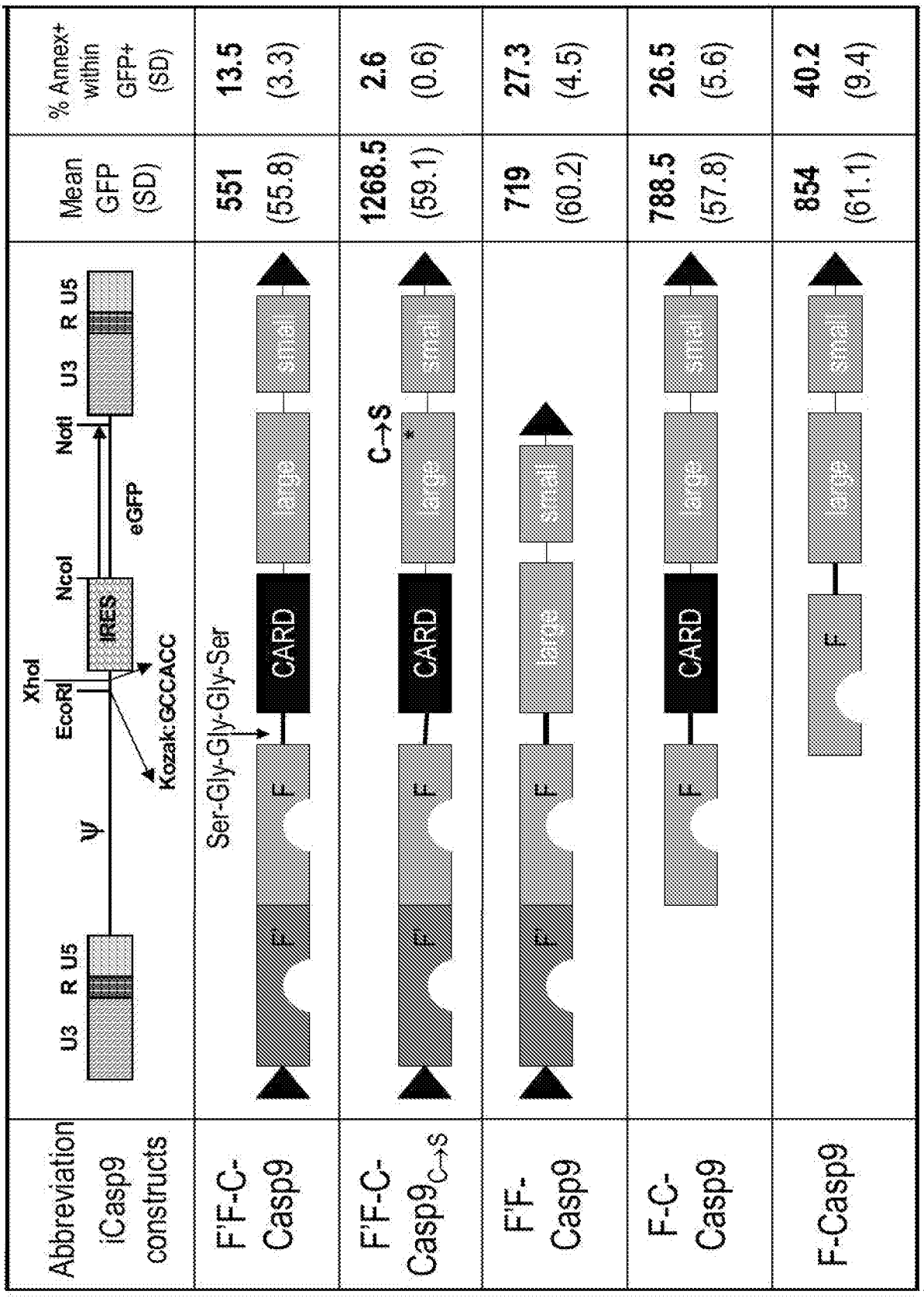

Abbreviation iCasp9 constructs
U3 R U5
Ψ
XhoI
EcoRI
NcoI
IRES
eGFP
NotI
U3 R U5
Kozak:GCCACC
Mean GFP (SD)
% Annex+ within GFP+ (SD)
F'F-C-Casp9
Ser-Gly-Gly-Gly-Ser
F'
F
CARD
large
small
551 (55.8)
13.5 (3.3)
F'F-C-Casp9C→S
C→S
*
1268.5 (59.1)
2.6 (0.6)
F'F-Casp9
719 (60.2)
27.3 (4.5)
F-C-Casp9
788.5 (57.8)
26.5 (5.6)
F-Casp9
854 (61.1)
40.2 (9.4)

FIG. 1A

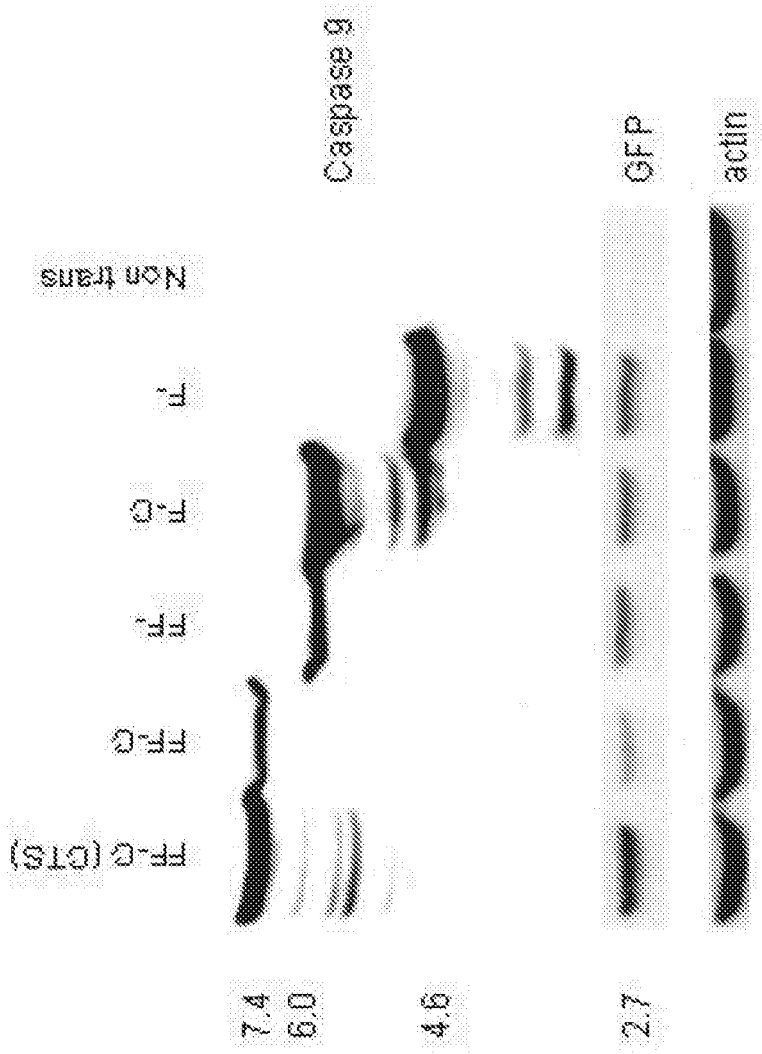


FIG. 1B

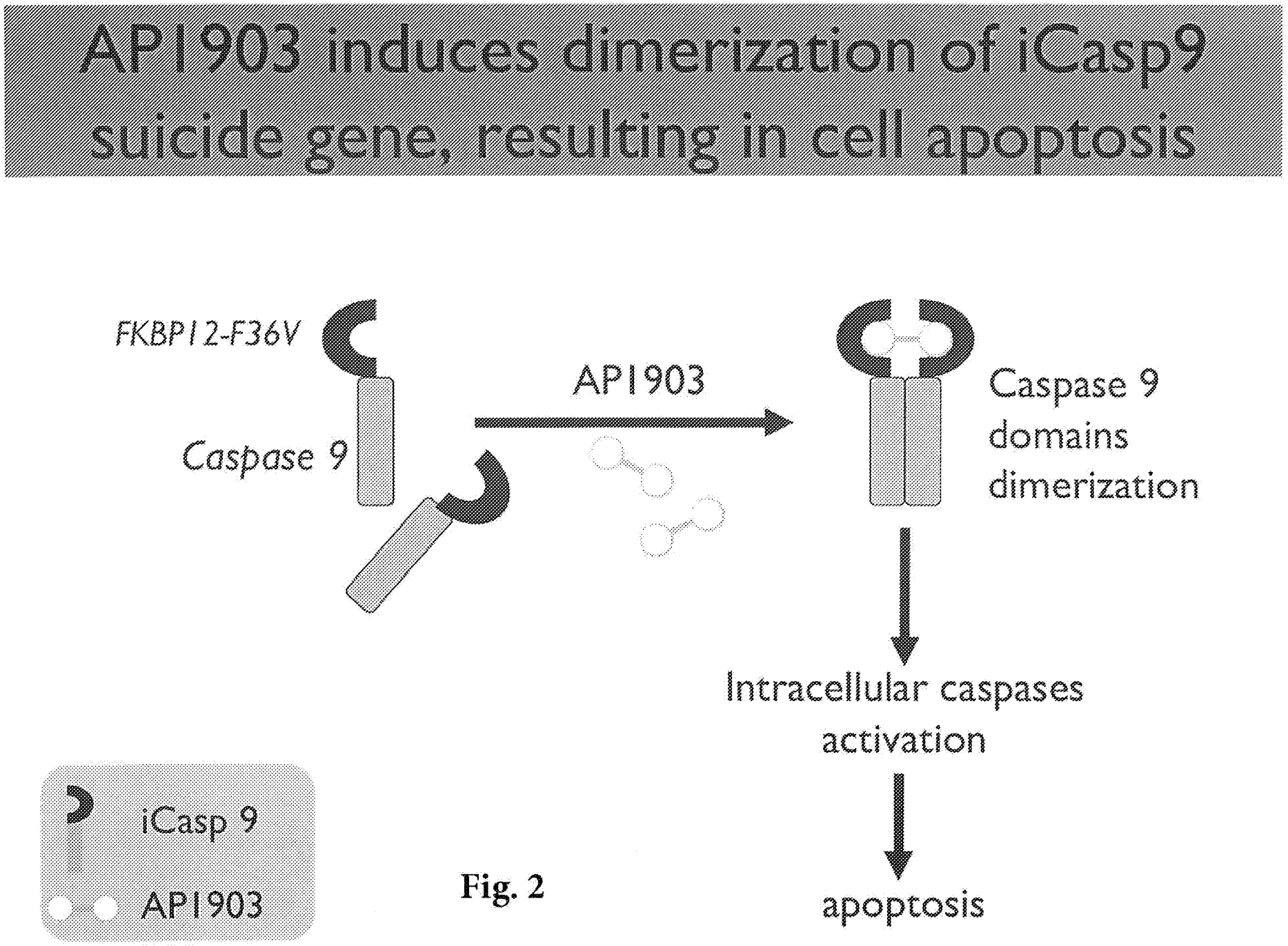

AP1903 induces dimerization of iCasp9 suicide gene, resulting in cell apoptosis
FKBP12-F36V
Caspase 9
AP1903
Caspase 9 domains dimerization
Intracellular caspases activation
apoptosis
iCasp 9
AP1903

Fig. 2

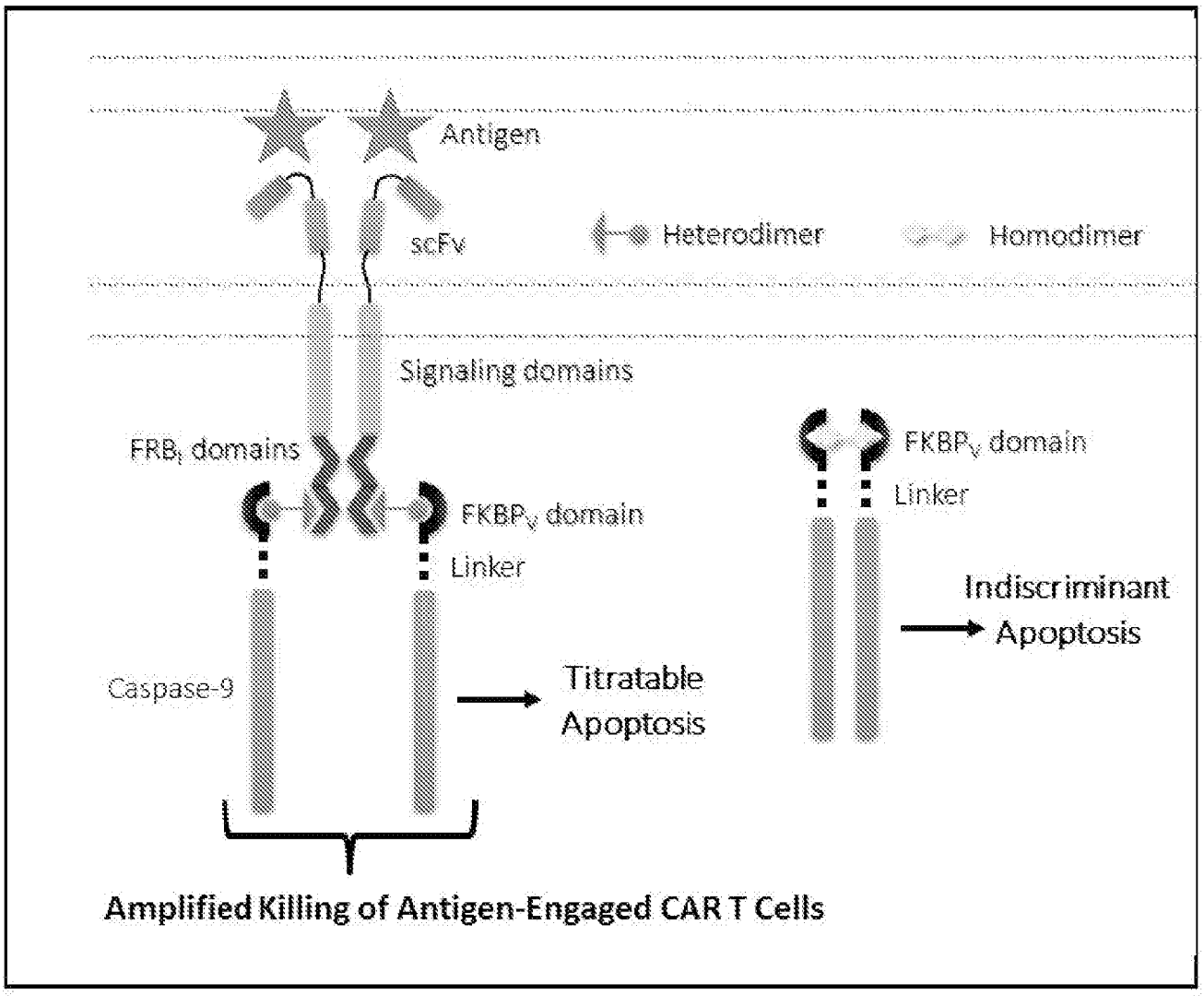

Antigen
scFv
Heterodimer
Homodimer
Signaling domains
FRB$_T$ domains
FKBP$_V$ domain
Linker
Caspase-9
Titratable Apoptosis
FKBP$_V$ domain
Linker
Indiscriminant Apoptosis
Amplified Killing of Antigen-Engaged CAR T Cells

Fig. 3

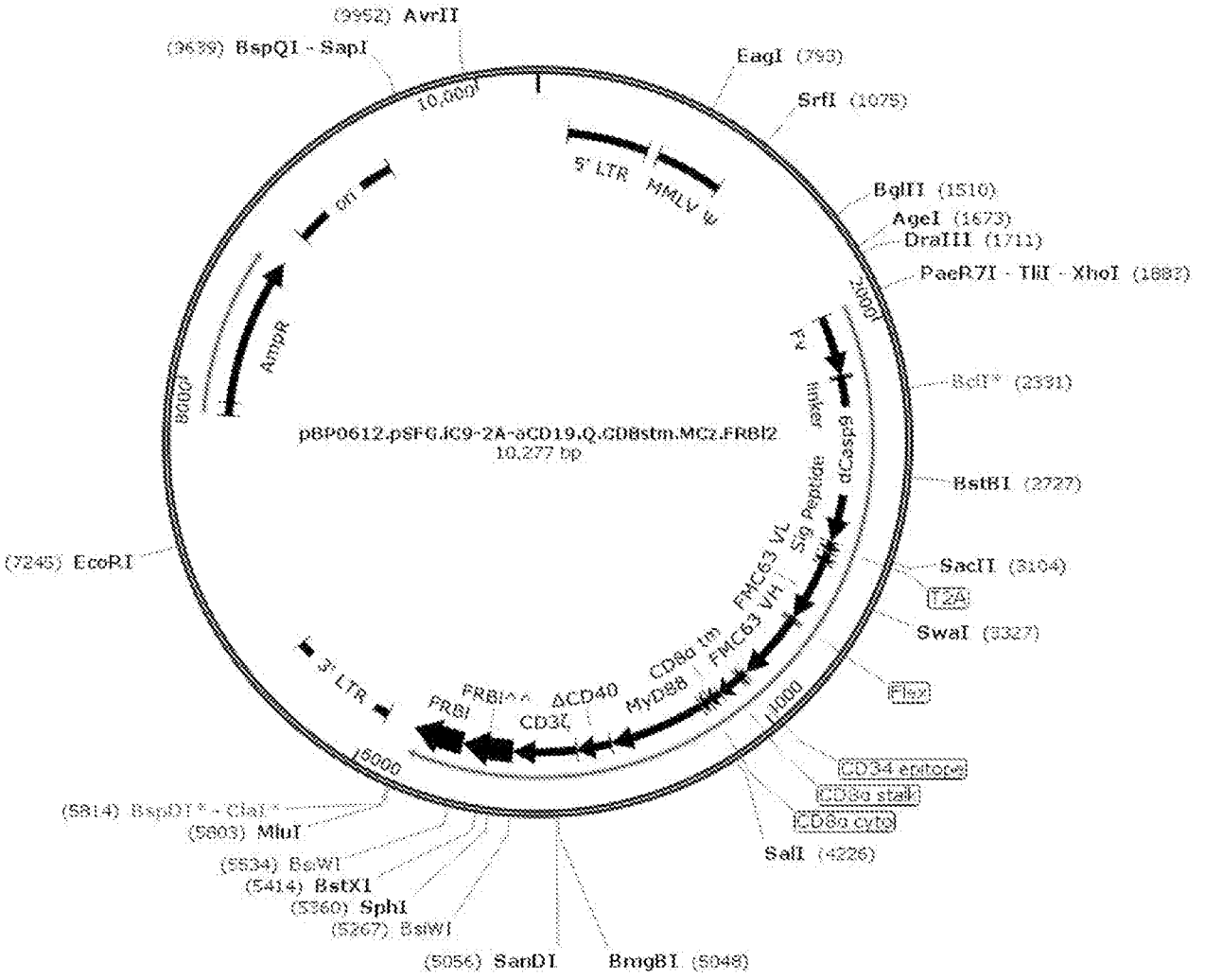

(9952) AvrII
(9639) BspQI - SapI
EagI (793)
SrfI (1075)
BglII (1510)
AgeI (1673)
DraIII (1711)
PaeR7I - TliI - XhoI (1882)
BclI* (2331)
BstBI (2727)
SacII (3104)
T2A
SwaI (3327)
Flex
CD34 epitope
CD8α stalk
CD8α cyto
SalI (4226)
BmgBI (5048)
(5056) SanDI
(5267) BsiWI
(5360) SphI
(5414) BstXI
(5534) BsiWI
(5803) MluI
(5814) BspDI* - ClaI*
(7245) EcoRI
pBP0612.pSFG.IC9-2A-aCD19.Q.CD8stm.MC2.FRBI2
10,277 bp
5' LTR
MMLV Ψ
ori
AmpR
Fv
linker
dCasp9
Sig Peptide
FMC63 VL
FMC63 VH
CD8α tm
MyD88
ΔCD40
CD3ζ
FRBI
FRBI^^
3' LTR
10,000
2000
1000
5000
8000

Fig. 4

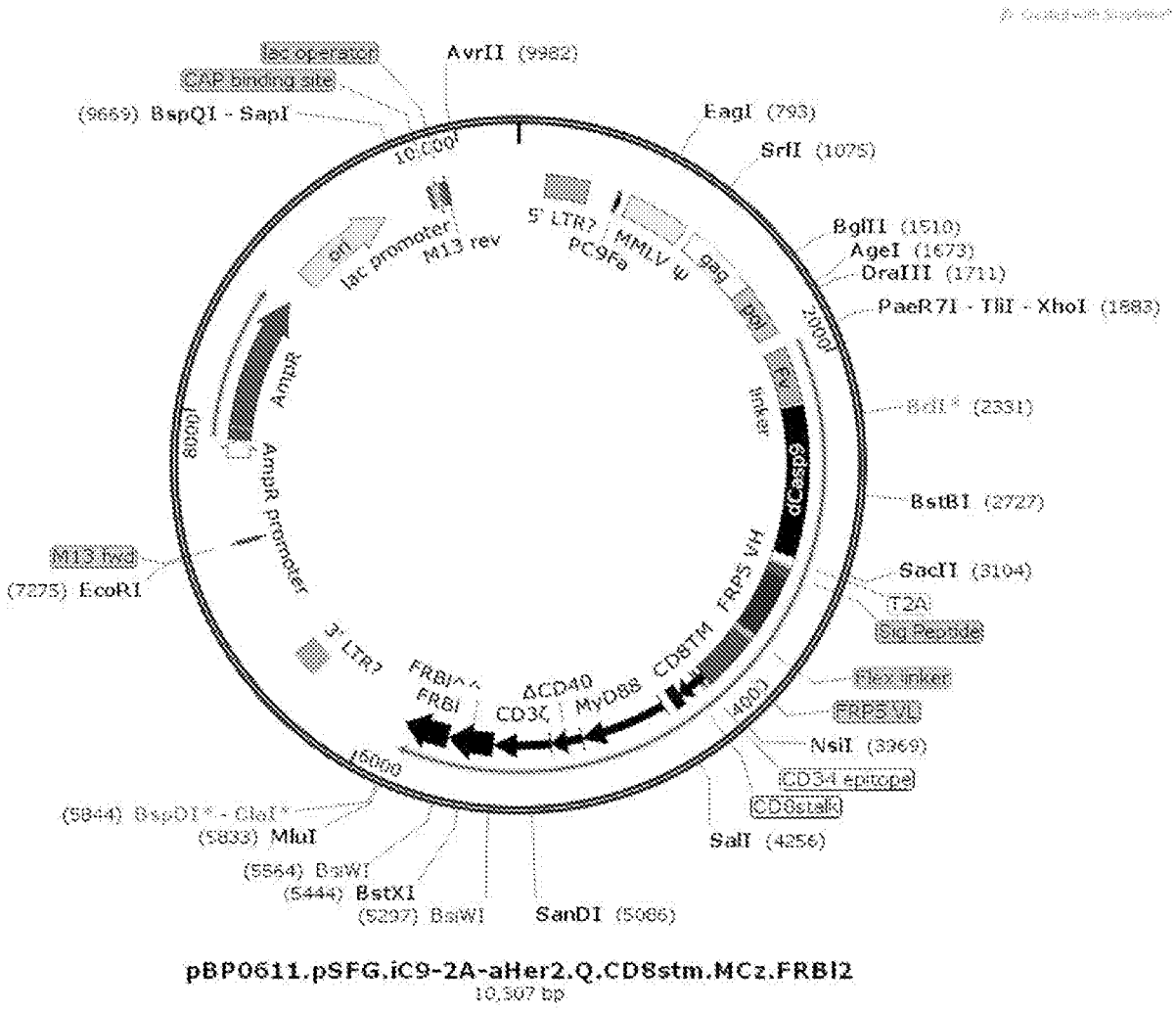

lac operator
CAP binding site
(9669) BspQI - SapI
AvrII (9982)
EagI (793)
SrfI (1075)
BglII (1510)
AgeI (1673)
DraIII (1711)
PaeR7I - TliI - XhoI (1883)
BrlI* (2331)
BstBI (2727)
SacII (3104)
T2A
Sig Peptide
Flex linker
FRP5 VL
NsiI (3969)
CD34 epitope
CD8stalk
SalI (4256)
SanDI (5086)
(5297) BsiWI
(5444) BstXI
(5564) BsiWI
(5833) MluI
(5844) BspDI* - ClaI*
M13 fwd
(7275) EcoRI
AmpR
AmpR promoter
lac promoter
M13 rev
5' LTR?
PC9Fa
MMLV ψ
gag
linker
dCasp9
FRP5 VH
CD8TM
MyD88
ΔCD40
CD3ζ
FRBI
3' LTR?
10,000
2000
4000
6000
8000
pBP0611.pSFG.iC9-2A-aHer2.Q.CD8stm.MCz.FRBI2
10,307 bp

Fig. 5

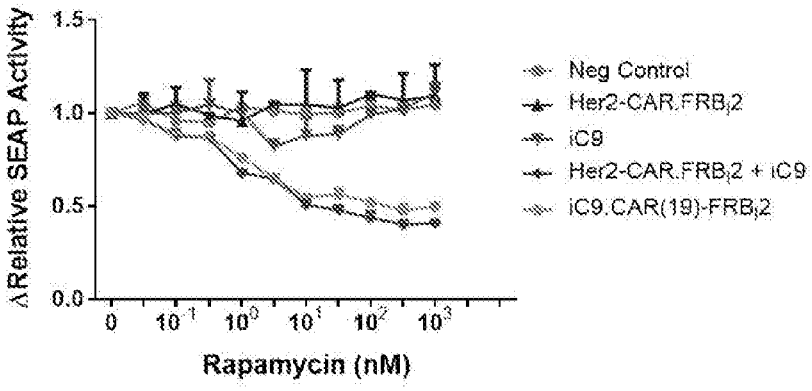

ΔRelative SEAP Activity
1.5
1.0
0.5
0.0
0
10^-1
10^0
10^1
10^2
10^3
Rapamycin (nM)
Neg Control
Her2-CAR.FRB|2
iC9
Her2-CAR.FRB|2 + iC9
iC9.CAR(19)-FRB|2

Fig. 6A

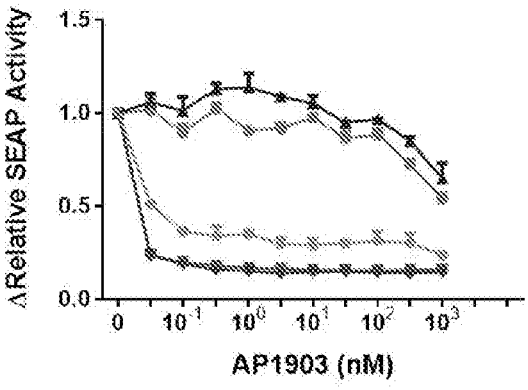

ΔRelative SEAP Activity
1.5
1.0
0.5
0.0
0
10^-1
10^0
10^1
10^2
10^3
AP1903 (nM)

Fig. 6B

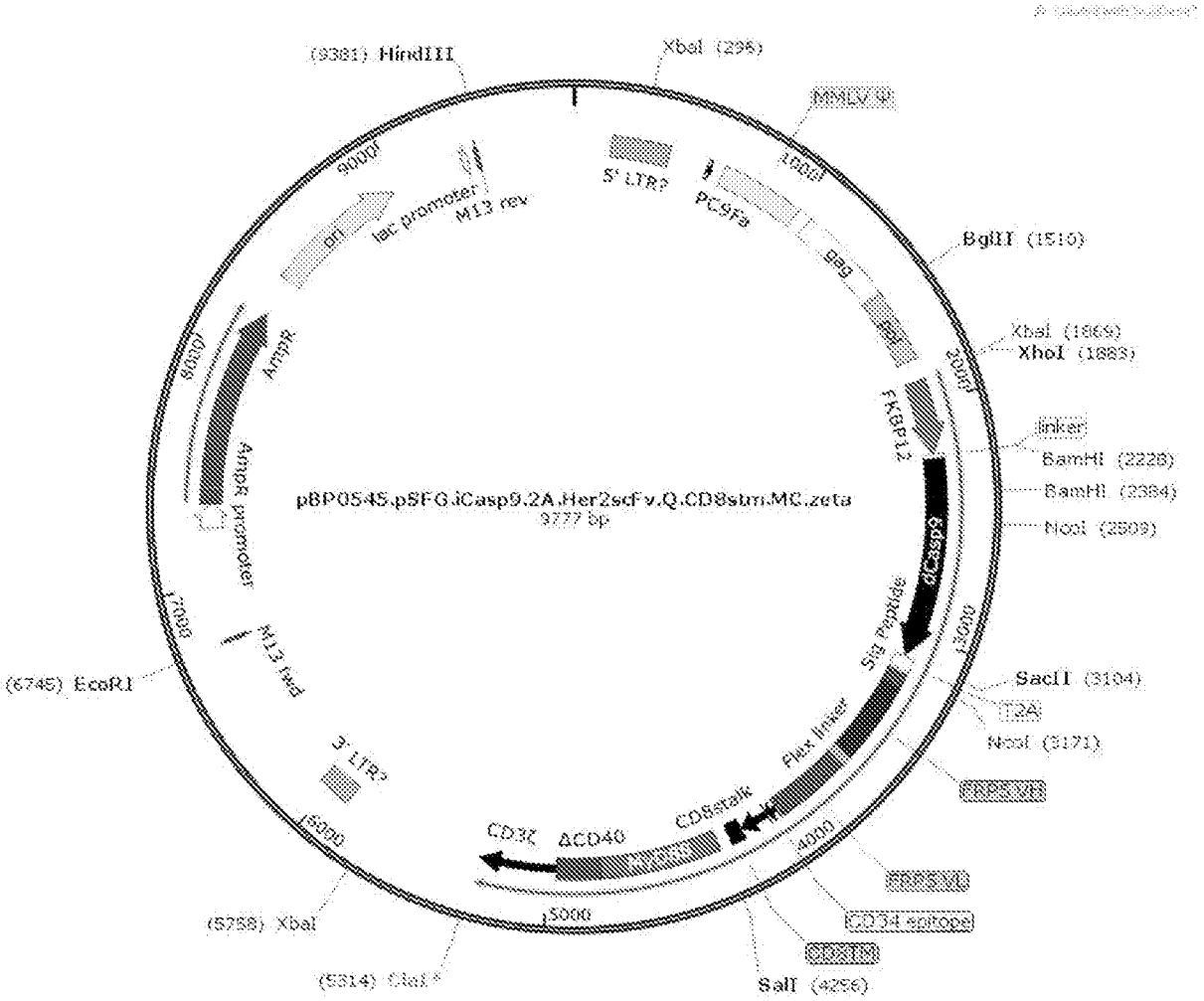

pBP0545.pSFG.iCasp9.2A.Her2scFv.Q.CD8stm.MC.zeta
9777 bp
(9381) HindIII
XbaI (296)
MMLV Ψ
1000
BglII (1510)
XbaI (1869)
XhoI (1883)
2000
linker
BamHI (2228)
BamHI (2384)
NcoI (2509)
iCasp9
3000
SacII (3104)
T2A
NcoI (3171)
4000
CD34 epitope
SalI (4256)
5000
(5314) ClaI
(5758) XbaI
6000
(6745) EcoRI
7000
8000
9000
ori
lac promoter
M13 rev
5' LTR?
PCγFa
gag
FKBP12
Sig Peptide
Flex linker
CD8stalk
CD3ζ
ΔCD40
3' LTR?
M13 fwd
AmpR promoter
AmpR

Fig. 7

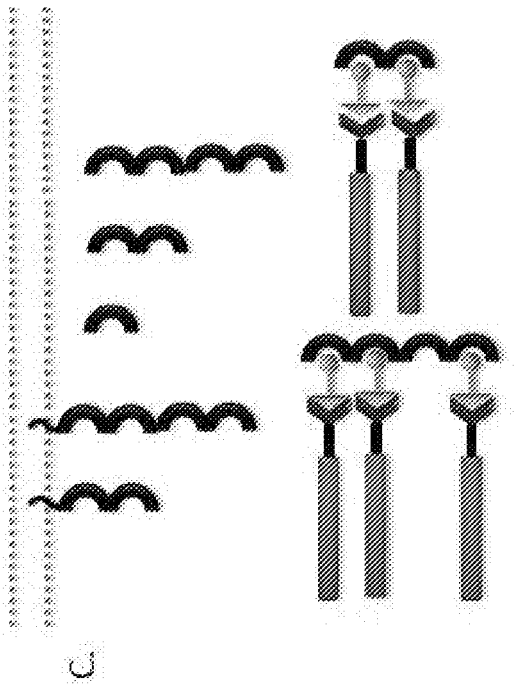


Fig. 8C

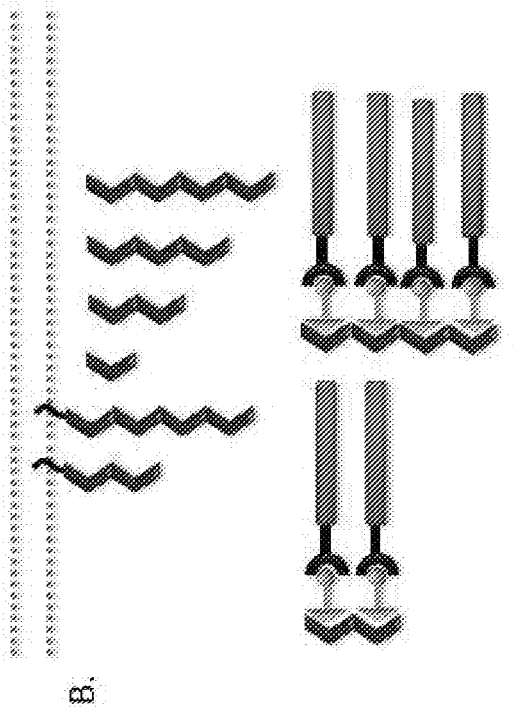


Fig. 8B

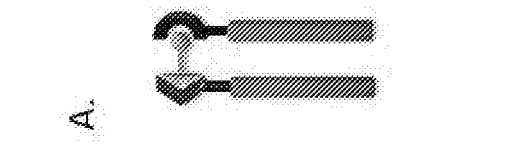


Fig. 8A

Fig. 9A

Fig. 9B

Fig. 9C

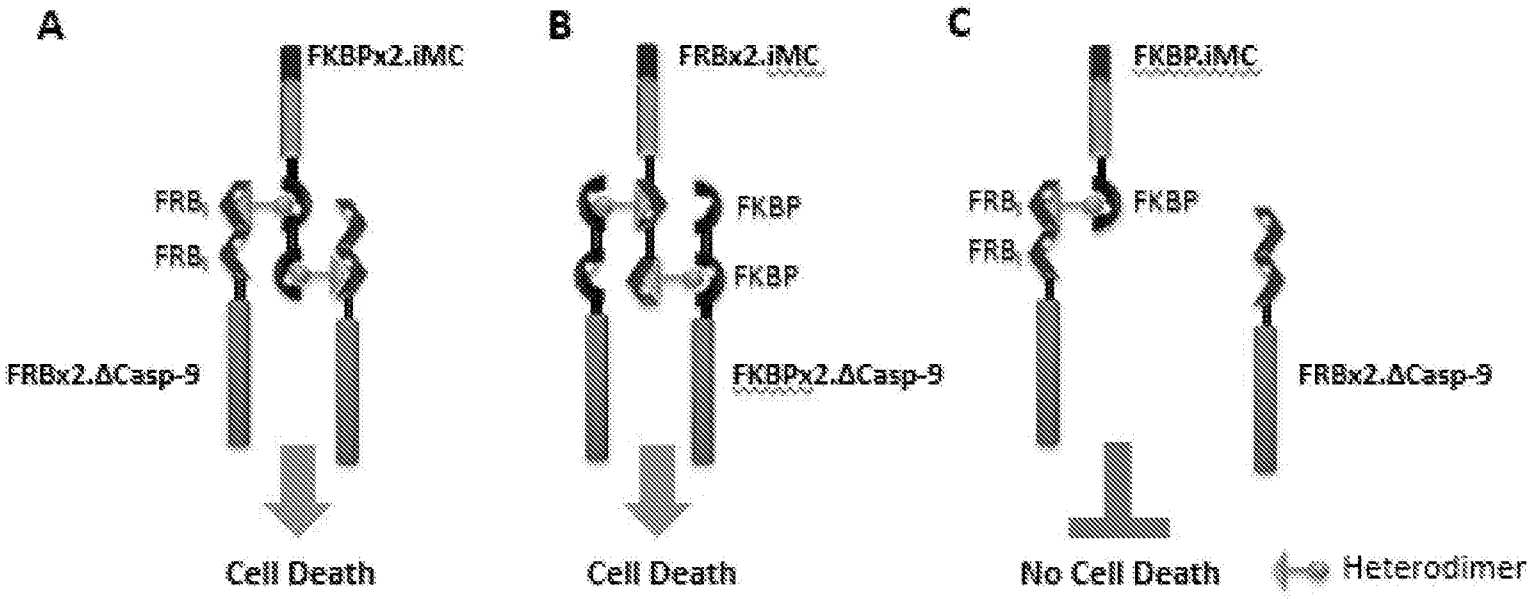
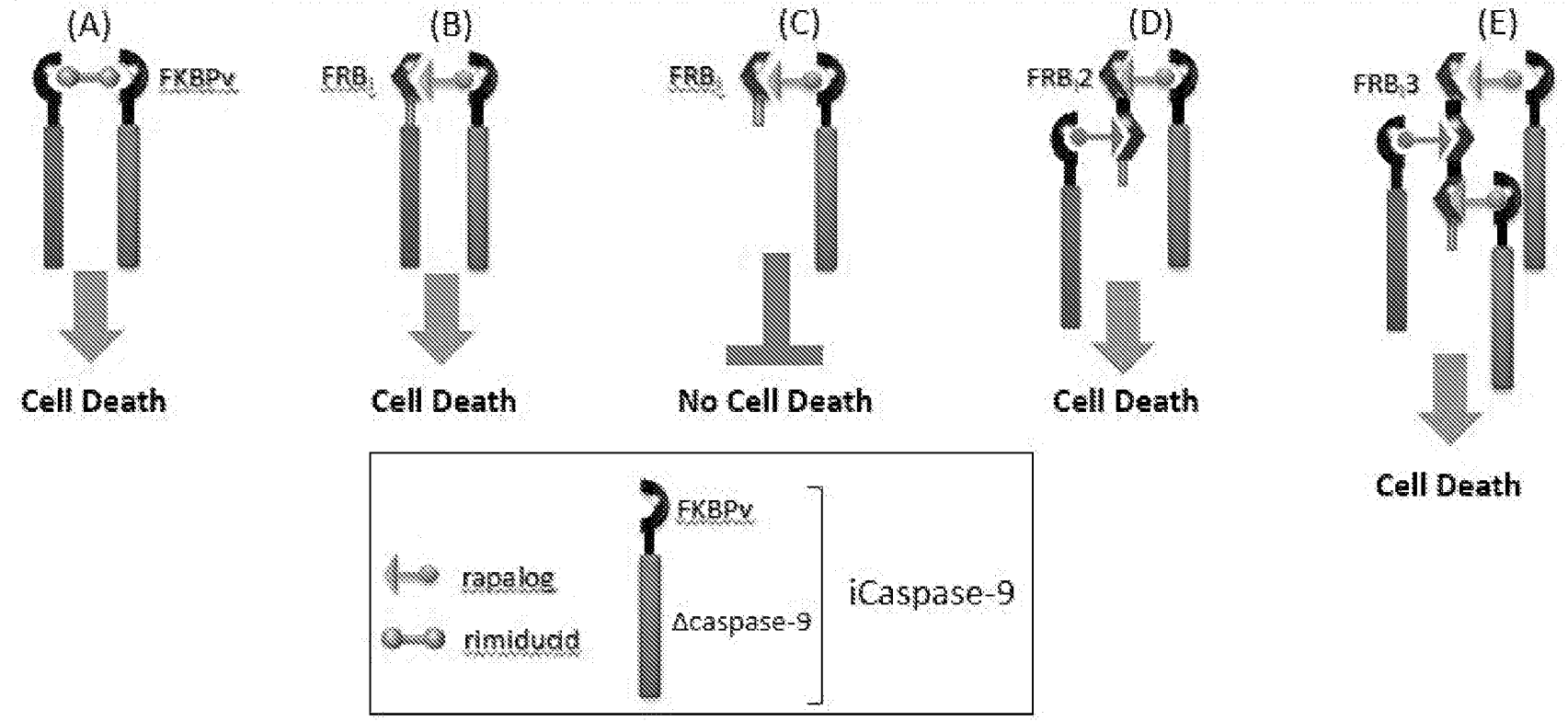


Fig. 10A Fig. 10B Fig. 10C Fig. 10D Fig. 10E



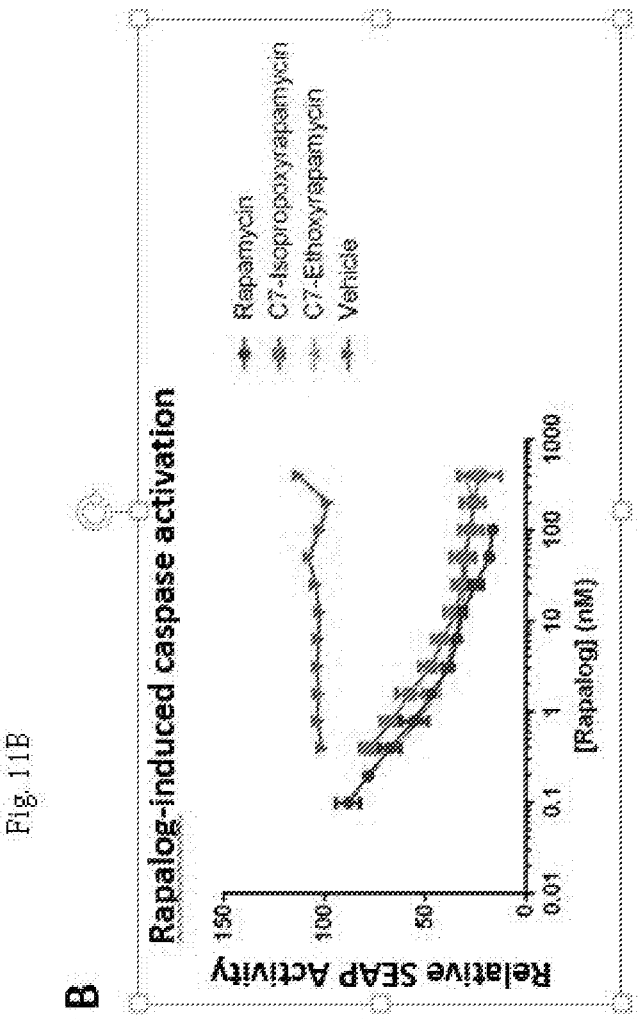


Fig. 11B

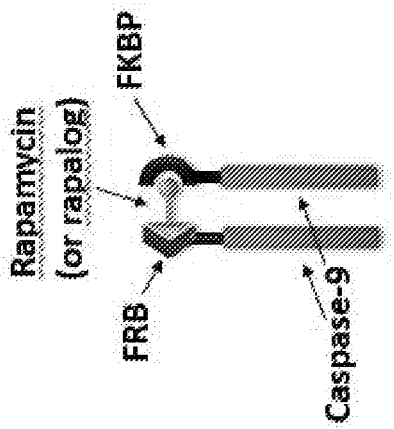


Fig. 11A

Fig. 12 **A**

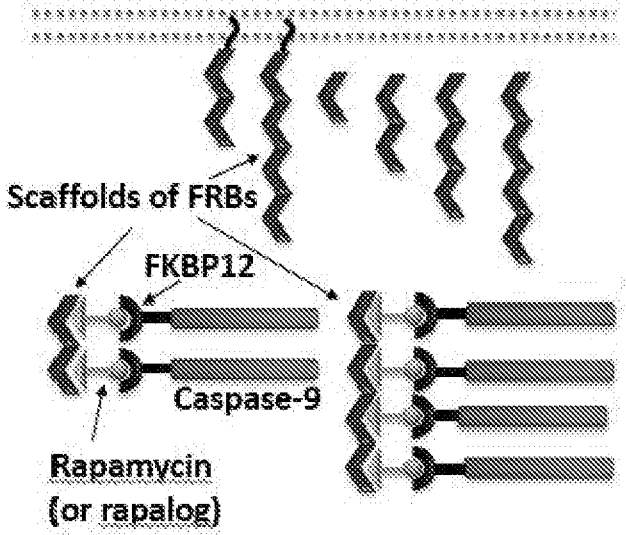


Fig. 12 **B**

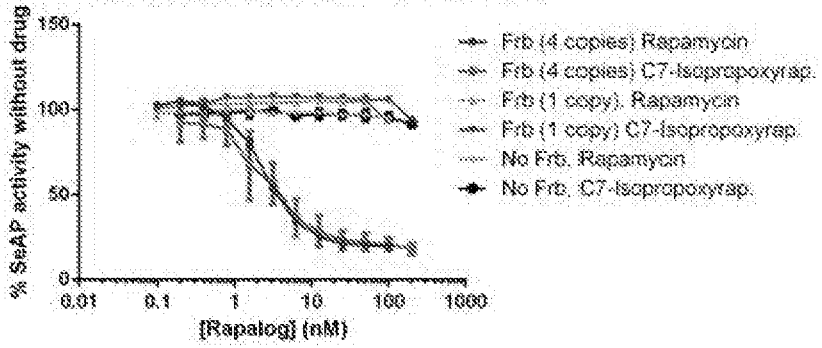


Fig. 12 **C**

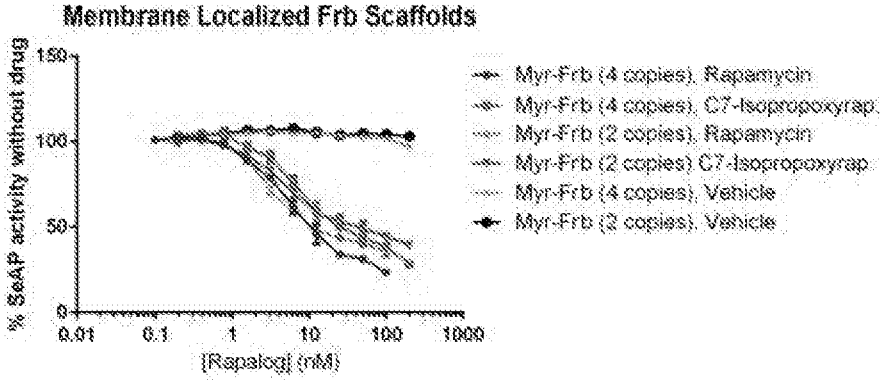


Fig. 13A

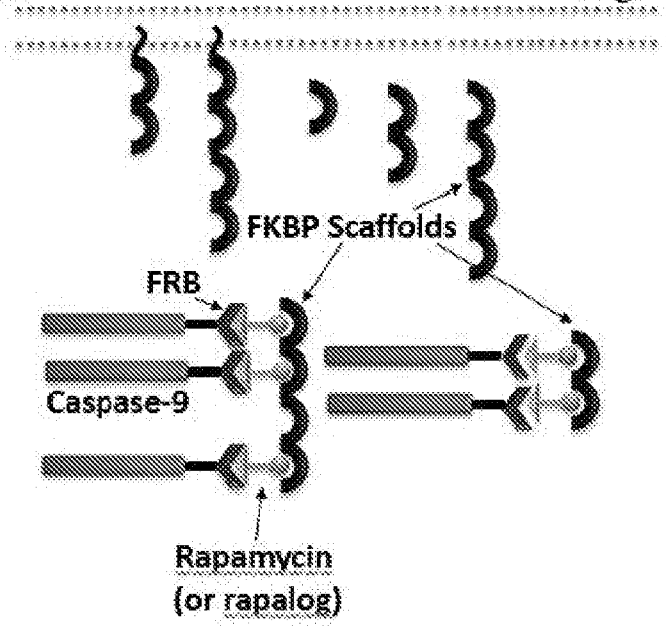
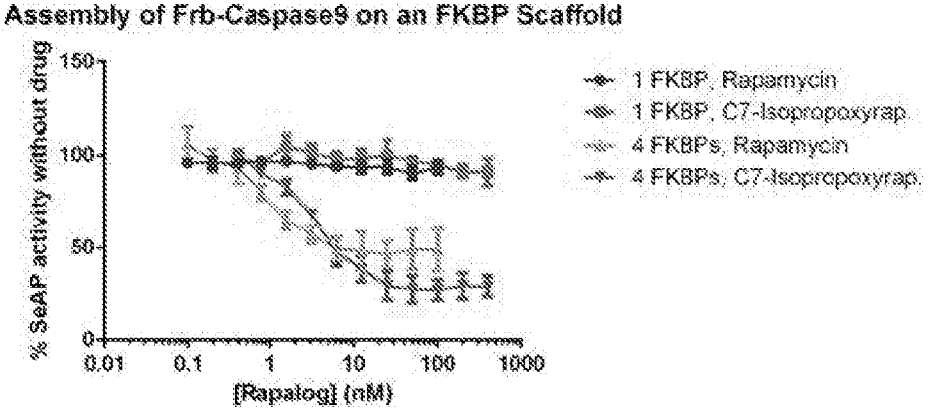


Fig. 13 B



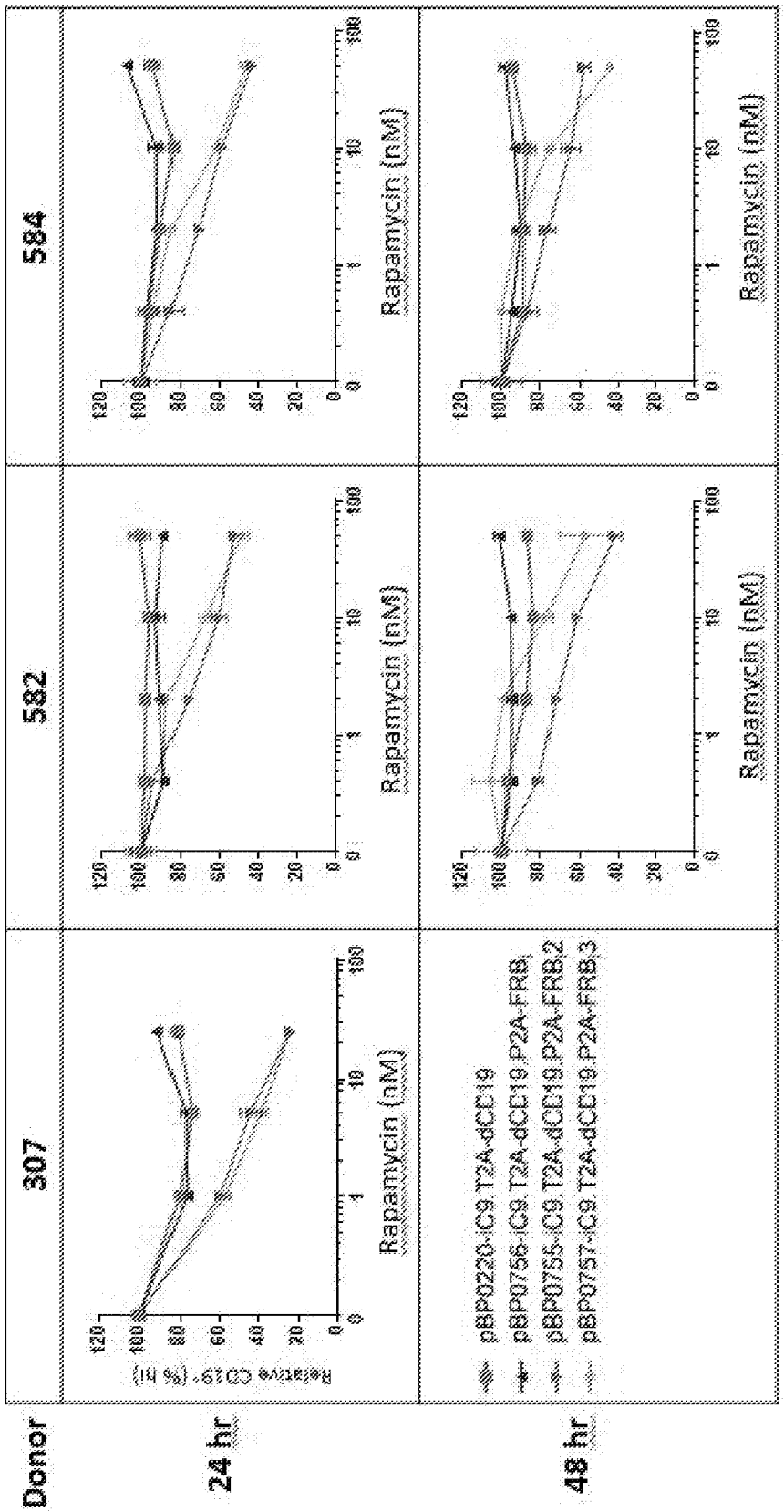


Fig. 14A

Fig. 14B

Fig. 14C

Fig. 14D

Fig. 14E

Fig. 15A

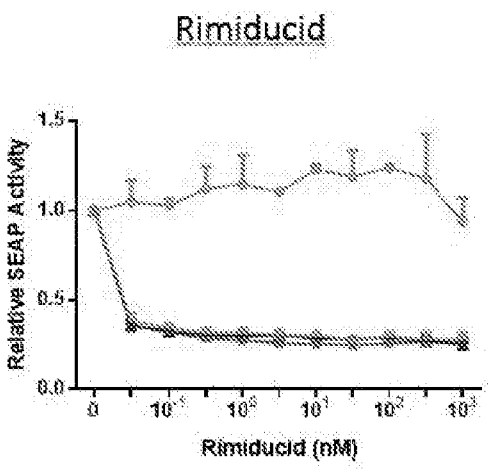


Fig. 15B

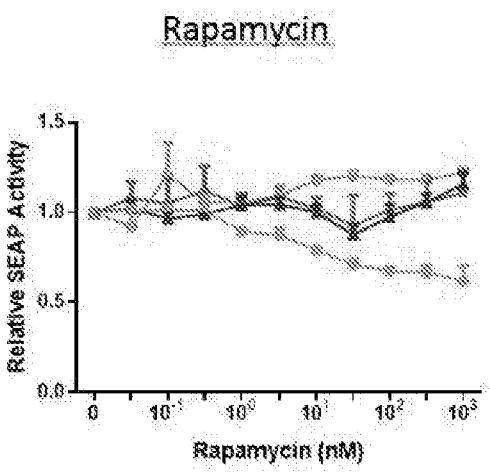
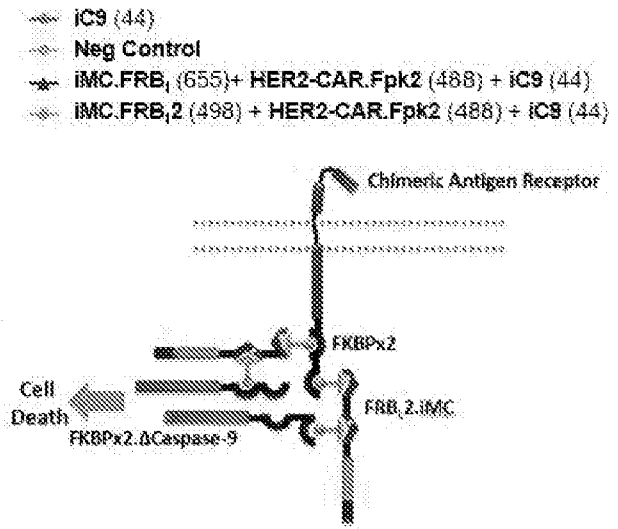


Fig. 15C



WO 2017/106185
PCT/US2016/066371

Fig. 16A

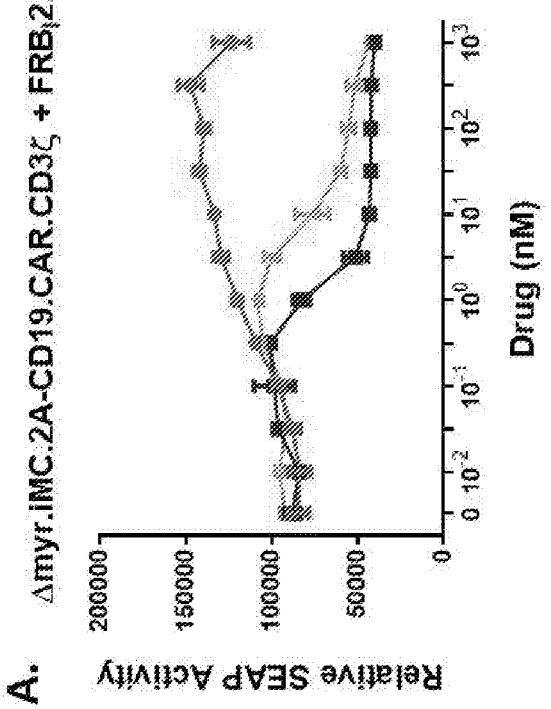


Fig. 16B

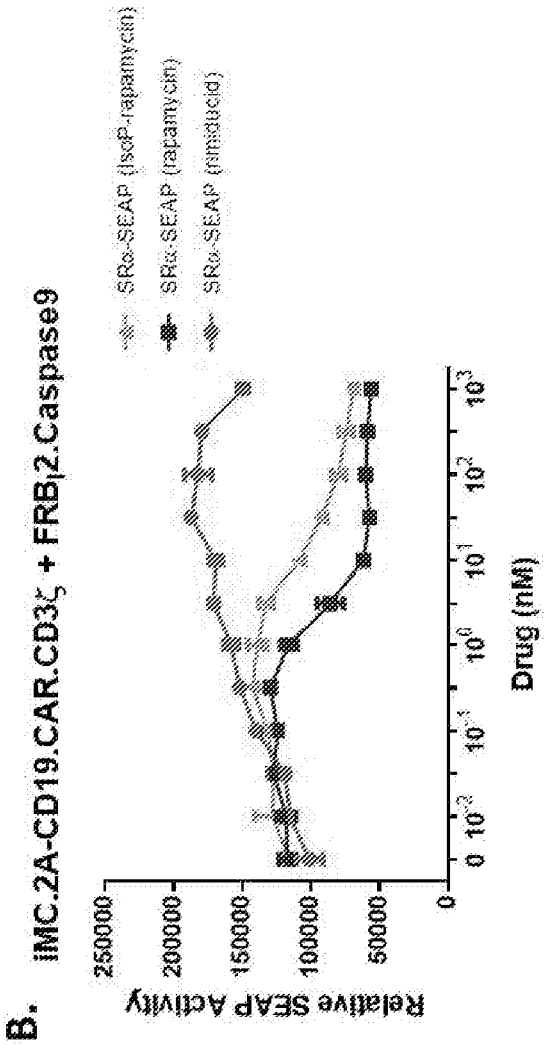


Fig. 17A

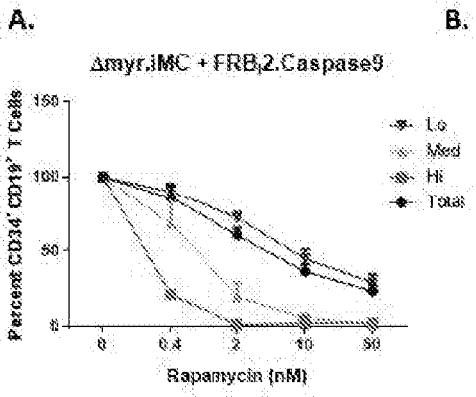


Fig. 17B

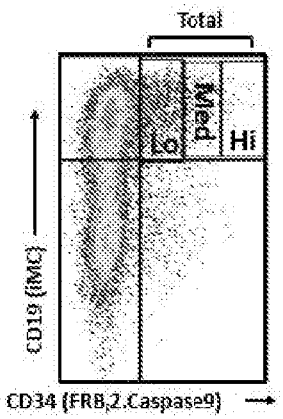
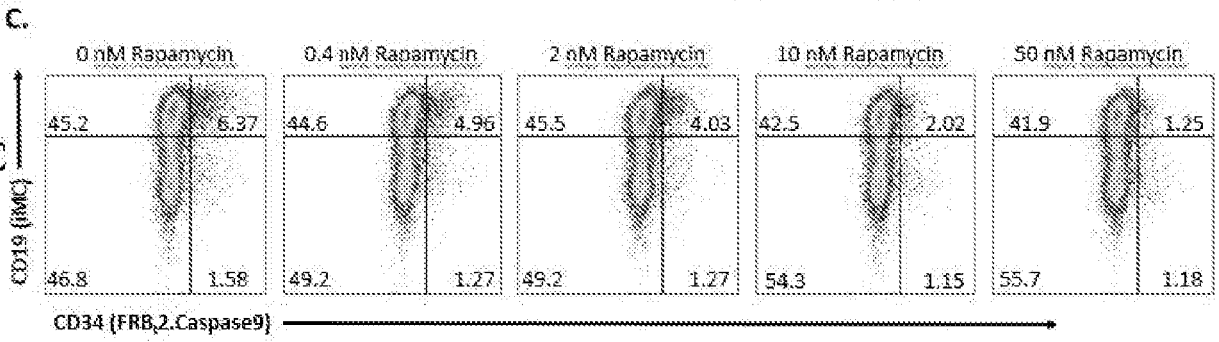


