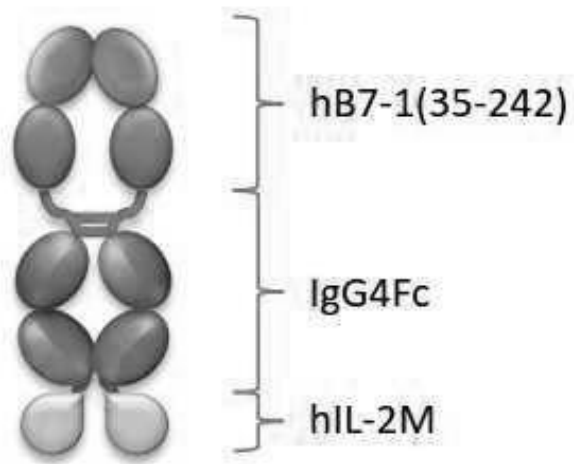
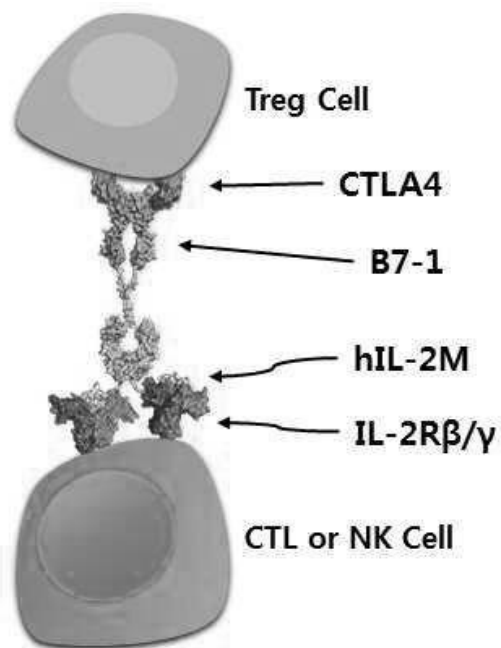


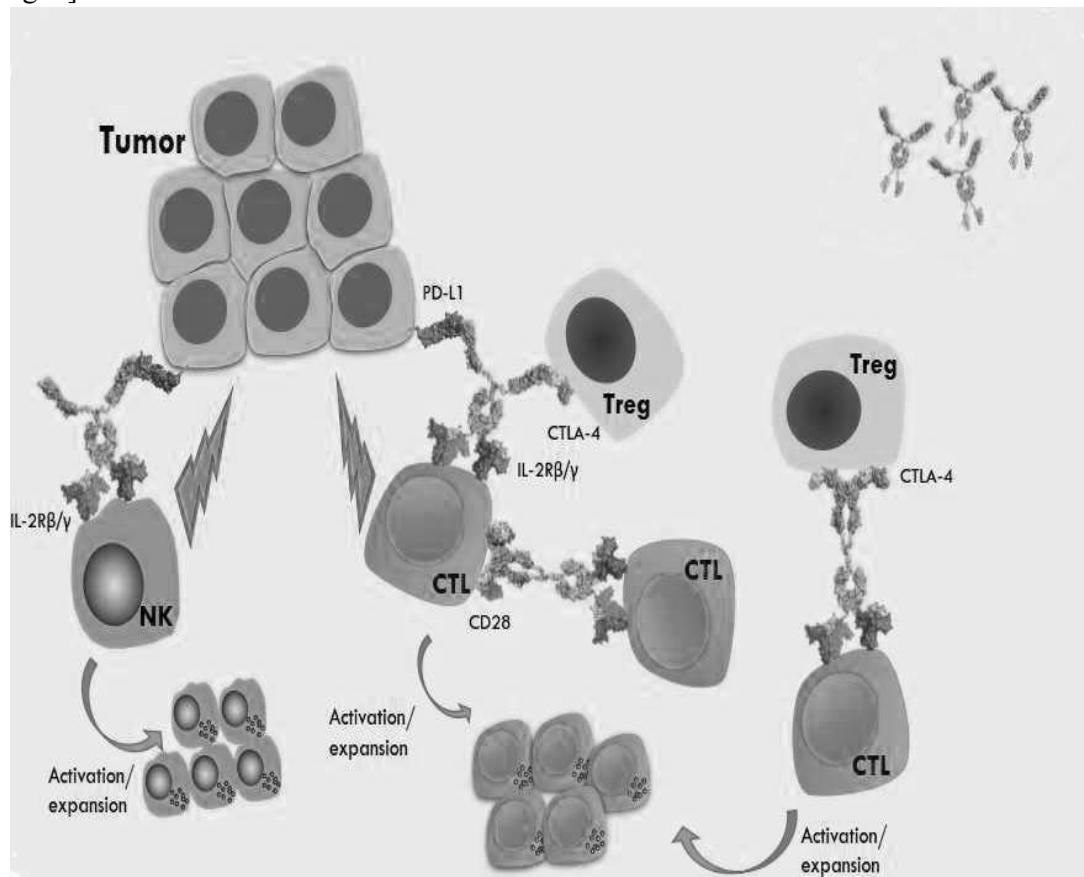
[Fig. 1]



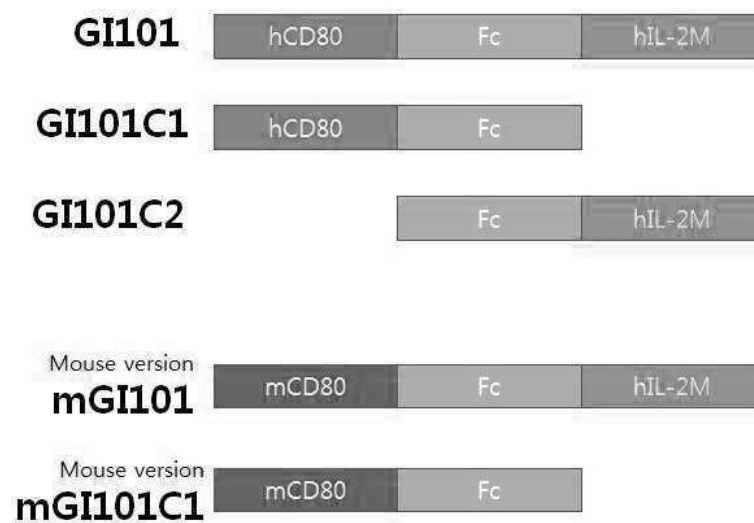
[Fig. 2]



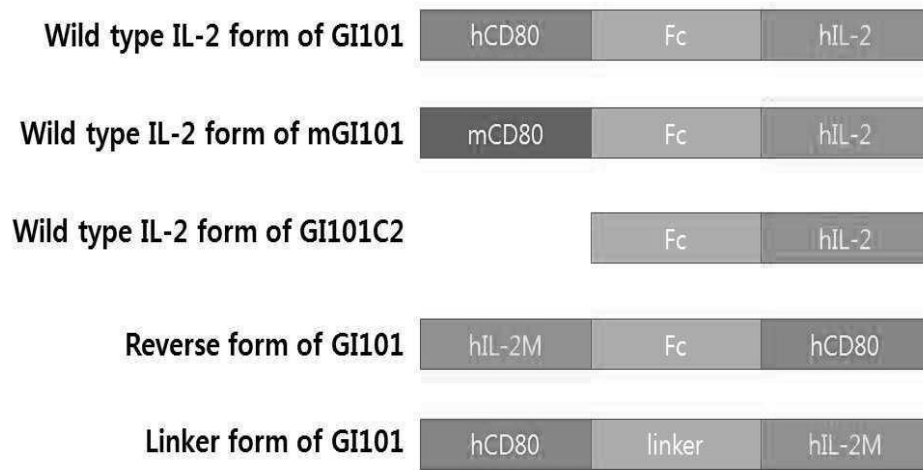
[Fig. 3]



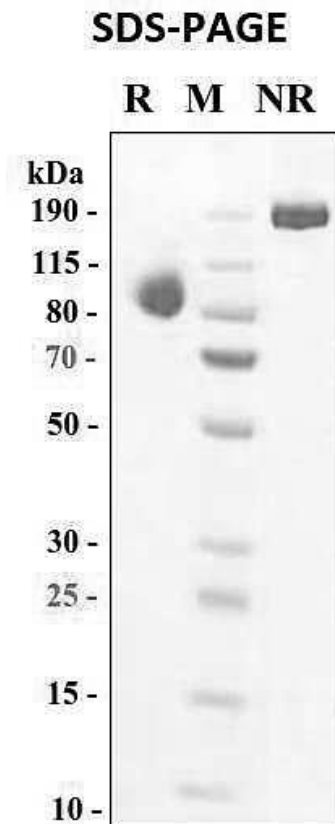
[Fig. 4]



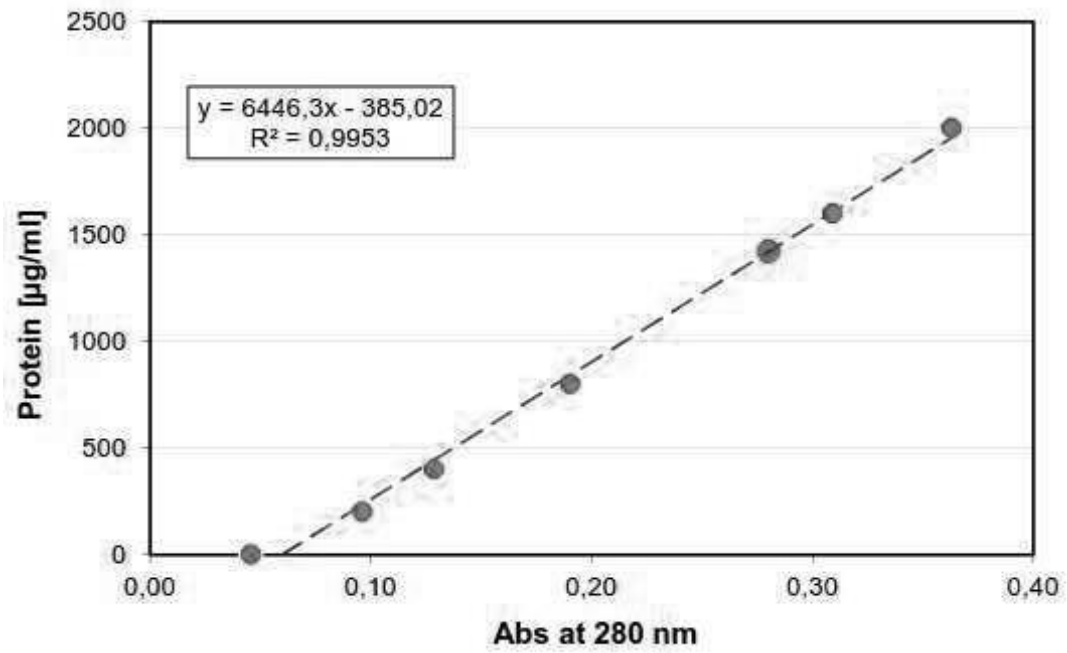
[Fig. 5]



[Fig. 6]

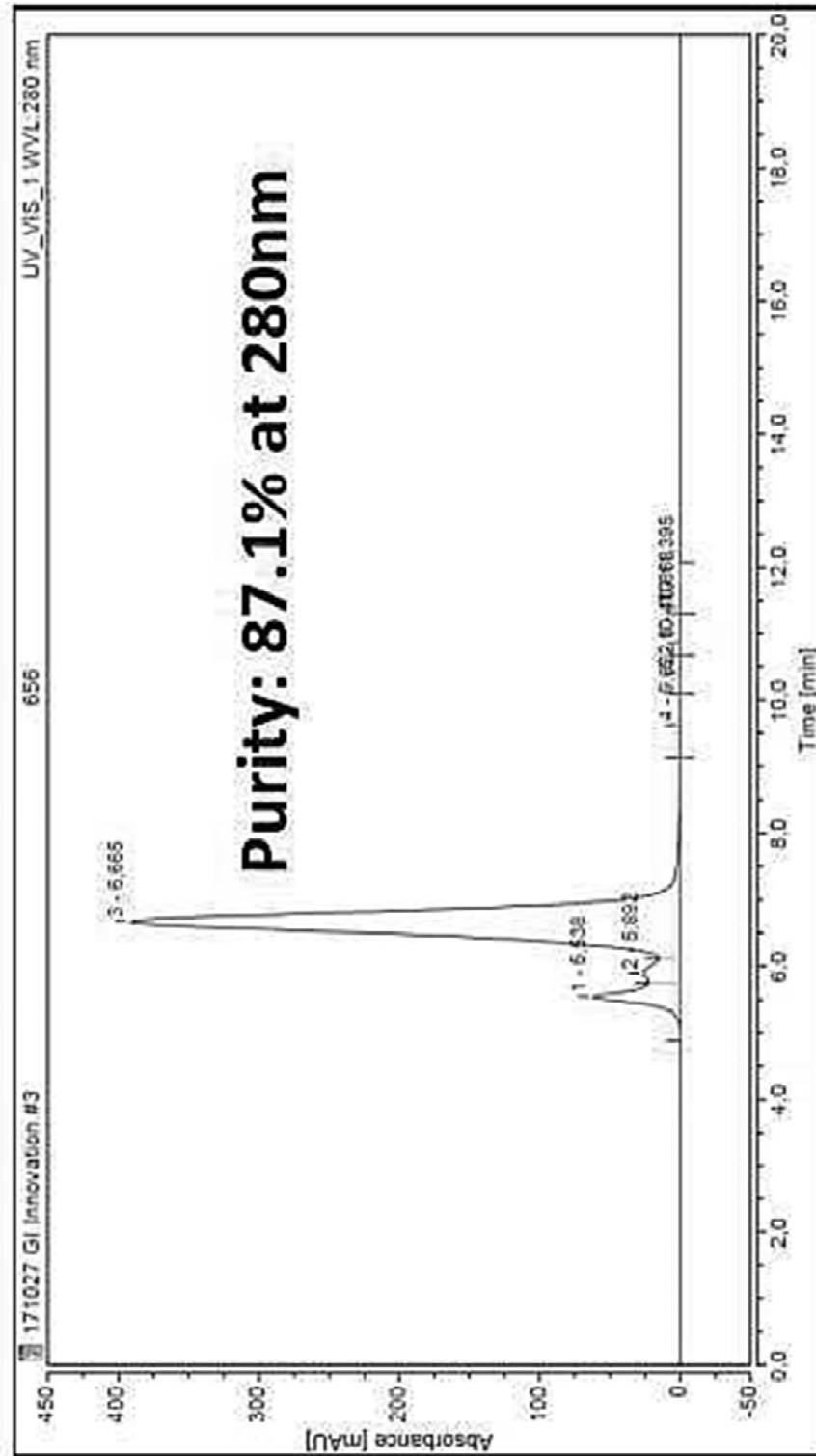


[Fig. 7]

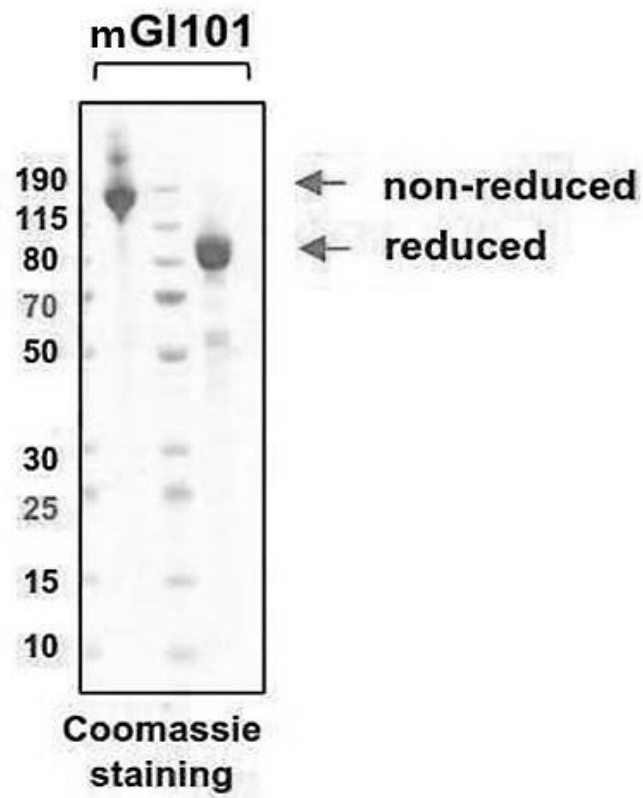


[Fig. 8]

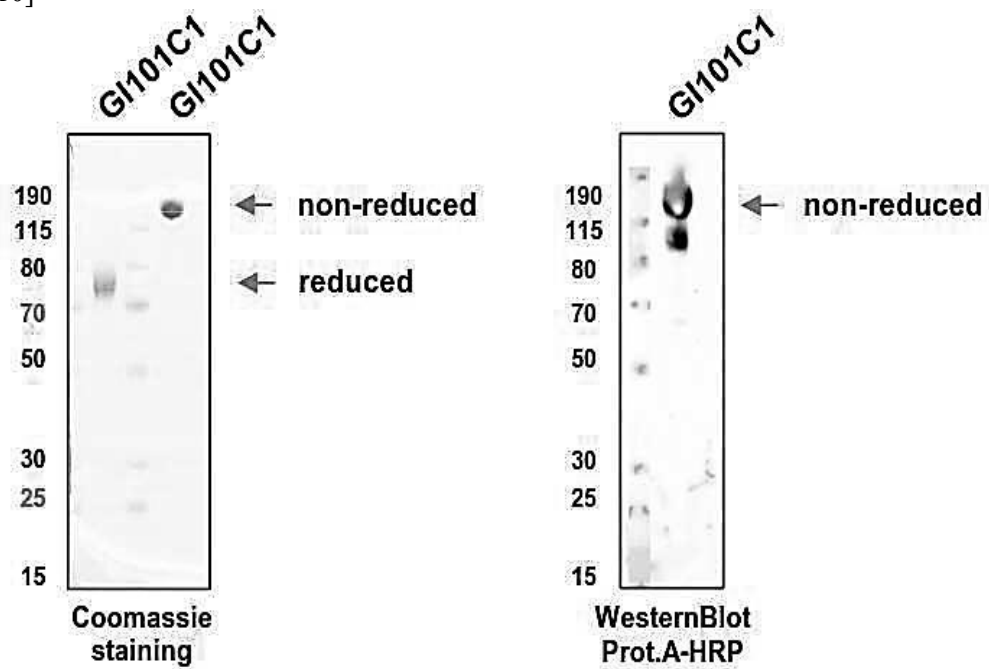
Anlytical size exclusion chromatography (SEC)



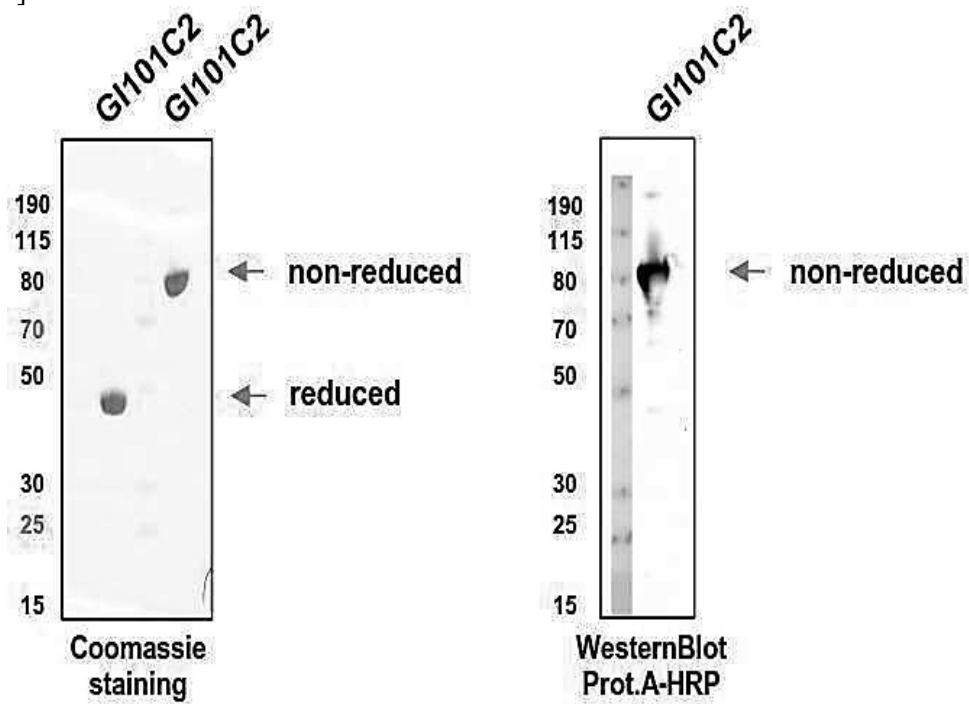
[Fig. 9]



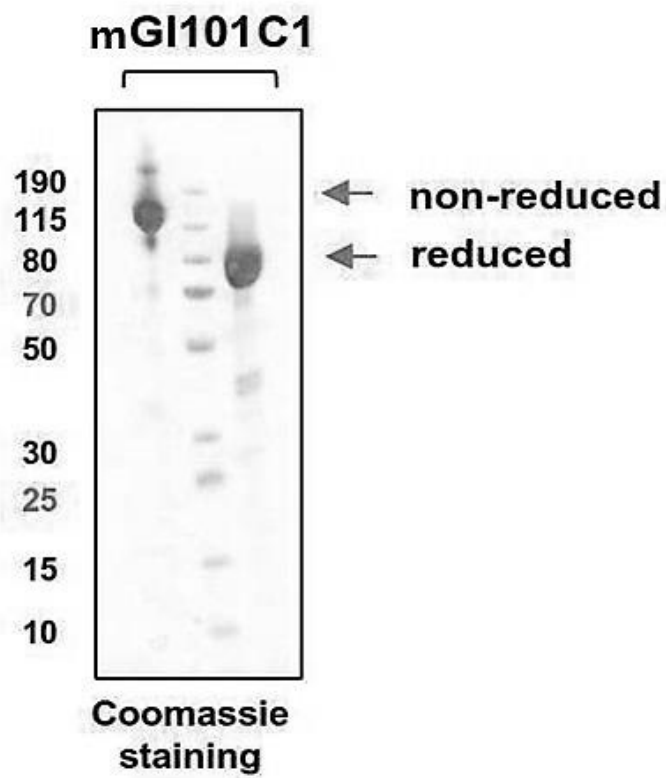
[Fig. 10]



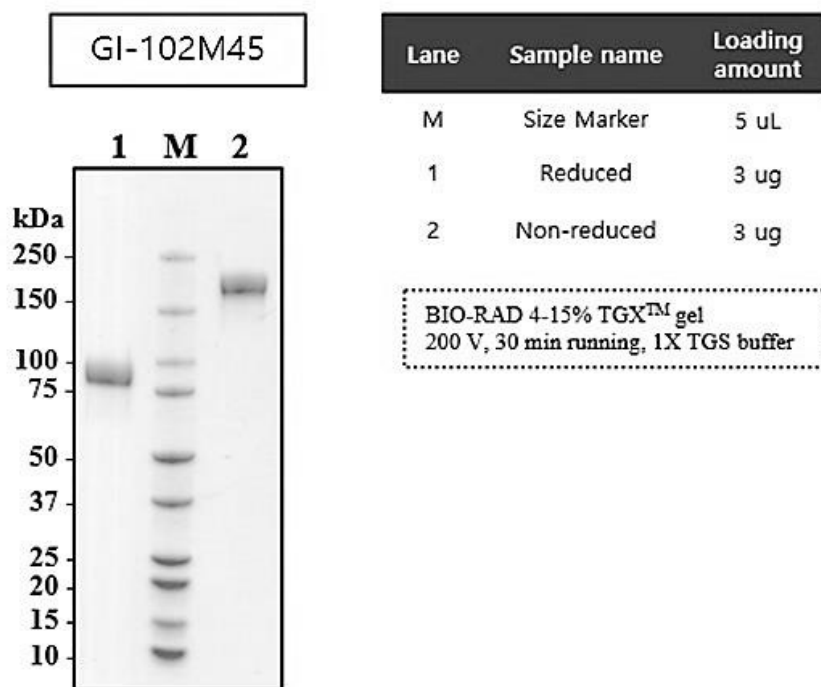
[Fig. 11]



