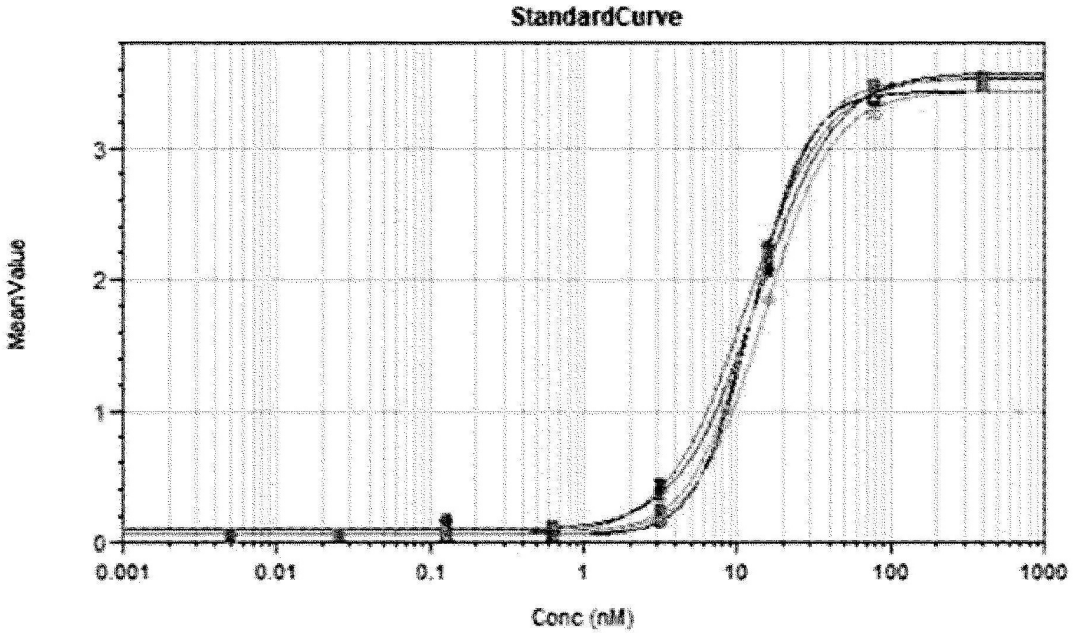
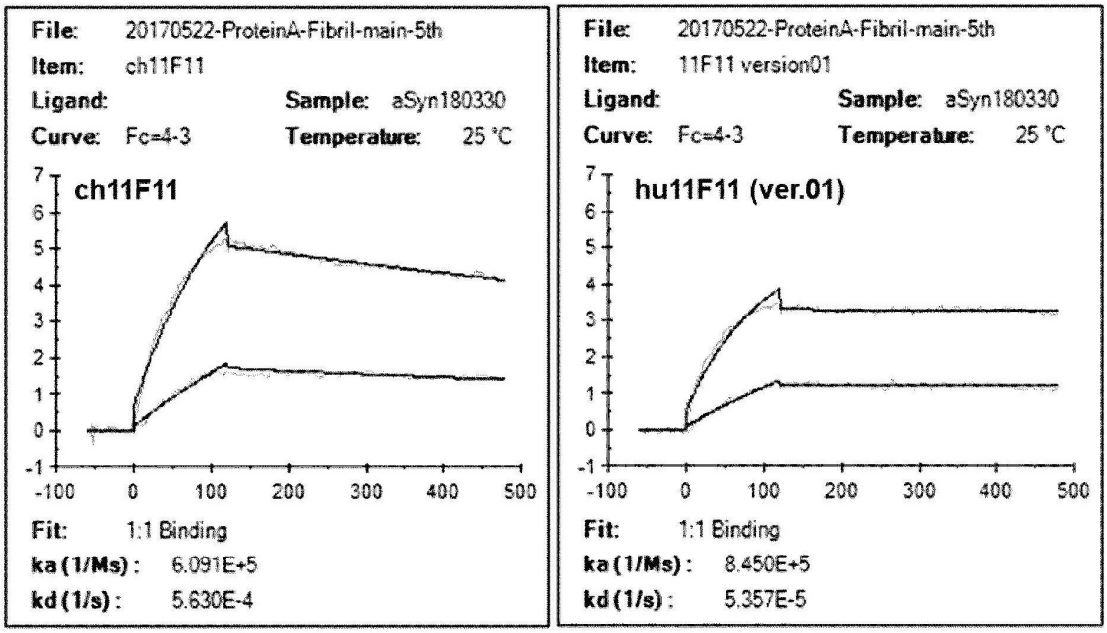
【DRAWINGS】

【FIG. 1】

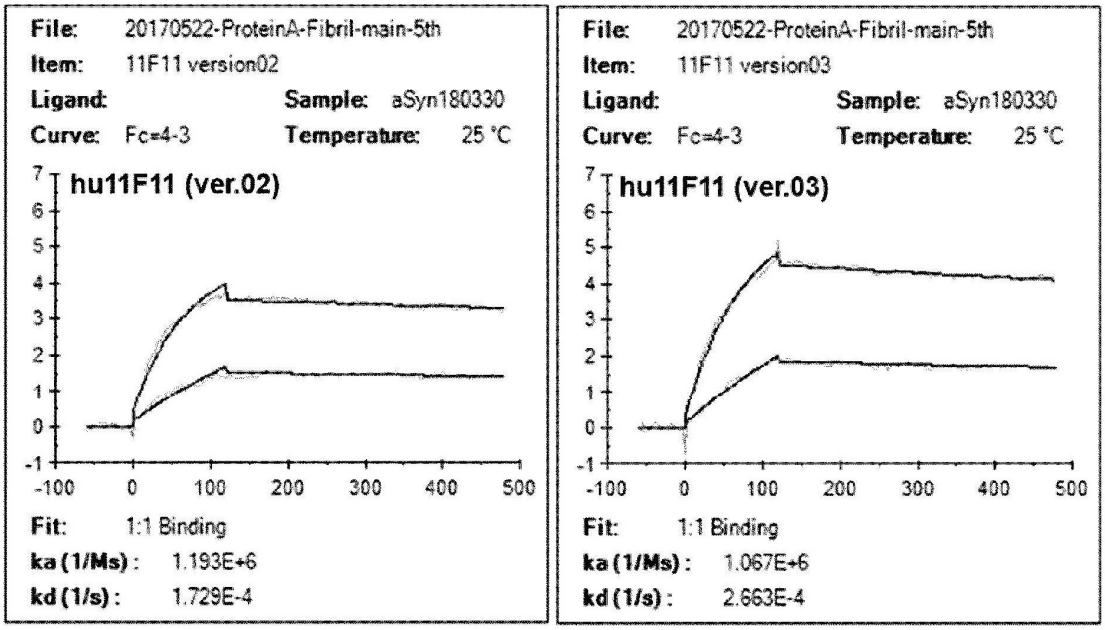


4-P Fit: y = (A - D)/(1 + (x/C)^B) + D:	A	B	C	D	R^2
○ Plot#1 (ch11F11(-RD): Concentration vs MeanVal...	0.0493	2.44	12.5	3.43	1
△ Plot#3 (hu11F11(ver.1): Concentration vs MeanV...	0.0532	1.69	11.5	3.55	1
◇ Plot#4 (hu11F11(ver.2): Concentration vs MeanV...	0.047	1.96	15.1	3.43	1
● Plot#5 (hu11F11(ver.3): Concentration vs MeanV...	0.0958	1.71	13.4	3.58	0.999
■ Plot#6 (hu11F11(ver.4): Concentration vs MeanV...	0.0791	2.18	12.9	3.52	1

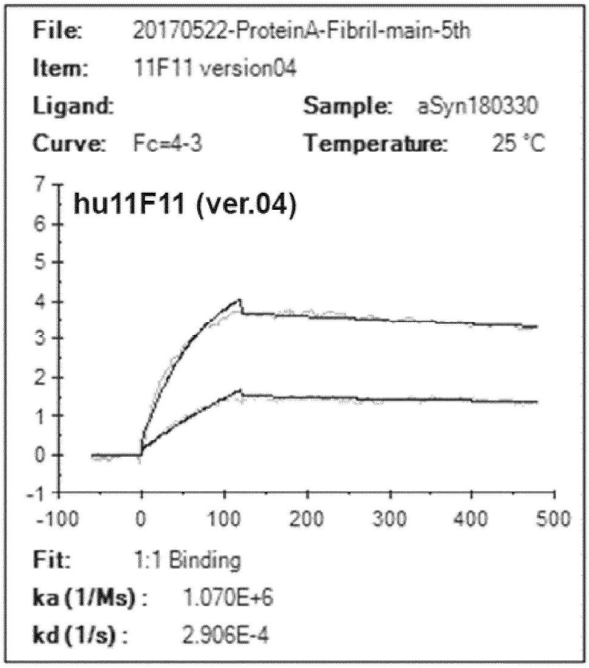
【FIG. 2a】


File: 20170522-ProteinA-Fibril-main-5th
Item: ch11F11
Ligand:
Sample: aSyn180330
Curve: Fc=4-3
Temperature: 25 °C
ch11F11
Fit: 1:1 Binding
ka (1/Ms): 6.091E+5
kd (1/s): 5.630E-4
File: 20170522-ProteinA-Fibril-main-5th
Item: 11F11 version01
Ligand:
Sample: aSyn180330
Curve: Fc=4-3
Temperature: 25 °C
hu11F11 (ver.01)
Fit: 1:1 Binding
ka (1/Ms): 8.450E+5
kd (1/s): 5.357E-5

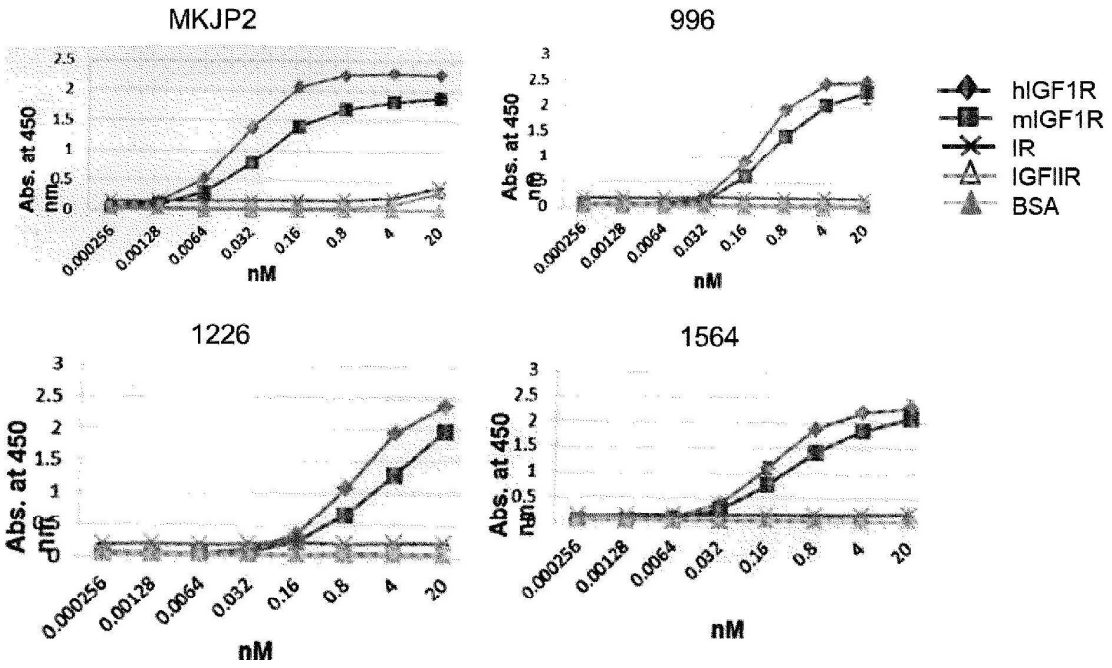
【FIG. 2b】


File: 20170522-ProteinA-Fibril-main-5th
Item: 11F11 version02
Ligand:
Sample: aSyn180330
Curve: Fc=4-3
Temperature: 25 °C
hu11F11 (ver.02)
Fit: 1:1 Binding
ka (1/Ms): 1.193E+6
kd (1/s): 1.729E-4
File: 20170522-ProteinA-Fibril-main-5th
Item: 11F11 version03
Ligand:
Sample: aSyn180330
Curve: Fc=4-3
Temperature: 25 °C
hu11F11 (ver.03)
Fit: 1:1 Binding
ka (1/Ms): 1.067E+6
kd (1/s): 2.663E-4

【FIG. 2c】

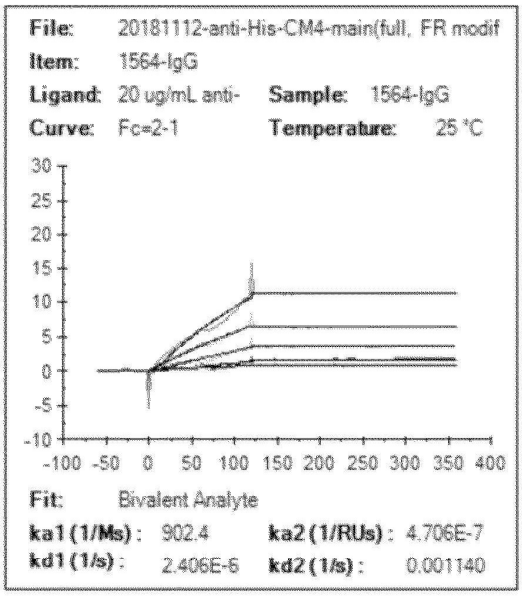

File: 20170522-ProteinA-Fibril-main-5th
Item: 11F11 version04
Ligand:
Sample: aSyn180330
Curve: Fc=4-3
Temperature: 25 °C
hu11F11 (ver.04)
7
6
5
4
3
2
1
0
-1
-100
0
100
200
300
400
500
Fit: 1:1 Binding
ka (1/Ms) : 1.070E+6
kd (1/s) : 2.906E-4

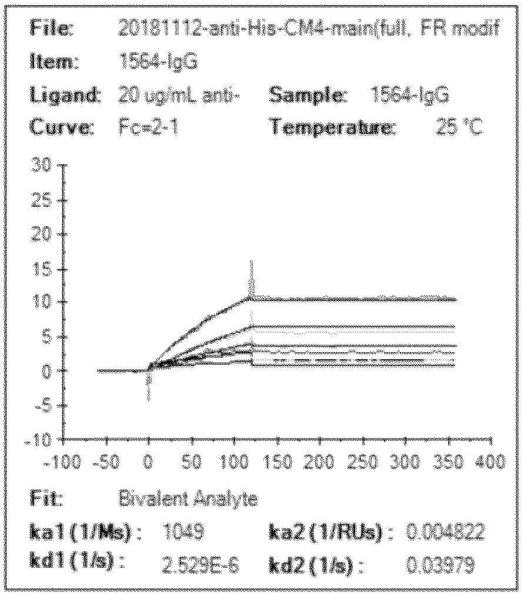
【FIG. 3a】


MKJP2
996
1226
1564
Abs. at 450 nm
nM
0.000256
0.00128
0.0064
0.032
0.16
0.8
4
20
hIGF1R
mIGF1R
IR
IGFIIR
BSA

