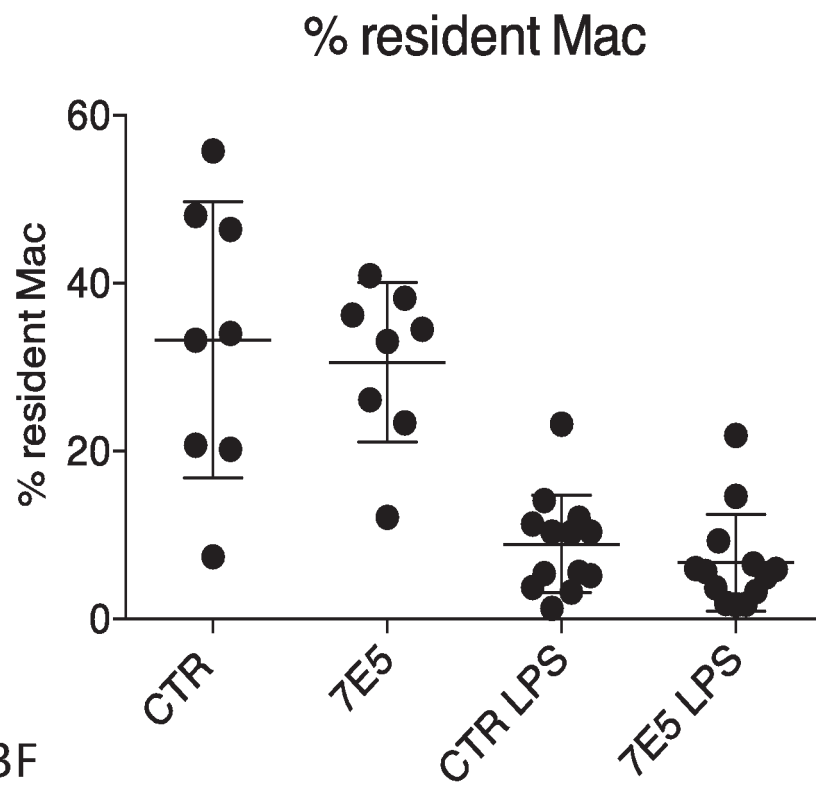


FIG. 13F

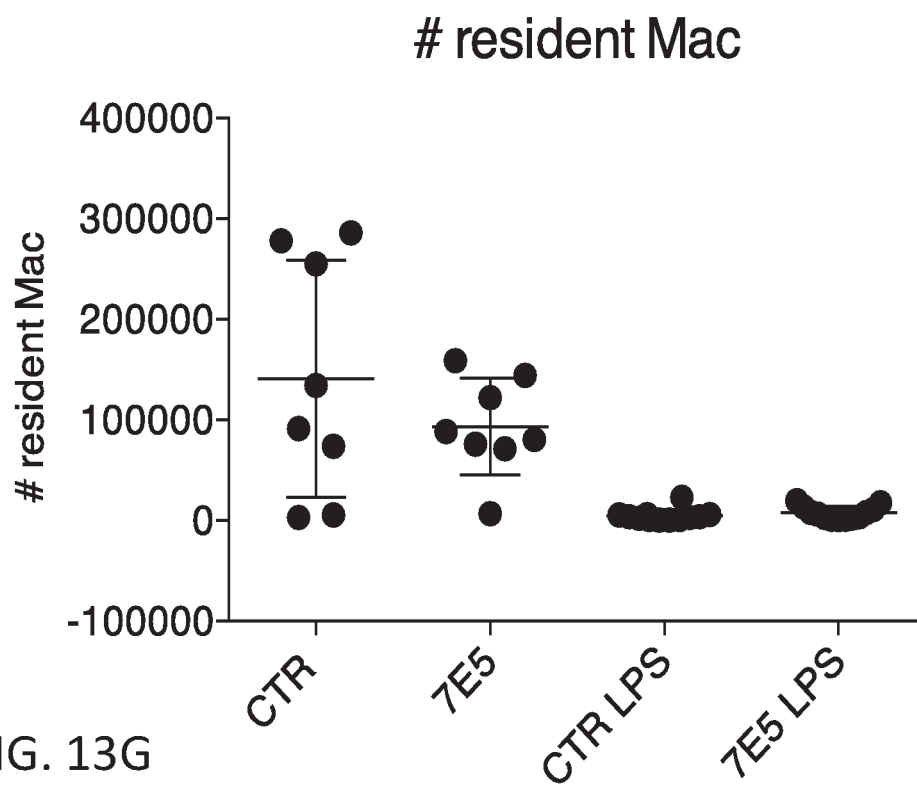


FIG. 13G

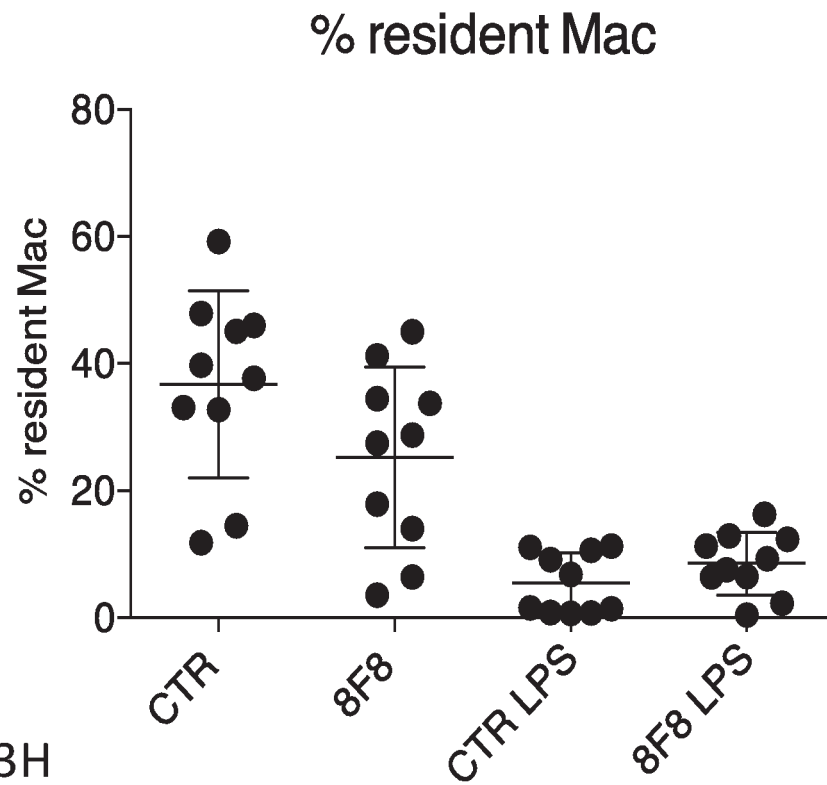


FIG. 13H

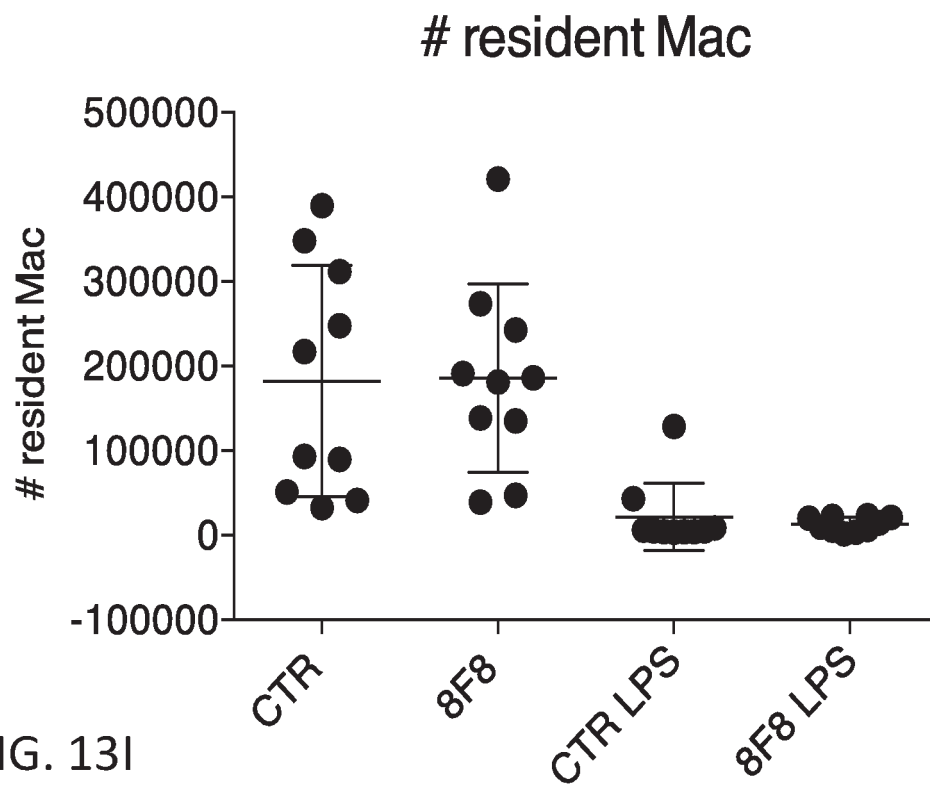


FIG. 13I

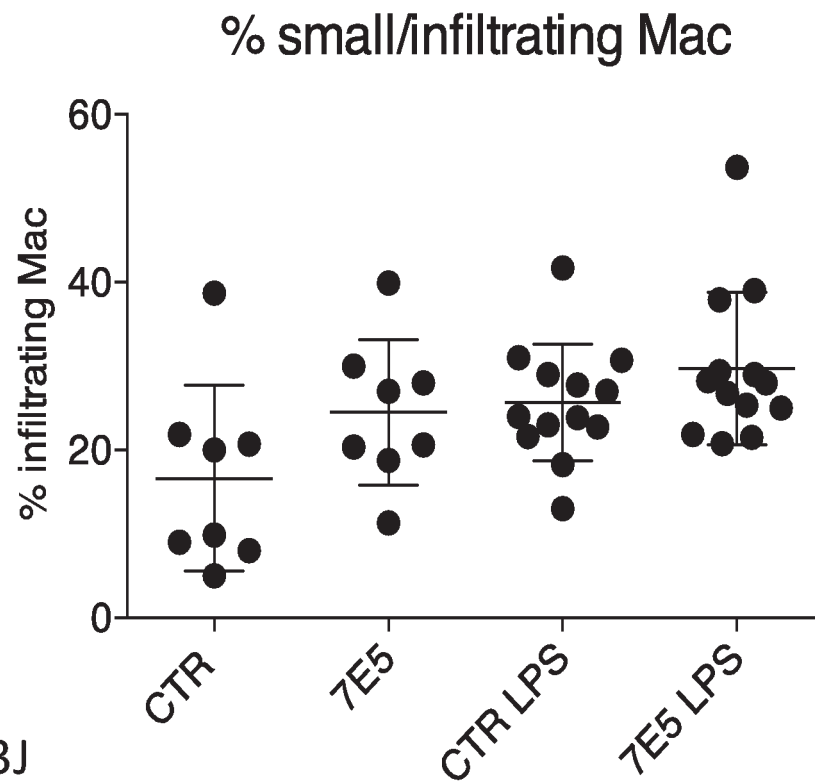


FIG. 13J

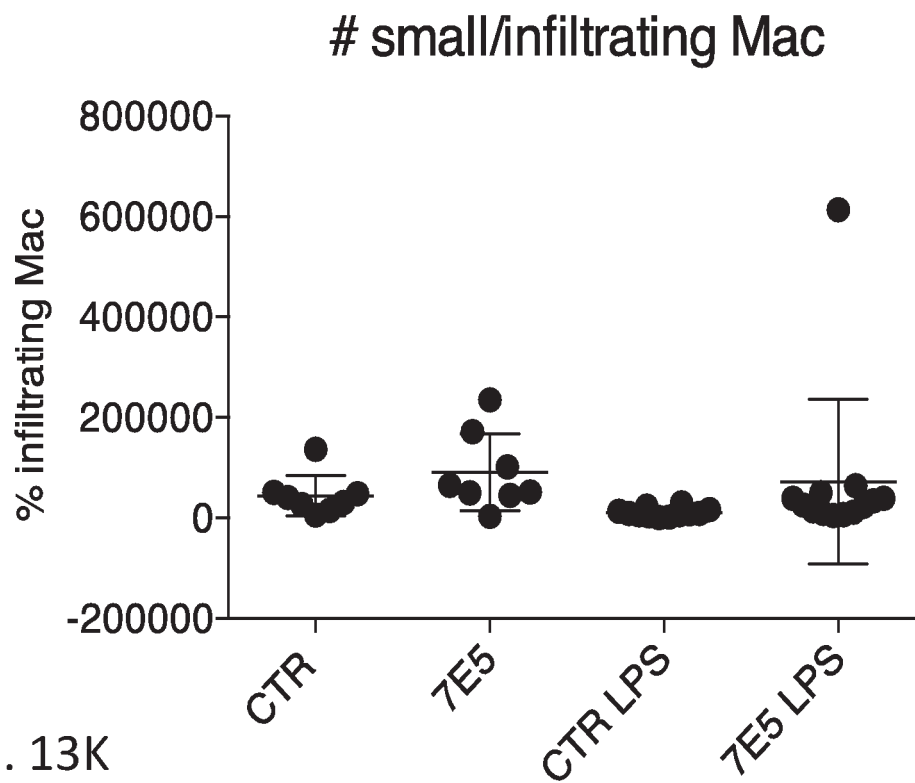