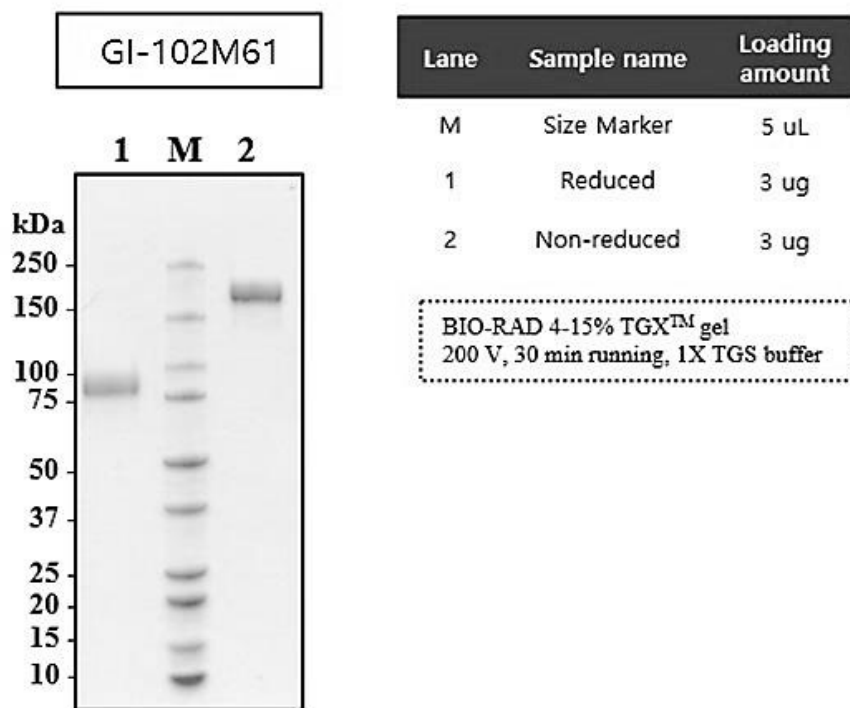
[Fig. 12]



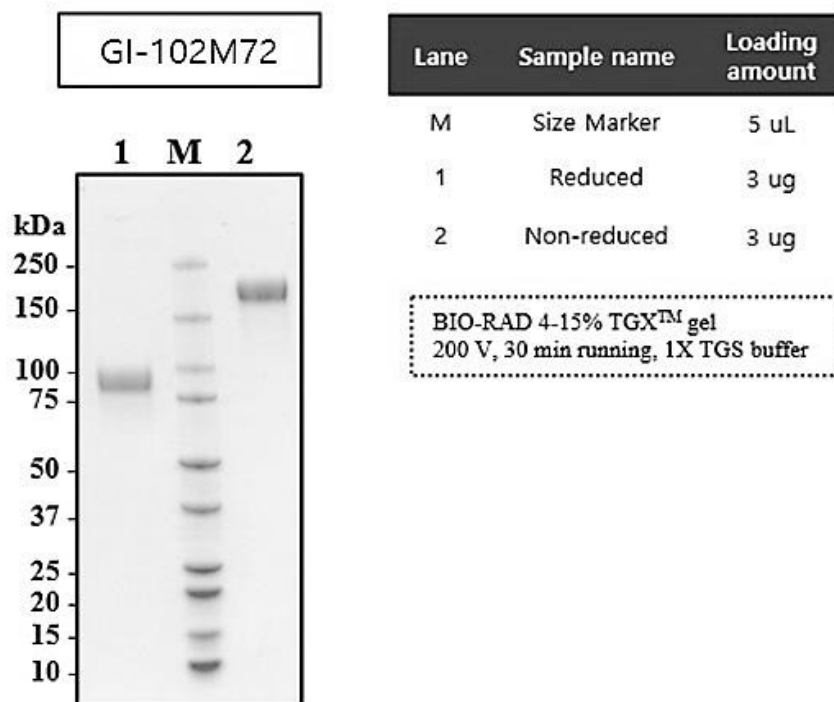
[Fig. 13]



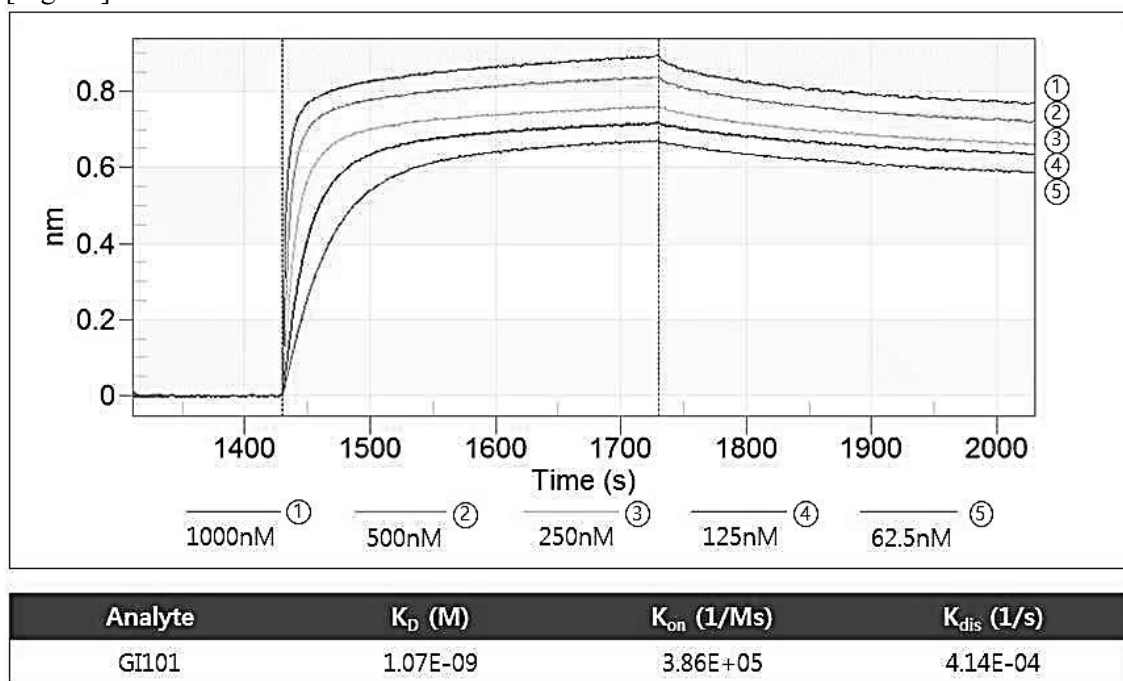
[Fig. 14]



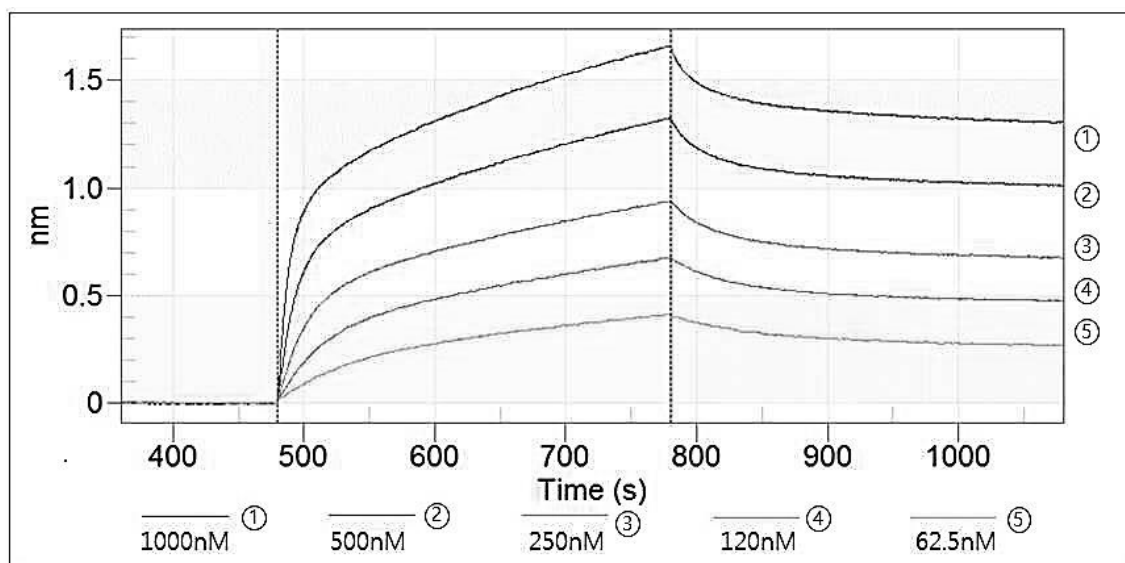
[Fig. 15]



[Fig. 16]

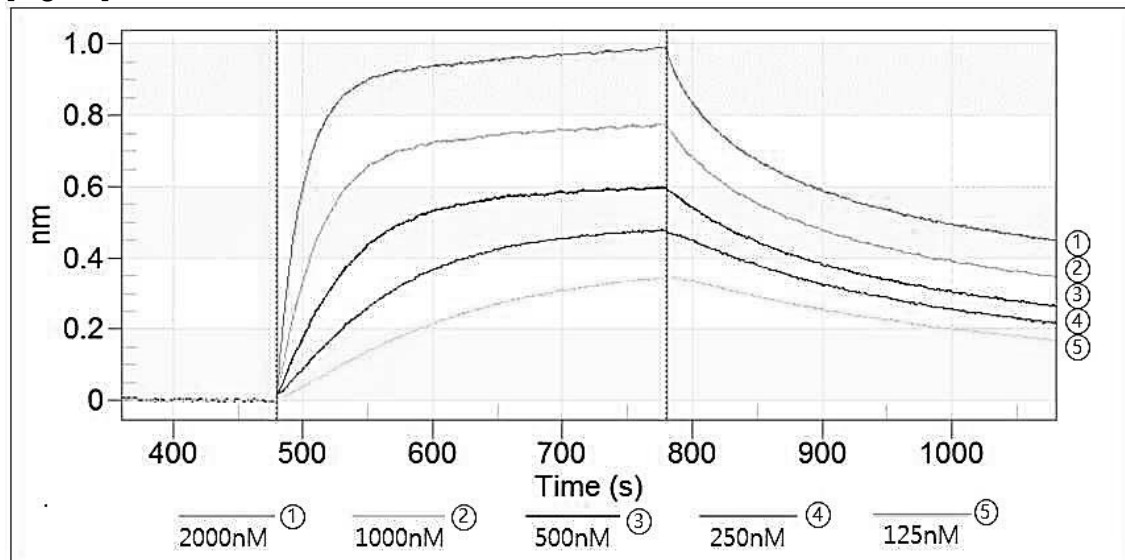


[Fig. 17]



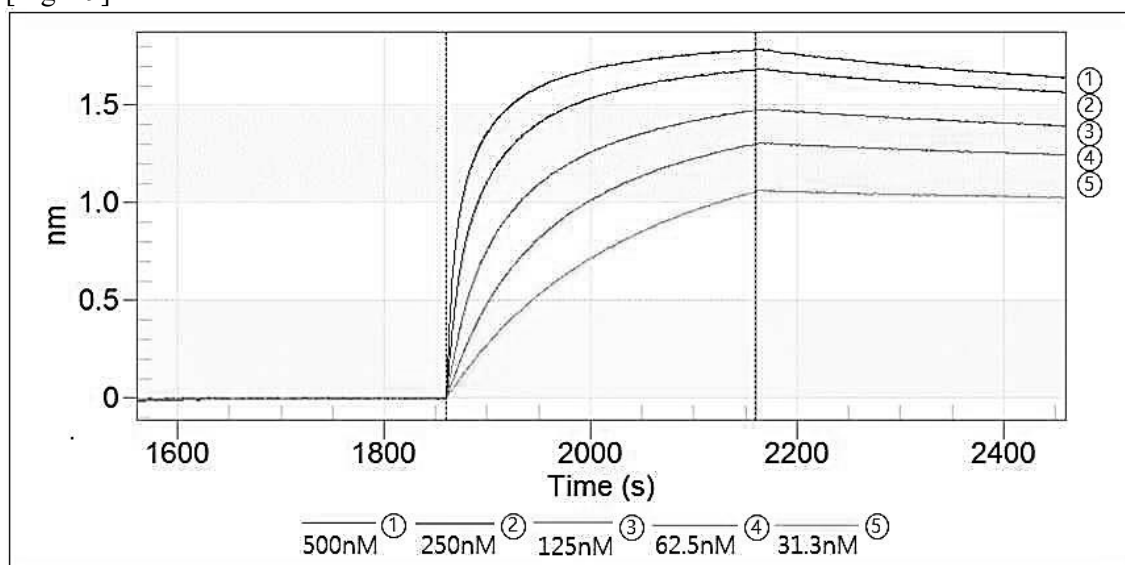
Analyte	K_D (M)	K_{on} (1/Ms)	K_{dis} (1/s)
Gl101	3.46E-08	7.0E+04	2.42E-03

[Fig. 18]



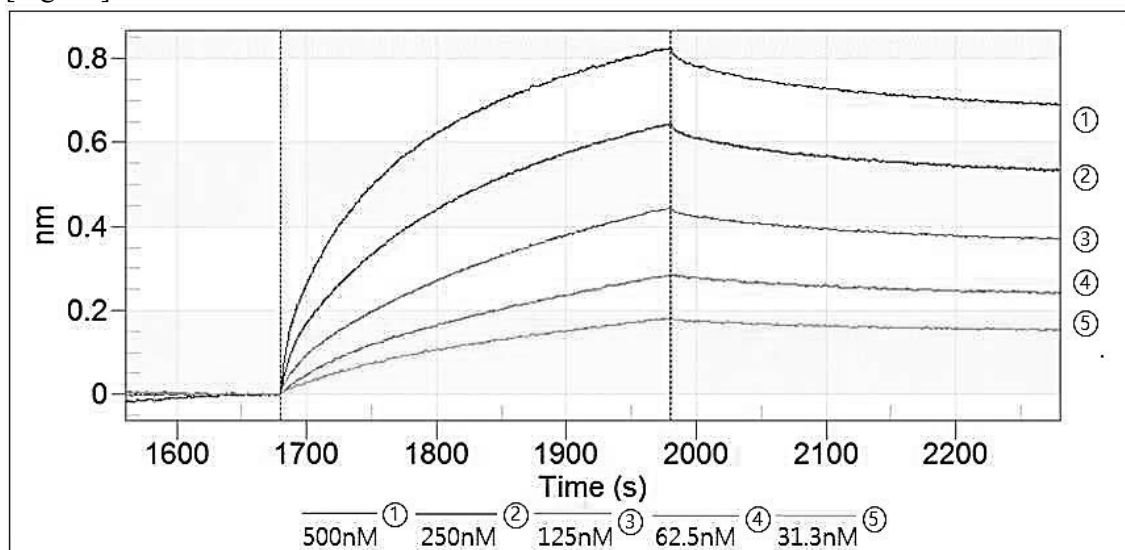
Analyte	K_D (M)	K_{on} (1/Ms)	K_{dis} (1/s)
PD-1	1.13E-07	2.72E+04	3.07E-03

[Fig. 19]



Analyte	K_D (M)	K_{on} (1/Ms)	K_{dis} (1/s)
mGI101	2.58E-08	3.05E+05	7.88E-04

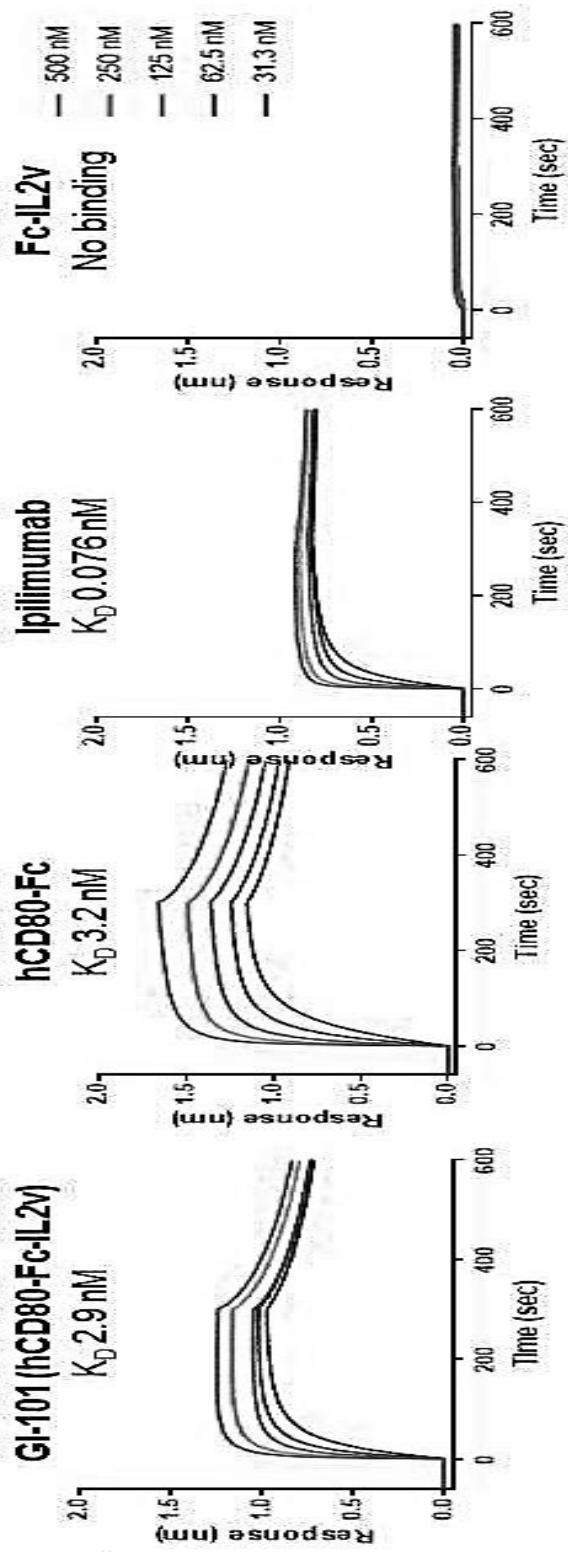
[Fig. 20]



Analyte	K_D (M)	K_{on} (1/Ms)	K_{dis} (1/s)
mGI101	9.91E-09	8.12E+05	8.04E-03

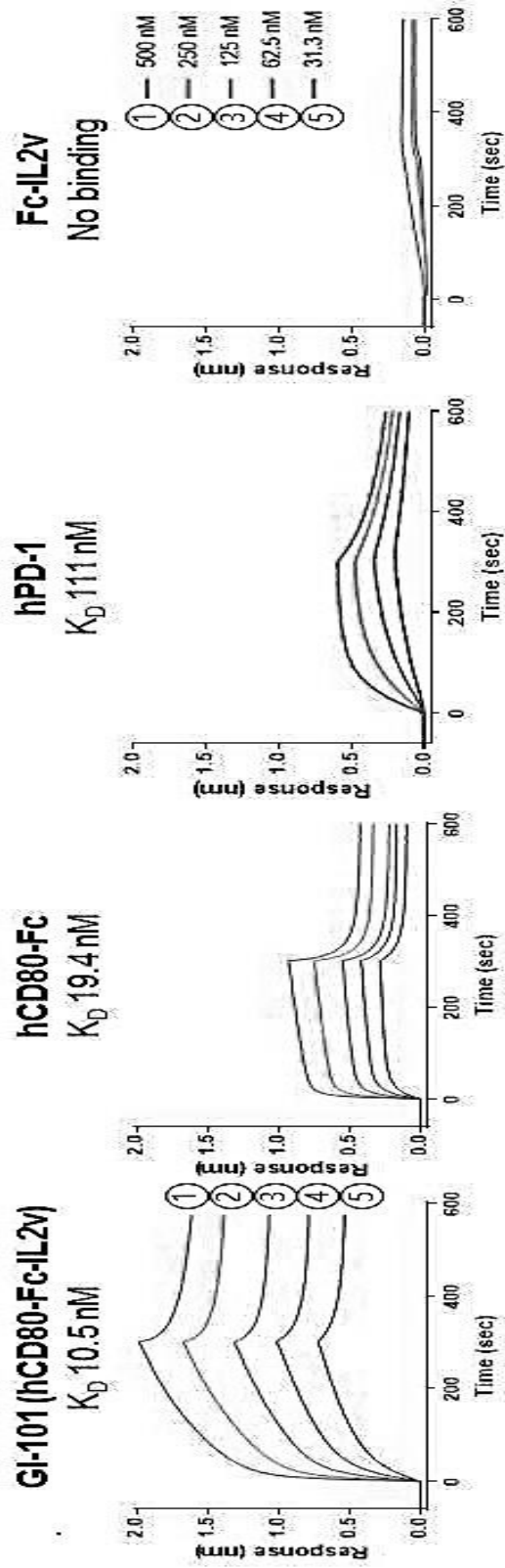
[Fig. 21]

Binding to hCTLA-4

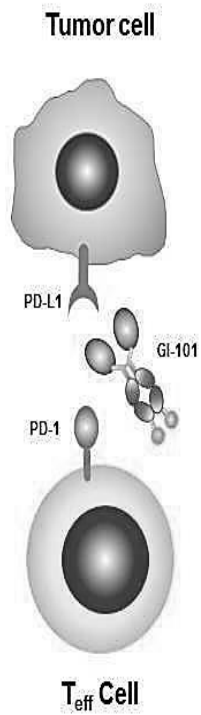


[Fig. 22]

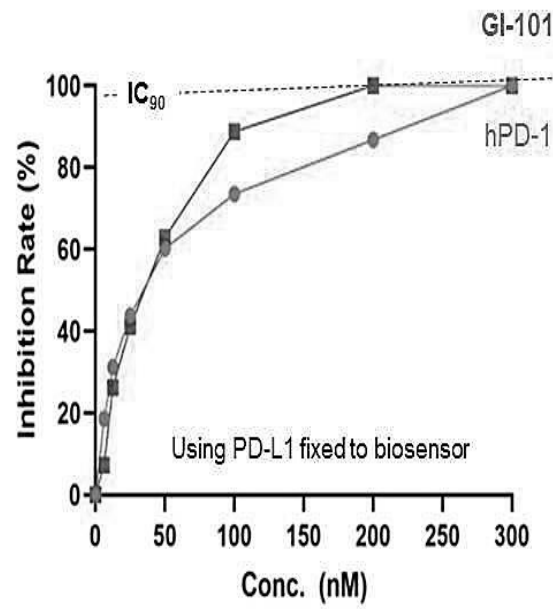
Binding to hPD-L1



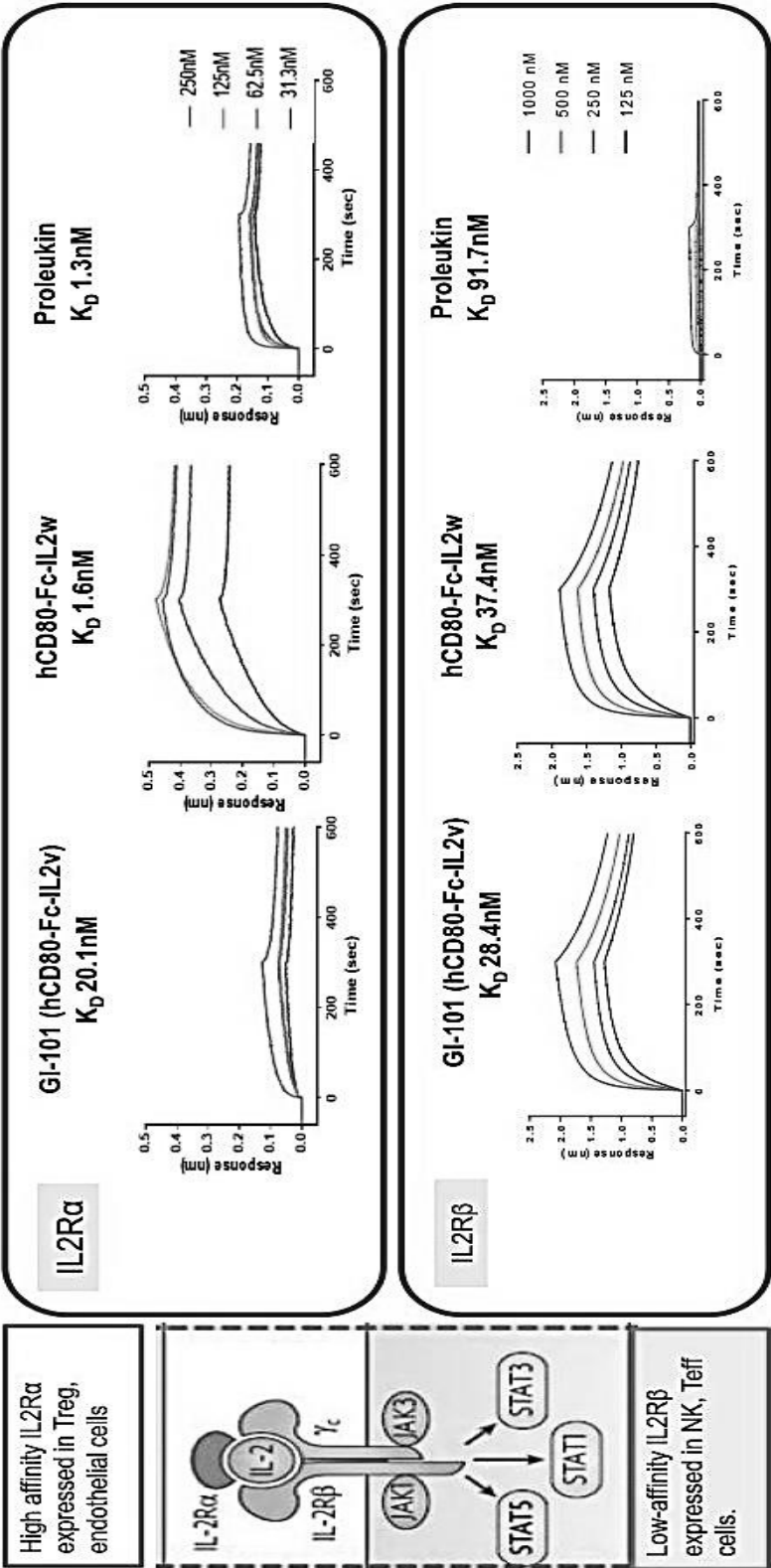
[Fig. 23]