Fig. 17C



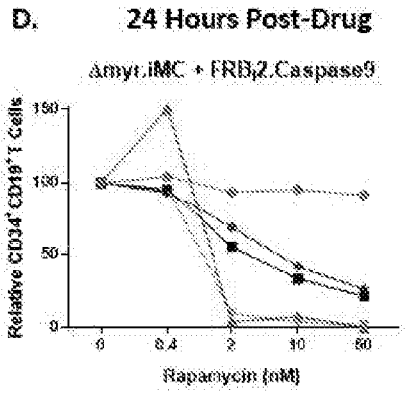


Fig. 17D

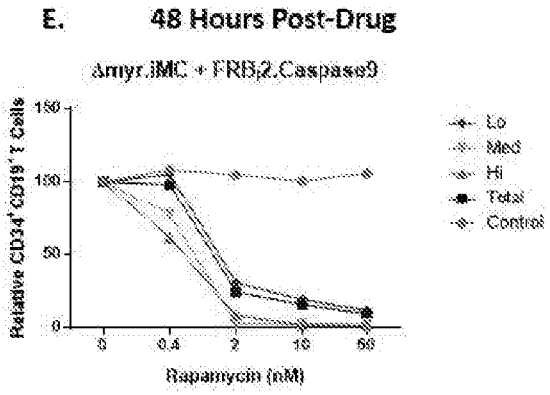


Fig. 17E

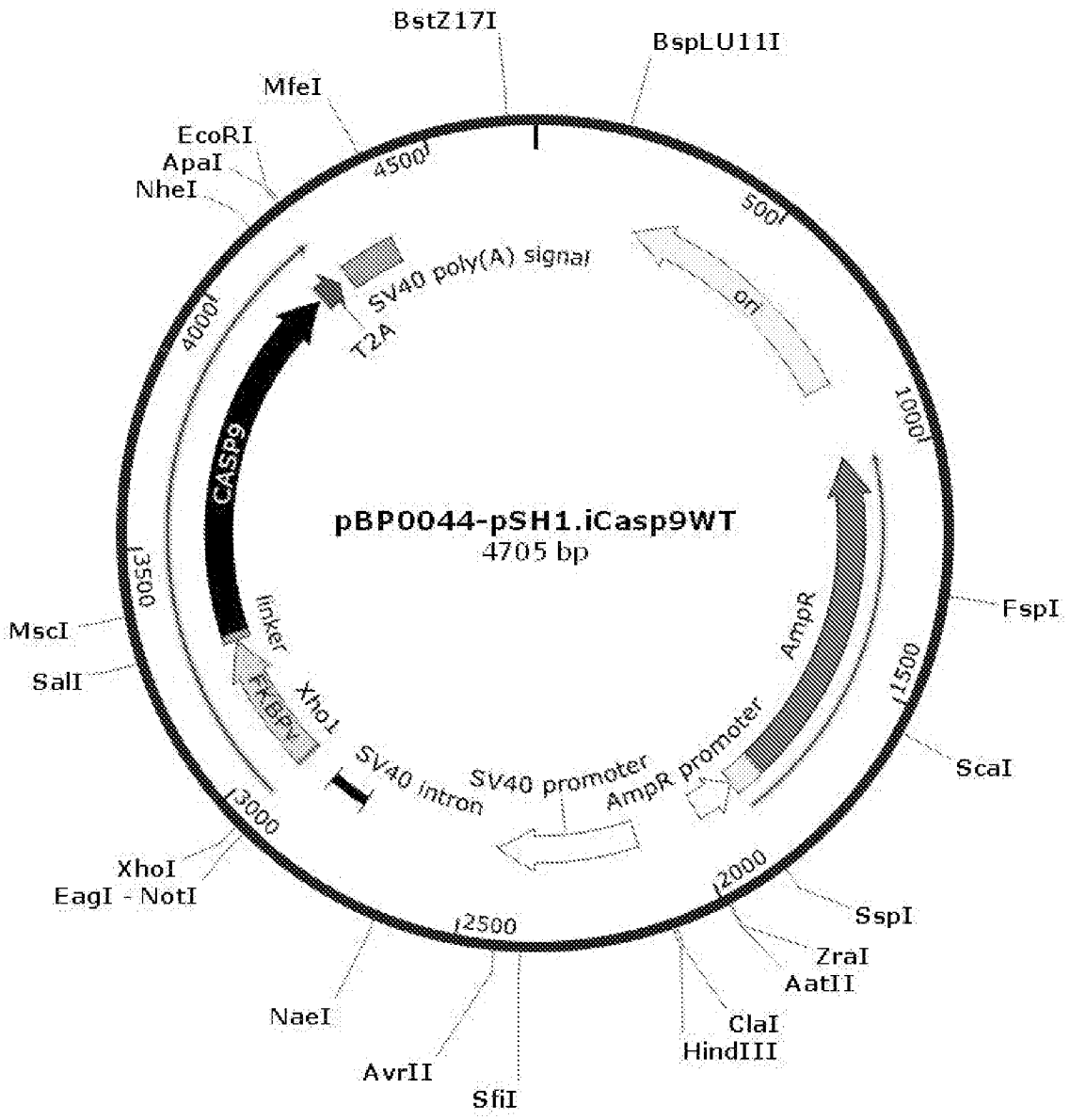

BstZ17I
BspLU11I
MfeI
EcoRI
ApaI
NheI
4500
500
4000
SV40 poly(A) signal
T2A
ori
1000
CASP9
pBP0044-pSH1.iCasp9WT
4705 bp
3500
linker
AmpR
FspI
MscI
SalI
FKBP
XhoI
1500
SV40 intron
SV40 promoter
AmpR promoter
ScaI
3000
XhoI
EagI - NotI
2000
SspI
2500
ZraI
AatII
NaeI
ClaI
HindIII
AvrII
SfiI

Fig. 18

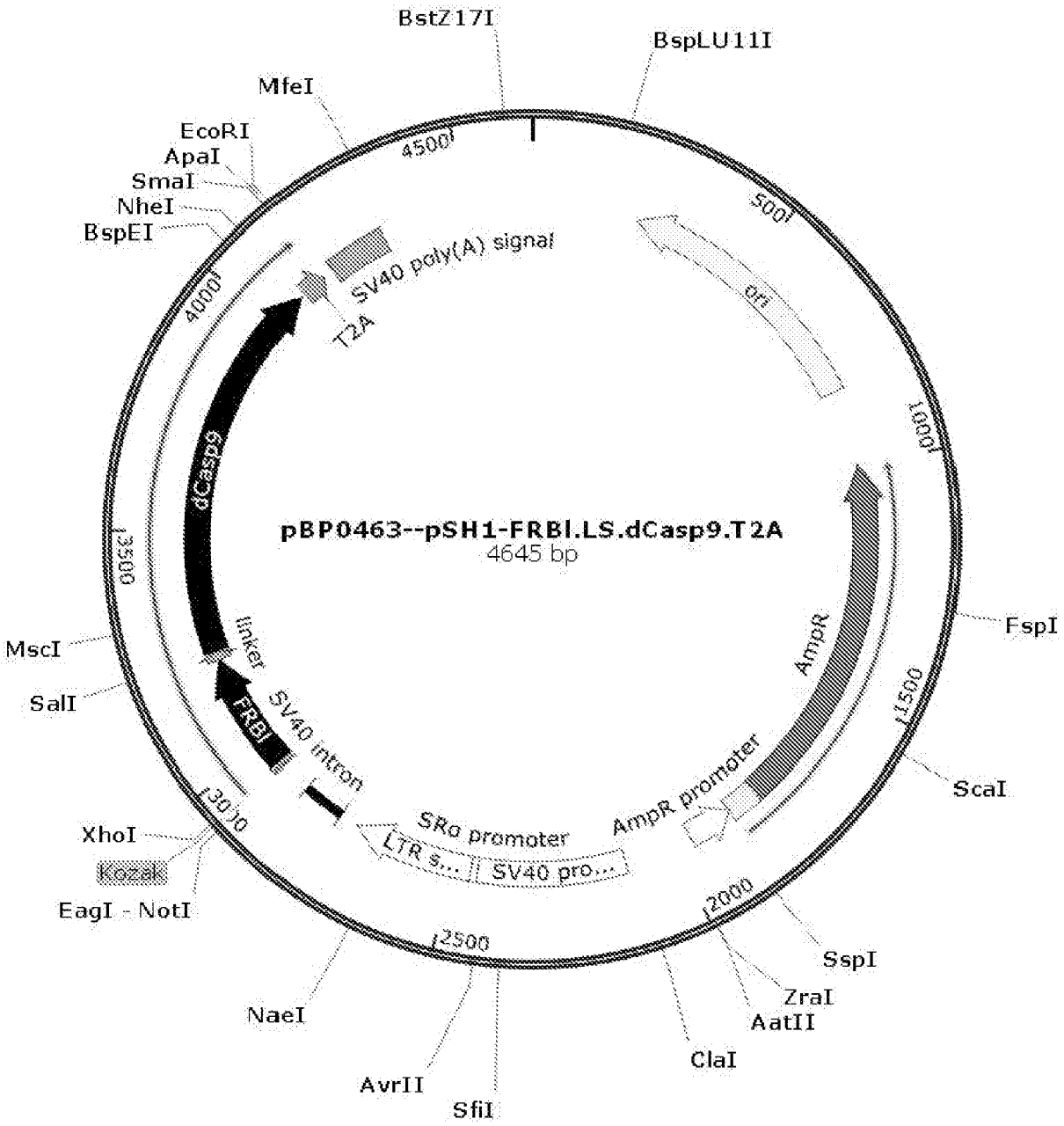

BstZ17I
BspLU11I
MfeI
EcoRI
ApaI
SmaI
NheI
BspEI
4500
5000
4000
SV40 poly(A) signal
T2A
ori
10000
dCasp9
pBP0463--pSH1-FRBl.LS.dCasp9.T2A
4645 bp
3500
AmpR
FspI
MscI
SalI
linker
FRBl
SV40 intron
1500
ScaI
3000
SRα promoter
AmpR promoter
LTR s...
SV40 pro...
XhoI
Kozak
EagI - NotI
2000
SspI
2500
ZraI
AatII
NaeI
ClaI
AvrII
SfiI

Fig. 19

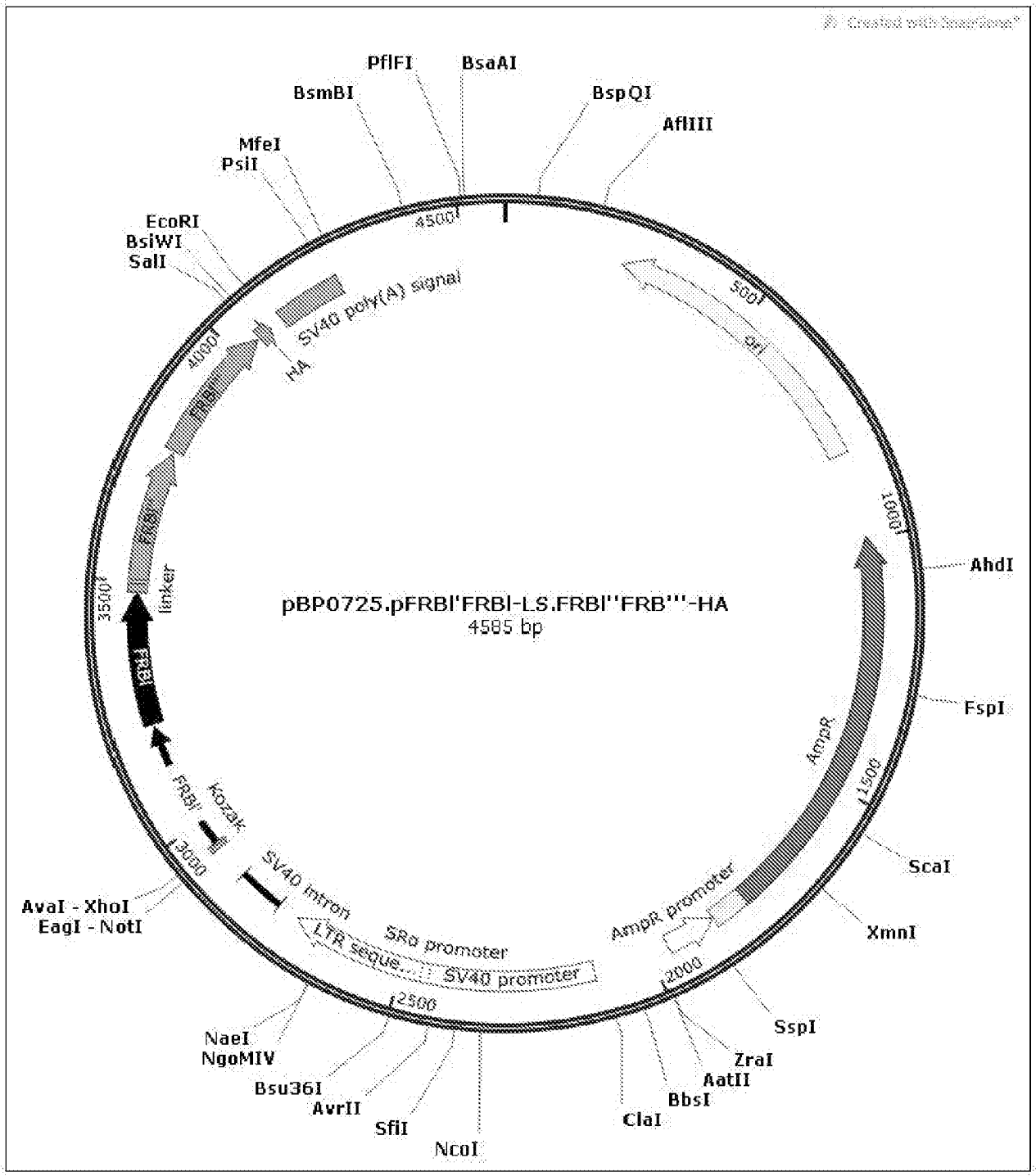

PflFI
BsaAI
BsmBI
BspQI
AflIII
MfeI
PsiI
EcoRI
BsiWI
SalI
4500
500
ori
SV40 poly(A) signal
HA
4000
FRBI'
FRBI
linker
3500
1000
AhdI
pBP0725.pFRBI'FRBI-LS.FRBI''FRB'''-HA
4585 bp
FspI
AmpR
1500
FRBI
Kozak
FRBI'
3000
SV40 intron
ScaI
AvaI - XhoI
EagI - NotI
SRα promoter
LTR seque...
SV40 promoter
AmpR promoter
XmnI
2000
2500
SspI
NaeI
NgoMIV
ZraI
AatII
Bsu36I
BbsI
AvrII
ClaI
SfiI
NcoI

Fig. 20

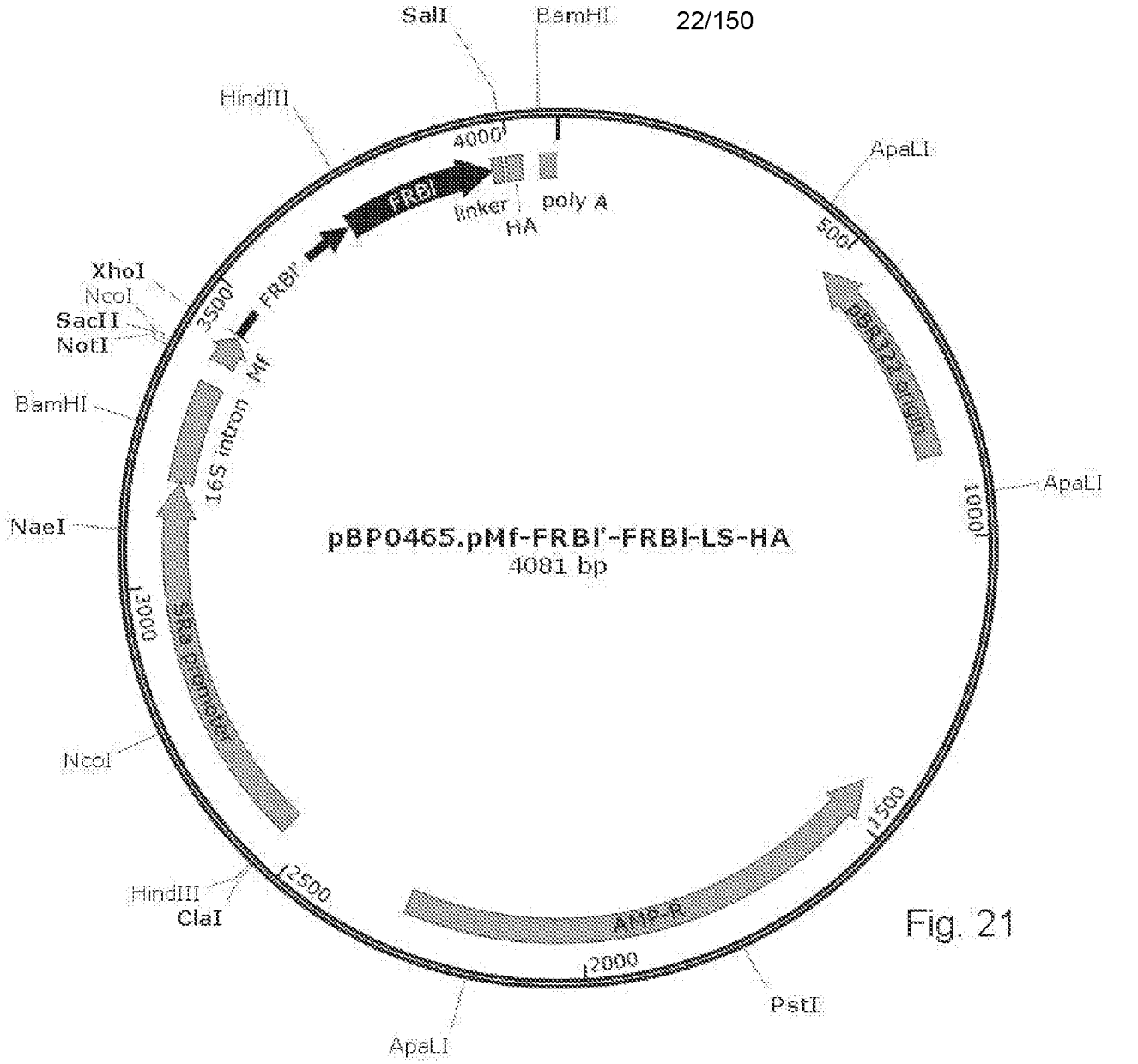

SalI
BamHI
HindIII
4000
ApaLI
FRBI
linker
HA
poly A
5000
XhoI
NcoI
SacII
NotI
3500
FRBI'
Mf
BamHI
16S intron
NaeI
pBP0465.pMf-FRBI'-FRBI-LS-HA
4081 bp
6000
ApaLI
3000
NcoI
1500
HindIII
ClaI
2500
AMP R
2000
PstI
ApaLI

Fig. 21

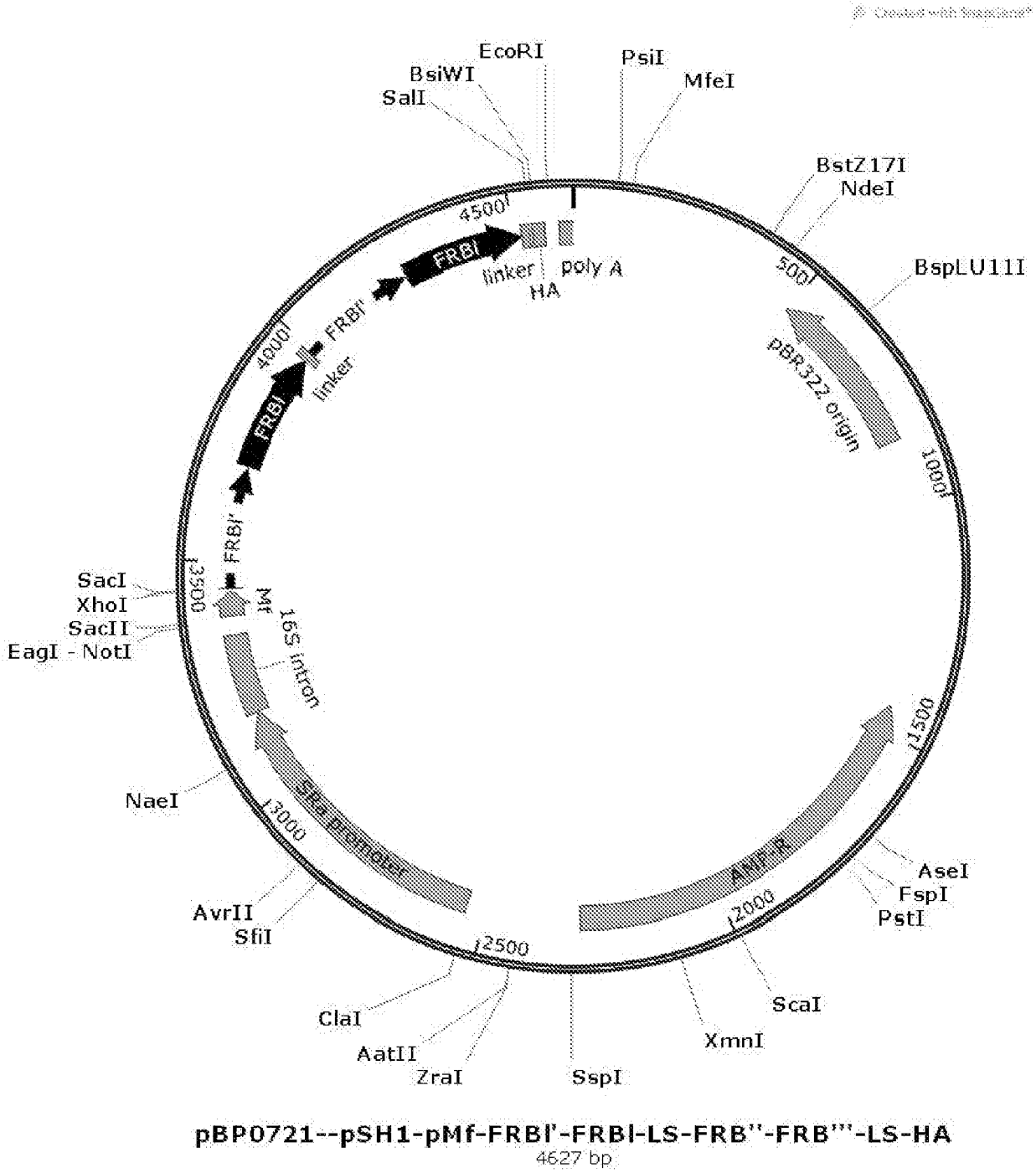
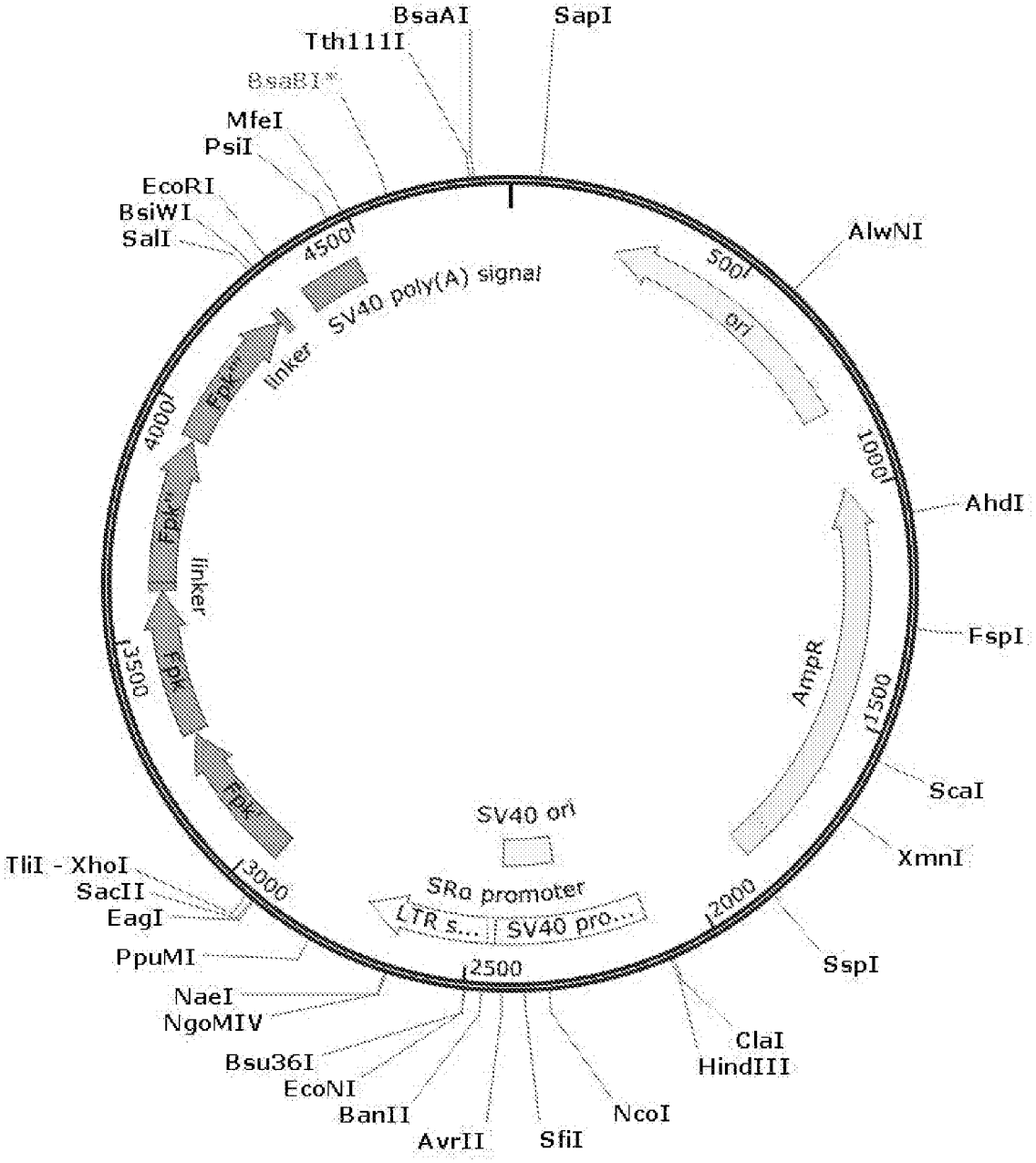

EcoRI
PsiI
BsiWI
MfeI
SalI
BstZ17I
NdeI
4500
FRBI
linker
poly A
HA
500
BspLU11I
4000
FRBI'
linker
pBR322 origin
1000
FRBI'
3500
SacI
XhoI
SacII
EagI - NotI
Mf
16S intron
1500
NaeI
3000
SSa promoter
AmpR
AseI
FspI
PstI
2000
AvrII
SfiI
2500
ClaI
AatII
ZraI
SspI
XmnI
ScaI
pBP0721--pSH1-pMf-FRBI'-FRBI-LS-FRB''-FRB'''-LS-HA
4627 bp

Fig. 22



pBP0722--pSH1-dMyr-Fpk'-Fpk-LS-Fpk''-Fpk'''-LS-HA
4820 bp

Fig. 23

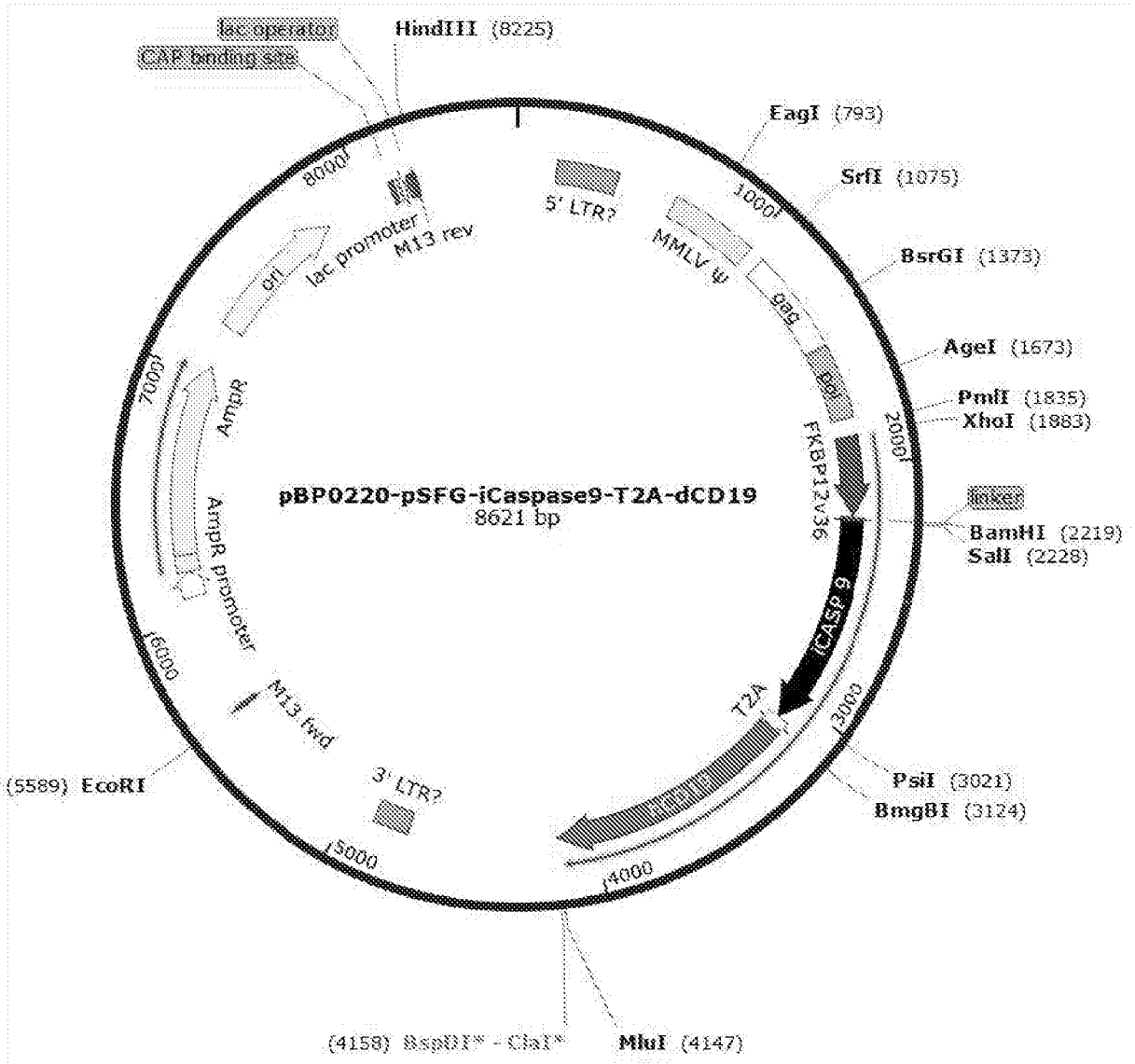

lac operator
CAP binding site
HindIII (8225)
EagI (793)
SrfI (1075)
BsrGI (1373)
AgeI (1673)
PmlI (1835)
XhoI (1883)
linker
BamHI (2219)
SalI (2228)
PsiI (3021)
BmgBI (3124)
MluI (4147)
(4158) BspDI™ - ClaI™
(5589) EcoRI
pBP0220-pSFG-iCaspase9-T2A-dCD19
8621 bp
5' LTR?
MMLV ψ
gag
pol
FKBP12v36
CASP 9
T2A
dCD19
3' LTR?
M13 fwd
AmpR promoter
AmpR
ori
lac promoter
M13 rev
1000
2000
3000
4000
5000
6000
7000
8000

Fig. 24

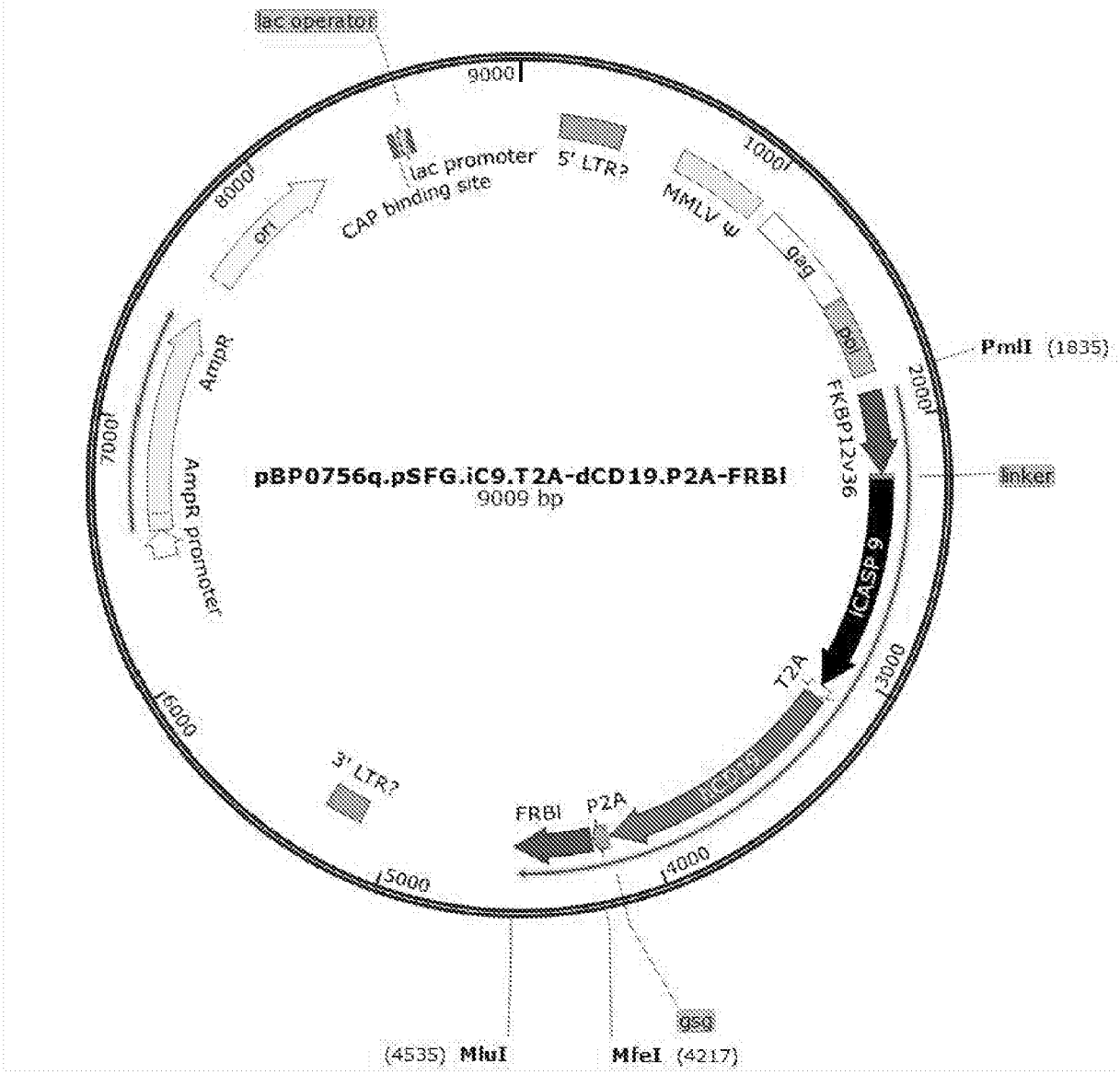

lac operator
9000
lac promoter
CAP binding site
5' LTR?
MMLV ψ
gag
pol
PmlI (1835)
10000
FKBP12v36
linker
iCASP 9
T2A
13000
14000
P2A
FRBI
3' LTR?
15000
16000
AmpR promoter
AmpR
ori
8000
7000
pBP0756q.pSFG.iC9.T2A-dCD19.P2A-FRBI
9009 bp
(4535) MluI
MfeI (4217)

Fig. 25

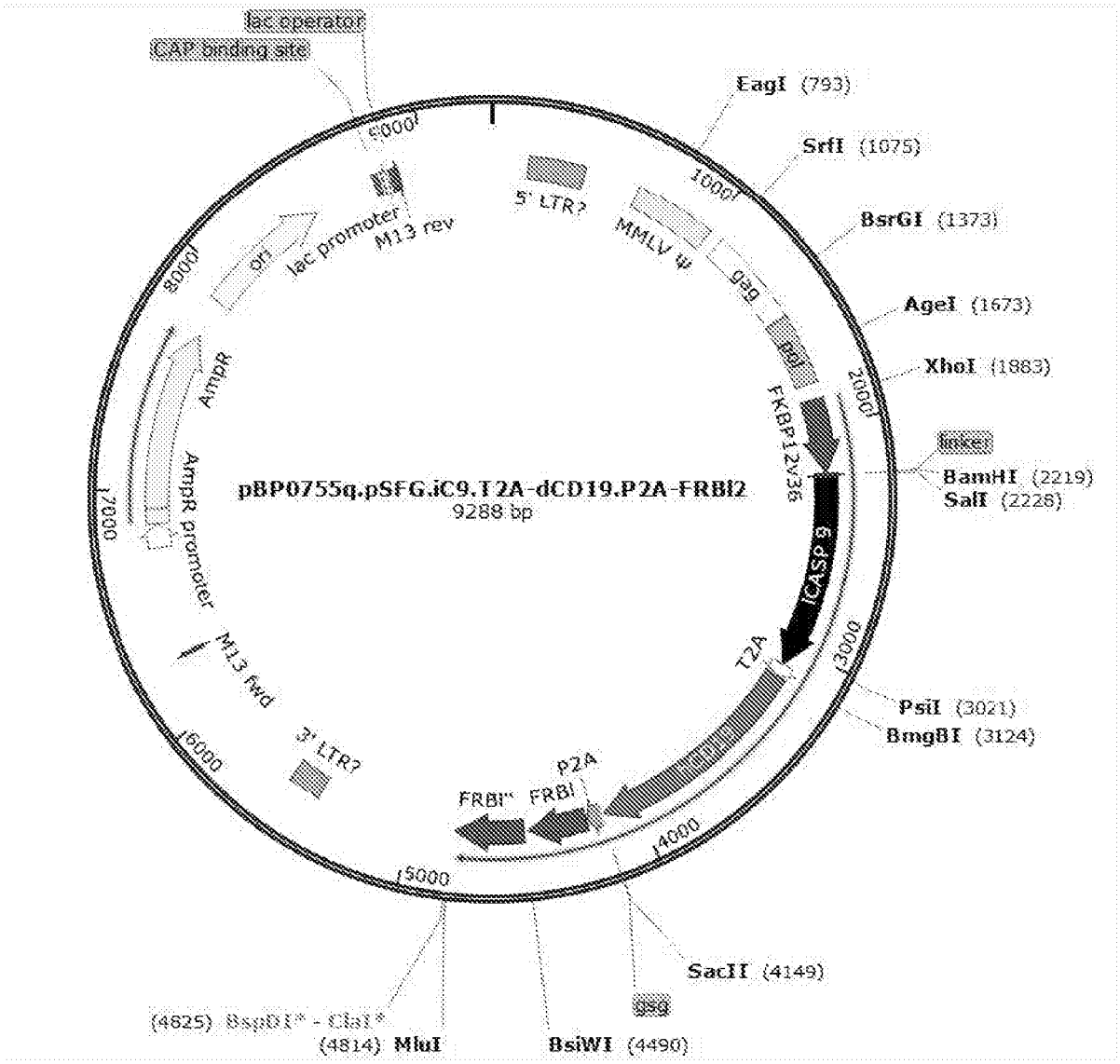

lac operator
CAP binding site
EagI (793)
SrfI (1075)
BsrGI (1373)
AgeI (1673)
XhoI (1883)
linker
BamHI (2219)
SalI (2228)
PsiI (3021)
BmgBI (3124)
SacII (4149)
BsiWI (4490)
MluI (4814)
(4825) BspDI* - ClaI*
pBP0755q.pSFG.iC9.T2A-dCD19.P2A-FRBI2
9288 bp
1000
2000
3000
4000
5000
6000
7000
8000
ori
lac promoter
M13 rev
5' LTR?
MMLV ψ
gag
pol
FKBP12v36
iCASP 9
T2A
dCD19
P2A
FRBI
FRBI*
3' LTR?
M13 fwd
AmpR promoter
AmpR

Fig. 26

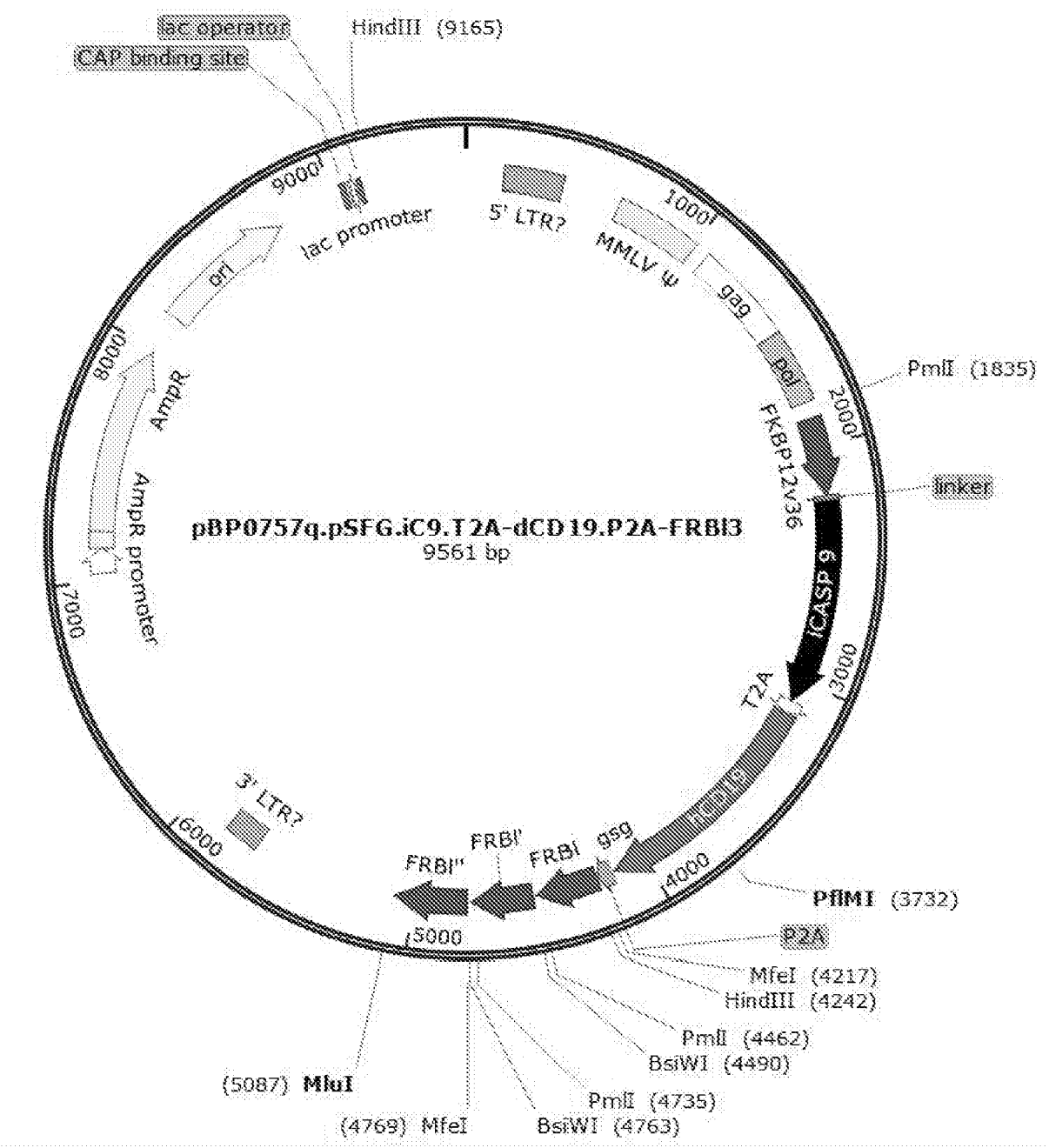

lac operator
CAP binding site
HindIII (9165)
9000
lac promoter
5' LTR?
MMLV Ψ
1000
gag
pol
ori
AmpR
AmpR promoter
pBP0757q.pSFG.iC9.T2A-dCD19.P2A-FRBI3
9561 bp
PmlI (1835)
2000
FKBP12v36
linker
iCASP 9
T2A
3000
3' LTR?
FRBI''
FRBI'
FRBI
gag
pol
4000
PflMI (3732)
P2A
MfeI (4217)
HindIII (4242)
PmlI (4462)
BsiWI (4490)
PmlI (4735)
BsiWI (4763)
5000
(5087) MluI
(4769) MfeI
6000
7000
8000

Fig. 27

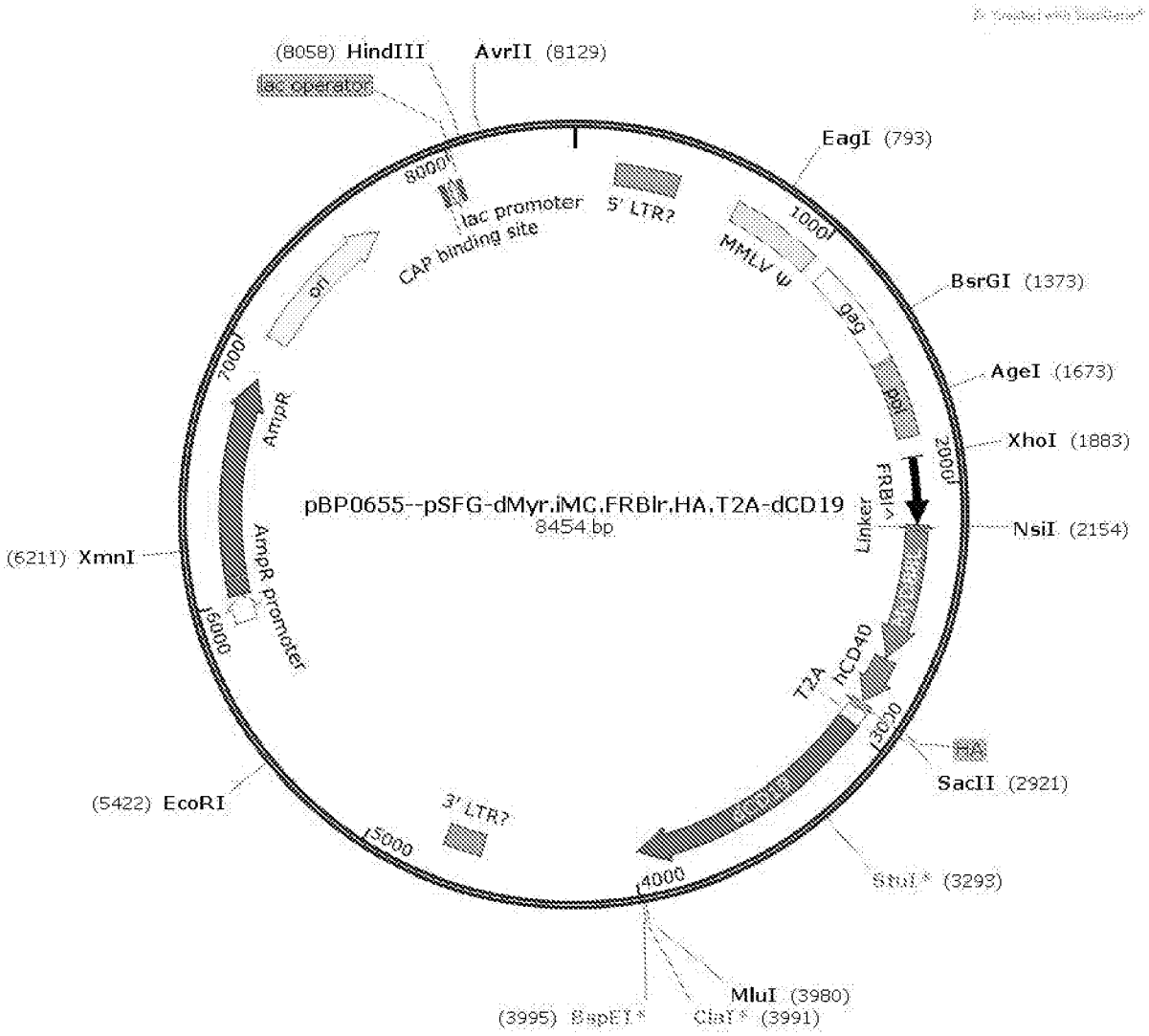

(8058) HindIII
AvrII (8129)
lac operator
8000
lac promoter
CAP binding site
5' LTR?
EagI (793)
1000
MMLV Ψ
gag
BsrGI (1373)
AgeI (1673)
pol
XhoI (1883)
2000
ori
7000
AmpR
pBP0655--pSFG-dMyr.iMC.FRBlr.HA.T2A-dCD19
8454 bp
FRBLr
Linker
NsiI (2154)
(6211) XmnI
AmpR promoter
6000
T2A
hCD40
3000
HA
SacII (2921)
(5422) EcoRI
3' LTR?
5000
4000
SnuI * (3293)
MluI (3980)
(3995) BspEI *
ClaI * (3991)

Fig. 28

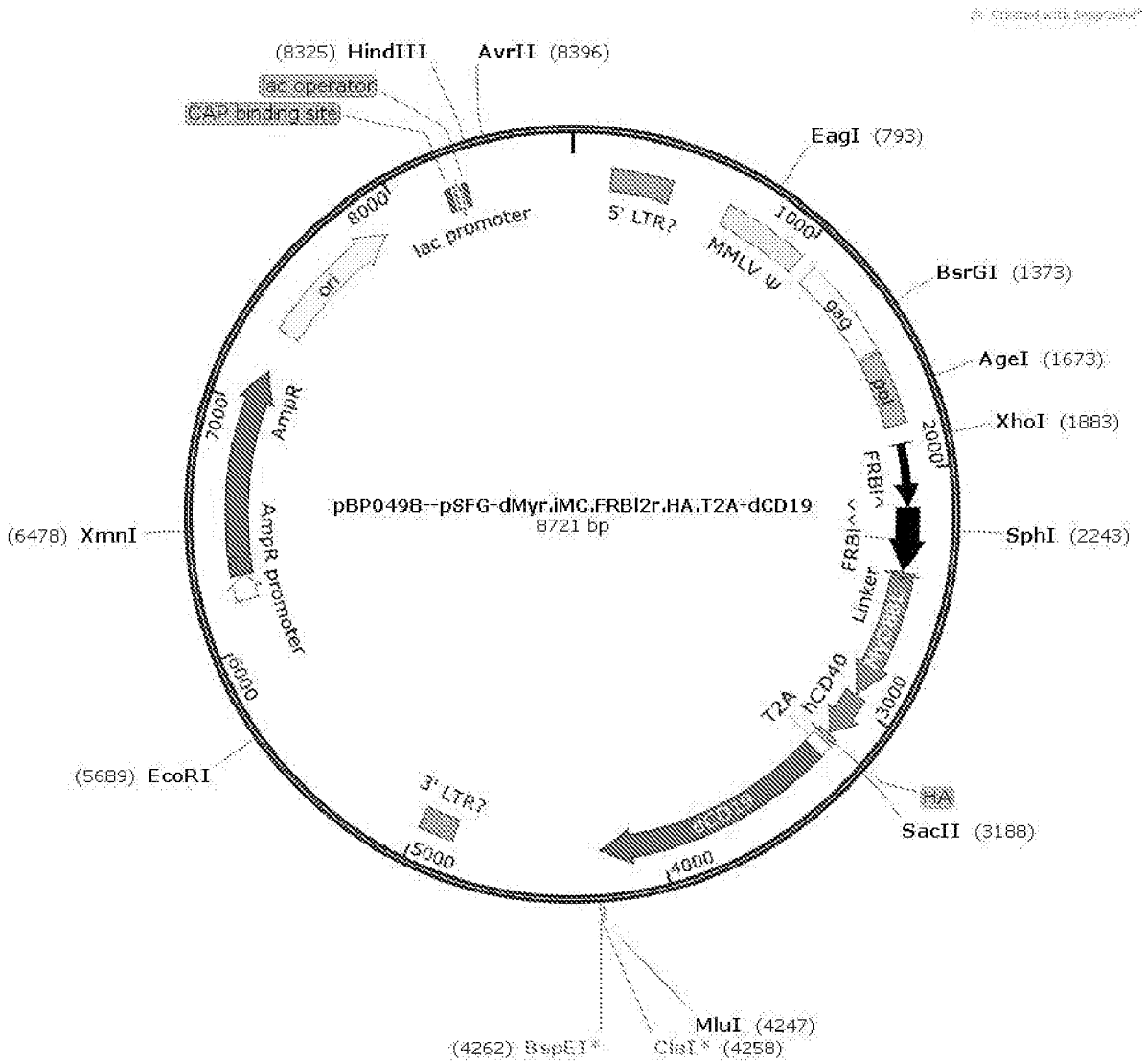
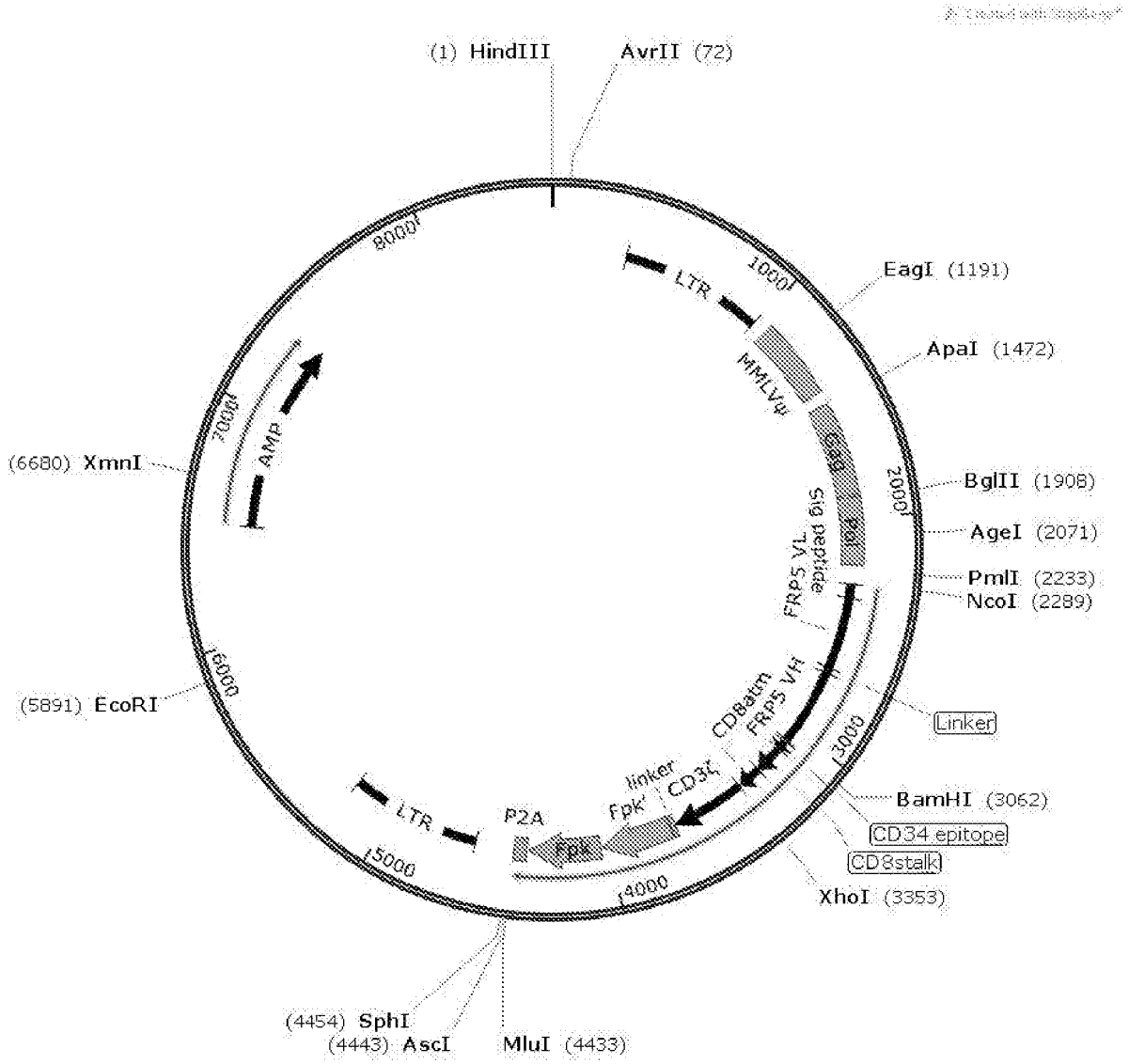

(8325) HindIII
AvrII (8396)
lac operator
CAP binding site
EagI (793)
8000
lac promoter
5' LTR?
1000
MMLV ψ
BsrGI (1373)
ori
gag
AgeI (1673)
pol
7000
AmpR
XhoI (1883)
2000
FRBI^
pBP0498--pSFG-dMyr.iMC.FRBI2r.HA.T2A-dCD19
8721 bp
(6478) XmnI
SphI (2243)
FRBI^^
AmpR promoter
Linker
6000
T2A
hCD40
3000
(5689) EcoRI
3' LTR?
HA
SacII (3188)
5000
4000
MluI (4247)
(4262) BspEI*
ClaI* (4258)

Fig. 29



pBP0488--pSFG-aHer2.Q.8stm.CD3z.Fpk2.P2A
8526 bp

Fig. 30

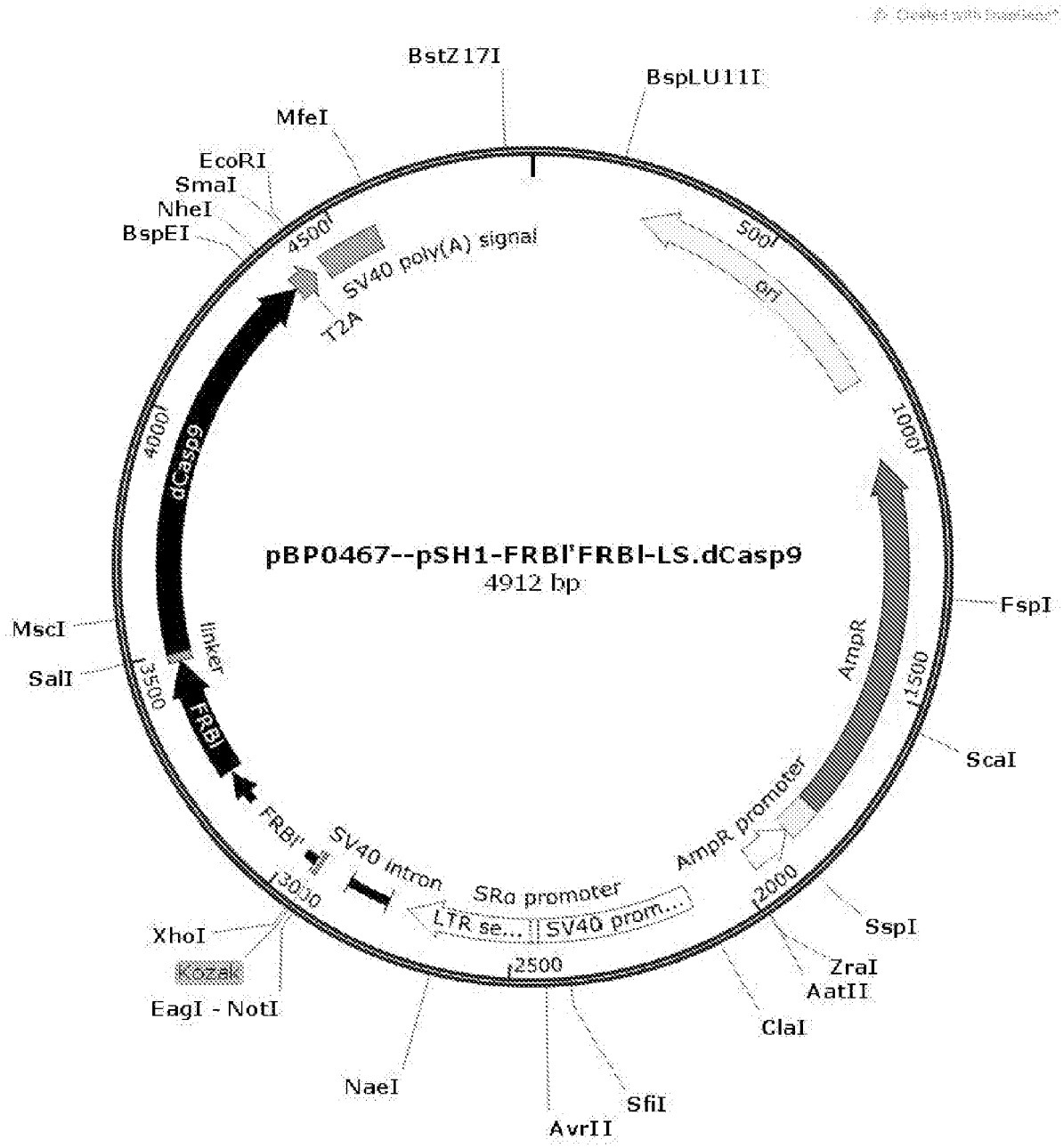

BstZ17I
BspLU11I
MfeI
EcoRI
SmaI
NheI
BspEI
4500
SV40 poly(A) signal
T2A
500
ori
1000
4000
dCasp9
pBP0467--pSH1-FRBl'FRBl-LS.dCasp9
4912 bp
FspI
MscI
SalI
3500
linker
FRBl
FRBl'
SV40 intron
3030
SRα promoter
LTR se...
SV40 prom...
AmpR
1500
AmpR promoter
2000
ScaI
SspI
ZraI
AatII
ClaI
XhoI
Kozak
EagI - NotI
2500
NaeI
SfiI
AvrII

