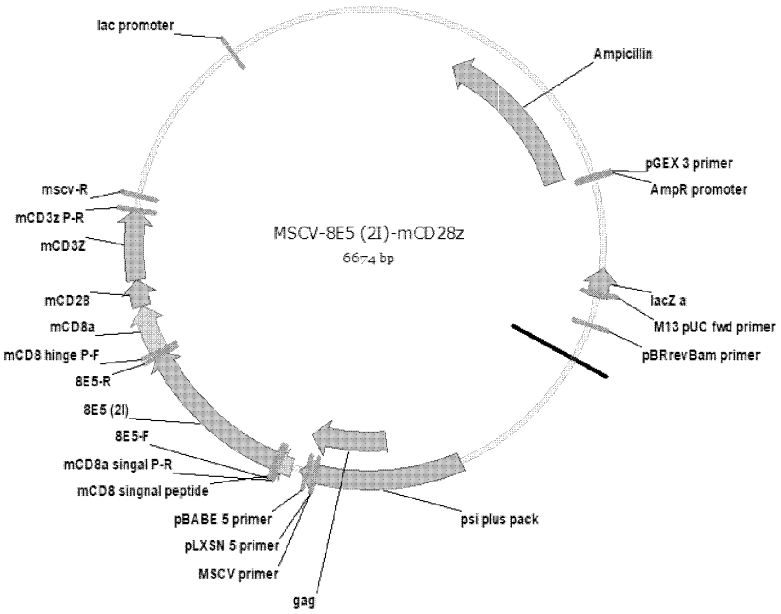

lac promoter
Ampicillin
pGEX 3 primer
AmpR promoter
mscv-R
mCD3z P-R
mCD3Z
MSCV-8E5 (2I)-mCD28z
6674 bp
lacZ a
M13 pUC fwd primer
pBRrevBam primer
mCD28
mCD8a
mCD8 hinge P-F
8E5-R
8E5 (2I)
8E5-F
mCD8a singal P-R
mCD8 singnal peptide
pBABE 5 primer
pLXSN 5 primer
MSCV primer
gag
psi plus pack

图 1A

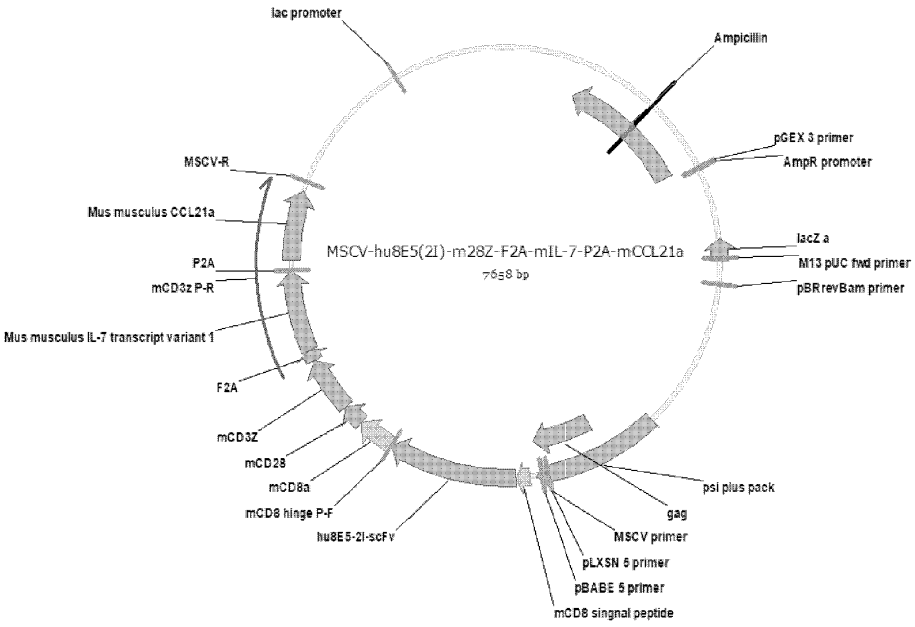

lac promoter
Ampicillin
pGEX 3 primer
AmpR promoter
MSCV-R
Mus musculus CCL21a
MSCV-hu8E5(2I)-m28Z-F2A-mIL-7-P2A-mCCL21a
7658 bp
lacZ a
M13 pUC fwd primer
pBRrevBam primer
P2A
mCD3z P-R
Mus musculus IL-7 transcript variant 1
F2A
mCD3Z
mCD28
mCD8a
mCD8 hinge P-F
hu8E5-2I-scFv
psi plus pack
gag
MSCV primer
pLXSN 5 primer
pBABE 5 primer
mCD8 singnal peptide

图 1B

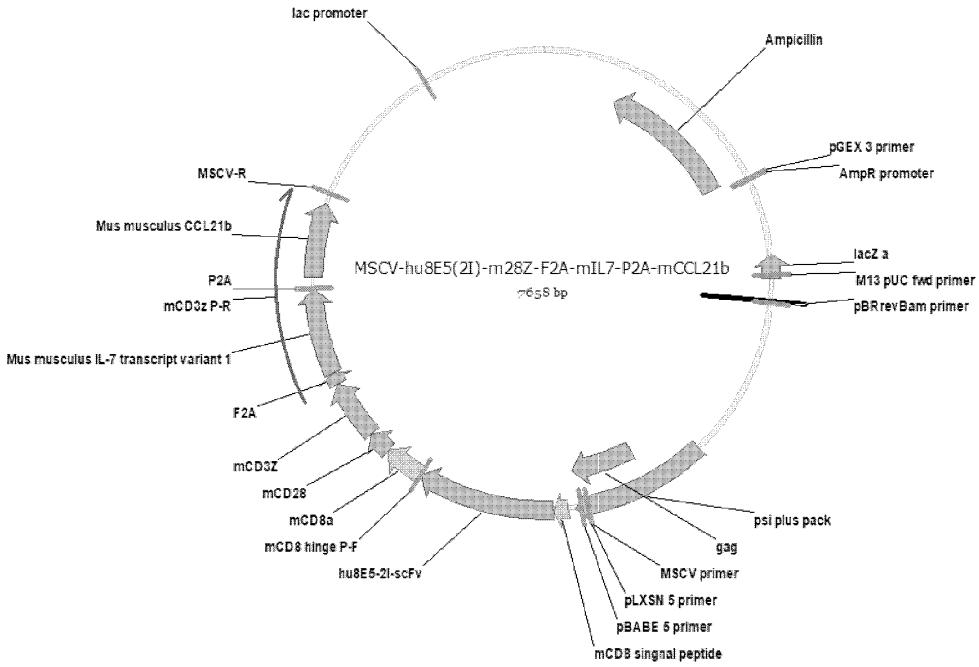

lac promoter
Ampicillin
pGEX 3 primer
AmpR promoter
MSCV-R
Mus musculus CCL21b
MSCV-hu8E5(2I)-m28Z-F2A-mIL7-P2A-mCCL21b
7658 bp
lacZ a
M13 pUC fwd primer
pBRrevBam primer
P2A
mCD3z P-R
Mus musculus IL-7 transcript variant 1
F2A
mCD3Z
mCD28
mCD8a
mCD8 hinge P-F
hu8E5-2I-scFv
psi plus pack
gag
MSCV primer
pLXSN 5 primer
pBABE 5 primer
mCD8 singnal peptide

图 1C

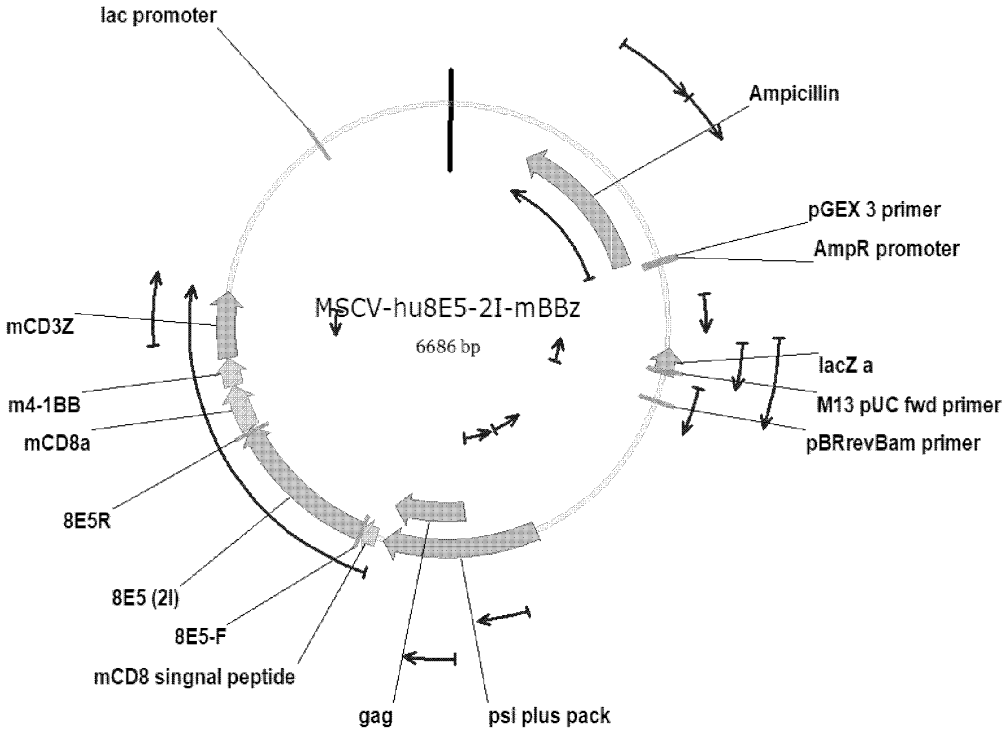

lac promoter
Ampicillin
pGEX 3 primer
AmpR promoter
MSCV-hu8E5-2I-mBBz
6686 bp
mCD3Z
m4-1BB
mCD8a
8E5R
8E5 (2I)
8E5-F
mCD8 singnal peptide
gag
psi plus pack
lacZ a
M13 pUC fwd primer
pBRrevBam primer

