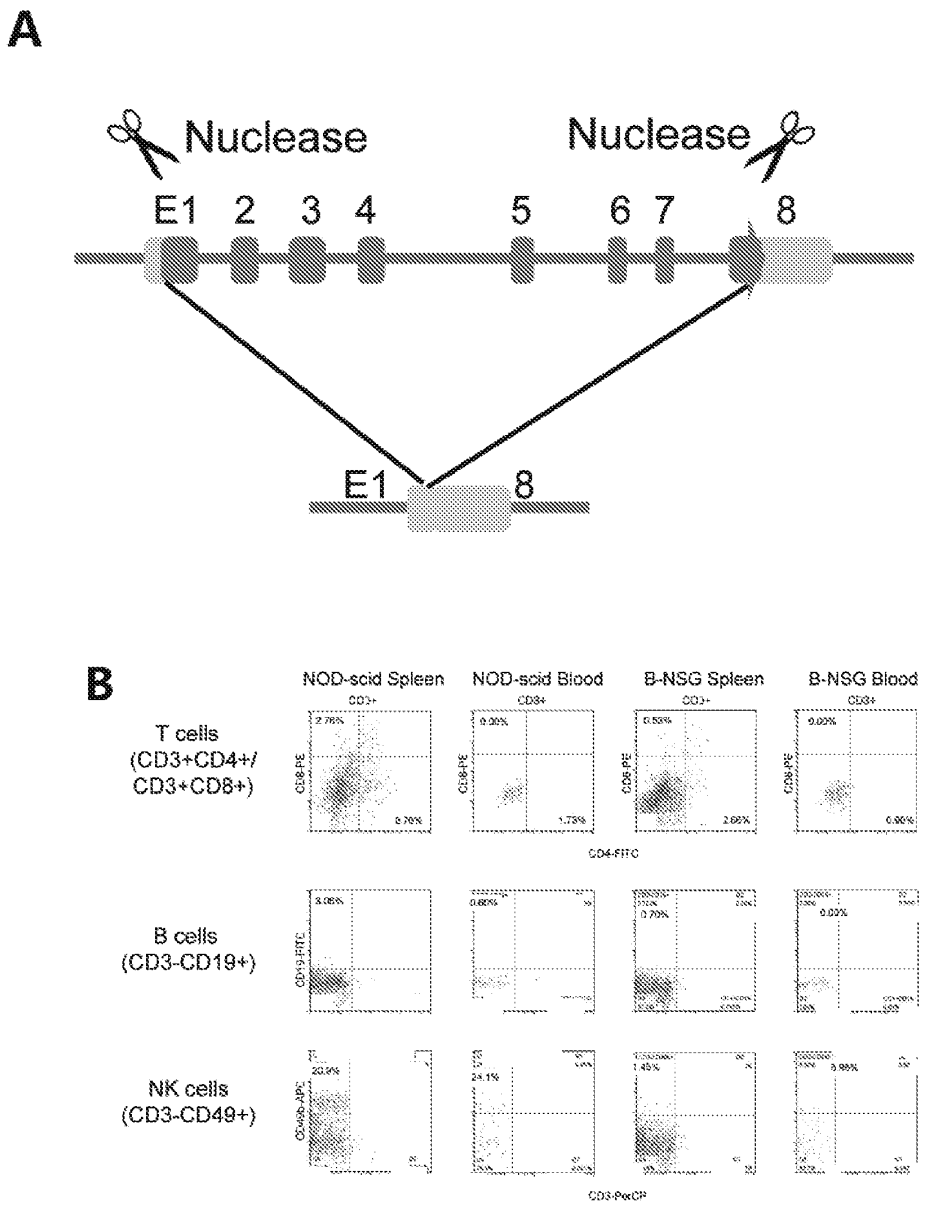
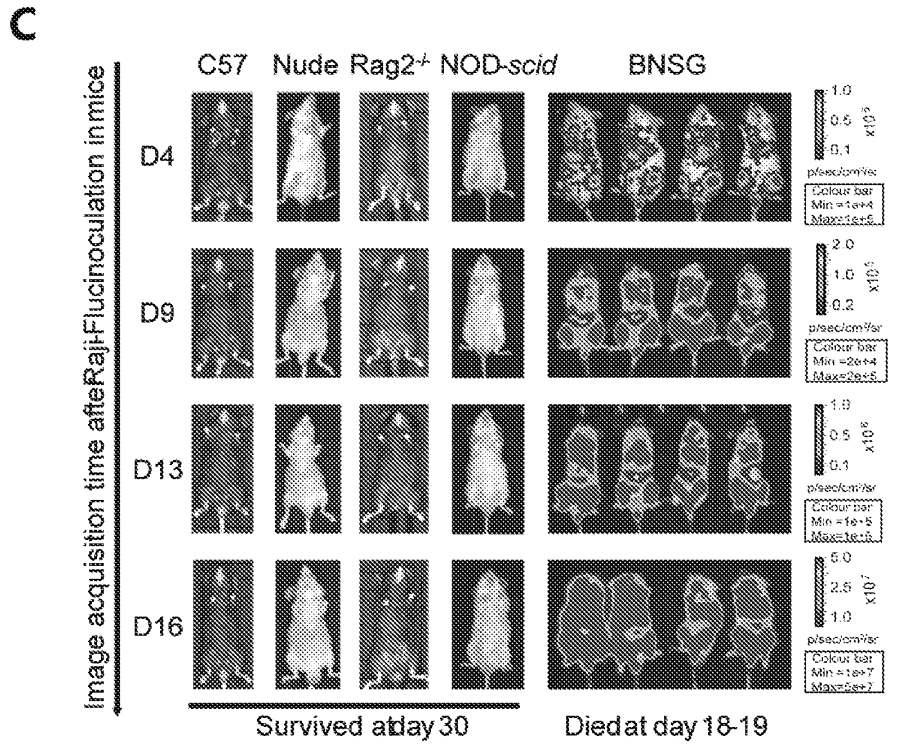
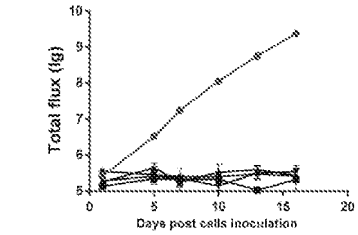
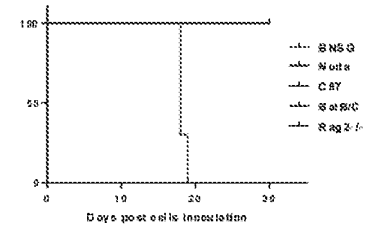
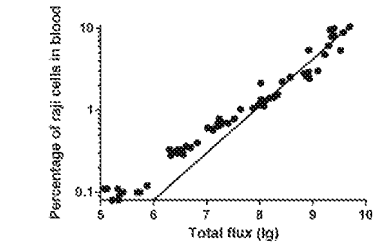