Fig. 31

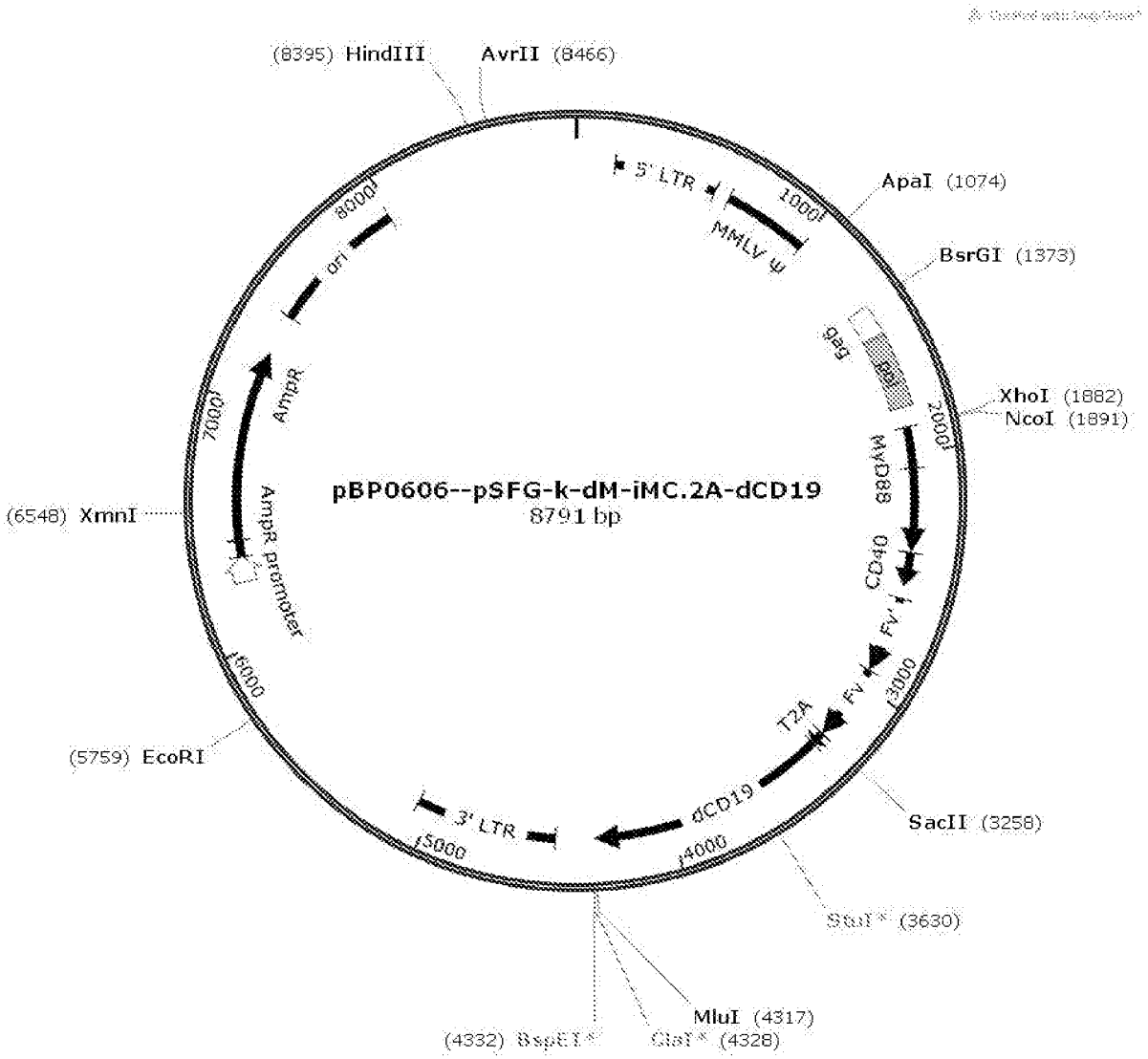

pBP0606--pSFG-k-dM-iMC.2A-dCD19
8791 bp
(8395) HindIII
AvrII (8466)
ApaI (1074)
BsrGI (1373)
XhoI (1882)
NcoI (1891)
(6548) XmnI
(5759) EcoRI
SacII (3258)
SnaI* (3630)
MluI (4317)
(4332) BspEI*
ClaI* (4328)
5' LTR
MMLV ψ
gag
MyD88
CD40
FV
T2A
dCD19
3' LTR
ori
AmpR
AmpR promoter
1000
2000
3000
4000
5000
6000
7000
8000

Fig. 32

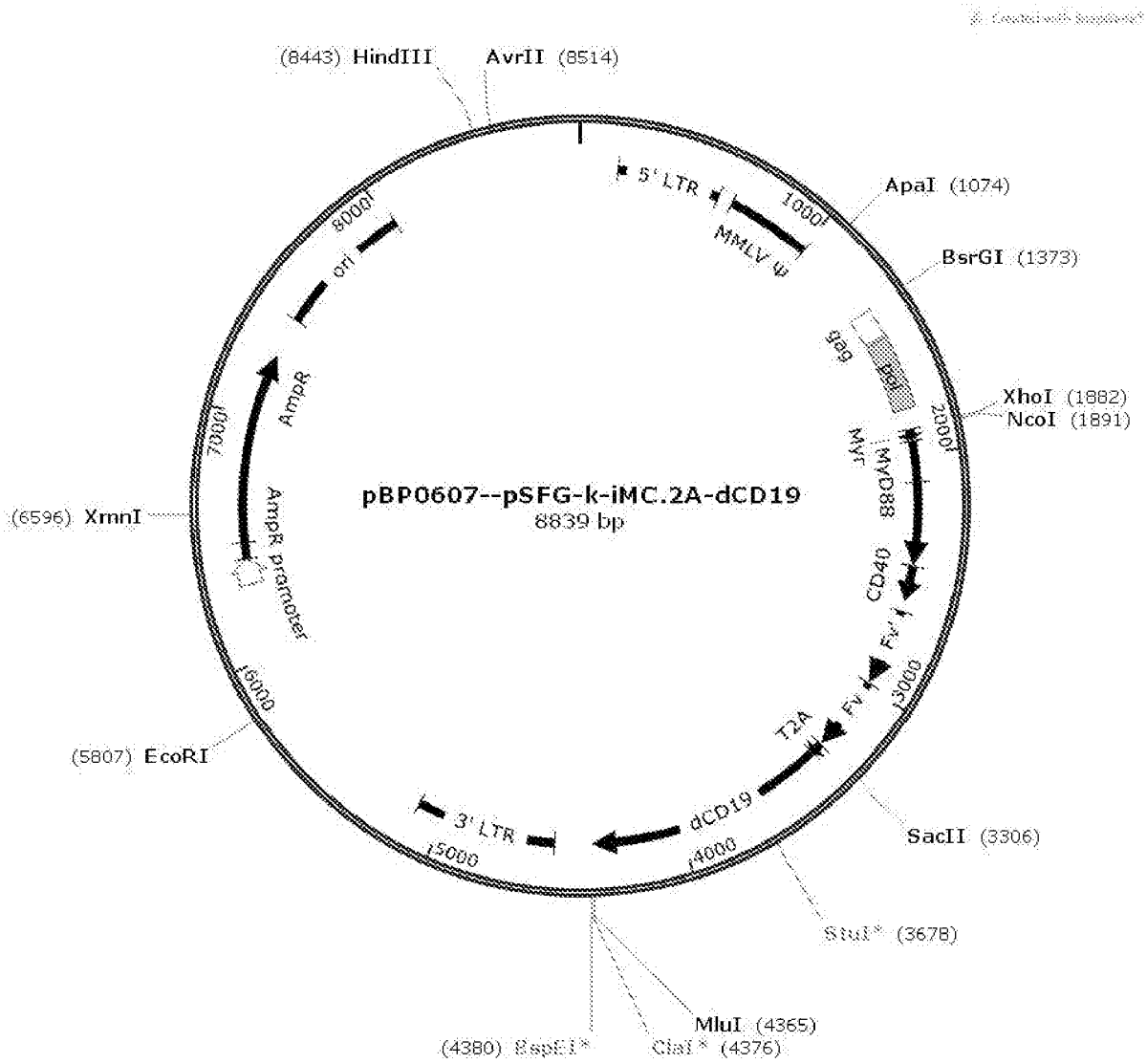

(8443) HindIII
AvrII (8514)
ApaI (1074)
BsrGI (1373)
XhoI (1882)
NcoI (1891)
(6596) XmnI
(5807) EcoRI
SacII (3306)
StuI* (3678)
MluI (4365)
(4380) EspEI*
ClaI* (4376)
pBP0607--pSFG-k-iMC.2A-dCD19
8839 bp
5' LTR
MMLV ψ
gag
pol
MyD88
CD40
Fv
T2A
dCD19
3' LTR
AmpR
AmpR promoter
ori
1000
2000
3000
4000
5000
6000
7000
8000

Fig. 33

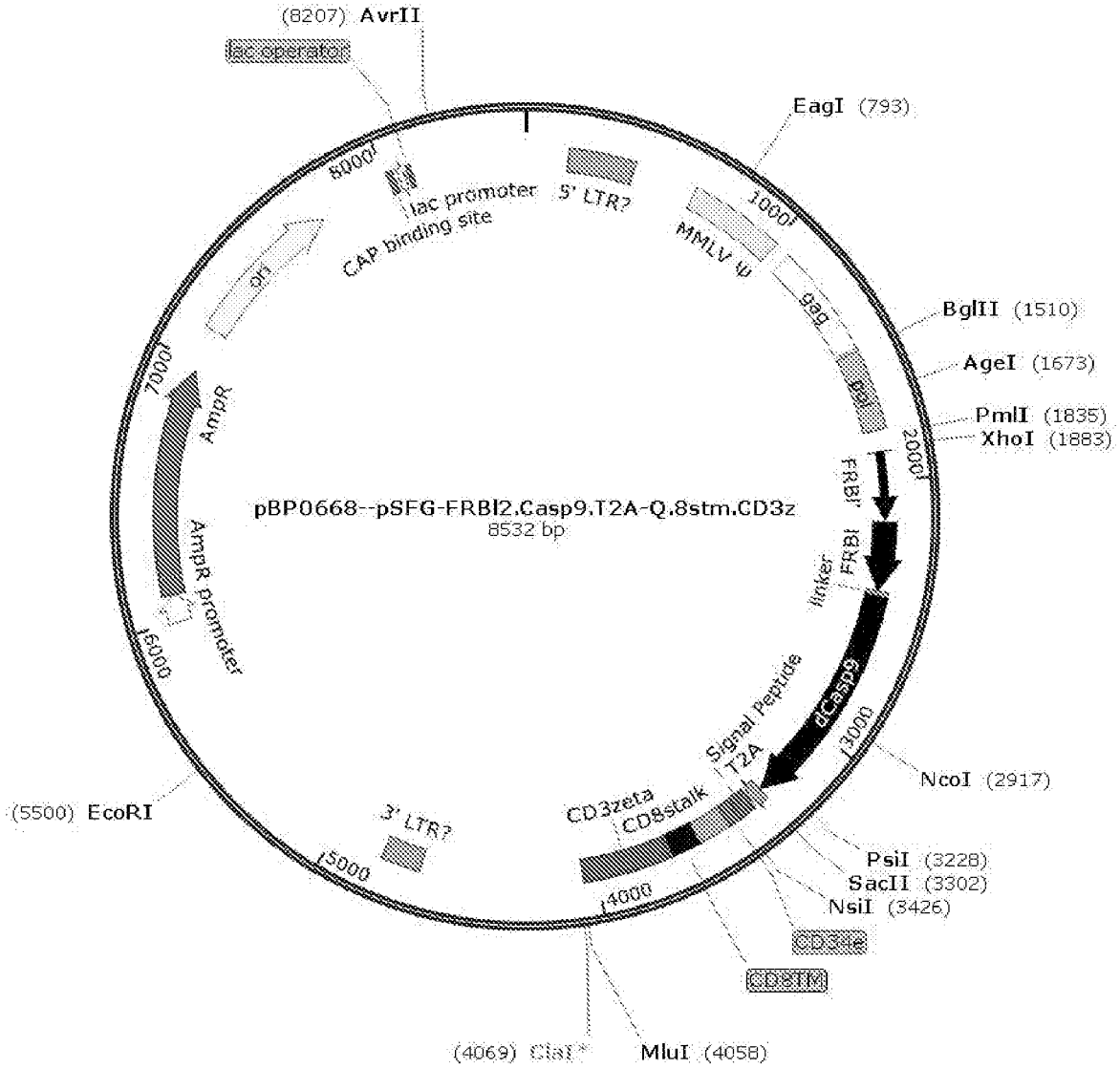

(8207) AvrII
lac operator
EagI (793)
lac promoter
CAP binding site
5' LTR?
MMLV ψ
gag
BglII (1510)
AgeI (1673)
PmlI (1835)
XhoI (1883)
ori
AmpR
AmpR promoter
pBP0668--pSFG-FRBI2.Casp9.T2A-Q.8stm.CD3z
8532 bp
FRBI'
FRBI
linker
dCasp9
Signal Peptide
T2A
CD3zeta
CD8stalk
3' LTR?
NcoI (2917)
(5500) EcoRI
PsiI (3228)
SacII (3302)
NsiI (3426)
CD3ζ
CD8TM
(4069) ClaI
MluI (4058)

Fig. 34

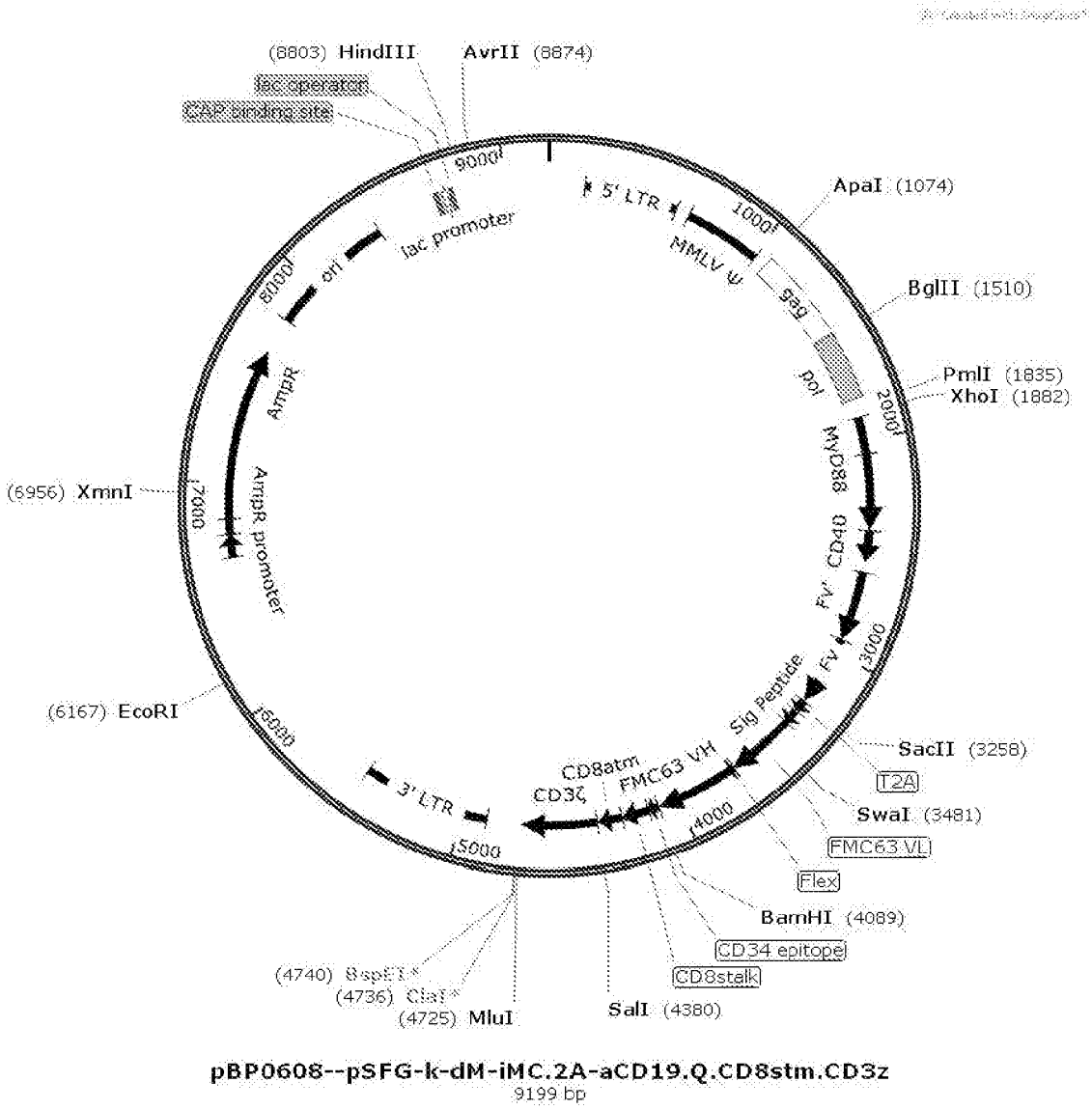

(8803) HindIII
AvrII (8874)
lac operator
CAP binding site
9000
5' LTR
1000
ApaI (1074)
lac promoter
MMLV Ψ
gag
BglII (1510)
ori
8000
pol
PmlI (1835)
XhoI (1882)
2000
AmpR
MyD88
CD40
FV'
(6956) XmnI
7000
AmpR promoter
FV
3000
Sig Peptide
(6167) EcoRI
6000
SacII (3258)
CD8atm
FMC63 VH
T2A
3' LTR
CD3ζ
SwaI (3481)
4000
FMC63 VL
5000
Flex
BamHI (4089)
CD34 epitope
(4740) BspEI
CD8stalk
(4736) ClaI
(4725) MluI
SalI (4380)
pBP0608--pSFG-k-dM-iMC.2A-aCD19.Q.CD8stm.CD3z
9199 bp

Fig. 35

Fig. 36

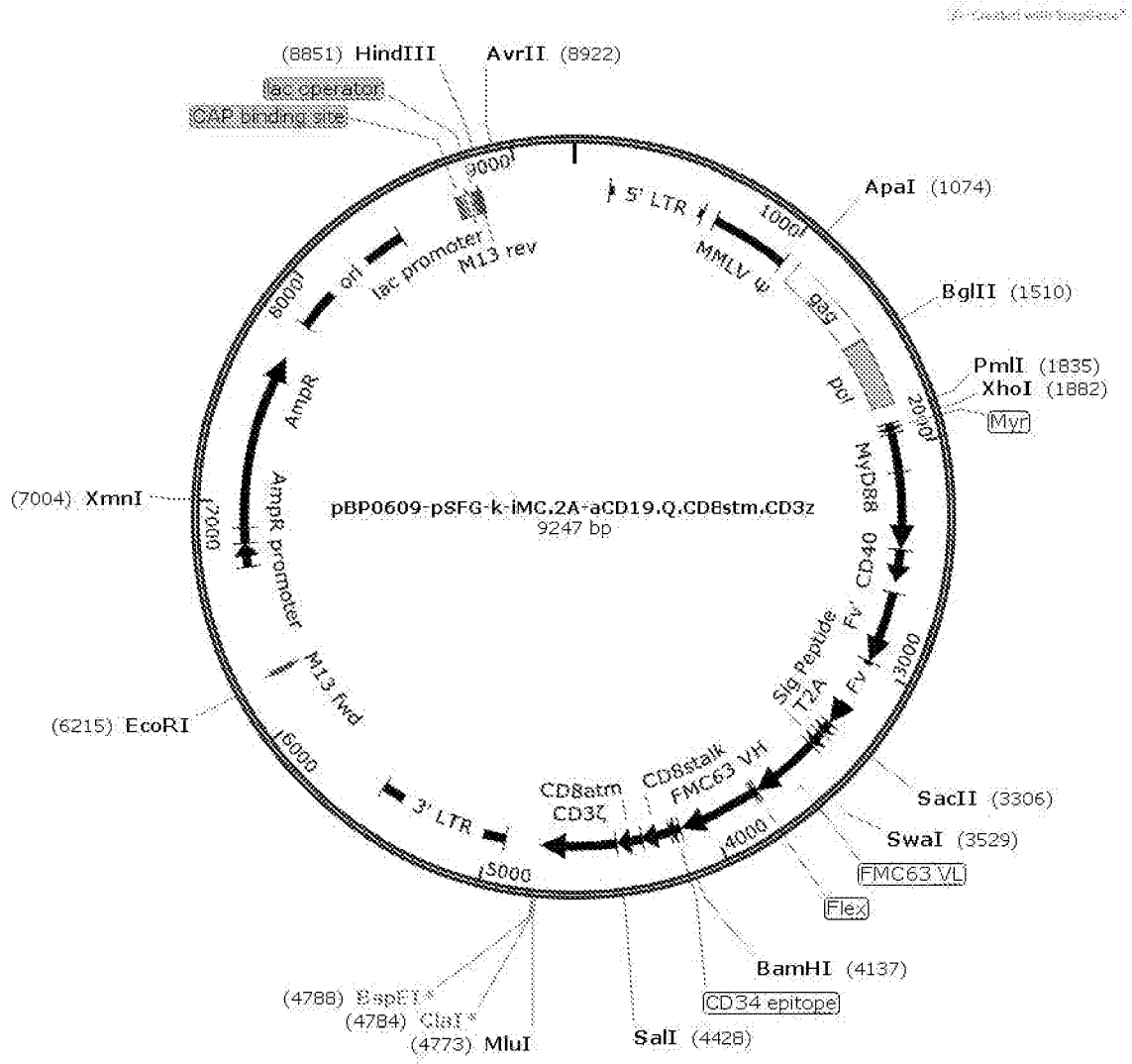

(8851) HindIII
AvrII (8922)
lac operator
CAP binding site
9000
5' LTR
1000
ApaI (1074)
MMLV Ψ
gag
BglII (1510)
pol
PmlI (1835)
XhoI (1882)
2000
Myr
MyD88
CD40
Fv'
Fv
3000
Sig Peptide
T2A
SacII (3306)
SwaI (3529)
FMC63 VL
Flex
4000
CD8stalk
FMC63 VH
CD8atm
CD3ζ
3' LTR
5000
BamHI (4137)
CD34 epitope
SalI (4428)
(4788) BspEI
(4784) ClaI
(4773) MluI
6000
M13 fwd
(6215) EcoRI
AmpR promoter
7000
AmpR
(7004) XmnI
8000
ori
lac promoter
M13 rev
pBP0609-pSFG-k-iMC.2A-aCD19.Q.CD8stm.CD3z
9247 bp

Fig. 37A

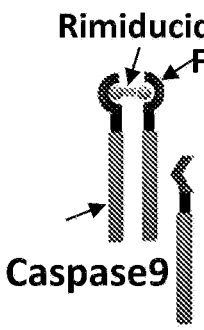


Fig. 37B

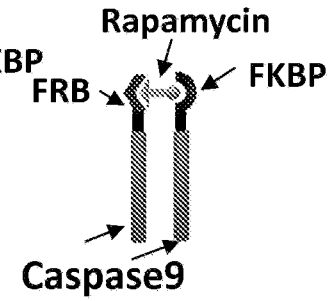


Fig. 37C

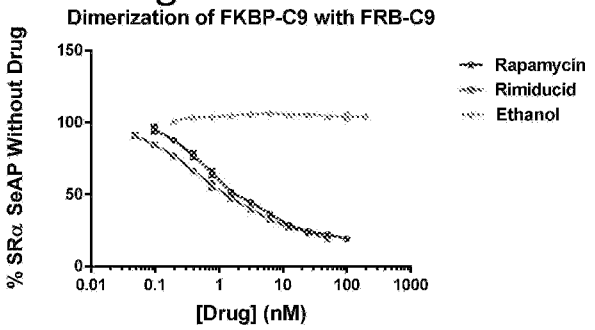


Fig. 38A

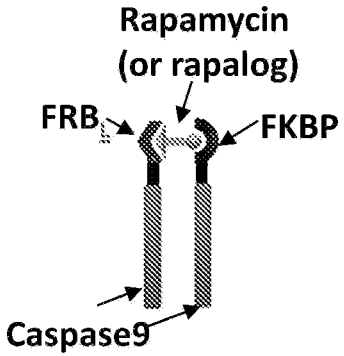


Fig. 38B

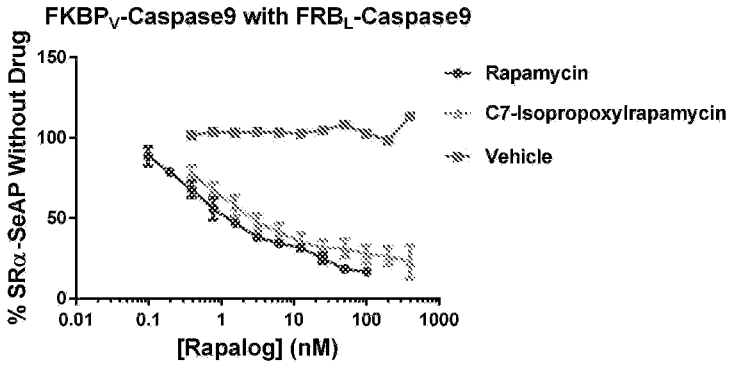


Fig. 39A

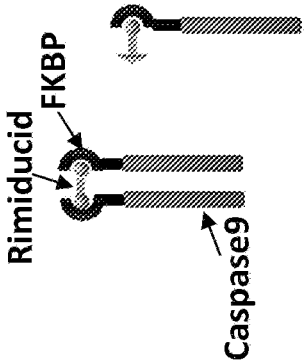


Fig. 39B

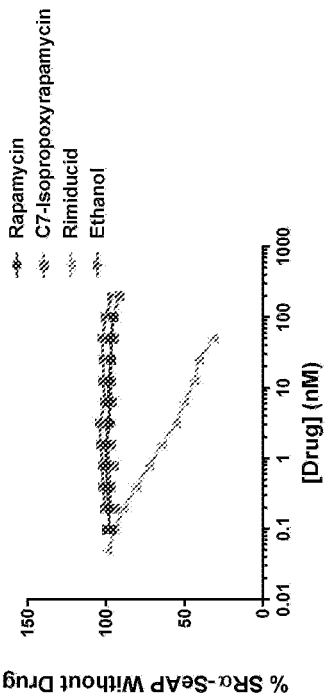


Fig. 40A

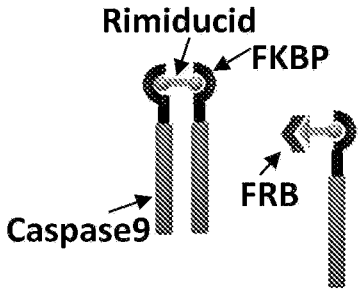
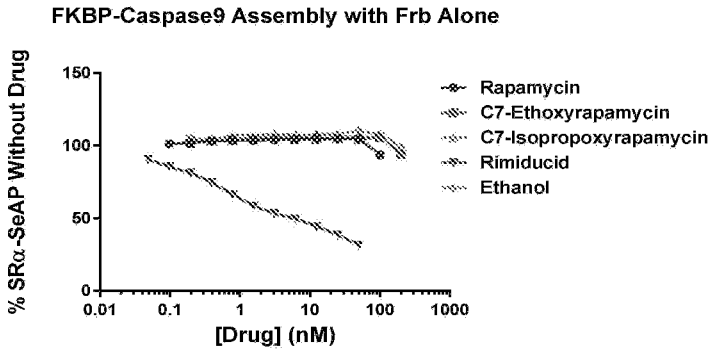


Fig. 40B



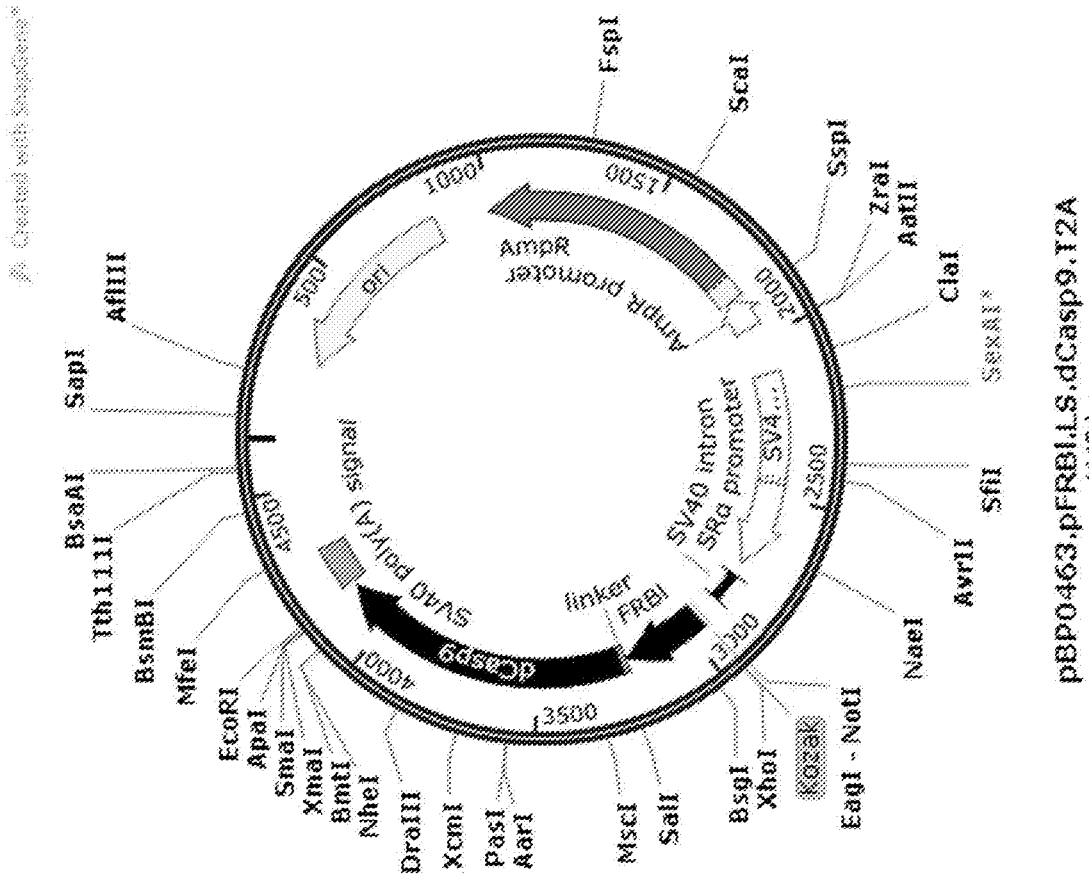

pBP0463.pFRB1.LS.dCasp9.T2A
4645 bp
AmpR promoter
AmpR
ori
linker
FRB1
dCasp9
SV40 intron
SRα promoter
SV40 Poly(A) signal
FspI
ScaI
SspI
ZraI
AatII
ClaI
SexAI*
SfiI
AvrII
NaeI
EagI - NotI
XhoI
BsgI
SalI
MscI
AarI
PasI
XcmI
DraIII
NheI
BmtI
XmaI
SmaI
ApaI
EcoRI
MfeI
BsmBI
Tth111I
BsaAI
SapI
AflIII

Fig. 41

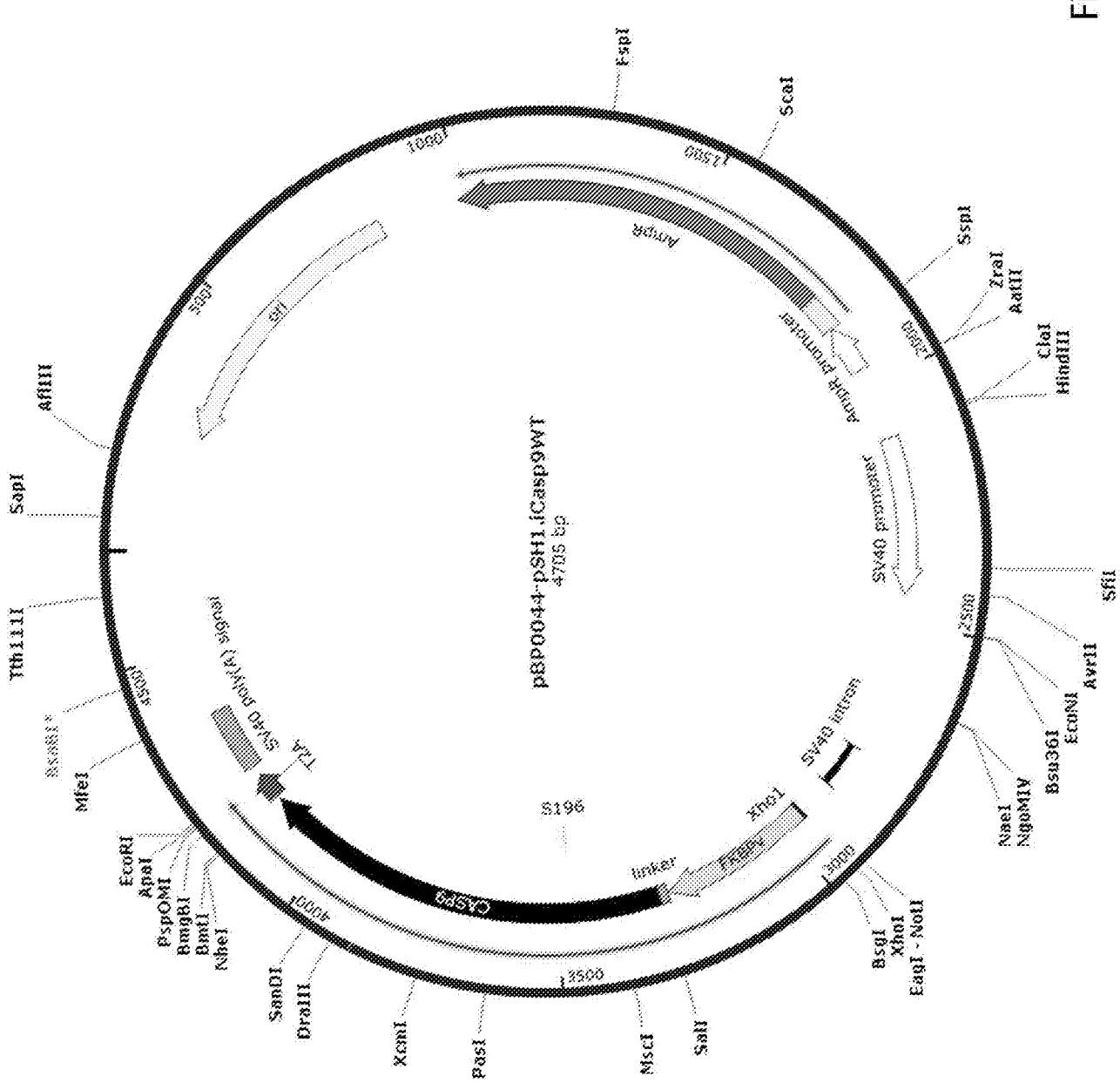

pBP0044-pSH1.iCasp9WT
4705 bp
FspI
ScaI
SspI
ZraI
AatII
ClaI
HindIII
SfiI
AvrII
EcoNI
Bsu36I
NaeI
NgoMIV
BsgI
XhoI
EagI - NotI
SalI
MscI
PasI
XcmI
DraIII
SanDI
NheI
BmtI
BmgBI
PspOMI
ApaI
EcoRI
MfeI
Tth111I
SapI
AflIII
AmpR
AmpR promoter
SV40 promoter
SV40 intron
SV40 poly(A) signal
T2A
CASP9
linker
FKBPV
XhoI
S196
1000
1500
2000
2500
3000
3500
4000
4500
5000

Fig. 42

Fig. 43A Fig. 43B Fig. 43C

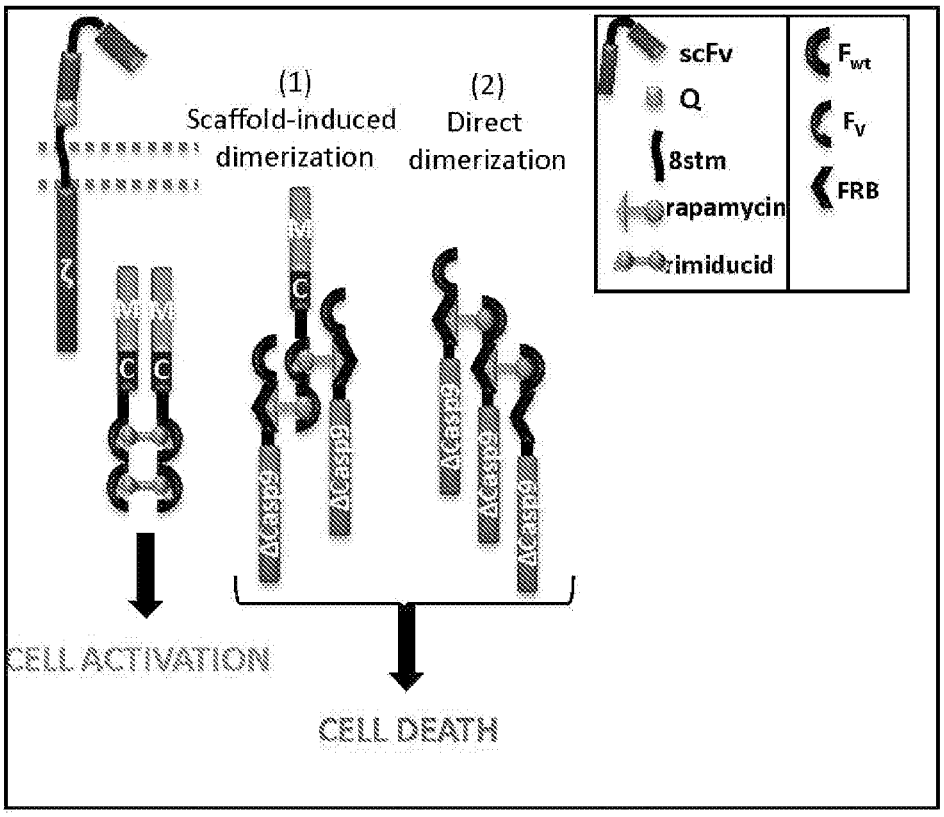


Fig. 44A

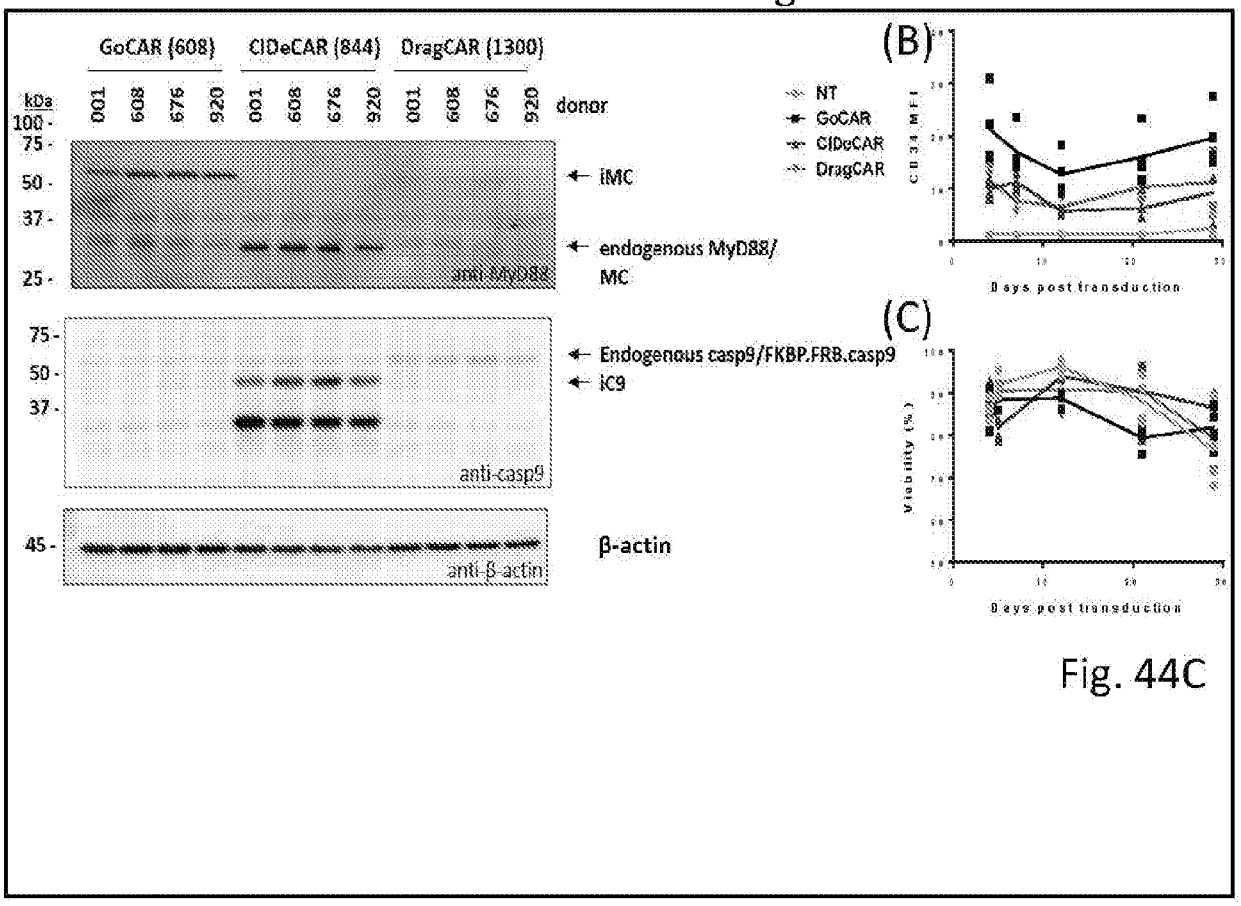


Fig. 44B

Fig. 44C

2

Fig. 45A

Fig. 45B

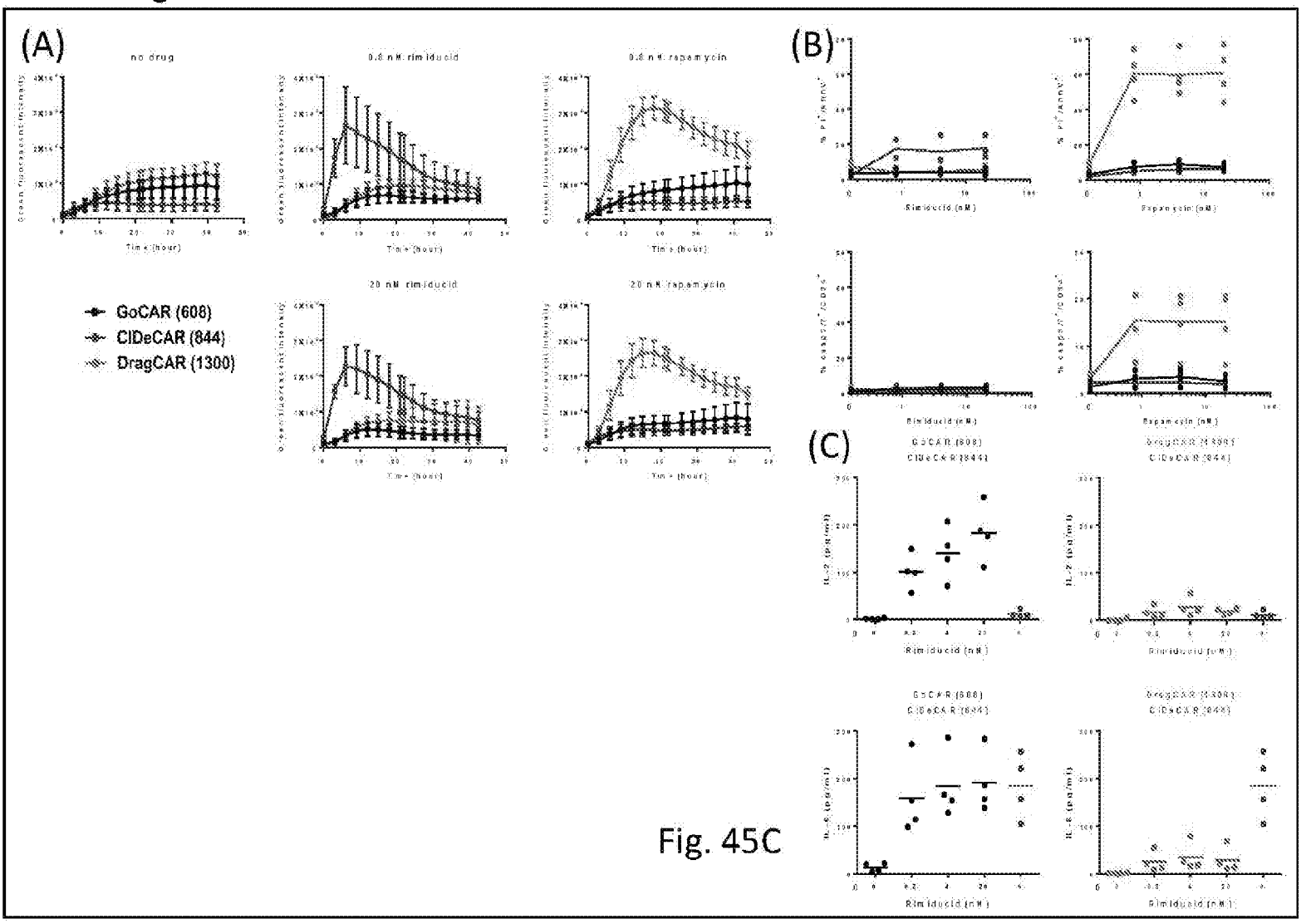


Fig. 45C

Fig. 46A Fig. 46B 47/150 Fig. 46C

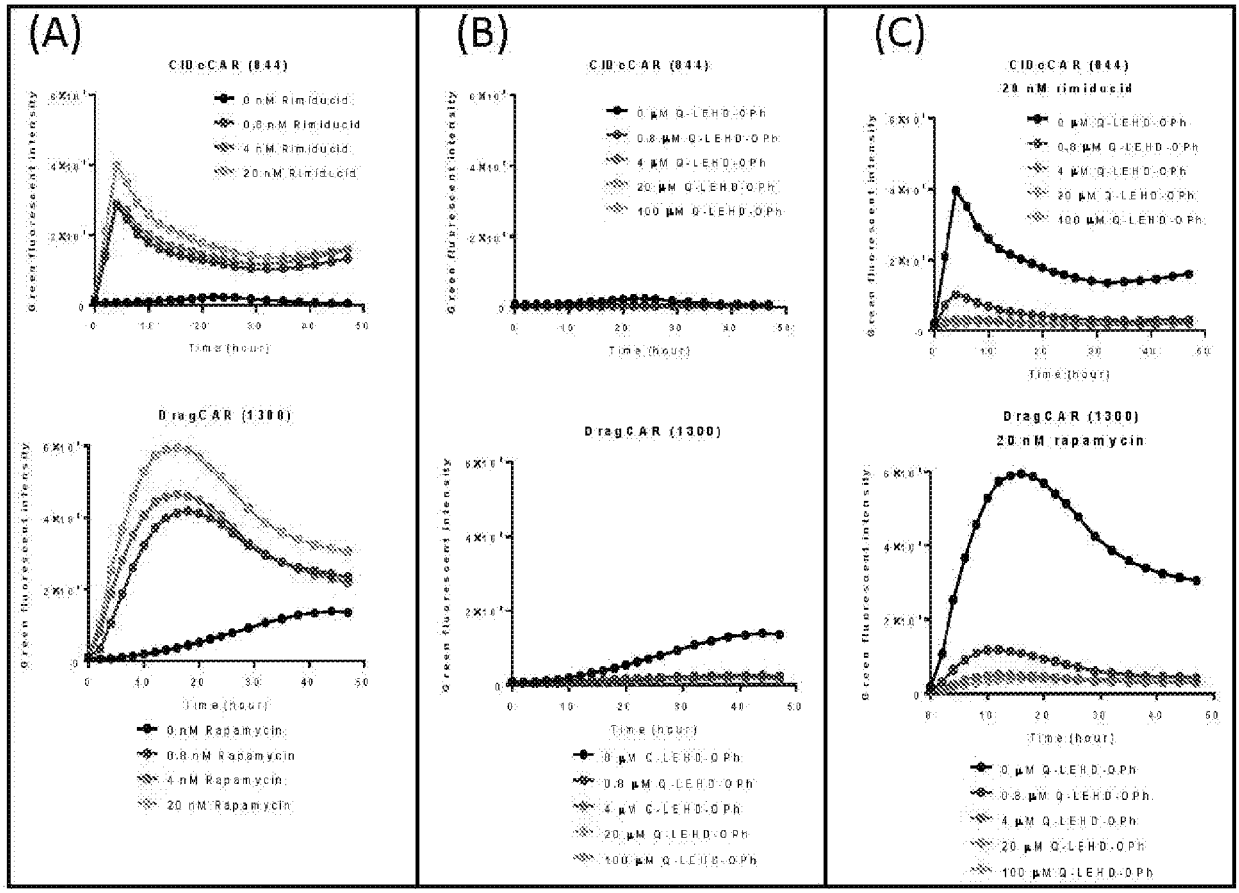


Fig. 47A

Fig. 47B

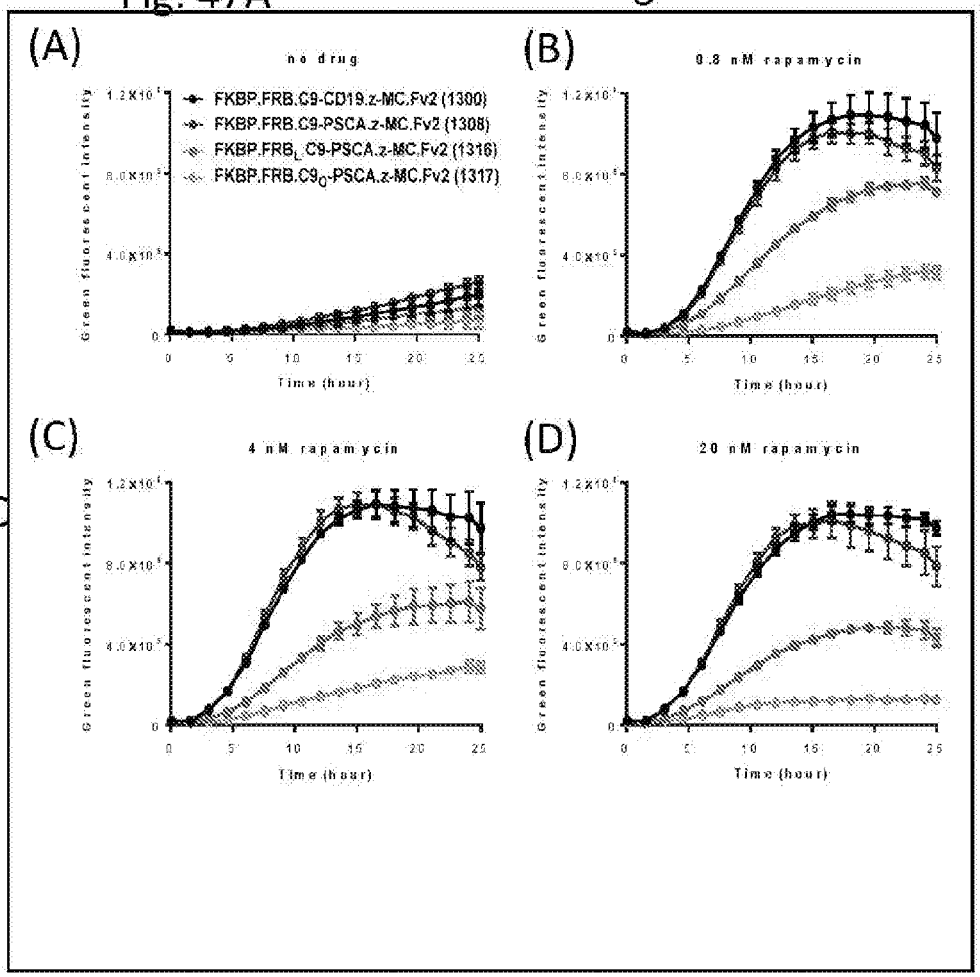


Fig. 47C

Fig. 47D

Fig. 48A

Fig. 48B

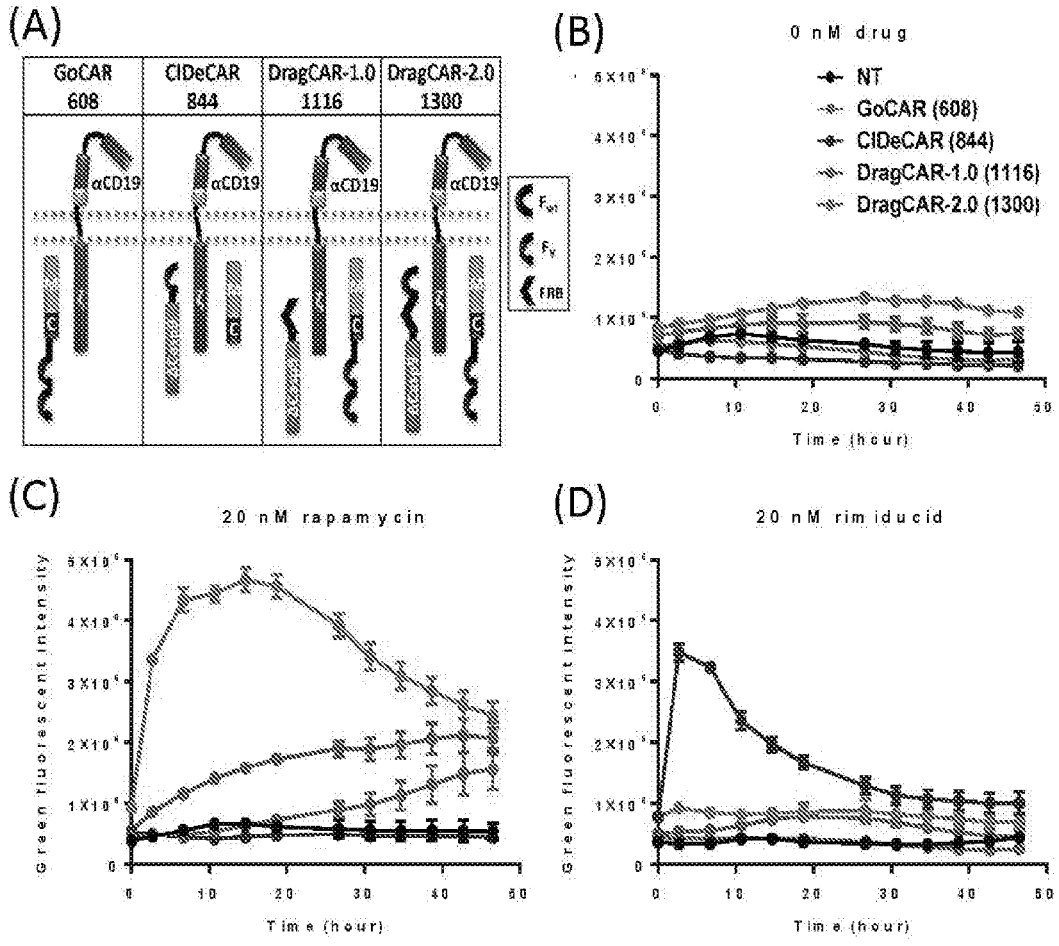


Fig. 48C

Fig. 48D

Fig. 49A

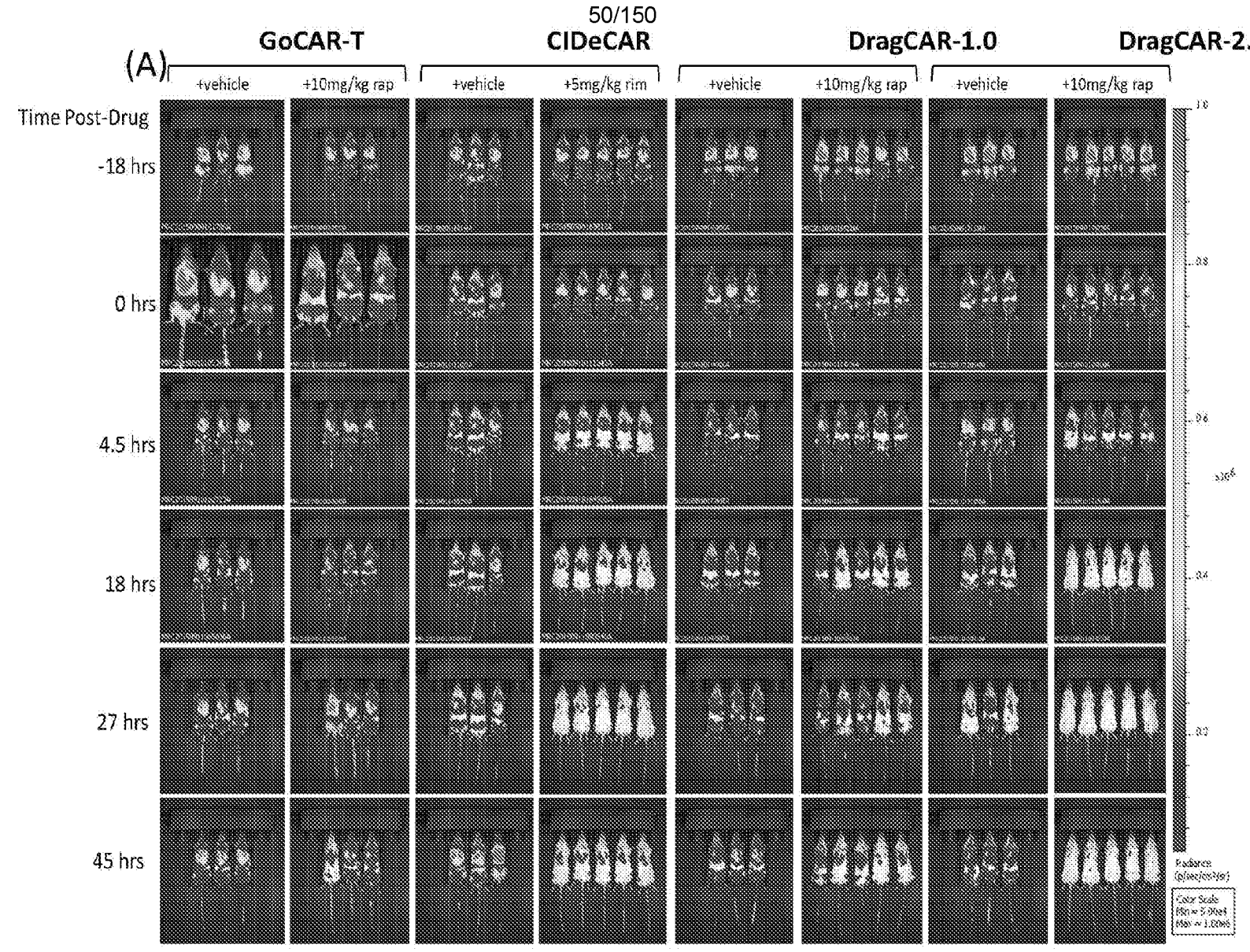

(A)
GoCAR-T
CIDeCAR
DragCAR-1.0
DragCAR-2.
+vehicle
+10mg/kg rap
+vehicle
+5mg/kg rim
+vehicle
+10mg/kg rap
+vehicle
+10mg/kg rap
Time Post-Drug
-18 hrs
0 hrs
4.5 hrs
18 hrs
27 hrs
45 hrs