图 1D

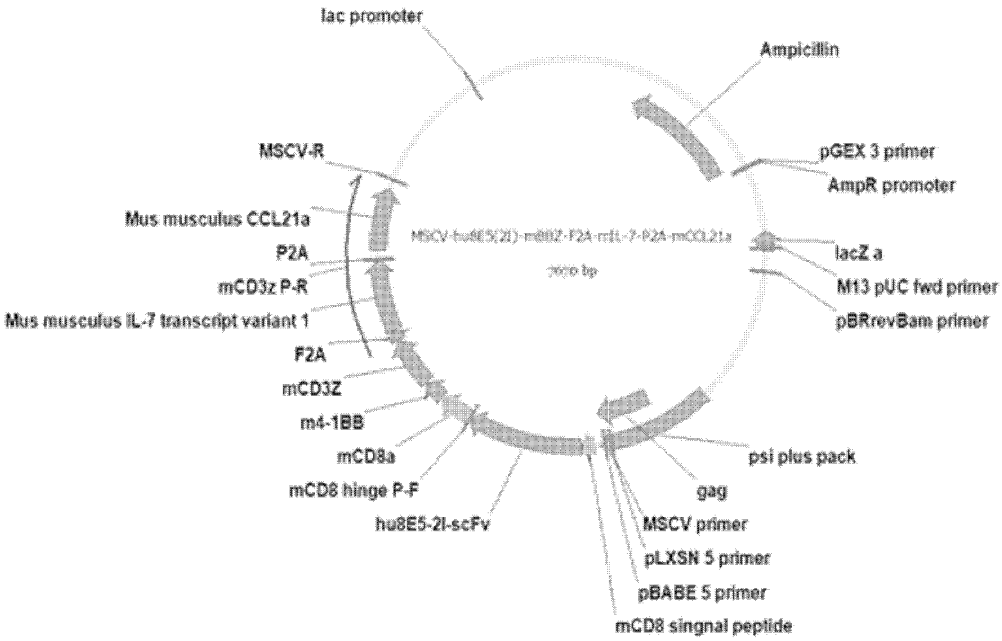

lac promoter
Ampicillin
MSCV-R
pGEX 3 primer
AmpR promoter
Mus musculus CCL21a
MSCV-hu8E5(2I)-m88Z-F2A-mIL-7-P2A-mCCL21a
7670 bp
P2A
lacZ a
mCD3z P-R
M13 pUC fwd primer
Mus musculus IL-7 transcript variant 1
pBRrevBam primer
F2A
mCD3Z
m4-1BB
psi plus pack
mCD8a
gag
mCD8 hinge P-F
MSCV primer
hu8E5-2I-scFv
pLXSN 5 primer
pBABE 5 primer
mCD8 singnal peptide

图 1E

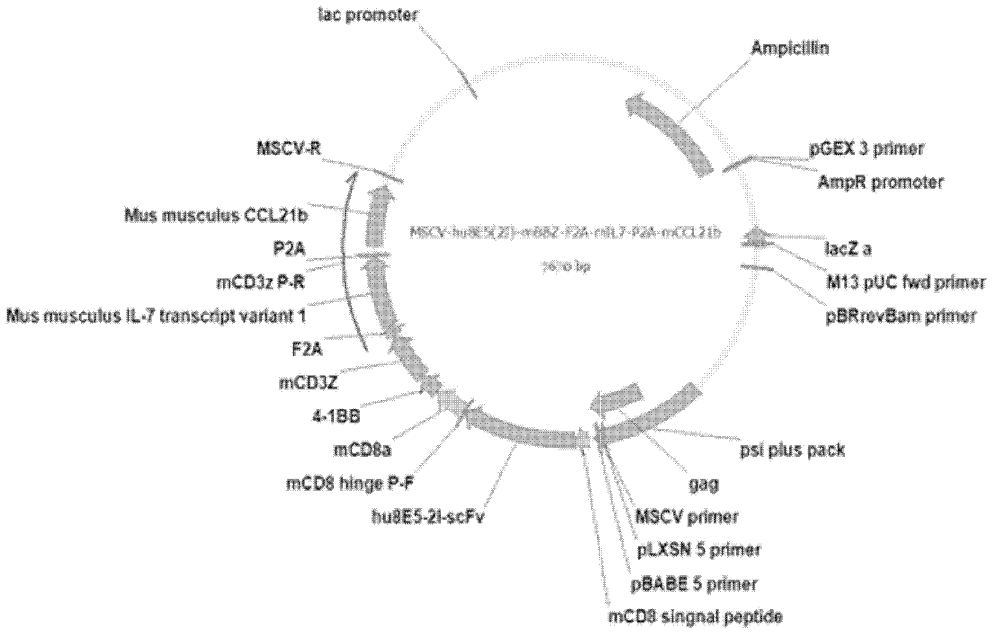

lac promoter
Ampicillin
MSCV-R
pGEX 3 primer
AmpR promoter
Mus musculus CCL21b
MSCV-hu8E5(2I)-m88Z-F2A-mIL7-P2A-mCCL21b
7670 bp
P2A
lacZ a
mCD3z P-R
M13 pUC fwd primer
Mus musculus IL-7 transcript variant 1
pBRrevBam primer
F2A
mCD3Z
4-1BB
psi plus pack
mCD8a
gag
mCD8 hinge P-F
MSCV primer
hu8E5-2I-scFv
pLXSN 5 primer
pBABE 5 primer
mCD8 singnal peptide

图 1F

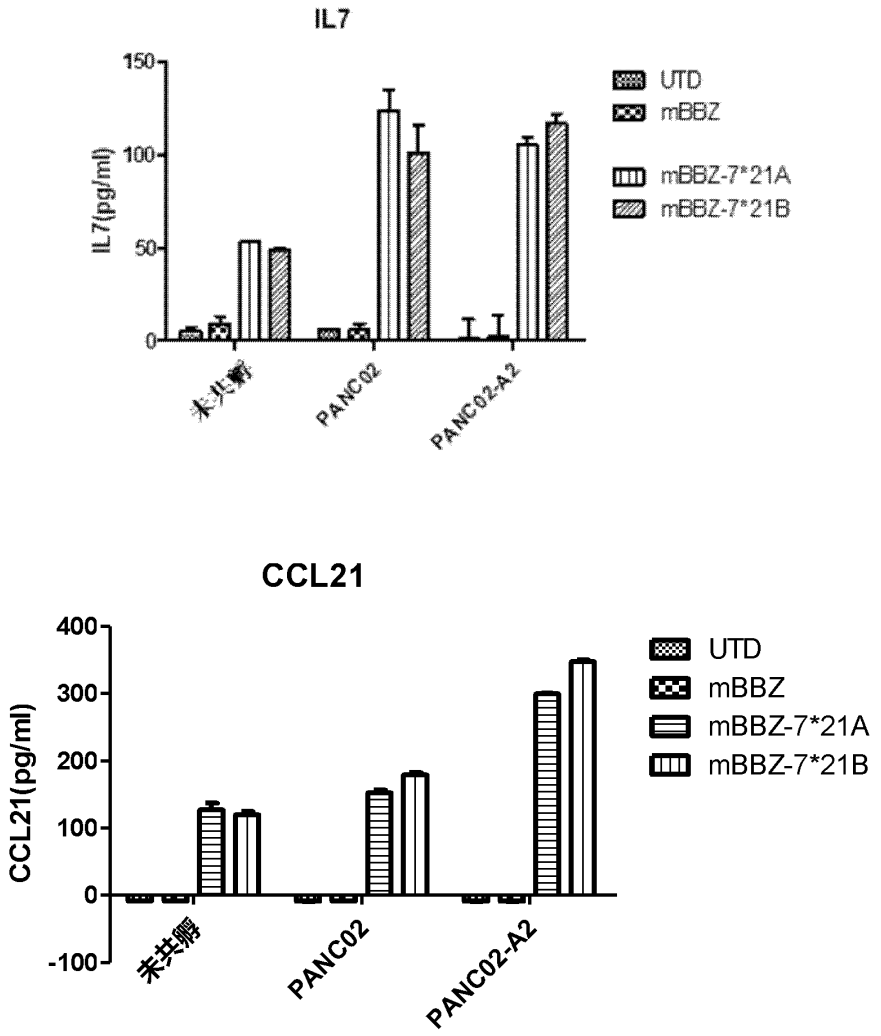

IL7
150
100
50
0
IL7(pg/ml)
UTD
mBBZ
mBBZ-7*21A
mBBZ-7*21B
未共孵
PANC02
PANC02-A2
CCL21
400
300
200
100
0
-100
CCL21(pg/ml)
UTD
mBBZ
mBBZ-7*21A
mBBZ-7*21B
未共孵
PANC02
PANC02-A2