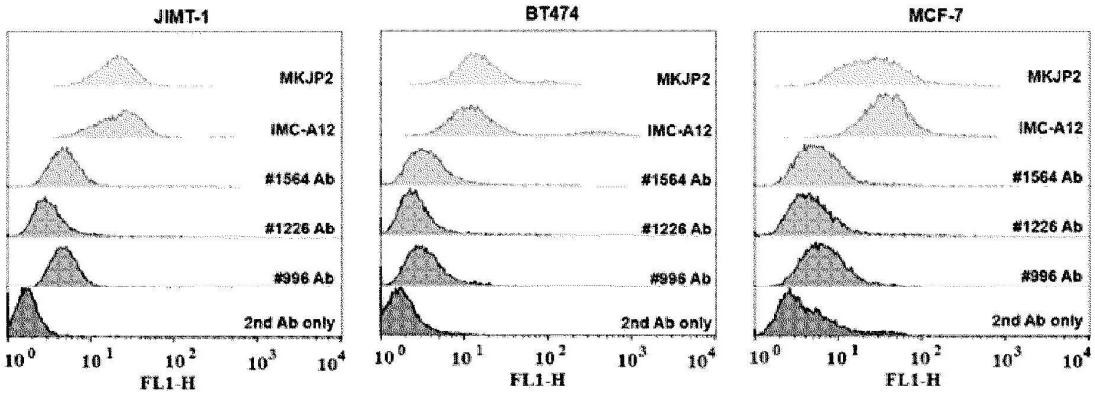
【FIG. 3b】

1564 IgG





【FIG. 4a】

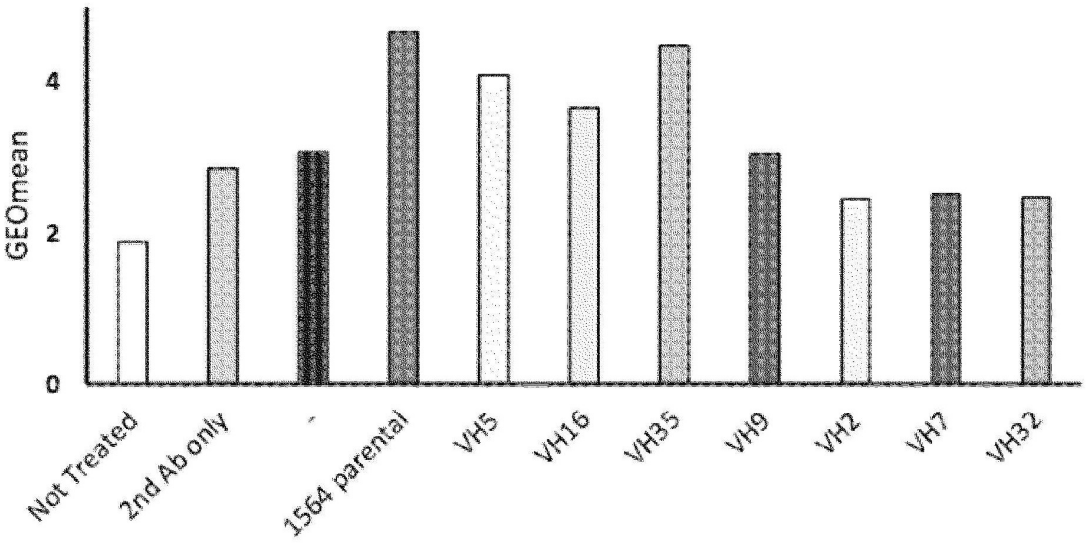


Sample Name	MFI		
	JIMT-1	BT474	MCF7
Untreated	1.36	1.8	2.51
2nd Ab only	1.89	1.93	4.53
#996 Ab	5.03	3.51	7.07
#1226 Ab	3.50	3.01	5.60
#1564 Ab	5.16	3.95	6.34
IMC-A12	22.99	18.34	40.08
MKJP2	20.67	16.43	26.67

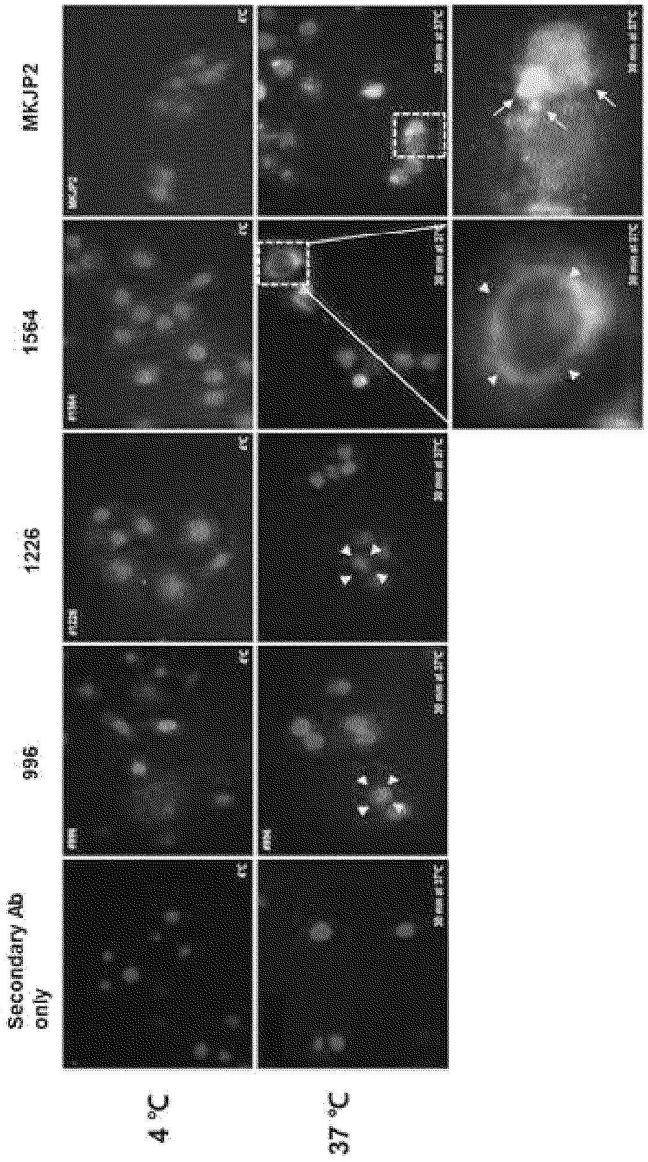
【FIG. 4b】

Samples	MFI
Secondary Ab only	3.20
ch11F11	3.26
ch11F11-1564	4.37
1564 IgG	7.55

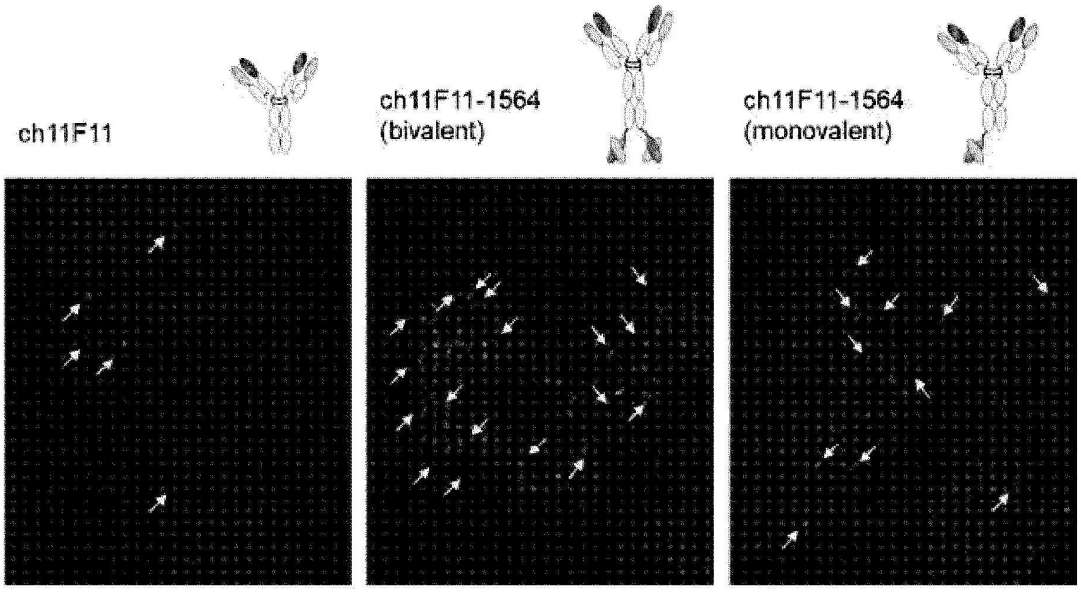
【FIG. 4c】


GEOmean
4
2
0
Not Treated
2nd Ab only
1564 parental
VH5
VH16
VH35
VH9
VH2
VH7
VH32

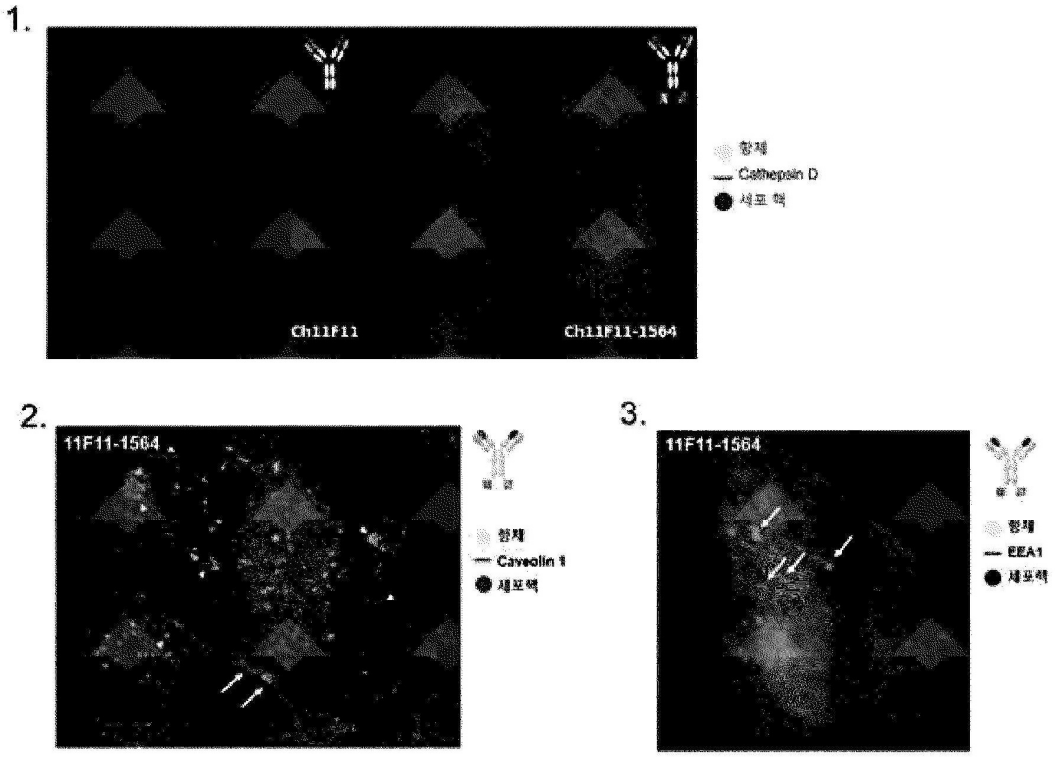
【FIG. 5a】



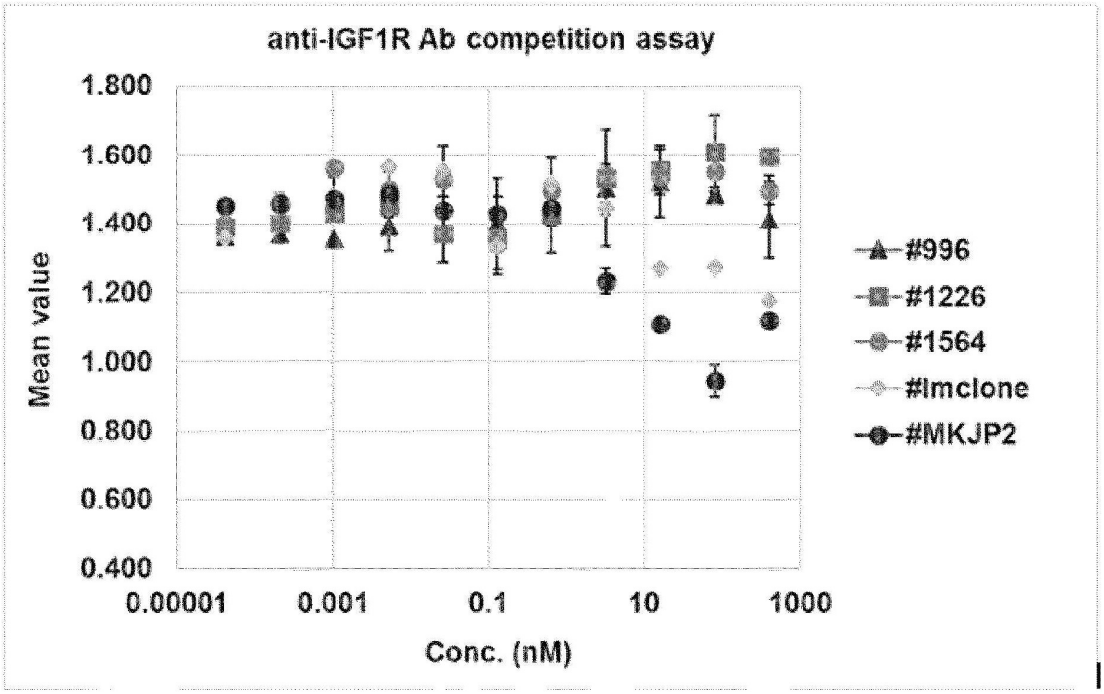
【FIG. 5b】



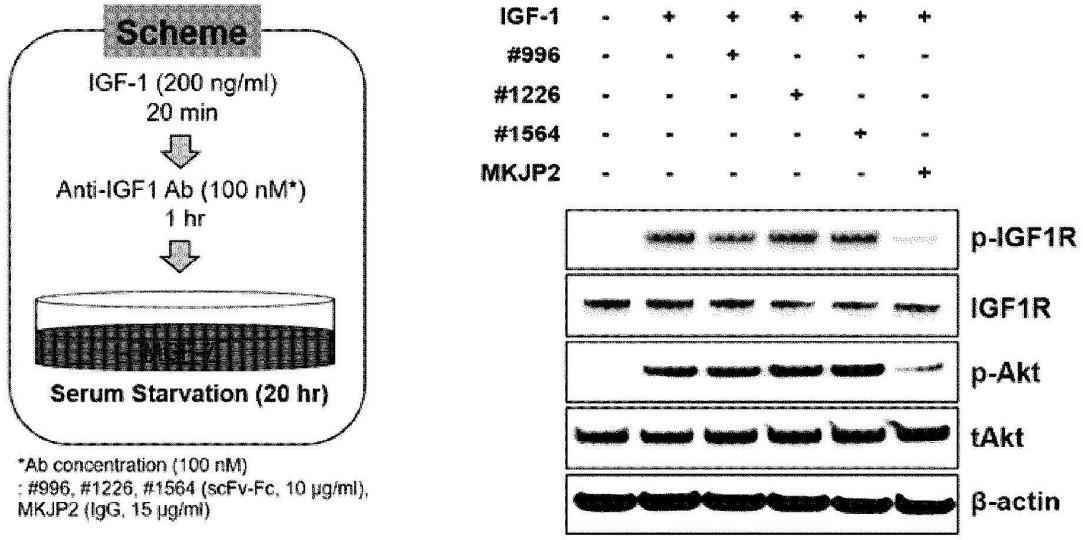
【FIG. 5c】


1.
ch11F11
ch11F11-1564
항체
Cathepsin D
세포 핵
2.
11F11-1564
항체
Caveolin 1
세포핵
3.
11F11-1564
항체
EEA1
세포핵