GI-101 dose-dependently inhibits PD-1/PD-L1 interactions

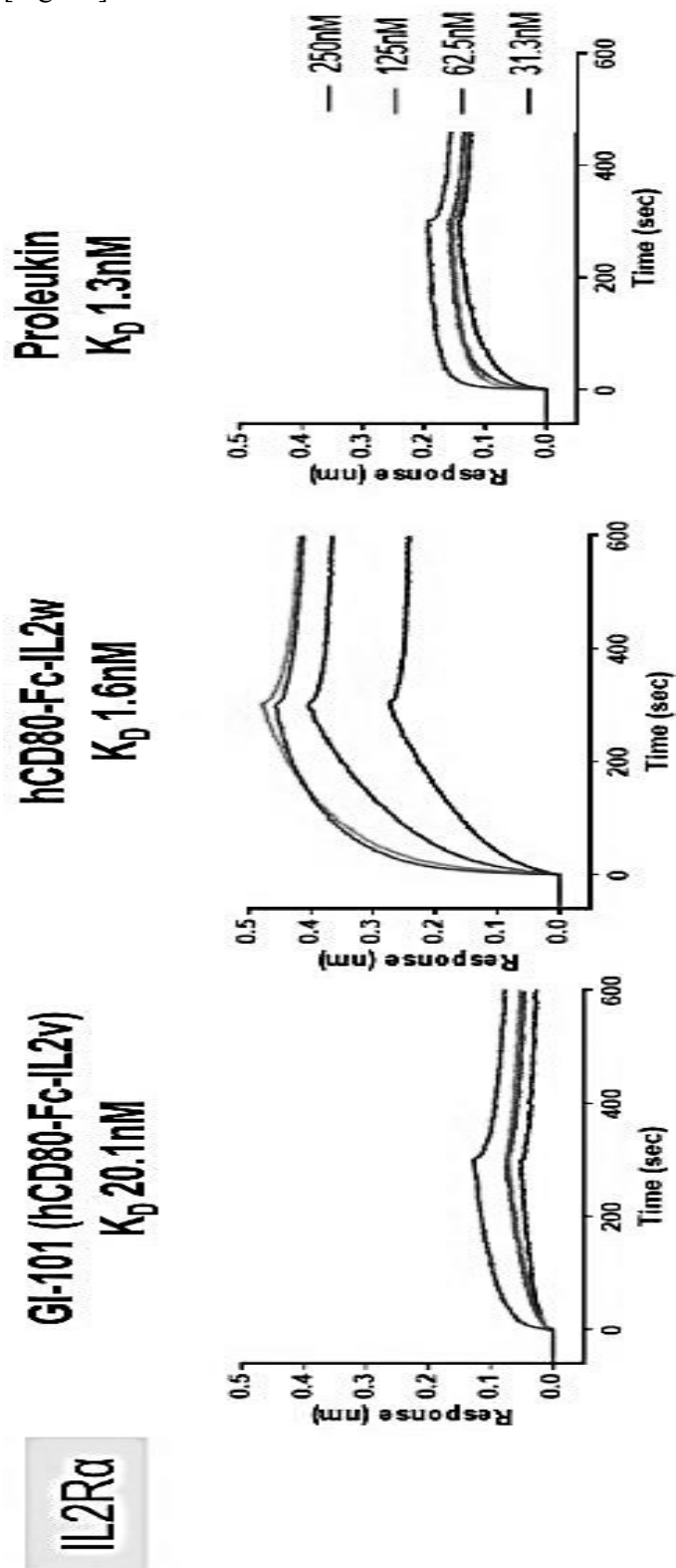


[Fig. 24]

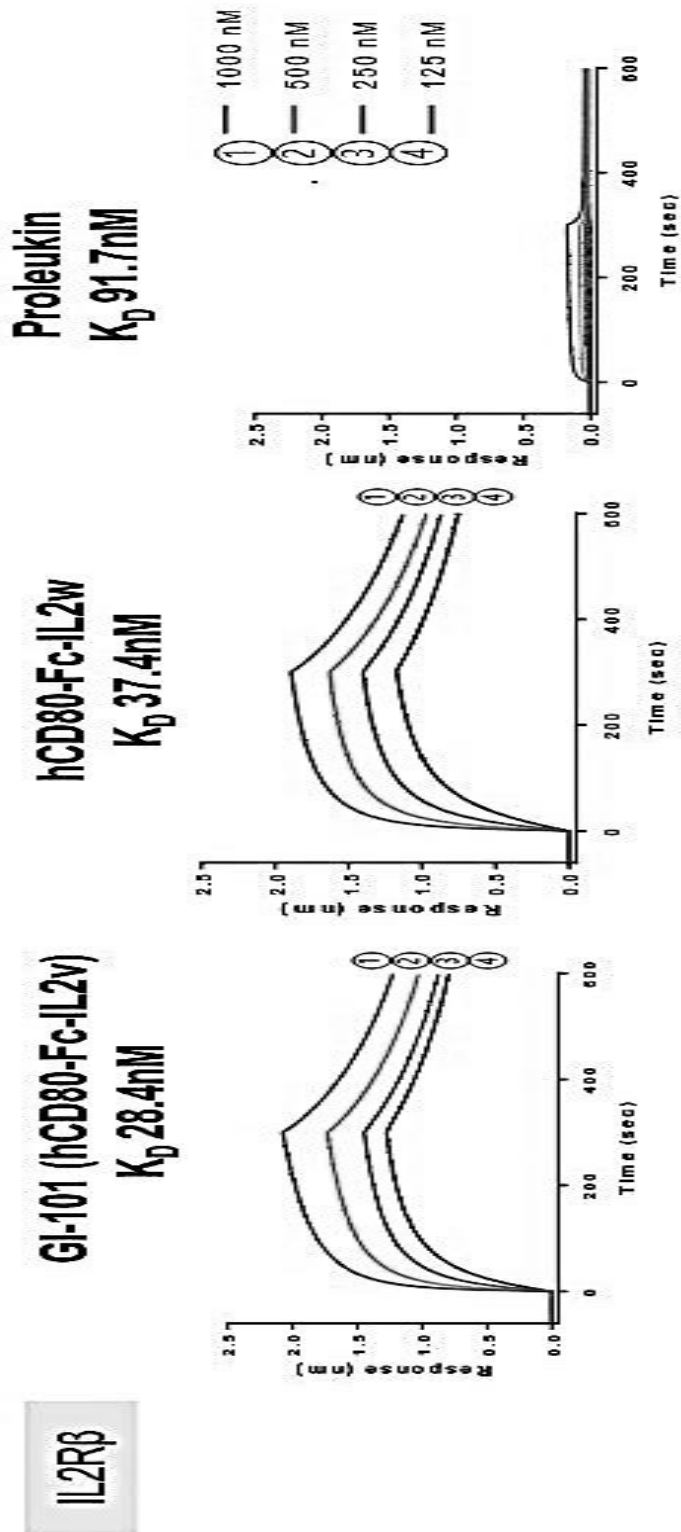


References		Kd (nM)	
Receptor	*hIL2w	**NKTR-214 (1-PEG-IL2)	**NKTR-214 (2-PEG-IL2)
hIL2R α	10 (x14)	8.6 (x28)	189.7 (x9) 486.6 (x8)
hIL2R β	144	238.9	1769.5 3951.8

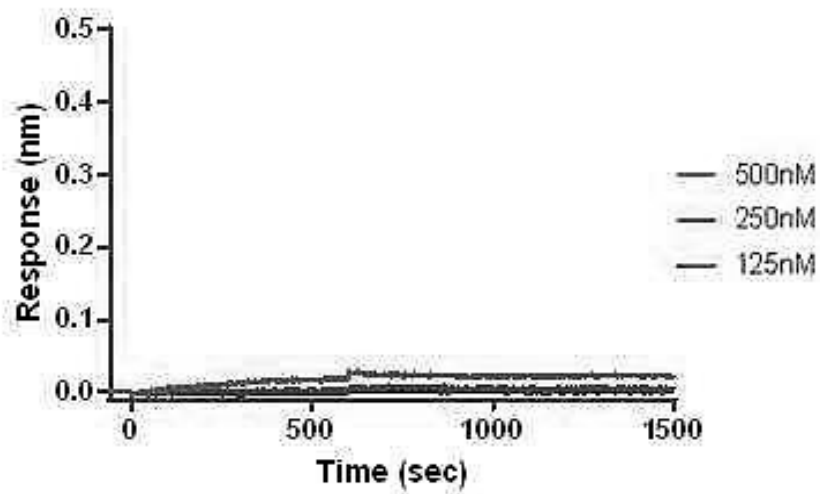
[Fig. 25]



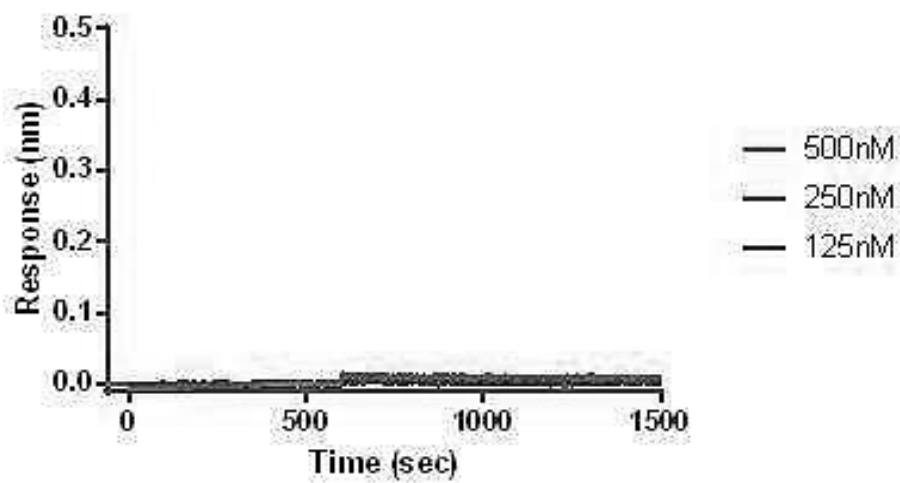
[Fig. 26]



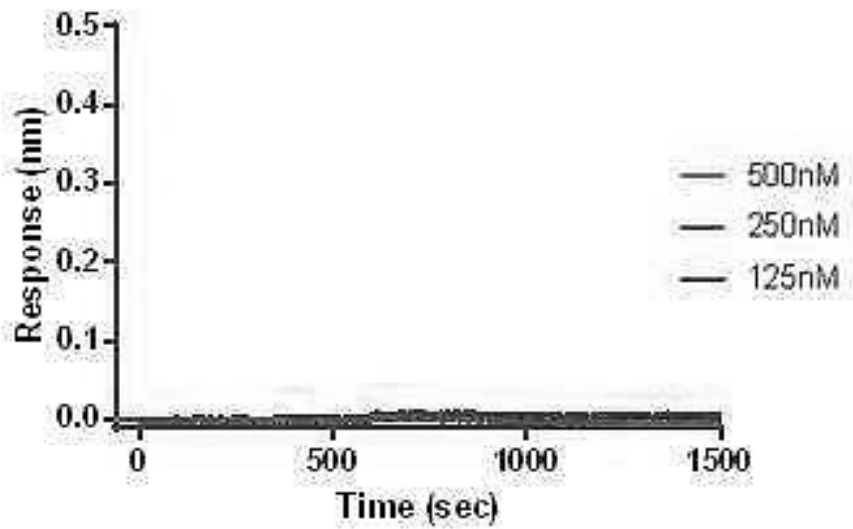
[Fig. 27]



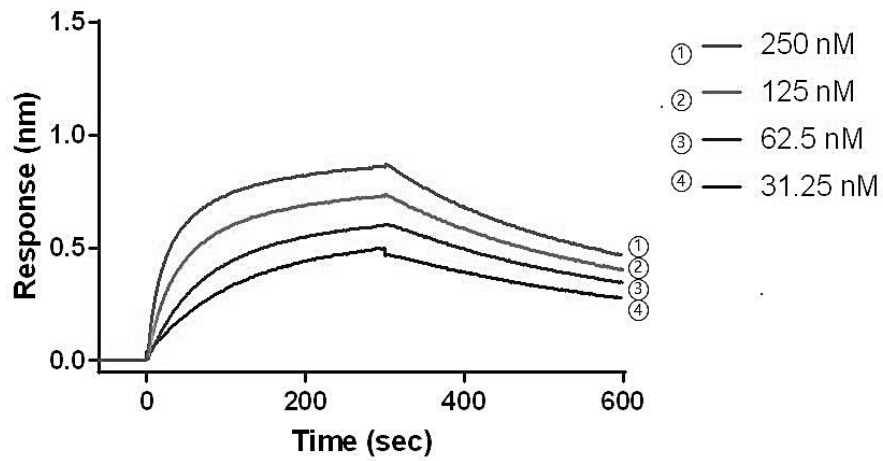
[Fig. 28]



[Fig. 29]

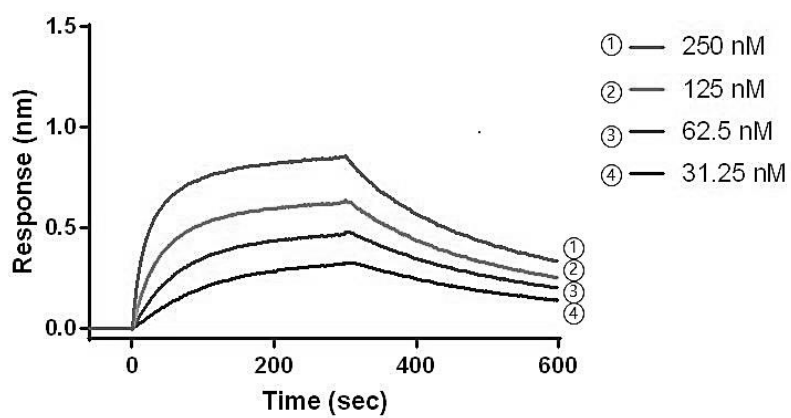


[Fig. 30]



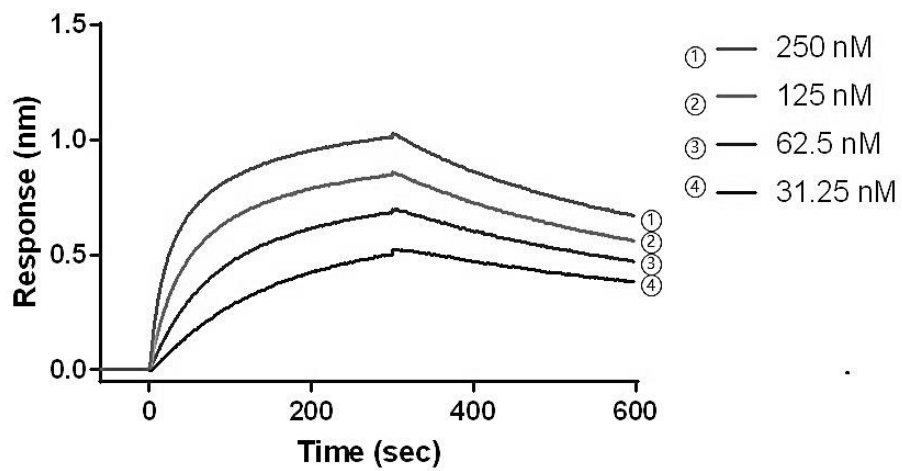
Kon	Koff	Kd
1.30X10 ⁵	2.01X10 ⁻³	1.55X10 ⁻⁸

[Fig. 31]



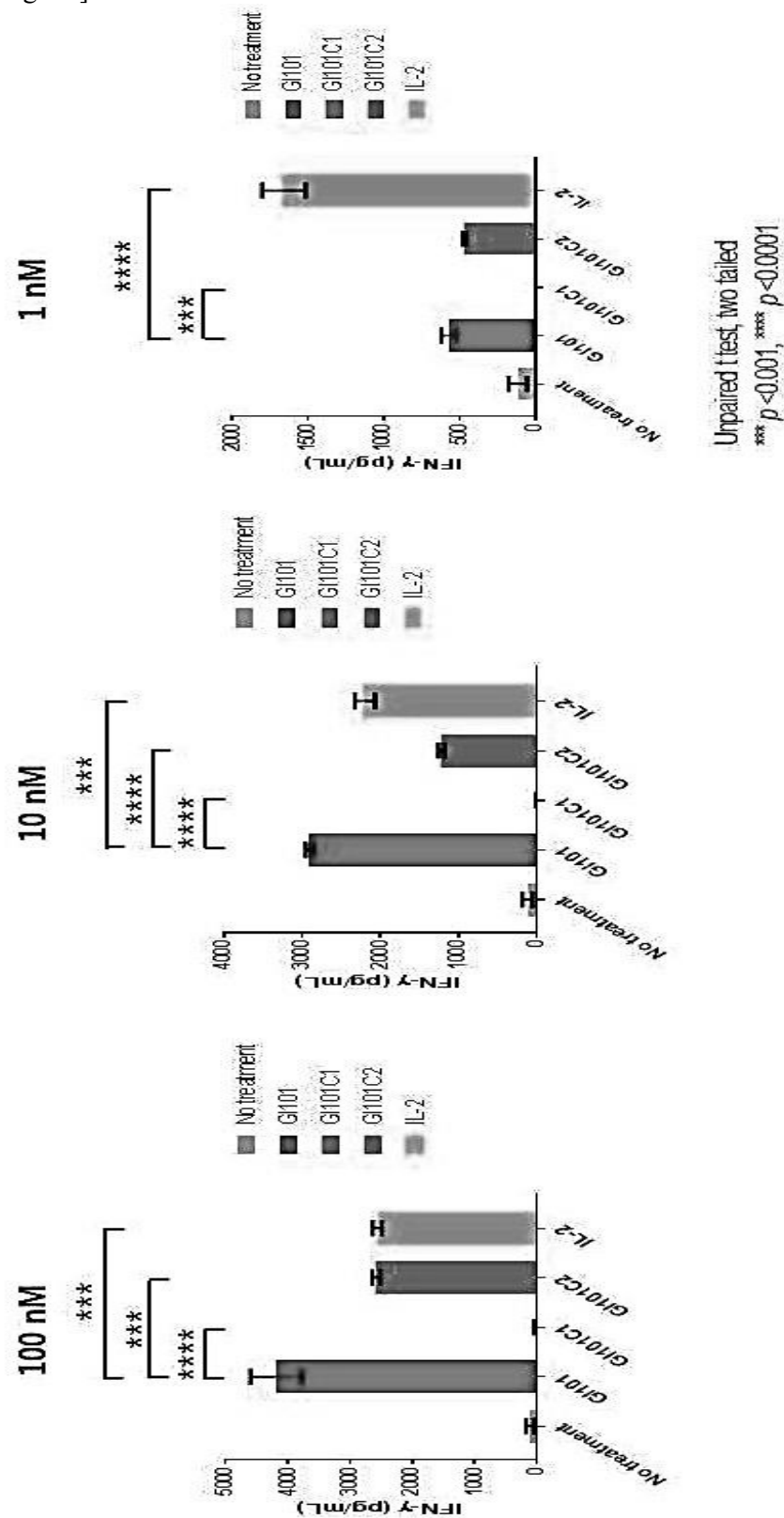
Kon	Koff	Kd
1.32X10 ⁵	3.11X10 ⁻³	2.36X10 ⁻⁸

[Fig. 32]

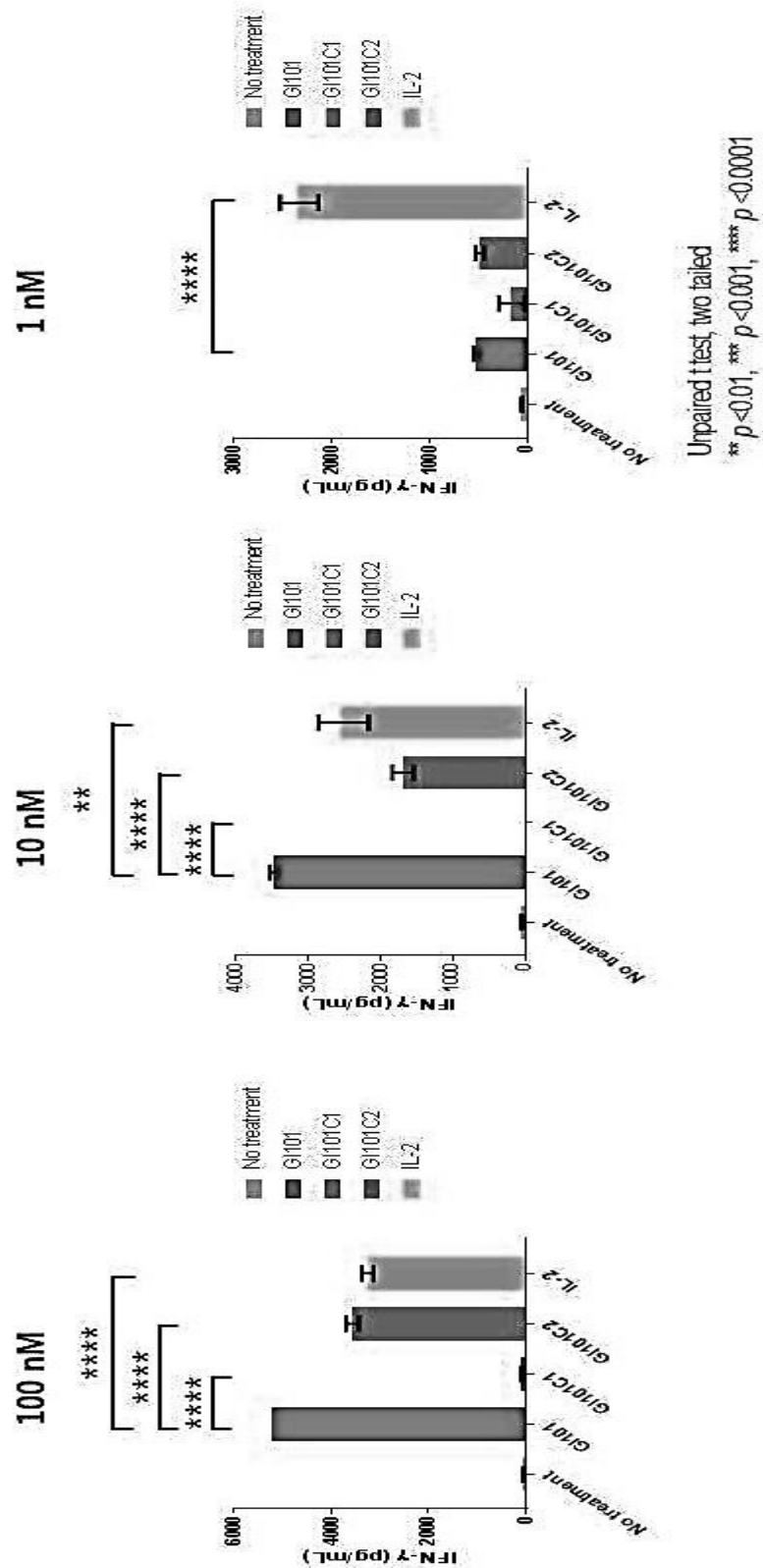


Kon	Koff	Kd
1.10X10 ⁵	1.27X10 ⁻³	1.15X10 ⁻⁸

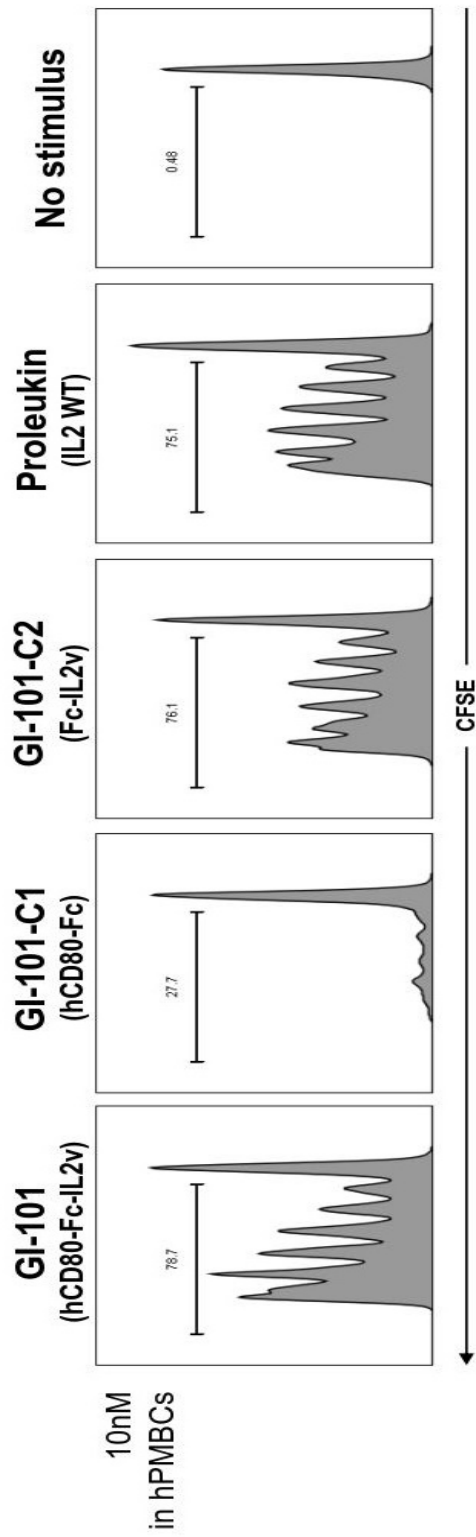
[Fig. 33]



