

FIG. 1A



FIG. 1B



FIG. 1C

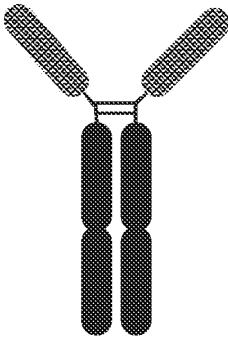


FIG. 1D

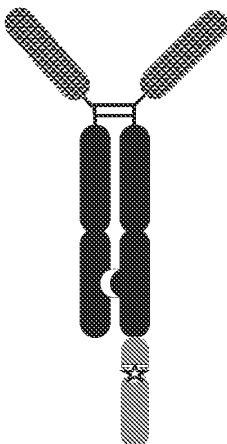


FIG. 1E

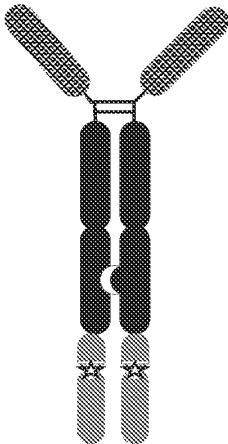


FIG. 1F

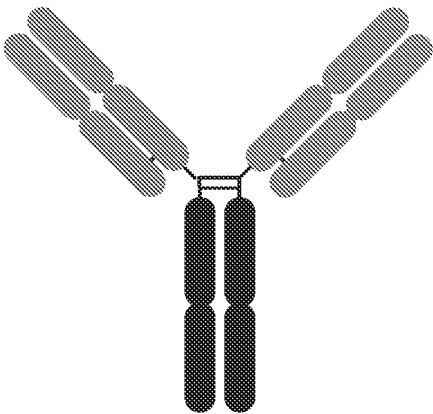


FIG. 1G

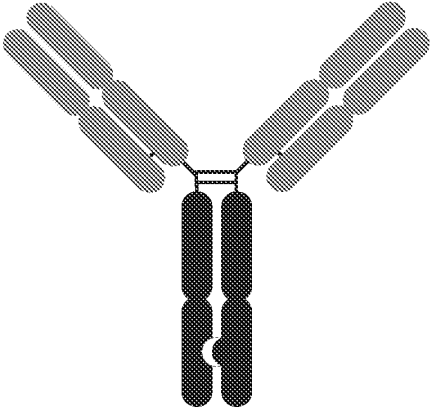


FIG. 1H

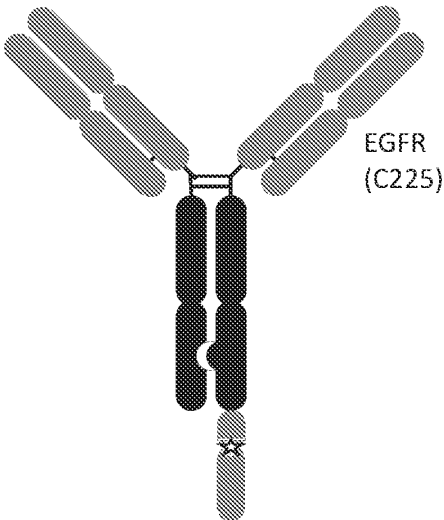


FIG. 1I

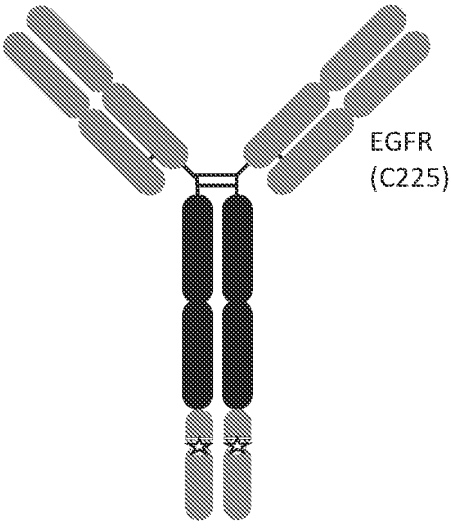


FIG. 1J

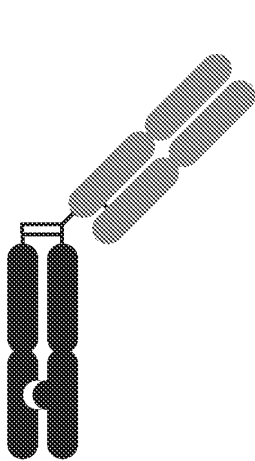


FIG. 1K

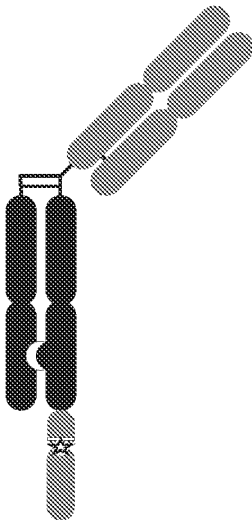


FIG. 1L

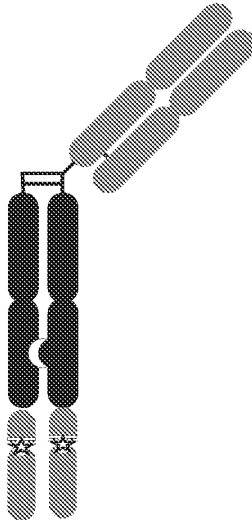


FIG. 1M

FIG. 2A

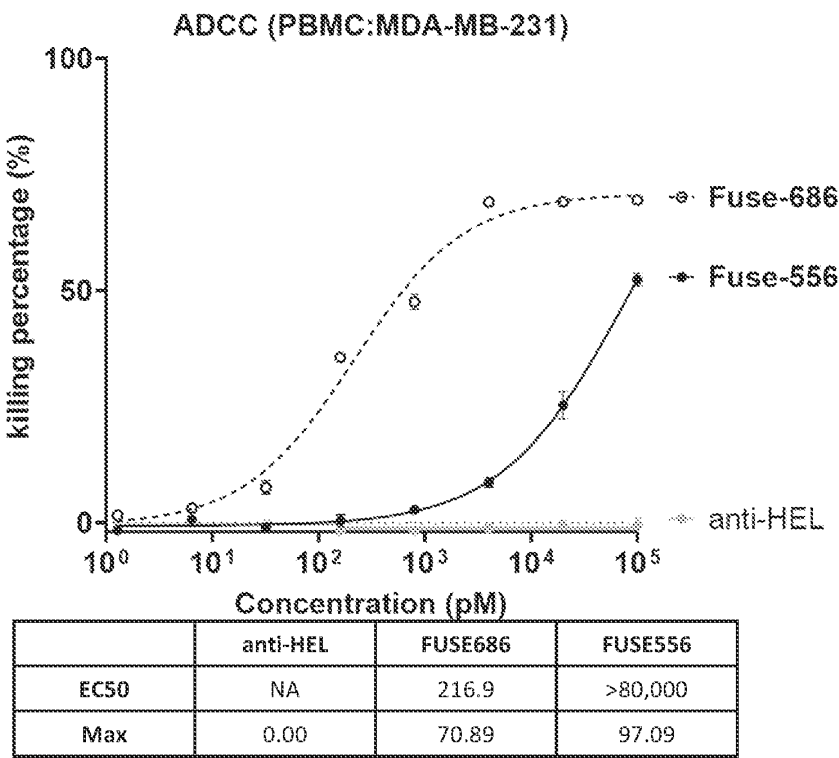


FIG. 2B

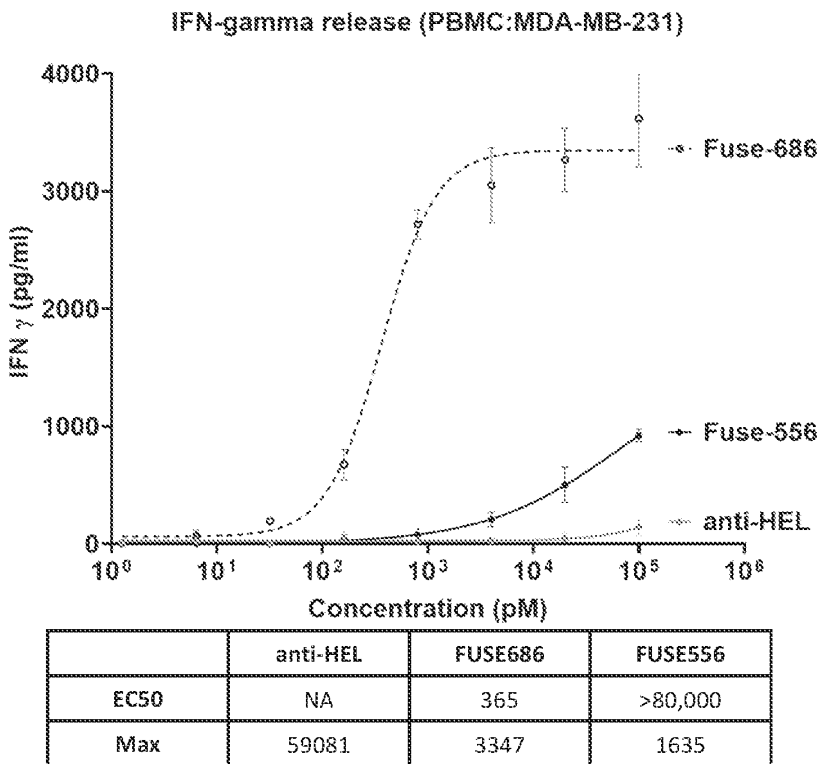
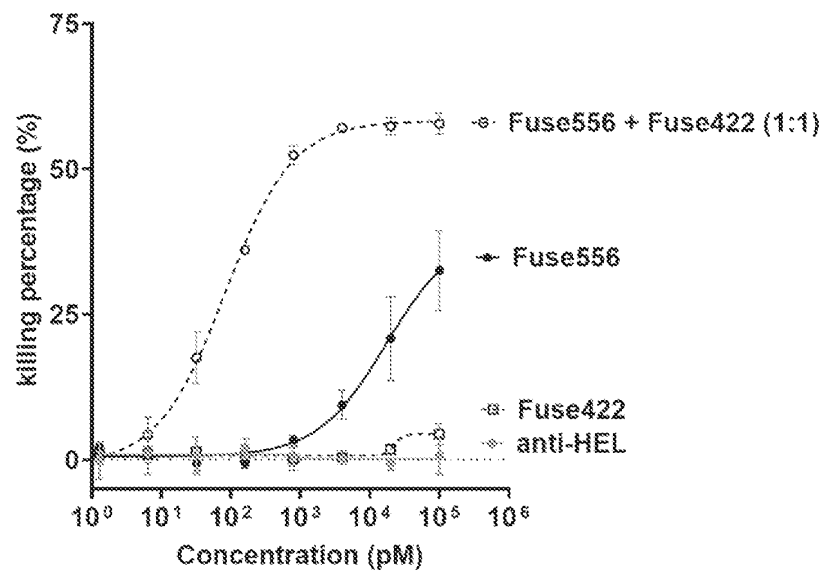


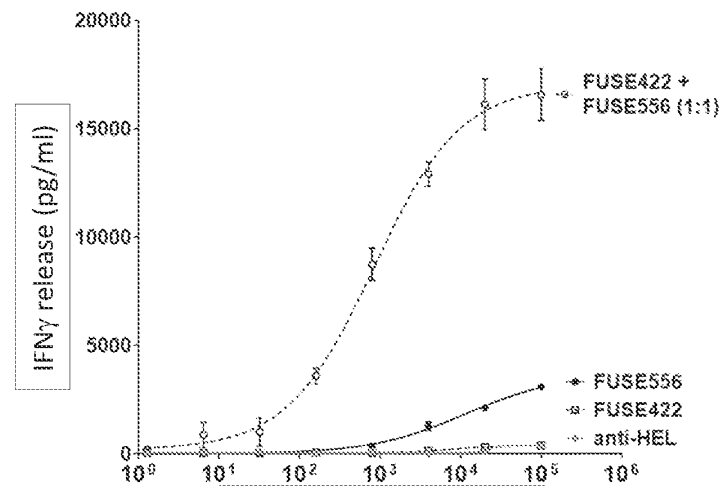
FIG. 3A ADCC (PBMC:MDA-MB-231)



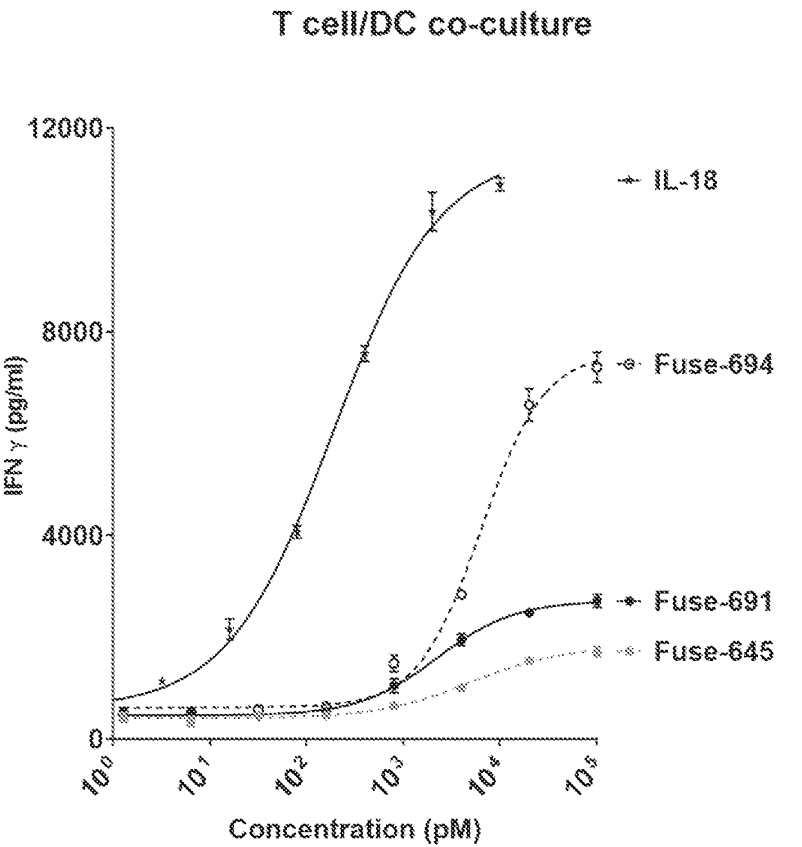
	anti-HEL	FUSE556	FUSE422	FUSE556+422
EC50	NA	>20,000	>25,000	83.05
Max	0.9329	39.35	4.402	58.29

IFN-gamma release (PBMC:MDA-MB-231)

FIG. 3B



	anti-HEL	FUSE556	FUSE422	FUSE556+422
EC50	NA	>50000	>100,000	340.8
Max	377.00	3,700.00	392.90	17,016