图 2

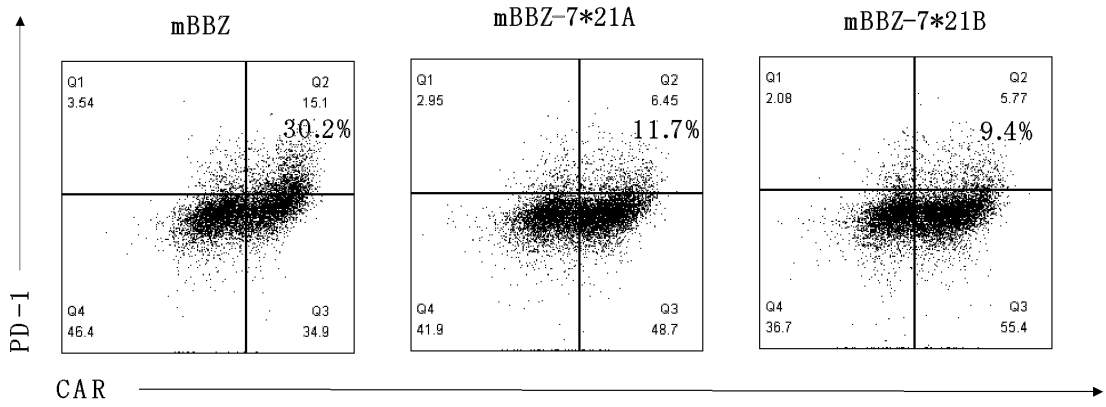

mBBZ
mBBZ-7*21A
mBBZ-7*21B
Q1
3.54
Q2
15.1
30.2%
Q4
46.4
Q3
34.9
Q1
2.95
Q2
6.45
11.7%
Q4
41.9
Q3
48.7
Q1
2.08
Q2
5.77
9.4%
Q4
36.7
Q3
55.4
PD-1
CAR

图 3A

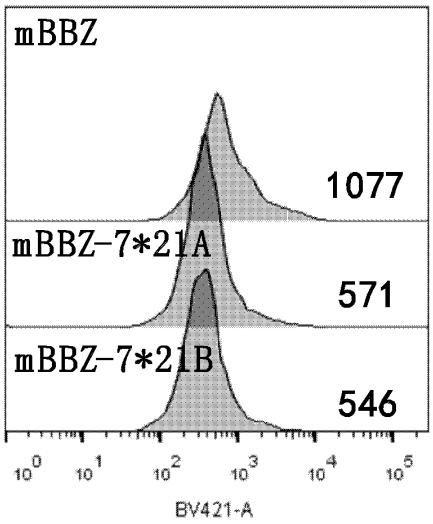

mBBZ
1077
mBBZ-7*21A
571
mBBZ-7*21B
546
10^0 10^1 10^2 10^3 10^4 10^5
BV421-A

图 3B

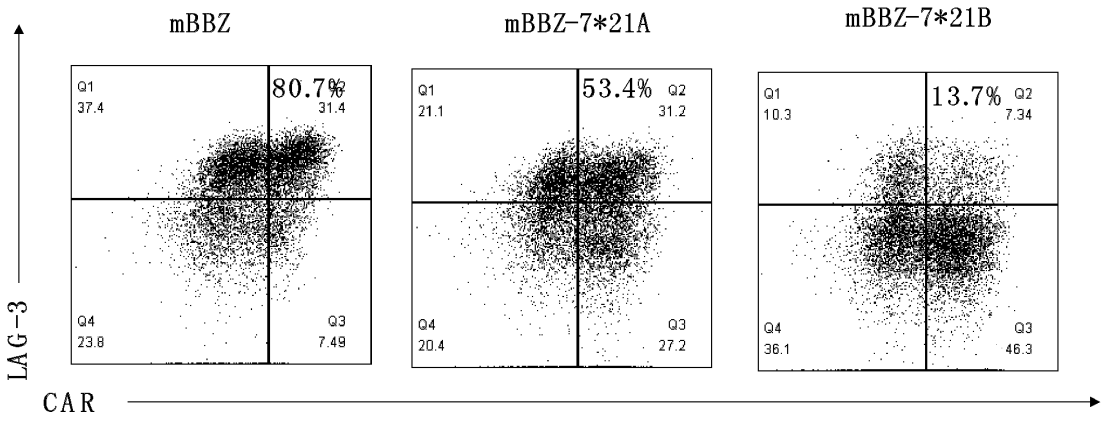

mBBZ
mBBZ-7*21A
mBBZ-7*21B
LAG-3
CAR
Q1
37.4
80.7%
31.4
Q4
23.8
Q3
7.49
Q1
21.1
53.4%
Q2
31.2
Q4
20.4
Q3
27.2
Q1
10.3
13.7%
Q2
7.34
Q4
36.1
Q3
46.3

图 3C

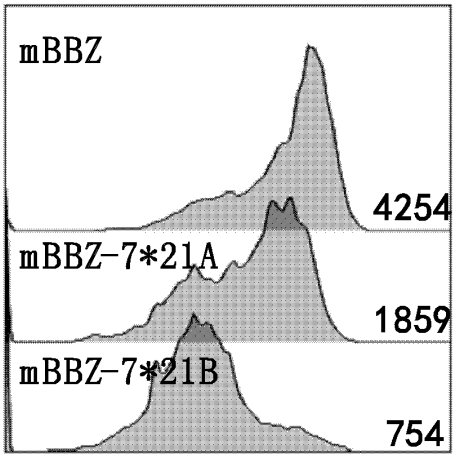

mBBZ
4254
mBBZ-7*21A
1859
mBBZ-7*21B
754

图 3D

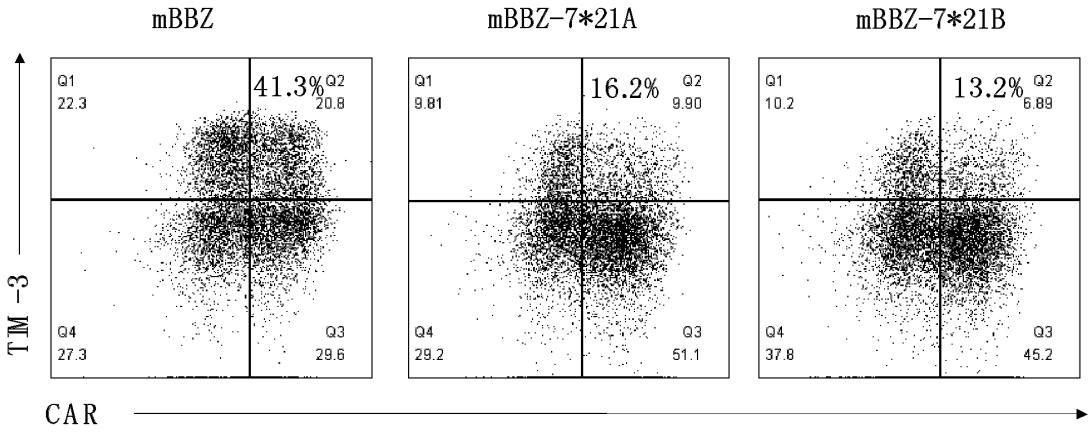

mBBZ
mBBZ-7*21A
mBBZ-7*21B
TM-3
CAR
Q1
22.3
41.3%
Q2
20.8
Q4
27.3
Q3
29.6
Q1
9.81
16.2%
Q2
9.90
Q4
29.2
Q3
51.1
Q1
10.2
13.2%
Q2
6.89
Q4
37.8
Q3
45.2

