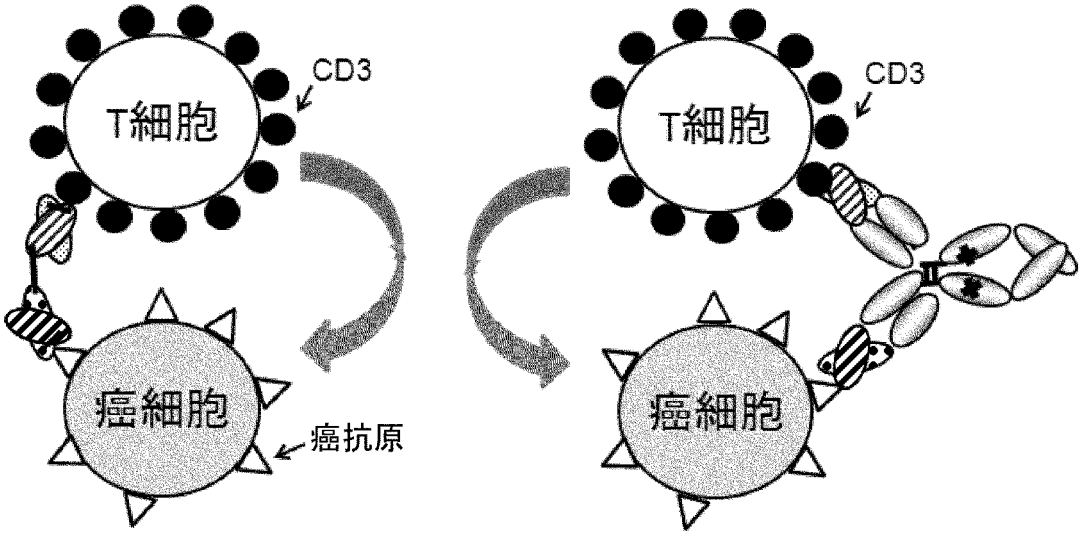
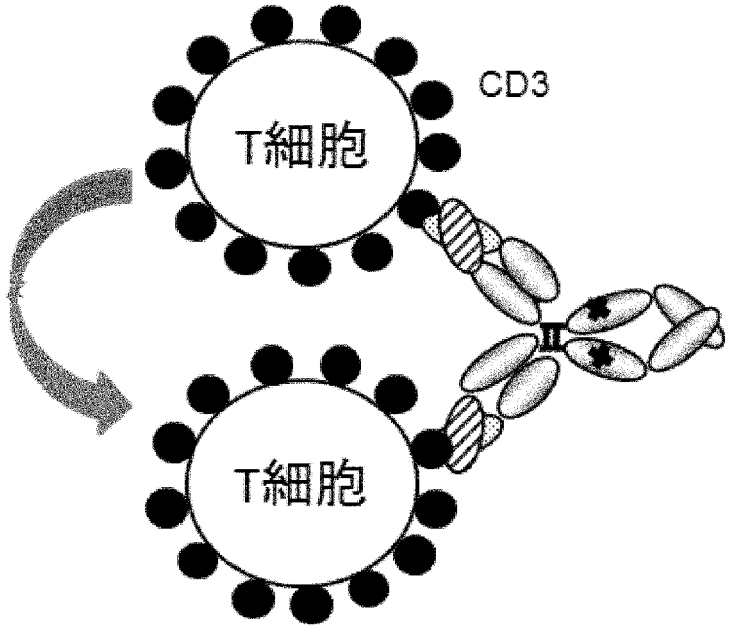
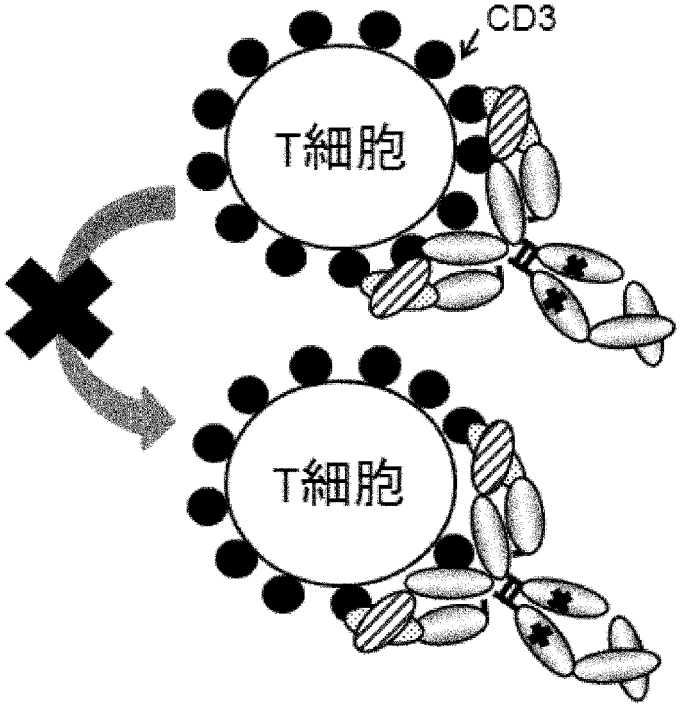
[図1]



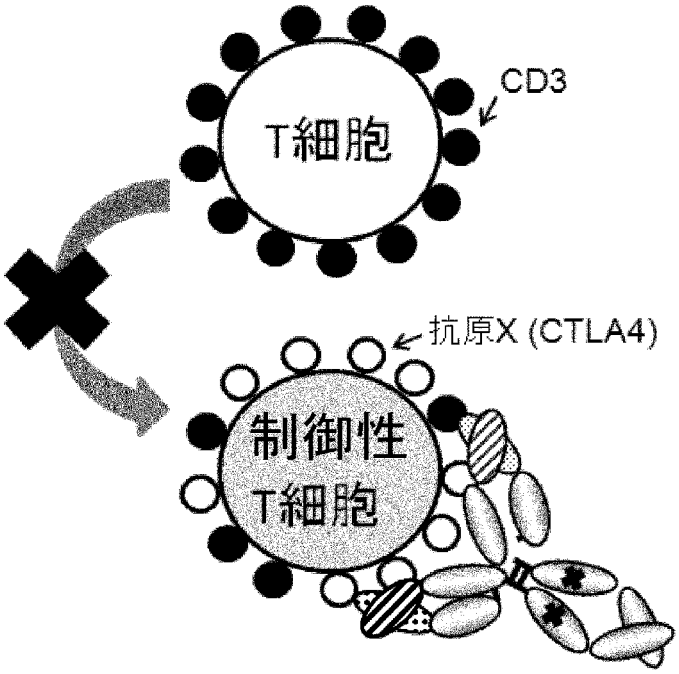
[図2-1]



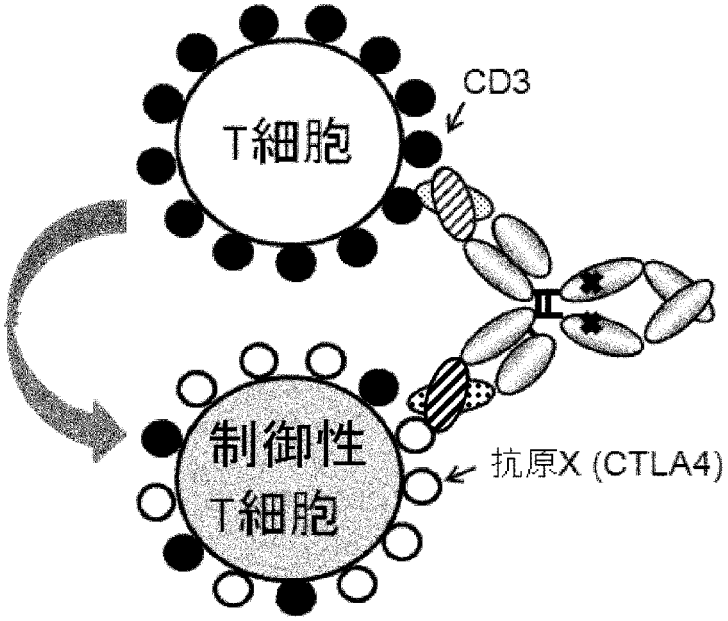
[図2-2]