	IL-18	FUSE645	FUSE691	FUSE694
EC50	~100	~10,000	~5000	~500
Max	11,529	1,826	2,718	7,595

FIG. 4

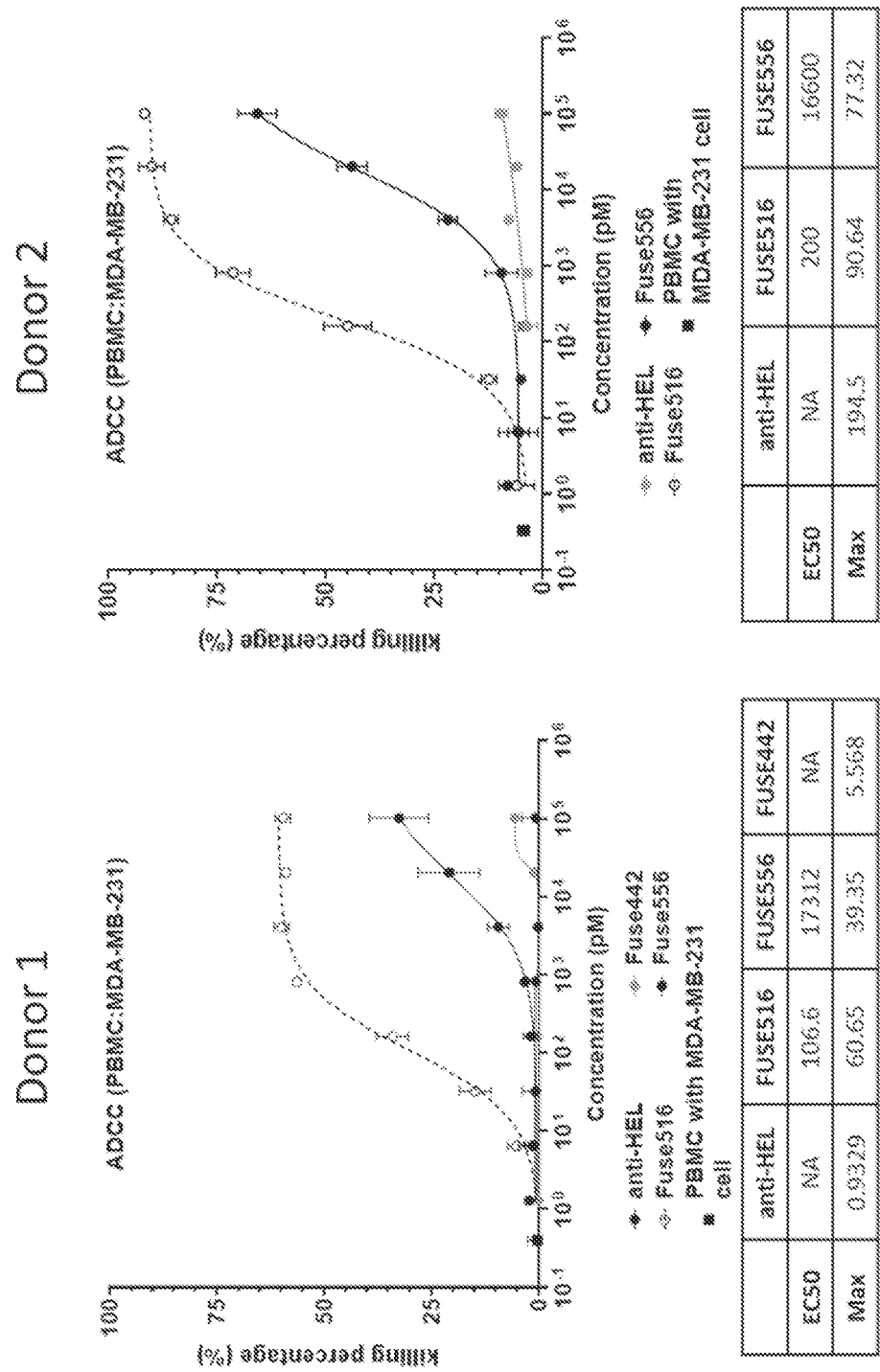


FIG. 5A

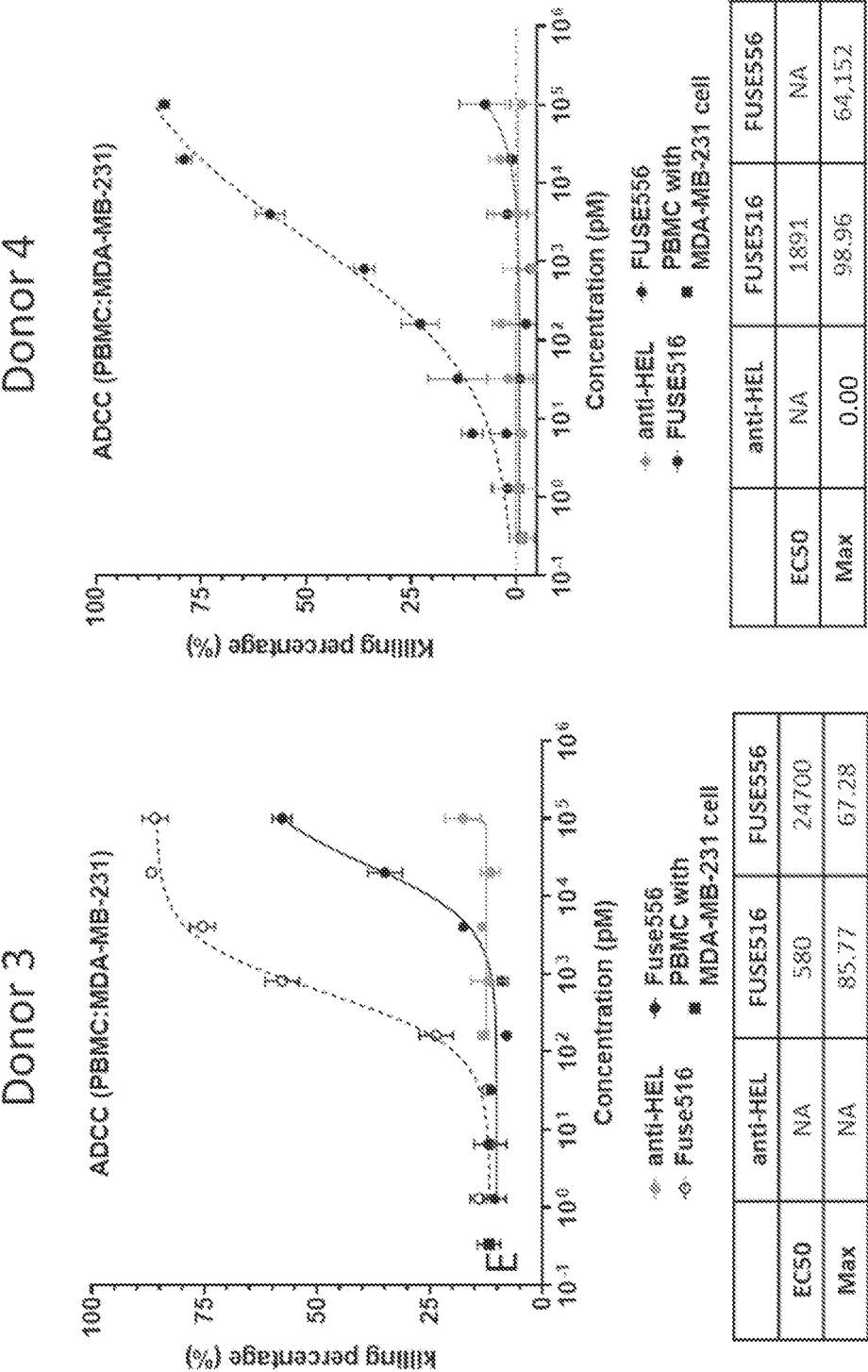


FIG. 5B

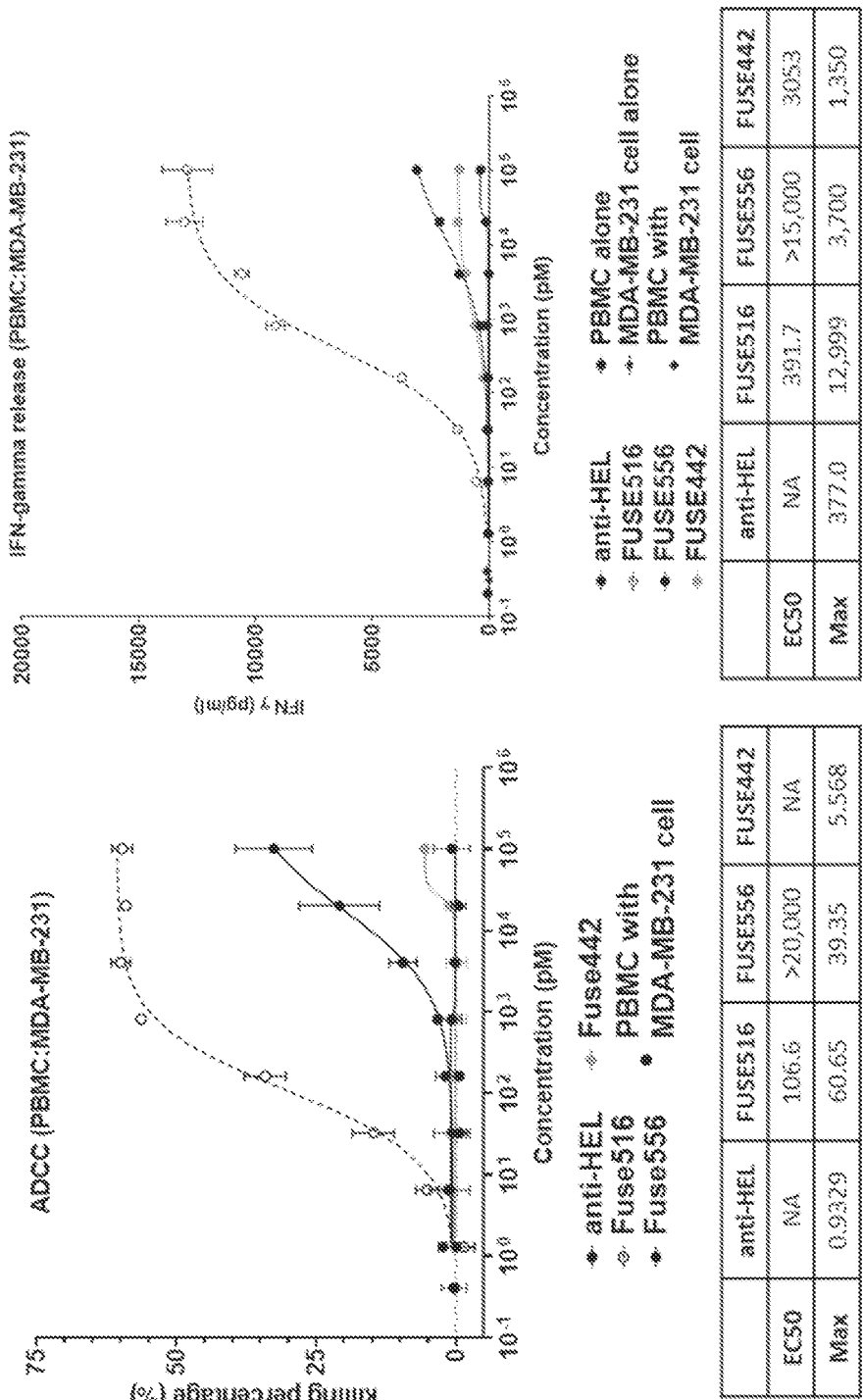
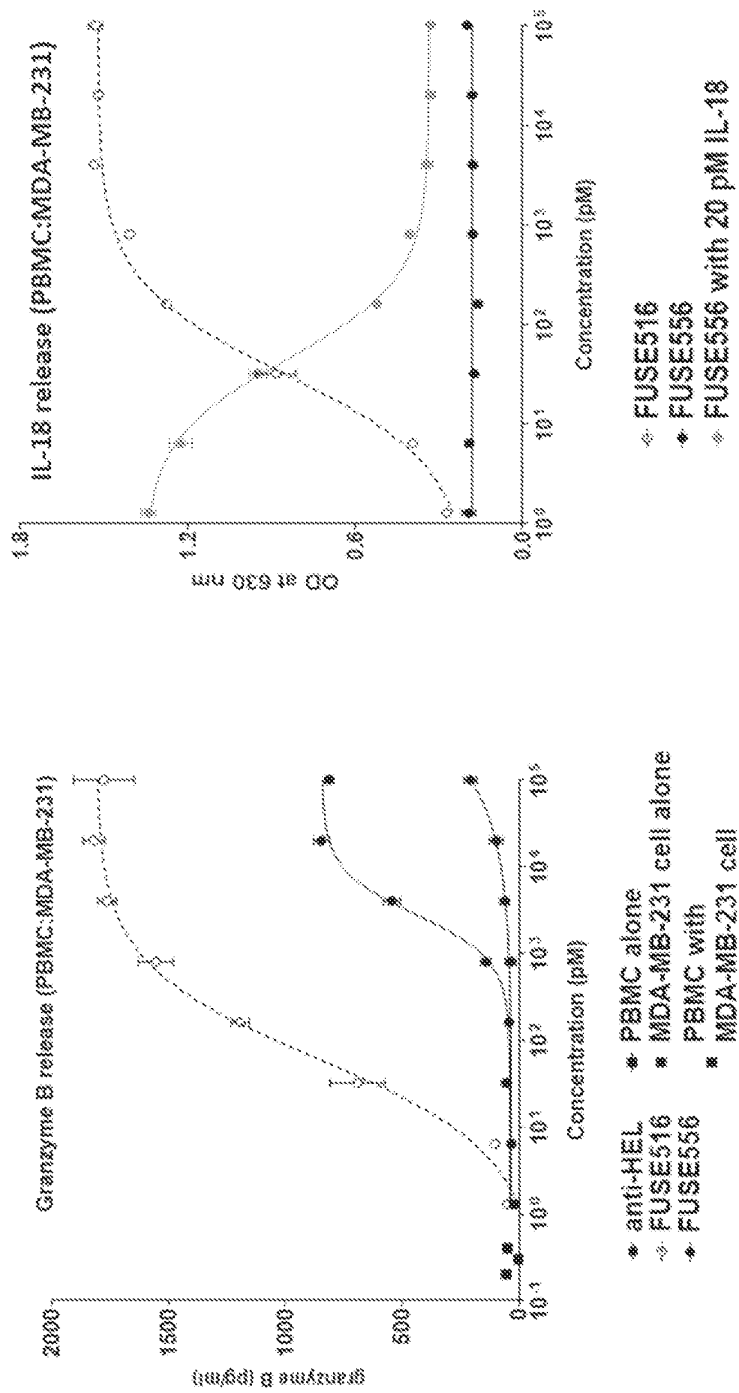


FIG. 6A

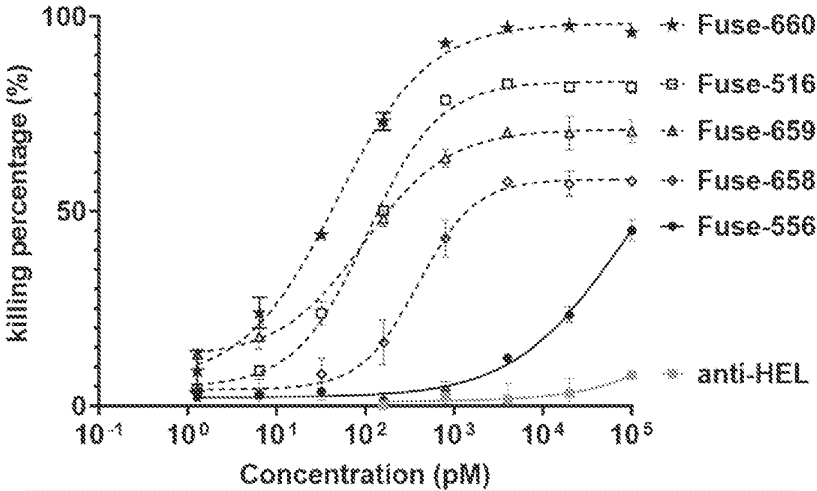


	anti-HEL	FUSE516	FUSE556
EC50	NA	60.9	3807
Max	24,164	1,809	844.5

FIG. 6B

FIG. 7A

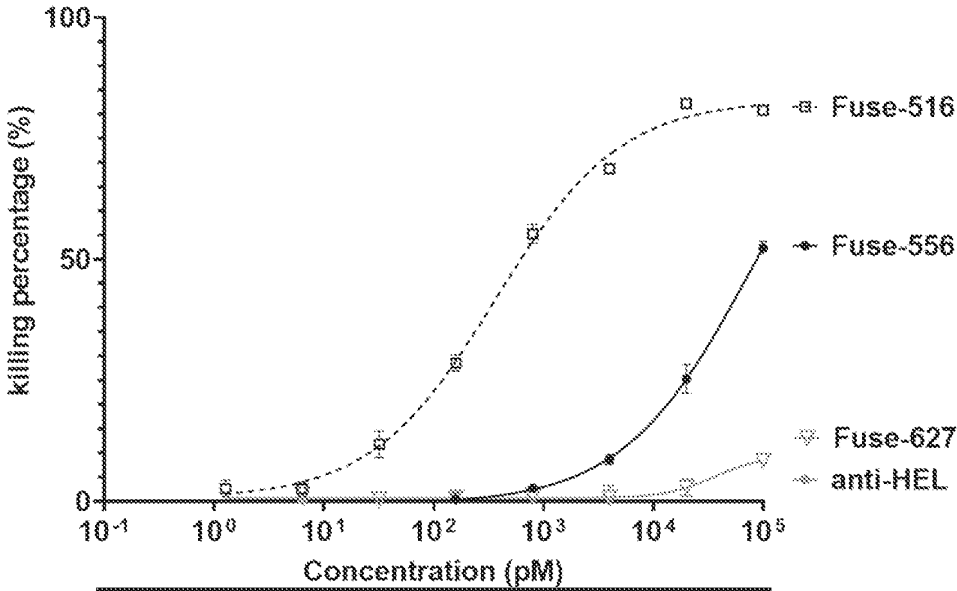
ADCC (PBMC:MDA-MB-231)



	anti-HEL	FUSE516	FUSE556	FUSE658	FUSE659	FUSE660
EC50	NA	105	>90000	391.5	53.05	46.61
Max	833.2	83.35	78.38	58.20	71.02	98.33

FIG. 7B

ADCC (PBMC:MDA-MB-231)



	anti-HEL	FUSE516	FUSE556	FUSE627
EC50	NA	367.1	>90,000	>270,000
Max	-0.3739	83.01	97.09	9.5

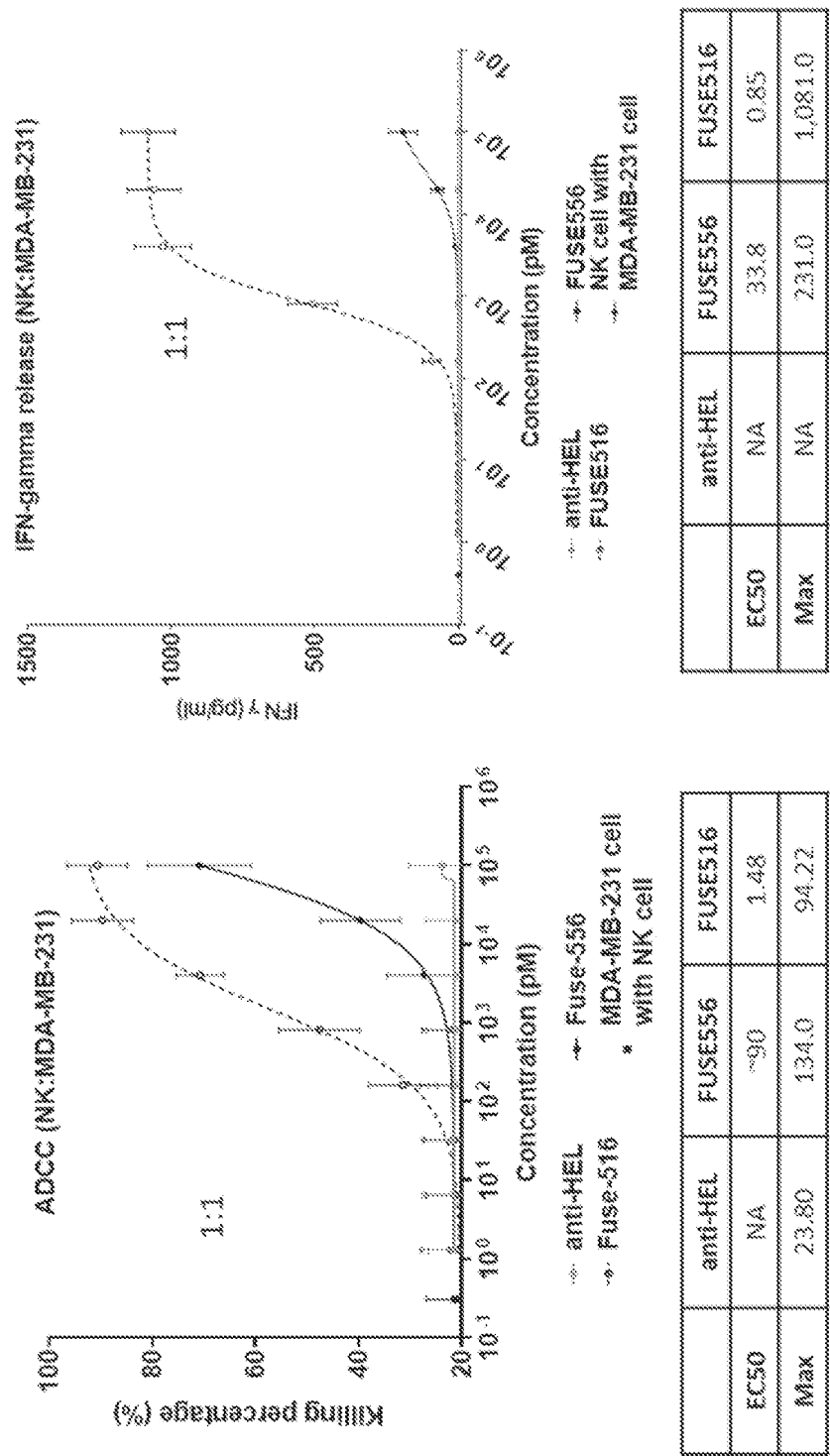


FIG. 8B

FIG. 8A

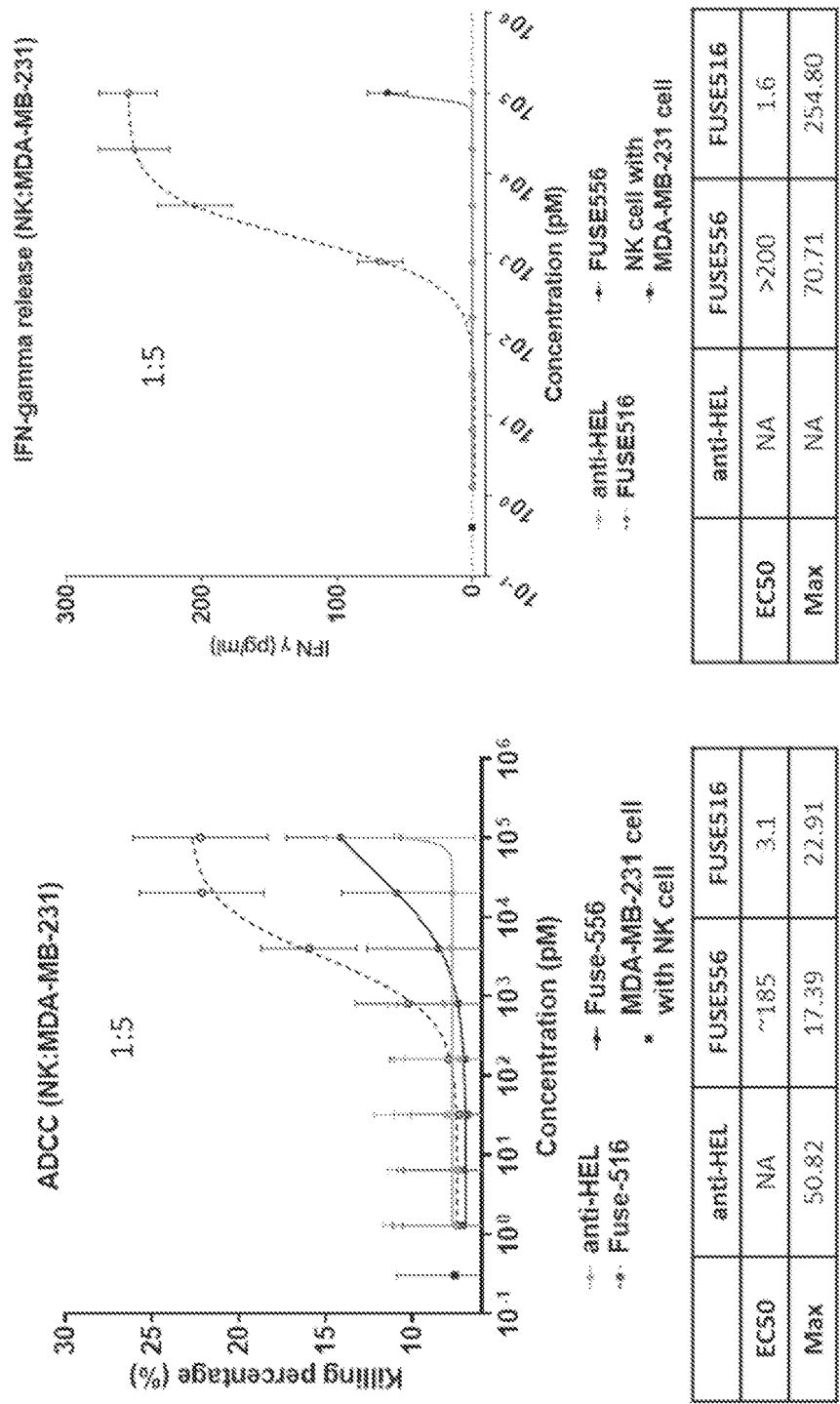


FIG. 8C

FIG. 8D

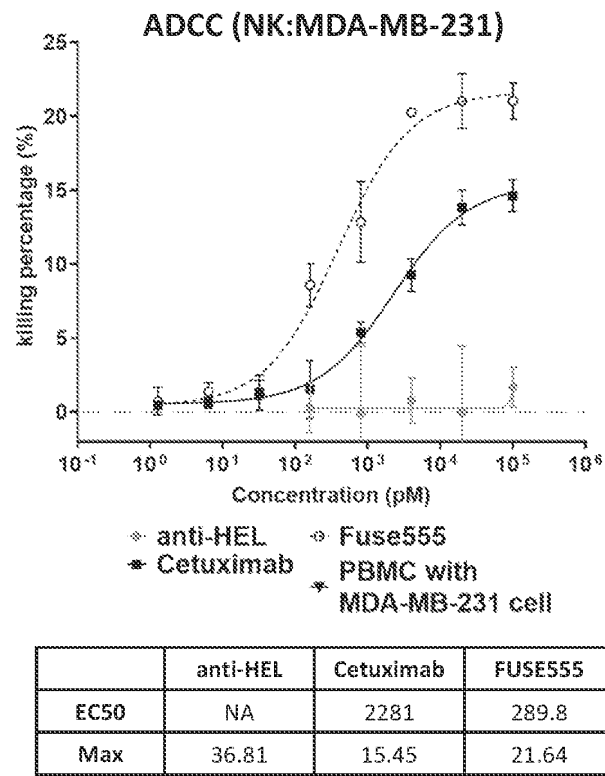


FIG. 9A

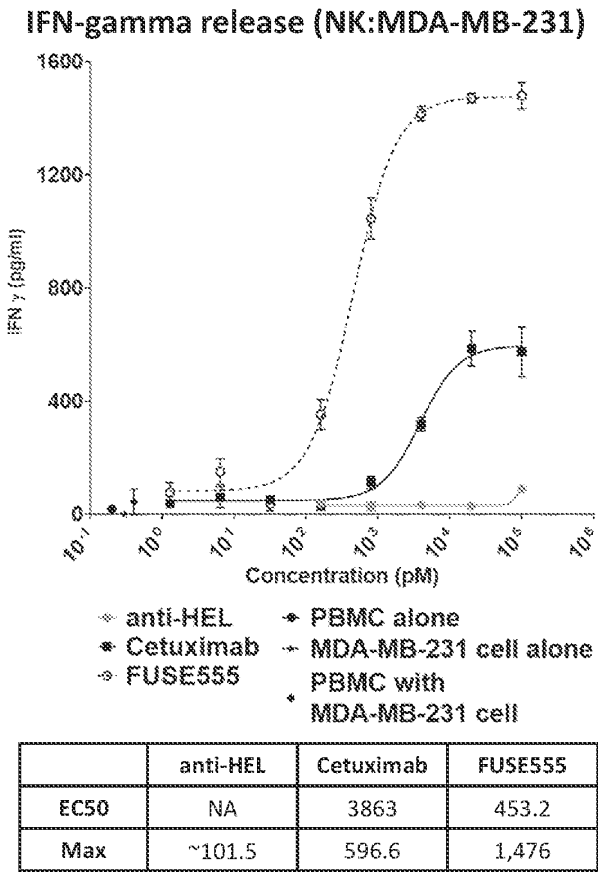


FIG. 9B

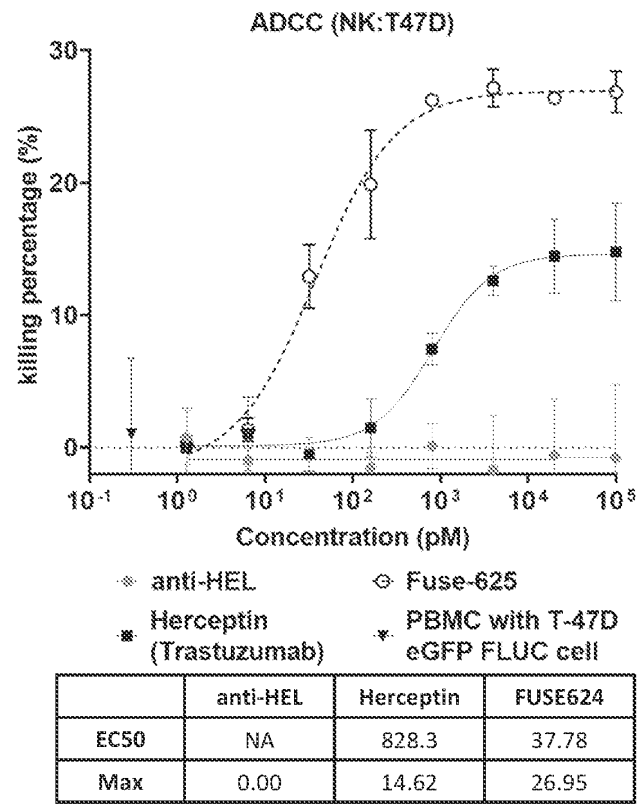


FIG. 10A

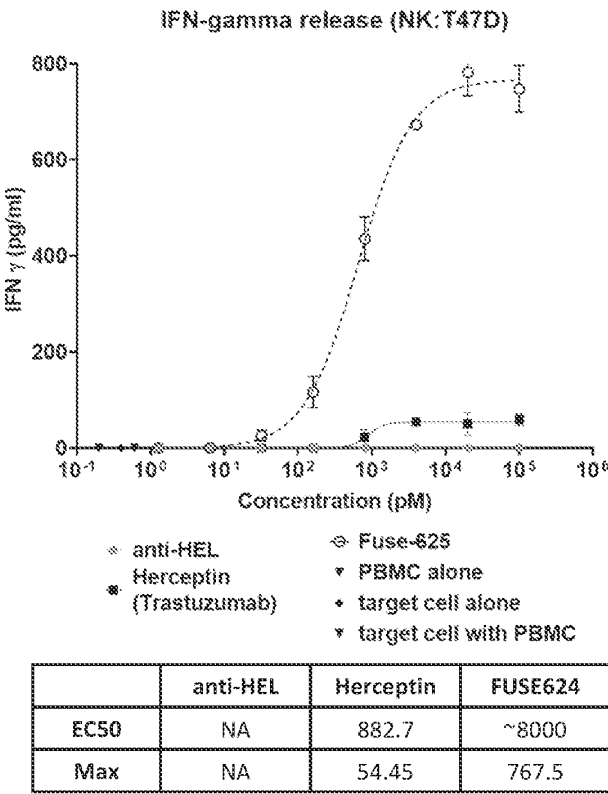
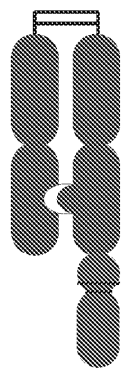