FIG. 13K

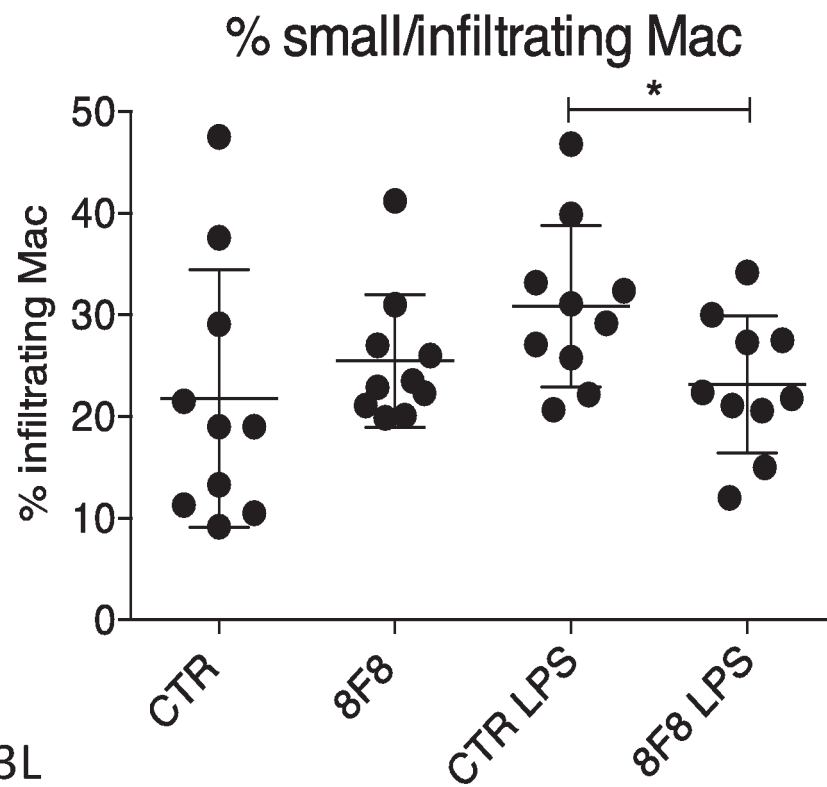


FIG. 13L

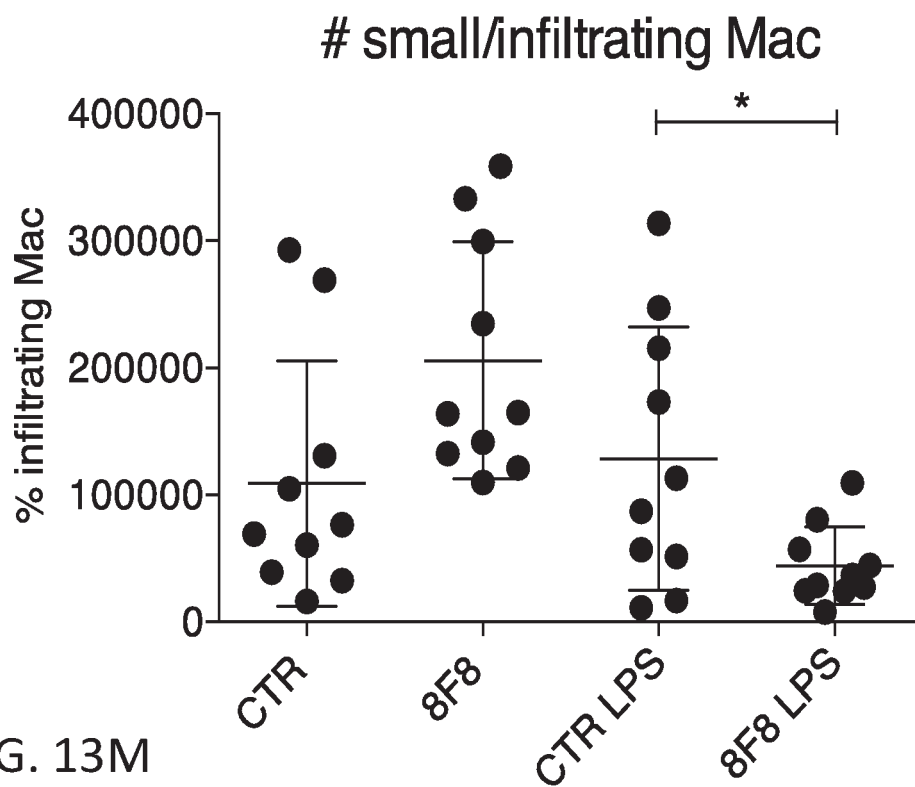


FIG. 13M

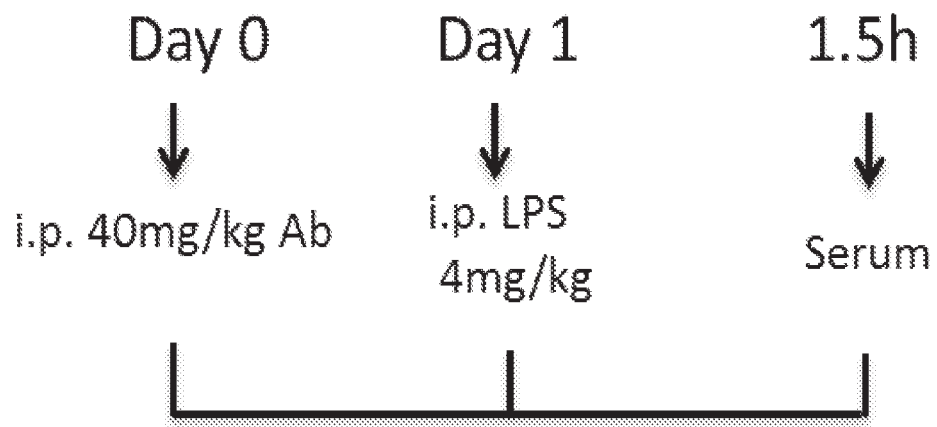


FIG. 13N

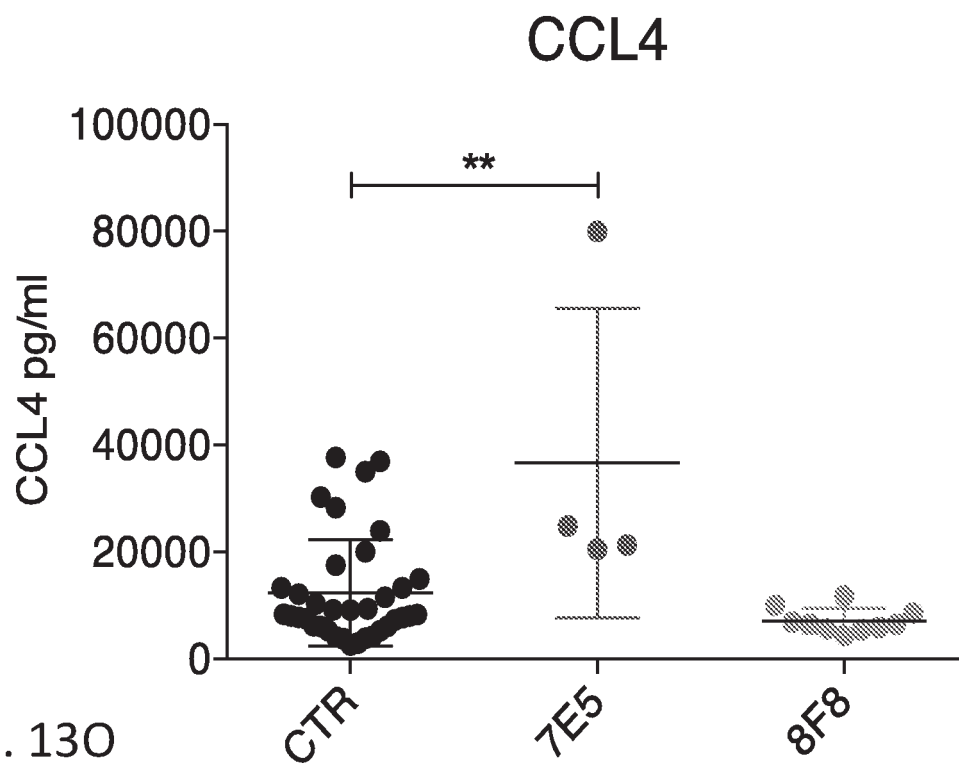
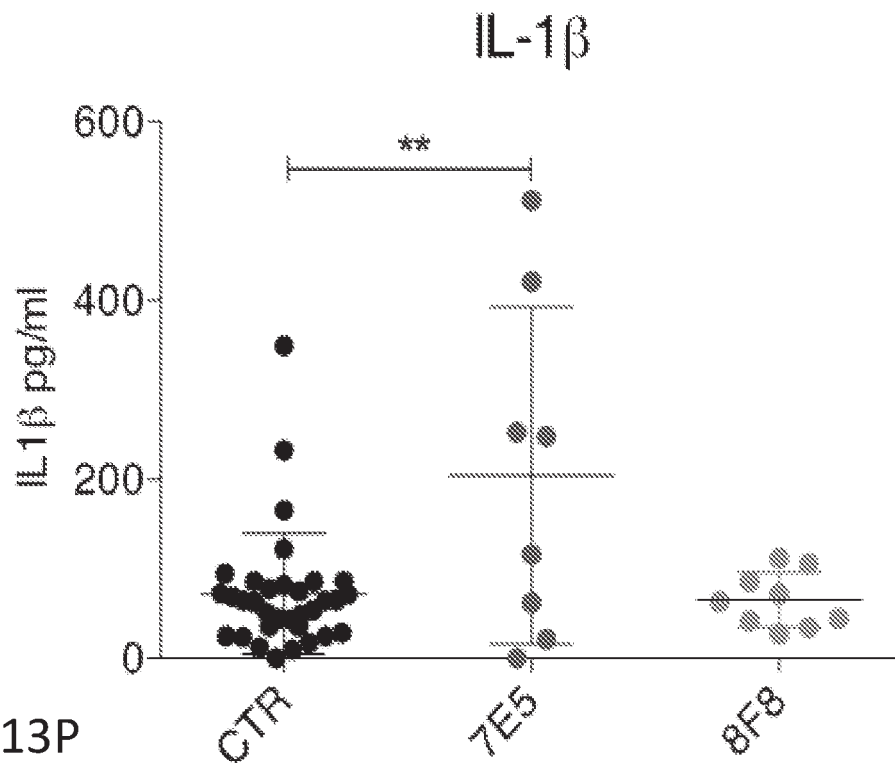
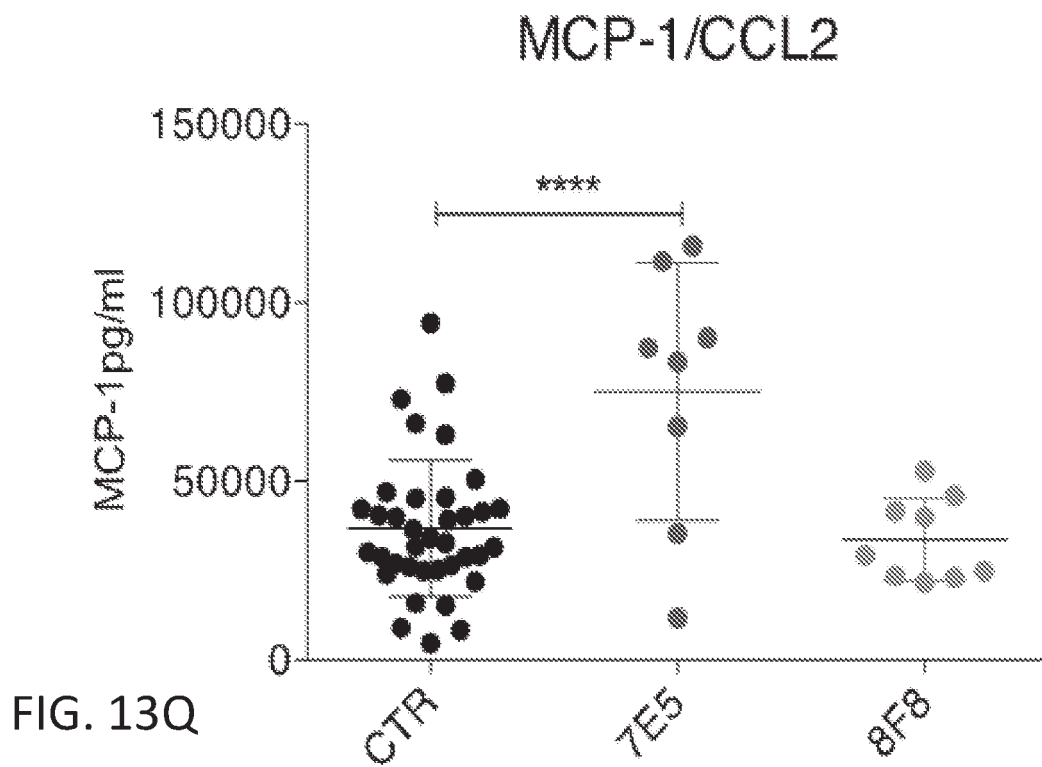