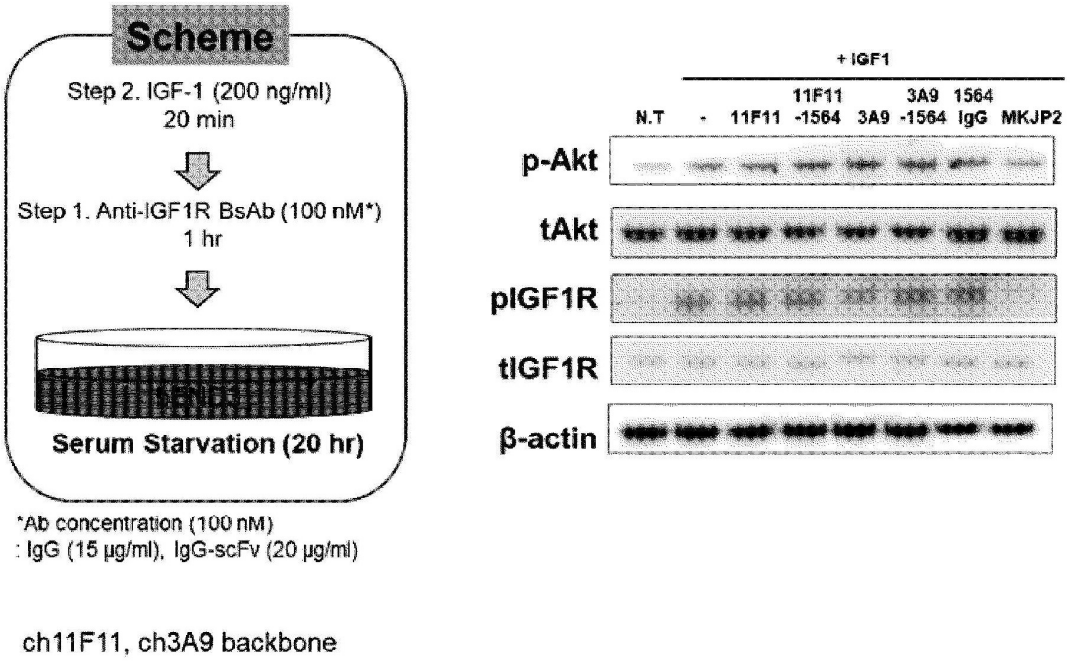
【FIG. 6a】


anti-IGF1R Ab competition assay
1.800
1.600
1.400
1.200
1.000
0.800
0.600
0.400
Mean value
0.00001
0.001
0.1
10
1000
Conc. (nM)
#996
#1226
#1564
#Imclone
#MKJP2

【FIG. 6b】

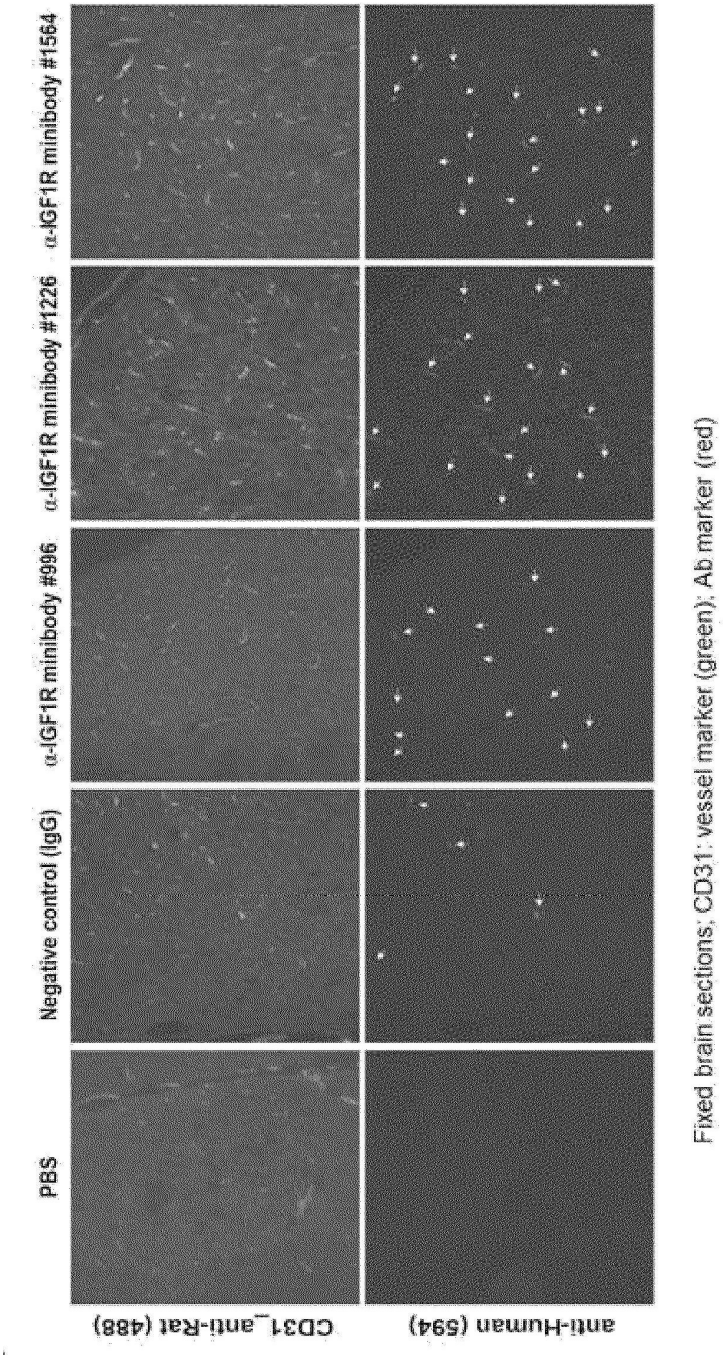


【FIG. 6c】



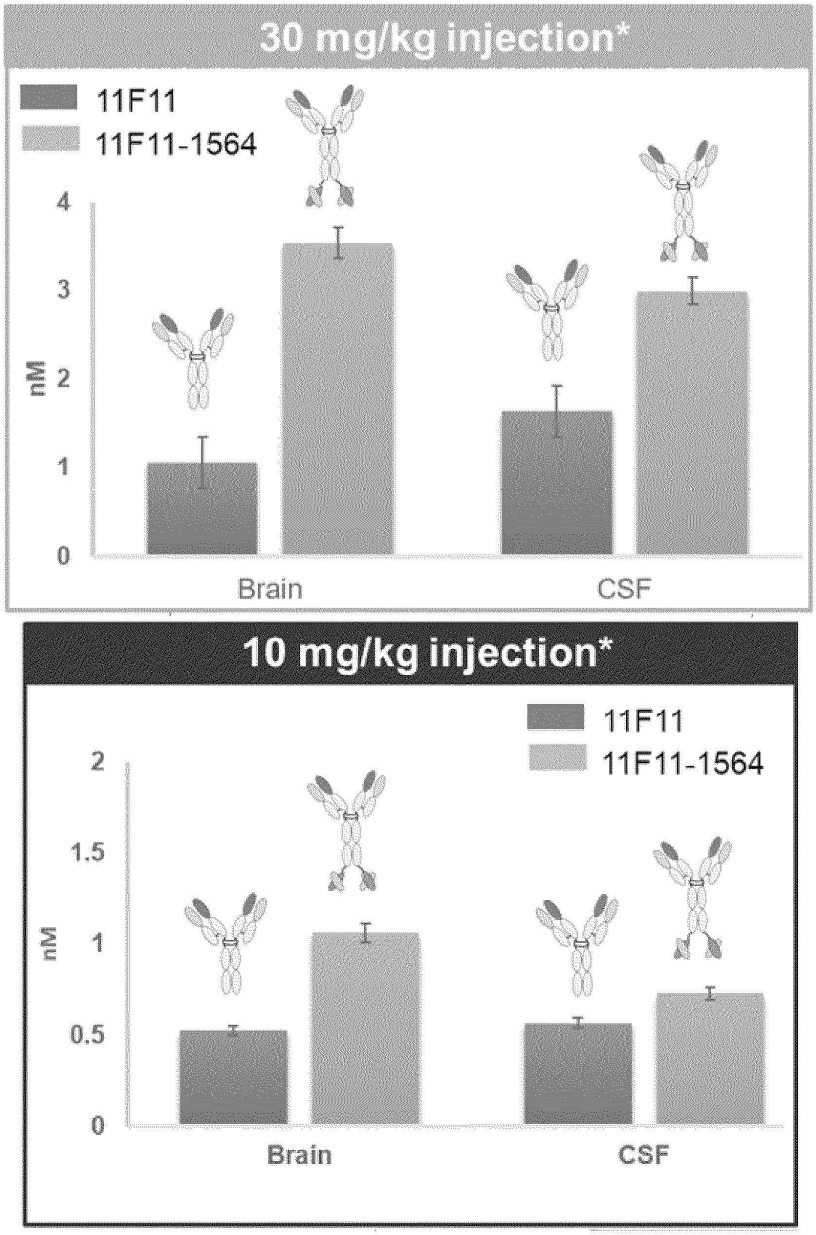
ch11F11, ch3A9 backbone

【FIG. 7a】

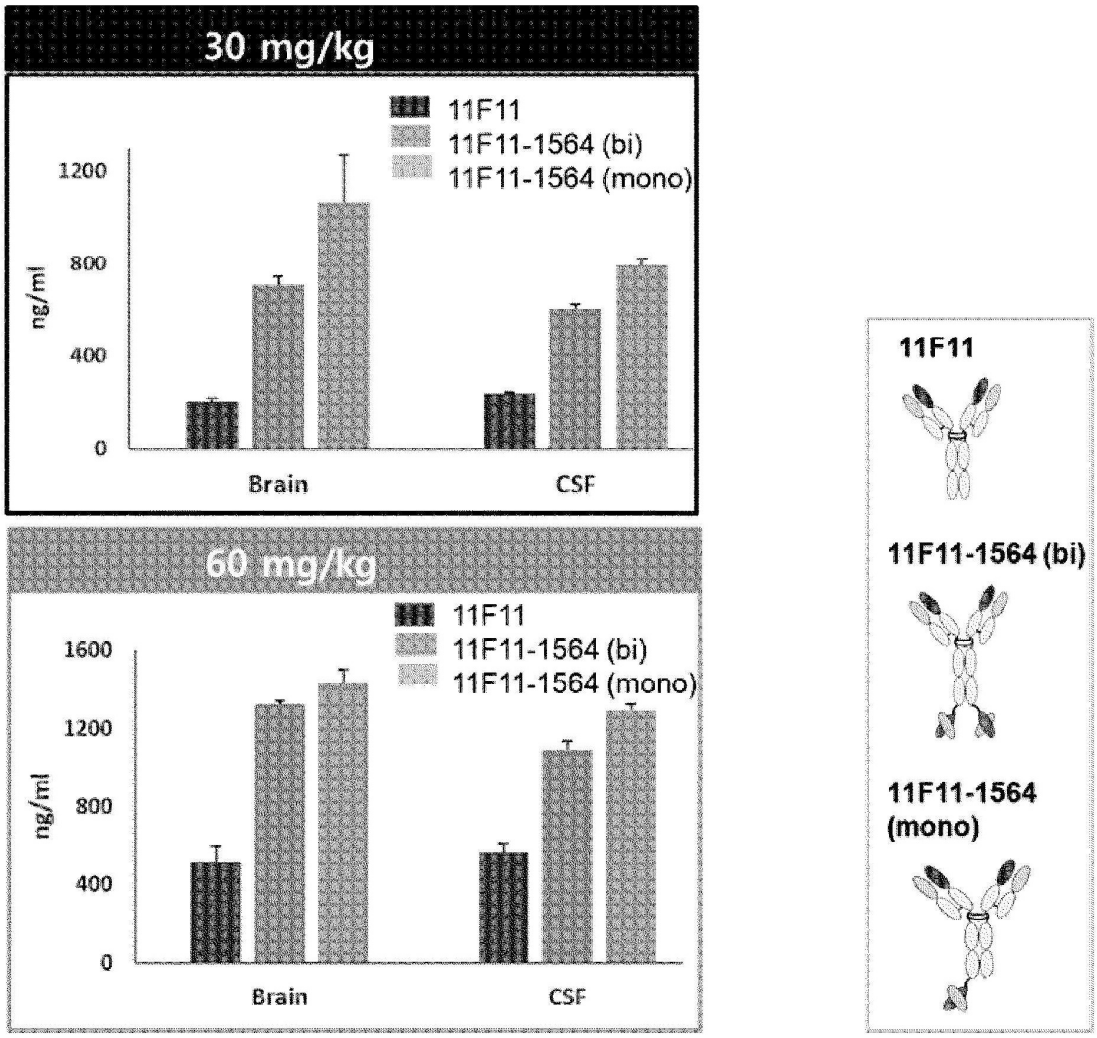


Fixed brain sections; CD31: vessel marker (green); Ab marker (red)

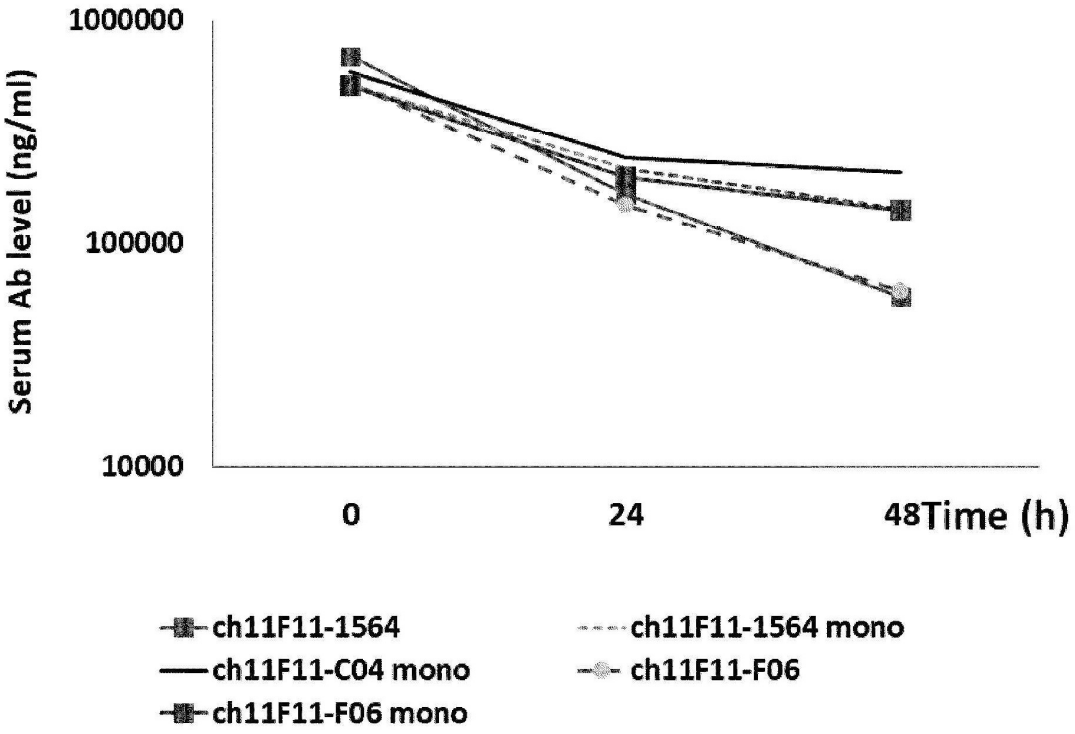
【FIG. 7b】


30 mg/kg injection*
11F11
11F11-1564
nM
4
3
2
1
0
Brain
CSF
10 mg/kg injection*
11F11
11F11-1564
nM
2
1.5
1
0.5
0
Brain
CSF