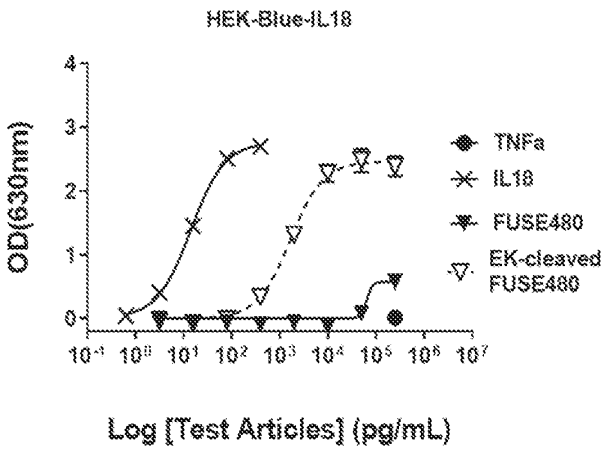
FIG. 10B

A

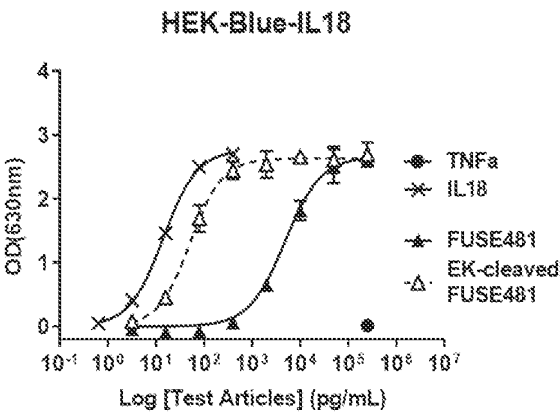
- FUSE 480: KiH_ppEK-IL18-AS
- FUSE 481: KiH_ppEK-IL18-AA
- FUSE 442: KiH_ppEK-IL18-AV



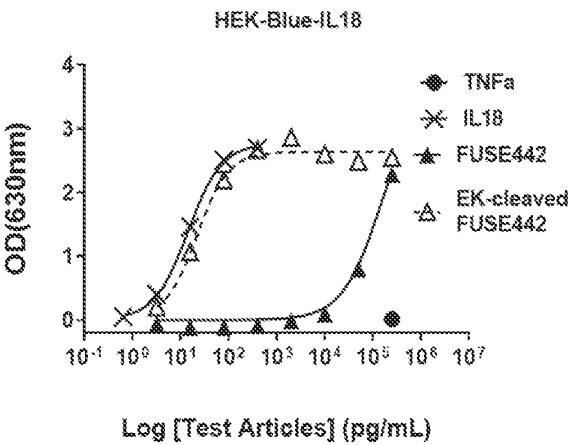
B FUSE480 – C to S



C FUSE481 – C to A



D FUSE442 – C to V



E

Compound	EC50-SEAP
Human rIL-18	0.014 ng/ml
Human rTNFα	N/A
FUSE480	>200 ng/ml
FUSE480 +EK	1.6 ng/ml
FUSE481	4.9 ng/ml
FUSE481 +EK	0.052 ng.ml
FUSE442	>200 ng/ml
FUSE442 + EK	0.022 ng/ml

FIG. 1 1

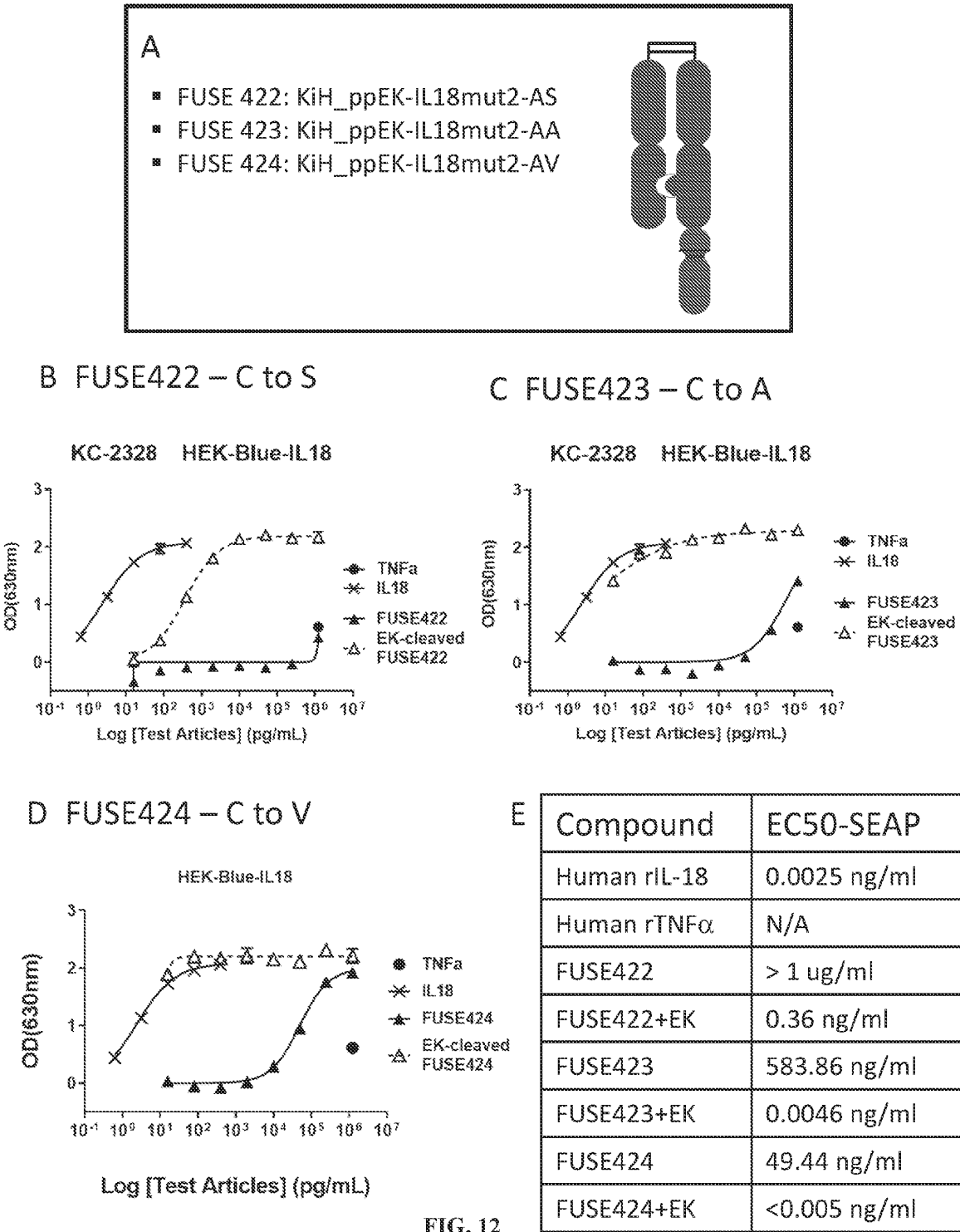


FIG. 12

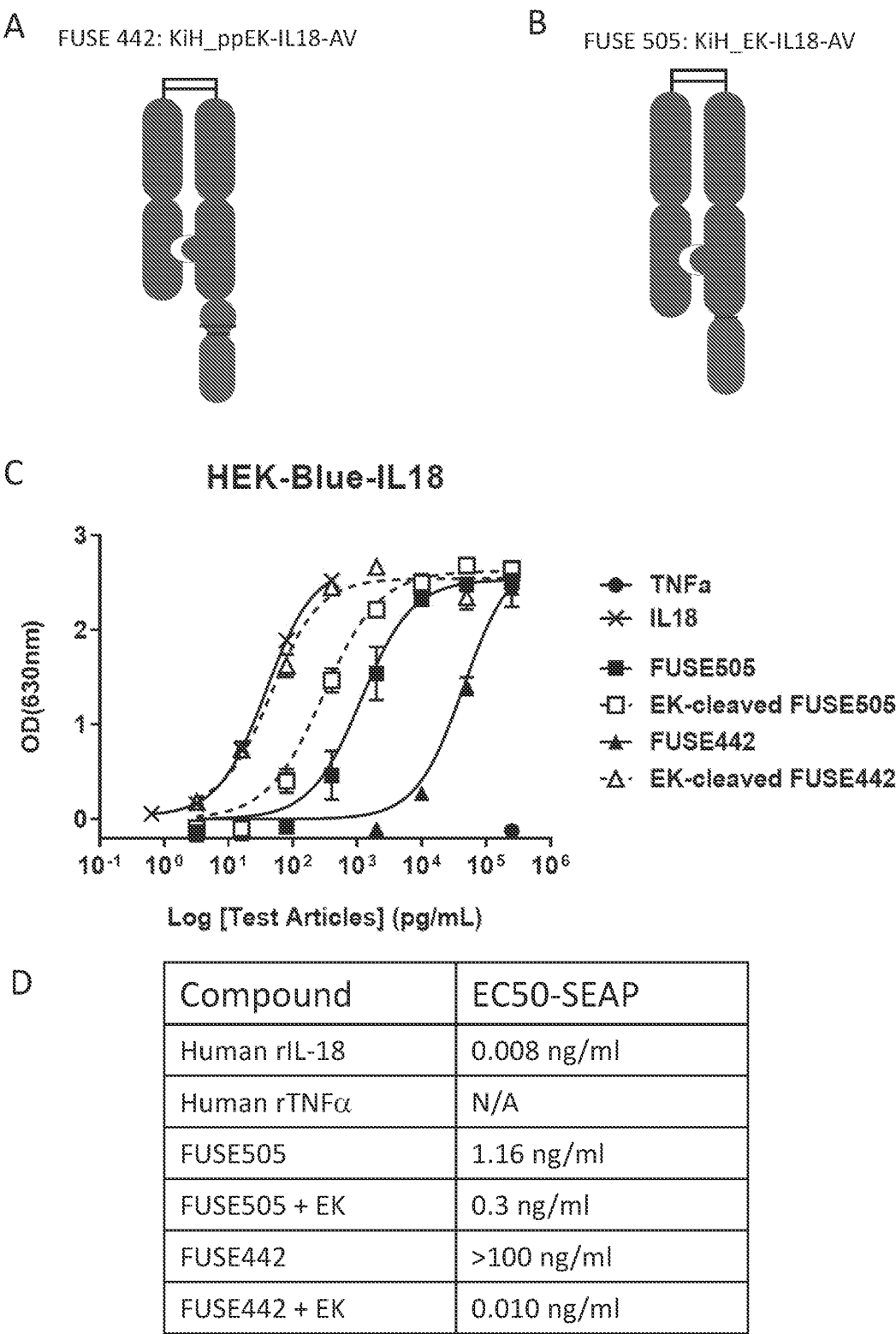


FIG. 13

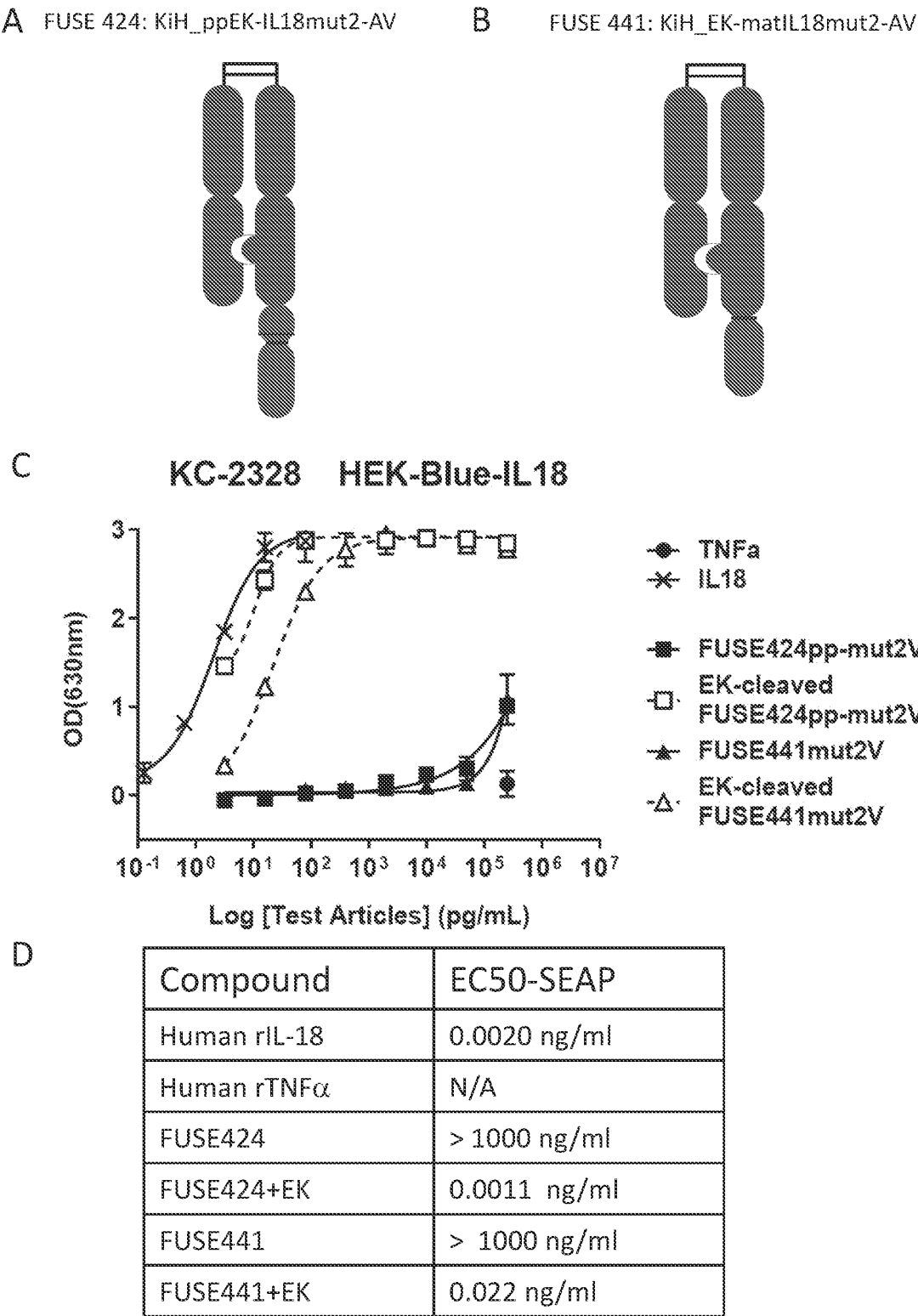


FIG. 14

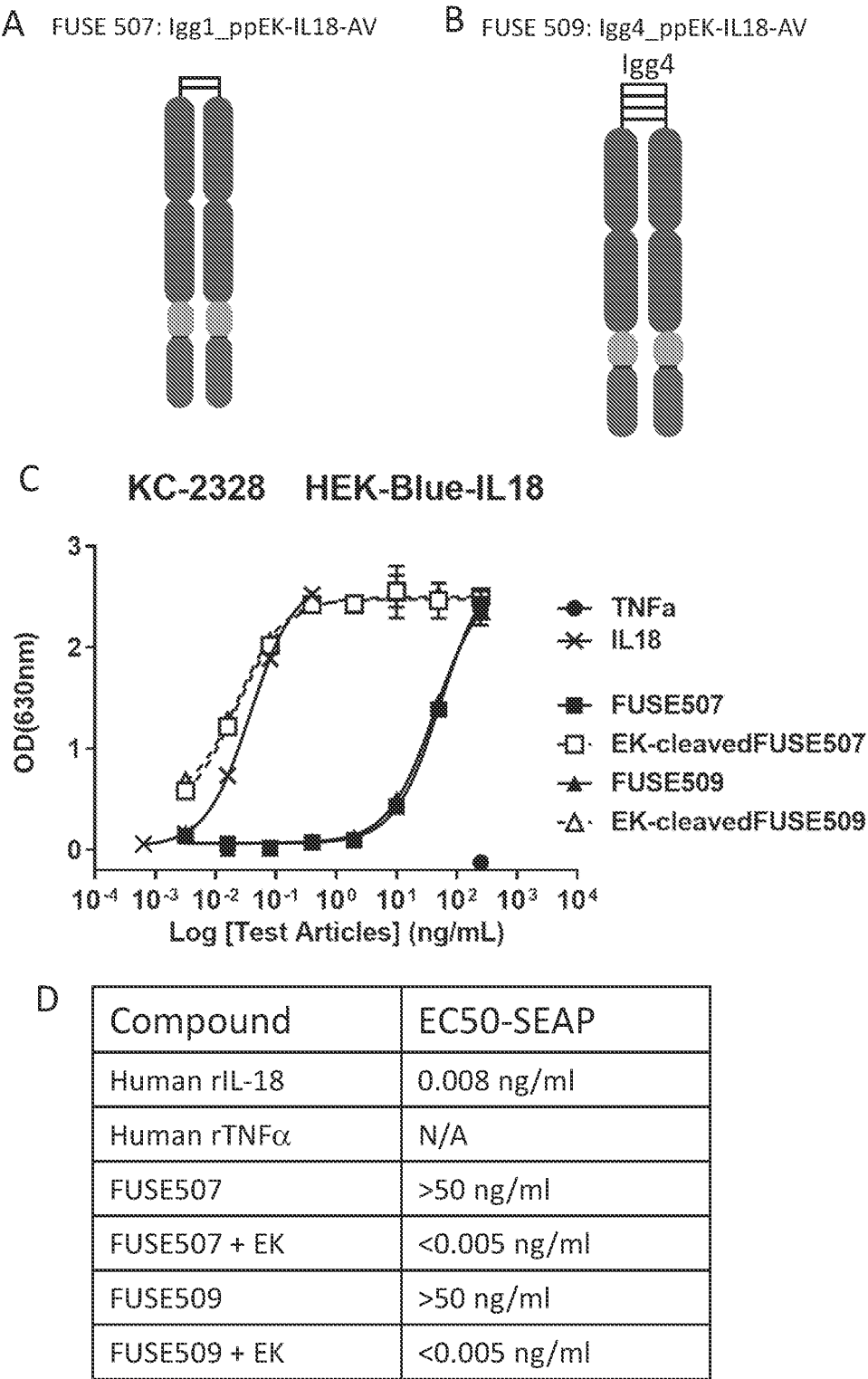
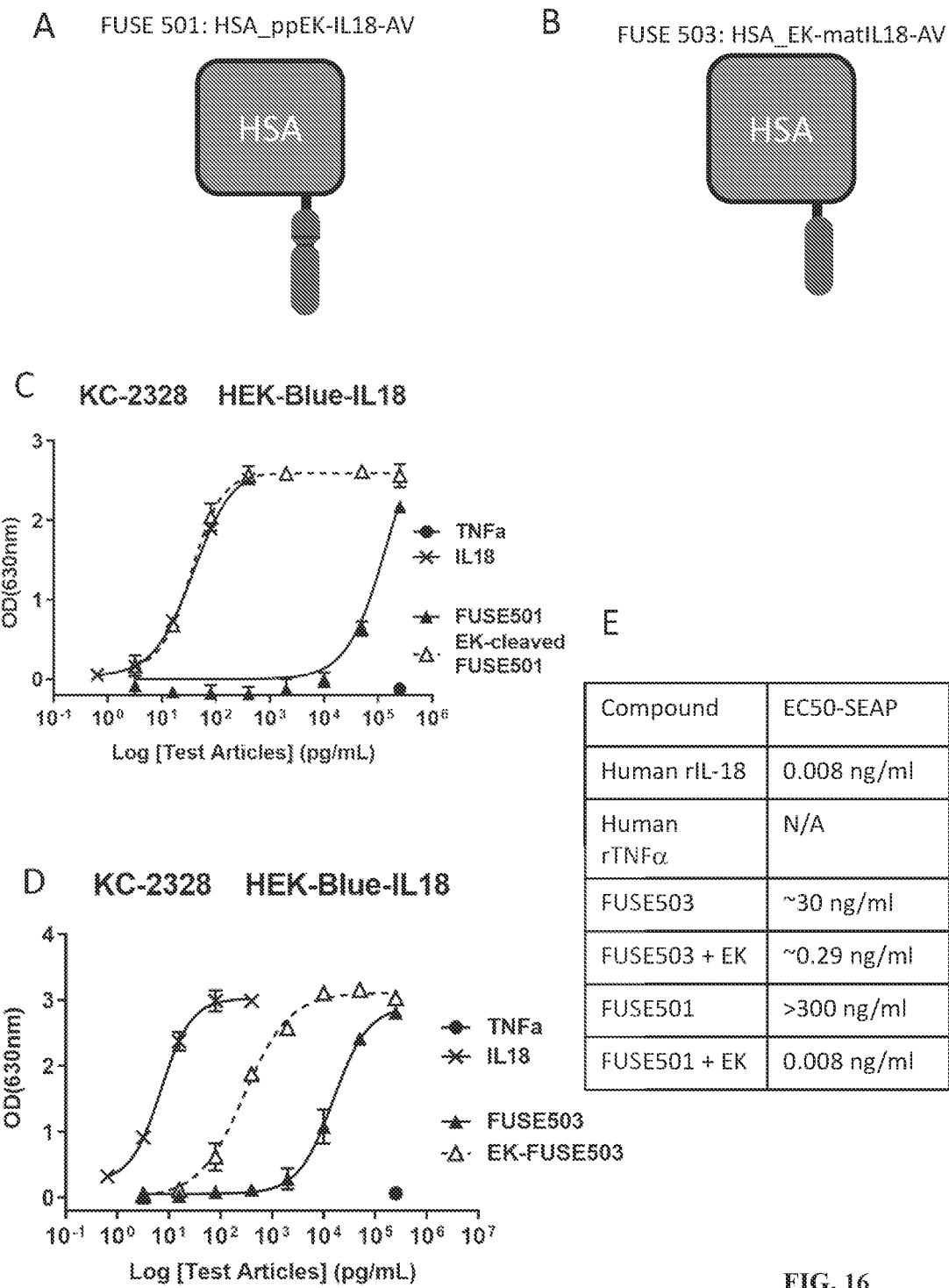


