

FIG. 1**Human PVRIG WT Full length**

Human PVRIG sequence starting from position 21 - alternative methionine

MGHRTLVPWVLLTLCVTAGTPEVWVQVRMEATELSSFTIRCGFLGSGSISLVTVSWG
GPNGAGGTTLAVLHPERGIRQWAPARQARWETQSSISLILEGSGASSPCANTTFCCKFASF
PEGSWEACGSLPPSSDPGLSAPPTPAPILRADLAGILGV
SGVLLFGCVYLLHLLRRHKHRPAPRLQPSRTSPQAPRARAWAPSQA

(SEQ ID NO: 1)

Human PVRIG sequence starting from position 1 methionine

MRTEAQVPALQPPEPGLEGAMGHRTLVPWVLLTLCVTAGTPEVWVQVRMEATELSSFTIRCGFLGSGSISLVTVSWG
GPNGAGGTTLAVLHPERGIRQWAPARQARWETQSSISLILEGSGASSPCANTTFCCKFASF
PEGSWEACGSLPPSSDPGLSAPPTPAPILRADLAGILGVSGVLLFGCVYLLHLLRRHKHRPAPRLQPSRTSPQAPRARAWAPSQA

(SEQ ID NO:2)

FIG. 2

Human PVLR2 alpha isoform

>gi|5360210|ref|NP_002847.1| nectin-2 isoform alpha precursor [Homo sapiens]

MARAAALLPSRSPTPLLWPLLLLLLLETTGAQDVRVQVLPEVRGQLGGTVELPCHLLPPVPGLYISLVTW
QRPDAPANHQNVAAAFHPKMGFSFSPKPGSERLSFVSAKQSTGQDTEAELQDATLALHGLTVEDEGNYTC
EFATFPKGSVRGMTWLRVIAKPKNQAEAQKVTFSQDPTTVALCISKEGRPPARISWLSSLDWEAKETQVS
GTLAGTVTVTSRFTLVPSGRADGVTVTCKVEHESFEEPALIPVTLSVRYPPPEVSISGYDDNWYLGRTDAT
LSCDVRSNPEPTGYDWSTTSGETFPTS AVAQGSQ LVIHAVDSL FNTTFVCTVTNAVGMGRAEQVIFVRETP
RASPRDVGPLVWGAVGGTLLVLLLLAGGSLAFILLRVRRRRKSPGGAGGGASGDGGFYDPKAQVLGNGDP
VFWTFVVPGPMEPDGKDEEEEEEEKAEKGLMLPPPPALED DMESQLDGSLISRRAVYV

(SEQ ID NO:3)

Human PVLR2 delta isoform

>gi|112789532|ref|NP_001036189.1| nectin-2 isoform delta precursor [Homo sapiens]

MARAAALLPSRSPTPLLWPLLLLLLLETTGAQDVRVQVLPEVRGQLGGTVELPCHLLPPVPGLYISLVTW
QRPDAPANHQNVAAAFHPKMGFSFSPKPGSERLSFVSAKQSTGQDTEAELQDATLALHGLTVEDEGNYTC
EFATFPKGSVRGMTWLRVIAKPKNQAEAQKVTFSQDPTTVALCISKEGRPPARISWLSSLDWEAKETQVS
GTLAGTVTVTSRFTLVPSGRADGVTVTCKVEHESFEEPALIPVTLSVRYPPPEVSISGYDDNWYLGRTDAT
LSCDVRSNPEPTGYDWSTTSGETFPTS AVAQGSQ LVIHAVDSL FNTTFVCTVTNAVGMGRAEQVIFVRETP
NTAGAGATGGIIGGIIAALIATAVAATGILICRQQRKEQTLQGAEEDEDLEGPPSYKPPTPKAKLEAQEM
PSQLFTLGASEHSPLKTPYFDAGASCTEQEMPRYHELPTLEERSGPLHPGATSLGSPIPVPPGPPAVEDV
SLDLEDEEGEEEEYYLDKINPIYDALSY

(SEQ ID NO:4)

Figure 3A

CHA.7.518.1.H4(S241P)

What	sequence	SEQ ID NO:
Variable heavy (vh) domain	QVQLVQSGAEVKKPGASVKVCKASGYTFDYNINWVRQAPGGQGLEWMGYIYPYIGGSGYAKFKQGRVTMTTRDTSTSTVYME LSSLRSEDTAVYYCAREDKTARNAMDYWGQGTLVTVSS	5
vhCDR1	GYTFDYN	6
vhCDR2	IYPYIGGS	7
vhCDR3	AREDKTARNAMDY	8
Full length HC	QVQLVQSGAEVKKPGASVKVCKASGYTFDYNINWVRQAPGGQGLEWMGYIYPYIGGSGYAKFKQGRVTMTTRDTSTSTVYME LSSLRSEDTAVYYCAREDKTARNAMDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPTVSWNSGALT SGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTITTCNVDHKPSNTKVDKRVESKYGPPCP?CPAPEFLGGPSVFLPPKPKDTLMISR TPEVTCVVDVDSQEDPEVQFNWVVDGVEVHNAKTPREEQFNSTYRVVSVLTV/HQDWLNGKEYCKVSNKGLPSSIEKTIKSA KGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVF SCSVMEALHNHYTQKSLSLSPGK	9
Variable light (vl) domain	DIQMTQSPSSLSASVGDRVTITCRVSENIYSNLAWYQQKPGKAPKLLIYEATNLAEGVPSRFSGSGSGTDFTLTISLQPEDFATYYC QHFWGTPYTFGGGTKLEIK	10
viCDR1	ENIYSN	11
viCDR2	EAT	12
viCDR3	QHFWGTPYT	13
Full length light chain	DIQMTQSPSSLSASVGDRVTITCRVSENIYSNLAWYQQKPGKAPKLLIYEATNLAEGVPSRFSGSGSGTDFTLTISLQPEDFATYYC QHFWGTPYTFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTY SLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	14

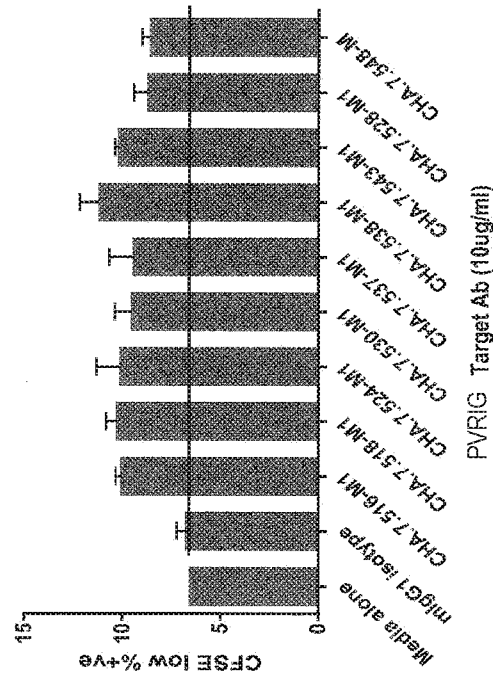
Figure 3B

CHA.7.538.1.2.H4(S241P)

What	sequence	SEQ ID NO:
Variable heavy (vh) domain	QVQLVQSGAEVKKPGASVKVCKASGYAFTNLYIEWVRQAPGGQGLEWIGVINPGSGGIYAAQKFQGRVTMTADTSTVYME LSSLRSEDTAVVYCARSETHDTWFAYWGQGTLLTVVSS	15
vhCDR1	GYAFTNLY	16
vhCDR2	INPGSGGI	17
vhCDR3	ARSETHDTWFAY	18
Full length HC	QVQLVQSGAEVKKPGASVKVCKASGYAFTNLYIEWVRQAPGGQGLEWIGVINPGSGGIYAAQKFQGRVTMTADTSTVYME LSSLRSEDTAVVYCARSETHDTWFAYWGQGTLLTVVSSASTKGPSVFFLA PCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLSSVTVPSSSLGKTITTCNVVDHKPSNTKVDKRVESKYGPCCP?CPAPEFLGGPSVFLFPPKPKDTLMISR TPEVTCVVDVSDQEDPEVQFNWVVDGVEVHNAKTKPREEQFNSTYRVSVLTVLHQDWLNGKEYCKVSNKGLPSSIEKTISKA KGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNV FSCVMHEALHNHYTQKSLSLSPGK	19
Variable light (vl) domain	DIQMTQSPSSLSASVGDRVTITCKASQSVRIAVAWFQQKPGKAPKALIVLASTRHTGVPSTRFSGSGGTDFLTITSSVQPEDFATY YCLQHWNYPYTFGGQGTKLEIK	20
viCDR1	QSVRIA	21
viCDR2	LAS	22
viCDR3	LQHWNYPYT	23
Full length light chain	DIQMTQSPSSLSASVGDRVTITCKASQSVRIAVAWFQQKPGKAPKALIVLASTRHTGVPSTRFSGSGGTDFLTITSSVQPEDFATY YCLQHWNYPYTFGGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKD STYLSSTLTLSKADYEEKHKVYACEVTHQGLSPVTKSFNRGEC	24

FIG. 4A

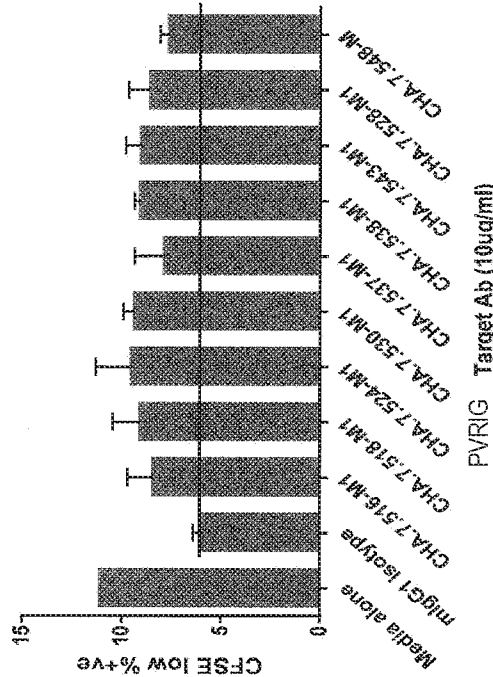
Donor134_CFSElo %positive



PVRIG Target Ab (10ug/ml)

FIG. 4B

Donor136_CFSElo %positive



PVRIG Target Ab (10ug/ml)

FIG. 5A

Antibody (mgG)	EC ₅₀ (HEK OE, nM)	HEK OE/par (3.3ug/ml, gMFir)	Jurkat (3.3ug/ml, gMFir)
CHA.7.502	40.18	71.99	6.21
CHA.7.503	1.05	260.98	23.59
CHA.7.506	No binding	0.76	No binding
CHA.7.508	3.30	45.86	6.50
CHA.7.510	92.81	16.32	4.19
CHA.7.512	52.99	5.12	1.47
CHA.7.514	5.31	49.82	7.67
CHA.7.516	0.79	37.90	5.73
CHA.7.518	0.36	42.24	6.58
CHA.7.520	No binding	1.01	No binding
CHA.7.522	91.44	10.12	2.99
CHA.7.524	0.46	48.33	7.87
CHA.7.525	3.05	41.86	4.30
CHA.7.526	2.99	47.28	3.98
CHA.7.527	No binding	0.98	No binding
CHA.7.528	7.31	44.88	6.17
CHA.7.530	0.33	51.14	8.04
CHA.7.534	1.87	43.72	5.05
CHA.7.535	3.67	40.44	2.79
CHA.7.537	2.47	36.61	5.53

FIG. 5B

CHA.7.538	0.52	35.80	7.37
CHA.7.543	0.52	49.81	6.73
CHA.7.544	0.76	42.60	5.68
CHA.7.545	0.76	44.31	6.53
CHA.7.546	0.61	43.14	6.42
CHA.7.547	14.37	10.94	1.02
CHA.7.548	0.27	45.26	7.37
CHA.7.549	2.60	29.71	2.23
CHA.7.550	1.34	27.72	2.10

FIG. 6A

Antibody (mIgG)	Human CD56 int. NK (gMFIr, 10ug/ml)	Human CD8+ T cells (gMFIr, 10ug/ml)	Expi cyno OE/par (gMFIr, 3.3ug/ml)	Cyno NK cells (gMFIr, 10ug/ml)	Cyno CD8+ T cells (gMFIr, 10ug/ml)
CHA.7.502	1.97	1.41	60.49	Not tested	Not tested
CHA.7.503	3.15	1.96	106.3	Not tested	Not tested
CHA.7.506	Not tested	Not tested	0.77	Not tested	Not tested
CHA.7.508	3.6	4.09	41.49	Not tested	Not tested
CHA.7.510	3.13	2.73	38.21	Not tested	Not tested
CHA.7.512	1.30	1.15	8.96	Not tested	Not tested
CHA.7.514	4.16	5.15	65.20	Not tested	Not tested
CHA.7.516	4.22	4.09	60.05	1.76	2.09
CHA.7.518	5.08	6.69	83.51	1.92	2.09
CHA.7.520	1.13	1.04	Not tested	Not tested	Not tested
CHA.7.522	2.06	1.90	27.24	Not tested	Not tested

FIG. 6B

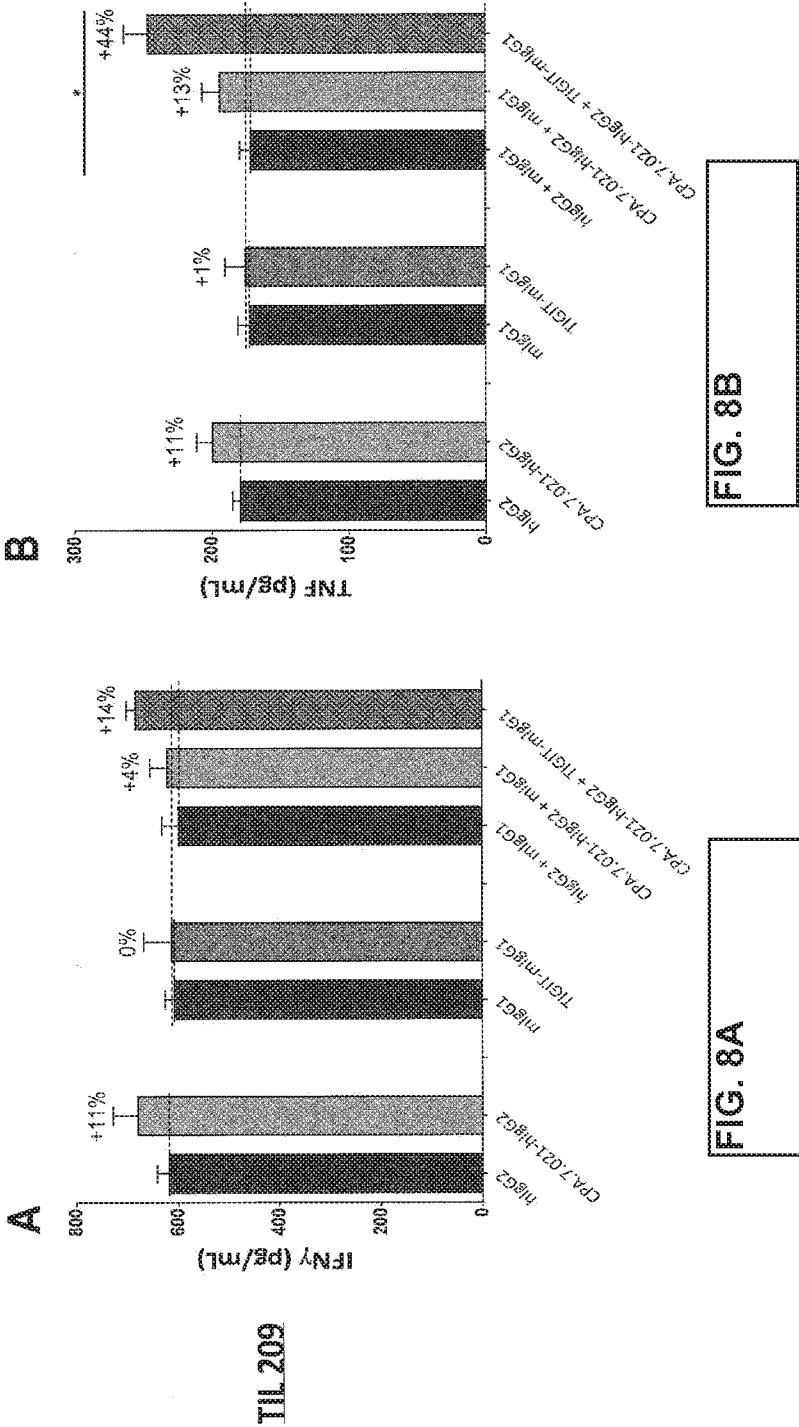
CHA.7.524	5.50	6.12	66.32	1.78	2.02
CHA.7.525	1.98	1.76	0.85	Not tested	Not tested
CHA.7.526	2.08	1.71	0.79	Not tested	Not tested
CHA.7.527	1.16	0.99	Not tested	Not tested	Not tested
CHA.7.528	3.08	3.63	12.2	1.21	1.18
CHA.7.530	6.04	6.47	60.80	1.73	1.89
CHA.7.534	2.60	1.96	46.27	Not tested	Not tested
CHA.7.535	2.24	1.28	0.82	Not tested	Not tested
CHA.7.537	3.90	3.41	1.55	1.18	1.19
CHA.7.538	6.49	6.17	15.16	1.36	1.45
CHA.7.543	4.48	4.33	0.83	1.35	1.39
CHA.7.544	2.36	2.54	61.09	Not tested	Not tested
CHA.7.545	2.54	2.82	0.91	Not tested	Not tested
CHA.7.546	2.75	2.95	0.85	Not tested	Not tested
CHA.7.547	2.21	1.13	26.65	Not tested	Not tested
CHA.7.548	3.15	3.35	4.25	1.18	1.09
CHA.7.549	3.05	1.42	1.00	Not tested	Not tested
CHA.7.550	1.60	1.29	0.90	Not tested	Not tested

FIG. 7A

Antibody (mIgG)	IC ₅₀ (nM)
CHA.7.502	39.90
CHA.7.503	No IC ₅₀
CHA.7.506	31.65
CHA.7.508	37.88
CHA.7.510	55.00
CHA.7.512	839.6
CHA.7.514	38.88
CHA.7.516	33.11
CHA.7.518	23.15
CHA.7.520	619.3
CHA.7.522	50.48
CHA.7.524	30.20
CHA.7.525	85.52
CHA.7.526	58.88
CHA.7.527	No IC ₅₀
CHA.7.528	28.88
CHA.7.530	34.56
CHA.7.534	181.4
CHA.7.535	821.1
CHA.7.537	38.95
CHA.7.538	51.87
CHA.7.543	No IC ₅₀

FIG. 7B

CHA.7.544	No IC ₅₀
CHA.7.545	96.06
CHA.7.546	92.05
CHA.7.547	27.94
CHA.7.548	18.98
CHA.7.549	36.12
CHA.7.550	58.34



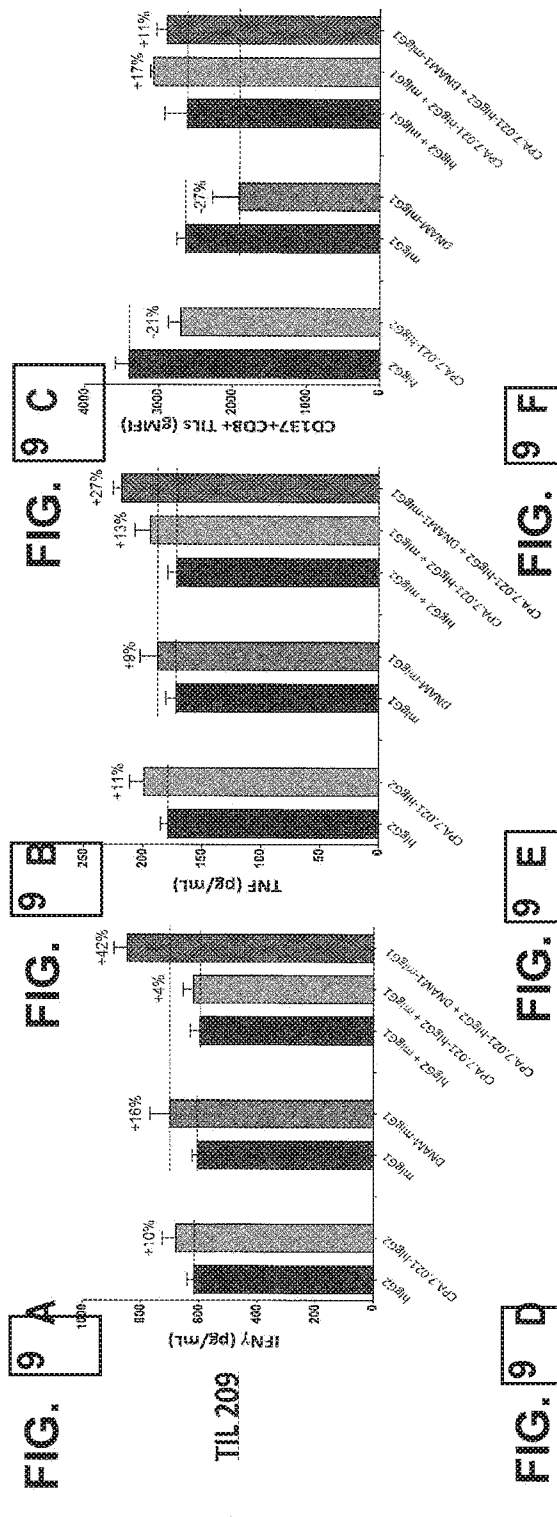
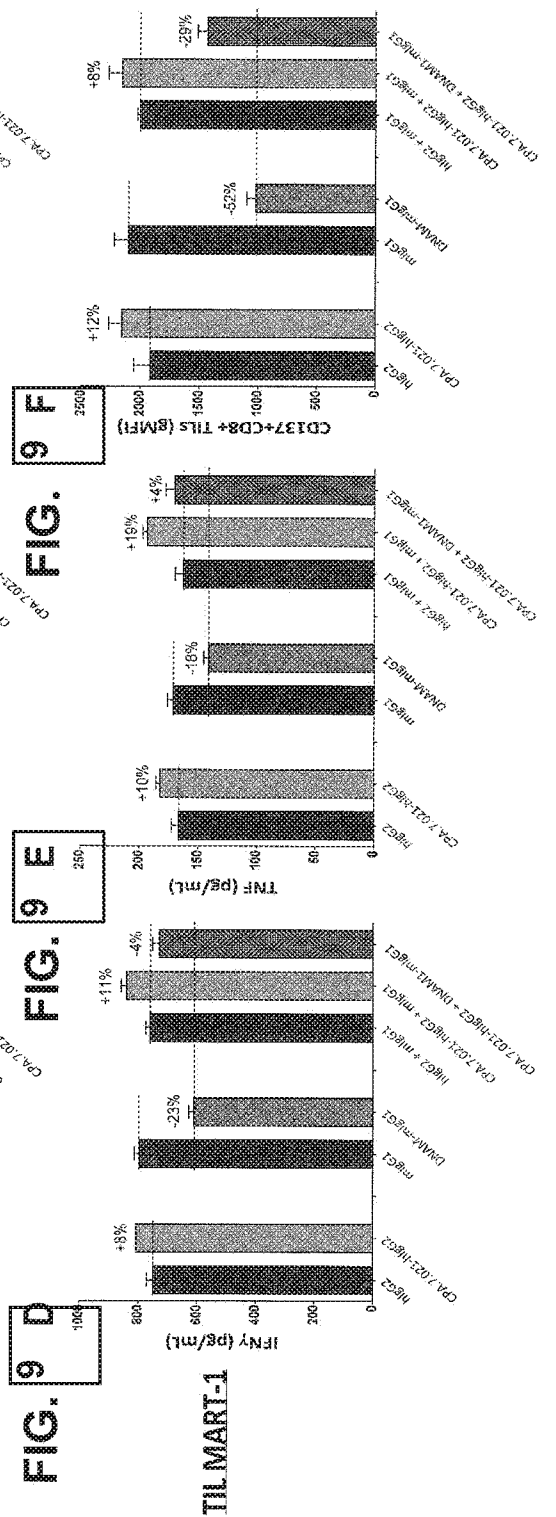


FIG. 10B

B

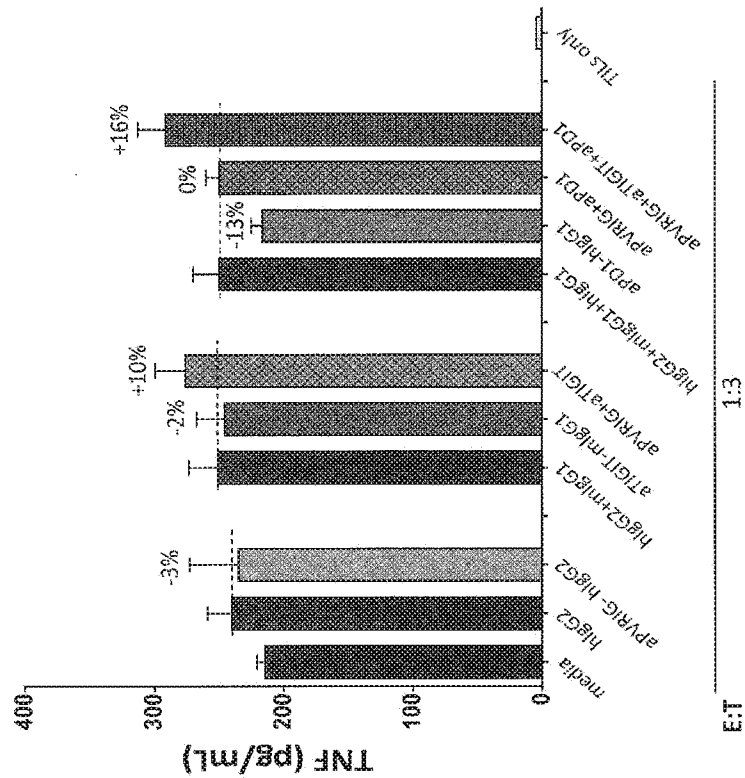


FIG. 10A

A

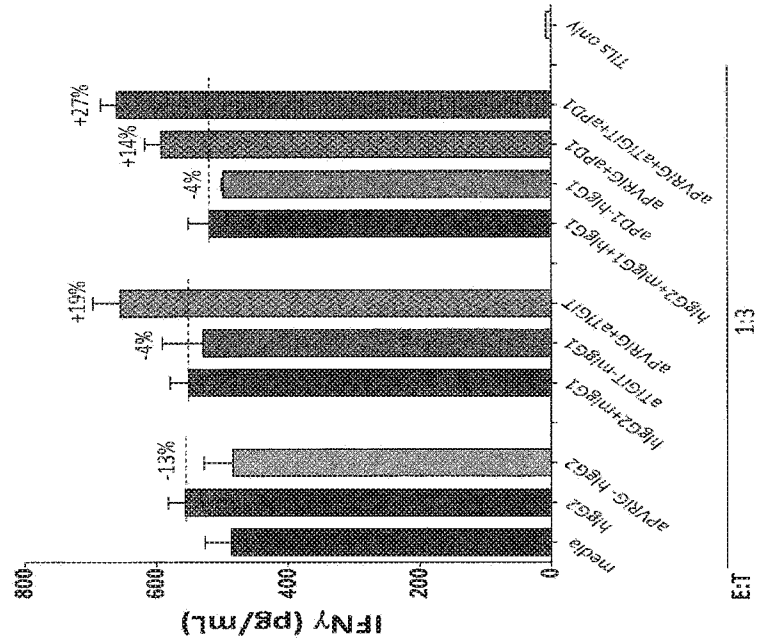


FIG. 11A

Humanized sequences of CHA.7.518 antibody VH

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

IGHV1-46*01 QVQLVQSGAEVKKPGASVKVSCKASGYFTFTSYMHVVRQAPGQGLEWMGIINPSGGSTSYAQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR
(SEQ ID NO: 25)

Joining region IMGT J00256|IGHJ4*01|YFDYWGQGTILTVSS (SEQ ID NO: 26)

seq	10	20	30	40	50	60	70	80	90
AbM	10	20	30	40	50	60	70	80	90
	b b b	p p b b	b b b	b i i	i i b b	b i b	b b b z	b b b	b b b b b
518	EVQLQQSGPELVKPGASVKISCKAS	GYTFTDYNIN	WVRQSHGKSLEWIG	YIYPYIGGSG	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR
	* * *	* * *	* * *	* * *	* * *	* * *	* * *	* * *	* * *
1-46*01	QVQLVQSGAEVKKPGASVKVSCKAS	GYTFTSYMH	WVRQAPGQGLEWMG	IINPSGGST	YAKQFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YAKQFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YAKQFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YAKQFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YAKQFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR
h518H1	QVQLVQSGAEVKKPGASVKVSCKAS	GYTFTDYNIN	WVRQAPGQGLEWMG	YIYPYIGGSG	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR
h518H2	QVQLVQSGAEVKKPGASVKVSCKAS	GYTFTDYNIN	WVRQAPGQGLEWMG	YIYPYIGGSG	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR
h518H3	QVQLVQSGAEVKKPGASVKISCKAS	GYTFTDYNIN	WVRQAPGQGLEWMG	YIYPYIGGSG	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR
h518H4	QVQLVQSGAEVKKPGASVKISCKAS	GYTFTDYNIN	WVRQAPGQGLEWMG	YIYPYIGGSG	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR	YNQKFQGRVTMTTRDTSTSTVYNMELSSLRSEDTAVYYCAR

seq	100	110	120
AbM	100	110	120
	i b b b	i b b b	i b b b
518	EDKTARNAMDY	WGQGTILTVSS	(SEQ ID NO: 27)
	*	*	(1-46*01 disclosed as SEQ ID NO: 28)
h518H1	EDKTARNAMDY	WGQGTILTVSS	(SEQ ID NO: 29)
h518H2	EDKTARNAMDY	WGQGTILTVSS	(SEQ ID NO: 30)
h518H3	EDKTARNAMDY	WGQGTILTVSS	(SEQ ID NO: 31)
h518H4	EDKTARNAMDY	WGQGTILTVSS	(SEQ ID NO: 32)

deamidation substitutions: Q/S/A

FIG. 11B

Humanized sequences of CHA.7.518 antibody VL

Potential humanized sequence based on IMGT IGKV1-39*01 acceptor framework

IGKV1-39*01
DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQGVPSRFSGSGTDFTLTISLQPEDFATYVQQSYSTPP (SEQ ID NO: 33)

Joining region IMGT J00242|IGKJ2*01|YTFGQGTKLEIK (SEQ ID NO: 34)

seq	10	20	30	40	50	60	70	80
AbM	10	20	30	40	50	60	70	80
518	b b b	p p p	b b b	b i b i	i i i b b i	i b b	b b b	b b b
	DIQMTQSPASLSVSGEVTIIC	RVSENIYSNLA	WYQQKQKSPQLLVY	EATNLAE	GVPSRFSGSGTDFTLTISLQPEDFATYV	QSYSTPP		
	*	*	*	*	*	*	*	*
IGKV1-39	DIQMTQSPSSLSASVGDRVTITC	RASQSISSYL	WYQQKPGKAPKLLIY	AASSLQ	GVPSRFSGSGTDFTLTISLQPEDFATYV	QSYSTPP		
h518L1	DIQMTQSPSSLSASVGDRVTITC	RVSENIYSNLA	WYQQKPGKAPKLLIY	EATNLAE	GVPSRFSGSGTDFTLTISLQPEDFATYV	QSYSTPP		
h518L2	DIQMTQSPSSLSASVGDRVTITC	RVSENIYSNLA	WYQQKPGKAPKLLIY	EATNLAE	GVPSRFSGSGTDFTLTISLQPEDFATYV	QSYSTPP		
h518L3	DIQMTQSPSSLSASVGDRVTITC	RVSENIYSNLA	WYQQKPGKAPKLLIY	EATNLAE	GVPSRFSGSGTDFTLTISLQPEDFATYV	QSYSTPP		

seq	90	100
AbM	90	100
518	i b i i b i	b b b
	QHFWGTPYT	FCGCTKLEIK
	*	
IGKV1-39	QQSYSTPP	(SEQ ID NO: 36)
h518L1	QHFWGTPYT	FCGCTKLEIK (SEQ ID NO: 37)
h518L2	QHFWGTPYT	FCGCTKLEIK (SEQ ID NO: 38)
h518L3	QHFWGTPYT	FCGCTKLEIK (SEQ ID NO: 39)

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

FIG. 11D

humanized sequences of CHA.7.538_1 antibody VL

Potential humanized sequence based on IMGT IGKV1-39*01 acceptor framework

IGKV1-39*01

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFGSGSGTDFTLTISSIQPEDFATYYCQQSYSTPP (SEQ ID NO: 48)

Joining region IMGT J00242|IGKJ2*01|YTFGQGTKLEIK (SEQ ID NO: 49)