FIG. 13O



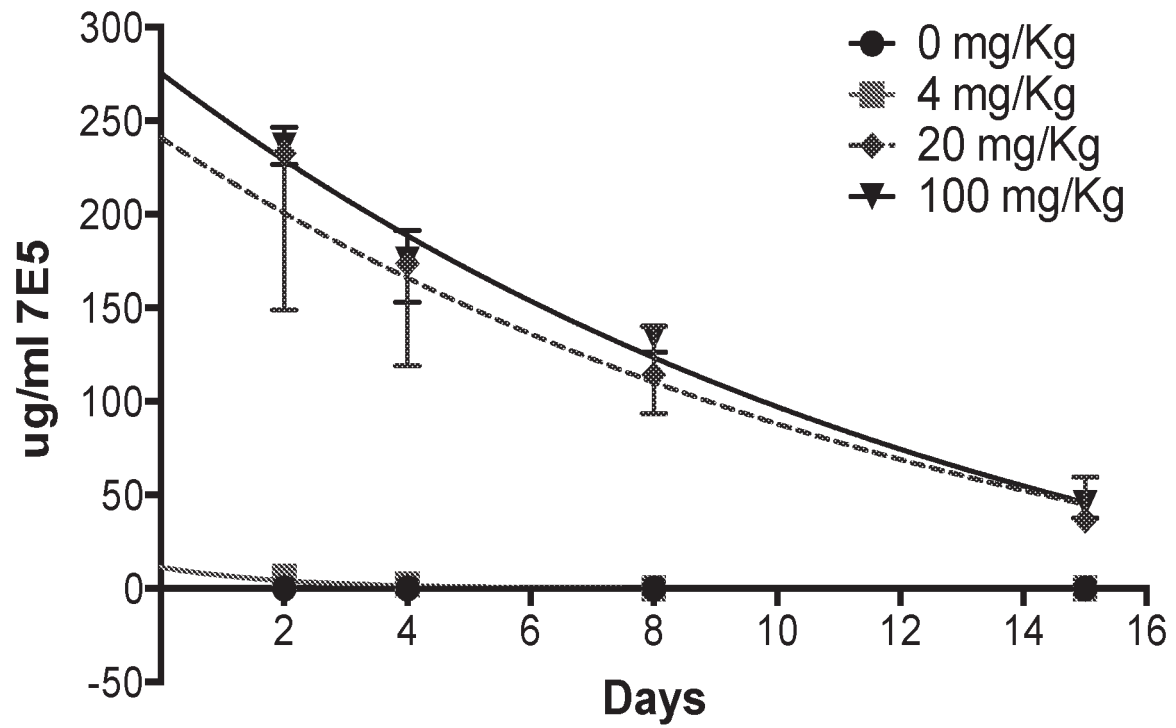


FIG. 14

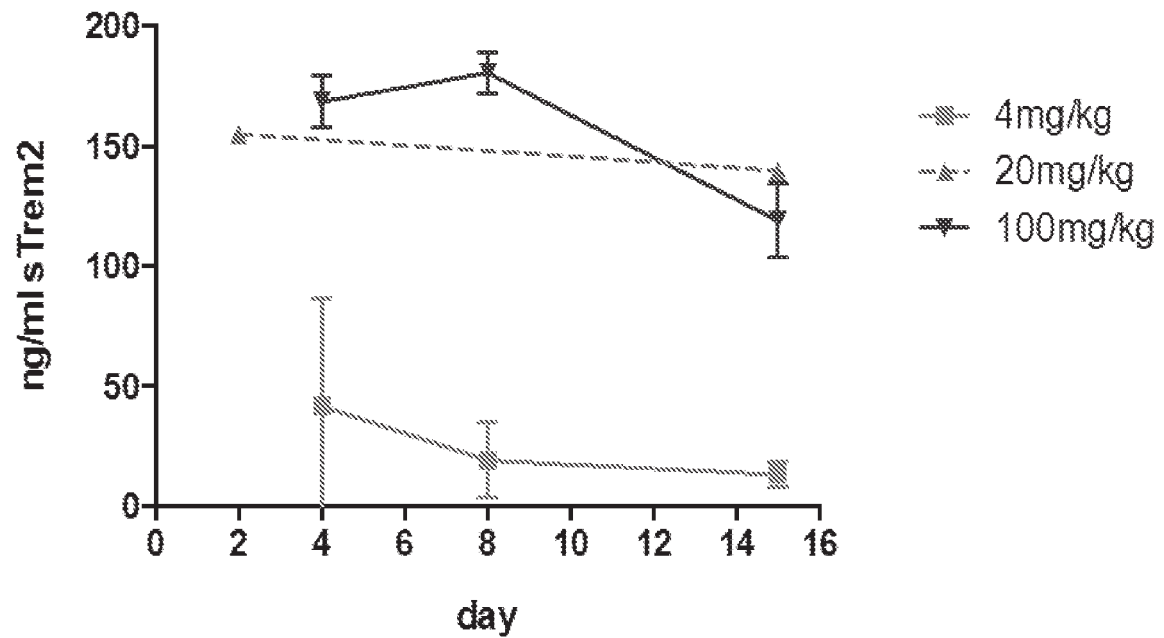


FIG. 15

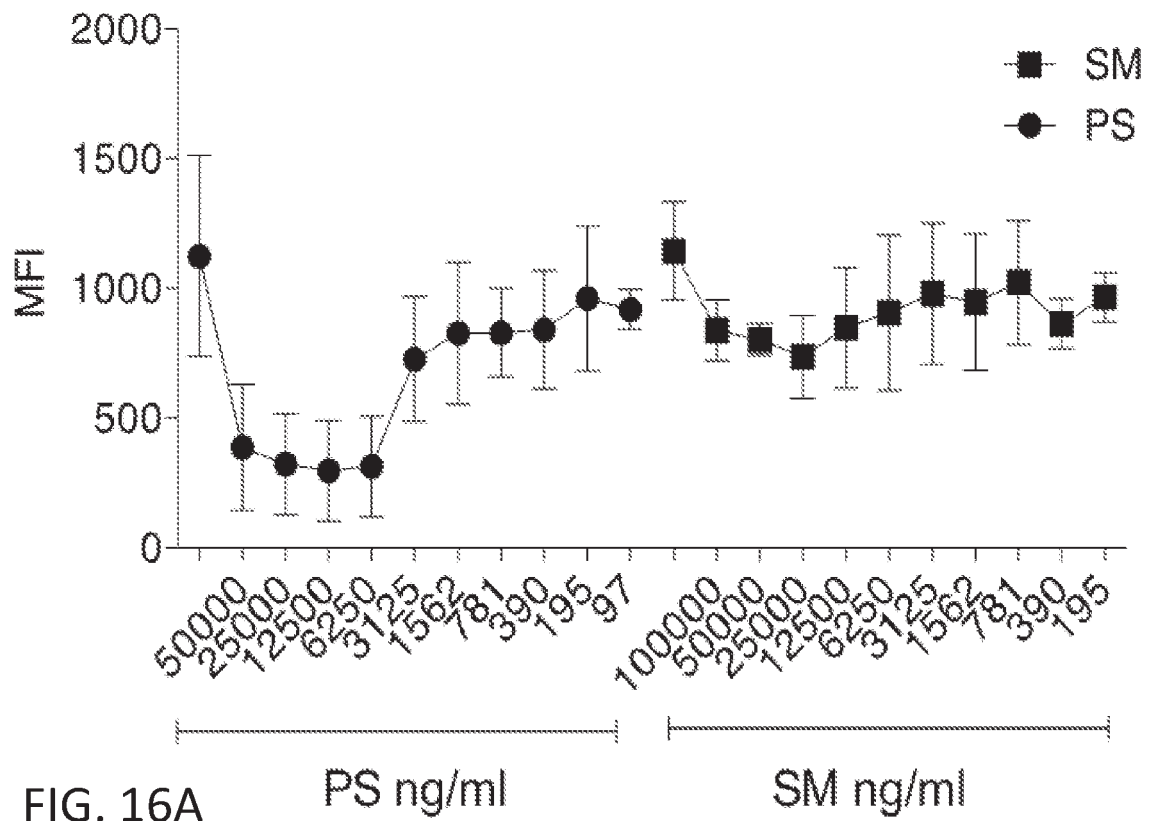


FIG. 16A

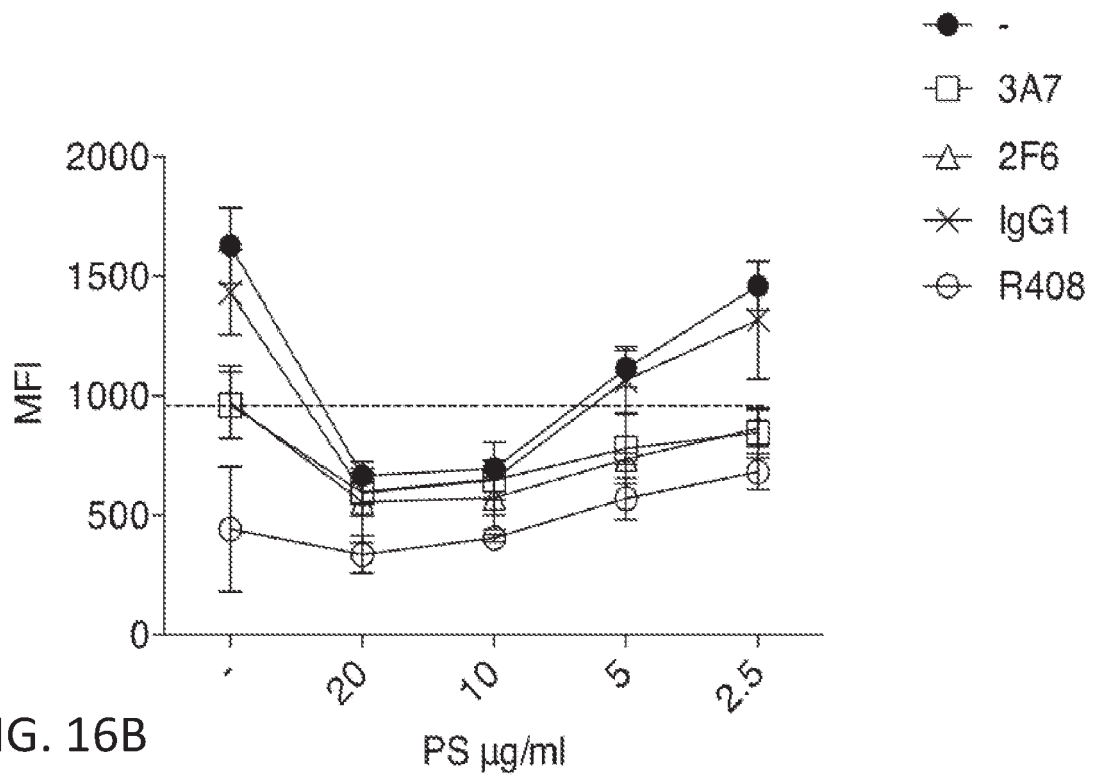


FIG. 16B

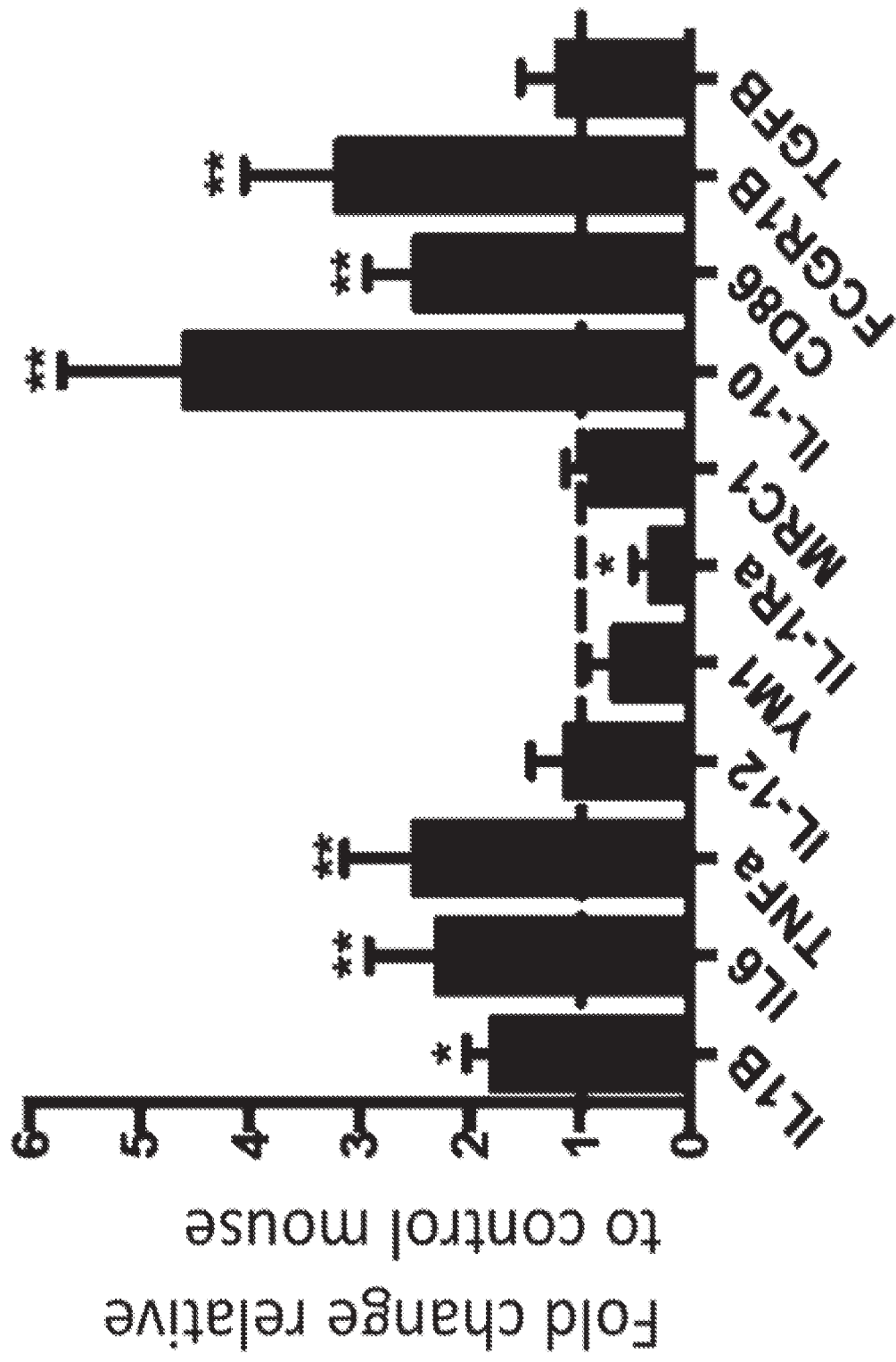


FIG. 17A

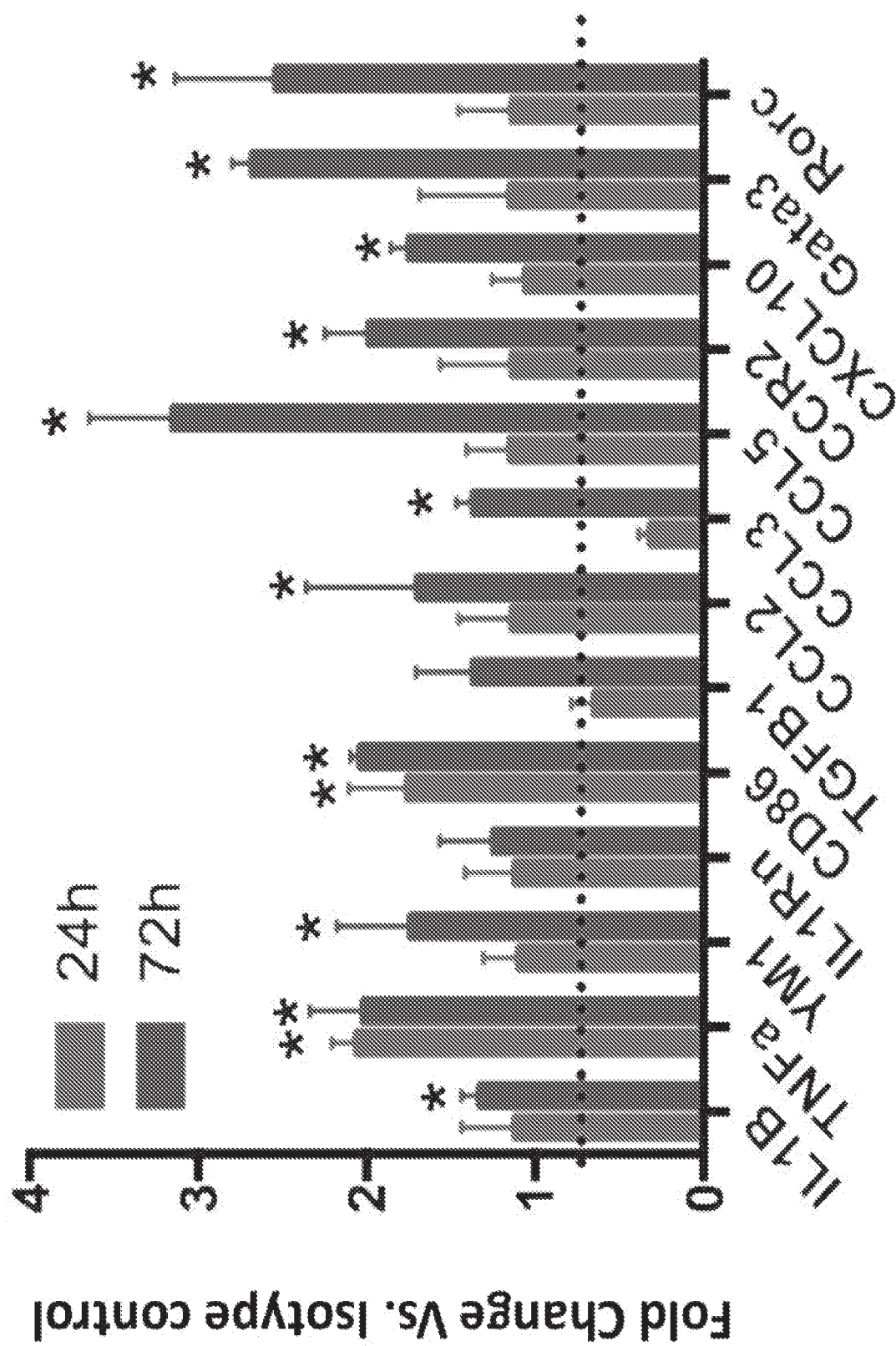


FIG. 17B

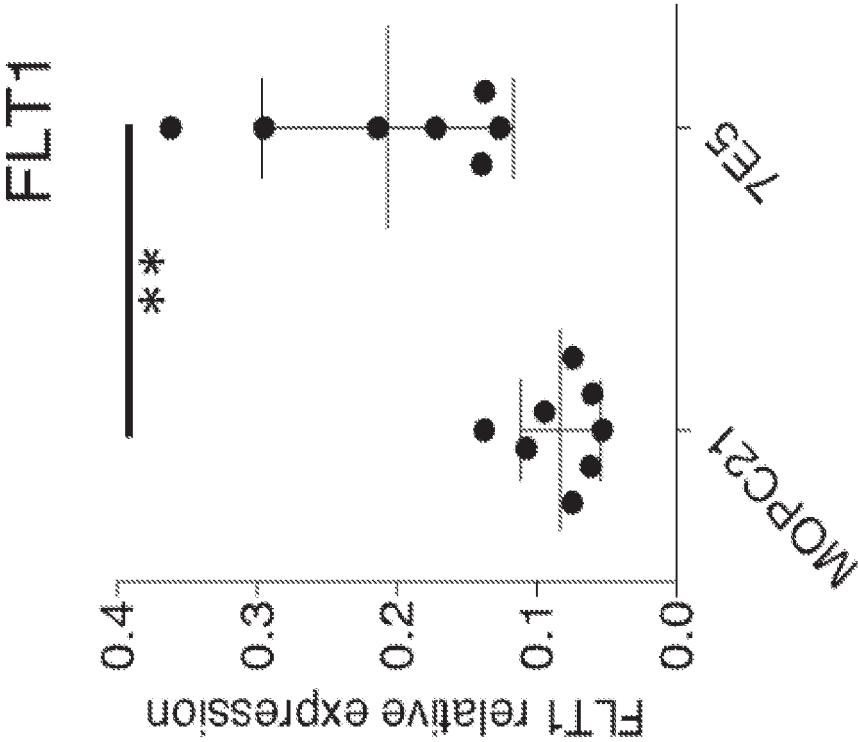
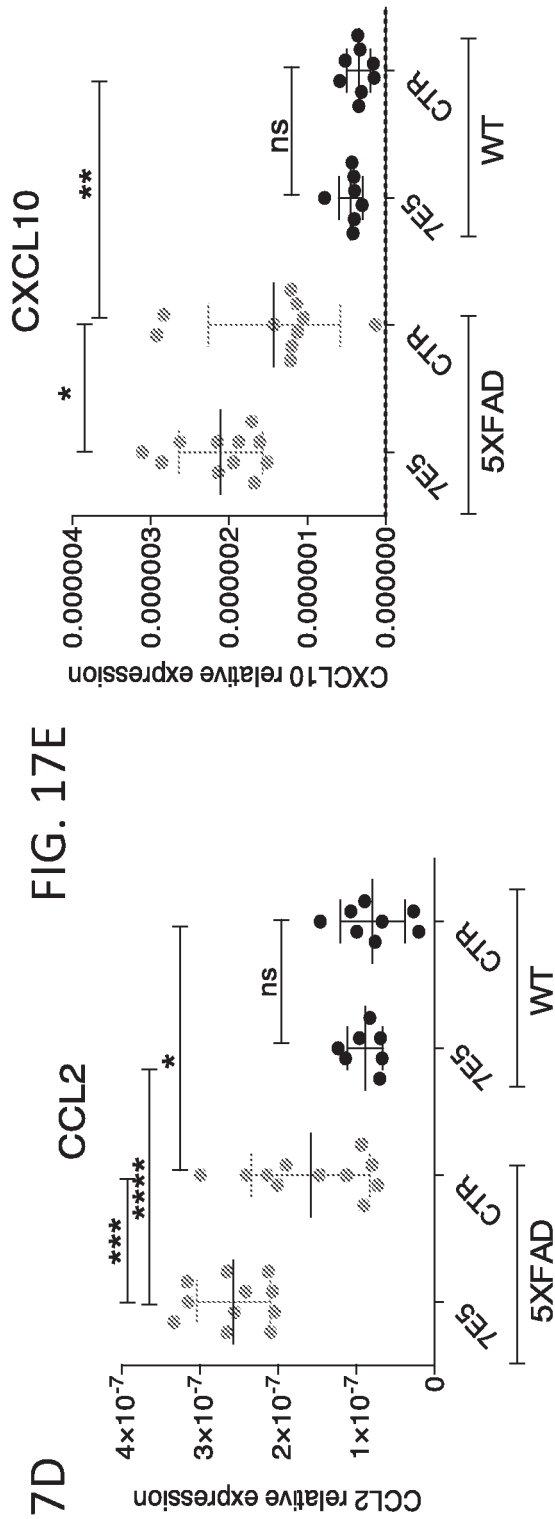