FIG. 15



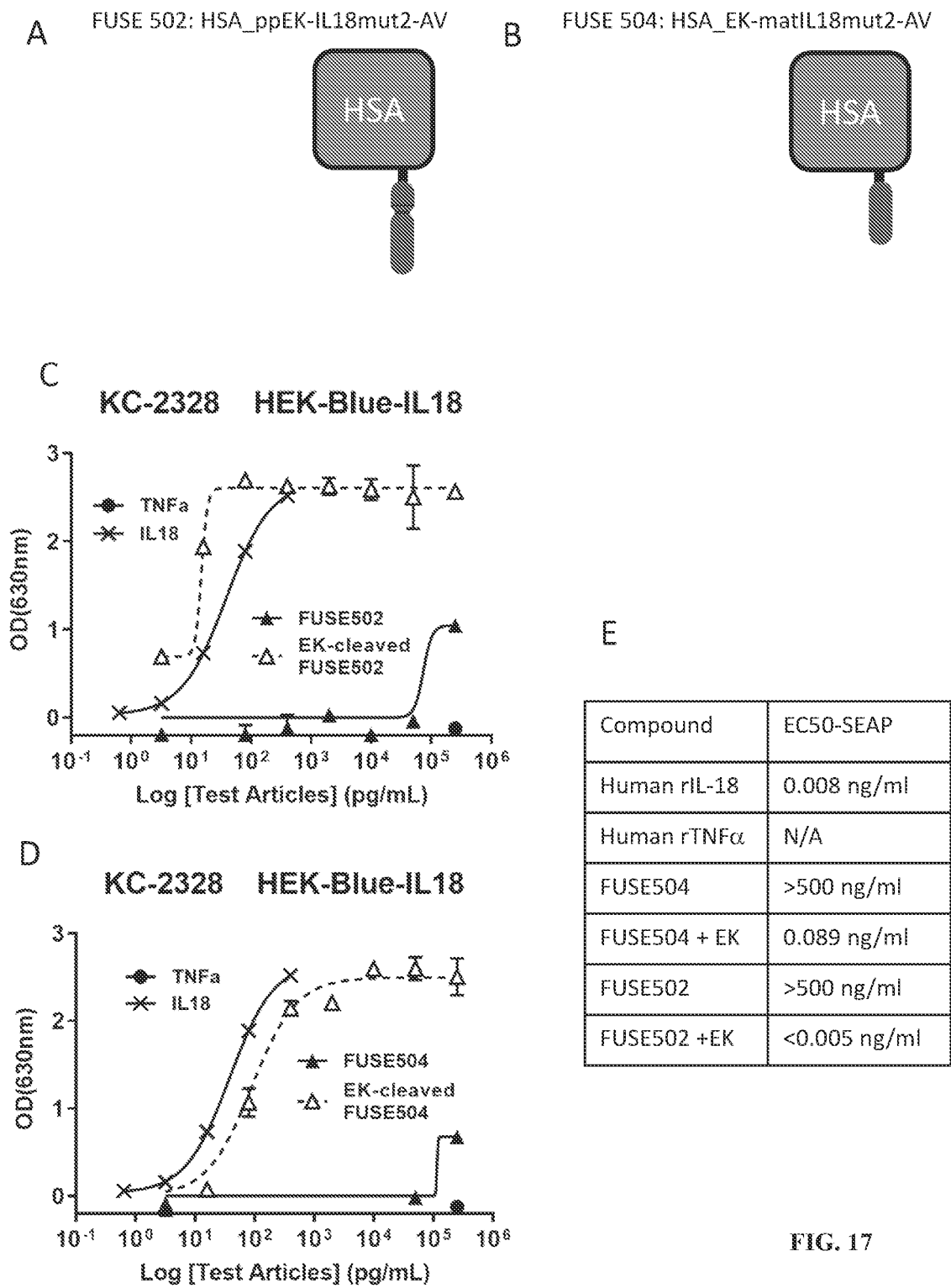


FIG. 17

FIG. 18

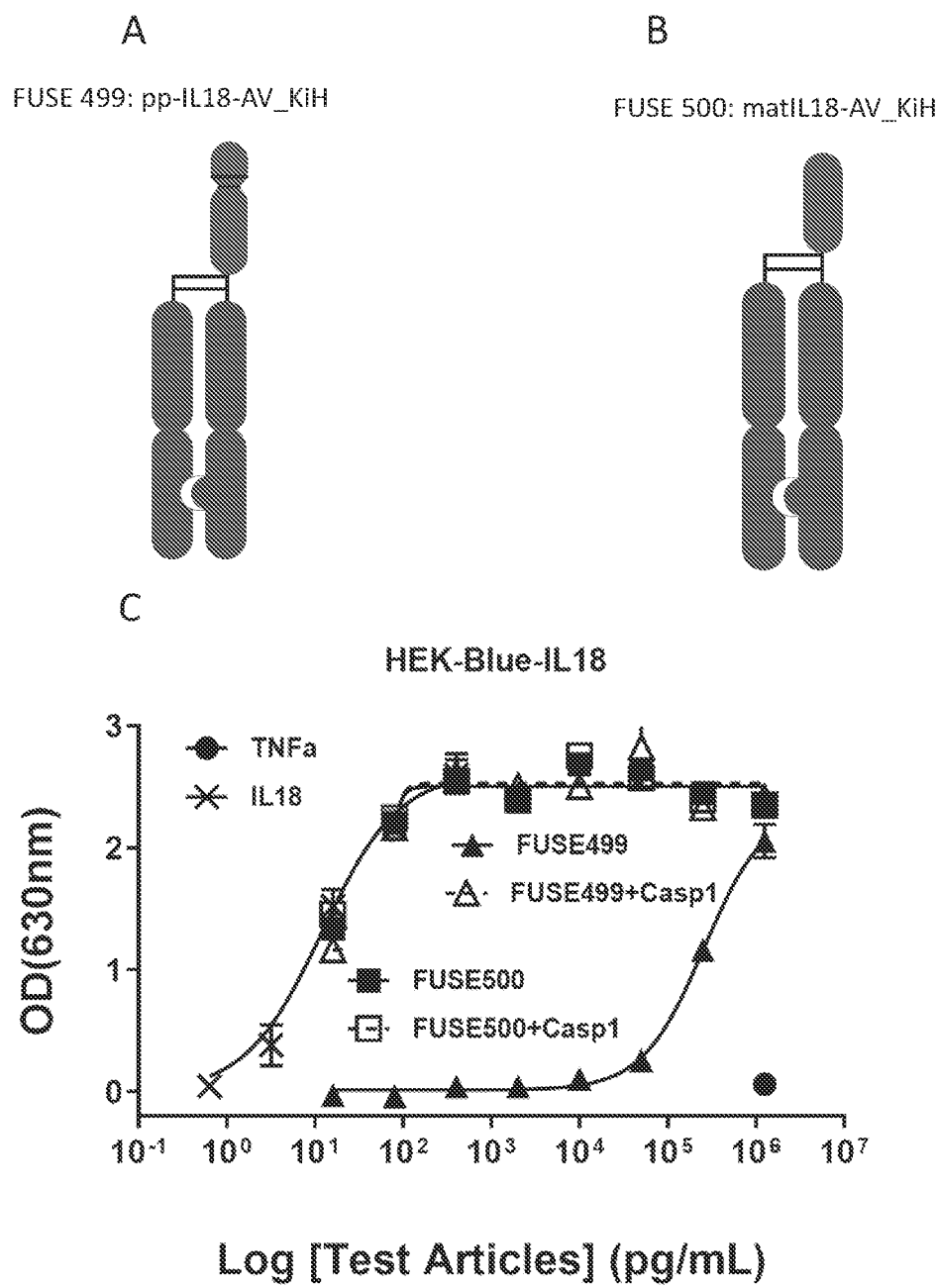


FIG. 18

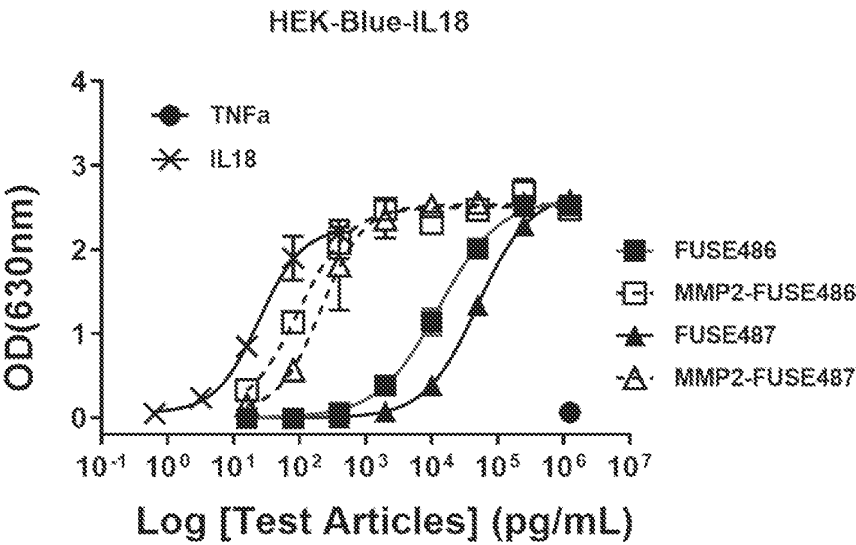
D

Compound	EC50-SEAP
Human rIL-18	0.01 ng/ml
Human rTNF α	N/A
FUSE499	>500 ng/ml
FUSE499 + Casp1	~0.01 ng/ml
FUSE500	~0.01 ng/ml
FUSE500 + Casp1	~0.01 ng/ml



FUSE 486: KiH_MMP2/9pp-IL18-AV
FUSE 487: KiH_MMP9/2pp-IL18-AV

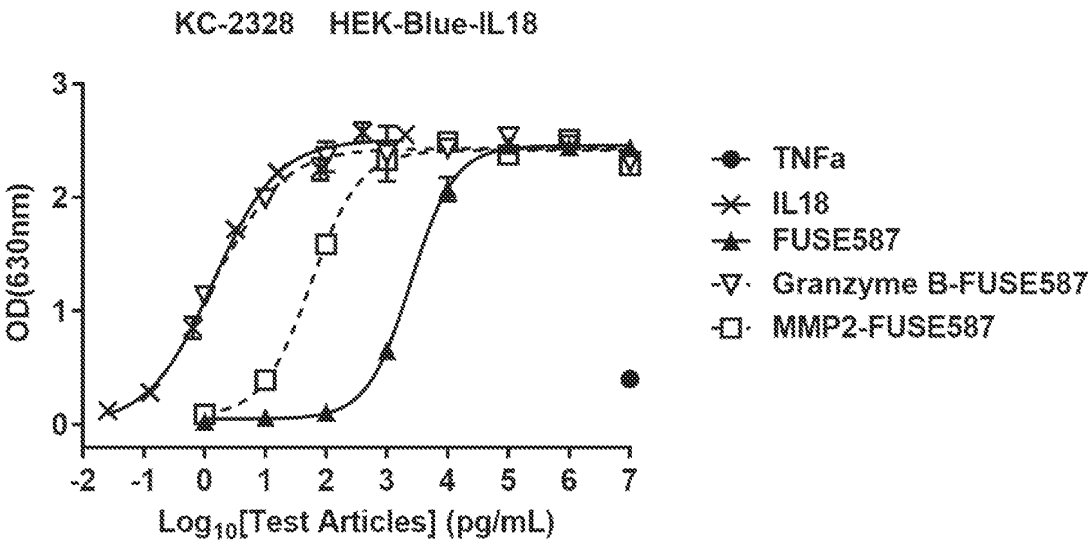
FIG. 19A



Compound	EC50-SEAP
Human rIL-18	0.02 ng/ml
Human rTNFα	N/A
FUSE486	~33 ng/ml
FUSE486 + MMP2	~0.06 ng/ml
FUSE487	~100 ng/ml
FUSE487 + MMP2	~0.12 ng/ml

FIG. 19B

FIG. 19C



Compound	EC50-SEAP
Human rIL-18	1.38
Human rTNFα	N/A
FUSE587	3483
FUSE587 + MMP2	2.23
FUSE587 + Granzyme B	56.24

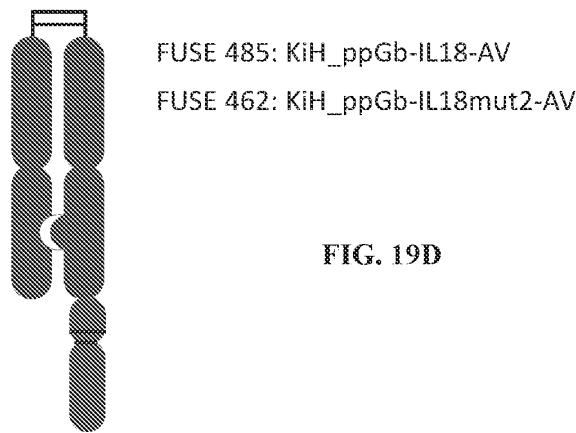


FIG. 19D

FIG. 19E

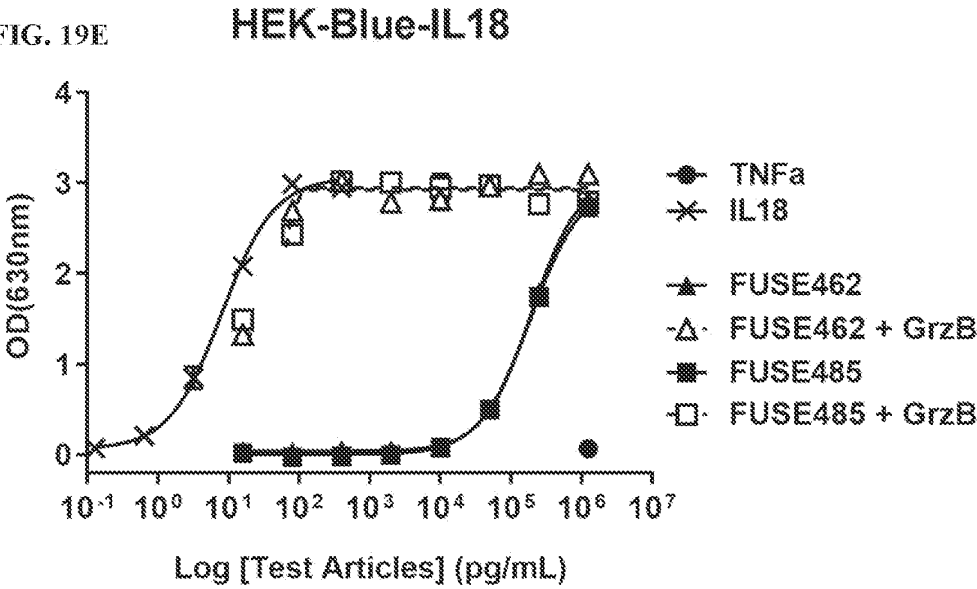


FIG. 19F

Compound.	EC50-SEAP
Human rIL-18	0.0020 ng/ml
Human rTNFα	N/A
FUSE462	>500 ng/ml
FUSE462 + GzmB	~0.03 ng/ml
FUSE485	>500 ng/ml
FUSE485 + GzmB	~0.03 ng/ml

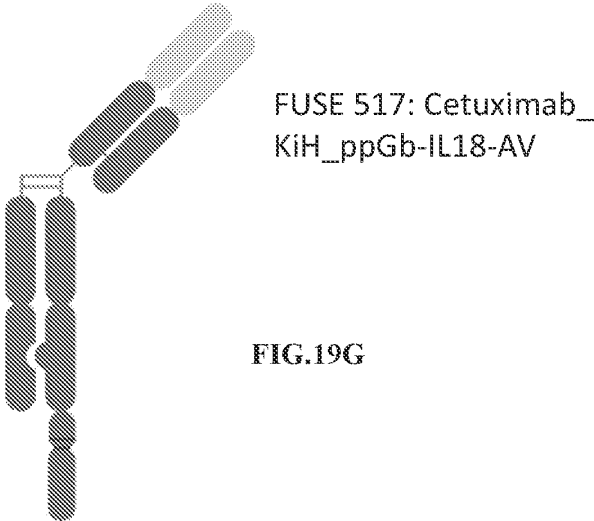


FIG.19G

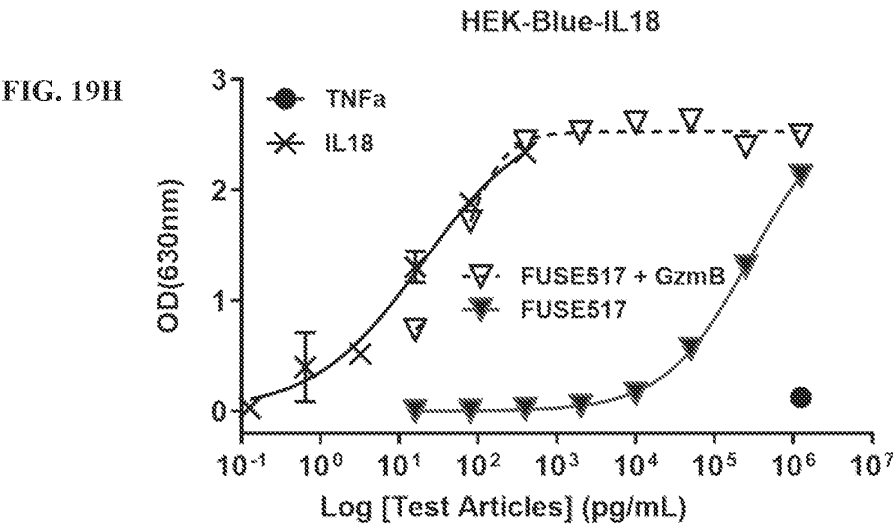


FIG. 19I

Compound	EC50-SEAP
Human rIL-18	0.002 ng/ml
Human rTNFα	N/A
FUSE517	>500 ng/ml
FUSE517 + GzmB	~0.03 ng/ml