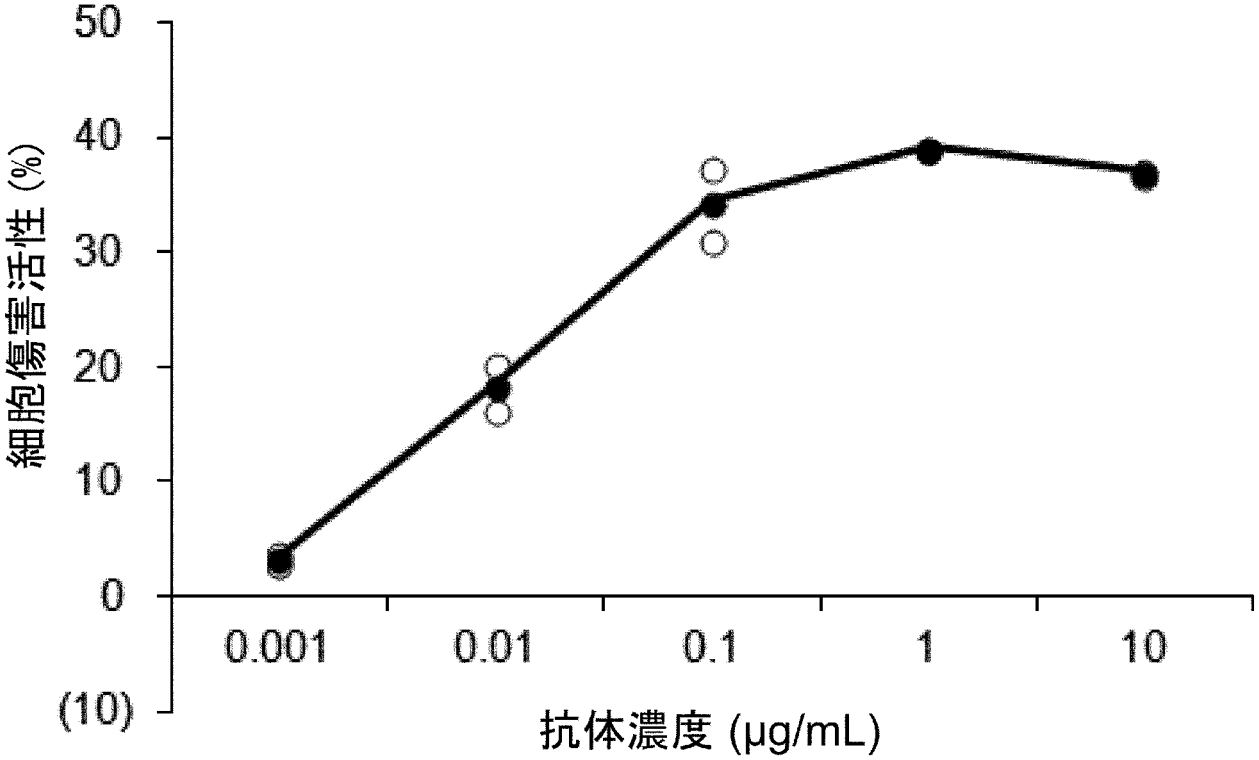
[図3]



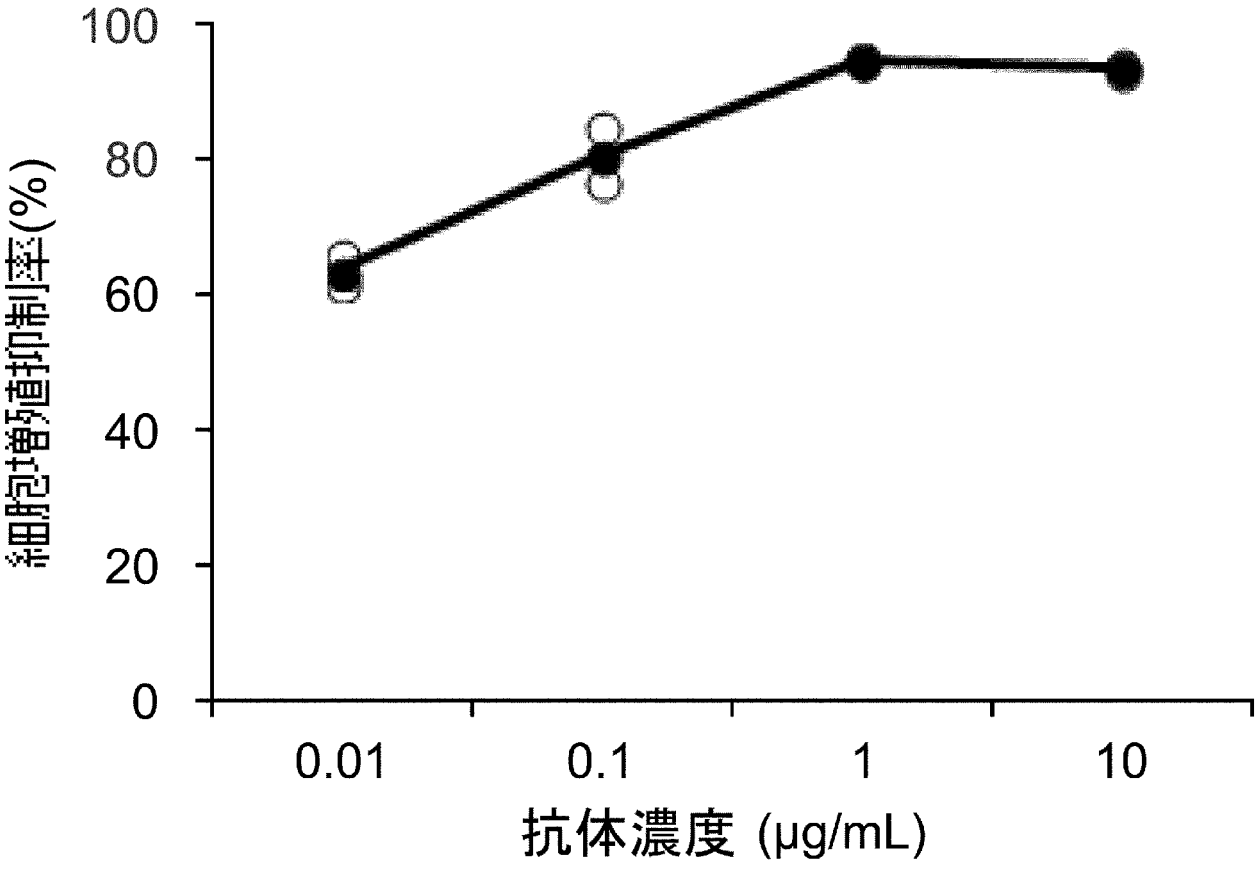
[図4]



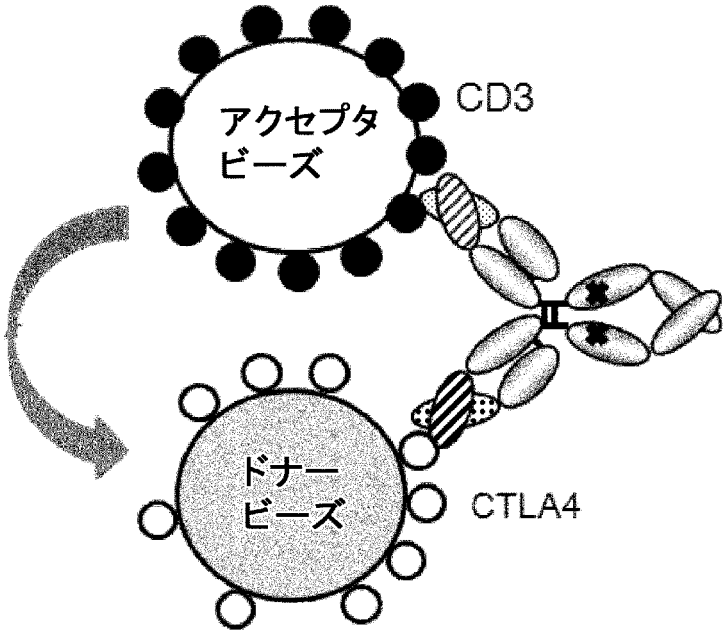
[図5]


50
40
30
20
10
0
(10)
細胞傷害活性 (%)
0.001
0.01
0.1
1
10
抗体濃度 (μg/mL)