FIG. 17C

FIG. 17D

FIG. 17E



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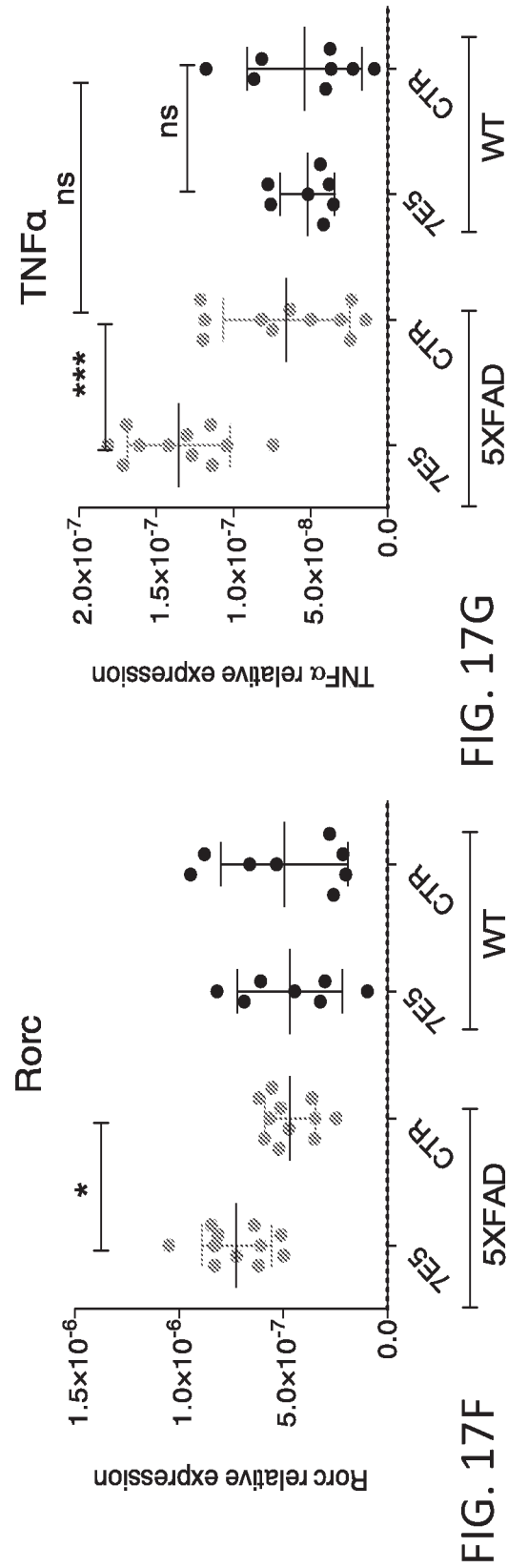


FIG. 17F

FIG. 17G

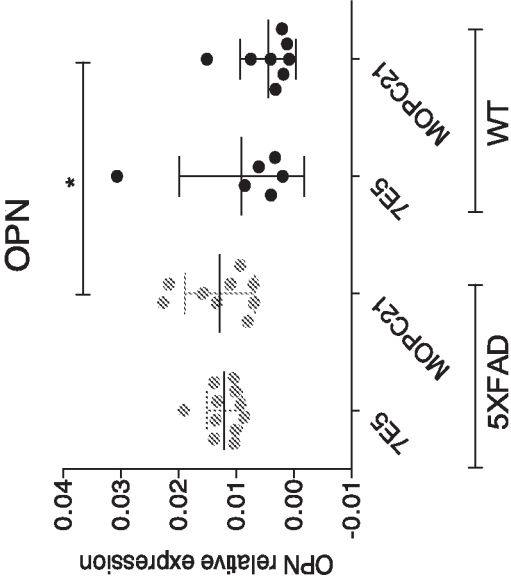


FIG. 17I

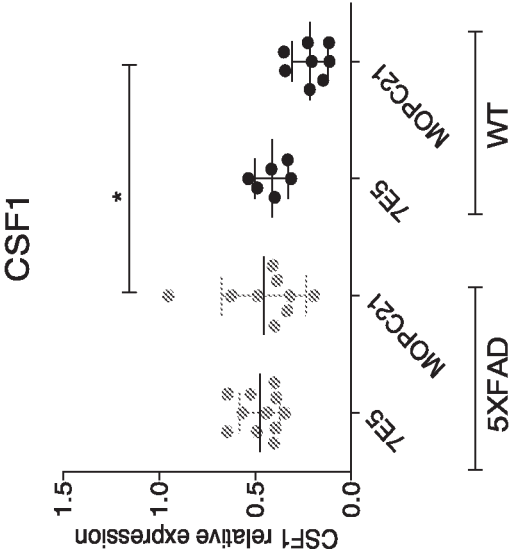


FIG. 17H

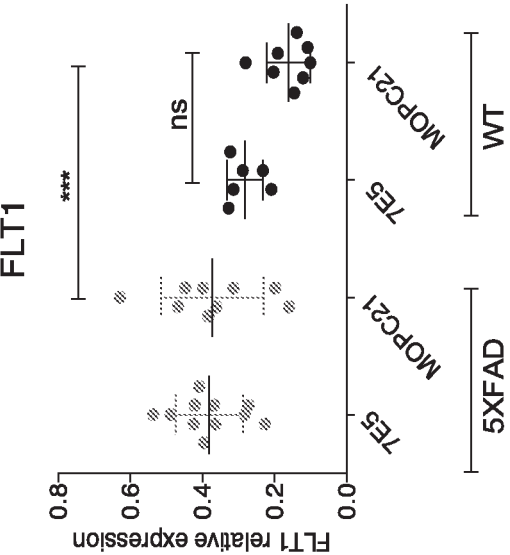


FIG. 17K

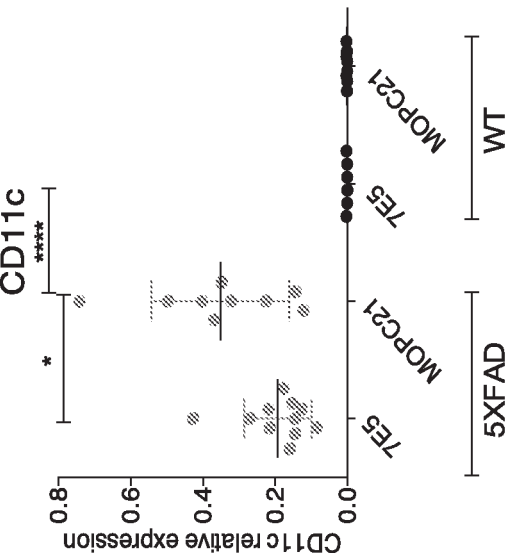


FIG. 17J

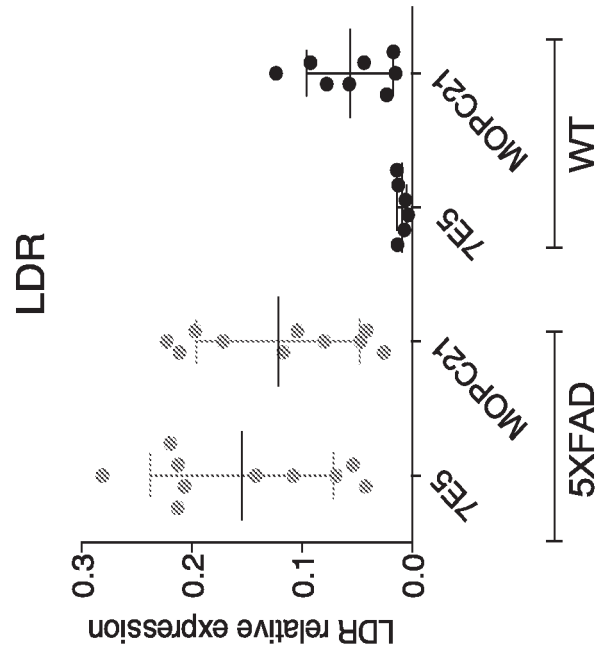


FIG. 17M

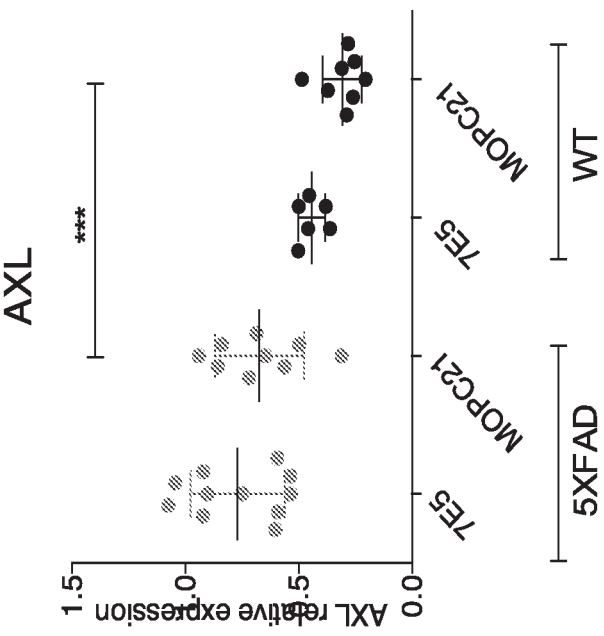


FIG. 17L

FIG. 17N

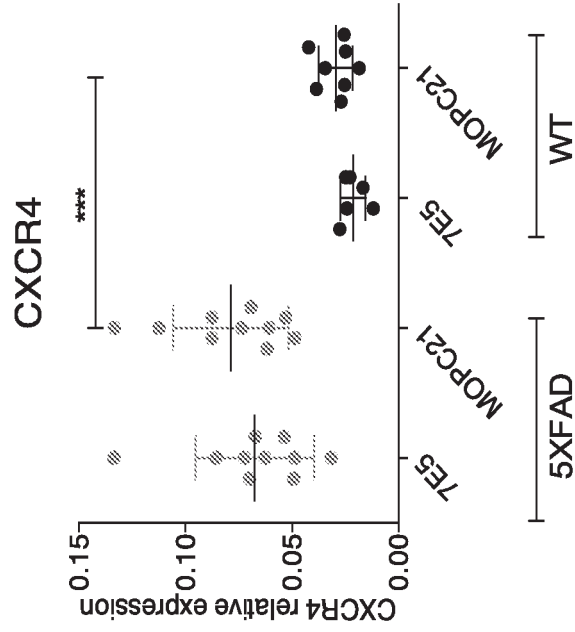
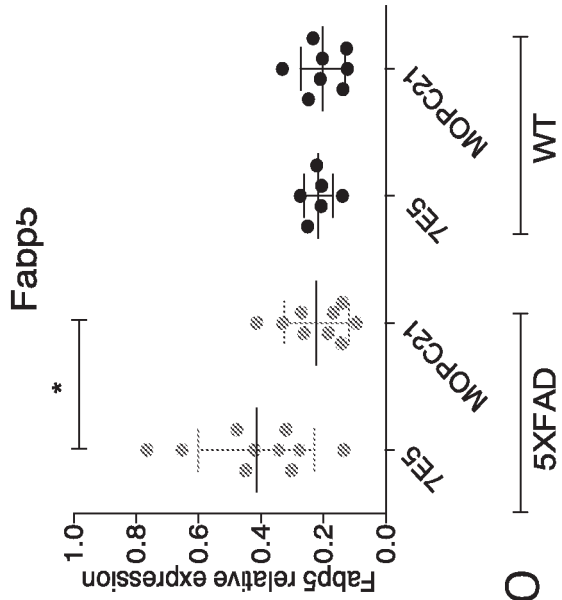