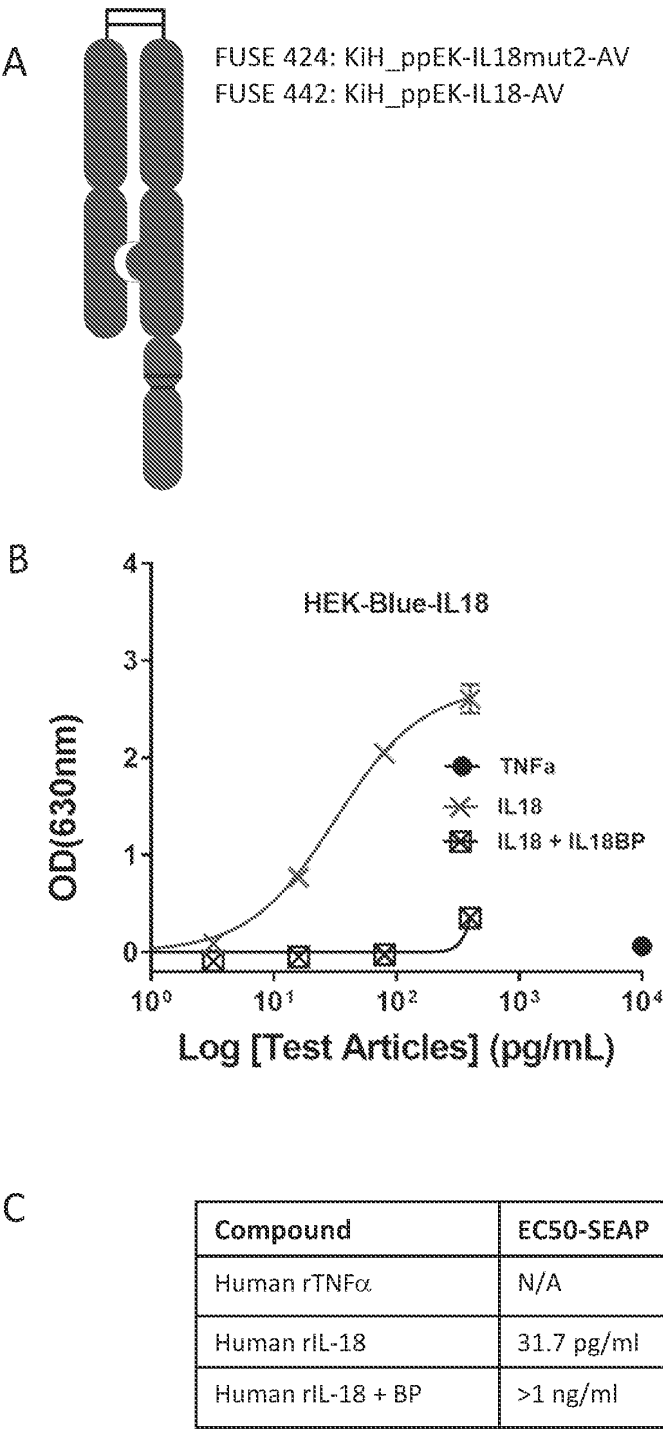


FIG. 20

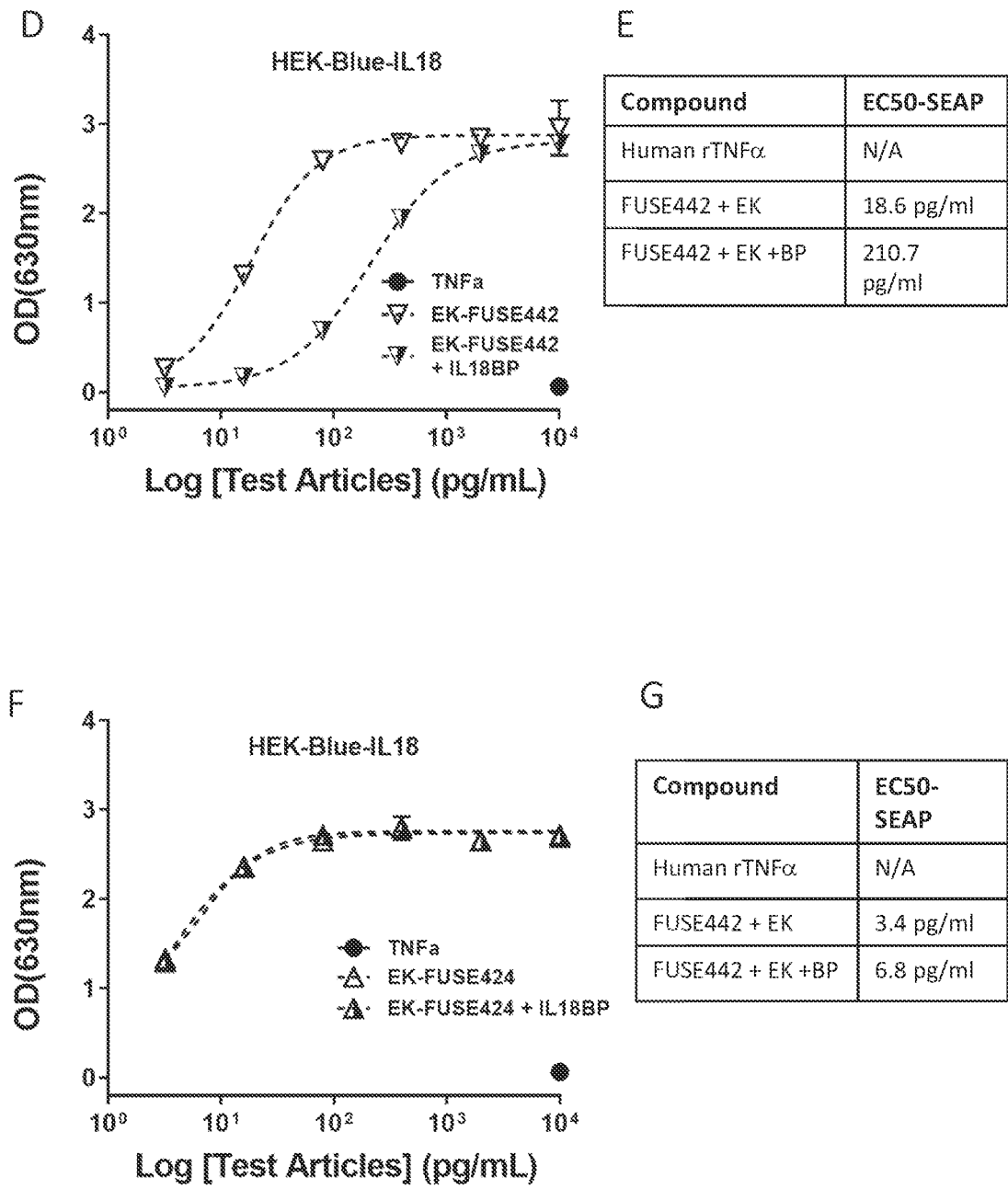
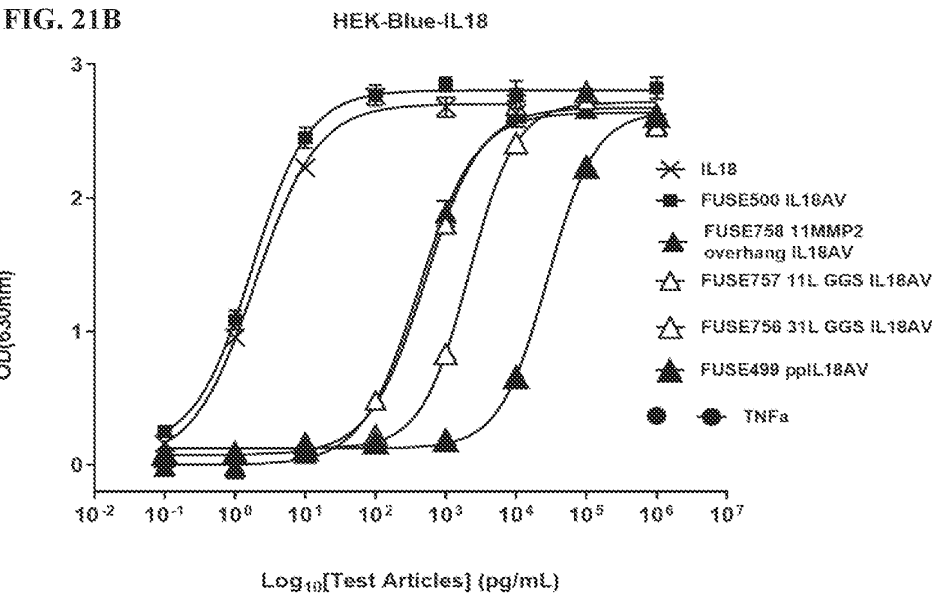
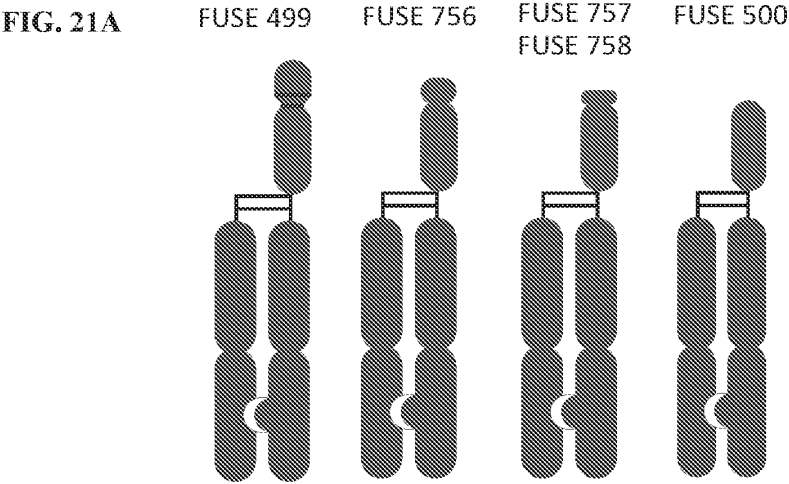


FIG. 20



Compound	EC50-SEAP
Human rTNF α	N/A
Human rIL-18	2 pg/ml
FUSE500	1.7 ng/ml

Compound	EC50-SEAP
FUSE758	413 ng/ml
FUSE757	500 ng/ml
FUSE756	2100 ng/ml
FUSE499	>30,000 ng/ml

	mut2	mut3	mut4	mut5	mut6	mut7	mut8	mut9	mut10	mut11	mut12
Fuse-500 (wt-AV)	Fuse-545	Fuse-546	Fuse-547	Fuse-583	Fuse-584	Fuse-585	Fuse-586	Fuse-599	Fuse-600	Fuse-601	Fuse-602
E42	-	K	R	A	H	R	Q	K	K		
M87	K	-	-					H	K	H	K
K89	G	G	G	A	G	E	A	G	G	A	A
M96	L	-	-					-	-	I	I
M149	V	-	-					-	-	I	I

FIG. 22A

	IL-18*	FUSE 500	FUSE 545	FUSE 546	FUSE 547	FUSE 583	FUSE 584	FUSE 585	FUSE 586	FUSE 599	FUSE 600	FUSE 601	FUSE 602
IL-18 BP Kd (nM)	4.00E-10	7.28E-10*	-	1.40E-07	4.00E-08	3.20E-09	4.00E-08	1.50E-07	2.60E-09	-	-	-	-

*www.pnas.org/doi/10.1073/pnas.97.3.1190

FIG. 22C

	IL18*	FUSE 500	FUSE 545	FUSE 546	FUSE 547	FUSE 583	FUSE 584	FUSE 585	FUSE 586	FUSE 599	FUSE 600	FUSE 601	FUSE 602
IL-18RA Kd (nM)	2E-08*	7.4E-09**	1.90E-08	1.80E-08	2.60E-08	1.20E-08	2.50E-08	2.00E-08	1.60E-08	3.00E-08	1.80E-08	2.10E-08	1.10E-08

*arthritis-research.biomedcentral.com/articles/10.1186/ar3295

FIG. 22E

FIG. 22B(i)

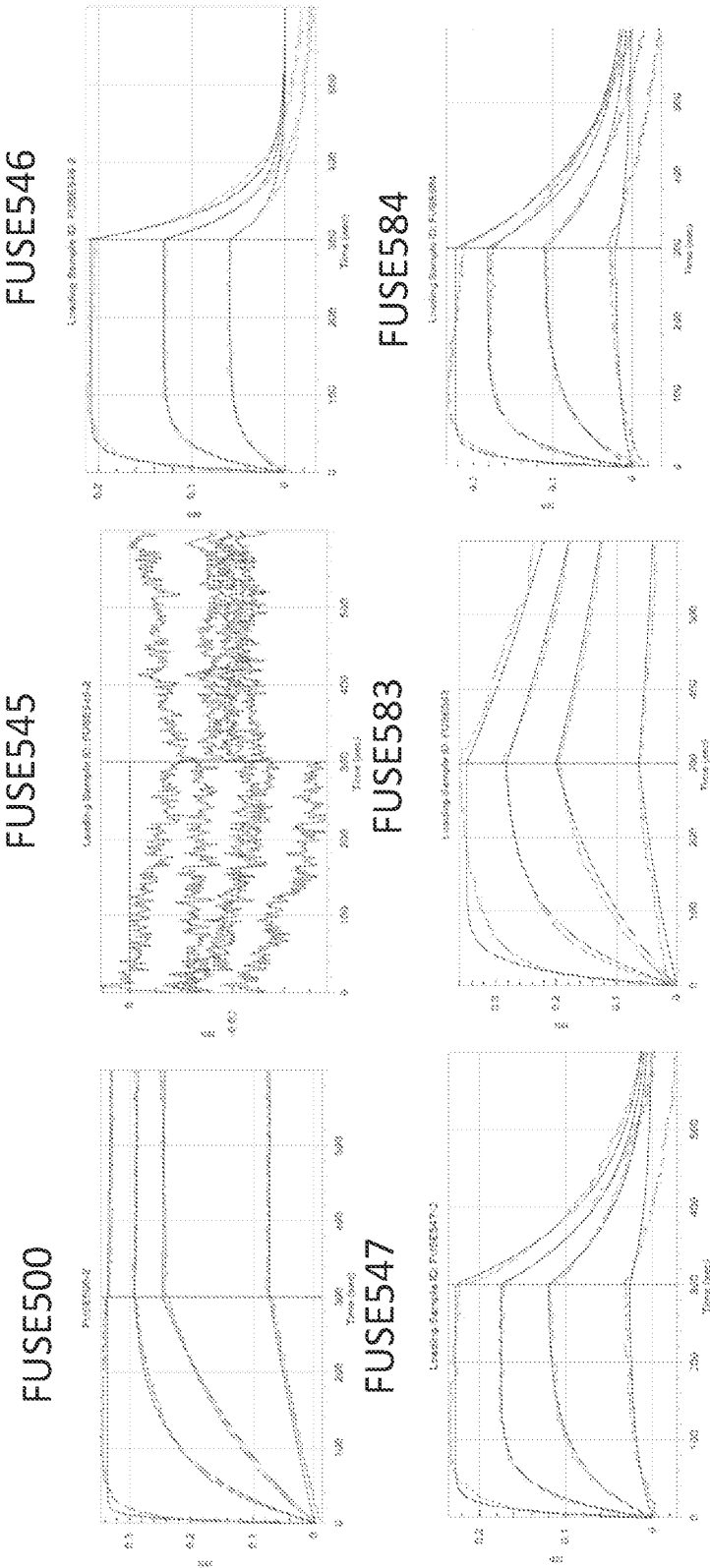


FIG. 22B(ii)

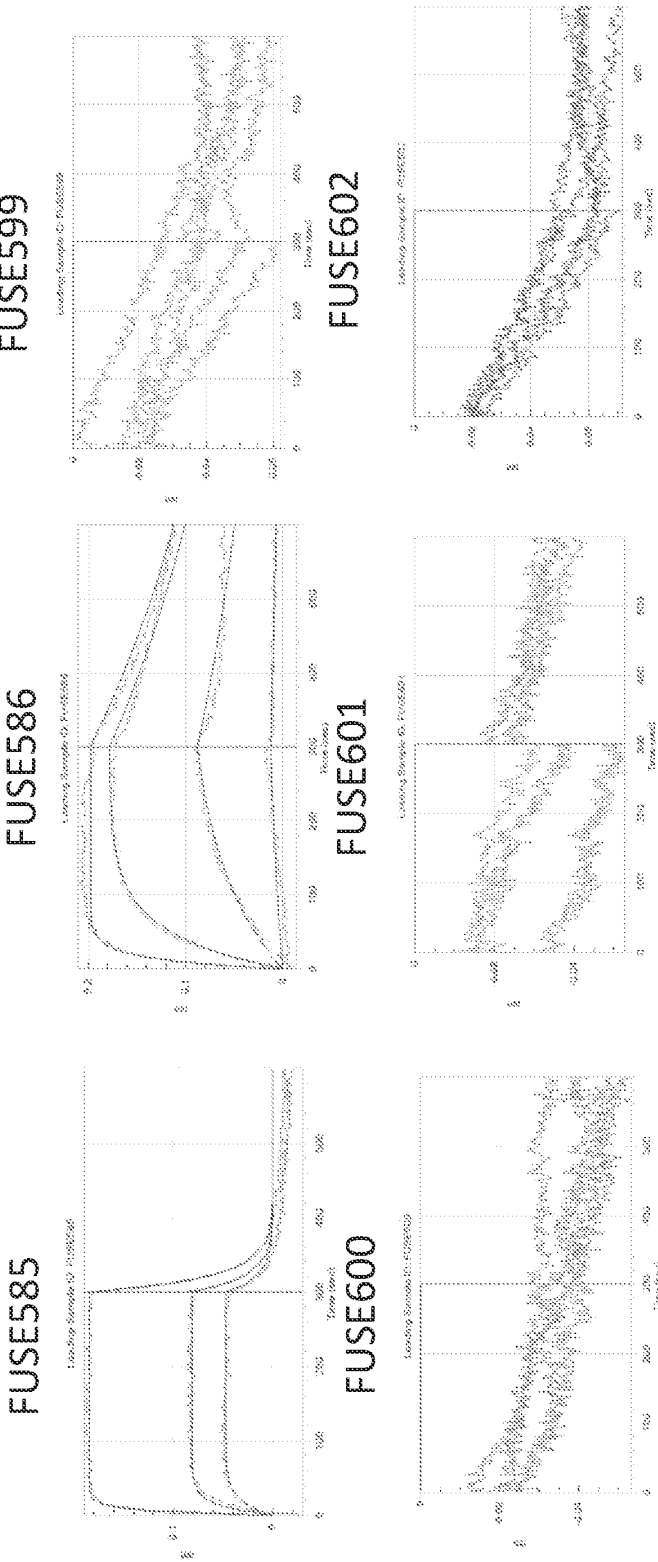
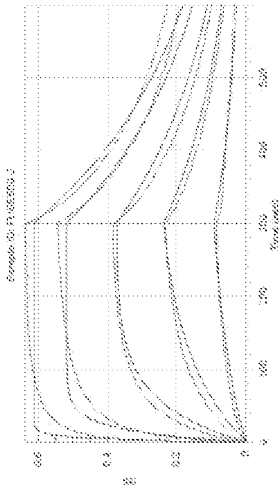
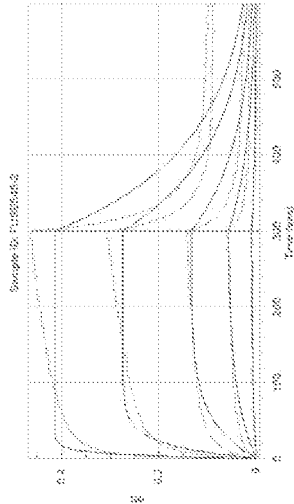


FIG. 22D(i)

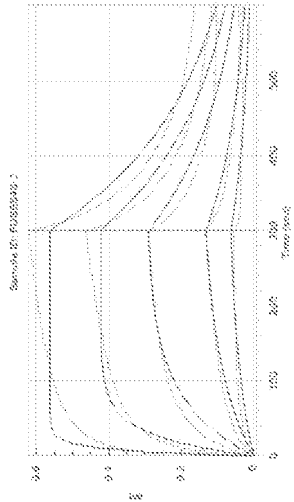
FUSE500



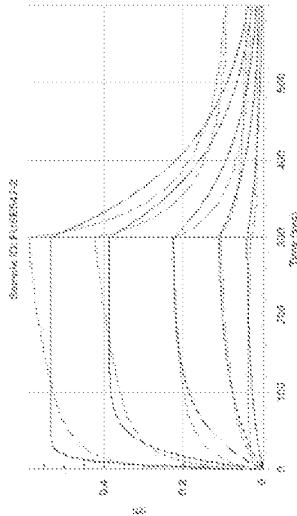
FUSE545



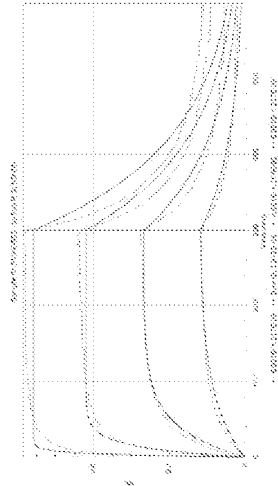
FUSE546



FUSE547



FUSE583



FUSE584

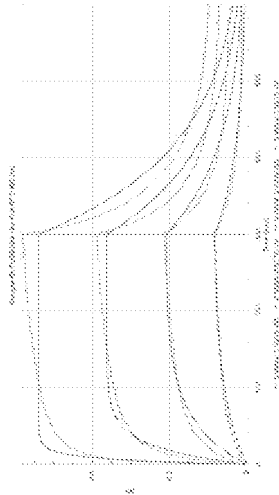


FIG. 22D(ii)