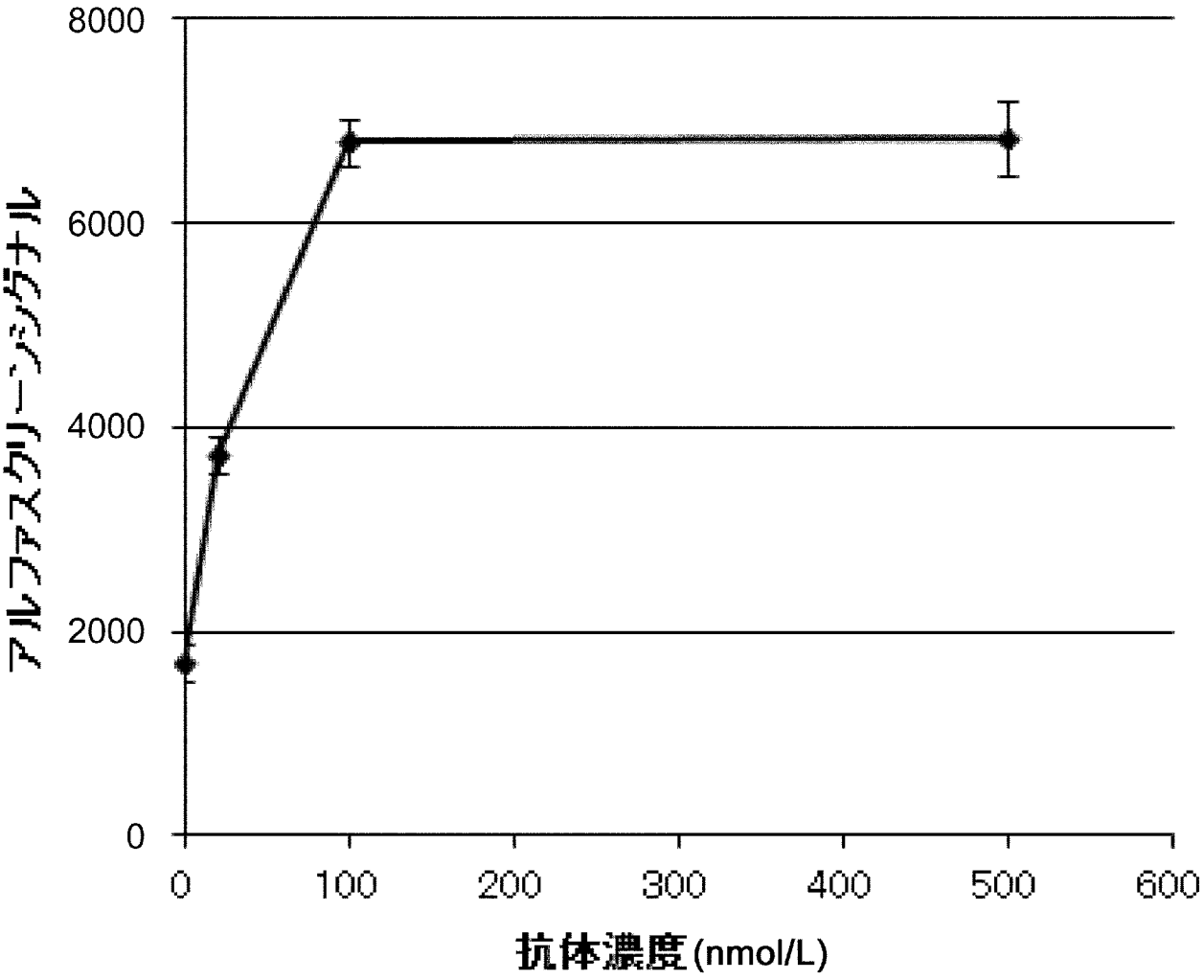
[図6]


100
80
60
40
20
0
細胞増殖抑制率(%)
0.01
0.1
1
10
抗体濃度 (μg/mL)

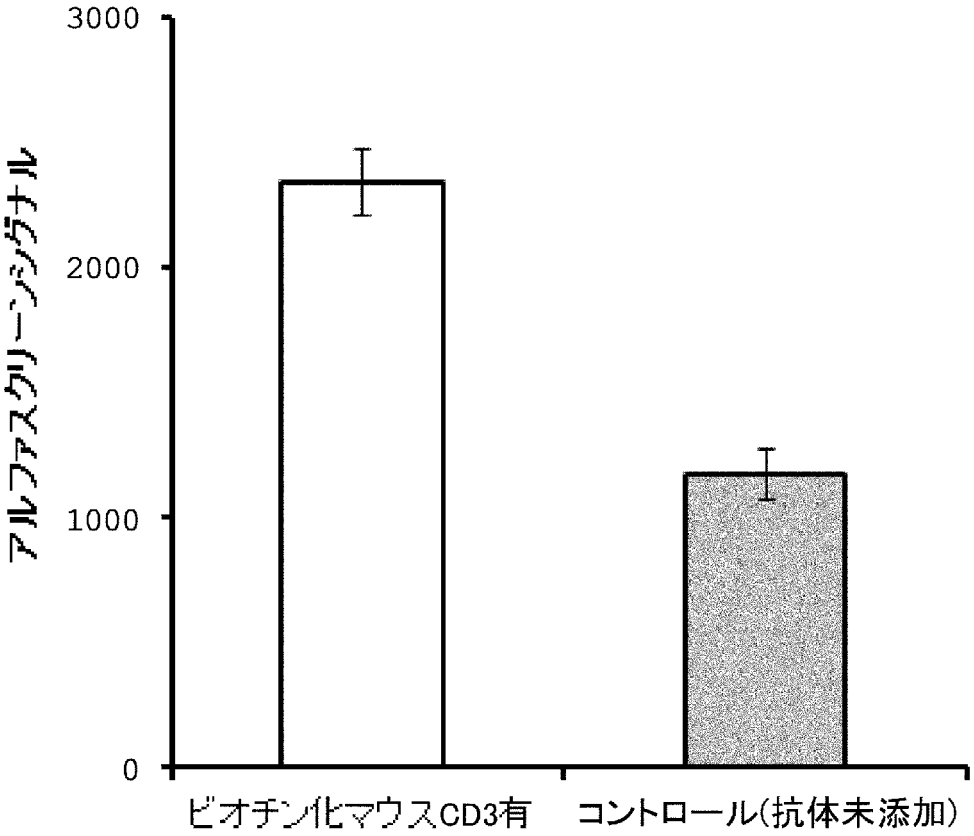
[図7-1]


アクセプタ
ビーズ
CD3
ドナー
ビーズ
CTLA4

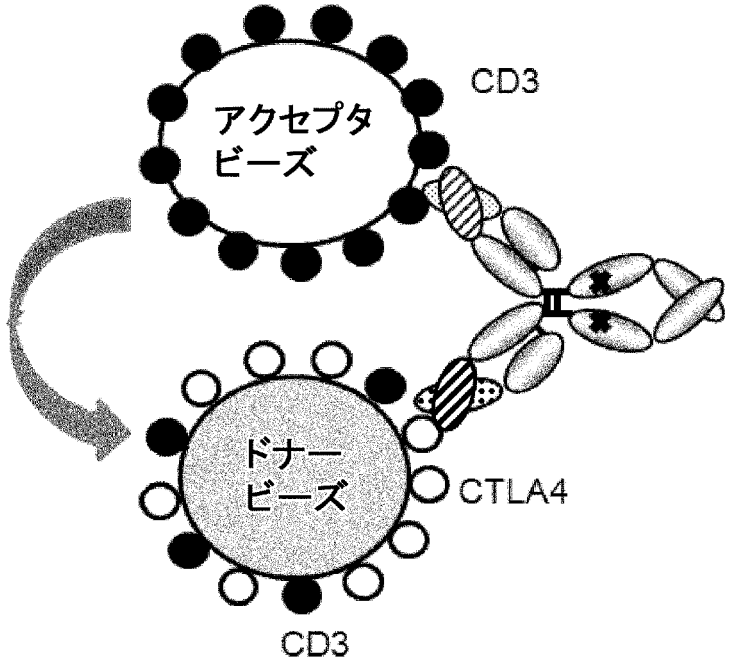
[図7-2]


8000
6000
4000
2000
0
アルファスクリーンシグナル
0
100
200
300
400
500
600
抗体濃度(nmol/L)