A
Nuclease
Nuclease
E1 2 3 4 5 6 7 8
E1 8
B
NOD-scid Spleen
NOD-scid Blood
B-NSG Spleen
B-NSG Blood
T cells
(CD3+CD4+/
CD3+CD8+)
B cells
(CD3-CD19+)
NK cells
(CD3-CD49+)
CD4-FITC
CD3-PerCP

图 1


C
C57
Nude
Rag2-/-
NOD-scid
BNSG
D4
D9
D13
D16
Image acquisition time afteRaji-Flucinoculation inmice
Survived atday 30
Diedat day 18-19


D
Total flux (lg)
Days post cells inoculation
BNSG
Nude
BalB/C
C57
Rag2-/-


F
Days post cells inoculation


E
Percentage of raji cells in blood
Total flux (lg)

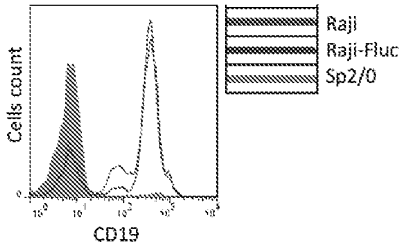

G
Cells count
CD19
Raji
Raji-Fluc
Sp2/0

图 1(续)

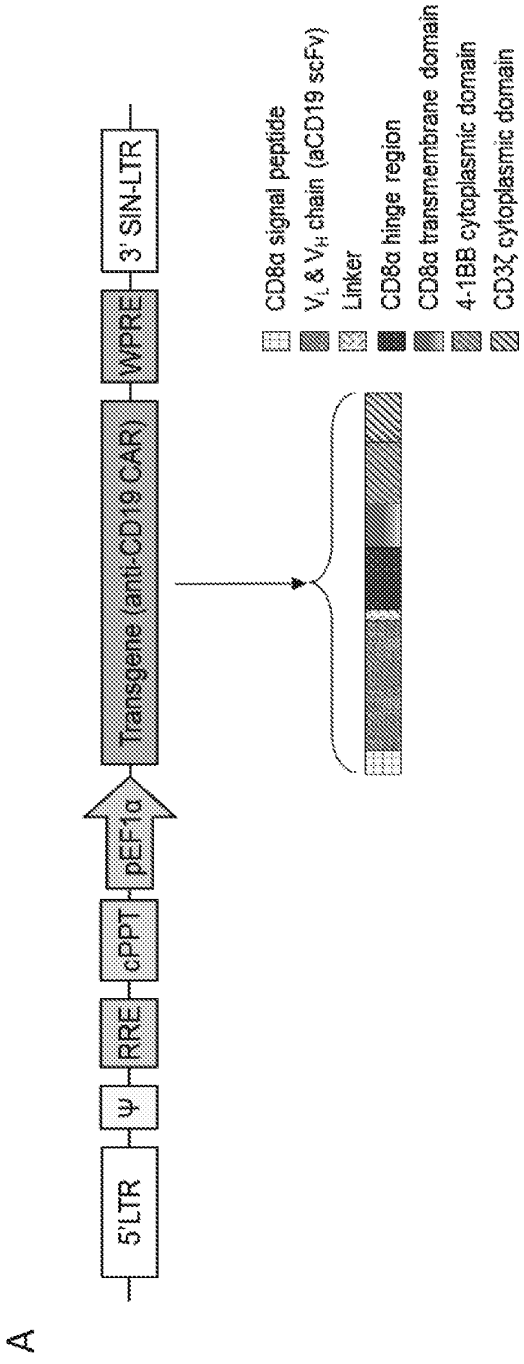

A
5'LTR
ψ
RRE
cPPT
pEF1α
Transgene (anti-CD19 CAR)
WPRE
3' SIN-LTR
CD8α signal peptide
V_L & V_H chain (αCD19 scFv)
Linker
CD8α hinge region
CD8α transmembrane domain
4-1BB cytoplasmic domain
CD3ζ cytoplasmic domain

