

FIG.1

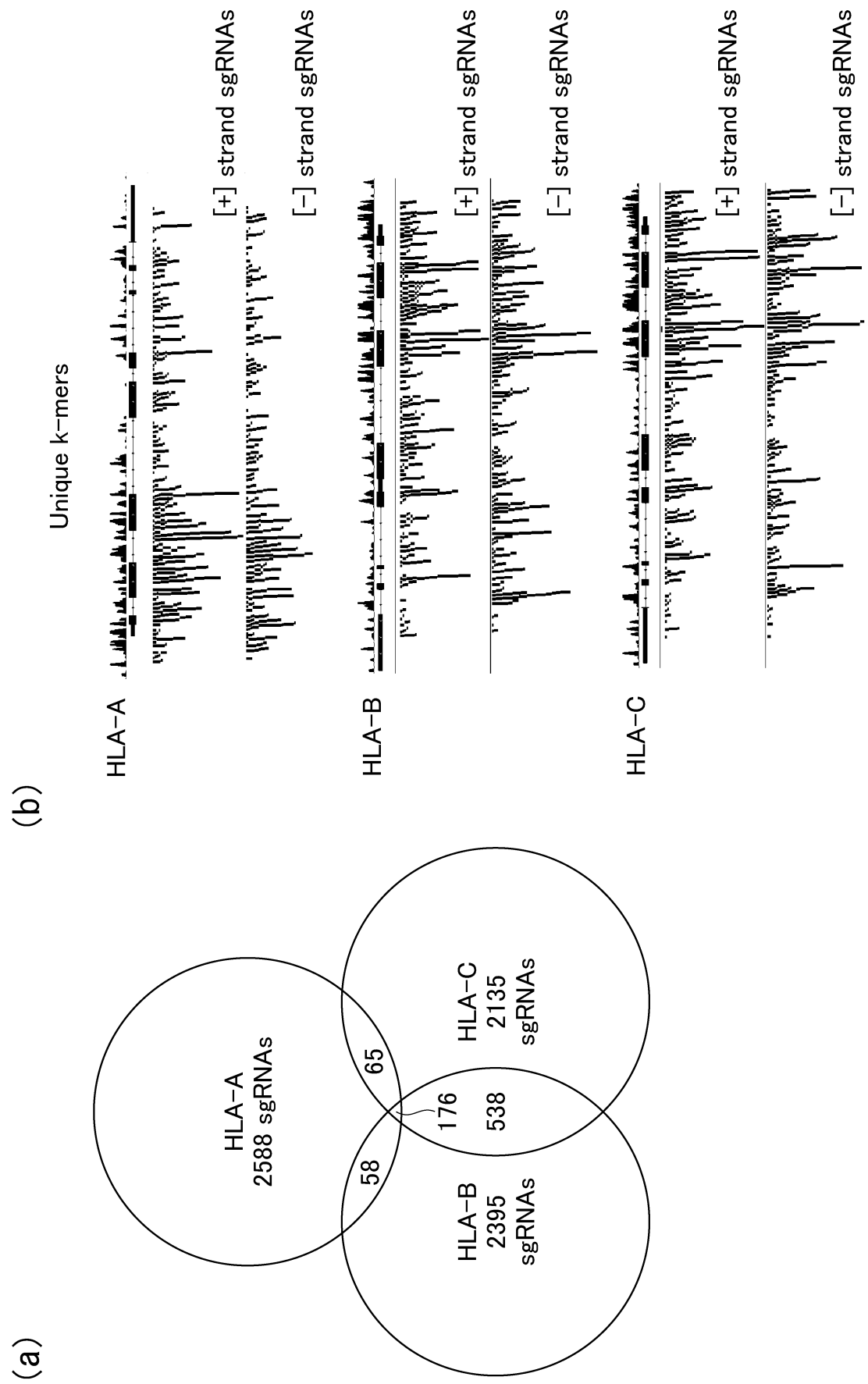


FIG.2

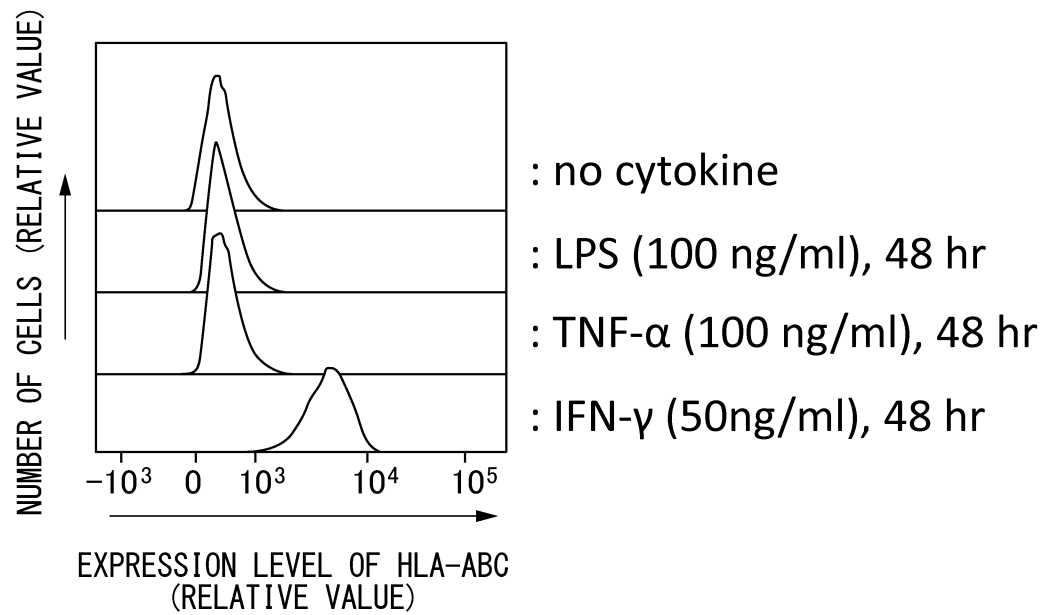


FIG.3

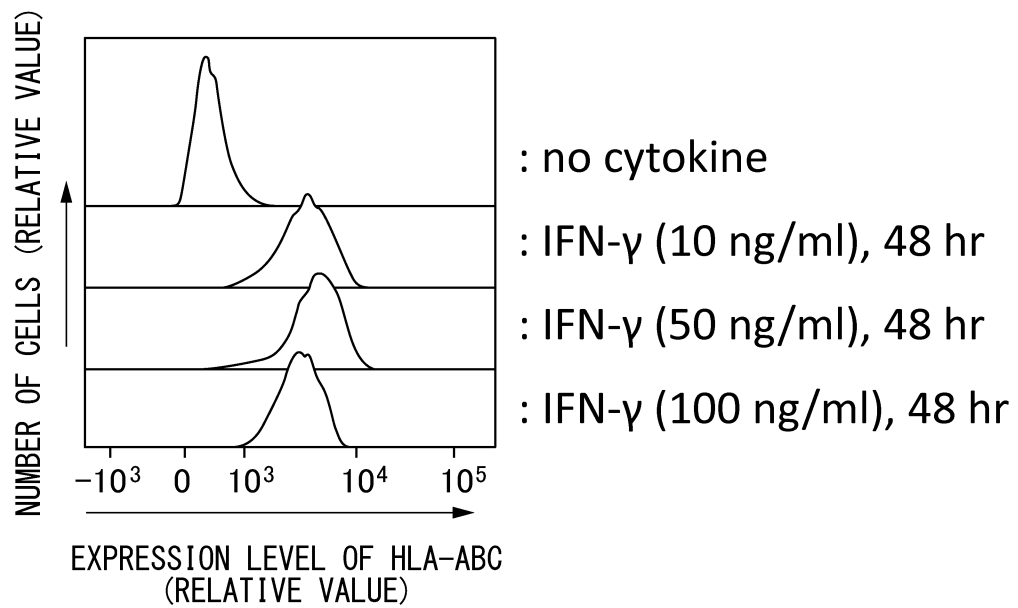


FIG.4

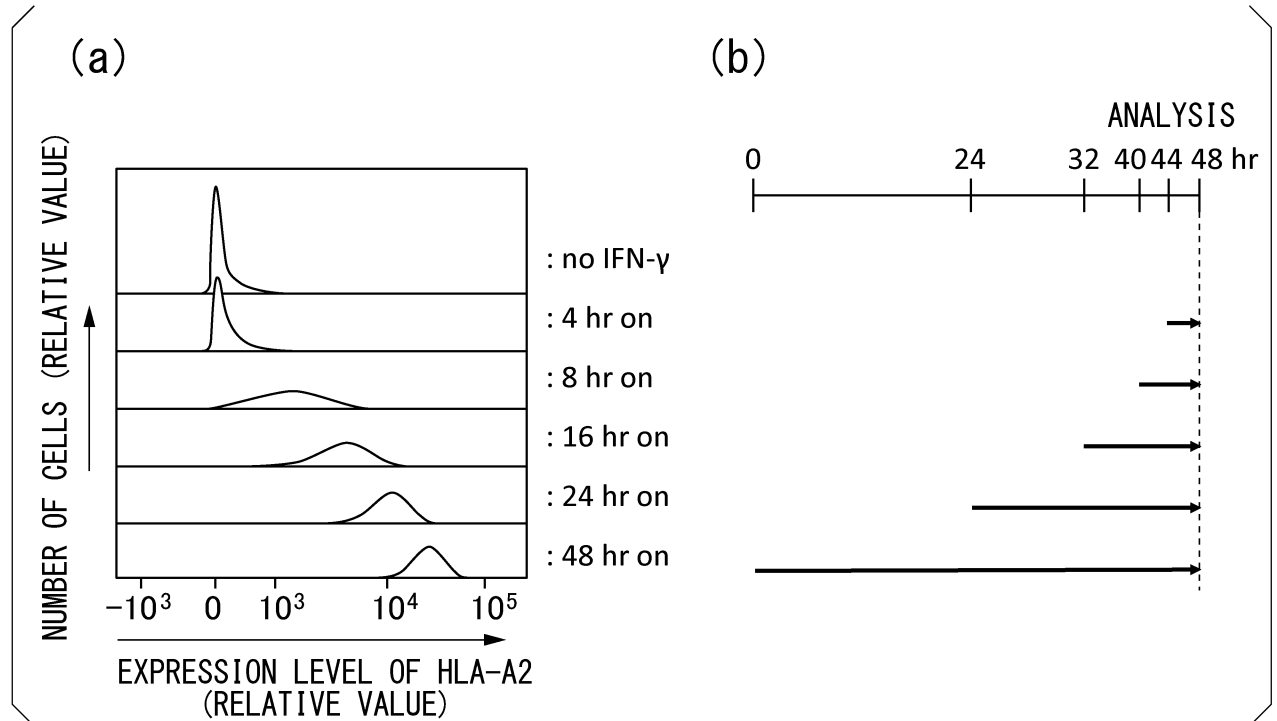
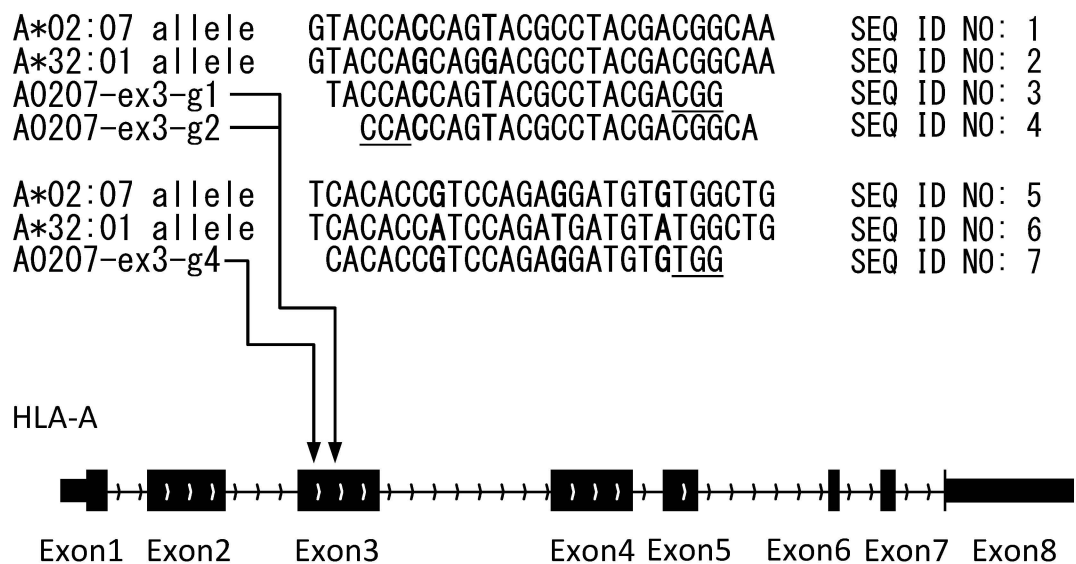


FIG.5

(a)



(b)

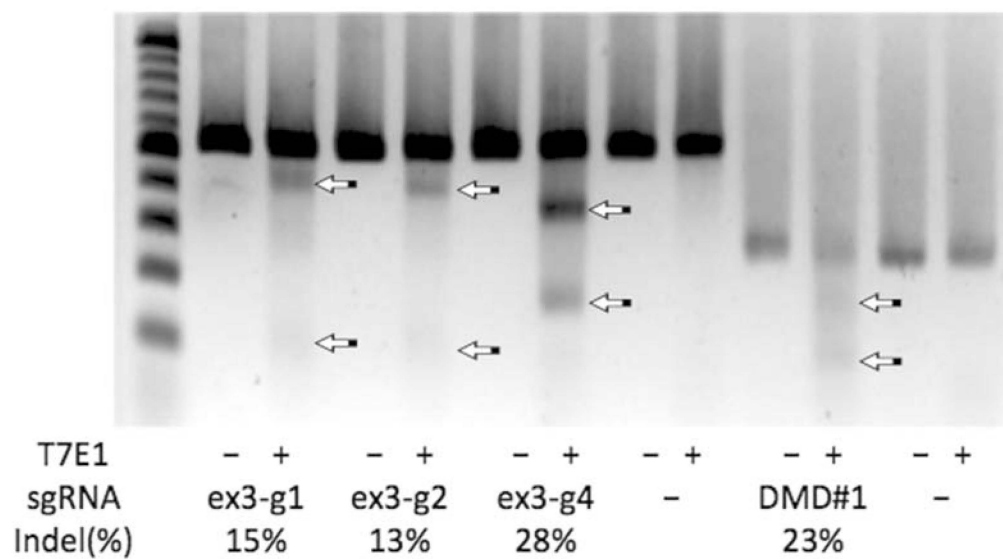
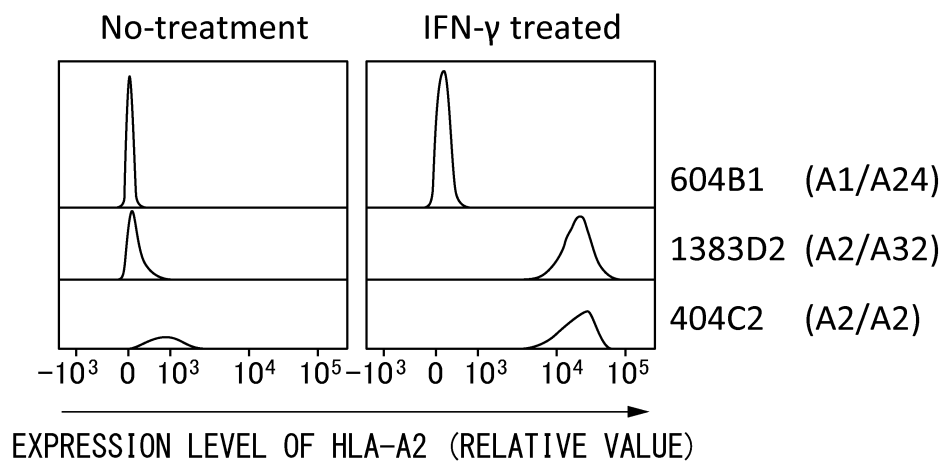


FIG.6

(a)



(b)

