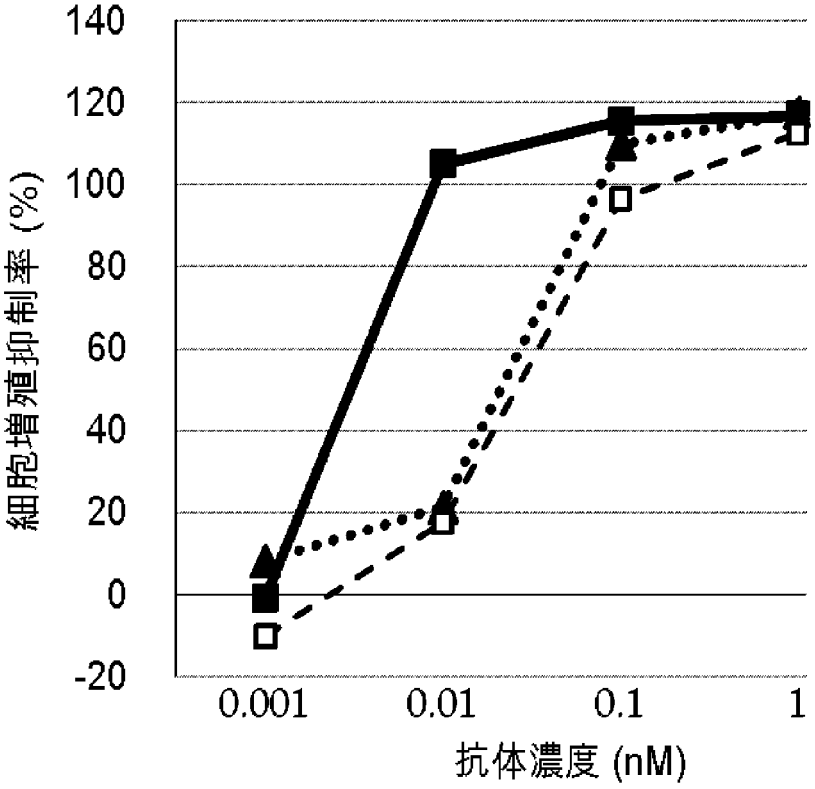
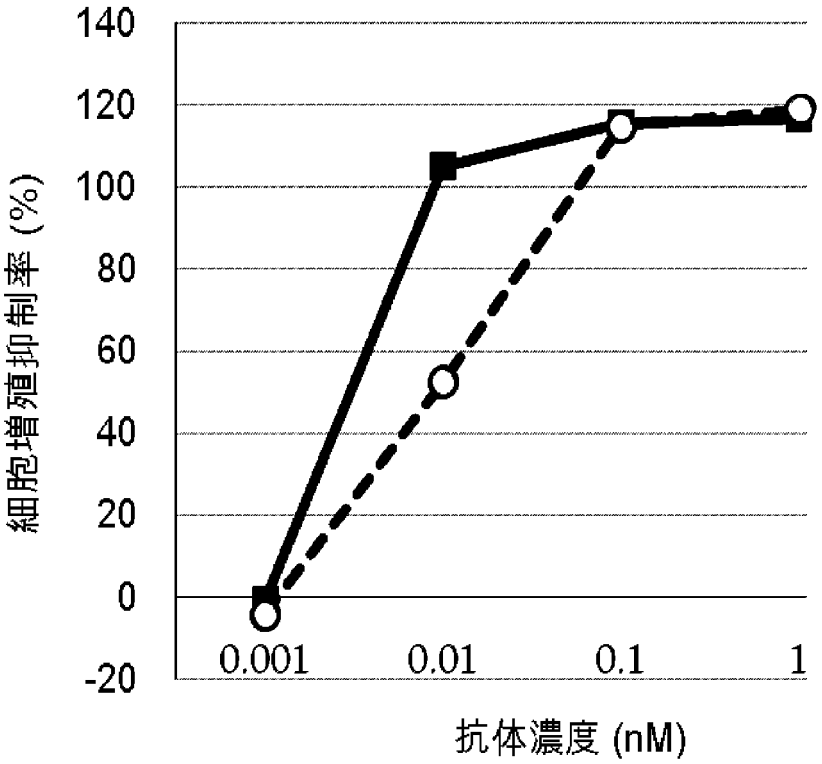
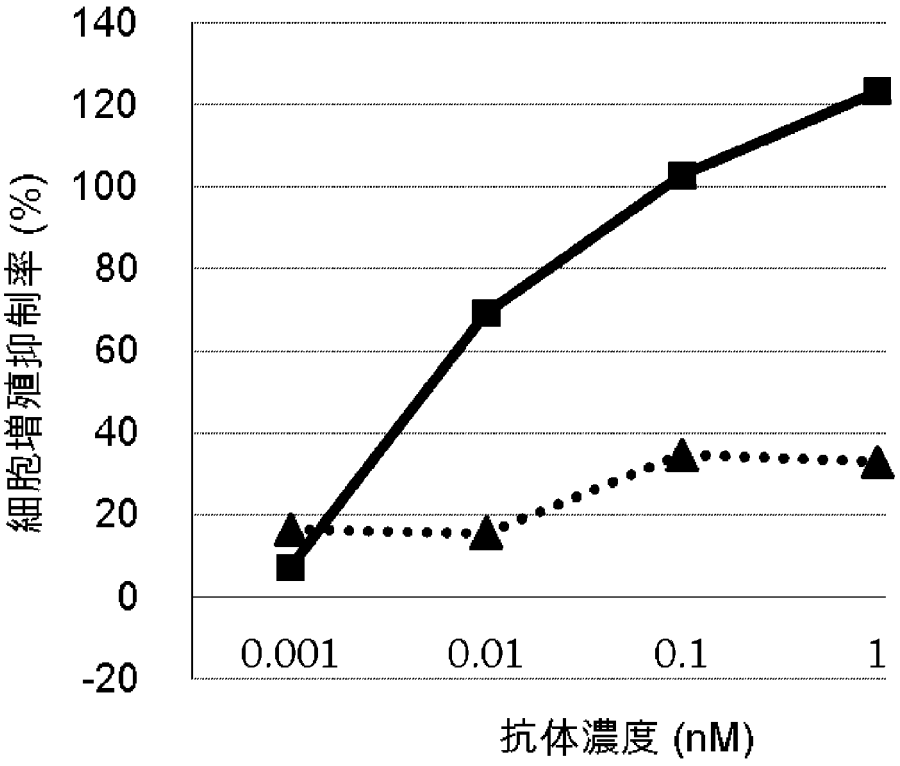
[図1]


140
120
100
80
60
40
20
0
-20
細胞増殖抑制率 (%)
0.001
0.01
0.1
1
抗体濃度 (nM)