FIG. 17O

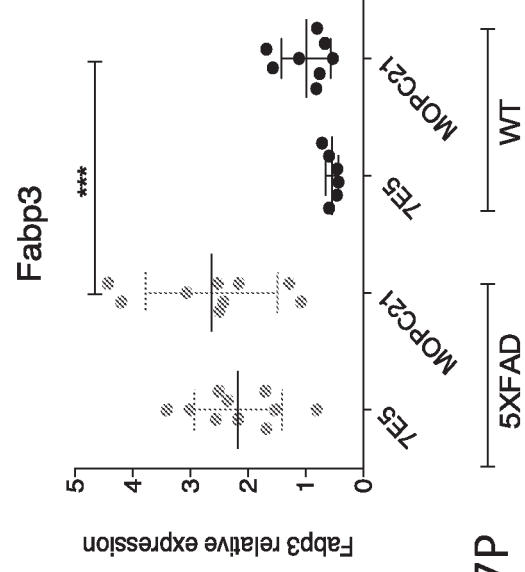


FIG. 17P

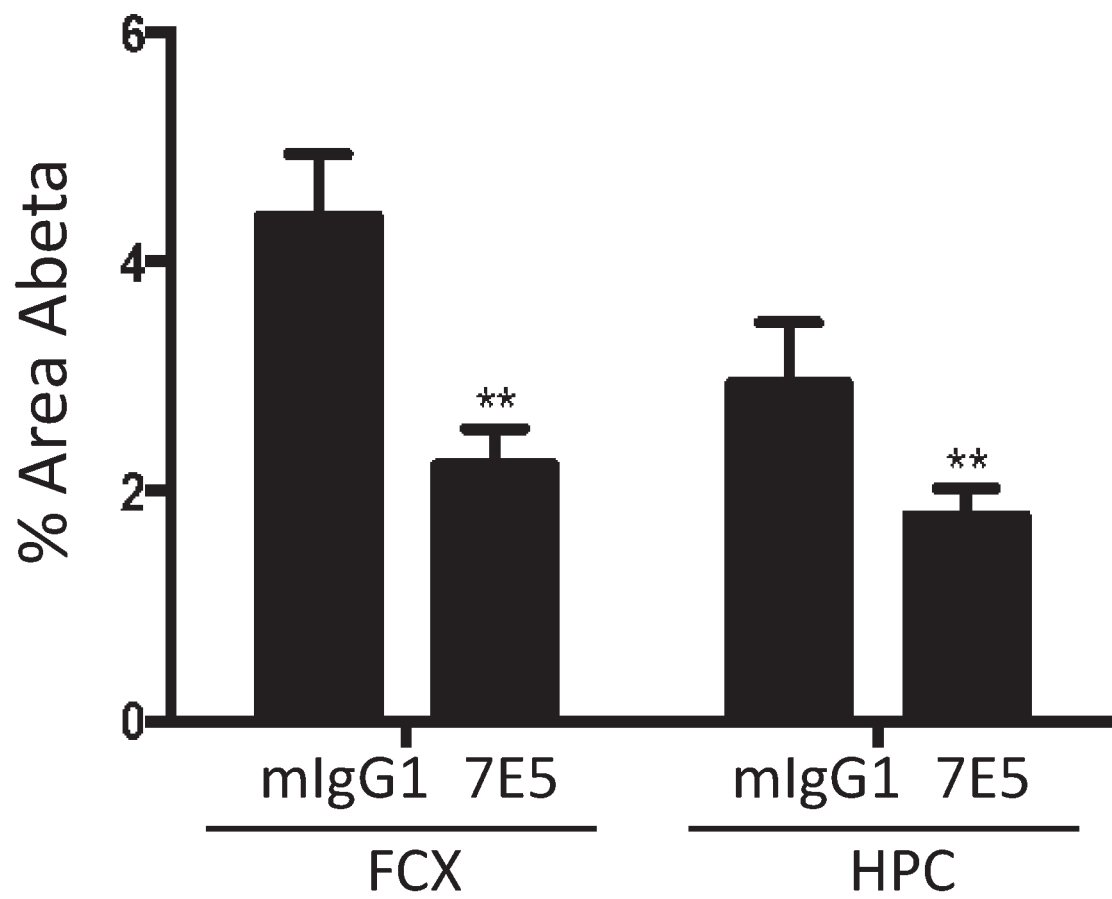


FIG. 17Q

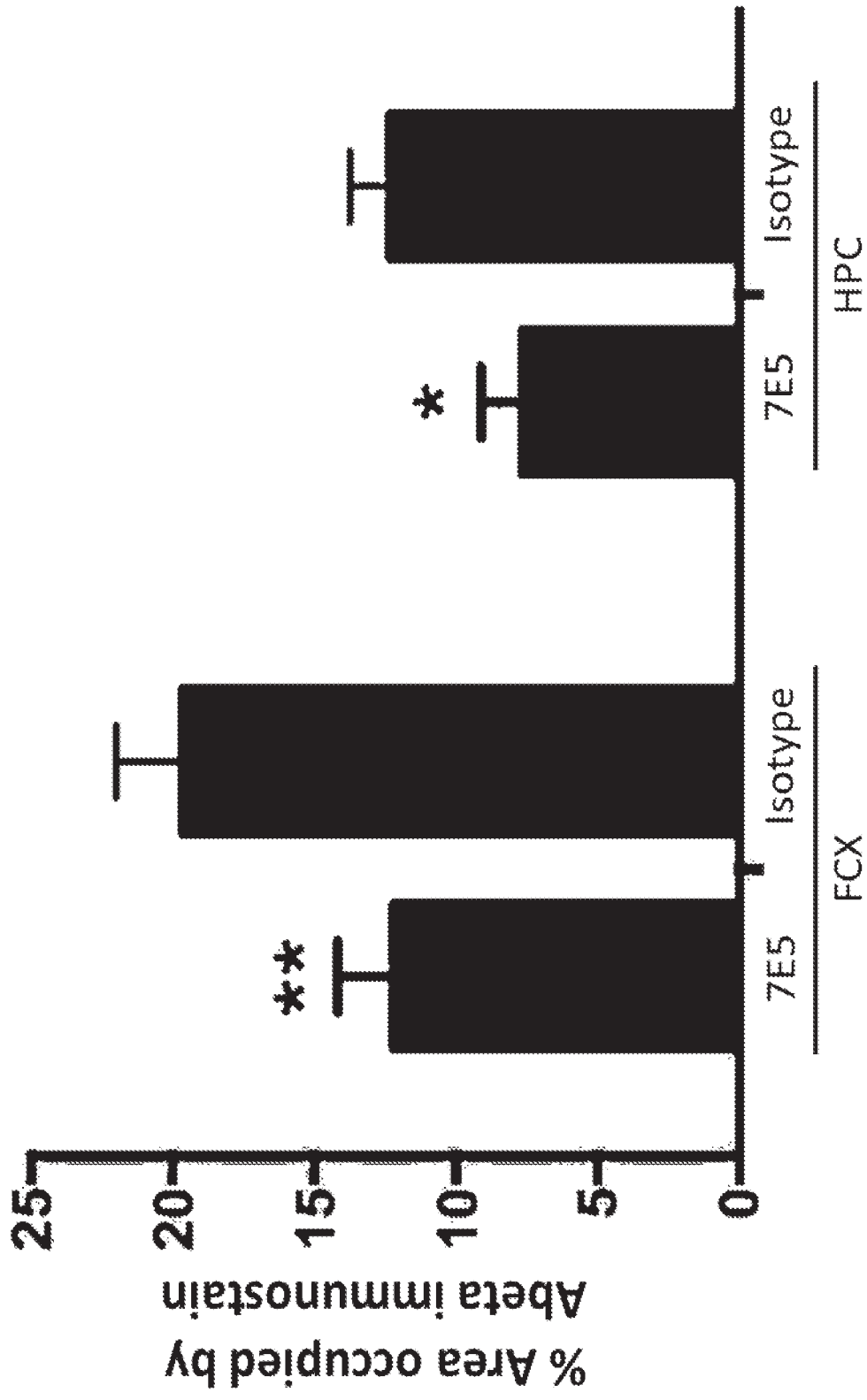


FIG. 17R

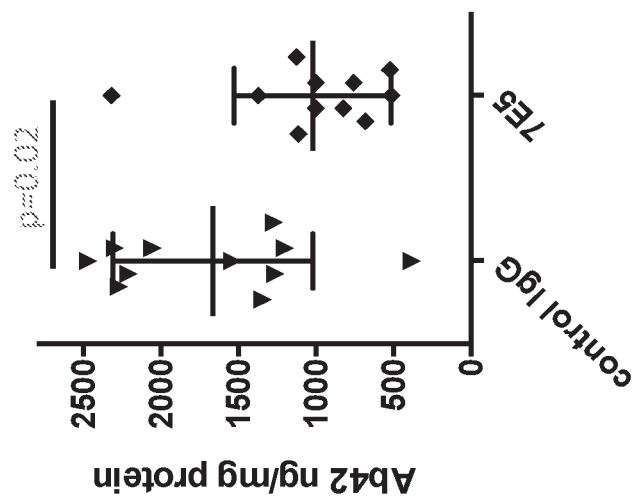


FIG. 17U

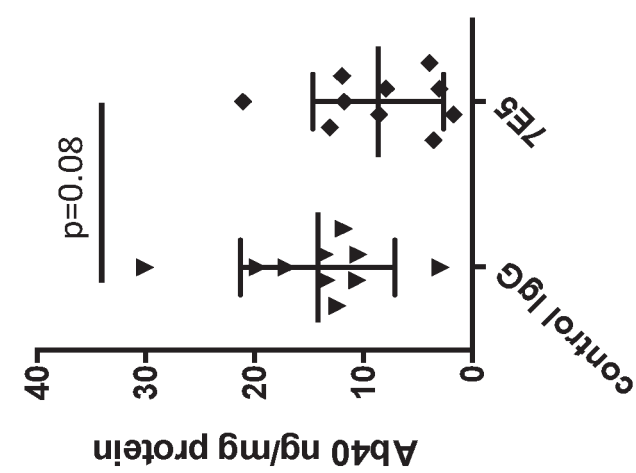


FIG. 17T

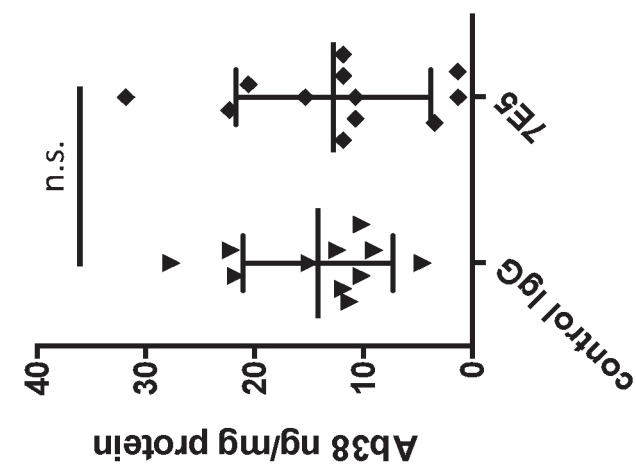


FIG. 17S