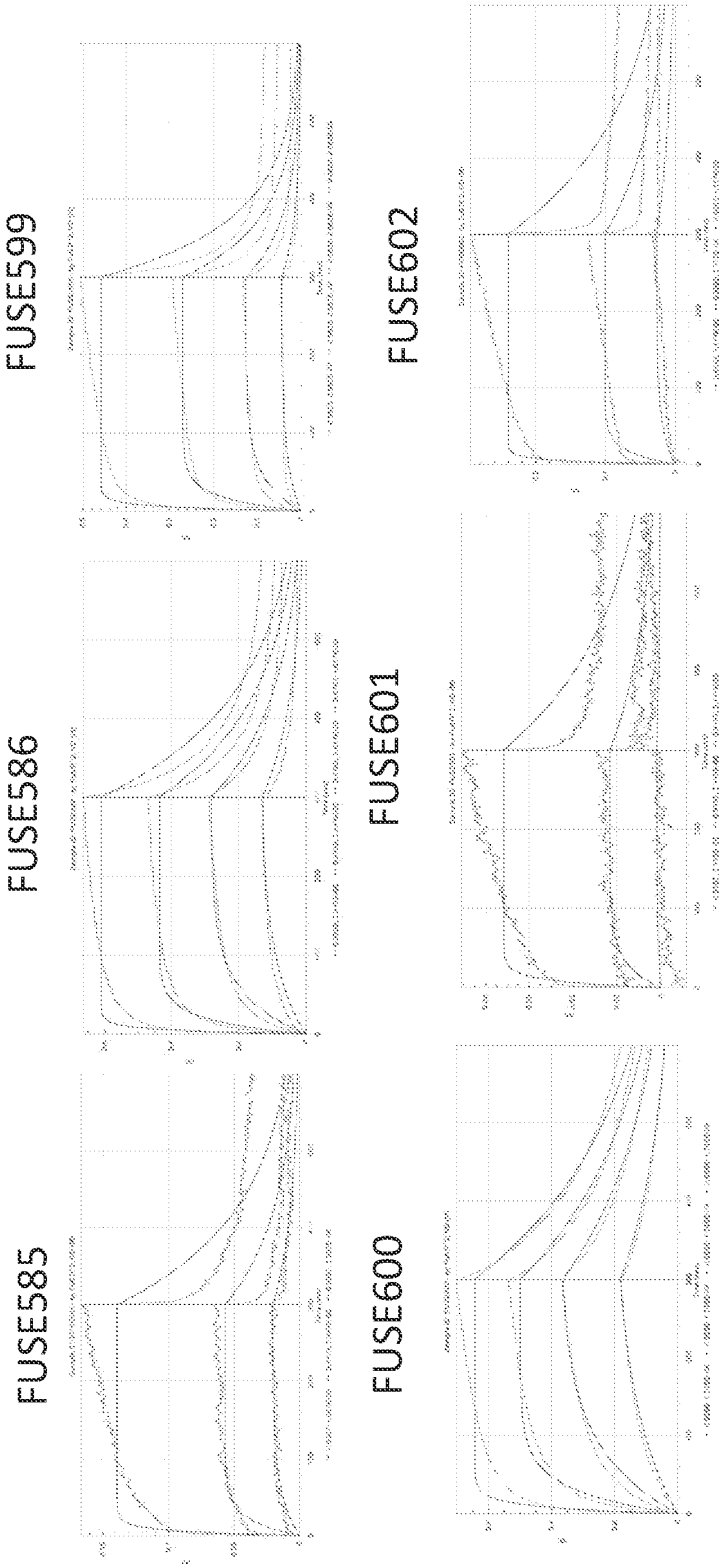
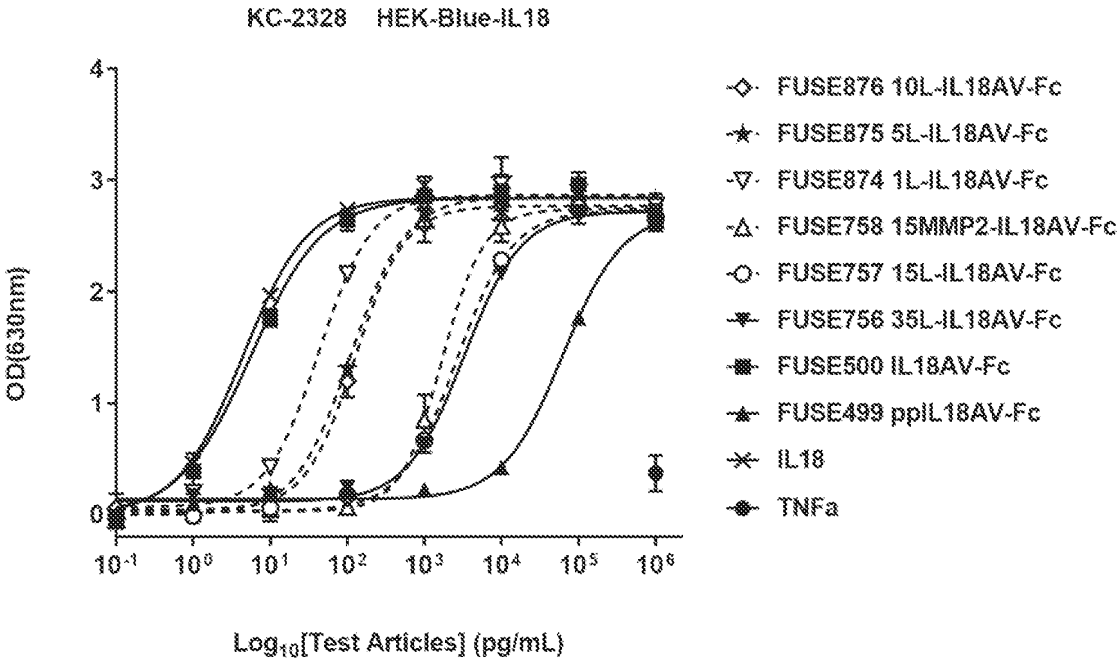
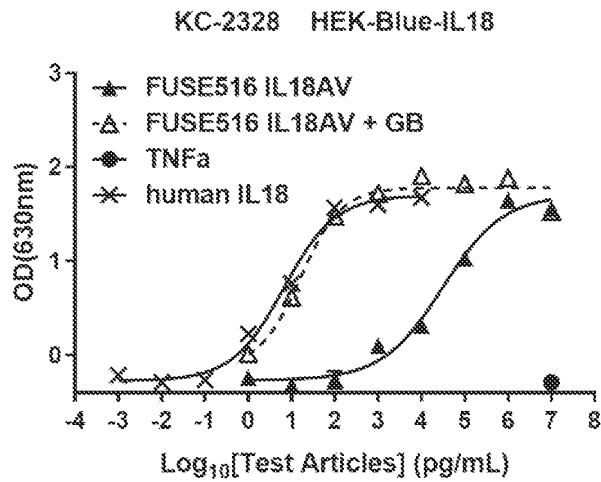


FIG. 23

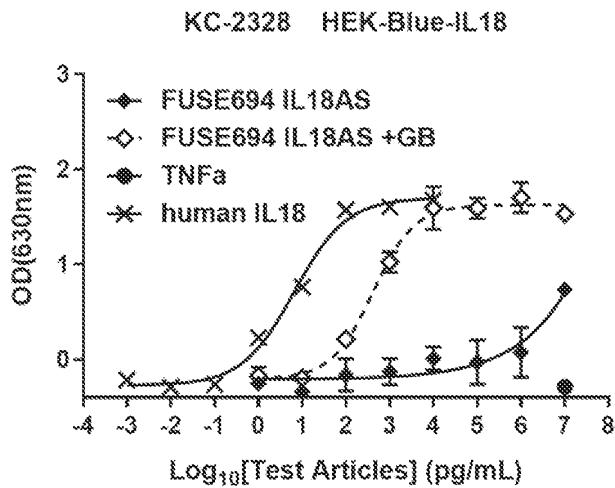


Compound	EC50-SEAP
Human rIL-18	0.0044 ng/mL
FUSE500	0.0056 ng/mL
Human rTNFα	N/A
FUSE874 (L)	0.053 ng/mL
FUSE875 (5L)	0.1103 ng/mL
FUSE876 (10L)	0.1258 ng/mL
FUSE758 (15MM)	1.689 ng/mL
FUSE756 (35L)	3.257 ng/mL
FUSE499 (pp)	62.14 ng/mL



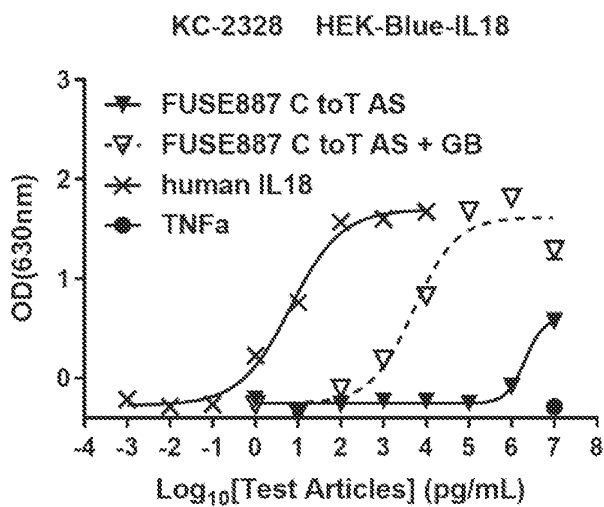
Compound	EC50-SEAP
Human rIL-18	6.67 pg/mL
Human rTNFα	N/A
FUSE516	31000 pg/ml
FUSE516 + GB	16.4 pg/ml

FIG. 24A



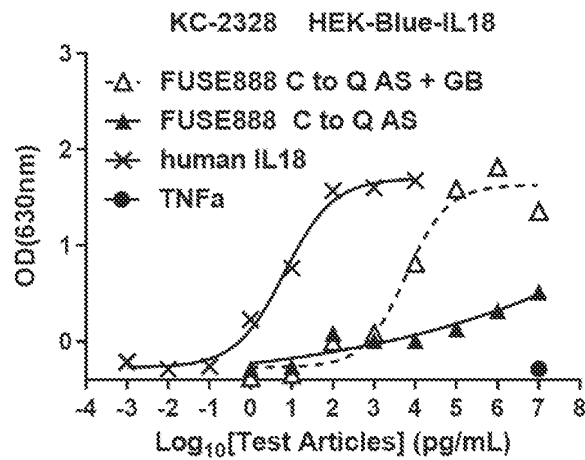
Compound	EC50-SEAP
Human rIL-18	6.66 pg/ml
Human rTNFα	N/A
FUSE694	>1,000,000 pg/ml
FUSE695 + GB	421.1 pg/ml

FIG. 24B



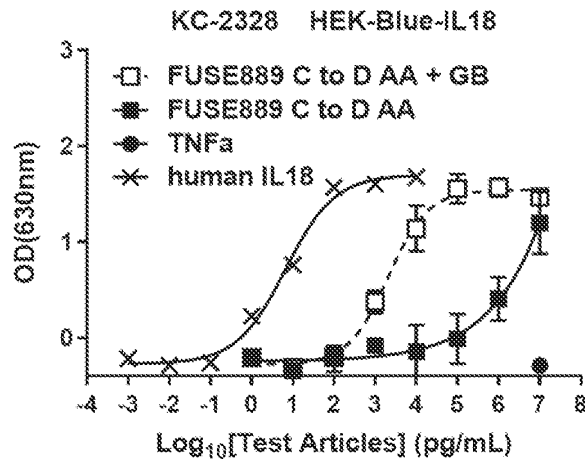
Compound	EC50-SEAP
Human rIL-18	6.7 pg/mL
Human rTNFα	N/A
FUSE887	>2000000 pg/ml
FUSE887 + GB	5000 pg/ml

FIG. 24C



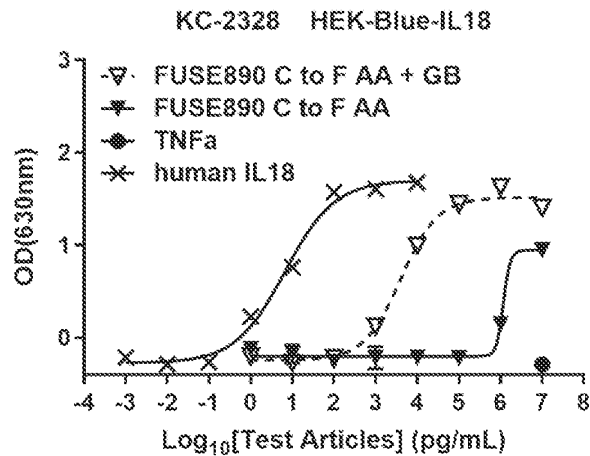
Compound	EC50-SEAP
Human rIL-18	6.7 pg/mL
Human rTNFα	N/A
FUSE888	>1000000 pg/ml
FUSE888+ GB	5900 pg/ml

FIG. 24D



Compound	EC50-SEAP
Human rIL-18	6.7 pg/mL
Human rTNFα	N/A
FUSE889	>1000000 pg/ml
FUSE889 + GB	2083 pg/ml

FIG. 24E



Compound	EC50-SEAP
Human rIL-18	6.7 pg/mL
Human rTNFα	N/A
FUSE890	>1000000 pg/ml
FUSE890 + GB	4000 pg/ml

FIG. 24F

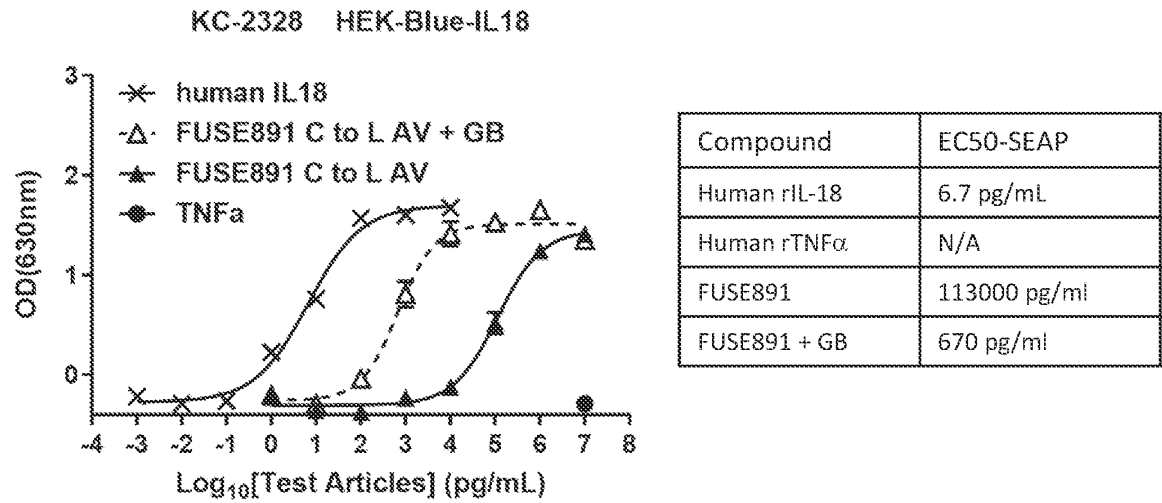


FIG. 24G

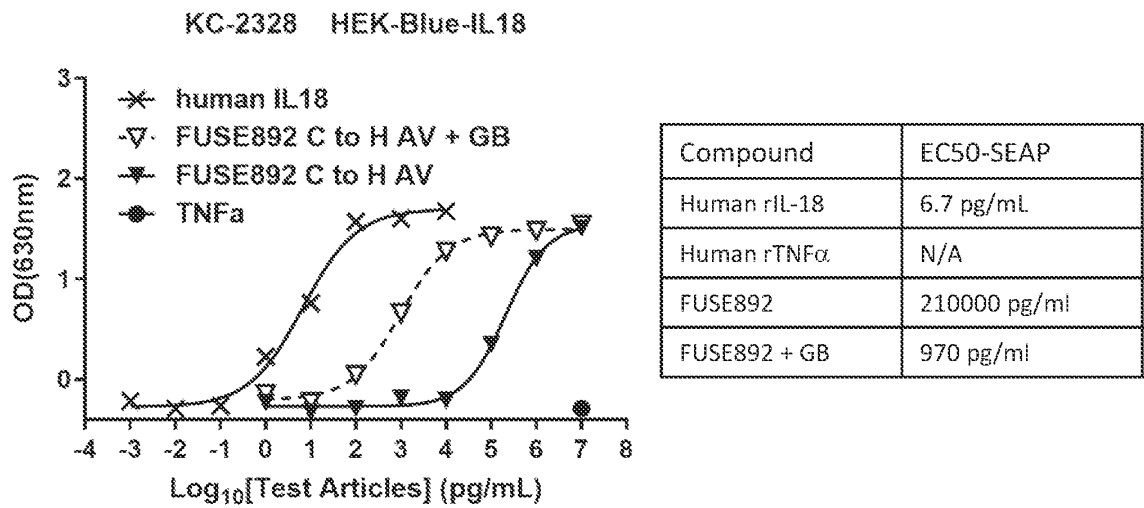


FIG. 24H

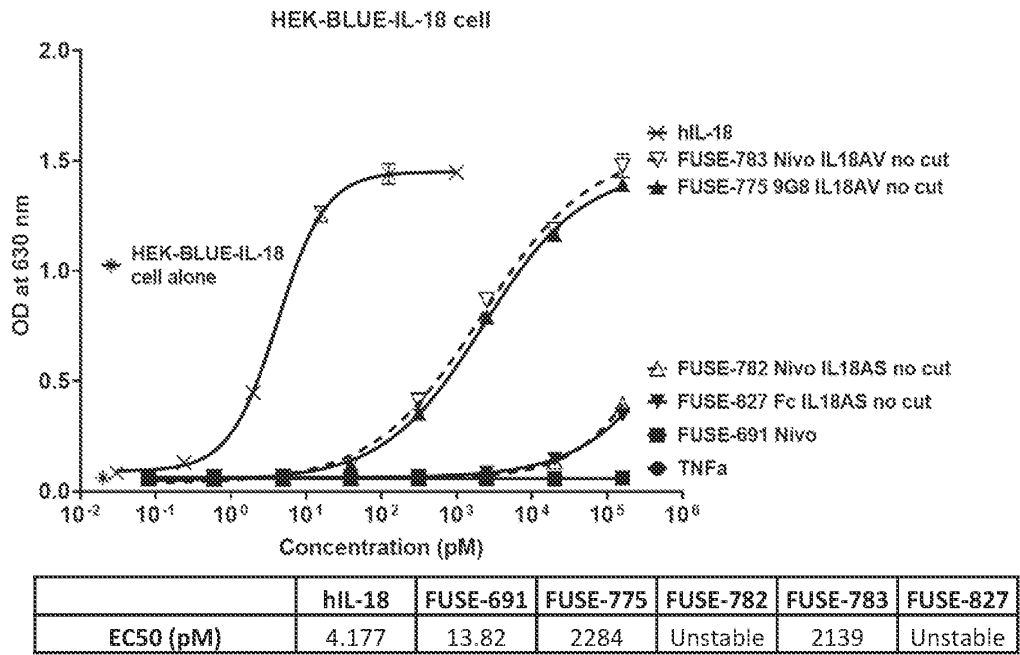


FIG. 25A

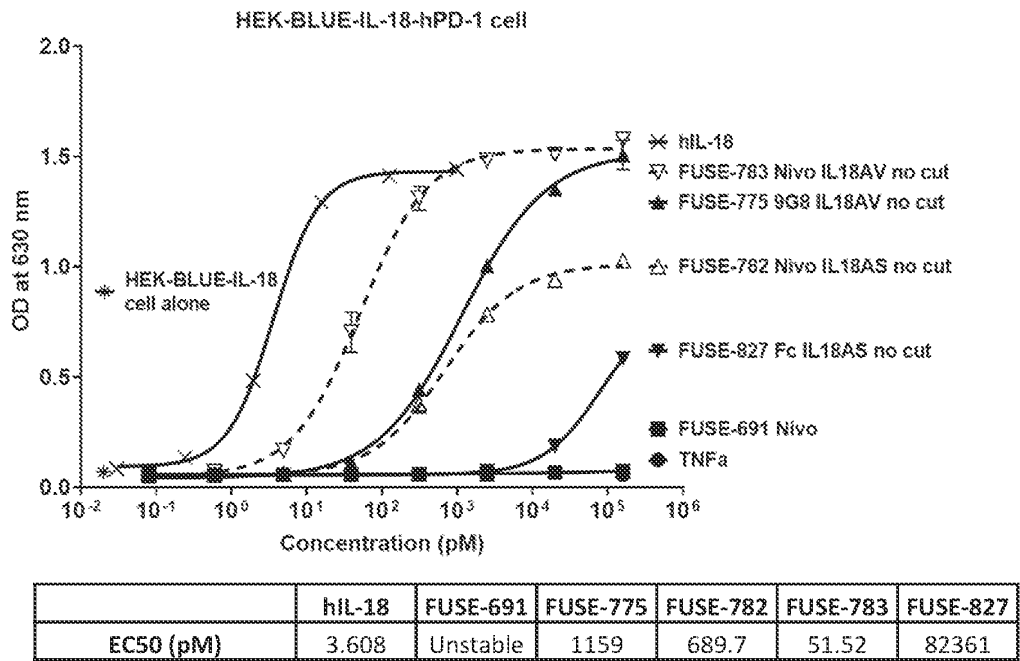
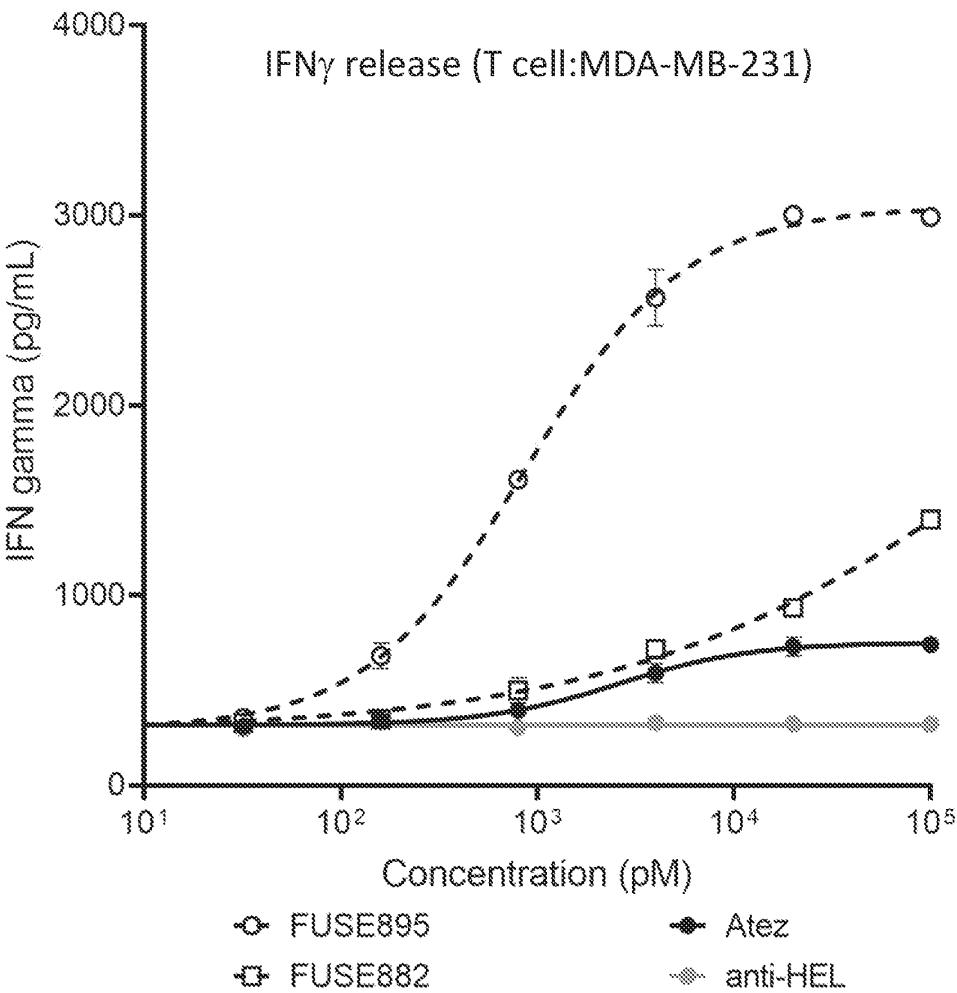