图 3E

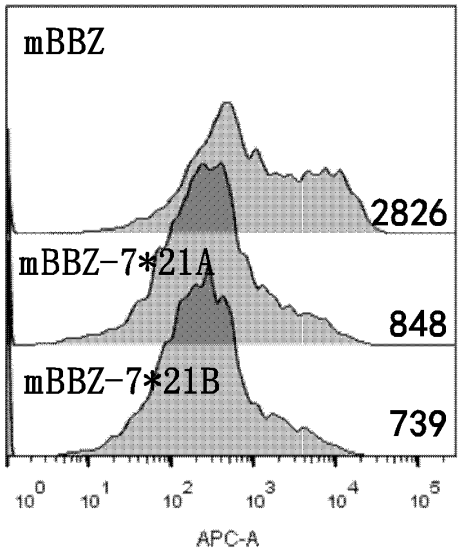

mBBZ
2826
mBBZ-7*21A
848
mBBZ-7*21B
739
10^0
10^1
10^2
10^3
10^4
10^5
APC-A

图 3F

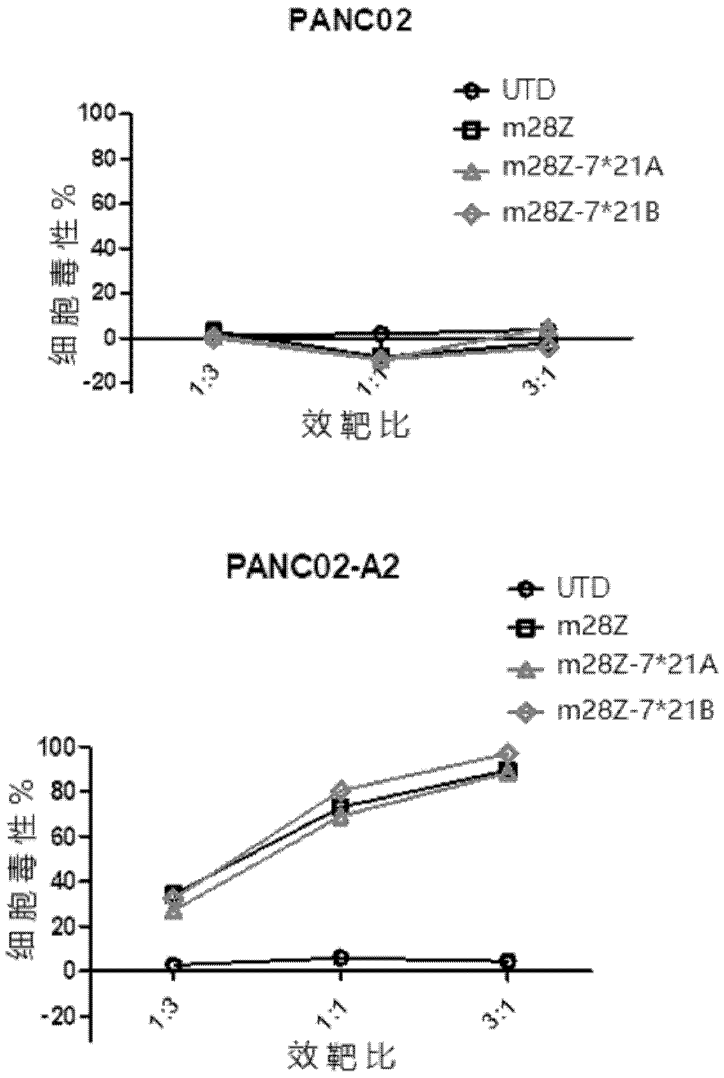

PANC02
UTD
m28Z
m28Z-7*21A
m28Z-7*21B
细胞毒性 %
100
80
60
40
20
0
-20
1:3
1:1
3:1
效靶比
PANC02-A2
UTD
m28Z
m28Z-7*21A
m28Z-7*21B
细胞毒性 %
100
80
60
40
20
0
-20
1:3
1:1
3:1
效靶比

图 4A

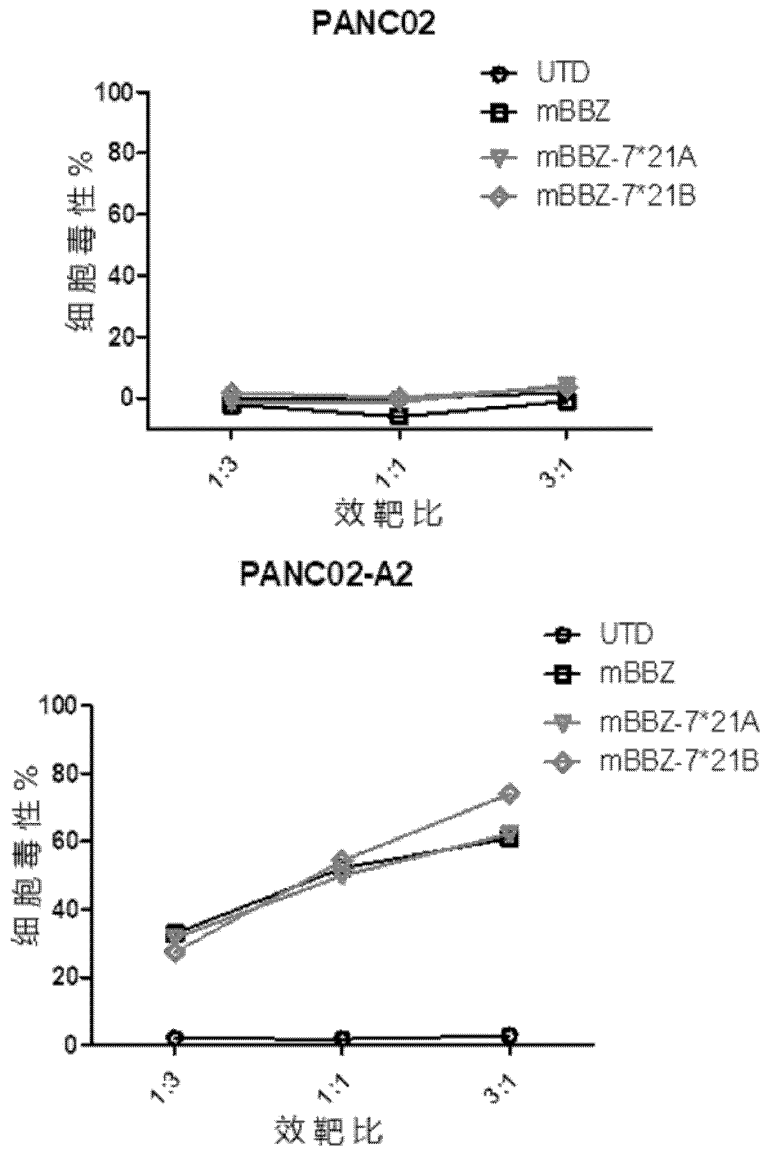

PANC02
UTD
mBBZ
mBBZ-7*21A
mBBZ-7*21B
细胞毒性 %
100
80
60
40
20
0
1:3
1:1
3:1
效靶比
PANC02-A2
UTD
mBBZ
mBBZ-7*21A
mBBZ-7*21B
细胞毒性 %
100
80
60
40
20
0
1:3
1:1
3:1
效靶比

图 4B

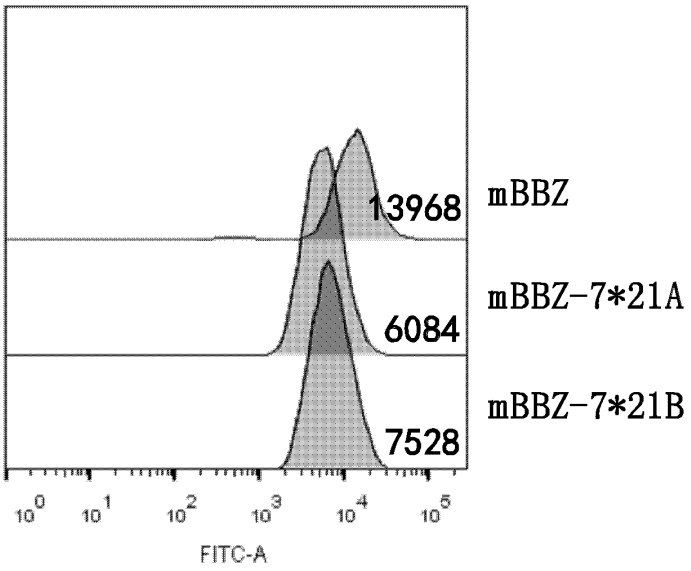

13968
mBBZ
6084
mBBZ-7*21A
7528
mBBZ-7*21B
10^0 10^1 10^2 10^3 10^4 10^5
FITC-A

图 5

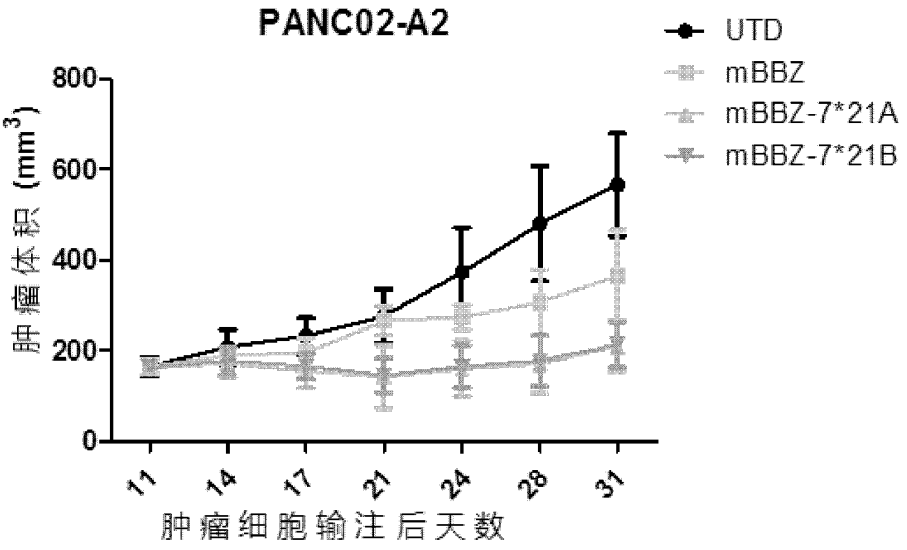

PANC02-A2
UTD
mBBZ
mBBZ-7*21A
mBBZ-7*21B
肿瘤体积 (mm^3)
800
600
400
200
0
11 14 17 21 24 28 31
肿瘤细胞输注后天数