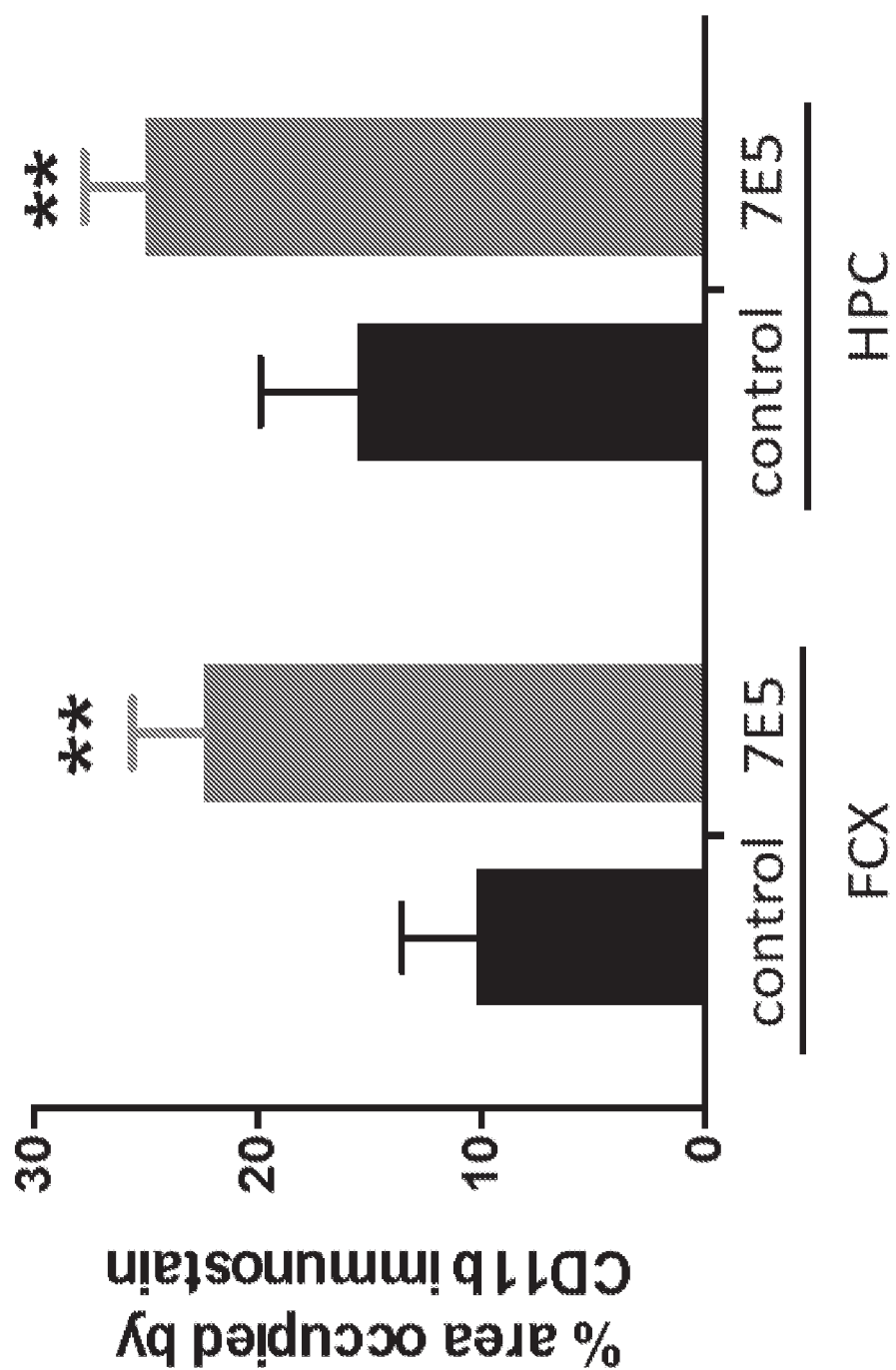


FIG. 17V

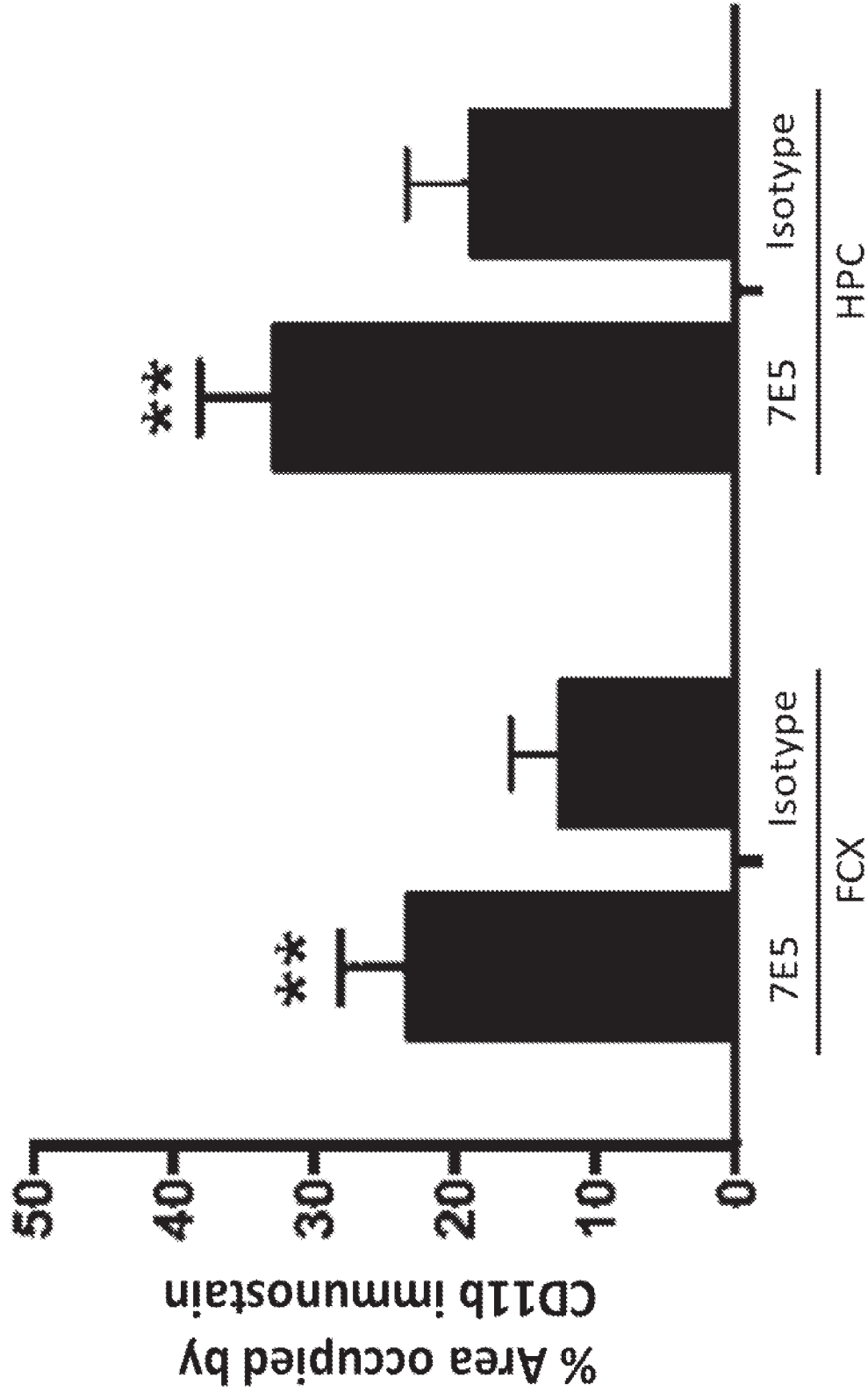


FIG. 17W

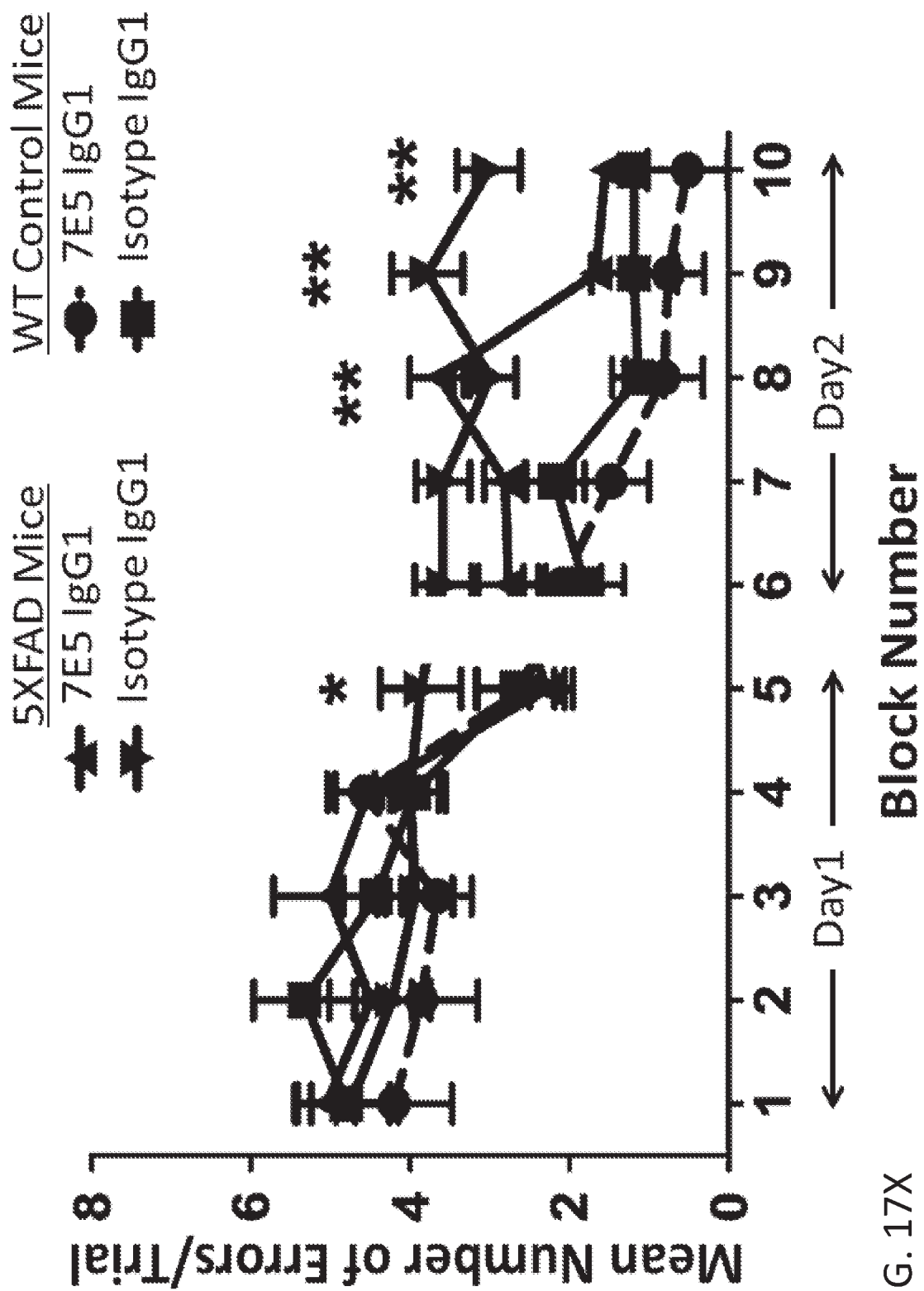


FIG. 17X

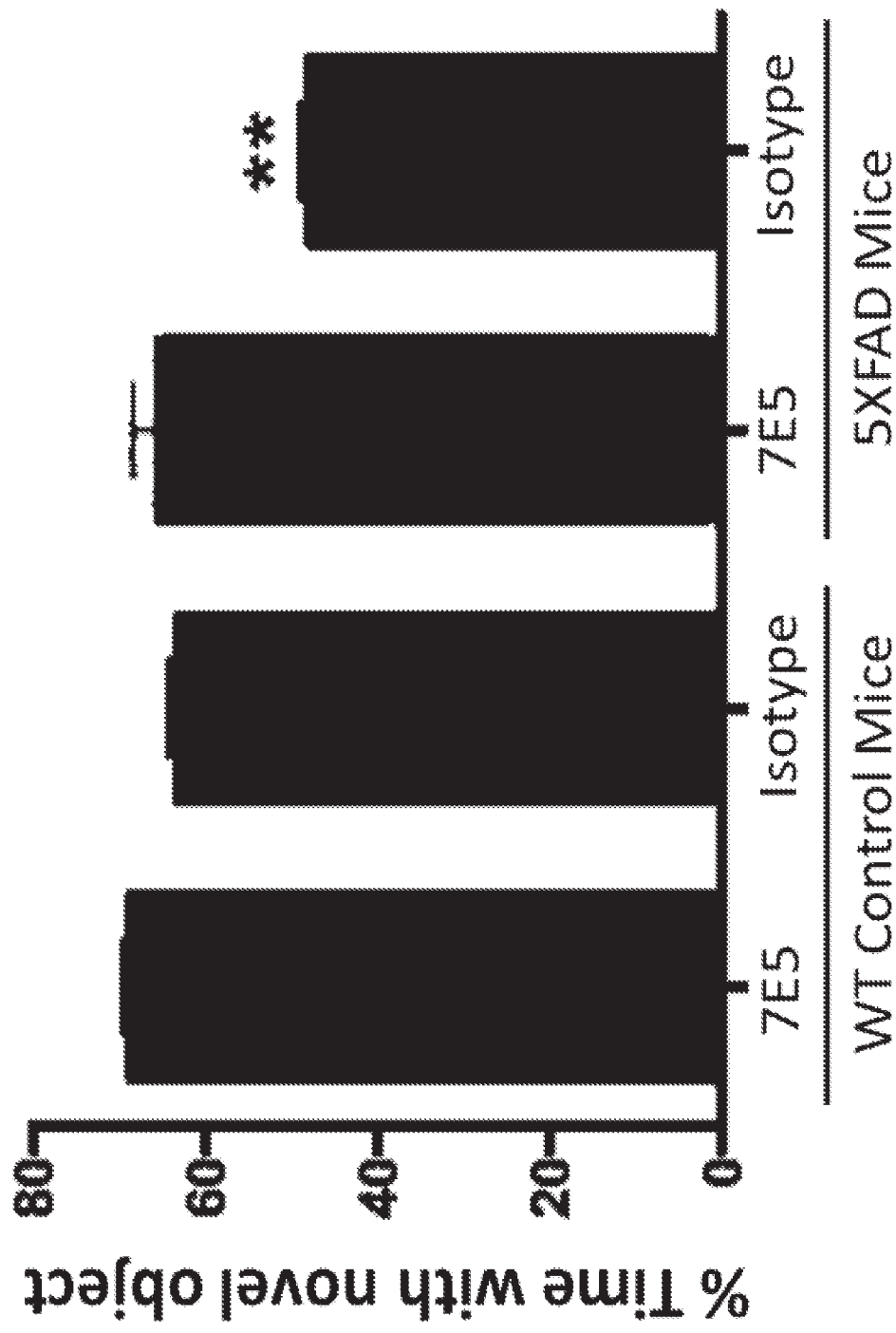


FIG. 17Y

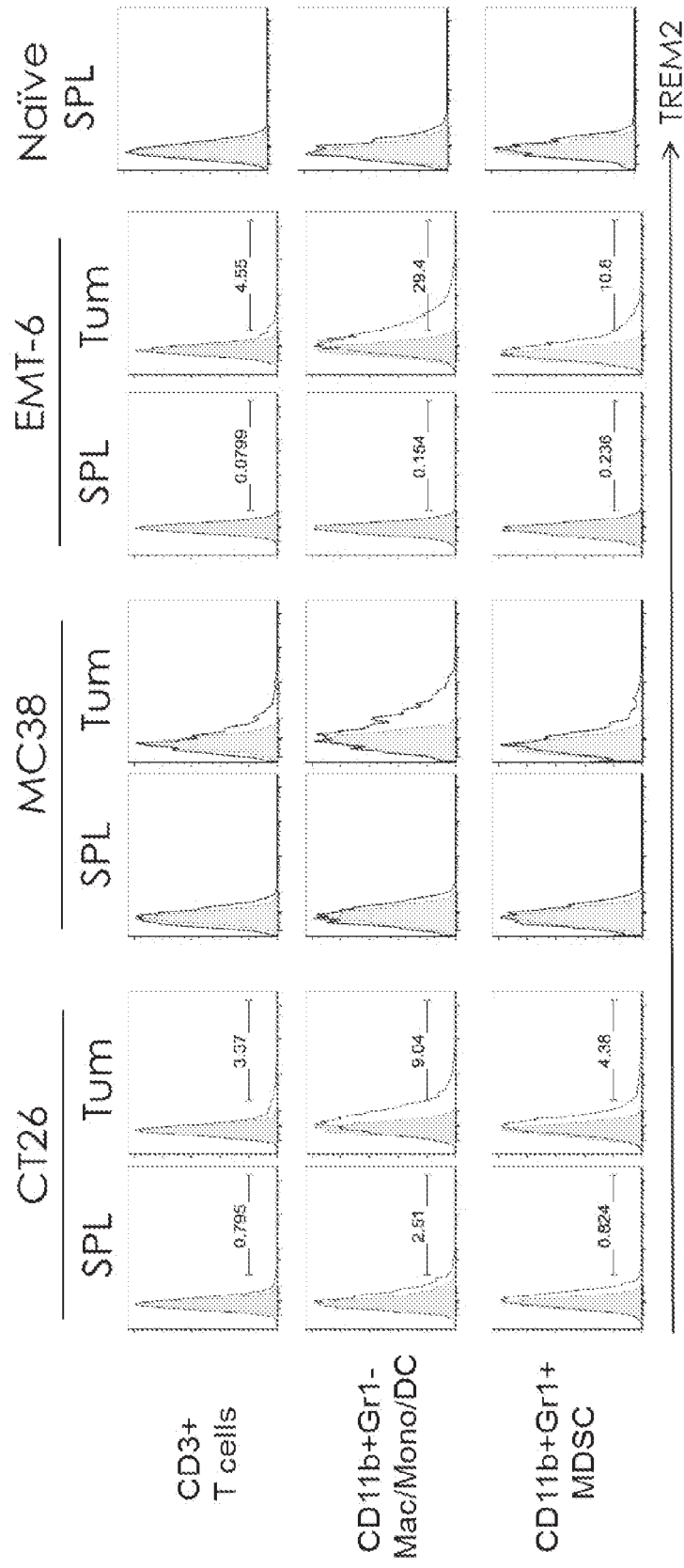


FIG. 18

FIG. 19A

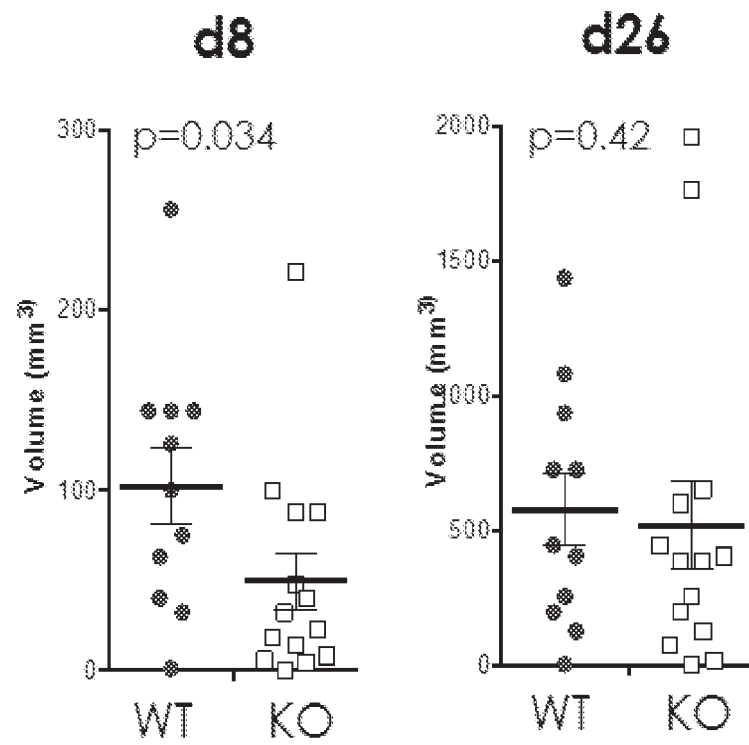
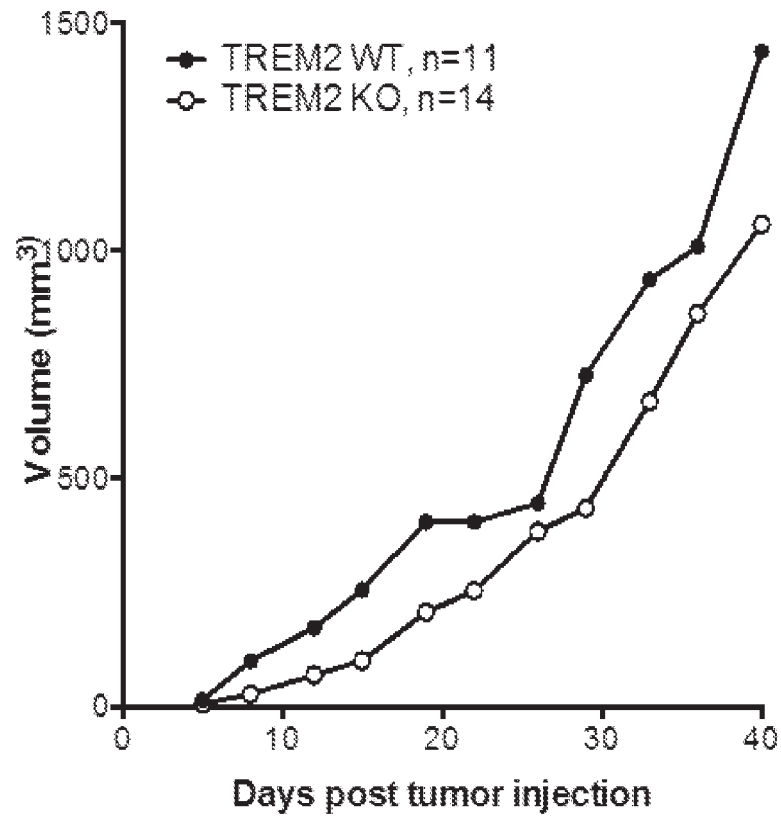