Fig. 49B

Fig. 49C

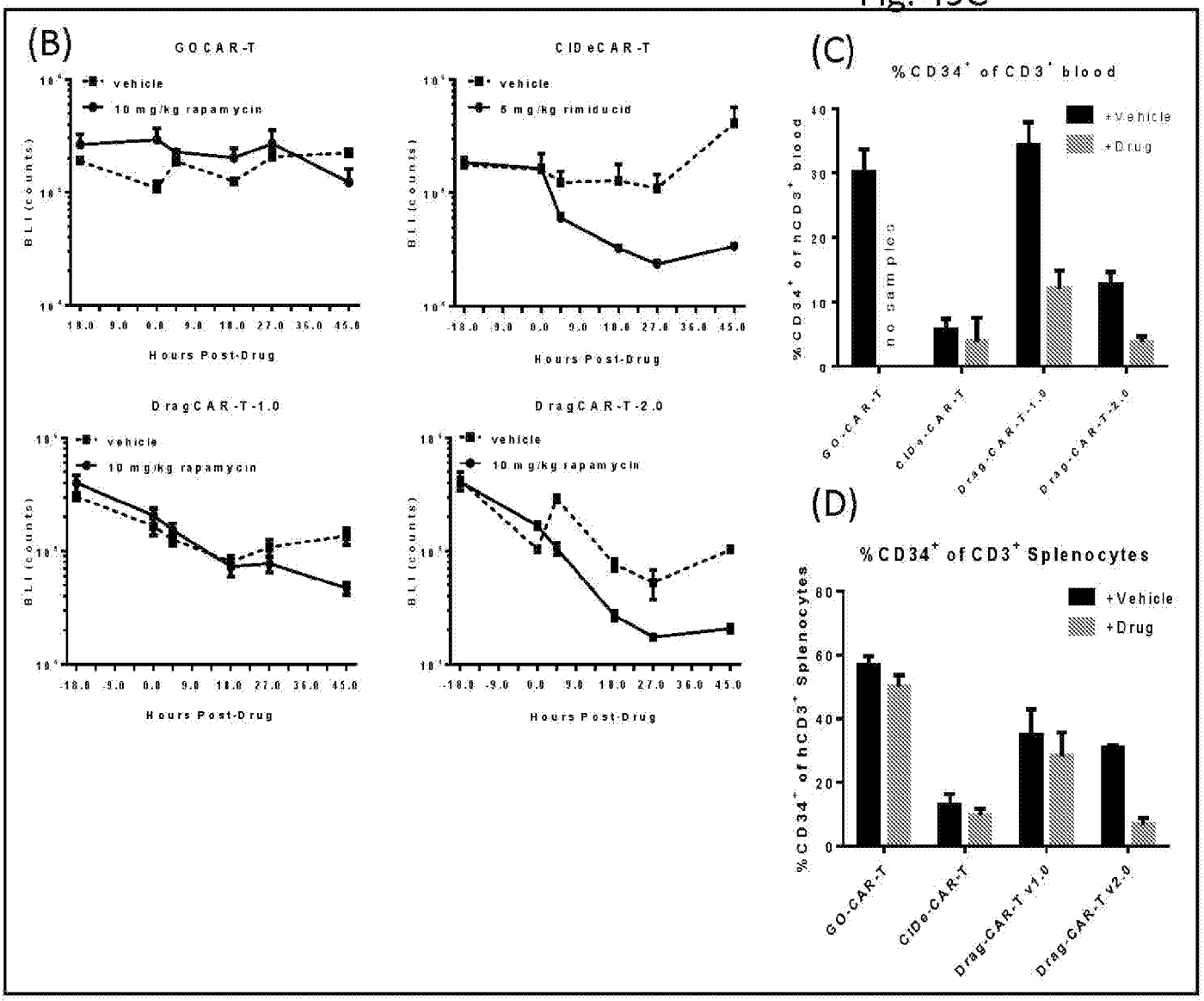


Fig. 49D

Fig. 50A

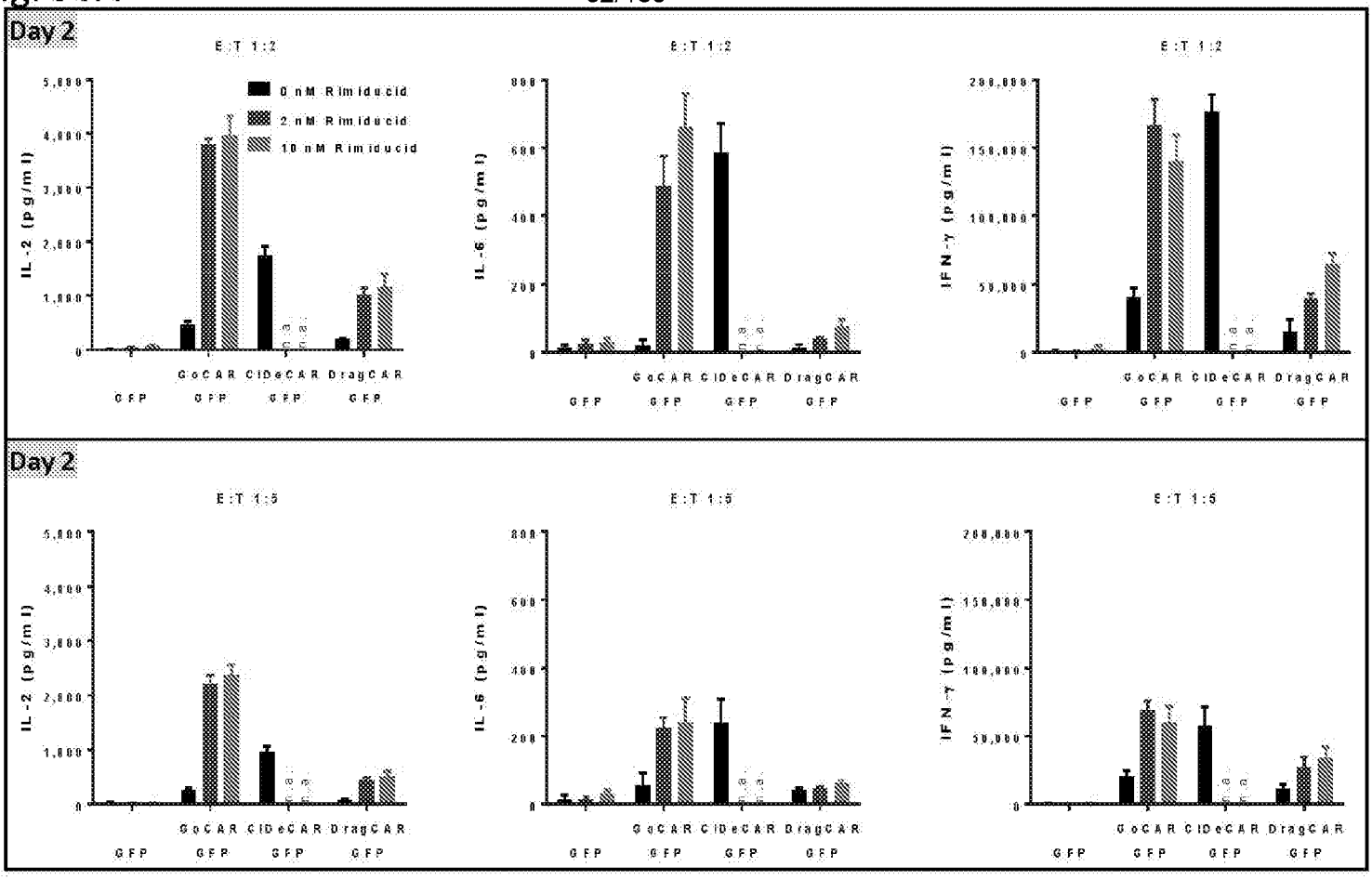


Fig. 50B

Figure 50C

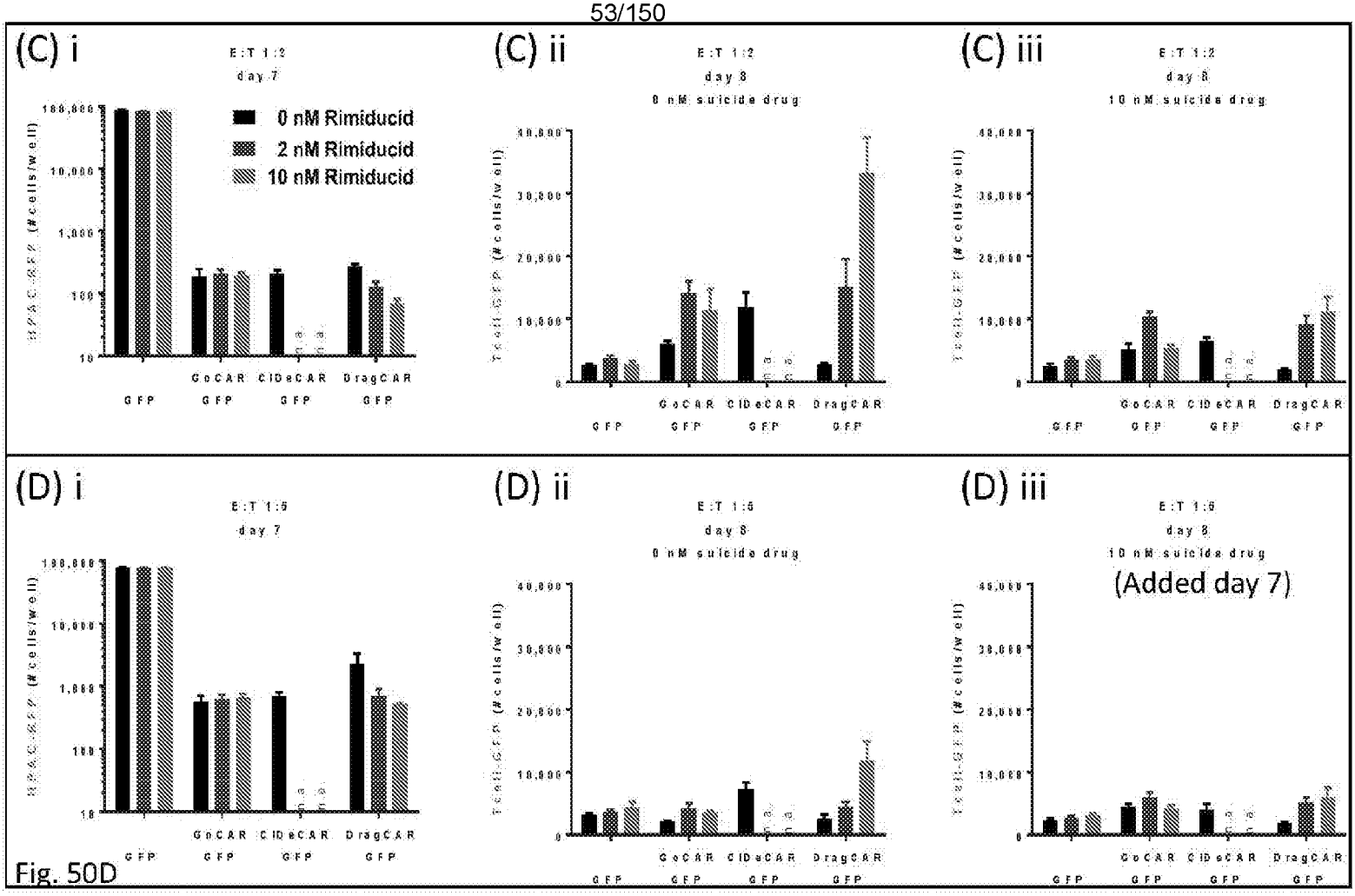


Fig. 50D

Fig. 51A

Fig. 51B

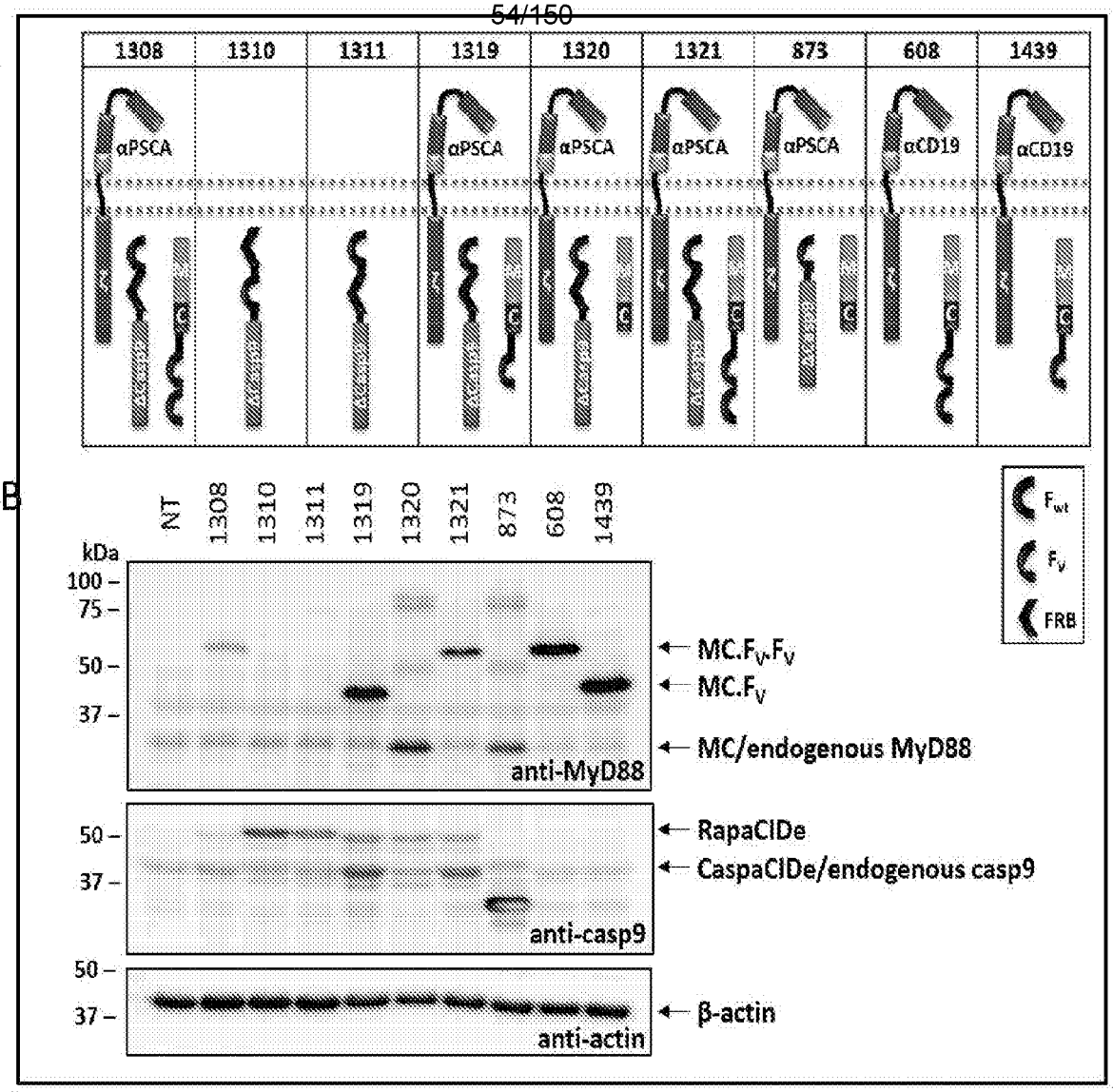


Fig. 51C

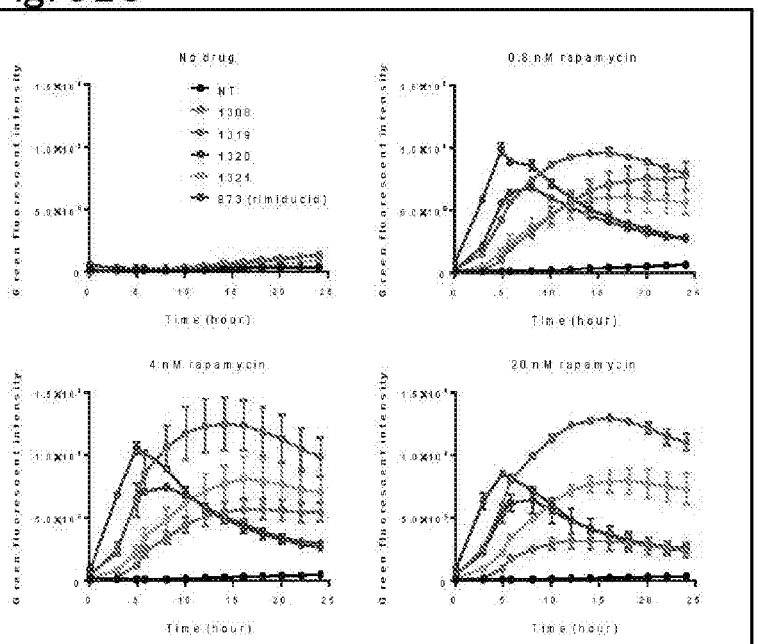
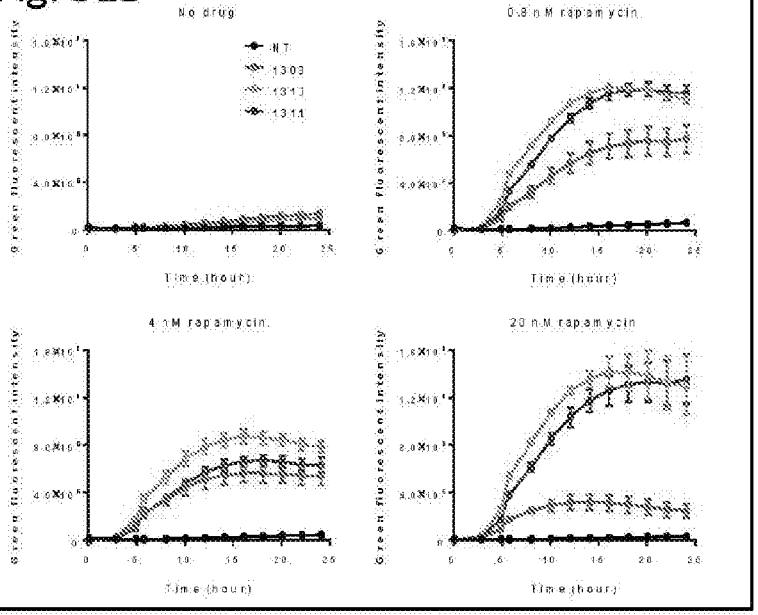


Fig. 51D



(E) Fig. 51E

55/150

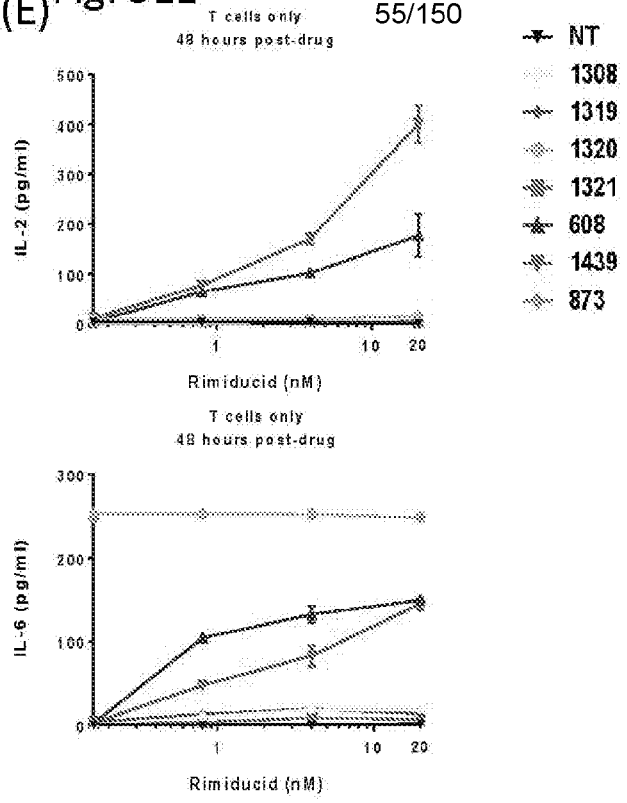


Fig. 52A

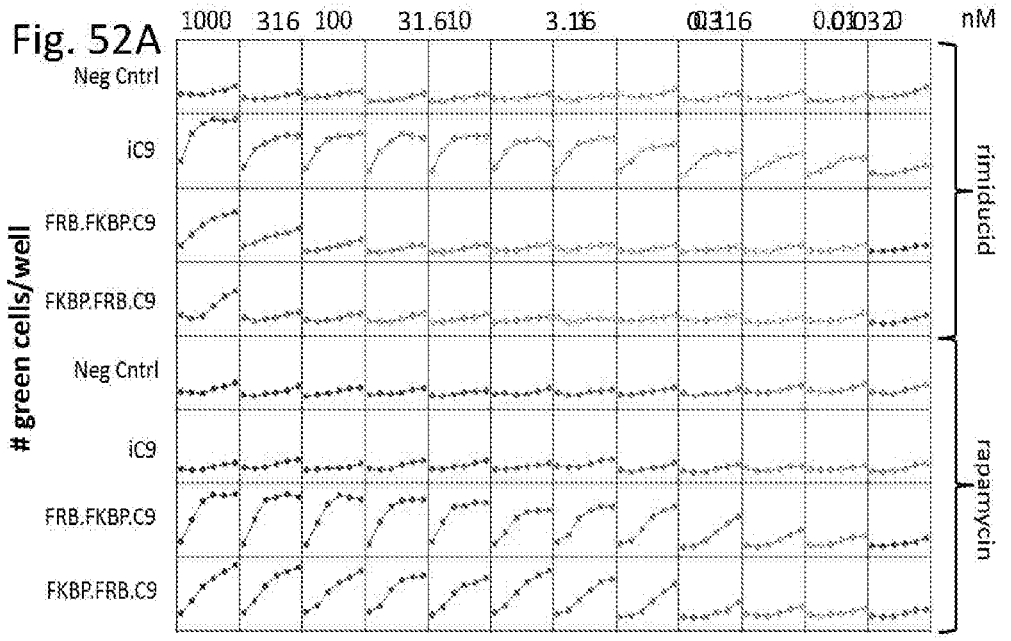


Fig. 52B

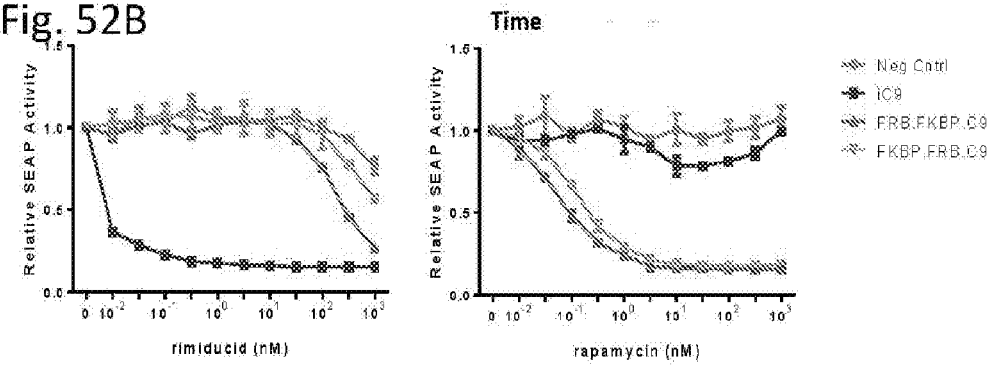


Fig. 53A

Fig. 53B

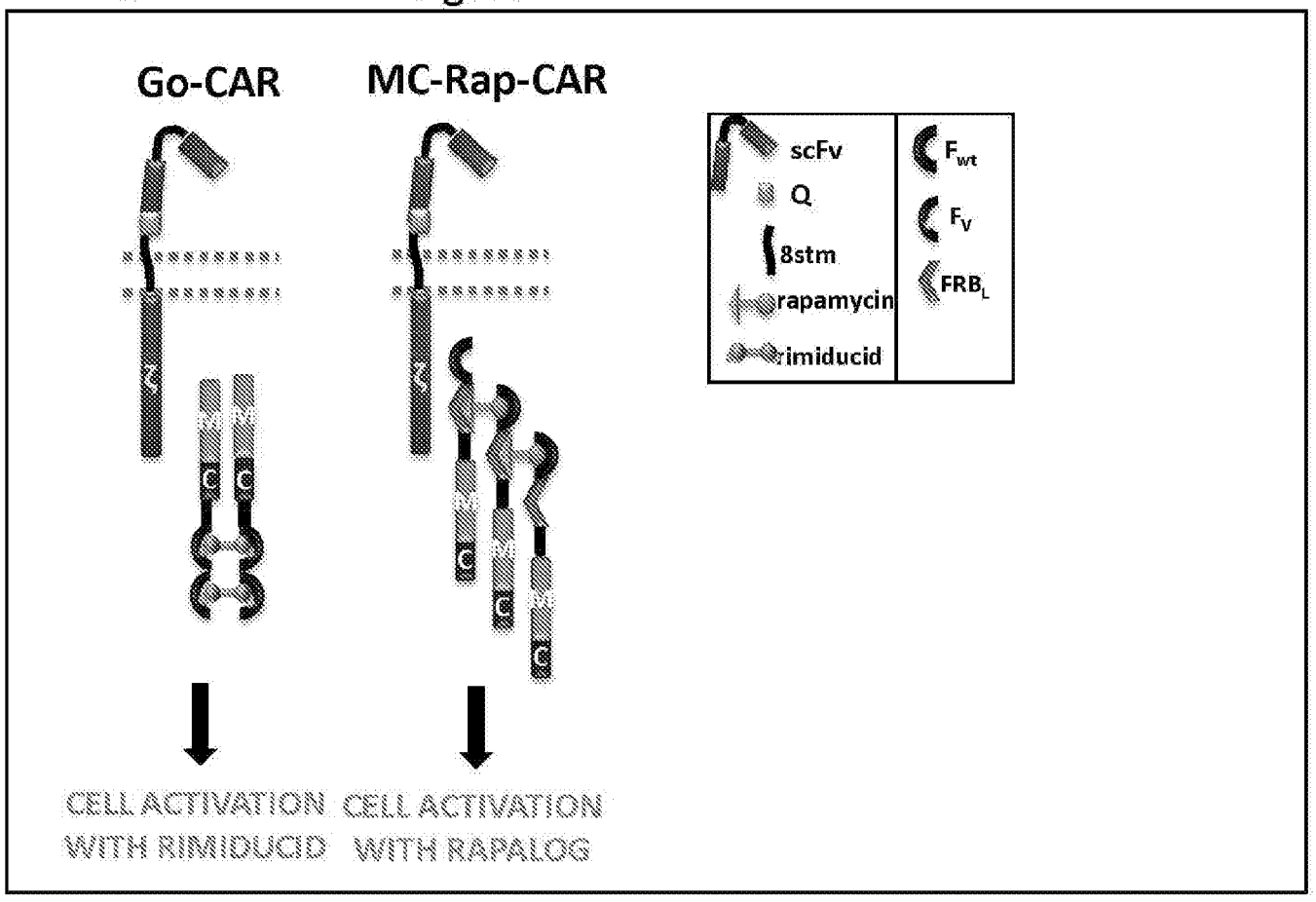


Fig. 54A

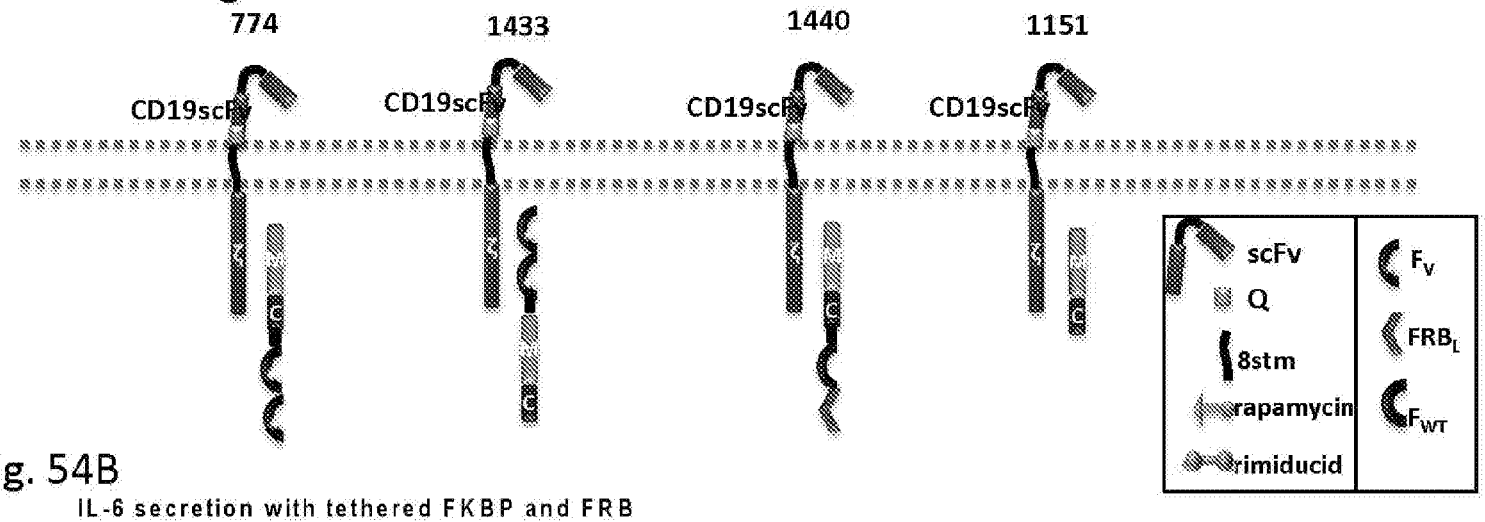


Fig. 54B

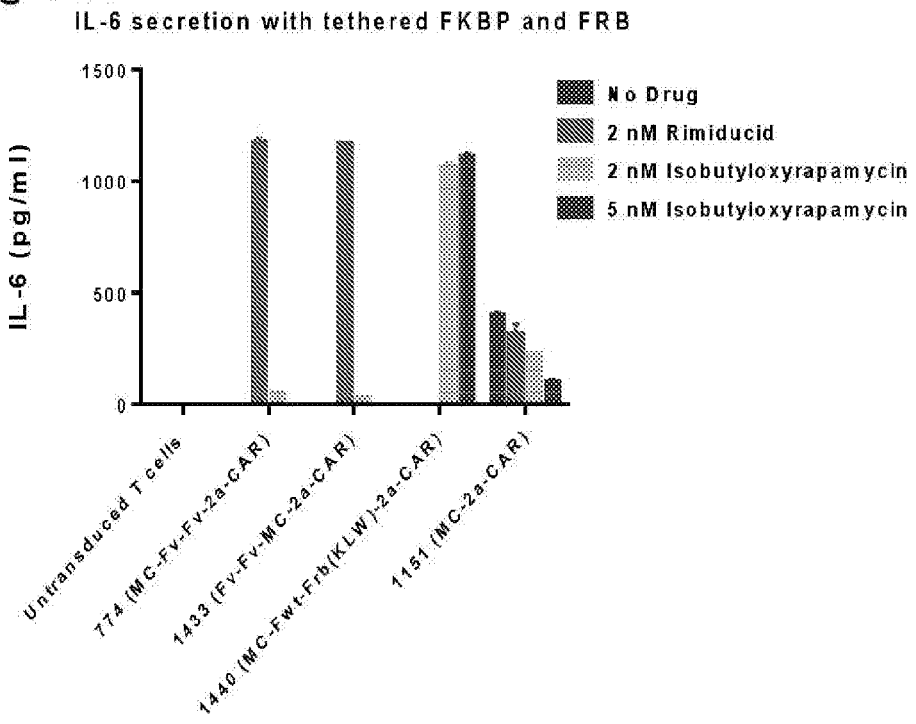
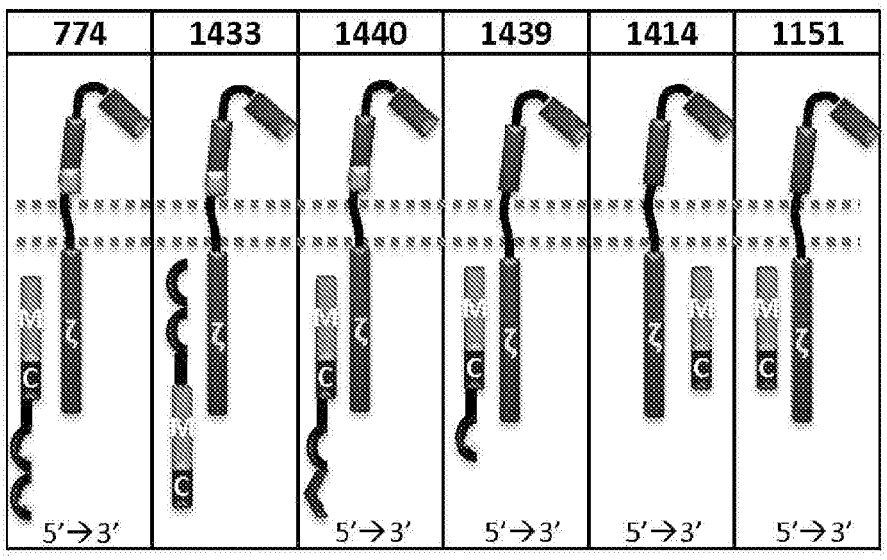
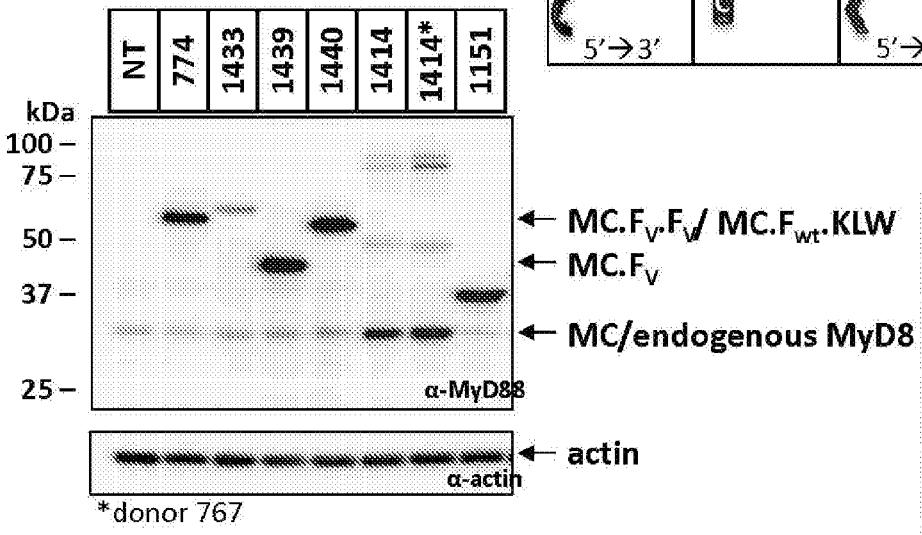


Fig. 55A





Donor	pBP	%CD3$^+$/CD34$^+$	CD34$^+$ MFI	% viability
920	NT	0.67	3.67	95.4
920	774	72.7	26.82	83.9
920	1433	76.01	28.74	73.3
920	1439	84.49	45.7	90.4
920	1440	73.86	23.5	77.8
920	1414	45.04	19.63	93.9
767	1414*	69.37	79.87	75.2
920	1151	71.75	43.08	74.2

Fig. 55B

Fig. 56A

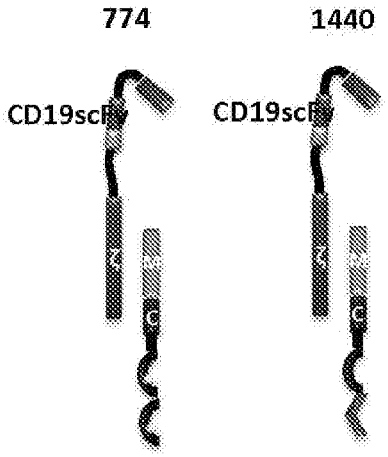
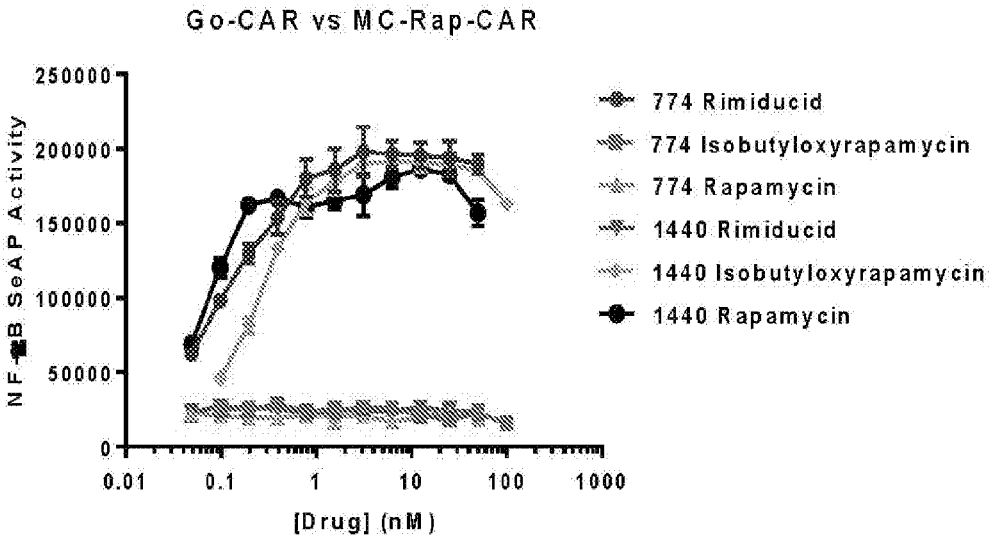


Fig. 56B



774 = MC-Fv-Fv-2A-CAR

1140 = MC-Fwt-FRB_L-2A-CAR

Fig. 57A Fig. 57B

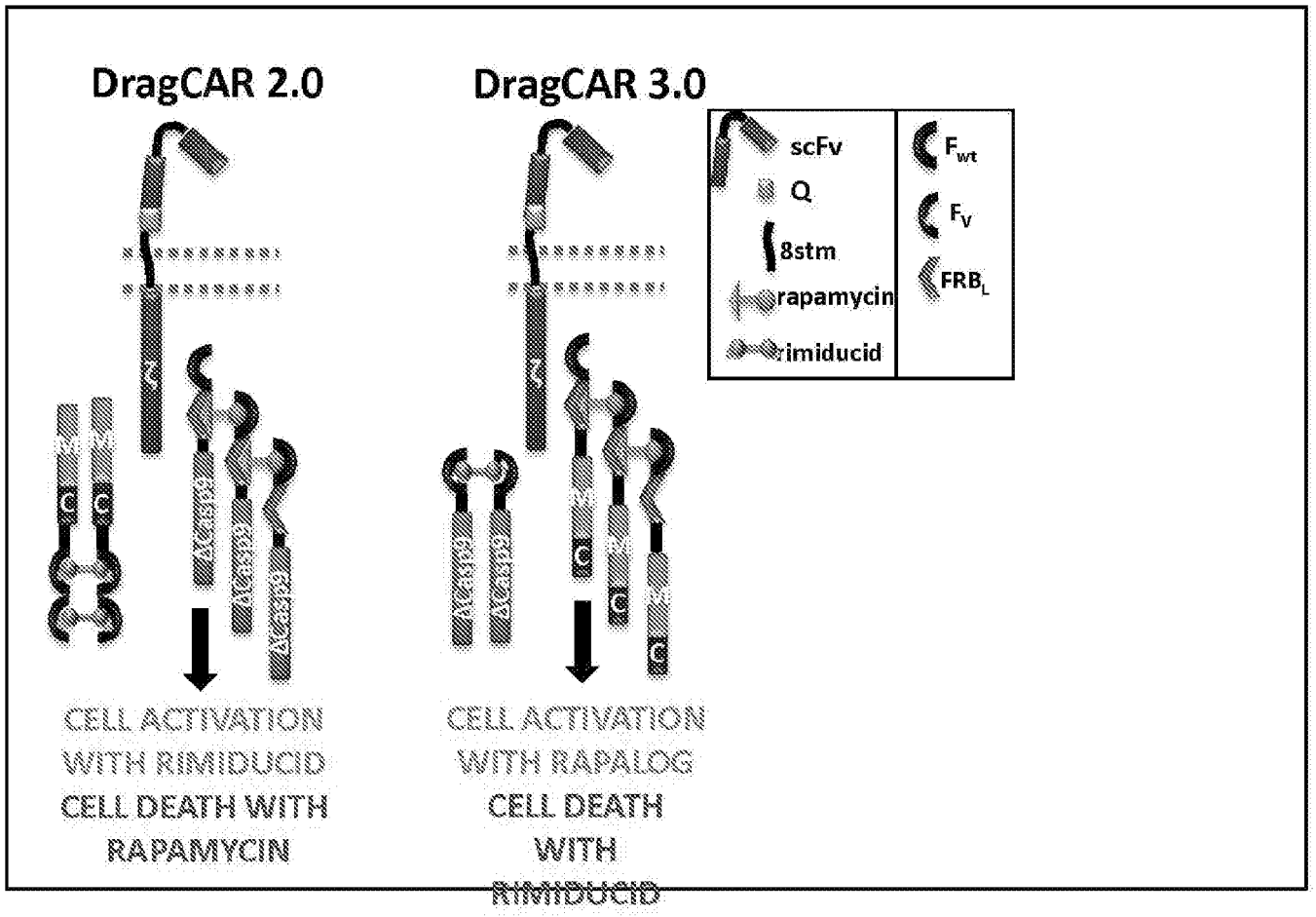
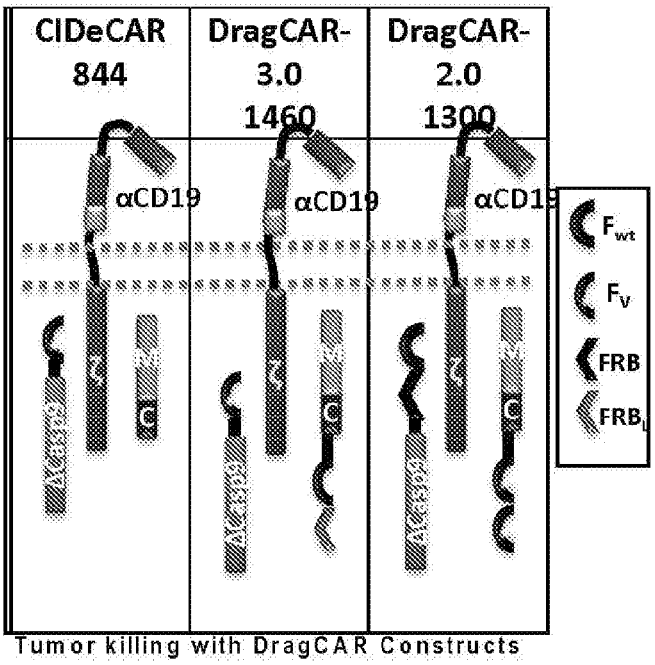


Fig. 58A



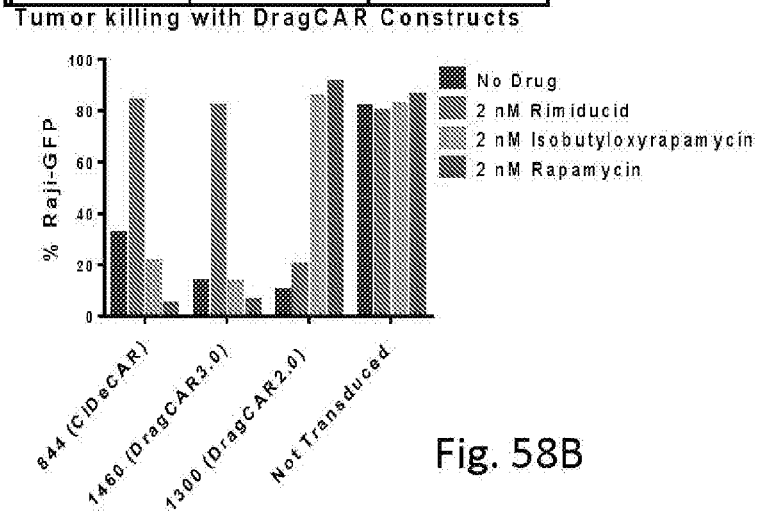


Fig. 58B

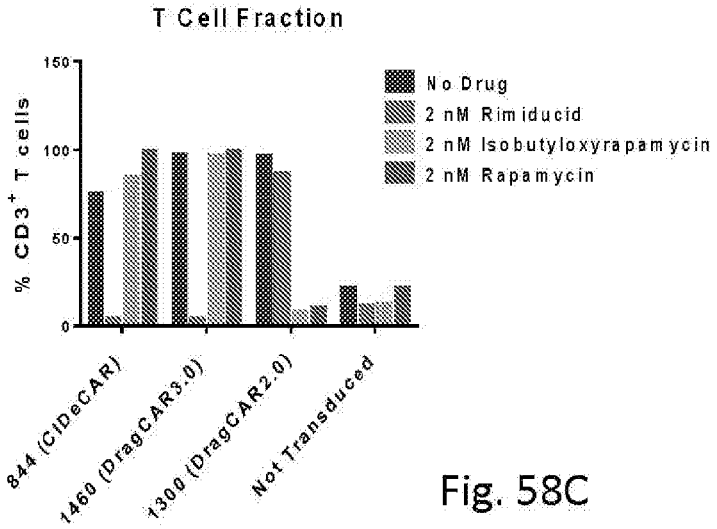
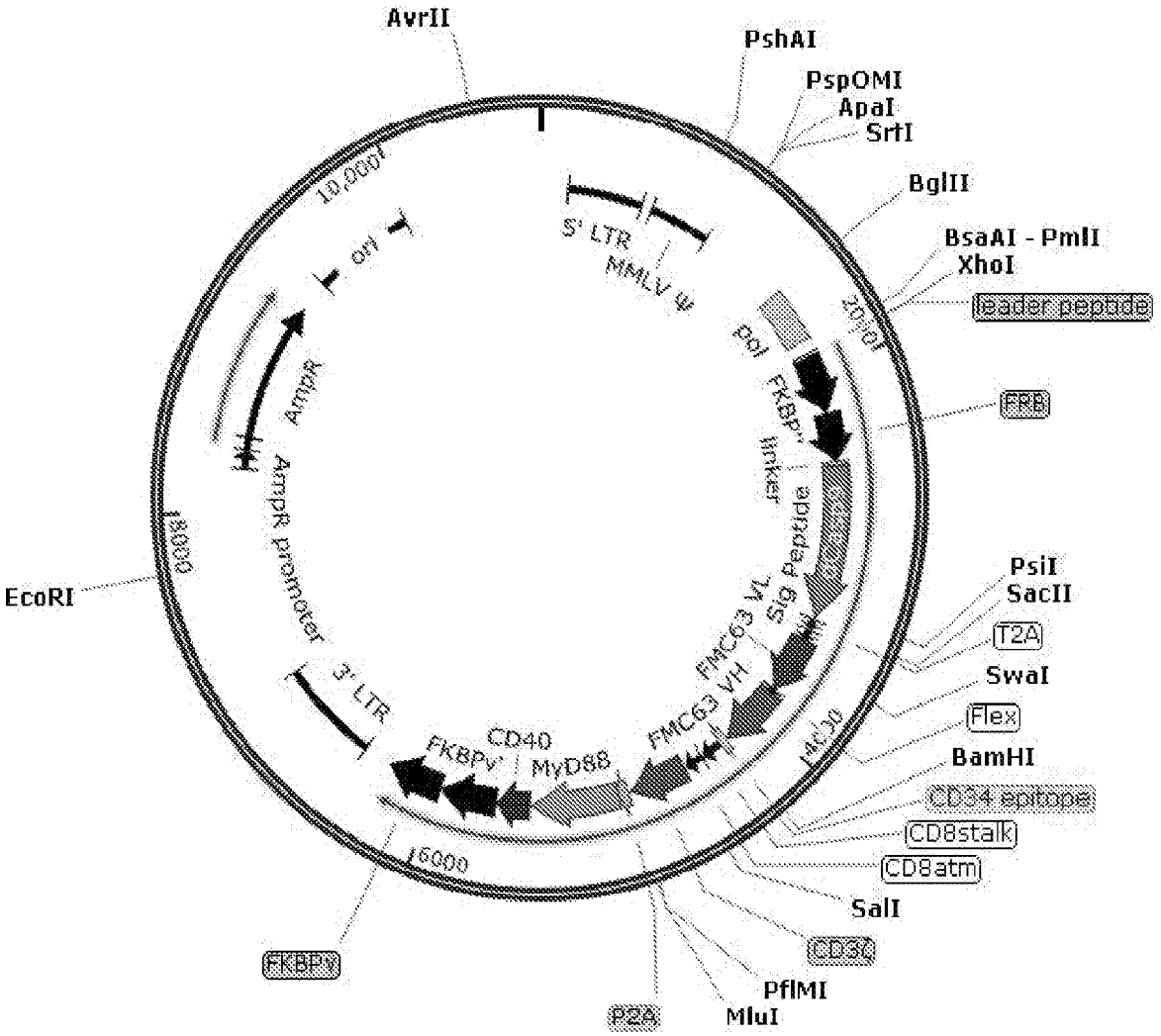
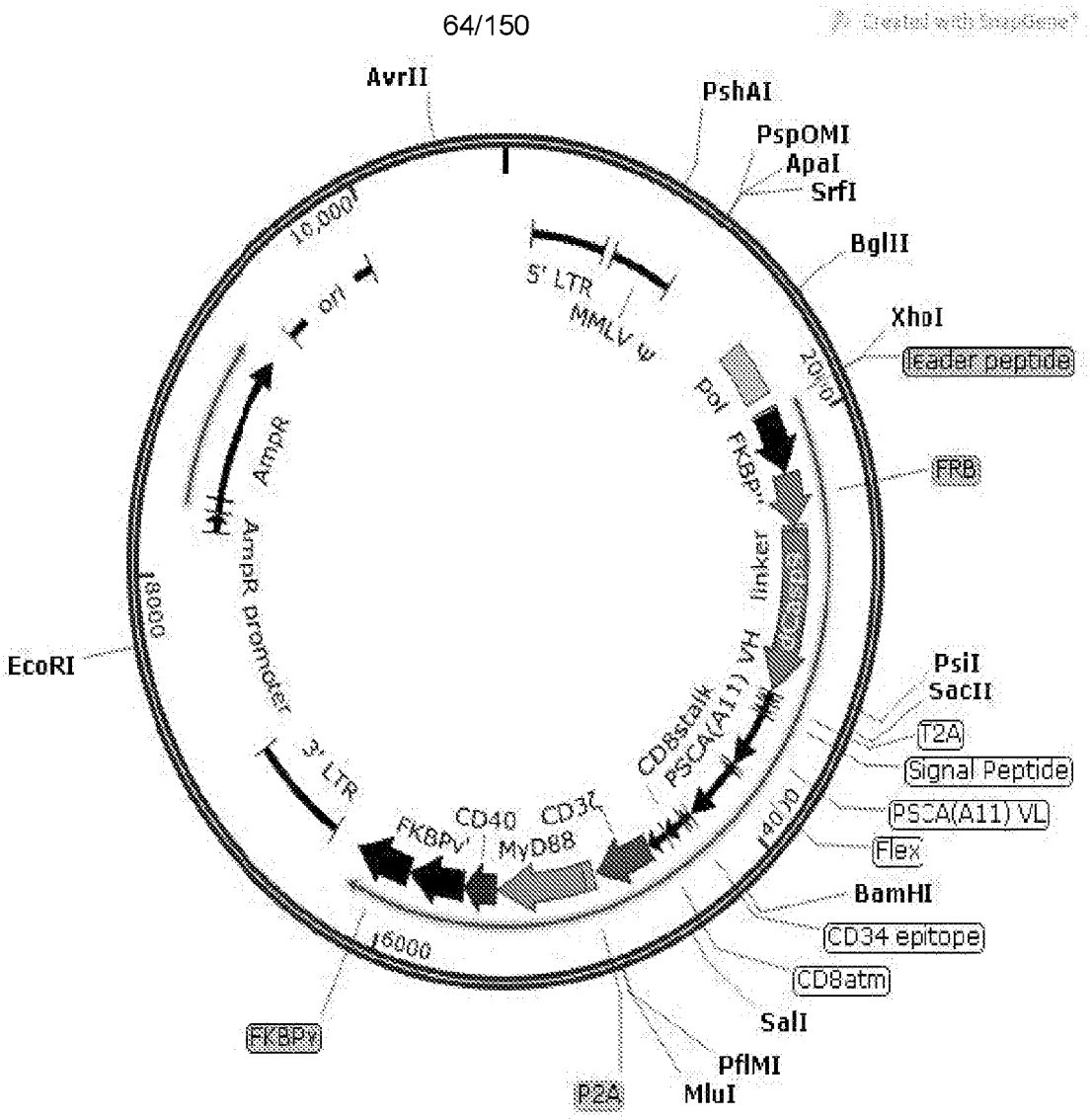


Fig. 58C



pBP1300--pSFG-FKBP.FRB.ΔC9.T2A-αCD19.Q.CD8stm.ζ.P2A-iMC
10,768 bp

Fig. 59



pBP1308--pSFG-FKBP.FRB.ΔC9.T2A-αPSCA.Q.CD8stm.ζ.P2A-iMC
10,741 bp

Fig. 60

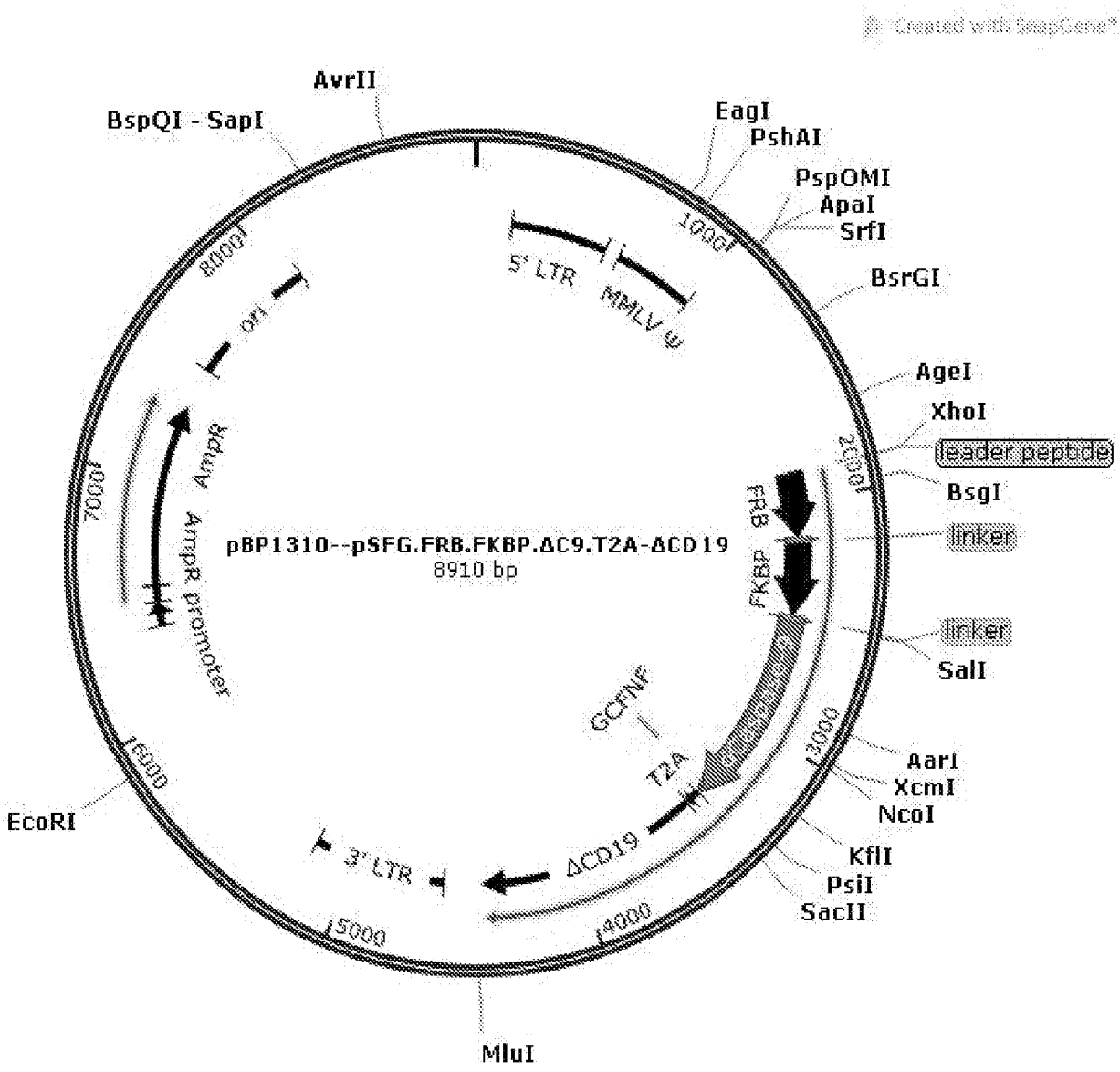
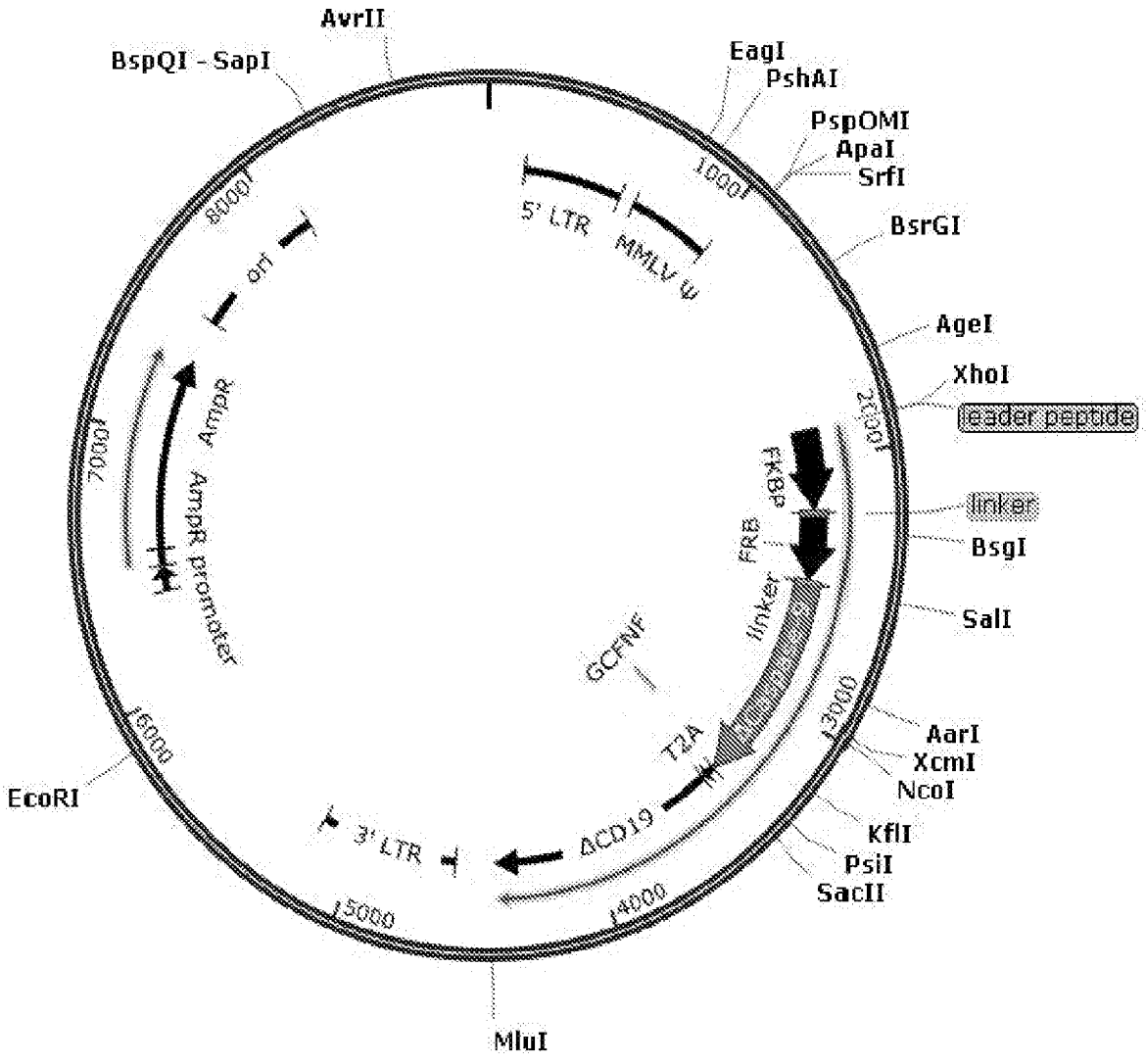
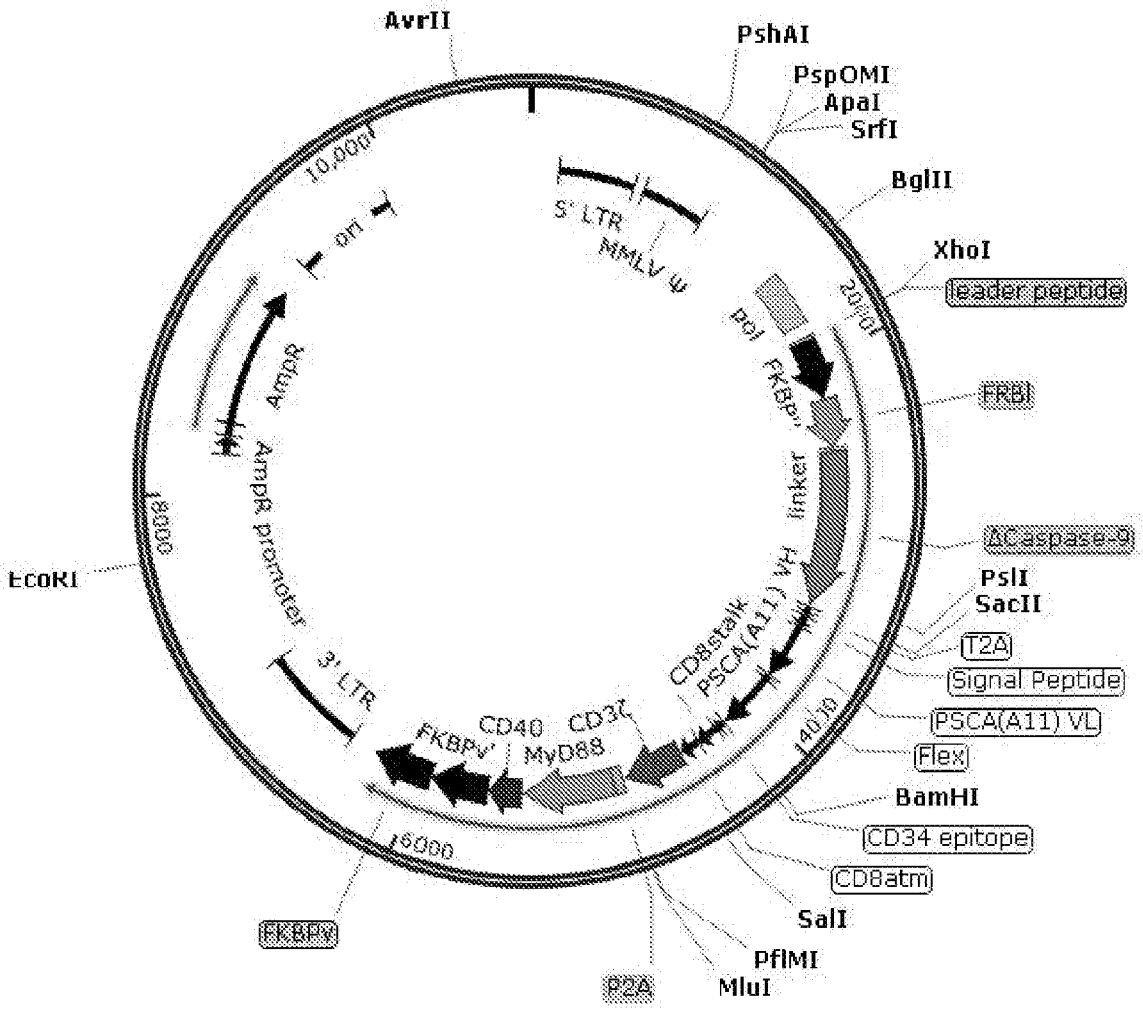