图 6

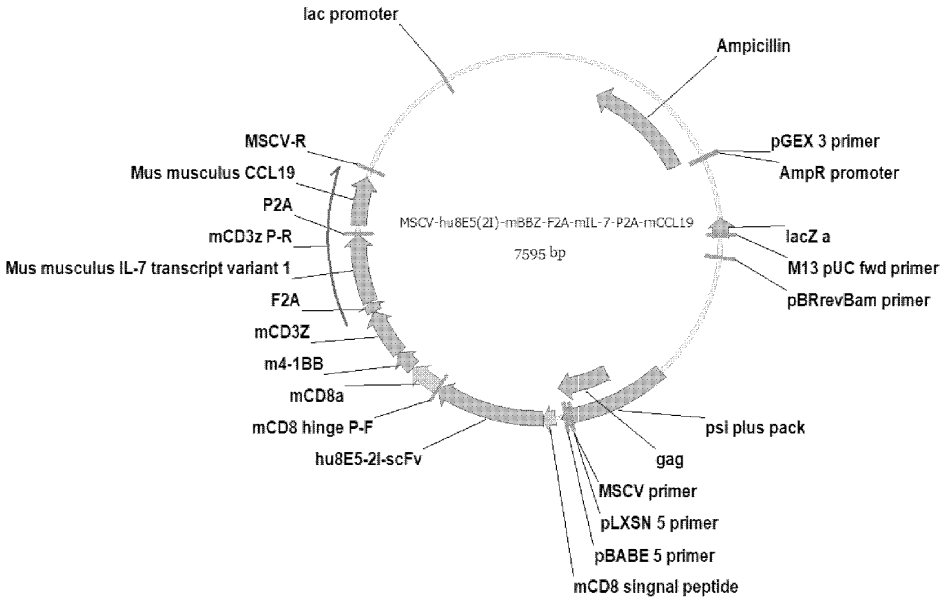

lac promoter
Ampicillin
MSCV-R
Mus musculus CCL19
P2A
mCD3z P-R
Mus musculus IL-7 transcript variant 1
F2A
mCD3Z
m4-1BB
mCD8a
mCD8 hinge P-F
hu8E5-2I-scFv
MSCV-hu8E5(2I)-mBBZ-F2A-mIL-7-P2A-mCCL19
7595 bp
pGEX 3 primer
AmpR promoter
lacZ a
M13 pUC fwd primer
pBRrevBam primer
psi plus pack
gag
MSCV primer
pLXSN 5 primer
pBABE 5 primer
mCD8 singnal peptide

图 7

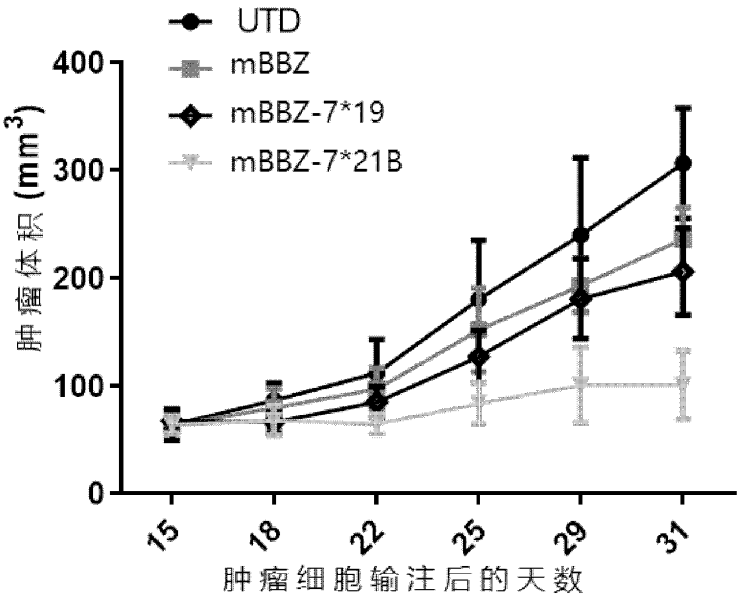

UTD
mBBZ
mBBZ-7*19
mBBZ-7*21B
肿瘤体积 (mm3)
400
300
200
100
0
15
18
22
25
29
31
肿瘤细胞输注后的天数