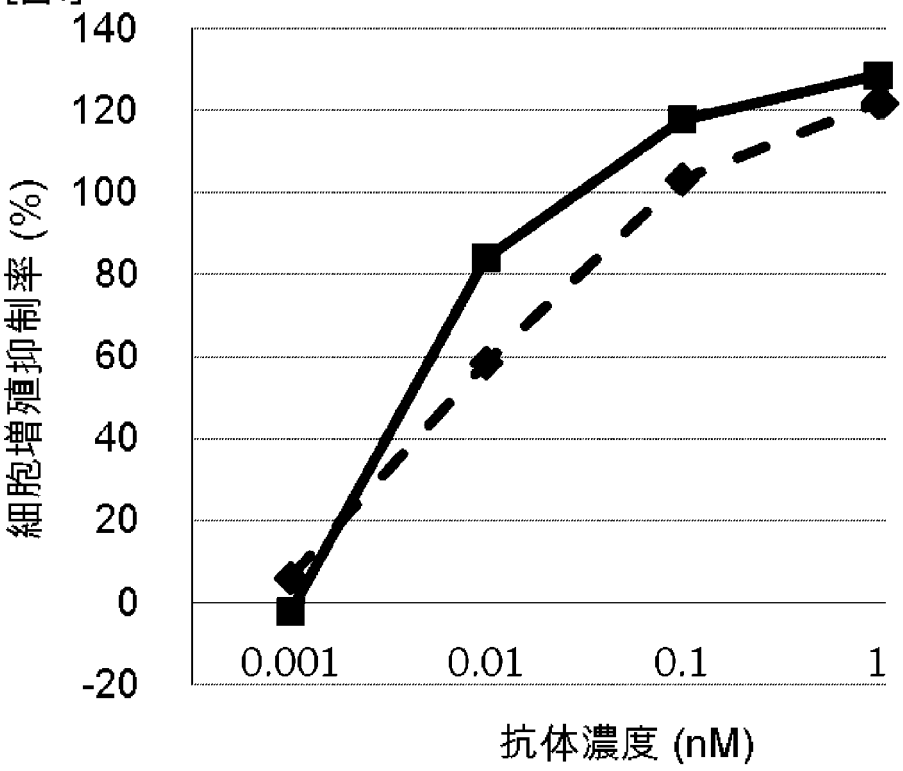
[図2]


140
120
100
80
60
40
20
0
-20
細胞増殖抑制率 (%)
0.001
0.01
0.1
1
抗体濃度 (nM)

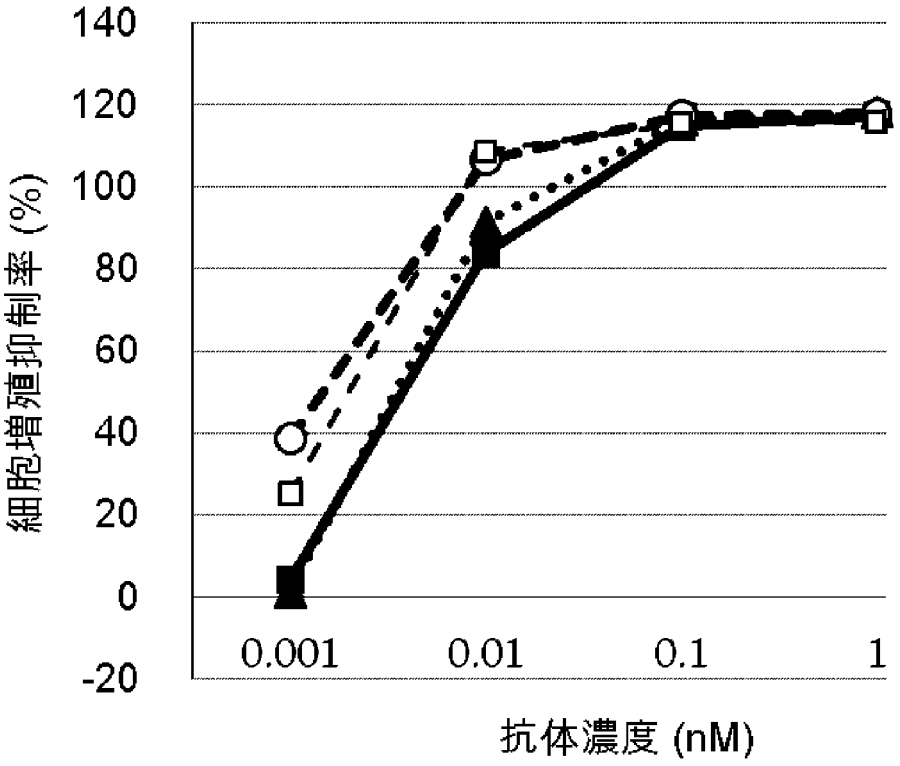
[図3]


140
120
100
80
60
40
20
0
-20
細胞増殖抑制率 (%)
0.001
0.01
0.1
1
抗体濃度 (nM)

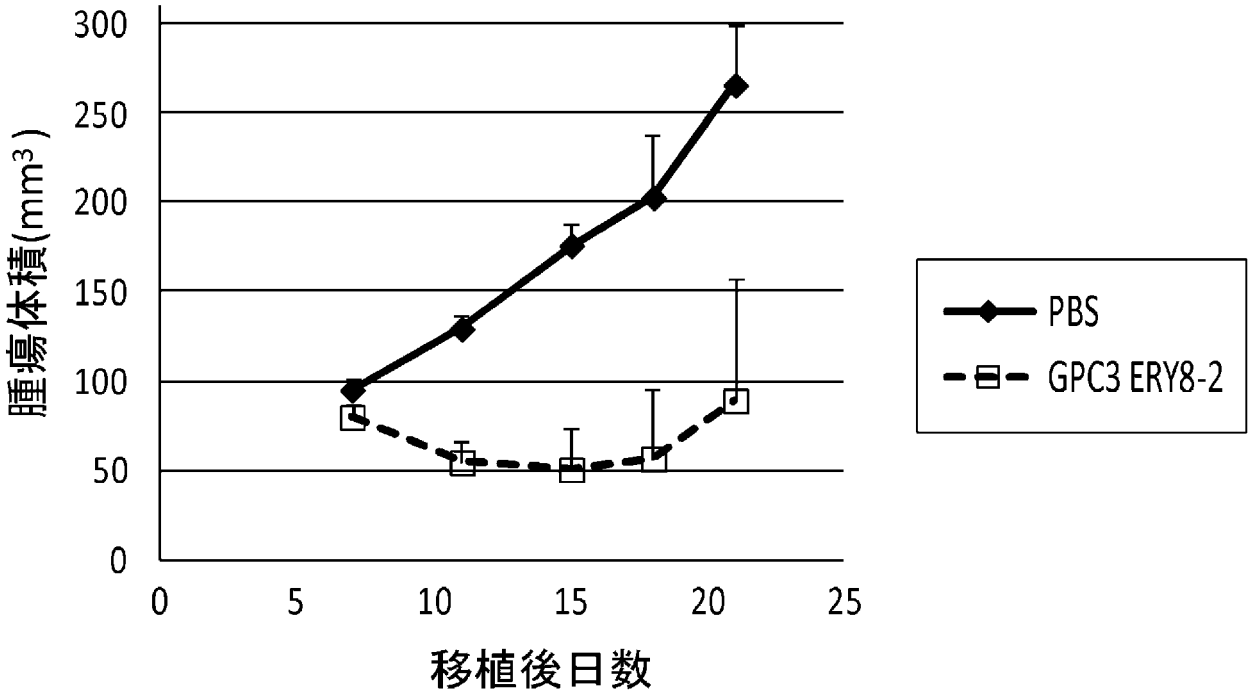
[図4]


140
120
100
80
60
40
20
0
-20
細胞増殖抑制率 (%)
0.001
0.01
0.1
1
抗体濃度 (nM)