IGKV1-17*02

DIQMTQSPSSLSASVGDRVTITCRASQGIKNDLGNWYQQKPGKAPKRLIYAASSLQSGVPSRFGSGSGTFTLTISNLQPEDFATYYCLQHNSYPP (SEQ ID NO: 50)

seq	10	20	30	40	50	60	70	80
AbM	10	20	30	40	50	60	70	80
538	b b b	p p p	b b b	b i b i	i i i b b i	i b b	b b b	b b b
	DIQMTQSPSSLSASVGDRVTITC	KASQSVRIAVA	WFQQKPGQSPKALII	LASTRHT	GVPSRFGSGSGTDFTLTI	SNVQSEDLADYFC	***	***
	*	****	*	*	*	*	*	*
IGKV1-39	DIQMTQSPSSLSASVGDRVTITC	RASQSISSYLN	WYQQKPGKAPKLLIY	AASSLQ	GVPSRFGSGSGTDFTLTI	SSIQPEDFATYYC		
h538L1	DIQMTQSPSSLSASVGDRVTITC	KASQSVRIAVA	WYQQKPGKAPKLLIY	LASTRHT	GVPSRFGSGSGTDFTLTI	SSIQPEDFATYYC		
h538L2	DIQMTQSPSSLSASVGDRVTITC	KASQSVRIAVA	WYQQKPGKAPKALII	LASTRHT	GVPSRFGSGSGTDFTLTI	SSVQPEDFATYYC		
	I T		S				L	F

seq	90	100
AbM	90	100
538	i b i i b i	b b b
	LQHWNYPTT	FGGGTKLEIK
	*(SEQ ID NO: 51)	
IGKV1-39	QQSYSTPP	(SEQ ID NO: 52)
h538L1	LQHWNYPTT	FGGGTKLEIK
h538L2	LQHWNYPTT	FGGGTKLEIK
	@#	(SEQ ID NO: 54)

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

FIG. 11E

humanized sequences of CHA.7.538_2 antibody VH

Potential humanized sequence based on IMGT IGHV1-46*01 acceptor framework IGHV1-46*01

QVQLVQSGAEVKKPGASVKVSCKASGYTFSTSYMHVVRQAPGQGLEWMGIINPSCGSTSYAQKFQGRVTMTRTDSTSTVYMELSSLRSEDTAVYYCAR (SEQ ID NO: 55)

Joining region

IMGT J00256|IGHJ4*01|YFDYWGQGTILVTVSS (SEQ ID NO: 56)

seq	10	20	30	40	50	60	70	80	90
AbM	10	20	30	40	50	60	70	80	90
	b b b	p p b b b	b b b	b i i	i i b b b	a	i b b b x	b b b	b b b b b
538_2	QVQLVQSGAEVKKPGASVKVSCKAA	GYTFSTNYWIG	WVKQRPCHGLEWIG	DIYPGGGGYTN	YNEKFKGKATLTADTSSSTAYMQLSSLTSEDSAIYYCAS	** * * * *	** * * * *	** * * * *	** * * * *
1-46*01	QVQLVQSGAEVKKPGASVKVSCKAS	GYTFSTNYMH	WVRQAPGQGLEWMG	IINPSCGSTS	YAKFQGRVTMTRTDSTSTVYMELSSLRSEDTAVYYCAR	** * * * *	** * * * *	** * * * *	** * * * *
h5382H1	QVQLVQSGAEVKKPGASVKVSCKAS	GYTFSTNYWIG	WVRQAPGQGLEWMG	DIYPGGGGYTN	YAKFQGRVTMTRTDSTSTVYMELSSLRSEDTAVYYCAR	** * * * *	** * * * *	** * * * *	** * * * *
h5382H2	QVQLVQSGAEVKKPGASVKVSCKAS	GYTFSTNYWIG	WVRQAPGQGLEWIG	DIYPGGGGYTN	YAKFQGRVTMTADTSTSTVYMELSSLRSEDTAVYYCAS	** * * * *	** * * * *	** * * * *	** * * * *
h5382H3	QVQLVQSGAEVKKPGASVKVSCKAS	GYTFSTNYWIG	WVRQAPGQGLEWIG	DIYPGGGGYTN	YAKFQGRATLTADTSTSTAYMELSSLRSEDTAVYYCAS	** * * * *	** * * * *	** * * * *	** * * * *

seq	100	110
AbM	110	
	i b b b	
538_2	PYYGSSYGFAP	WGQGTILVTVSA (SEQ ID NO: 57)
	*	(1-46*01 disclosed as SEQ ID NO: 58)
h5382H1	PYYGSSYGFAP	WGQGTILVTVSS (SEQ ID NO: 59)
h5382H2	PYYGSSYGFAP	WGQGTILVTVSS (SEQ ID NO: 60)
h5382H3	PYYGSSYGFAP	WGQGTILVTVSS (SEQ ID NO: 61)

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

Figure 12A

What	Sequences
humanized CHA.7.518 VH h518HH1	QVQLVQSGAEVKKPGASVKVSCKASGYTFDYNINWVRQAPGQGLEWMGYIYPYIGSGGYAQKFQ GRVTMTRDTSTSTVYMELSSLRSED TA VYYCAREDKTARNAMDYWGQGTLVTVSS (SEQ ID NO:62)
humanized CHA.7.518 VH h518HH2	QVQLVQSGAEVKKPGASVKVSCKASGYTFDYNINWVRQAPGQGLEWIGYIYPYIGSGGYAQKFQ RVTMTADTSTSTVYMELSSLRSED TA VYYCAREDKTARNAMDYWGQGTLVTVSS (SEQ ID NO:63)
humanized CHA.7.518 VH h518HH3	QVQLVQSGAEVKKPGASVKISCKASGYTFDYNINWVRQAPGQGLEWIGYIYPYIGSGGYAQKFQ RATLTADTSTSTAYMELSSLRSED TA VYYCAREDKTARNAMDYWGQGTLVTVSS (SEQ ID NO:64)
humanized CHA.7.518 VH h518HH4	QVQLVQSGAEVKKPGASVKISCKASGYTFDYNINWVRQAPGQGLEWIGYIYPYIGSGGYAQKFQGR ATLTADNSTSTAYMELSSLRSED TA VYYCAREDKTARNAMDYWGQGTLVTVSS (SEQ ID NO:65)
humanized CHA.7.518 VL h518HL1	DIQMTQSPSSLSASVGDRTVTITCRVSENIYSNLAWYQQKPKAPKLLIYEATNLAEGVPSRFSGSGSGT DFTLTISLQPEDFATYYCQHF WG TPYTFGGQGTKLEIK (SEQ ID NO:66)
humanized CHA.7.518 VL h518HL2	DIQMTQSPSSLSASVGDRTVTITCRVSENIYSNLAWYQQKPKAPKLLIYEATNLAEGVPSRFSGSGSGT DYTLTISLQPEDFATYYCQHF WG TPYTFGGQGTKLEIK (SEQ ID NO:67)
humanized CHA.7.518 VL h518HL3	DIQMTQSPSSLSASVGDRTVTITCRVSENIYSNLAWYQQKPKAPKLLVYEATNLAEGVPSRFSGSGSG TDYTLTISLQPEDFGTYVCQHF WG TPYTFGGQGTKLEIK (SEQ ID NO:68)

Figure 12B

What	Sequences
humanized CHA.7.538_1 VH h5381HH1	QVQLVQSGAEVKKPGASVKVSCKASGYAFN ^{YL} IEWVRQAPGQGLEWMGVINP <u>SGGGIYYAQKFQ</u> GRVTMTRDTSTSTVYMELSSLRSEDTAVYYC <u>ARSETHDTWFAYWGQGTILVTVSS</u> (SEQ ID NO:69)
humanized CHA.7.538_1 VH h5381HH2	QVQLVQSGAEVKKPGASVKVSCKASGYAFN ^{YL} IEWVRQAPGQGLEWIGVINP <u>SGGGIYYAQKFQ</u> RVTMTADTSTSTVYMELSSLRSEDTAVYYC <u>ARSETHDTWFAYWGQGTILVTVSS</u> (SEQ ID NO:70)
humanized CHA.7.538_1 VH h5381HH3	QVQLVQSGAEVKKPGASVKVSCKTSGYAFN ^{YL} IEWVRQAPGQGLEWIGVINP <u>SGGGIYYAQKFQ</u> RVTLTADTSTSTAYMELSSLRSEDTAVYYC <u>ARSETHDTWFAYWGQGTILVTVSS</u> (SEQ ID NO:71)
humanized CHA.7.538_1 VH h5381HH4	QVQLVQSGAEVKKPGASVKVSCKTSGYAFN ^{YL} IEWVRQAPGQGLEWIGVINP <u>SGGGIYYAQKFQ</u> RVTLTADKSTSTAYMELSSLRSEDTAVYYC <u>ARSETHDTWFAYWGQGTILVTVSS</u> (SEQ ID NO:72)
humanized CHA.7.538_1/538_2 VL h538HL1	DIQMTQSPSSLSASVGDRVTITCKASQSVRIA ^{VA} WYQQKPGKAPKLLIYLA <u>STRHTGVPSRFSGSGSGT</u> DFTLTISSLQPEDFATYYC <u>LQHWNPYPYTFGGQGTKLEIK</u> (SEQ ID NO:73)
humanized CHA.7.538_1/538_2 VL h538HL2	DIQMTQSPSSLSASVGDRVTITCKASQSVRIA ^{VA} WYQQKPGKAPKALIYLA <u>STRHTGVPSRFSGSGSGT</u> DFTLTISSVQPEDFATYYC <u>LQHWNPYPYTFGGQGTKLEIK</u> (SEQ ID NO:74)

Figure 12C

What	Sequences
humanized CHA.7.538_2 VH h5382HH1	QVQLVQSGAEVKKPGASVKVSCKASGYTFITNYWIGWVRQAPGQGLEWMGDIYPGGGYTNYAQKF QGRVTMTTRDTSTSTVYMELSSLRSEDTAVYYCARPYYGSSYGFAFWGQGTLVTVSS (SEQ ID NO:75)
humanized CHA.7.538_2 VH h5382HH2	QVQLVQSGAEVKKPGASVKVSCKASGYTFITNYWIGWVRQAPGQGLEWIGDIYPGGGYTNYAQKFQ GRVTMTADTSTSTVYMELSSLRSEDTAVYYCASPYYGSSYGFAFWGQGTLVTVSS (SEQ ID NO:76)
humanized CHA.7.538_2 VH h5382HH3	QVQLVQSGAEVKKPGASVKMSCKASGYTFITNYWIGWVRQAPGQGLEWIGDIYPGGGYTNYAQKFQ GRATLTADTSTSTVYMELSSLRSEDTAVYYCASPYYGSSYGFAFWGQGTLVTVSS (SEQ ID NO:77)
humanized CHA.7.538_1/538_2 VL h538HL1	DIQMTQSPSSLASVGDRTITCKASQSVRIAVAWYQQKPGKAPKLLIYLASTRHTGVPSRFSGSGSGT DFTLTISLQPEDFATYYCLOHWNPYPYTFGGQGTKLEIK (SEQ ID NO:78)
humanized CHA.7.538_1/538_2 VL h538HL2	DIQMTQSPSSLASVGDRTITCKASQSVRIAVAWFQQKPGKAPKALIYLASTRHTGVPSRFSGSGSGT DFTLTISLQPEDFATYYCLOHWNPYPYTFGGQGTKLEIK (SEQ ID NO:79)

Figure 13 humanized CHA.7 VH-VL Pairs

Antibody CHA.7.518

	VH	VL
ch518	chimVH	chimVL
h518-1	h518HH1	h518HL1 (optional)
h518-2	h518HH2	h518HL2
h518-3	h518HH3	h518HL2
h518-4	h518HH3	h518HL3
h518-5	h518HH4	h518HL3

Antibody CHA.7.538_1

	VH	VL
ch538.1	chimVH	chimVL
h538.1-1	h538.1HH1	h538.1HL1 (optional)
h538.1-2	h538.1HH2	h538.1HL2
h538.1-3	h538.1HH3	h538.1HL2
h538.1-4	h538.1HH4	h538.1HL2

Antibody CHA.7.538_2

	VH	VL
ch538.2	chimVH	chimVL
h538.2-1	h538.2HH1	h538.1HL1 (optional)
h538.2-2	h538.2HH2	h538.1HL2
h538.2-3	h538.2HH3	h538.1HL2

FIG. 14

Antibody (mgG)	Human CD56 int. NK (gMFir, 10ug/ml)	Human CD8+ T cells (gMFir, 10ug/ml)	Expi cyno OE/par (gMFir, 3.3ug/ml)	Cyno NK cells (gMFir, 10ug/ml)	Cyno CD8+ T cells (gMFir, 10ug/ml)
CHA.7.502	1.97	1.41	60.49	Not tested	Not tested
CHA.7.503	3.15	1.96	106.3	Not tested	Not tested
CHA.7.506	Not tested	Not tested	0.77	Not tested	Not tested
CHA.7.508	3.6	4.09	41.49	Not tested	Not tested
CHA.7.510	3.13	2.73	38.21	Not tested	Not tested
CHA.7.512	1.30	1.15	8.96	Not tested	Not tested
CHA.7.514	4.16	5.15	65.20	Not tested	Not tested
CHA.7.516	4.22	4.09	60.05	1.76	2.09
CHA.7.518	5.08	6.69	83.51	1.92	2.09
CHA.7.520	1.13	1.04	Not tested	Not tested	Not tested
CHA.7.522	2.06	1.90	27.24	Not tested	Not tested
CHA.7.524	5.50	6.12	66.32	1.78	2.02
CHA.7.525	1.98	1.76	0.85	Not tested	Not tested
CHA.7.526	2.08	1.71	0.79	Not tested	Not tested
CHA.7.527	1.16	0.99	Not tested	Not tested	Not tested
CHA.7.528	3.08	3.63	12.2	1.21	1.18
CHA.7.530	6.04	6.47	60.80	1.73	1.89
CHA.7.534	2.60	1.96	46.27	Not tested	Not tested
CHA.7.535	2.24	1.28	0.82	Not tested	Not tested
CHA.7.537	3.90	3.41	1.55	1.18	1.19
CHA.7.538	6.49	6.17	15.16	1.36	1.45
CHA.7.543	4.48	4.33	0.83	1.35	1.39
CHA.7.544	2.36	2.54	61.09	Not tested	Not tested
CHA.7.545	2.54	2.82	0.91	Not tested	Not tested
CHA.7.546	2.75	2.95	0.85	Not tested	Not tested
CHA.7.547	2.21	1.13	26.65	Not tested	Not tested
CHA.7.548	3.15	3.35	4.25	1.18	1.09
CHA.7.549	3.05	1.42	1.00	Not tested	Not tested
CHA.7.550	1.60	1.29	0.90	Not tested	Not tested

FIG. 15

Antibody (mgG)	IC ₅₀ (nM)
CHA.7.502	39.90
CHA.7.503	No IC ₅₀
CHA.7.506	31.65
CHA.7.508	37.88
CHA.7.510	55.00
CHA.7.512	839.6
CHA.7.514	38.88
CHA.7.516	33.11
CHA.7.518	23.15
CHA.7.520	619.3
CHA.7.522	50.48
CHA.7.524	30.20
CHA.7.525	85.52
CHA.7.526	58.88
CHA.7.527	No IC ₅₀
CHA.7.528	28.88
CHA.7.530	34.56
CHA.7.534	181.4
CHA.7.535	821.1
CHA.7.537	38.95
CHA.7.538	51.87
CHA.7.543	No IC ₅₀
CHA.7.544	No IC ₅₀
CHA.7.545	96.06
CHA.7.546	92.05
CHA.7.547	27.94
CHA.7.548	18.98
CHA.7.549	36.12
CHA.7.550	58.34

FIG. 16

Antibody (hlgG1)	Target Cell line	Fold change in cytotoxicity relative to control
CPA.7.002	Reh	2.9
	MOLM-13	1.9
CPA.7.005	Reh	1.6
	MOLM-13	1.6
CPA.7.021	Reh	1.9
	MOLM-13	0.7
CPA.7.036	Reh	0.9
CPA.7.037	Reh	1.1
CPA.7.038	Reh	0.8
CPA.7.041	Reh	0.7
CPA.7.042	Reh	0.7
CPA.7.050	Reh	1.6
TIGIT	Reh	1.1
	MOLM-13	1.1
DNAM-1	Reh	1.2

FIG. 17

NP_076975.2-Homosapiens
XP_005549281.1-Macacafascicularis
XP_003732227.1-Callithrixjacchus
XP_001103603.1-Macacamulatta

[illegible]

NP_076975.2-Homosapiens
XP_005549281.1-Macacafascicularis
XP_003732227.1-Callithrixjacchus
XP_001103603.1-Macacamulatta

APARQARWETQSSISLILEGSGASSPCANTTFCKKFASFPEGSWEACGSLPSSDPGLSA
 APARQARWETQSSISLALEDSGASSPFANTTFCKKFASFPEGSWEACGSLPSSDPGLSA
 APARQARWETQSSISLILEEPGASSPANTTFCKKFASFPEGSWEACGSLPSSDPGLSA
 APARQARWETQSSISLALEDSGASSPFANTTFCKKFASFPEGSWEACGSLPSSDPGLSA
 * * * * *

NP_076975.2-Homosapiens
XP_005549281.1-Macacafascicularis
XP_003732227.1-Callithrixjacchus
XP_001103603.1-Macacamulatta

PPTPAPILRAD
PPTPVPILRAD
PIL-----RAD
PPTPVPILRAD
* * *

SEQ ID NOS:80-83, respectively in order of appearance

FIG. 18A

CPA.7.002

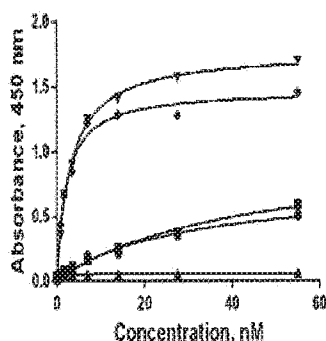


FIG. 18B

CPA.7.021

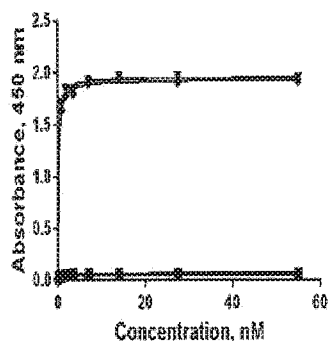
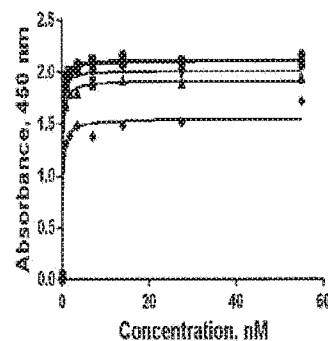


FIG. 18C

CPA.7.024



CPA.7.028

Concentration (nM)	Absorbance (Open Circles)	Absorbance (Open Squares)
0	0.0	0.0
2	1.9	1.8
4	1.9	1.8
8	1.9	1.8
12	2.0	1.9
24	2.0	1.9
48	2.0	1.9

CPA.7.081

CPA.7.050

FIG. 18D

FIG. 18E

FIG. 18F

FIG. 19

mAb	Cyno cross-reactivity	Epitope bin	Epitope group
CPA.7.002	+	1	2
CPA.7.021	-	1	1
CPA.7.024	+++	1	3
CPA.7.028	-	1	1
CPA.7.041	++	1	2
CPA.7.050	+++	4	3

FIG. 20A

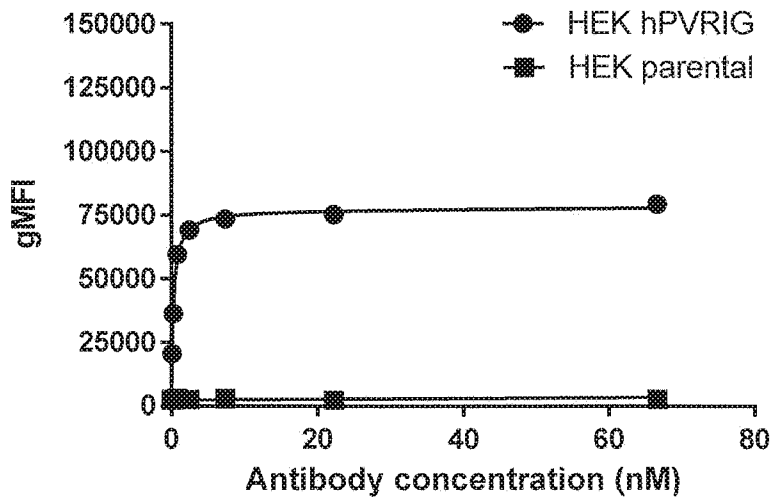


FIG. 20B

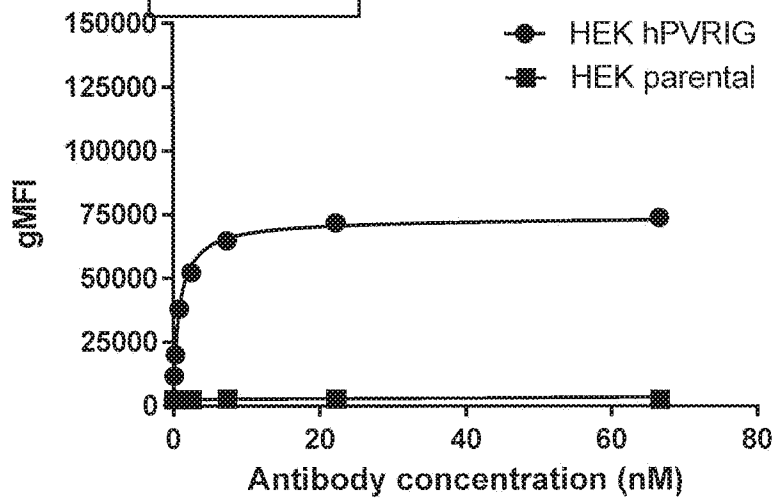


FIG. 21A

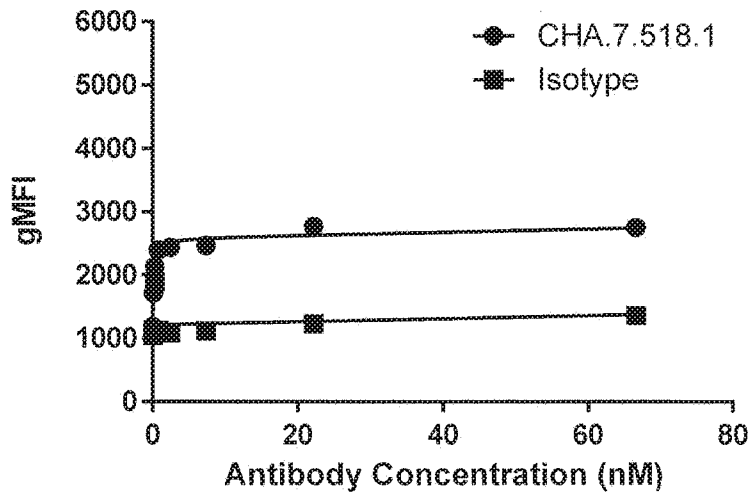


FIG. 21B

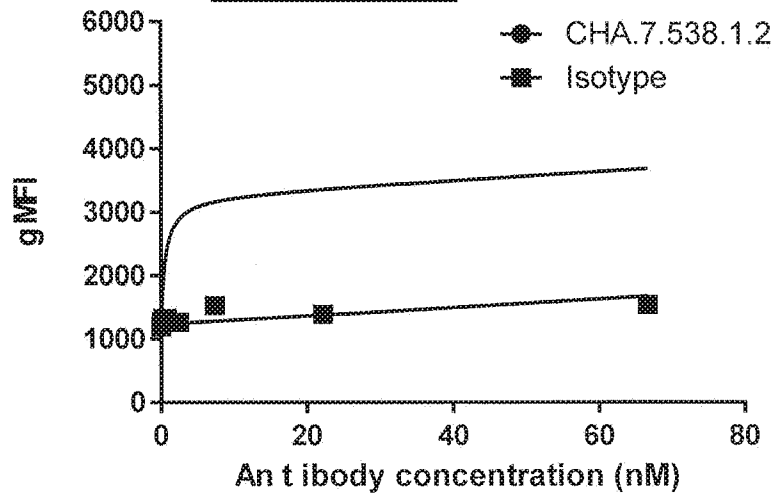


FIG. 22

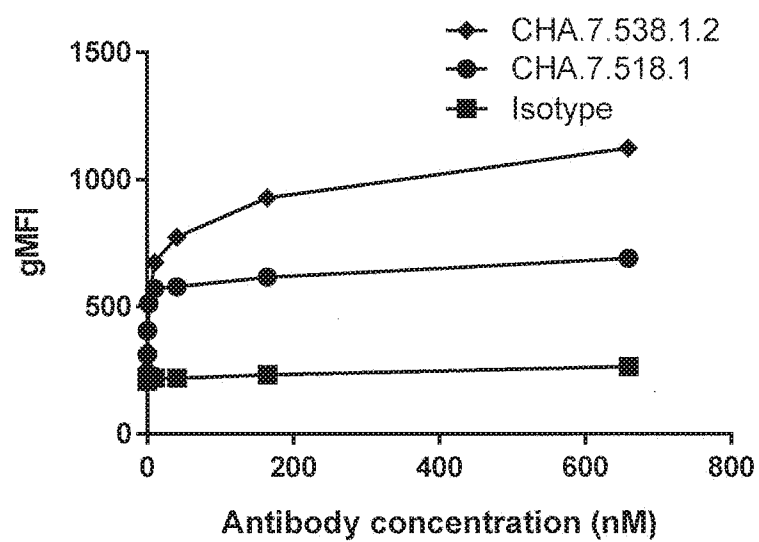


FIG. 23A

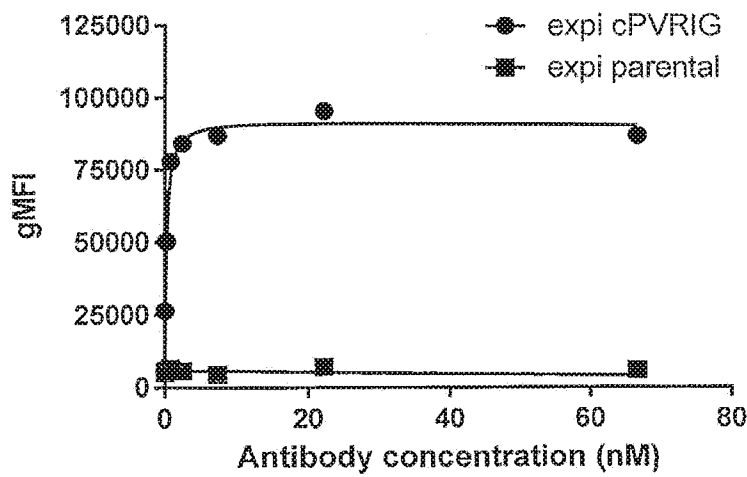
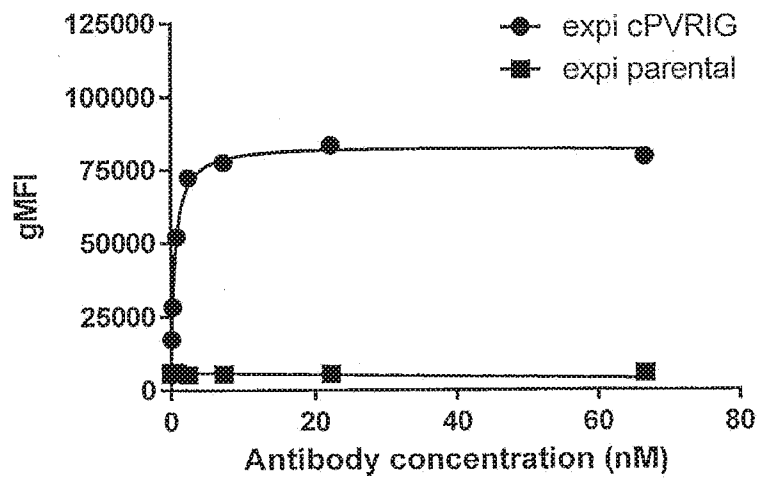
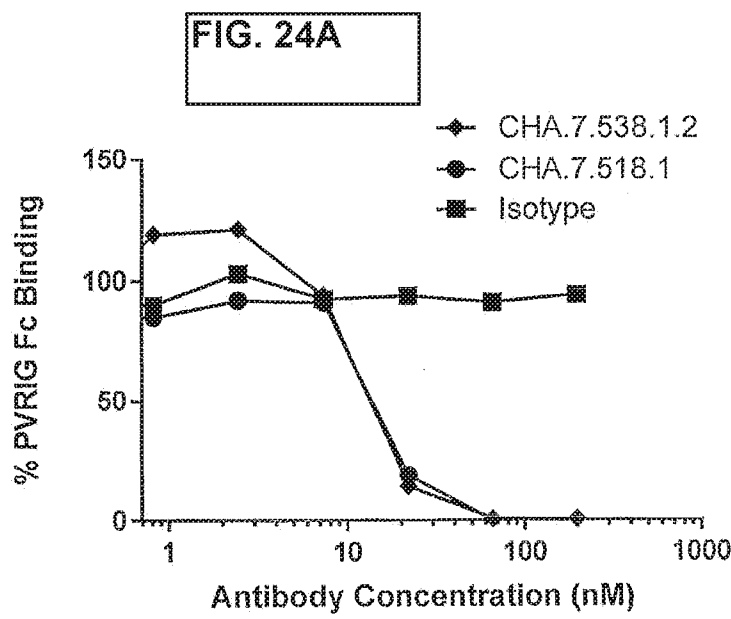
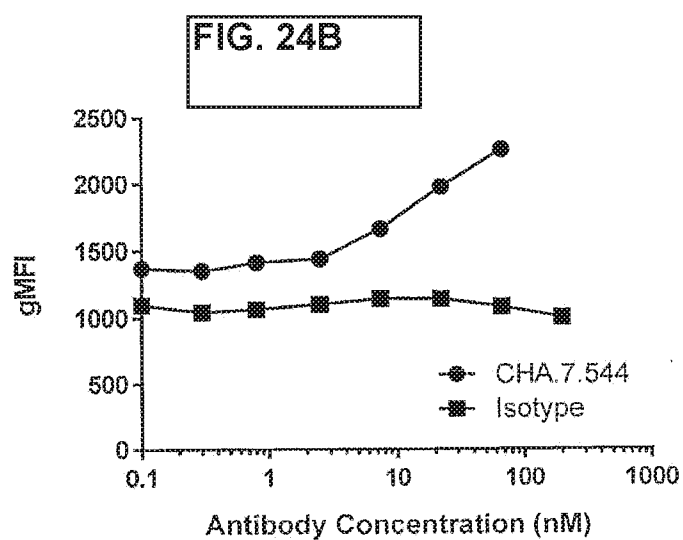


FIG. 23B





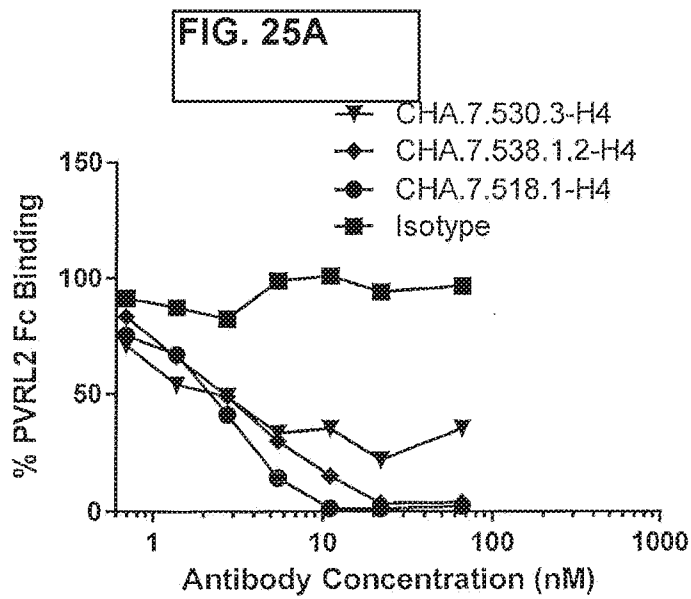
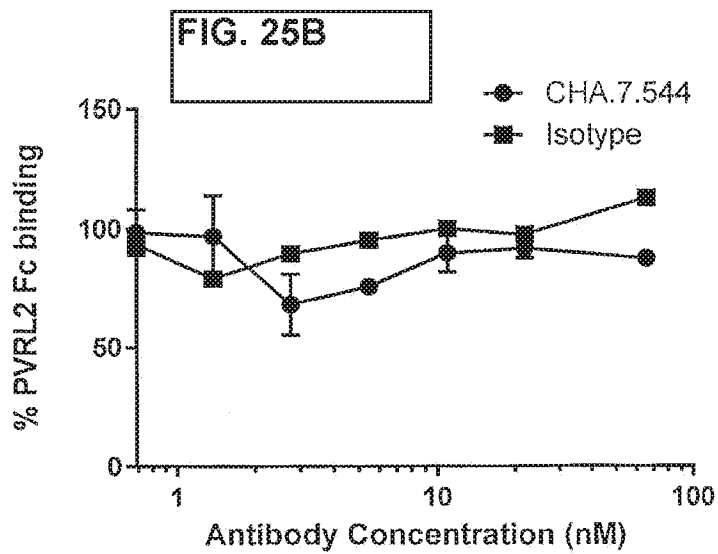


FIG. 26

	CHA.7.518.1 (Alexa 647)	CHA.7.538.1.2 (Alexa 647)
Isotype (unconjugated)	100	100
CHA.7.518.1 (unconjugated)	14	32
CHA.7.538.1.2 (unconjugated)	7	7