AvrII
BspQI - SapI
EagI
PshAI
PspOMI
ApaI
SrfI
BsrGI
AgeI
XhoI
leader peptide
BsgI
linker
linker
SalI
AarI
XcmI
NcoI
KflI
PsiI
SacII
MluI
EcoRI
5' LTR
MMLV ψ
ori
AmpR
AmpR promoter
pBP1310--pSFG.FRB.FKBP.ΔC9.T2A-ΔCD19
8910 bp
FRB
FKBP
GCFNF
T2A
ΔCD19
3' LTR
1000
2000
3000
4000
5000
6000
7000
8000

Fig. 61



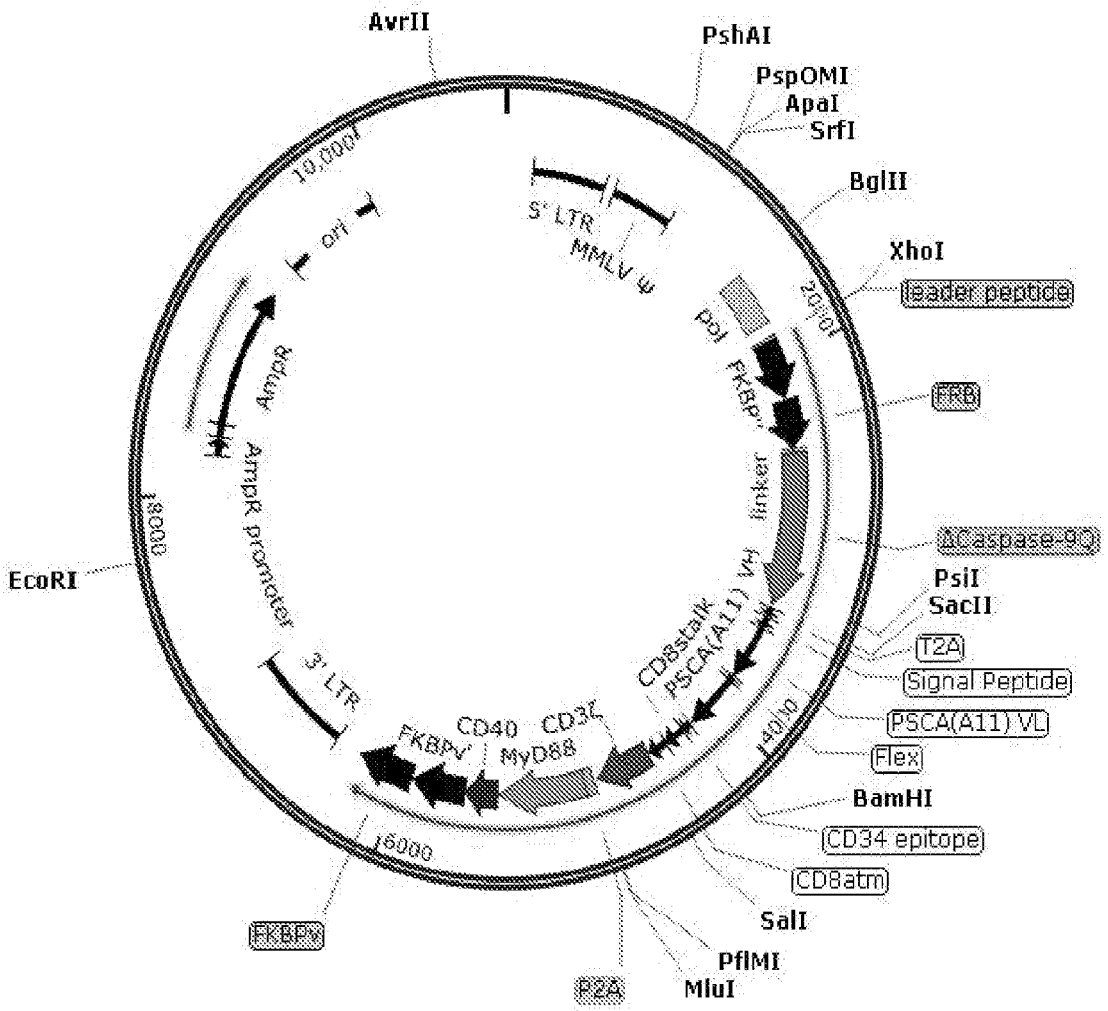
pBP1311--pSFG.FKBP.FRB.ΔC9.T2A-ΔCD19
8910 bp

Fig. 62



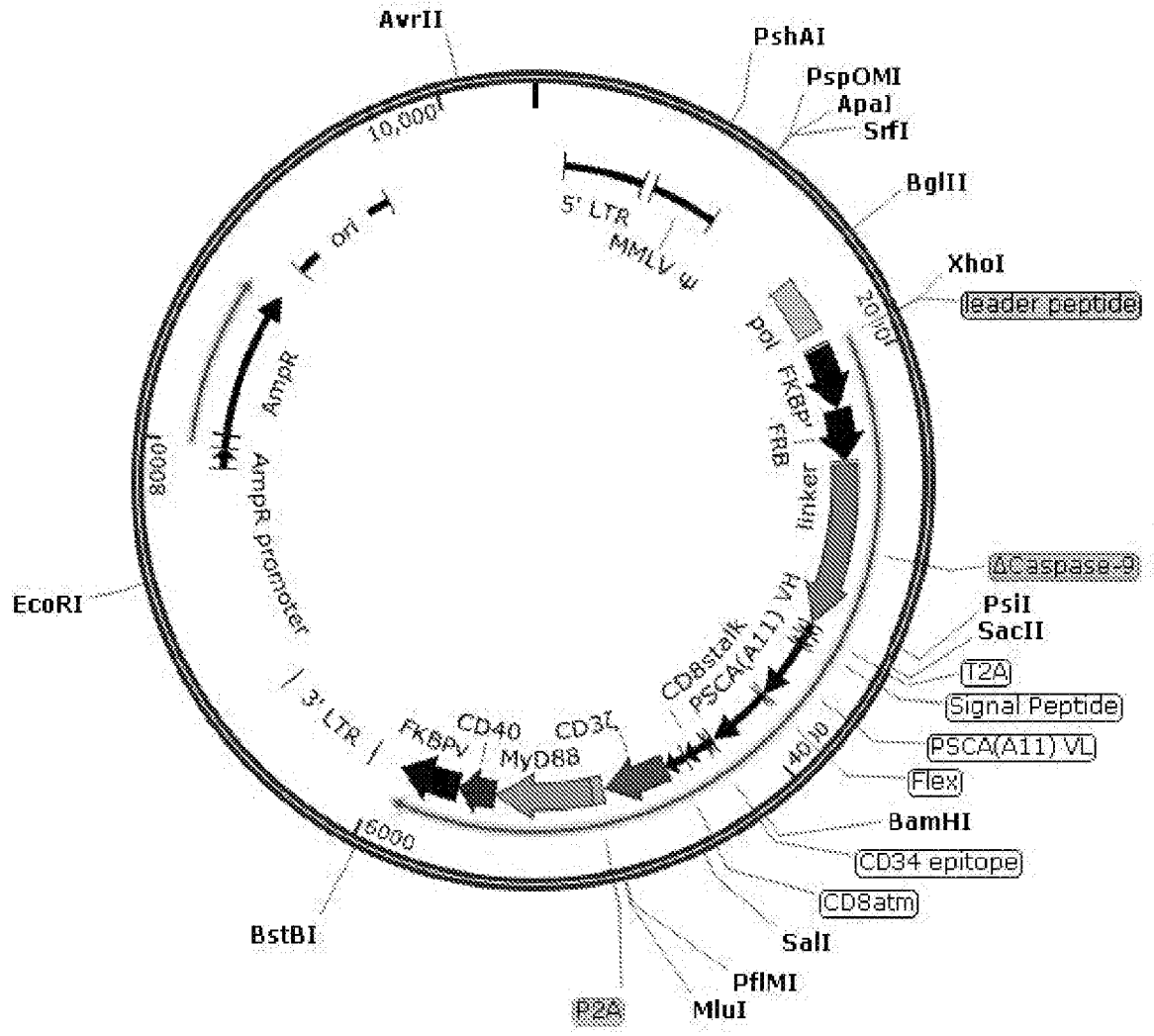
pBP1316--pSFG-FKBP.FRBI.ΔC9.T2A-αPSCA.Q.CD8stm.ζ.P2A-iMC
10,741 bp

Fig. 63



pBP1317--pSFG-FKBP.FRB.ΔC9Q.T2A-αPSCA.Q.CD8stm.ζ.P2A-iMC
10,741 bp

Fig. 64



pBP1319--pSFG-FKBP.FRB.ΔC9.T2A-αPSCA.Q.CD8stm.ζ.P2A-MC.FKBPv
10,414 bp

Fig. 65

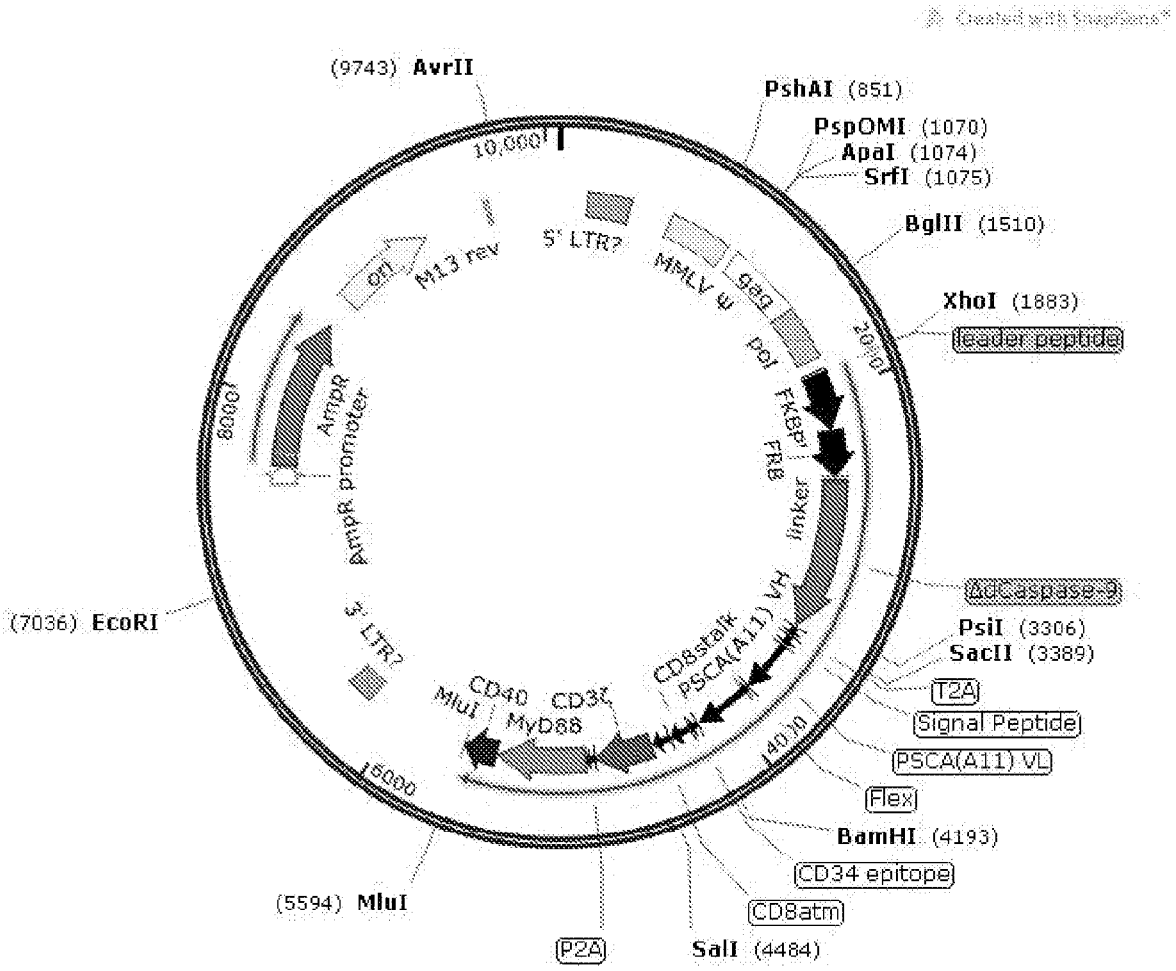
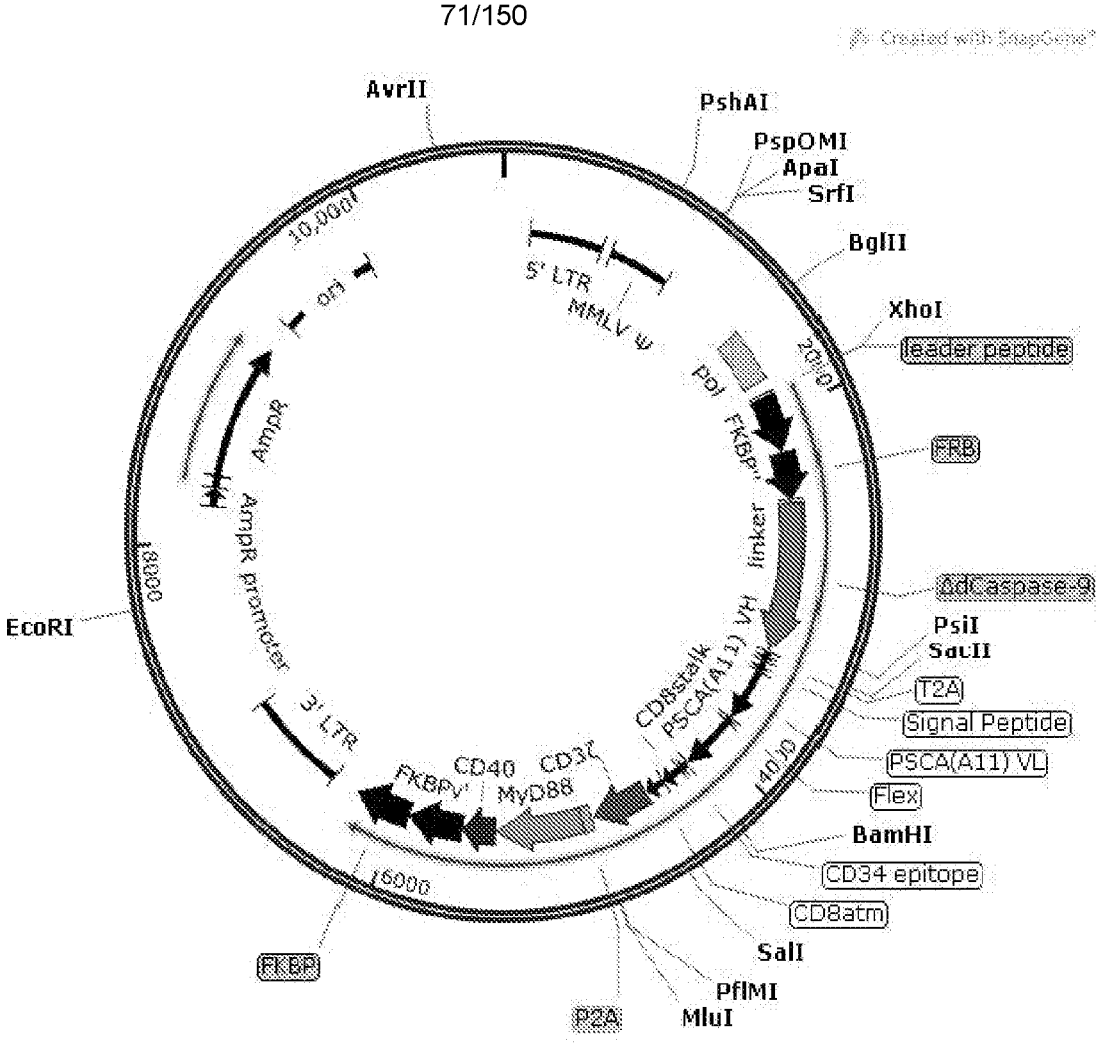

(9743) AvrII
PshAI (851)
PspOMI (1070)
ApaI (1074)
SrfI (1075)
BglII (1510)
XhoI (1883)
leader peptide
ΔdCaspase-9
PsiI (3306)
SacII (3389)
T2A
Signal Peptide
PSCA(A11) VL
Flex
BamHI (4193)
CD34 epitope
CD8atm
SalI (4484)
P2A
(5594) MluI
(7036) EcoRI
10,000
5' LTR?
MMLV ψ
gag
pol
FKBP
FRB
linker
VH
CD8stalk
PSCA(A11)
CD3ζ
CD40
MyD88
MluI
3' LTR?
AmpR promoter
AmpR
ori
M13 rev
5000
15000
20,000
pBP1320--pSFG-FKBP.FRB.ΔC9.T2A-αPSCA.Q.CD8stm.ζ.P2A-MC
10,068 bp

Fig. 66



pBP1321--pSFG-FKBP.FRB.ΔC9.T2A-αPSCA.Q.CD8stm.ζ.P2A-MC.FKBPV.FKBP
10,741 bp

Fig. 67

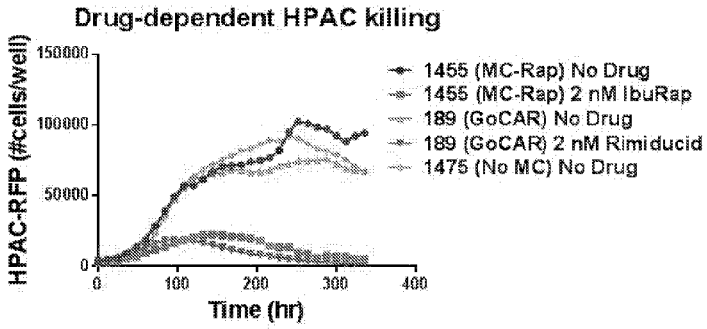


Fig. 68A

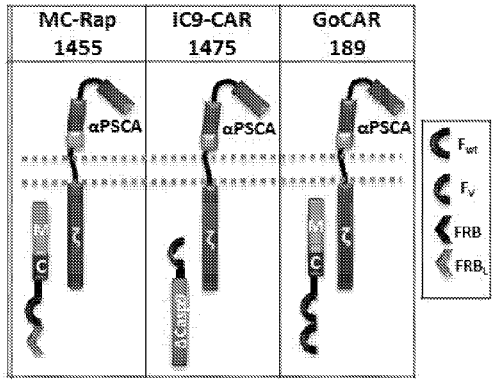


Fig. 68B

Fig. 69 **A**

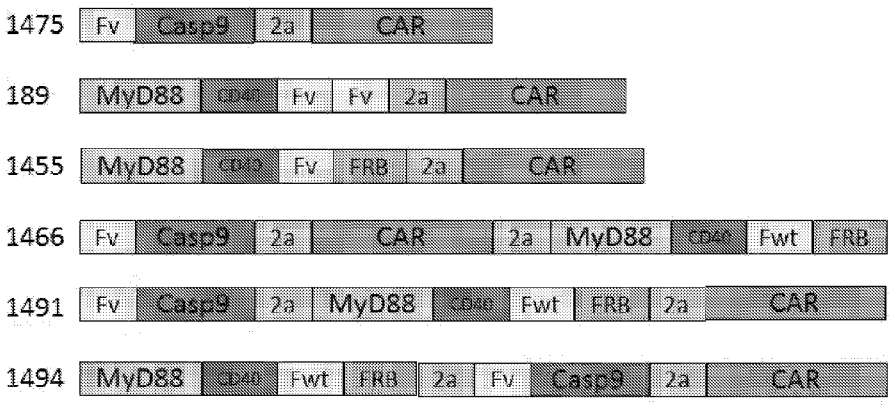


Fig. 69 **B**

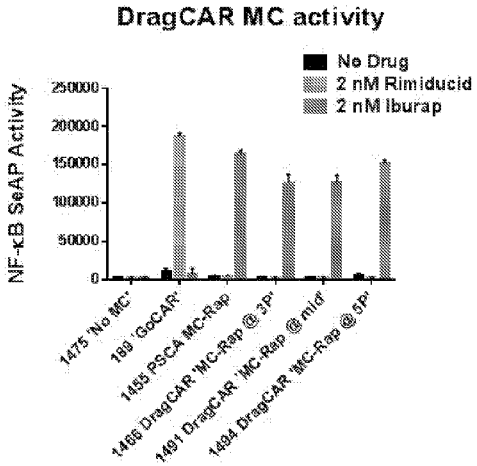


Fig. 69 C

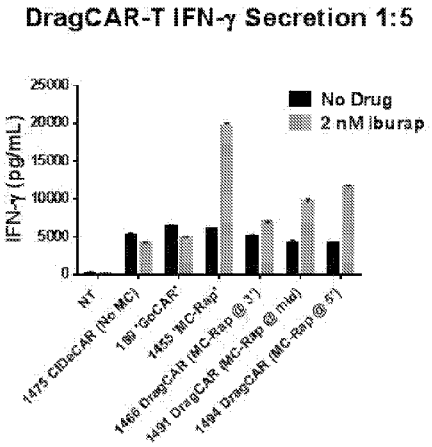


Fig. 69 D

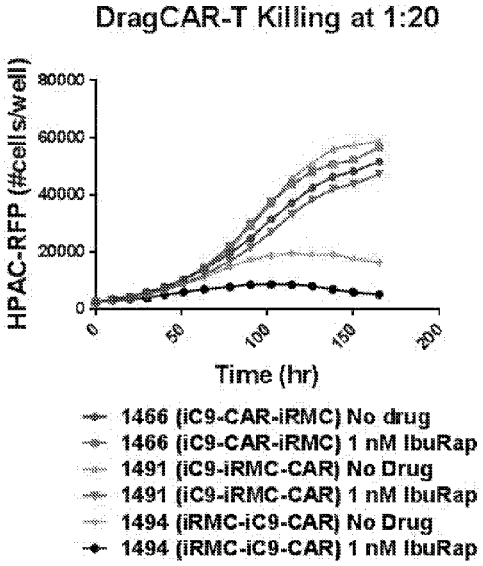


Fig. 70 **A**

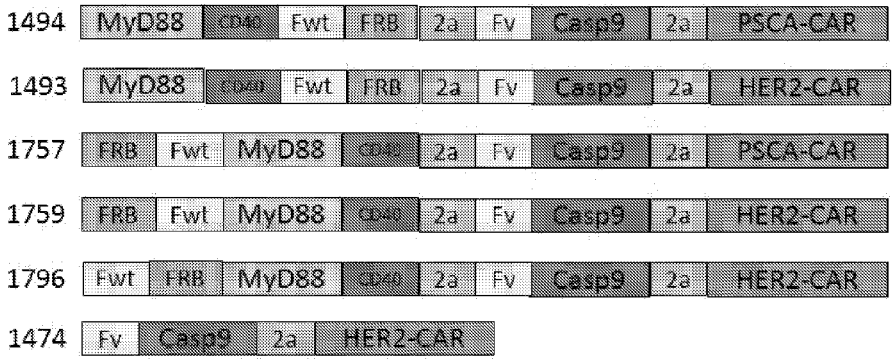


Fig. 70 **B**

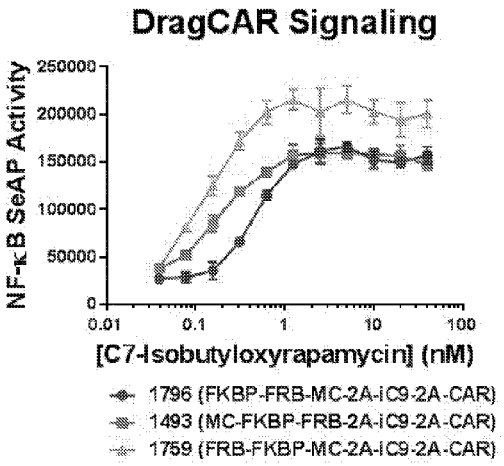


Fig. 70 C

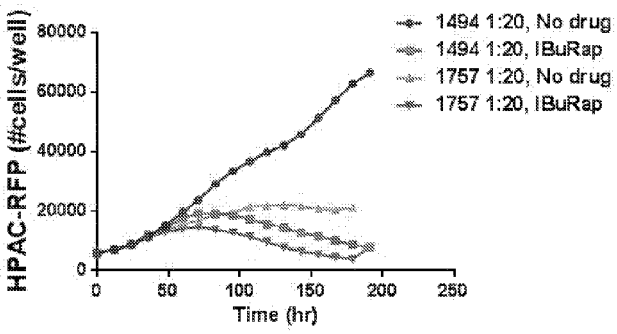


Fig. 70 D

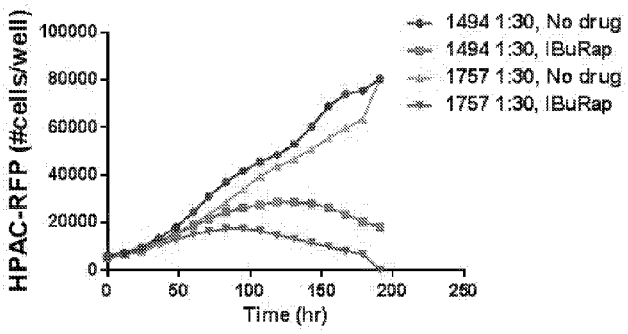


Fig. 70E

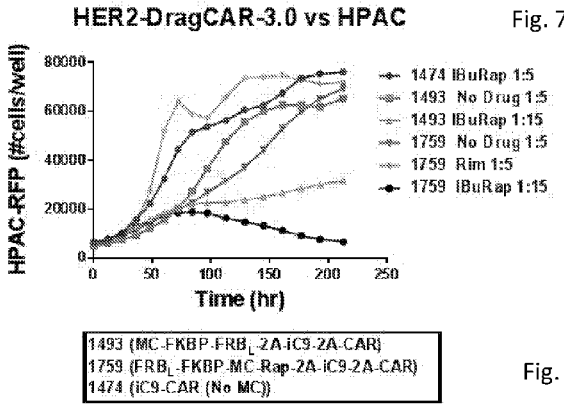


Fig. 70 F

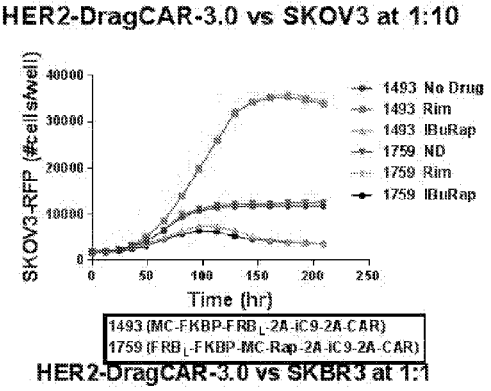


Fig. 70 G

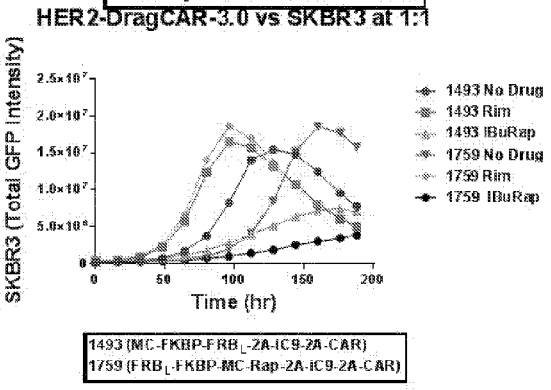


Fig. 71 A

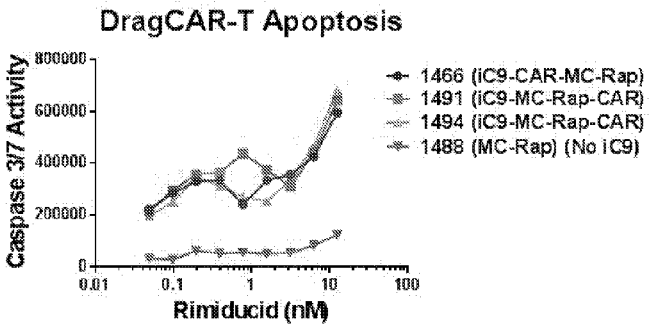


Fig. 71 B

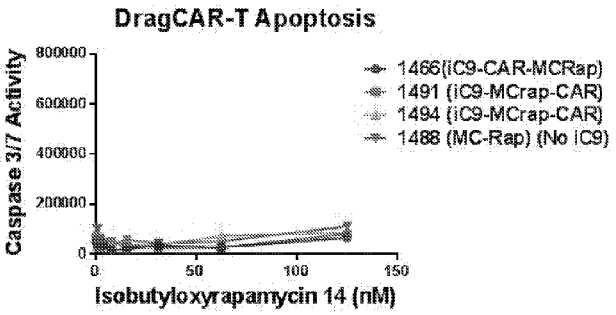
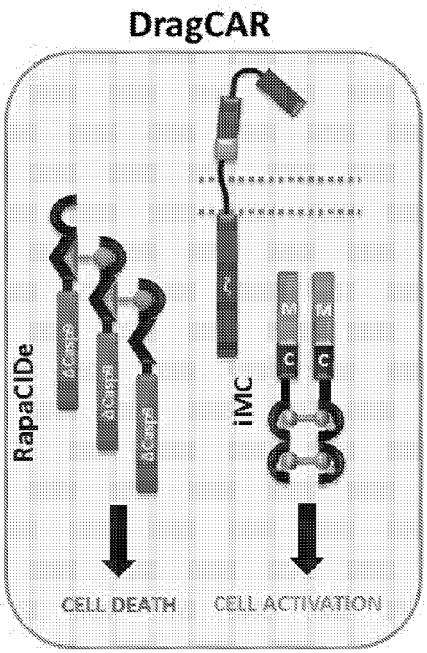
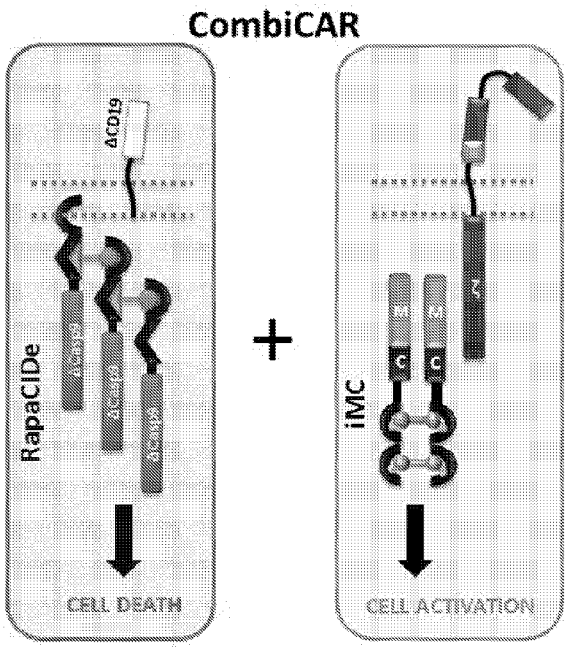


Fig. 72A



SFG-FKBP.FRB.C9.2A-scFv.Q.ζ.2A-iMC

Fig. 72B



SFG-FKBP.FRB.C9.2A-ΔCD19
RapaCIDe

SFG-iMC.2A-scFv.Q.ζ
GoCAR

Fig. 73 A

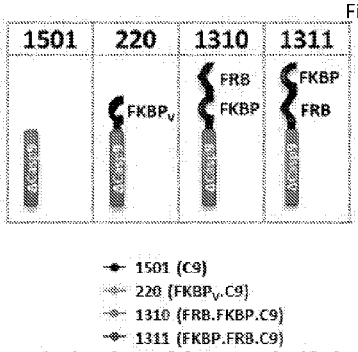
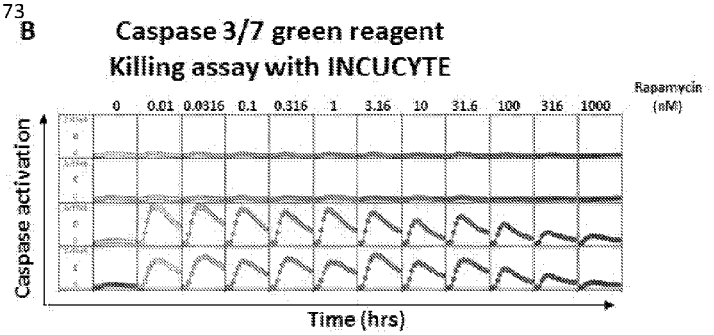


Fig. 73 B



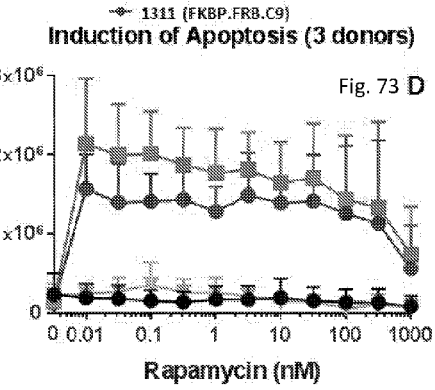


Fig. 73 C

Fig. 73 D

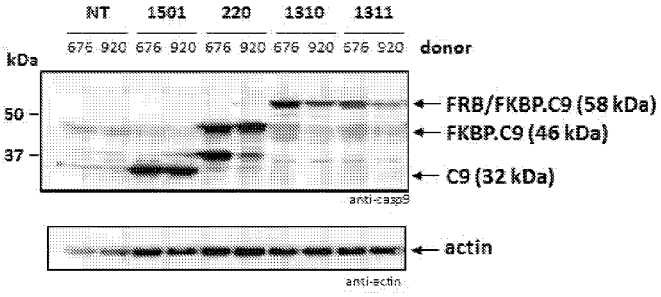


Fig. 74 A

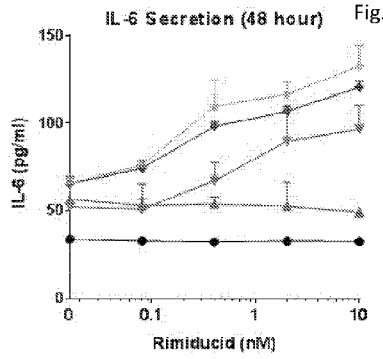


Fig. 74 B

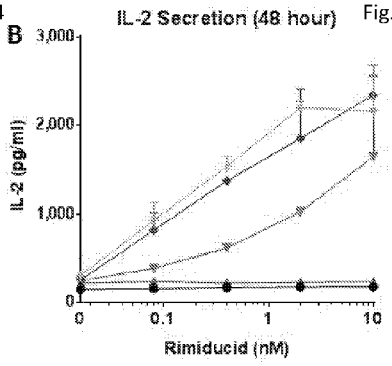


Fig. 74 C

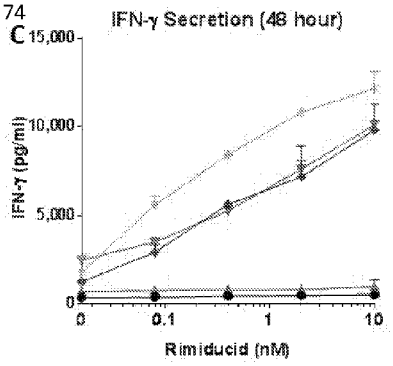


Fig. 74 D Killing of HPAC Tumor Cells at Day 8 of Coculture

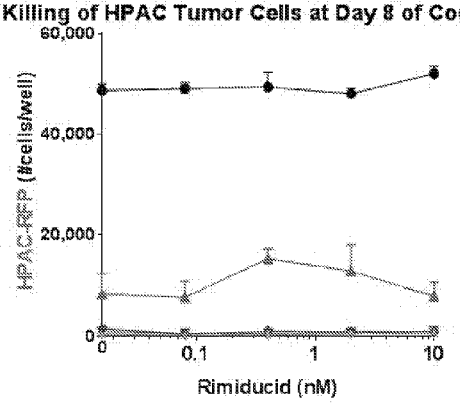


Fig. 74 E

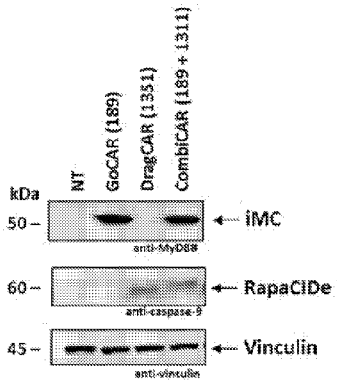


Fig. 75 A

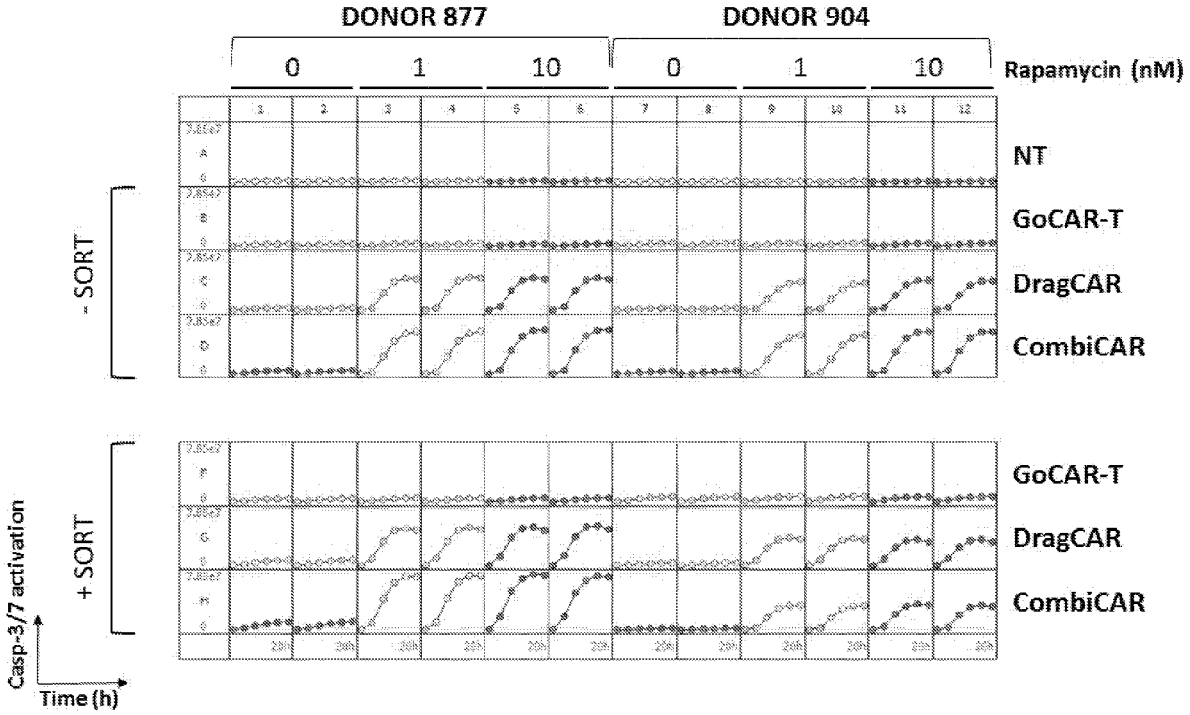

DONOR 877
DONOR 904
0
1
10
0
1
10
Rapamycin (nM)
NT
GoCAR-T
DragCAR
CombiCAR
- SORT
+ SORT
GoCAR-T
DragCAR
CombiCAR
Casp-3/7 activation
Time (h)

Fig. 75 B

Apoptosis determined by Incucyte after 12 hours drug treatment

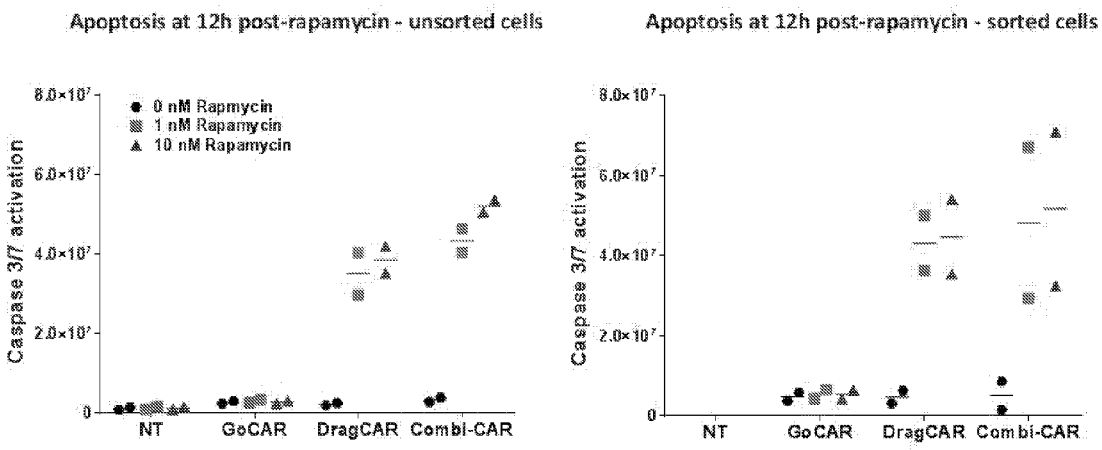


Fig. 75 C

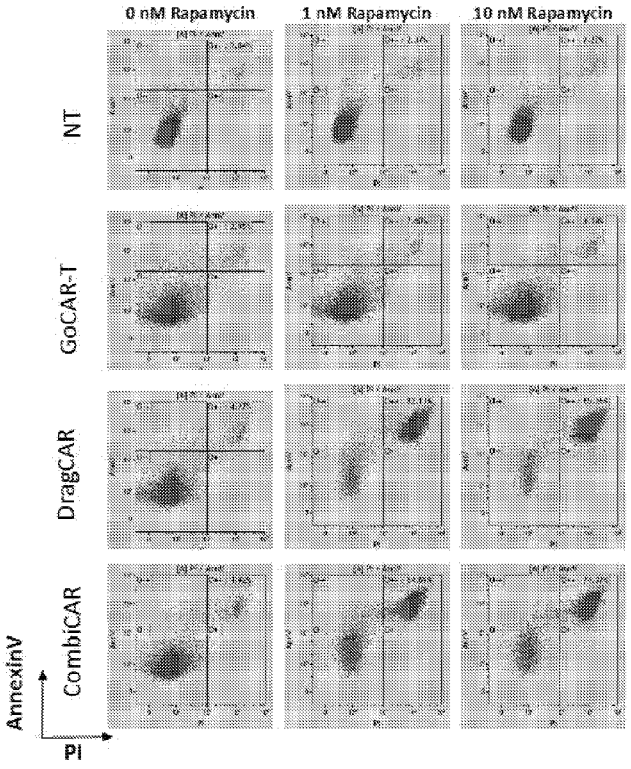

0 nM Rapamycin
1 nM Rapamycin
10 nM Rapamycin
NT
GoCAR-T
DragCAR
CombiCAR
AnnexinV
PI

Fig. 75 D

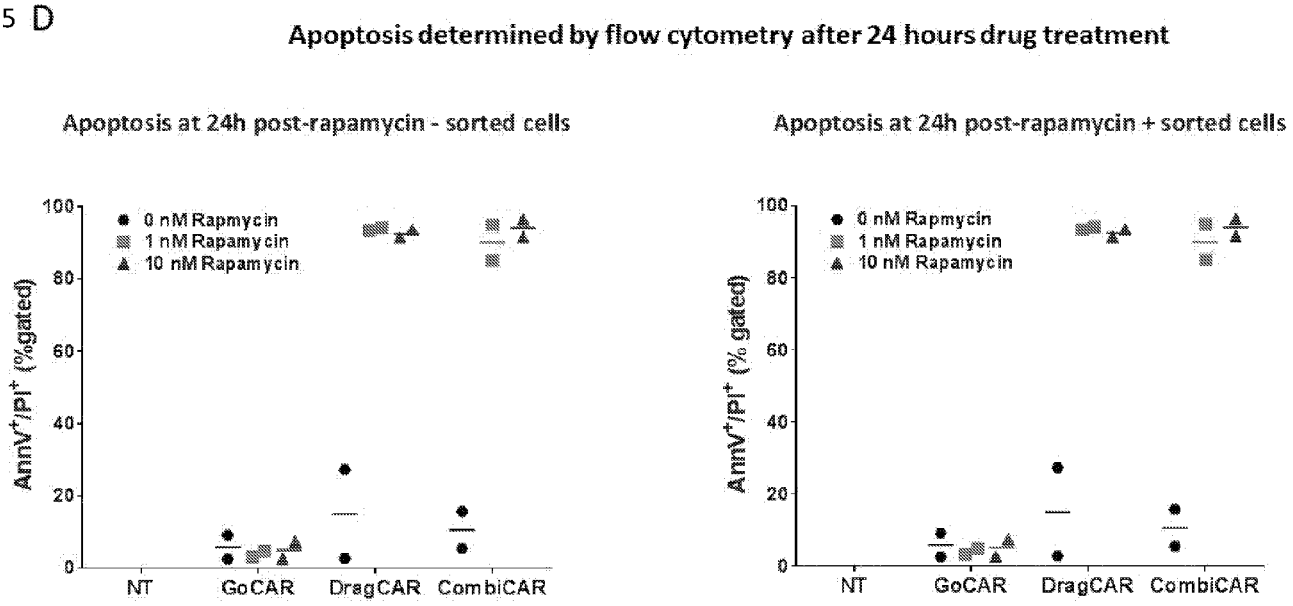

Apoptosis determined by flow cytometry after 24 hours drug treatment
Apoptosis at 24h post-rapamycin - sorted cells
Apoptosis at 24h post-rapamycin + sorted cells
0 nM Rapmycin
1 nM Rapamycin
10 nM Rapamycin
AnnV+/PI+ (%gated)
AnnV+/PI+ (% gated)
100
80
60
40
20
0
NT
GoCAR
DragCAR
CombiCAR

Fig. 76 A

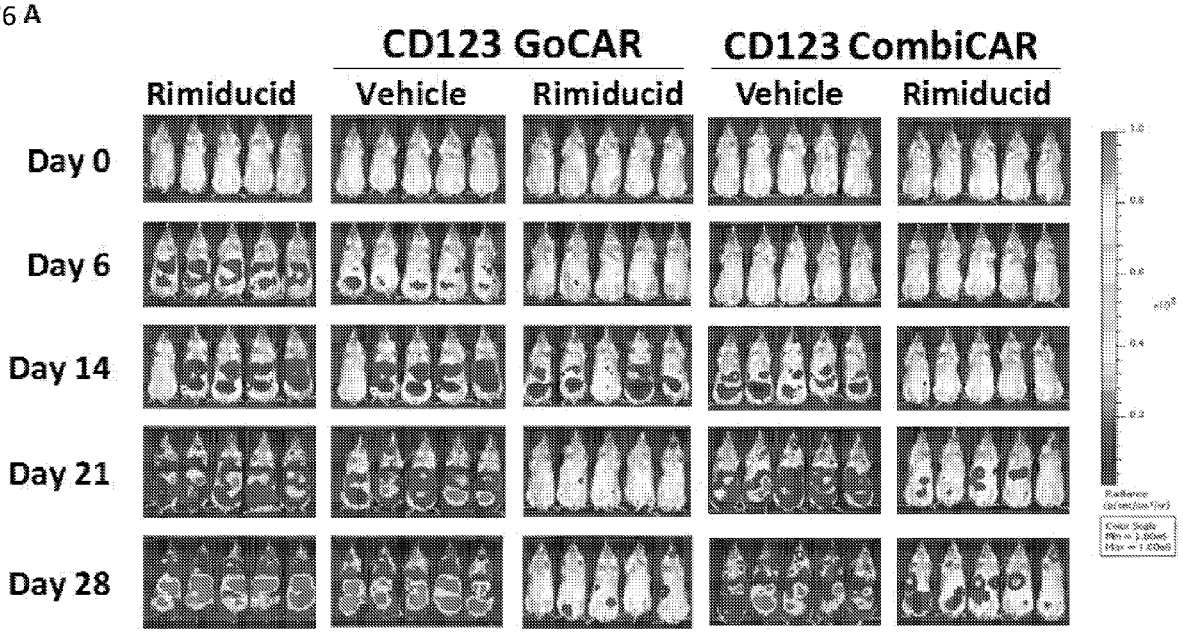

CD123 GoCAR
CD123 CombiCAR
Rimiducid
Vehicle
Rimiducid
Vehicle
Rimiducid
Day 0
Day 6
Day 14
Day 21
Day 28

Fig. 76 B

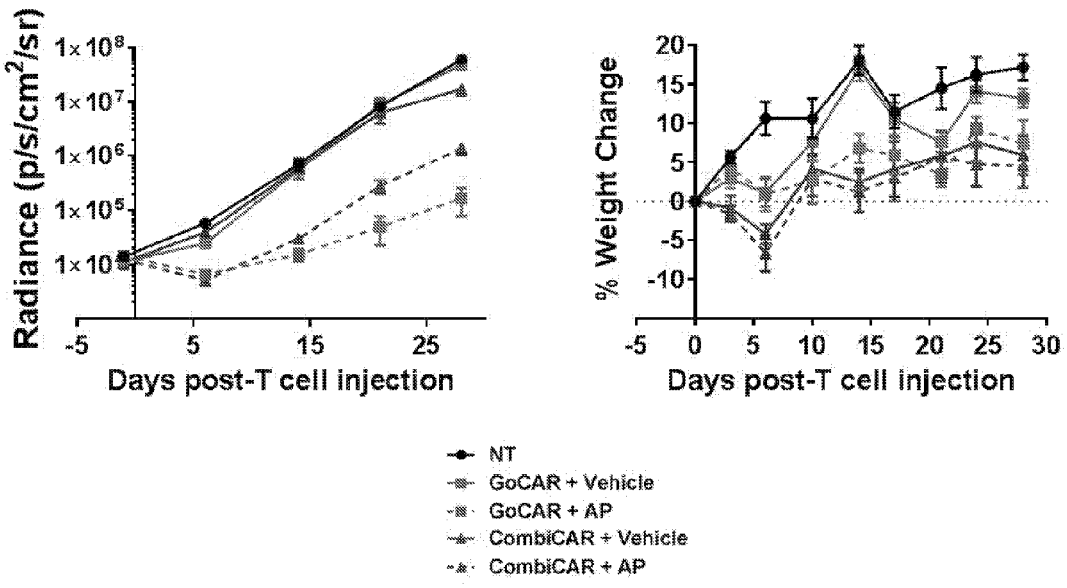

Radiance (p/s/cm²/sr)
1×10⁸
1×10⁷
1×10⁶
1×10⁵
1×10⁴
-5
5
15
25
Days post-T cell injection
% Weight Change
20
15
10
5
0
-5
-10
-5
0
5
10
15
20
25
30
Days post-T cell injection
NT
GoCAR + Vehicle
GoCAR + AP
CombiCAR + Vehicle
CombiCAR + AP

Fig. 76 C

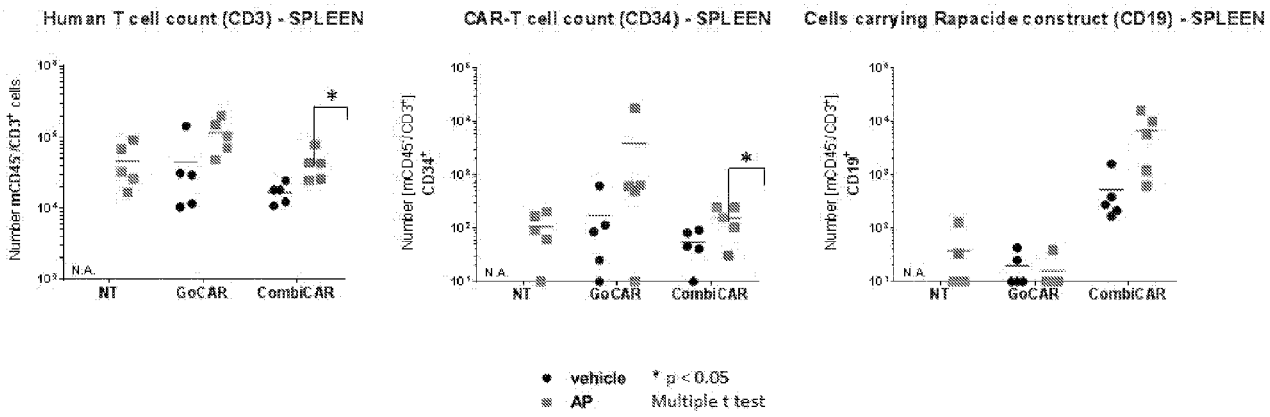

Human T cell count (CD3) - SPLEEN
CAR-T cell count (CD34) - SPLEEN
Cells carrying Rapacide construct (CD19) - SPLEEN
Number mCD45+CD3+ cells
Number [mCD45+/CD3+] CD34+
Number [mCD45+/CD3+] CD19+
N.A.
NT
GoCAR
CombiCAR
*
vehicle
AP
* p < 0.05
Multiple t test

Fig. 76 D

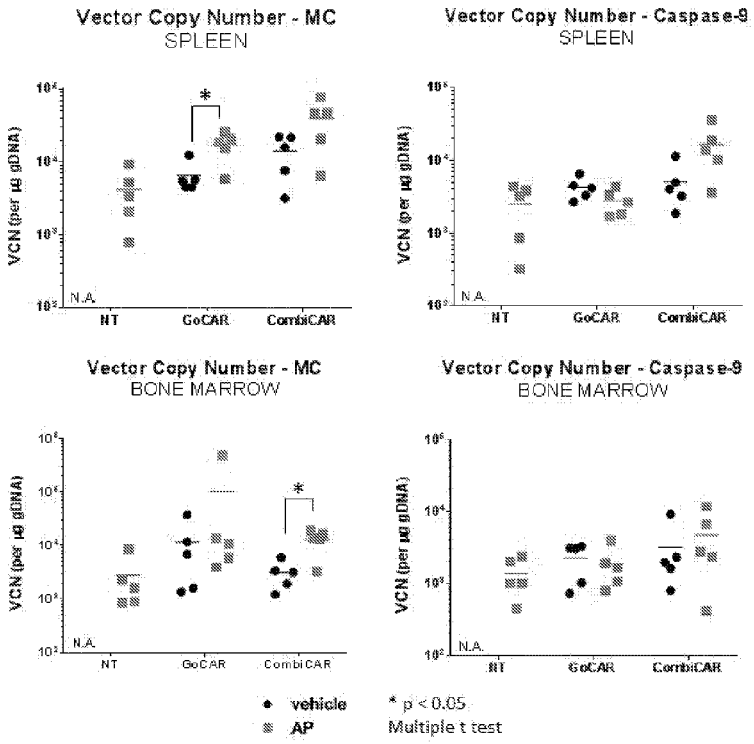

Vector Copy Number - MC
SPLEEN
Vector Copy Number - Caspase-9
SPLEEN
VCN (per µg gDNA)
N.A.
NT
GoCAR
CombiCAR
*
Vector Copy Number - MC
BONE MARROW
Vector Copy Number - Caspase-9
BONE MARROW
vehicle
AP
* p < 0.05
Multiple t test

Fig. 77 A

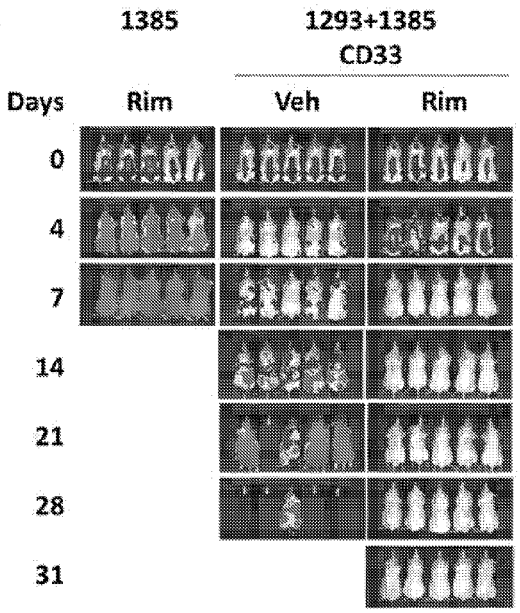


Fig. 77B

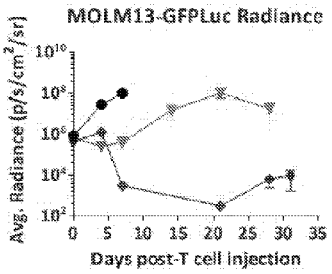


Fig. 77 C

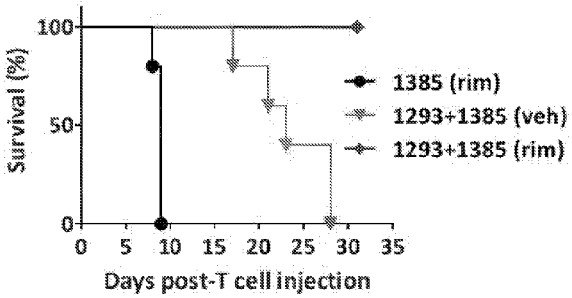


Fig. 77 D

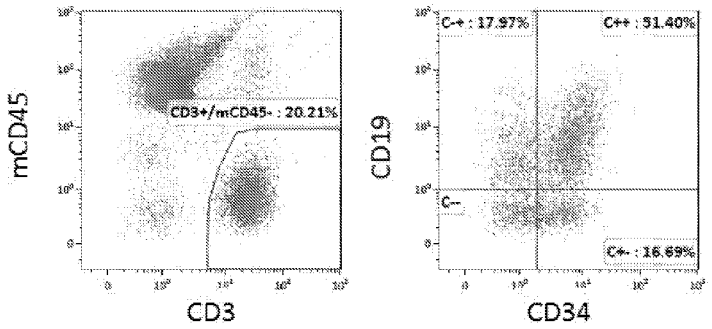


Fig. 78 A

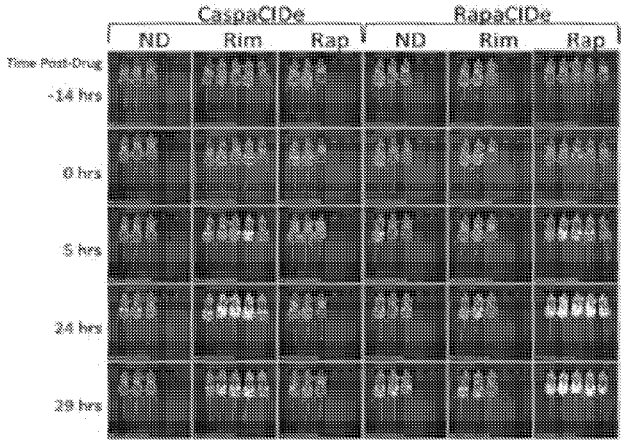


Fig. 78 B

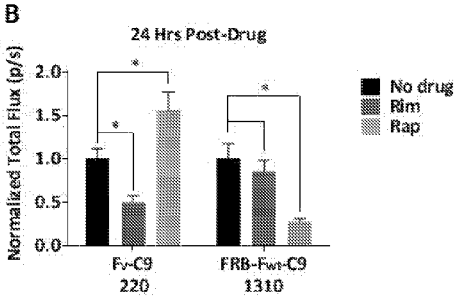


Fig. 78 C

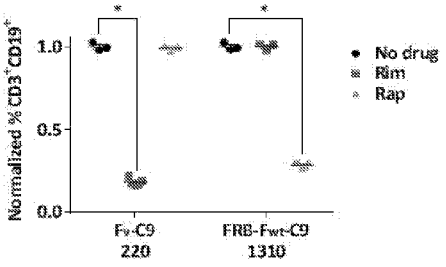


Fig. 79 A

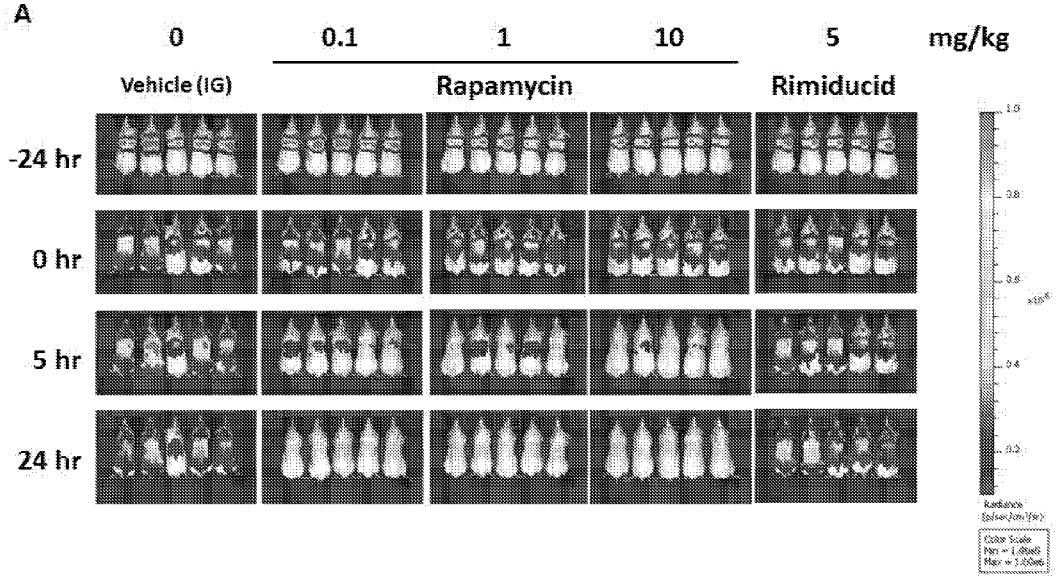
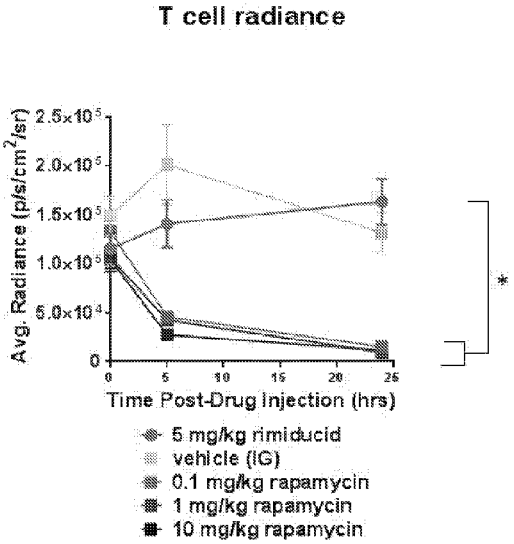
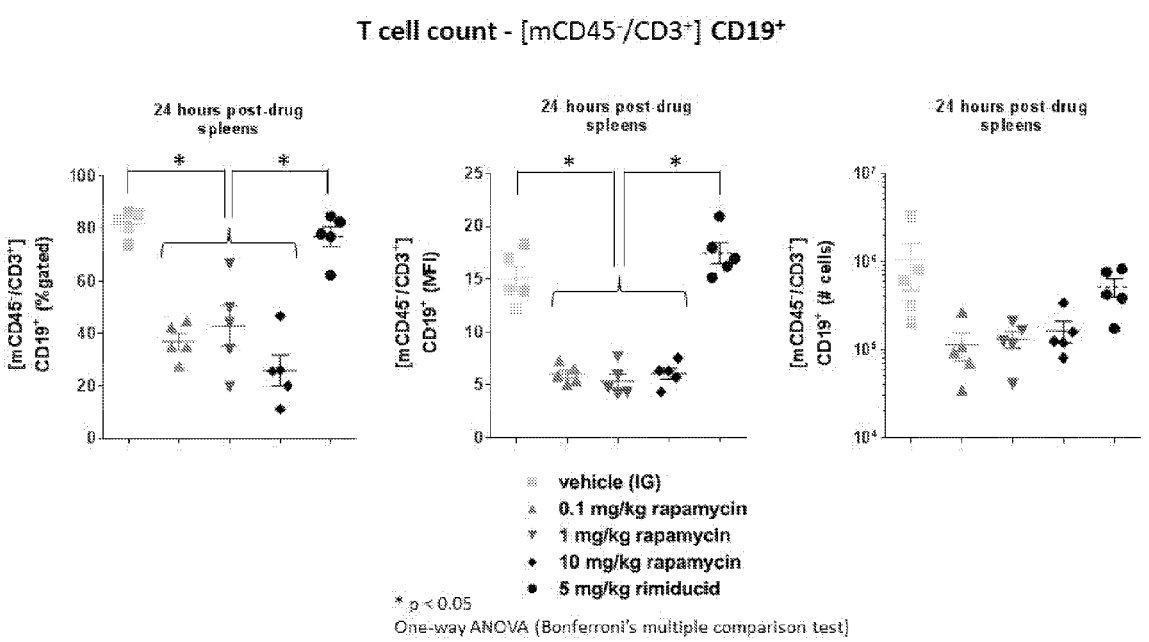

0
0.1
1
10
5
mg/kg
Vehicle (IG)
Rapamycin
Rimiducid
-24 hr
0 hr
5 hr
24 hr

Fig. 79 B



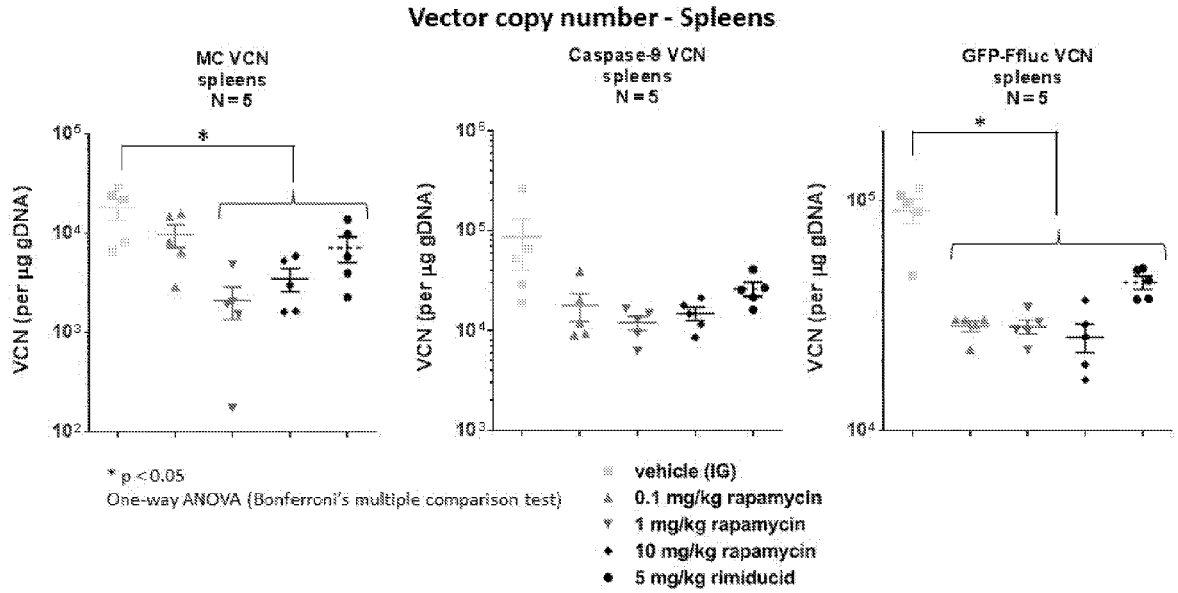
* $p < 0.05$
Two-way ANOVA (Bonferroni's multiple comparison test)

Fig. 79 C



- There was significant difference in rapamycin-induced elimination of CD19+ cells.
- There was no significant reduction of CD19+ T cells with rimiducid treatment.