FIG. 19B



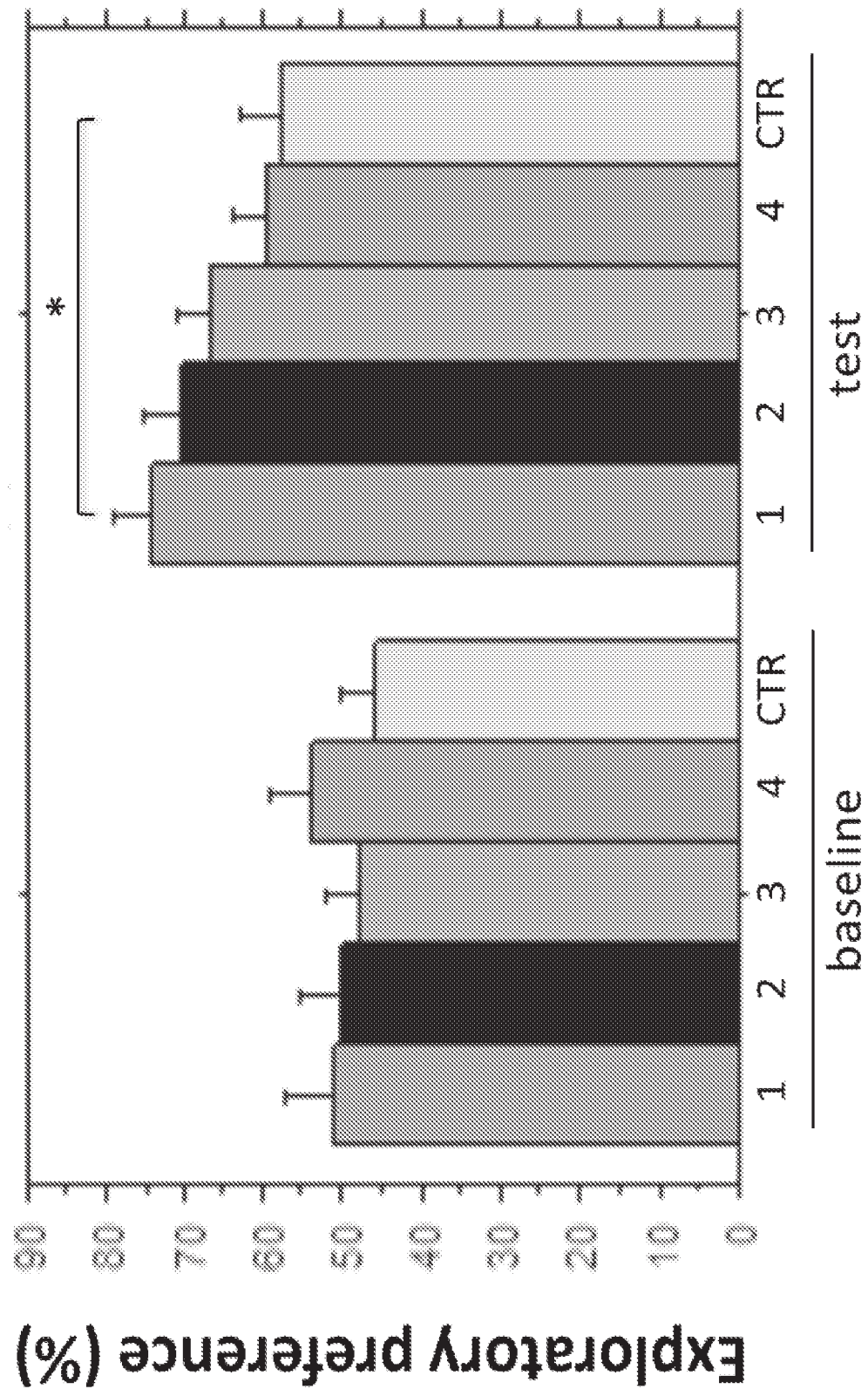


FIG. 20

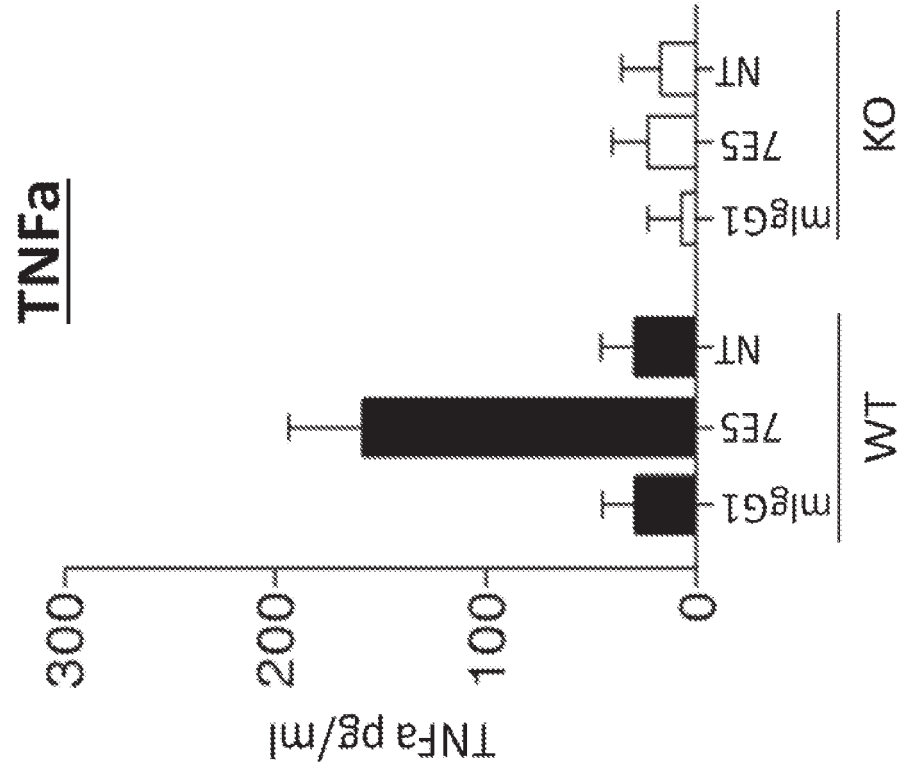


FIG. 21A

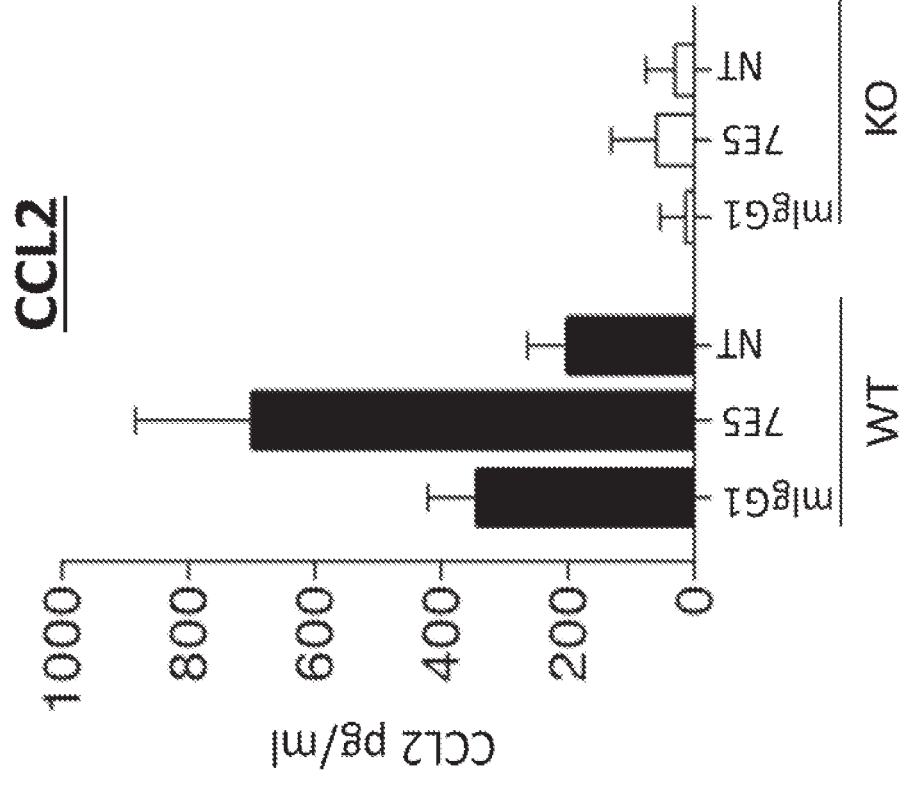


FIG. 21B

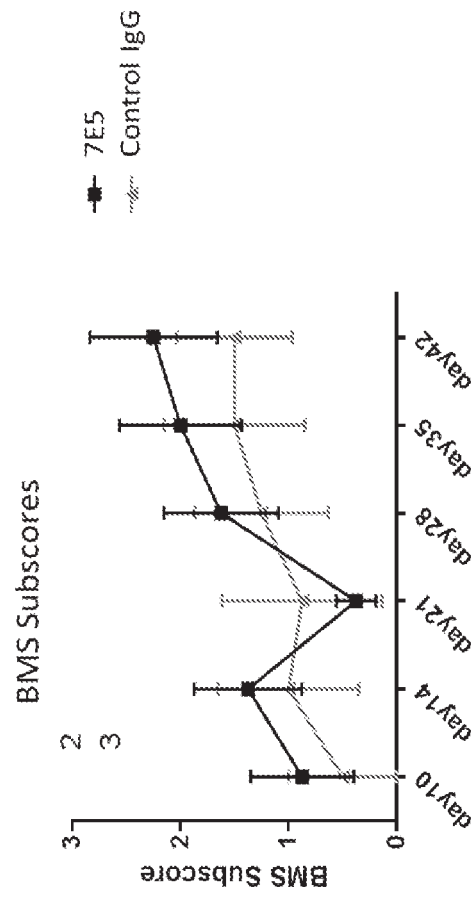


FIG. 22B

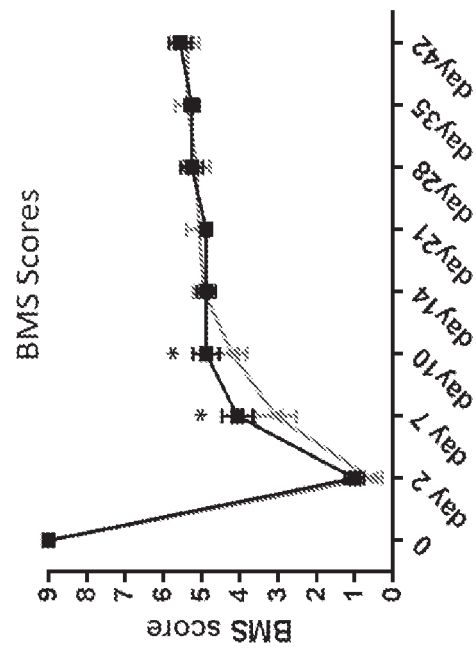


FIG. 22A

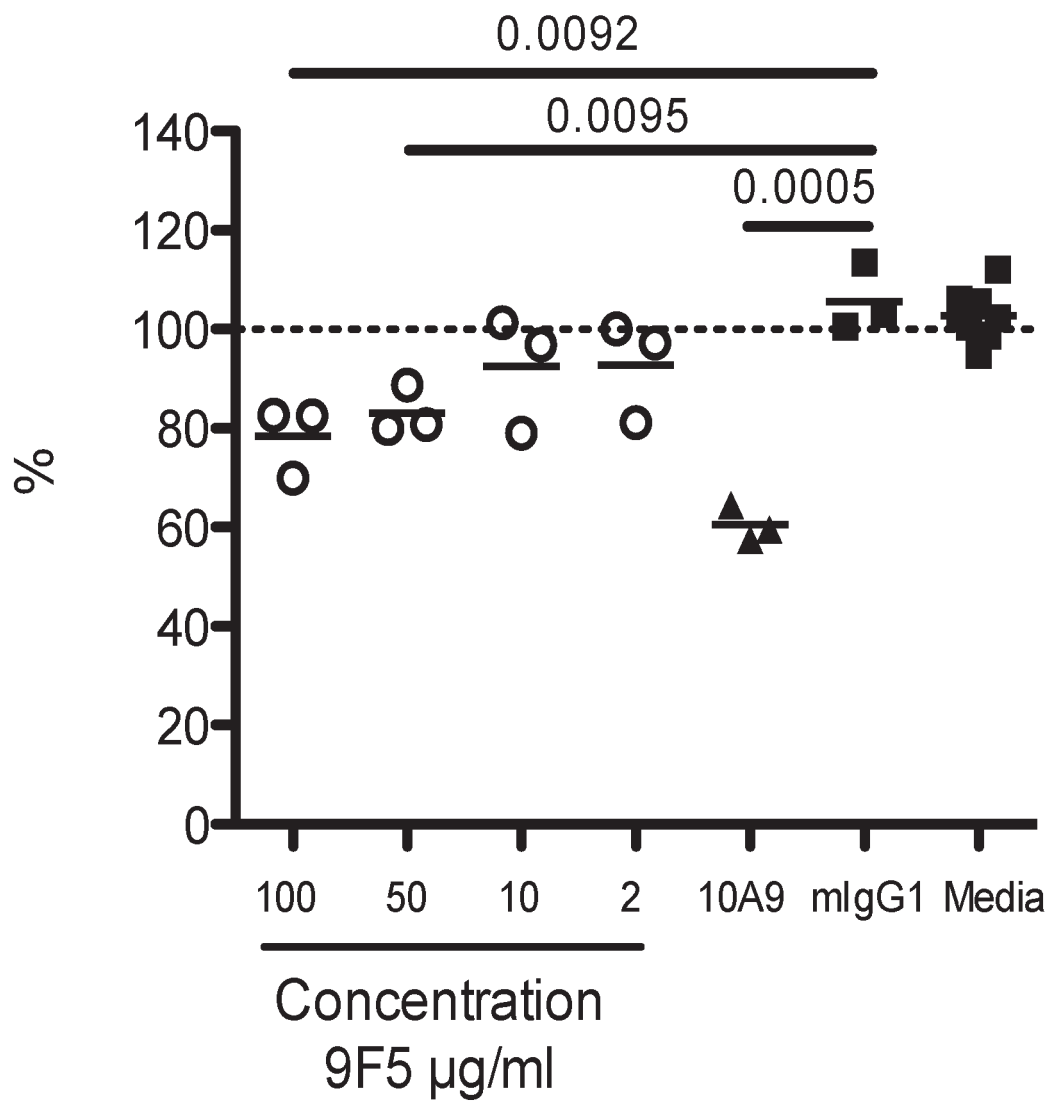


FIG. 23

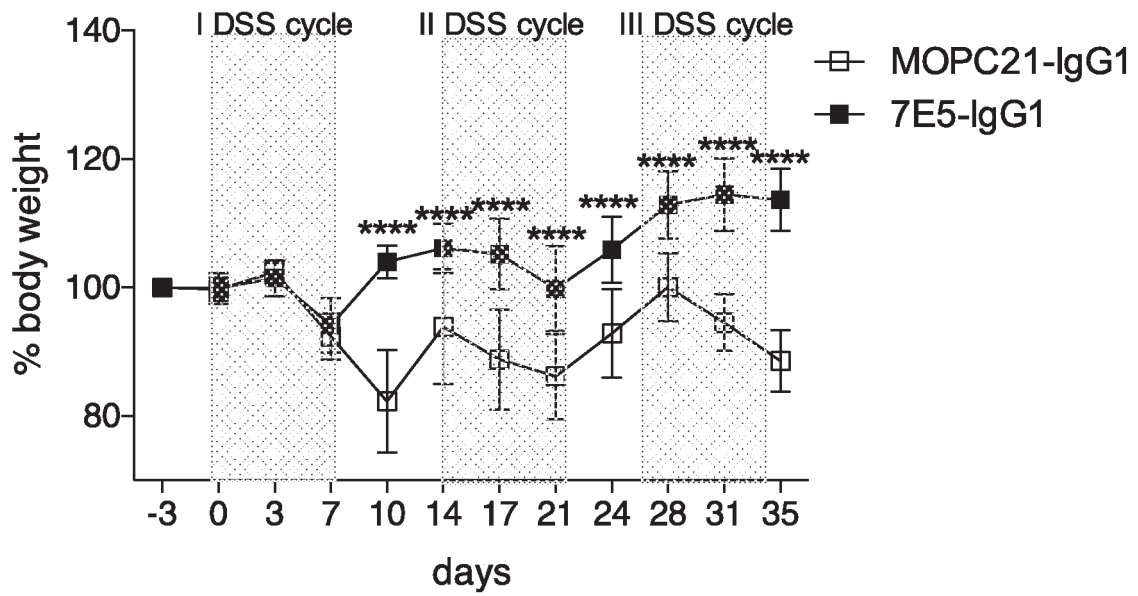


FIG. 24A