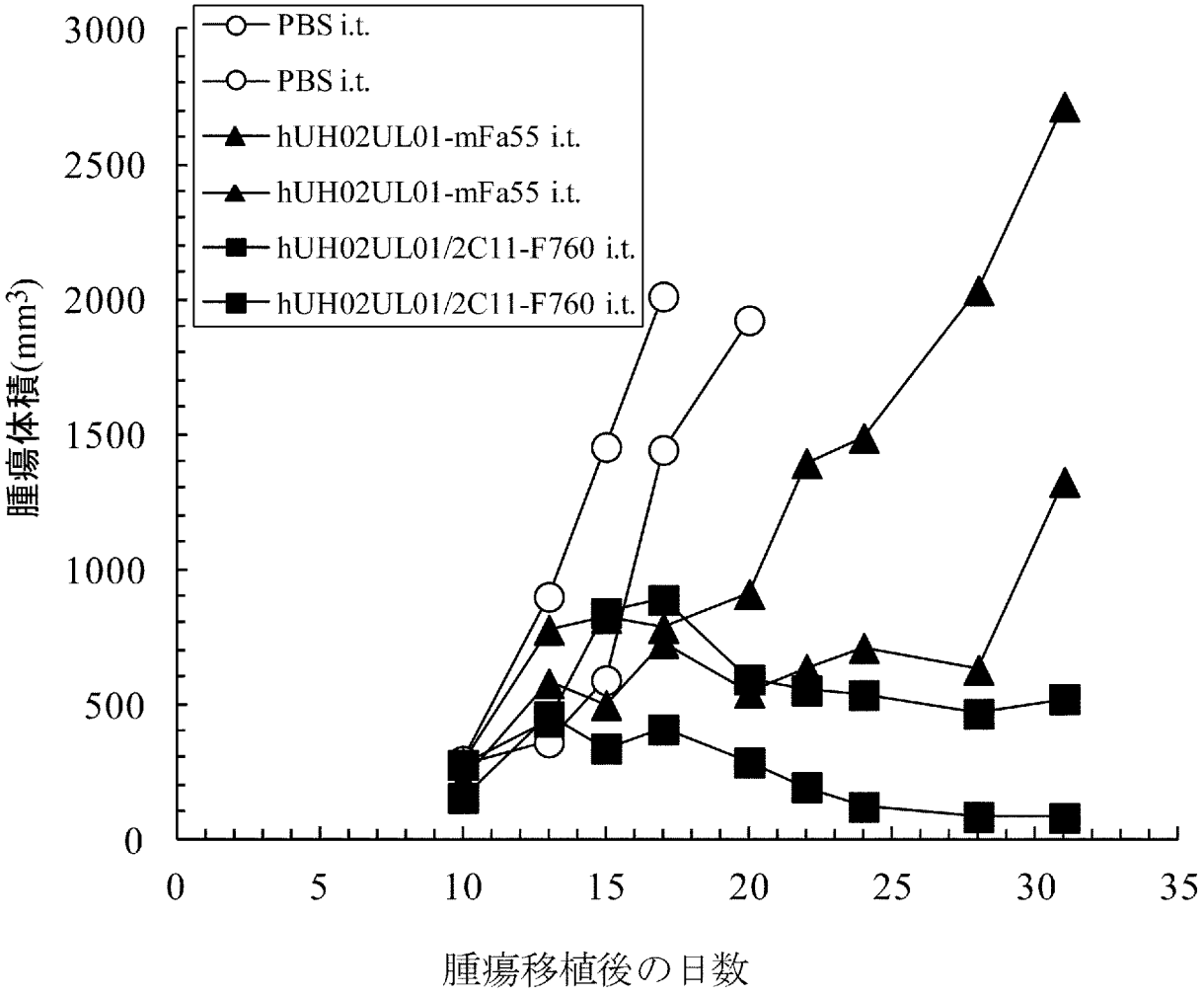
[図7-3]


3000
2000
1000
0
アルファスクリーンシグナル
ビオチン化マウスCD3有
コントロール(抗体未添加)

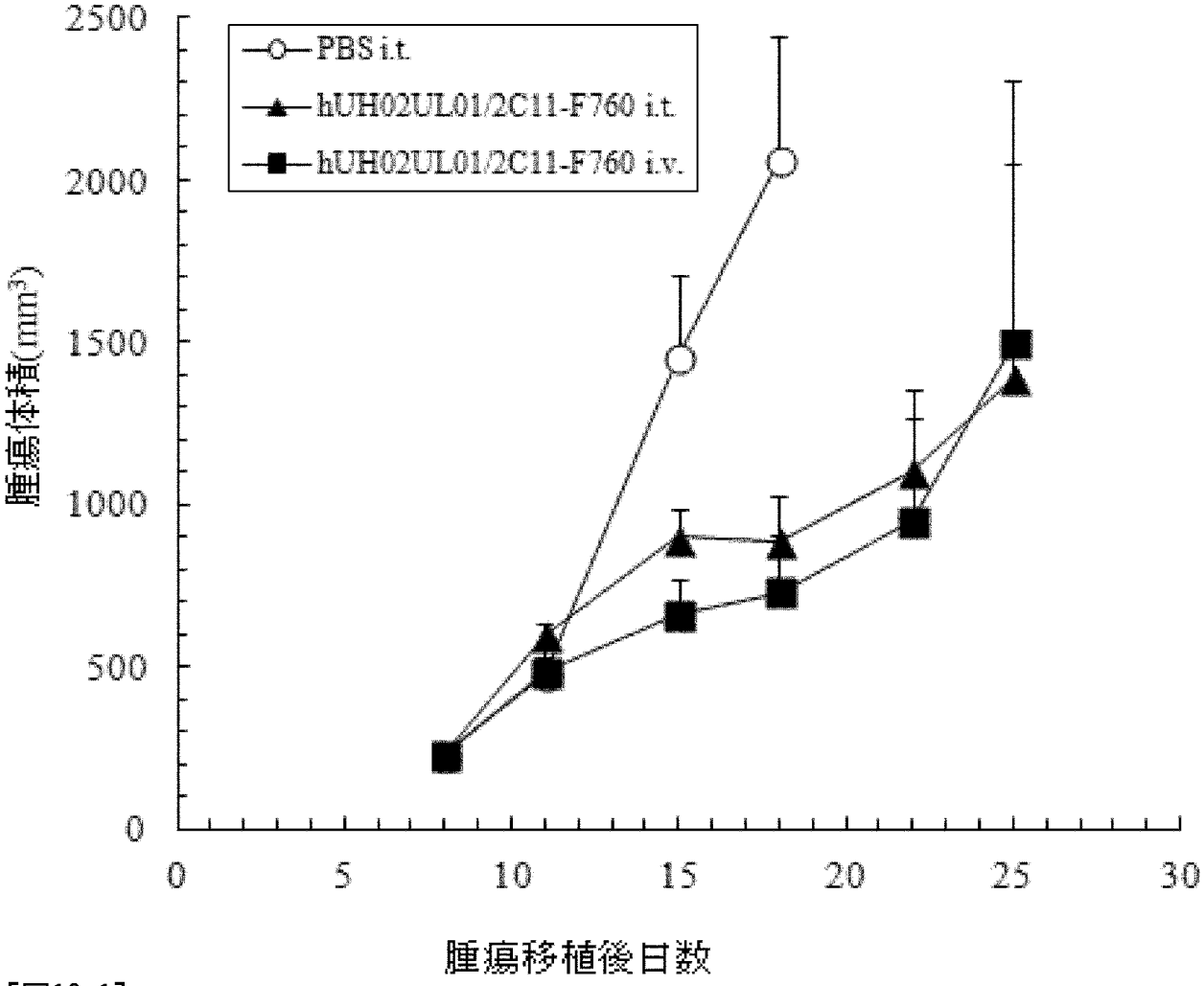
[図7-4]