Fig. 79 D


Vector copy number - Spleens
MC VCN spleens N=5
Caspase-9 VCN spleens N=5
GFP-Ffluc VCN spleens N=5
VCN (per µg gDNA)
*
* p < 0.05
One-way ANOVA (Bonferroni's multiple comparison test)
vehicle (IG)
0.1 mg/kg rapamycin
1 mg/kg rapamycin
10 mg/kg rapamycin
5 mg/kg rimiducid

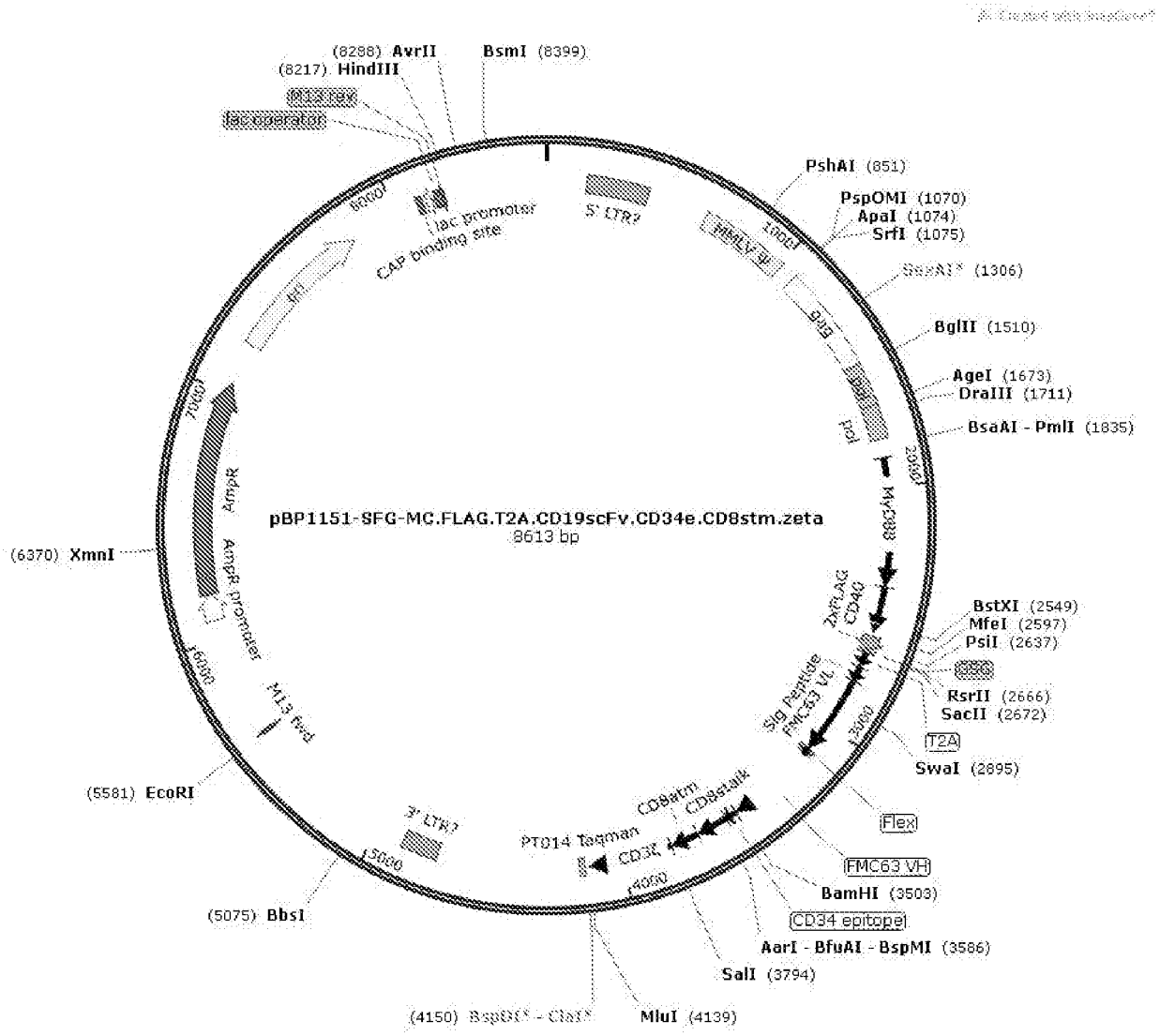

(8288) AvrII
BsmI (8399)
(8217) HindIII
M13 rev
lac operator
lac promoter
CAP binding site
5' LTR?
PshAI (851)
PspOMI (1070)
ApaI (1074)
SrfI (1075)
MMLV
(1306)
BglII (1510)
AgeI (1673)
DraIII (1711)
BsaAI - PmlI (1835)
pol
MyC88
pBP1151-SFG-MC.FLAG.T2A.CD19scFv.CD34e.CD8stm.zeta
8613 bp
(6370) XmnI
AmpR
AmpR promoter
M13 fwd
BstXI (2549)
MfeI (2597)
PsiI (2637)
RsrII (2666)
SacII (2672)
T2A
SwaI (2895)
Sig Peptide
FMC63 VL
Flex
FMC63 VH
BamHI (3503)
CD34 epitope
AarI - BfuAI - BspMI (3586)
SalI (3794)
(5581) EcoRI
3' LTR?
PT014 Taqman
CD8stm
CD8stalk
(5075) BbsI
(4150) BspDI* - ClaI*
MluI (4139)

Fig. 80

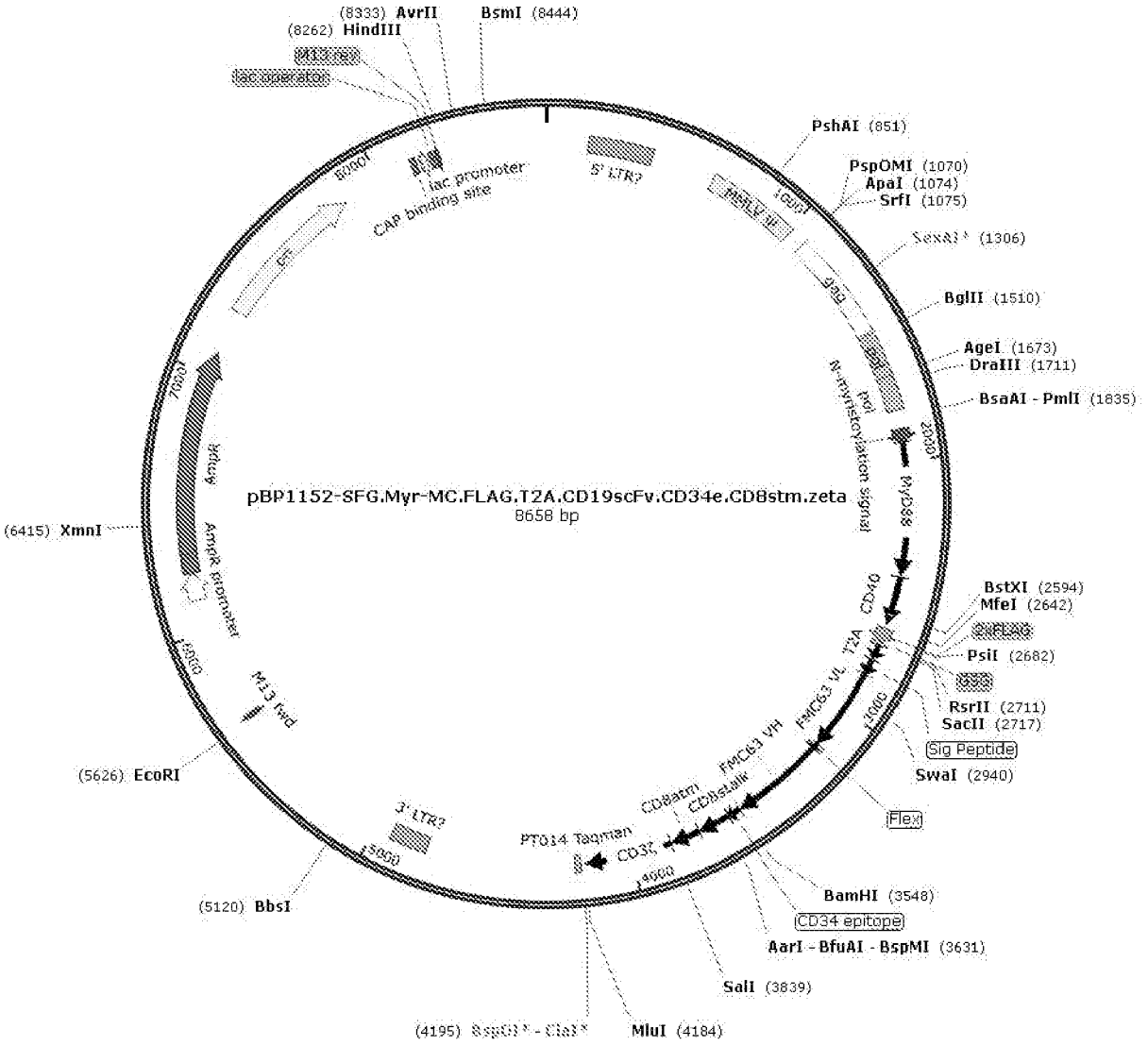

pBP1152-SFG.Myr-MC.FLAG.T2A.CD19scFv.CD34e.CD8stm.zeta
8658 bp
(8333) AvrII
(8262) HindIII
BsmI (8444)
lac operator
lac promoter
CAP binding site
5' LTR?
PshAI (851)
PspOMI (1070)
ApaI (1074)
SrfI (1075)
SexAI (1306)
BglII (1510)
AgeI (1673)
DraIII (1711)
BsaAI - PmlI (1835)
N-myristoylation signal
pol
Myr88
CD40
BstXI (2594)
MfeI (2642)
FLAG
PsiI (2682)
T2A
RsrII (2711)
SacII (2717)
Sig Peptide
SwaI (2940)
FMC63 VL
FMC63 VH
Flex
CD8stalk
CD8stm
CD3ζ
PT014 Taqman
BamHI (3548)
CD34 epitope
AarI - BfuAI - BspMI (3631)
SalI (3839)
MluI (4184)
(4195) BspQI* - ClaI*
(5120) BbsI
3' LTR?
(5626) EcoRI
M13 fwd
AmpR promoter
AmpR
(6415) XmnI

Fig. 81

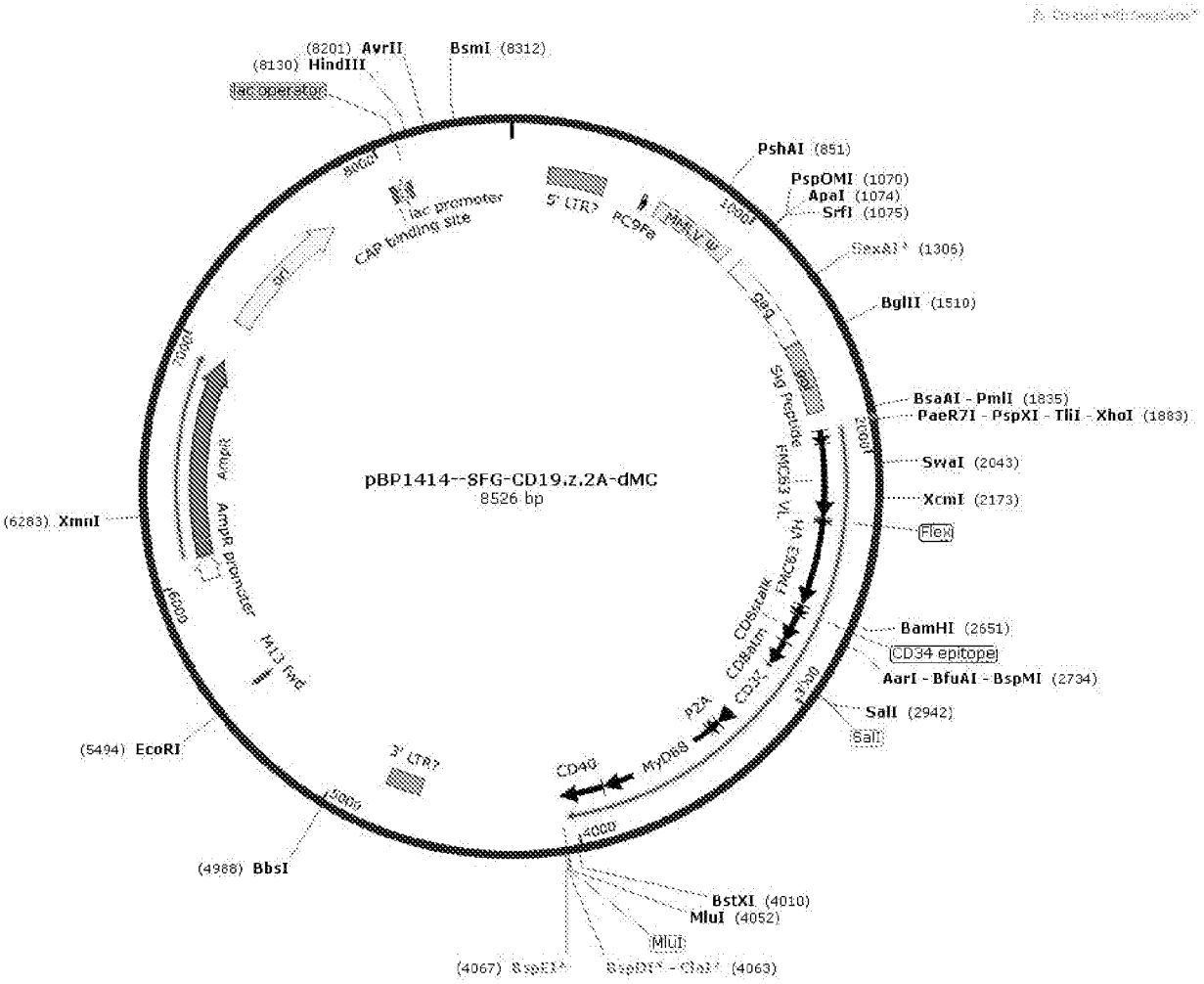

(8201) AvrII
(8130) HindIII
BsmI (8312)
lac operator
PshAI (851)
PspOMI (1070)
ApaI (1074)
SrfI (1075)
(1306)
BglII (1510)
BsaAI - PmlI (1835)
PaeR7I - PspXI - TliI - XhoI (1883)
SwaI (2043)
XcmI (2173)
Flex
BamHI (2651)
CD34 epitope
AarI - BfuAI - BspMI (2734)
SalI (2942)
SalI
(6283) XmnI
(5494) EcoRI
(4988) BbsI
BstXI (4010)
MluI (4052)
MluI
(4067)
(4063)
pBP1414--SFG-CD19.z.2A-dMC
8526 bp
lac promoter
CAP binding site
5' LTR7
PC9Fa
Sig Peptide
FMC63 VL
FMC63 VH
CD8stalk
CD8atm
CD3Z
P2A
MyD88
CD40
3' LTR7
AmpR
AmpR promoter
M13 fwd
8000
1000
2000
3000
4000
5000
6000
7000

Fig. 82

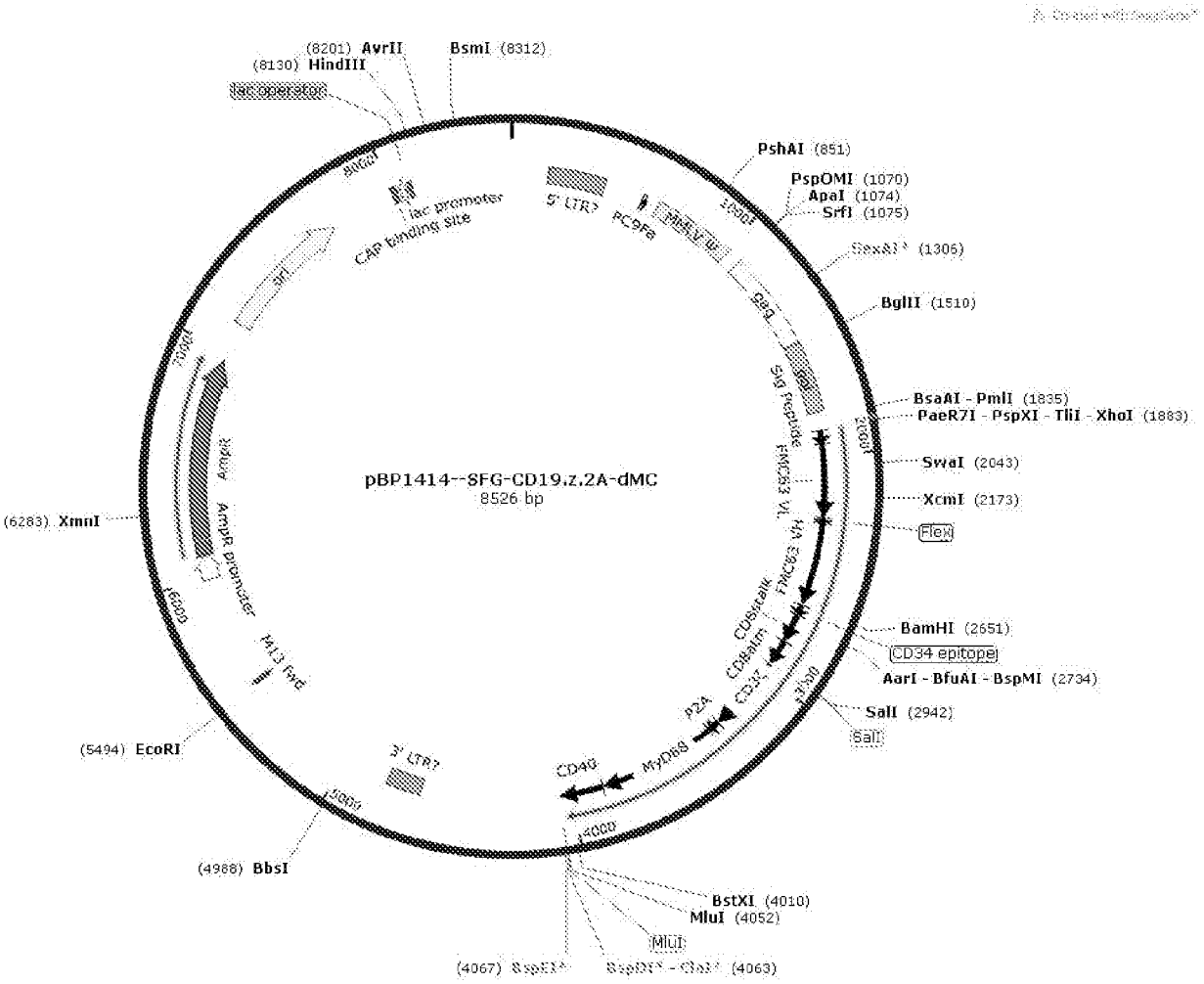

(8201) AvrII
(8130) HindIII
BsmI (8312)
lac operator
PshAI (851)
PspOMI (1070)
ApaI (1074)
SrfI (1075)
(1306)
BglII (1510)
BsaAI - PmlI (1835)
PaeR7I - PspXI - TliI - XhoI (1883)
SwaI (2043)
XcmI (2173)
Flex
BamHI (2651)
CD34 epitope
AarI - BfuAI - BspMI (2734)
SalI (2942)
SalI
(6283) XmnI
(5494) EcoRI
(4988) BbsI
BstXI (4010)
MluI (4052)
MluI
(4067)
(4063)
pBP1414--SFG-CD19.z.2A-dMC
8526 bp
lac promoter
CAP binding site
5' LTR7
PC9Fa
Sig Peptide
FMC63 VL
FMC63 VH
CD8stalk
CD8atm
CD3z
P2A
MyD88
CD40
3' LTR7
AmpR
AmpR promoter
M13 fwd
1000
2000
3000
4000
5000
6000
7000
8000

Fig. 83

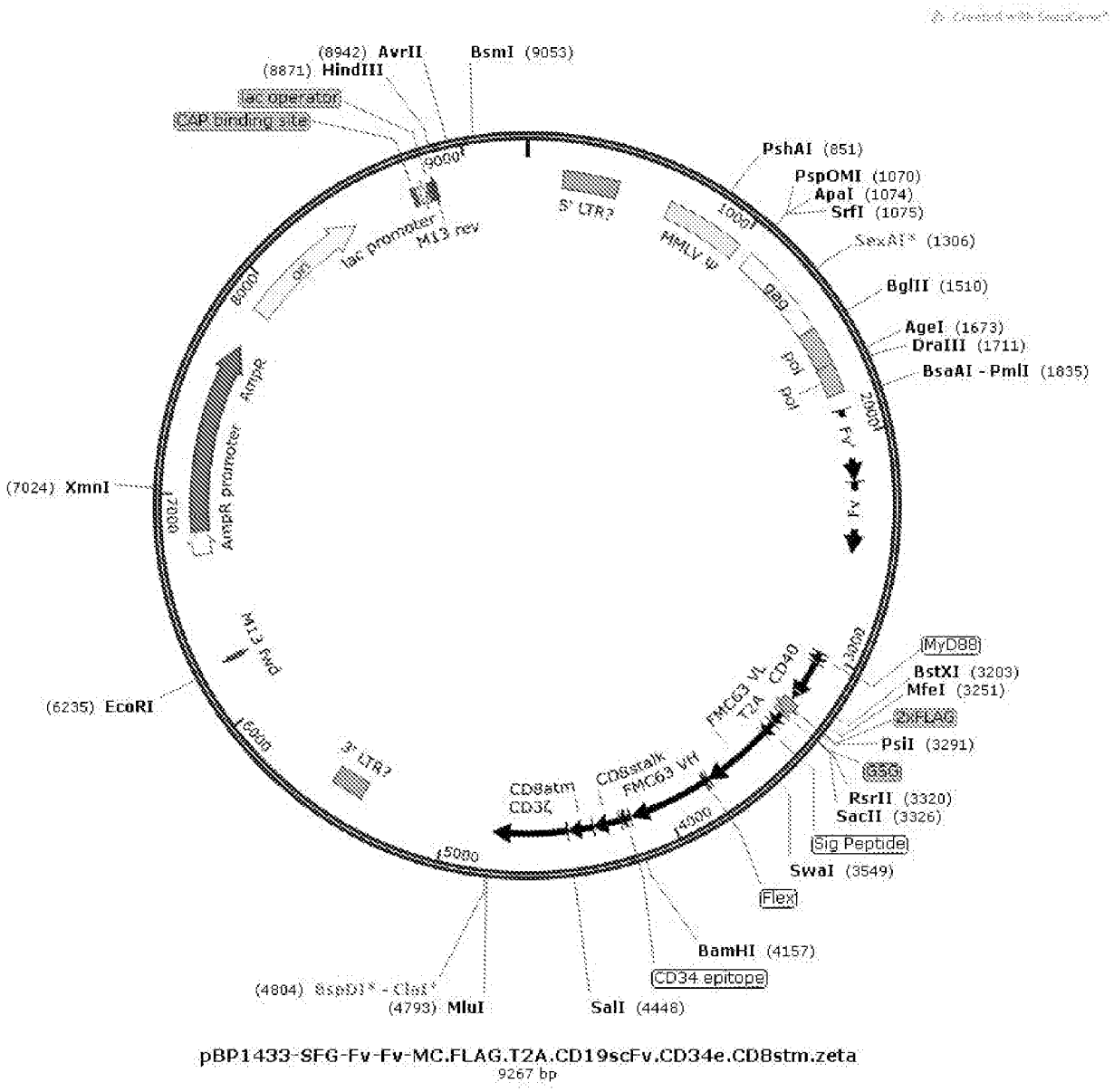

(8942) AvrII
(8871) HindIII
BsmI (9053)
lac operator
CAP binding site
PshAI (851)
PspOMI (1070)
ApaI (1074)
SrfI (1075)
SexAI* (1306)
BglII (1510)
AgeI (1673)
DraIII (1711)
BsaAI - PmlI (1835)
lac promoter
M13 rev
5' LTR?
MMLV ψ
gag
pol
Pol
Fv
Fv
AmpR
AmpR promoter
(7024) XmnI
M13 fwd
(6235) EcoRI
3' LTR?
CD8atm
CD3ζ
CD8stalk
FMC63 VH
FMC63 VL
T2A
CD40
MyD88
BstXI (3203)
MfeI (3251)
2xFLAG
PsiI (3291)
GSG
RsrII (3320)
SacII (3326)
Sig Peptide
SwaI (3549)
Flex
BamHI (4157)
CD34 epitope
(4804) BspDI* - ClaI*
(4793) MluI
SalI (4448)
pBP1433-SFG-Fv-Fv-MC.FLAG.T2A.CD19scFv.CD34e.CD8stm.zeta
9267 bp

Fig. 84

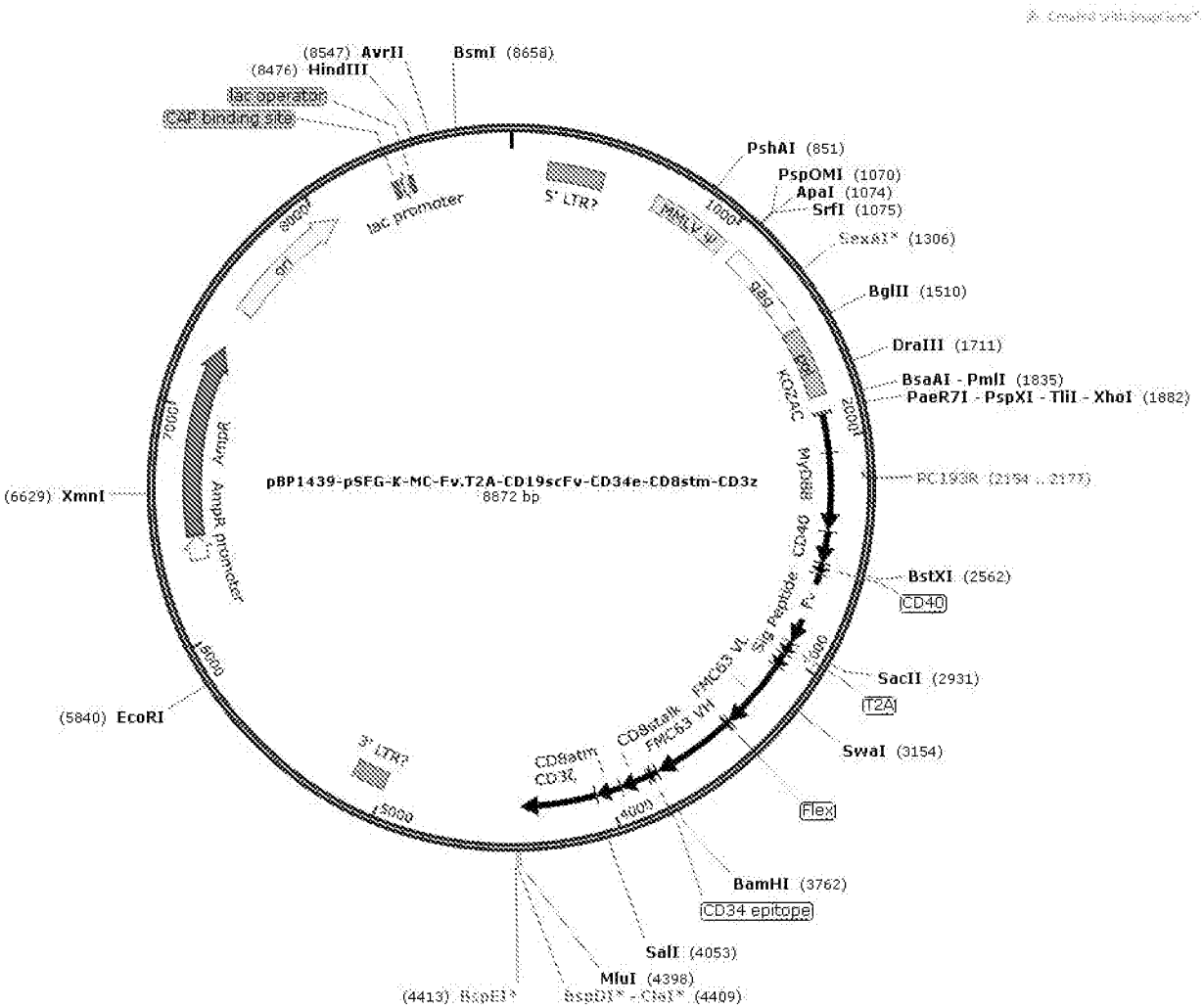

(8547) AvrII
BsmI (8658)
(8476) HindIII
lac operator
CAP binding site
lac promoter
5' LTR?
PshAI (851)
PspOMI (1070)
ApaI (1074)
SrfI (1075)
SexAI* (1306)
BglII (1510)
DraIII (1711)
BsaAI - PmlI (1835)
PaeR7I - PspXI - TliI - XhoI (1882)
KOZAC
MyD88
CD40
Sig Peptide
FMC63 VL
FMC63 VH
CD8stalk
CD8atm
CD3z
3' LTR?
AmpR promoter
AmpR
pBP1439-pSFG-K-MC-Fv.T2A-CD19scFv-CD34e-CD8stm-CD3z
8872 bp
(6629) XmnI
(5840) EcoRI
BstXI (2562)
CD40
SacII (2931)
T2A
SwaI (3154)
Flex
BamHI (3762)
CD34 epitope
SalI (4053)
MluI (4398)
(4413) BspEI*
BspDI* - ClaI* (4409)

Fig. 85

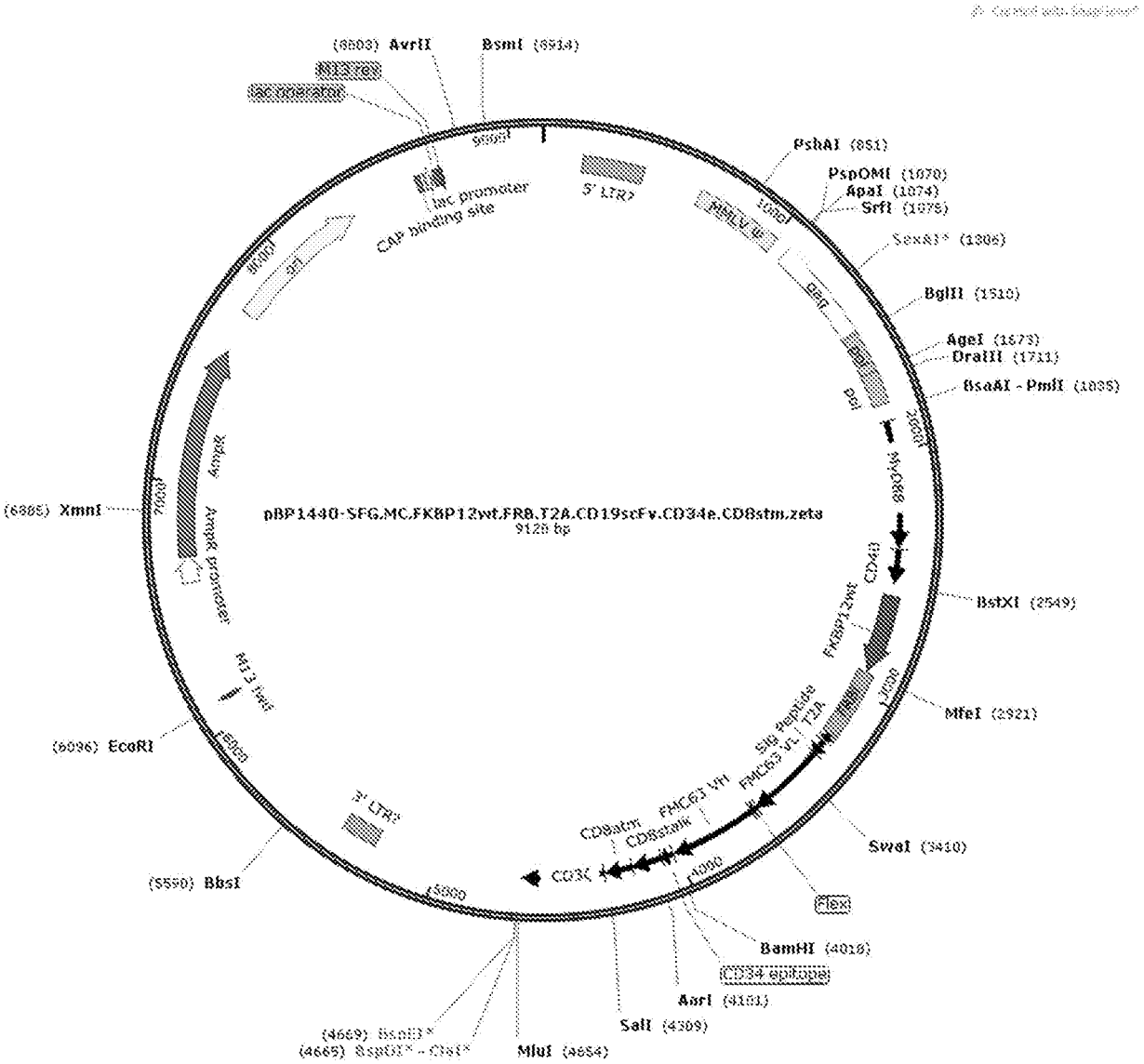

(8803) AvrII
BsmI (8914)
M13 rev
lac operator
lac promoter
CAP binding site
5' LTR?
PshAI (851)
PspOMI (1070)
ApaI (1074)
SrfI (1075)
SexAI* (1306)
BglII (1510)
AgeI (1673)
DraIII (1711)
BsaAI - PmlI (1835)
MyD88
CD40
BstXI (2549)
FKBP12wt
MfeI (2921)
Sig Peptide
FMC63 VL
T2A
FMC63 VH
CD8atm
CD8stalk
CD3ζ
SwaI (3410)
Flex
BamHI (4018)
CD34 epitope
AarI (4101)
SalI (4309)
MluI (4654)
(4669) BspEI*
(4665) BspDI* - ClaI*
(5590) BbsI
3' LTR?
(6096) EcoRI
M13 fwd
AmpR
AmpR promoter
(6885) XmnI
pBP1440-SFG.MC.FKBP12wt.FRB.T2A.CD19scFv.CD34e.CD8stm.zeta
9128 bp

Fig. 86

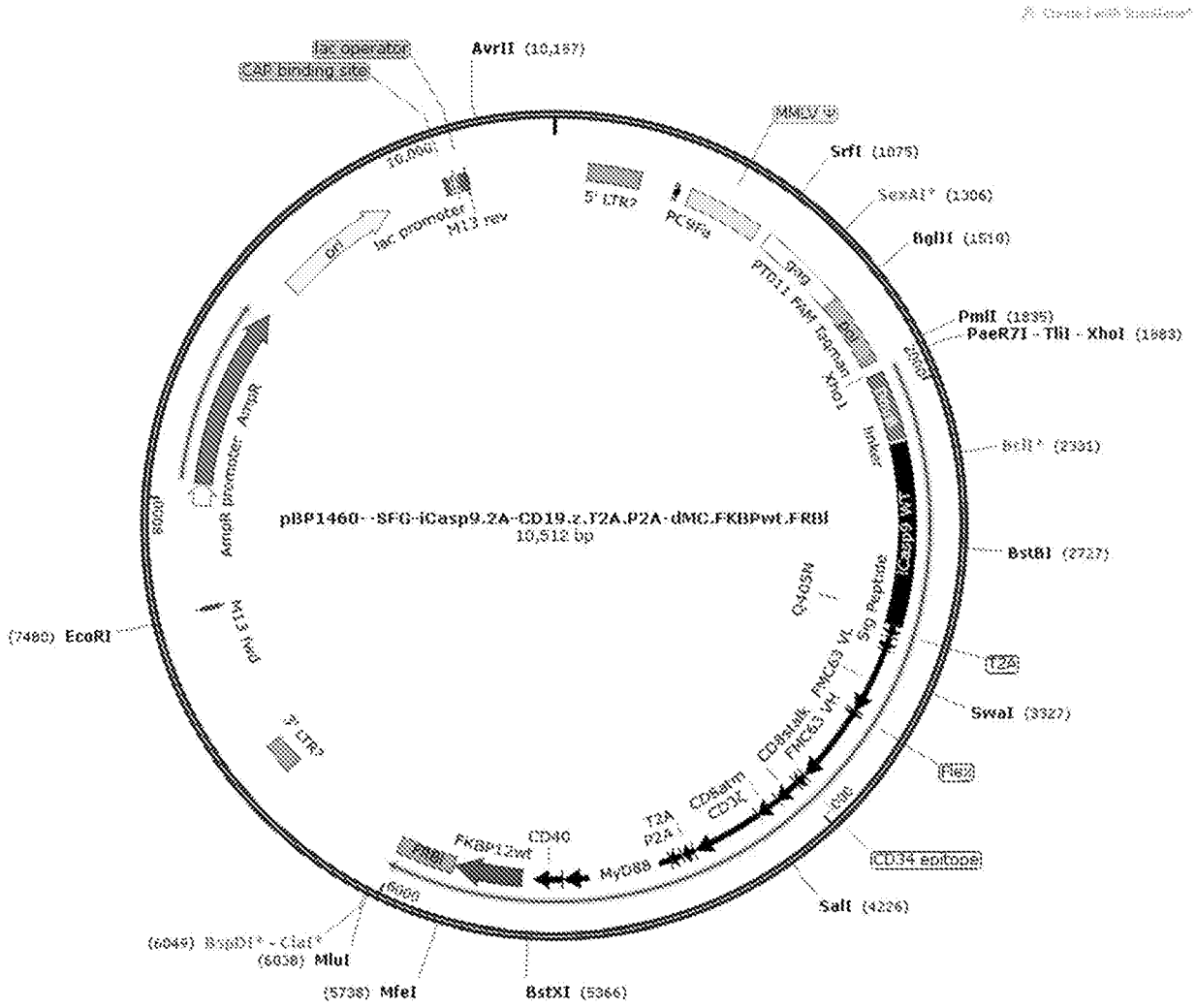
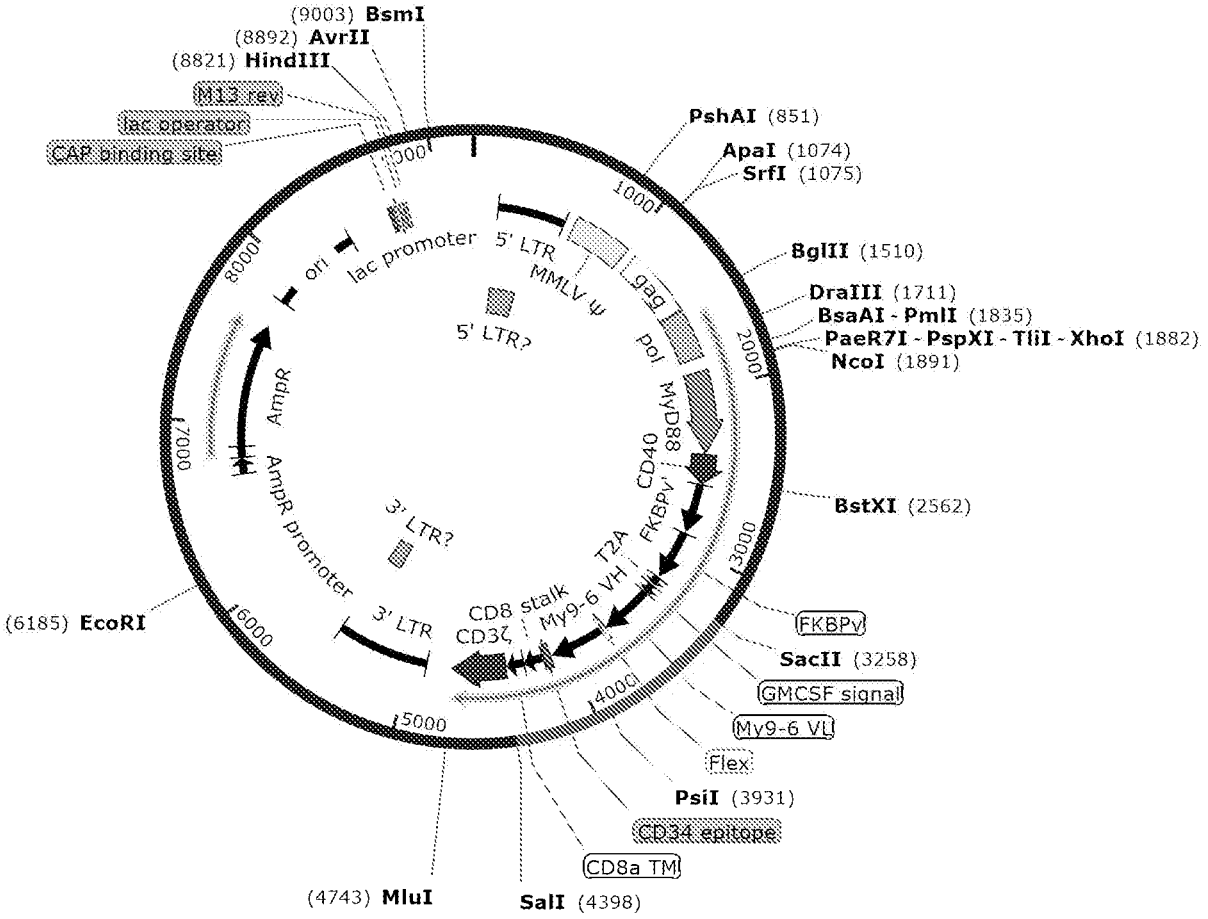
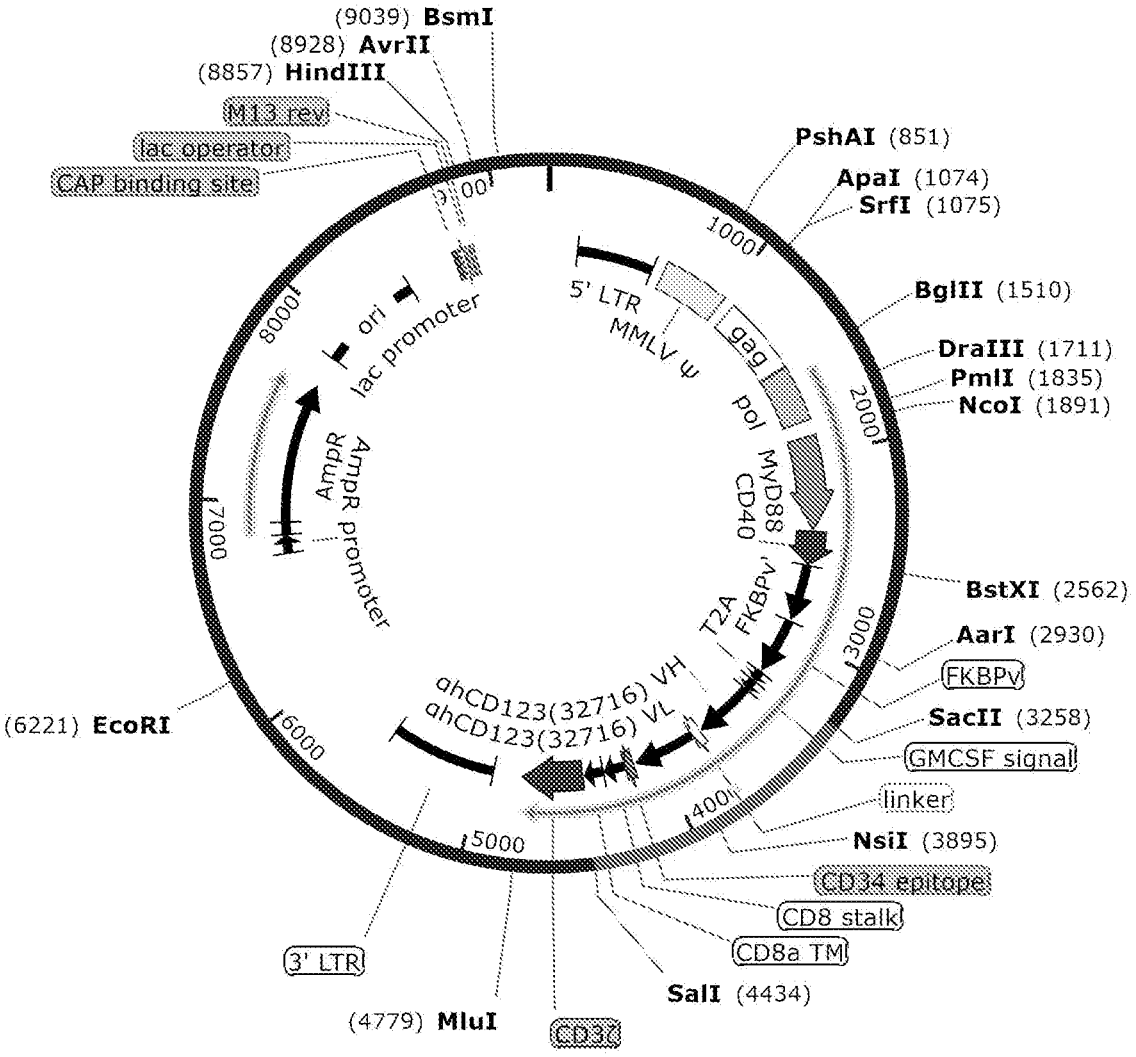

lac operator
CAP binding site
AvrII (10,157)
10,000
MMLV 9
SrfI (1075)
SexAI* (1306)
BglII (1510)
PmlI (1835)
PaeR7I - TliI - XhoI (1883)
BtlI* (2331)
BstBI (2727)
T2A
SwaI (3327)
Flex
CD34 epitope
SalI (4226)
BstXI (5366)
(5738) MfeI
(6038) MluI
(6049) BspDI* - ClaI*
(7480) EcoRI
5' LTR?
PC9Pa
lac promoter
M13 rev
ori
AmpR
AmpR promoter
pBP1460--SFG-iCasp9.2A-CD19.z.T2A.P2A-dMC.FKBPwt.FRBI
10,512 bp
Q405N
Sig Peptide
FMC63 VL
FMC63 VH
CD8stalk
CD8atm
CD3ζ
T2A
P2A
MyD88
CD40
FKBP12wt
7' LTR?
M13 fwd
6000

Fig. 87



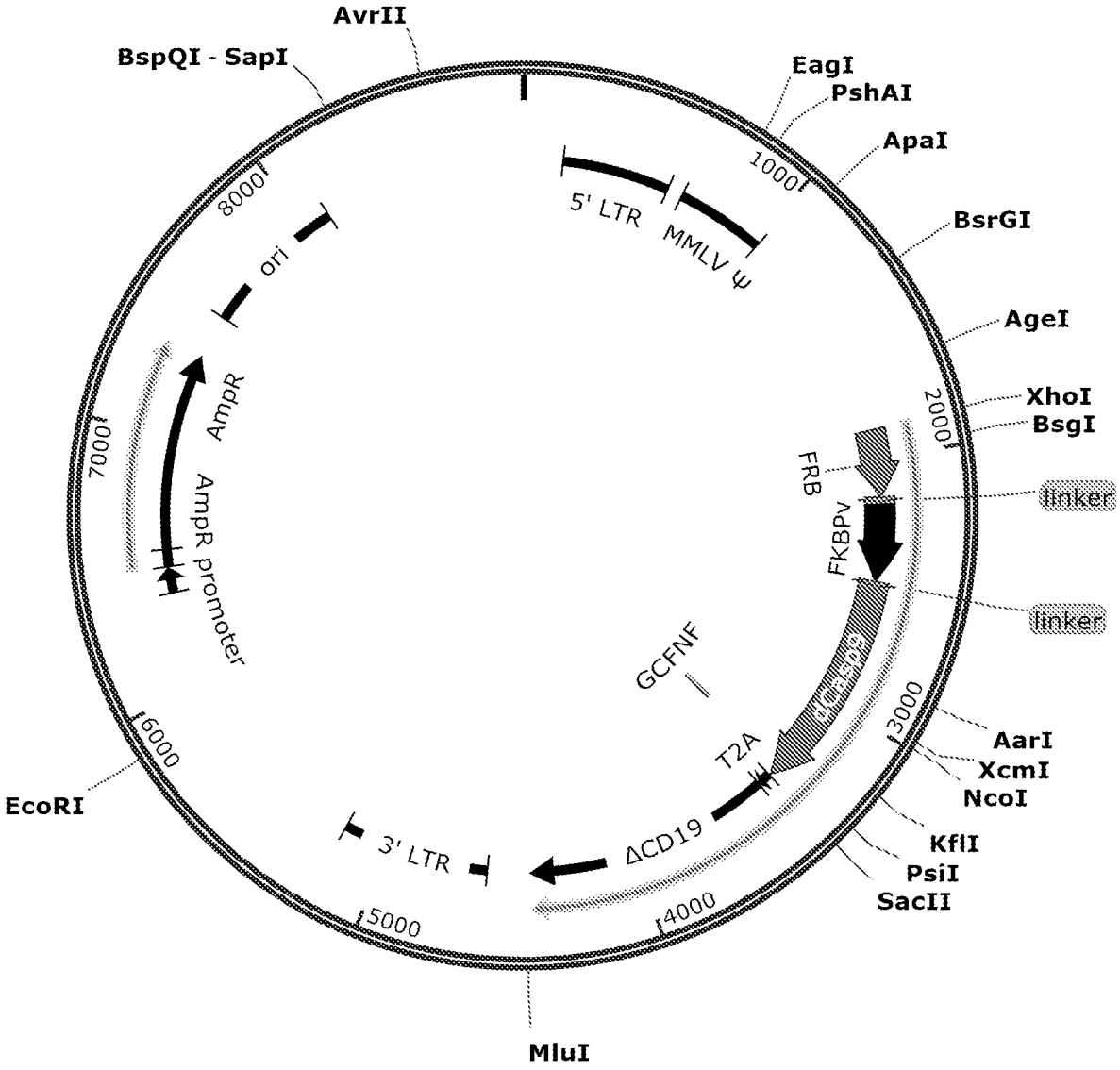
pBP1293--pSFG-iMC.T2A-ahCD33(My9.6).ζ
9217 bp

Fig. 88



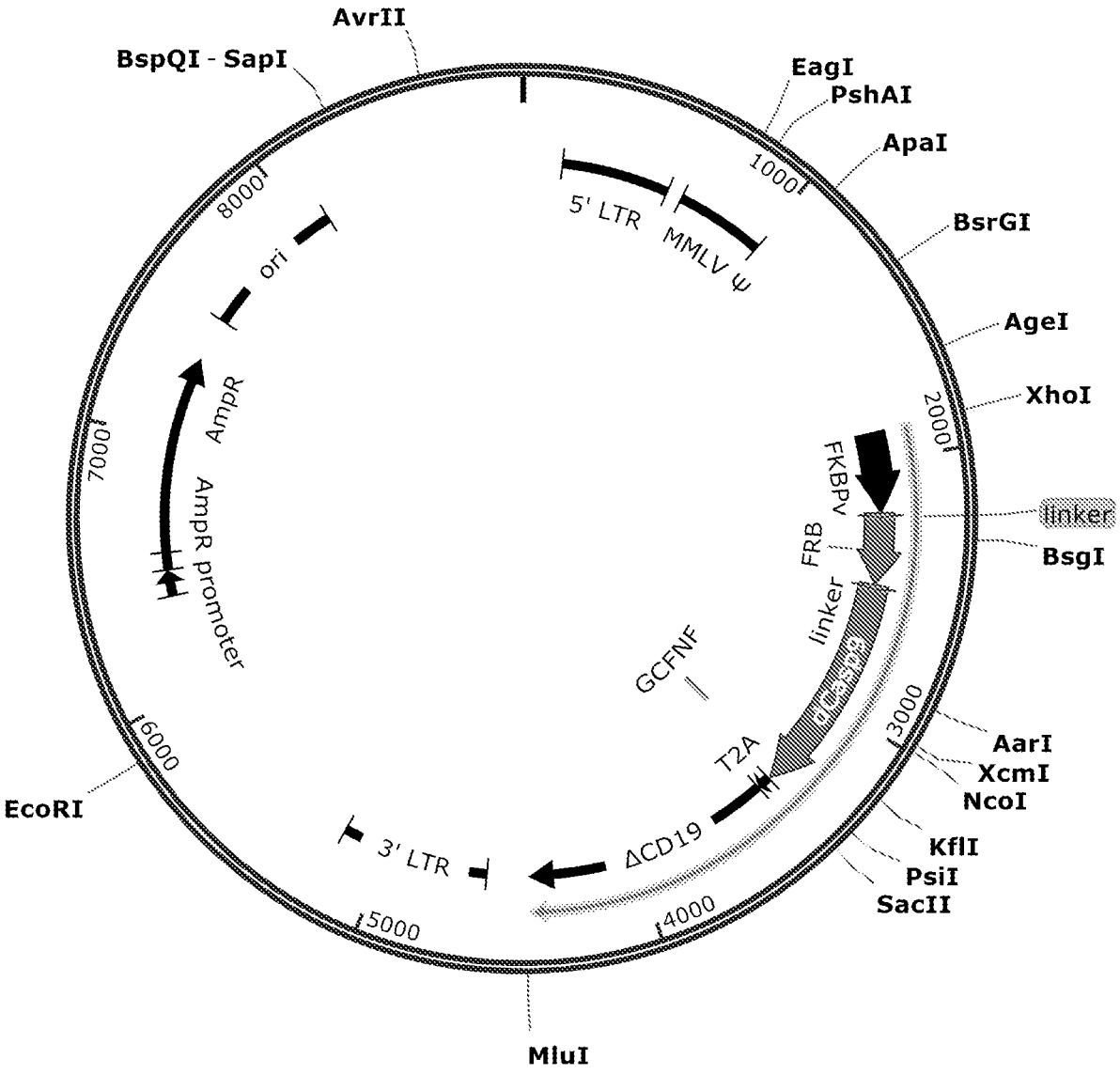
pBP1296--pSFG-iMC.T2A-ahCD123(32716).ζ
9253 bp