Figure 27A

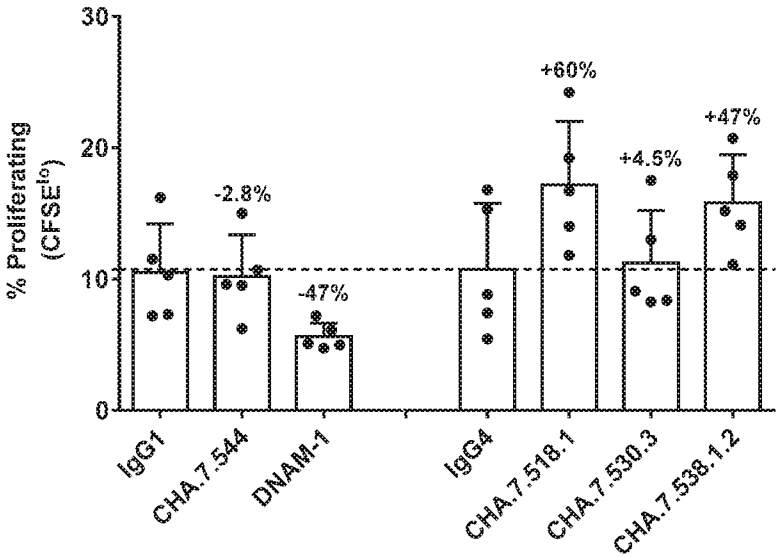


Figure 27B

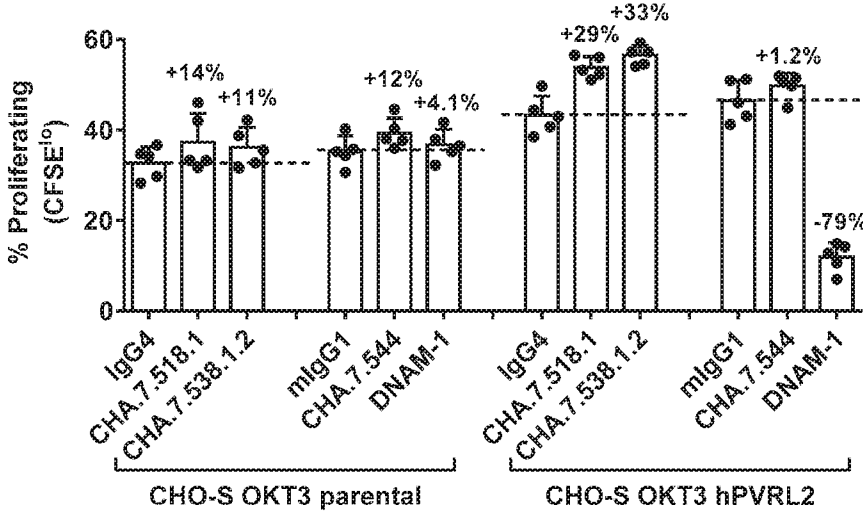


FIG. 28B

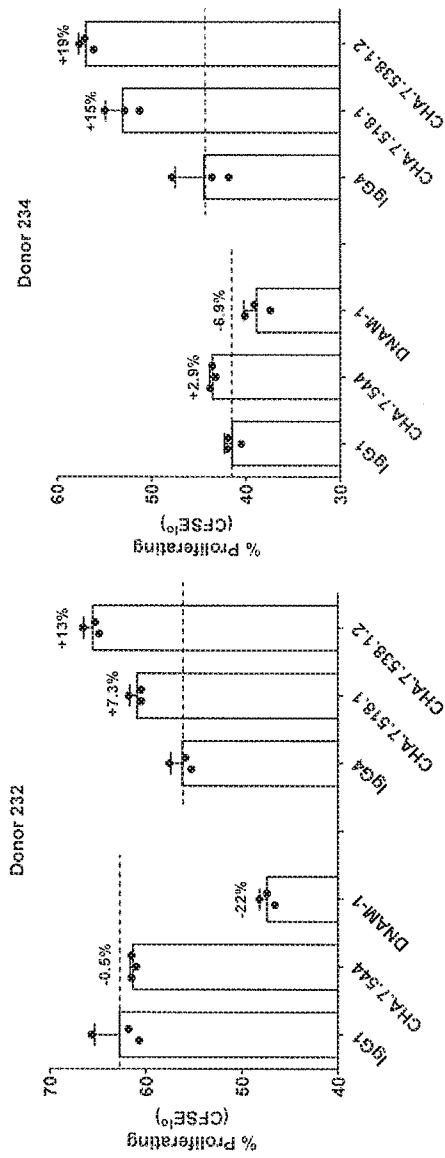


FIG. 28A

FIG. 28C

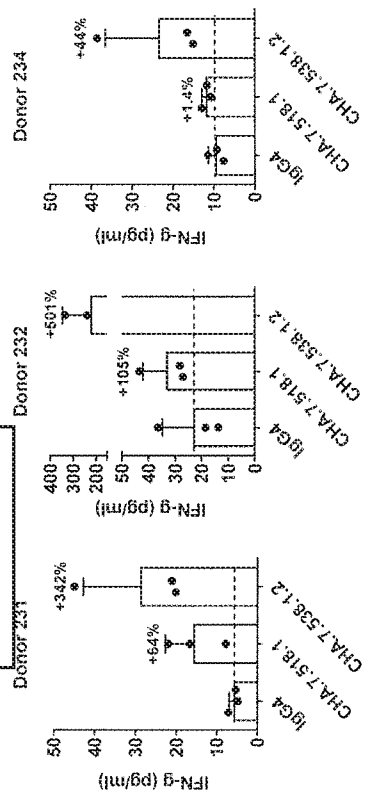


FIG. 29

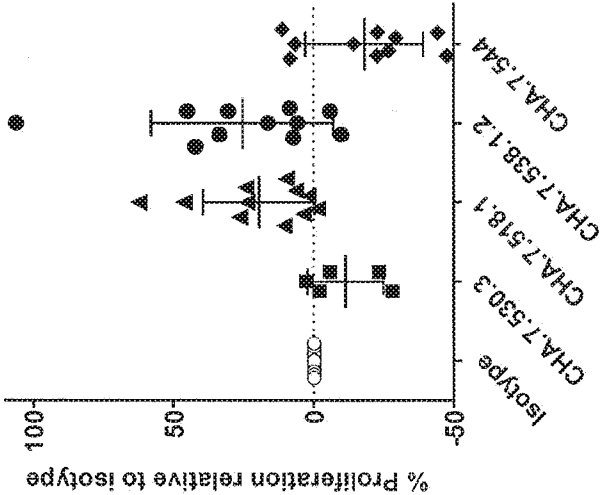


FIG. 30A

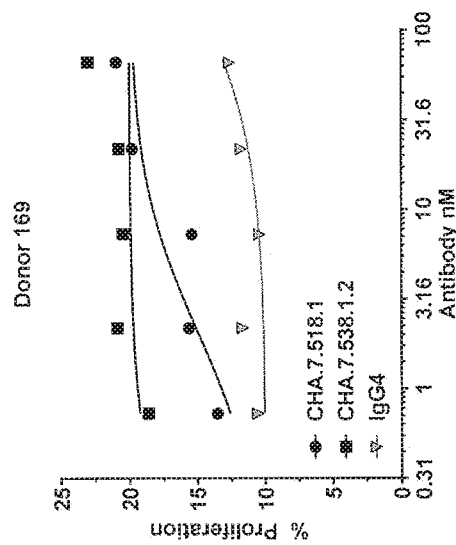


FIG. 30B

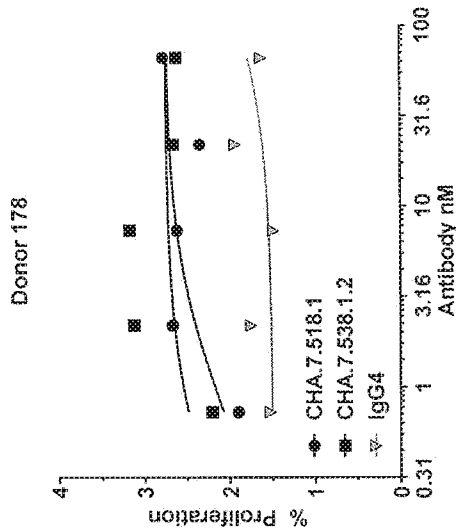


FIG. 30C

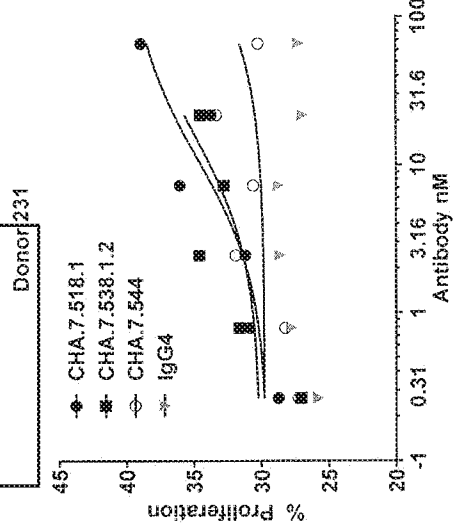


FIG. 30D

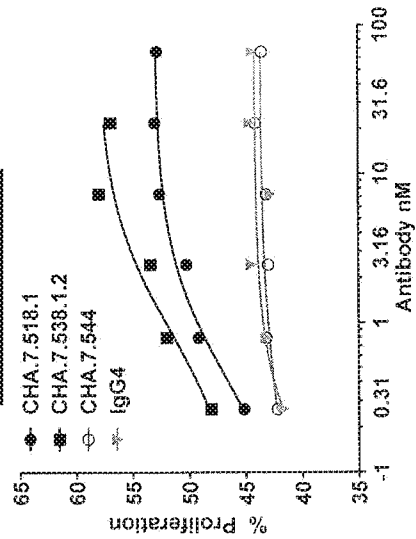


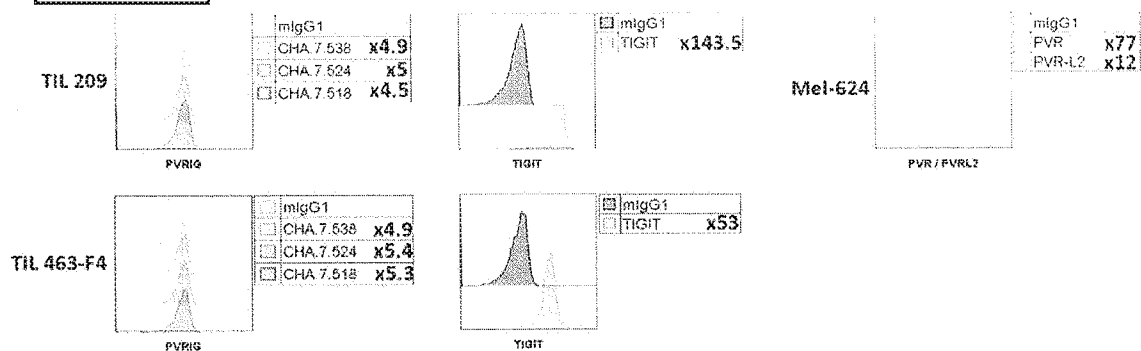
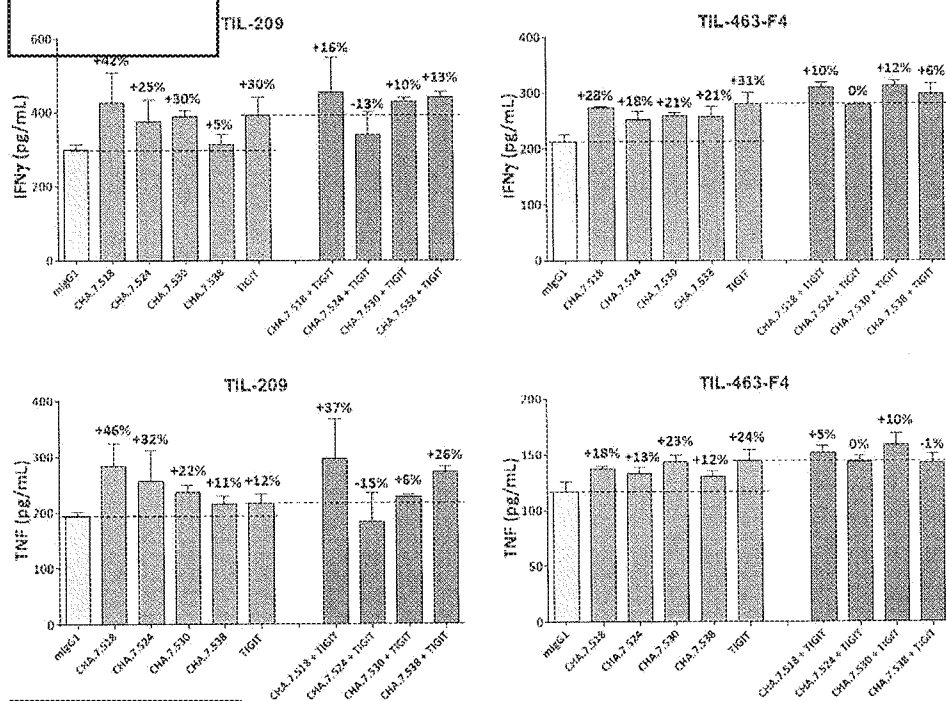
FIG. 31A**FIG. 31B****FIG. 31C**

FIG. 32A

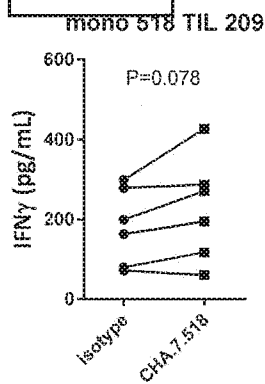


FIG. 32B

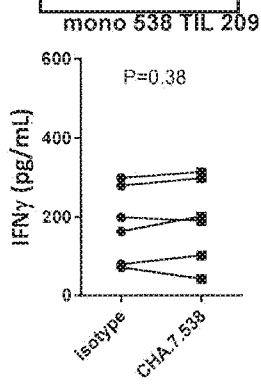


FIG. 32C

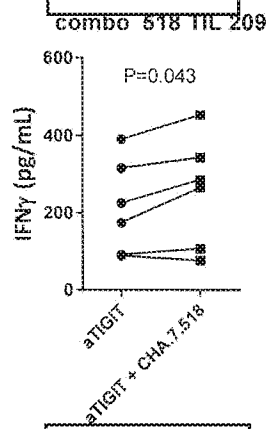


FIG. 32D

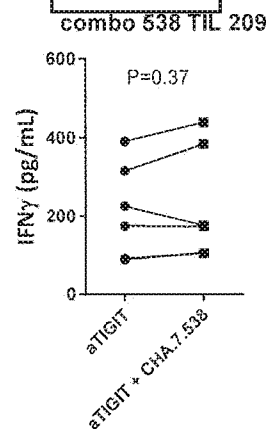


FIG. 32E

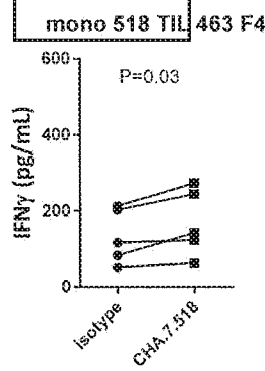


FIG. 32F

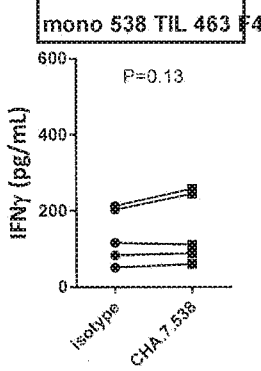


FIG. 32G

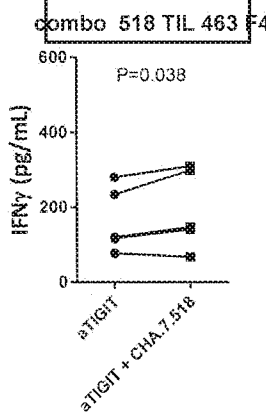


FIG. 32H

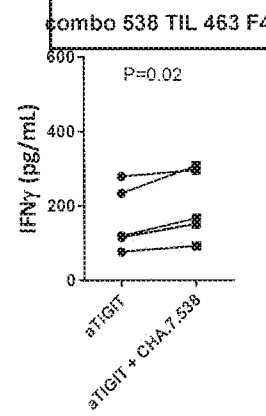


FIG. 33A

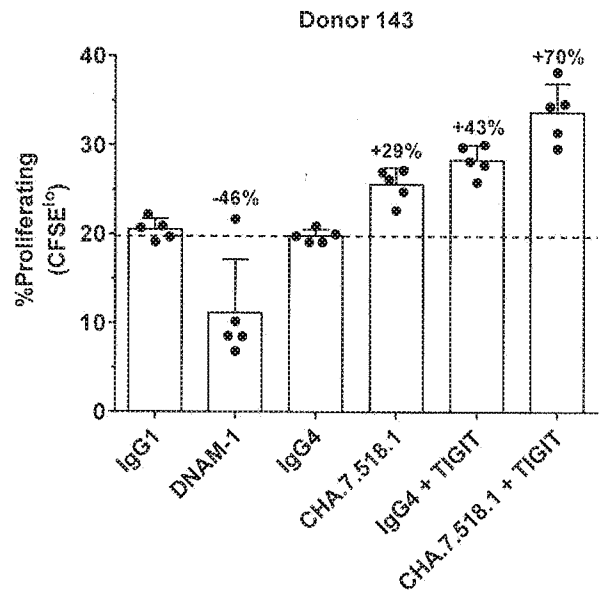


FIG. 33B

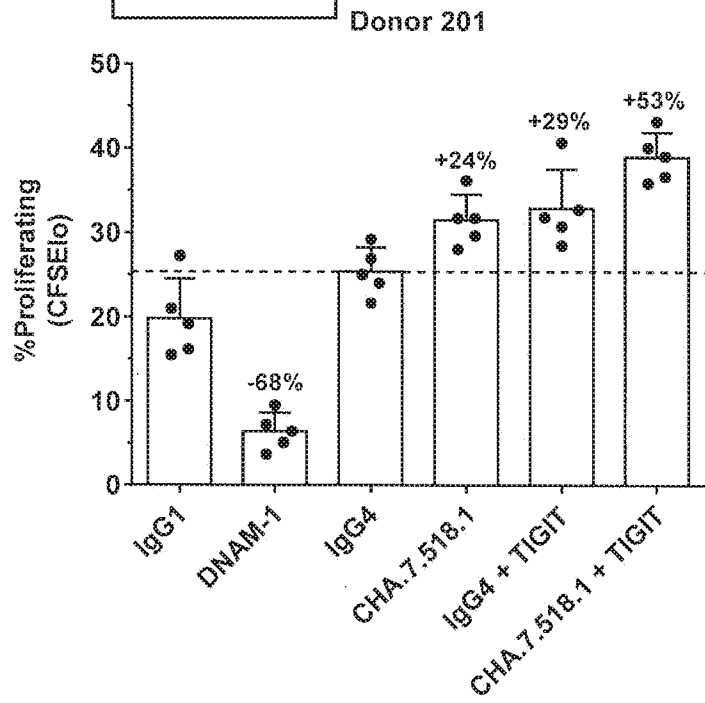


FIG. 34A

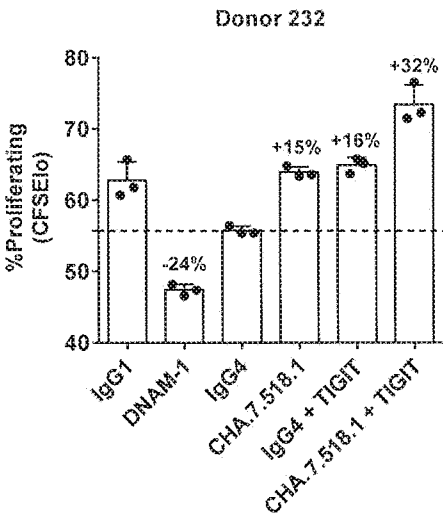


FIG. 34B

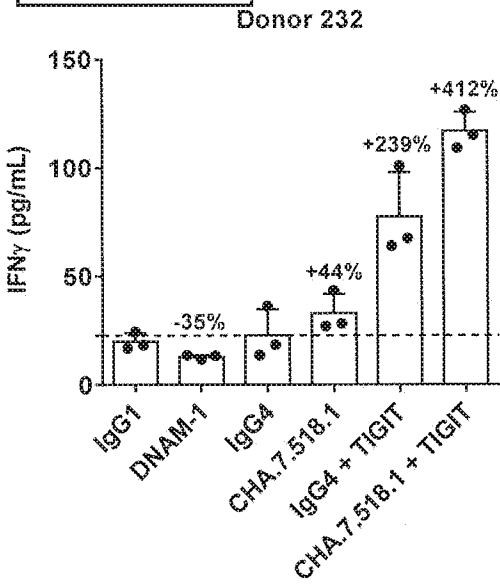


FIG. 35

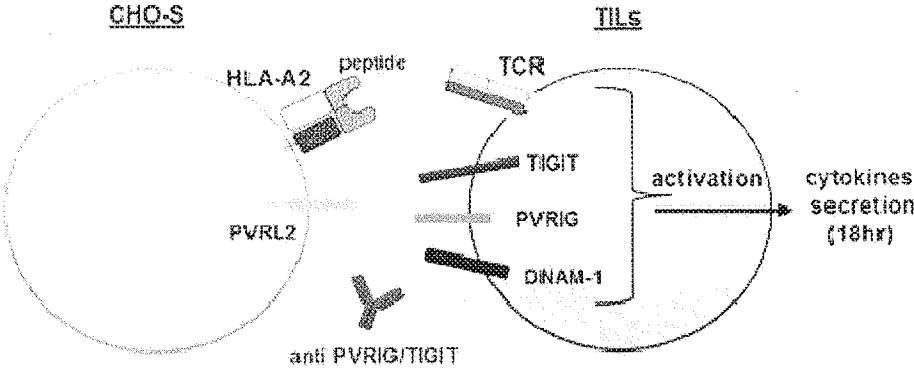
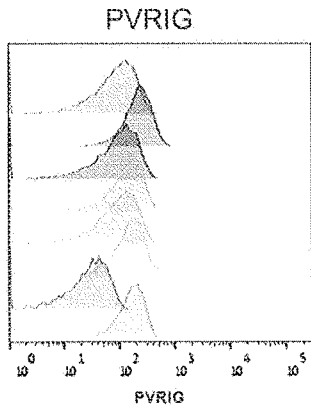
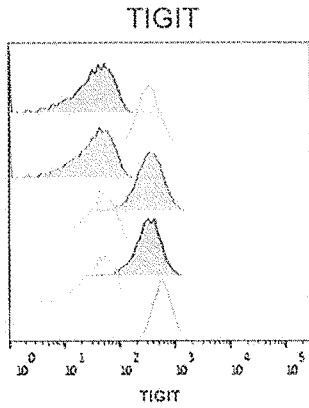


FIG. 36A



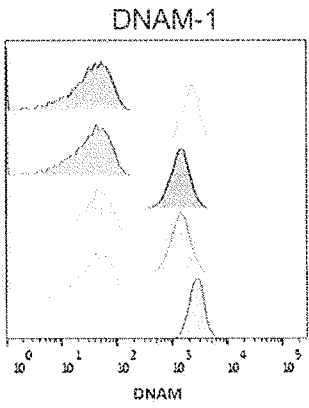
MART1 anti iso control	19.8
MART1 anti PVRIG	184
F5 anti iso control	20.1
F5 anti PVRIG	84.3
F4 anti iso control	21.1
F4 anti PVRIG	82.1
209 anti iso control	11.0
209 anti PVRIG	101

FIG. 36B



MART1 anti iso control	12.5
MART1 anti TIGIT	320
F5 anti iso control	11.5
F5 anti TIGIT	312
F4 anti iso control	14.7
F4 anti TIGIT	277
209 anti iso control	13.5
209 anti TIGIT	543

FIG. 36C



MART1 anti iso control	12.5
MART1 anti DNAM	2078
F5 anti iso control	11.5
F5 anti DNAM	1308
F4 anti iso control	14.7
F4 anti DNAM	1291
209 anti iso control	13.5
209 anti DNAM	2557

FIG. 37

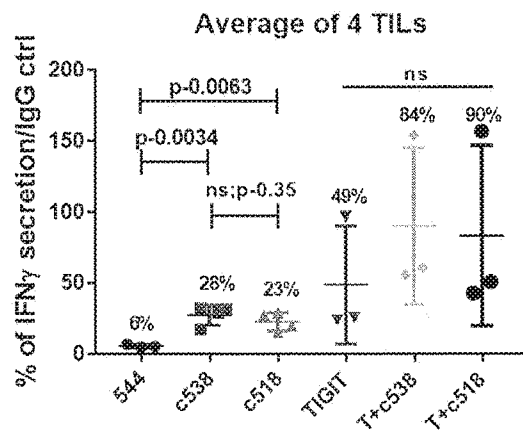


FIG. 38A

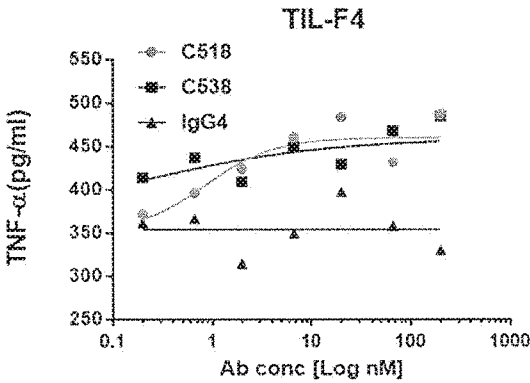


FIG. 38B

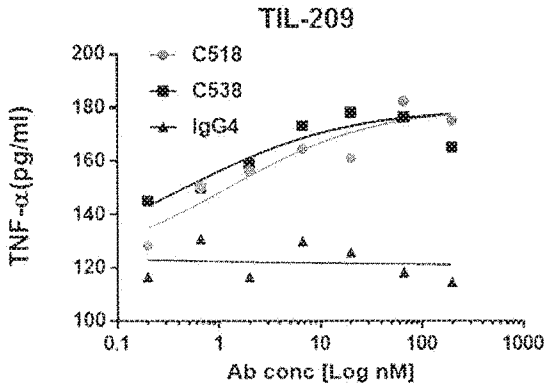


FIG. 39A

peptide 0.5ug/ml		TIGIT	544	c538	c518	TIGIT+c518
TIL-209	IFN γ	111%	11%	29%	29%	171%
	TNF α	181%	17%	20%	23%	216%
TIL-F4	IFN γ	32%	<5%	<5%	11%	47%
	TNF α	63%	<5%	<5%	21%	83%
TIL-F5	IFN γ	37%	15%	39%	56%	86%
	TNF α	44%	5%	<5%	9%	54%

peptide 0.1ug/ml		544	c538	c518
TIL-209	IFN γ	12%	48%	39%
	TNF α	20%	47%	38%
TIL-F4	IFN γ	8%	13%	9%
	TNF α	7%	31%	15%
TIL-F5	IFN γ	3%	31%	21%
	TNF α	0%	10%	14%

FIG. 39B

peptide 0.1ug/ml		544	c538	c518	TIGIT	c538+ TIGIT	c518+ TIGIT
TIL-209	IFN γ	2%	16%	19%	97%	154%	157%
	TNF α	7%	28%	27%	150%	190%	180%
TIL-F4	IFN γ	2%	12%	7%	26%	56%	51%
	TNF α	15%	31%	18%	39%	55%	60%
TIL-F5	IFN γ	8%	4%	10%	24%	61%	43%
	TNF α	11%	16%	20%	35%	56%	59%
MART-1	IFN γ	50%	53%	81%	39%	87%	81%

FIG. 39C

FIG. 40A

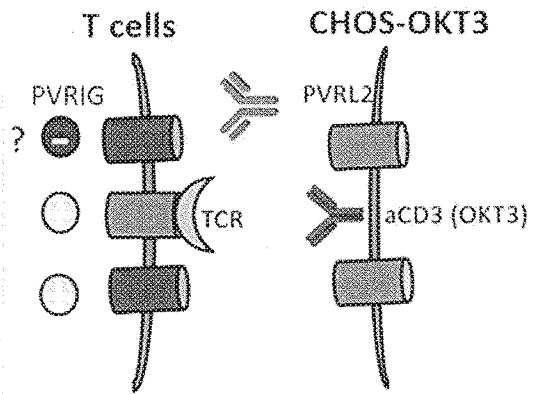
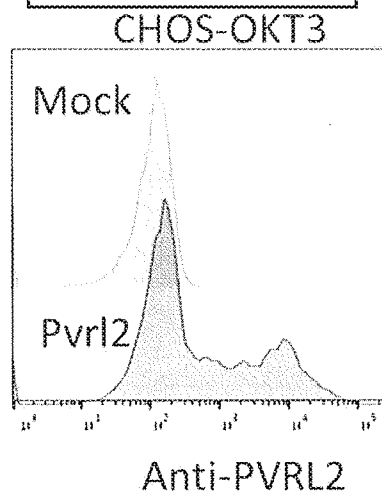
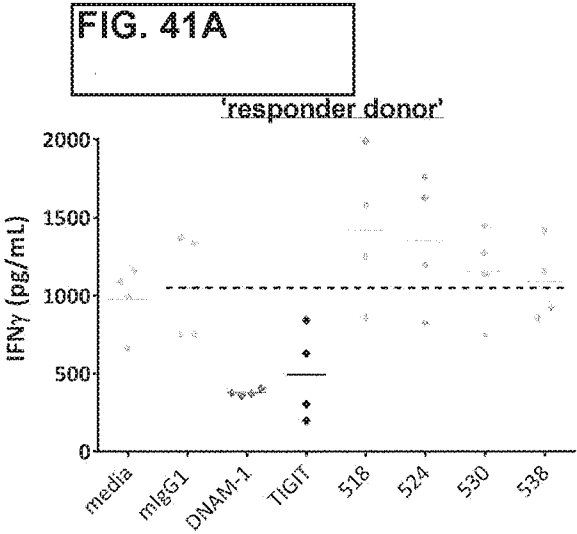
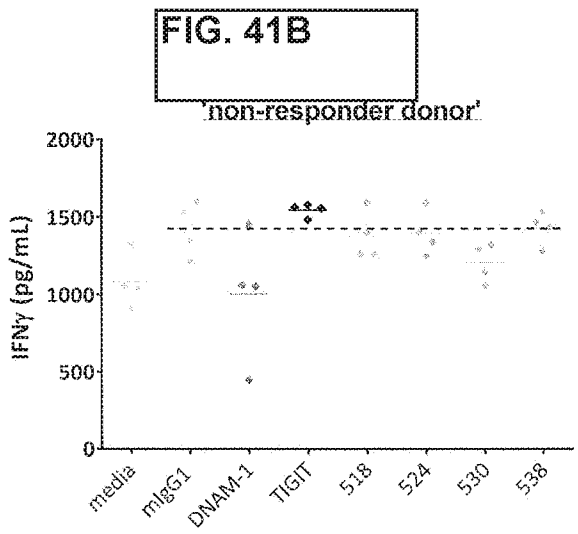
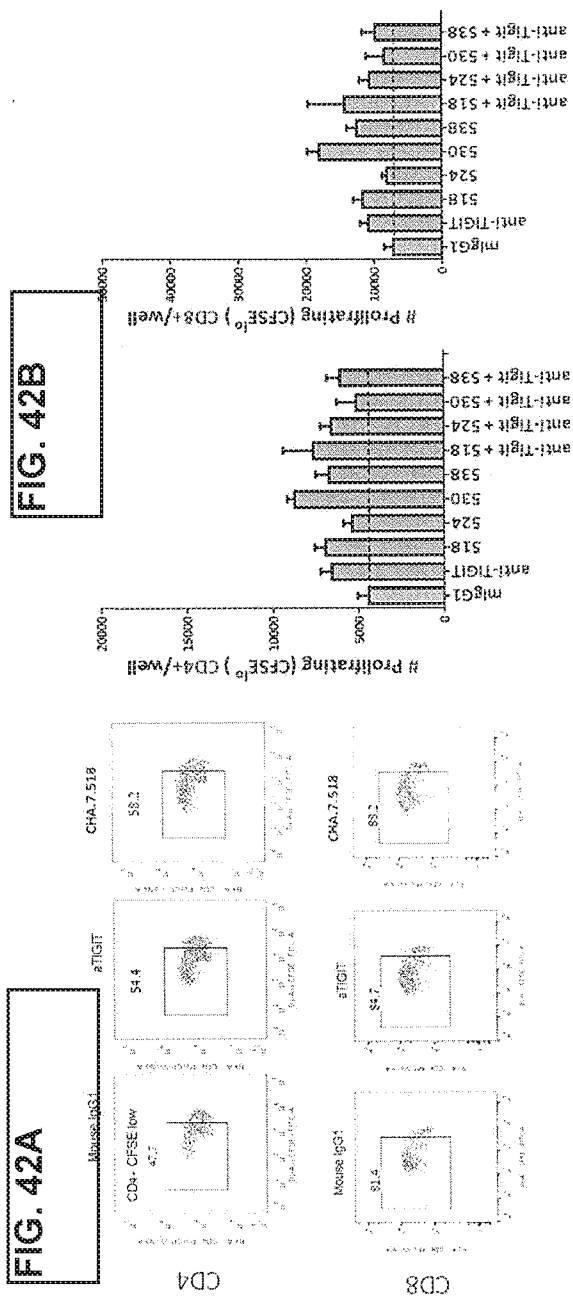