图 8A

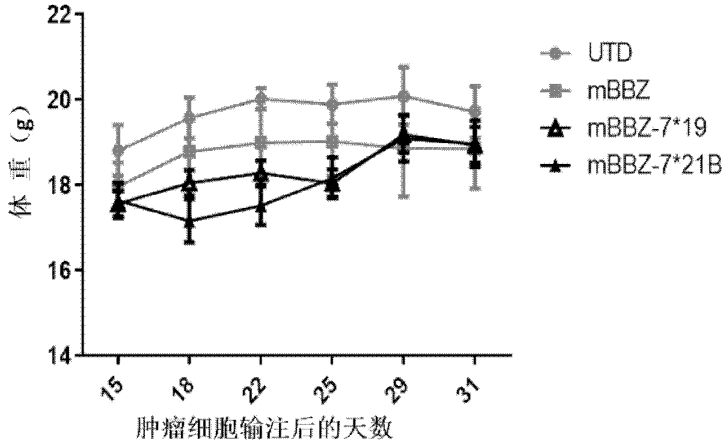

22
20
18
16
14
体重（g）
15
18
22
25
29
31
肿瘤细胞输注后的天数
UTD
mBBZ
mBBZ-7*19
mBBZ-7*21B

图 8B

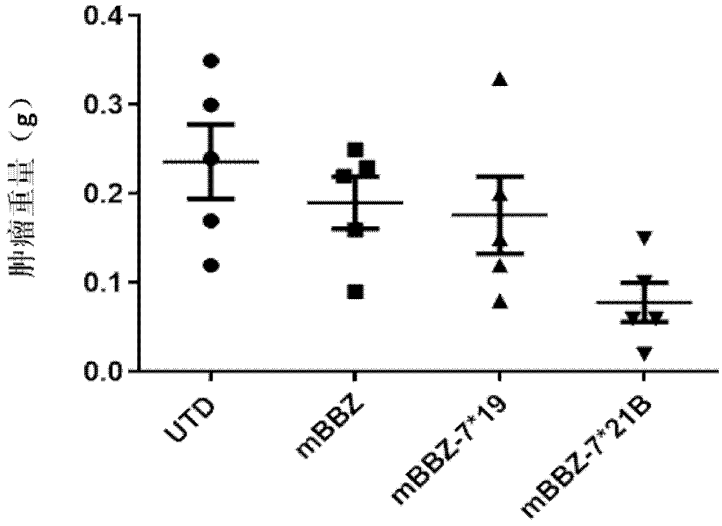

0.4
0.3
0.2
0.1
0.0
肿瘤重量（g）
UTD
mBBZ
mBBZ-7*19
mBBZ-7*21B

图 8C

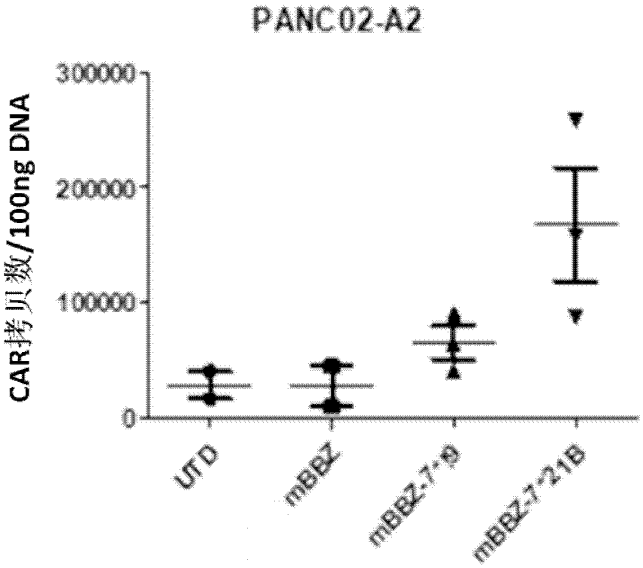

PANC02-A2
CAR拷贝数/100ng DNA
300000
200000
100000
0
UTD
mBBZ
mBBZ-7*9
mBBZ-7*21B

图 8D

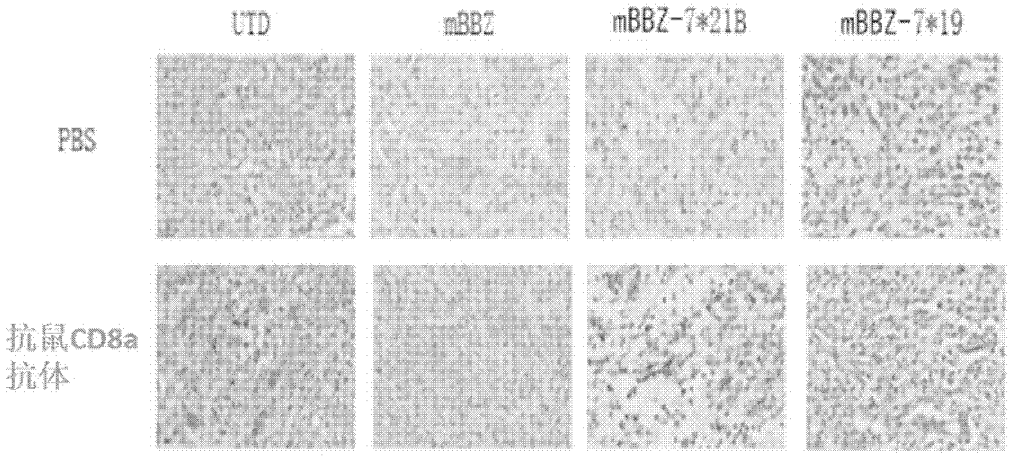

UTD
mBBZ
mBBZ-7*21B
mBBZ-7*19
PBS
抗鼠CD8a
抗体

图 8E

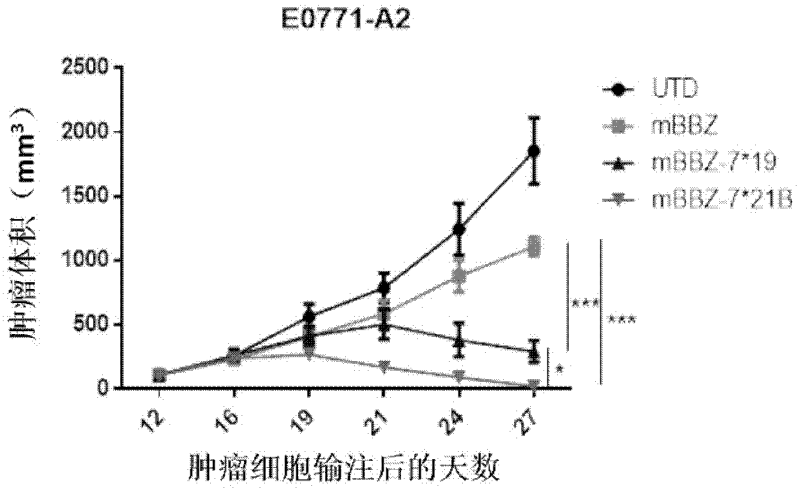

E0771-A2
肿瘤体积（mm³）
2500
2000
1500
1000
500
0
12
16
19
21
24
27
肿瘤细胞输注后的天数
UTD
mBBZ
mBBZ-7*19
mBBZ-7*21B
***
***
*

图 9A

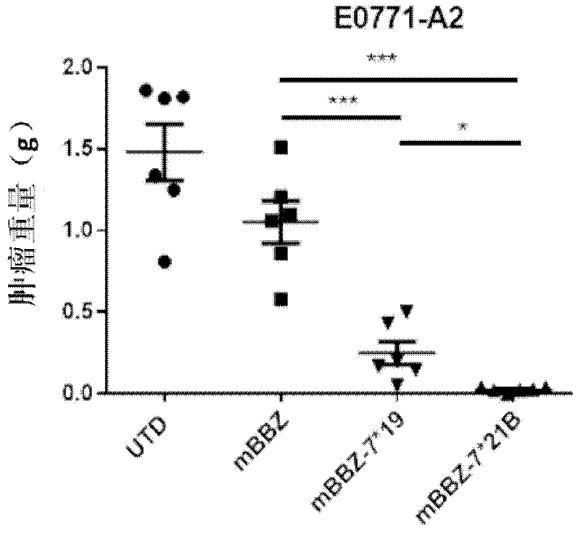

E0771-A2
肿瘤重量（g）
2.0
1.5
1.0
0.5
0.0
***
***
*
UTD
mBBZ
mBBZ-7*19
mBBZ-7*21B

图 9B

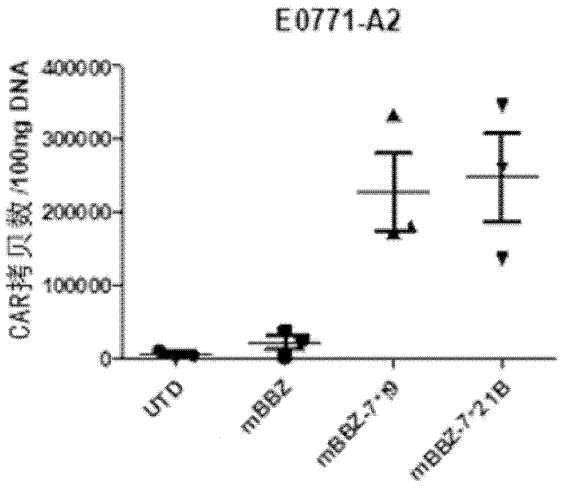

E0771-A2
CAR拷贝数/100mg DNA
400000
300000
200000
100000
0
UTD
mBBZ
mBBZ-7*9
mBBZ-7*21B

图 9C

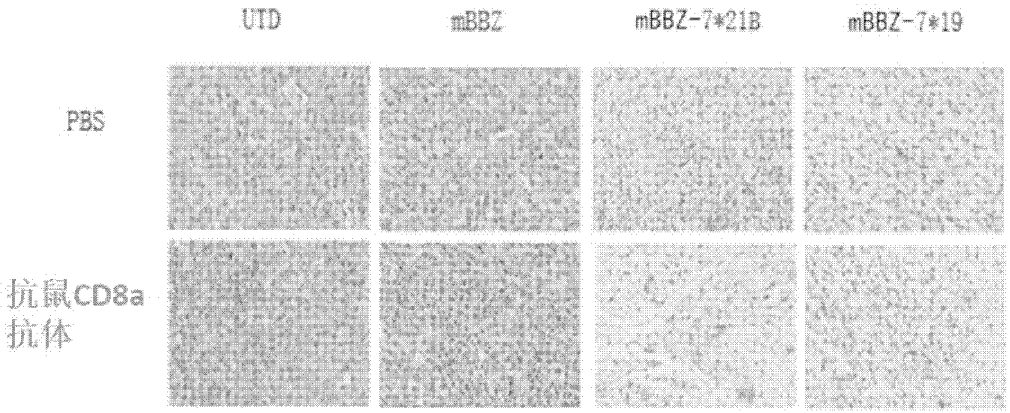

UTD
mBBZ
mBBZ-7*21B
mBBZ-7*19
PBS
抗鼠CD8a
抗体

图 9D

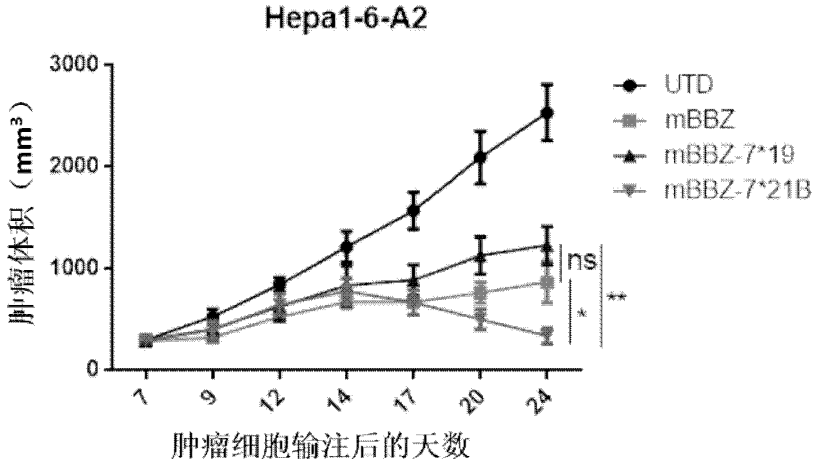

Hepa1-6-A2
肿瘤体积（mm³）
3000
2000
1000
0
7
9
12
14
17
20
24
肿瘤细胞输注后的天数
UTD
mBBZ
mBBZ-7*19
mBBZ-7*21B
ns
*
**