图 2

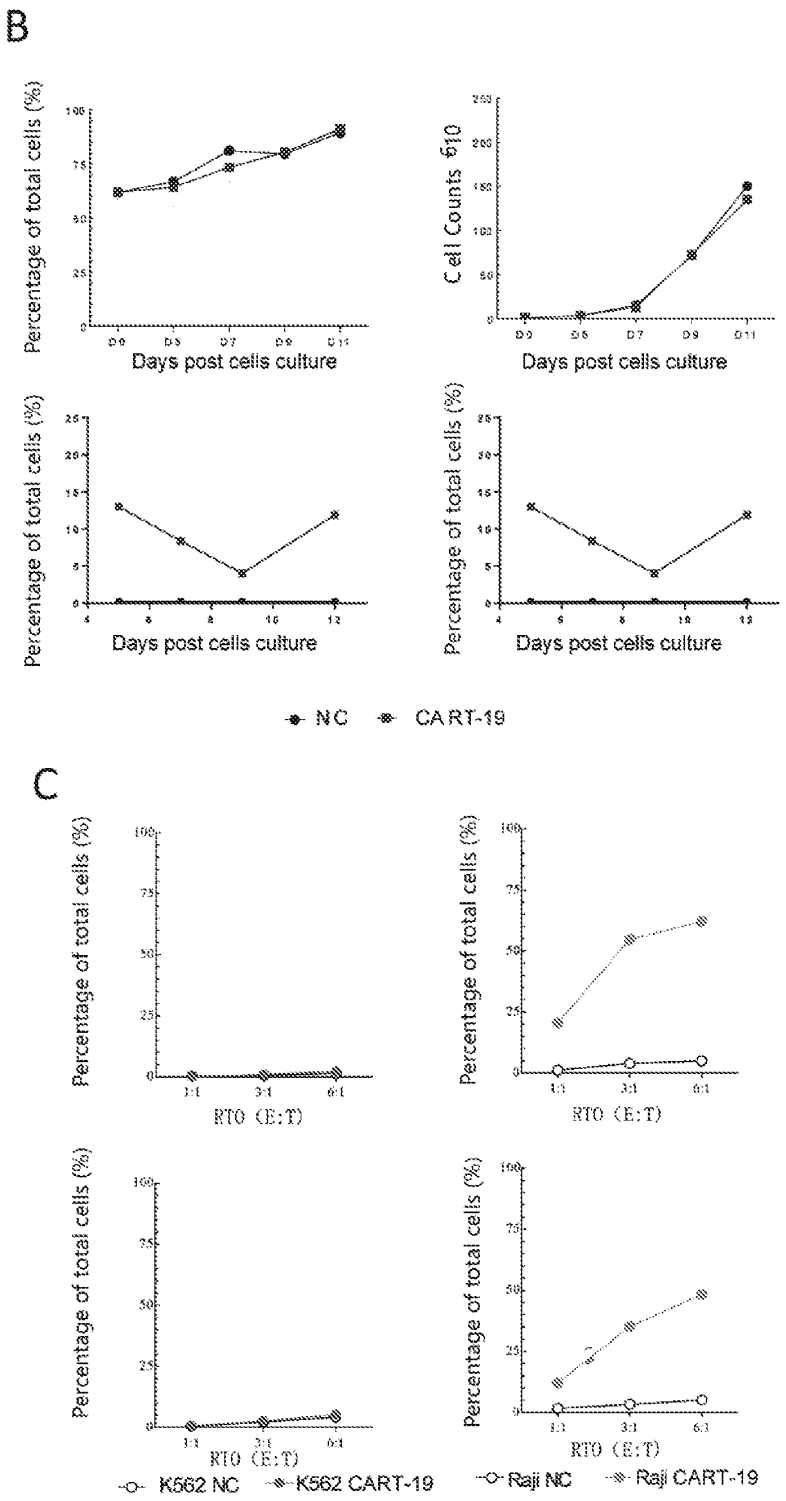

B
Percentage of total cells (%)
Days post cells culture
Cell Counts *10
Days post cells culture
Percentage of total cells (%)
Days post cells culture
Percentage of total cells (%)
Days post cells culture
NC
CART-19
C
Percentage of total cells (%)
RTO (E:T)
Percentage of total cells (%)
RTO (E:T)
Percentage of total cells (%)
RTO (E:T)
Percentage of total cells (%)
RTO (E:T)
K562 NC
K562 CART-19
Raji NC
Raji CART-19

图 2(续)

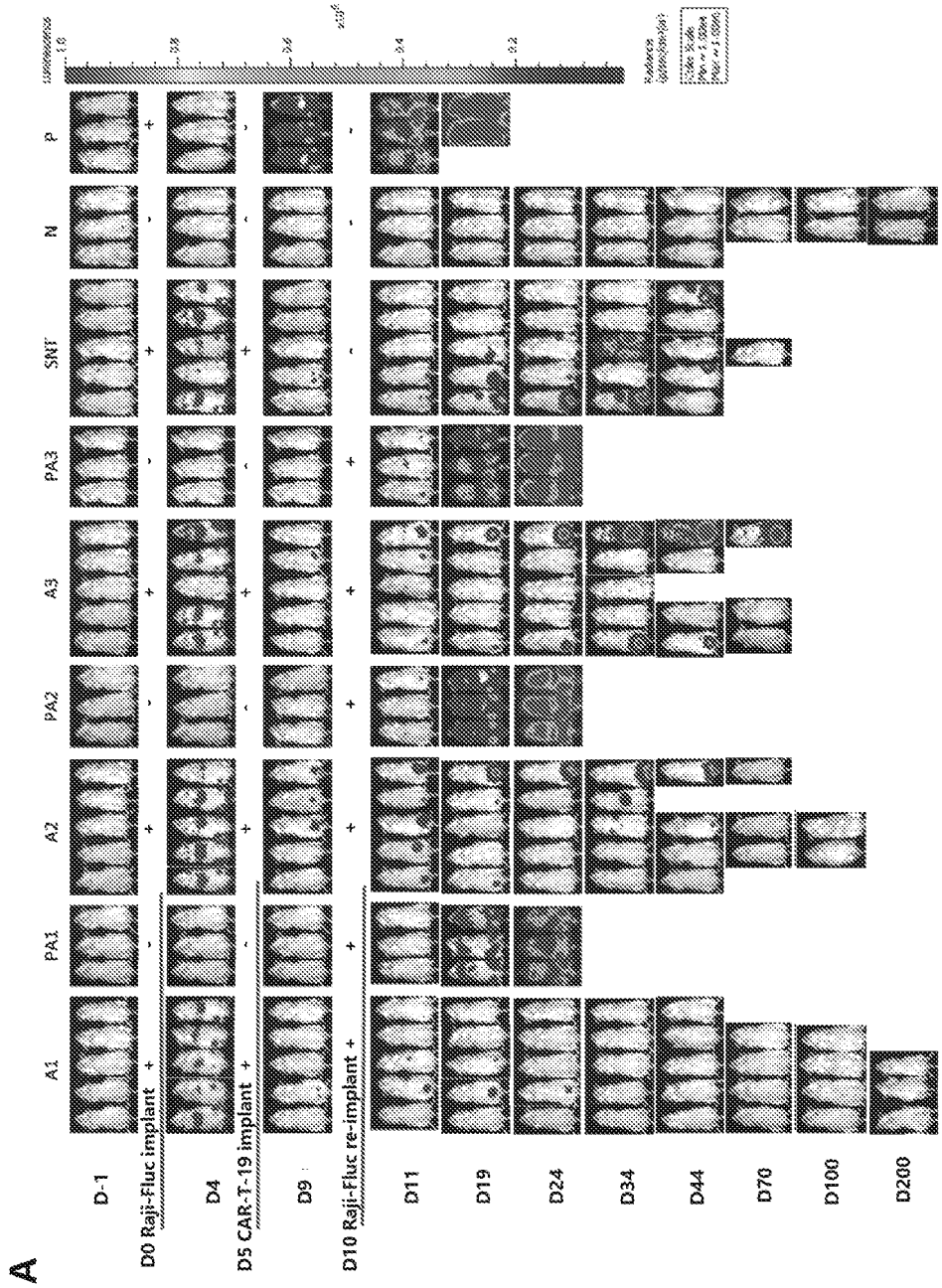

A
D-1
D0 Raji-Fluc implant
D4
D5 CAR-T-19 implant
D9
D10 Raji-Fluc re-implant
D11
D19
D24
D34
D44
D70
D100
D200
A1
PA1
A2
PA2
A3
PA3
SNT
N
P