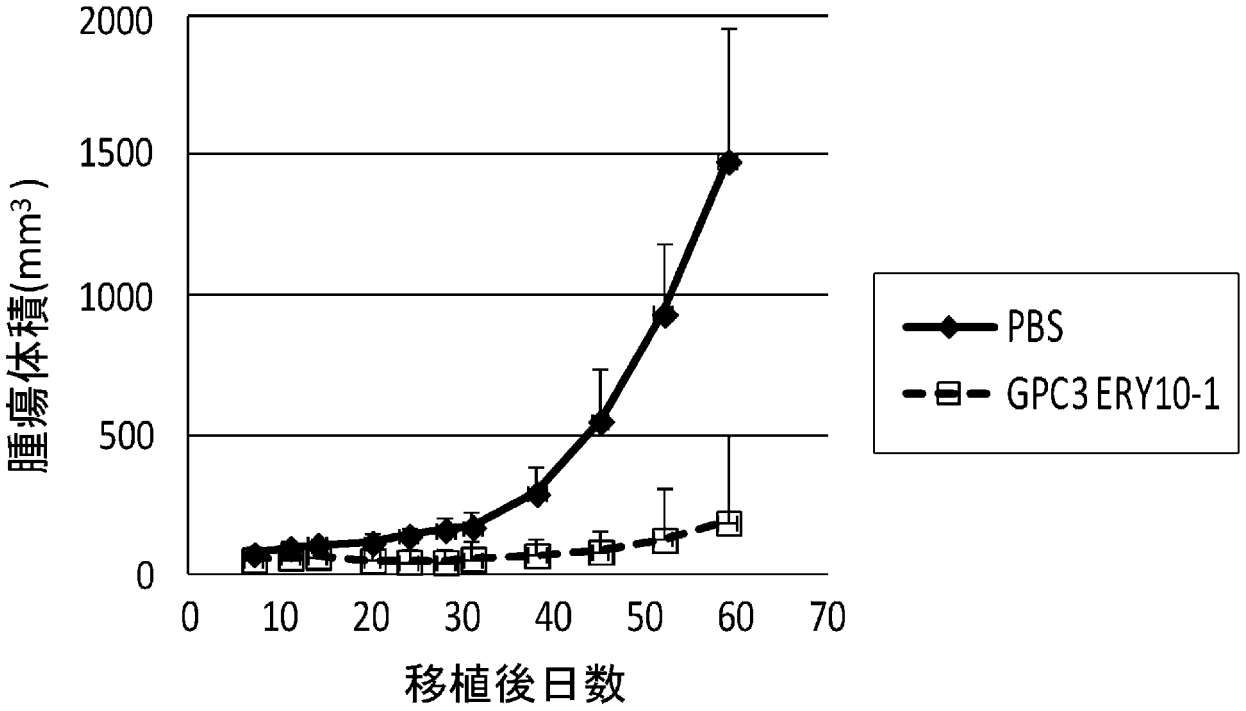
[図5]


140
120
100
80
60
40
20
0
-20
細胞増殖抑制率 (%)
0.001
0.01
0.1
1
抗体濃度 (nM)

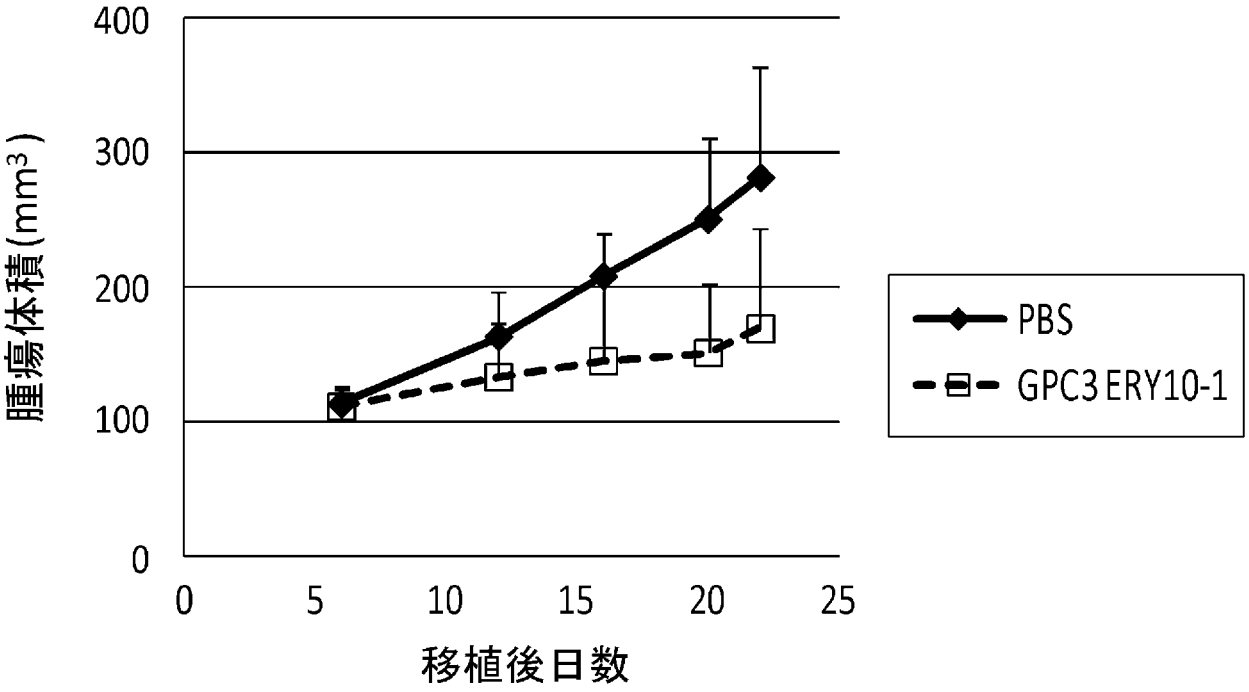
[図6]


300
250
200
150
100
50
0
腫瘍体積(mm3)
0
5
10
15
20
25
移植後日数
PBS
GPC3 ERY8-2

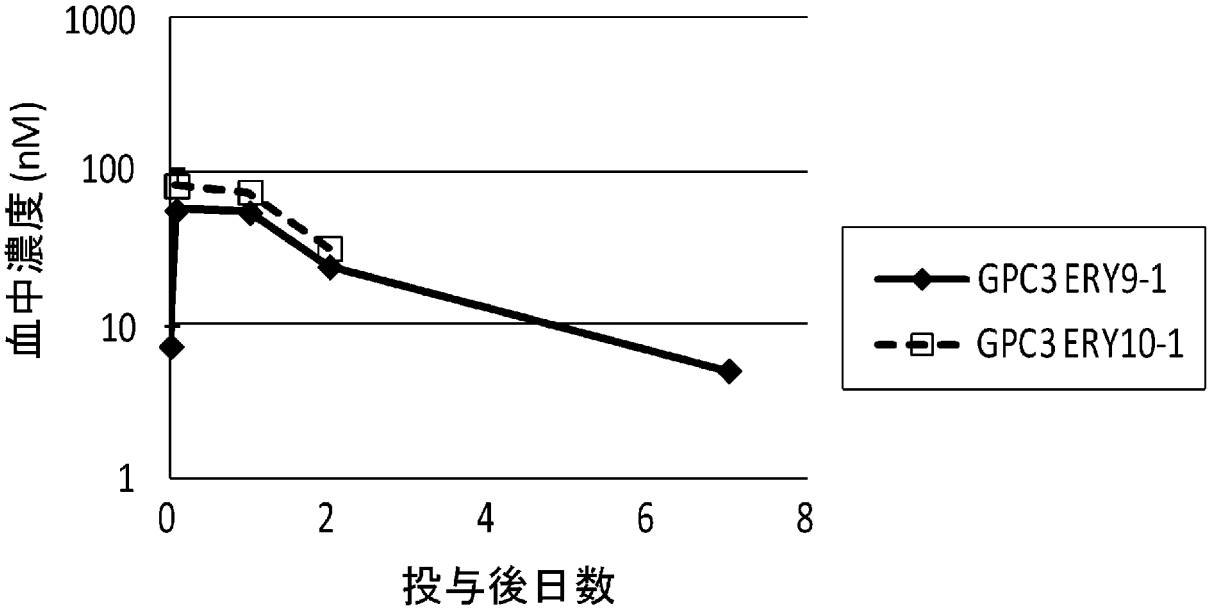
[図7]