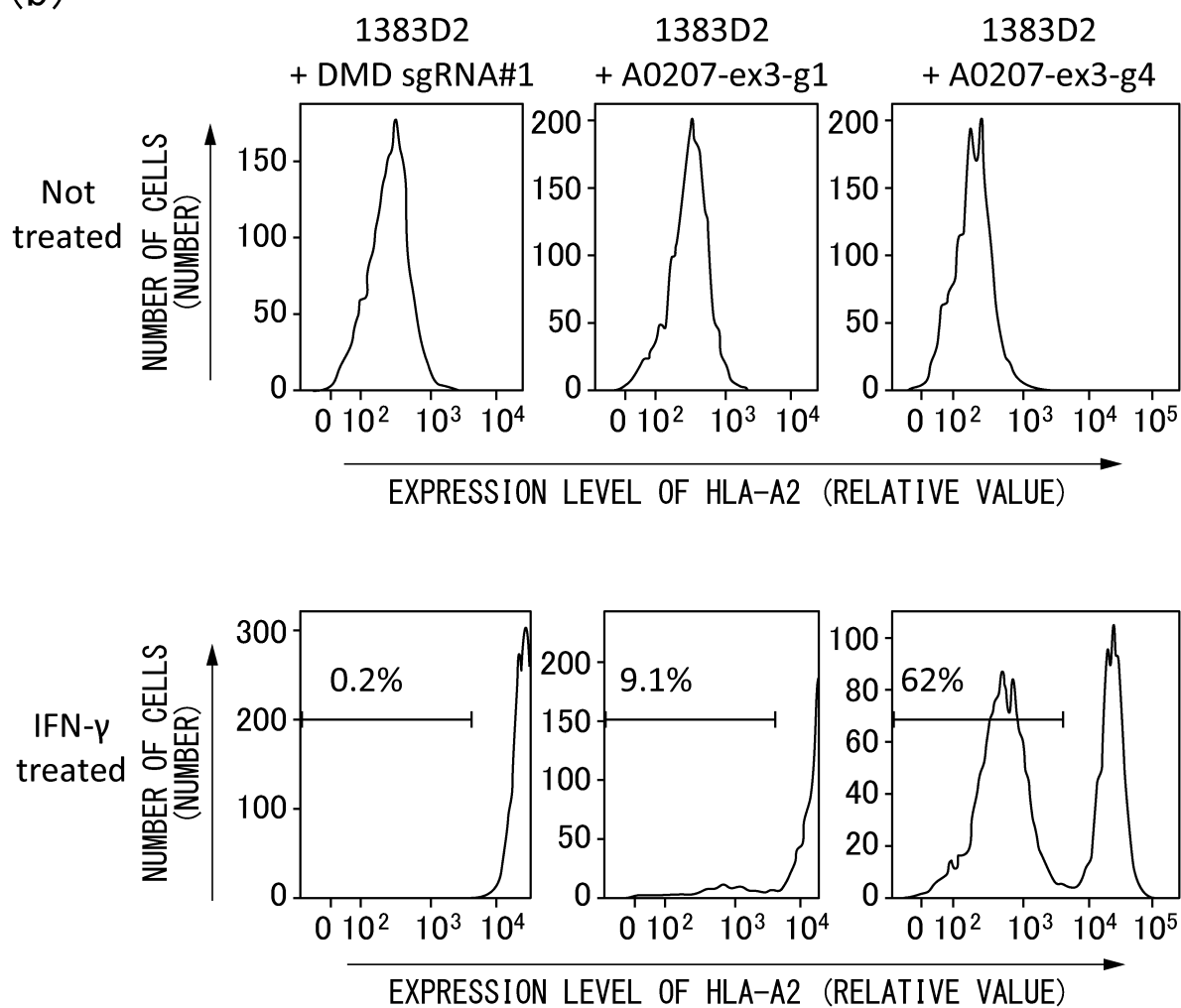


FIG.7

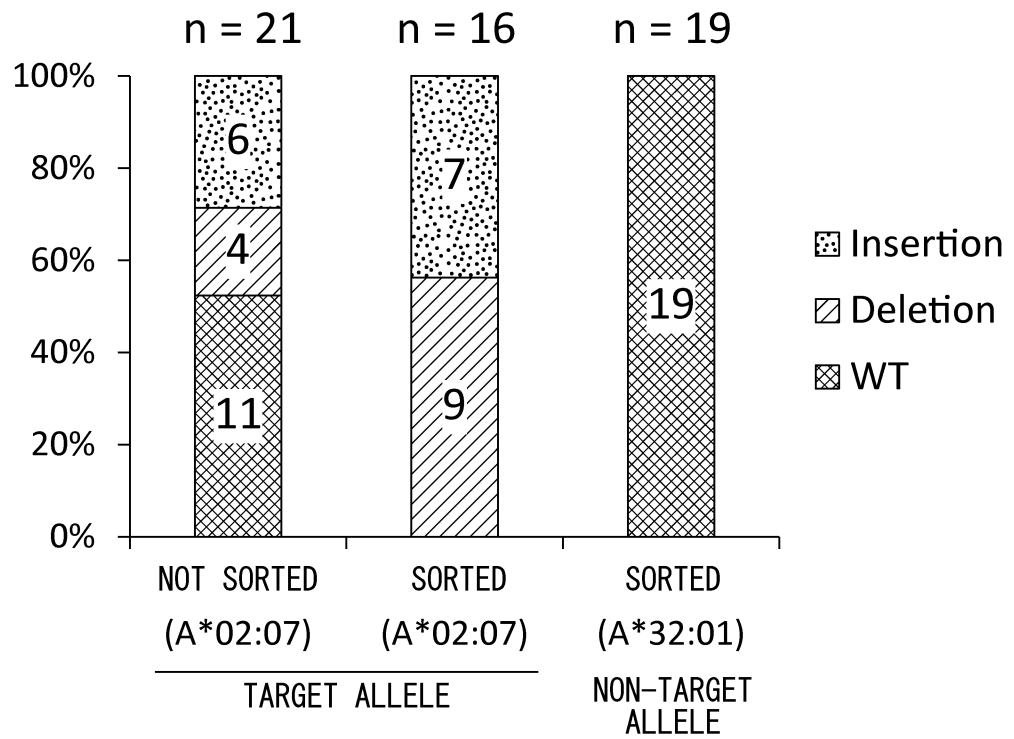


FIG.8

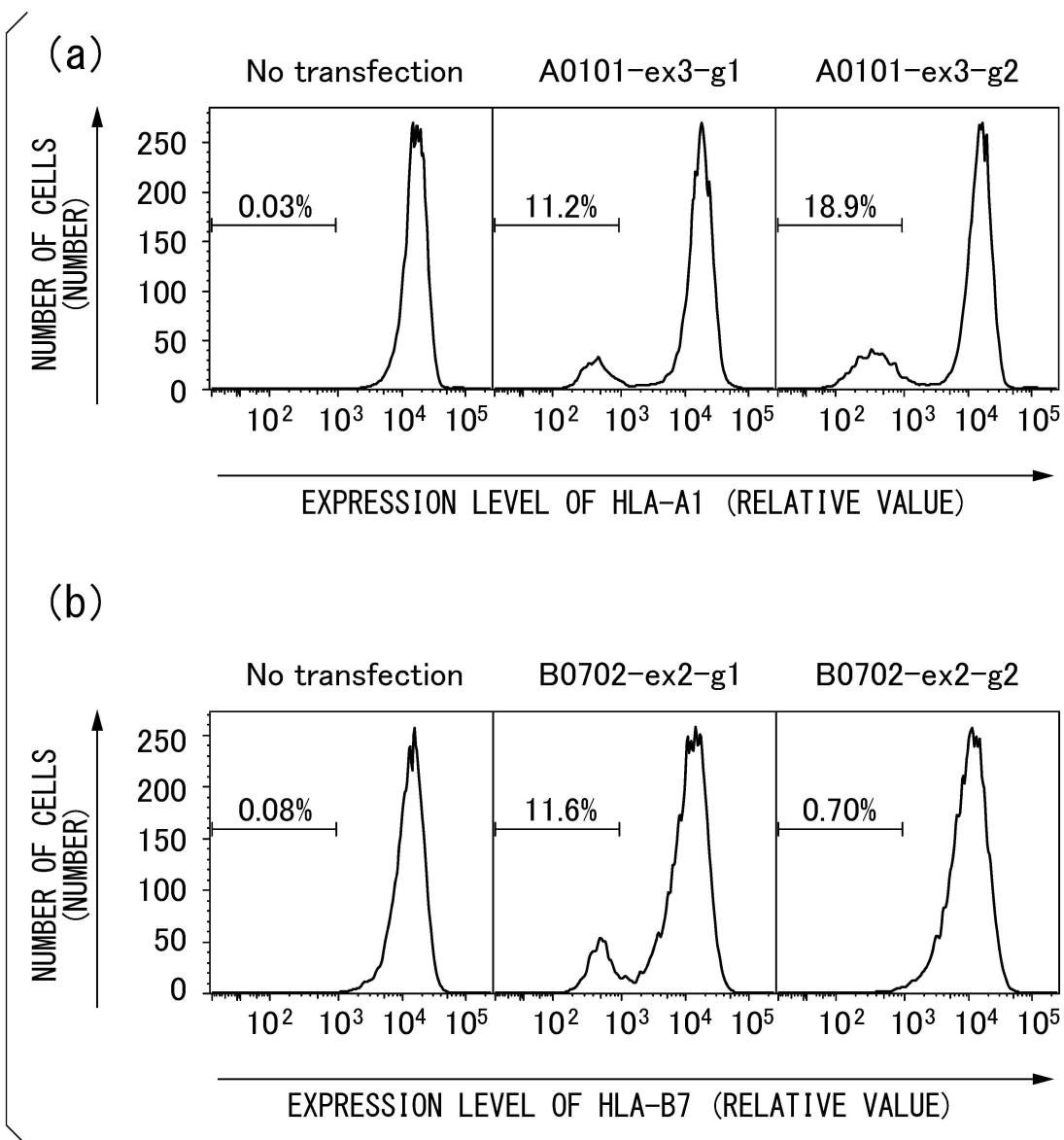


FIG.9



FIG.10

(a)

CLONE NO.	HLA-A1	HLA-B7
#1	-5 bp	-6 bp
#2	-5 bp	-6 bp
#3	WT	WT
#5	-5 bp	-6 bp
#6	-5 bp	-6 bp
#7	WT	WT
#8	-4 bp	-2 bp
#10	-14 bp	-11 bp
#11	+18 bp	-1 bp
#12	-5 bp	-6 bp
#13	-4 bp	-2 bp
#14	WT	WT
#15	-4 bp	-2 bp

(b)

HLA-A*01:01		
WT	GGGTACCGGCAGGACGCCT	SEQ ID NO: 8
#8	GGGTACCGG----CCGCCT	SEQ ID NO: 9
#10	GG-----CCT	
HLA-B*07:02		
WT	ACAAGGCCCAGGCACA	SEQ ID NO: 10
#8	ACAA--CCCAGGCACA	SEQ ID NO: 11
#10	ACA-----CA	

FIG.11

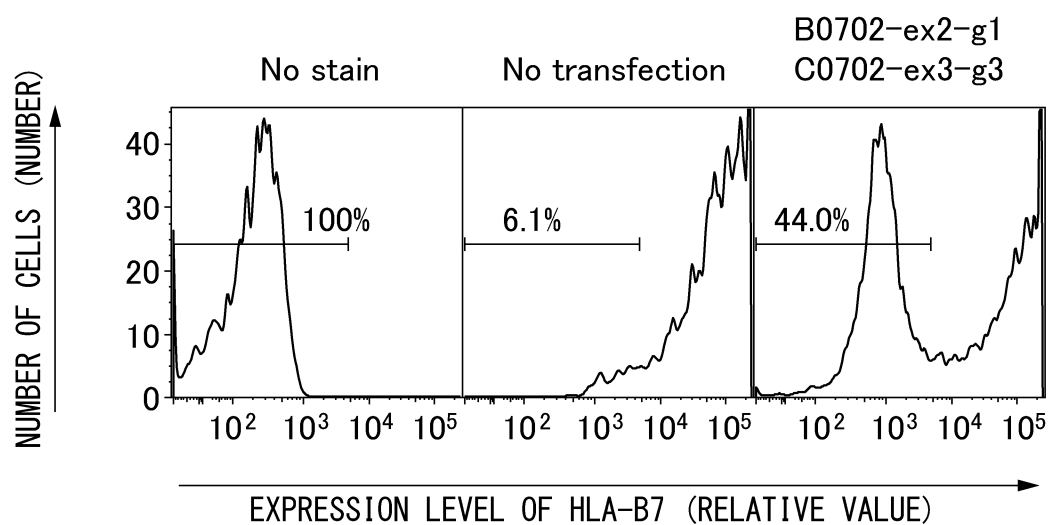


FIG.12

(a)

CLONE NO.	HLA-B7	HLA-C7
#1	-6 bp	-9 bp
#2	-6 bp	+2 bp
#3	-6 bp	WT
#4	-6 bp	WT
#5	-6 bp	-9 bp
#6	-6 bp	WT
#7	-6 bp	WT
#8	-6 bp	WT
#9	-6 bp	+2 bp
#10	-3 bp	+1 bp
#11	-3 bp	+1 bp
#12	-6 bp	WT
#13	-3 bp	+1 bp
#14	-3 bp	+1 bp
#16	-6 bp	WT
#17	-6 bp	+2 bp
#18	-6 bp	+2 bp
#19	-6 bp	+2 bp
#20	-6 bp	+2 bp
#21	-6 bp	+2 bp
#22	-6 bp	+2 bp
#23	-6 bp	+2 bp
#24	-6 bp	+2 bp
#25	-6 bp	+2 bp
#26	-2 bp	+1 bp
#27	-6 bp	+2 bp
#28	-6 bp	+2 bp

(b)

	HLA-B*07:02	HLA-C*07:02
WT	AAGGCCAG	GGACACC
#2	A-----AG	GGACACC
		AA
#11	A---CCCAG	GGACACC
		A
#26	AA--CCCAG	GGACACG
		A

FIG.13

(a)

CLONE NO.	HLA-C12
#1	-1 bp
#2	-3 bp
#3	-28 bp
#4	-28 bp
#5	-3 bp
#6	-28 bp
#7	-1 bp
#8	-9 bp
#9	-2 bp
#10	-40 bp
#11	-28 bp
#12	+1 bp
#13	-1 bp
#14	-3 bp
#16	-3 bp
#17	-1 bp

(b)

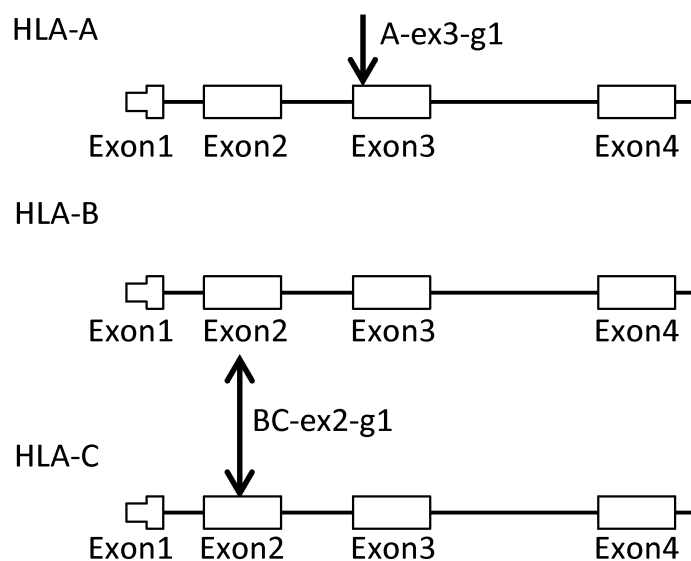
CLONE NO.	HLA-B52
#1-1	Mut
#1-2	-12 bp
#1-3	WT
#1-4	WT
#1-5	WT
#1-6	Mut
#1-7	WT
#1-8	WT
#1-9	WT
#1-10	-11 bp
#1-11	WT
#1-12	WT

(c)

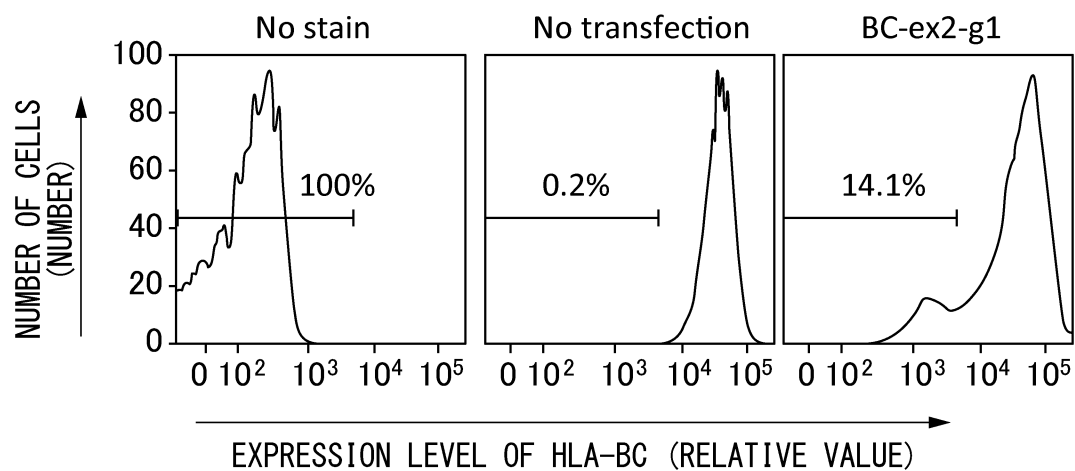
	HLA-C*12:02	HLA-B*52:02
WT	GAGGATG	GCATAAC
#1-1	GAG-ATG	GTATGAC

FIG.16

(a)



(b)



(c)

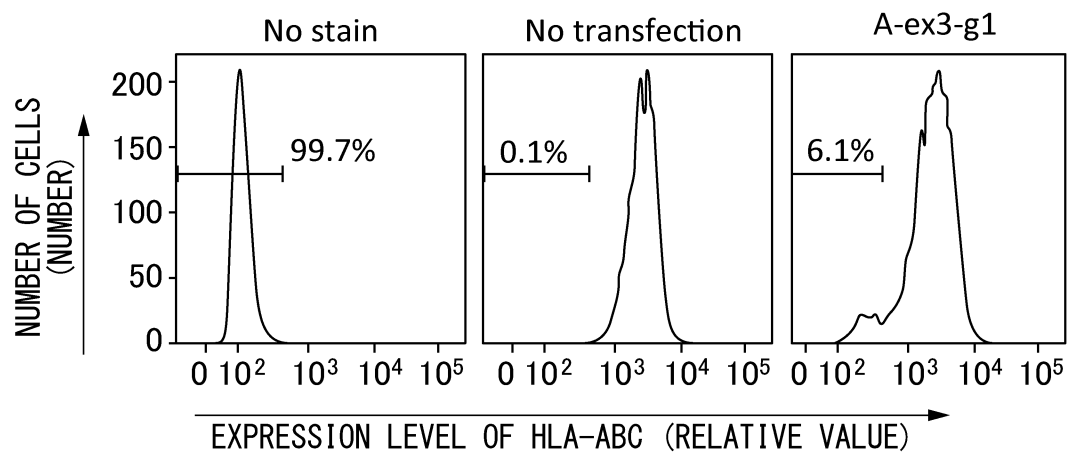


FIG.17

(a)

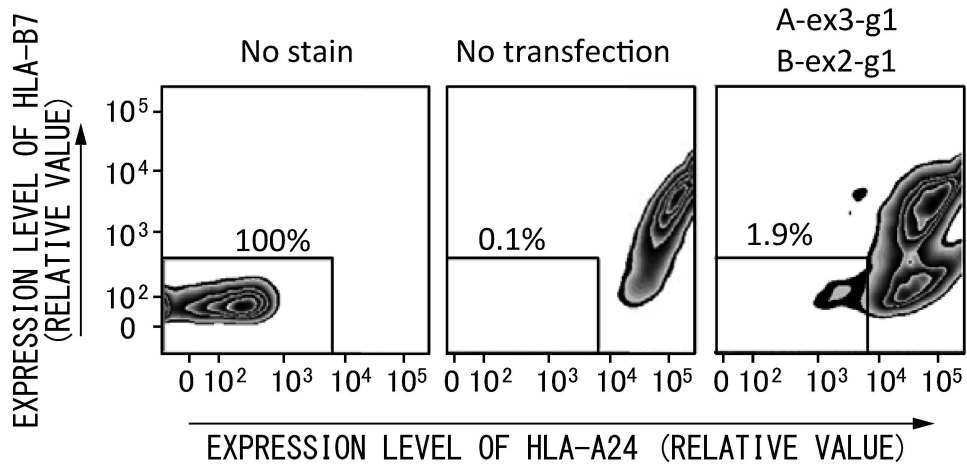
CLONE NO.	HLA-A01	HLA-A24	HLA-B07	HLA-B37	HLA-C06	HLA-C07
#1	+1 bp	+1 bp	-1 bp	-6 bp	+9 bp	-14 bp

(b)

A*01:01			A*24:02		
WT	TCTTGGACCGCGG	SEQ ID NO: 14	WT	TCTTGGACCGCGG	SEQ ID NO: 16
#1	TCTTGGACCGCGG	SEQ ID NO: 15	#1	TCTTGGACCGCGG	SEQ ID NO: 17
					
B*07:02			B*37:01		
WT	AGTATTGGGACCGG	SEQ ID NO: 18	WT	TGGGACCGGGAGAC	SEQ ID NO: 20
#1	AGTATTGG-ACCGG	SEQ ID NO: 19	#1	TGGGA-----GAC	
C*06:02			C*07:02		
WT	GTATTGGGACCGGG	SEQ ID NO: 21	WT	GAGGGGCCGGAGTATTG	SEQ ID NO: 23
#1	GTATTGGGACCGGG	SEQ ID NO: 22	#1	GA-----G	
					

FIG.18

(a)



(b)

CLONE NO.	HLA-A24	HLA-A24	HLA-B07	HLA-B52
#1	+9 bp	+10 bp	-7 bp	-20 bp
#3	-9 bp	-10 bp	-1 bp	+1 bp
#5	+1 bp	+1 bp	WT	+1 bp
#7	+1 bp	+1 bp	+1 bp	-545 bp
#8	+1 bp	? bp	-4 bp	+1 bp
#10	+1 bp	+1 bp	+1 bp	+1 bp

(c)

A*24:02 GGACCTGCGCTCTTGGACCGCGGCGGACATGGCGGCTCAG SEQ ID NO: 24
 #3 GGAYCTGASCTCTKGAAMTGGSSGGTTCRAATCACCARS SEQ ID NO: 25

B*07:02 CACCCAGTTCGTGAGG SEQ ID NO: 26 B*52:01 CACCCAGTTCGTGA SEQ ID NO: 28
 #3 CACCCAGT-CGTGAGG SEQ ID NO: 27 #3 CACCCAGTTCGTGA SEQ ID NO: 29