FIG. 40B







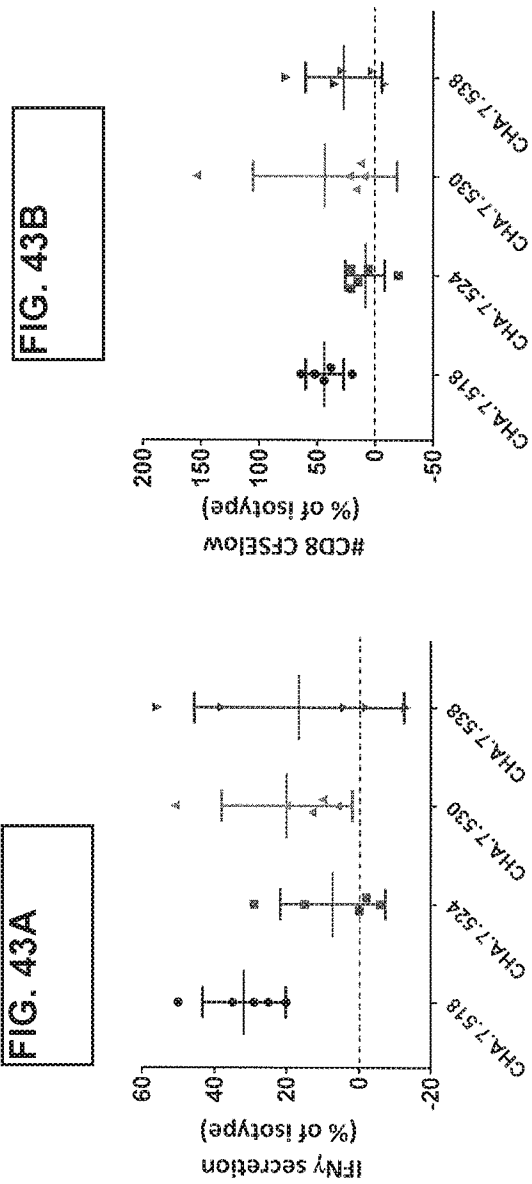


FIG. 43C

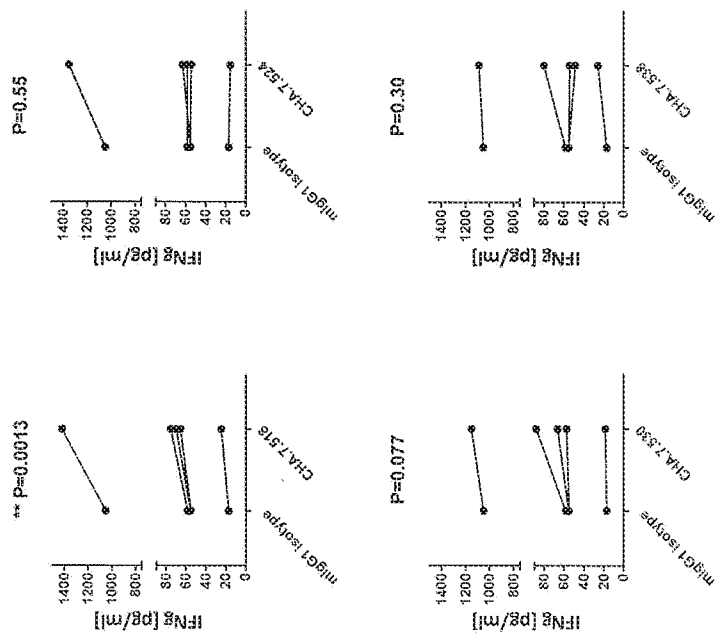


FIG. 44

% of effect (vs. isotype)	exp #	Donor	IFN γ	CD4+ total no. CFSE low	CD8+ total no. CFSE low
CHA.7.518	410-IB-003	3	25%	24%	52%
	410-IB-003	72	29%	58%	64%
	400-ES-002	226	50%	16%	38%
	400-ES-002	345	20%	-26%	20%
	400-ES-002	ES_001	35%	39%	44%
	400-ES-003	ES_002	-3%	-22%	-17%
	400-ES-003	ES_004	-20%	-14%	-15%
	400-ES-003	ES_005	1%	5%	1%
	400-ES-003	ES_006	-11%	4%	12%
	400-ES-003	ES_007	4%	6%	15%
CHA.7.524	410-IB-003	3	-2%	-9%	-20%
	410-IB-003	72	0%	23%	15%
	400-ES-002	226	-6%	0%	6%
	400-ES-002	345	15%	-21%	21%
	400-ES-002	ES_001	29%	25%	21%
	400-ES-003	ES_002	-2%	-10%	-14%
	400-ES-003	ES_004	-18%	-8%	-7%
	400-ES-003	ES_005	12%	10%	12%
	400-ES-003	ES_006	2%	8%	-10%
	400-ES-003	ES_007	-4%	-4%	2%
CHA.7.530	410-IB-003	3	20%	16%	10%
	410-IB-003	72	51%	98%	154%
	400-ES-002	226	13%	3%	13%
	400-ES-002	345	6%	-25%	23%
	400-ES-002	ES_001	10%	20%	17%
	400-ES-003	ES_002	-15%	-23%	-29%
	400-ES-003	ES_004	-20%	-7%	-10%
	400-ES-003	ES_005	11%	5%	13%
	400-ES-003	ES_006	-20%	5%	17%
	400-ES-003	ES_007	0%	0%	11%
CHA.7.538	410-IB-003	3	-13%	1%	-8%
	410-IB-003	72	38%	53%	77%
	400-ES-002	226	56%	24%	29%
	400-ES-002	345	-2%	-22%	35%
	400-ES-002	ES_001	4%	0%	3%
	400-ES-003	ES_002	0%	1%	1%
	400-ES-003	ES_004	-21%	-9%	-5%
	400-ES-003	ES_005	18%	-1%	0%
	400-ES-003	ES_006	-21%	6%	13%
	400-ES-003	ES_007	-4%	11%	20%

FIG. 45A

Cells	antibody	Kd	gMFI
HEK hPVRIG	CPA.7.021 IgG4	2.939	18.17
HEK hPVRIG	CHA7.518 M1	0.36	42.24
Jurkat	CPA.7.021 IgG4	3.18	10.08
Jurkat	CHA7.518 M1	0.24	6.58

FIG. 45B

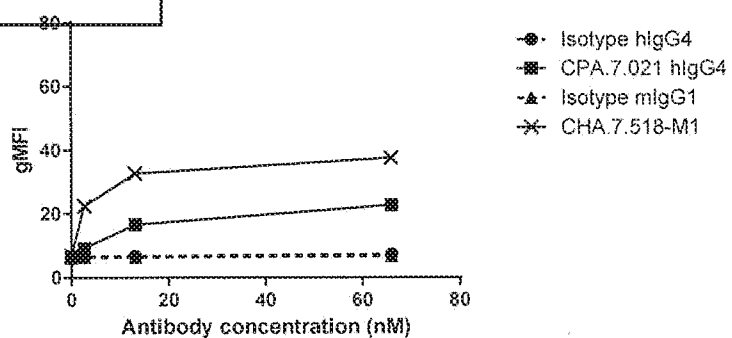


FIG. 45C

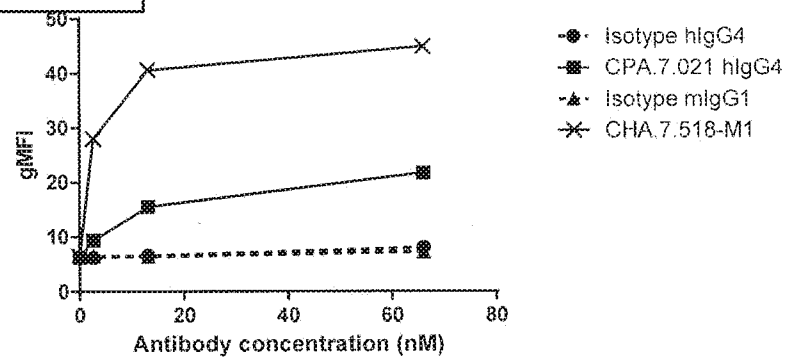


FIG. 46A

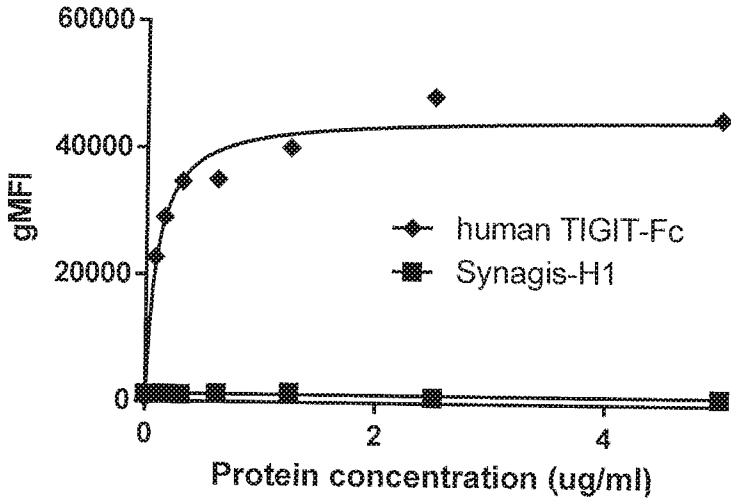
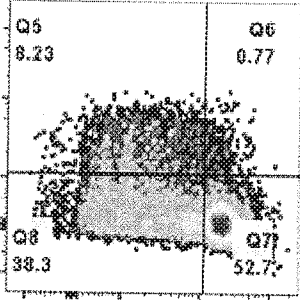


FIG. 46B

PVR



CFSE

Figure 47A & 47B

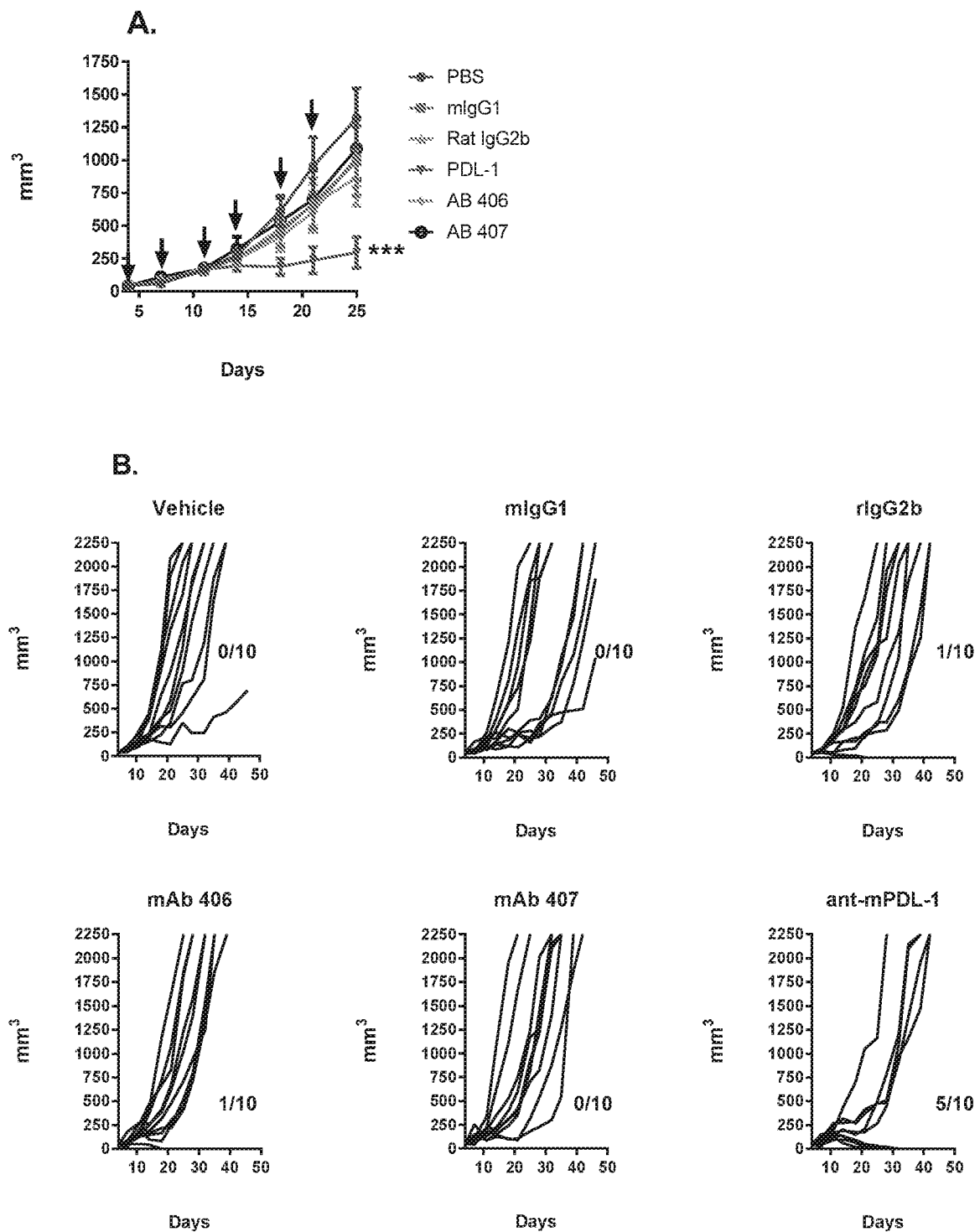


Figure 47C

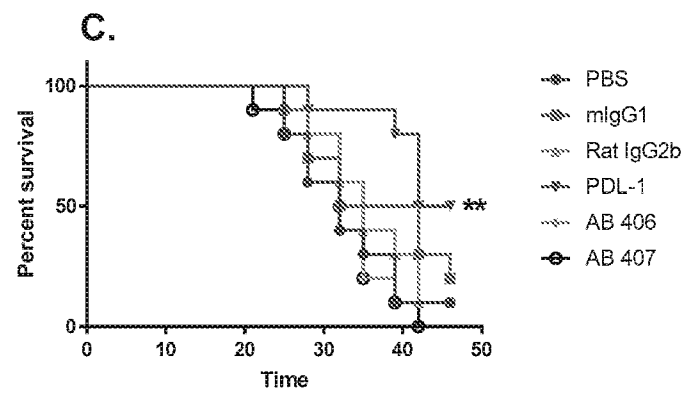


Figure 48A & 48B

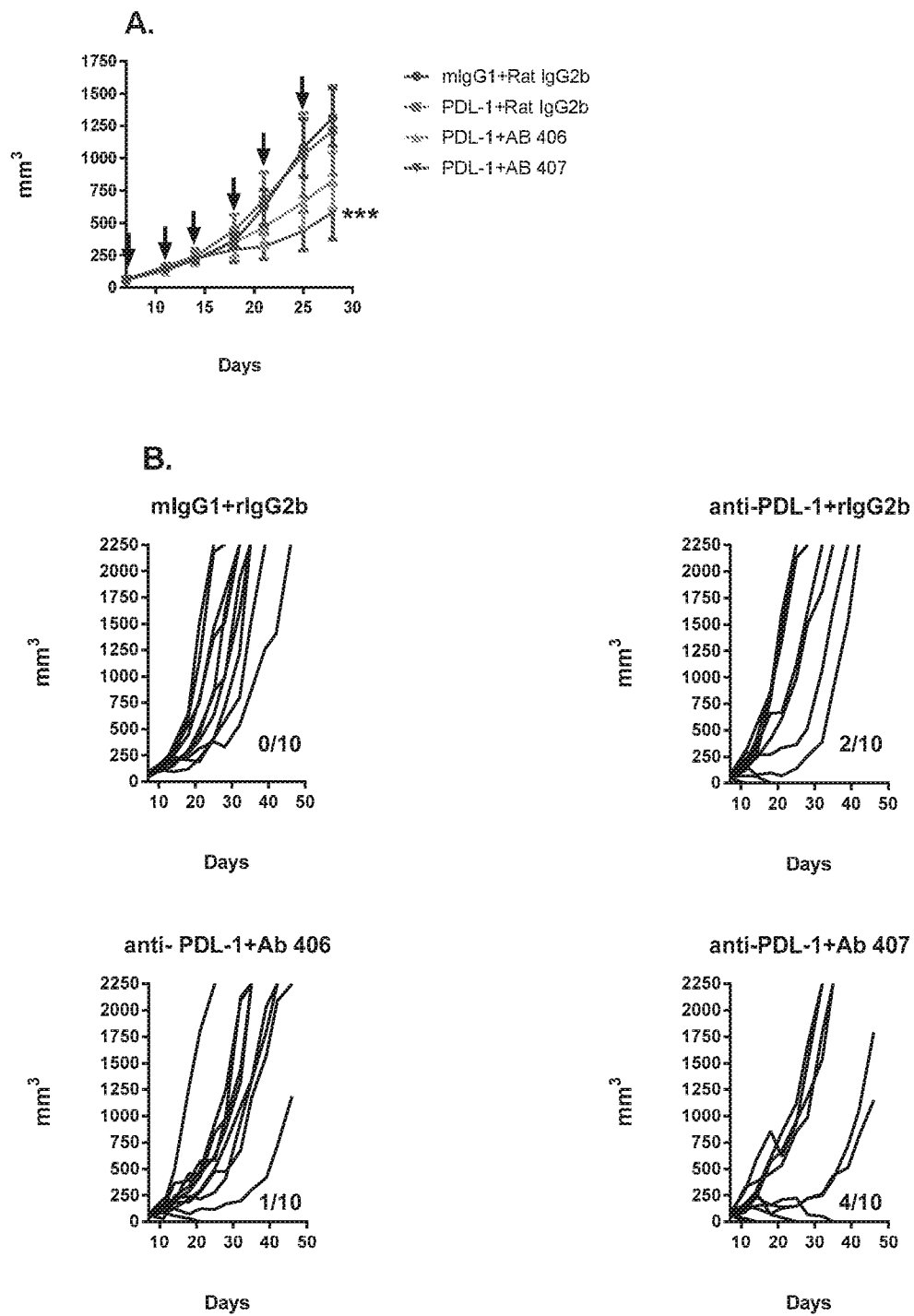


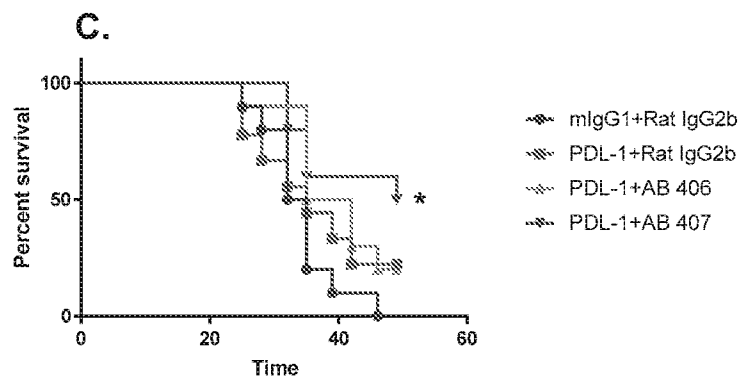
Figure 48C

Figure 49A, 49B, 49C, & 49D**A)****AB-407 (BOJ-5G4-F4)**

Heavy chain: Amino acid sequence

MEWNWVFLFLSVTAGVHSQVQLQQSGAELAKPGSSVMISCKASGYFTFN
 YAVHWIKTTGQALEWTGYIAPGSGVTKYNEKFKGKATLTVDKSSTTAYMQLSSLTPVDTAVYYCASGTTRFAYWGQ
 GTLVTVSSAQTTAPSVYPLAPGCGDTSSTVTLGCLVKG (SEQ ID NO:84)

B)**AB-407 (BOJ-5G4-F4)**

Heavy chain: DNA sequence

ATGGAATGGAAGTGGGTCTTTCTTCTCCTCTGTCAGTAACTGCAGGAGTCCACTCCCAGGTCCAGC
 TGCAGCAGTCTGGAGCTGAGCTGGCAAAGCCTGGCTCTTCAGTGATGATTCCTGCAAGGCTTCTGG
 TTACACCTTTACCAACTATGCTGTGCACTGGATAAAGCAGACGACTGGACAGGCCCTTGAGTGGACT
 GGATATATTGCTCCTGGAAGTGGAGTTACTAAATACAATGAGAAGTTCAAGGGCAAGGCCACATTGA
 CTGTAGACAAATCCTCAACCACAGCCTACATGCAACTCAGCAGCCTGACACCTGTGGACACTGCGGT
 CTATTACTGTGCAAGCGGAAGTACGAGGTTTGCTTATTGGGGCCAAGGCACTCTGGTCACTGTCTCT
 TCA GCCCAAACAACAGCCCCATCTGTCTATCCACTGGCTCCTGGATGTGGTGATACAACCAGC
 TCCACGGTGACTCTGGGATGCCTGGTCAAGGGC (SEQ ID NO:85)

C)**AB-407 (BOJ-5G4-F4)**

Light chain: Amino acid sequence

METDTLLLWVLLLWVPGSTGDIVLTQSPALAVSLGQRATISCRASQSVSLSSYNLMQWYQQKPGQEP
 KILYDASNLPSGIPARFSGSGSGTDFTLTIDPVQADDIATYYCQQSKDDPLTFGSGTKLEIK (SEQ ID NO:86)

D)**AB-407 (BOJ-5G4-F4)**

Light chain: DNA sequence

ATGGAGACAGACACTCCTGCTATGGGTGCTGCTGCTCTGGGTTCCAGGCTCCACTGGTGACATTG
 TGCTGACCCAGTCTCCTGCTTTGGCTGTGTCTCTAGGGCAGAGGGCCACAATCTCCTGTAGAGCCAG
 CCAAAGTGTCAGTTTATCCAGCTATAATCTCATGCAGTGGTACCAACAGAAACCAGGACAGGAACCC
 AAAATCCTCATCTATGATGCATCCAACCTACCATCTGGGATCCCTGCCAGGTTCAAGTGGCAGTGGGT
 CTGGGACAGACTTCACCTCACCATTGATCCTGTGCAGGCTGATGATATTGCAACCTATTACTGTCA
 GCAGAGTAAGGATGACCCGCTCACGTTTCGGTCTGGGACCAAGCTGGAGATCAAA (SEQ ID NO:87)

Figure 50**Human IgG1 constant region (SEQ ID NO:88)**

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV
 VTPVSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI
 SRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC
 KVSNAKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN
 NYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK

Human IgG1 D265A constant region (SEQ ID NO:89)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV
 VTPVSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI
 SRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC
 KVSNAKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN
 NYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK

Human IgG1 N297A constant region (SEQ ID NO:90)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV
 VTPVSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI
 SRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC
 KVSNAKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN
 NYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK

Human IgG2 constant region (SEQ ID NO:91)

ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV
 VTPVSSSNFGTQTYTCNVNHNKPSNTKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTF
 EVTCVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVSVLTVVHQDWLNGKEYKCKVSN
 KGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT
 TTPMLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK

Human IgG3 constant region (SEQ ID NO:92)

ASTKGPSVFPLAPCSRSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV
 VTPVSSSLGTQTYTCNVNHNKPSNTKVDKRVELKTPLGDTTHTCPRCPEPKSCDTPPPCPRCPEPKSCD
 TPPPCPRCPEPKSCDTPPPCPRCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVDVSHEDPEVQ
 FKWYVDGVEVHNAKTKPREEQYNSTFRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKTKGQ
 PREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESSGQPENNYNTTPMLDSDGSFFLYSKL
 TVDKSRWQQGNIFCFSVMHEALHNRETQKSLSLSPGK

Figure 50 continued

Human IgG4 constant region (Wild Type) (SEQ ID NO:93)

ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV
VTVPSSSLGKTYTCNVDPKPSNTKVDKRVESKYGPPCPSCPAPEFLGGPSVFLFPPKPKDTLMISRT
PEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVS
NKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSPGK

Human IgG4 constant region (S241P hinge mutant) (SEQ ID NO:94)

ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV
VTVPSSSLGKTYTCNVDPKPSNTKVDKRVESKYGPPCP[**P**]CPAPEFLGGPSVFLFPPKPKDTLMISRT
PEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVS
NKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSPGK

Human kappa light chain (SEQ ID NO:95)

RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLS
SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Human lambda light chain (SEQ ID NO:96)

GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAA
SSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

Figure 51

Human TIGIT ECD (SEQ ID NO:97)

MMTGTIETTGNISAEKGGSIILQCHLSSTTAQVTQVNWEQQDQLLAICNADLGWHISPSFKDRVAPGP
GLGLTLQSLTVNDTGEYFCIYHTYPDGTYTGRIFLEVLESSVAEHGARFQIP

Cyno macaque TIGIT ECD (SEQ ID NO:98)

MMTGTIETTGNISAKKGGSVILQCHLSSTMAQVTQVNWEQHDHSLLAIRNAELGWHIYPAFKDRVAPG
PGLGLTLQSLTMNDTGEYFCTYHTYPDGTYRGRIFLEVLESSVAEHSARFQIP

Human PVR ECD (SEQ ID NO:99)

DVVVQAPTQVPGFLGDSVTLP CYLQVPNMEVTHVSQLTWARHGESGSMVVFHQTQGPPSYSESKRLEFV
AARLGAELRNASLRMFGLRVEDEGNYTCLFVTFPQGSRSVDIWLRLVLAQPONTAEVQKVQLTGEPVPM
ARCVSTGGRPPAQITWHS DLGGMPNTSQVPGFLSGTVTVTSLWILVPSSQVDGKNVTCKVEHESFEKP
QLLTVNLTVYYPPEVSISGYDNNWYLGQNEATLTCDARSNPEPTGYNWSTTMGPLPPFAVAQGAQLLI
RPVDPKPIINTTLCNVTNALGARQAELTVQVKEGPPSEHSGMSRN

Figure 52

Campaign	Antibody ID	MFir (OE/Par) hTIGIT	MFir (OE/Par) cTIGIT
1	CPA.9.002	98	ND
1	CPA.9.009	8.7	ND
1	CPA.9.011	12	ND
1	CPA.9.012	12	ND
1	CPA.9.013	25	ND
1	CPA.9.014	110	ND
1	CPA.9.015	10	ND
1	CPA.9.018	16	ND
1	CPA.9.053	4.4	ND
2	CPA.9.057	30	ND
2	CPA.9.059	11	ND
2	CPA.9.064	5	ND
2	CPA.9.069	5	ND
2	CPA.9.071	5.7	ND
2	CPA.9.077	19	ND
2	CPA.9.081	7.6	ND
3	CPA.9.027	110	ND
3	CPA.9.049	94	ND
4	CPA.9.083	170	97
4	CPA.9.086	36	34
4	CPA.9.089	110	52
4	CPA.9.093	80	60
4	CPA.9.101	130	22
4	CPA.9.103	95	30

Figure 53A: CPA.9.086

What	sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVETGGGLIQGRSLRLSCAASGFTSSYAMHWVRQAPGKGLWVAVISYAGEVKYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARDPLPLHYGMDVWVGQGTITVSS	160
vhCDR1	GFTSSYA	161
vhCDR2	ISYAGEVK	162
vhCDR3	ARDPLPLHYGMDV	163
Full length HC (IgG4(S241P))	EVQLVETGGGLIQGRSLRLSCAASGFTSSYAMHWVRQAPGKGLWVAVISYAGEVKYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARDPLPLHYGMDVWVGQGTITVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTWSWN SGALTSGVHTFPAVLQSSGLYSLSVTVTPSSSLGTKTYTCNVDPKPSNTKVDKRVESKYGPPCPAPAEFLGGPSVFLFPPK PKDTLMISRTPEVTCVVDVDSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVWSVLTVLHQDWLNGKEYKCKVSNK GLPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGGSFFLYSRL TVDKSRWQEGNVPFSCVMHEALHNHYTQKSLSLSPGK	164
Variable light (vl) domain	QSALTQPRASGNPGRVTISCSGSSNMGRRPVNWYQQIPGTAPKLLIYSQNQRPSGVPDRFSGSQSGTSASLTISGLQSE DEAEYFCVWDDIGRVLQLGGGTQLAVLG	165
vlCDR1	SSNMGRRP	166
vlCDR2	SQN	167
vlCDR3	AVWDDIGRVLQ	168
Full length light chain	QSALTQPRASGNPGRVTISCSGSSNMGRRPVNWYQQIPGTAPKLLIYSQNQRPSGVPDRFSGSQSGTSASLTISGLQSE DEAEYFCVWDDIGRVLQLGGGTQLAVLGQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVE TTTPSKQSNKNKYAASSVLSLTPEQWKSRSYSCQVTHEGSTVEKTVAPTECS	169

Figure 53B: CPA.9.083

What	sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVETGGGLIQGRSLRLSCAASGFTSSYAMHWVRQAPGKGLEWVAVISYDGTPTVYADSVKGRFTISRDN SKNTLYLQ MNSLRAEDTAVYVCARDPLPLHYYGMDVWVGQGTITVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWN	150
vhCDR1	GFTSSYA	151
vhCDR2	ISYDGTPTV	152
vhCDR3	ARDPLPLHYYGMDV	153
Full length HC (IgG4(S241P))	EVQLVETGGGLIQGRSLRLSCAASGFTSSYAMHWVRQAPGKGLEWVAVISYDGTPTVYADSVKGRFTISRDN SKNTLYLQ MNSLRAEDTAVYVCARDPLPLHYYGMDVWVGQGTITVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWN SGALTSVHTFPAVLQSSGLYSLSVTVTPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPAPEFLGGPSVFLFPPK PKDTLMISRTPEVTCVVDVDSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVWSVLTVLHQDWLNGKEYCKVSNK GLPSSIEKTIKAKGQPREPQWYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGGSFFLYSRL TVDKSRWQEGNVPFSCVMHEALHNHYTQKSLSLSPGK	154
Variable light (vl) domain	QSALTQPRASGNPGQRVTISCSGSSNMGRRPVNWYQQIPGTAPKLLIYSQNRPSGVPDFRSGSQSGTSASLTISGLQSE DEAEYFCVWVDGDRRSLLQLGGGTQLAVLG	155
vlCDR1	SSNMGRRP	156
vlCDR2	SQN	157
vlCDR3	AVWVDGDRRSLLQ	158
Full length light chain	QSALTQPRASGNPGQRVTISCSGSSNMGRRPVNWYQQIPGTAPKLLIYSQNRPSGVPDFRSGSQSGTSASLTISGLQSE DEAEYFCVWVDGDRRSLLQLGGGTQLAVLGQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGV ETTPSKQSNKYYAASSYLSLTPEQWKSHRYSYSCQVTHEGSTVEKTVAPTECS	159

Figure 53C: CHA.9.547.13

What	Sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSYIMSWVRQAPGKGLWVATISGGGTNTYYADSVKGRFTISRDN SKN TLYLQMNSLRAEDTAVYYCAKWLSSYYAMDYWGQGTLVTVSS	560
vhCDR1	GFTFSYIMS	561
vhCDR2	TISGGGTNTY	562
vhCDR3	WLLSSYYAMIDY	563
Full length HC	EVQLVESGGGLVQPGGSLRLSCAASGFTFSYIMSWVRQAPGKGLWVATISGGGTNTYYADSVKGRFTISRDN SKN TLYLQMNSLRAEDTAVYYCAKWLSSYYAMDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPTVS WNSGALTSGVHTFPAVLQSSGLYSLSSWTVPSSSLGKTCTYCNVDHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVSVLTVHLQDWWLNGKEYCKV SNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLY SRLTVDKSRWQEGNVPFSCSVMEALHNHYTQKSLSLSPGK	564
Variable light (vl) domain	DIQMTQSPSSLSASVGDRTITTCRASQININWLSWYQQKPGKAPKLLIYKASKSHTGVPSRFSGSGSGTDFLTISS LQPEDFATYYCQQGQSYPTFGQGTKEIK	565
vlCDR1	RASQININWLS	566
vlCDR2	KASKSHT	567
vlCDR3	QQGQSYPT	568
Full length light chain	DIQMTQSPSSLSASVGDRTITTCRASQININWLSWYQQKPGKAPKLLIYKASKSHTGVPSRFSGSGSGTDFLTISS LQPEDFATYYCQQGQSYPTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	569

Figure 54

Antibody	Date	$K_D \pm 95\%$ Confidence Interval of the Fit
BM26	12/12/2016	490 pM $\pm$ 80 pM
BM29	12/12/2016	760 pM $\pm$ 180 pM
CPA.9.027	10/18/2016	170 pM $\pm$ 40 pM
CPA.9.049	7/21/2016	260 pM $\pm$ 170 pM
CPA.9.059	10/18/2016	290 pM $\pm$ 110 pM
CHA.9.536	12/12/2016	880 pM $\pm$ 260 pM
CHA.9.541	12/12/2016	1.24 nM $\pm$ 470 pM
CHA.9.543	12/12/2016	10.2 nM $\pm$ 3.27 nM
CHA.9.546	12/12/2016	1.22 nM $\pm$ 390 pM
CHA.9.547	12/12/2016	720 pM $\pm$ 200 pM
CHA.9.560	12/12/2016	1.02 nM $\pm$ 210 pM