图 3

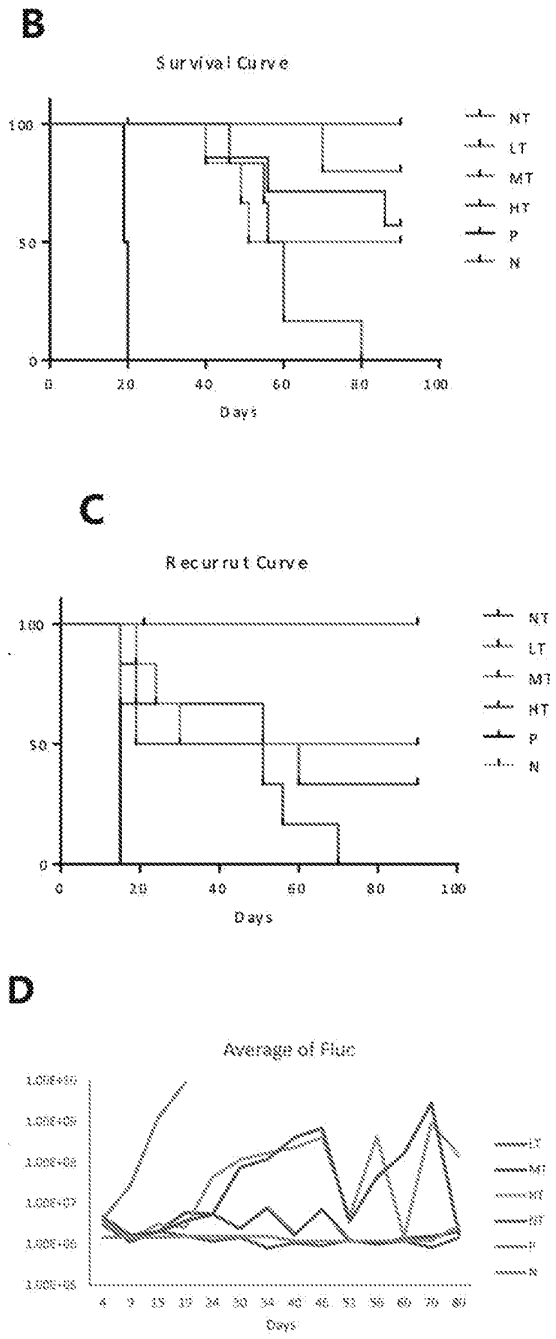

B
Survival Curve
100
50
0
0
20
40
60
80
100
Days
NT
LT
MT
HT
P
N
C
Recurrut Curve
100
50
0
0
20
40
60
80
100
Days
NT
LT
MT
HT
P
N
D
Average of Fluc
Days

图 3(续)

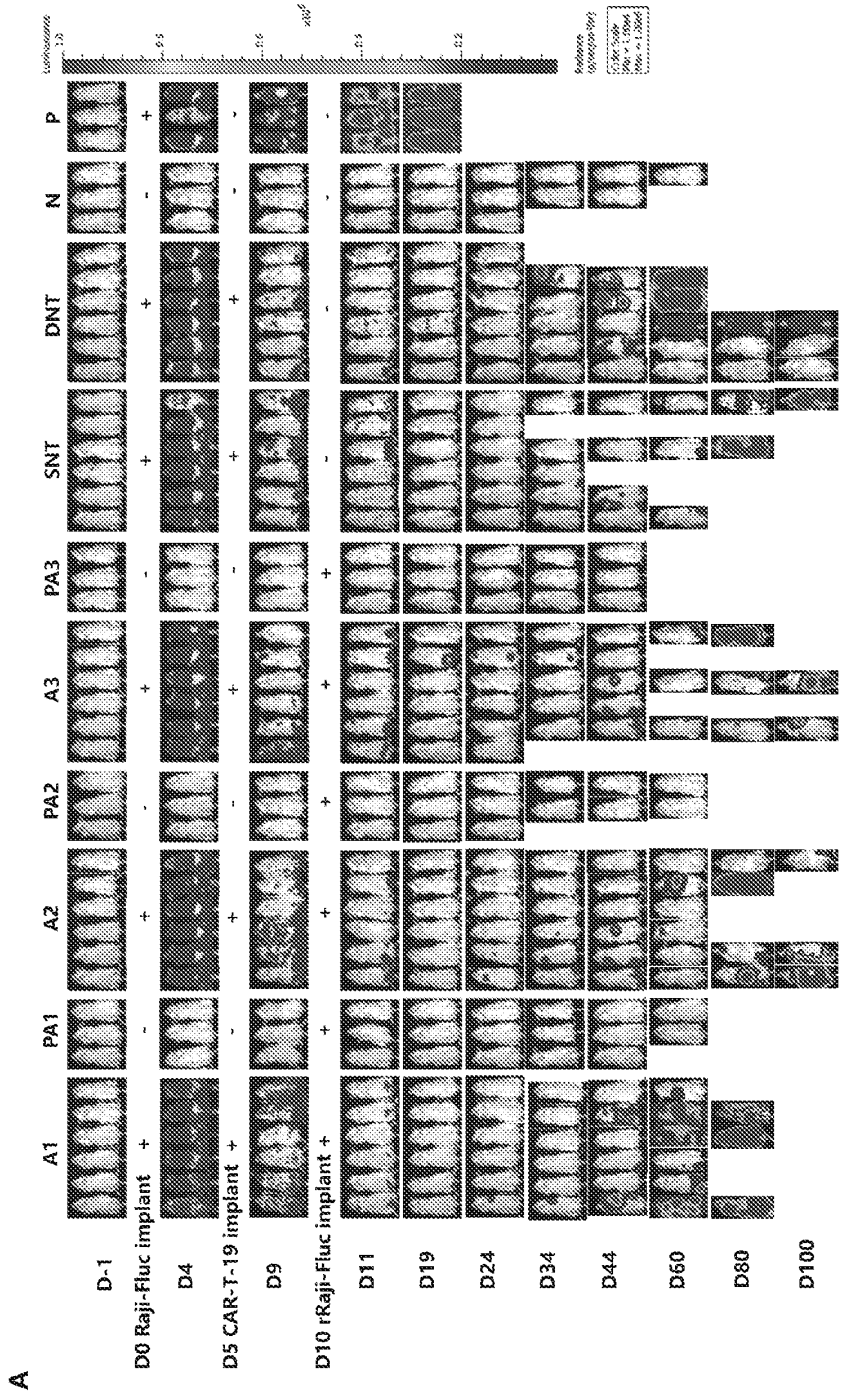

A
D-1
D0 Raji-Fluc implant +
D4
D5 CAR-T-19 implant +
D9
D10 rRaji-Fluc implant +
D11
D19
D24
D34
D44
D60
D80
D100
A1
PA1
A2
PA2
A3
PA3
SNT
DNT
N
P