↑

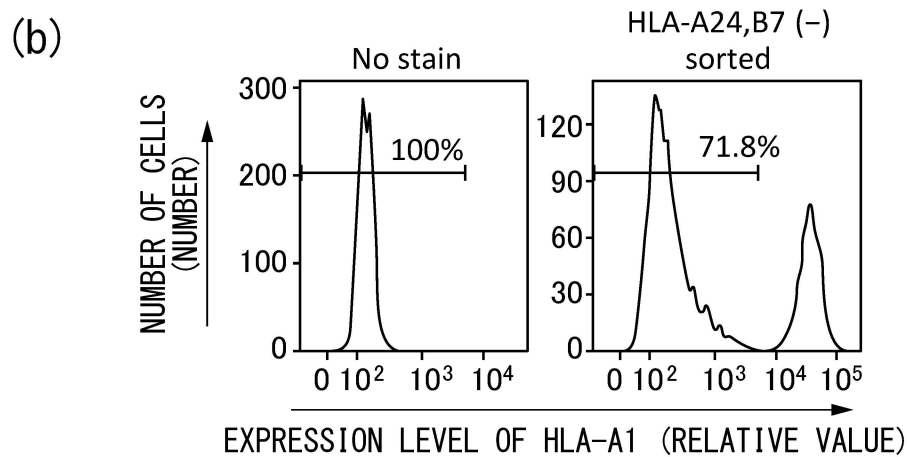
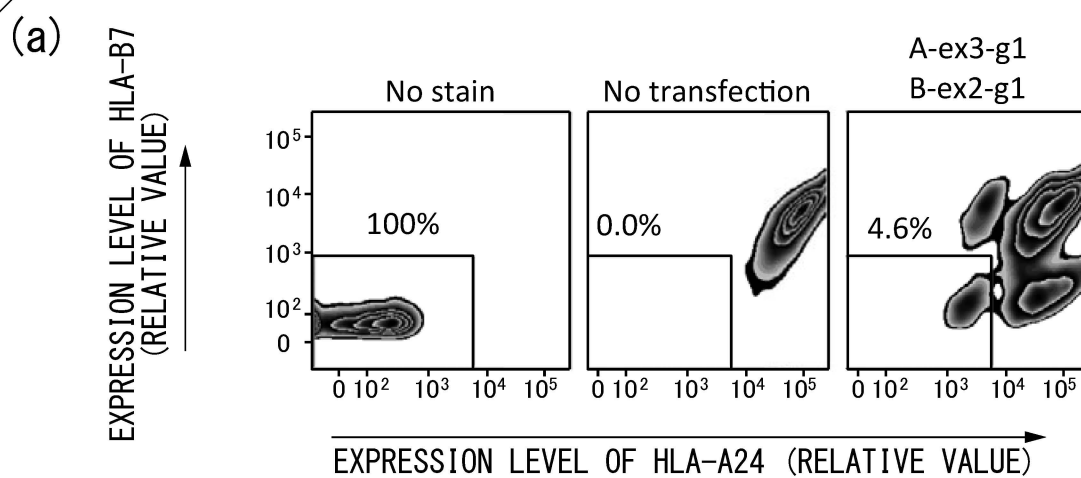
(d)

CLONE NO.	HLA-C07	HLA-C12
#3-1	WT	-34 bp
#3-2	WT	-1 bp
#3-3	WT	-1 bp
#3-4	WT	WT

(e)

C*12:02 CAGAGGATGTACGGCTGCGACCTGGGGCCCGACGGG SEQ ID NO: 30
 #3-1 C-----G
 #3-2 CAGAG-ATGTACGGCTGCGACCTGGGGCCCGACGGG SEQ ID NO: 31

FIG.19



(c)

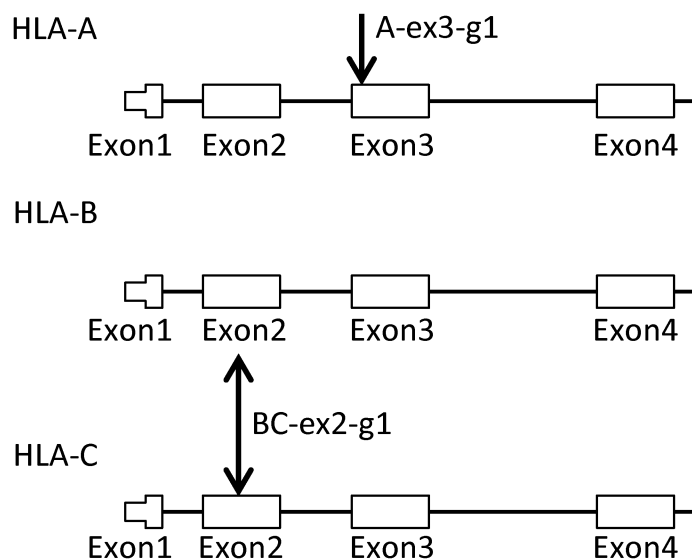
CLONE NO.	HLA-A01	HLA-A24	HLA-B07	HLA-B37
#1	-2 bp	+1 bp	+355 bp	+1 bp
#3	+1 bp	+1 bp	+1 bp	WT
#4	-2 bp	+1 bp	+1 bp	-1 bp
#9	+1 bp	+1 bp	-4 bp	+1 bp
#14	+1 bp	+1 bp	+1 bp	+145 bp
#17	-1 bp	+3 bp	+1 bp	-4 bp
#23	+1 bp	-25 bp	+1 bp	+1 bp

(d)

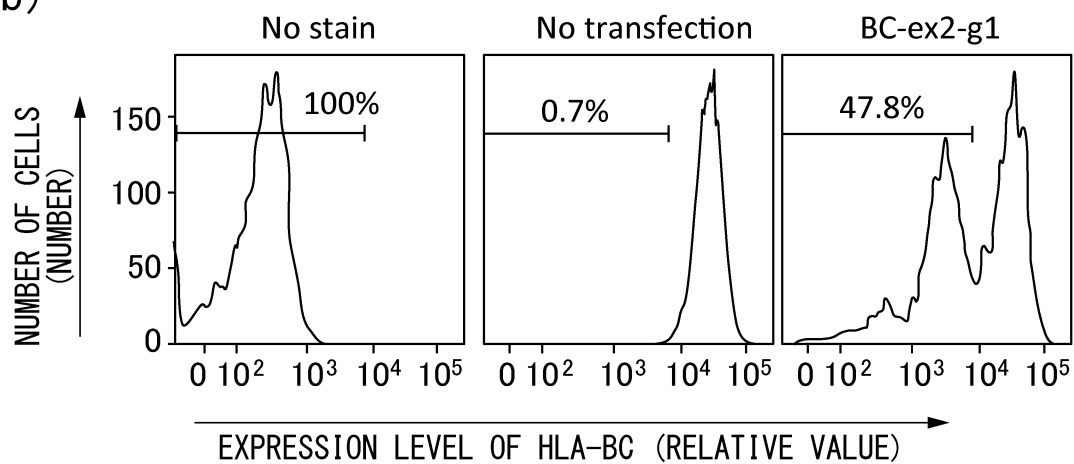
A*01:01	TTGGACCG	A*24:02	TTGGACCG
#4	TTG--CCG	#4	TTGGACCG
			A
B*07:02	CCAGTTCG	B*37:01	CCAGTTCG
#4	CCAGTTCG	#4	CCAGT-CG
	A		

FIG.20

(a)



(b)



(c)

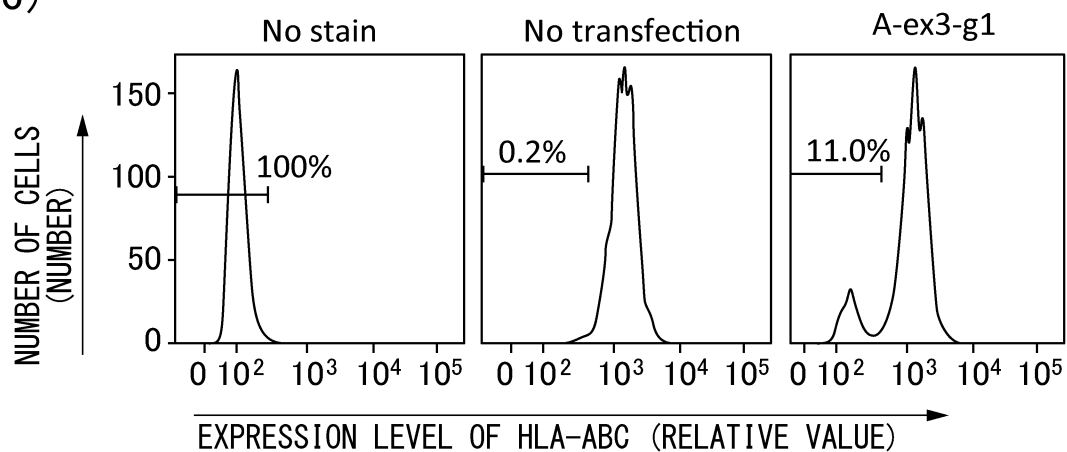


FIG.21

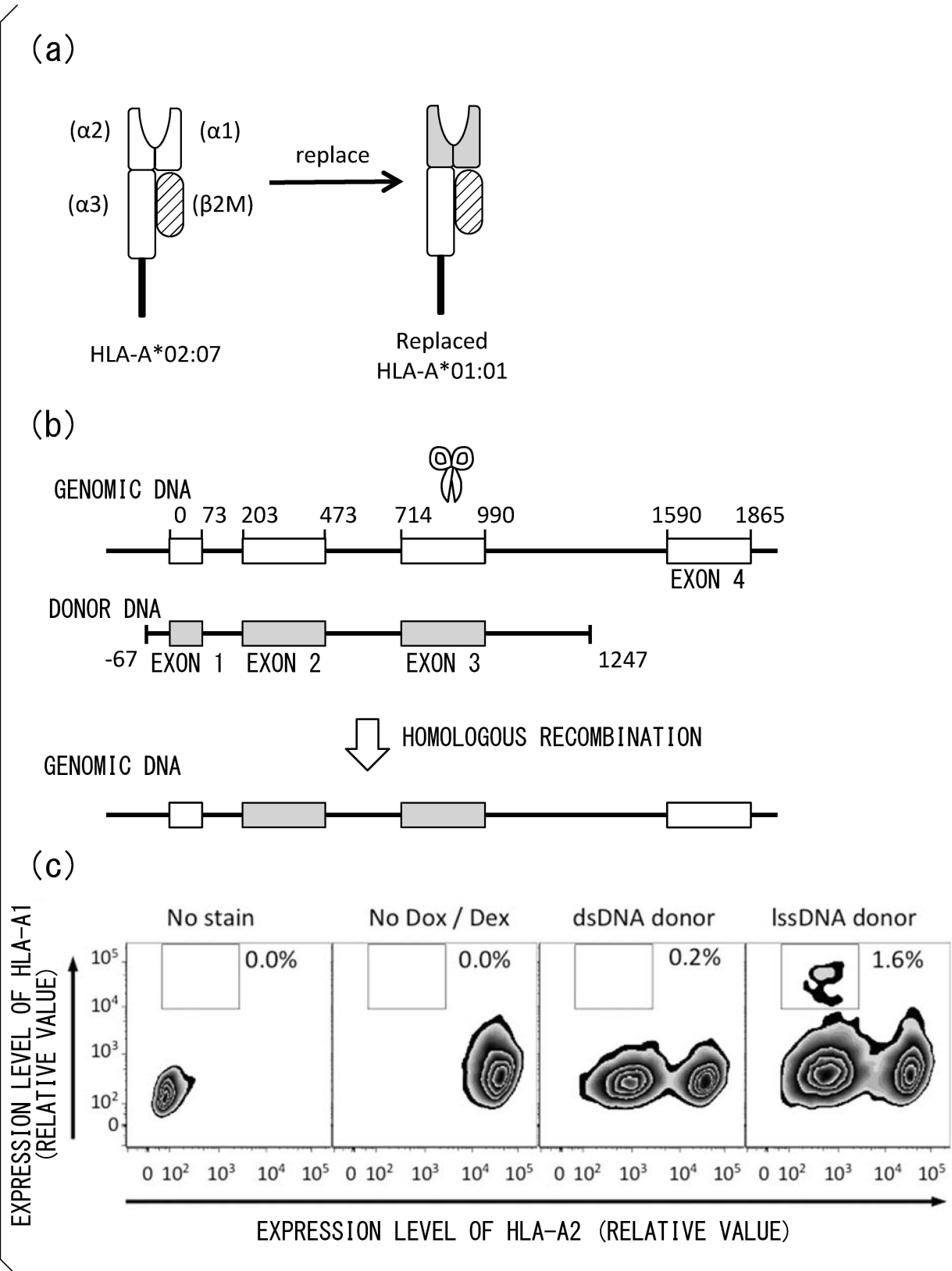


FIG.22

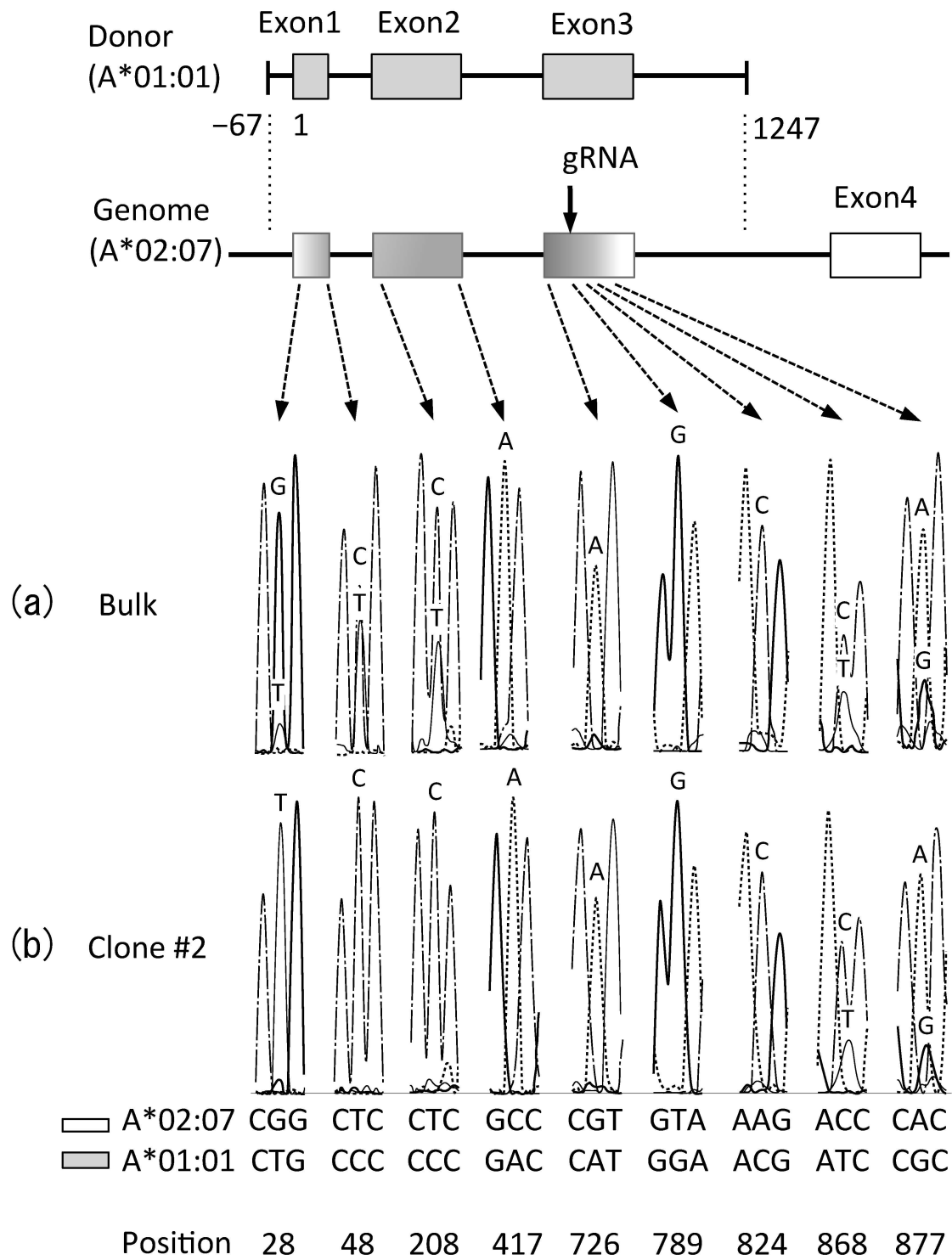


FIG.23

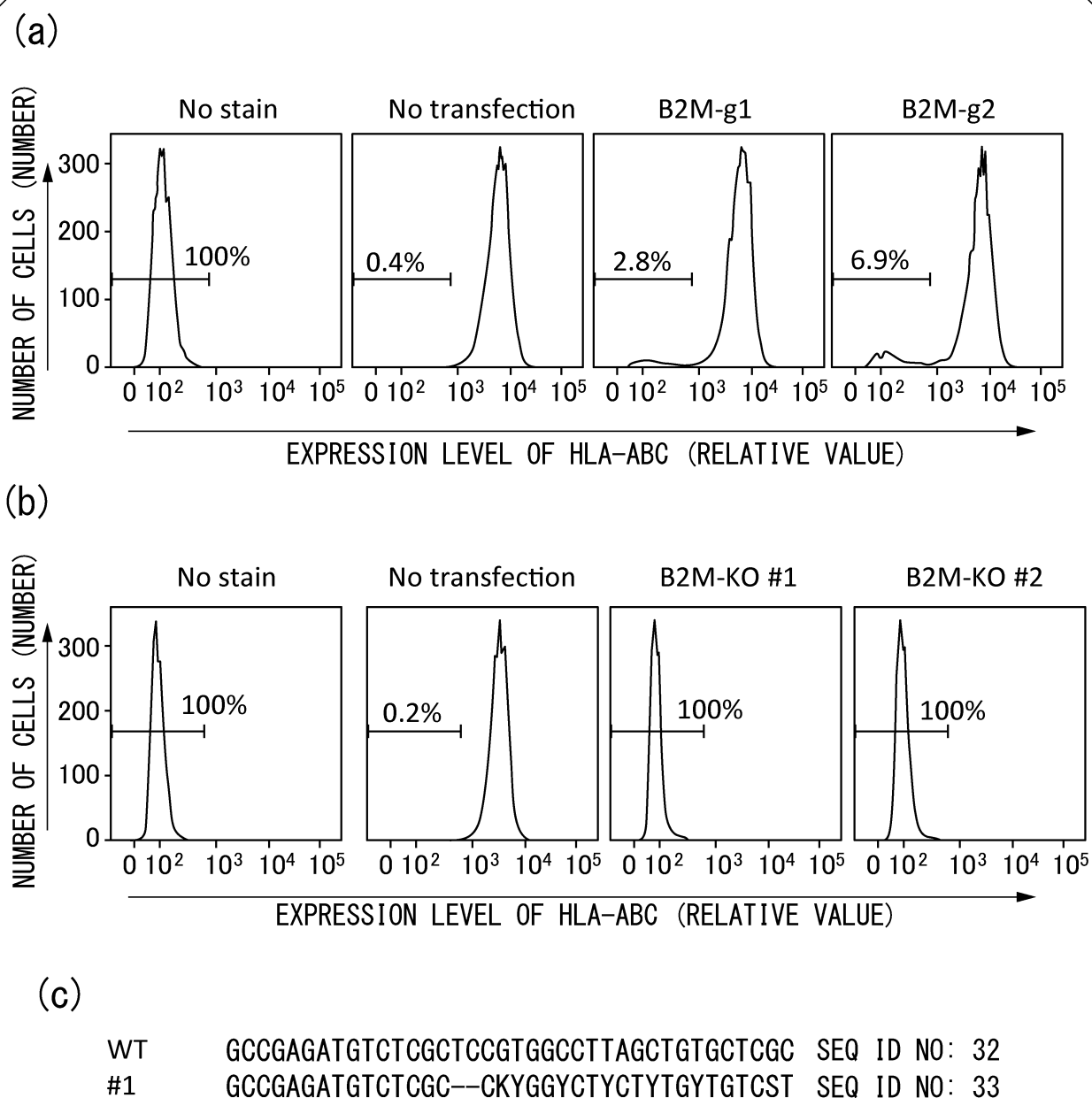
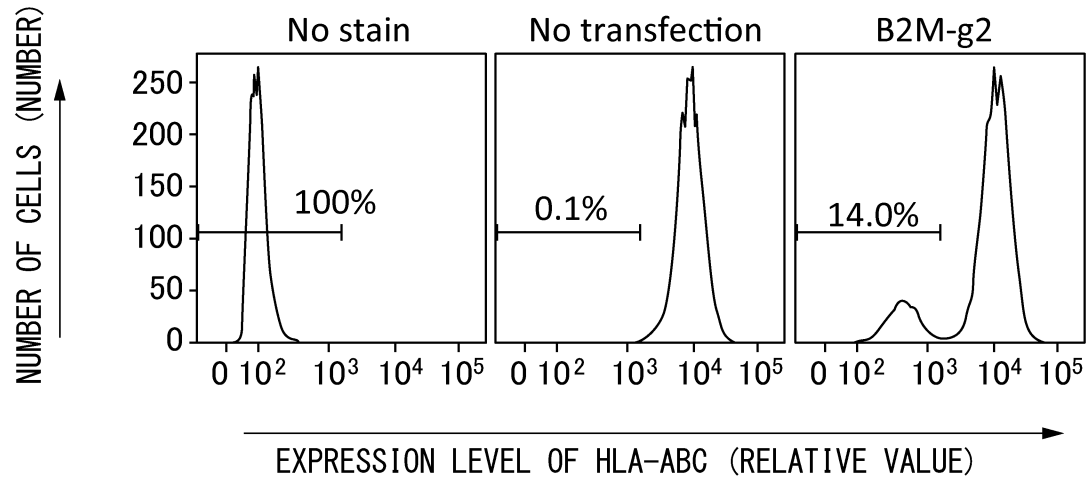