Figure 55

Antibody	Date	$K_D \pm 95\%$ Confidence Interval of the Fit	
		K_D	Interval of the Fit
BM26	12/12/2016	670 pM $\pm$ 240 pM	
BM29	12/12/2016	Not Reliable Fit	
CPA.9.027	10/18/2016	2.25 nM $\pm$ 760 pM	
CPA.9.049	7/21/2016	1.88 nM $\pm$ 1.09 nM	
CPA.9.059	9/2/2016	No Binding	
CHA.9.536	12/12/2016	2.15 nM $\pm$ 590 pM	
CHA.9.541	12/12/2016	2.09 nM $\pm$ 280 pM	
CHA.9.543	12/12/2016	17.2 nM $\pm$ 3.82 nM	
CHA.9.546	12/12/2016	1.36 nM $\pm$ 270 pM	
CHA.9.547	12/12/2016	1.40 nM $\pm$ 390 pM	
CHA.9.560	12/12/2016	1.84 nM $\pm$ 140 pM	

Figure 56

MAb	Human TIGIT			Cyno TIGIT			Mouse TIGIT		
	k_a (/s)	k_d (/M-s)	K_D (M)	k_a (/s)	k_d (/M-s)	K_D (M)	k_a (/s)	k_d (/M-s)	K_D (M)
CPA.9.027	1.94E+06	2.51E-04	1.30E-10			Complex Kinetics	4.50E+05	3.60E-02	8.00E-08
CPA.9.049	1.68E+06	1.58E-04	9.45E-11			Complex Kinetics	4.65E+05	3.85E-02	8.27E-08
CPA.9.059	1.88E+06	4.01E-05	2.13E-11			Complex Kinetics			N/A
CHA.9.536	8.81E+05	*1.00E-05	1.13E-11	1.18E+06	2.90E-04	2.45E-10			No binding
CHA.9.541	4.51E+05	3.64E-05	8.08E-11	1.75E+06	*1.00E-05	5.73E-12			No binding
CHA.9.543	1.97E+06	4.54E-05	2.31E-11	6.46E+06	*1.00E-05	1.55E-12			No binding
CHA.9.546	1.19E+06	2.68E-04	2.26E-10	2.20E+06	1.23E-03	5.56E-10			No binding
CHA.9.547	2.69E+06	1.03E-04	3.84E-11	3.34E+06	5.15E-04	1.54E-10			No binding
CHA.9.560	1.04E+06	1.59E-06	*1.52E-12	3.05E+06	1.90E-04	6.23E-11			No binding
BM26	2.05E+06	4.94E-05	2.41E-11	7.99E+06	*1.00E-05	1.25E-12			No binding
BM29	1.63E+06	2.45E-05	1.5E-11		Complex				No binding

Figure 57A & 57B

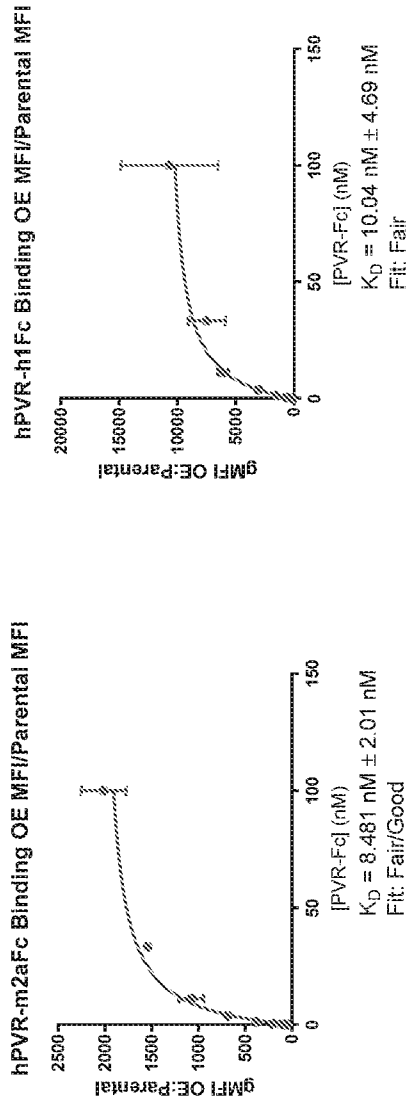


Figure 58

	6.7 nM mAb	1.3 nM mAb	266 pM mAb
Antibody	Blocking (Yes/No)	Blocking (Yes/No)	Blocking (Yes/No)
BM26	Yes	Yes	Yes
Synagis	No	No	No
CPA.9.027	Yes	Yes	Yes
CPA.9.049	Yes	Yes	Yes
CPA.9.059	Yes	Yes	Yes
	gMFI	gMFI	gMFI
BM26	234	401	719
Synagis	828	964	959
CPA.9.027	208	253	529
CPA.9.049	215	276	511
CPA.9.059	209	262	509

Figure 59

Antibody	Date Tested	IC50 (nM)
BM26	12/10/2016	0.37
BM29	12/10/2016	0.60
CHA.9.536	12/10/2016	0.92
CHA.9.541	12/10/2016	1.24
CHA.9.546	12/10/2016	0.63
CHA.9.547	12/10/2016	0.49
CHA.9.560	12/10/2016	1.12

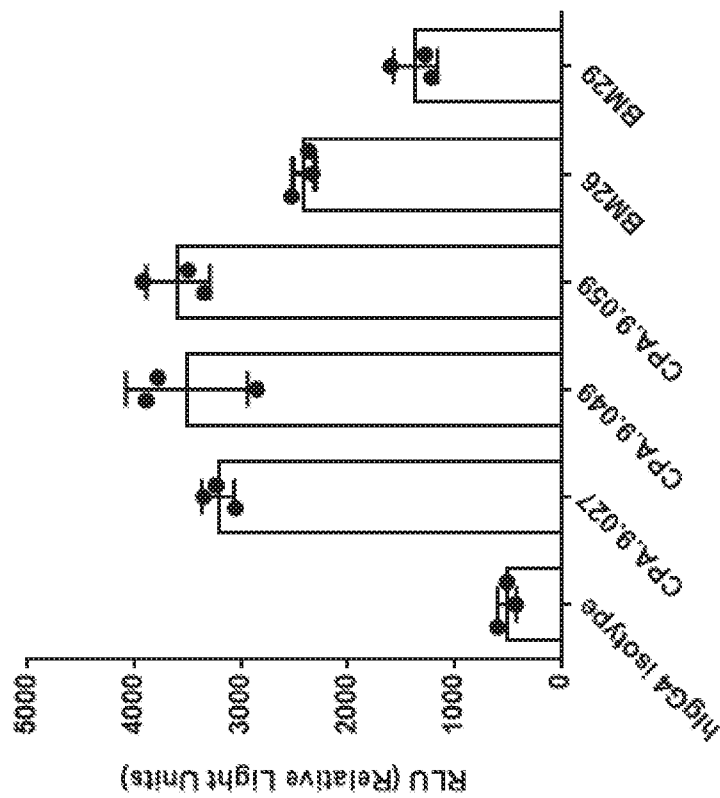
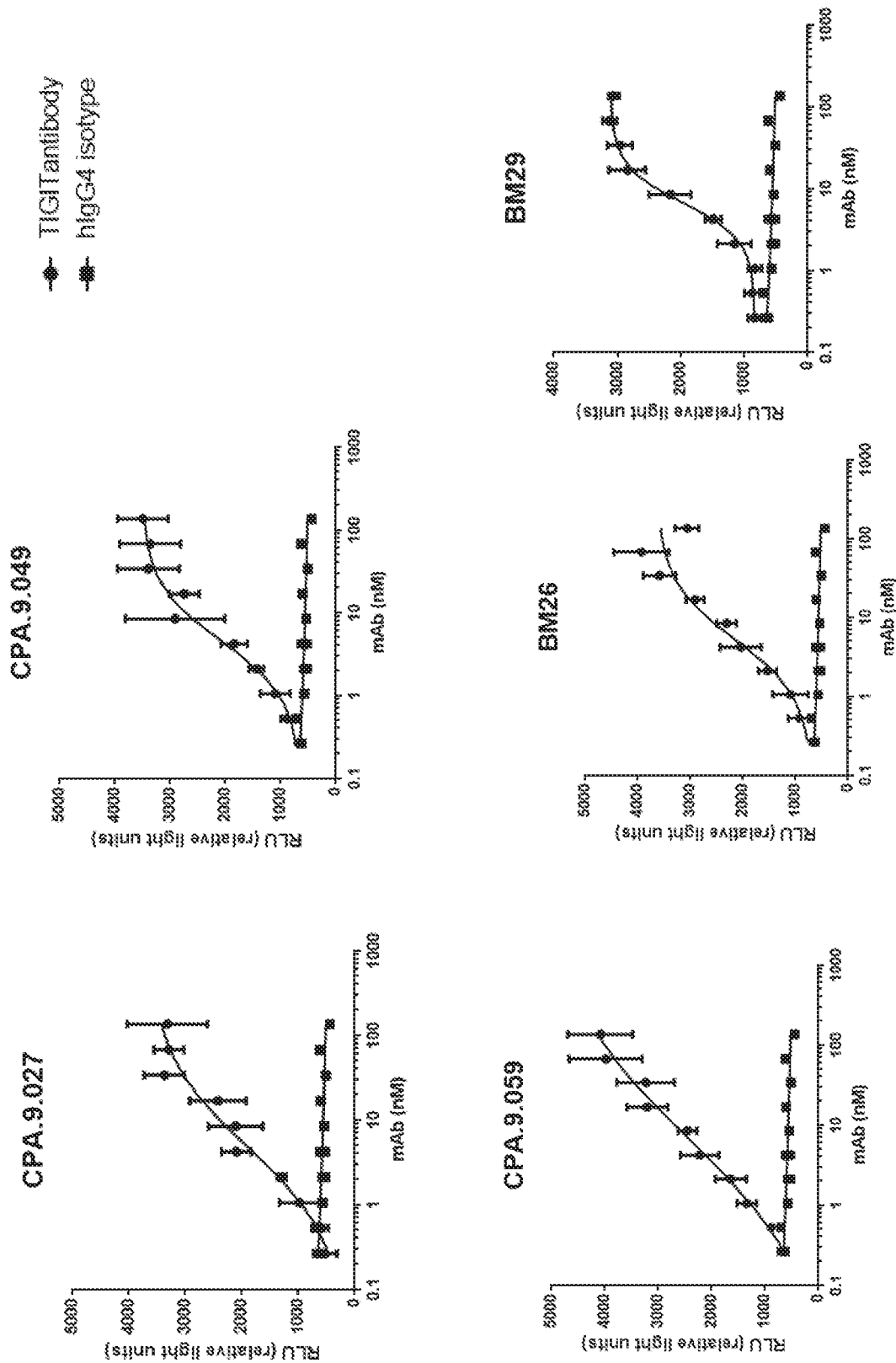


Figure 60

Figure 61



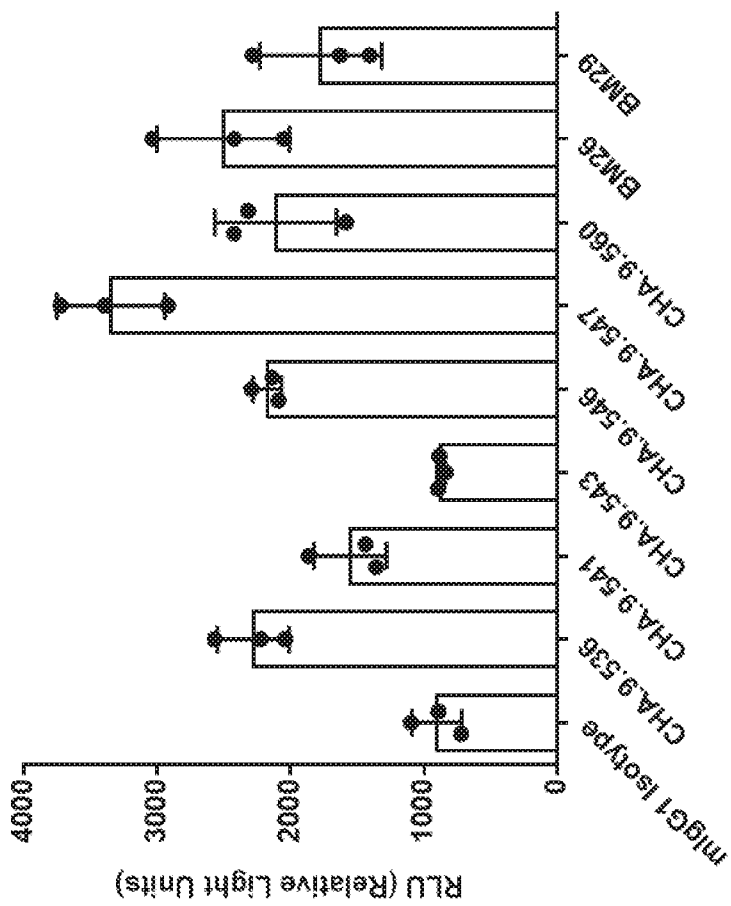


Figure 62

◆ TIGIT antibody
■ mIgG1 isotype

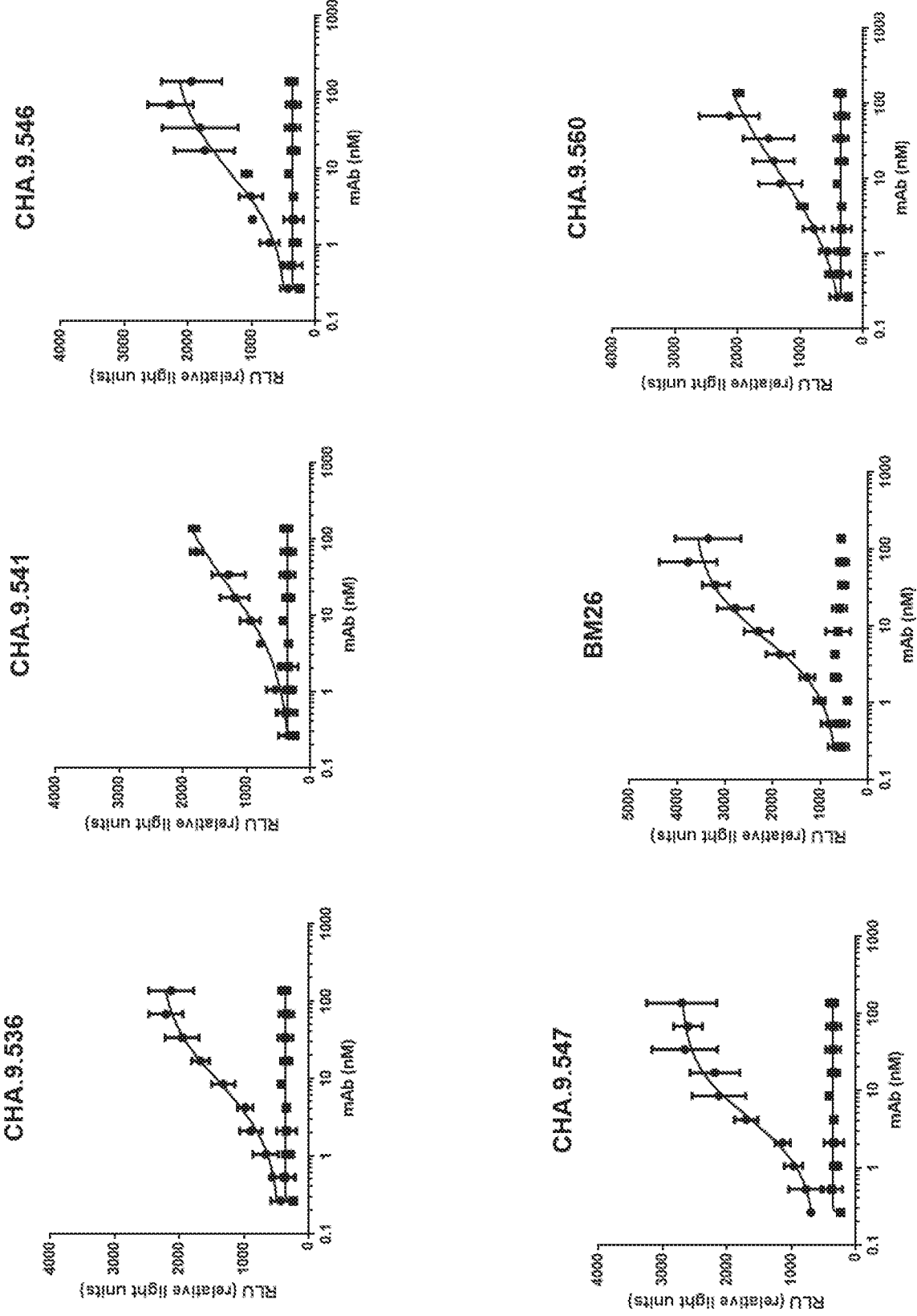


Figure 63

Figure 64

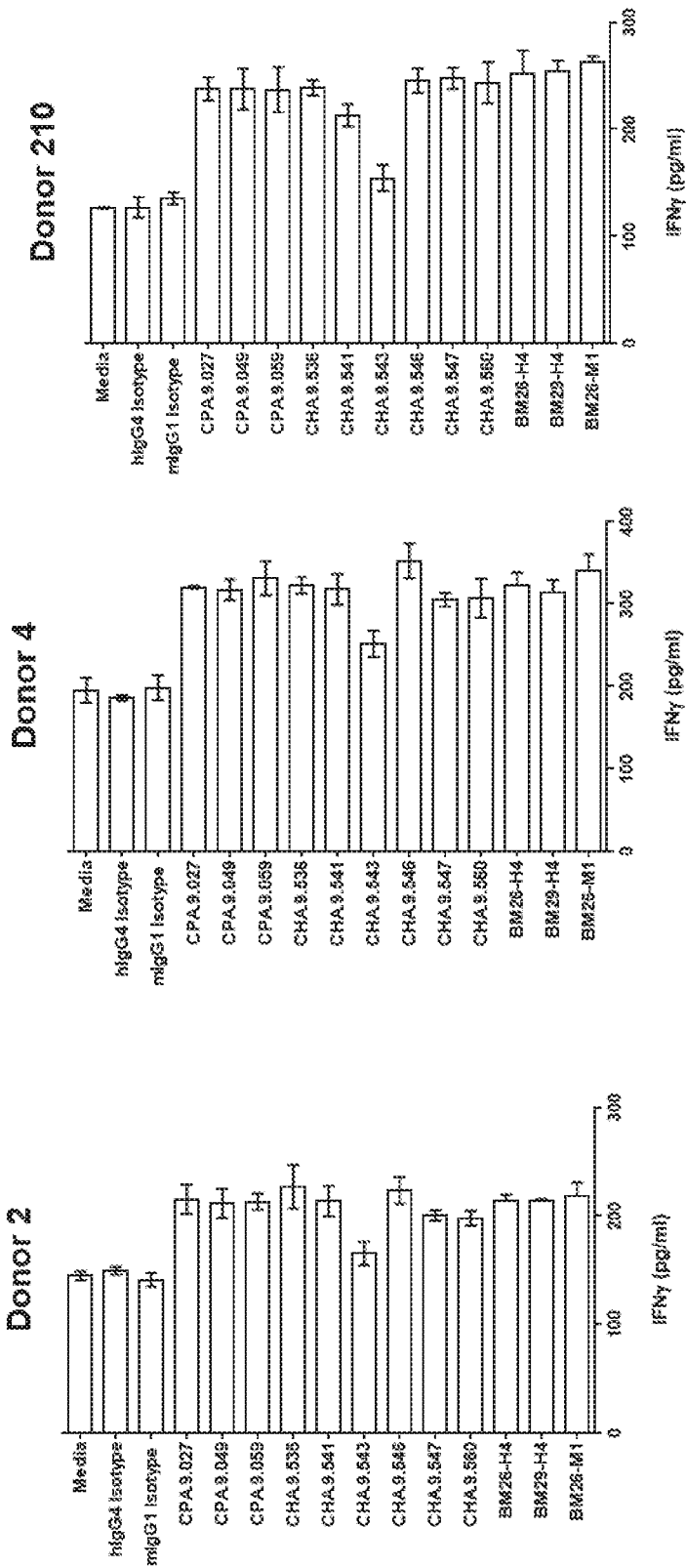


Figure 65

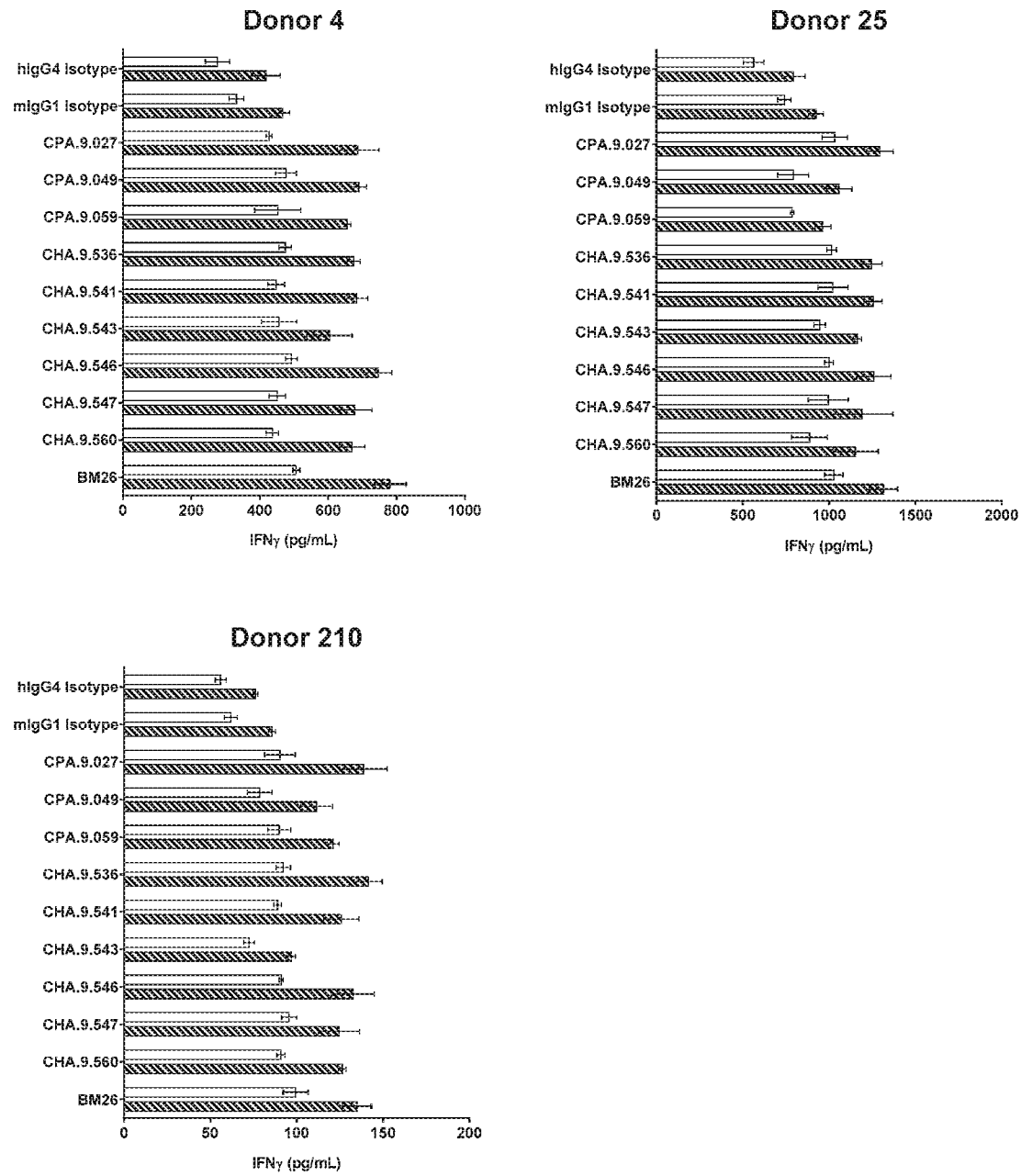


Figure 66

	Average of 3 Donors	
	Monotherapy	Combo with CHA.7.518.1
CHA.7.518.1 + hlgG4 Isotype	 43	
CPA.9.027-H4	 66	 142
CPA.9.049-H4	 51	 112
CPA.9.059-H4	 55	 108
CHA.7.518.1 + mlgG1 Isotype	 39	
CHA.9.536-M1	 43	 100
CHA.9.541-M1	 39	 93
CHA.9.543-M1 (Non-blocker)	 27	 65
CHA.9.546-M1	 43	 103
CHA.9.547-M1	 47	 96
CHA.9.560-M1	 38	 94
BM26	 49	 107

Figure 67

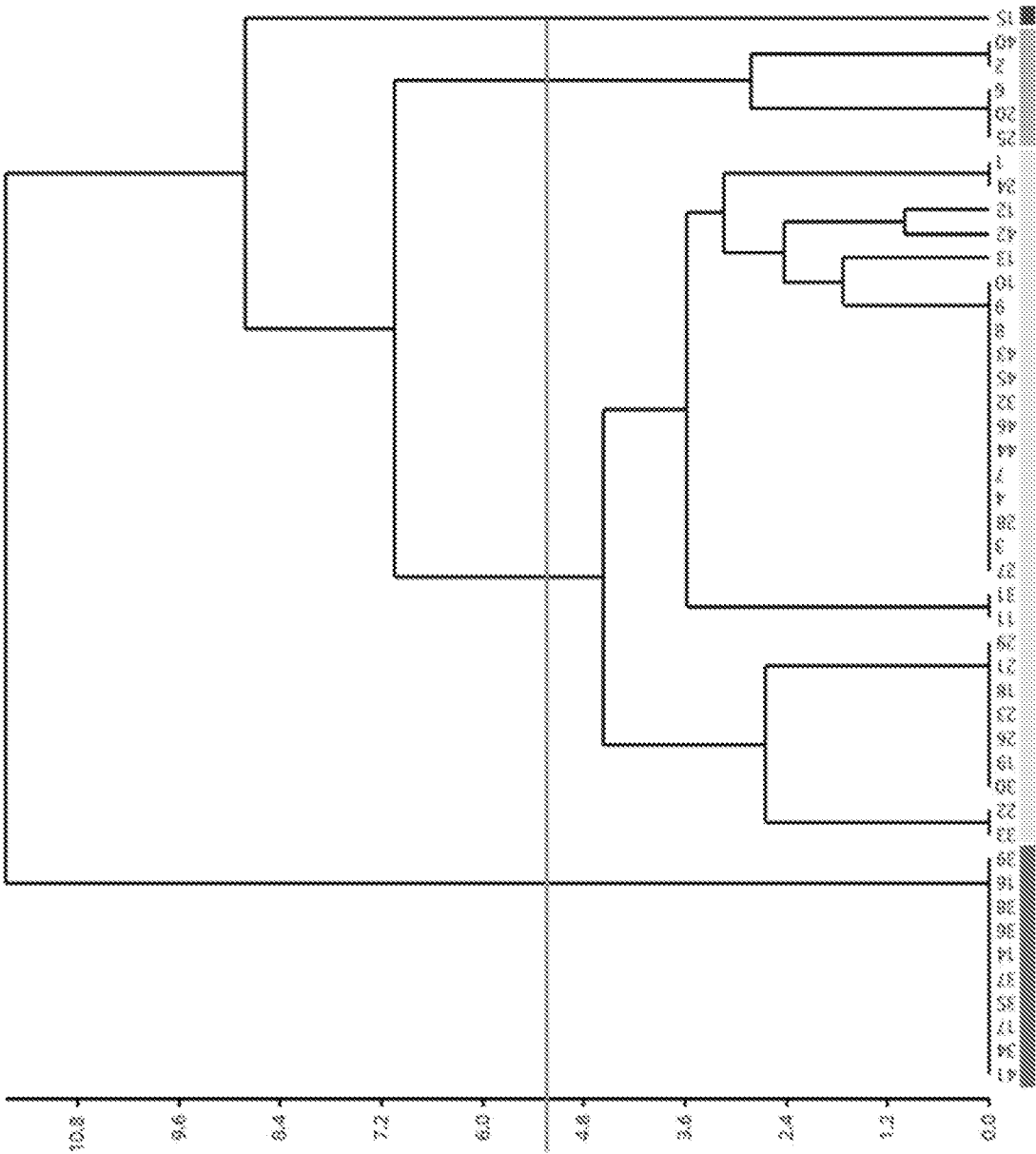


Figure 68

41 BM9-H4 34 CHA.9.525 17 CPA.9.081-H4 35 CHA.9.538 37 CHA.9.553 14 CPA.9.069-H4 36 CHA.9.543 38 CHA.9.556 16 CPA.9.077-H4 39 CHA.9.561	33 CHA.9.560 22 CHA.9.528 30 CHA.9.552 19 CHA.9.521 26 CHA.9.541 23 CHA.9.529 18 CHA.9.519 21 CHA.9.527 29 CHA.9.549 11 CPA.9.057-H4 31 CHA.9.554	27 CHA.9.546 3 CPA.9.012-H4 28 CHA.9.547 4 CPA.9.013-H4 7 CPA.9.018-H4 44 MBSA43-M1 46 Sino PVR-Fc (ligand) 32 CHA.9.555 45 PVR-Fc M2A (ligand) 43 BM29-H4 8 CPA.9.027-H4 9 CPA.9.049-H4 10 CPA.9.053-H4 13 CPA.9.064-H4 42 BM26-H4 12 CPA.9.059-H4 24 CHA.9.535 1 CPA.9.009-H4	25 CHA.9.536 20 CHA.9.522 6 CPA.9.015-H4 2 CPA.9.011-H4 40 BM8-H4 15 CPA.9.071-H4
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Figure 69