图 4

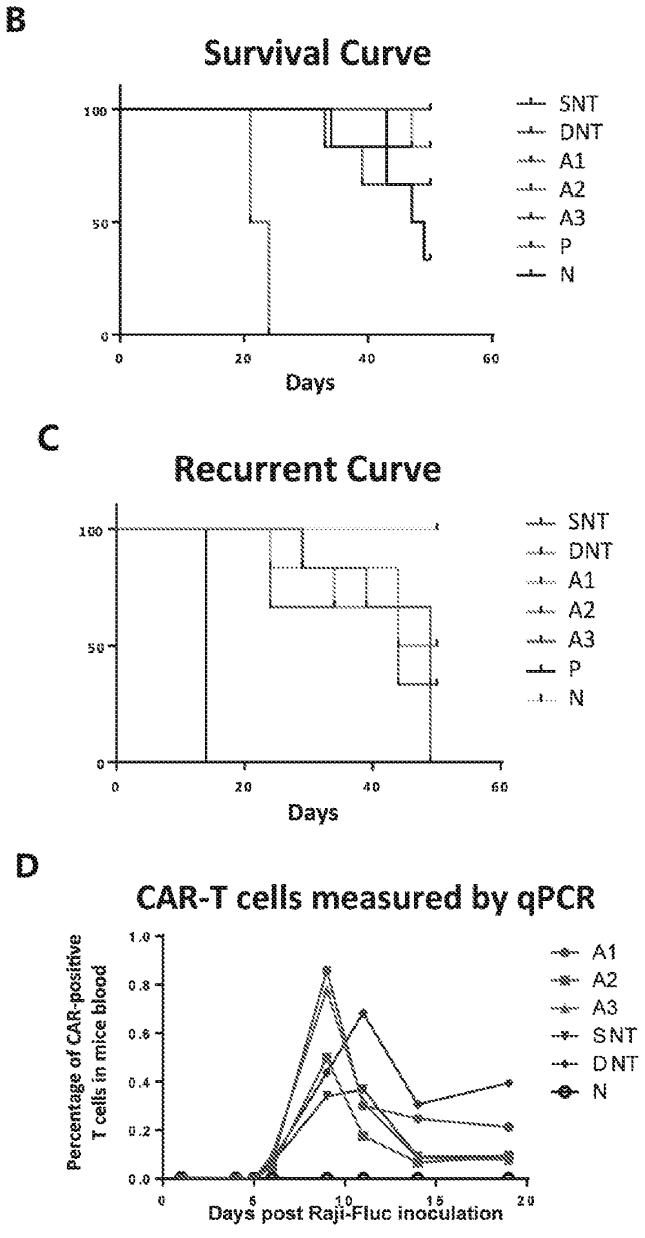

B
Survival Curve
100
50
0
0
20
40
60
Days
SNT
DNT
A1
A2
A3
P
N
C
Recurrent Curve
100
50
0
0
20
40
60
Days
SNT
DNT
A1
A2
A3
P
N
D
CAR-T cells measured by qPCR
Percentage of CAR-positive T cells in mice blood
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
Days post Raji-Fluc inoculation
A1
A2
A3
SNT
DNT
N

图 4(续)

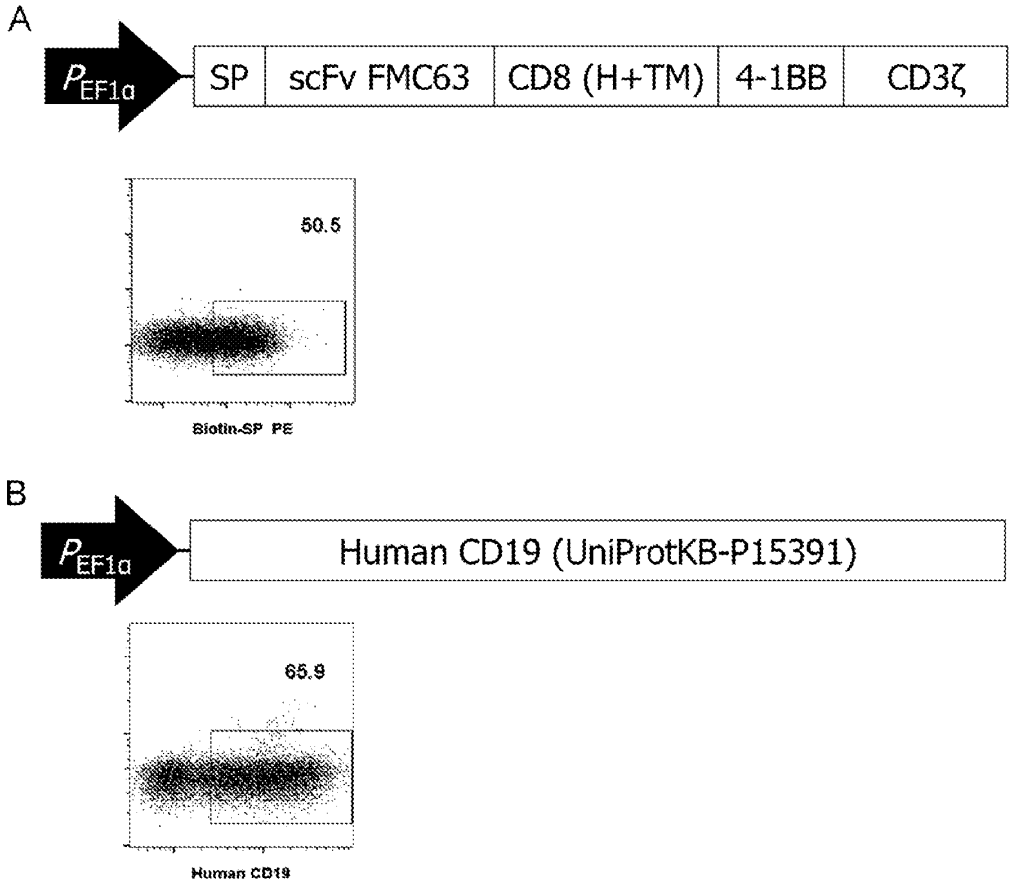
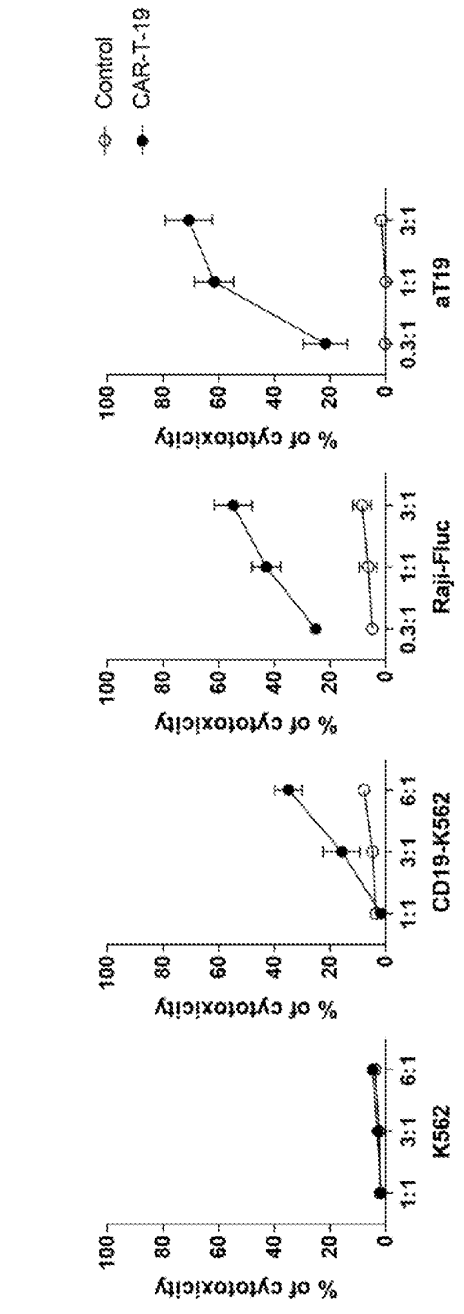

A
$P_{EF1\alpha}$
SP
scFv FMC63
CD8 (H+TM)
4-1BB
CD3ζ
50.5
Biotin-SP PE
B
$P_{EF1\alpha}$
Human CD19 (UniProtKB-P15391)
65.9
Human CD19