2000
1500
1000
500
0
腫瘍体積(mm³)
0
10
20
30
40
50
60
70
移植後日数
PBS
GPC3 ERY10-1

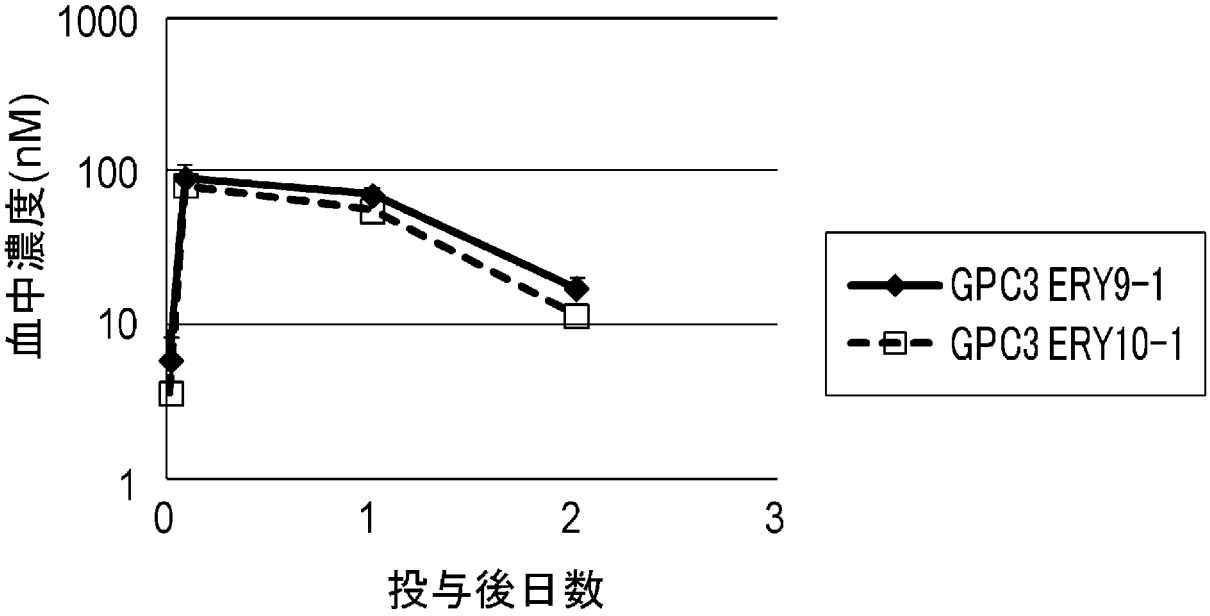
[図8]


400
300
200
100
0
腫瘍体積(mm³)
0
5
10
15
20
25
移植後日数
PBS
GPC3 ERY10-1

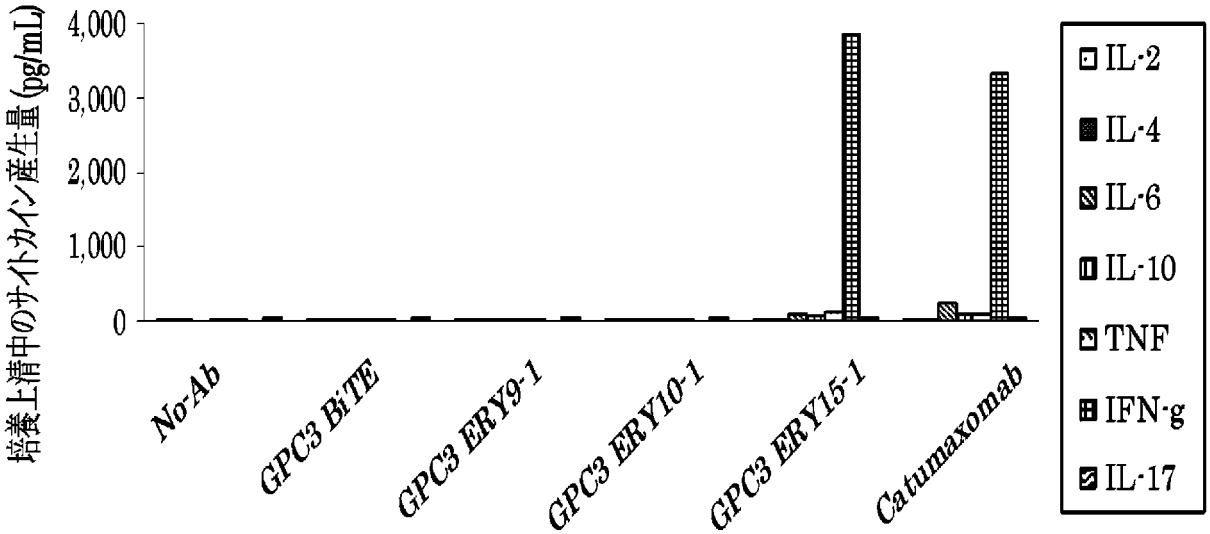
[図9]


1000
100
10
1
血中濃度(nM)
0
2
4
6
8
投与後日数
GPC3 ERY9-1
GPC3 ERY10-1

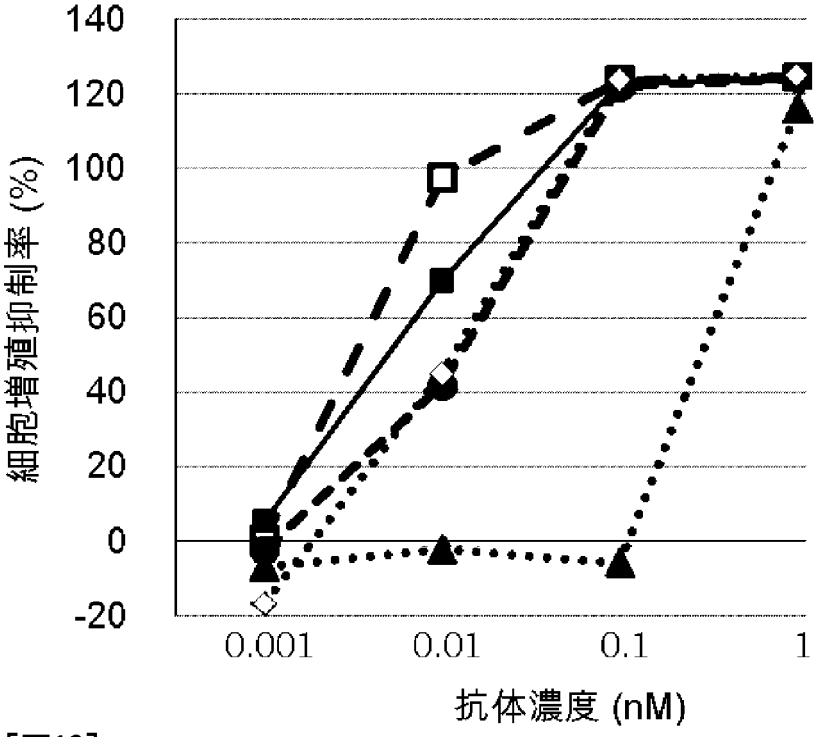
[図10]


1000
100
10
1
血中濃度(nM)
0
1
2
3
投与後日数
GPC3 ERY9-1
GPC3 ERY10-1

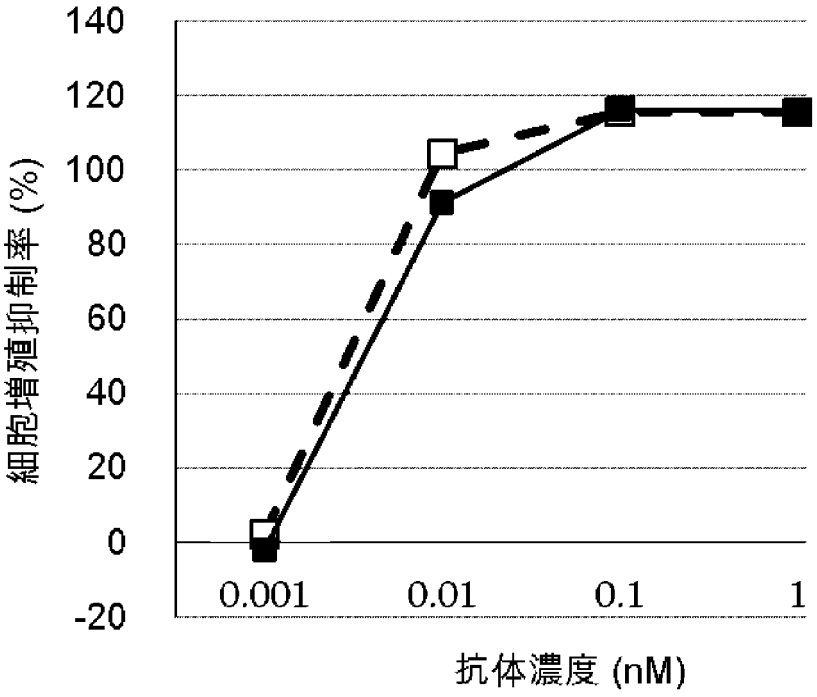
[図11]