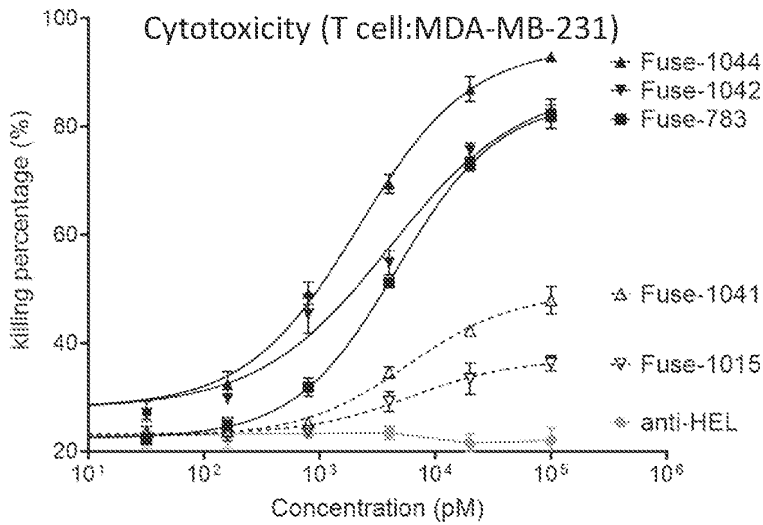
FIG. 25B

FIG. 26



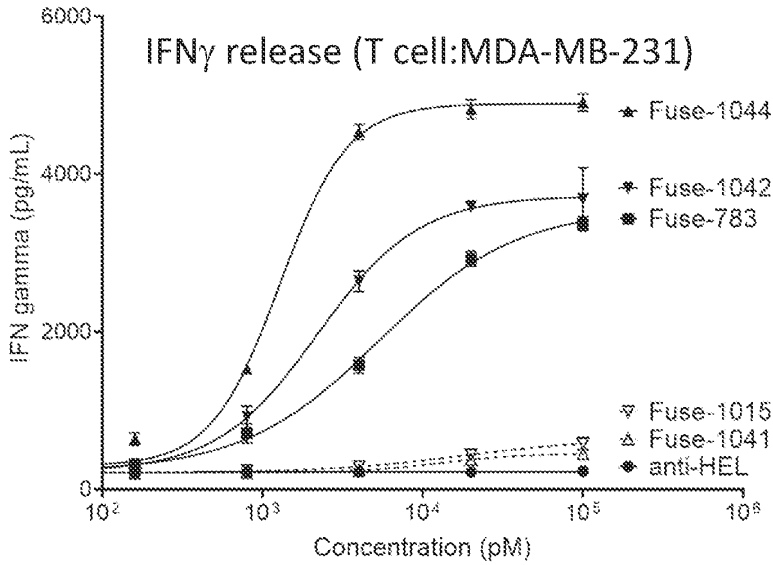
	anti-HEL	Atez	Fuse-882	Fuse-895
IFNg Emax (%)	318.1	751.5	3351	3044
IFNg EC50 (pM)	0.5504	2593	>10,000	876.1
IFNg AUC	3.2E+07	71317675	1.09E+08	2.92E+08

FIG. 27A



	anti-HEL	Fuse-783	Fuse-1041	Fuse-1042	Fuse-1044	Fuse-1015
Killing Emax (%)		84.83	49.35	87.52	94.77	37.01
Killing EC50 (pM)		4645	5813	4031	2171	6088
Killing AUC	2194985	7344089	4337316	7547916	8662867	3392542

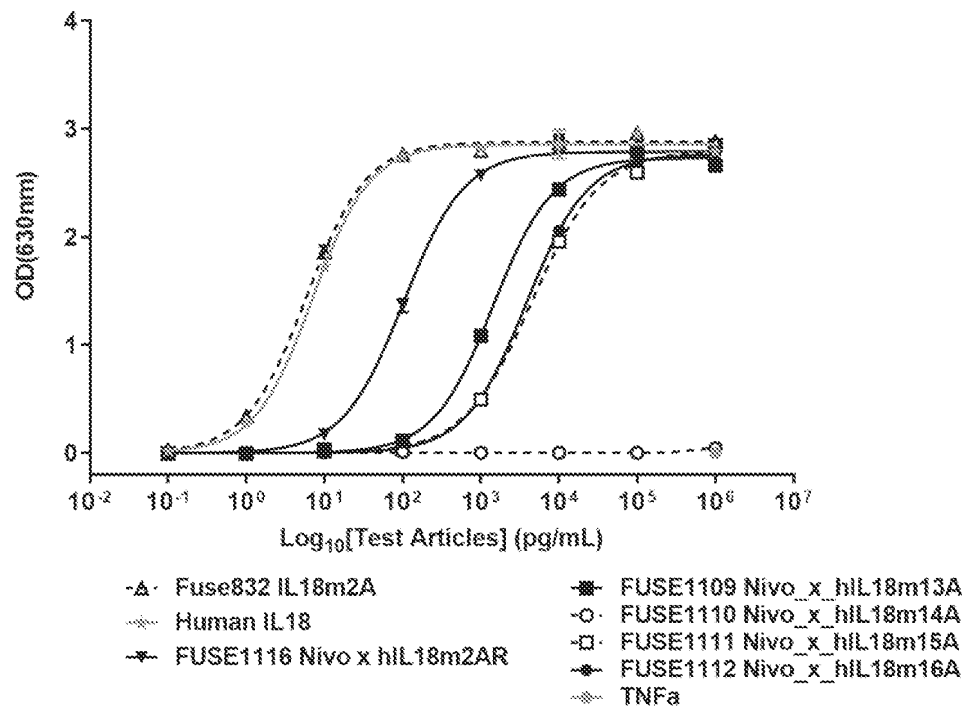
FIG. 27B



	anti-HEL	Fuse-783	Fuse-1041	Fuse-1042	Fuse-1044	Fuse-1015
IFN gamma release Emax (pg/mL)	223.2	3565	455.8	3725	4896	648.9
IFN gamma release EC50 (pM)	Unstable	5398	12697	2213	1280	18429
IFN gamma release AUC	22390830	2.92E+08	38837375	3.47E+08	4.75E+08	47693103

FIG. 28

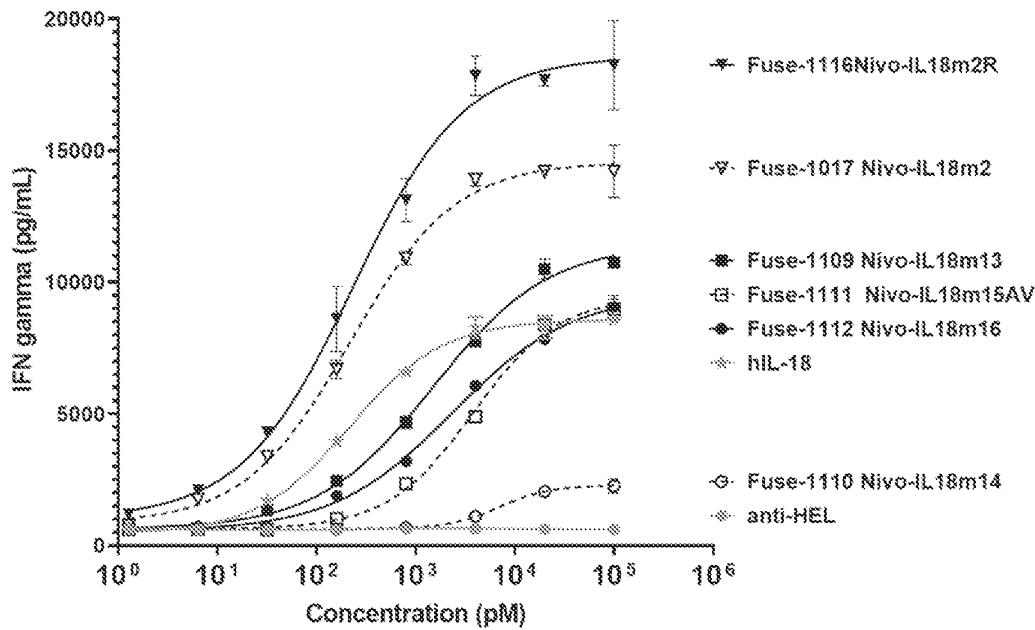
HEK-Blue IL-18 mediated SEAP release



Group	EC50(pg/ml)
TNF-α	N/A
Human IL18	7.22
FUSE832	5.87
FUSE1109	1448.00
FUSE1110	N/A
FUSE1111	4492.00
FUSE1112	3841.00
FUSE1116	104.40

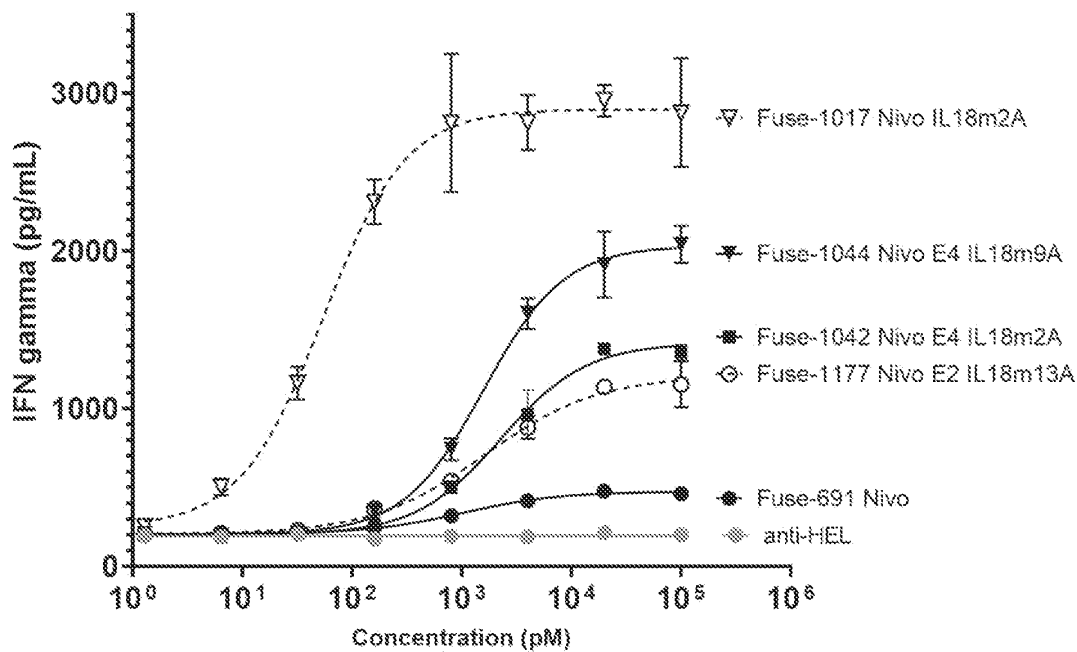
FIG. 29A

T cell mediated IFN γ release



	anti-HEL	hIL-18	Fuse-1017	Fuse-1109	Fuse-1110	Fuse-1111	Fuse-1112	Fuse-1116
IFN gamma release Emax (pg/mL)	N/A	8582	14573	11448	2288	9457	9556	18583
IFN gamma release EC50 (pM)	N/A	216.5	217.3	1509	6826	3794	2353	233.1

FIG. 29B



	Anti-HEL	Fuse-691	Fuse-1042	Fuse-1044	Fuse-1177	Fuse-1017
IFN gamma release Emax (pg/mL)	N/A	474.2	1417	2033	1210	2899
IFN gamma release EC50 (pM)	N/A	1027	2271	1584	1616	54.31

FIG. 30A

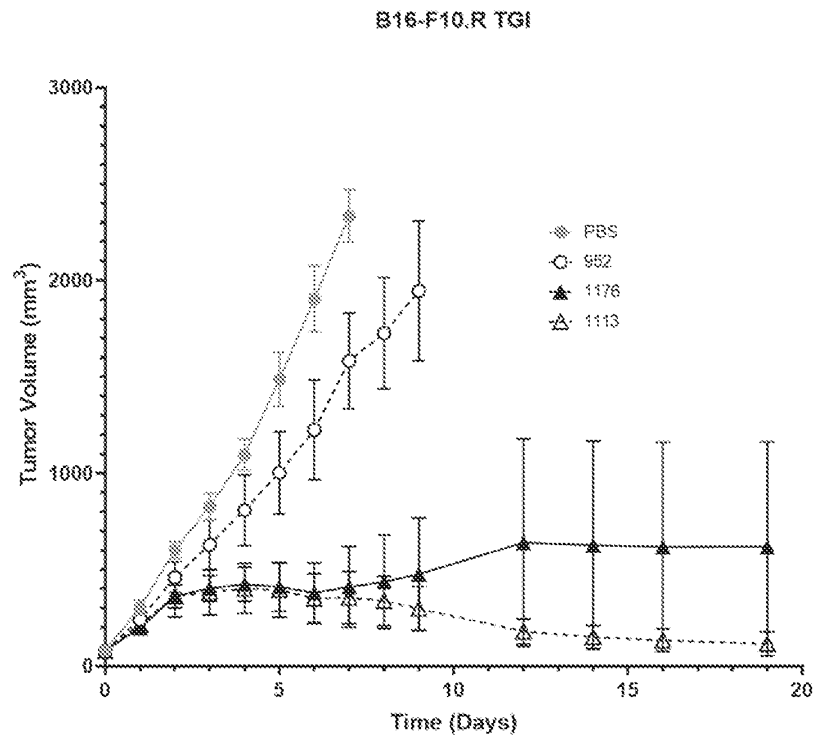


FIG. 30B

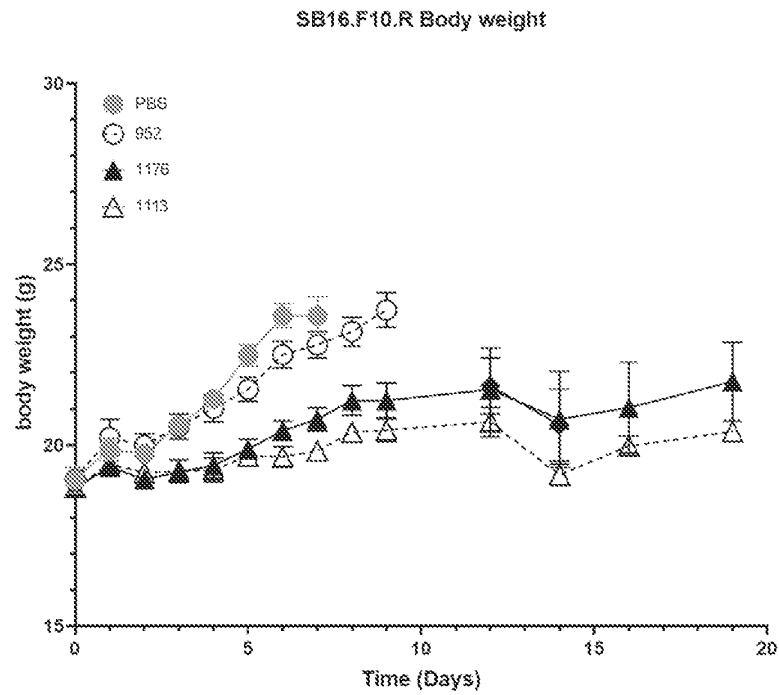


FIG. 30C

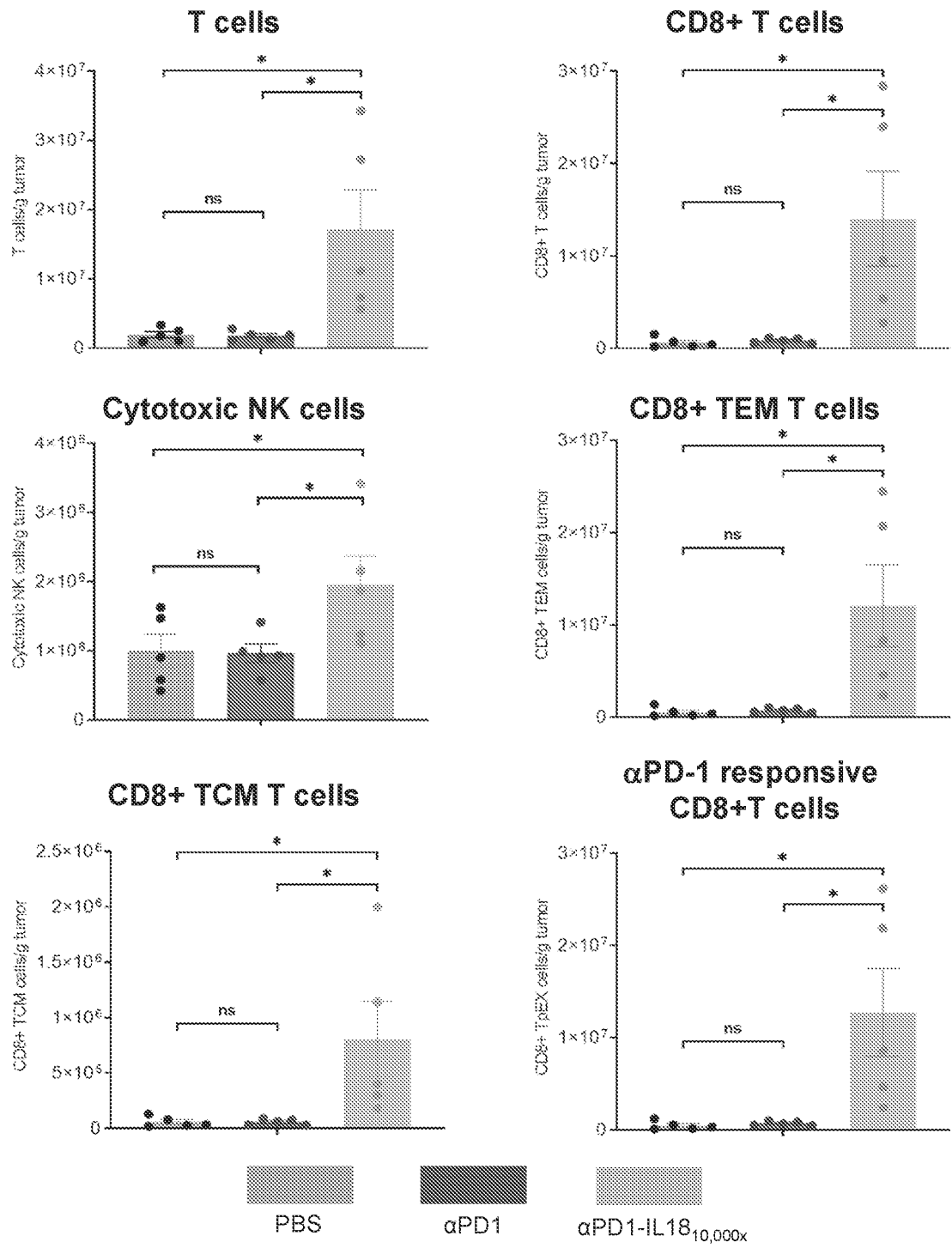


FIG. 30D

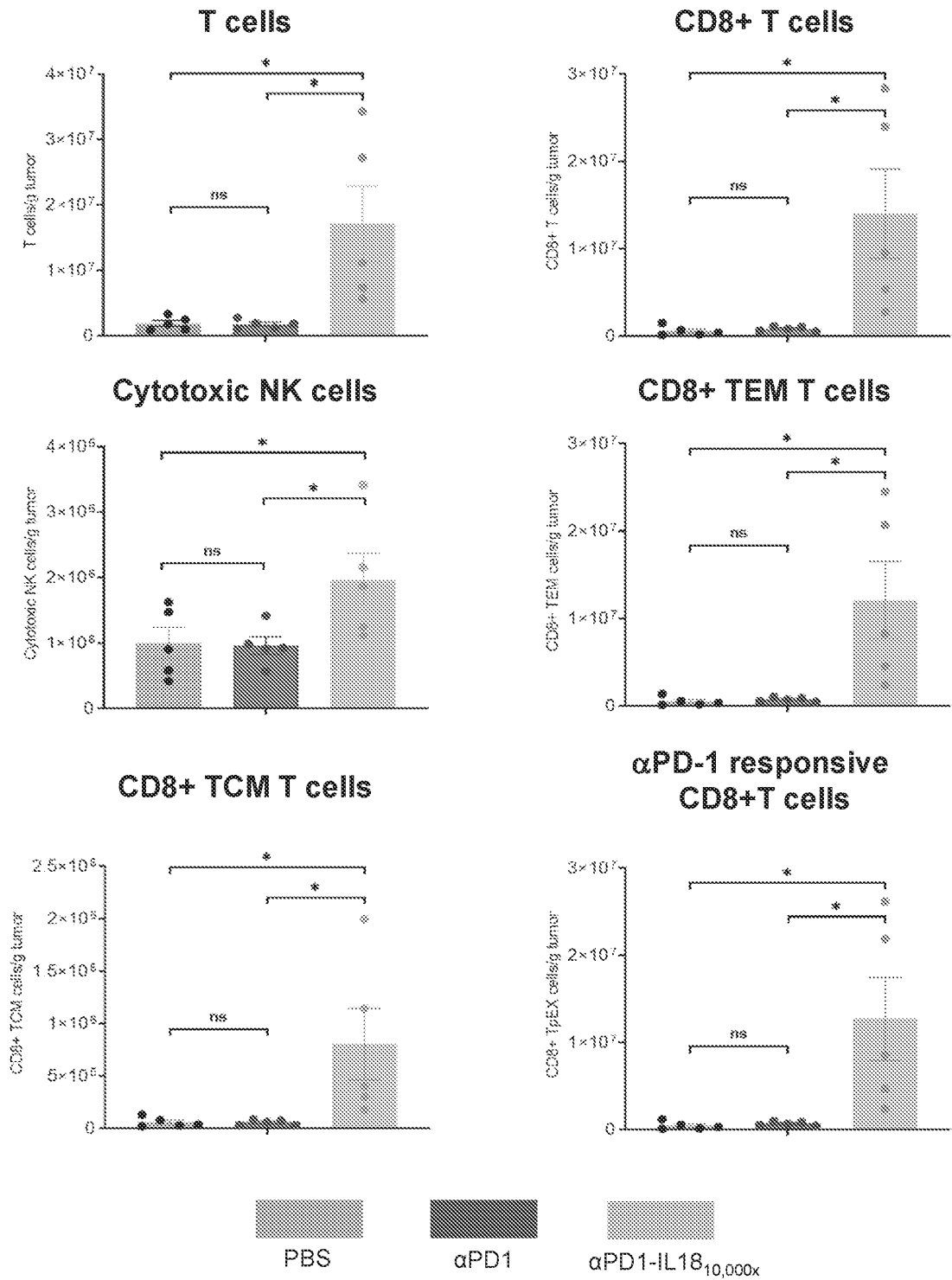


FIG. 31 A

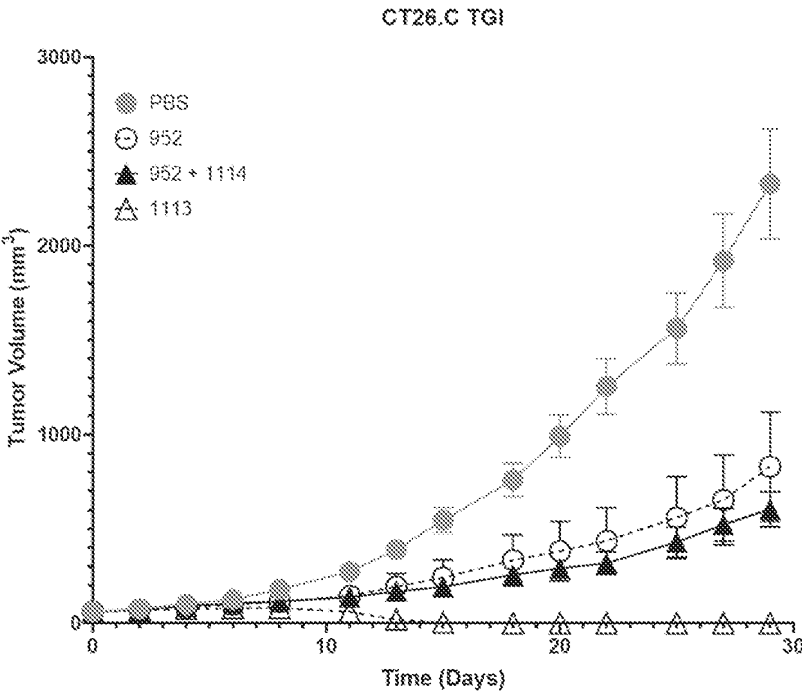
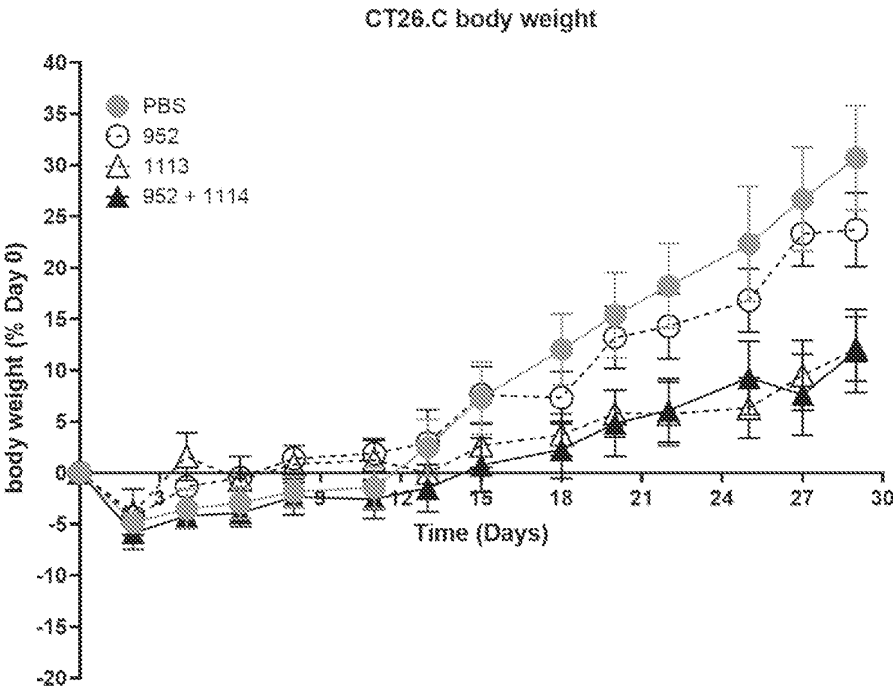