图 10A

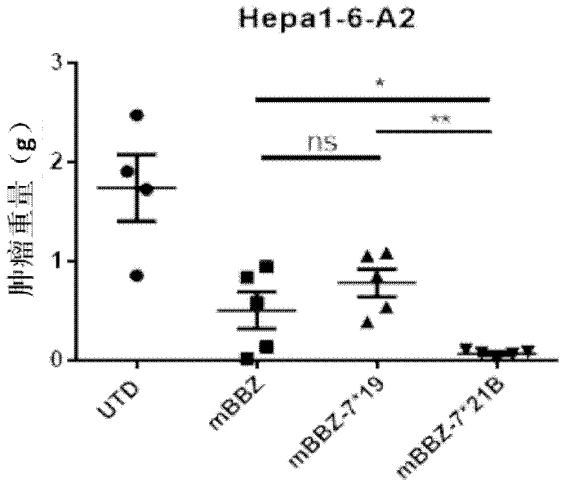

Hepa1-6-A2
肿瘤重量（g）
3
2
1
0
*
**
ns
UTD
mBBZ
mBBZ-7*19
mBBZ-7*21B

图 10B

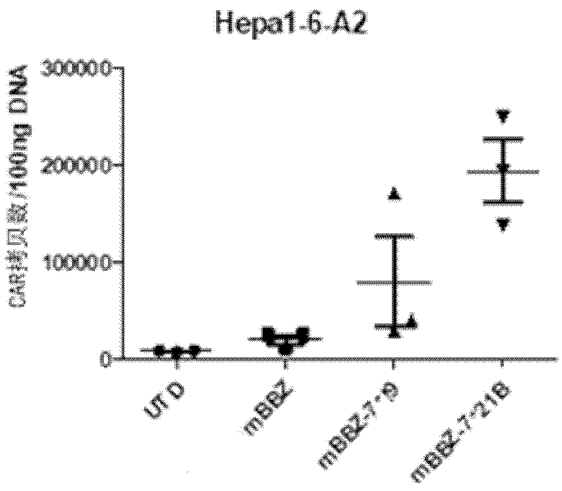

Hepa1-6-A2
CAR拷贝数/100ng DNA
300000
200000
100000
0
UTD
mBBZ
mBBZ-7*9
mBBZ-7*21B

图 10C

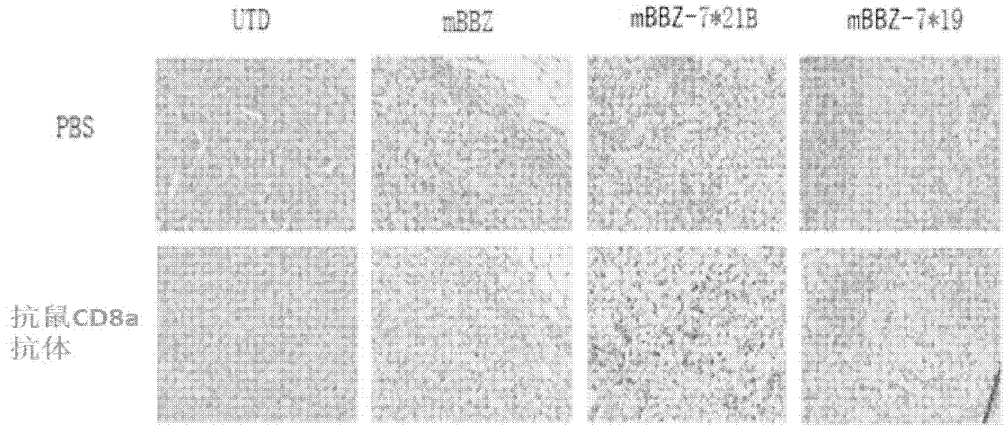

UTD
mBBZ
mBBZ-7*21B
mBBZ-7*19
PBS
抗鼠CD8a
抗体

图 10D

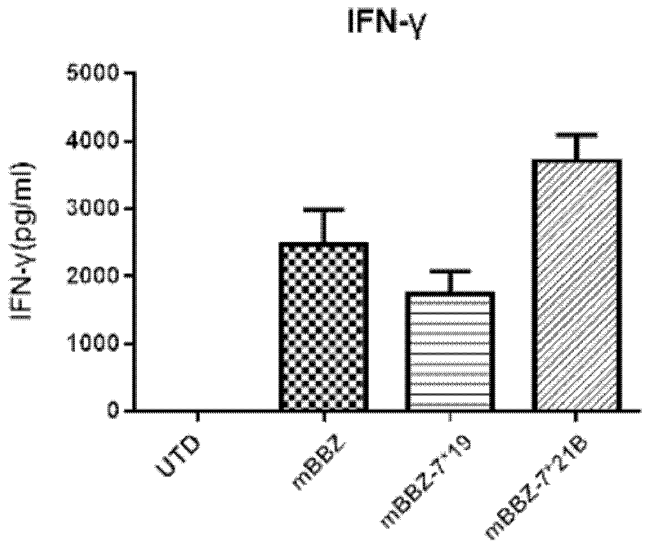

IFN-γ
IFN-γ(pg/ml)
5000
4000
3000
2000
1000
0
UTD
mBBZ
mBBZ-7*19
mBBZ-7*21B

图 11

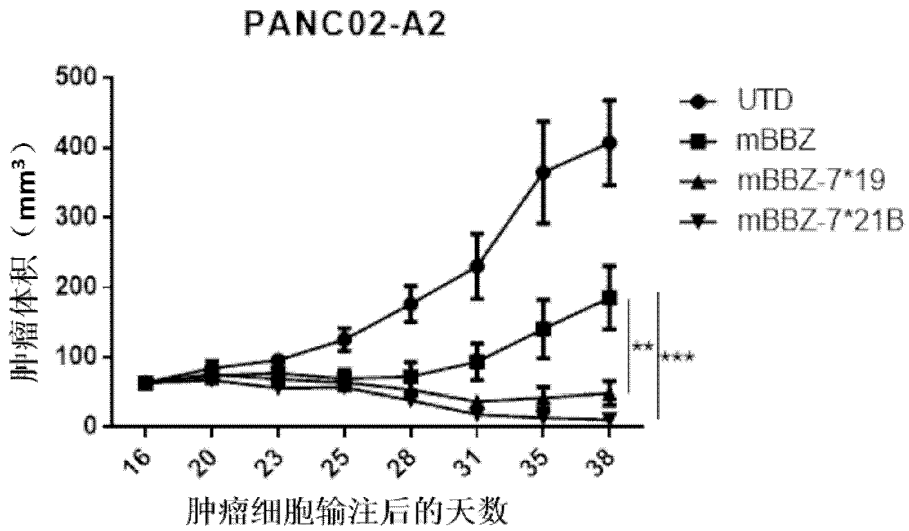

PANC02-A2
肿瘤体积（mm³）
500
400
300
200
100
0
16
20
23
25
28
31
35
38
肿瘤细胞输注后的天数
UTD
mBBZ
mBBZ-7*19
mBBZ-7*21B
**
***

图 12A

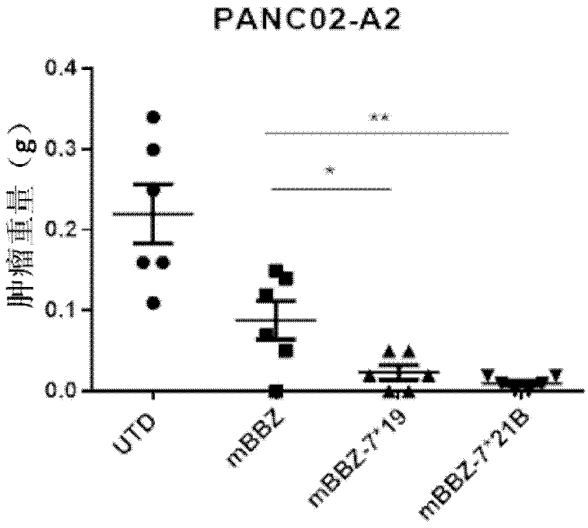

PANC02-A2
肿瘤重量（g）
0.4
0.3
0.2
0.1
0.0
**
*
UTD
mBBZ
mBBZ-7*19
mBBZ-7*21B

图 12B

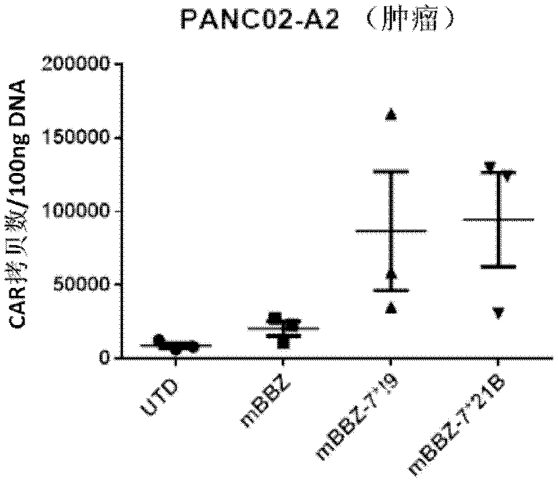

PANC02-A2 （肿瘤）
CAR拷贝数/100ng DNA
200000
150000
100000
50000
0
UTD
mBBZ
mBBZ-7*19
mBBZ-7*21B