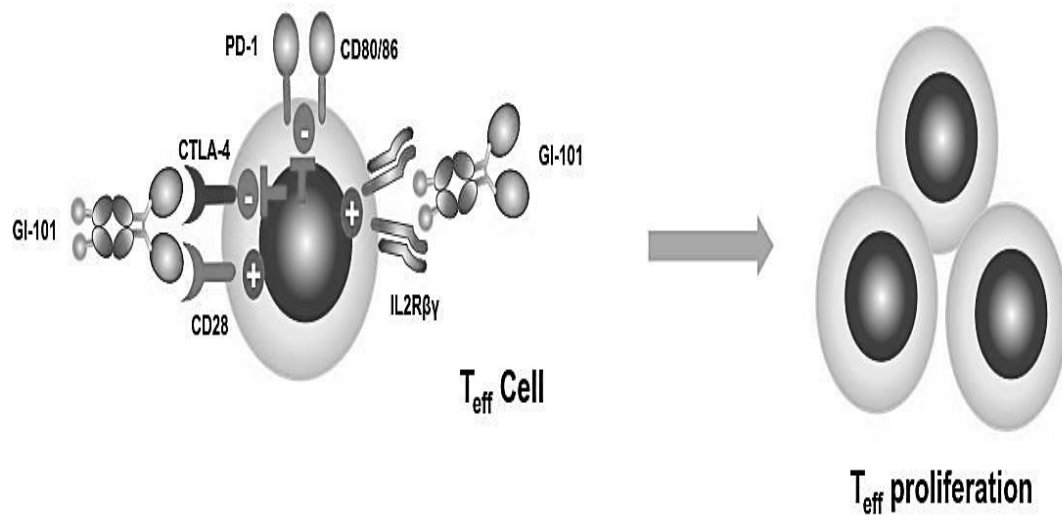
[Fig. 34]



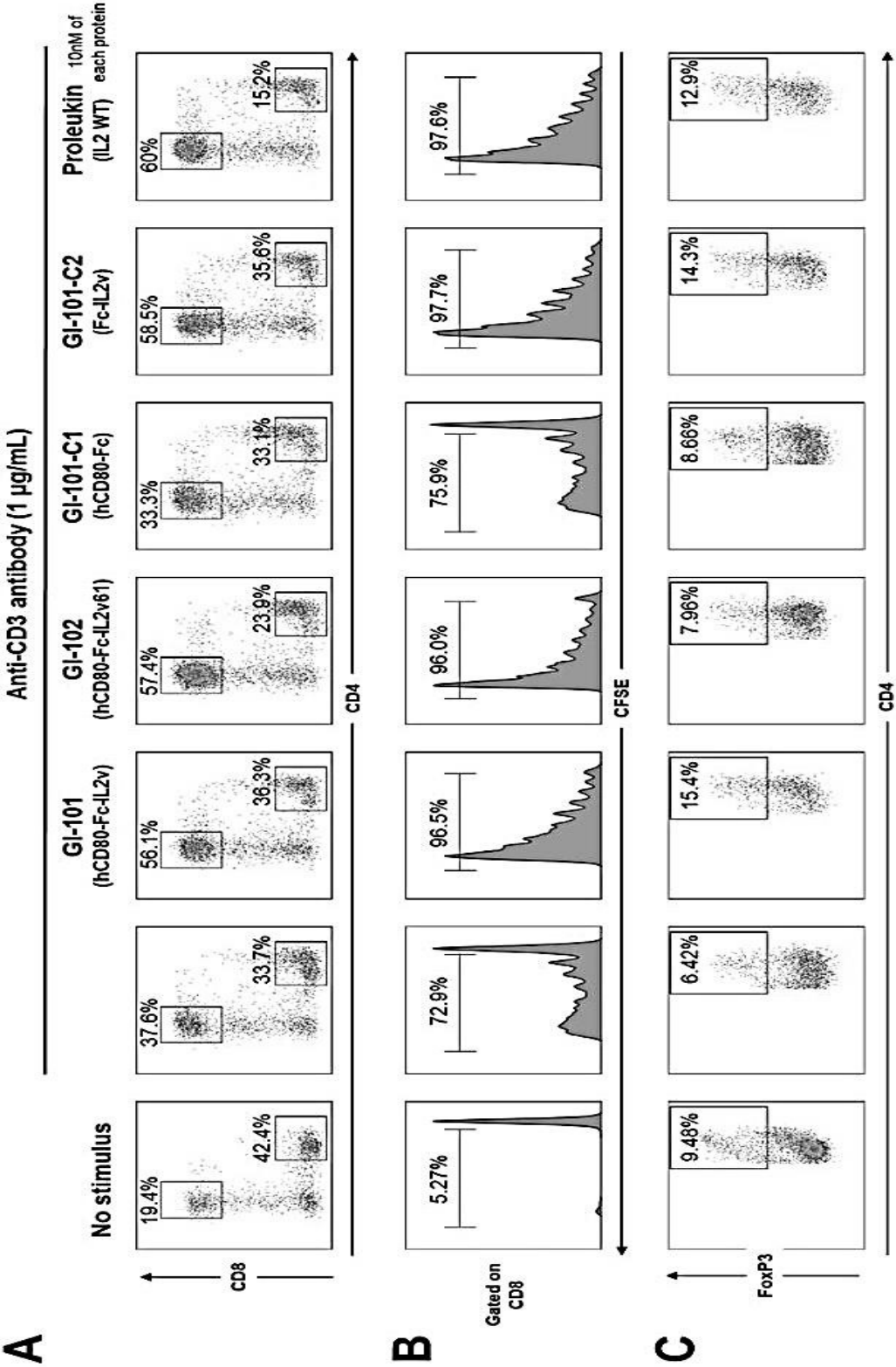
[Fig. 35]



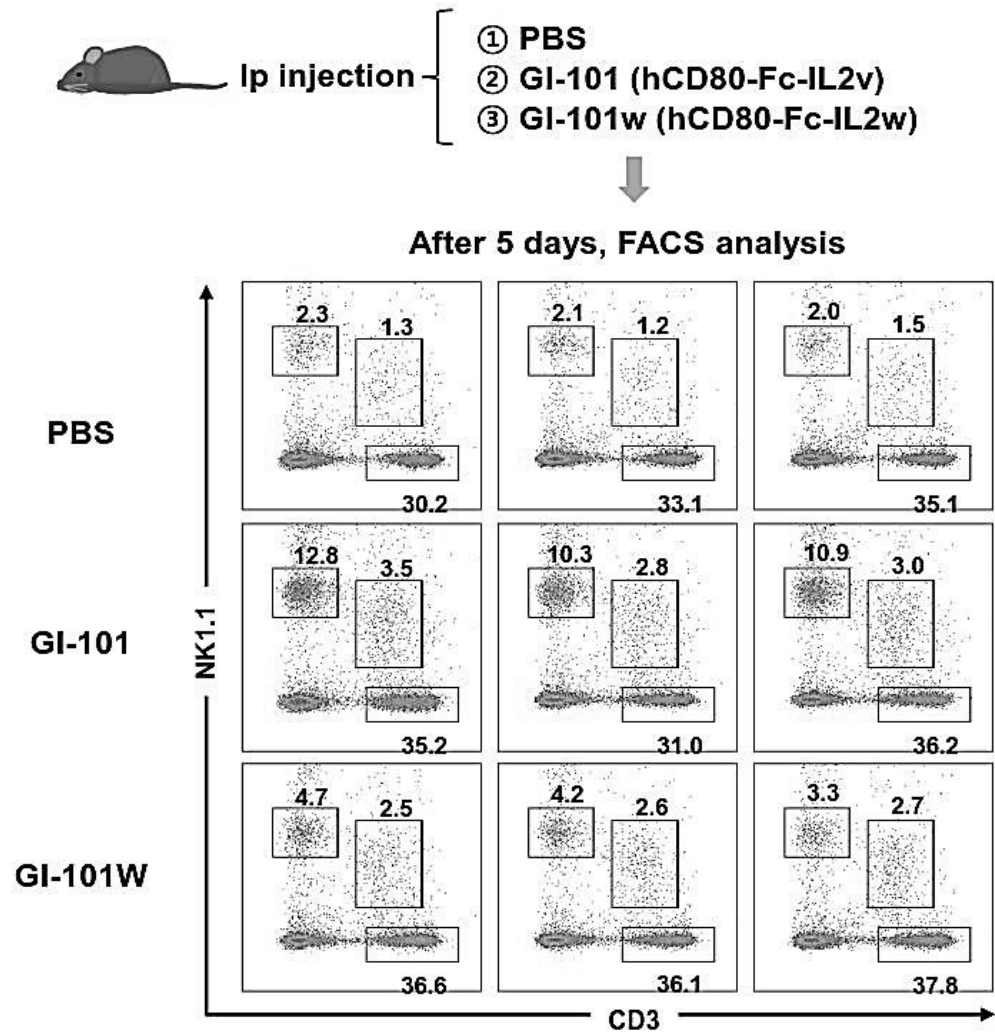
[Fig. 36]



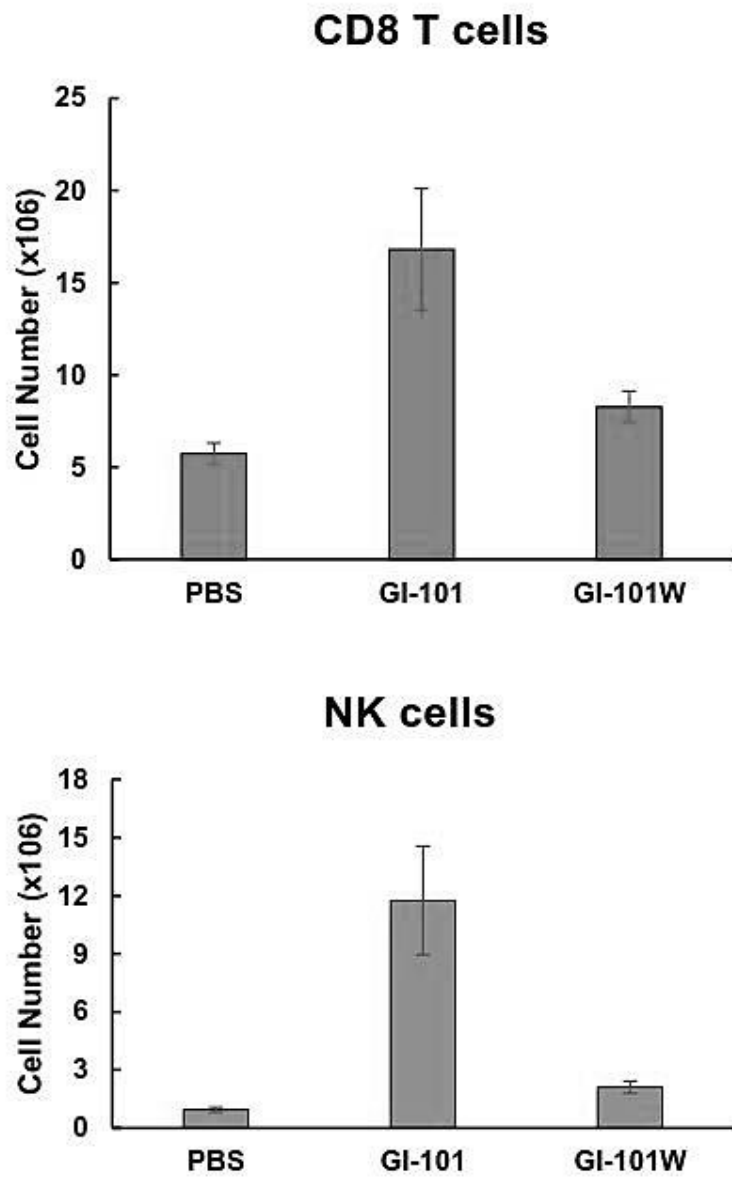
[Fig. 37]



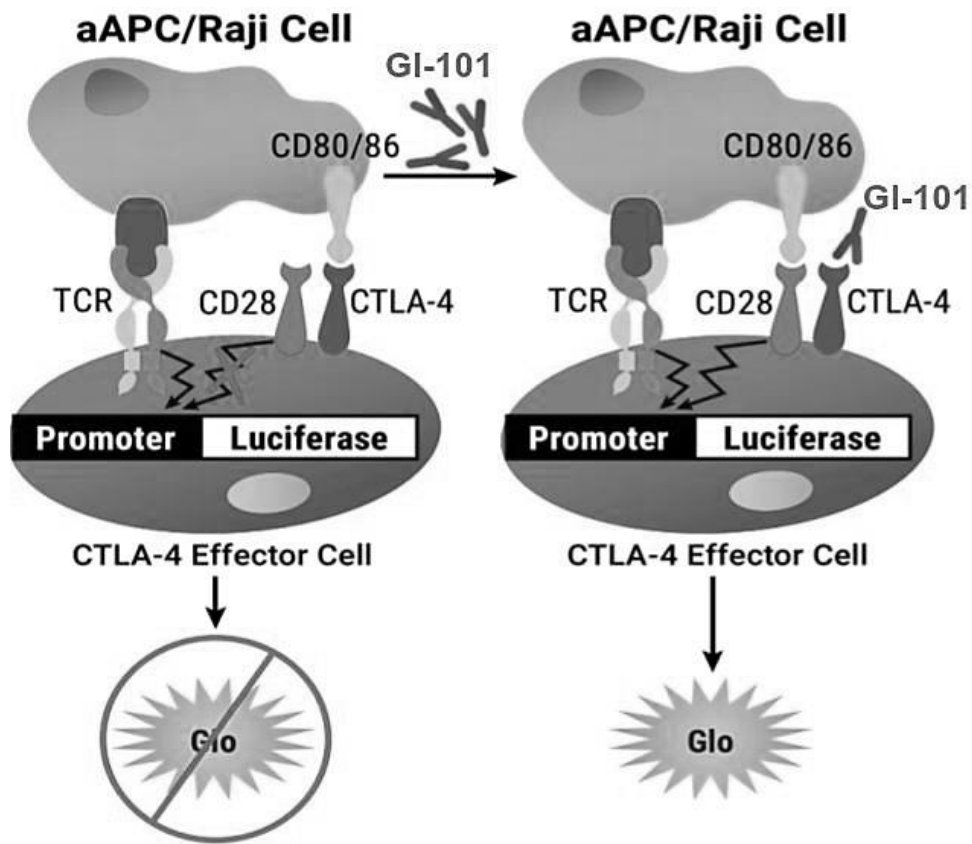
[Fig. 38]



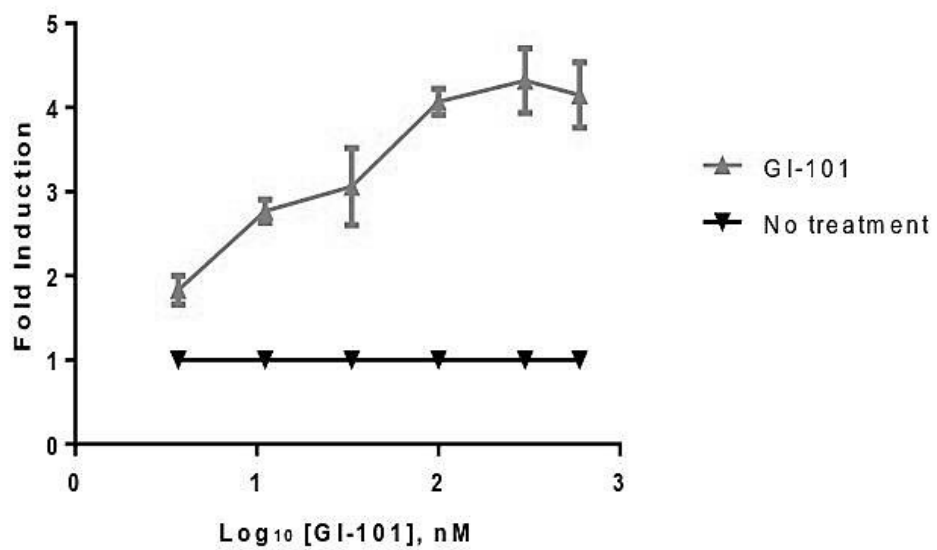
[Fig. 39]



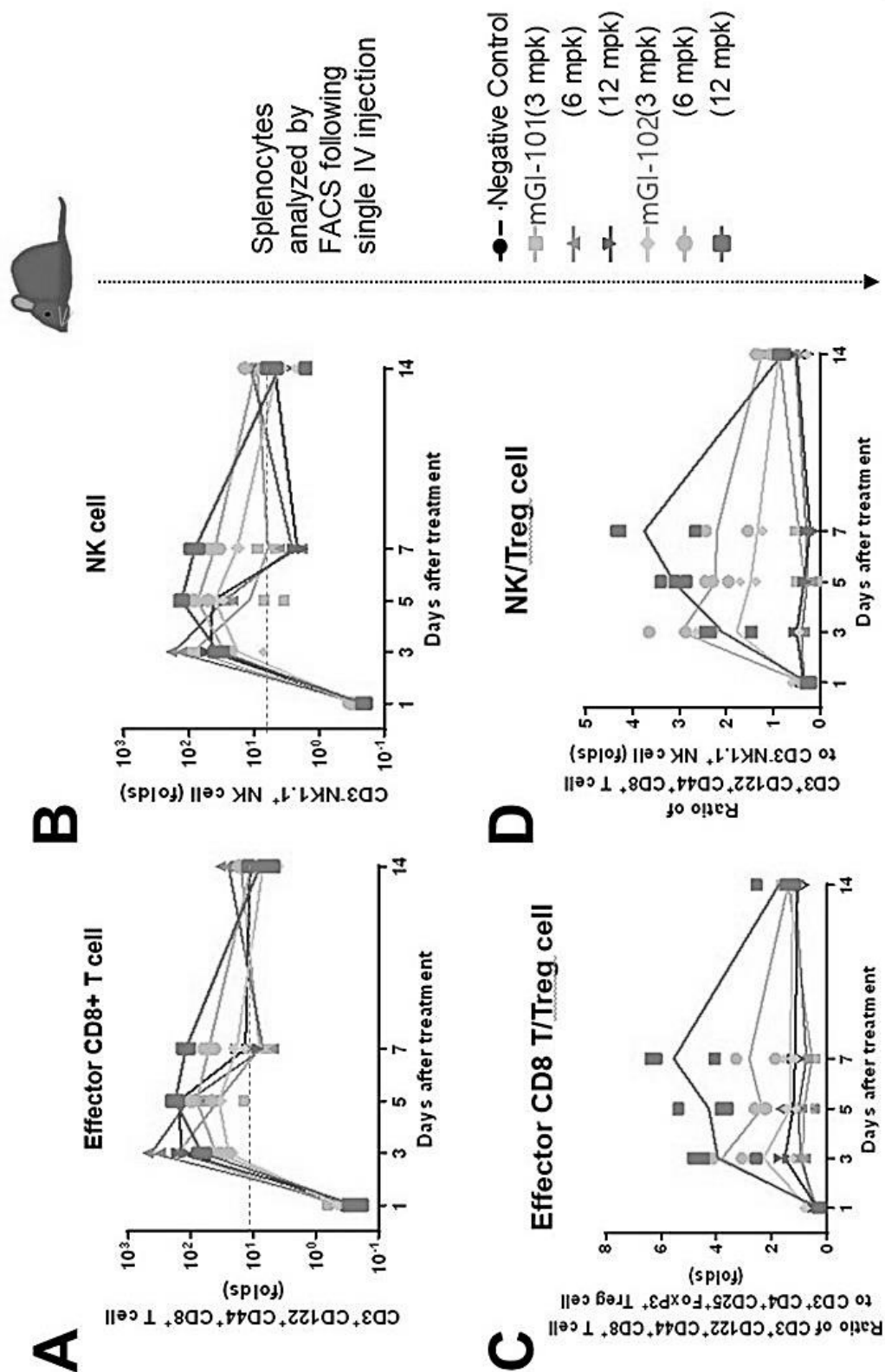
[Fig. 40]



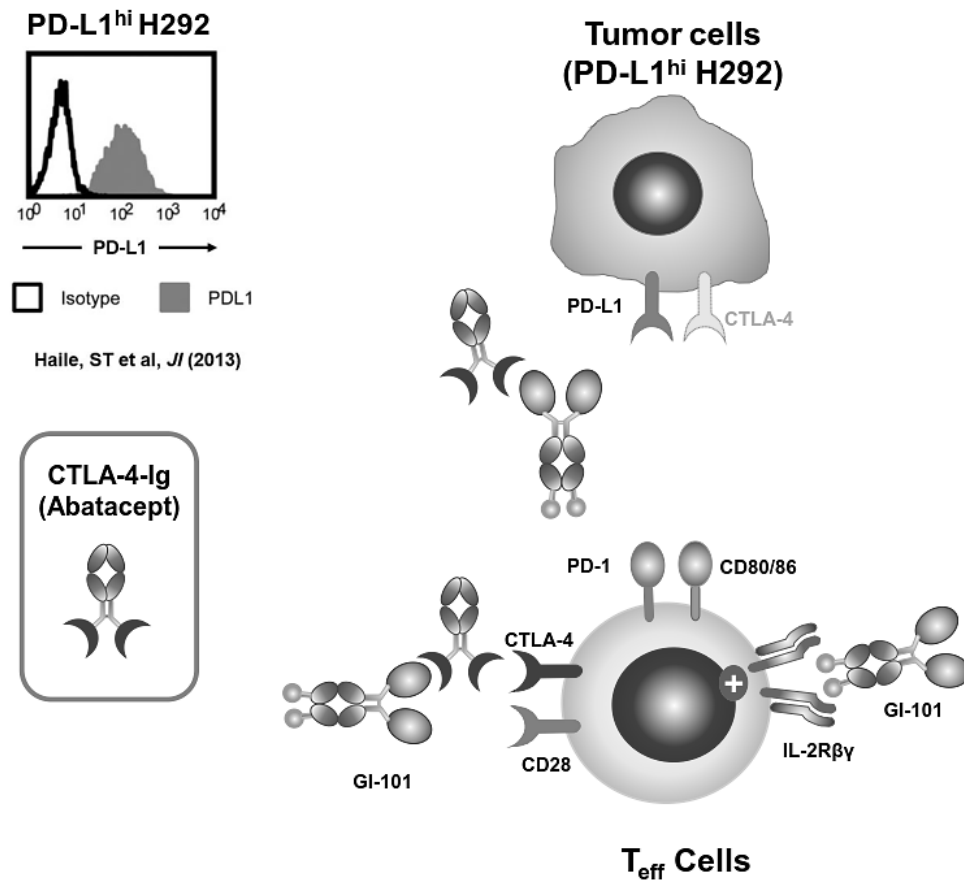
[Fig. 41]



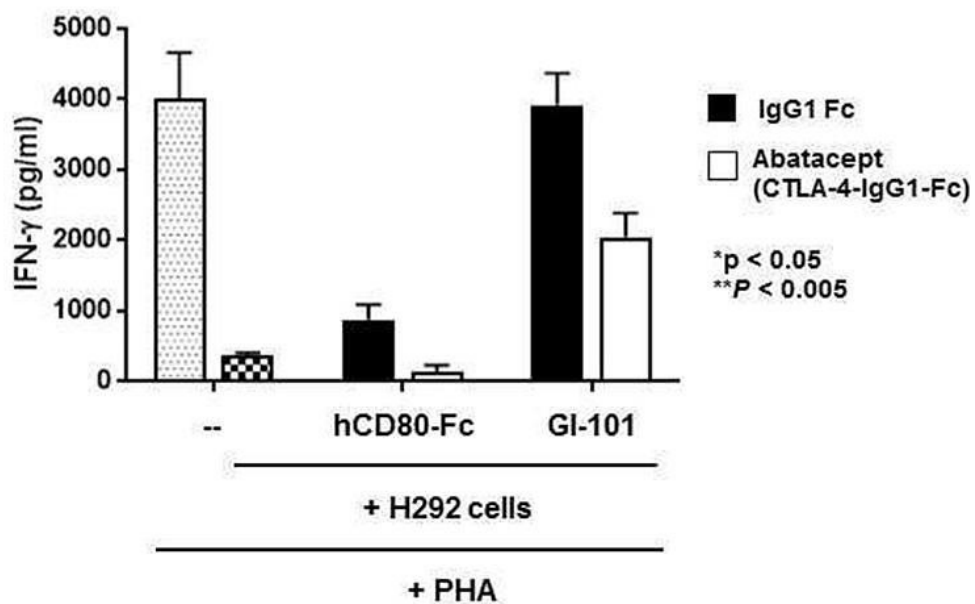
[Fig. 42]