CD3
アクセプタ
ビーズ
ドナー
ビーズ
CTLA4
CD3

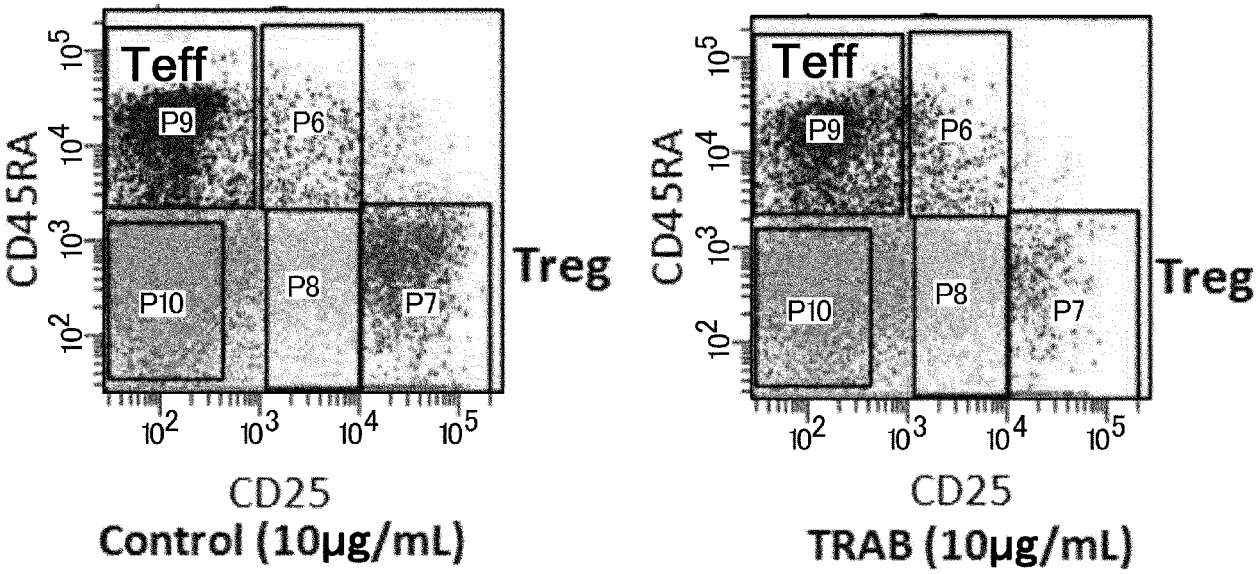
[図8]


PBS i.t.
PBS i.t.
hUH02UL01-mFa55 i.t.
hUH02UL01-mFa55 i.t.
hUH02UL01/2C11-F760 i.t.
hUH02UL01/2C11-F760 i.t.
腫瘍体積(mm3)
3000
2500
2000
1500
1000
500
0
0
5
10
15
20
25
30
35
腫瘍移植後の日数

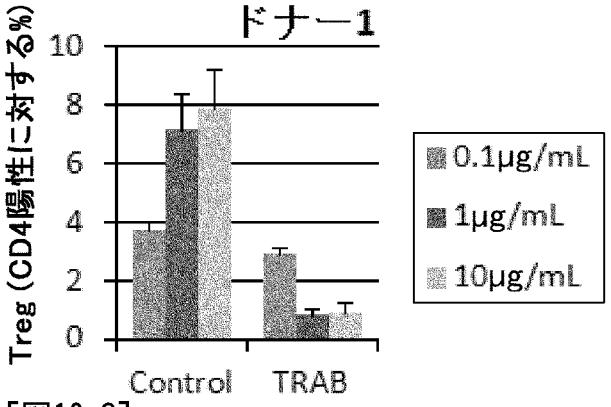
[図9]

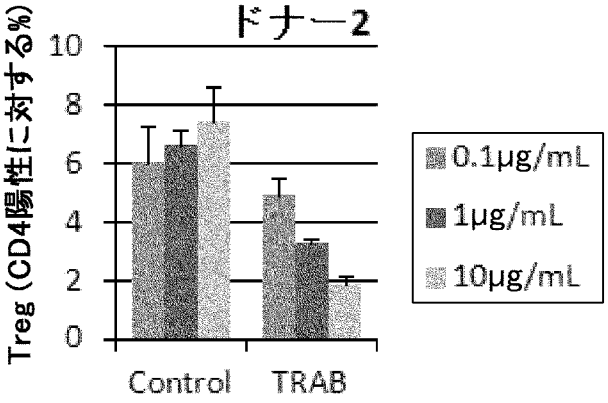

PBS i.t.
hUH02UL01/2C11-F760 i.t.
hUH02UL01/2C11-F760 i.v.
腫瘍体積(mm³)
2500
2000
1500
1000
500
0
0
5
10
15
20
25
30
腫瘍移植後日数

[図10-1]

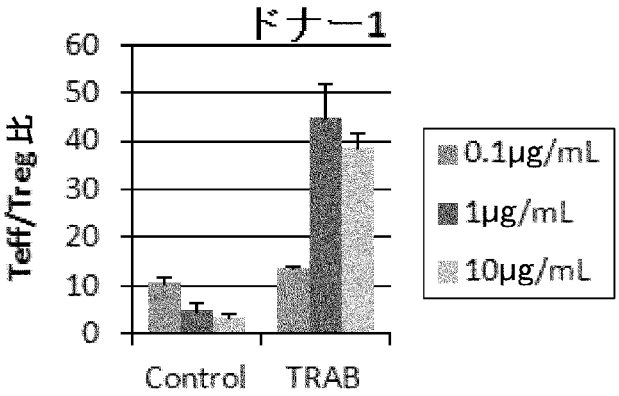

Teff
P9
P6
P10
P8
P7
Treg
CD45RA
CD25
Control (10μg/mL)
TRAB (10μg/mL)

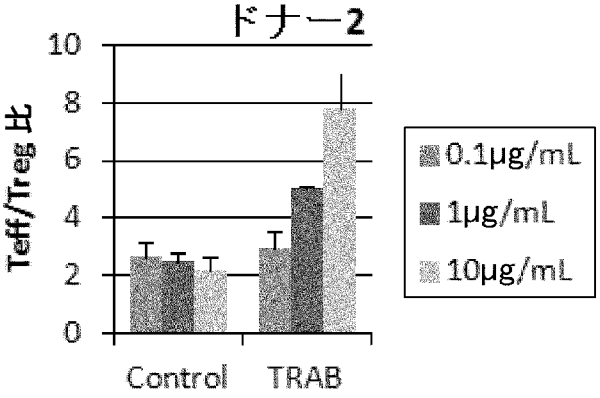
[図10-2]



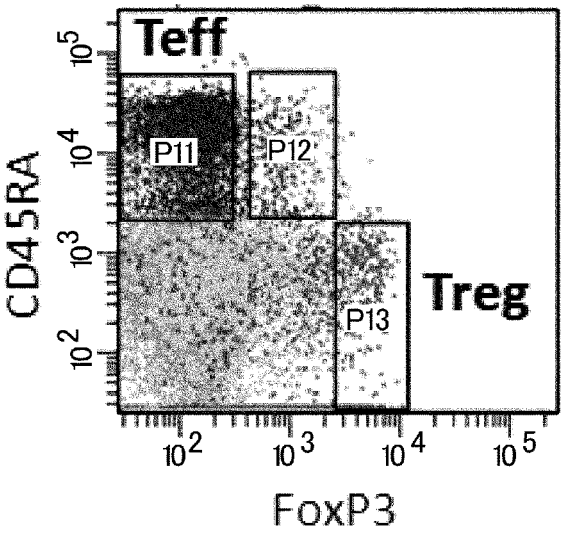


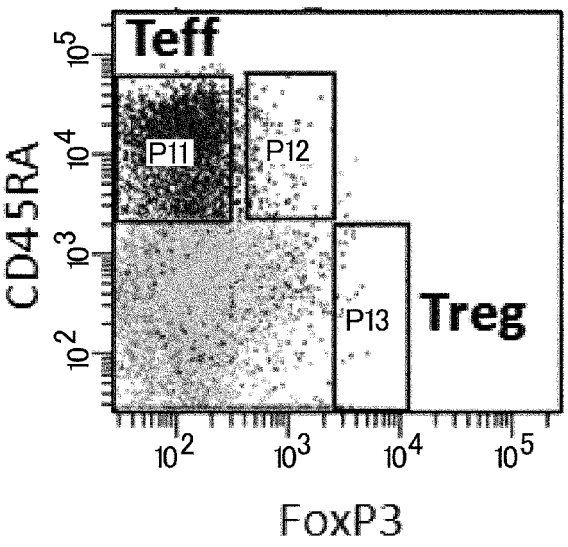
[図10-3]