FIG.24

(a)



(b)

WT	TCGGGCCGAGATGTCTCGCTCCGTGGCCTT	SEQ ID NO: 34
#1	TCGGGCCGAGATGTCTCGCTCCGTGGCCTT	SEQ ID NO: 35
	└─┬─┘ T	
#2	TCGGGCCGAGAT-----SKCKCTWGTCTC	SEQ ID NO: 36
#3	TCGGGCCGAGATGTCTCGCTCCGTGGCCTT	SEQ ID NO: 37
	└─┬─┘ T	
#4	TCGGGCCGAGATGTCTCG-----TGGCCTT	SEQ ID NO: 38

FIG.25

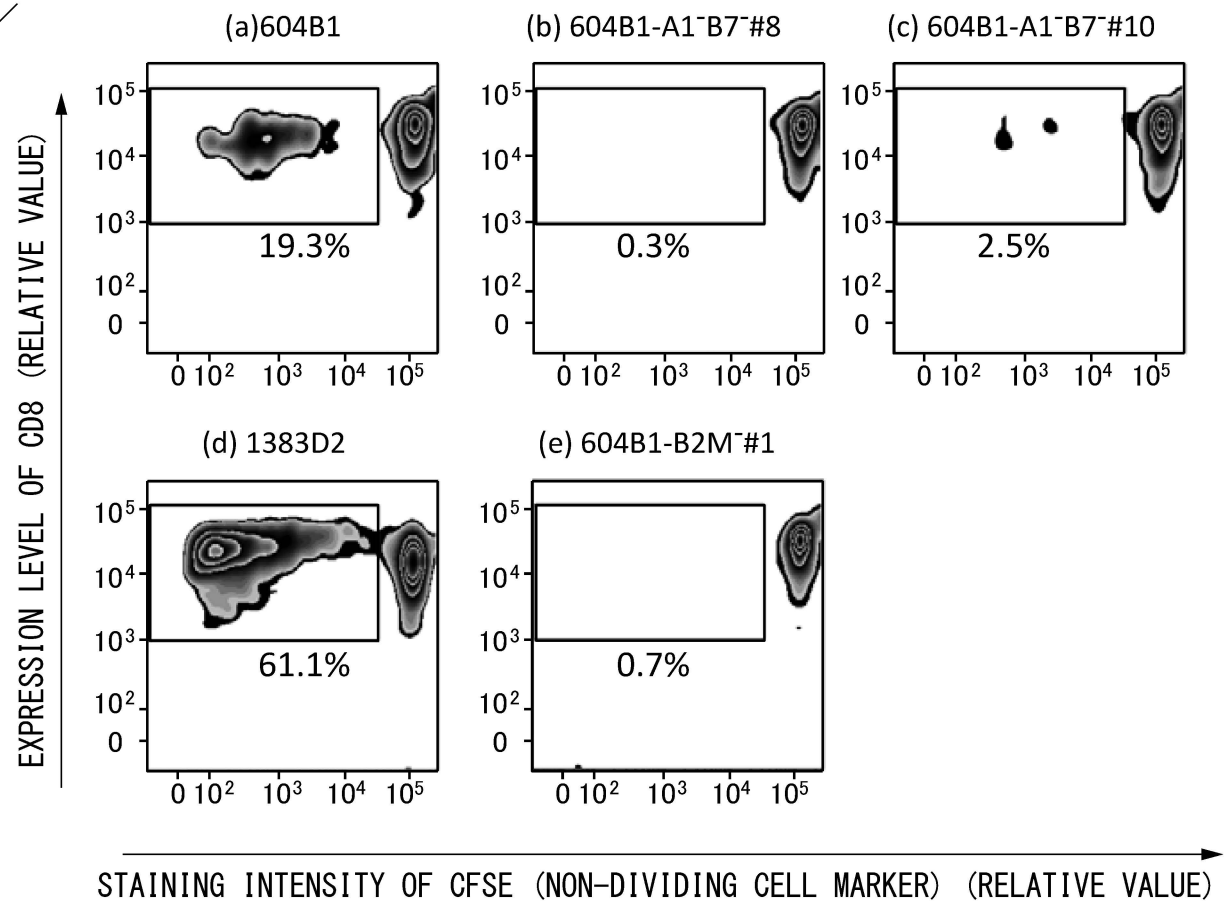


FIG.26

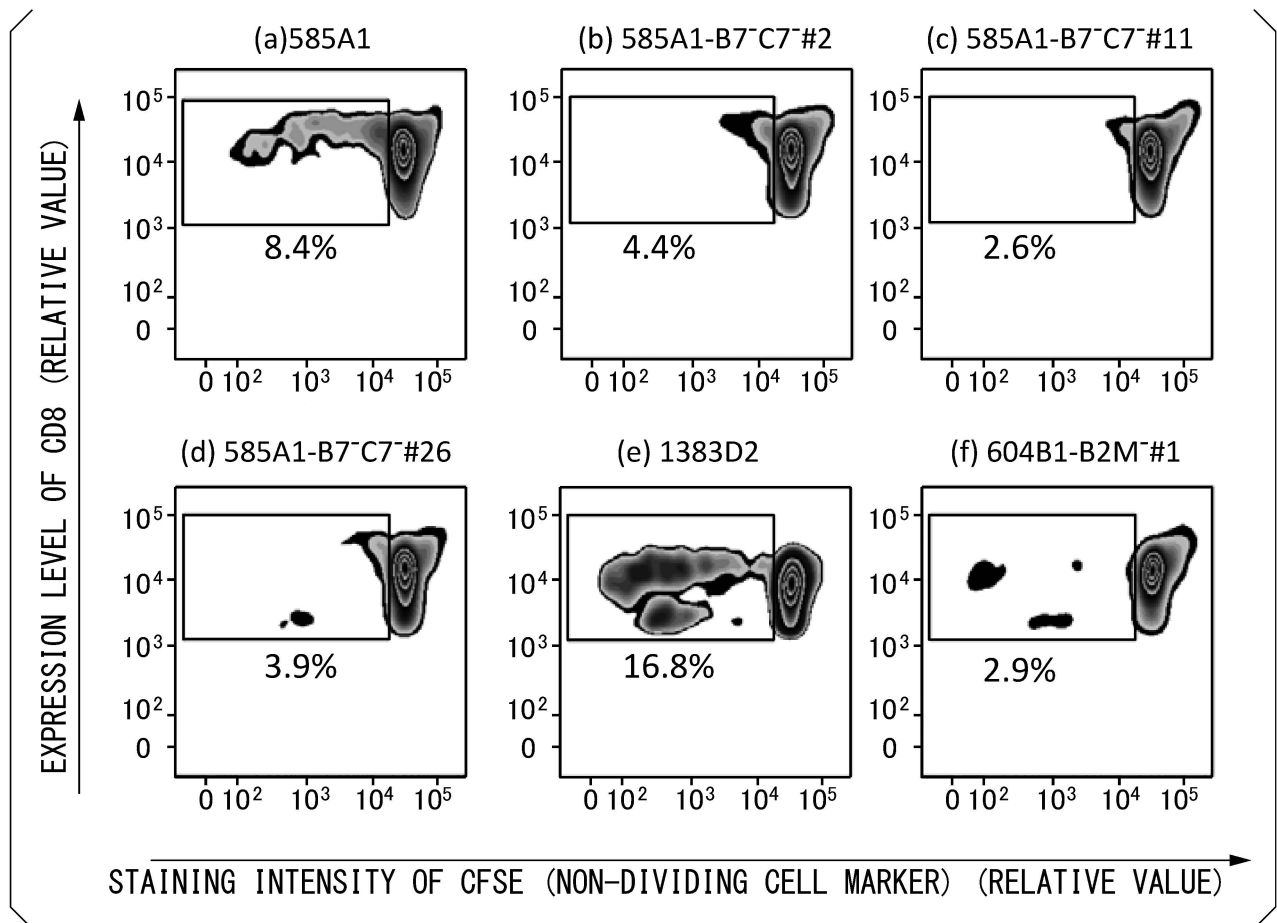


FIG.27