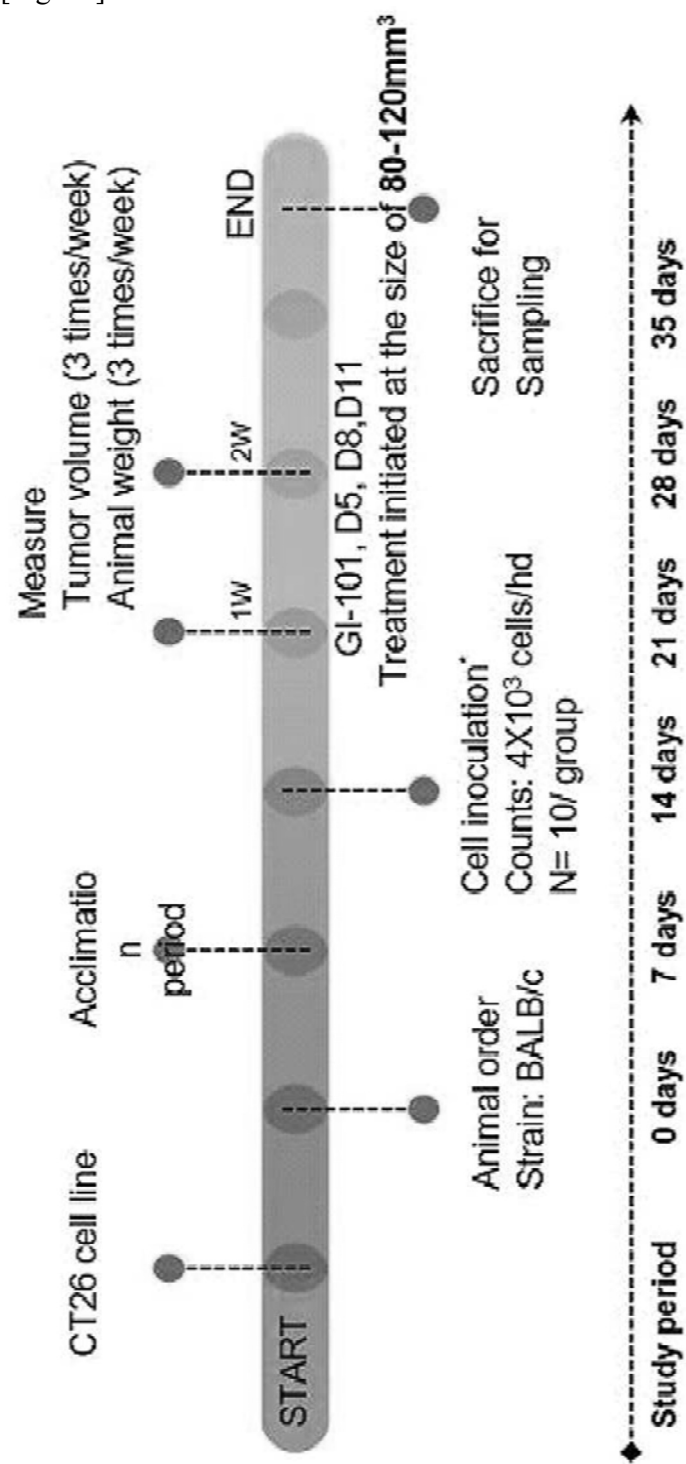
[Fig. 43]



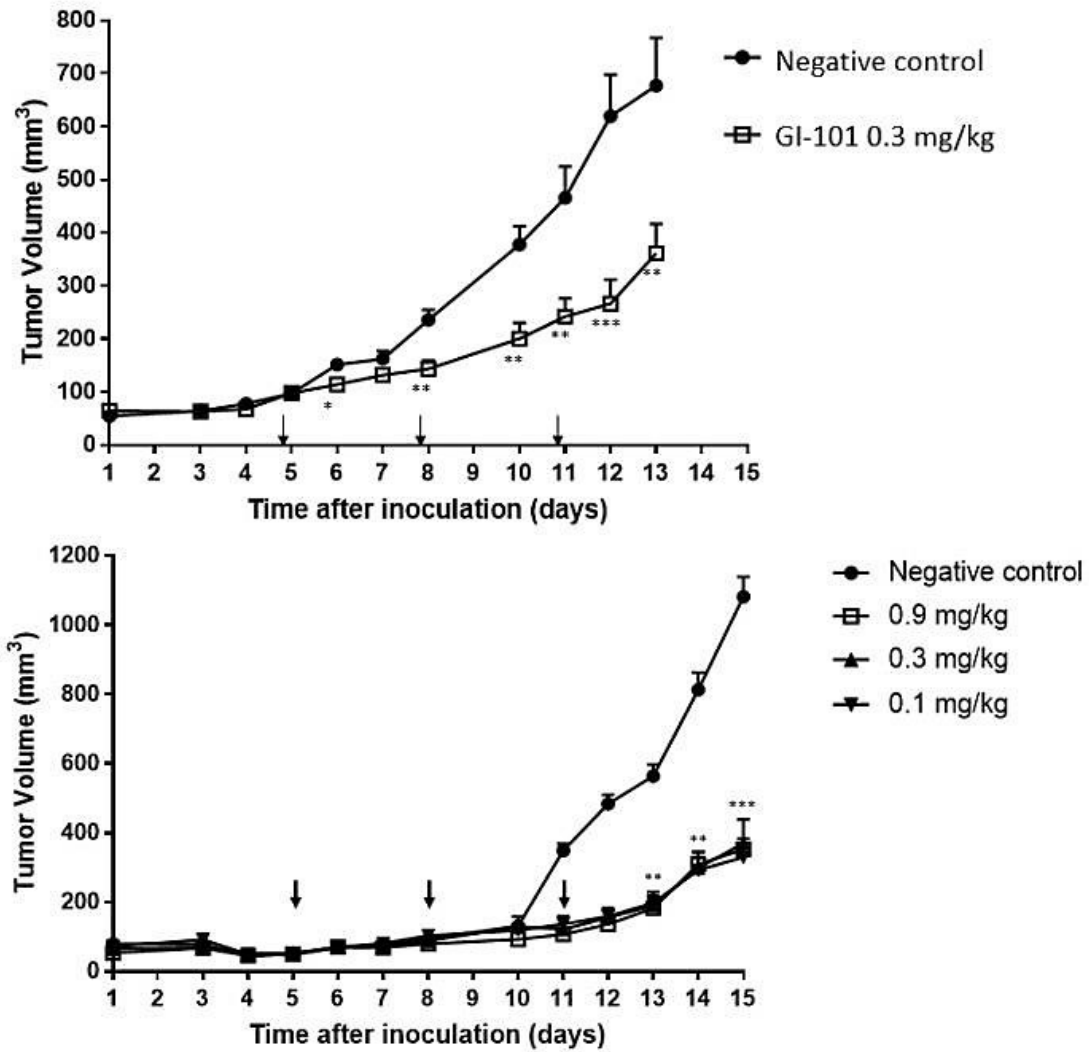
[Fig. 44]



[Fig. 45]



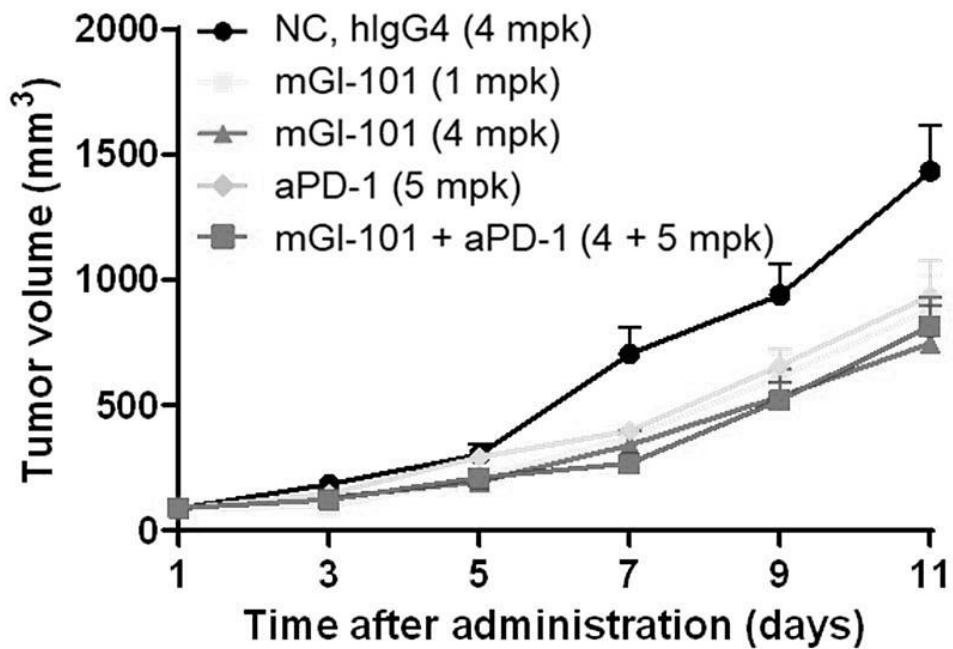
[Fig. 46]



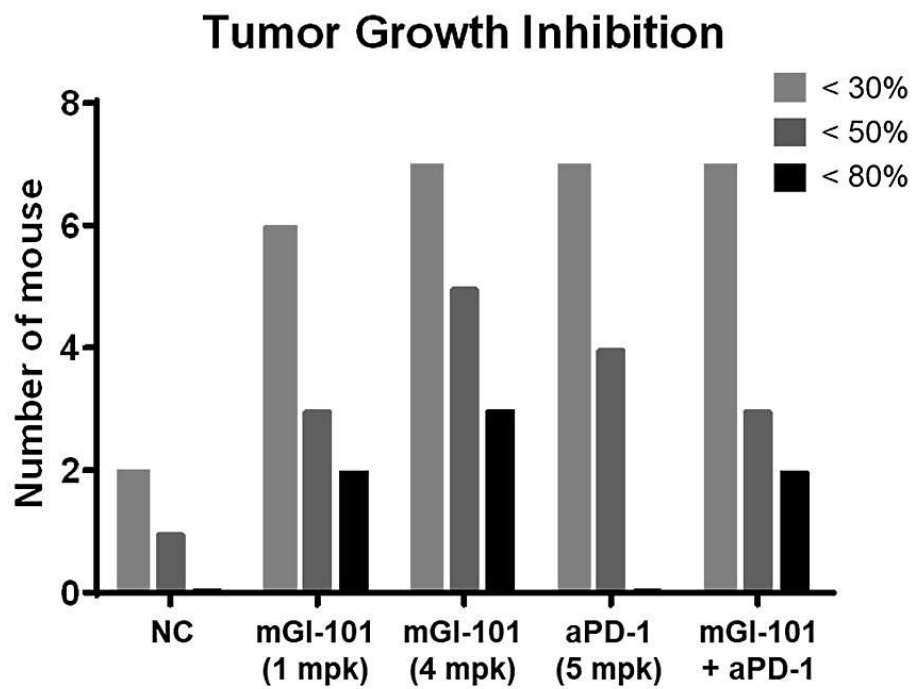
* $p < 0.05$, ** $p < 0.005$, *** $p < 0.001$

Each point represents mean + SE (n=10)

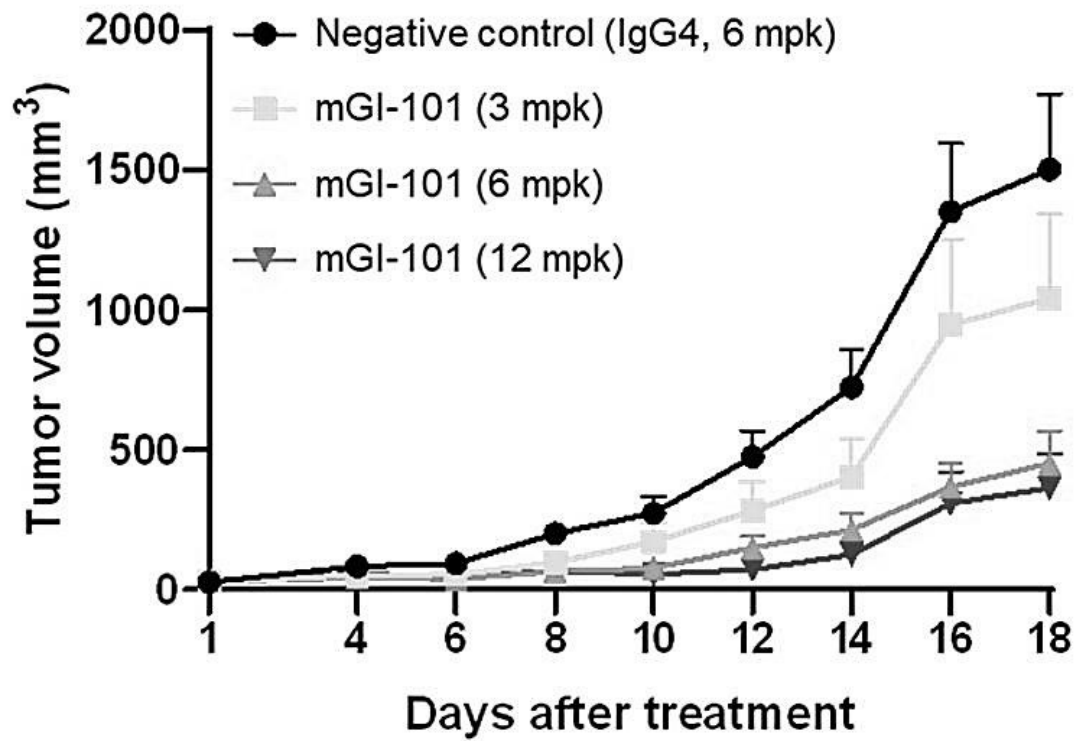
[Fig. 47]



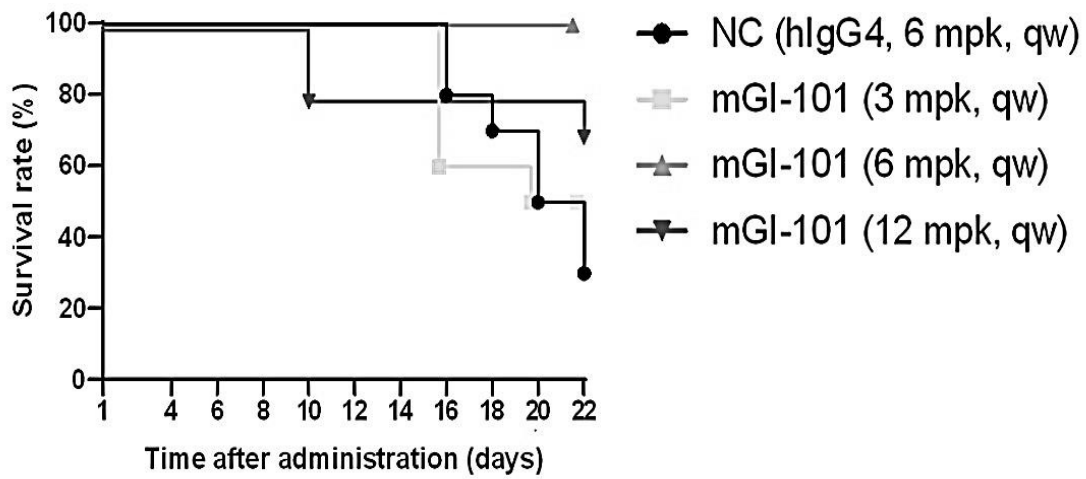
[Fig. 48]



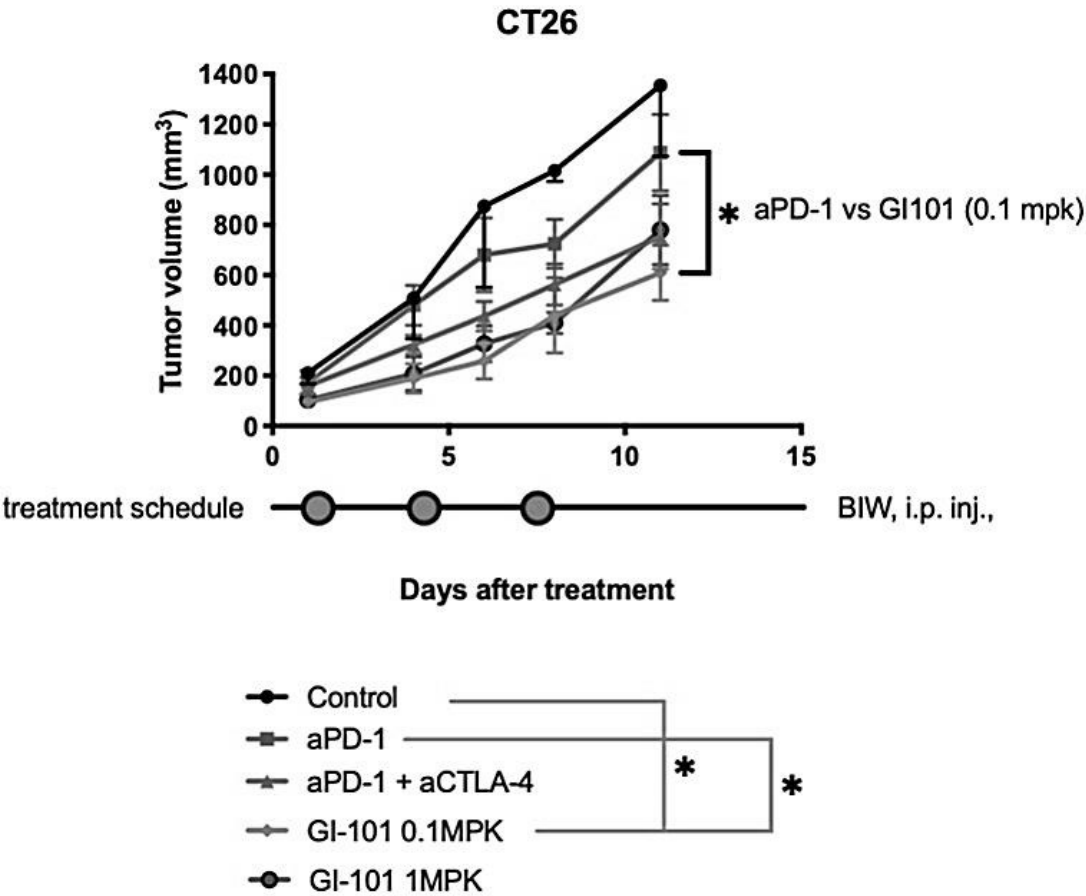
[Fig. 49]



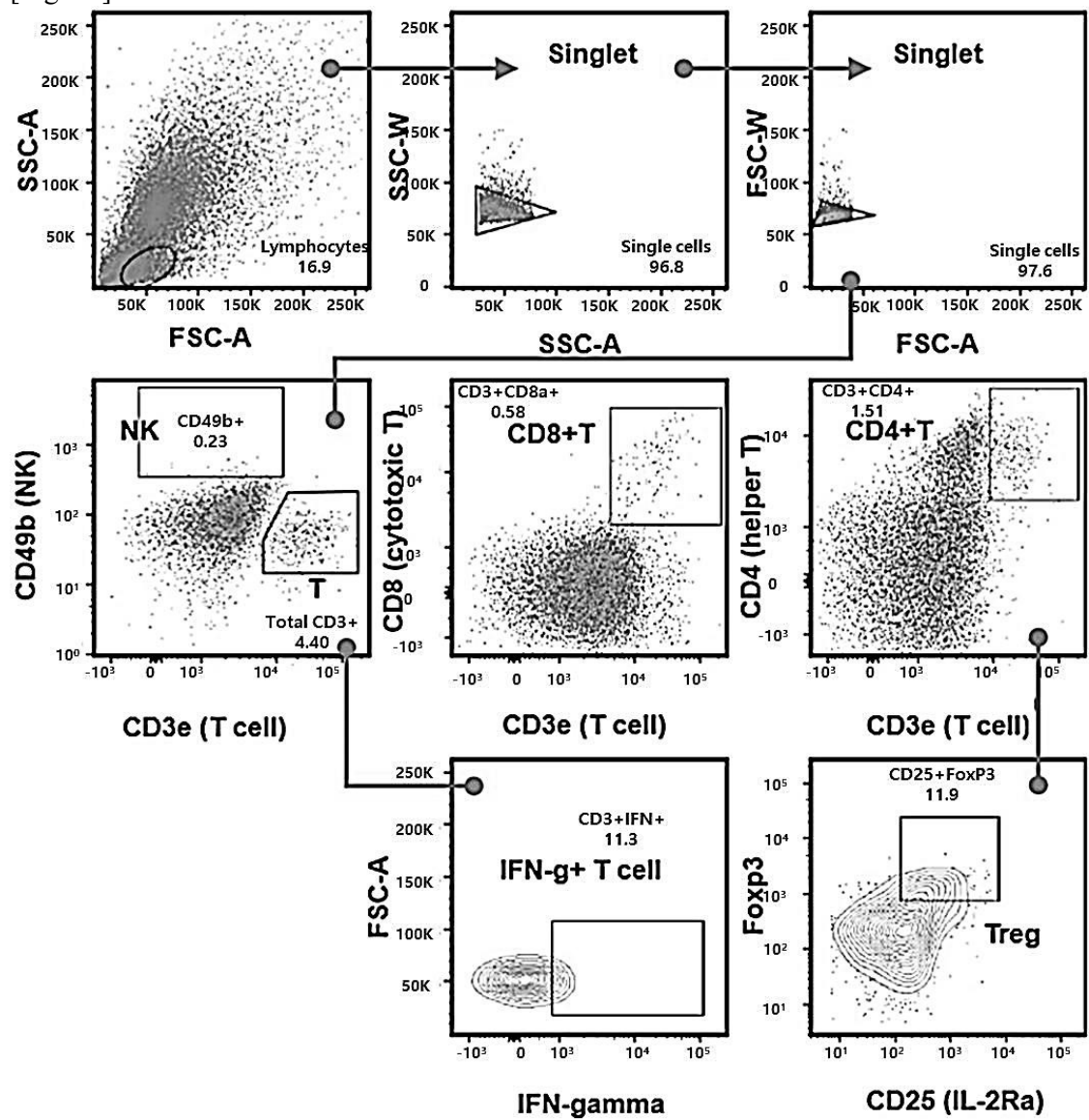
[Fig. 50]



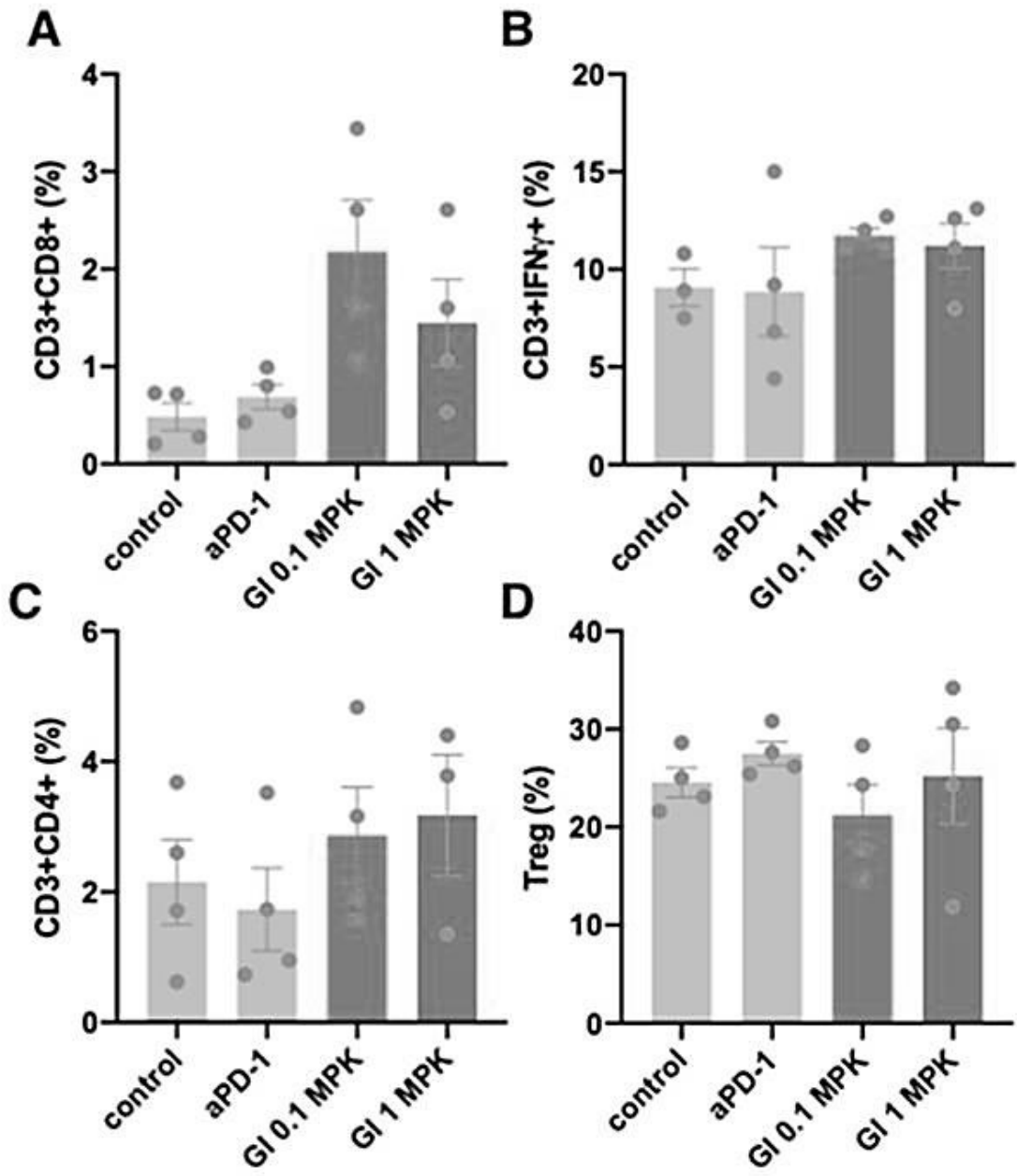
[Fig. 51]