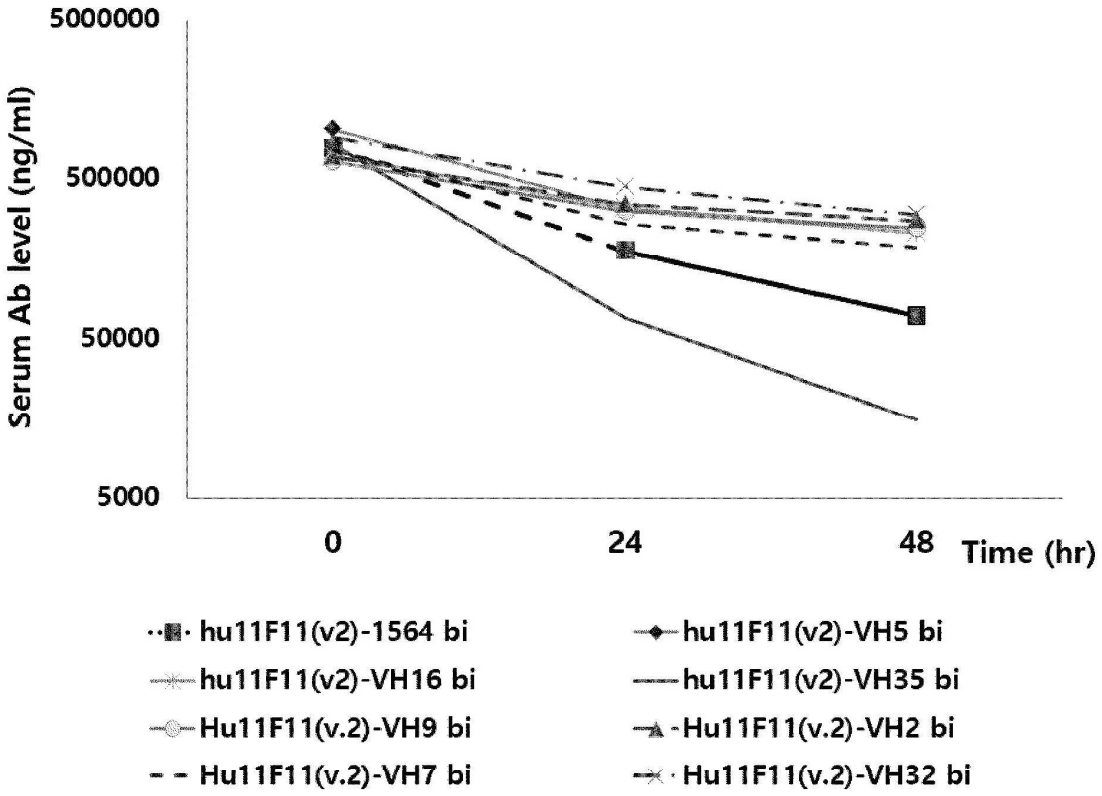
【FIG. 7c】


30 mg/kg
11F11
11F11-1564 (bi)
11F11-1564 (mono)
1200
800
400
0
ng/ml
Brain
CSF
60 mg/kg
11F11
11F11-1564 (bi)
11F11-1564 (mono)
1600
1200
800
400
0
ng/ml
Brain
CSF
11F11
11F11-1564 (bi)
11F11-1564 (mono)

【FIG. 7d】

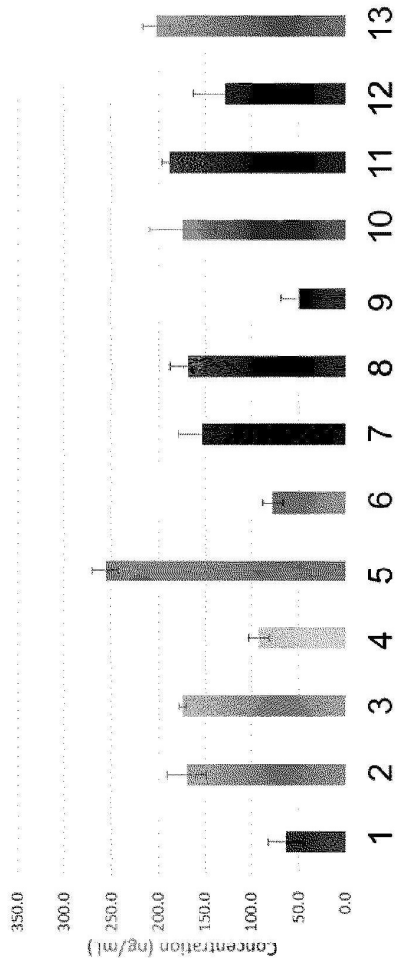

1000000
100000
10000
Serum Ab level (ng/ml)
0
24
48
Time (h)
ch11F11-1564
ch11F11-1564 mono
ch11F11-C04 mono
ch11F11-F06
ch11F11-F06 mono

【FIG. 7e】


5000000
500000
50000
5000
Serum Ab level (ng/ml)
0
24
48
Time (hr)
hu11F11(v2)-1564 bi
hu11F11(v2)-VH5 bi
hu11F11(v2)-VH16 bi
hu11F11(v2)-VH35 bi
Hu11F11(v.2)-VH9 bi
Hu11F11(v.2)-VH2 bi
Hu11F11(v.2)-VH7 bi
Hu11F11(v.2)-VH32 bi

【FIG. 7f】

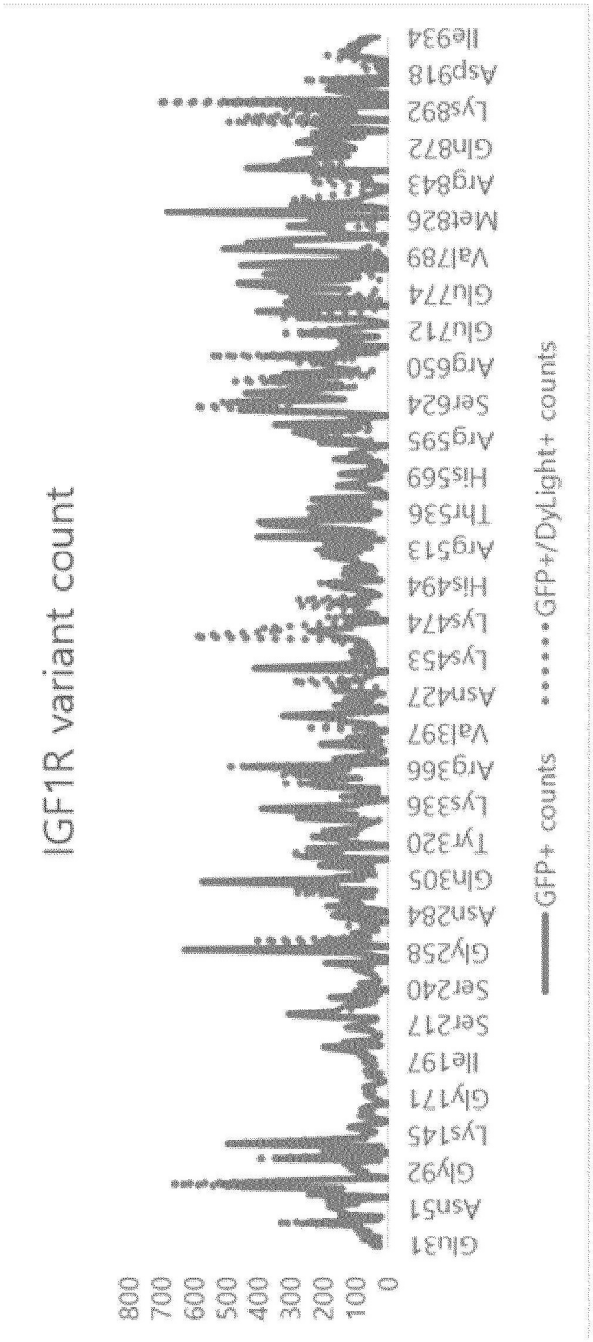
	Clones
1	ch11F11-1564 bivalent
2	ch11F11-1564 monovalent
3	ch11F11-C04 monovalent
4	ch11F11-F06 bivalent
5	ch11F11-F06 monovalent
6	hu11F11(ver.2)-1564 bivalent
7	hu11F11(ver.2)-VH5 bivalent
8	hu11F11(ver.2)-VH16 bivalent
9	hu11F11(ver.2)-VH35 bivalent
10	hu11F11(ver.2)-VH9 bivalent
11	hu11F11(ver.2)-VH2 bivalent
12	hu11F11(ver.2)-VH7 bivalent
13	hu11F11(ver.2)-VH32 bivalent



【FIG. 8】

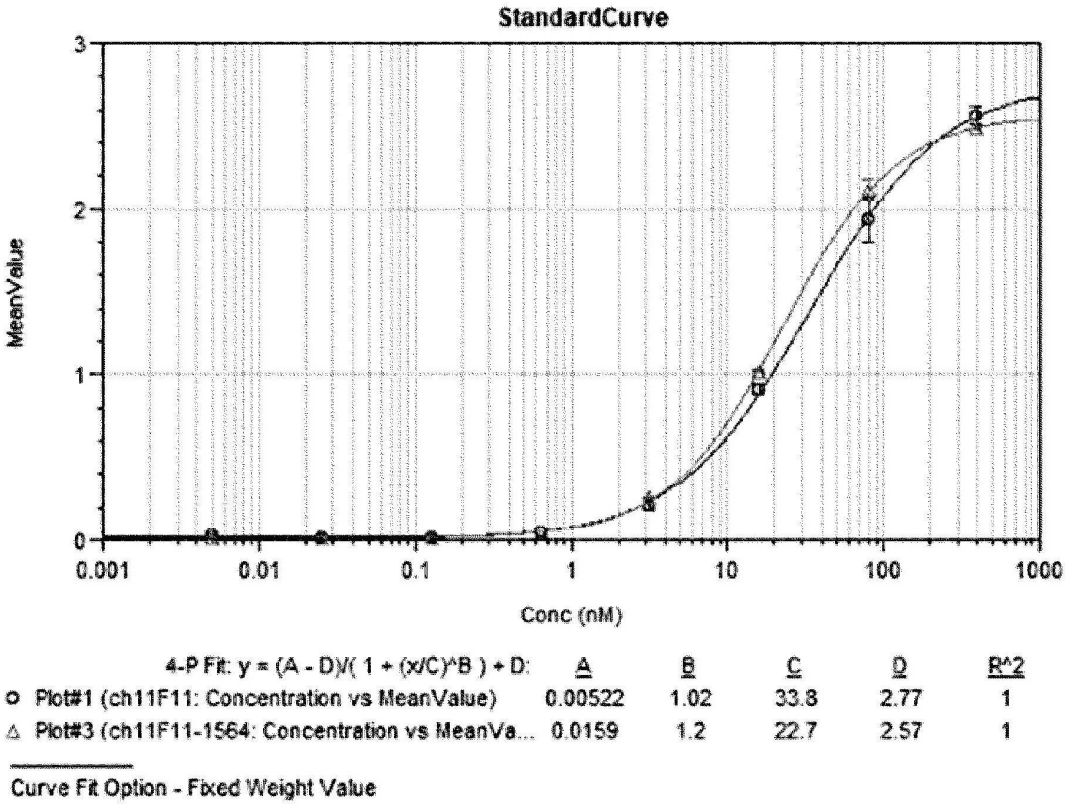
Location in 1564 antibody	Site	Temperature (℃)	Modification	% content
LCDR1	scFV(483-511)	4	Unmodified	99.2
			Deamidated	0.8
LCDR1	scFV(483-511)	40	Unmodified	99.0
			Deamidated	1.0
LCDR2	scFV(512-527)	4	Unmodified	84.7
			Deamidated	**15.3**
LCDR2	scFV(512-527)	40	Unmodified	83.1
			Deamidated	**16.9**
LCDR3	scFV(546-571)	4	Unmodified	95.4
			Deamidated	**4.6**
LCDR3	scFV(546-571)	40	Unmodified	90.2
			Deamidated	**9.8**
HCDR2	scFV(639-660)	4	Unmodified	55.8
			Deamidated	**44.2**
HCDR2	scFV(639-660)	40	Unmodified	52.7
			Deamidated	**47.3**
1564_Frame work	scFV(672-682)	4	Unmodified	95.6
			Deamidated	4.4
1564_Frame work	scFV(672-682)	40	Unmodified	95.7
			Deamidated	4.3

【FIG. 9】

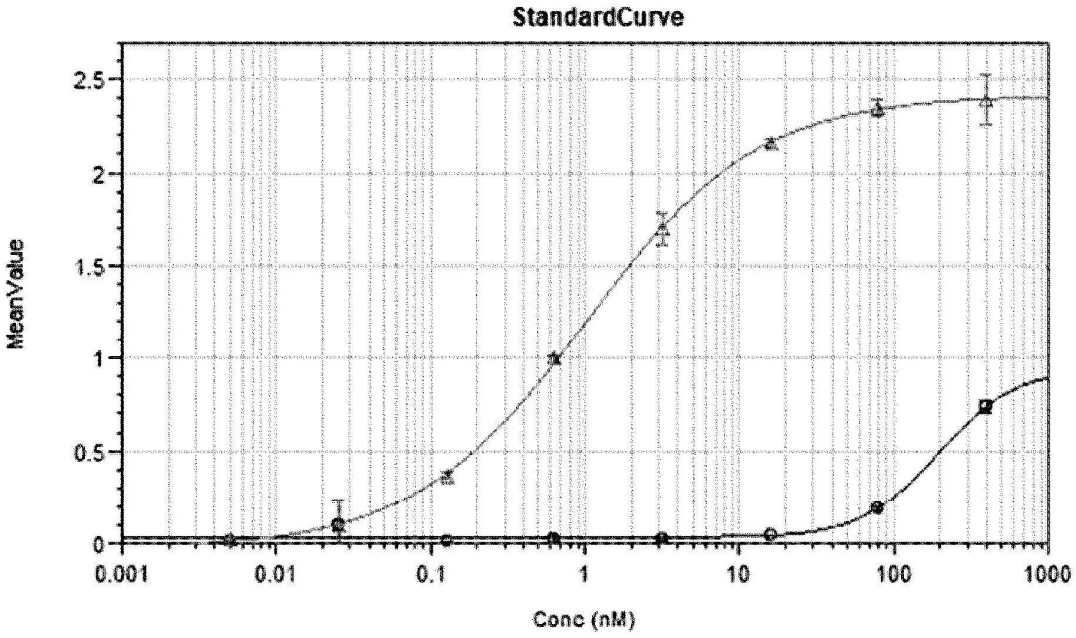


Binding region of 1564 clone	
Inside FN2	Y775, P776, F778, R650, S791, L798 and Glu779

【FIG. 10a】


StandardCurve
MeanValue
Conc (nM)
0.001
0.01
0.1
1
10
100
1000
0
1
2
3
4-P Fit: y = (A - D)/(1 + (x/C)^B) + D:
A
B
C
D
R^2
Plot#1 (ch11F11: Concentration vs MeanValue) 0.00522 1.02 33.8 2.77 1
Plot#3 (ch11F11-1564: Concentration vs MeanVa... 0.0159 1.2 22.7 2.57 1
Curve Fit Option - Fixed Weight Value