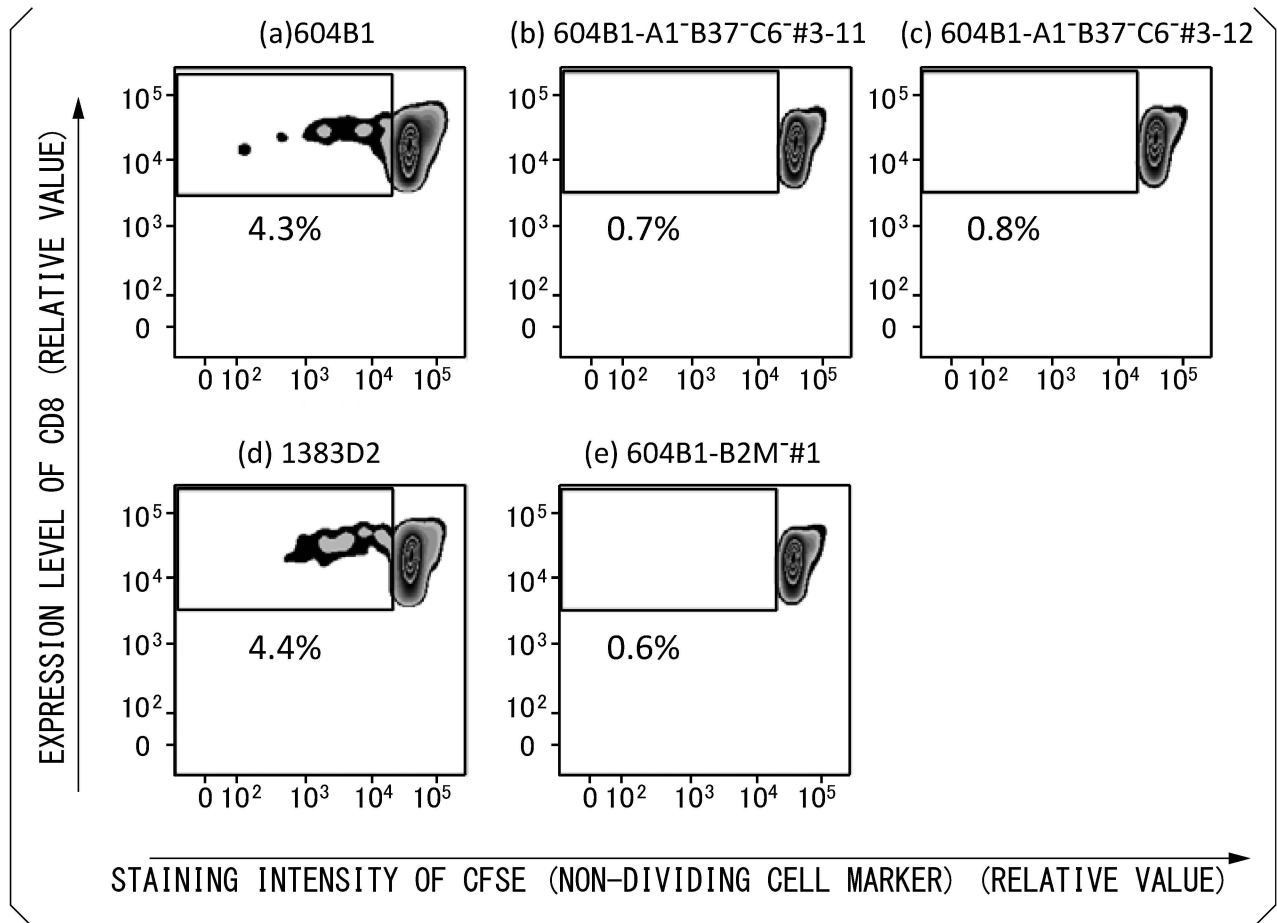


FIG.28

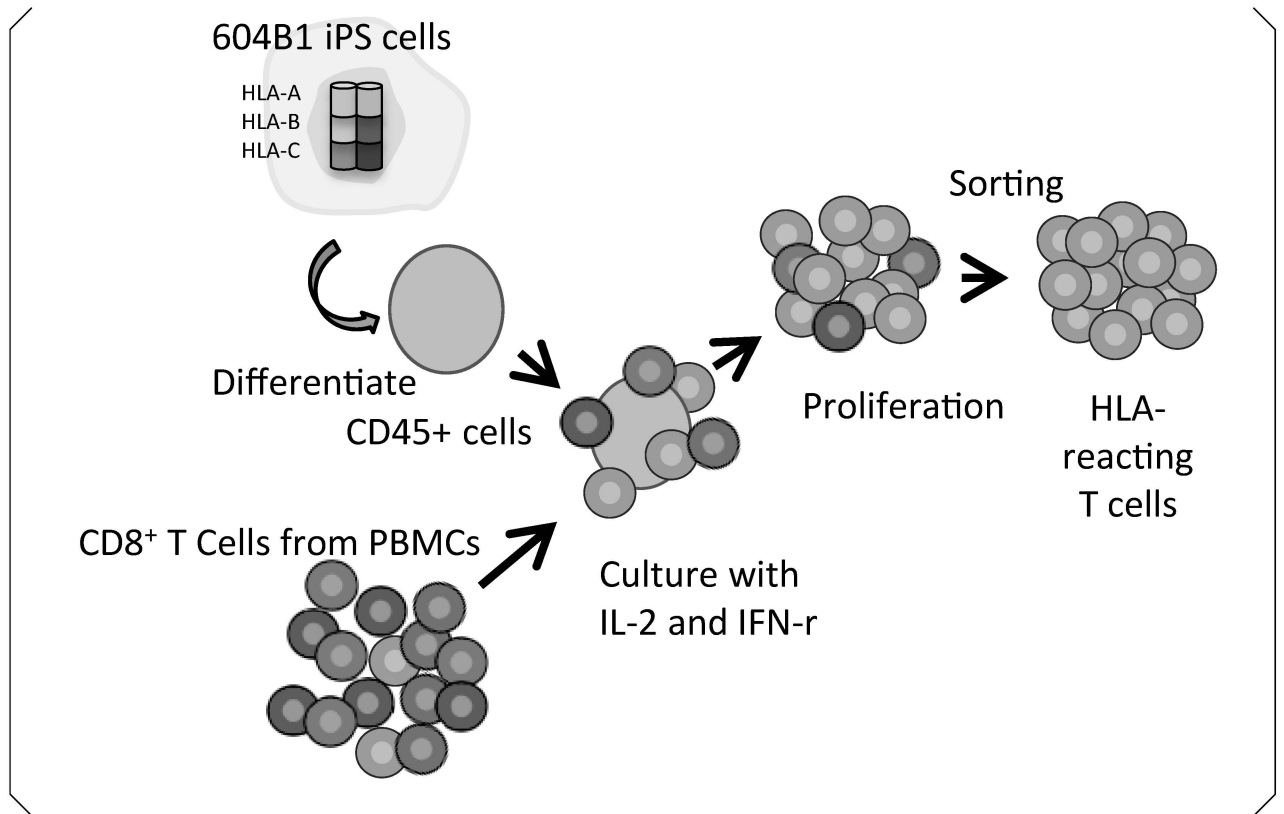


FIG.29

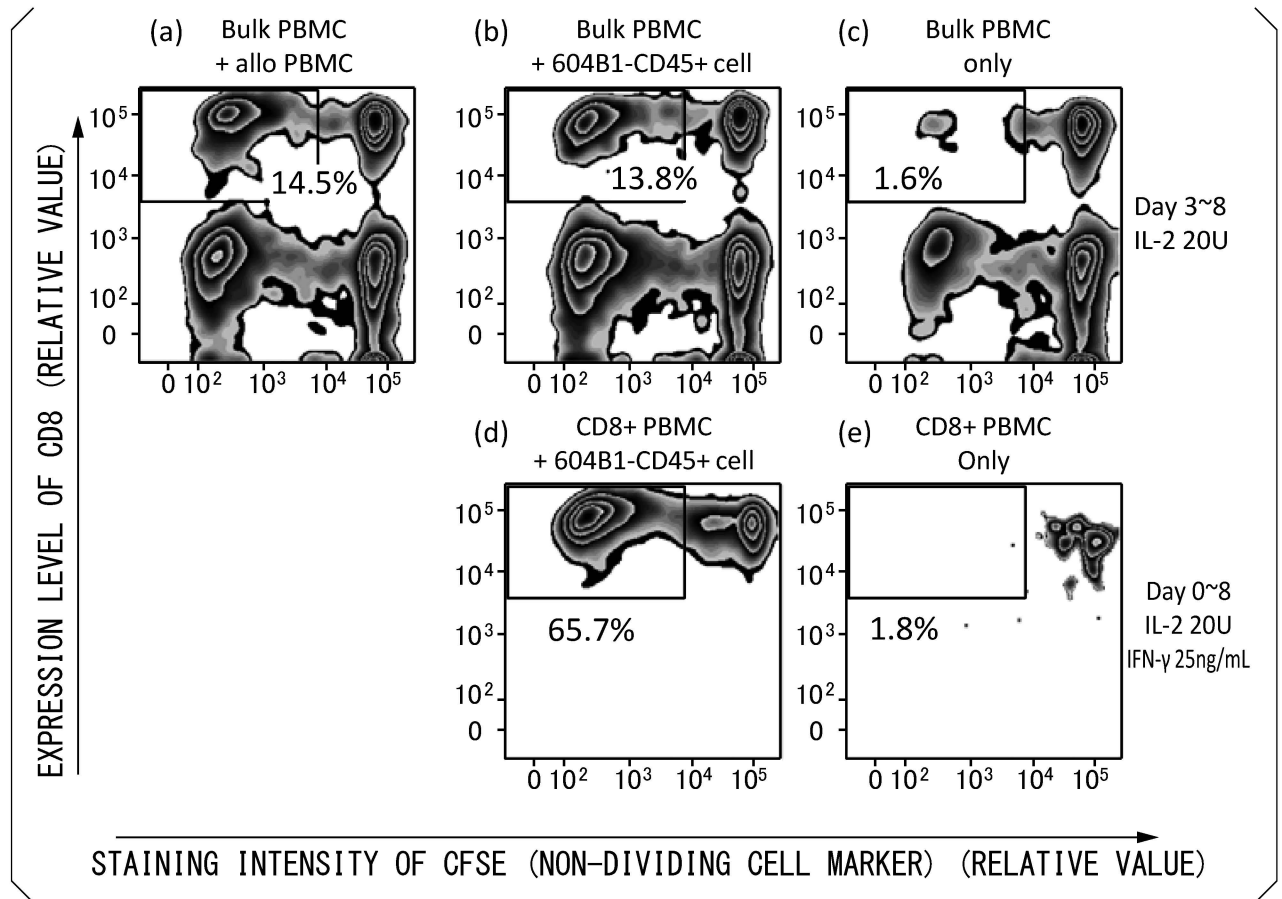


FIG.30

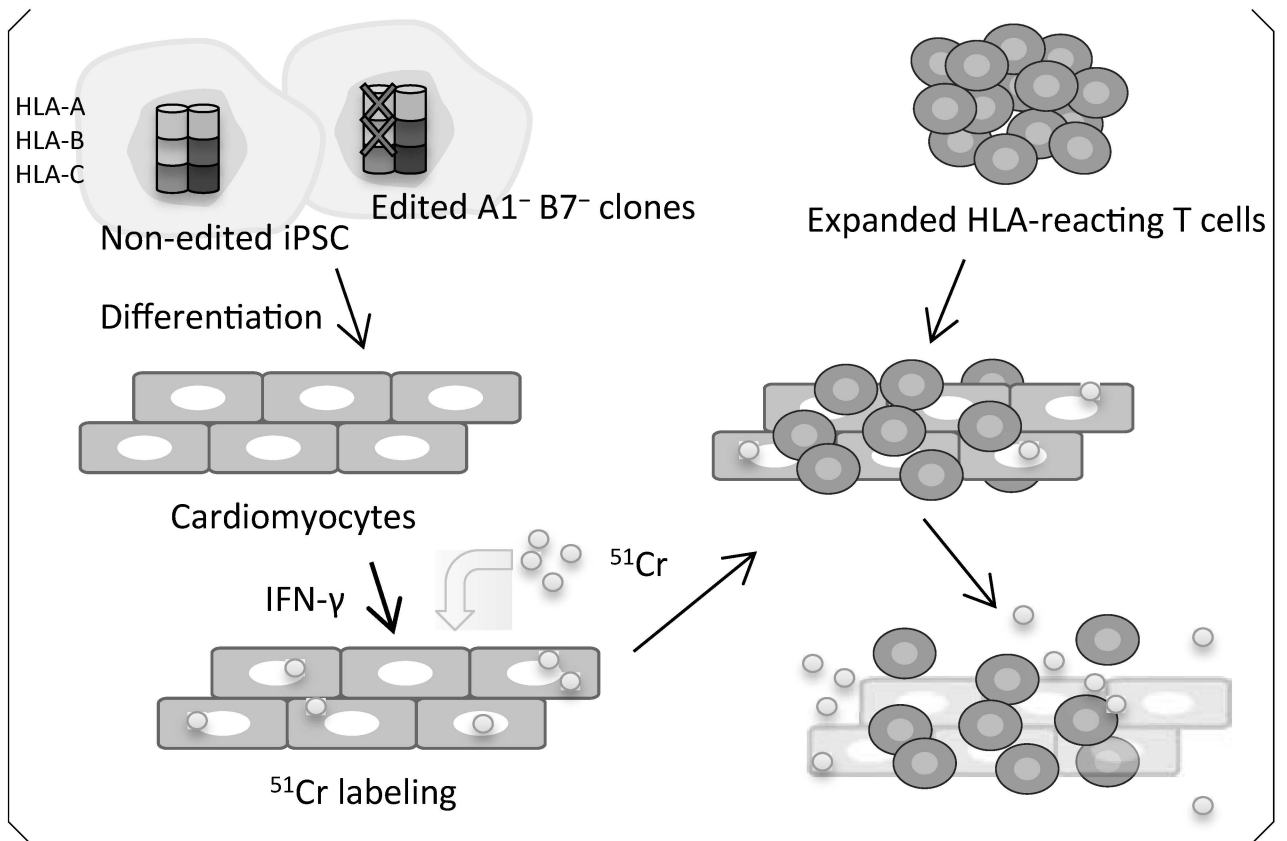


FIG.31

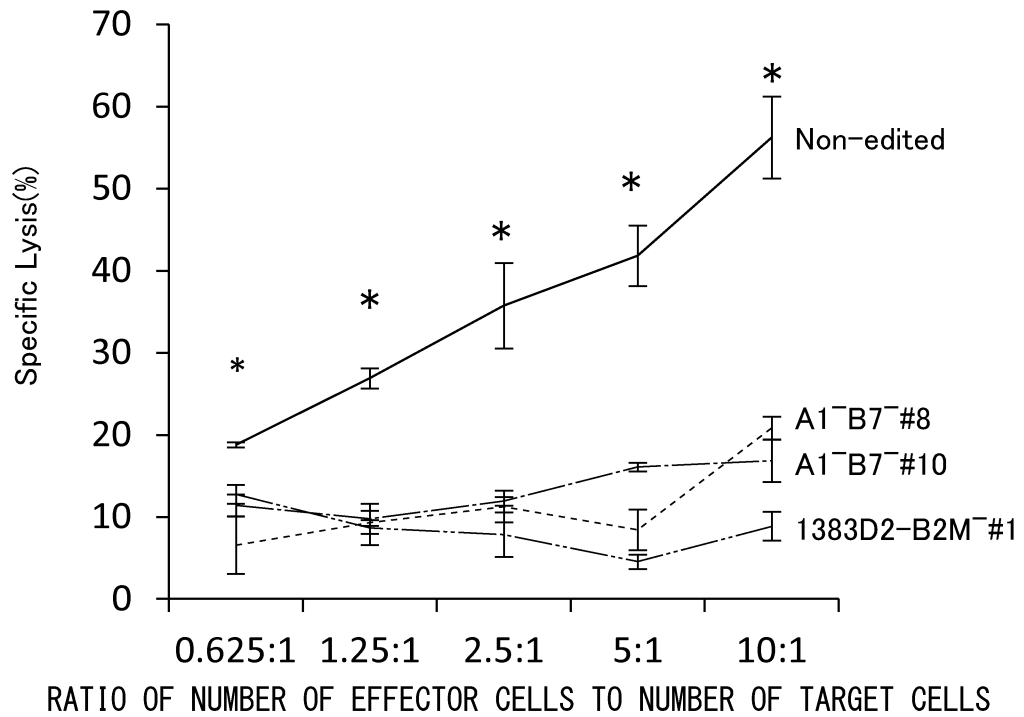


FIG.32

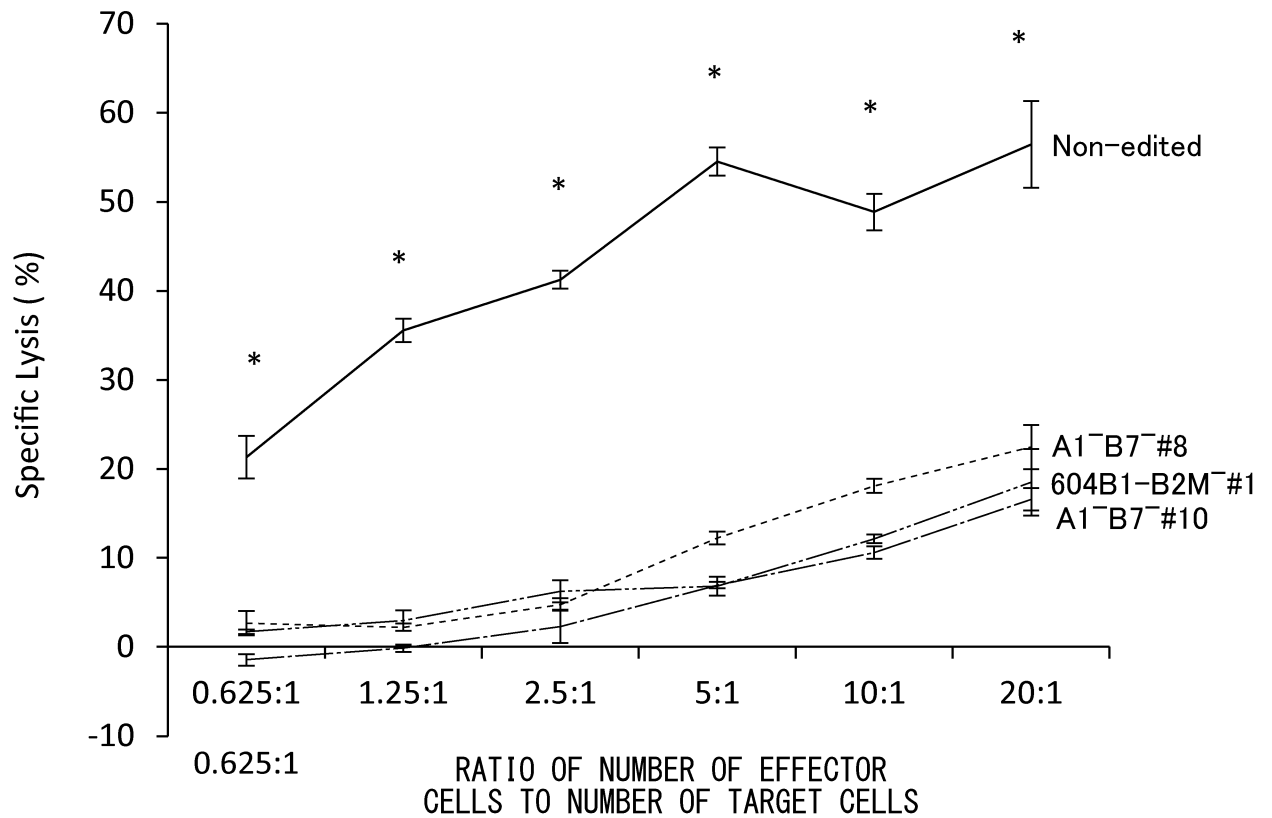


FIG.33

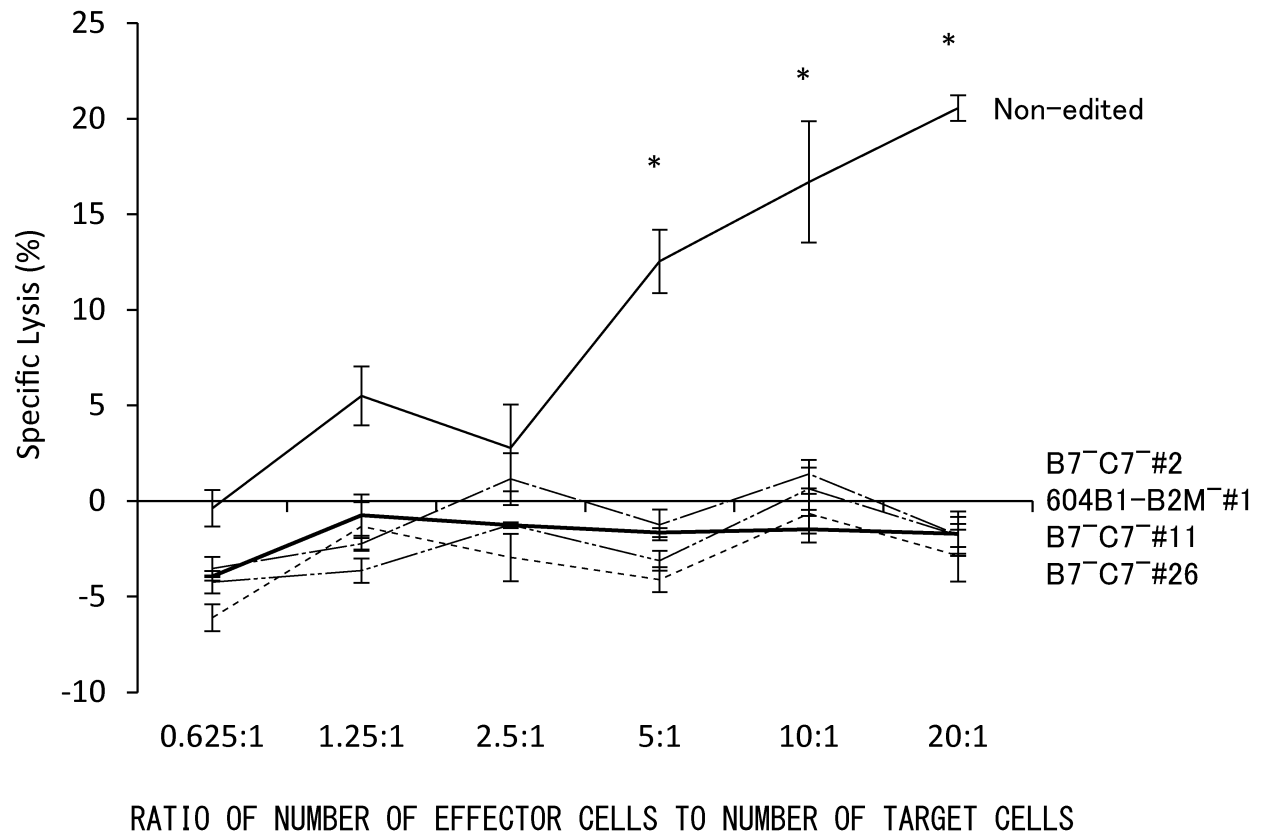


FIG.34

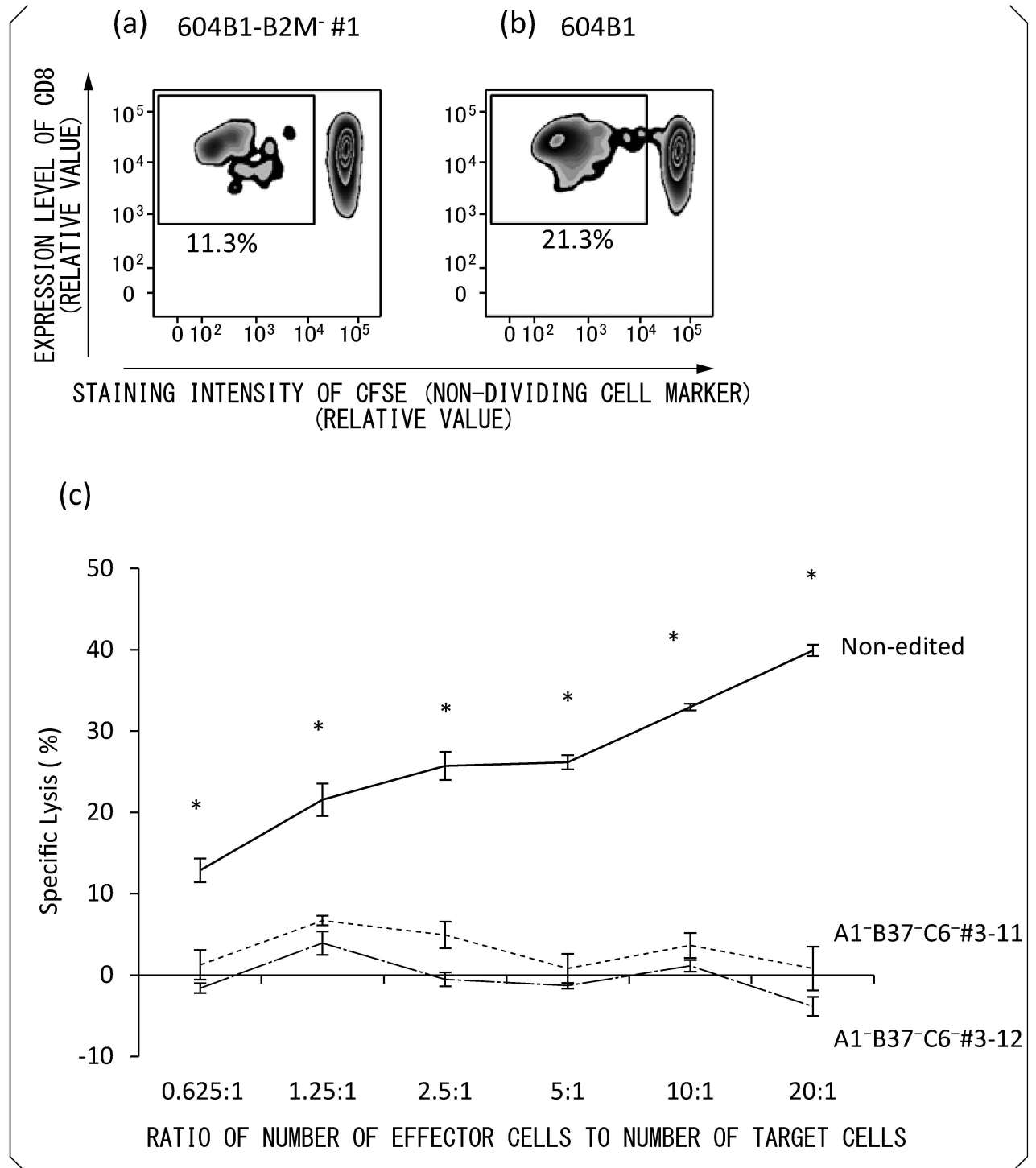


FIG.35