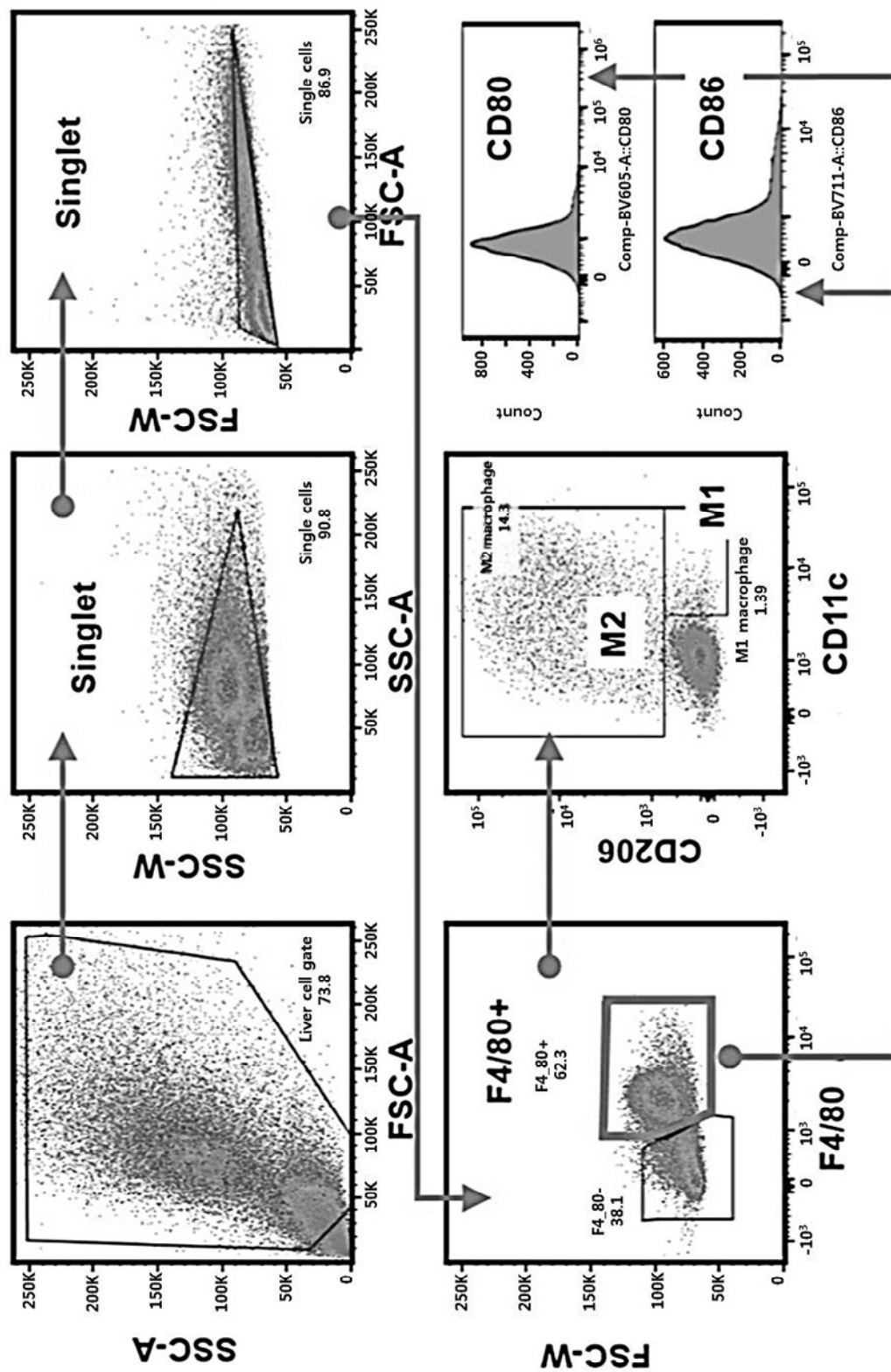
[Fig. 52]



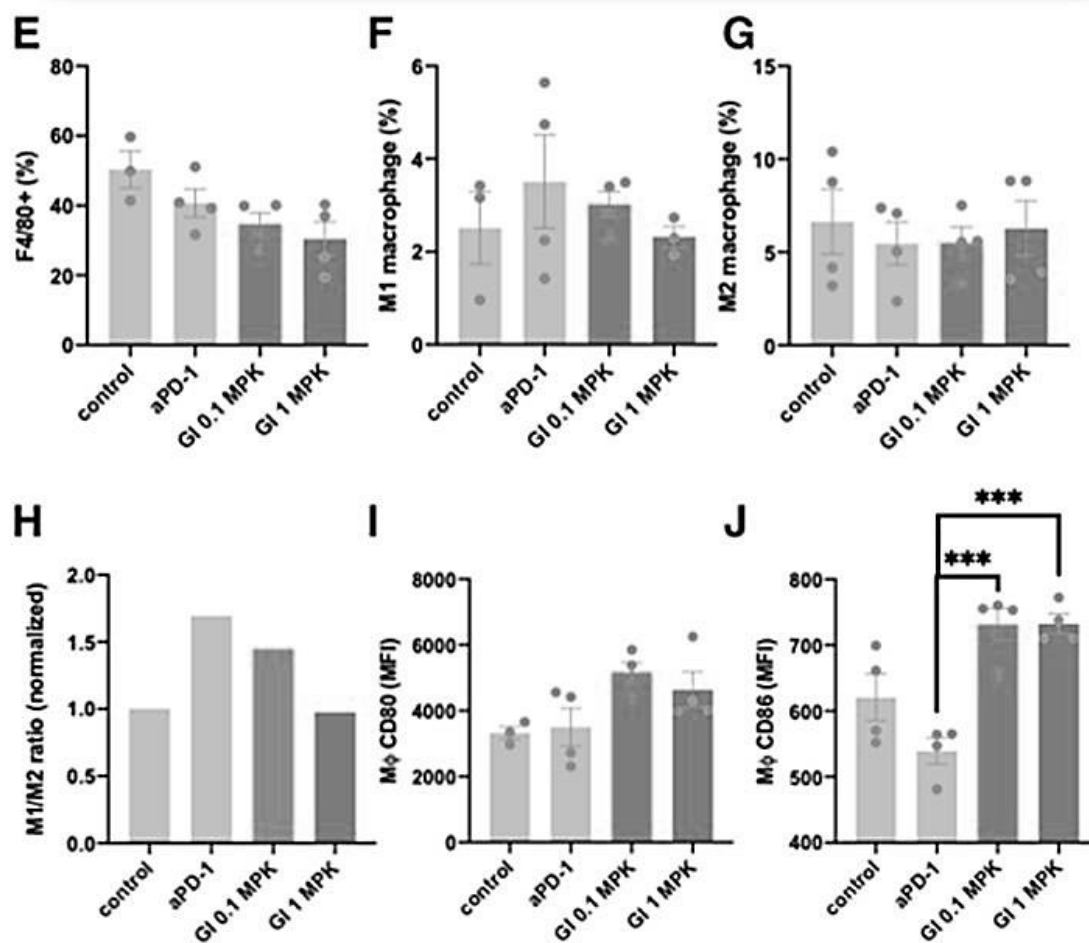
[Fig. 53]



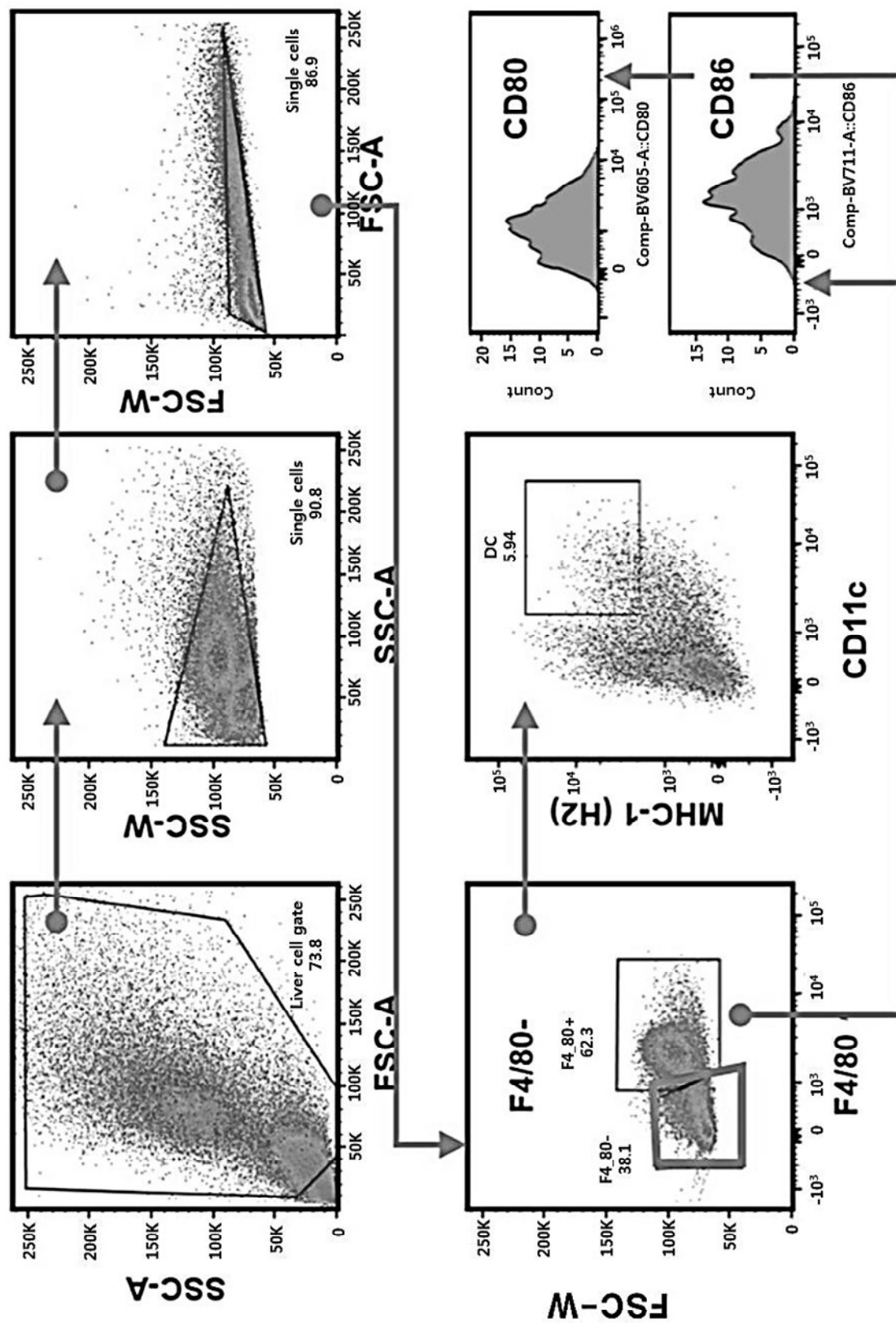
[Fig. 54]



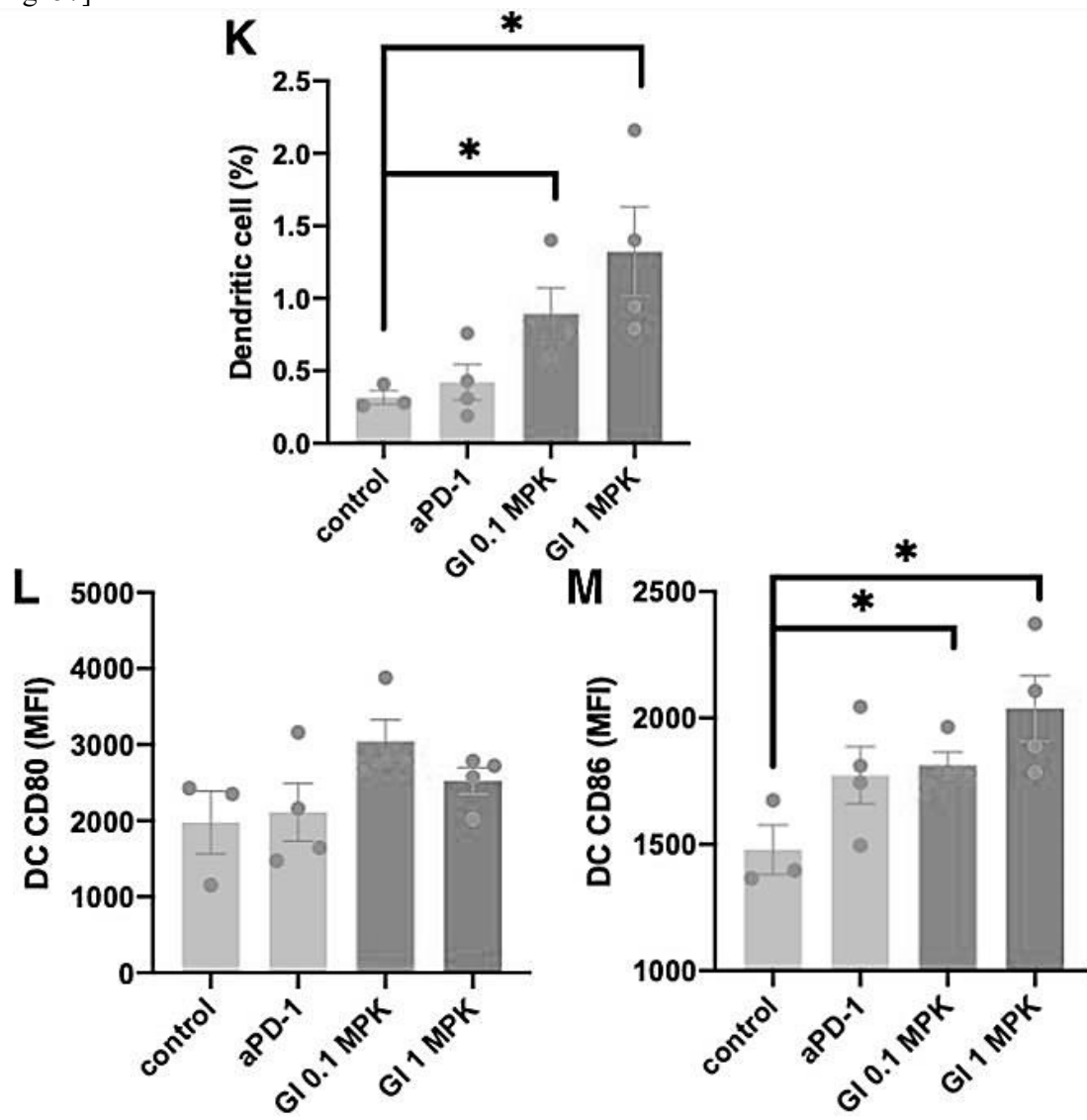
[Fig. 55]



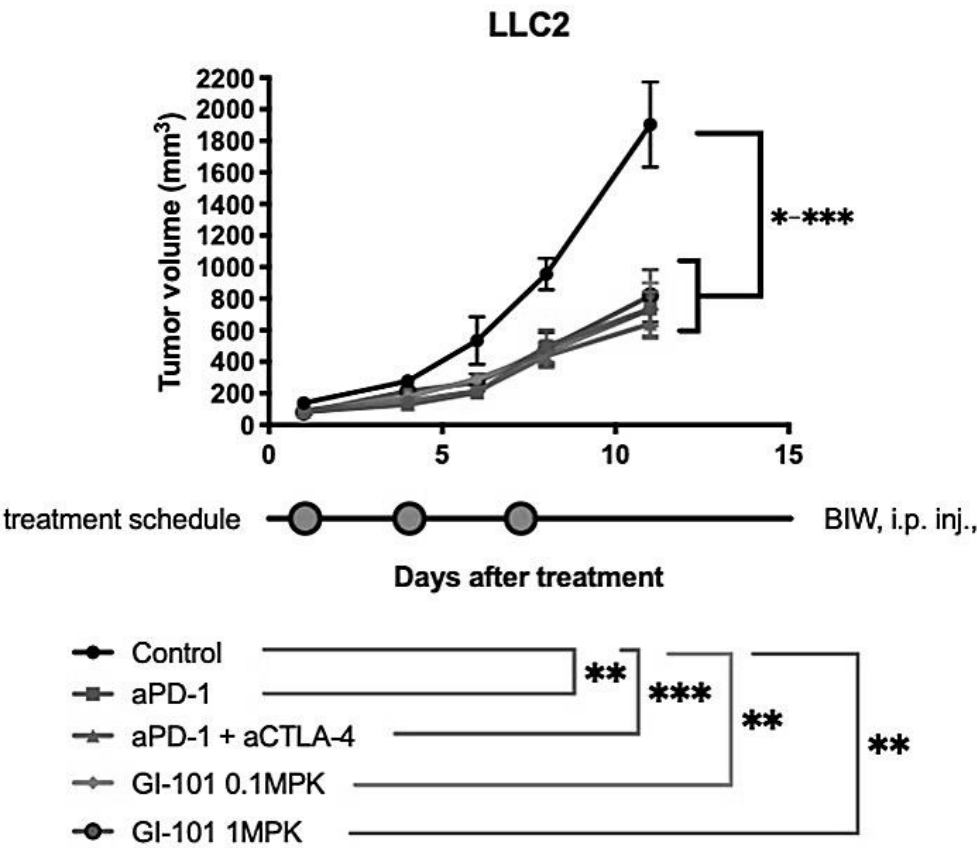
[Fig. 56]



[Fig. 57]

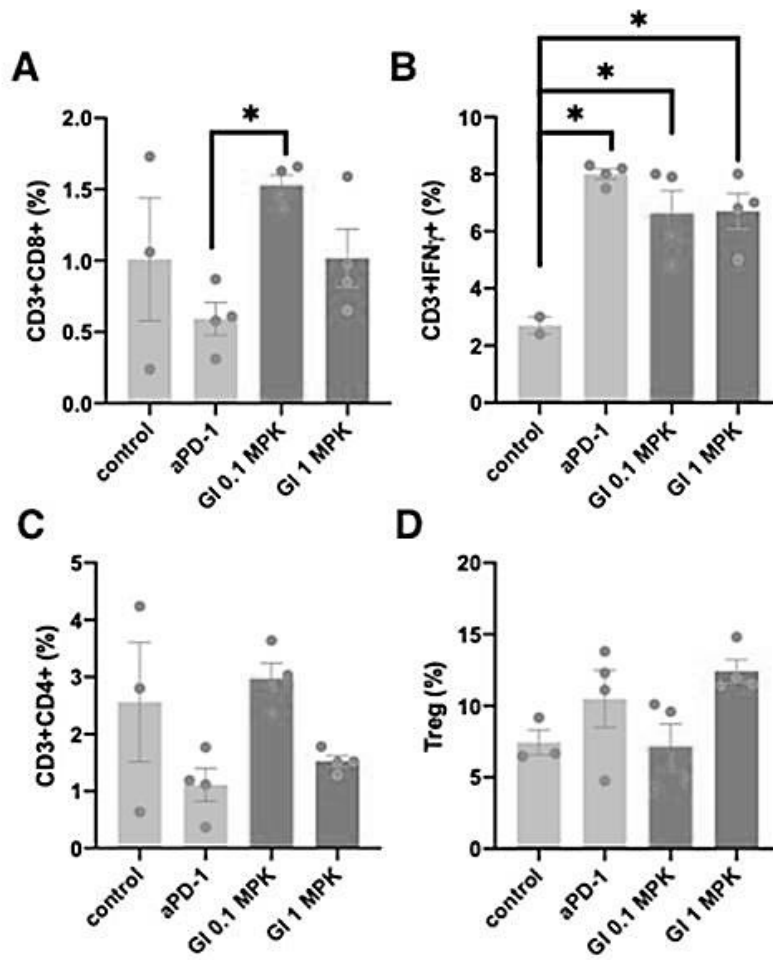


[Fig. 58]

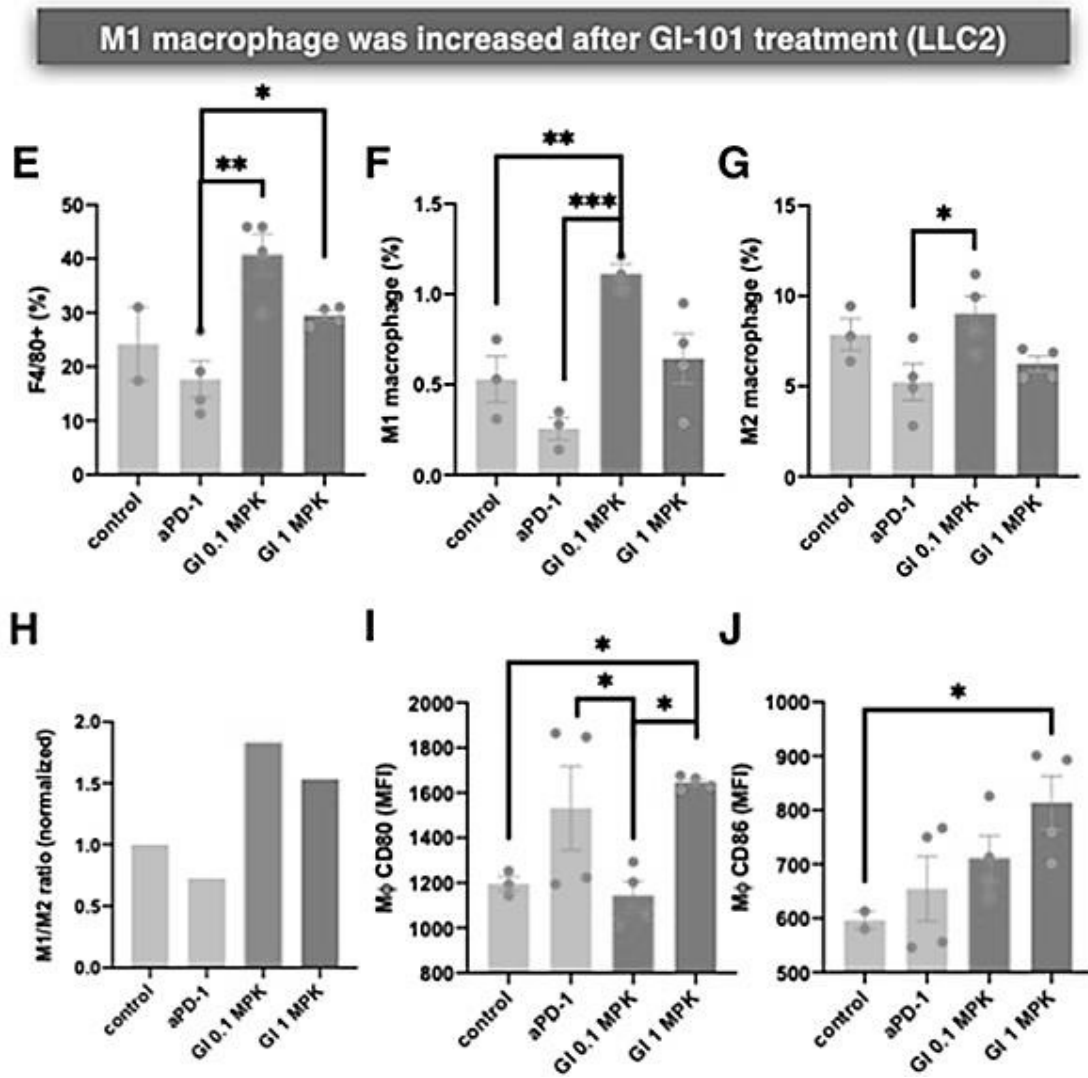


[Fig. 59]

IFN-gamma expressing T cell was increased after GI-101 treatment
But, not increased regulatory T cell population in tumor