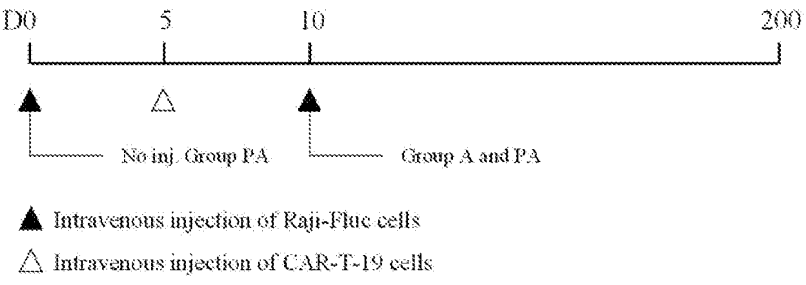
图 5


Control
CAR-T-19
% of cytotoxicity
100
80
60
40
20
0
0.3:1
1:1
3:1
6:1
aT19
Raji-Fluc
CD19-K562
K562

C

图 5(续)

A


D0
5
10
200
No inj. Group PA
Group A and PA
Intravenous injection of Raji-Fluc cells
Intravenous injection of CAR-T-19 cells

B

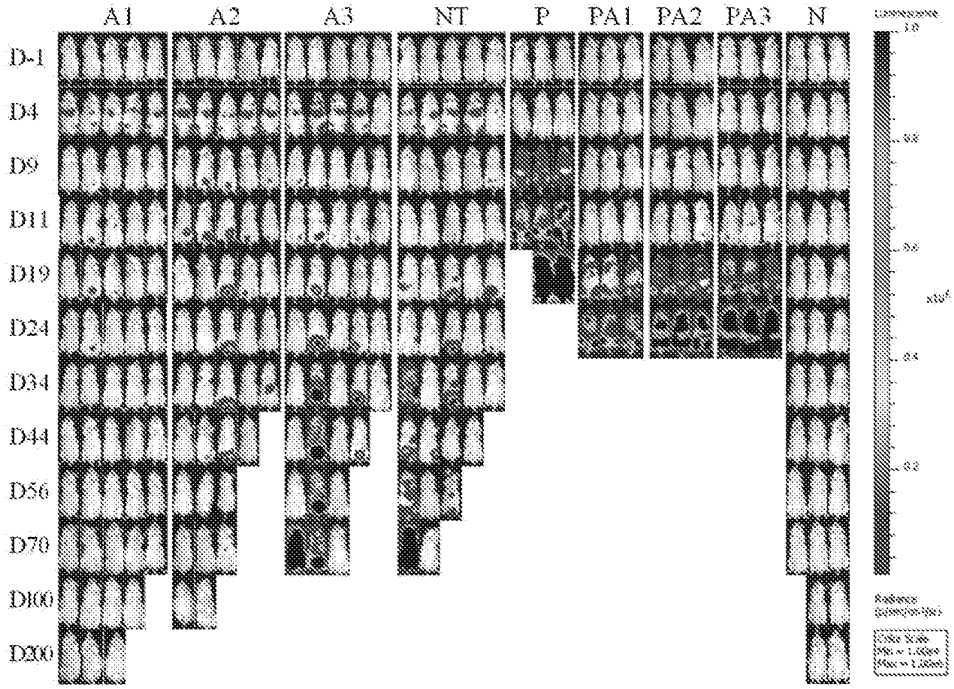

A1
A2
A3
NT
P
PA1
PA2
PA3
N
D-1
D4
D9
D11
D19
D24
D34
D44
D56
D70
D100
D200

图 6

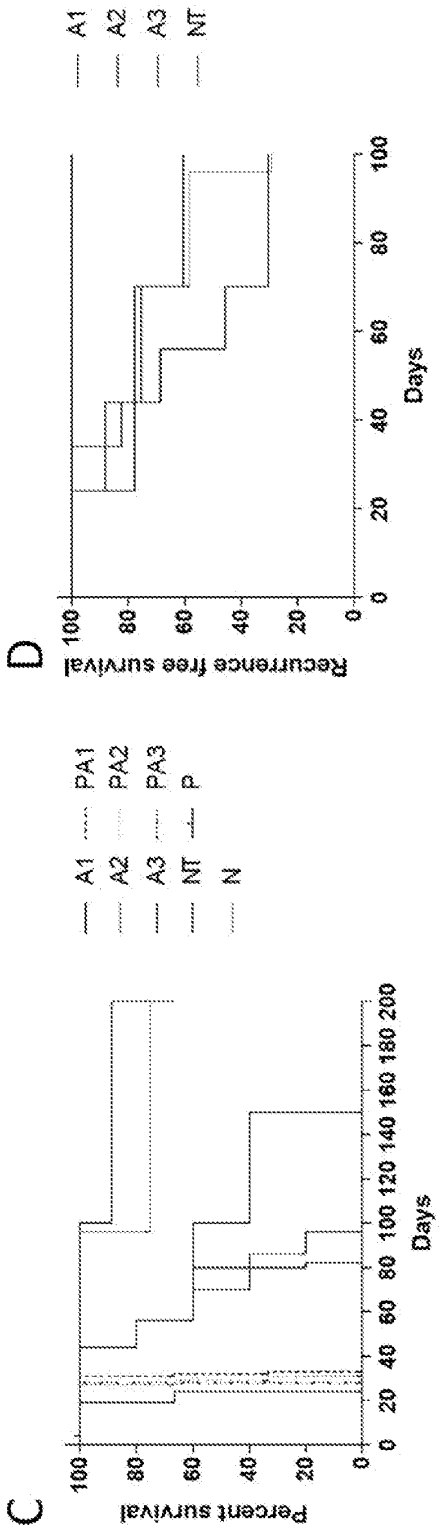
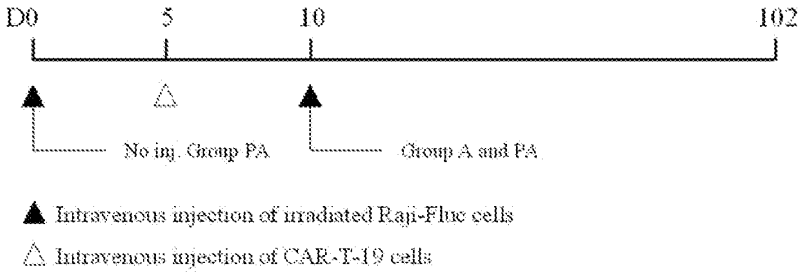

C
Percent survival
100
80
60
40
20
0
0 20 40 60 80 100 120 140 160 180 200
Days
A1
A2
A3
NT
N
PA1
PA2
PA3
P
D
Recurrence free survival
100
80
60
40
20
0
0 20 40 60 80 100
Days
A1
A2
A3
NT

图 6(续)