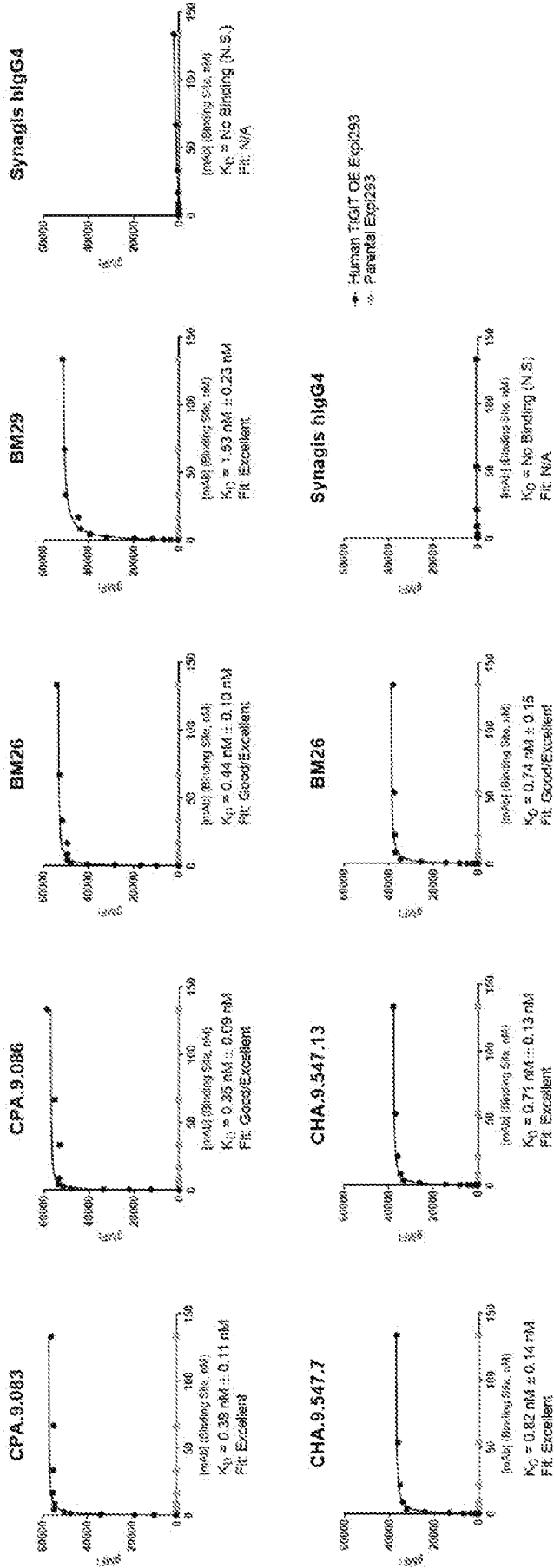


Figure 70

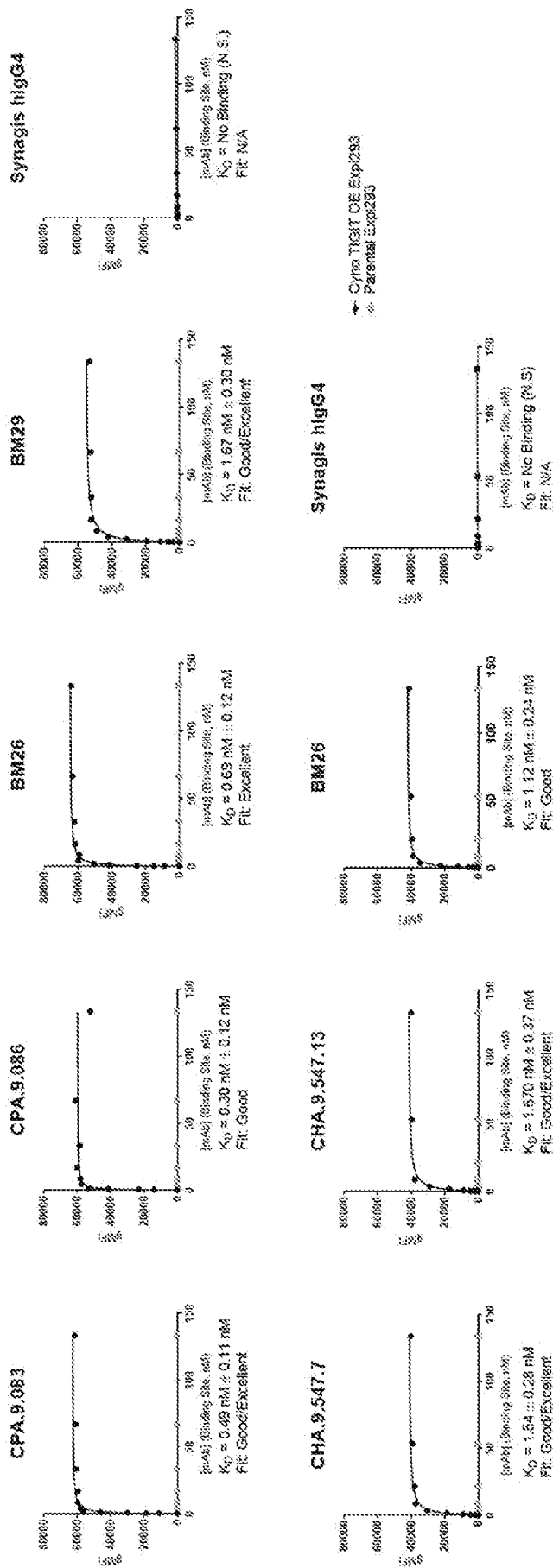


Figure 71

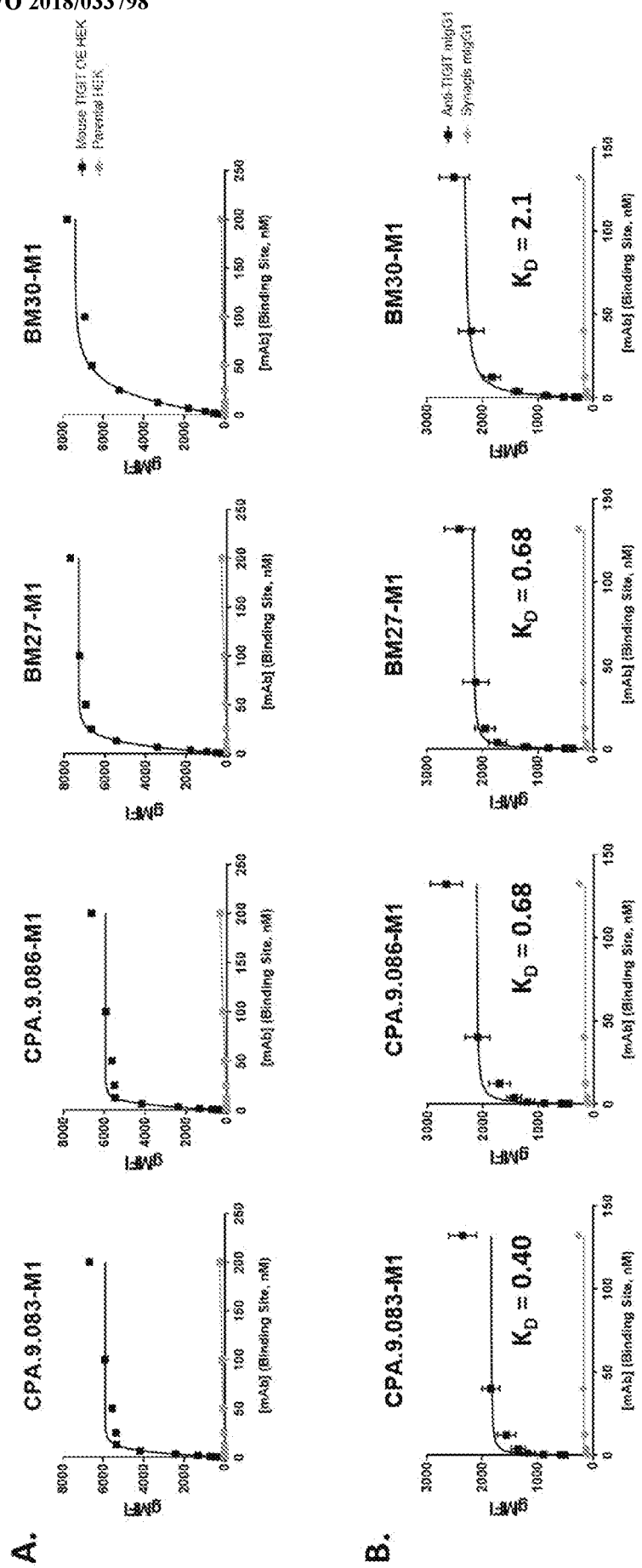
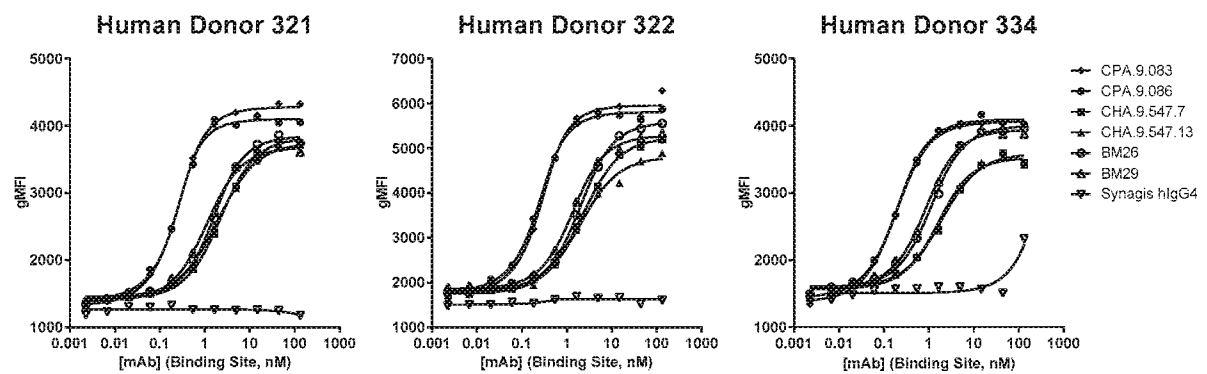
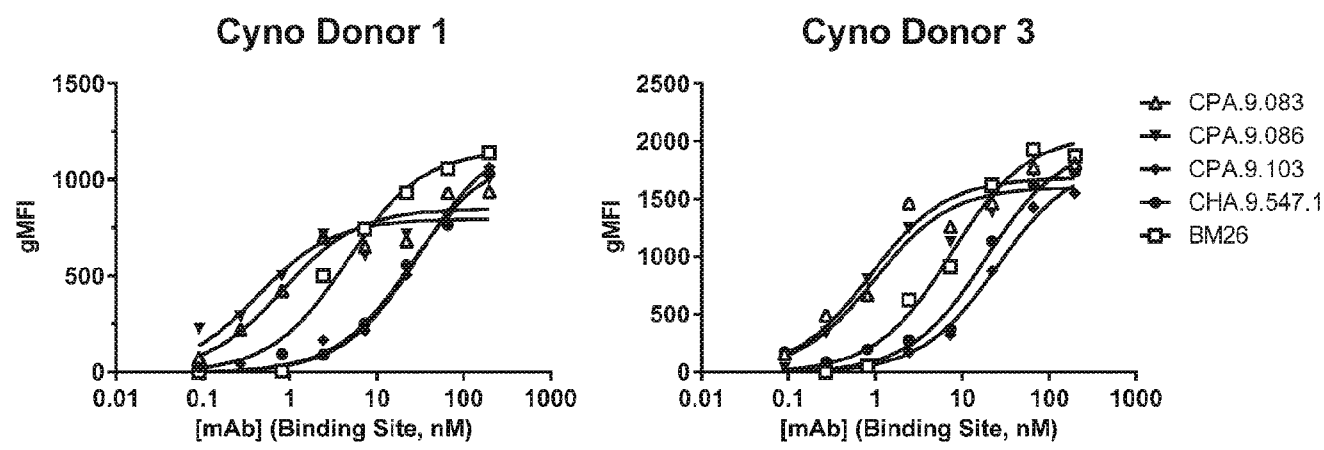


Figure 72



Anti-TIGIT Ab	K _D CD8 ⁺ Tem (nM)		
	Donor 321	Donor 322	Donor 334
CPA.9.083	0.13	0.12	0.13
CPA.9.086	0.09	0.11	0.13
CHA.9.547.7	1.8	2.1	1.8
CHA.9.547.13	2.0	1.9	1.2
BM26	0.93	1.4	0.81
BM29	0.88	0.91	0.59

Figure 73

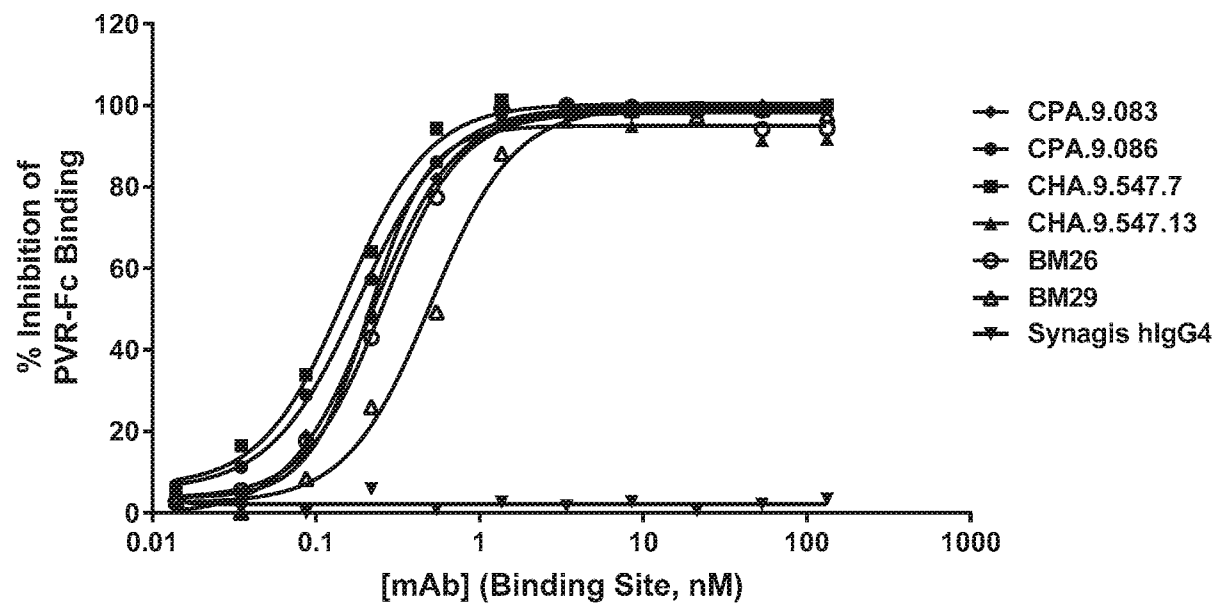


Anti-TIGIT Ab	K_D	K_D
	CD8 ⁺ Tem Donor 1 (nM)	CD8 ⁺ Tem Donor 3 (nM)
CPA.9.083	0.82	0.88
CPA.9.086	0.43	0.98
CPA.9.103	31	25
CHA.9.547.1	25	19
BM26	4.6	7.5

Figure 74

Name	Human TIGIT-His				Cyno TIGIT-His				Mouse TIGIT-His			
	k_a [1/s]	K_d [1/M-s]	K_D [pM]		k_a [1/s]	K_d [1/M-s]	K_D [pM]		k_a [1/s]	K_d [1/M-s]	K_D [pM]	
CPA.9.083	6.00E+06	1.00E-05	1.7		Complex kinetics				2.73E+06	1.19E-03	434	
CPA.9.086	4.40E+06	1.00E-05	2.3		Complex kinetics				1.83E+06	1.21E-03	663	
CPA.9.103	2.48E+06	1.60E-05	6.4		1.63E+06	5.50E-04	337		1.60E+07	0.4	25,000	
CHA.9.547.1	2.47E+06	2.42E-04	98		1.03E+06	1.17E-03	1131		No binding			
CHA.9.547.7	1.60E+06	5.51E-05	35		7.45E+05	3.40E-04	456		No binding			
BM26	2.50E+06	1.00E-05	4.0		2.83E+06	1.00E-05	3.5		No binding			
BM29	9.10E+05	1.00E-05	11		3.45E+06	5.30E-03	1537		No binding			

Figure 75



Anti-TIGIT Ab	IC ₅₀ Binding site (nM), n=1	IC ₅₀ Binding site (nM), n=2
CPA.9.083	0.47	0.22
CPA.9.086	0.36	0.18
CHA.9.547.7	0.21	0.15
CHA.9.547.13	0.26	0.21
BM26	0.45	0.26
BM29	1.0	0.50

Figure 76

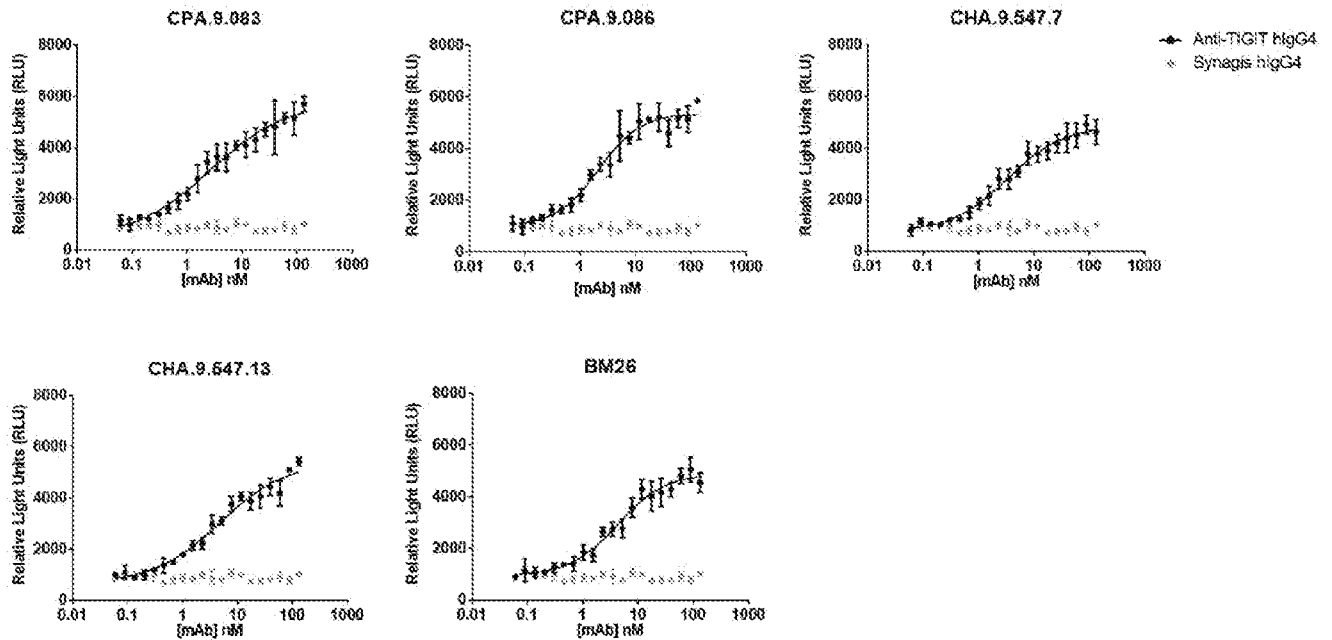
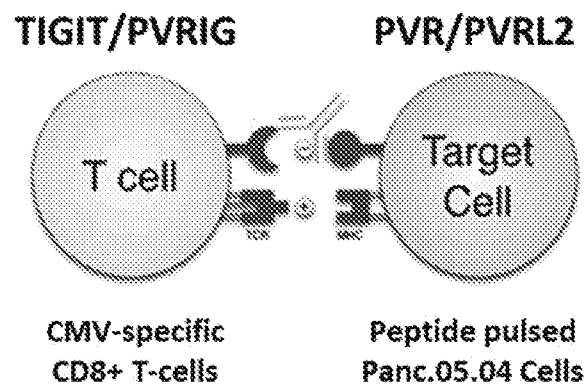
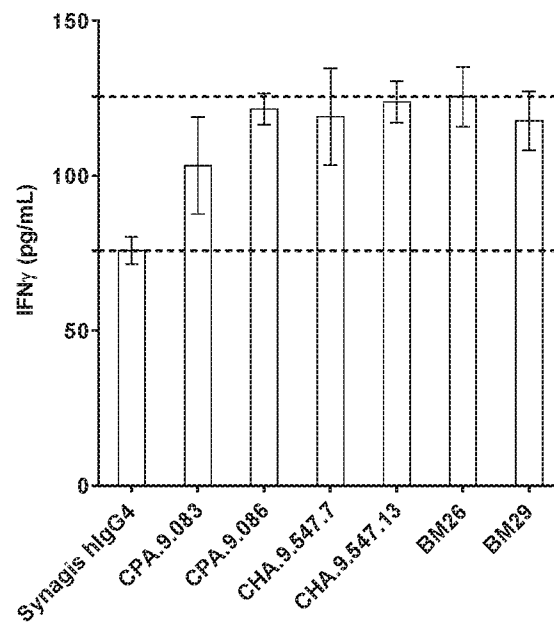
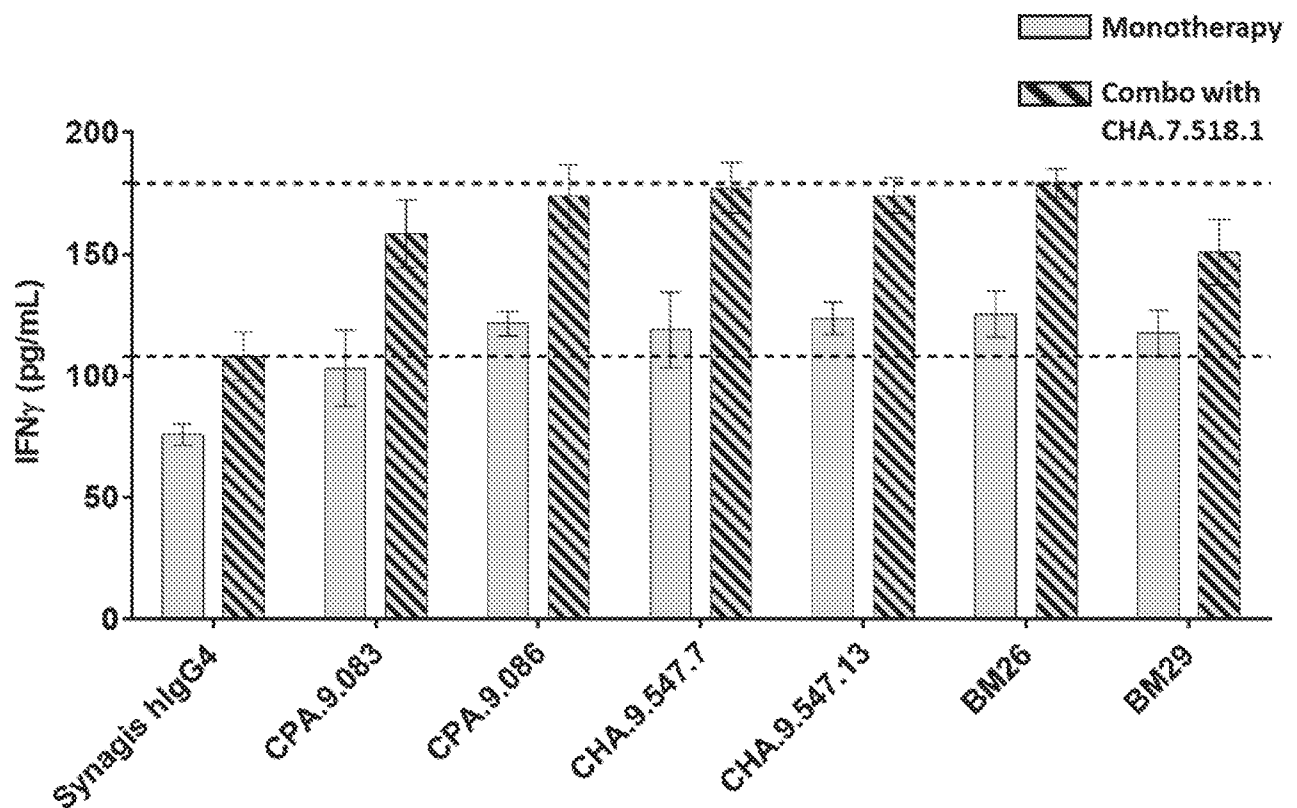


Figure 77



	Donor 4 (n=1)	Donor 4 (n=2)
CPA.9.083	36	111
CPA.9.086	60	100
CHA.9.547.7	57	125
CHA.9.547.13	63	108
BM26	65	84
BM29	55	103

Figure 78



	Donor 4 (n=1)	Donor 4 (n=2)
CPA.9.083	46	149
CPA.9.086	61	115
CHA.9.547.7	64	114
CHA.9.547.13	61	107
BM26	66	88
BM29	39	67