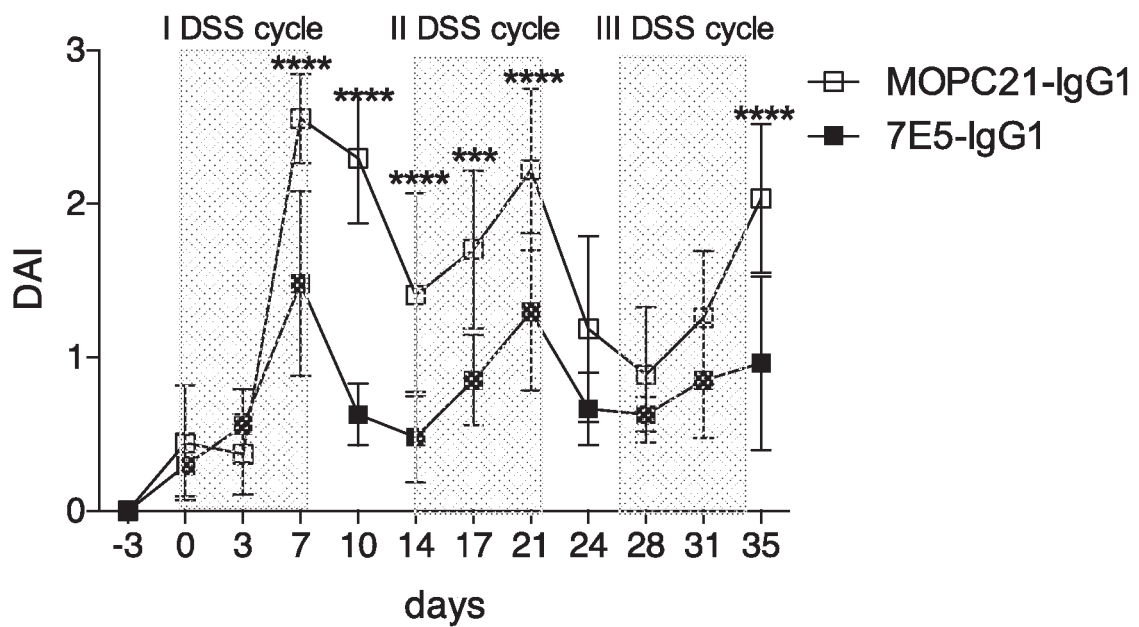


FIG. 24B



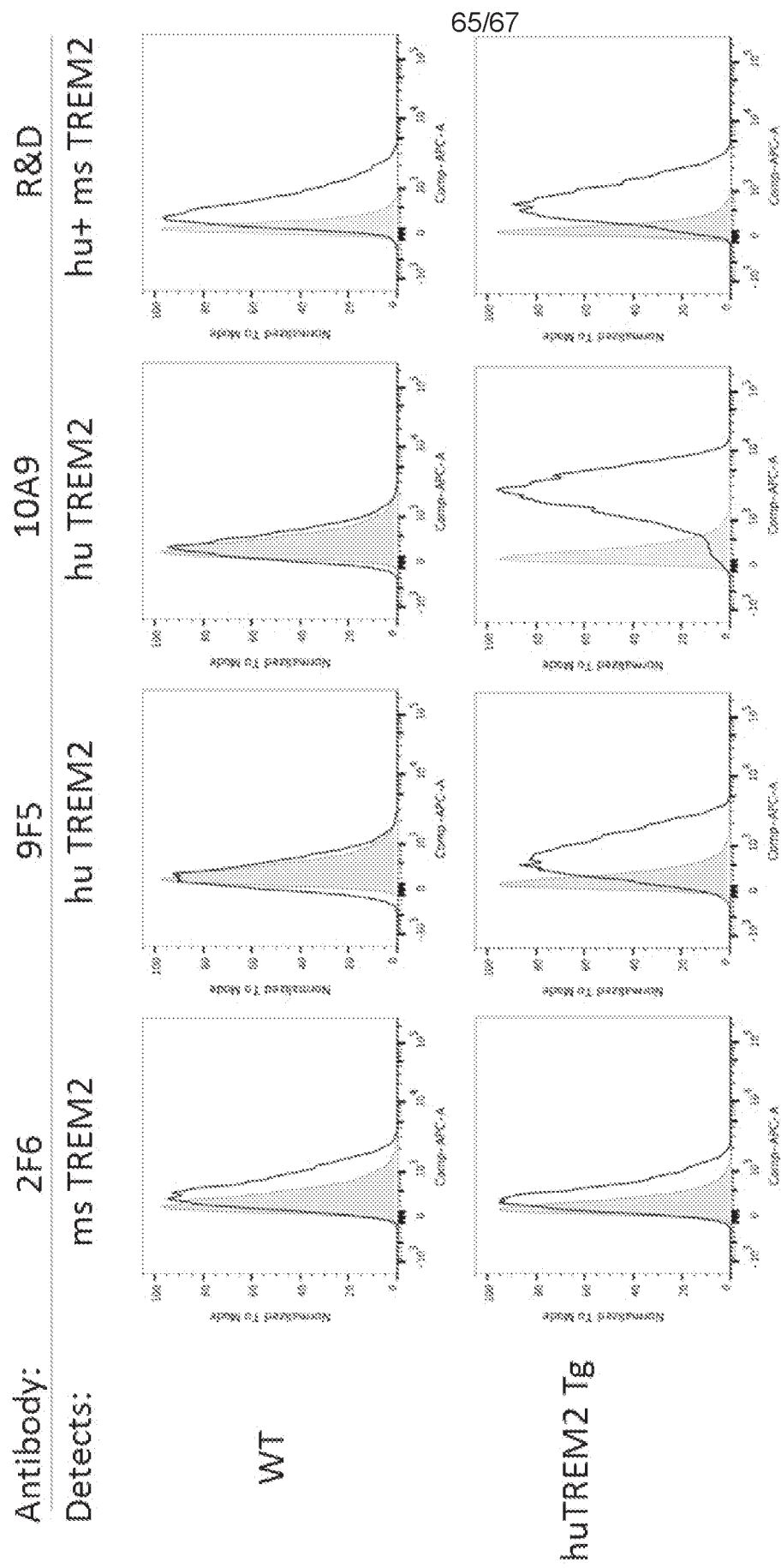


FIG. 25A

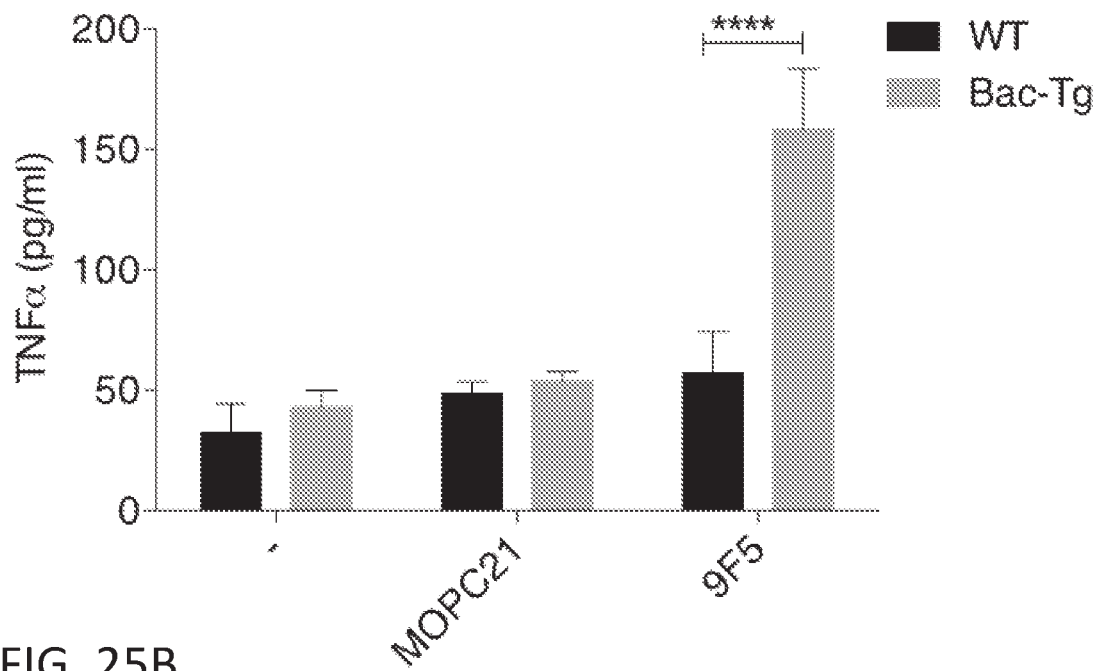
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FIG. 25B

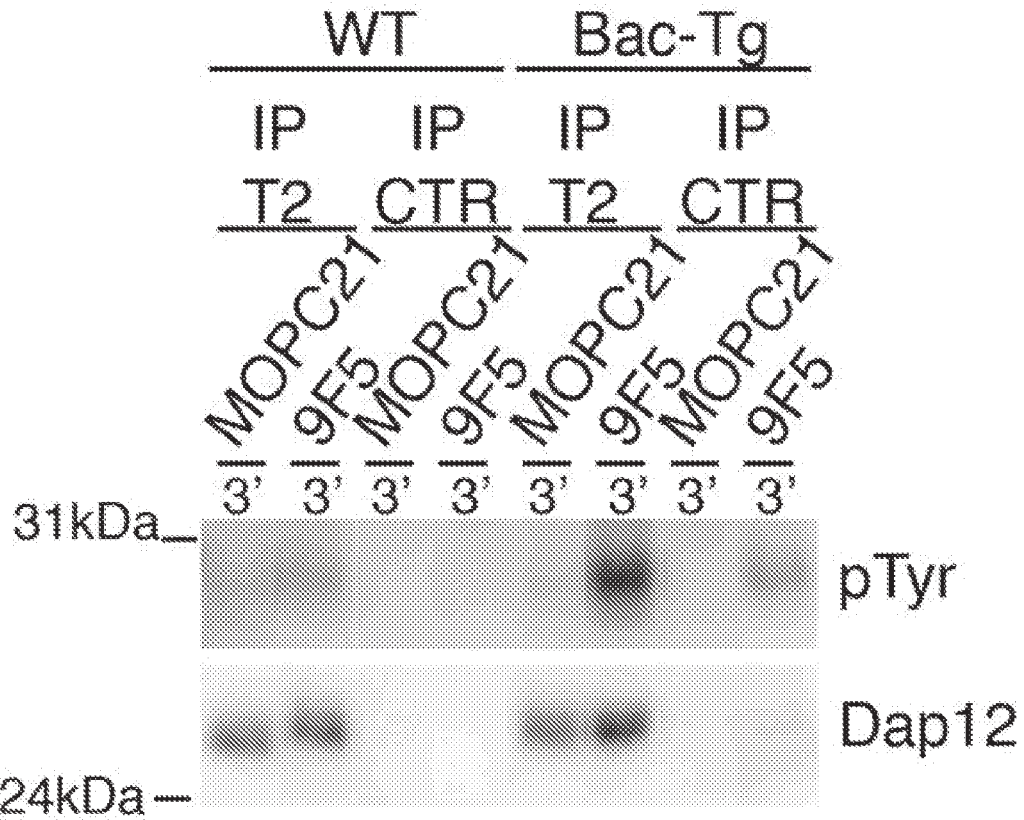


FIG. 25C

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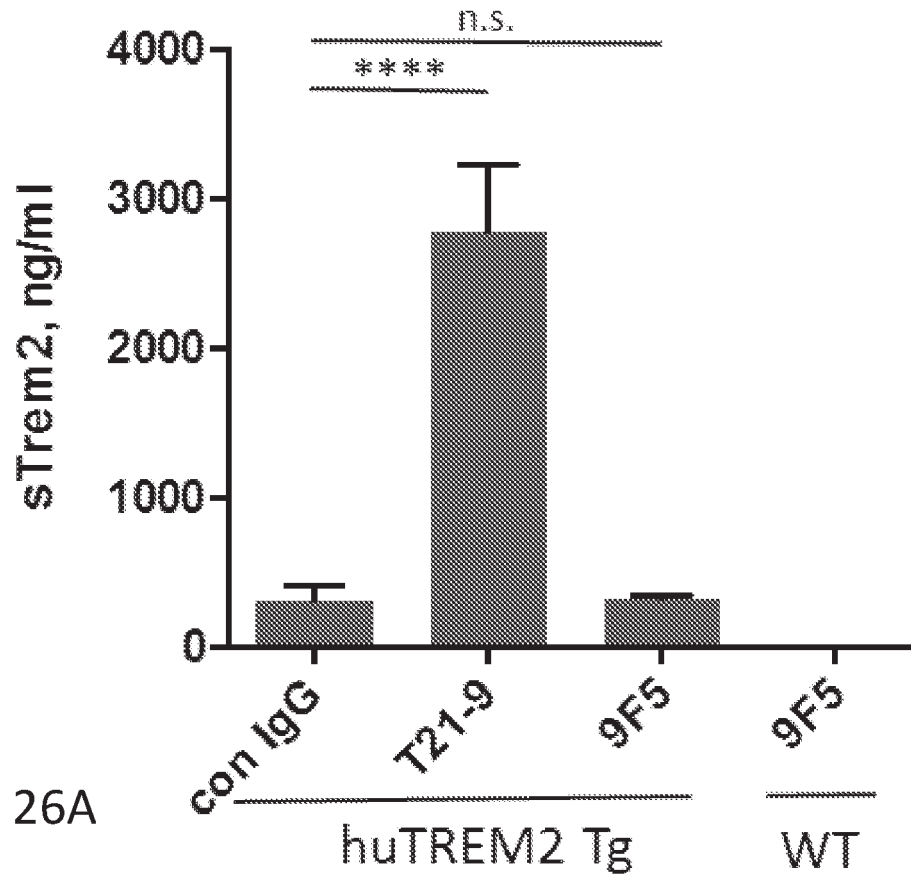


FIG. 26A

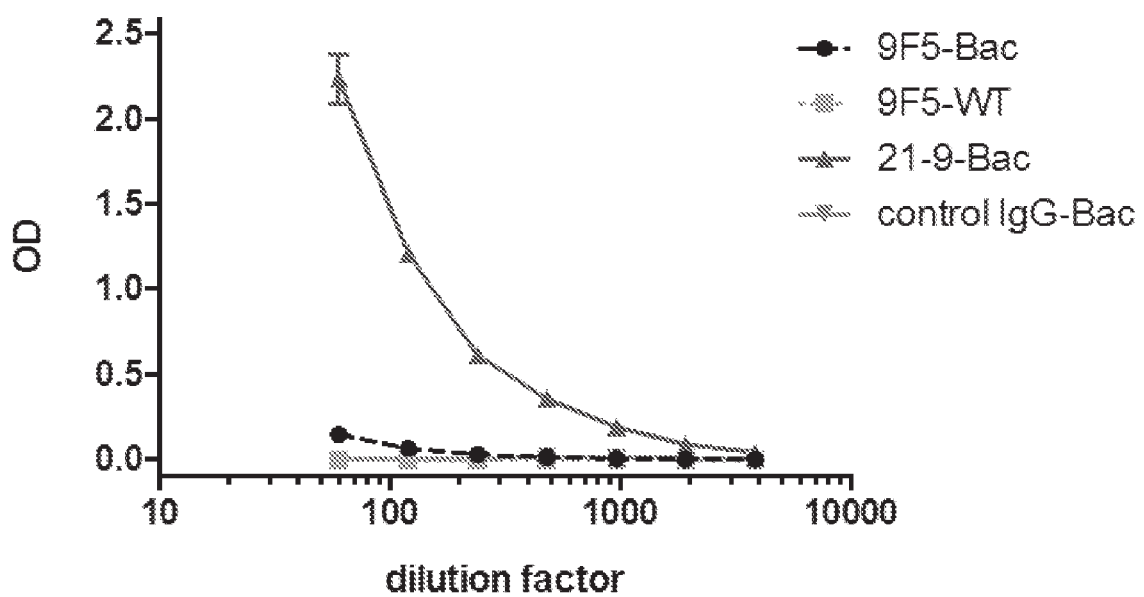


FIG. 26B