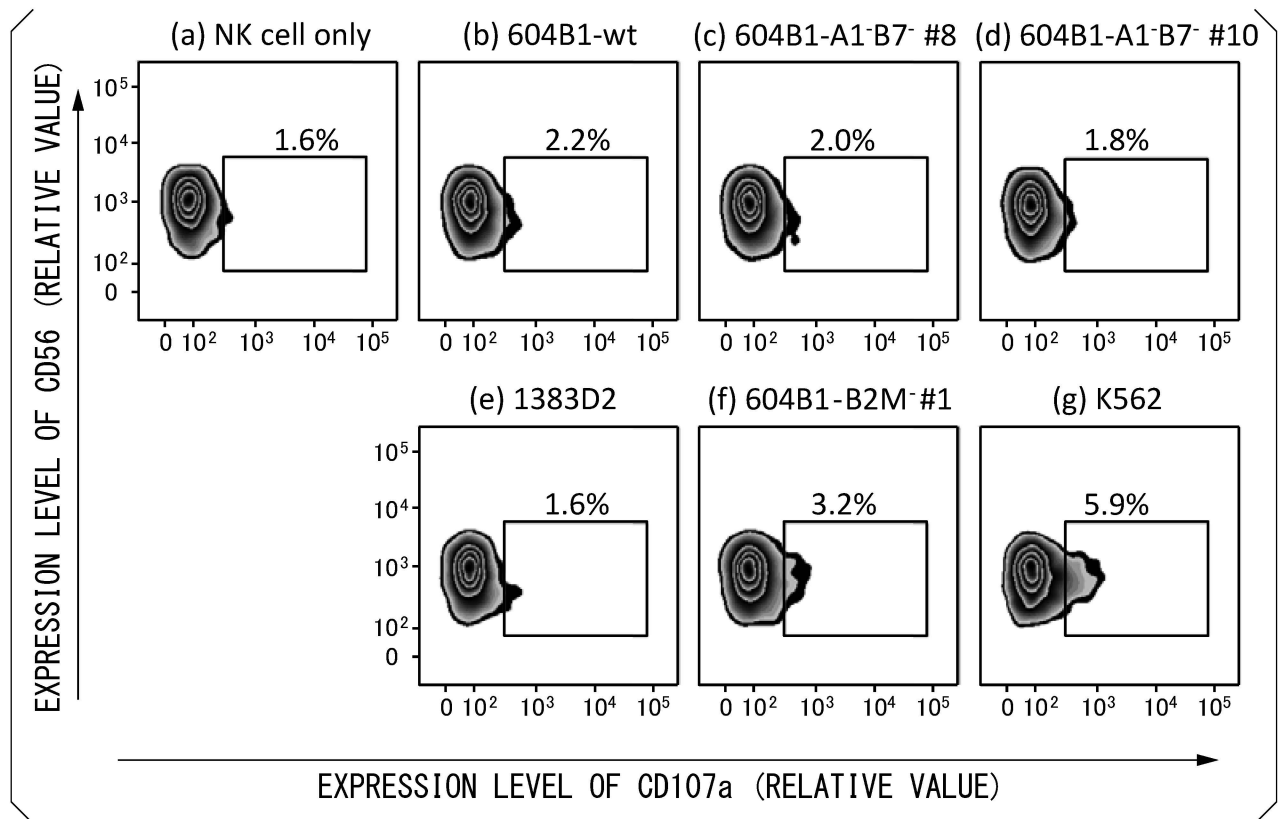


FIG.36

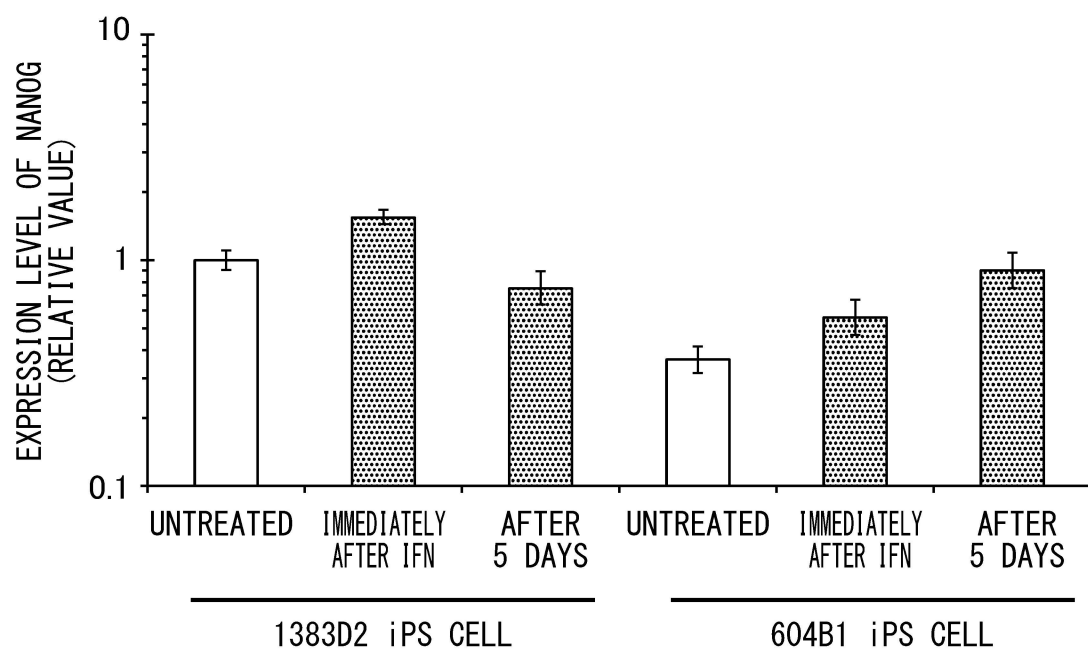


FIG.37

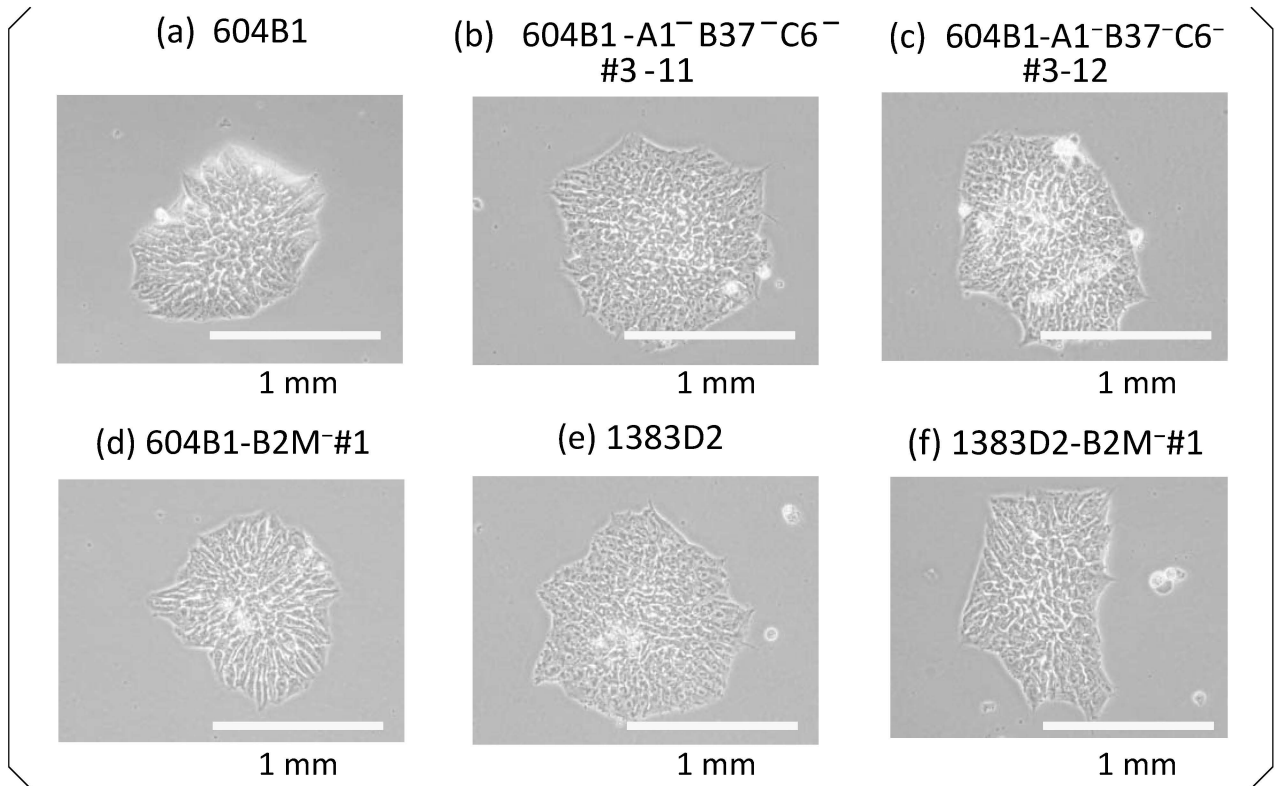


FIG.38

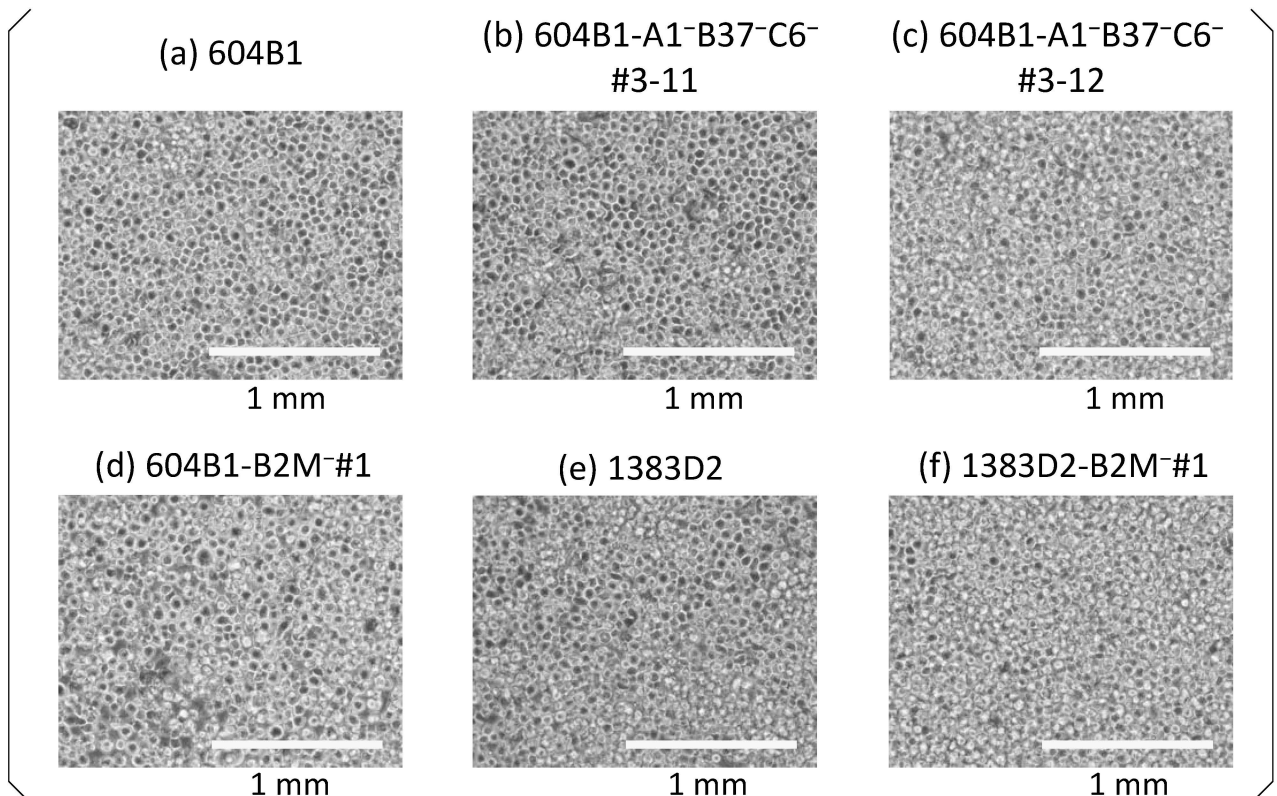


FIG.39

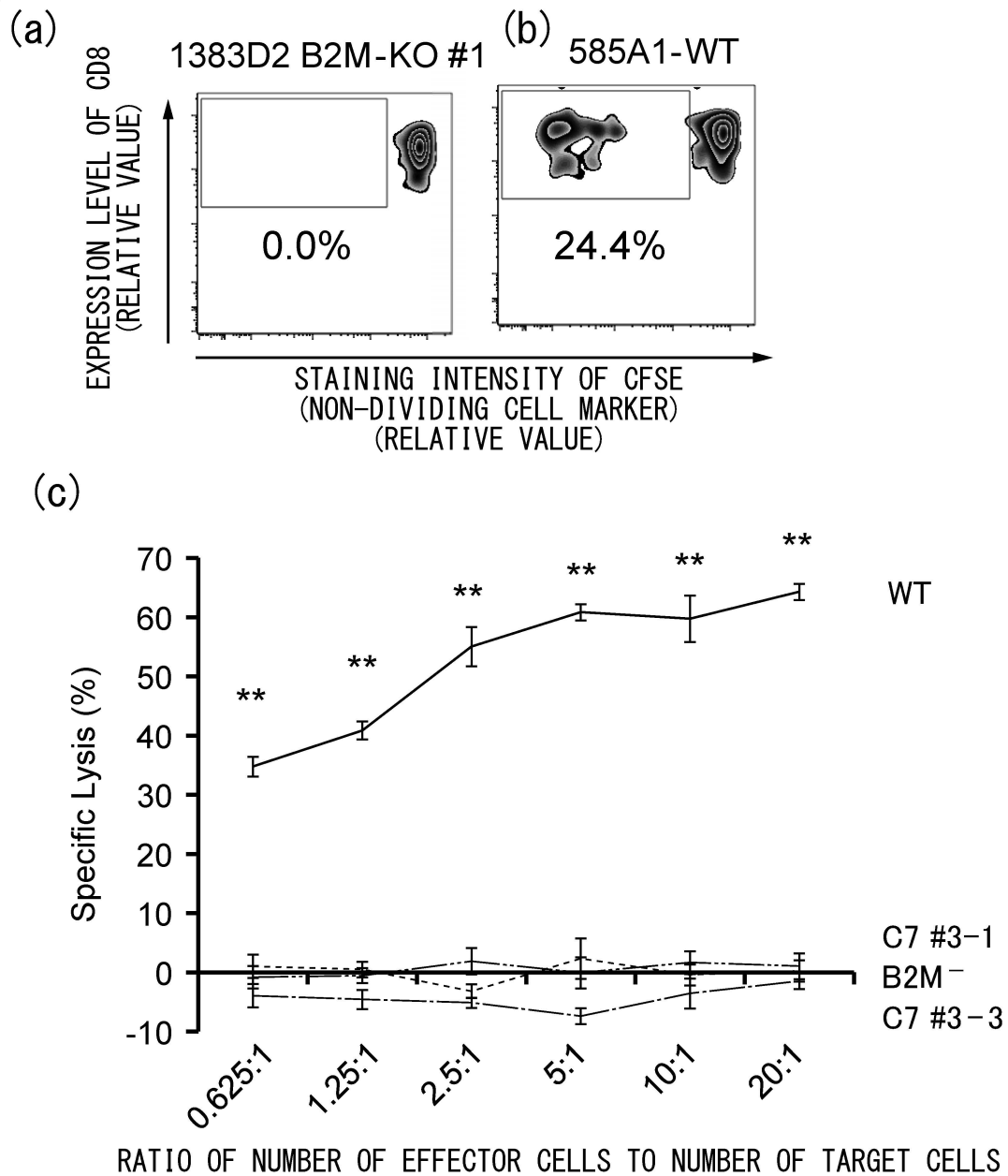


FIG.40

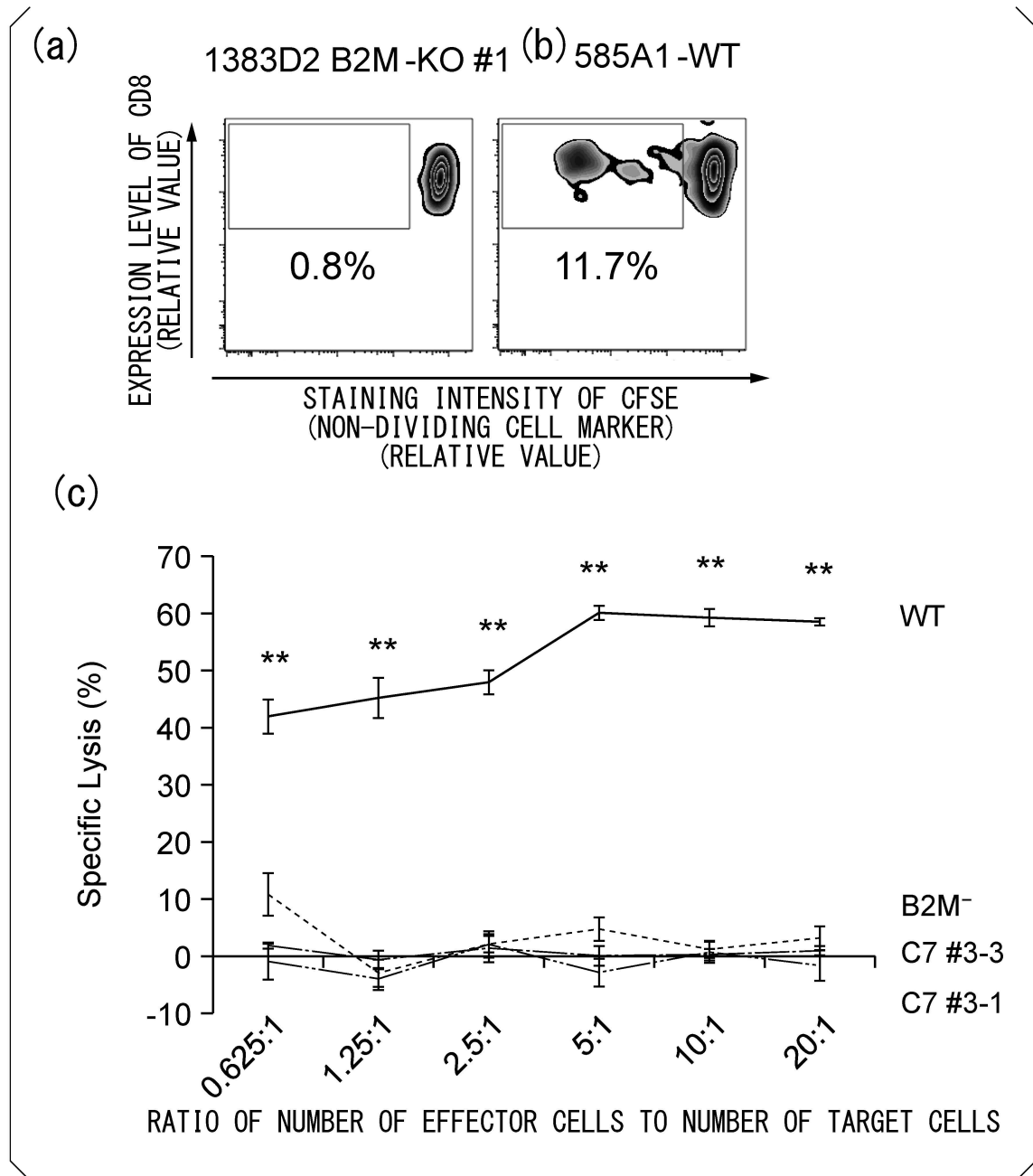


FIG.41

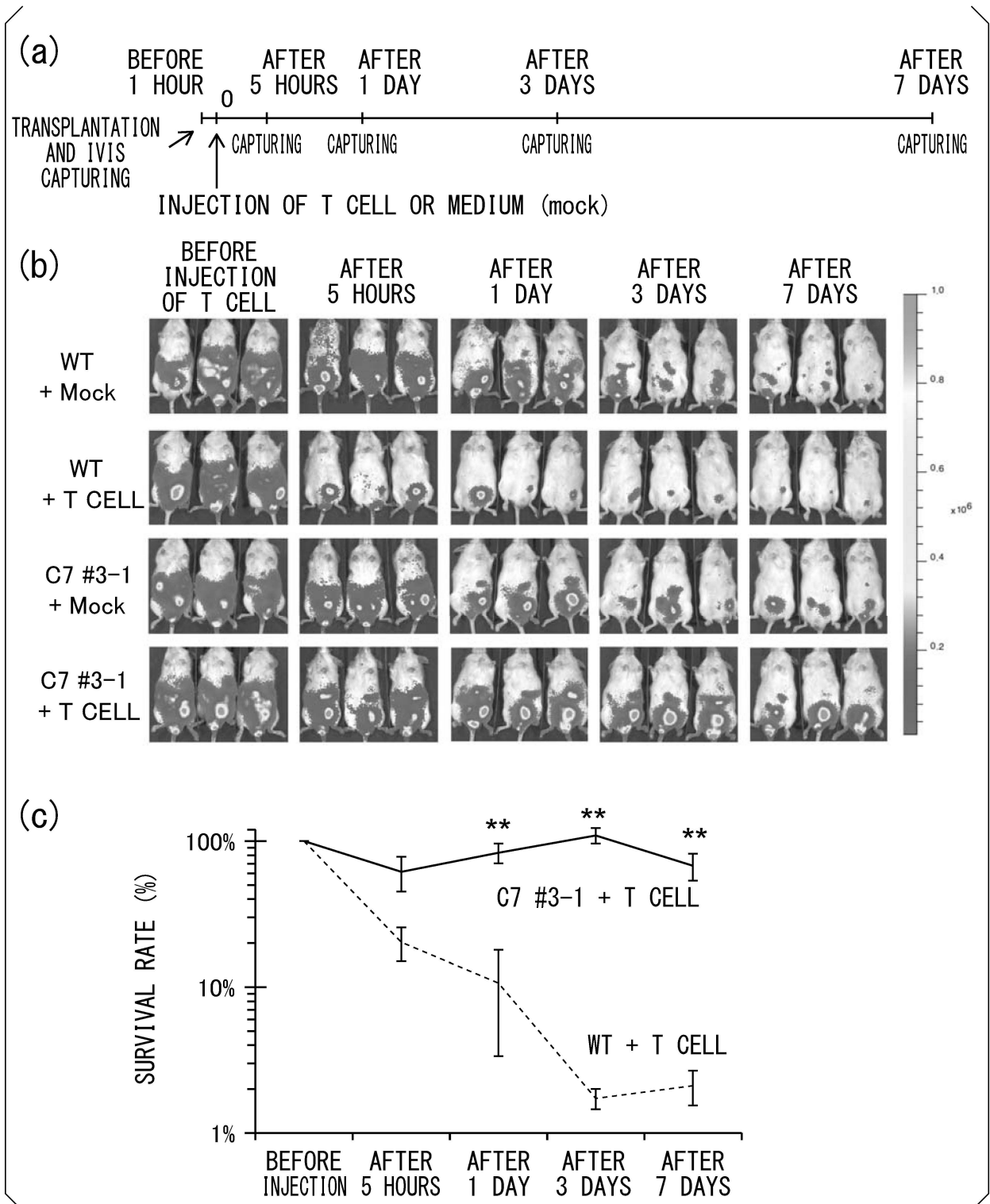
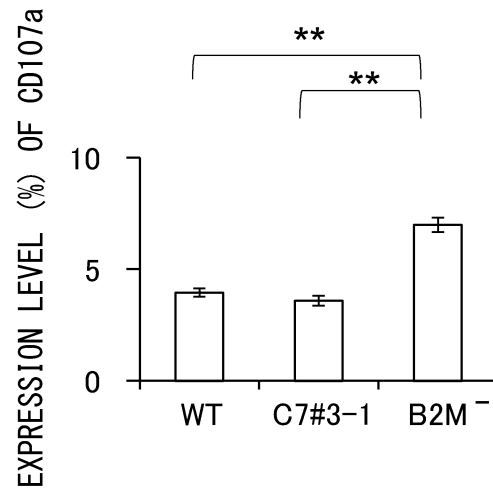


FIG.42

(a)



(b)