培養上清中のサイトカイン産生量(pg/mL)
4,000
3,000
2,000
1,000
0
No-Ab
GPC3 BiTE
GPC3 ERY9-1
GPC3 ERY10-1
GPC3 ERY15-1
Catumaxomab
IL-2
IL-4
IL-6
IL-10
TNF
IFN-g
IL-17

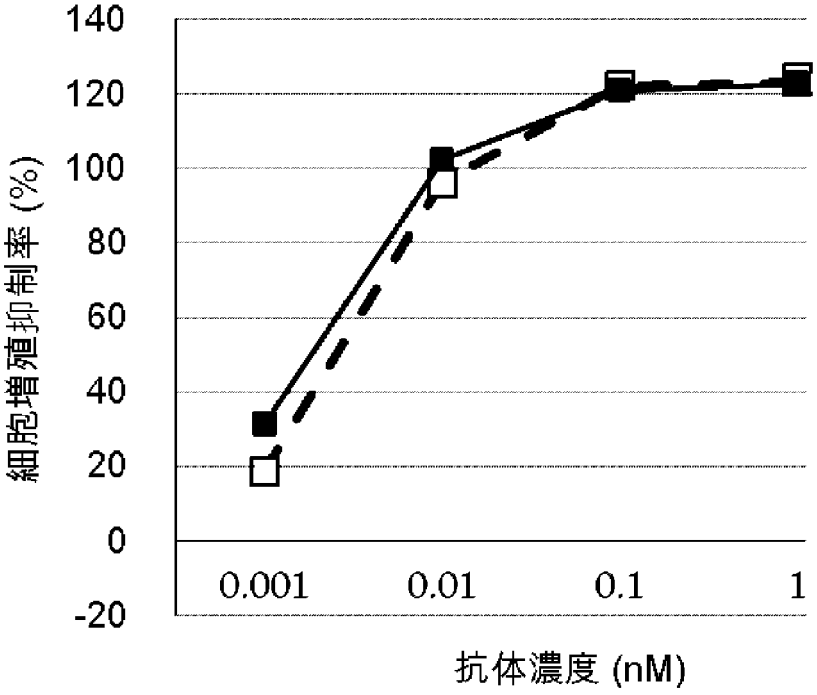
[図12]


140
120
100
80
60
40
20
0
-20
細胞増殖抑制率 (%)
0.001
0.01
0.1
1
抗体濃度 (nM)

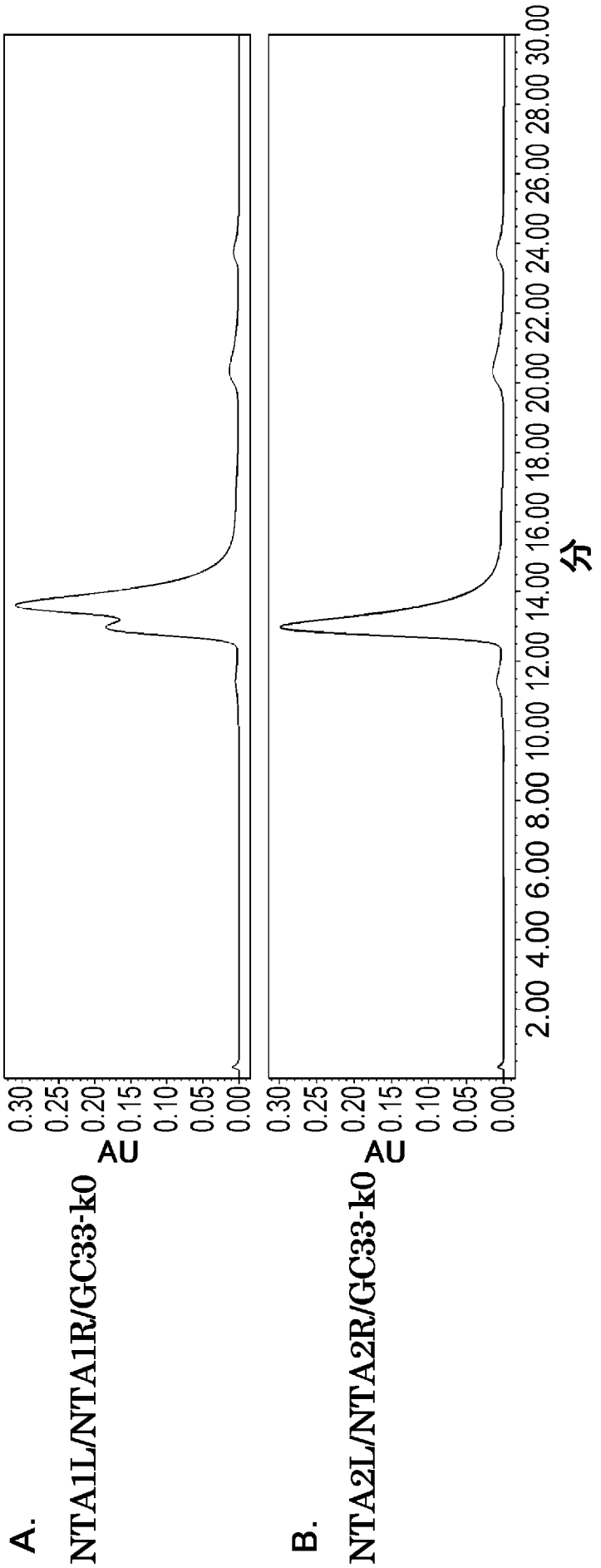
[図13]


140
120
100
80
60
40
20
0
-20
細胞増殖抑制率 (%)
0.001
0.01
0.1
1
抗体濃度 (nM)

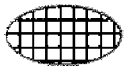
[図14]



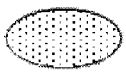
[図15]


A.
NTA1L/NTA1R/GC33-k0
AU
0.30
0.25
0.20
0.15
0.10
0.05
0.00
B.
NTA2L/NTA2R/GC33-k0
AU
0.30
0.25
0.20
0.15
0.10
0.05
0.00
2.00 4.00 6.00 8.00 10.00 12.00 14.00 16.00 18.00 20.00 22.00 24.00 26.00 28.00 30.00
分

[図16]