Fig. 89



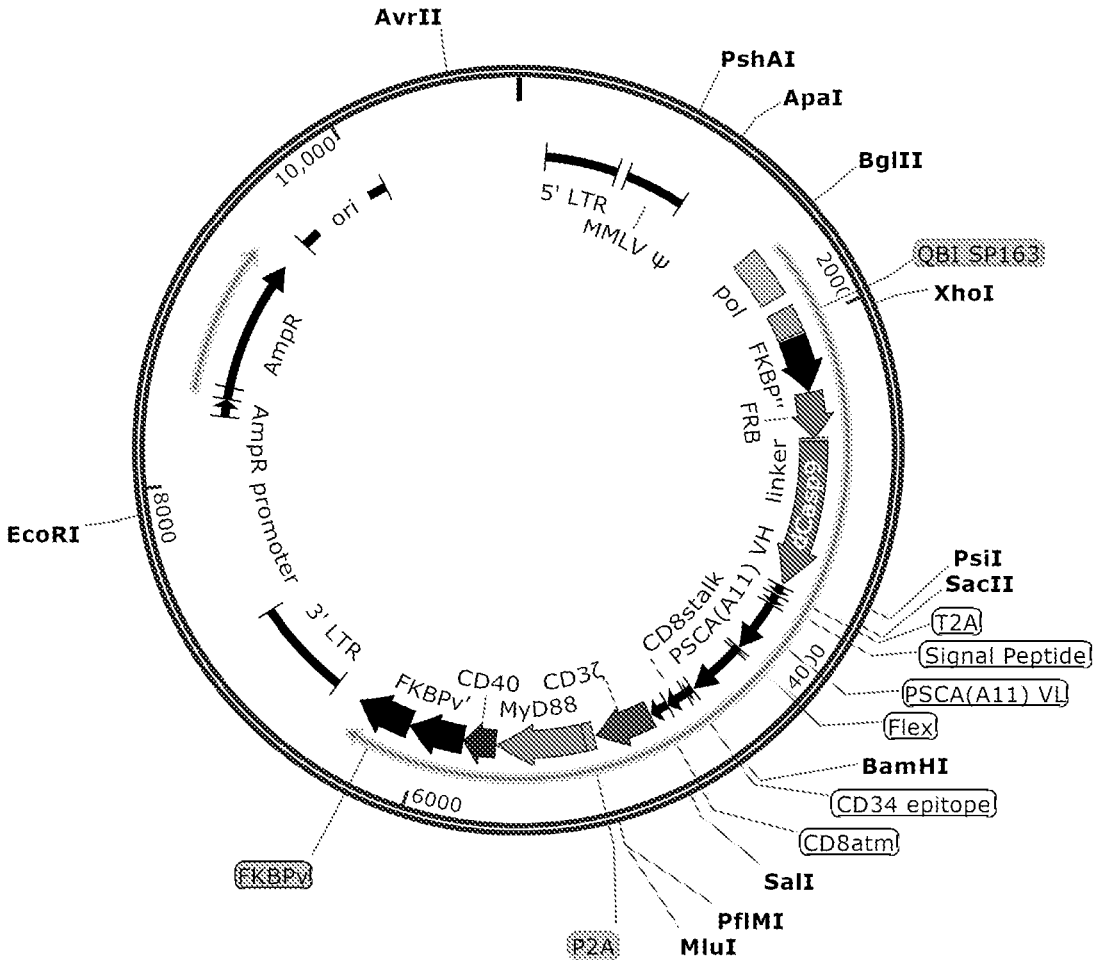
pBP1327-pSFG.FRB.FKBPvΔC9.2A-ΔCD19
8910 bp

Fig. 90



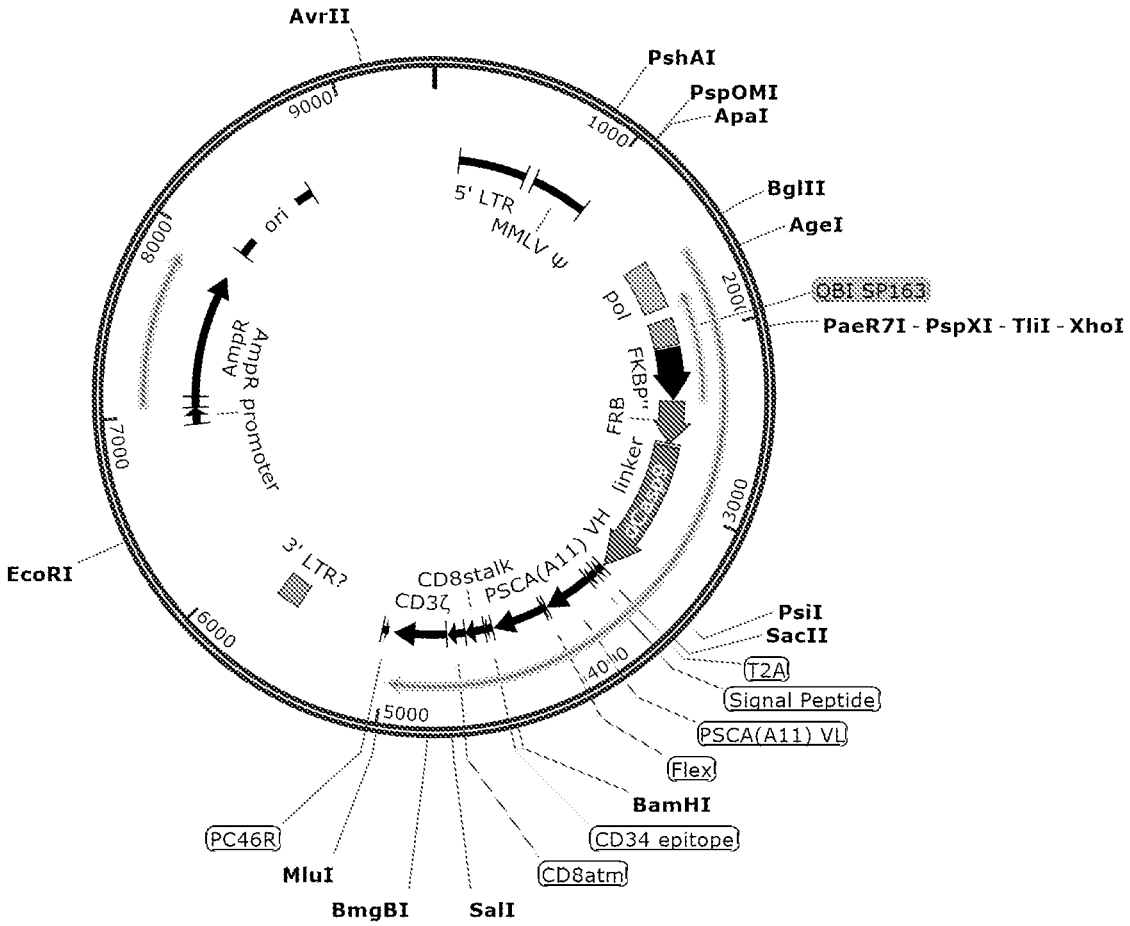
pBP1328—pSFG-FKBPv.FRBΔC9.2A-ΔCD19
8910 bp

Fig. 91



pBP1351--pSFG-SP163.FKBP.FRB.C9.T2A-ahPSCA.Q.CD8stm.z.2A-iMC
10,907 bp

Fig. 92



pBP1373--pSFG-sp-FKBP.FRB.C9.T2A-PSCAscFv.Q.CD8stm.z
9469 bp

Fig. 93

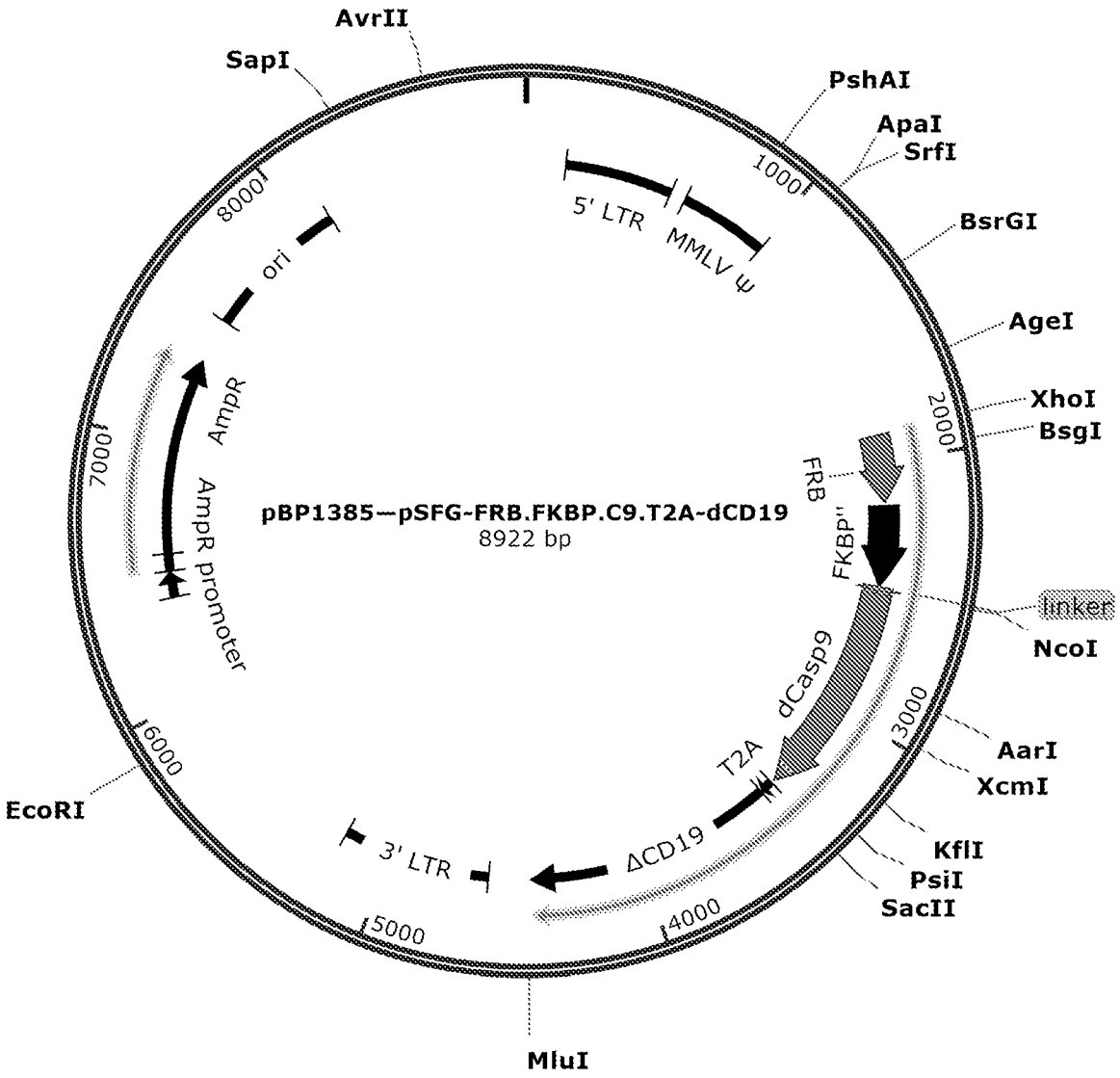

AvrII
SapI
PshAI
ApaI
SrfI
BsrGI
AgeI
XhoI
BsgI
NcoI
linker
AarI
XcmI
KflI
PsiI
SacII
MluI
EcoRI
1000
2000
3000
4000
5000
6000
7000
8000
5' LTR
MMLV ψ
ori
AmpR
AmpR promoter
FRB
FKBP''
dCasp9
T2A
ΔCD19
3' LTR
pBP1385—pSFG-FRB.FKBP.C9.T2A-dCD19
8922 bp

Fig. 94

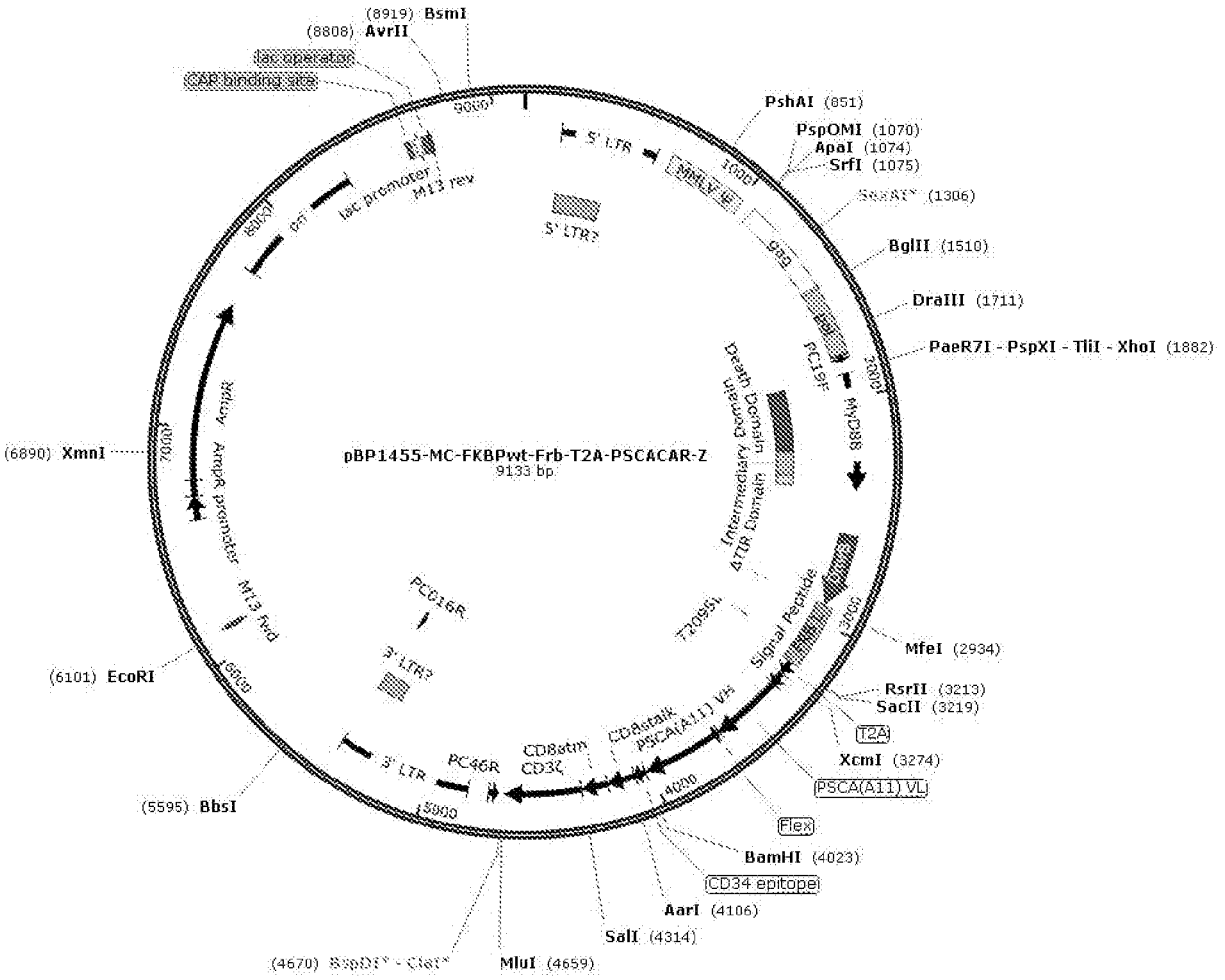

(8919) BsmI
(8808) AvrII
lac operator
CAP binding site
PshAI (851)
PspOMI (1070)
ApaI (1074)
SrfI (1075)
(1306)
BglII (1510)
DraIII (1711)
PaeR7I - PspXI - TliI - XhoI (1882)
(6890) XmnI
pBP1455-MC-FKBPwt-Frb-T2A-PSCACAR-Z
9133 bp
MfeI (2934)
RsrII (3213)
SacII (3219)
T2A
XcmI (3274)
PSCA(A11) VL
Flex
BamHI (4023)
CD34 epitope
AarI (4106)
SalI (4314)
MluI (4659)
(6101) EcoRI
(5595) BbsI
lac promoter
M13 rev
5' LTR
5' LTR?
3' LTR
3' LTR?
PC19F
MyD88
Intermediary Domain
ATIR Domain
Signal Peptide
PC016R
PC46R
CD8atm
CD3ζ
CD8atm
PSCA(A11) VH
AmpR
AmpR promoter
M13 fwd
9000
1000
2000
3000
4000
5000
6000
7000
8000

Fig. 95

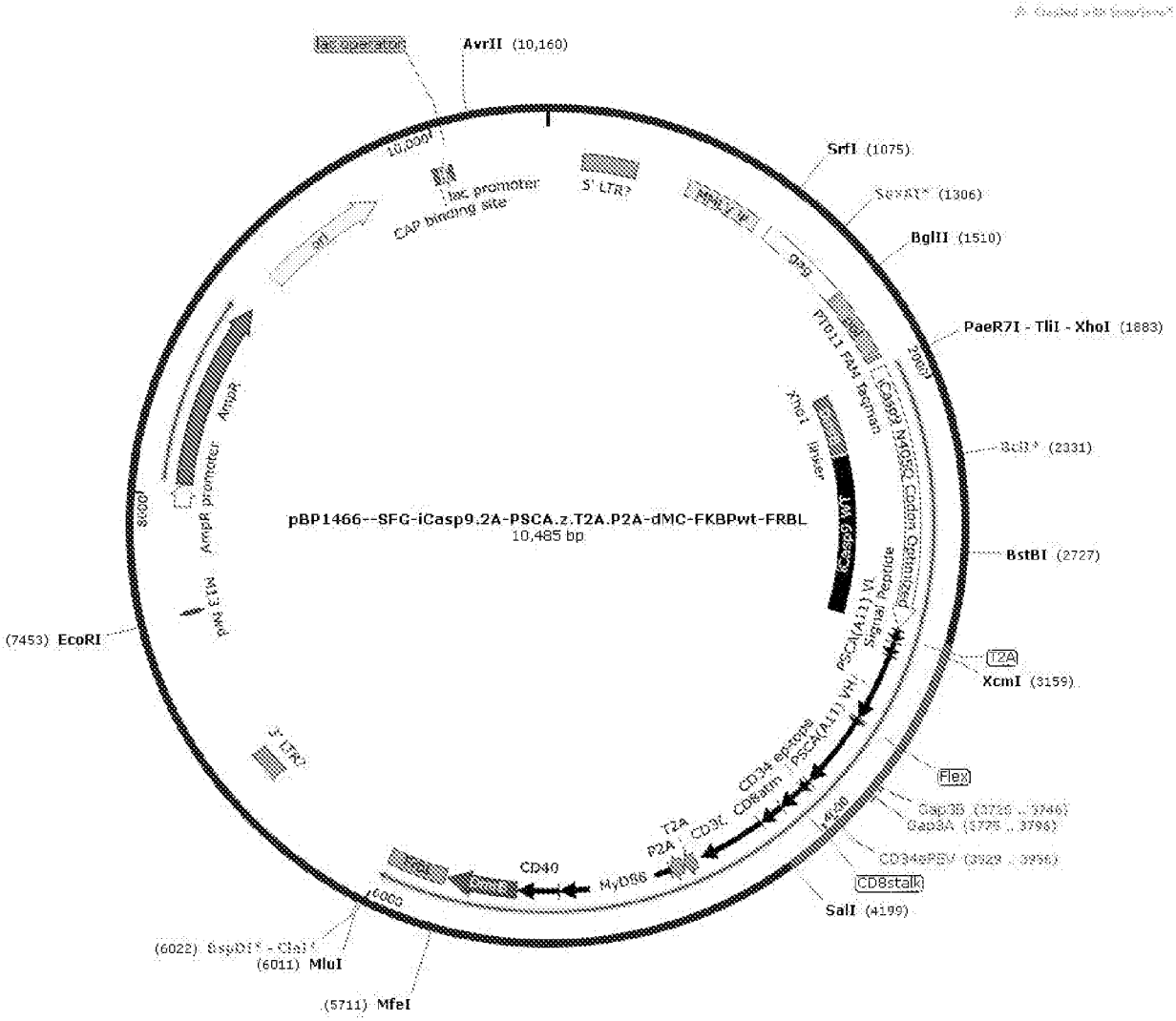

AvrII (10,160)
SrfI (1075)
BglII (1510)
PaeR7I - TliI - XhoI (1883)
BstBI (2727)
XcmI (3159)
SalI (4199)
(7453) EcoRI
(6022) BspDI* - ClaI*
(6011) MluI
(5711) MfeI
pBP1466--SFG-iCasp9.2A-PSCA.z.T2A.P2A-dMC-FKBPwt-FRBL
10,485 bp
lac promoter
CAP binding site
5' LTR?
AmpR
AmpR promoter
Signal Peptide
T2A
Flex
CD8stalk
CD40
MyD88
P2A
CD3C
CD8atm
CD34 epsilon
PSCA(A11) VH
PSCA(A11) VL
Xhoi
linker
iCasp9 N405Q Codon Optimized
PTG11 FAM Tagman
gag
2000
4000
6000
8000
10,000

Fig. 96

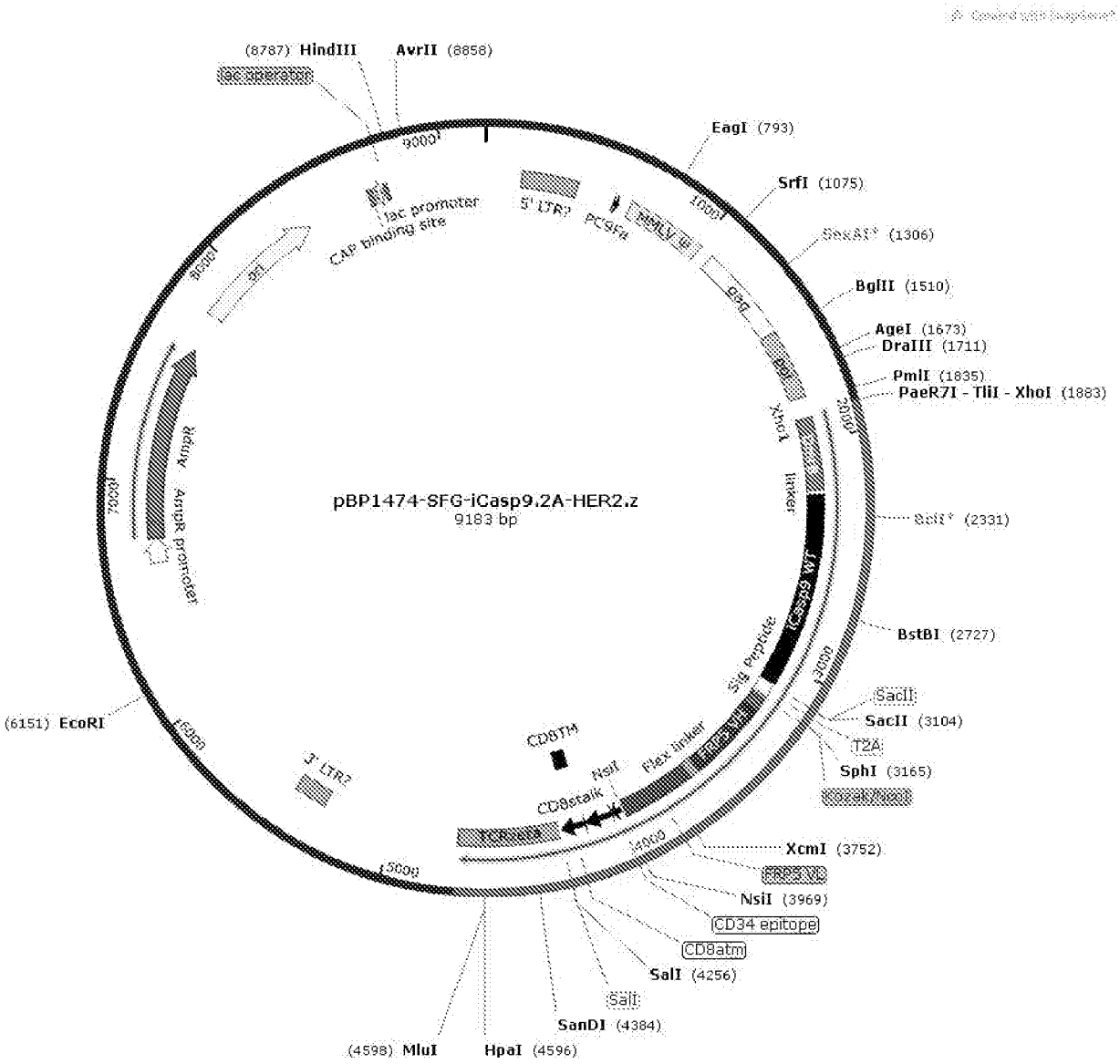

(8787) HindIII
AvrII (8858)
EagI (793)
SrfI (1075)
(1306)
BglII (1510)
AgeI (1673)
DraIII (1711)
PmlI (1835)
PaeR7I - TliI - XhoI (1883)
(2331)
BstBI (2727)
SacII
SacII (3104)
T2A
SphI (3165)
XcmI (3752)
NsiI (3969)
CD34 epitope
CD8atm
SalI (4256)
SalI
SanDI (4384)
(4598) MluI
HpaI (4596)
(6151) EcoRI
pBP1474-SFG-iCasp9.2A-HER2.z
9183 bp
lac promoter
CAP binding site
5' LTR?
PC9Fa
MMLV
XhoI
linker
Sig peptide
Flex linker
CD8TM
NsiI
CD8stalk
3' LTR?
AmpR
AmpR promoter
9000
1000
2000
3000
4000
5000
6000
7000
8000

Fig. 97

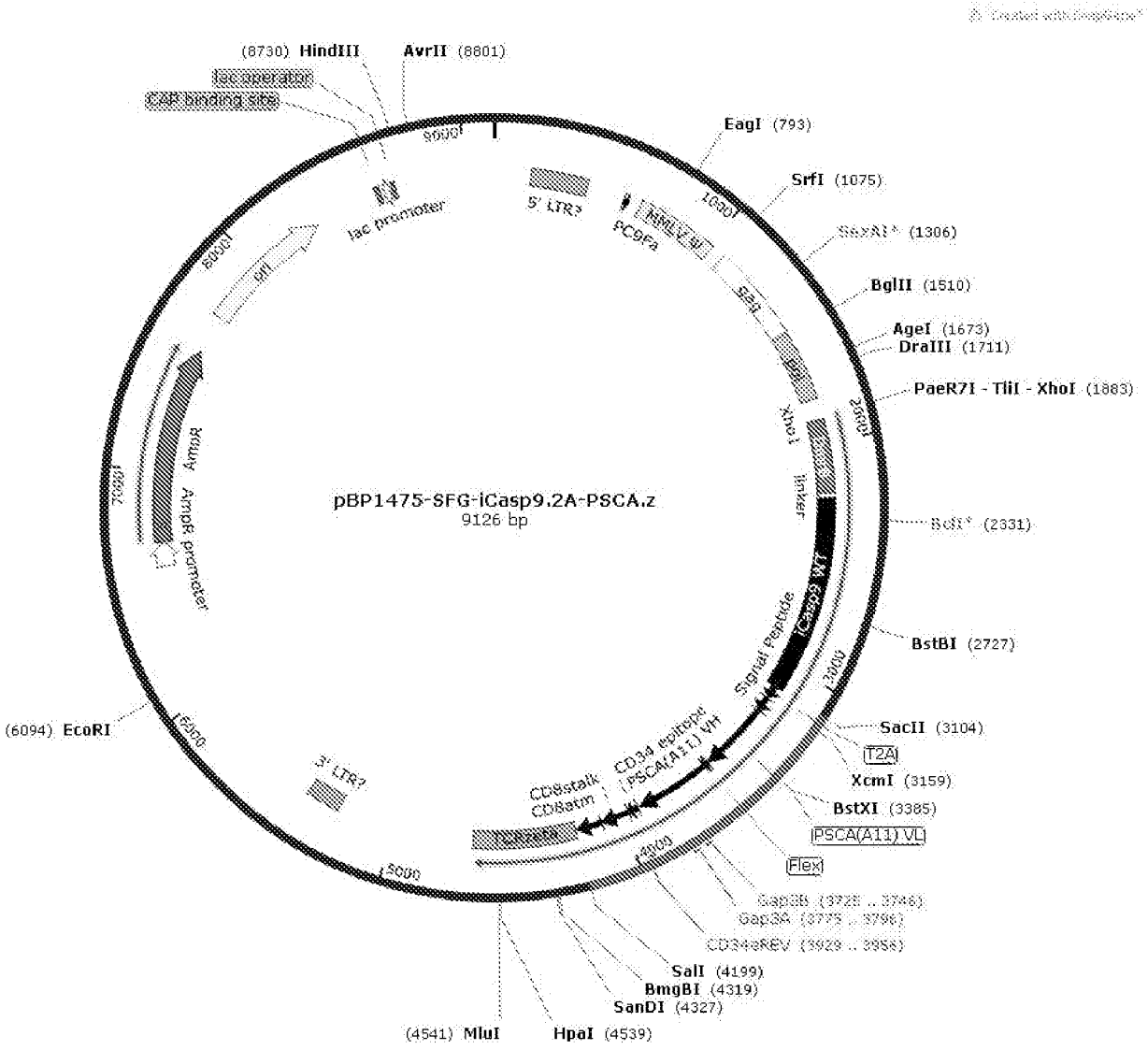
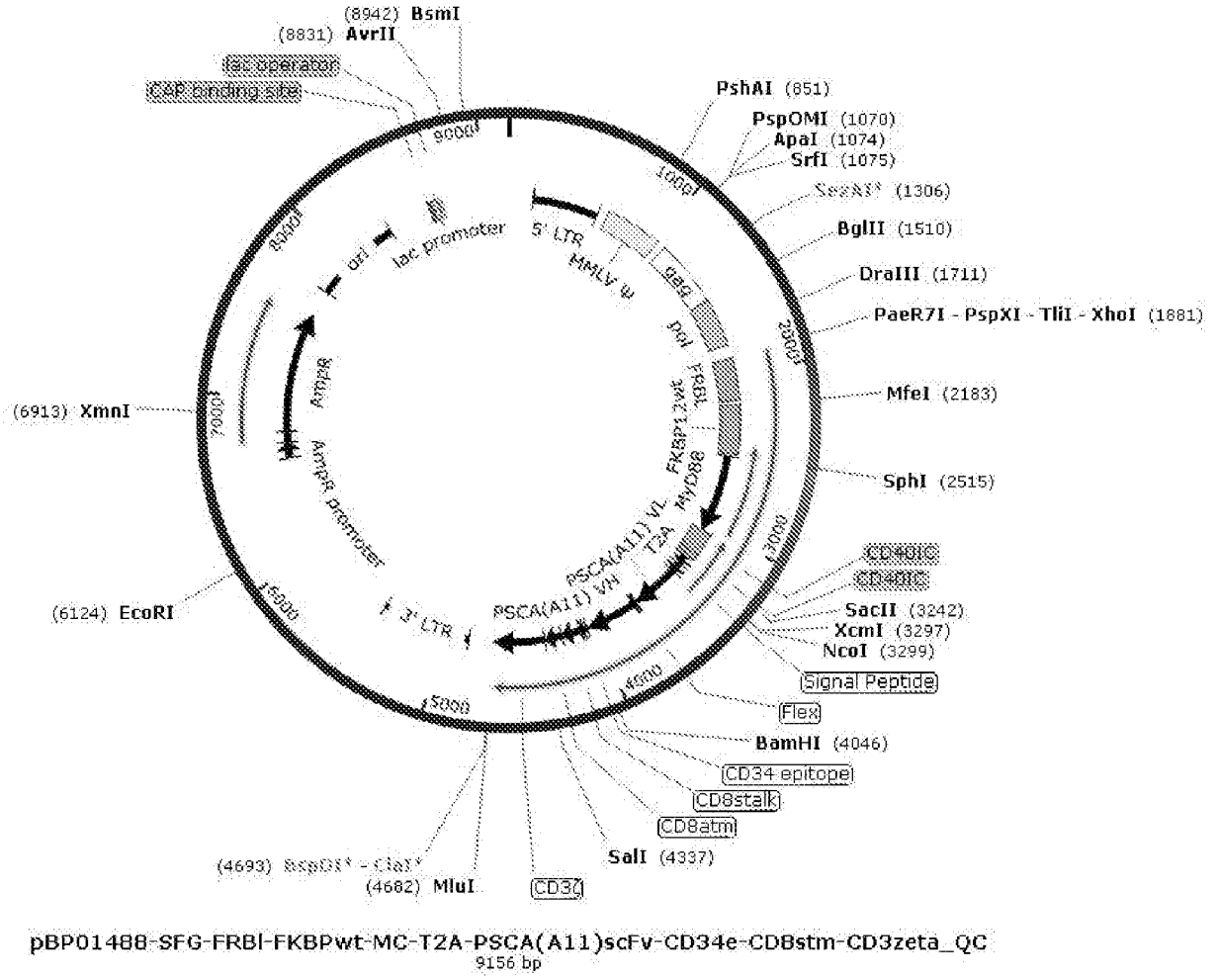
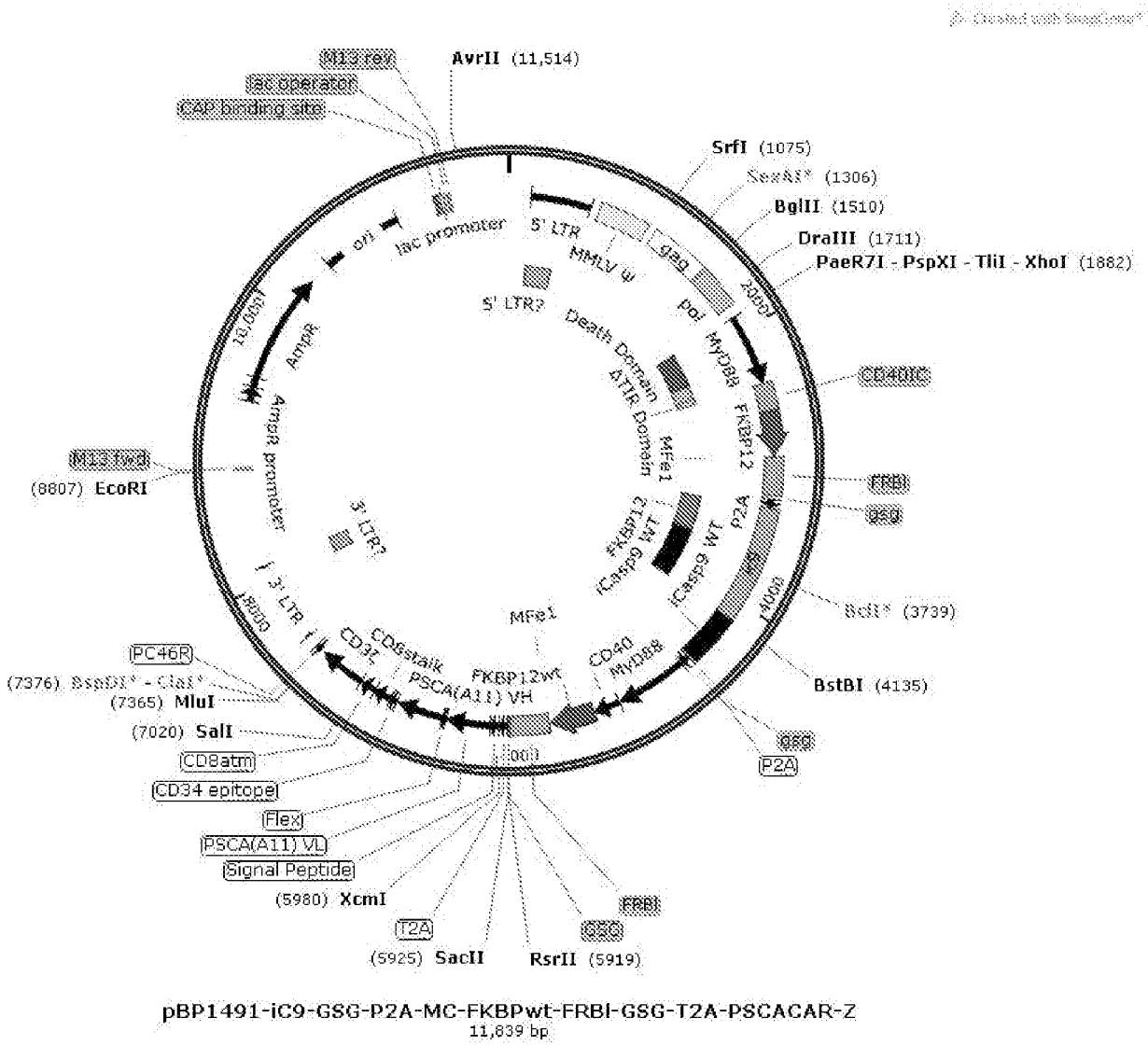

(8730) HindIII
AvrII (8801)
lac operator
CAP binding site
EagI (793)
SrfI (1075)
(1306)
BglII (1510)
AgeI (1673)
DraIII (1711)
PaeR7I - TliI - XhoI (1883)
(2331)
BstBI (2727)
SacII (3104)
T2A
XcmI (3159)
BstXI (3385)
PSCA(A11) VL
Flex
(6094) EcoRI
lac promoter
5' LTR?
PC9Fa
MMLV ψ
SAS
Xho I
linker
Signal Peptide
iCasp9 VH
CD34 epitope
PSCA(A11) VH
CD8stalk
CD8atm
3' LTR?
AmpR
AmpR promoter
pBP1475-SFG-iCasp9.2A-PSCA.z
9126 bp
SalI (4199)
BmgBI (4319)
SanDI (4327)
(4541) MluI
HpaI (4539)

Fig. 98



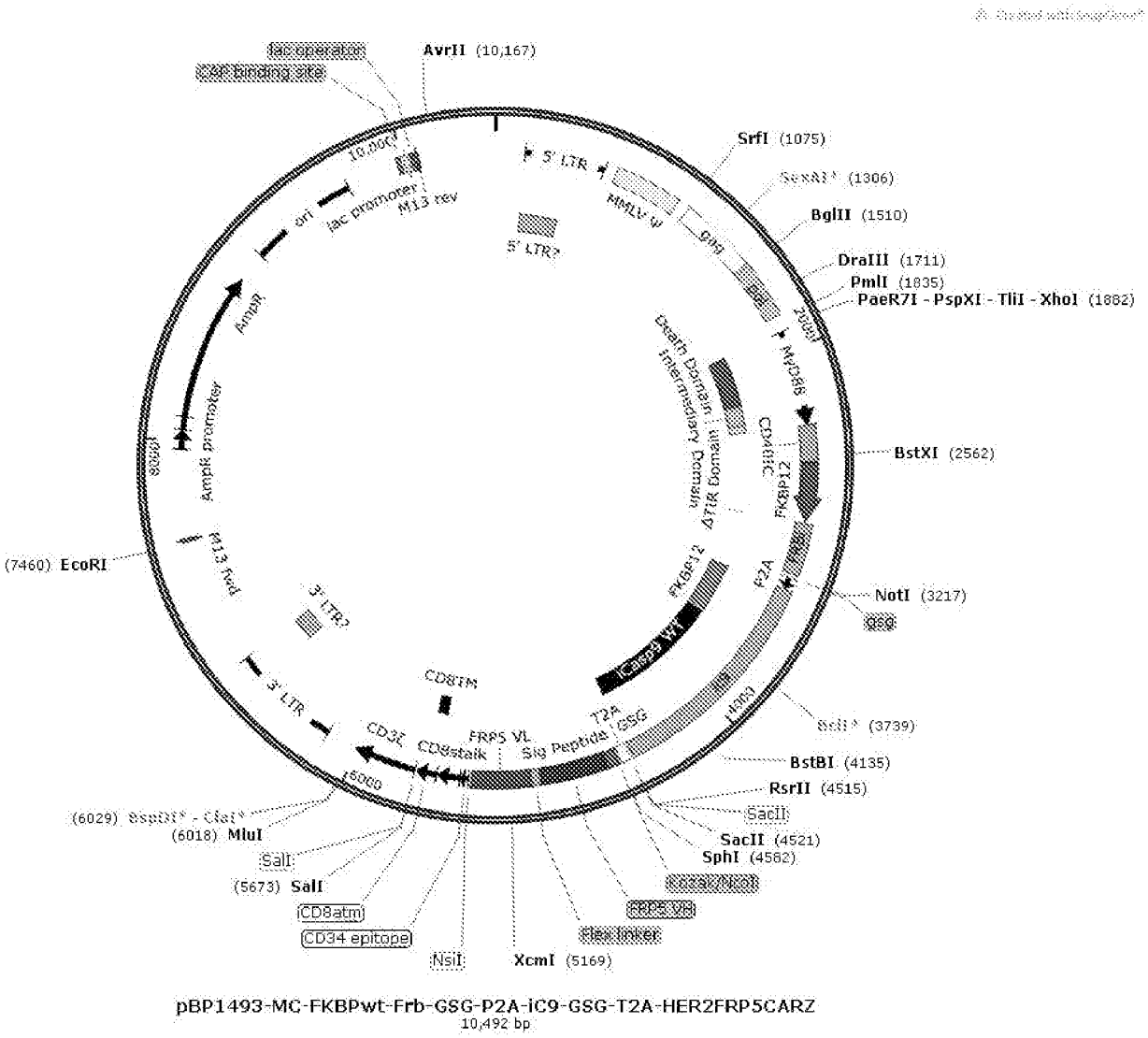
pBP01488-SFG-FRBl-FKBPwt-MC-T2A-PSCA(A11)scFv-CD34e-CD8stm-CD3zeta_QC
9156 bp

Fig. 99



pBP1491-iC9-GSG-P2A-MC-FKBPwt-FRBI-GSG-T2A-PSCACAR-Z
11,839 bp

Fig. 100



pBP1493-MC-FKBPwt-Frb-GSG-P2A-iC9-GSG-T2A-HER2FRP5CARZ
10,492 bp

Fig. 101

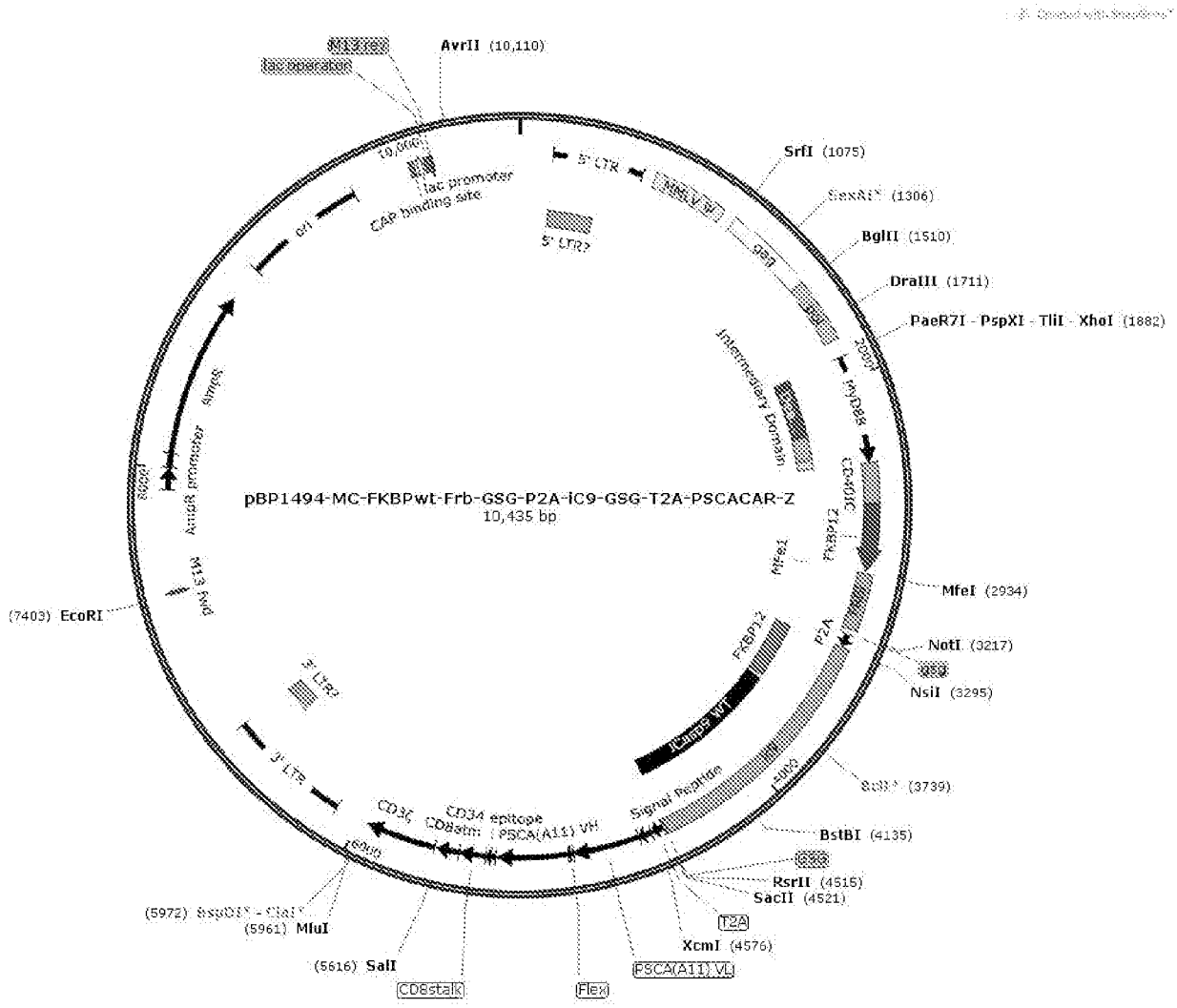

AvrII (10,110)
lac operator
lac promoter
CAP binding site
5' LTR
SrfI (1075)
(1306)
BglII (1510)
DraIII (1711)
PaeR7I - PspXI - TliI - XhoI (1882)
Intermediary Domain
MyD88
CD40
FKBP12
MfeI
MfeI (2934)
NotI (3217)
NsiI (3295)
P2A
Signal Peptide
BstBI (4135)
RsrII (4515)
SacII (4521)
T2A
XcmI (4576)
PSCA(A11) VL
Flex
CD8stalk
(5616) SalI
(5961) MluI
(5972)
CD3ζ
CD34 epitope
CD8atm
PSCA(A11) VH
3' LTR
(7403) EcoRI
M13 fwd
AmpR promoter
AmpR
pBP1494-MC-FKBPwt-Frb-GSG-P2A-iC9-GSG-T2A-PSCACAR-Z
10,435 bp

Fig. 102

AvrII (10,108)
SrfI (1075)
BglII (1510)
DraIII (1711)
PaeR7I - PspXI - TliI - XhoI (1883)
MfeI (1897)
NotI (3215)
NsiI (3293)
BstBI (4133)
RsrII (4513)
SacII (4519)
(7401) EcoRI
(5970)
(5959) MluI
(5614) SalI
CDBstalk
Flex
PSCA(A11) VL
T2A
pBP1757-FRBI-FKBPwt-MC-GSG-P2A-iC9-GSG-T2A-PSCACAR-Z
10,433 bp

Fig. 103

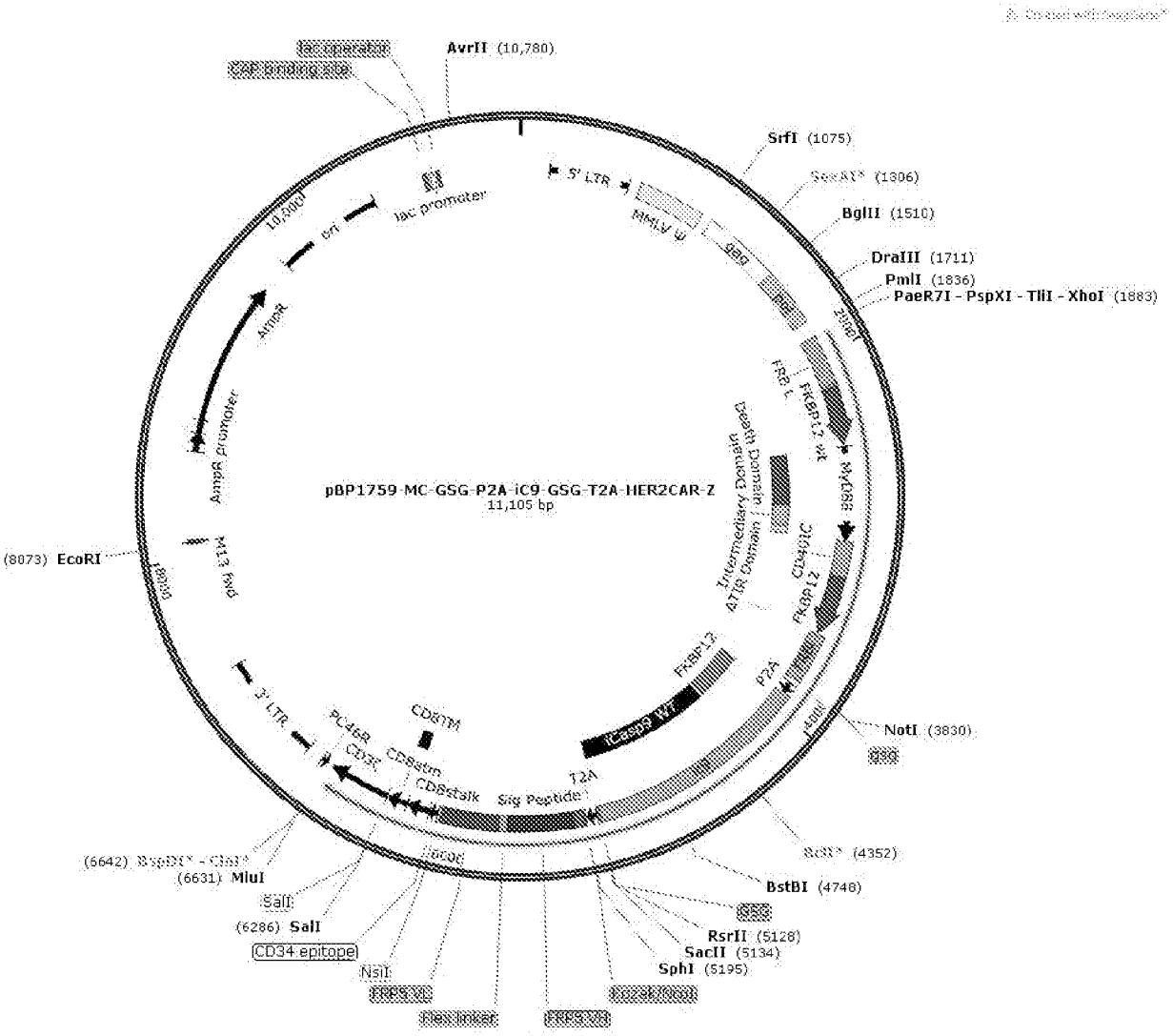

AvrII (10,780)
SrfI (1075)
BglII (1510)
DraIII (1711)
PmlI (1836)
PaeR7I - PspXI - TliI - XhoI (1883)
5' LTR
MMLV ψ
gag
lac promoter
ori
AmpR
AmpR promoter
M13 fwd
pBP1759-MC-GSG-P2A-iC9-GSG-T2A-HER2CAR-Z
11,105 bp
Intermediary Domain
ATIR Domain
Death Domain
FKBP12 wt
FKBP12
P2A
iCasp9 WT
T2A
Sig Peptide
CD8TM
CD8stm
CD8stalk
PC46R
CD3C
3' LTR
(8073) EcoRI
NotI (3830)
BstBI (4748)
RsrII (5128)
SacII (5134)
SphI (5195)
(6642)
(6631) MluI
SalI
(6286) SalI
CD34 epitope
NsiI
Flex linker

Fig. 104

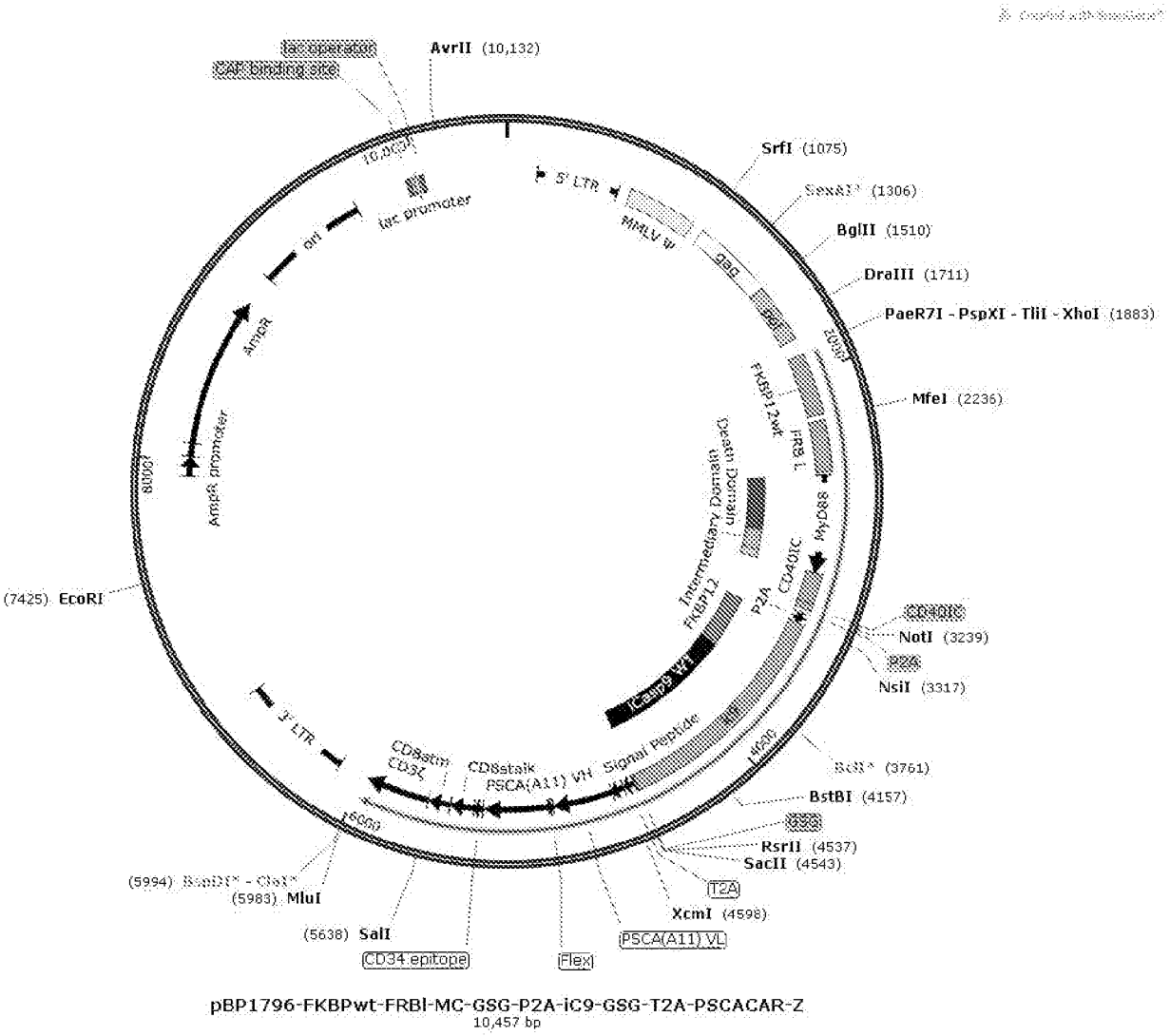

AvrII (10,132)
SrfI (1075)
BglII (1510)
DraIII (1711)
PaeR7I - PspXI - TliI - XhoI (1883)
MfeI (2236)
NotI (3239)
NsiI (3317)
BstBI (4157)
RsrII (4537)
SacII (4543)
XcmI (4598)
(7425) EcoRI
(5994)
(5983) MluI
(5638) SalI
CD34 epitope
Flex
PSCA(A11) VL
T2A
PSCA(A11) VH
Signal Peptide
CD8stalk
CD8atm
CD3ζ
3' LTR
AmpR promoter
AmpR
ori
lac promoter
5' LTR
MMLV w
gag
FKBP12wt
FRB L
Death Domain
Intermediary Domain
FKBP12
P2A
CD40IC
MyD88
pBP1796-FKBPwt-FRBl-MC-GSG-P2A-iC9-GSG-T2A-PSCACAR-Z
10,457 bp

Fig. 105

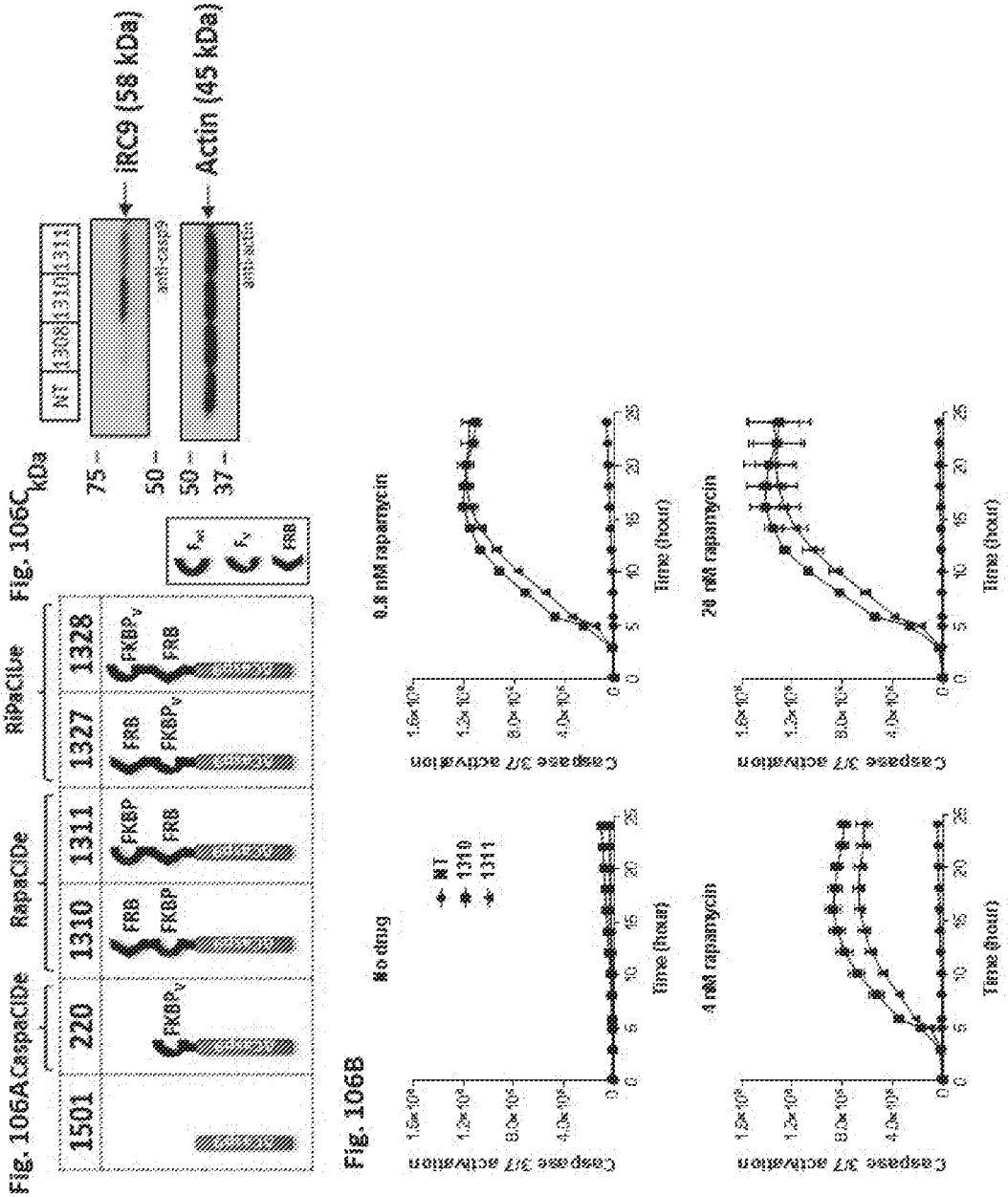


Fig. 106A CaspaCIDe
RapaCIDe
RiPaCIve
1501
220
1310
1311
1327
1328
FKBP$_V$
FRB
FKBP
Fig. 106C
kDa
75 –
50 –
50 –
37 –
NT
1308
1310
1311
iRC9 (58 kDa)
Actin (45 kDa)
anti-caspase
anti-actin
f_M
f_V
FRB
Fig. 106B
No drug
0.8 nM rapamycin
4 nM rapamycin
20 nM rapamycin
NT
1310
1311
Caspase 3/7 activation
Time (hour)

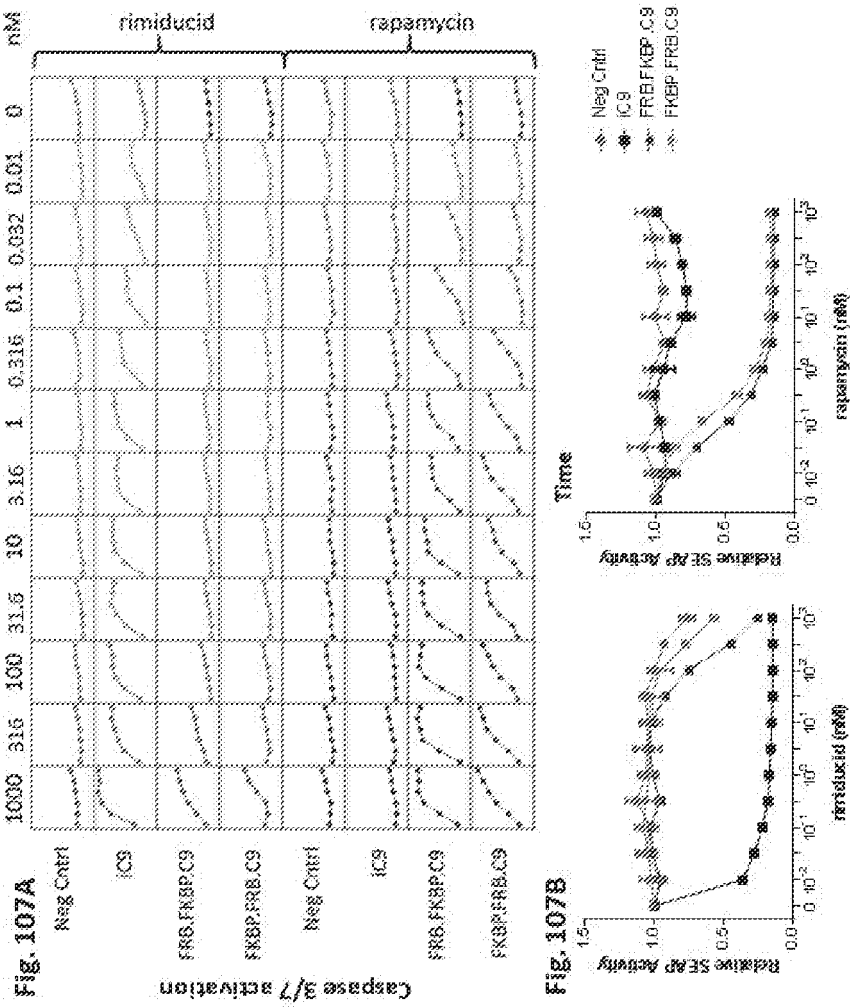


Fig. 107A
rimiducid
rapamycin
nM
1000
316
100
31.6
10
3.16
1
0.316
0.1
0.032
0.01
0
Neg Cntrl
iC9
FRB.FKBP.C9
FKBP.FRB.C9
Caspase 3/7 activation
Fig. 107B
Time
Neg Cntrl
iC9
FRB.FKBP.C9
FKBP.FRB.C9
Relative SEAP Activity
rimiducid (nM)
rapamycin (nM)