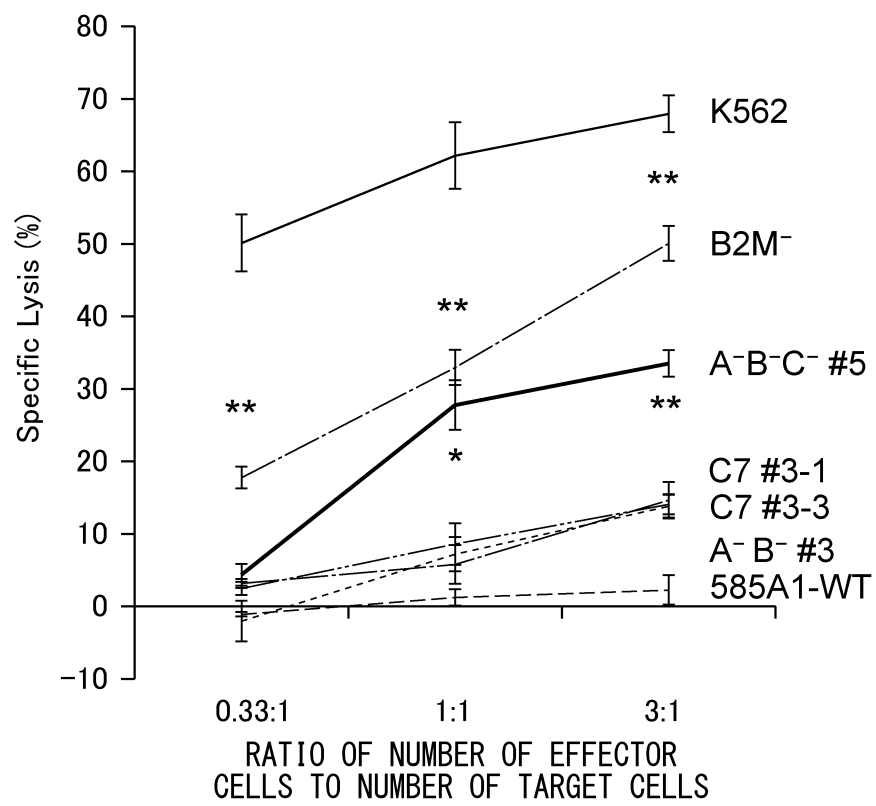


FIG.43

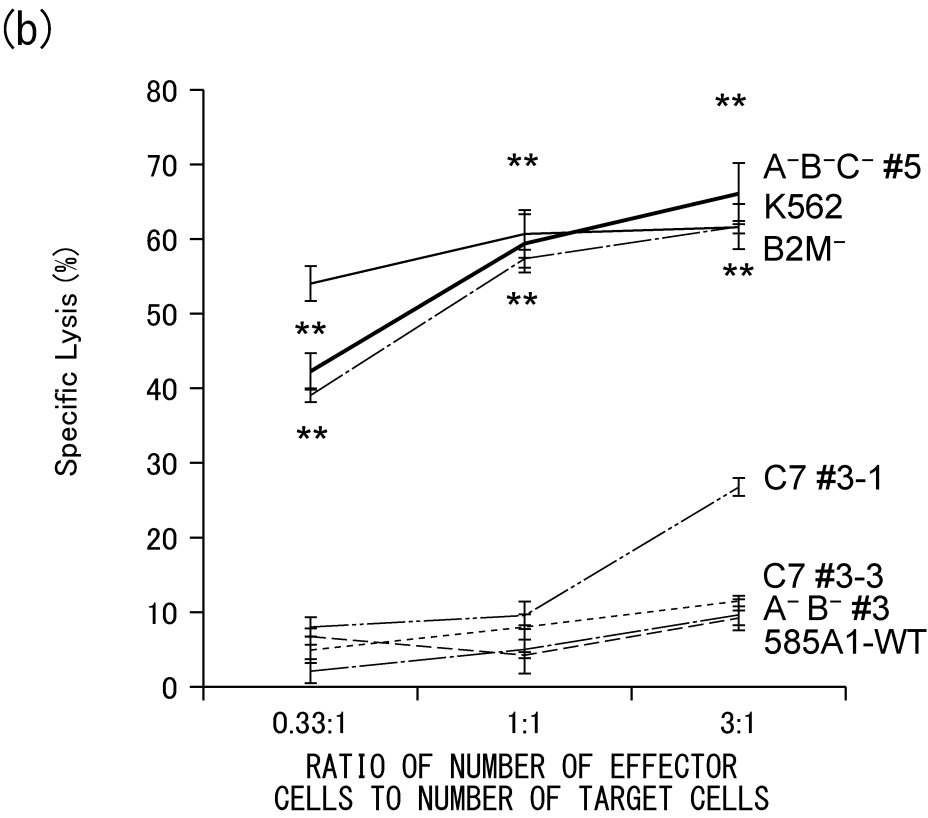
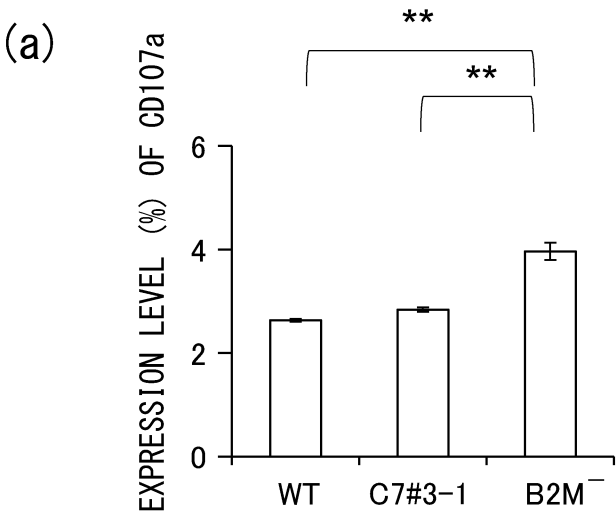
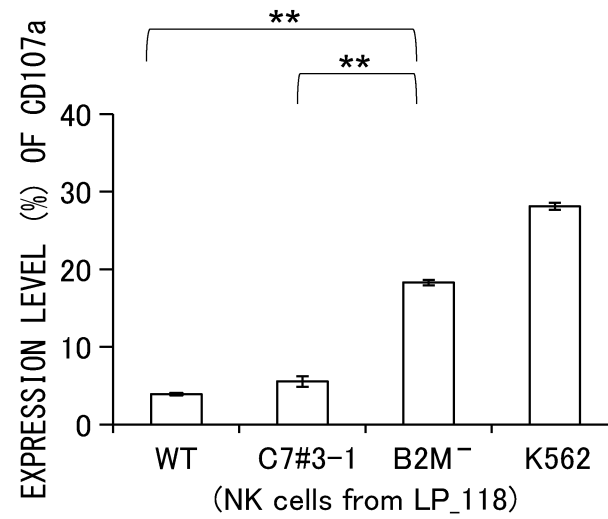


FIG.44

(a)



(b)

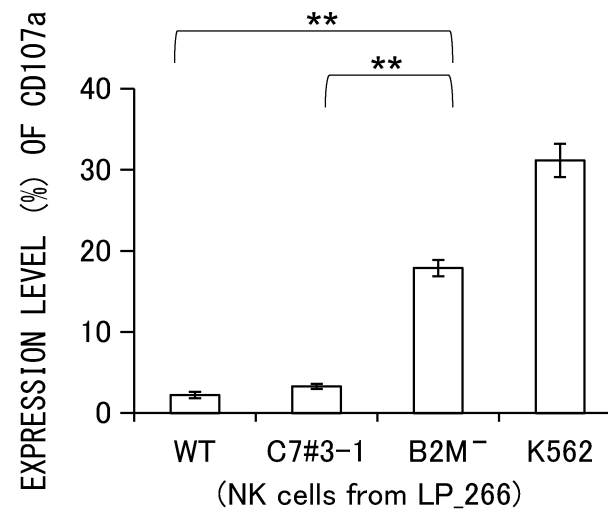


FIG.45

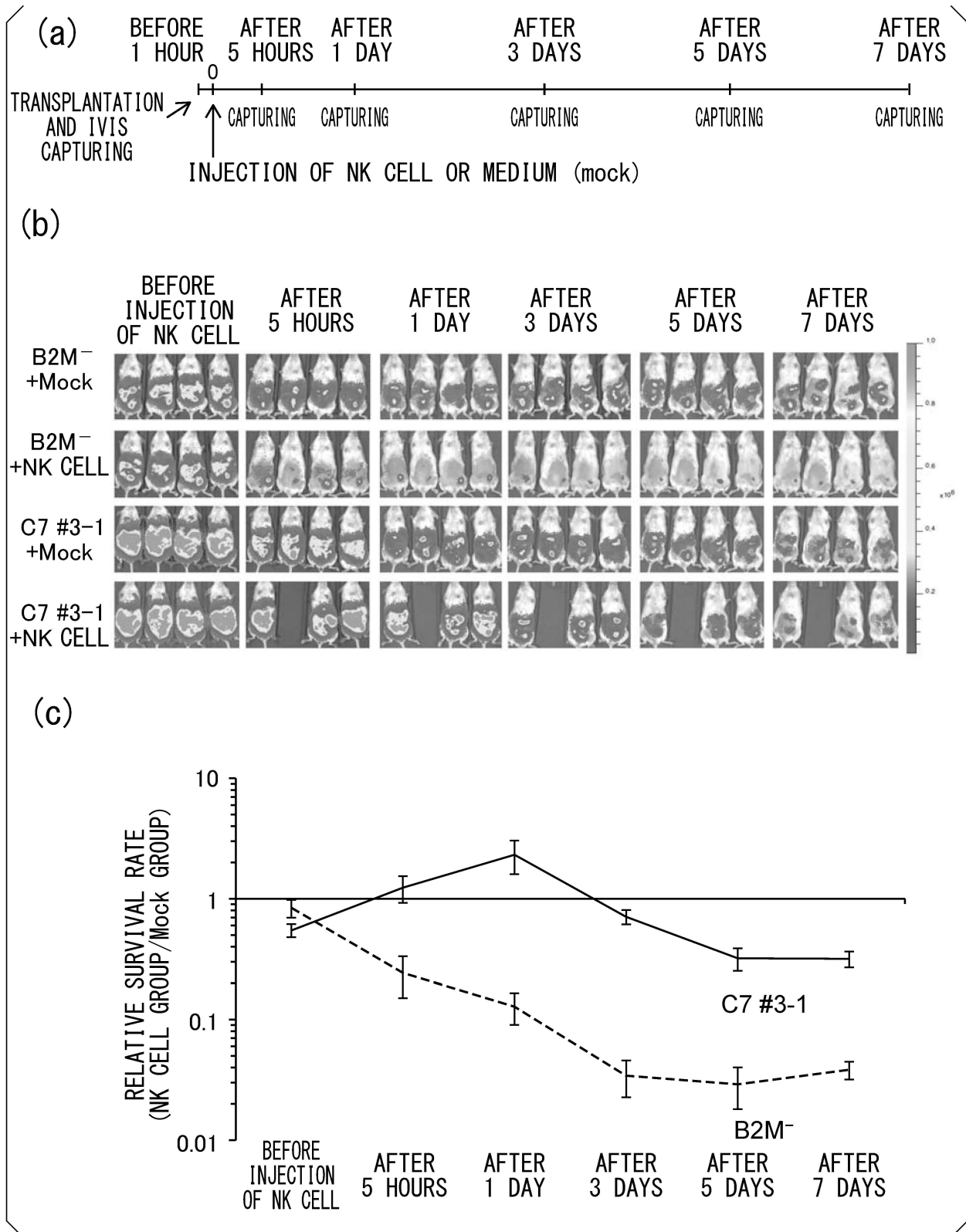


FIG.46

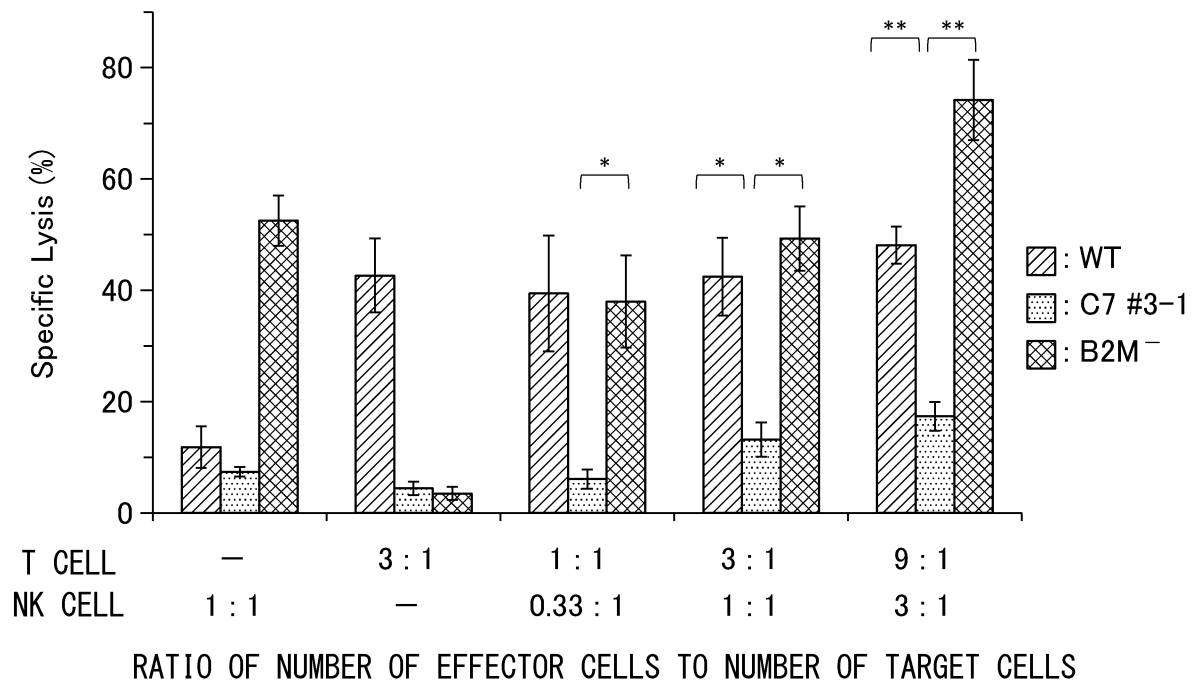


FIG.47

(a)

585A1-C7 RESIDUAL CELL			
HLA-A	HLA-B	HLA-C	DP/DQ/DR
~~A*24:02~~	~~B*07:02~~	C*07:02	CIITA
~~A*24:02~~	~~B*52:01~~	~~C*12:02~~	CIITA

585A1-C7 RESIDUAL CELL
(CLASS II DEFICIENCY)

↓ CIITA KO

HLA-A	HLA-B	HLA-C	DP/DQ/DR
~~A*24:02~~	~~B*07:02~~	C*07:02	~~CIITA~~
~~A*24:02~~	~~B*52:01~~	~~C*12:02~~	~~CIITA~~

(b)

Clone ID	CIITA	CIITA
#3-1-1	WT	+1 bp
#3-1-2	WT	WT
#3-1-3	+1 bp	-5 bp
#3-1-4	+1 bp	WT
#3-1-5	WT	WT
#3-1-6	+1 bp	-1 bp
#3-1-7	-13 bp	-13 bp
#3-1-8	WT	-1 bp
#3-1-9	-13 bp	+1 bp
#3-1-10	WT	WT
#3-1-11	WT	WT
#3-1-12	WT	+1 bp
#3-1-13	WT	-15 bp
#3-1-14	WT	WT
#3-1-18	+1 bp	+1 bp
#3-1-19	WT	WT
#3-1-20	WT	WT
#3-1-21	+2 bp	-10 bp
#3-1-22	+1 bp	+1 bp
#3-1-23	WT	WT
#3-1-24	WT	WT
#3-1-25	WT	+2 bp
#3-1-26	WT	WT
#3-1-27	WT	+1 bp
#3-1-28	WT	WT
#3-1-31	WT	WT
#3-1-32	+16 bp	-6 bp
#3-1-33	WT	WT

(c)