FIG. 31 B



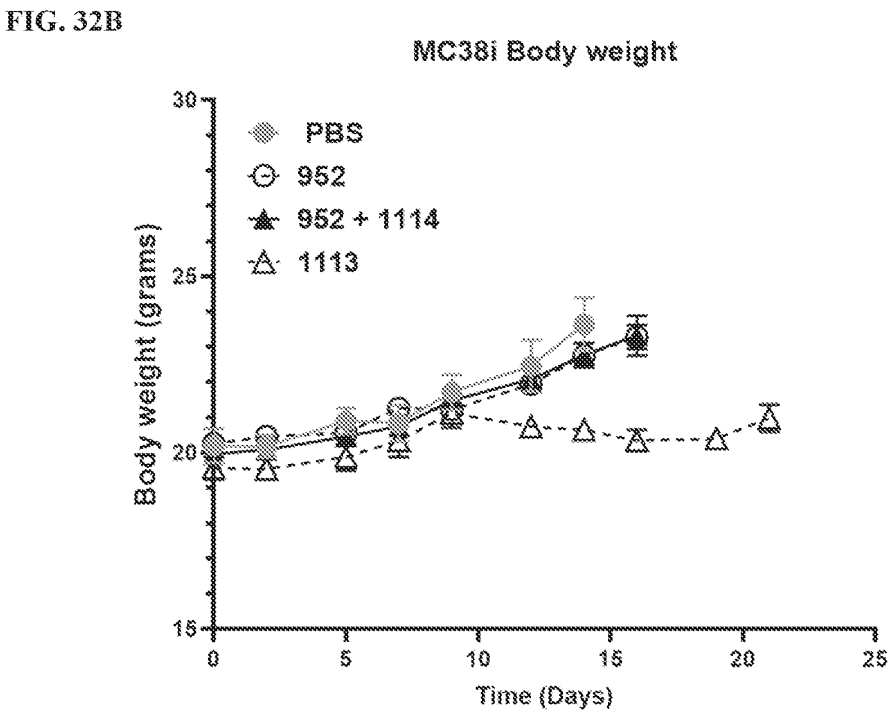
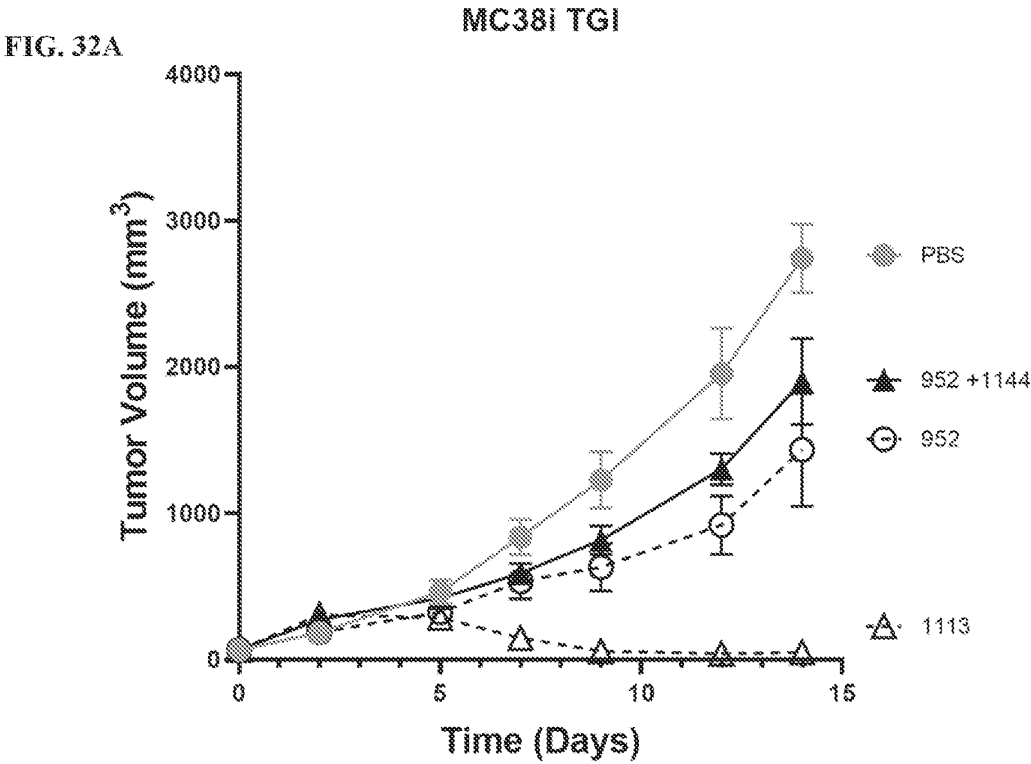


FIG. 33A

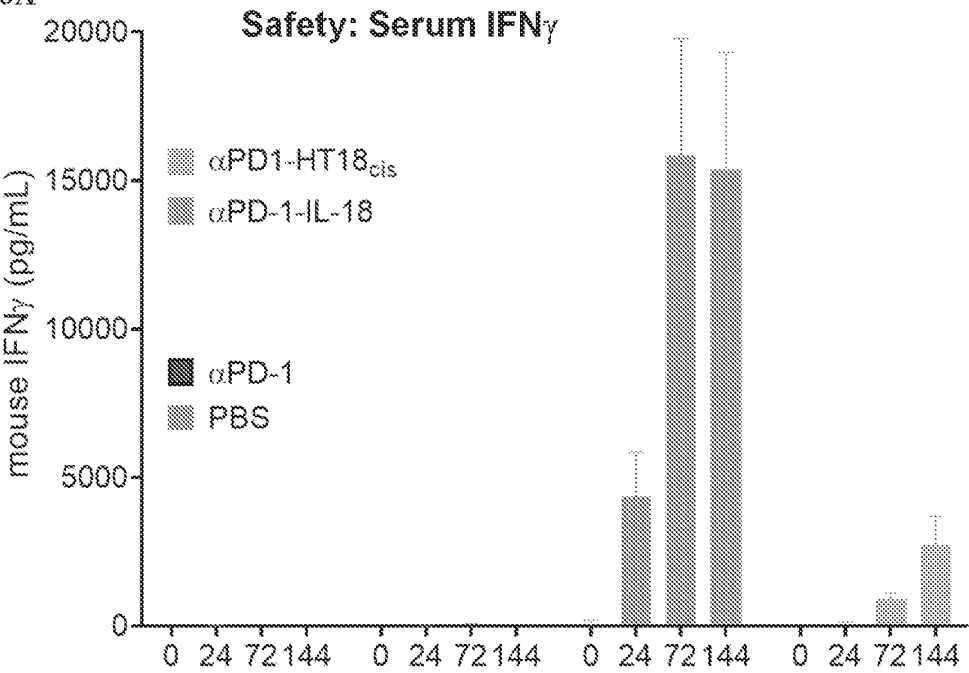


FIG. 33B

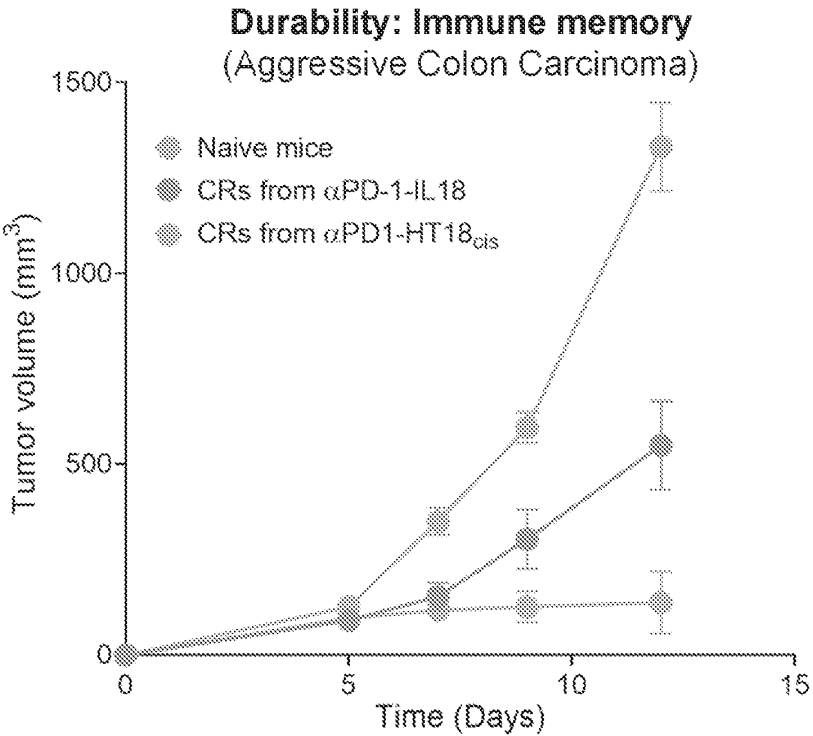


FIG. 34

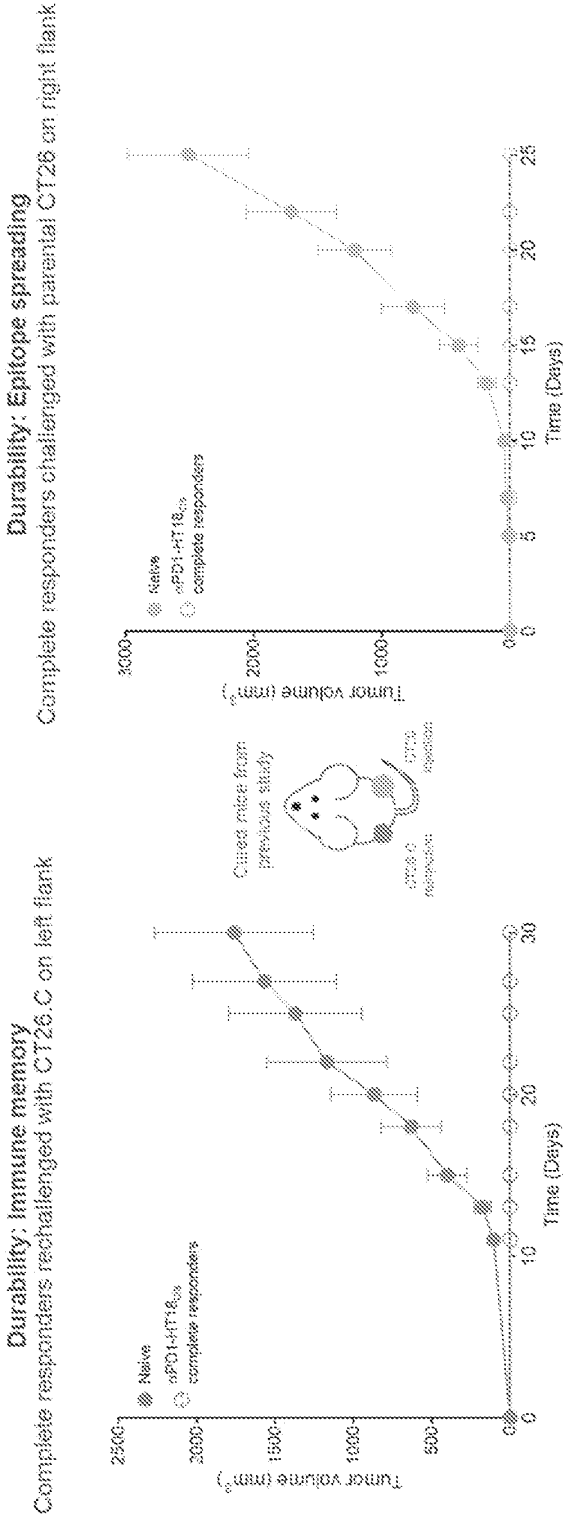


FIG. 35

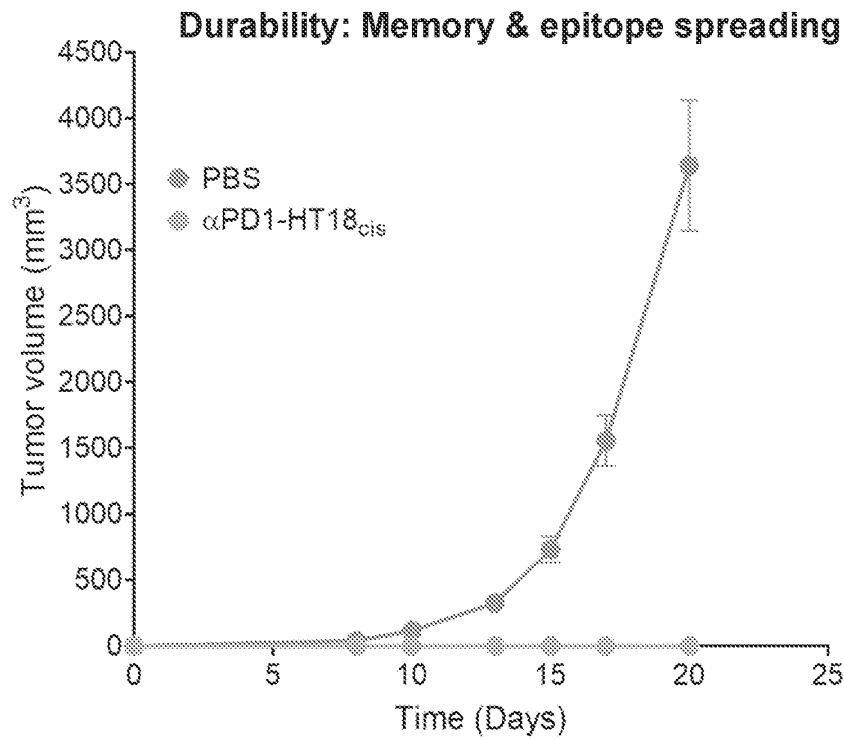
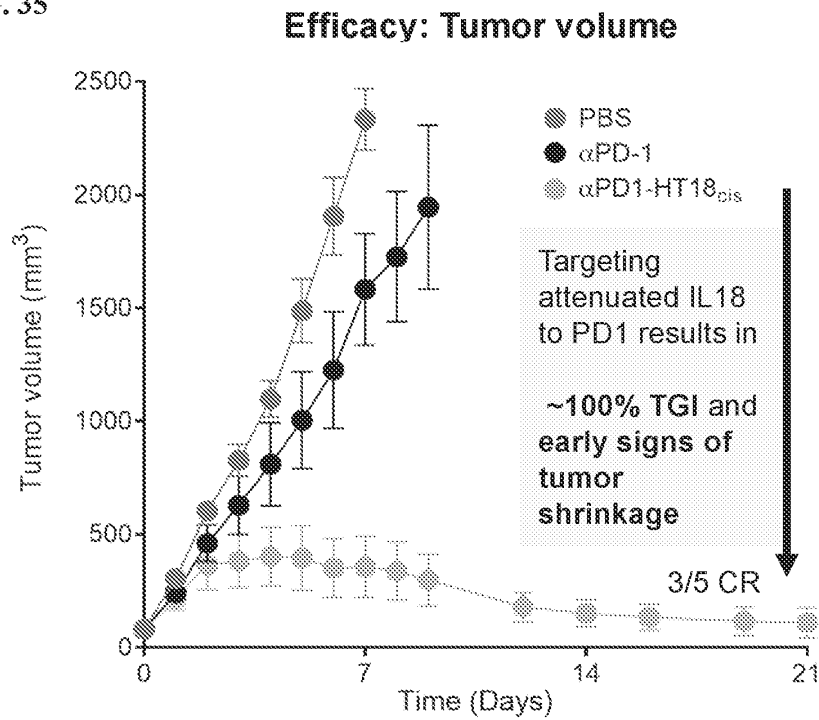


FIG. 36

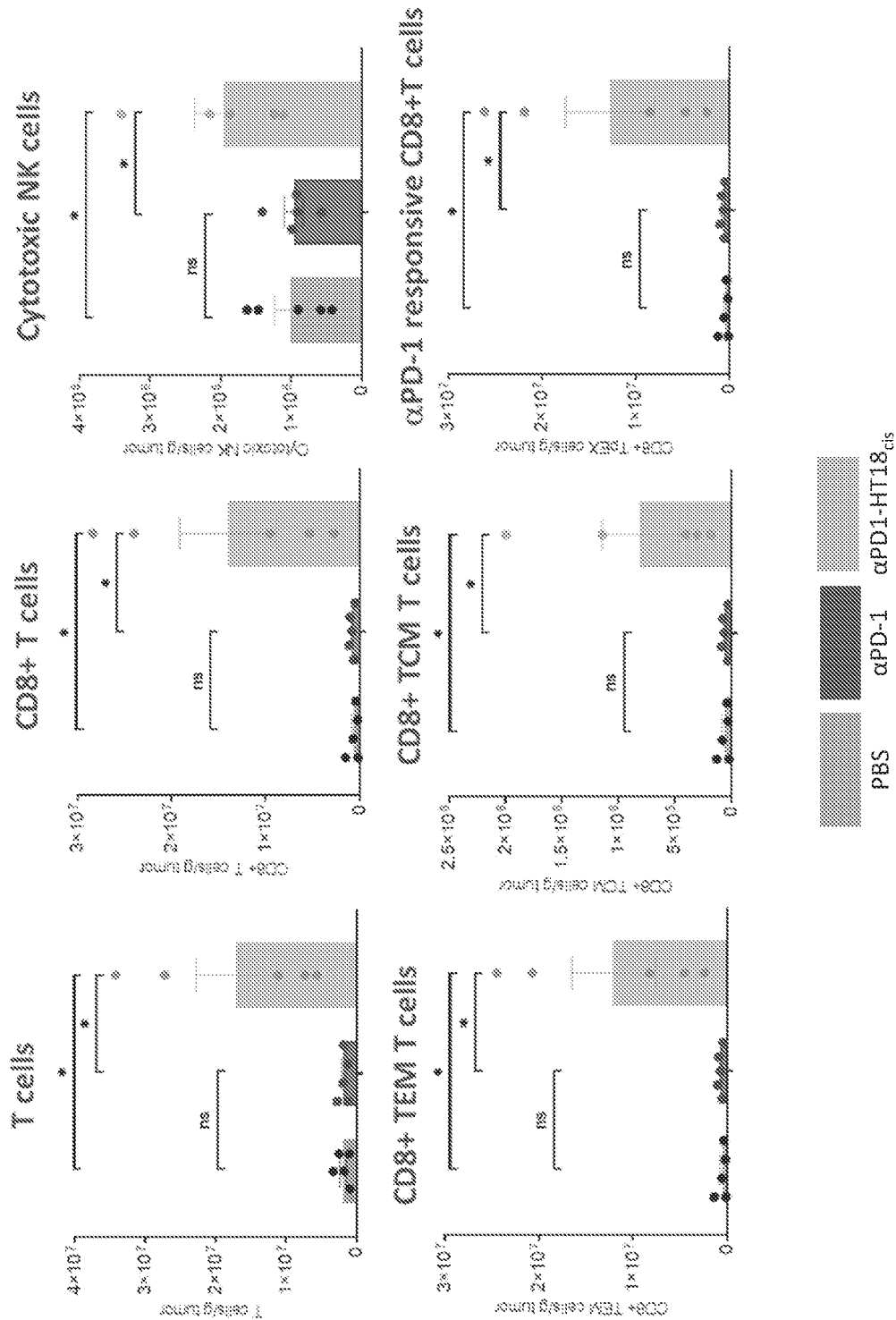


FIG. 37