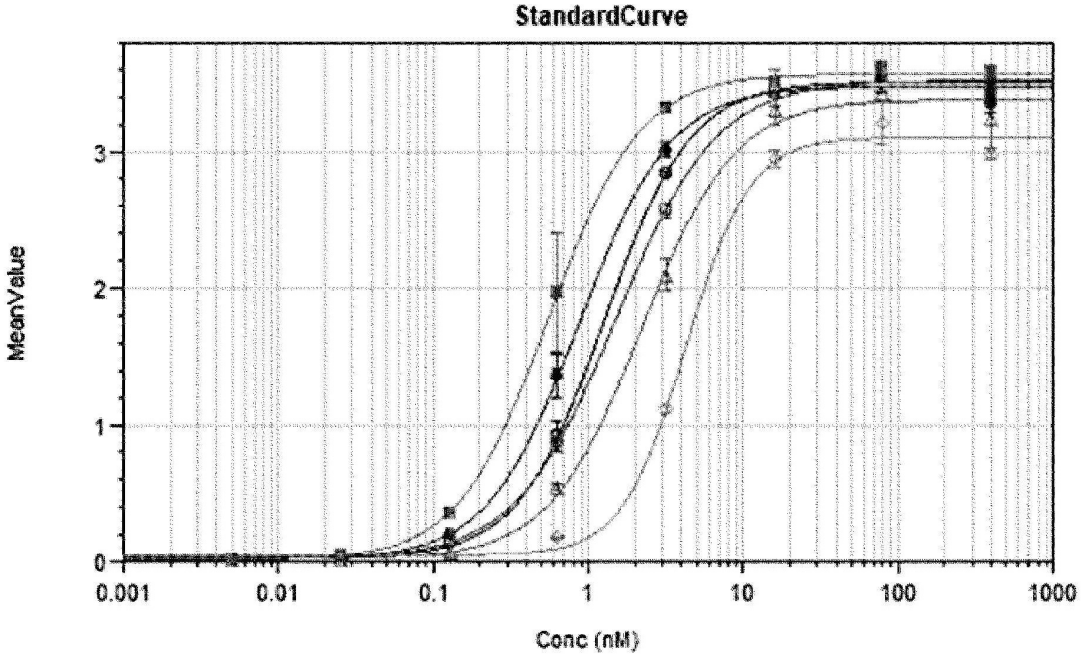
【FIG. 10b】



4-P Fit: y = (A - D)/(1 + (x/C)^B) + D:	A	B	C	D	R^2
○ Plot#1 (ch11F11: Concentration vs MeanValue)	0.0321	1.73	196	0.945	0.985
△ Plot#3 (ch11F11-1564: Concentration vs MeanVa...	-0.0248	0.781	1.01	2.42	1

Curve Fit Option - Fixed Weight Value

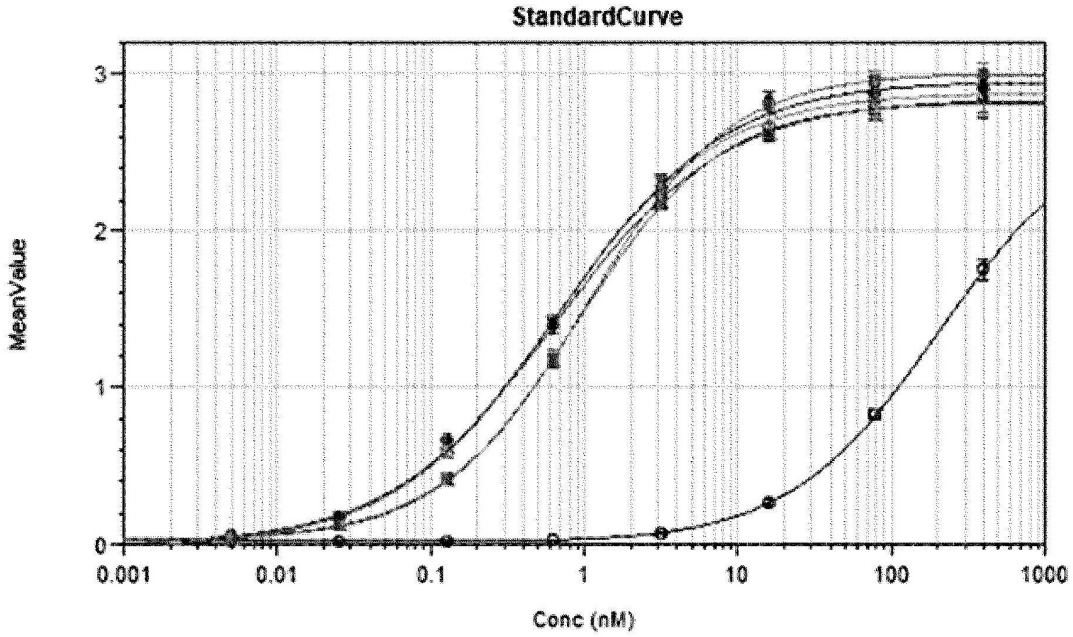
【FIG. 10c】



4-P Fit: y = (A - D)/(1 + (x/C)^B) + D:	A	B	C	D	R^2
○ Plot#4 (ch11F11(-RD)_: Concentration vs MeanV...	0.0238	1.56	1.27	3.51	0.999
□ Plot#1 (ch11F11-1564(-RD)_: Concentration vs M...	0.0186	1.34	1.5	3.52	0.999
△ Plot#2 (ch11F11-1564(-RD) mono: Concentration ...	0.02	1.45	2.21	3.39	0.998
◇ Plot#3 (hu11F11-1564(ver.2): Concentration vs M...	0.0445	2.11	4.27	3.11	0.997
● Plot#5 (hu11F11-1564(ver.3): Concentration vs M...	0.0138	1.47	0.874	3.48	0.999
■ Plot#6 (hu11F11-1564 (ver.3) mono: Concentratio...	0.00929	1.48	0.559	3.57	1

Curve Fit Option - Fixed Weight Value

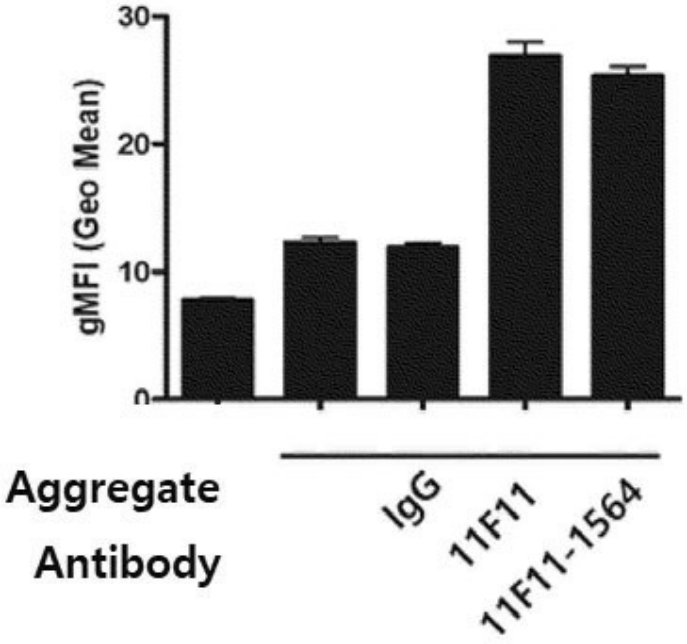
【FIG. 10d】



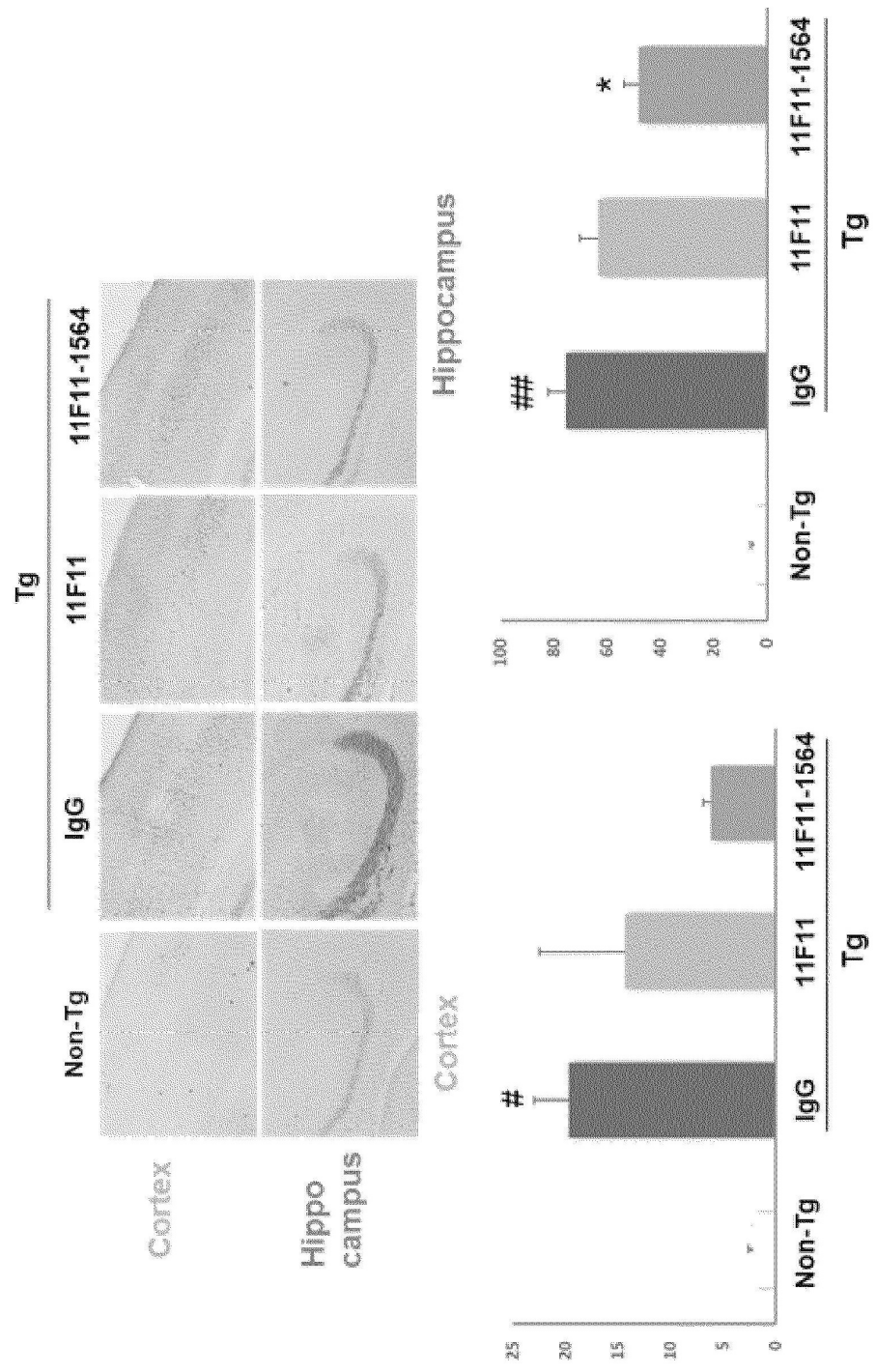
4-P Fit: y = (A - D)/(1 + (x/C)^B) + D:	A	B	C	D	R^2
○ Plot#4 (ch11F11(-RD)_: Concentration vs MeanV...	0.013	0.898	201	2.68	1
□ Plot#1 (ch11F11-1564(-RD)_: Concentration vs M...	-0.0288	0.789	0.644	2.84	1
△ Plot#2 (ch11F11-1564(-RD) mono: Concentration ...	0.029	0.942	0.904	2.82	0.999
◇ Plot#3 (hu11F11-1564(ver.2): Concentration vs M...	-0.00338	0.84	0.649	2.88	1
● Plot#5 (hu11F11-1564(ver.3): Concentration vs M...	-0.00109	0.812	0.687	2.96	0.999
■ Plot#6 (hu11F11-1564 (ver.3) mono: Concentratio...	0.0203	0.929	1.02	3.01	1