TARGET SEQUENCE OF sgRNA-CIITA-ex3g5

CIITA ACACCATCAACTGCGACCAGTTCAGCAGG SEQ ID NO: 8014

Allele 1 ACAC-----ACTGCGACCAGTTCAGCAGG SEQ ID NO: 8015

Allele 2 ACACCATCAACTGCGACCAGTTCAGCAGG SEQ ID NO: 8016

FIG.48

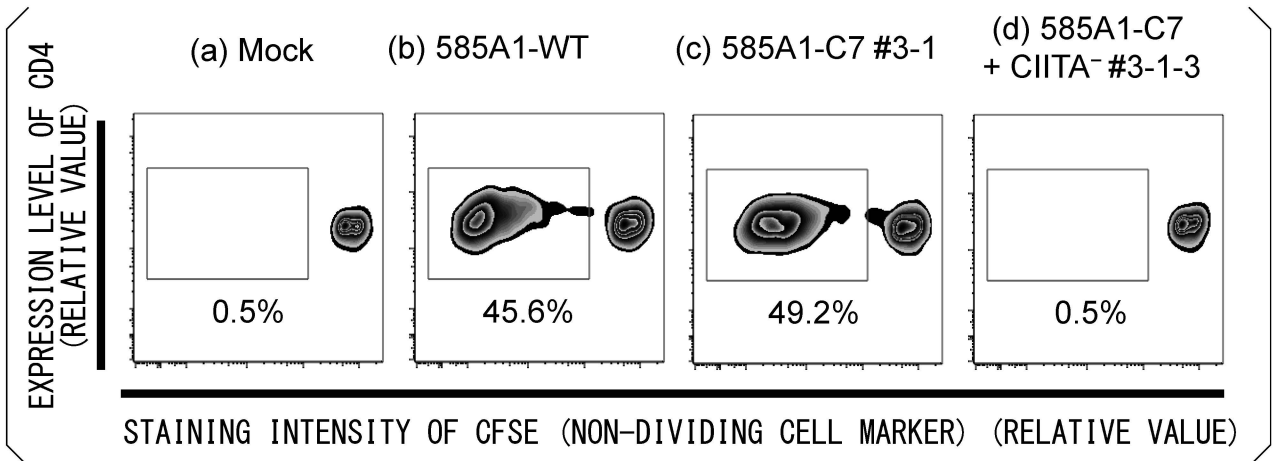


FIG.49

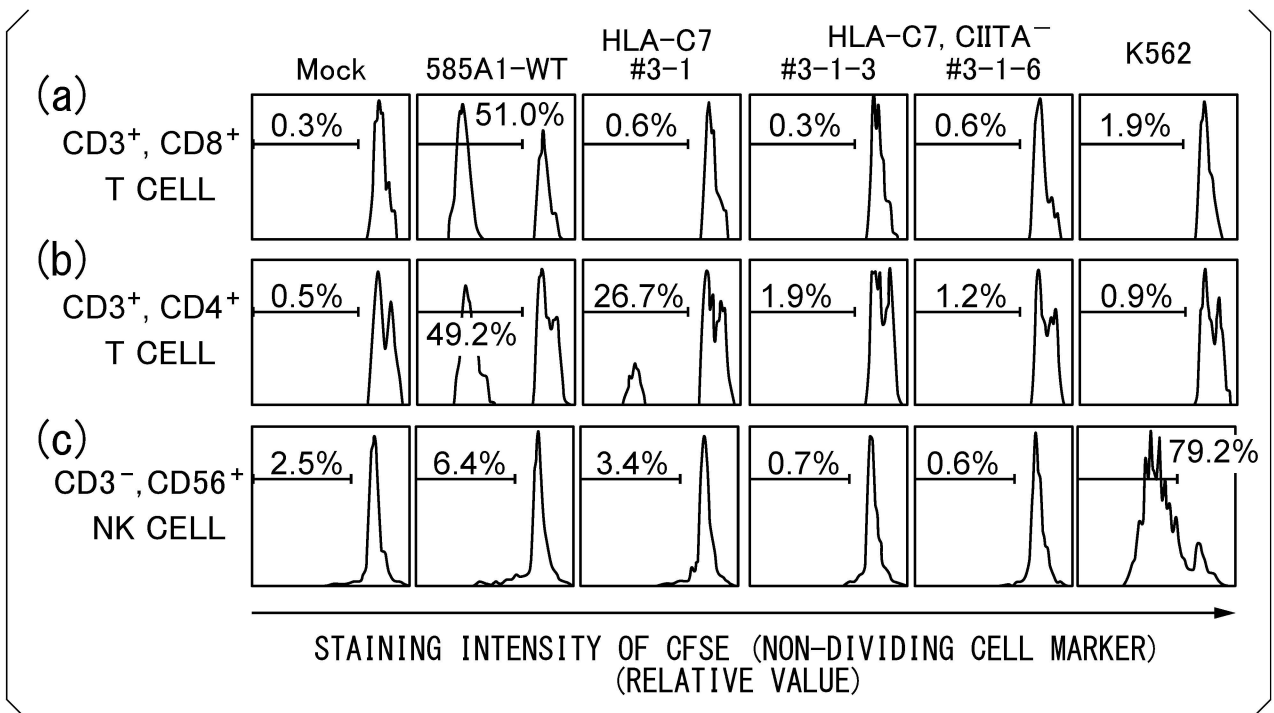


FIG.50

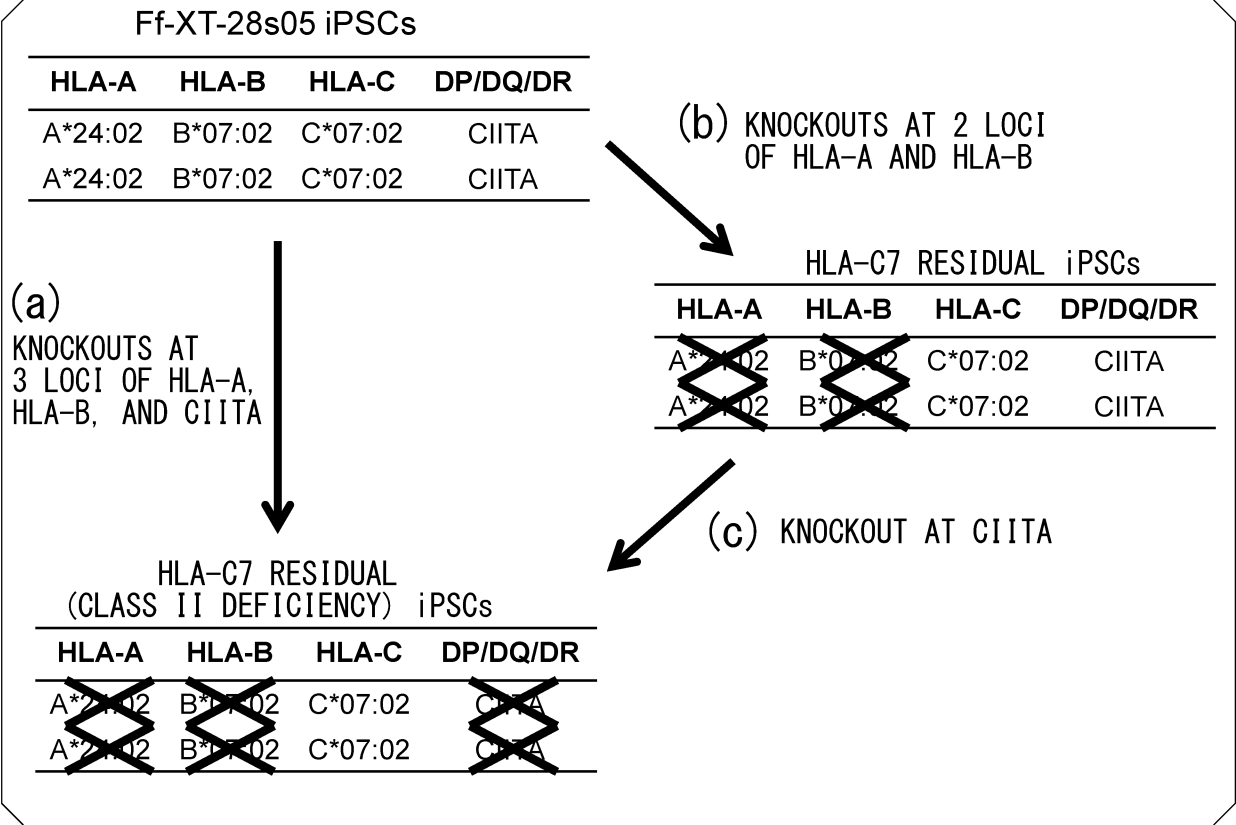
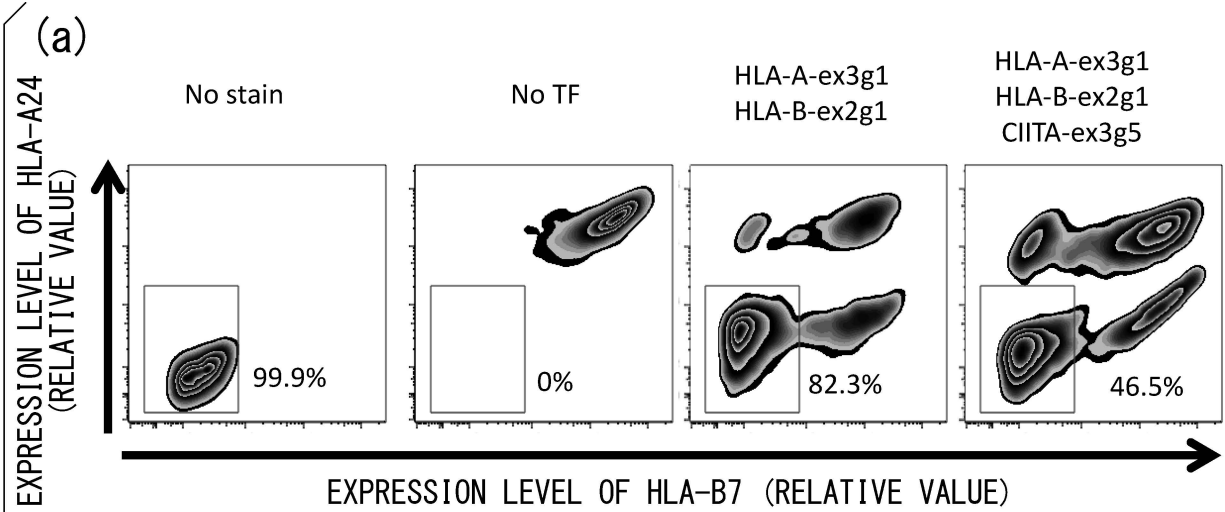


FIG.51



(b)

Clone ID	HLA-A24	HLA-A24	HLA-B7	HLA-B7	CIITA	CIITA
Ff-XT28s05-ABTo #1	+1 bp	+1 bp	-3 bp	-1 bp	+1 bp	+2 bp
Ff-XT28s05-ABTo #2	+1 bp	+1 bp	+2 bp	+2 bp	+1 bp	-1 bp
Ff-XT28s05-ABTo #3	+1 bp	+1 bp	-1 bp	-1 bp	+4 bp	-19 bp
Ff-XT28s05-ABTo #4	N.D.	N.D.	N.D.	N.D.	+200 bp	+200 bp
Ff-XT28s05-ABTo #5	N.D.	N.D.	N.D.	N.D.	WT	WT
Ff-XT28s05-ABTo #6	-11 bp	+1 bp	+1 bp	+1 bp	+1 bp	+1 bp
Ff-XT28s05-ABTo #7	N.D.	N.D.	N.D.	N.D.	-1 bp	WT
Ff-XT28s05-ABTo #8	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Ff-XT28s05-ABTo #9	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Ff-XT28s05-ABTo #10	N.D.	N.D.	N.D.	N.D.	+3 bp	+1 bp
Ff-XT28s05-ABTo #11	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Ff-XT28s05-ABTo #12	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Ff-XT28s05-ABTo #13	-11 bp	+1 bp	-2 bp	-2 bp	+1 bp	-1 bp
Ff-XT28s05-ABTo #14	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Ff-XT28s05-ABTo #15	-544 bp	-544 bp	-9 bp	-9 bp	-10 bp	+1 bp

FIG.52

(a)

Clone ID	HLA-A24	HLA-A24	HLA-B7	HLA-B7
Ff-XT28s05-ABo #1	+1 bp	-1 bp	WT	+1 bp
Ff-XT28s05-ABo #2	+1 bp	+1 bp	Mut.	Mut.
Ff-XT28s05-ABo #3	WT	+1 bp	WT	WT
Ff-XT28s05-ABo #4	WT	WT	WT	WT
Ff-XT28s05-ABo #5	WT	WT	WT	WT
Ff-XT28s05-ABo #6	WT	WT	WT	WT
Ff-XT28s05-ABo #9	+1 bp	-1 bp	WT	Mut.
Ff-XT28s05-ABo #10	WT	WT	WT	WT
Ff-XT28s05-ABo #11	WT	+1 bp	WT	Mut.
Ff-XT28s05-ABo #12	WT	WT	WT	WT
Ff-XT28s05-ABo #13	+1 bp	+1 bp	WT	+1 bp
Ff-XT28s05-ABo #14	+1 bp	+1 bp	+1 bp	-12 bp
Ff-XT28s05-ABo #15	WT	WT	WT	WT
Ff-XT28s05-ABo #16	WT	+1 bp	WT	WT
Ff-XT28s05-ABo #17	+1 bp	+1 bp	WT	-23 bp

(b)

Clone ID	CIITA	CIITA
Ff-XT28s05-ABo_To # 14-1	N.D.	N.D.
Ff-XT28s05-ABo_To # 14-2	N.D.	N.D.
Ff-XT28s05-ABo_To # 14-3	+2 bp	+2 bp
Ff-XT28s05-ABo_To # 14-4	+1 bp	+1 bp
Ff-XT28s05-ABo_To # 14-5	+5 bp	+12 bp
Ff-XT28s05-ABo_To # 14-6	+1 bp	+1 bp
Ff-XT28s05-ABo_To # 14-7	+1 bp	+12 bp
Ff-XT28s05-ABo_To #14-8	+1 bp	WT
Ff-XT28s05-ABo_To #14-9	+1 bp	+1 bp
Ff-XT28s05-ABo_To #14-10	+1 bp	WT
Ff-XT28s05-ABo_To #14-11	N.D.	N.D.
Ff-XT28s05-ABo_To #14-12	+1 bp	+1 bp

FIG.53

HLA-C ALLELE	JPN RANK	JPN ALLELE FREQUENCY	EUR RANK	EUR ALLELE FREQUENCY	AFA RANK	AFA ALLELE FREQUENCY	API RANK	API ALLELE FREQUENCY	HIS RANK	HIS ALLELE FREQUENCY
*01:02	1	17.558%	12	2.922%	19	0.850%	2	13.375%	7	4.927%
*02:02	19	0.025%	10	3.729%	5	8.461%	21	0.395%	10	4.227%
*03:03	2	13.116%	7	5.457%	16	1.182%	8	5.023%	12	3.402%
*03:04	4	12.451%	6	8.215%	8	5.330%	3	8.352%	4	6.978%
*04:01	9	4.441%	3	10.534%	1	18.457%	4	8.070%	1	16.508%
*05:01	15	0.376%	5	9.136%	10	3.526%	18	0.847%	9	4.652%
*06:02	13	0.797%	4	9.301%	4	8.855%	6	6.518%	5	5.878%
*07:01	18	0.076%	1	16.658%	2	12.401%	12	3.894%	3	10.355%
*07:02	3	12.634%	2	15.006%	7	6.968%	1	14.560%	2	11.281%
*08:01	6	7.370%	47	0.006%	24	0.124%	5	7.985%	14	2.826%
*12:02	5	11.142%	16	0.934%	23	0.145%	11	4.486%	17	1.301%
*16:01	N/A	0.000%	11	3.539%	3	9.788%	25	0.169%	6	5.053%
TOTAL ALLELE FREQUENCY		79.986%		85.437%		76.087%		73.674%		77.388%
TOTAL COVER RATE		95.994%		97.879%		94.282%		93.069%		94.887%

FIG.54

Clone ID	B2M	B2M
Ff-XT28s05-Mo #1	+1 bp	-1 bp
Ff-XT28s05-Mo #2	-8 bp	-15 bp
Ff-XT28s05-Mo #3	+1 bp	+1 bp
Ff-XT28s05-Mo #4	WT	WT
Ff-XT28s05-Mo #5	+1 bp	+6 bp

FIG.55

Clone ID	B2M	B2M	CIITA	CIITA
Ff-XT28s05-MTo #1	-21 bp	-2 bp	WT	WT
Ff-XT28s05-MTo #2	+1 bp	WT	+1 bp	+1 bp
Ff-XT28s05-MTo #3	+1 bp	WT	WT	WT
Ff-XT28s05-MTo #4	+1 bp	WT	WT	-13 bp
Ff-XT28s05-MTo #5	+1 bp	+1 bp	-15 bp	+1 bp
Ff-XT28s05-MTo #6	+1 bp	+1 bp	+1 bp	WT
Ff-XT28s05-MTo #7	+1 bp	+1 bp	+1 bp	WT
Ff-XT28s05-MTo #8	+1 bp	+1 bp	-7 bp	+1 bp
Ff-XT28s05-MTo #9	+1 bp	WT	-20 bp	WT
Ff-XT28s05-MTo #10	+1 bp	+1 bp	+1 bp	WT
Ff-XT28s05-MTo #11	+1 bp	-1 bp	+1 bp	WT
Ff-XT28s05-MTo #12	+1 bp	+1 bp	+1 bp	WT
Ff-XT28s05-MTo #13	+1 bp	+1 bp	-1 bp	WT
Ff-XT28s05-MTo #14	+1 bp	+1 bp	+1 bp	WT
Ff-XT28s05-MTo #15	+1 bp	+1 bp	-18 bp	-27 bp
Ff-XT28s05-MTo #16	WT	WT	WT	WT
Ff-XT28s05-MTo #17	-13 bp	-8 bp	WT	WT
Ff-XT28s05-MTo #18	+1 bp	+1 bp	-29 bp	WT
Ff-XT28s05-MTo #19	+1 bp	+1 bp	-1 bp	WT

FIG.56

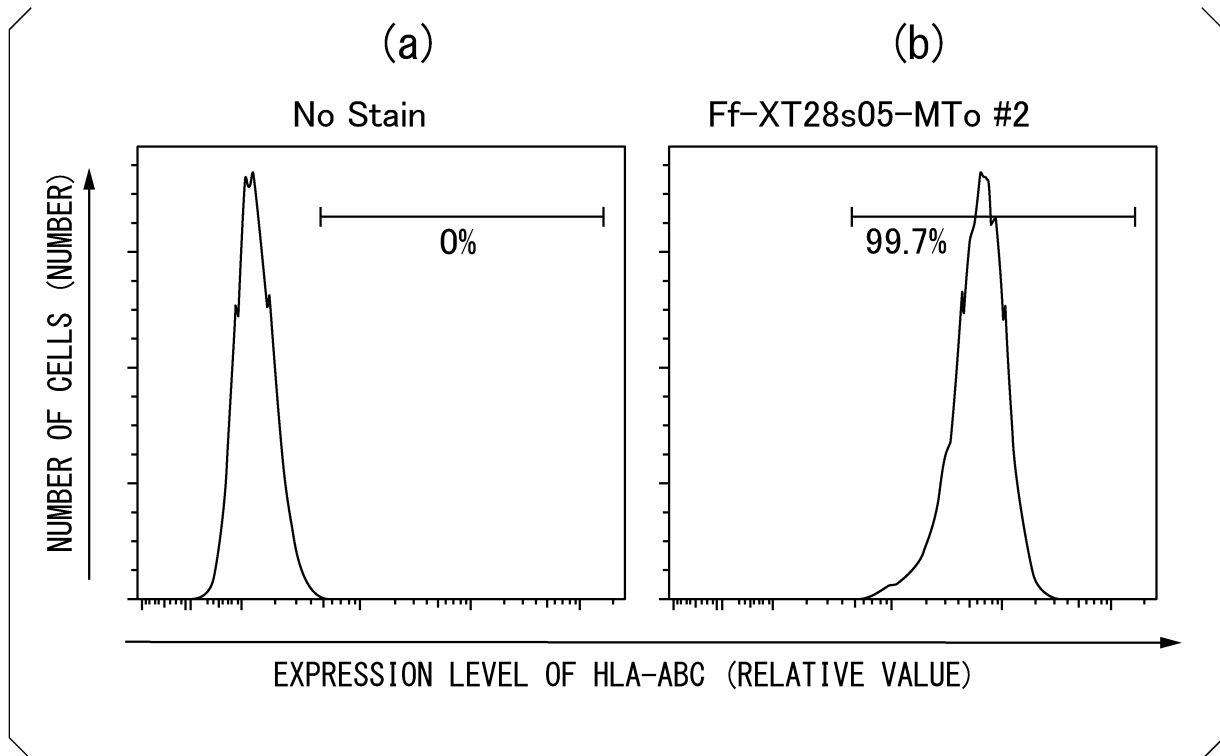


FIG.57

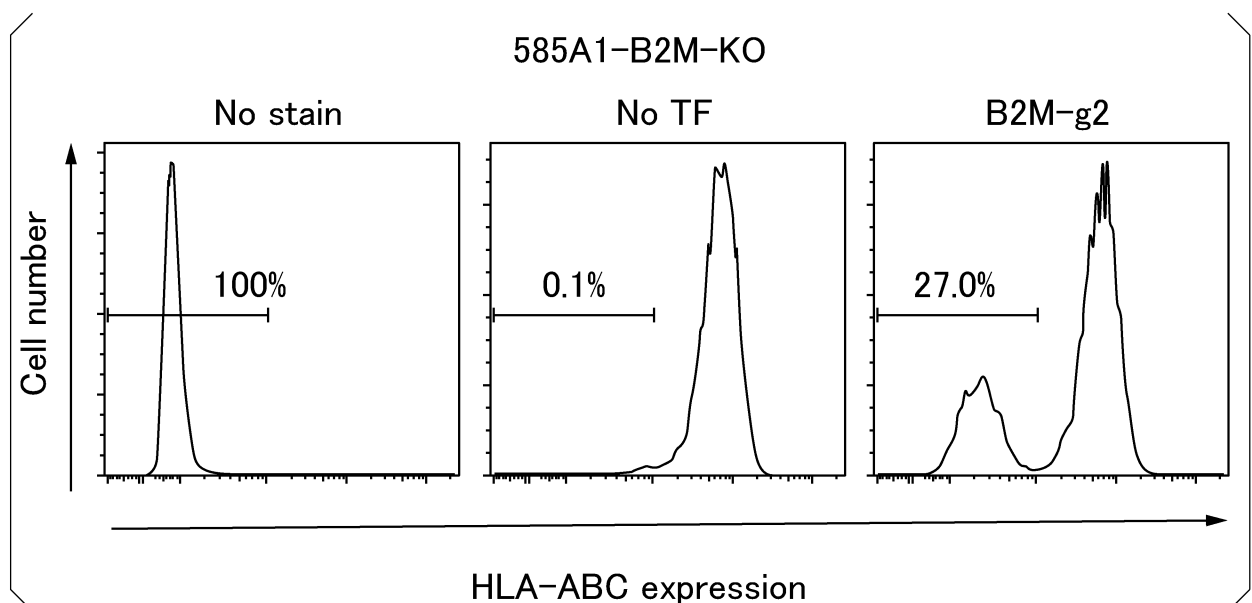


FIG.58

Clone ID	HLA-C07	HLA-C12
#3-2	WT	-3 bp
#3-3	WT	+198 bp
#3-4	-2 bp	+197 bp
#3-5	+1 bp	-21 bp
#3-6	+1 bp	-7 bp
#3-7	+2 bp	-7 bp

FIG.59

Clone ID	HLA-C07	HLA-C12
#3-1	+1 bp	WT
#3-2	+1 bp	WT
#3-3	+1 bp	WT
#3-4	WT	WT
#3-5	+1 bp	WT
#3-6	+1 bp	WT

FIG.60

Clone ID	HLA-C06	HLA-C07
#4-1	WT	WT
#4-2	WT	-4 bp
#4-3	WT	WT
#4-4	WT	WT
#4-5	WT	WT
#4-6	WT	+1 bp
#4-7	WT	WT
#4-8	WT	WT
#4-10	WT	+1 bp
#4-11	WT	+1 bp
#4-12	WT	WT