A


D0
5
10
102
No inj. Group PA
Group A and PA
Intravenous injection of irradiated Raji-Fluc cells
Intravenous injection of CAR-T-19 cells

B

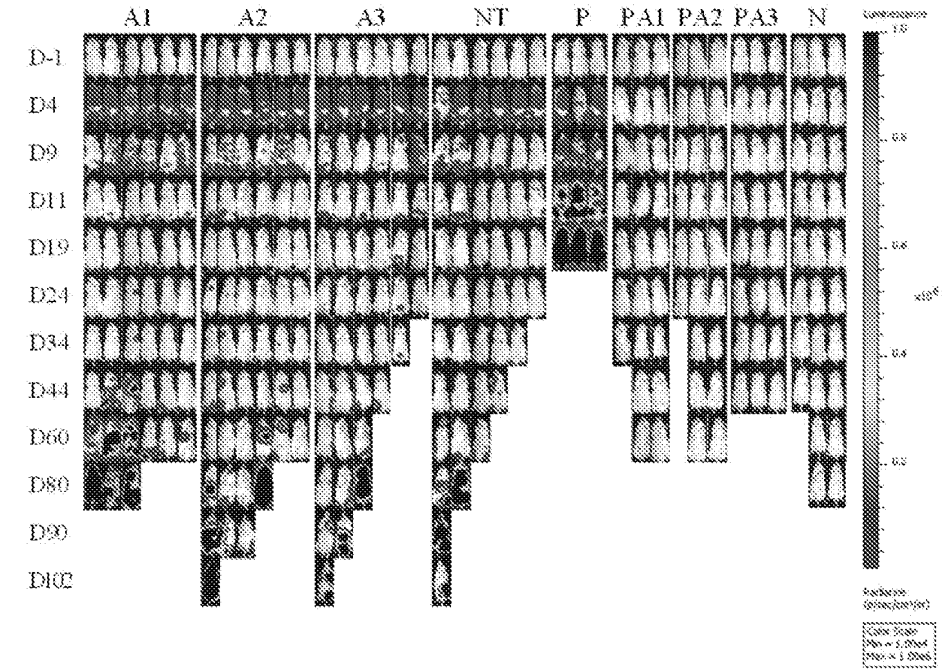

A1
A2
A3
NT
P
PA1
PA2
PA3
N
D-1
D4
D9
D11
D19
D24
D34
D44
D60
D80
D90
D102

图 7

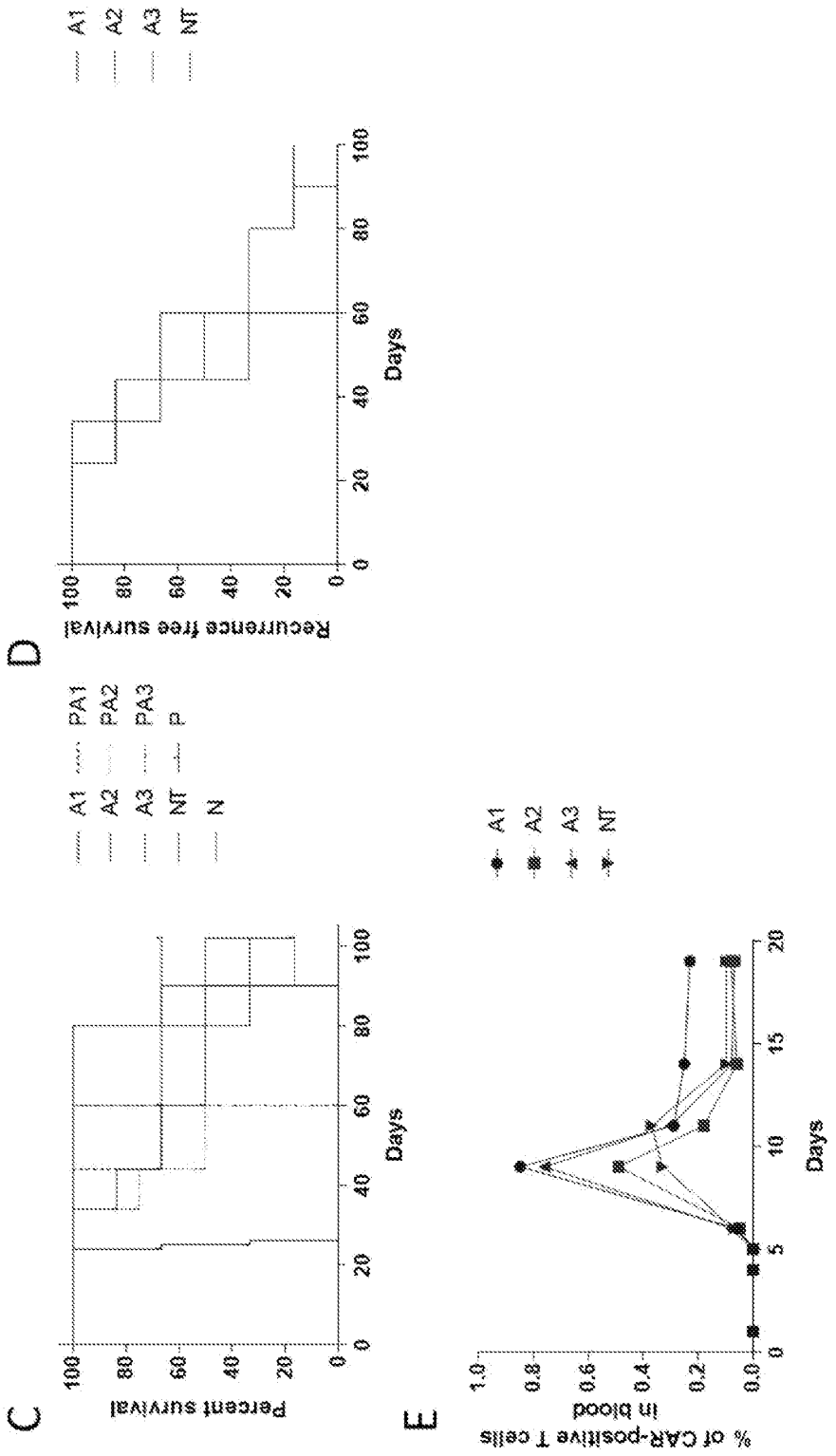
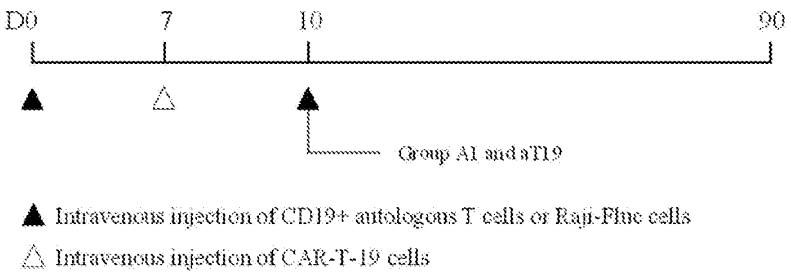