抗癌抗原（GPC3、EpCAM、EGFR）抗体 H鎖可変領域


抗癌抗原（GPC3、EpCAM、EGFR）抗体 L鎖可変領域


抗CD3抗体 H鎖可変領域

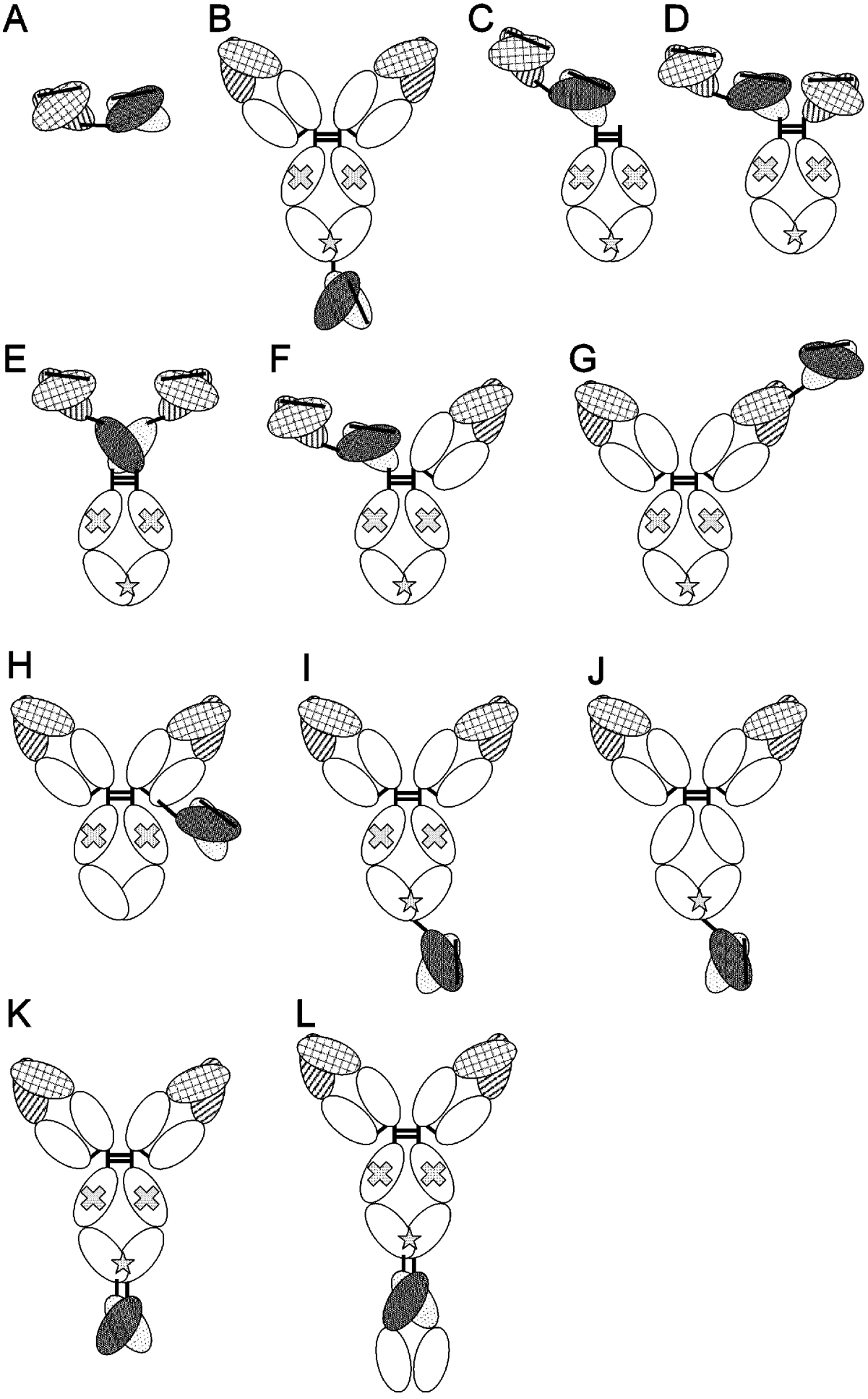

抗CD3抗体 L鎖可変領域


抗体定常領域


サイレントFc変異


ヘテロFc会合化変異

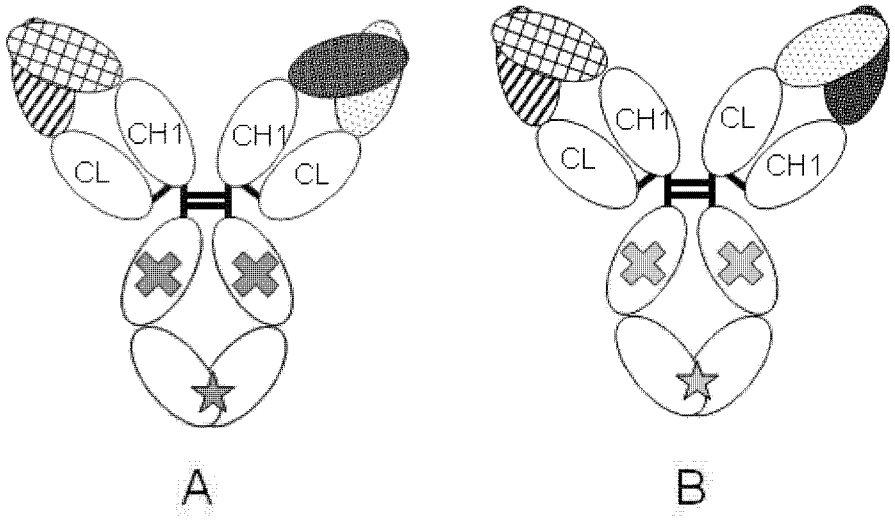
[図17]



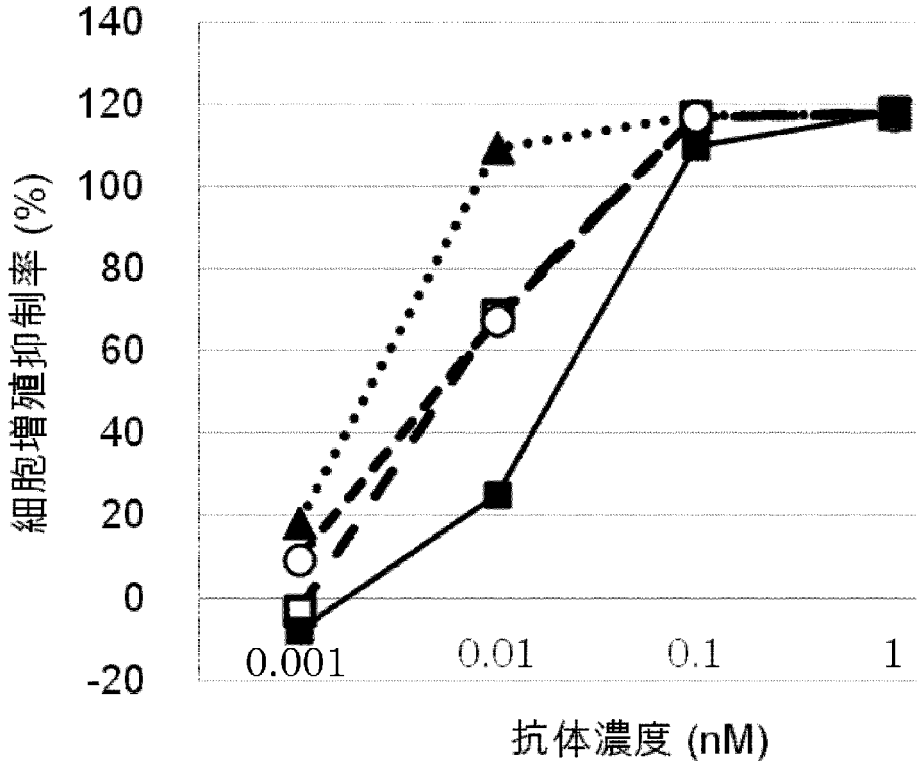
[図18]

```
Kabat    1                                                
```