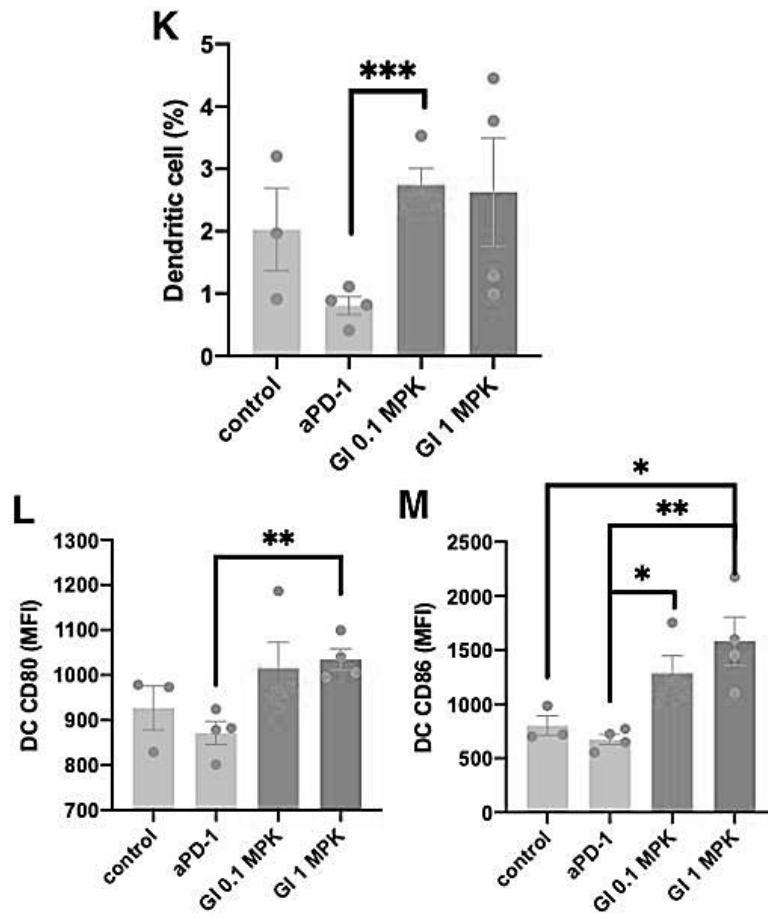


[Fig. 60]

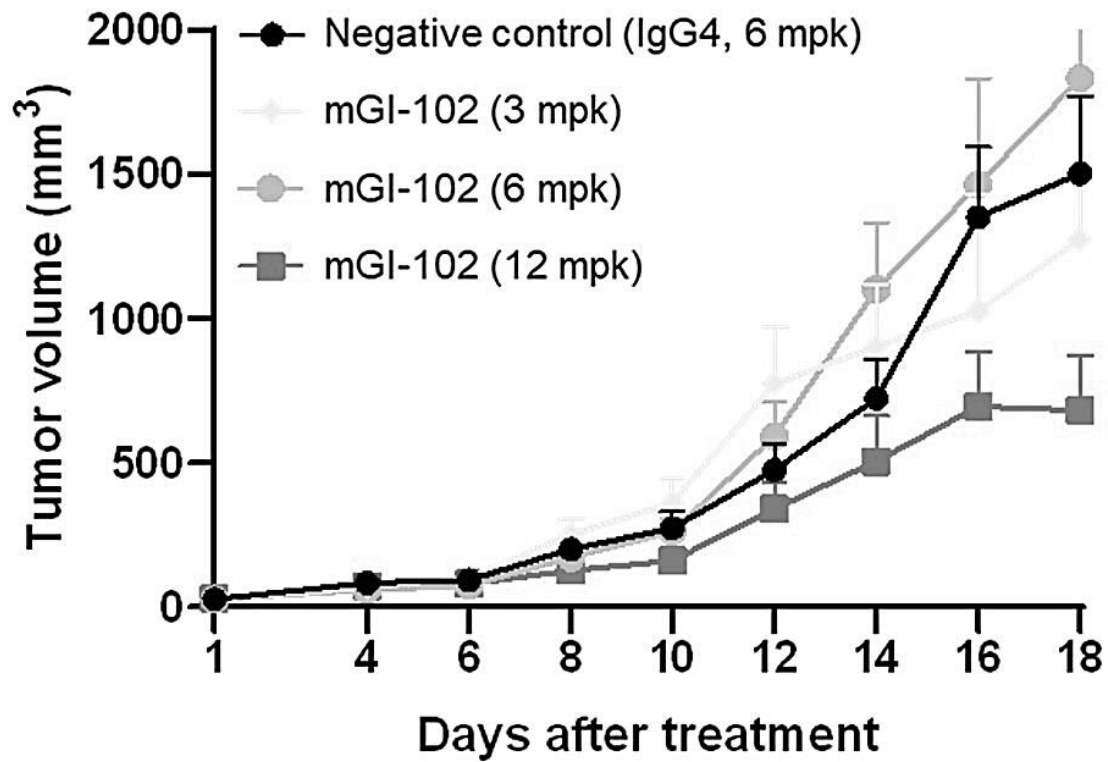


[Fig. 61]

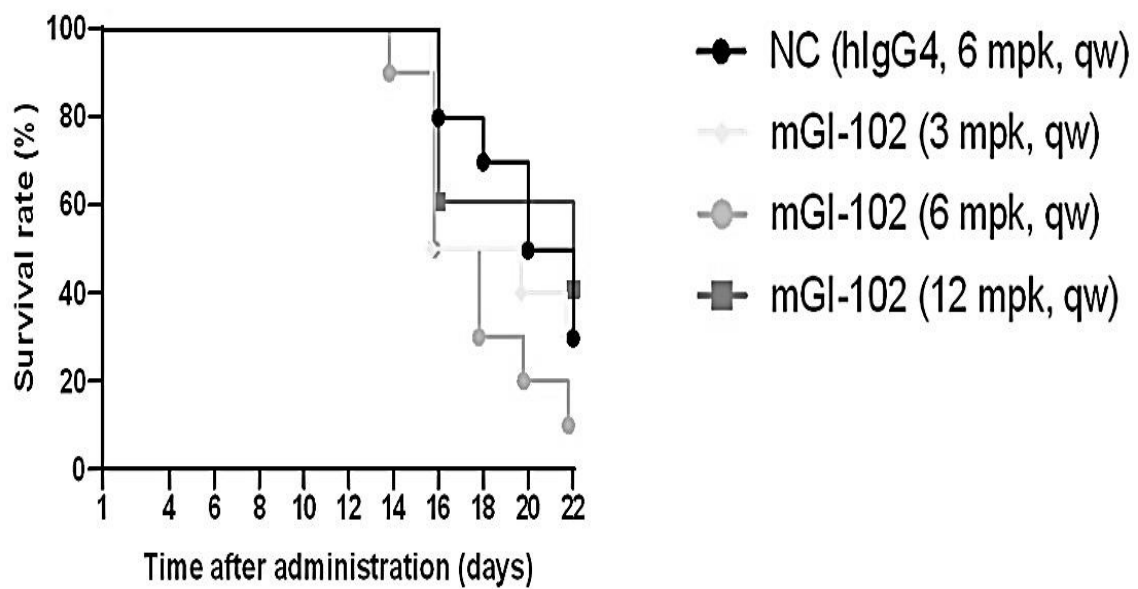
Dendritic cell population and antigen presentation effects were increased after GI-101 treatment (LLC2)



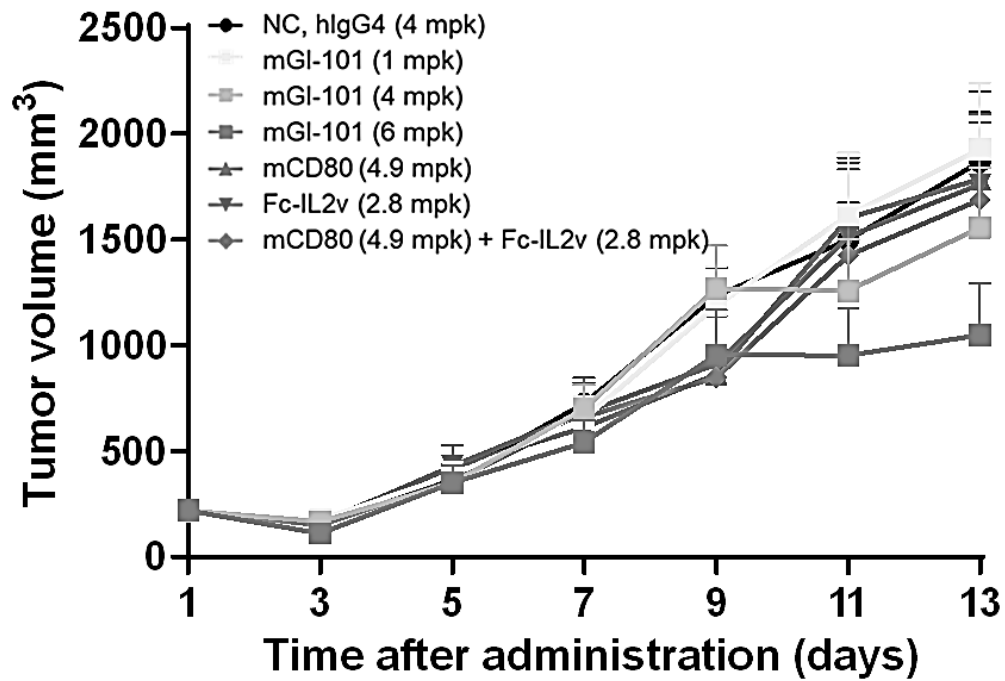
[Fig. 62]



[Fig. 63]

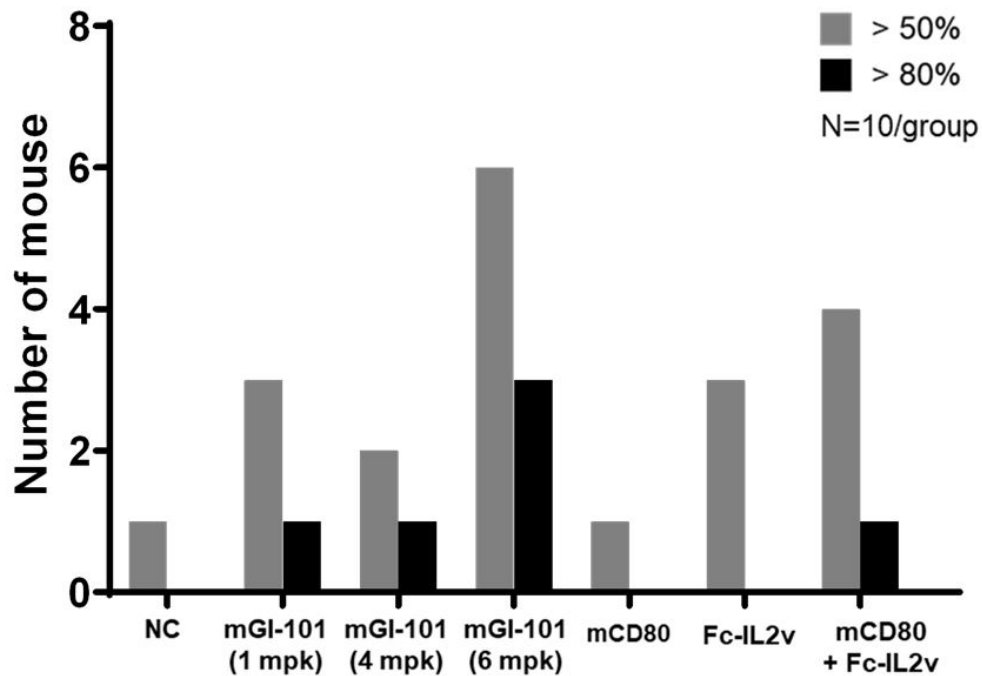


[Fig. 64]



[Fig. 65]

Tumor Growth Inhibition



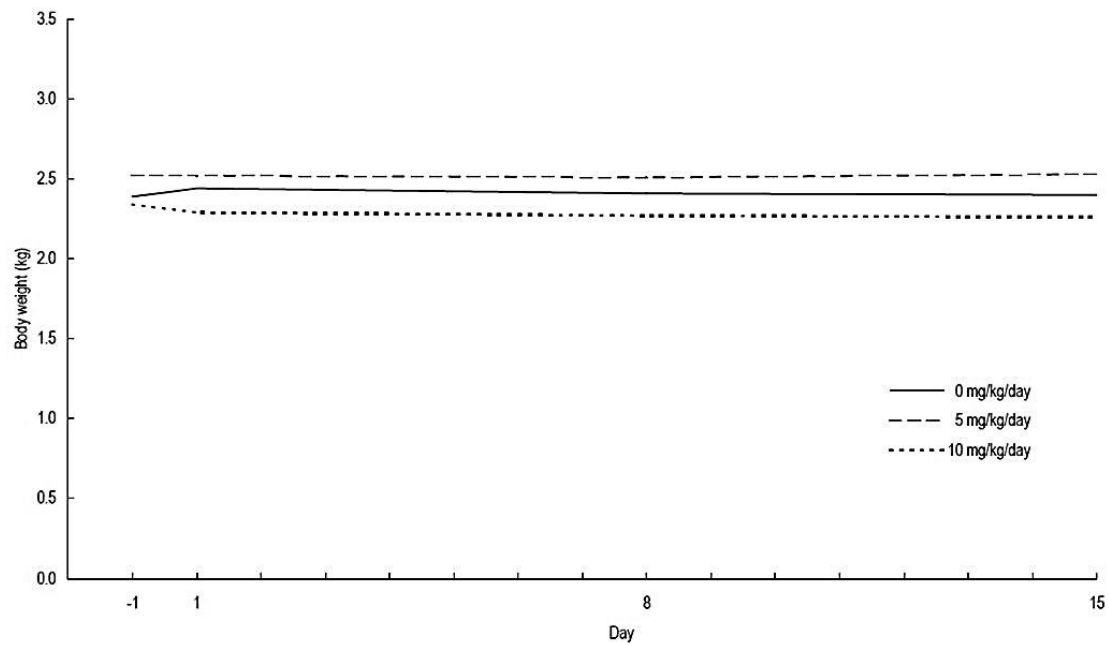
A 2-Week Intravenous Dose Toxicity Study of GI-101 in Cynomolgus Monkeys

Table 1 Clinical observations

Sex: Male		Day																Day of necropsy
Group	Animal No.	-1	1	2	3	4	5	6	7	8		9	10	11	12	13	14	
		am	Pre	0.5 h	am	am	am	am	am	am	Pre	0.5 h	am	am	am	am	am	
0 mg/kg/day	CJ1M01	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	CJ1M02	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	CJ1M03	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
5 mg/kg/day	CJ2M01	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	CJ2M02	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	CJ2M03	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
10 mg/kg/day	CJ3M01	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	CJ3M02	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	CJ3M03	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

General Footnote: Pre: Pre-dosing 0.5 h: 0.5 hours post-dosing
NA: No clinical or fecal abnormalities

[Fig. 67]



[Fig. 68]

Body weight (kg)

Sex: Male		0 mg/kg/day	5 mg/kg/day	10 mg/kg/day
Day(s) Relative to Start Date				
-1	Mean	2.39	2.52	2.34
	S.D.	0.10	0.31	0.16
	N	3	3	3
1	Mean	2.44	2.52	2.29
	S.D.	0.07	0.31	0.16
	N	3	3	3
8	Mean	2.41	2.51	2.27
	S.D.	0.12	0.34	0.08
	N	3	3	3
15	Mean	2.40	2.53	2.26
	S.D.	0.12	0.34	0.11
	N	3	3	3

Statistical Test: Generalised Anova/Ancova Test Transformation: Identity (No Transformation)

[Fig. 70]

Sex: Male			0 mg/kg/day	5 mg/kg/day	10 mg/kg/day
Day(s) Relative to Start Date					
%Retic. (%)	-2	Mean	0.75	1.40	0.93
		S.D.	0.07	0.52	0.30
		N	3	3	3
	15	Mean	1.67	3.10 d ¹	3.14 d ¹
		S.D.	0.61	0.55	0.32
		N	3	3	3
#Retic (10 ⁹ /L)	-2	Mean	44.0	81.9	55.1
		S.D.	7.0	28.4	19.7
		N	3	3	3
	15	Mean	91.5	171.6 d ¹	161.5 d ¹
		S.D.	33.6	32.3	17.2
		N	3	3	3
PLT (10 ³ /μL)	-2	Mean	404	380	380
		S.D.	25	90	28
		N	3	3	3
	15	Mean	501	522	601
		S.D.	29	135	85
		N	3	3	3

[Fig. 71]

Sex: Male			0 mg/kg/day	5 mg/kg/day	10 mg/kg/day
Day(s) Relative to Start Date					
WBC (10 ³ /μL)	-2	Mean	10.59	8.18	8.29
		S.D.	1.63	1.43	2.11
		N	3	3	3
	15	Mean	8.09	12.08	16.52
		S.D.	0.25	0.74	6.81
		N	3	3	3
%Neut (%)	-2	Mean	38.1	23.1	23.6
		S.D.	23.2	3.2	13.1
		N	3	3	3
	15	Mean	35.9	14.5	22.4
		S.D.	14.3	2.1	14.2
		N	3	3	3
%Lymph (%)	-2	Mean	57.7	71.6	69.8
		S.D.	21.7	2.8	13.7
		N	3	3	3
	15	Mean	59.6	81.2	69.5
		S.D.	13.1	1.4	15.0
		N	3	3	3

[Fig. 72]

Sex: Male			0 mg/kg/day	5 mg/kg/day	10 mg/kg/day
Day(s) Relative to Start Date					
#Neut (10 ³ /μL)	-2	Mean	4.24	1.86	1.77
		S.D.	3.09	0.22	0.52
		N	3	3	3
	15	Mean	2.93	1.76	3.11
		S.D.	1.26	0.35	0.63
		N	3	3	3
#Lymph (10 ³ /μL)	-2	Mean	5.92	5.87	5.98
		S.D.	1.78	1.24	2.54
		N	3	3	3
	15	Mean	4.80	9.80	12.05
		S.D.	0.94	0.48	6.47
		N	3	3	3
#Mono (10 ³ /μL)	-2	Mean	0.36	0.37	0.45
		S.D.	0.10	0.09	0.08
		N	3	3	3
	15	Mean	0.32	0.33	0.77 d ¹
		S.D.	0.11	0.06	0.26
		N	3	3	3

[Fig. 73]

Sex: Male			0 mg/kg/day	5 mg/kg/day	10 mg/kg/day
Day(s) Relative to Start Date					
AST (U/L)	-2	Mean	36	45	30
		S.D.	19	21	7
		N	3	3	3
	15	Mean	24	34	33
		S.D.	5	5	8
		N	3	3	3
ALT (U/L)	-2	Mean	58	72	34
		S.D.	51	71	8
		N	3	3	3
	15	Mean	34	52	36
		S.D.	6	44	5
		N	3	3	3
ALP (U/L)	-2	Mean	1511	1658	1972
		S.D.	542	258	357
		N	3	3	3
	15	Mean	1395	1444	1565
		S.D.	365	346	235
		N	3	3	3

[Fig. 74]

Sex: Male			0 mg/kg/day	5 mg/kg/day	10 mg/kg/day
Day(s) Relative to Start Date					
LD (U/L)	-2	Mean	255	289	292
		S.D.	6	57	47
		N	3	3	3
	15	Mean	236	304	361 ^{dd'}
		S.D.	15	47	38
		N	3	3	3
CK (U/L)	-2	Mean	132	140	182
		S.D.	23	4	61
		N	3	3	3
	15	Mean	120	128	140
		S.D.	31	19	23
		N	3	3	3
GLU (mg/dL)	-2	Mean	98	91	112
		S.D.	17	4	15
		N	3	3	3
	15	Mean	87	88	104
		S.D.	9	17	5
		N	3	3	3

[Fig. 75]

Sex: Male			0 mg/kg/day	5 mg/kg/day	10 mg/kg/day
Day(s) Relative to Start Date					
BIL (mg/dL)	-2	Mean	0.10	0.15 ^{d'}	0.10
		S.D.	0.02	0.03	0.01
		N	3	3	3
	15	Mean	0.11	0.15	0.10
		S.D.	0.04	0.03	0.03
		N	3	3	3
UN (mg/dL)	-2	Mean	19.1	15.4	18.8
		S.D.	7.2	2.3	4.5
		N	3	3	3
	15	Mean	16.2	13.9	14.2
		S.D.	5.6	0.7	2.4
		N	3	3	3
CRE (mg/dL)	-2	Mean	0.73	0.69	0.73
		S.D.	0.07	0.17	0.10
		N	3	3	3
	15	Mean	0.72	0.66	0.65
		S.D.	0.06	0.13	0.11
		N	3	3	3

[Fig. 76]

Sex: Male			0 mg/kg/day	5 mg/kg/day	10 mg/kg/day
Day(s) Relative to Start Date					
CHO (mg/dL)	-2	Mean	109	162	147
		S.D.	23	59	47
		N	3	3	3
	15	Mean	108	159	143
		S.D.	24	46	34
		N	3	3	3
TG (mg/dL)	-2	Mean	44	27	40
		S.D.	24	12	2
		N	3	3	3
	15	Mean	35	29	34
		S.D.	2	14	14
		N	3	3	3
PL (mg/dL)	-2	Mean	180	236	220
		S.D.	48	43	65
		N	3	3	3
	15	Mean	164	216	195
		S.D.	31	52	40
		N	3	3	3

[Fig. 77]

Sex: Male			0 mg/kg/day	5 mg/kg/day	10 mg/kg/day
Day(s) Relative to Start Date					
IP (mg/dL)	-2	Mean	5.16	5.14	5.00
		S.D.	1.16	0.91	0.90
		N	3	3	3
	15	Mean	5.52	5.94	5.66
		S.D.	0.61	0.61	0.94
		N	3	3	3
CA (mg/dL)	-2	Mean	9.63	9.82	9.79
		S.D.	0.59	0.55	0.19
		N	3	3	3
	15	Mean	9.45	9.48	9.31
		S.D.	0.57	0.25	0.03
		N	3	3	3
NA (mEq/L)	-2	Mean	152.8	154.5	153.9
		S.D.	2.4	4.2	2.5
		N	3	3	3
	15	Mean	151.8	153.5	153.4
		S.D.	3.3	2.0	3.3
		N	3	3	3

[Fig. 78]

Sex: Male			0 mg/kg/day	5 mg/kg/day	10 mg/kg/day
Day(s) Relative to Start Date					
K (mEq/L)	-2	Mean	4.28	4.17	3.90
		S.D.	0.69	0.29	0.40
		N	3	3	3
	15	Mean	3.99	4.09	3.85
		S.D.	0.50	0.18	0.14
		N	3	3	3
CL (mEq/L)	-2	Mean	112.3	111.1	110.7
		S.D.	2.2	3.9	2.6
		N	3	3	3
	15	Mean	111.5	109.6	110.2
		S.D.	0.7	3.7	2.8
		N	3	3	3
TP (g/dL)	-2	Mean	7.20	7.36	7.53
		S.D.	0.59	0.42	0.22
		N	3	3	3
	15	Mean	6.99	7.22	7.30
		S.D.	0.62	0.37	0.11
		N	3	3	3

[Fig. 79]

Sex: Male			0 mg/kg/day	5 mg/kg/day	10 mg/kg/day
Day(s) Relative to Start Date					
ALB (g/dL)	-2	Mean	4.18	4.11	4.14
		S.D.	0.34	0.46	0.19
		N	3	3	3
	15	Mean	4.09	3.98	3.88
		S.D.	0.36	0.47	0.17
		N	3	3	3
A/G	-2	Mean	1.39	1.27	1.22
		S.D.	0.06	0.19	0.04
		N	3	3	3
	15	Mean	1.41	1.24	1.13
		S.D.	0.04	0.22	0.07
		N	3	3	3

[Fig. 80]

Sex: Male		Tumor necrosis factor- α					Interferon- γ					Interleukin-1 β					Interleukin-2					Interleukin-4				
Group	Animal	(pg/mL)					(pg/mL)					(pg/mL)					(pg/mL)					(pg/mL)				
No.		Pretest	Day 3	Day 8	Day 15		Pretest	Day 3	Day 8	Day 15		Pretest	Day 3	Day 8	Day 15		Pretest	Day 3	Day 8	Day 15		Pretest	Day 3	Day 8	Day 15	
0 mg/kg/day	CJ1M01	BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ	
	CJ1M02	BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ	
	CJ1M03	BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ	
	Mean	N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.	
	S.D.	N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.	
5 mg/kg/day	N	0	0	0	0		0	0	0	0		0	0	0	0		0	0	0	0		0	0	0	0	
	CJ2M01	BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ	
	CJ2M02	BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ	
	CJ2M03	BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ	
	Mean	N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.	
10 mg/kg/day	S.D.	N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.	
	N	0	0	0	0		0	0	0	0		0	0	0	0		0	0	0	0		0	0	0	0	
	CJ3M01	BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	5.51	4.60		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ	
	CJ3M02	BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	12.74	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ	
	CJ3M03	BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ	
	Mean	N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	9.13	N.C.		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.	
	S.D.	N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.	
	N	0	0	0	0		0	0	0	0		0	0	0	0		0	0	0	0		0	0	0	0	

General Footnote: Day 8: Prior to dosing

BLQ: Below the lower limit of quantification (4.9 pg/mL for Interleukin-4, 2.4 pg/mL for the others)

When plasma concentrations were BLQ in 1 of the 3 animals, the mean of the 2 remaining animals was calculated.

The mean was regarded as N.C. when plasma concentrations in 2 of the 3 animals were BLQ.