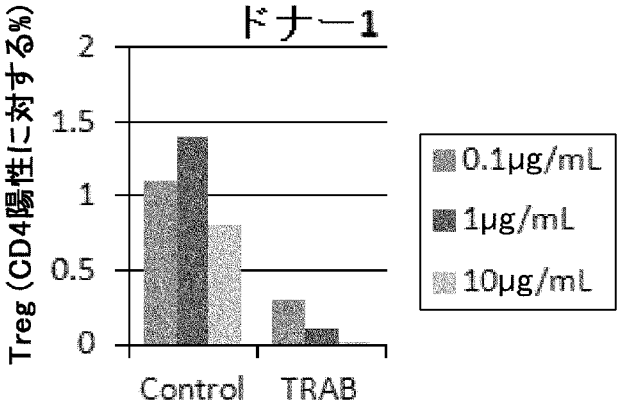


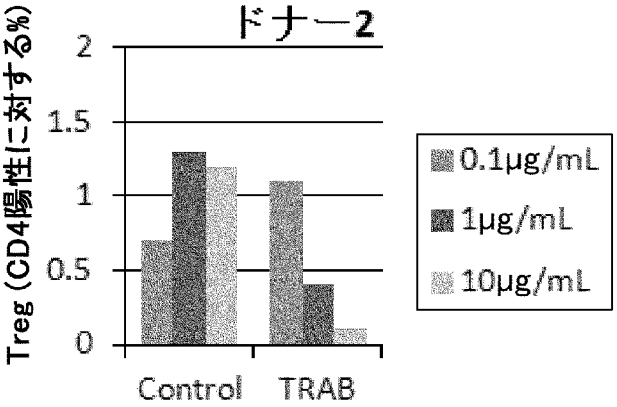
[図11-1]



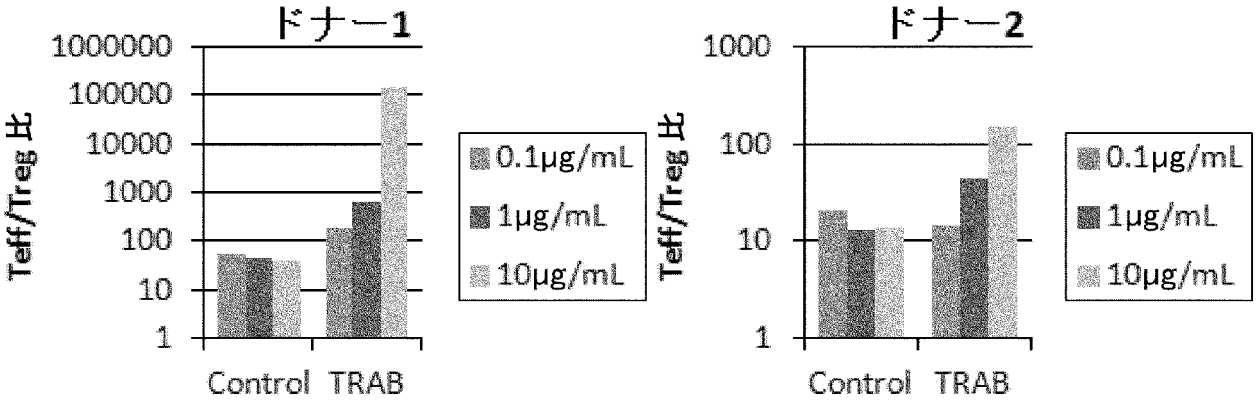


[図11-2]