图 12C

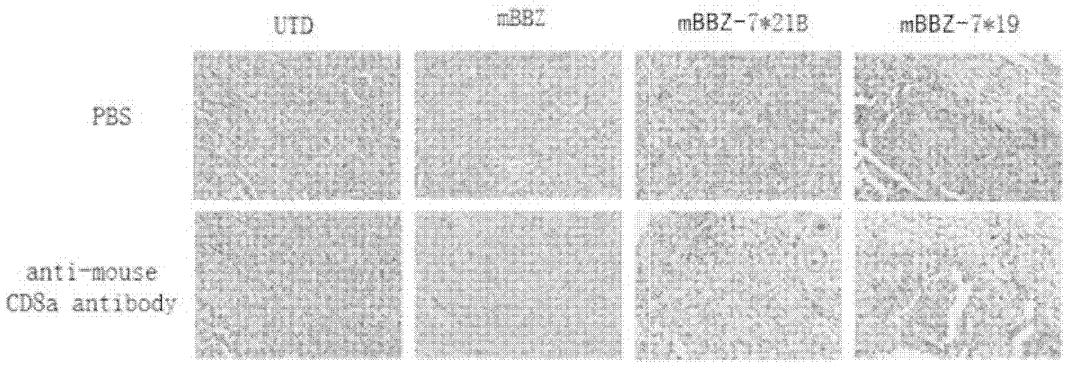


图 12D

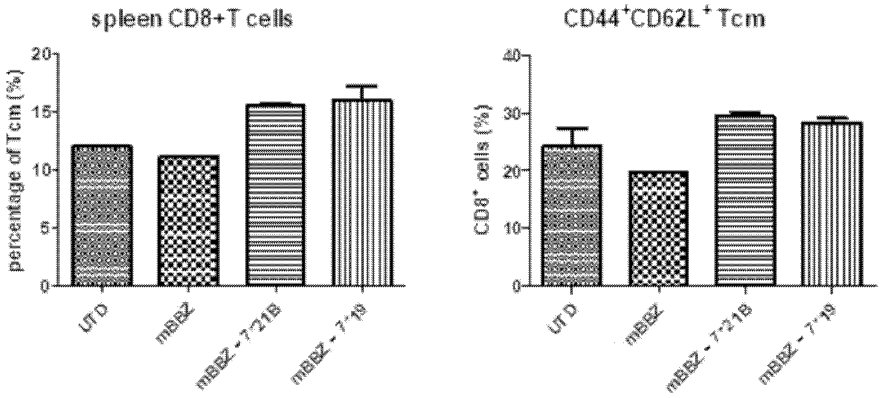


图 13A

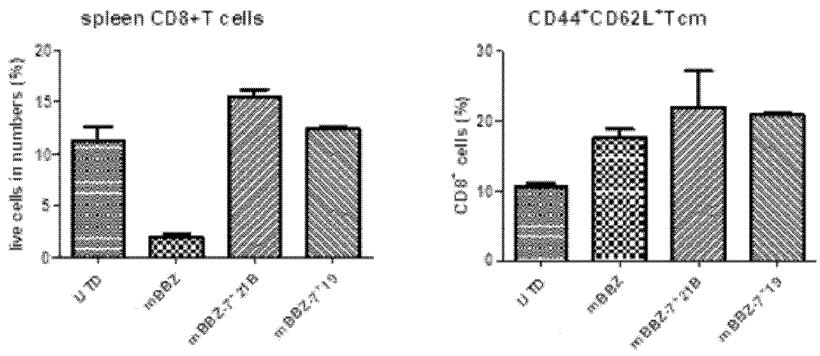


图 13B

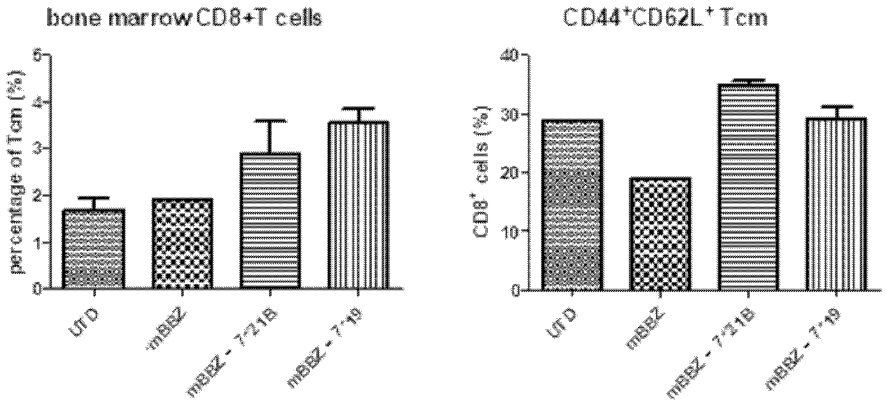


图 14A

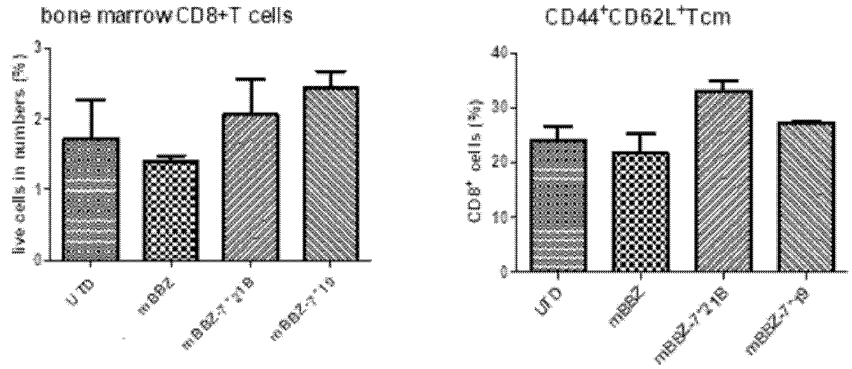


图 14B

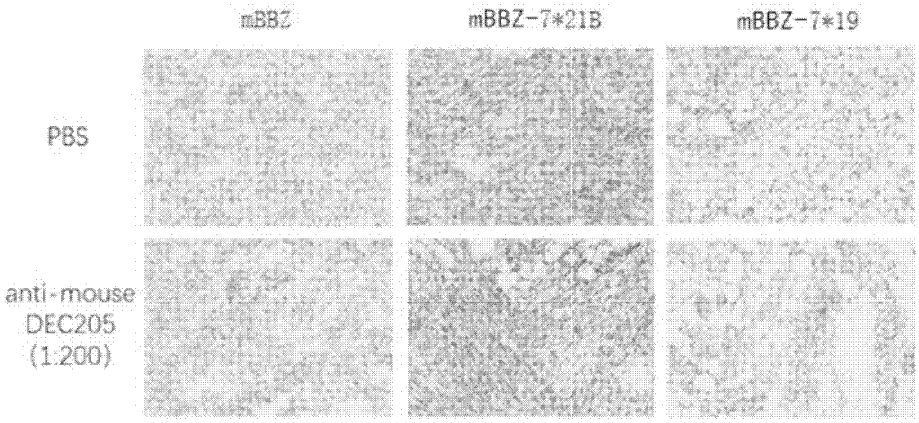


图 15

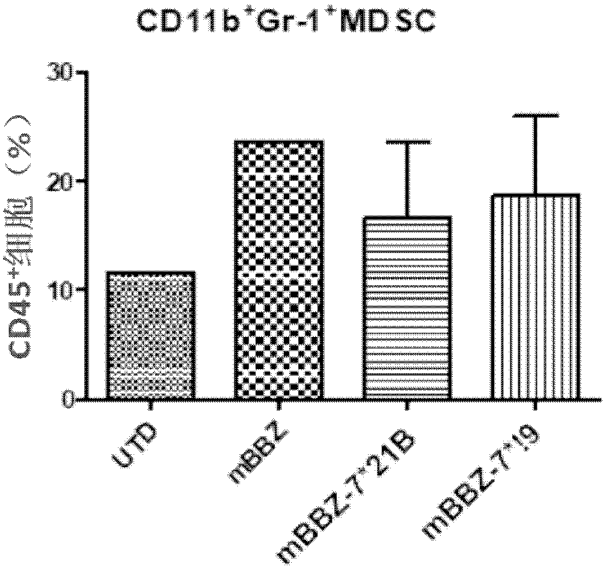


图 16