Curve Fit Option - Fixed Weight Value

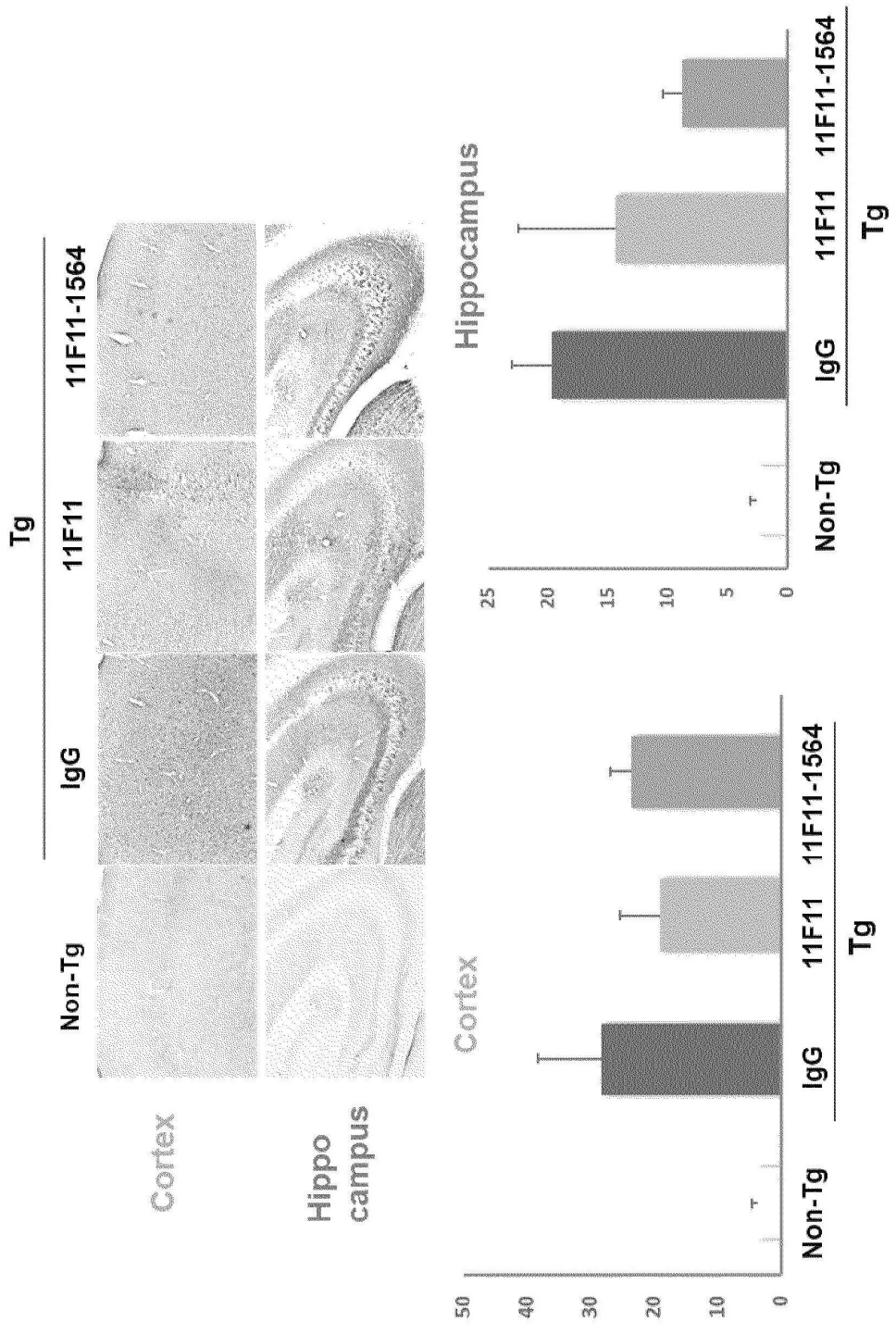
【FIG. 10e】


30
20
10
0
gMFI (Geo Mean)
Aggregate
Antibody
IgG
11F11
11F11-1564

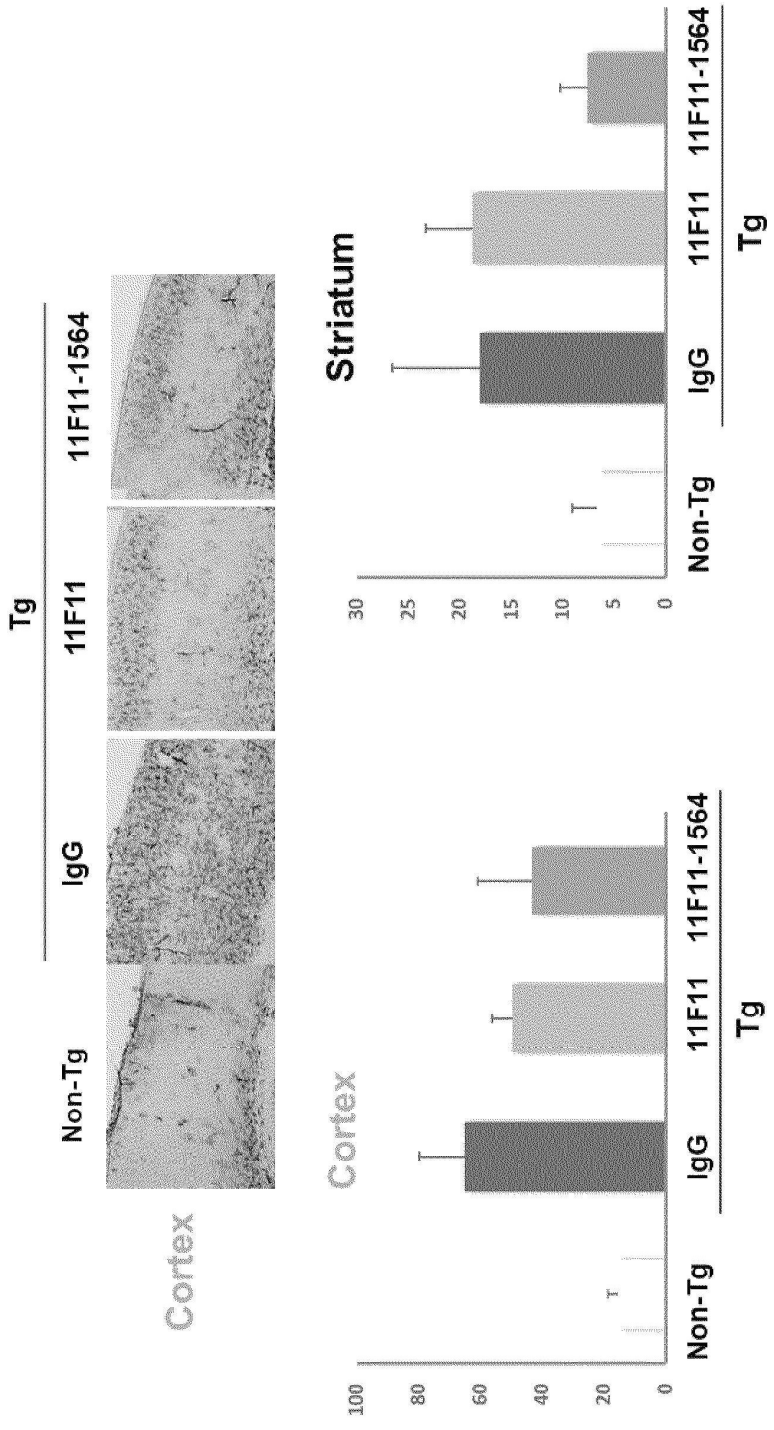
【FIG. 11a】


Tg
Non-Tg
IgG
11F11
11F11-1564
Cortex
Hippo campus
Hippocampus
Cortex
#
##
*
Non-Tg
IgG
11F11
11F11-1564
Tg
0
5
10
15
20
25
0
20
40
60
80
100

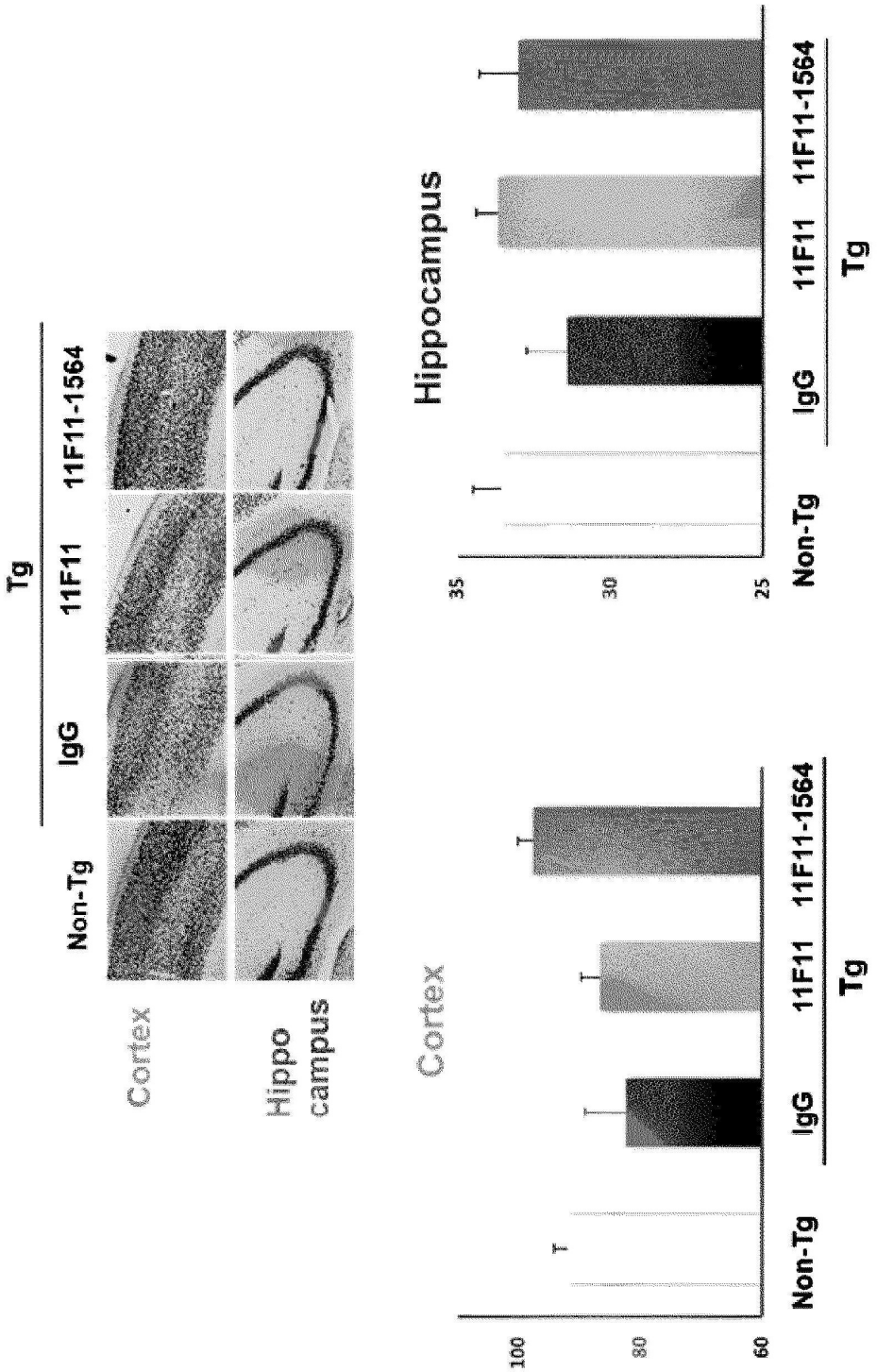
【FIG. 11b】


Tg
Non-Tg
IgG
11F11
11F11-1564
Cortex
Hippo campus
Cortex
Hippocampus
Non-Tg
IgG
11F11
11F11-1564
Tg
50
40
30
20
10
0
25
20
15
10
5
0

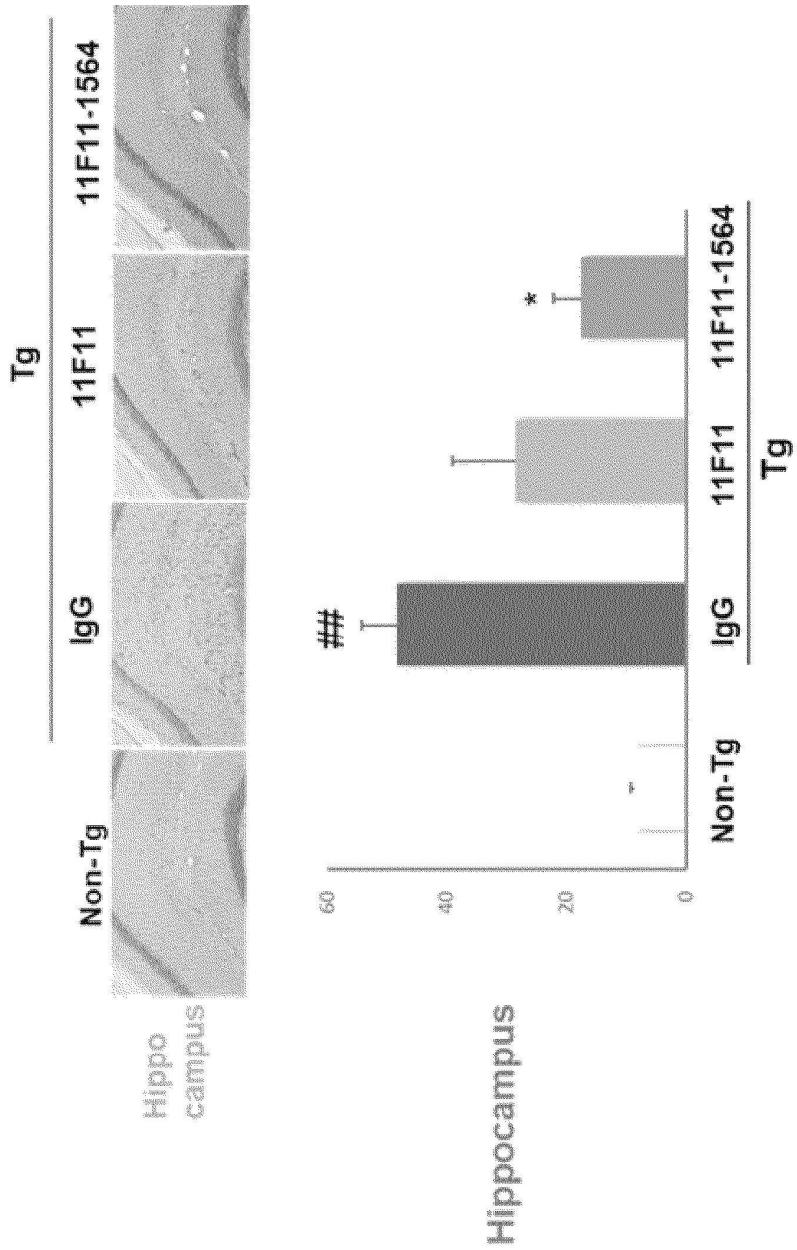
【FIG. 11c】


Tg
Non-Tg
IgG
11F11
11F11-1564
Cortex
Cortex
100
80
60
40
20
0
Non-Tg
IgG
11F11
11F11-1564
Tg
Striatum
30
25
20
15
10
5
0
Non-Tg
IgG
11F11
11F11-1564
Tg

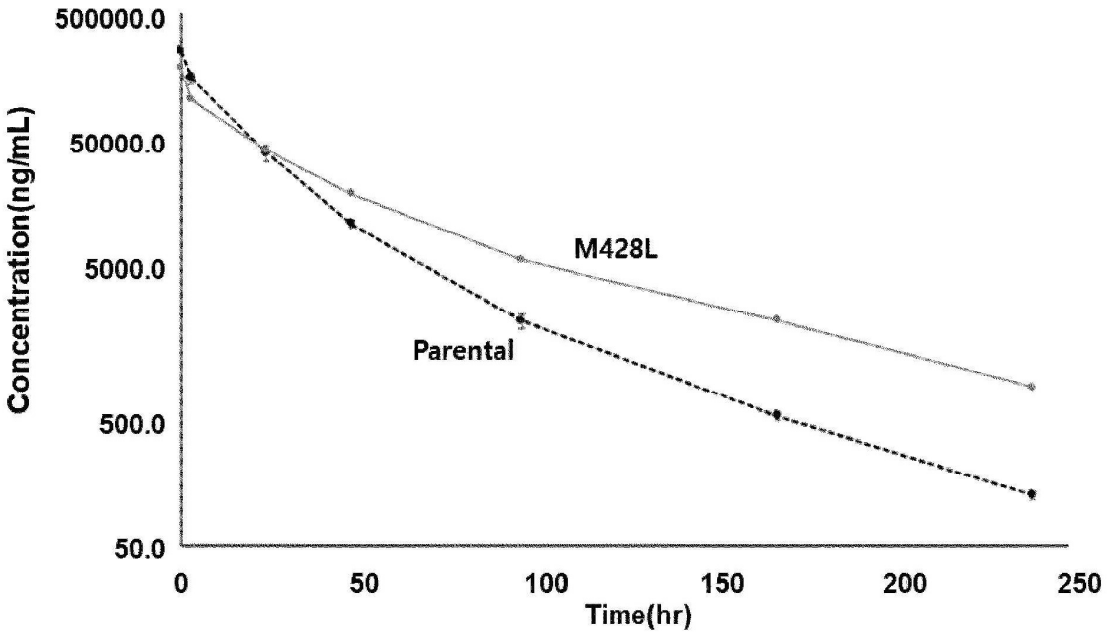
【FIG. 11d】


Tg
Non-Tg
IgG
11F11
11F11-1564
Cortex
Hippo campus
Cortex
Hippocampus
100
80
60
35
30
25
Non-Tg
IgG
11F11
11F11-1564
Tg

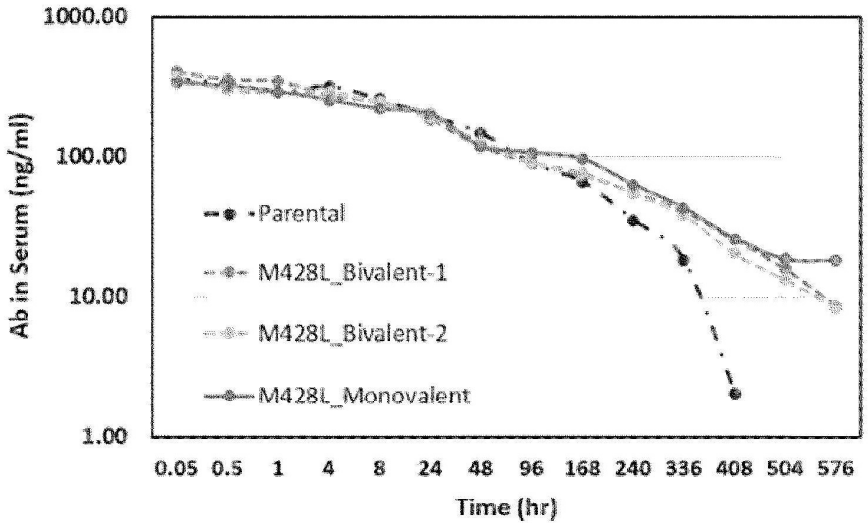
【FIG. 11e】


Tg
Non-Tg
IgG
11F11
11F11-1564
Hippo campus
##
*
Hippocampus
60
40
20
0
Non-Tg
IgG
11F11
11F11-1564
Tg