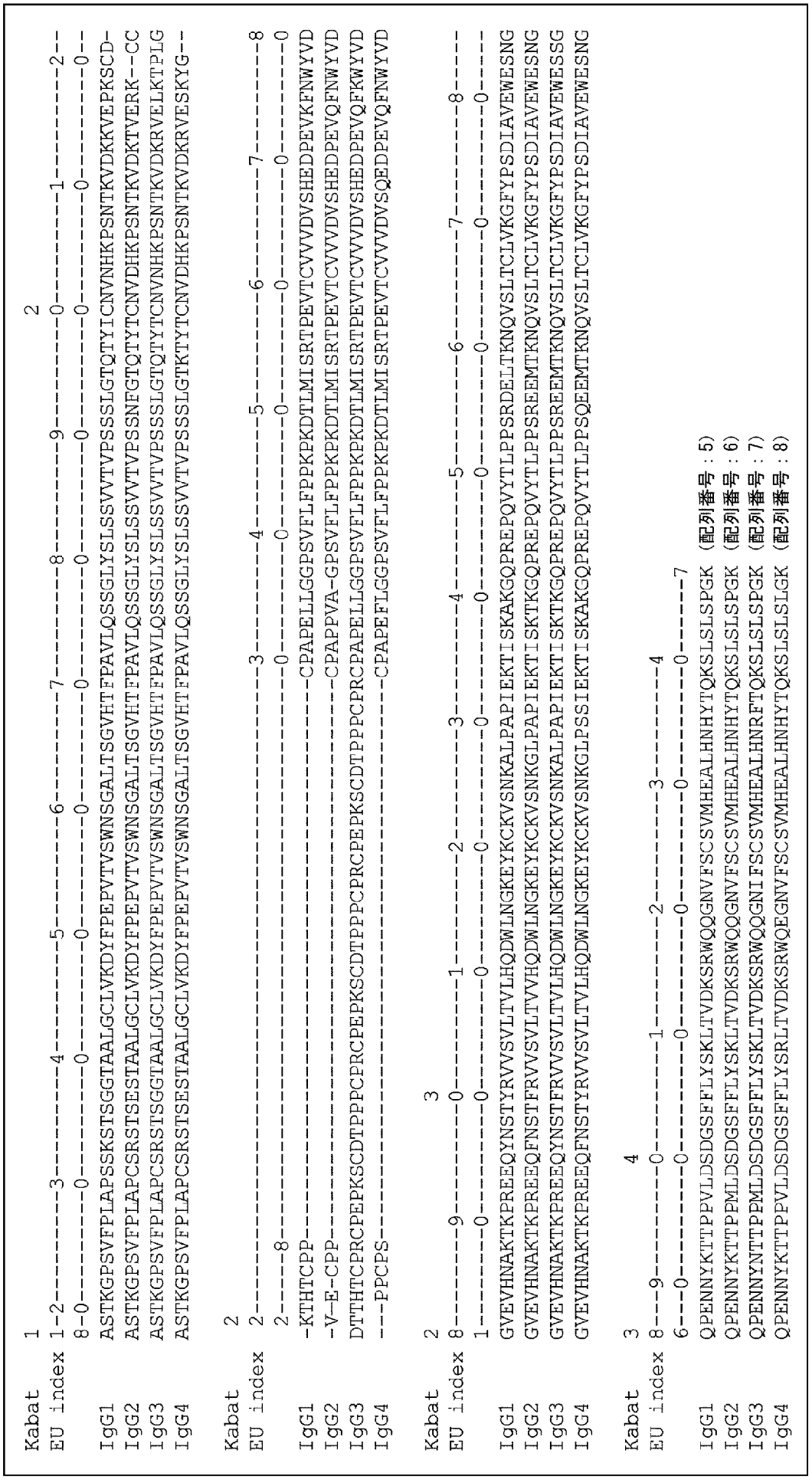




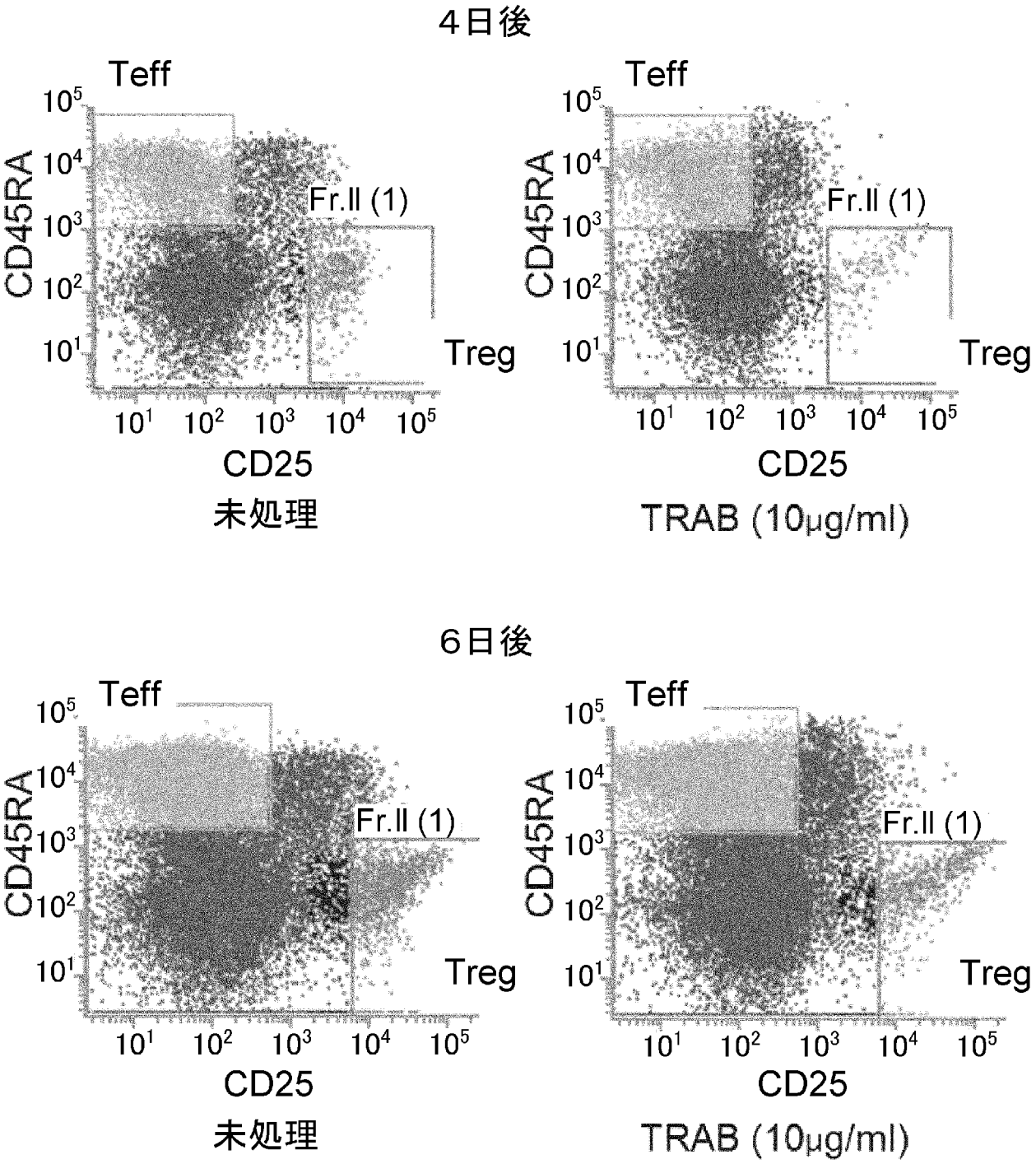
[図11-3]


ドナー1
1000000
100000
10000
1000
100
10
1
Teff/Treg 比
Control
TRAB
0.1μg/mL
1μg/mL
10μg/mL
ドナー2
1000
100
10
1
Teff/Treg 比
Control
TRAB
0.1μg/mL
1μg/mL
10μg/mL

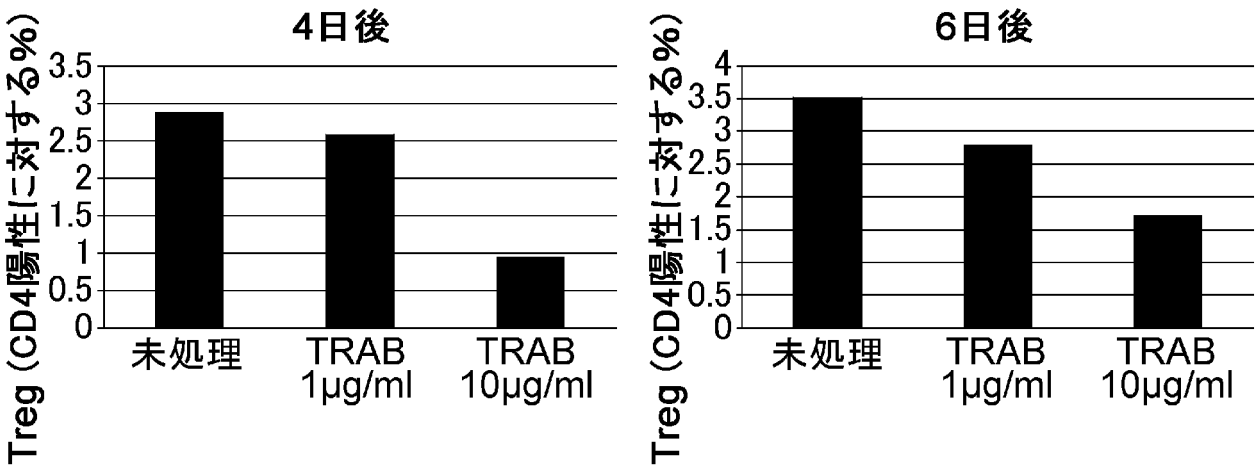
[図12]


Kabat 1 2
EU index 1-2---------3---------4---------5---------6---------7---------8---------9---------0---------1---------2--
8-0---------0---------0---------0---------0---------0---------0---------0---------0---------0--
IgG1 ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD-
IgG2 ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVDKTVERK--CC
IgG3 ASTKGPSVFPLAPCSRSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYTCNVNHKPSNTKVDKRVELKTPLG
IgG4 ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYG--
Kabat 2
EU index 2---3---------4---------5---------6---------7---------8
2-----8---------------------------------------0---------0---------0---------0---------0---------0
IgG1 -KTHTCPP---CPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD
IgG2 -V-E-CPP---CPAPPVA-GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVD
IgG3 DTTHTCPRCPEPKSCDTPPPCPRCPEPKSCDTPPPCPRCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFKWYVD
IgG4 ---PPCPS---CPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVD
Kabat 2 3
EU index 8---------9---------0---------1---------2---------3---------4---------5---------6---------7---------8-----
1---------0---------0---------0---------0---------0---------0---------0---------0---------0---------0-----
IgG1 GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG
IgG2 GVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNG
IgG3 GVEVHNAKTKPREEQYNSTFRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESSG
IgG4 GVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNG
Kabat 3 4
EU index 8---9---------0---------1---------2---------3---------4
6---0---------0---------0---------0---------0---------7
IgG1 QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (配列番号：5)
IgG2 QPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (配列番号：6)
IgG3 QPENNYNTTPPMLDSDGSFFLYSKLTVDKSRWQQGNIFSCSVMHEALHNRFTQKSLSLSPGK (配列番号：7)
IgG4 QPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK (配列番号：8)

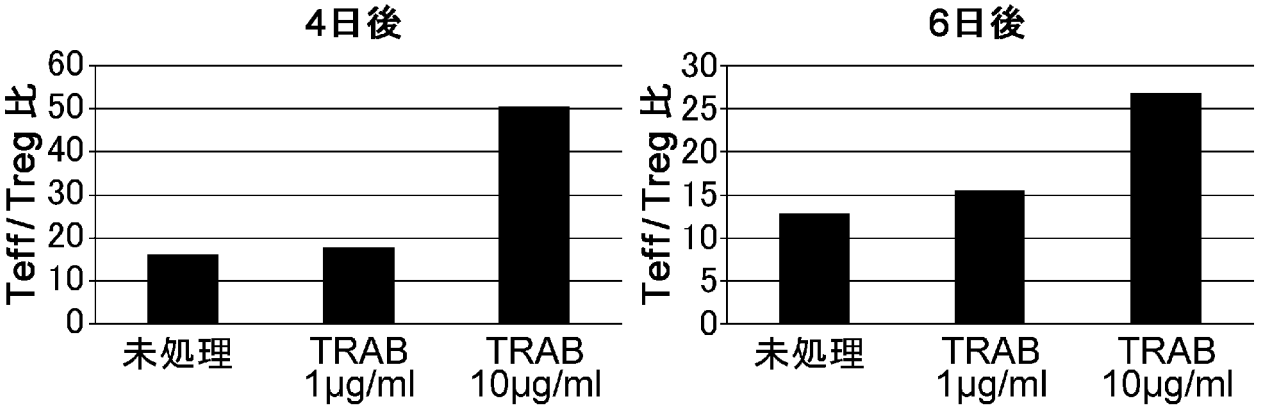
[図13]