D
A1
A2
A3
NT
Recurrence free survival
Days
C
PA1
PA2
PA3
P
A1
A2
A3
NT
N
Percent survival
Days
E
A1
A2
A3
NT
% of CAR-positive T cells in blood
Days

图 7(续)

A


D0
7
10
90
Group A1 and aT19
▲ Intravenous injection of CD19+ autologous T cells or Raji-Fluc cells
△ Intravenous injection of CAR-T-19 cells

B

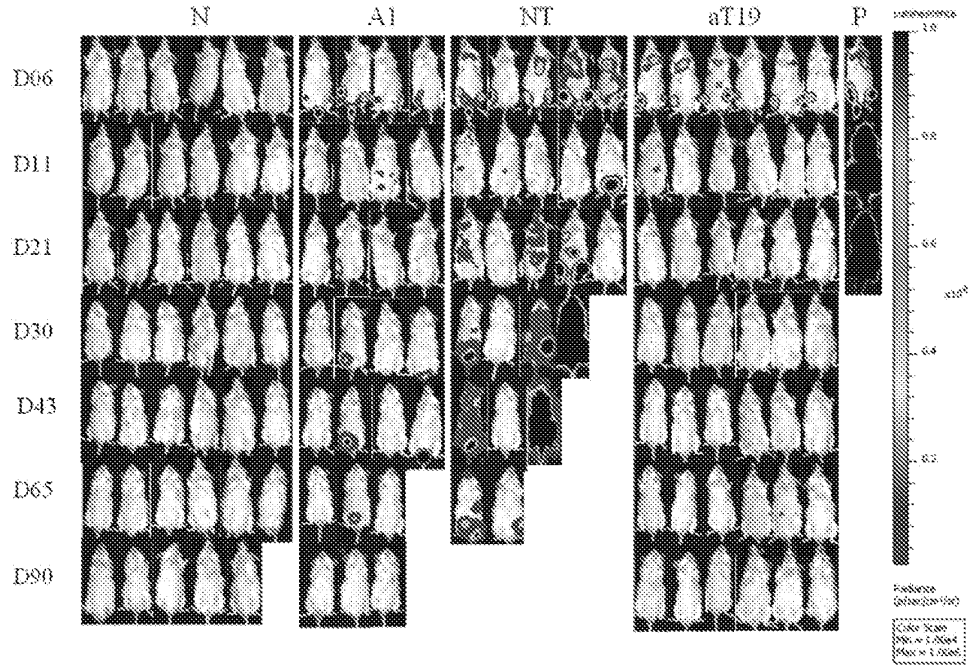

N
A1
NT
aT19
P
D06
D11
D21
D30
D43
D65
D90

图 8

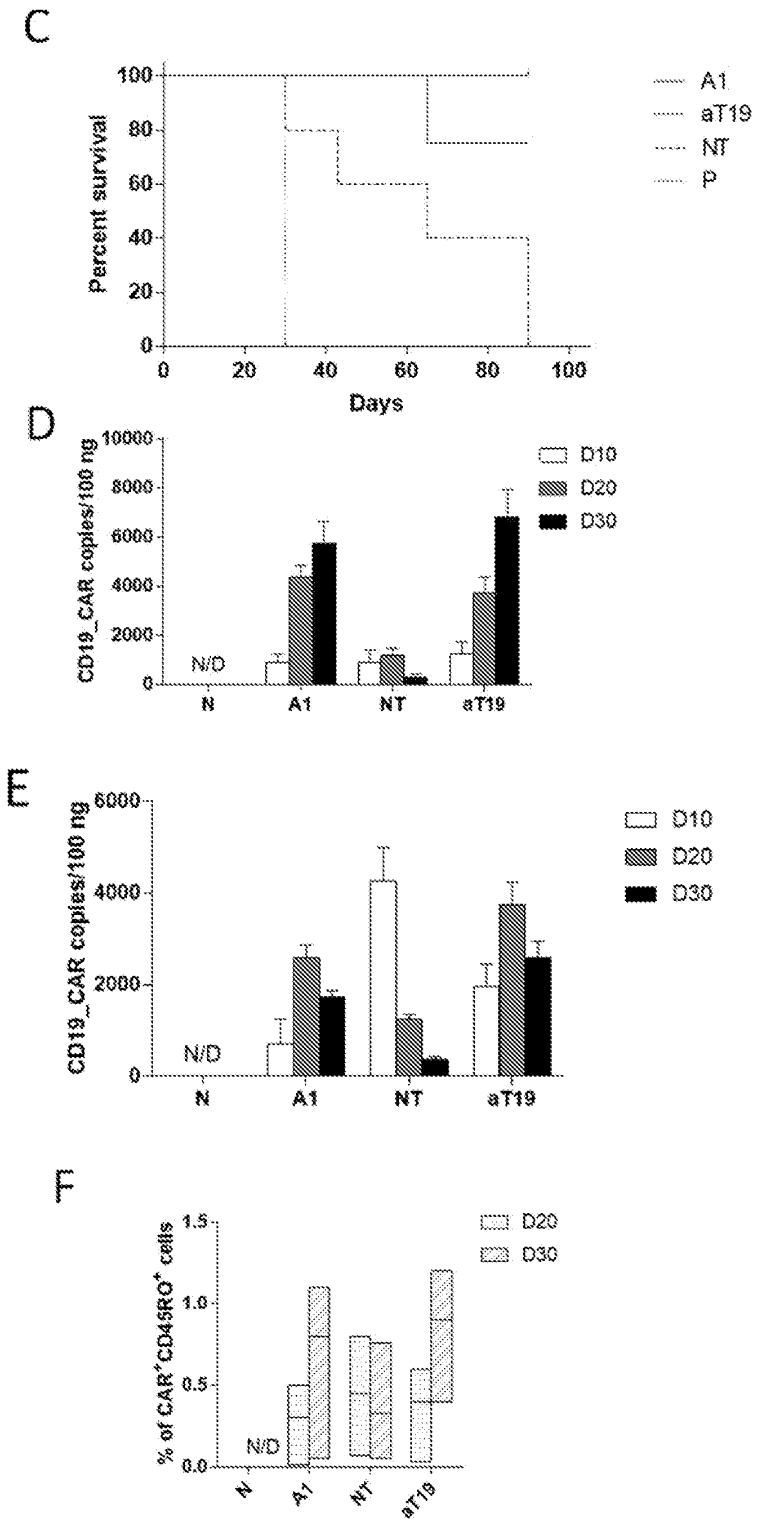

C
Percent survival
Days
A1
aT19
NT
P
D
CD19_CAR copies/100 ng
D10
D20
D30
N/D
N
A1
NT
aT19
E
CD19_CAR copies/100 ng
D10
D20
D30
N/D
N
A1
NT
aT19
F
% of CAR+CD45RO+ cells
D20
D30
N/D
N
A1
NT
aT19

图 8(续)