Figure 79

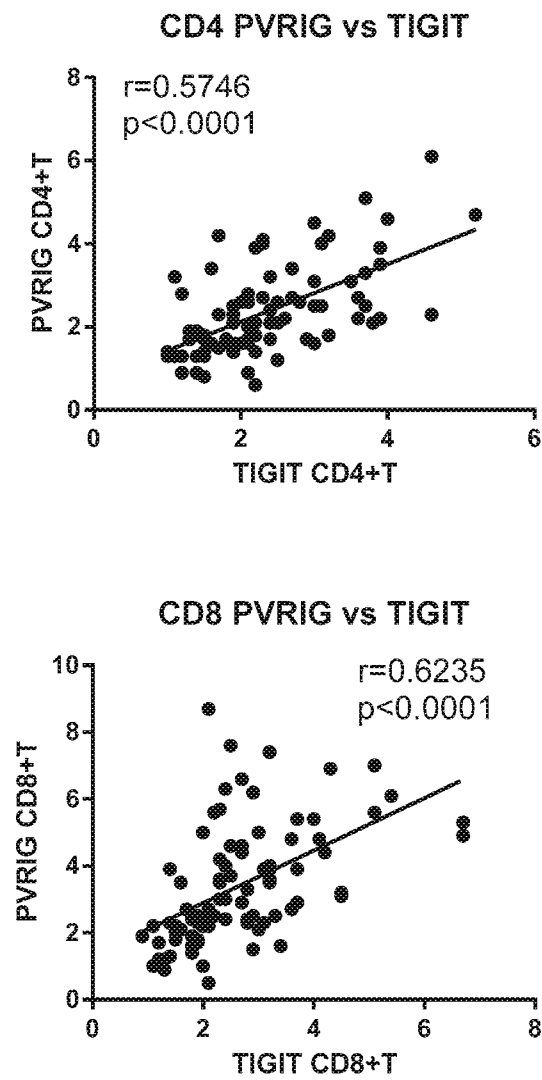


Figure 80

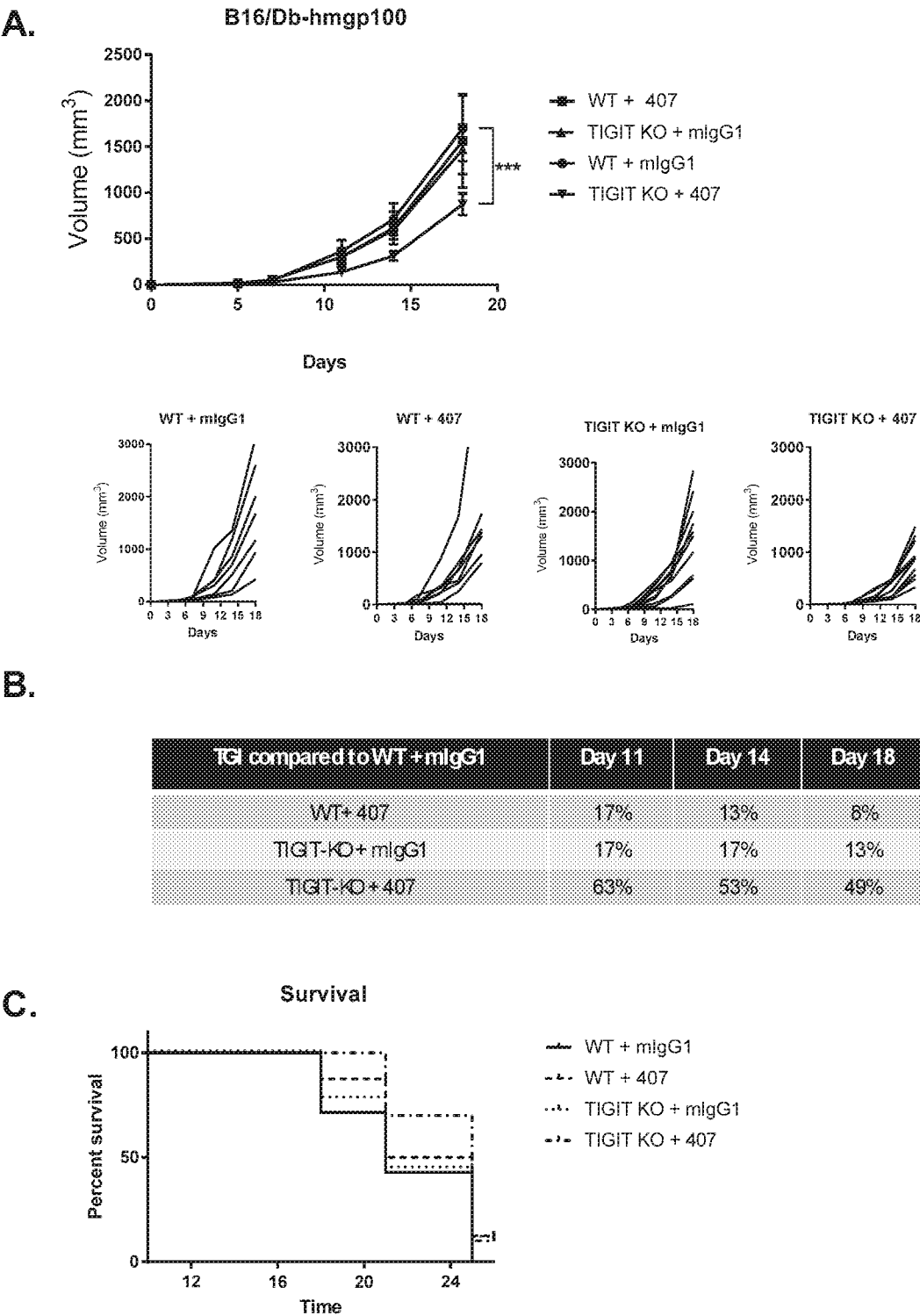


Figure 81

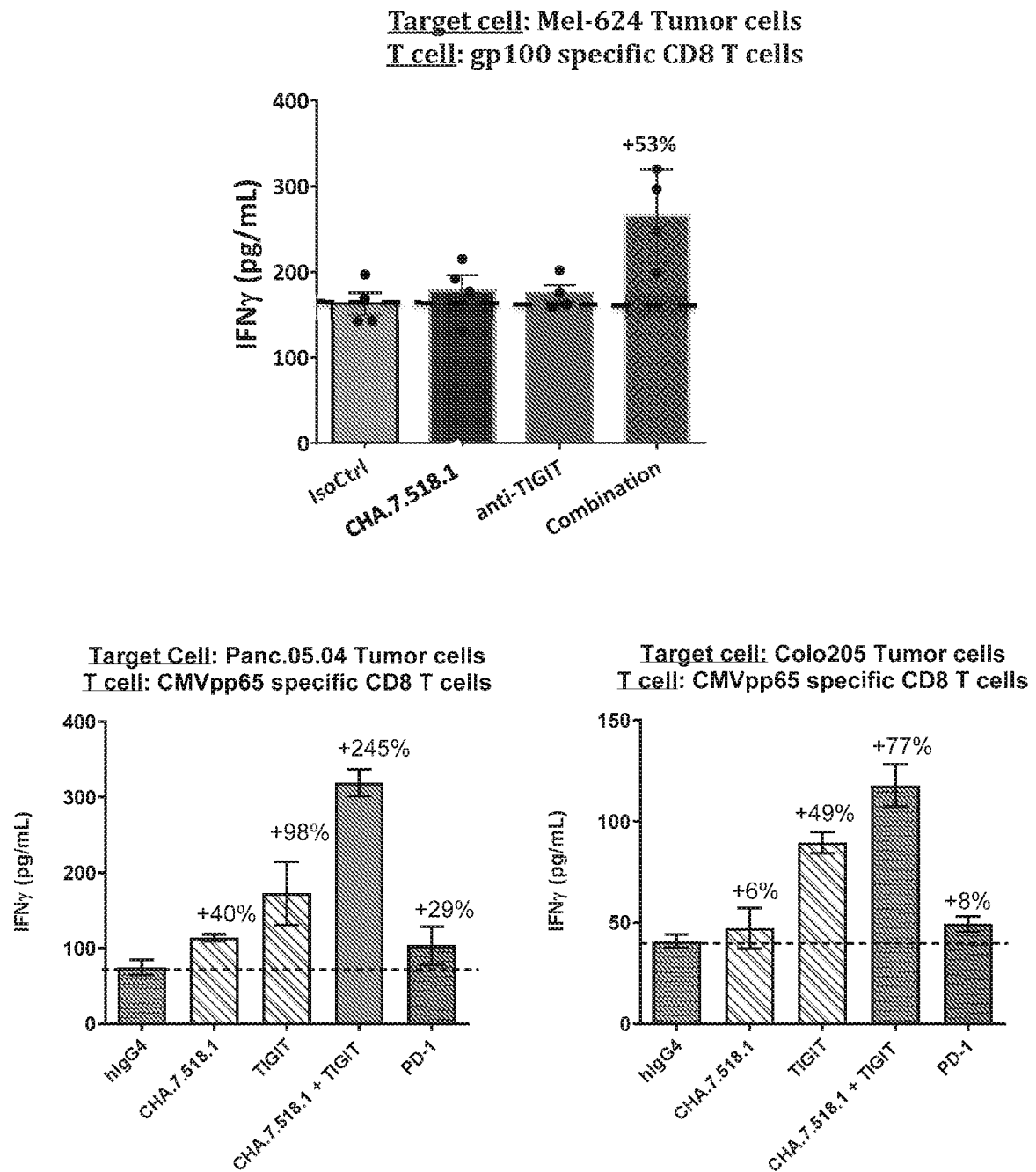


Figure 82A, 82B

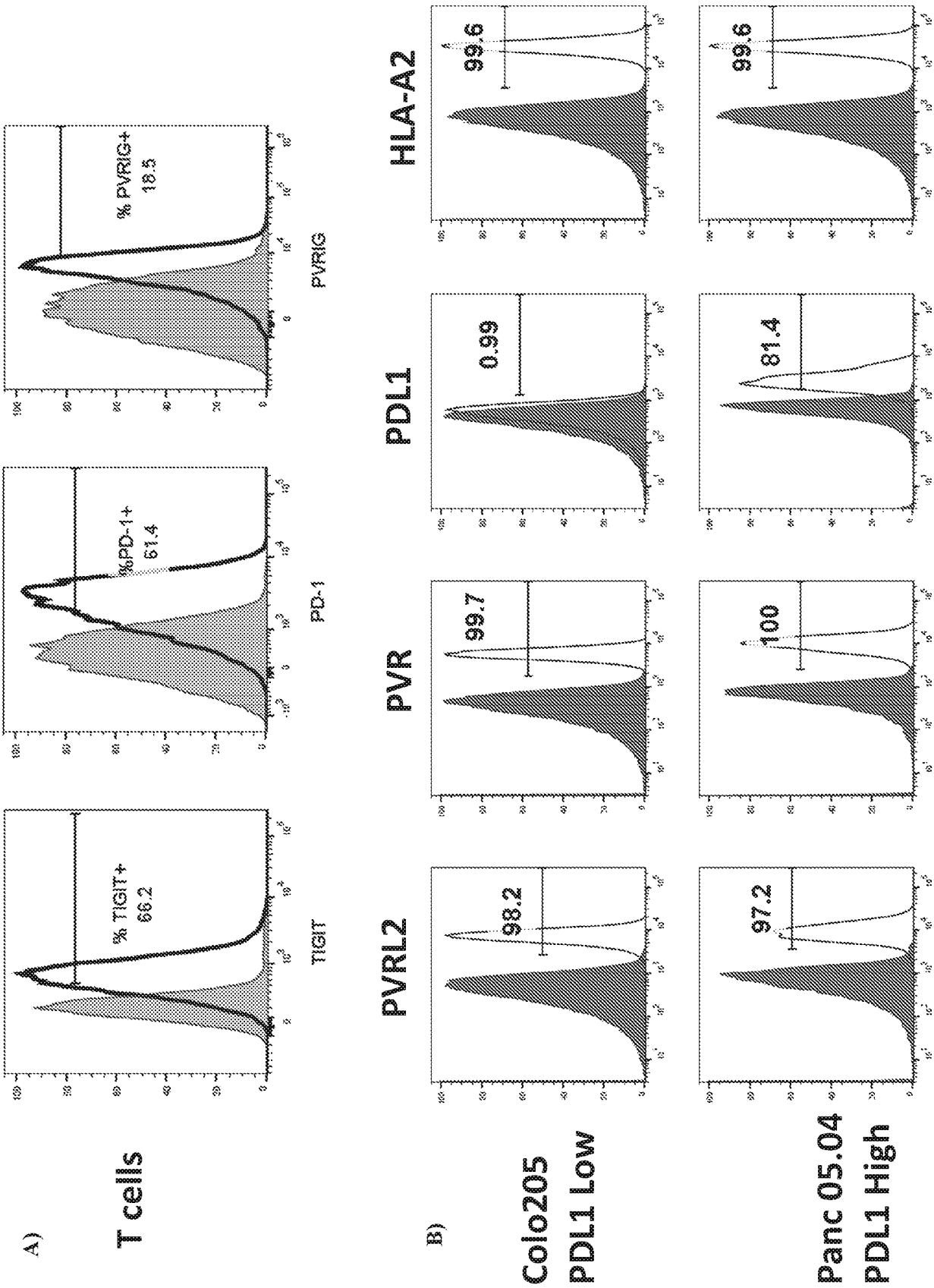


Figure 82C

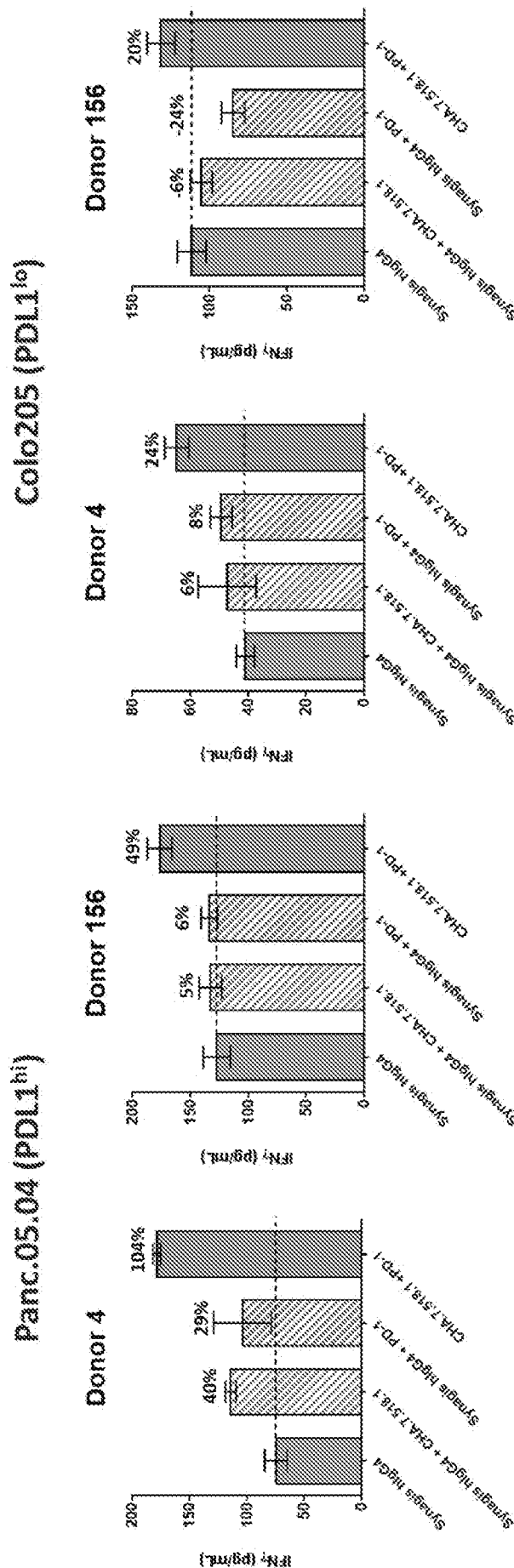


Figure 83

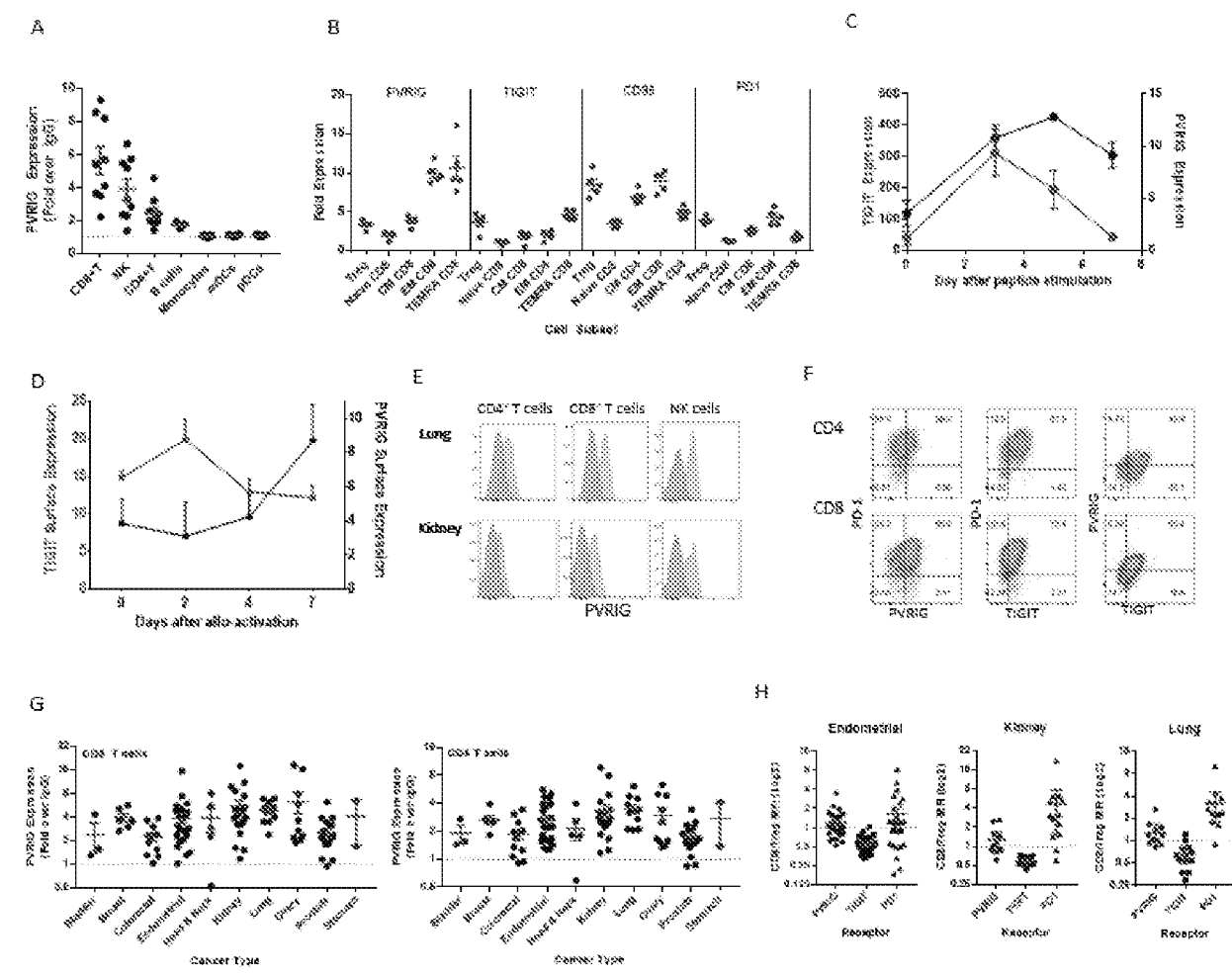


Figure 84

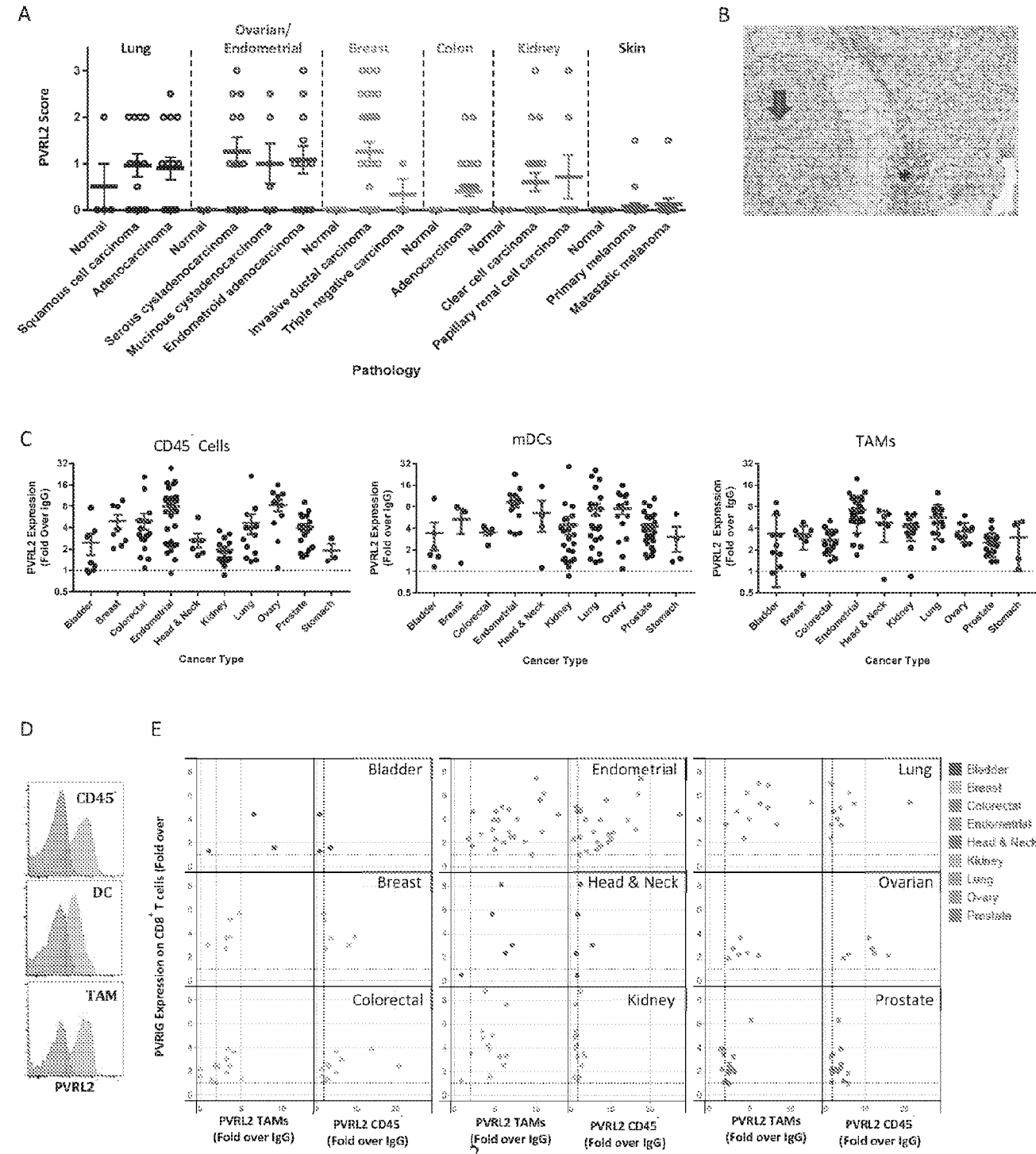


Figure 84F

	All Tumors				PD-L1+				PD-L1-		
Tissue Type	PVRL2+	Total	% Positive		PVRL2+	Total	% Positive		PVRL2+	Total	% Positive
Lung											
Normal	1	4	25		N/A	N/A	N/A		N/A	N/A	N/A
Adenocarcinoma	8	14	57		3	5	60		5	9	56
Squamous cell carcinoma	8	13	62		5	7	71		3	6	50
Ovarian											
Normal	0	2	0		N/A	N/A	N/A		N/A	N/A	N/A
Serous cystadenocarcinoma	8	12	67		2	3	67		6	9	67
Mucinous cystadenocarcinoma	4	6	67		1	1	100		3	5	60
Endometrioid adenocarcinoma	8	12	67		3	4	75		5	8	63
Colon											
Normal	0	2	0		N/A	N/A	N/A		N/A	N/A	N/A
Adenocarcinoma	16	30	53		8	14	57		7	16	44
Skin											
Normal	0	4	0		N/A	N/A	N/A		N/A	N/A	N/A
Melanoma-Primary	3	24	13		1	4	25		2	20	10
Metastatic melanoma	1	12	8		1	4	25		0	8	0
Renal											
Normal	0	3	0		N/A	N/A	N/A		N/A	N/A	N/A
Clear cell carcinoma	8	20	40		0	0	N/A		8	20	40
Papillary renal cell carcinoma	2	7	29		1	1	100		1	6	17
Breast											
TNBC	1	3	33		0	0	N/A		1	3	33
Invasive ductal carcinoma	19	30	63		6	10	60		13	20	65