N.C.: Not calculated

[Fig. 81]

Sex: Male		Interleukin-6 (pg/mL)					Interleukin-8 (pg/mL)					Interleukin-10 (pg/mL)					Interleukin-12 (pg/mL)				
Group	Animal No.	Pretest	Day 3	Day 8	Day 15		Pretest	Day 3	Day 8	Day 15		Pretest	Day 3	Day 8	Day 15		Pretest	Day 3	Day 8	Day 15	
0 mg/kg/day	CJ1M01	BLQ	2.95	BLQ	3.34		4047.41	4861.65	7894.37	6783.89		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ	
	CJ1M02	BLQ	BLQ	BLQ	BLQ		3418.18	1382.07	6035.41	4096.95		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ	
	CJ1M03	BLQ	2.78	BLQ	BLQ		809.60	905.96	972.78	981.31		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ	
	Mean	N.C.	2.87	N.C.	N.C.		2758.40	2383.23	4967.52	3954.05		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.	
5 mg/kg/day	S.D.	N.C.	N.C.	N.C.	N.C.		1716.78	2159.54	3582.23	2903.93		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.	
	N	0	2	0	1		3	3	3	3		0	0	0	0		0	0	0	0	
	CJ2M01	BLQ	BLQ	BLQ	BLQ		4800.40	3355.74	5986.48	5511.93		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ	
	CJ2M02	BLQ	BLQ	BLQ	BLQ		2633.61	2388.95	4778.15	5266.00		BLQ	BLQ	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ	
10 mg/kg/day	CJ2M03	BLQ	2.91	BLQ	BLQ		7482.97	6571.61	9663.74	8892.13		BLQ	BLQ	BLQ	BLQ		7.07	6.31	BLQ	BLQ	
	Mean	N.C.	N.C.	N.C.	N.C.		4972.33	4105.43	6809.46	6556.69		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.	
	S.D.	N.C.	N.C.	N.C.	N.C.		2429.25	2189.79	2544.64	2026.29		N.C.	N.C.	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.	
	N	0	1	0	0		3	3	3	3		0	0	0	0		1	1	0	0	
d ¹	CJ3M01	BLQ	5.26	BLQ	BLQ		8312.98	2753.66	7101.75	8973.45		BLQ	19.41	BLQ	BLQ		3.41	BLQ	BLQ	2.96	
	CJ3M02	BLQ	BLQ	BLQ	BLQ		7136.73	2722.78	9985.51	9298.79		BLQ	108.34	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ	
	CJ3M03	BLQ	2.41	BLQ	BLQ		5832.12	4900.91	8873.95	9812.62		BLQ	39.40	BLQ	BLQ		BLQ	BLQ	BLQ	BLQ	
	Mean	N.C.	3.84	N.C.	N.C.		7093.94	3459.12	8653.74	9361.62		N.C.	55.72	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.	
General Footnote: Day 8: Prior to dosing	S.D.	N.C.	N.C.	N.C.	N.C.		1240.98	1248.73	1454.44	423.10		N.C.	46.66	N.C.	N.C.		N.C.	N.C.	N.C.	N.C.	
	N	0	2	0	0		3	3	3	3		0	3	0	0		1	0	0	1	

BLQ: Below the lower limit of quantification (12.2 pg/mL for Interleukin-10, 2.4 pg/mL for the others)

When plasma concentrations were BLQ in 1 of the 3 animals, the mean of the 2 remaining animals was calculated.

The mean was regarded as N.C. when plasma concentrations in 2 of the 3 animals were BLQ.

N.C.: Not calculated

[Fig. 82]

Sex: Male		Ratio in lymphocytes (%)																							
Group	Animal No.	T cell				CD4 T cell				CD8 T cell				Regulatory T cell				NK cell							
		Pre	D3	D8	D15	Pre	D3	D8	D15	Pre	D3	D8	D15	Pre	D3	D8	D15	Pre	D3	D8	D15				
0 mg/kg/day	CJ1M01	49.2	57.1	57.0	53.3	28.0	34.9	34.6	32.9	15.1	15.3	16.0	13.5	1.3	1.5	1.5	1.6	38.4	33.5	34.4	37.1				
	CJ1M02	69.4	68.5	67.3	55.2	27.3	29.6	25.4	19.0	35.7	31.7	35.6	30.4	0.8	0.9	0.8	0.7	18.3	10.9	20.3	30.5				
	CJ1M03	55.4	70.8	61.2	51.6	27.5	38.7	29.9	22.3	22.5	26.9	26.3	24.8	1.3	1.7	1.3	1.5	31.7	16.6	29.0	35.5				
	Mean	58.0	65.5	61.8	53.4	27.6	34.4	30.0	24.7	24.4	24.6	26.0	22.9	1.1	1.4	1.2	1.3	29.5	20.3	27.9	34.4				
5 mg/kg/day	S.D.	10.3	7.3	5.2	1.8	0.4	4.6	4.6	7.3	10.4	8.4	9.8	8.6	0.3	0.4	0.4	0.5	10.2	11.8	7.1	3.4				
	N	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3				
	CJ2M01	62.6	86.7	60.8	59.7	25.0	55.3	22.7	17.1	32.2	25.1	32.2	35.4	1.0	4.4	2.0	2.0	26.0	4.4	28.2	29.6				
	CJ2M02	52.7	75.9	55.3	51.9	22.7	41.0	24.3	19.4	24.8	28.2	25.6	25.6	0.8	3.6	2.6	1.6	27.2	6.3	28.9	34.4				
10 mg/kg/day	CJ2M03	61.0	78.0	62.9	59.3	17.2	31.0	16.2	17.2	38.0	39.4	40.8	36.4	0.8	3.5	2.5	2.6	19.0	6.9	17.8	21.3				
	Mean	58.8	80.2	59.7	57.0	21.6	42.4	21.1	17.9	31.7	30.9	32.9	32.5	0.9	3.8	2.4	2.1	24.1	5.9	25.0	28.4				
	S.D.	5.3	5.7	3.9	4.4	4.0	12.2	4.3	1.3	6.6	7.5	7.6	6.0	0.1	0.5	0.3	0.5	4.4	1.3	6.2	6.6				
	N	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3				
	CJ3M01	69.3	80.8	73.6	69.8	15.2	32.7	18.3	18.0	43.8	34.8	45.4	44.1	0.8	4.1	3.0	2.5	17.1	6.5	14.1	15.1				
	CJ3M02	65.2	86.4	65.4	66.0	18.4	28.4	13.7	16.6	39.0	48.8	42.1	37.3	0.6	2.8	1.6	1.9	16.0	3.8	14.8	15.3				
	CJ3M03	70.2	89.7	76.8	74.0	19.2	46.7	23.8	28.2	44.9	33.8	44.9	37.5	1.0	7.6	4.6	5.9	17.5	3.0	10.6	16.5				
	Mean	68.2	85.6	71.9	69.9	17.6	35.9	18.6	20.9	42.6	39.1	44.1	39.6	0.8	4.8	3.1	3.4	16.9	4.4	13.2	15.6				
General Footnote: Pre: Pretest	S.D.	2.7	4.5	5.9	4.0	2.1	9.6	5.1	6.3	3.1	8.4	1.8	3.9	0.2	2.5	1.5	2.2	0.8	1.8	2.3	0.8				
	N	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3				
	1 [d - Test: Dunnett 2 Sided p < 0.05]																					2 [dd - Test: Dunnett 2 Sided p < 0.01]			
	D3, D8 and D15: Days 3, 8 (prior to dosing) and 15																								

2 [dd - Test Dunnett 2 Sided p < 0.01]

General Footnote: Pre: Pretest
1 [d - Test Dunnett 2 Sided p < 0.05]
D3, D8 and D15: Days 3, 8 (prior to dosing) and 15

[Fig. 83]

Sex: Male

Group	Animal No.	Lymphocytes (10 ³ /μL)		Absolute count (10 ³ /μL)									
				T cell		CD4 T cell		CD8 T cell		Regulatory T cell		NK cell	
		Pre	D15	Pre	D15	Pre	D15	Pre	D15	Pre	D15	Pre	D15
0 mg/kg/day	CJ1M01	7.40	5.60	3.64	2.98	2.07	1.84	1.12	0.76	0.10	0.09	2.84	2.08
	CJ1M02	6.42	5.03	4.46	2.78	1.75	0.96	2.29	1.53	0.05	0.04	1.17	1.53
	CJ1M03	3.94	3.77	2.18	1.95	1.08	0.84	0.89	0.93	0.05	0.06	1.25	1.34
	Mean	5.92	4.80	3.43	2.57	1.63	1.21	1.43	1.07	0.07	0.06	1.75	1.65
	S.D.	1.78	0.94	1.15	0.55	0.51	0.55	0.75	0.40	0.03	0.03	0.94	0.38
5 mg/kg/day	CJ2M01	5.01	9.42	3.14	5.62	1.25	1.61	1.61	3.33	0.05	0.19	1.30	2.79
	CJ2M02	7.29	10.34	3.84	5.37	1.65	2.01	1.81	2.65	0.06	0.17	1.98	3.56
	CJ2M03	5.32	9.63	3.25	5.71	0.92	1.66	2.02	3.51	0.04	0.25	1.01	2.05
	Mean	5.87	9.80	3.41	5.57	1.27	1.76	1.81	3.16	0.05	0.20	1.43	2.80
	S.D.	1.24	0.48	0.38	0.18	0.37	0.22	0.21	0.45	0.01	0.04	0.50	0.76
10 mg/kg/day	CJ3M01	8.38	13.41	5.81	9.36	1.27	2.41	3.67	5.91	0.07	0.34	1.43	2.02
	CJ3M02	6.25	17.73	4.08	11.70	1.15	2.94	2.44	6.61	0.04	0.34	1.00	2.71
	CJ3M03	3.32	5.01	2.33	3.71	0.64	1.41	1.49	1.88	0.03	0.30	0.58	0.83
	Mean	5.98	12.05	4.07	8.26	1.02	2.25	2.53	4.80	0.05	0.33	1.00	1.85
	S.D.	2.54	6.47	1.74	4.11	0.33	0.78	1.09	2.55	0.02	0.02	0.43	0.95

General Footnote: Pre: Pretest D15: Day 15

1 [d - Test: Dunnett 2 Sided p < 0.05]

2 [dd - Test: Dunnett 2 Sided p < 0.01]

[Fig. 84]

Sex: Male

Group	Animal No.	Ratio to baseline (pretest, %)															
		T cell				CD4 T cell				CD8 T cell				Regulatory T cell			
		Pre	D3	D8	D15	Pre	D3	D8	D15	Pre	D3	D8	D15	Pre	D3	D8	D15
0 mg/kg/day	CJ1M01	1.00	1.16	1.16	1.08	1.00	1.25	1.24	1.18	1.00	1.01	1.06	0.89	1.00	1.15	1.15	1.23
	CJ1M02	1.00	0.99	0.97	0.80	1.00	1.08	0.93	0.70	1.00	0.89	1.00	0.85	1.00	1.13	1.00	0.88
	CJ1M03	1.00	1.28	1.10	0.93	1.00	1.41	1.09	0.81	1.00	1.20	1.17	1.10	1.00	1.31	1.00	1.15
	Mean	1.00	1.14	1.08	0.94	1.00	1.25	1.09	0.90	1.00	1.03	1.08	0.95	1.00	1.20	1.05	1.09
	S.D.	0.00	0.15	0.10	0.14	0.00	0.17	0.16	0.25	0.00	0.16	0.09	0.13	0.00	0.10	0.09	0.18
5 mg/kg/day	CJ2M01	1.00	1.38	0.97	0.95	1.00	2.21	0.91	0.68	1.00	0.78	1.00	1.10	1.00	4.40	2.00	2.00
	CJ2M02	1.00	1.44	1.05	0.98	1.00	1.81	1.07	0.85	1.00	1.14	1.03	1.03	1.00	4.50	3.25	2.00
	CJ2M03	1.00	1.28	1.03	0.97	1.00	1.80	0.94	1.00	1.00	1.04	1.07	0.96	1.00	4.38	3.13	3.25
	Mean	1.00	1.37	1.02	0.97	1.00	1.94	0.97	0.84	1.00	0.99	1.03	1.03	1.00	4.43	2.79	2.42
	S.D.	0.00	0.08	0.04	0.02	0.00	0.23	0.09	0.16	0.00	0.19	0.04	0.07	0.00	0.06	0.69	0.72
10 mg/kg/day	CJ3M01	1.00	1.17	1.06	1.01	1.00	2.15	1.20	1.18	1.00	0.79	1.04	1.01	1.00	5.13	3.75	3.13
	CJ3M02	1.00	1.33	1.00	1.01	1.00	1.54	0.74	0.90	1.00	1.25	1.08	0.96	1.00	4.67	2.67	3.17
	CJ3M03	1.00	1.28	1.09	1.05	1.00	2.43	1.24	1.47	1.00	0.75	1.00	0.84	1.00	7.60	4.60	5.90
	Mean	1.00	1.26	1.05	1.02	1.00	2.04	1.06	1.18	1.00	0.93	1.04	0.94	1.00	5.80	3.67	4.07
	S.D.	0.00	0.08	0.05	0.02	0.00	0.46	0.28	0.29	0.00	0.28	0.04	0.09	0.00	1.58	0.97	1.59

General Footnote: Pre: Pretest D3, D8 and D15: Days 3, 8 (prior to dosing) and 15

1 [d - Test: Dunnett 2 Sided p < 0.05]

2 [dd - Test: Dunnett 2 Sided p < 0.01]

[Fig. 85]

Sex: Male		Ratio in each cell type (%)																							
Group	Animal No.	K67 + I cell				K67 + CD4 T cell				K67 + CD8 T cell				K67 + Treg				K67 + ICOS + Treg				ICOS + Treg			
		Pre	D3	D8	D15	Pre	D3	D8	D15	Pre	D3	D8	D15	Pre	D3	D8	D15	Pre	D3	D8	D15	Pre	D3	D8	D15
0 mg/kg/day	CJ1M01	9.6	7.6	9.1	10.3	9.3	5.8	7.7	7.9	6.3	5.8	7.2	9.2	30.6	23.4	23.9	23.2	28.5	20.7	20.3	21.1	54.9	40.6	37.5	38.2
	CJ1M02	10.9	8.2	7.6	10.0	7.5	7.1	7.3	10.7	11.7	7.3	6.5	7.5	14.7	16.8	28.0	24.4	13.8	13.6	24.7	20.3	23.3	17.6	32.9	25.4
	CJ1M03	10.1	7.2	12.6	16.8	7.5	5.3	7.2	15.1	12.3	8.2	17.2	16.6	34.5	24.1	28.7	46.8	29.4	20.1	25.5	38.2	40.8	29.5	32.1	46.2
	Mean	10.2	7.7	9.8	12.4	8.1	6.1	7.4	11.2	10.1	7.1	10.3	11.1	26.6	21.4	26.9	31.5	23.9	18.1	23.5	26.5	39.7	29.2	34.2	36.6
5 mg/kg/day	S.D.	0.7	0.5	2.6	3.8	1.0	0.9	0.3	3.6	3.3	1.2	6.0	4.8	10.5	4.0	2.6	13.3	8.8	3.9	2.8	10.1	15.8	11.5	2.9	10.5
	N	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
	CJ2M01	10.4	16.9	40.5	30.5	9.6	13.3	16.2	15.2	10.2	21.5	53.3	34.4	40.4	41.9	68.9	62.0	35.5	33.4	51.5	45.2	49.5	42.4	57.0	52.0
	CJ2M02	6.6	14.6	36.9	24.6	5.4	13.7	22.7	11.5	5.2	13.3	46.4	28.4	29.2	39.2	65.0	43.4	25.0	32.0	55.4	30.8	41.7	39.4	65.1	42.0
10 mg/kg/day	CJ2M03	9.9	13.4	48.9	31.6	11.7	11.7	28.6	17.2	8.1	13.4	54.6	36.3	39.4	28.2	61.7	49.8	32.3	22.8	40.4	25.3	39.4	28.4	45.6	28.1
	Mean	9.0	15.0	42.1	28.9	8.9	12.9	22.5	14.6	7.8	16.1	51.4	33.0	36.3	36.4	65.2	51.7	30.9	29.4	49.1	33.8	43.5	36.7	55.9	40.7
	S.D.	2.1	1.8	6.2	3.8	3.2	1.1	6.2	2.9	2.5	4.7	4.4	4.1	6.2	7.3	3.6	9.4	5.4	5.8	7.8	10.3	5.3	7.4	9.8	12.0
	N	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
10 mg/kg/day	CJ3M01	11.4	20.8	51.0	32.9	12.3	16.8	32.8	18.4	9.6	23.7	56.5	36.9	41.9	39.2	68.8	54.5	37.6	28.7	51.3	22.0	52.6	33.4	58.0	27.9
	CJ3M02	9.1	21.7	57.2	29.5	8.9	23.1	35.7	13.3	7.5	17.9	63.2	32.5	35.3	51.8	68.3	47.4	32.4	38.3	54.5	31.2	48.8	47.4	67.9	44.2
	CJ3M03	9.8	23.0	54.6	32.3	10.6	23.6	28.0	20.4	8.3	19.4	65.3	37.1	38.7	45.3	66.5	61.4	35.5	29.2	42.5	36.6	53.7	36.0	49.1	48.4
	Mean	10.1	21.8	54.3	31.6	10.6	21.2	32.2	17.4	8.5	20.3	61.7	35.5	38.6	45.4	67.9	54.4	35.2	32.1	49.4	29.9	51.7	38.9	58.3	40.2
10 mg/kg/day	S.D.	1.2	1.1	3.1	1.8	1.7	3.8	3.9	3.7	1.1	3.0	4.6	2.6	3.3	6.3	1.2	7.0	2.6	5.4	6.2	7.4	2.6	7.4	9.4	10.8
	N	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
	CJ4M01	10.1	21.8	54.3	31.6	10.6	21.2	32.2	17.4	8.5	20.3	61.7	35.5	38.6	45.4	67.9	54.4	35.2	32.1	49.4	29.9	51.7	38.9	58.3	40.2
	S.D.	1.2	1.1	3.1	1.8	1.7	3.8	3.9	3.7	1.1	3.0	4.6	2.6	3.3	6.3	1.2	7.0	2.6	5.4	6.2	7.4	2.6	7.4	9.4	10.8
	N	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3

Treg: Regulatory T cell

2 (d - Test Dunnett 2 Sided p < 0.05)

1 (dd - Test Dunnett 2 Sided p < 0.01)

General Footnote: Pre: Pretest

D3, D8 and D15: Days 3, 8 (prior to dosing) and 15

[Fig. 87]

Sex: Male		Ratio to baseline (pretest, %)																																			
		K67 + T cell						K67 + CD4 T cell						K67 + CD8 T cell						K67 + Treg						K67 + ICOS + Treg						K67 + NK cell					
		Pre	D3	D8	D15	Pre	D3	D8	D15	Pre	D3	D8	D15	Pre	D3	D8	D15	Pre	D3	D8	D15	Pre	D3	D8	D15	Pre	D3	D8	D15								
Group	Animal No.																																				
0 mg/kg/day	CJ1M01	1.00	0.79	0.95	1.07	1.00	0.62	0.83	0.85	1.00	0.92	1.14	1.46	1.00	0.76	0.78	0.76	1.00	0.73	0.71	0.74	1.00	0.74	0.68	0.70	1.00	2.71	2.33	1.37								
	CJ1M02	1.00	0.75	0.70	0.92	1.00	0.95	0.97	1.43	1.00	0.62	0.56	0.64	1.00	1.14	1.90	1.66	1.00	0.99	1.79	1.47	1.00	0.76	1.41	1.09	1.00	0.47	0.54	0.41								
	CJ1M03	1.00	0.71	1.25	1.66	1.00	0.71	0.96	2.01	1.00	0.67	1.40	1.35	1.00	0.70	0.83	1.36	1.00	0.68	0.87	1.30	1.00	0.72	0.79	1.13	1.00	1.02	2.59	1.65								
5 mg/kg/day	Mean	1.00	0.75	0.97	1.22	1.00	0.76	0.92	1.43	1.00	0.74	1.03	1.15	1.00	0.87	1.17	1.26	1.00	0.80	1.12	1.17	1.00	0.74	0.96	0.97	1.00	1.40	1.82	1.14								
	S.D.		0.00	0.04	0.28	0.39	0.00	0.17	0.08	0.58	0.00	0.16	0.43	0.45	0.00	0.24	0.63	0.46	0.00	0.17	0.58	0.38	0.00	0.02	0.39	0.24	0.00	1.17	1.12	0.65							
	N	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3							
10 mg/kg/day	CJ2M01	1.00	1.63	3.89	2.93	1.00	1.39	1.69	1.58	1.00	2.11	5.23	3.37	1.00	1.04	1.71	1.53	1.00	0.94	1.45	1.27	1.00	0.86	1.15	1.05	1.00	3.23	6.29	5.27								
	CJ2M02	1.00	2.21	5.59	3.73	1.00	2.54	4.20	2.13	1.00	2.56	8.92	5.46	1.00	1.34	2.23	1.49	1.00	1.28	2.22	1.23	1.00	0.94	1.56	1.01	1.00	3.46	5.10	4.55								
	CJ2M03	1.00	1.35	4.94	3.19	1.00	1.00	2.44	1.47	1.00	1.65	6.74	4.48	1.00	0.72	1.57	1.26	1.00	0.71	1.25	0.78	1.00	0.72	1.16	0.71	1.00	1.56	6.80	5.42								
			d [†]	dd [‡]	dd [‡]							dd [‡]	dd [‡]	dd [‡]													dd [‡]	dd [‡]									
	Mean	1.00	1.73	4.81	3.28	1.00	1.64	2.78	1.73	1.00	2.11	6.96	4.44	1.00	1.03	1.84	1.43	1.00	0.98	1.64	1.09	1.00	0.84	1.29	0.92	1.00	2.75	6.06	5.08								
	S.D.		0.00	0.44	0.86	0.41	0.00	0.80	1.29	0.35	0.00	0.46	1.86	1.05	0.00	0.31	0.35	0.15	0.00	0.29	0.51	0.27	0.00	0.11	0.23	0.19	0.00	1.04	0.87	0.47							
	N	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3							
10 mg/kg/day	CJ3M01	1.00	1.82	4.47	2.89	1.00	1.37	2.67	1.50	1.00	2.47	5.89	3.84	1.00	0.94	1.64	1.30	1.00	0.76	1.36	0.59	1.00	0.63	1.10	0.53	1.00	2.10	7.03	4.00								
	CJ3M02	1.00	2.38	6.29	3.24	1.00	2.60	4.01	1.49	1.00	2.39	8.43	4.33	1.00	1.47	1.93	1.34	1.00	1.18	1.68	0.96	1.00	0.97	1.39	0.91	1.00	2.69	4.55	3.46								
	CJ3M03	1.00	2.35	5.57	3.30	1.00	2.23	2.64	1.92	1.00	2.34	7.87	4.47	1.00	1.17	1.72	1.59	1.00	0.82	1.20	1.03	1.00	0.67	0.91	0.90	1.00	3.02	7.18	4.74								
			dd [‡]	dd [‡]	dd [‡]							dd [‡]	dd [‡]	dd [‡]													dd [‡]	dd [‡]									
	Mean	1.00	2.18	5.44	3.14	1.00	2.07	3.11	1.64	1.00	2.40	7.40	4.21	1.00	1.19	1.76	1.41	1.00	0.92	1.41	0.86	1.00	0.76	1.13	0.78	1.00	2.60	6.25	4.07								
	S.D.		0.00	0.32	0.92	0.22	0.00	0.63	0.78	0.25	0.00	0.07	1.33	0.33	0.00	0.27	0.15	0.16	0.00	0.23	0.24	0.24	0.00	0.19	0.24	0.22	0.00	0.47	1.48	0.64							
	N	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3							

General Footnote: Pre: Pretest
D3, D8 and D15: Days 3, 8 (prior to dosing) and 15
Treg: Regulatory T cell
2 [d - Test; Dunnett 2 Sided p < 0.05]
2 [dd - Test; Dunnett 2 Sided p < 0.01]

General Footnote: Pre: Pretest D3, D8 and D15: Days 3, 8 (prior to dosing) and 15 Treg: Regulatory T cell
 1 [d - Test Dunnett 2 Sided p < 0.05] 2 [dd - Test Dunnett 2 Sided p < 0.01]

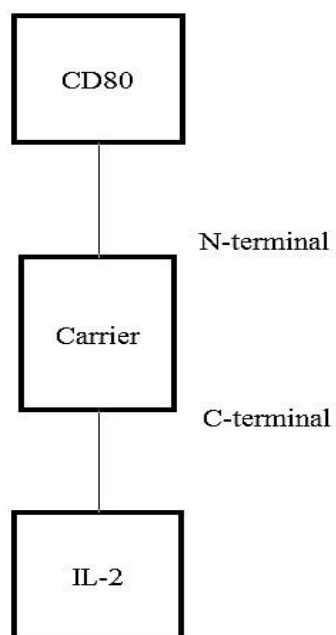
[Fig. 88]

Day(s): 15 Relative to Start Date

Sex: Male		0 mg/kg/day	5 mg/kg/day	10 mg/kg/day
Liver (g)	Mean	41.5	42.7	42.1
	S.D.	0.9	7.1	5.6
	N	3	3	3
Liver (%)	Mean	1.73	1.68	1.86
	S.D.	0.09	0.10	0.18
	N	3	3	3
Spleen (g)	Mean	1.727	3.358	3.886 d ^a
	S.D.	0.520	0.758	1.087
	N	3	3	3
Spleen (%)	Mean	0.072	0.132	0.171 d ^a
	S.D.	0.023	0.025	0.040
	N	3	3	3
Pancreas (g)	Mean	4.27	4.27	3.24
	S.D.	0.54	1.20	0.38
	N	3	3	3

[Fig. 89]

A



B