【FIG. 12a】

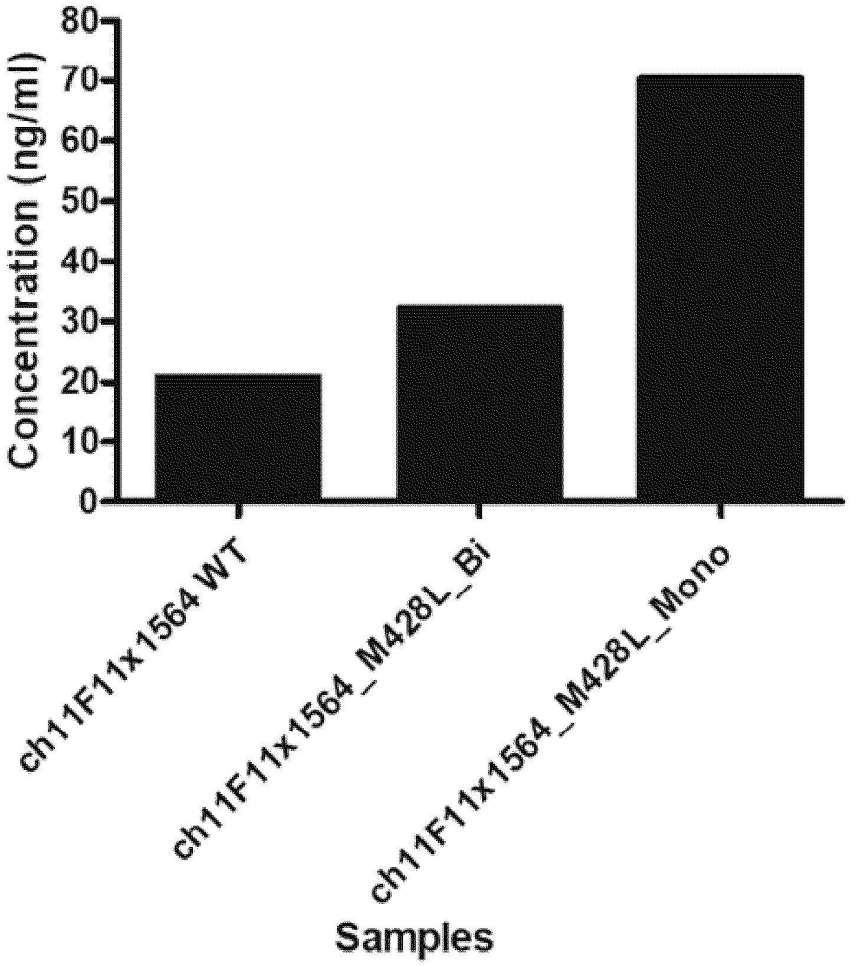

500000.0
50000.0
5000.0
500.0
50.0
Concentration(ng/mL)
M428L
Parental
0
50
100
150
200
250
Time(hr)

【FIG. 12b】

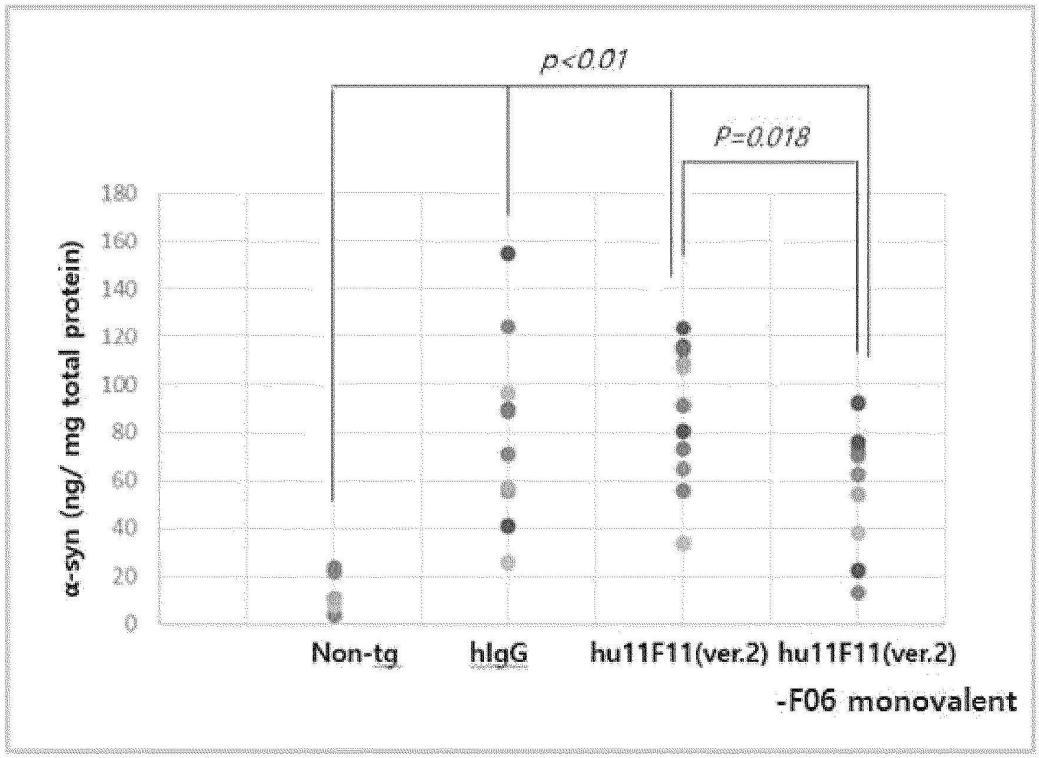


	Half-Life (d)	Clearance (ml/h/kg)
Parental	3.6	0.438
M428L_Bivalent	5.1	0.37
M428L_Monovalent	4.9	0.3155

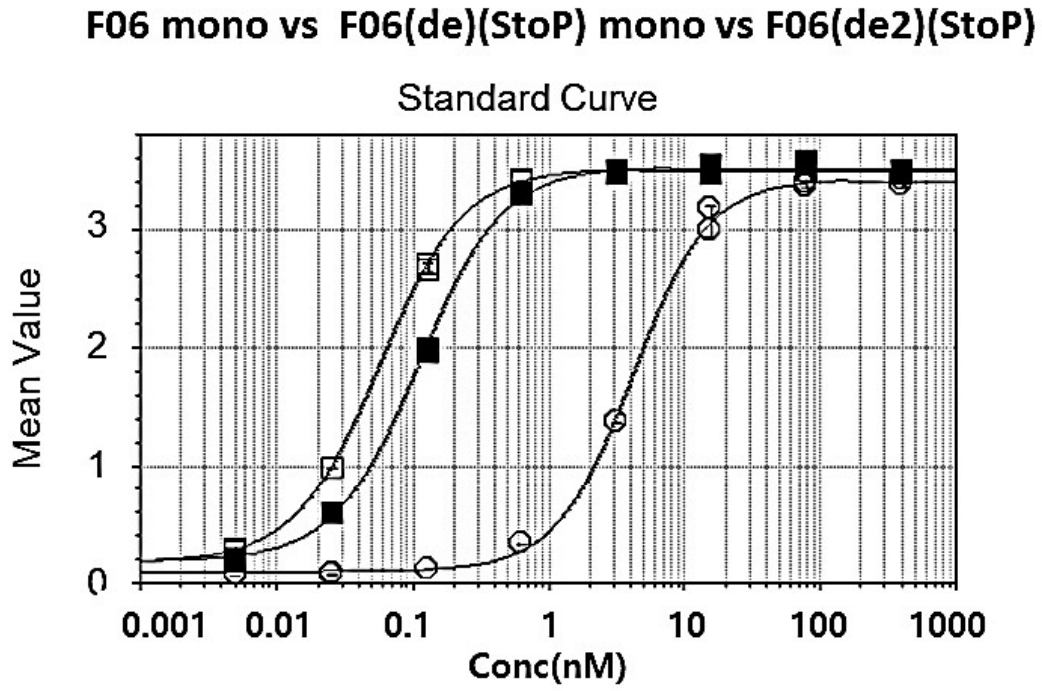
【FIG. 12c】


Concentration (ng/ml)
80
70
60
50
40
30
20
10
0
ch11F11x1564 WT
ch11F11x1564_M428L_Bi
ch11F11x1564_M428L_Mono
Samples

【FIG. 13】


p<0.01
P=0.018
α-syn (ng/ mg total protein)
180
160
140
120
100
80
60
40
20
0
Non-tg
hIgG
hu11F11(ver.2)
hu11F11(ver.2)
-F06 monovalent

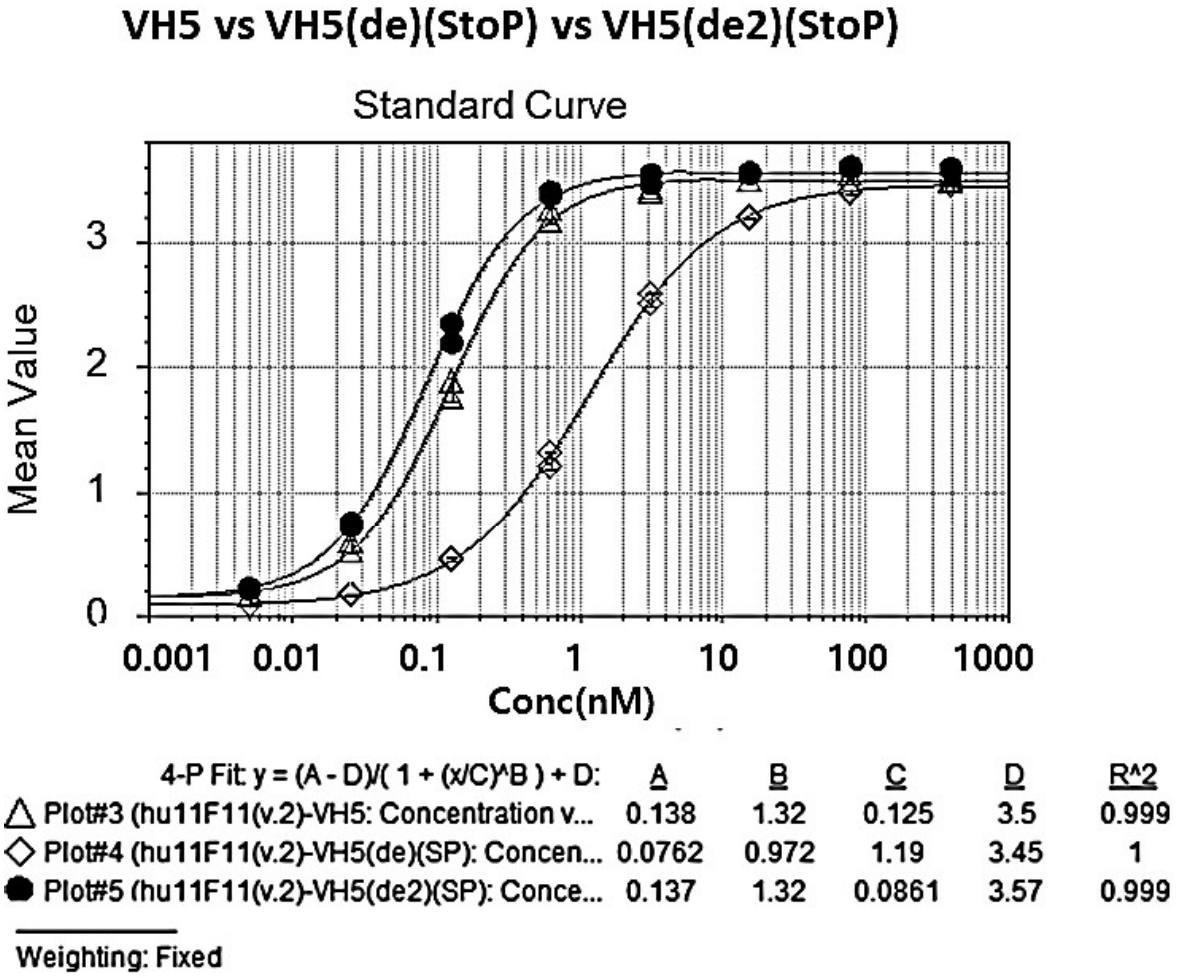
【FIG. 14a】



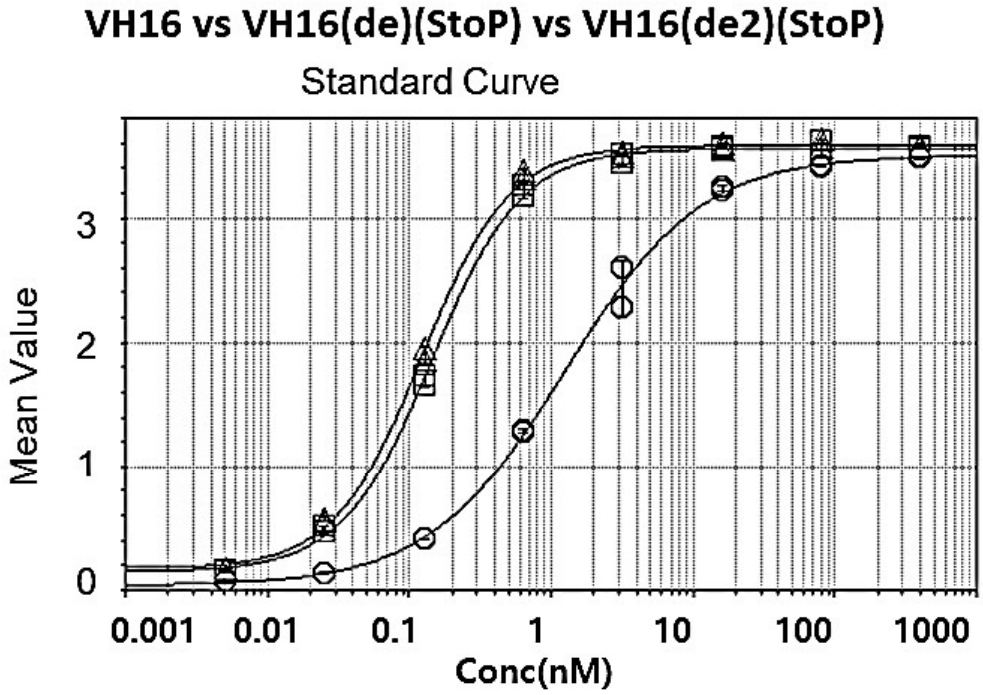
4-P Fit: y = (A - D)/(1 + (x/C)^B) + D:	A	B	C	D	R^2
■ Plot#6 (hu11F11(v.2)-F06_mono: Concentr...	0.178	1.4	0.112	3.51	0.999
○ Plot#1 (hu11F11(v.2)-F06(de)(SP)_mono: ...	0.0921	1.55	4.24	3.41	0.999
□ Plot#2 (hu11F11(v.2)-F06(de2)(StoP)_mon...	0.169	1.4	0.0575	3.5	1

Weighting: Fixed

【FIG. 14b】


VH5 vs VH5(de)(StoP) vs VH5(de2)(StoP)
Standard Curve
Mean Value
0
1
2
3
0.001
0.01
0.1
1
10
100
1000
Conc(nM)
4-P Fit: y = (A - D)/(1 + (x/C)^B) + D: A B C D R^2
Plot#3 (hu11F11(v.2)-VH5: Concentration v... 0.138 1.32 0.125 3.5 0.999
Plot#4 (hu11F11(v.2)-VH5(de)(SP): Concen... 0.0762 0.972 1.19 3.45 1
Plot#5 (hu11F11(v.2)-VH5(de2)(SP): Conce... 0.137 1.32 0.0861 3.57 0.999
Weighting: Fixed