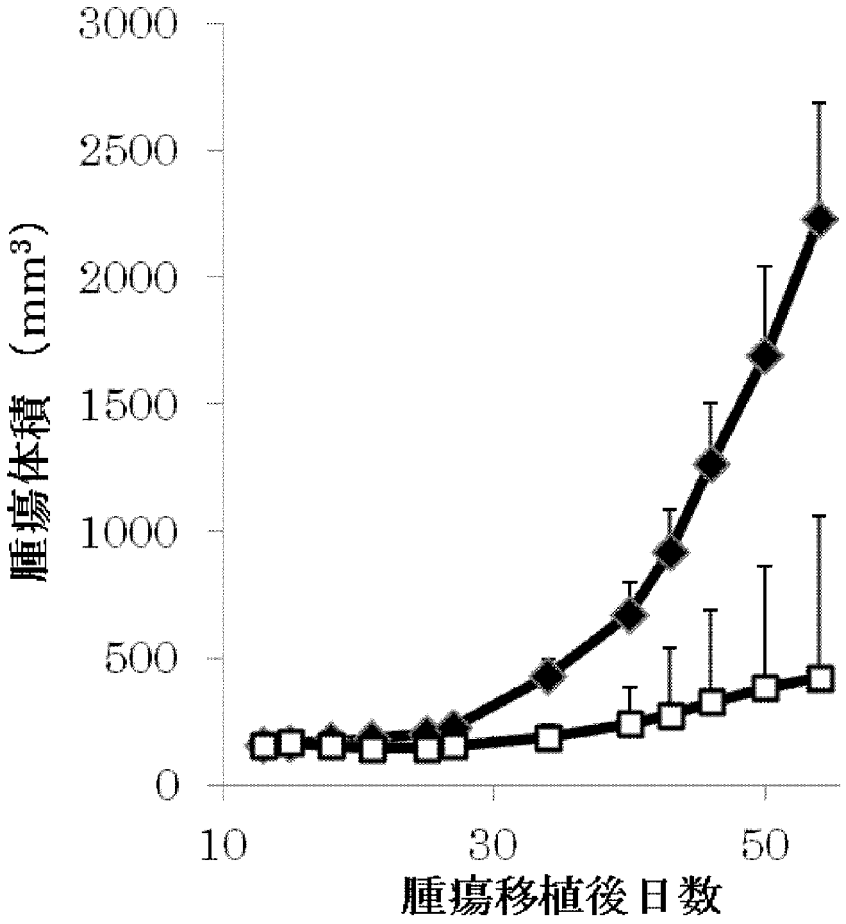
[図19]


CH1
CH1
CL
CL
CL
CH1
CL
CH1
A
B

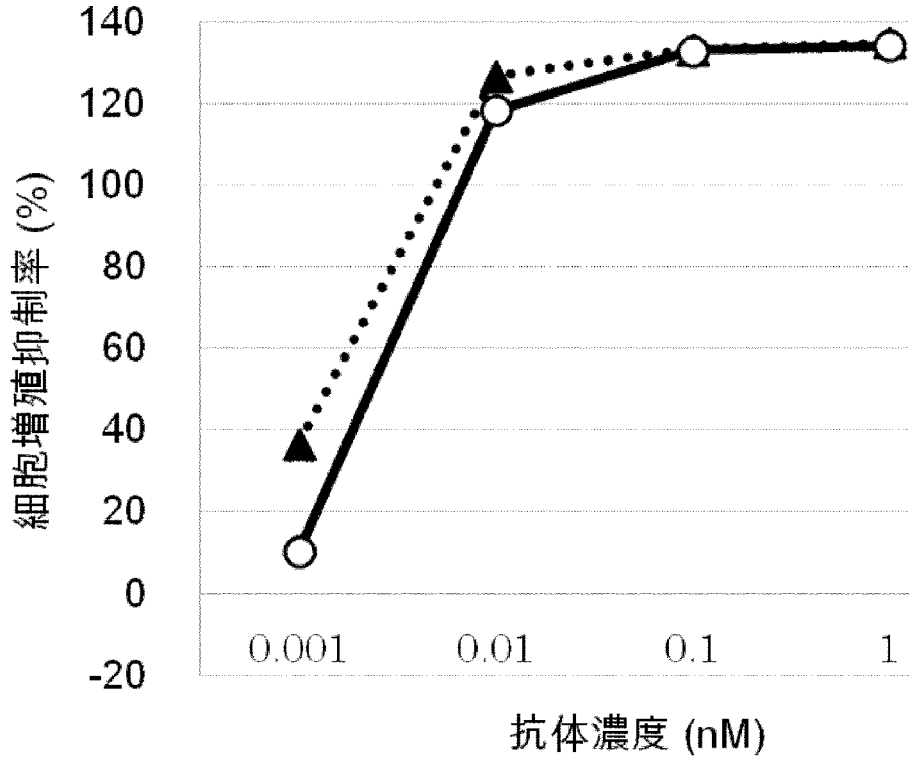
[図20]


140
120
100
80
60
40
20
0
-20
細胞増殖抑制率 (%)
0.001
0.01
0.1
1
抗体濃度 (nM)

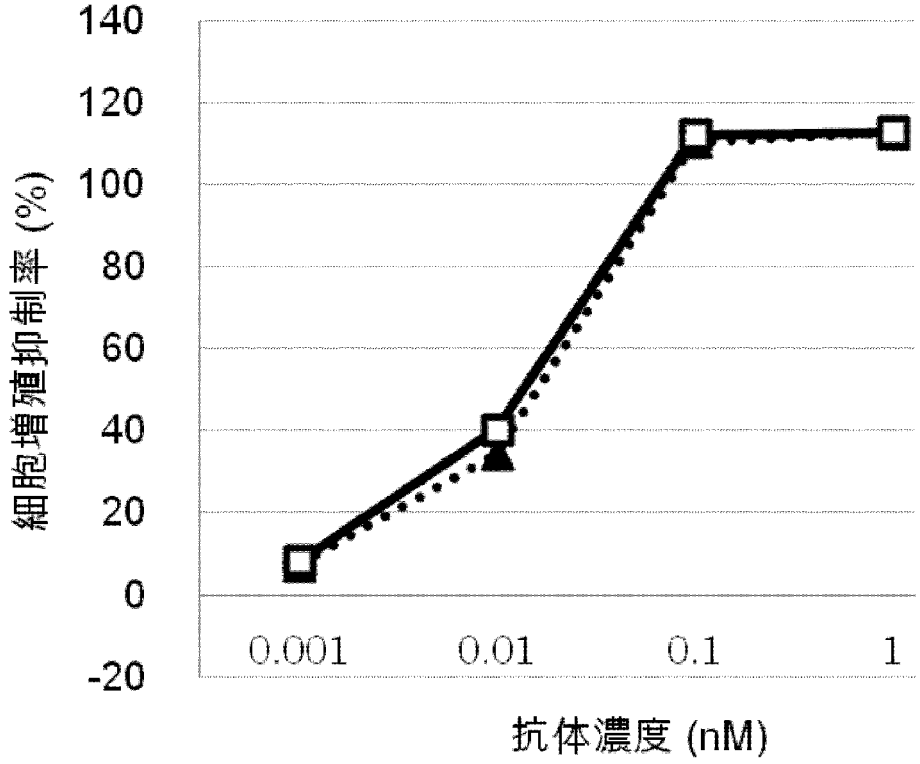
[図21]