4日後
Teff
CD45RA
Fr.II (1)
Treg
CD25
未処理
TRAB (10μg/ml)
6日後

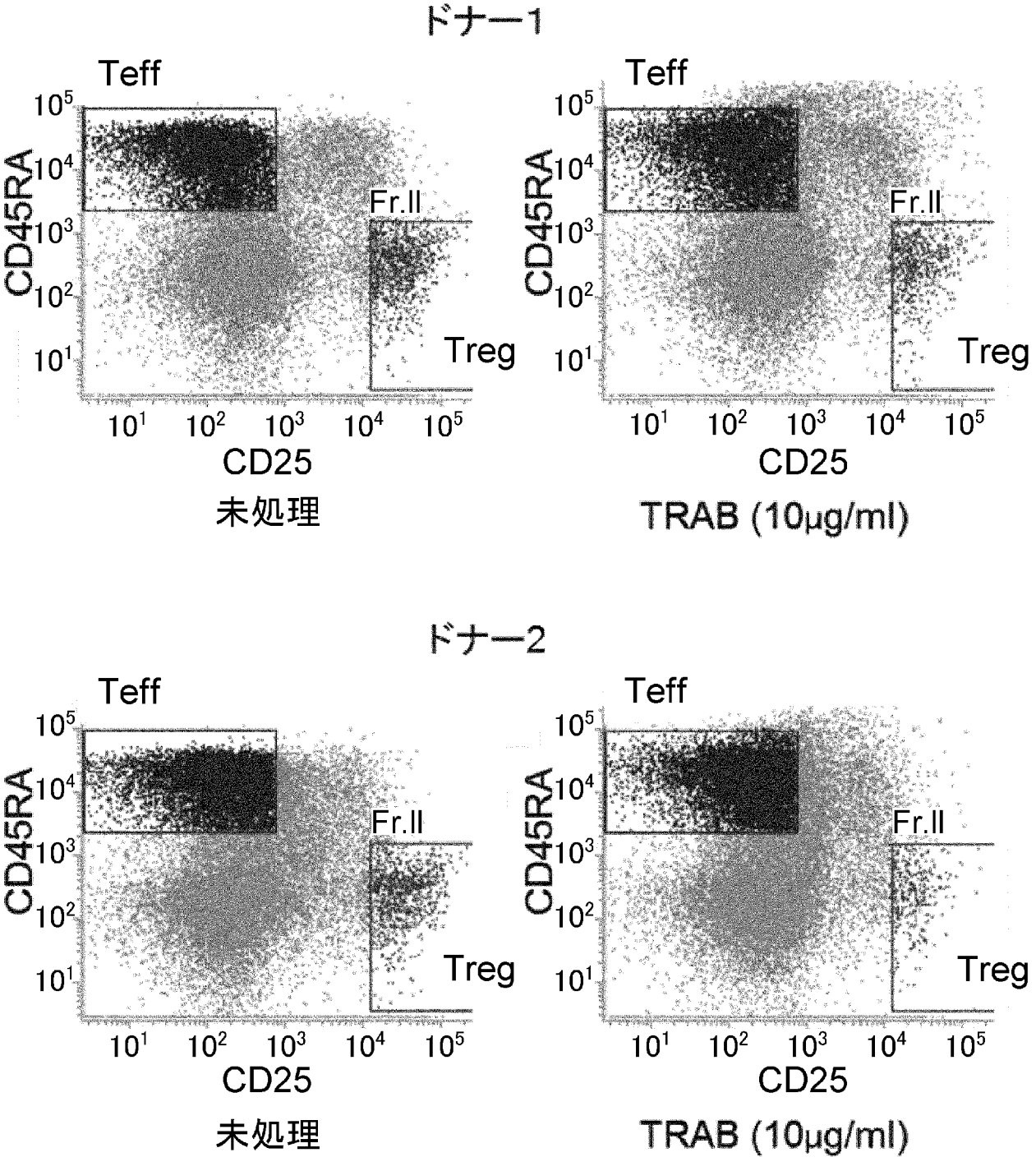
[図14]


4日後
6日後
Treg (CD4陽性に対する%)
未処理
TRAB 1μg/ml
TRAB 10μg/ml

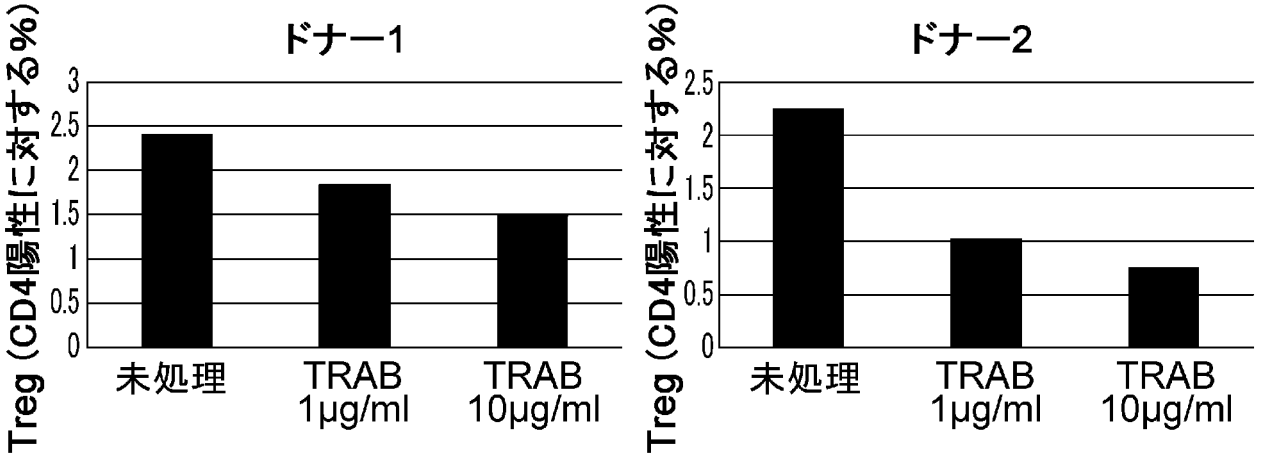
[図15]


4日後
Teff/Treg 比
60
50
40
30
20
10
0
未処理
TRAB 1μg/ml
TRAB 10μg/ml
6日後
Teff/Treg 比
30
25
20
15
10
5
0
未処理
TRAB 1μg/ml
TRAB 10μg/ml

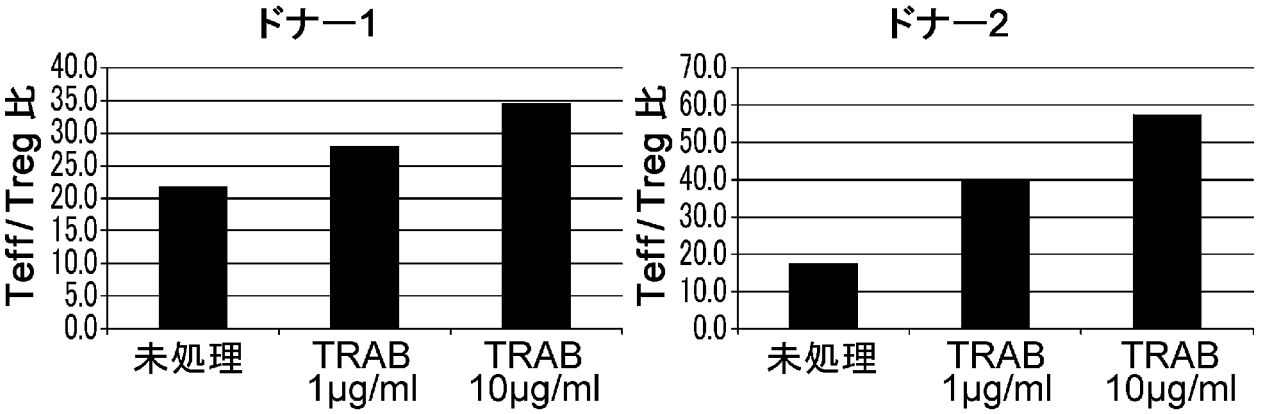
[図16]


ドナー1
Teff
CD45RA
Fr.II
Treg
CD25
未処理
TRAB (10μg/ml)
ドナー2
Teff
CD45RA
Fr.II
Treg
CD25
未処理
TRAB (10μg/ml)

[図17]


ドナー1
Treg（CD4陽性に対する%）
3
2.5
2
1.5
1
0.5
0
未処理
TRAB 1μg/ml
TRAB 10μg/ml
ドナー2
Treg（CD4陽性に対する%）
2.5
2
1.5
1
0.5
0
未処理
TRAB 1μg/ml
TRAB 10μg/ml

[図18]


ドナー1
Teff/Treg 比
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
未処理
TRAB 1μg/ml
TRAB 10μg/ml
ドナー2
Teff/Treg 比
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
未処理
TRAB 1μg/ml
TRAB 10μg/ml