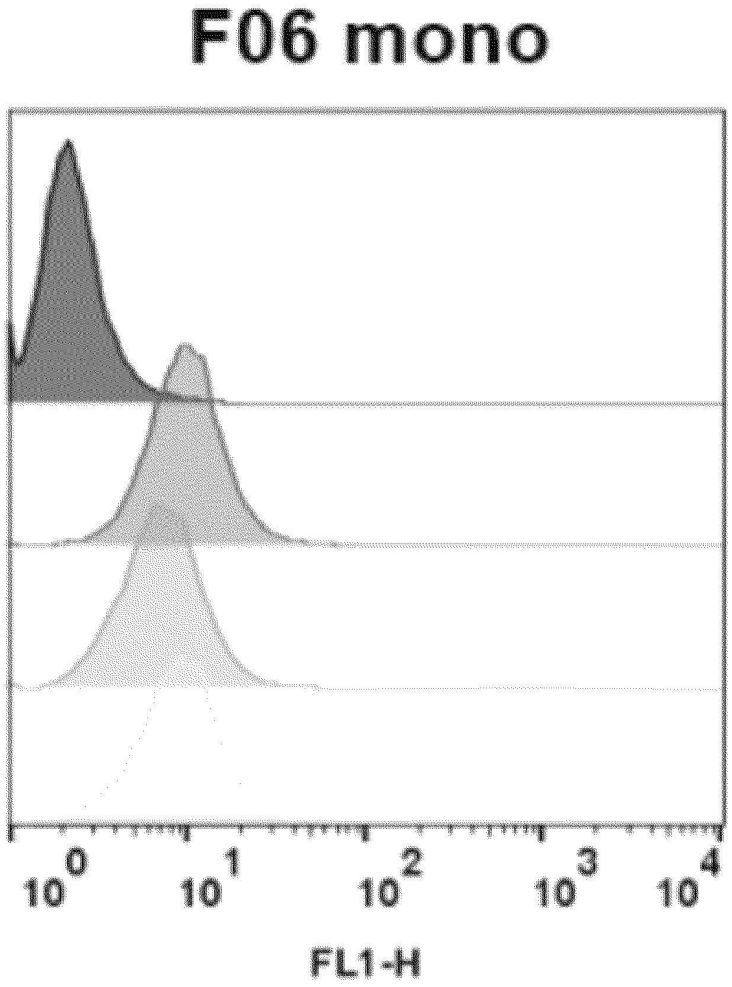
【FIG. 14c】



4-P Fit: y = (A - D)/(1 + (x/C)^B) + D:	A	B	C	D	R^2
□ Plot#2 (hu11F11(v.2)-VH16: Concentration vs ...	0.15	1.38	0.143	3.56	0.999
○ Plot#1 (hu11F11(v.2)-VH16(de)(StoP): Conce...	0.0381	0.907	1.25	3.5	0.998
△ Plot#3 (hu11F11(v.2)-VH16(de2)(StoP): Conc...	0.173	1.41	0.122	3.58	0.999

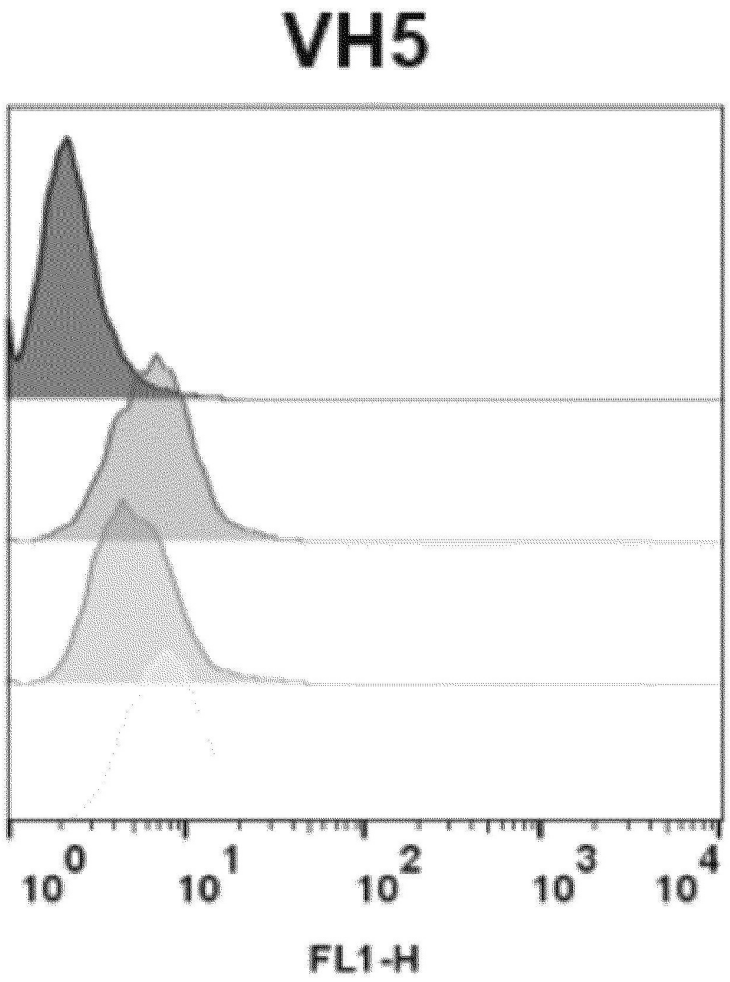
Weighting: Fixed

【FIG. 15a】



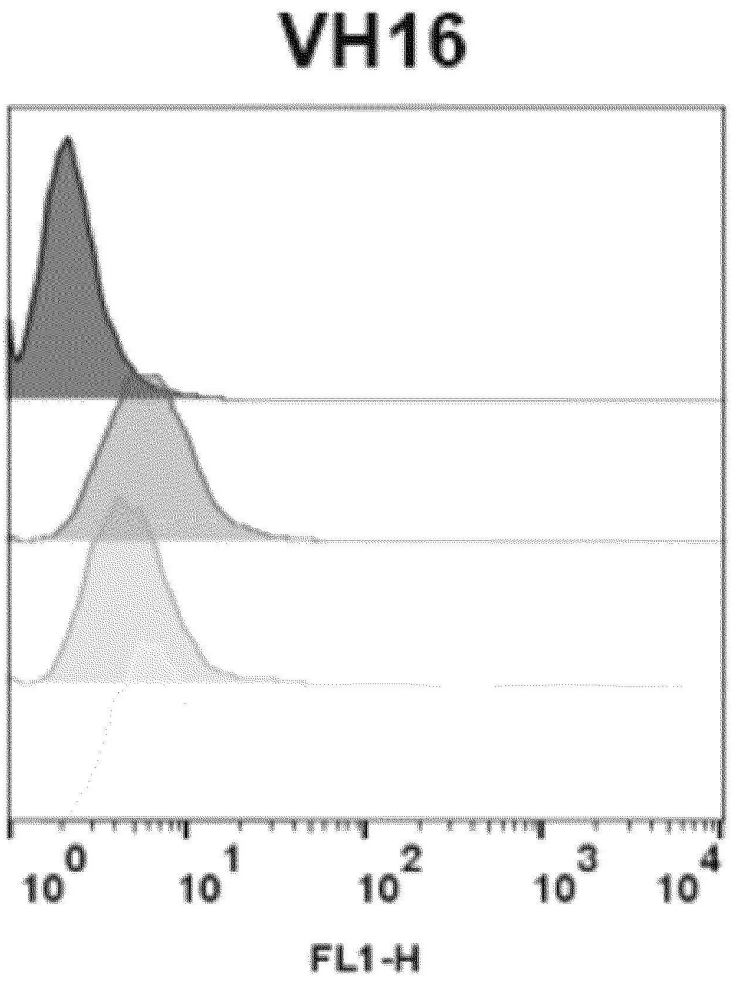
	Sample Name	Geometric Mean : FL1-H
	2nd Ab only.002	2.30
	F06-mono.004	9.65
	F06(de)(StoP)-mono.005	7.10
	F06(de2)(StoP)-mono.006	8.65

【FIG. 15b】



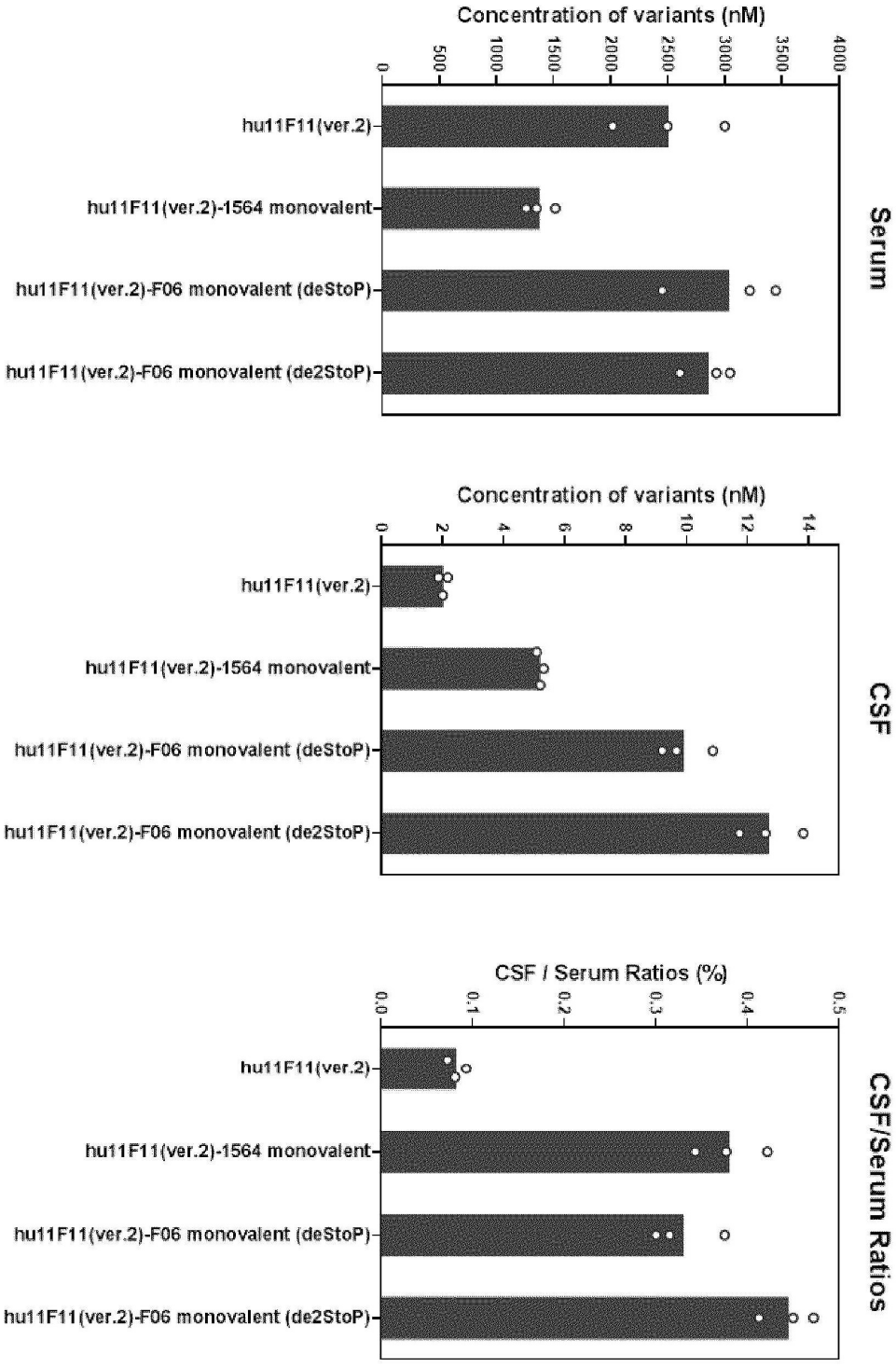
	Sample Name	Geometric Mean : FL1-H
	2nd Ab only.002	2.30
	VH5.010	6.47
	VH5(de)(StoP).011	5.27
	VH5(de2)(StoP).012	8.07

【FIG. 15c】

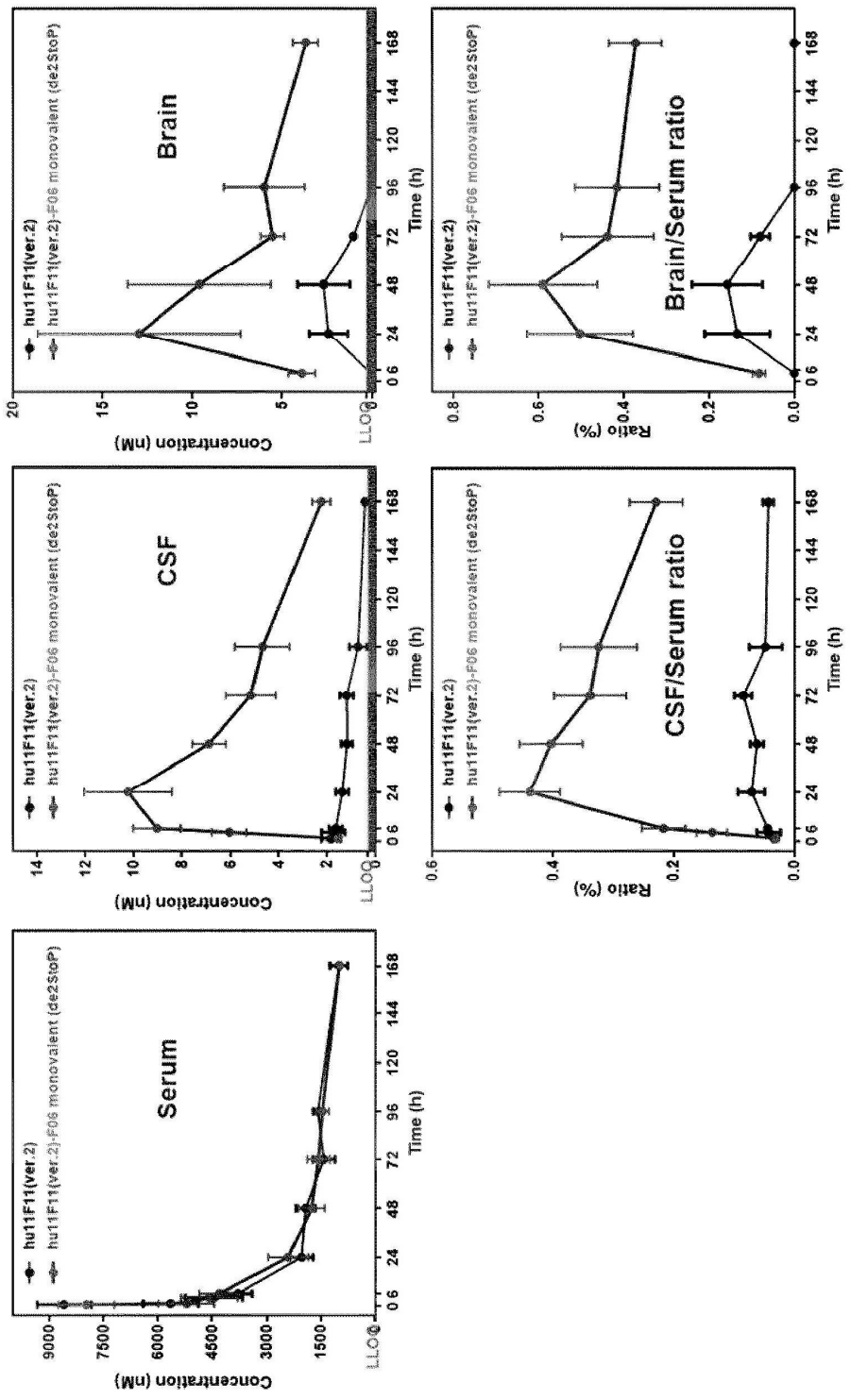


	Sample Name	Geometric Mean : FL1-H
	2nd Ab only.002	2.30
	VH16.007	6.16
	VH16(de)(StoP).008	4.83
	VH16(de2)(StoP).009	6.45

【FIG. 16】


Concentration of variants (nM)
0
500
1000
1500
2000
2500
3000
3500
4000
hu11F11(ver.2)
hu11F11(ver.2)-1564 monovalent
hu11F11(ver.2)-F06 monovalent (deStoP)
hu11F11(ver.2)-F06 monovalent (de2StoP)
Serum
Concentration of variants (nM)
0
2
4
6
8
10
12
14
hu11F11(ver.2)
hu11F11(ver.2)-1564 monovalent
hu11F11(ver.2)-F06 monovalent (deStoP)
hu11F11(ver.2)-F06 monovalent (de2StoP)
CSF
CSF / Serum Ratios (%)
0.0
0.1
0.2
0.3
0.4
0.5
hu11F11(ver.2)
hu11F11(ver.2)-1564 monovalent
hu11F11(ver.2)-F06 monovalent (deStoP)
hu11F11(ver.2)-F06 monovalent (de2StoP)
CSF/Serum Ratios

【FIG. 17】


Serum
CSF
Brain
CSF/Serum ratio
Brain/Serum ratio
hu11F11(ver.2)
hu11F11(ver.2)-F06 monovalent (de2StoP)
Concentration (nM)
Ratio (%)
Time (h)
LLOQ