3000
2500
2000
1500
1000
500
0
腫瘍体積 (mm3)
10
30
50
腫瘍移植後日数

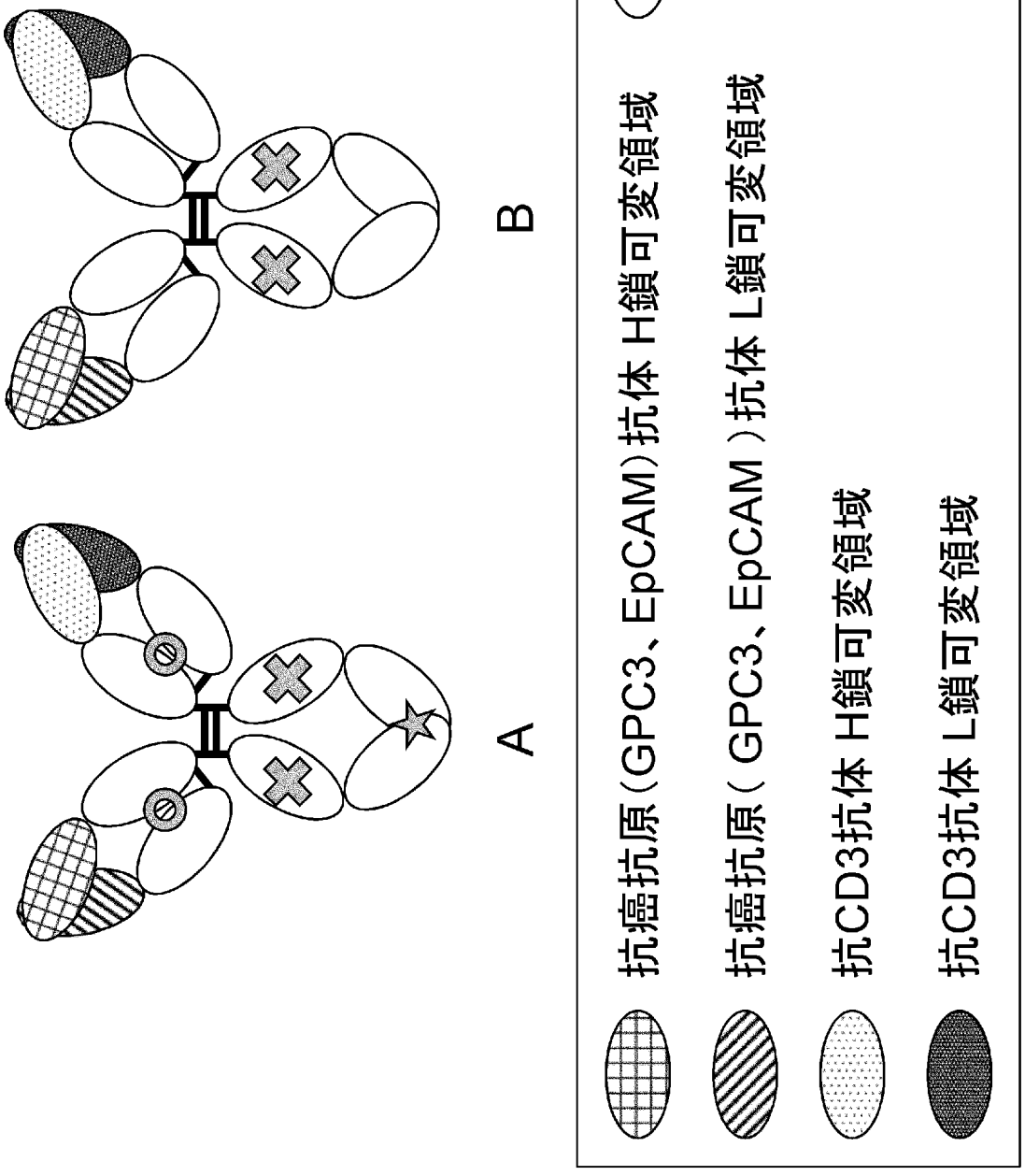
[図22]


140
120
100
80
60
40
20
0
-20
細胞増殖抑制率 (%)
0.001
0.01
0.1
1
抗体濃度 (nM)

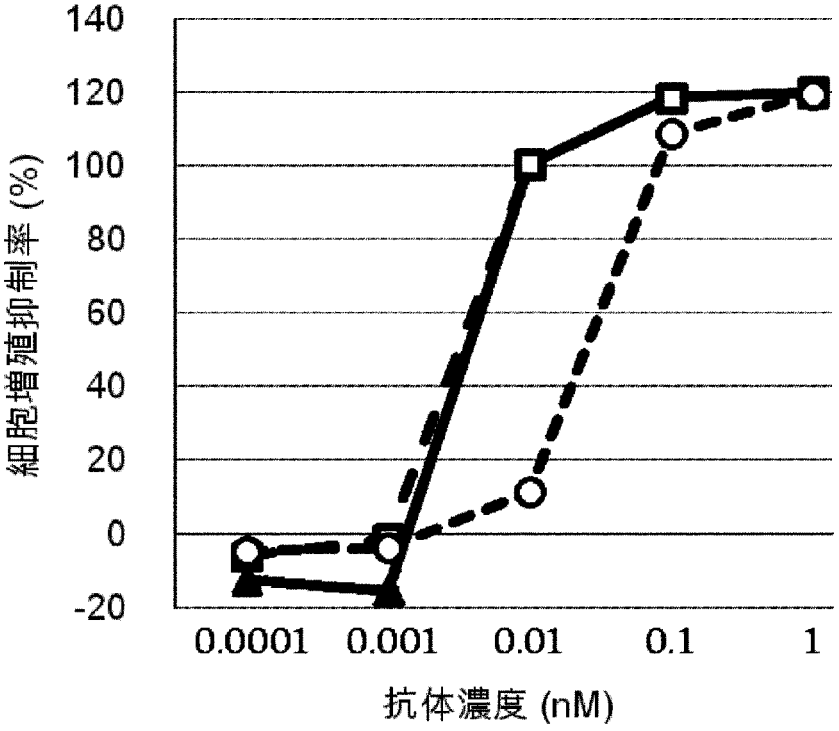
[図23]



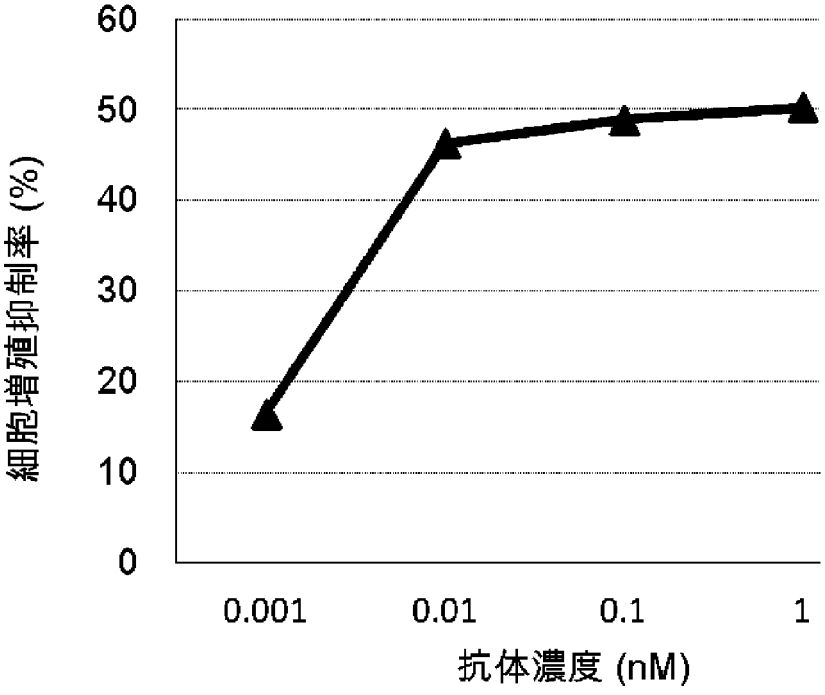
[図24]


A
B
抗癌抗原(GPC3、EpCAM)抗体 H鎖可変領域
抗癌抗原(GPC3、EpCAM)抗体 L鎖可変領域
抗CD3抗体 H鎖可変領域
抗CD3抗体 L鎖可変領域
抗体定常領域
サイレントFc変異
ヘテロFc会合化変異
CH/CL界面制御

[図25]


140
120
100
80
60
40
20
0
-20
細胞増殖抑制率 (%)
0.0001
0.001
0.01
0.1
1
抗体濃度 (nM)

[図26]


60
50
40
30
20
10
0
細胞増殖抑制率 (%)
0.001
0.01
0.1
1
抗体濃度 (nM)