Figure 85

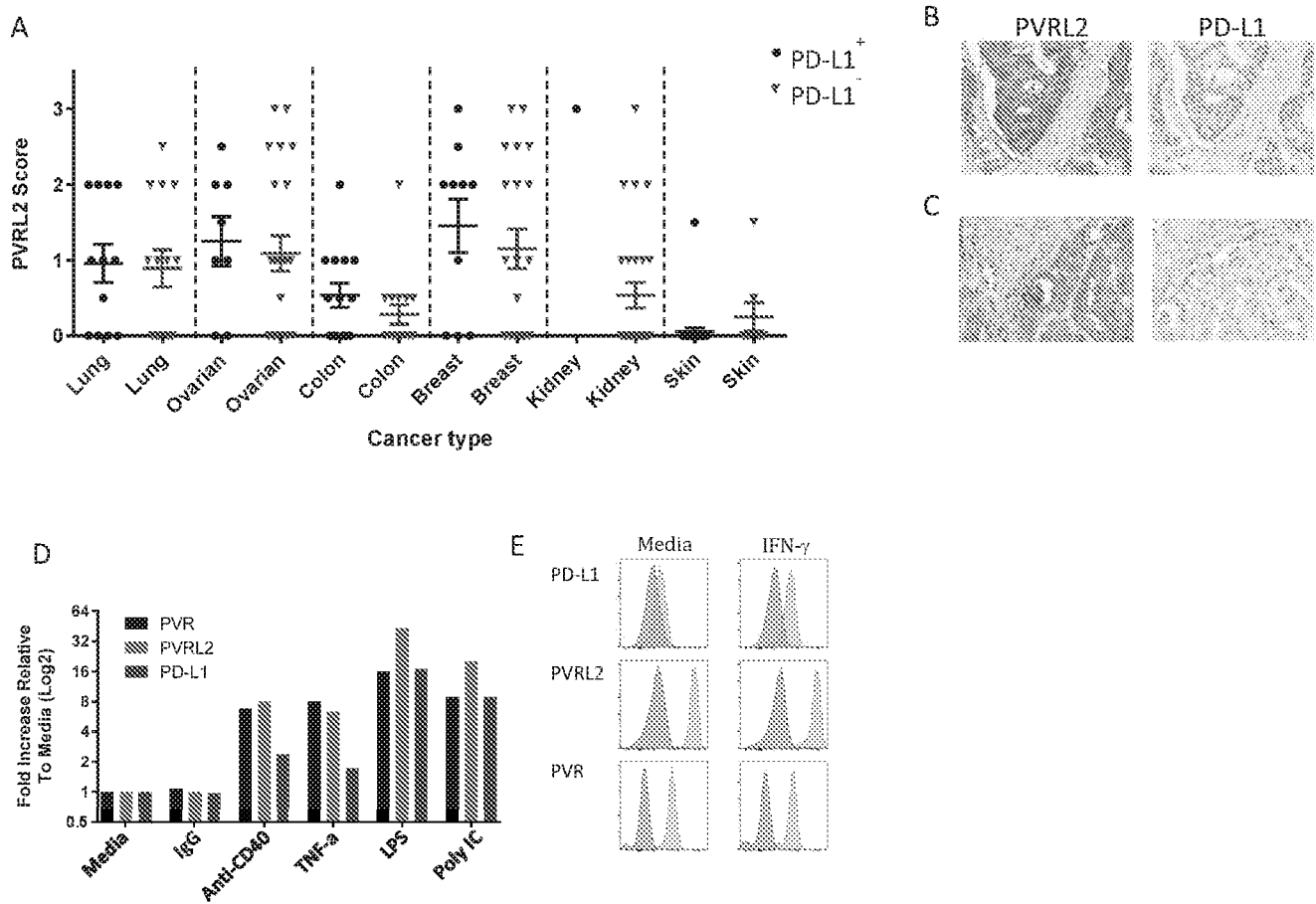


Figure 86

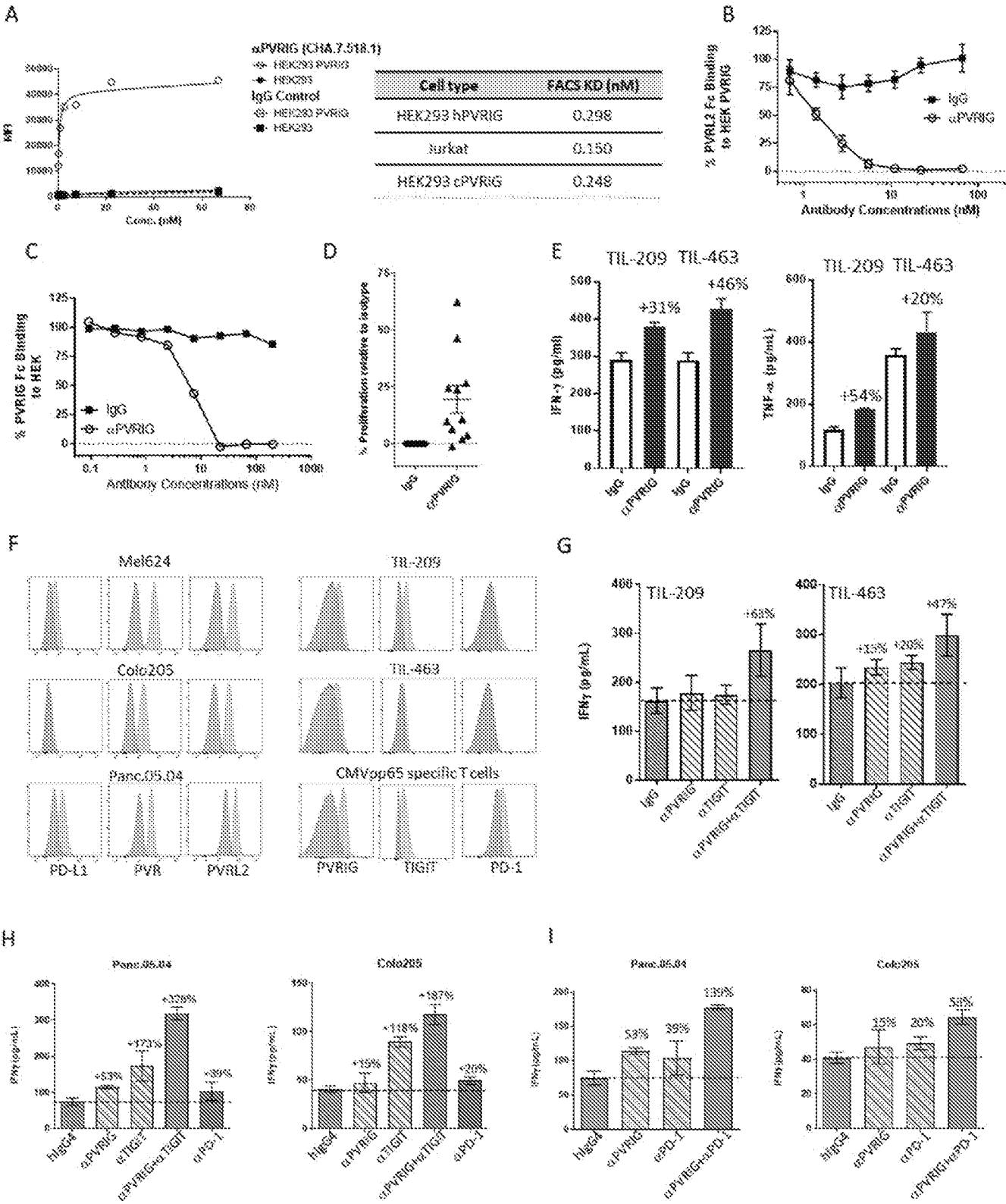


Figure 87

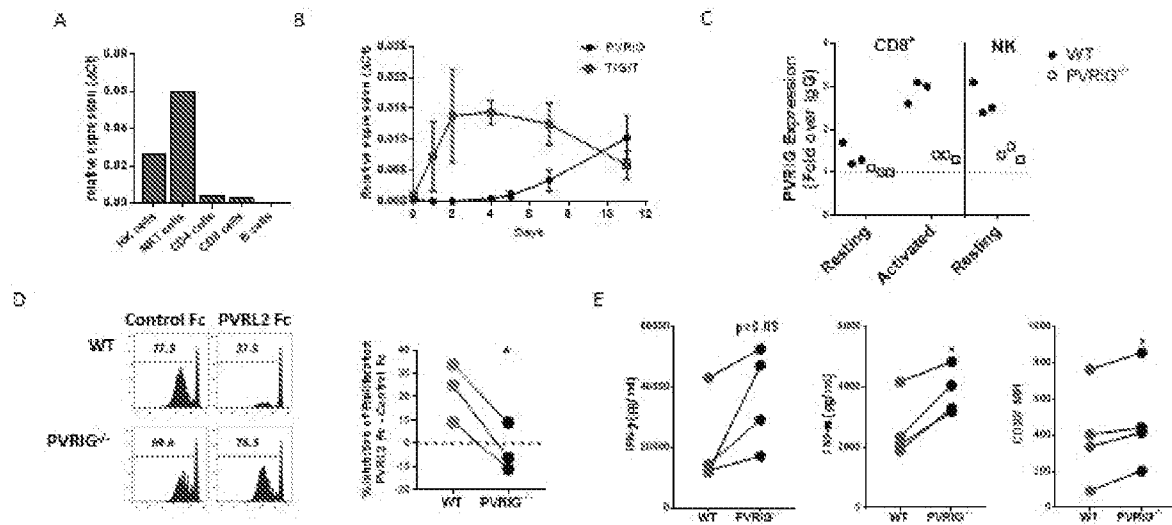


Figure 88

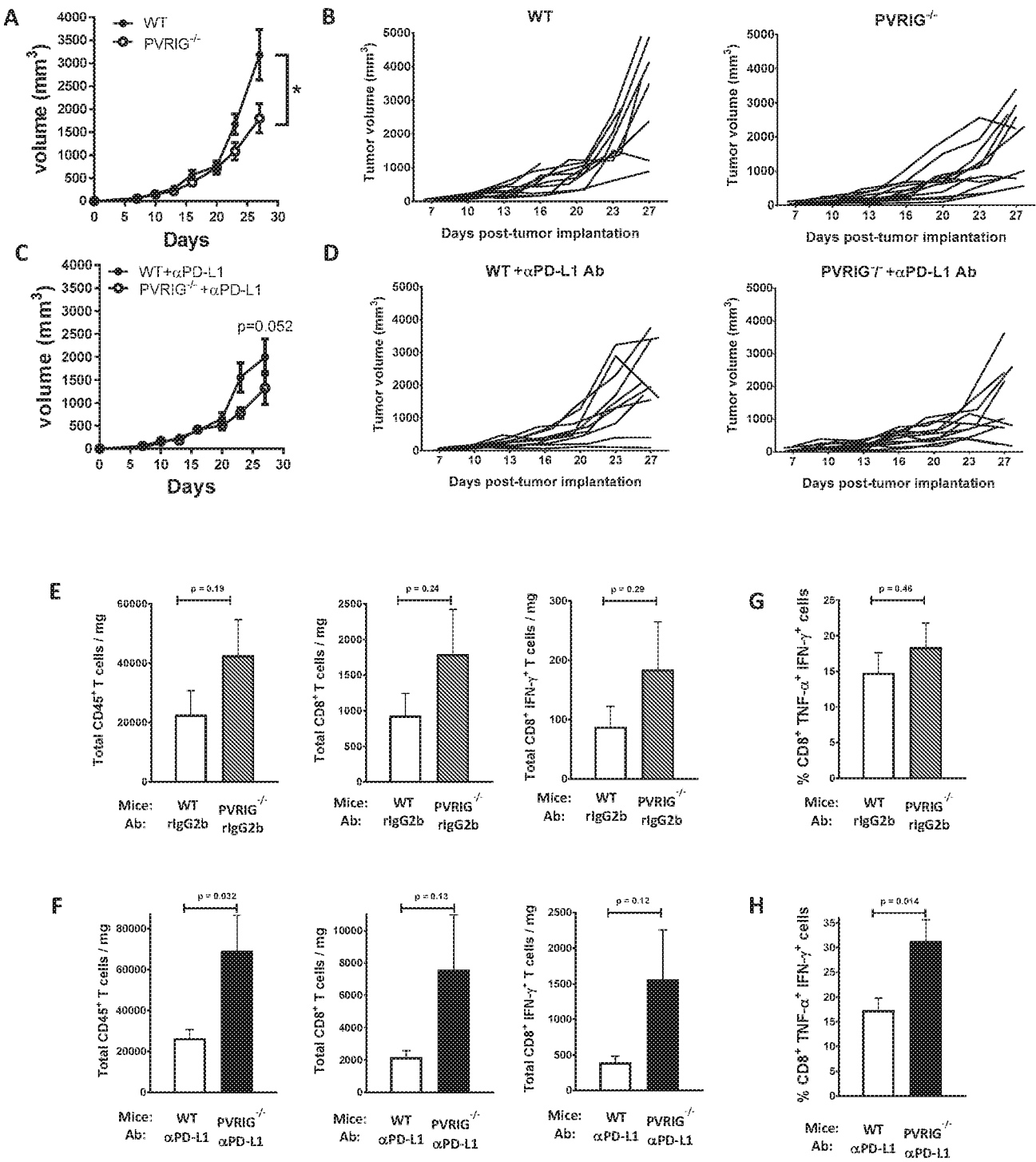


Figure 89

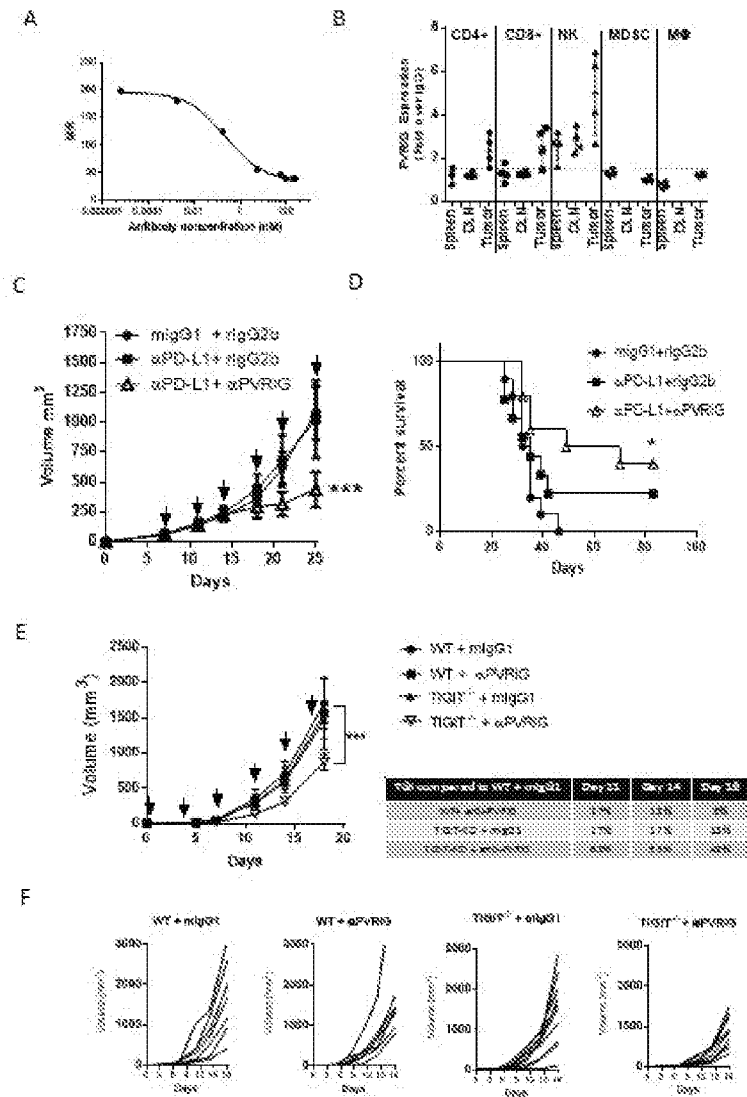


Figure 90

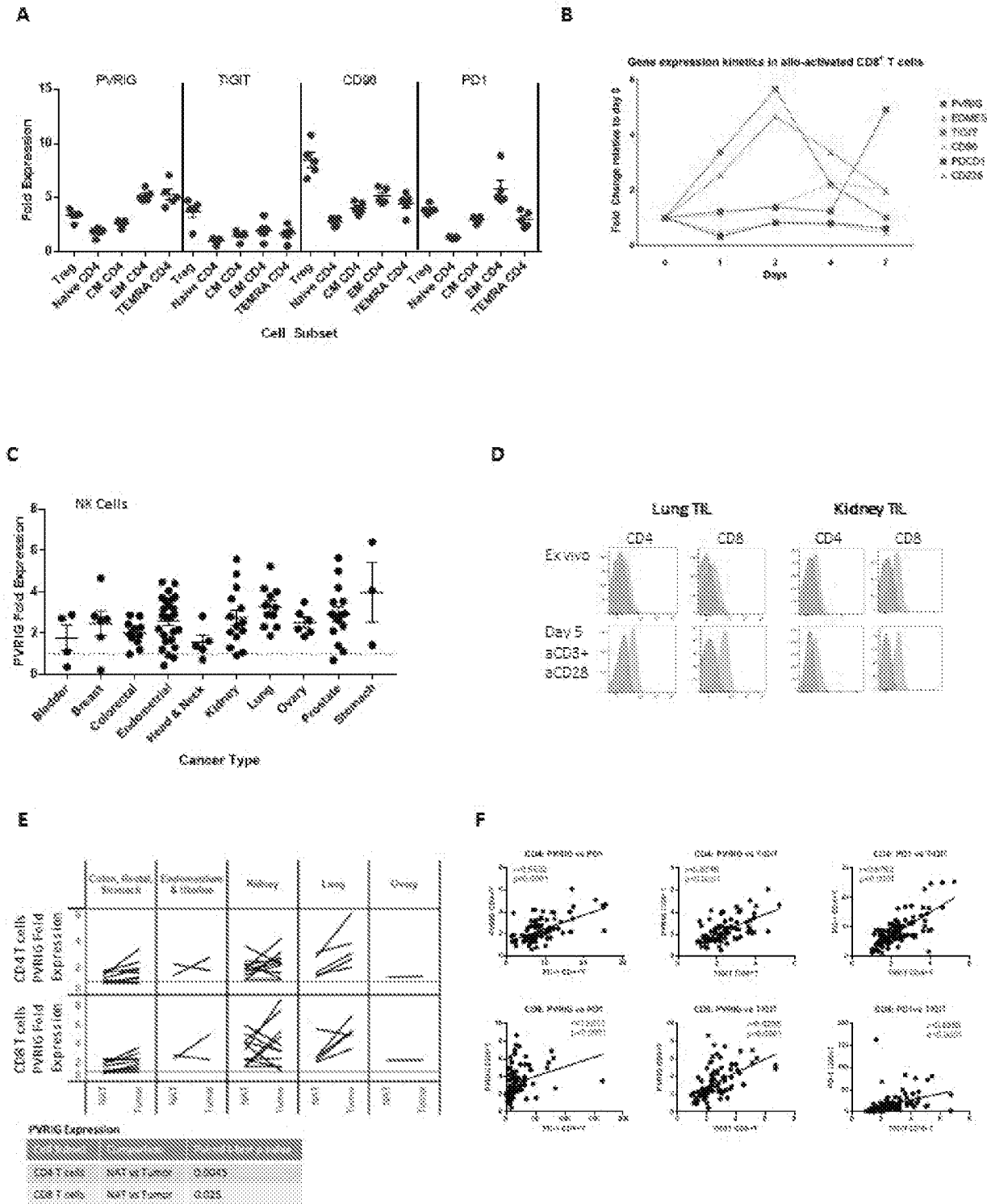


Figure 91

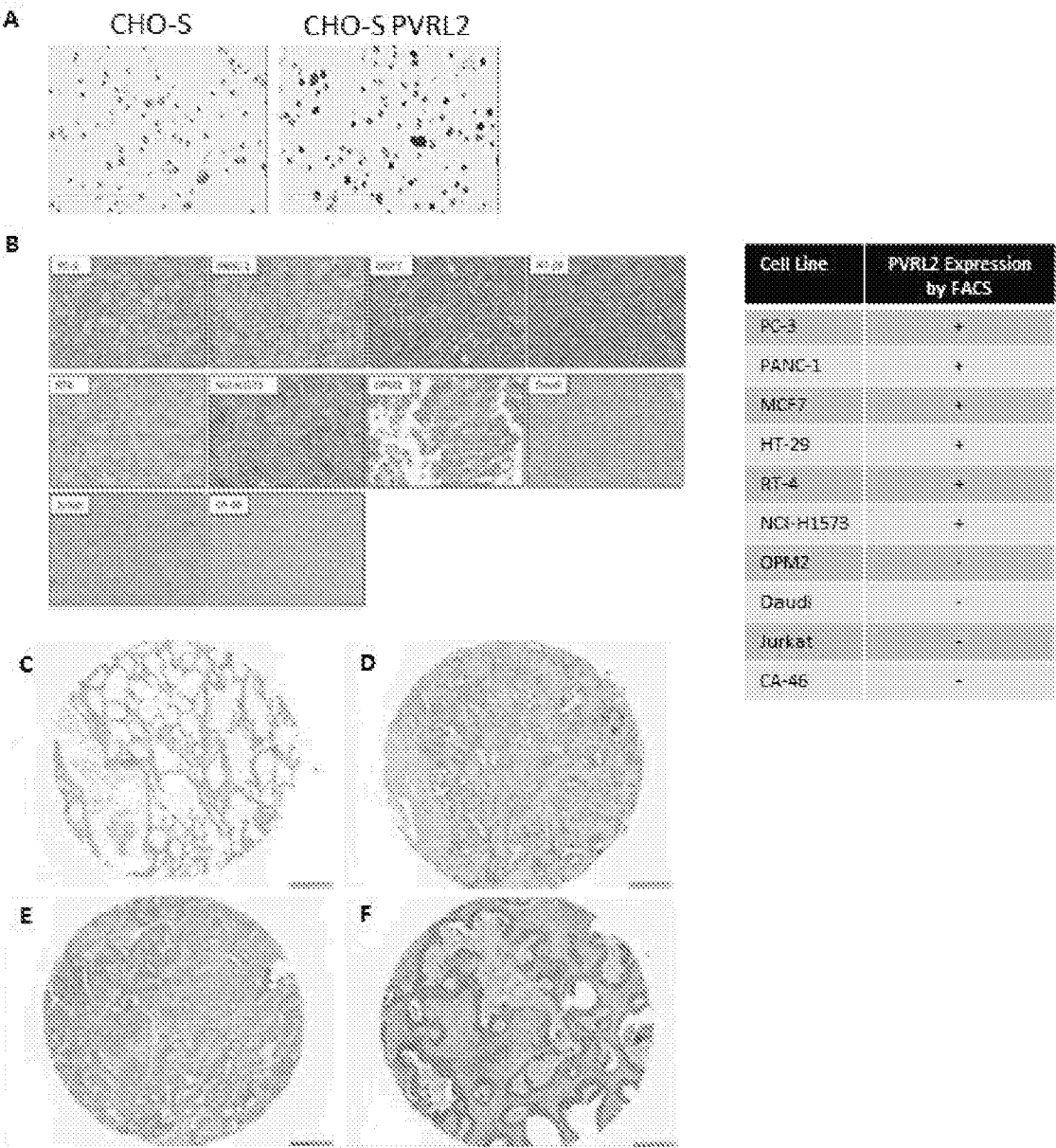


Figure 92

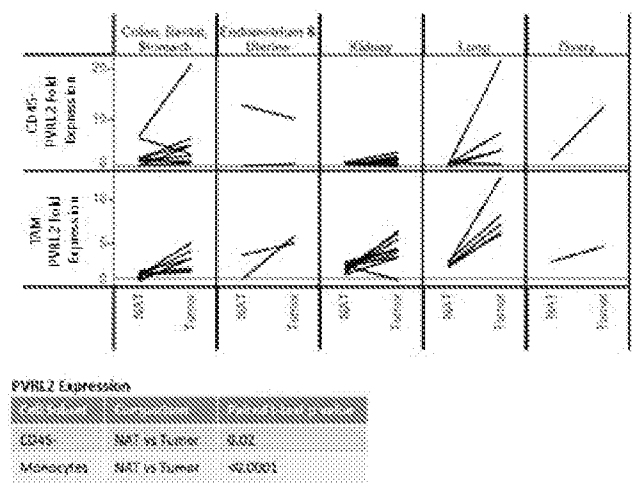


Figure 93

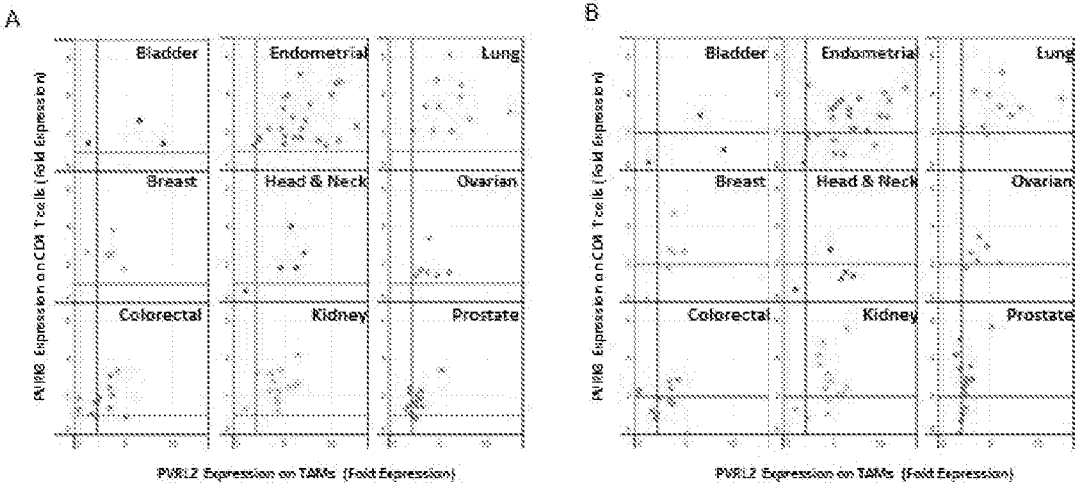


Figure 94

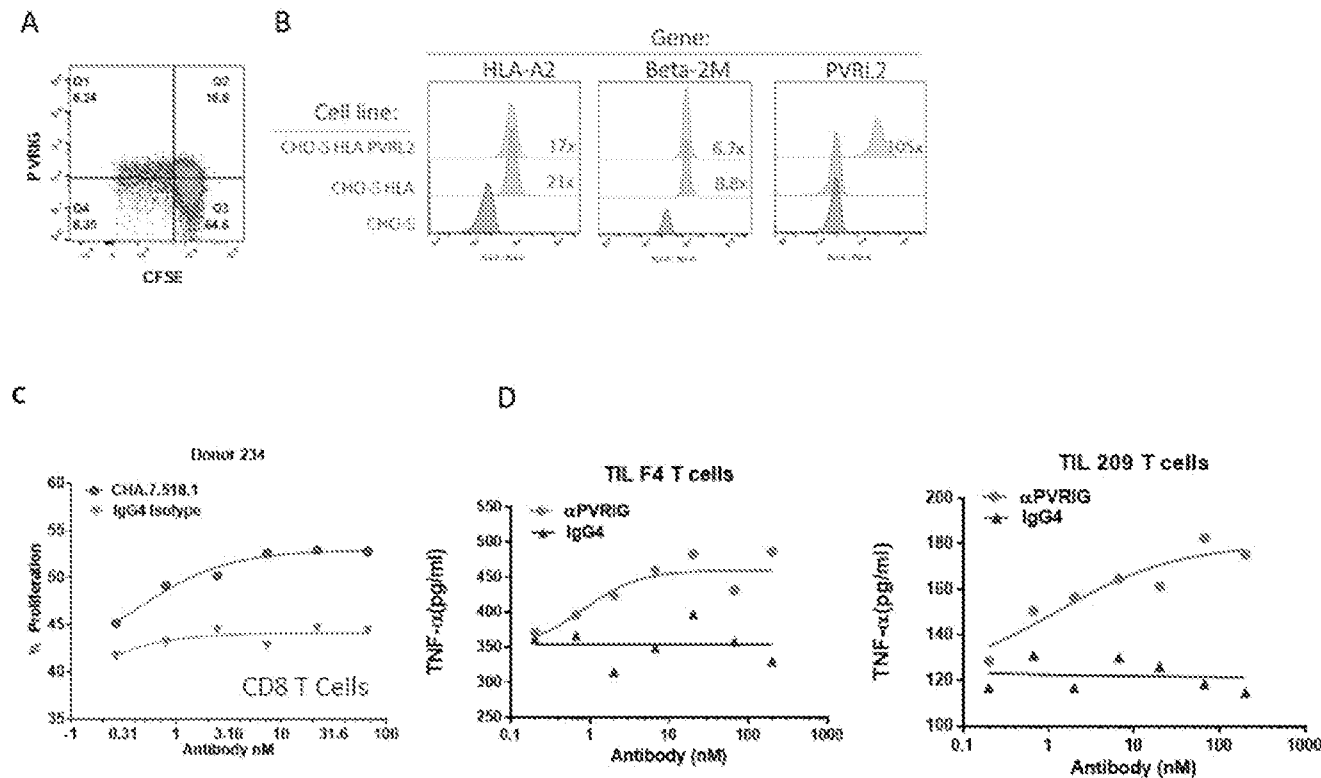


Figure 95

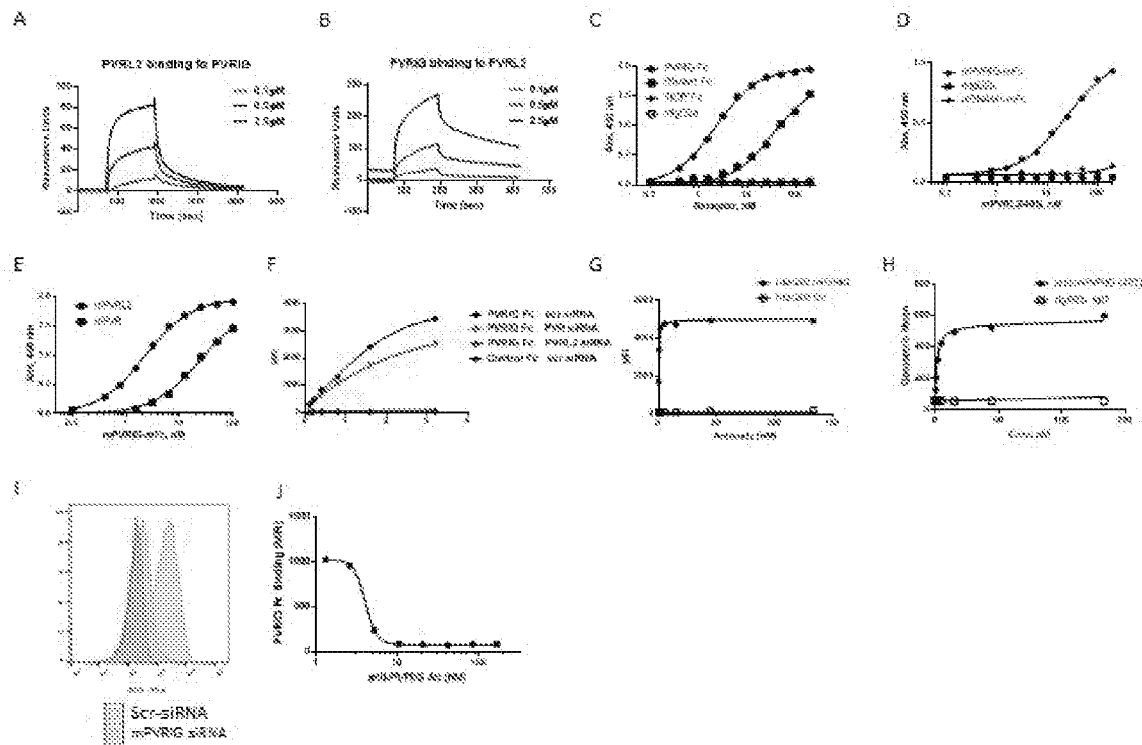


Figure 96

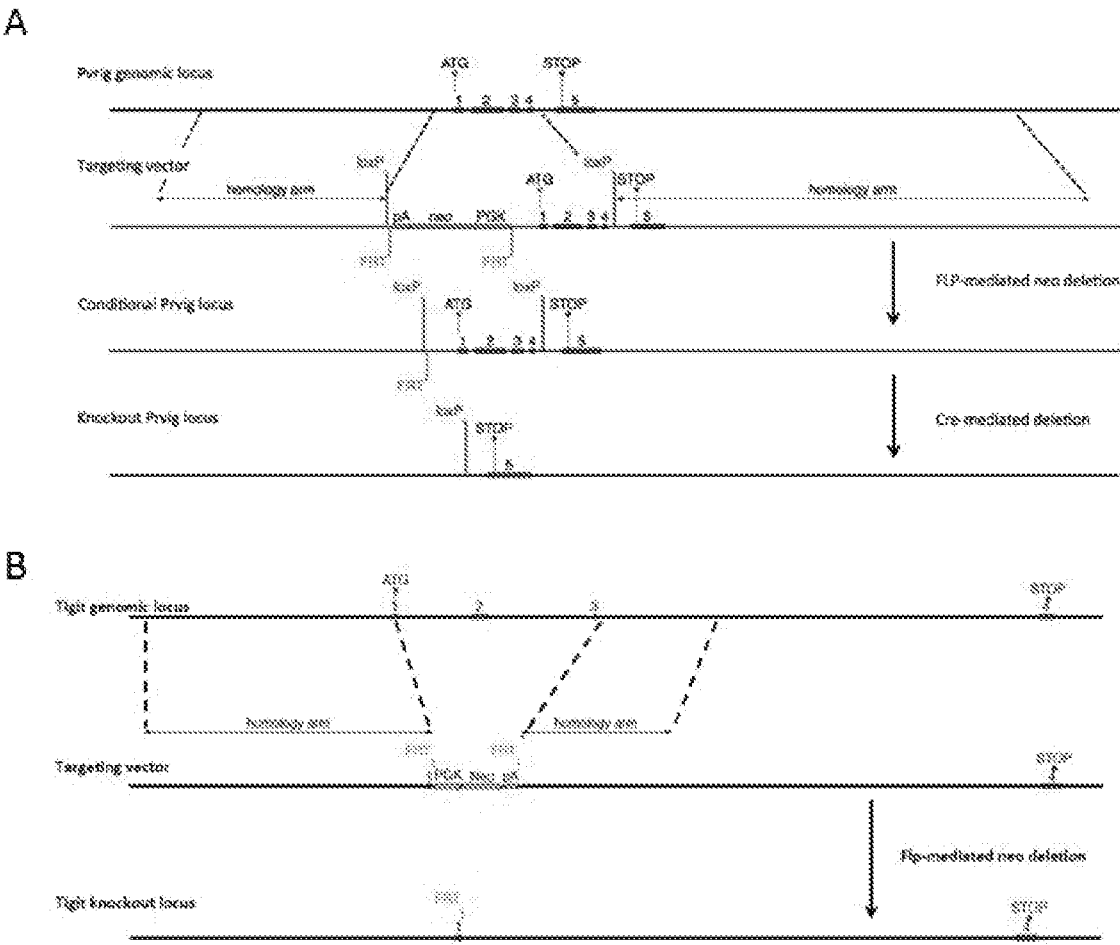


Figure 97

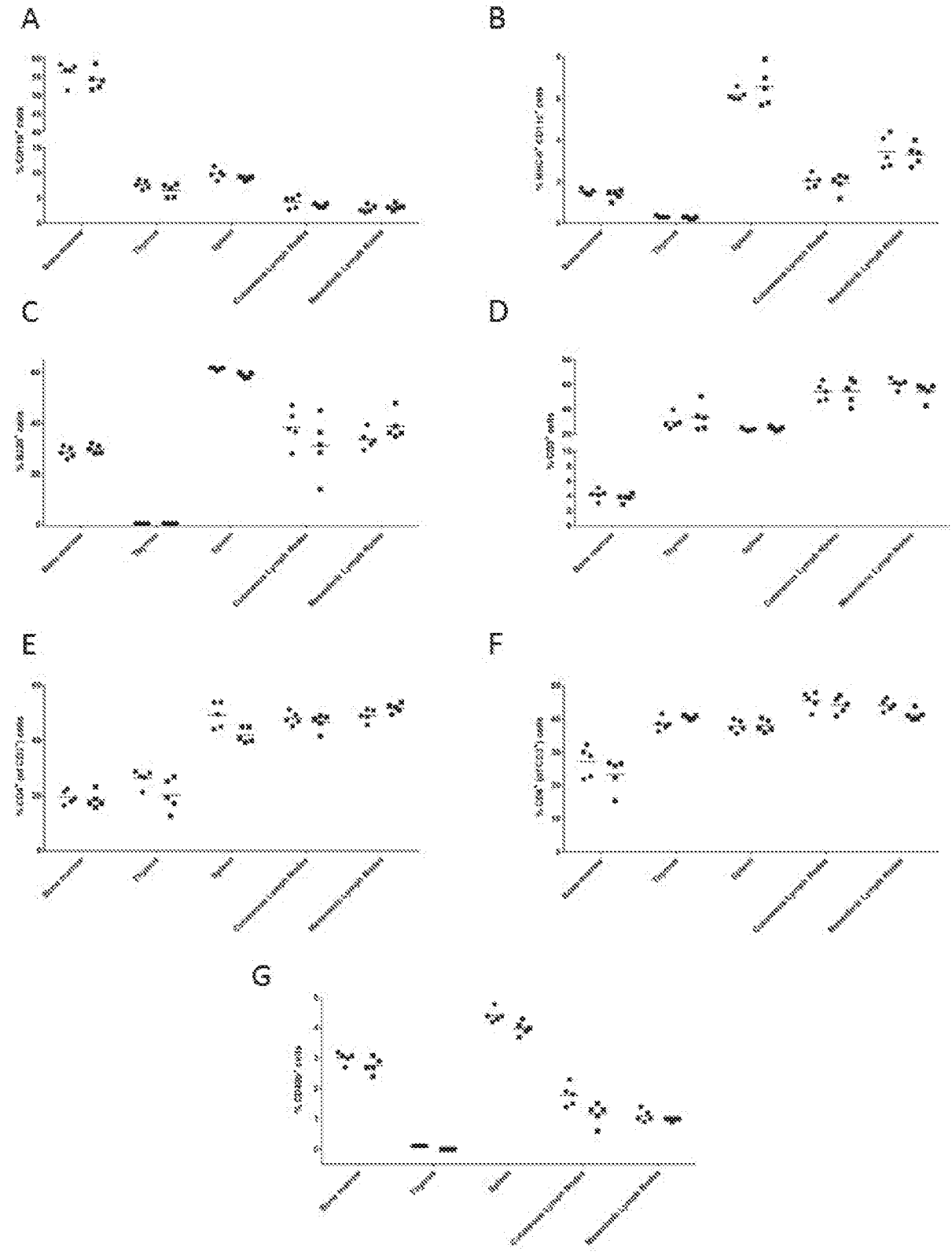


Figure 97 (cont.)

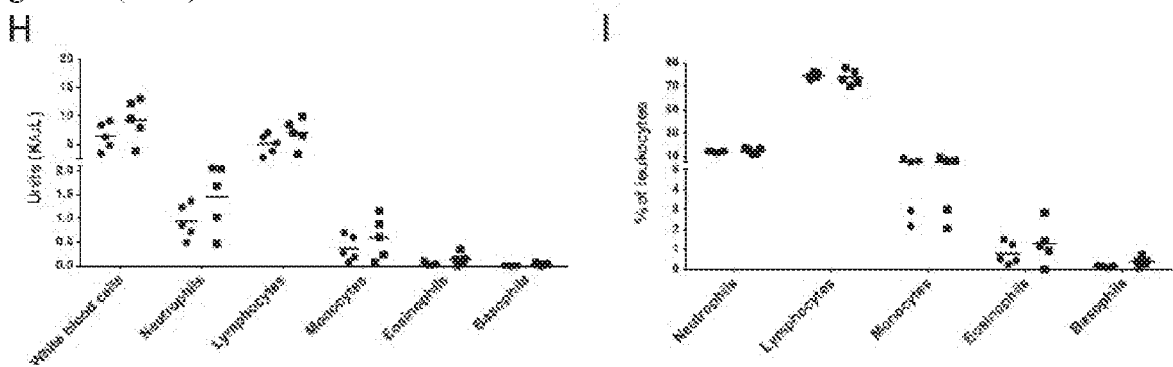


Figure 98

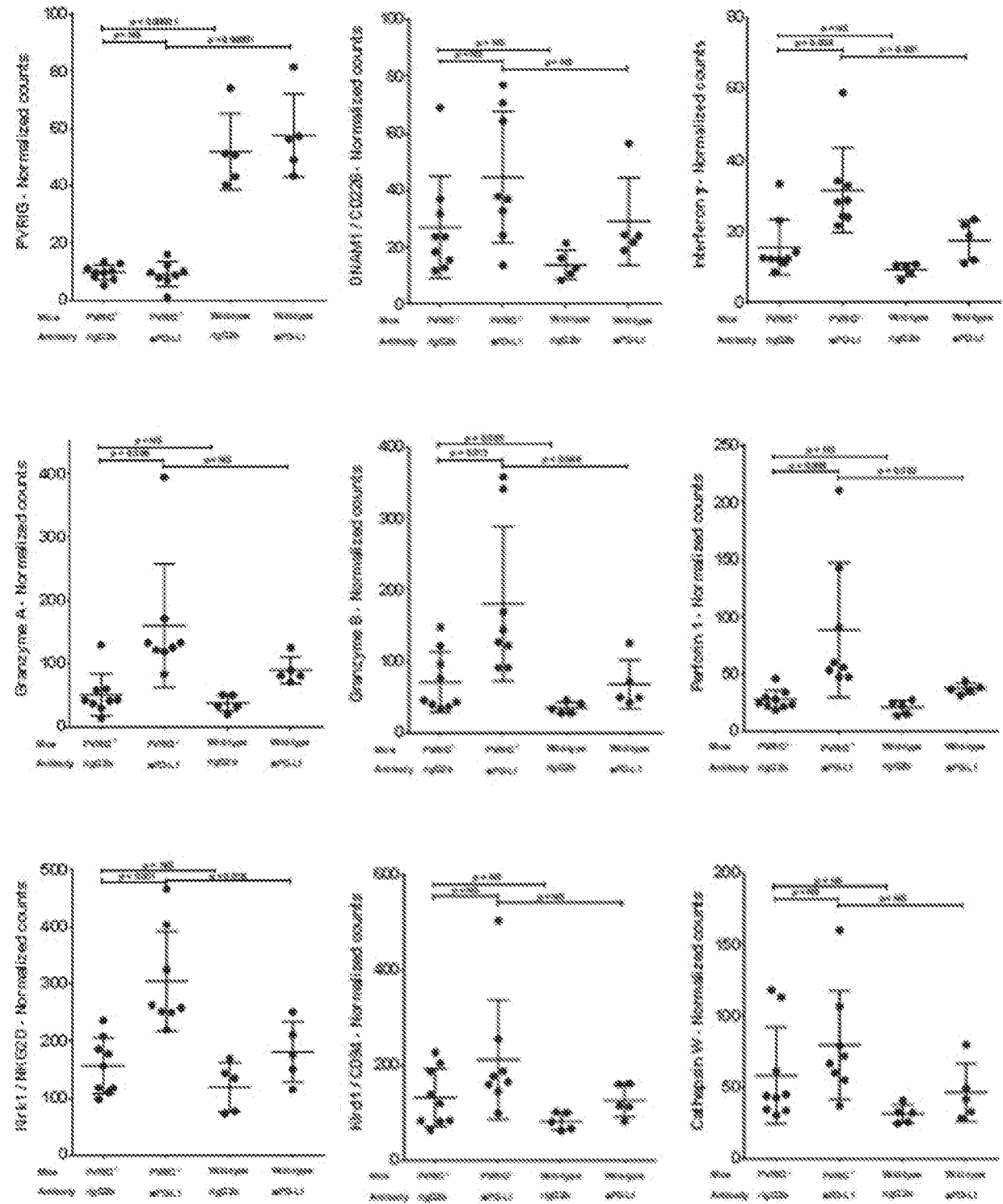


Figure 99

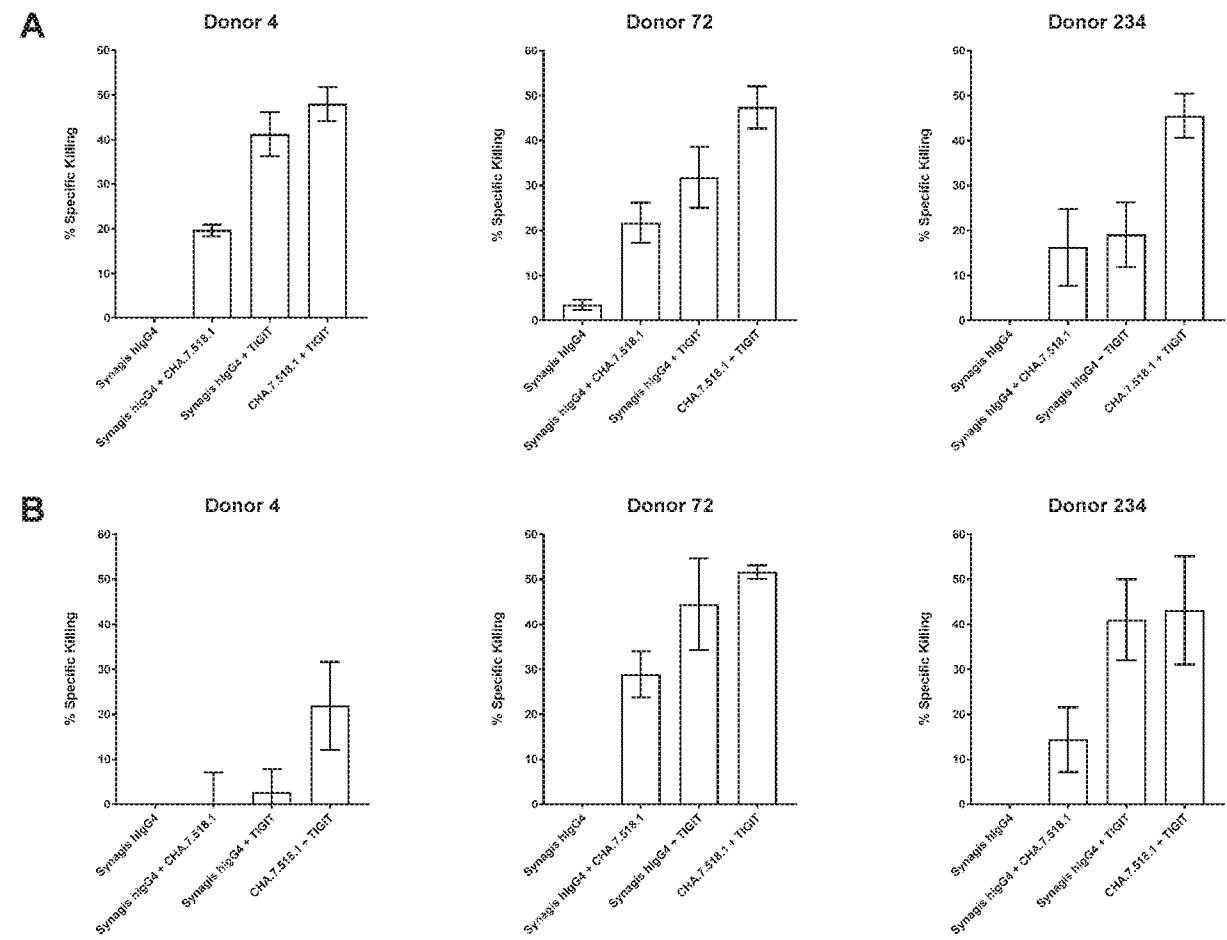


Figure 100

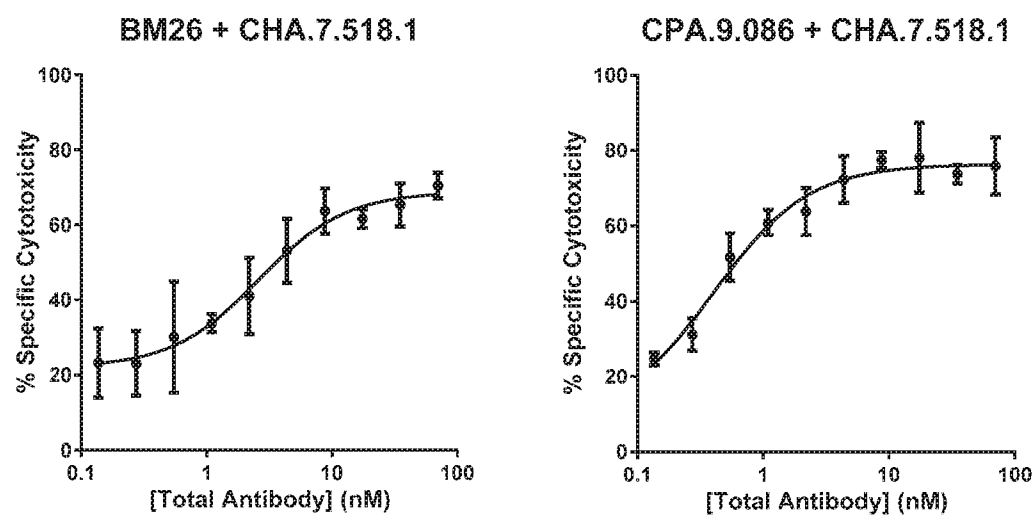
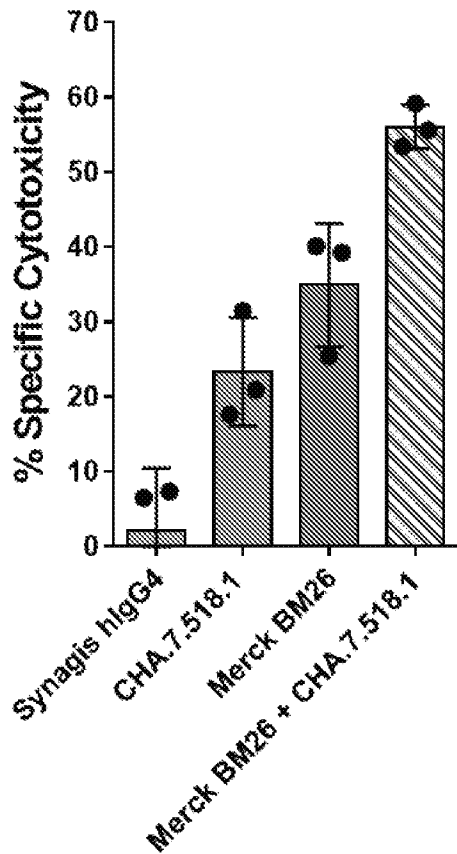
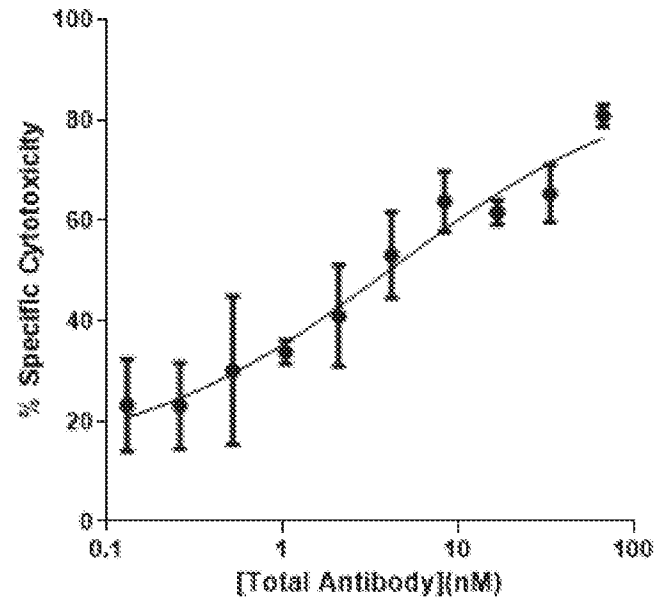


Figure 101

CPA9.086 CDR sequences

Definition	H-CDR1	H-CDR2	H-CDR3	L-CDR1	L-CDR2	L-CDR3
IMGT	GTFSSYA (SEQ ID NO:600)	ISYAGEVK (SEQ ID NO:601)	ARDPLPLHYGMDV (SEQ ID NO:602)	SSNMGRRP (SEQ ID NO:603)	SQN (SEQ ID NO:604)	AVWDDIGRVLQ (SEQ ID NO:605)
Kabat	SYAMH (SEQ ID NO:606)	VISYAGEVKYYADSVKG (SEQ ID NO:607)	DPLPLHYGMDV (SEQ ID NO:608)	SGSSSNMGRRPVN (SEQ ID NO:609)	SQNQRPS (SEQ ID NO:610)	AVWDDIGRVLQ (SEQ ID NO:611)

Figure 102

Merck BM26 + CHA.7.518.1**Merck BM26 + CHA.7.518.1****CPA.9.086 + CHA.7.518.1**