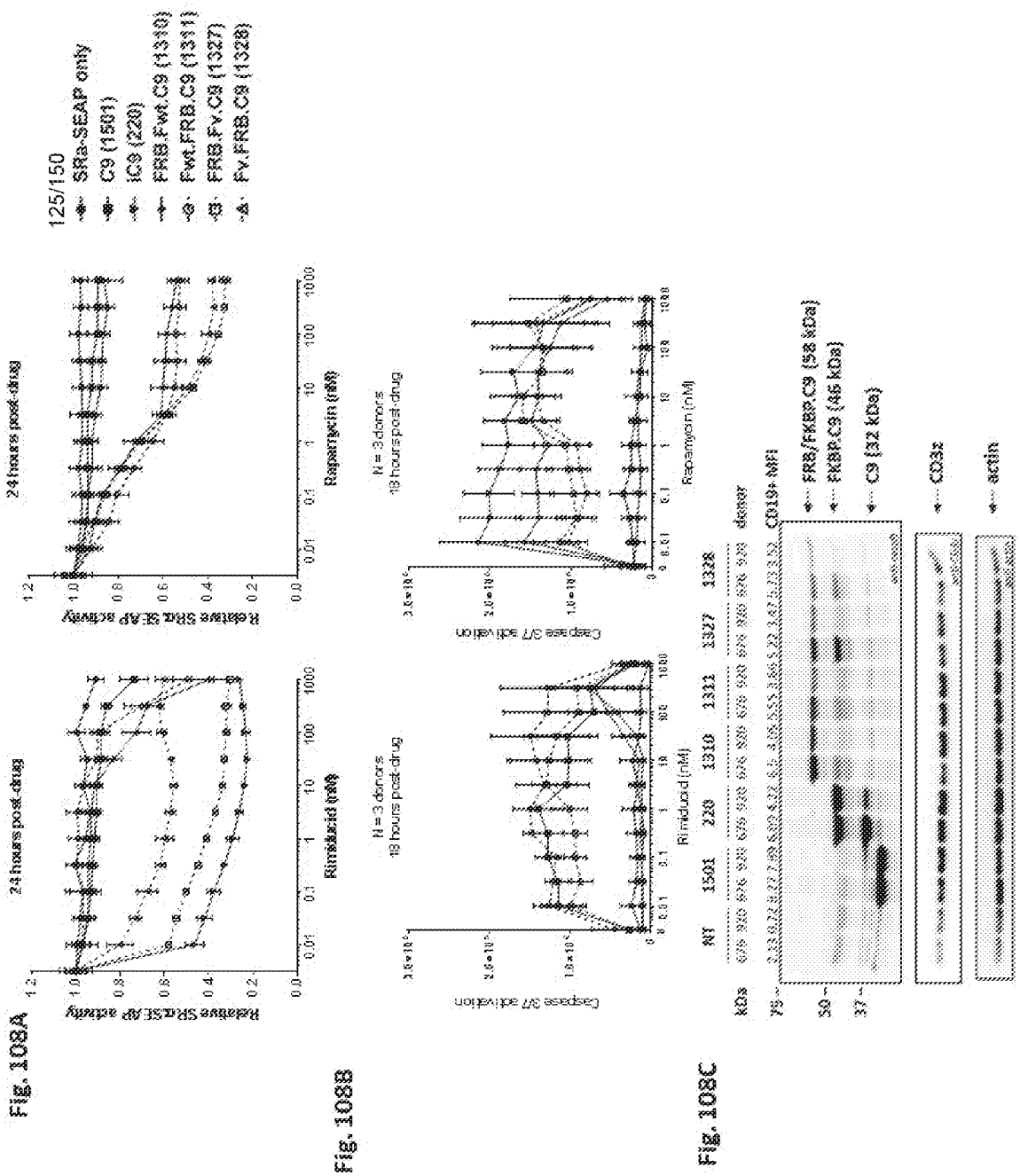


Fig. 108A

Fig. 108B

Fig. 108C

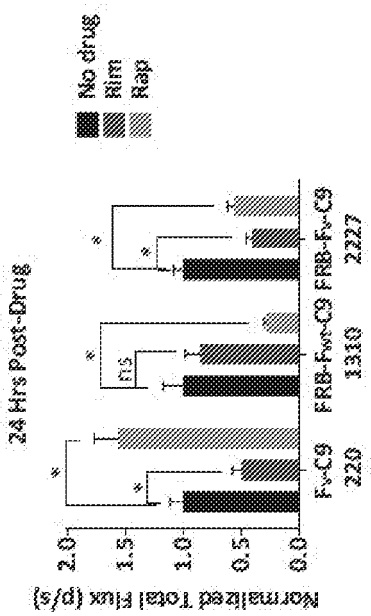


Fig 109B

Fig. 109A

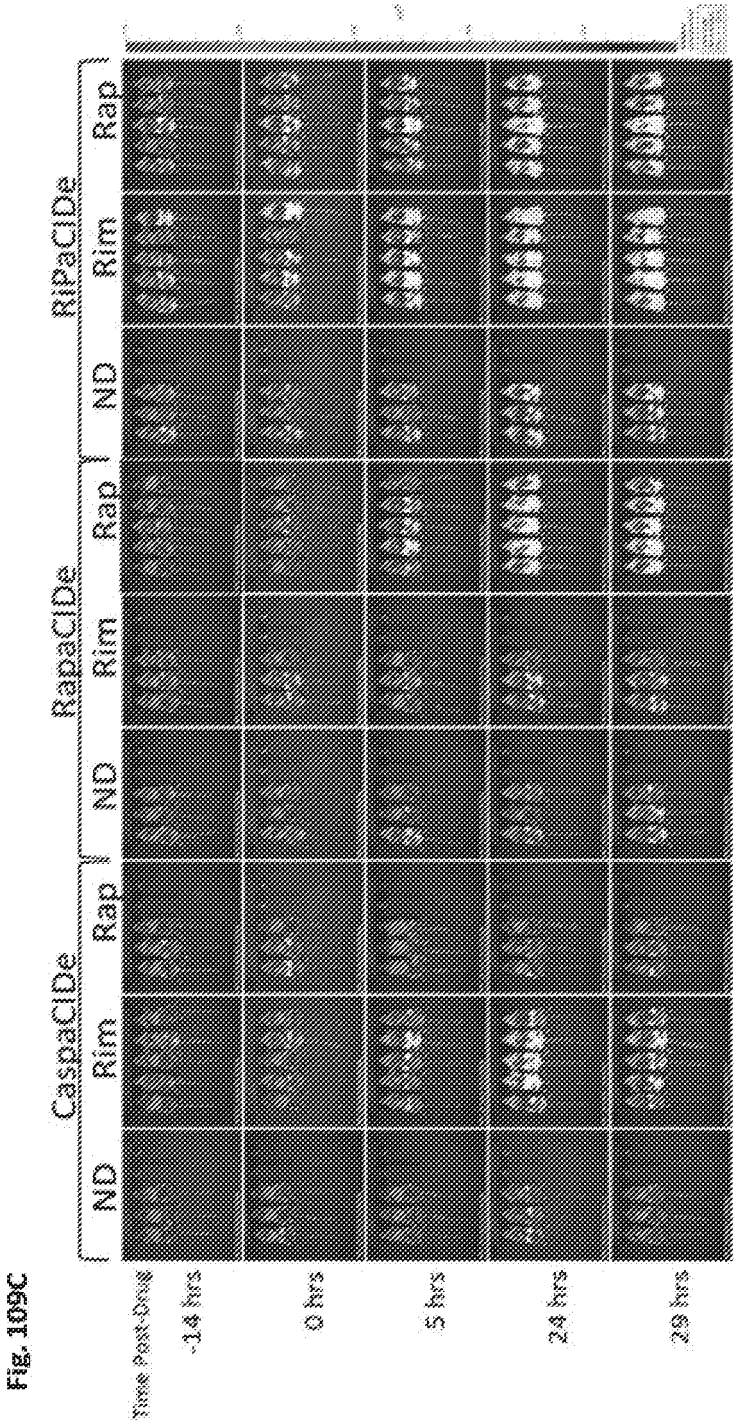


Fig. 109C

Fig. 109C

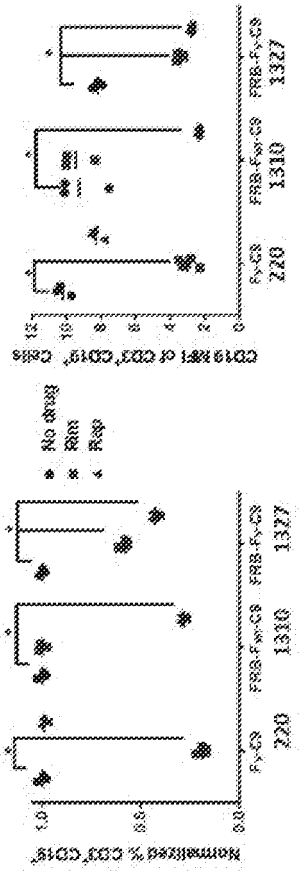

Normalized % CD3+CD19+
1.0
0.5
0.0
Fy-C3
220
FRB-Fy-C3
1310
FRB-Fy-C3
1327
No drug
Rim
Rap
CD19 MFI of CD3+CD19+ Cells
12
10
8
6
4
2
0
Fy-C3
220
FRB-Fy-C3
1310
FRB-Fy-C3
1327

Fig. 109D

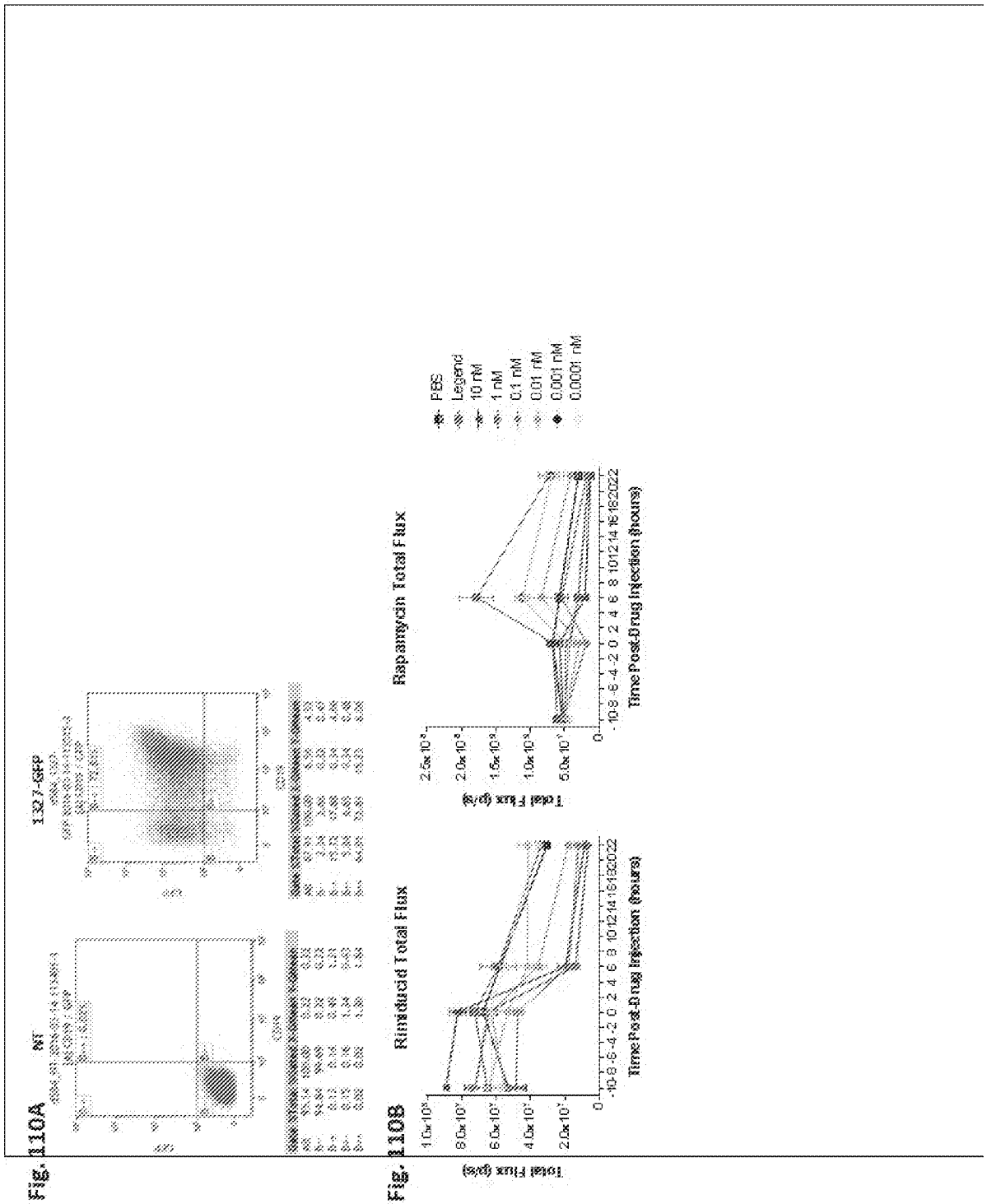


Fig. 110A
WT
1327-GFP
Fig. 110B
Rimducid Total Flux
Rapamycin Total Flux
Total Flux (p/s)
Time Post-Drug Injection (hours)
PBS
Legend
10 nM
1 nM
0.1 nM
0.01 nM
0.001 nM
0.0001 nM

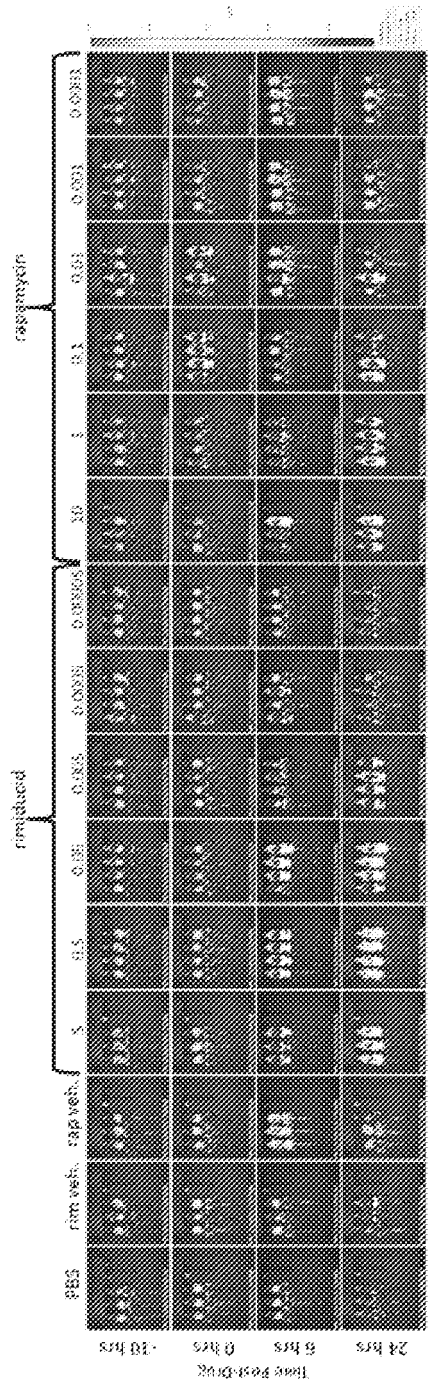

rimiducid
rapamycin
PBS
rim veh.
rap veh.
5
0.5
0.05
0.005
0.0005
0.00005
10
1
0.1
0.01
0.001
0.0001
-10 hrs
0 hrs
6 hrs
24 hrs
Time Post-Drug

Fig. 110C

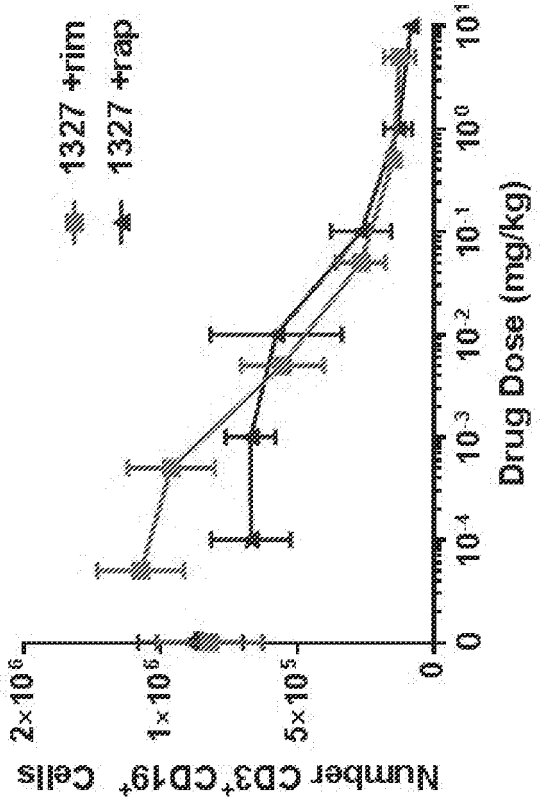

1327 +rim
1327 +rap
Number CD3+CD19+ cells
2×10^6
1×10^6
5×10^5
0
Drug Dose (mg/kg)
0
10^-4
10^-3
10^-2
10^-1
10^0
10^1

Fig. 110D

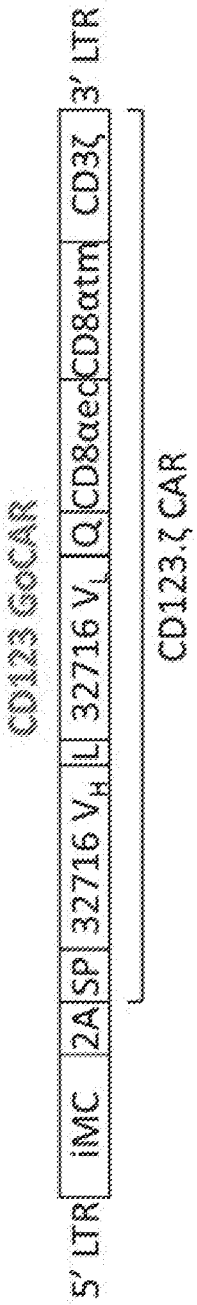

CD123 GoCAR
5' LTR
iMC
2A
SP
32716 V_H
L
32716 V_L
Q
CD8αecd
CD8αtm
CD3ζ
3' LTR
CD123.ζ CAR

Fig. 111

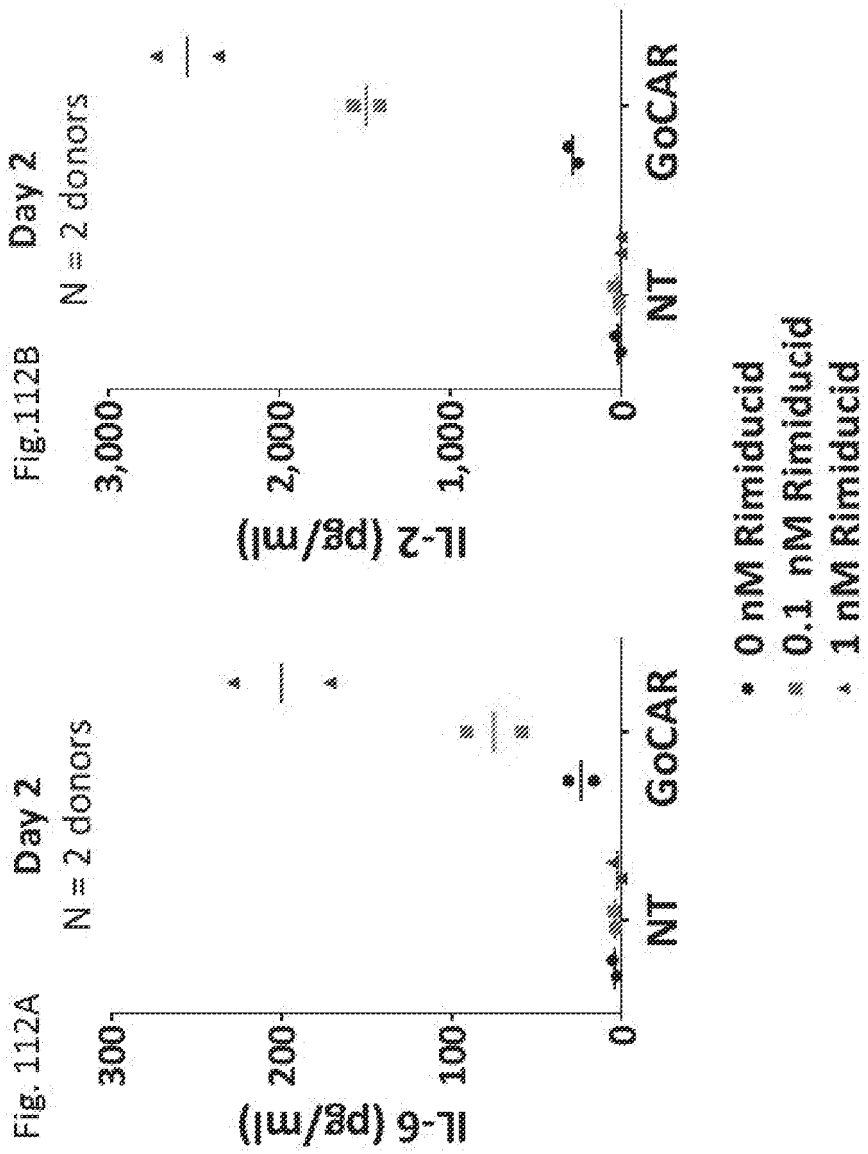


Fig. 112A
Day 2
N = 2 donors
IL-6 (pg/ml)
300
200
100
0
NT
GoCAR
Fig.112B
Day 2
N = 2 donors
IL-2 (pg/ml)
3,000
2,000
1,000
0
NT
GoCAR
0 nM Rimiducid
0.1 nM Rimiducid
1 nM Rimiducid

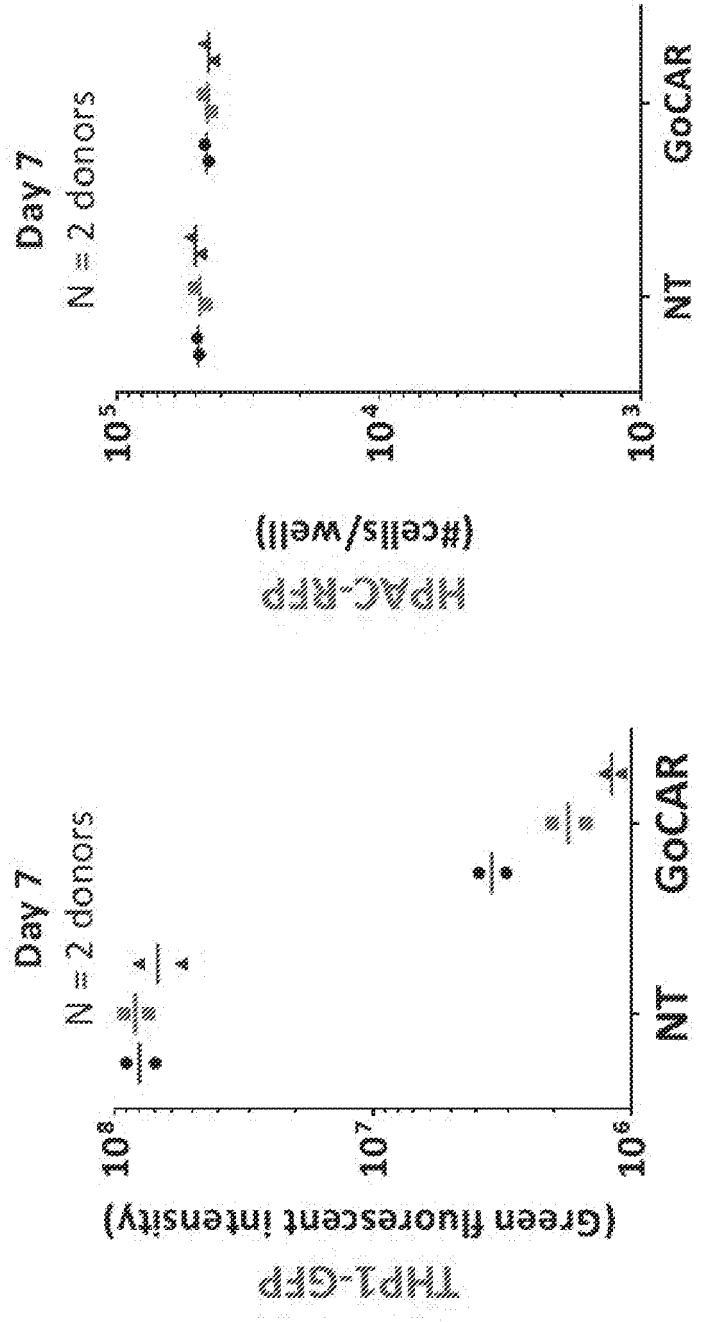
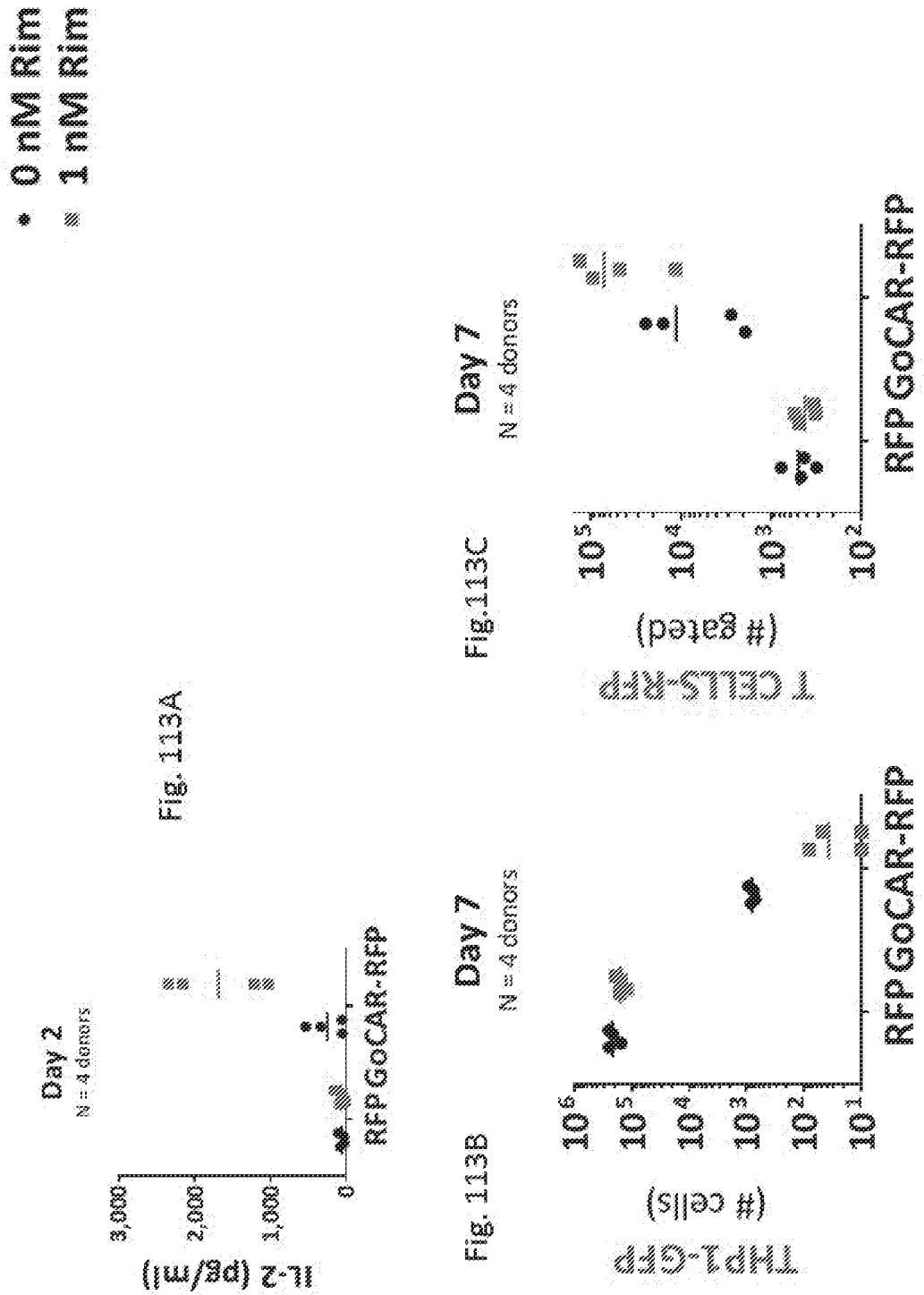


Fig. 112C Fig. 112D


0 nM Rim
1 nM Rim
Day 2
N = 4 donors
IL-2 (pg/ml)
3,000
2,000
1,000
0
RFP GoCAR-RFP
Fig. 113A
Day 7
N = 4 donors
THP1-GFP
(# cells)
10^6
10^5
10^4
10^3
10^2
10^1
RFP GoCAR-RFP
Fig. 113B
Day 7
N = 4 donors
T CELLS-RFP
(# gated)
10^5
10^4
10^3
10^2
RFP GoCAR-RFP
Fig.113C

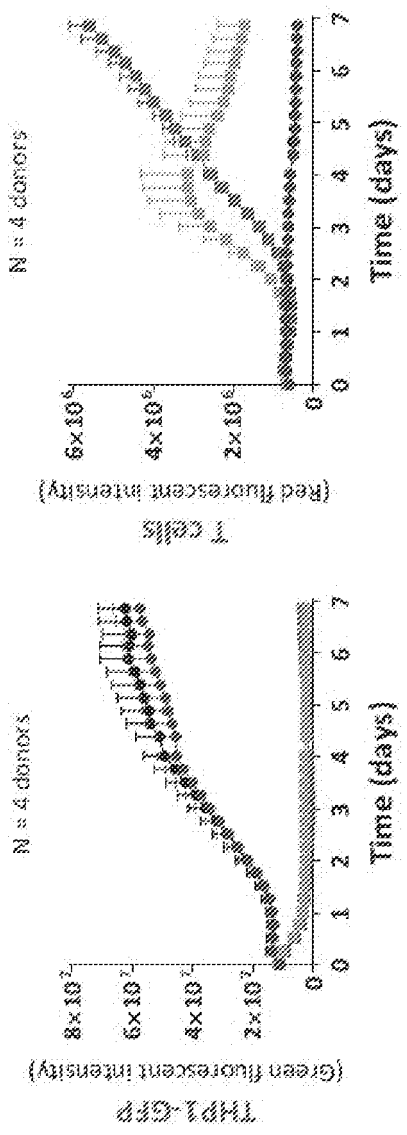


Fig. 113D

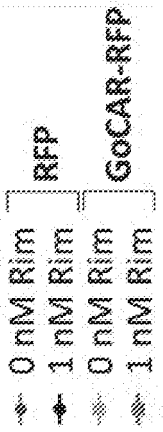


Fig. 113E

Fig. 114A

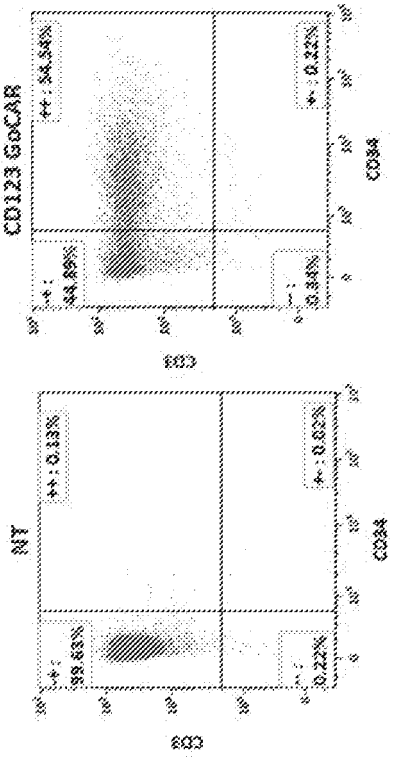
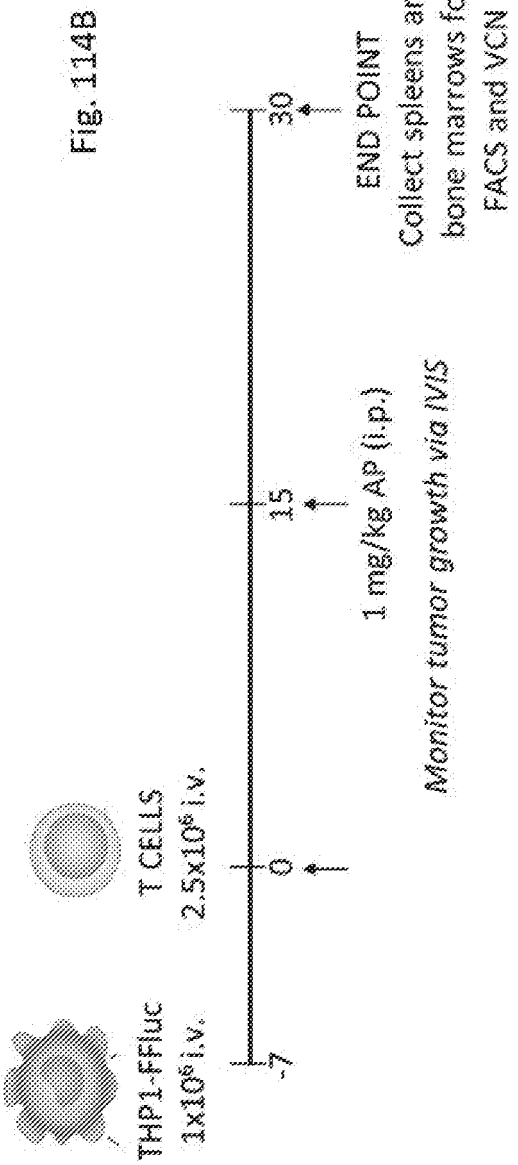


Fig. 114B



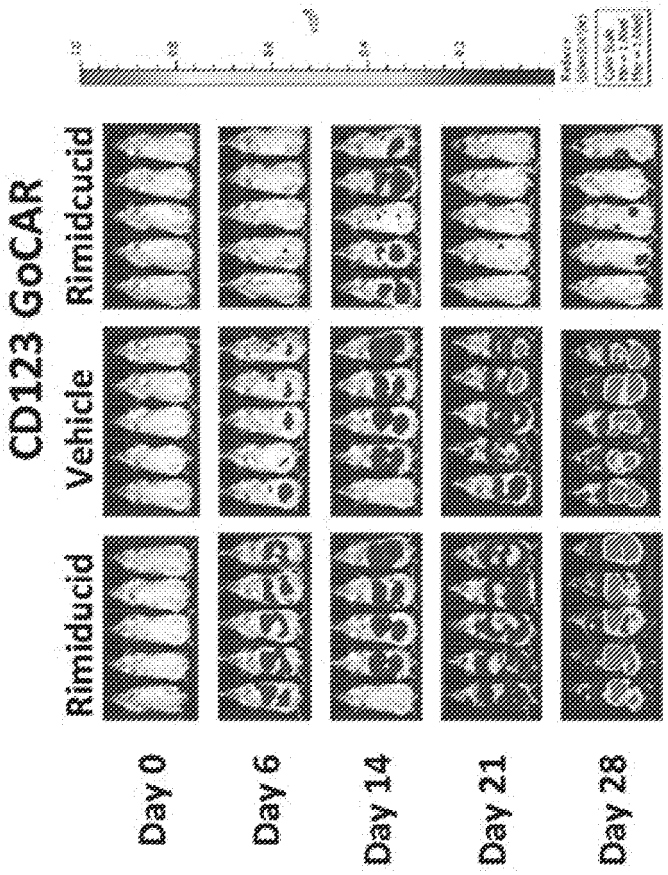

CD123 GoCAR
Rimiducid
Vehicle
Rimiducid
Day 0
Day 6
Day 14
Day 21
Day 28

Fig. 114C

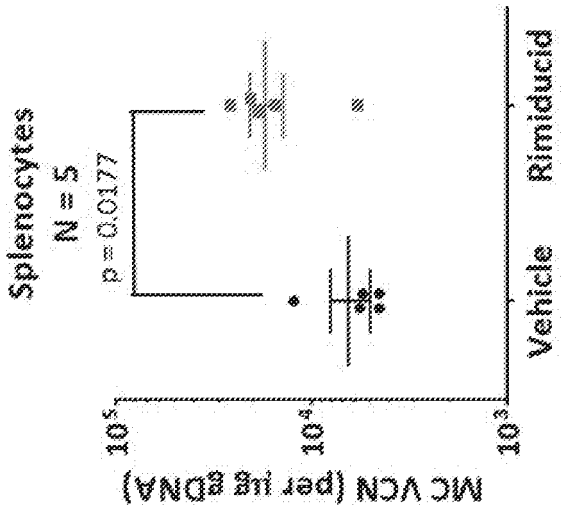


Fig. 114E

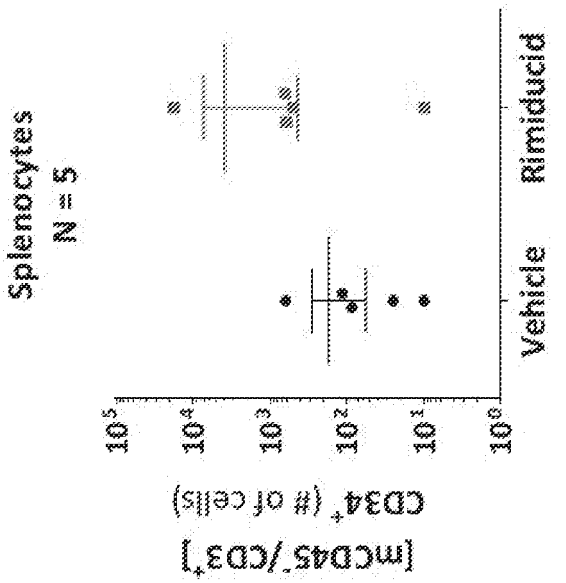


Fig. 114D

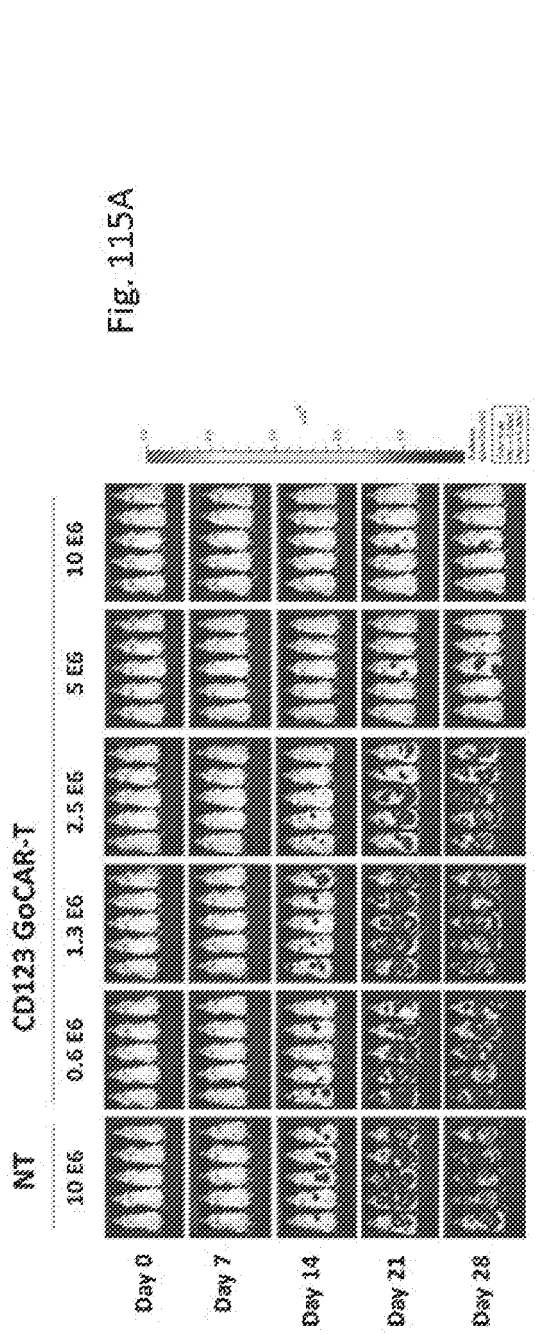


Fig. 115A

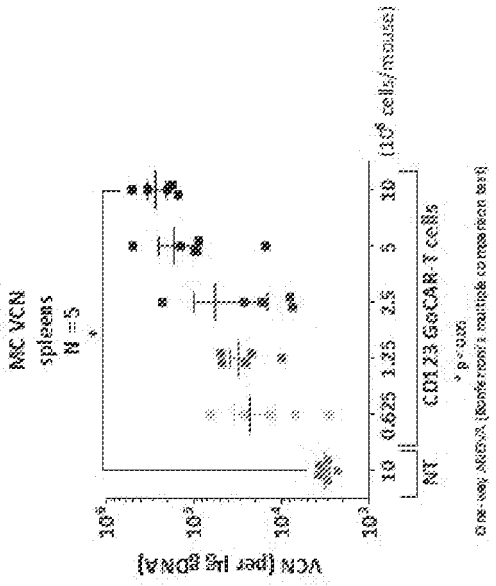


Fig. 115B

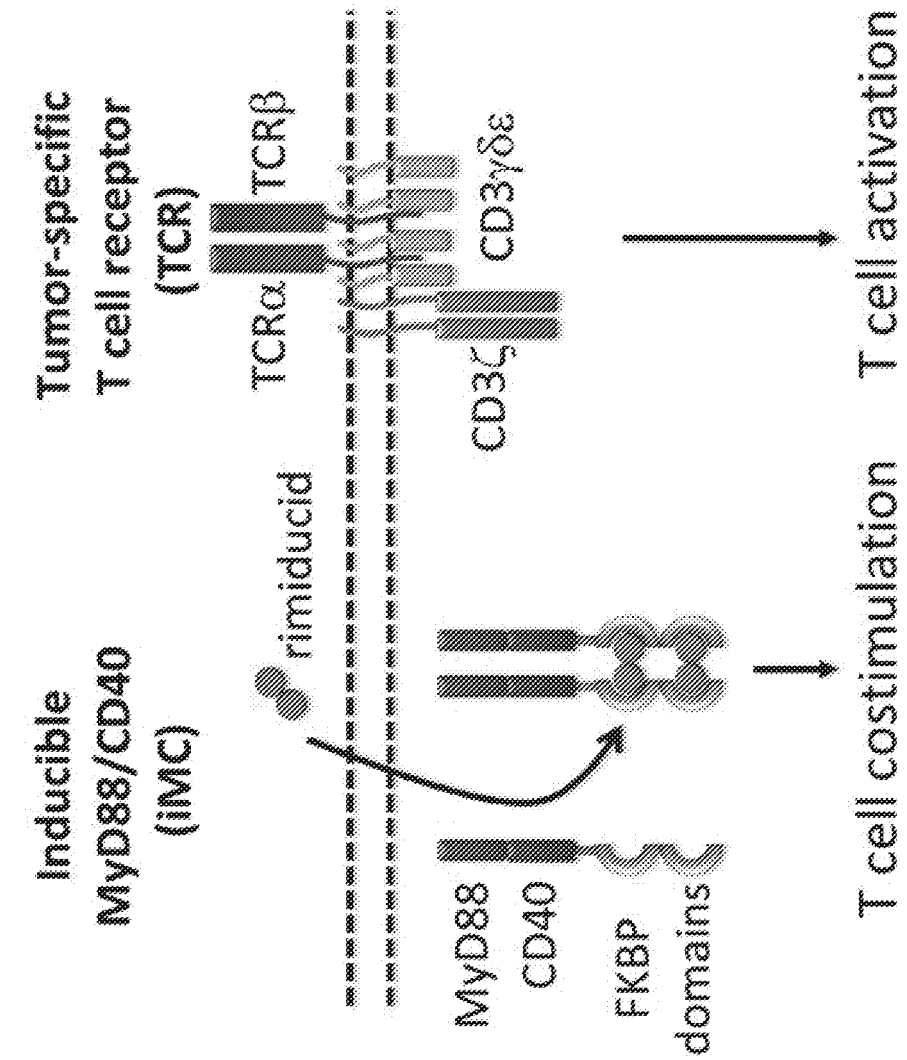

Inducible
MyD88/CD40
(iMC)
Tumor-specific
T cell receptor
(TCR)
TCRα
TCRβ
CD3ζ
CD3γδε
rimiducid
MyD88
CD40
FKBP
domains
T cell costimulation
T cell activation

Fig. 116

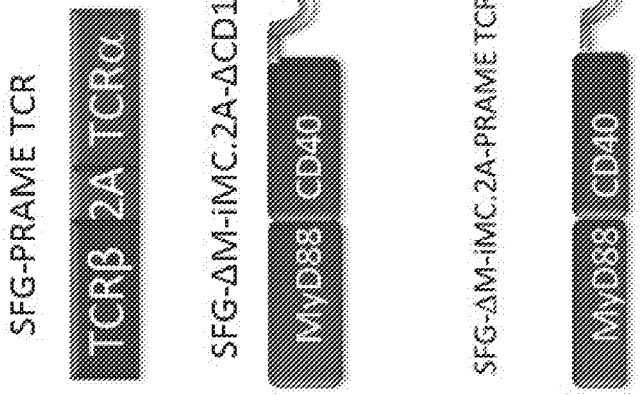


Fig. 117A

Fig. 117B

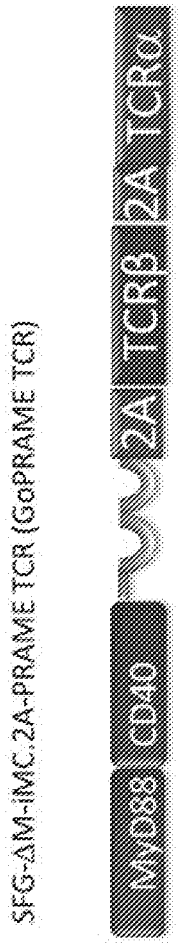


Fig. 117C

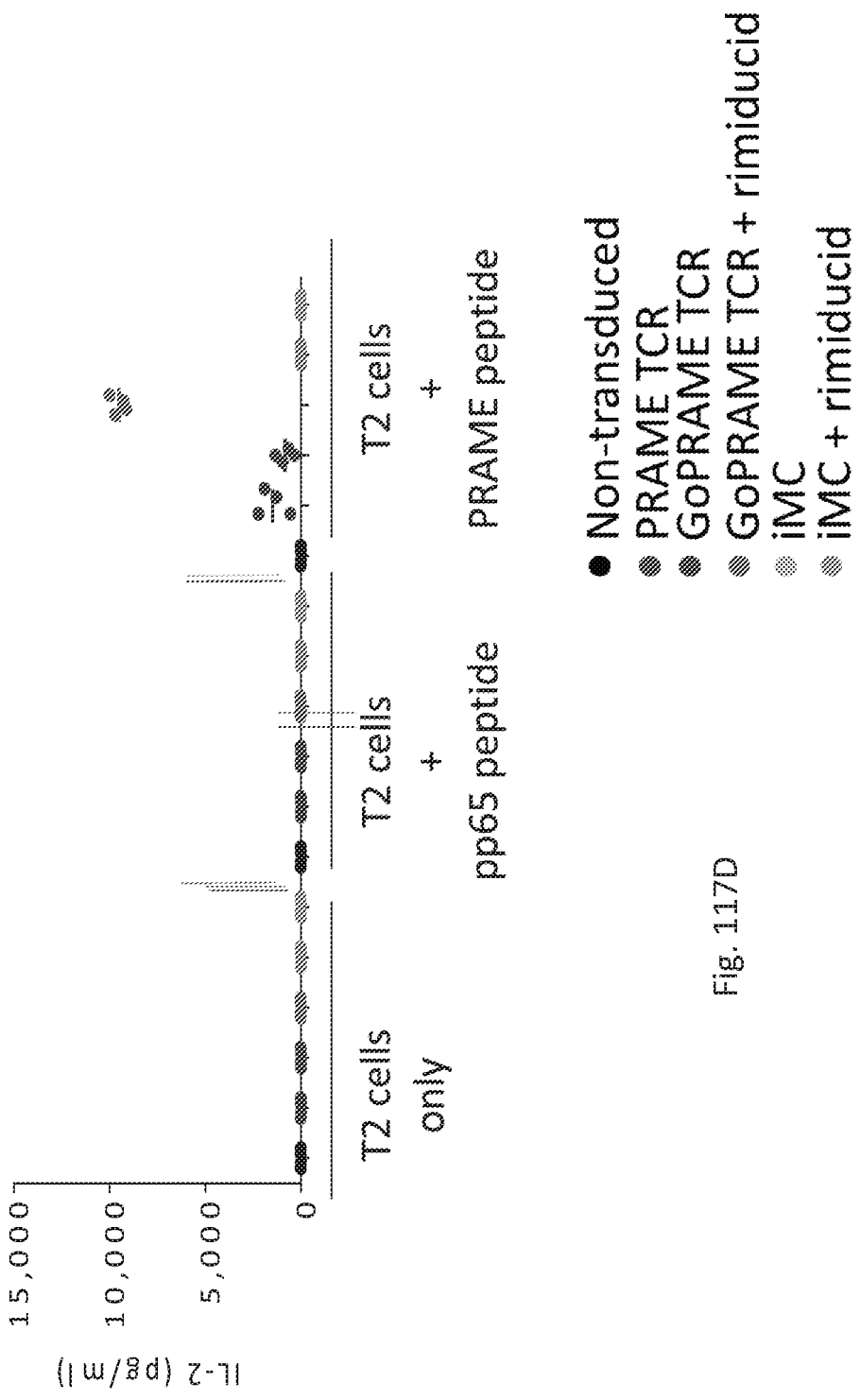

IL-2 (pg/ml)
15,000
10,000
5,000
0
T2 cells only
T2 cells + pp65 peptide
T2 cells + PRAME peptide
Non-transduced
PRAME TCR
GoPRAME TCR
GoPRAME TCR + rimiducid
iMC
iMC + rimiducid

Fig. 117D

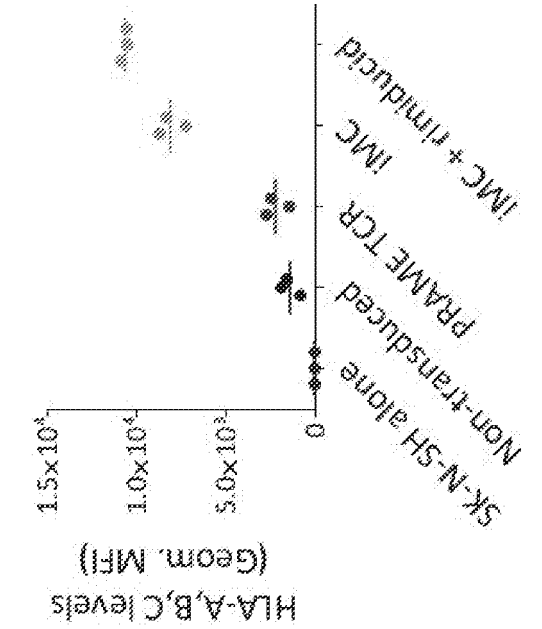


Fig. 118B

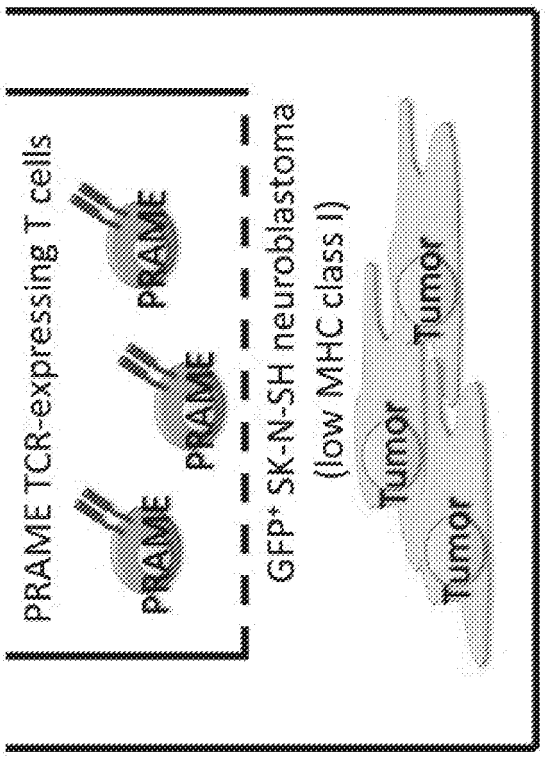


Fig. 118A

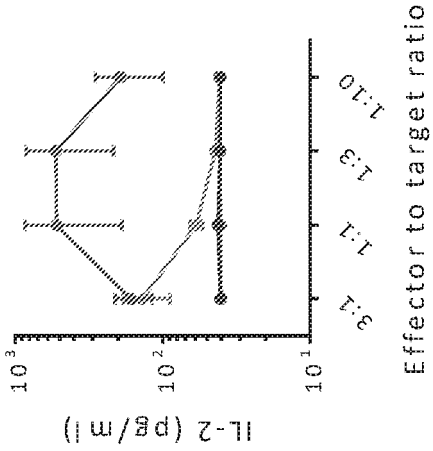


Fig. 119B

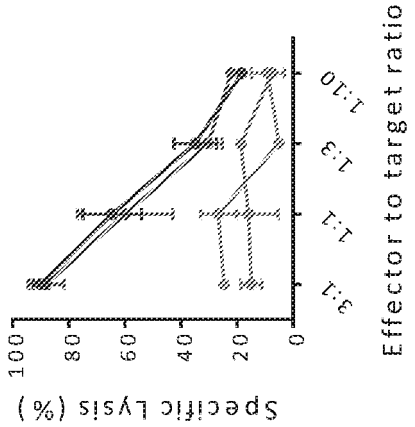


Fig. 119A

GoPRAME TCR
GoPRAME TCR + rimiducid
Go156 TCR
Go156 TCR + rimiducid

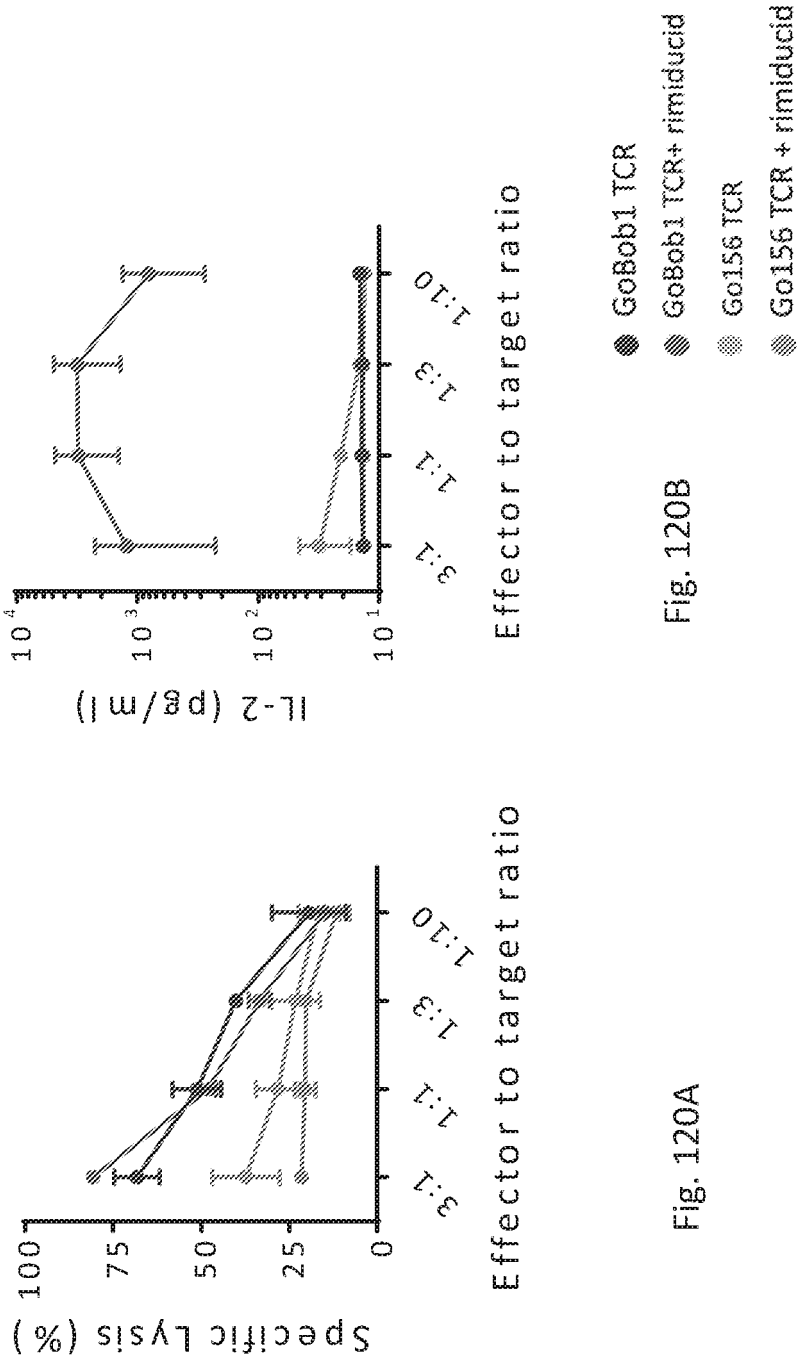


Fig. 120A

Fig. 120B

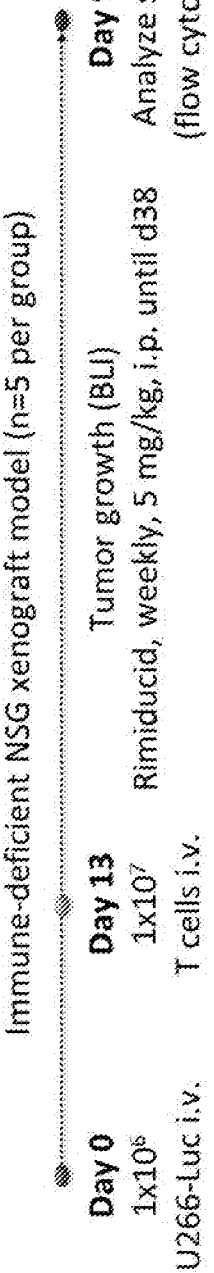

Immune-deficient NSG xenograft model (n=5 per group)
Day 0
1x10^6
U266-Luc i.v.
Day 13
1x10^7
T cells i.v.
Tumor growth (BLI)
Rimiducid, weekly, 5 mg/kg, i.p. until d38
Day 94
Analyze spleen
(flow cytometry)

Fig. 121A

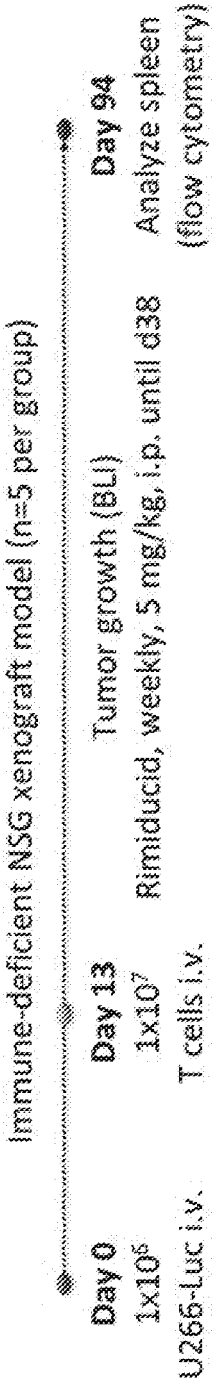

Immune-deficient NSG xenograft model (n=5 per group)
Day 0
1x10^6
U266-Luc i.v.
Day 13
1x10^7
T cells i.v.
Tumor growth (BLI)
Rimiducid, weekly, 5 mg/kg, i.p. until d38
Day 94
Analyze spleen
(flow cytometry)

Fig. 121A

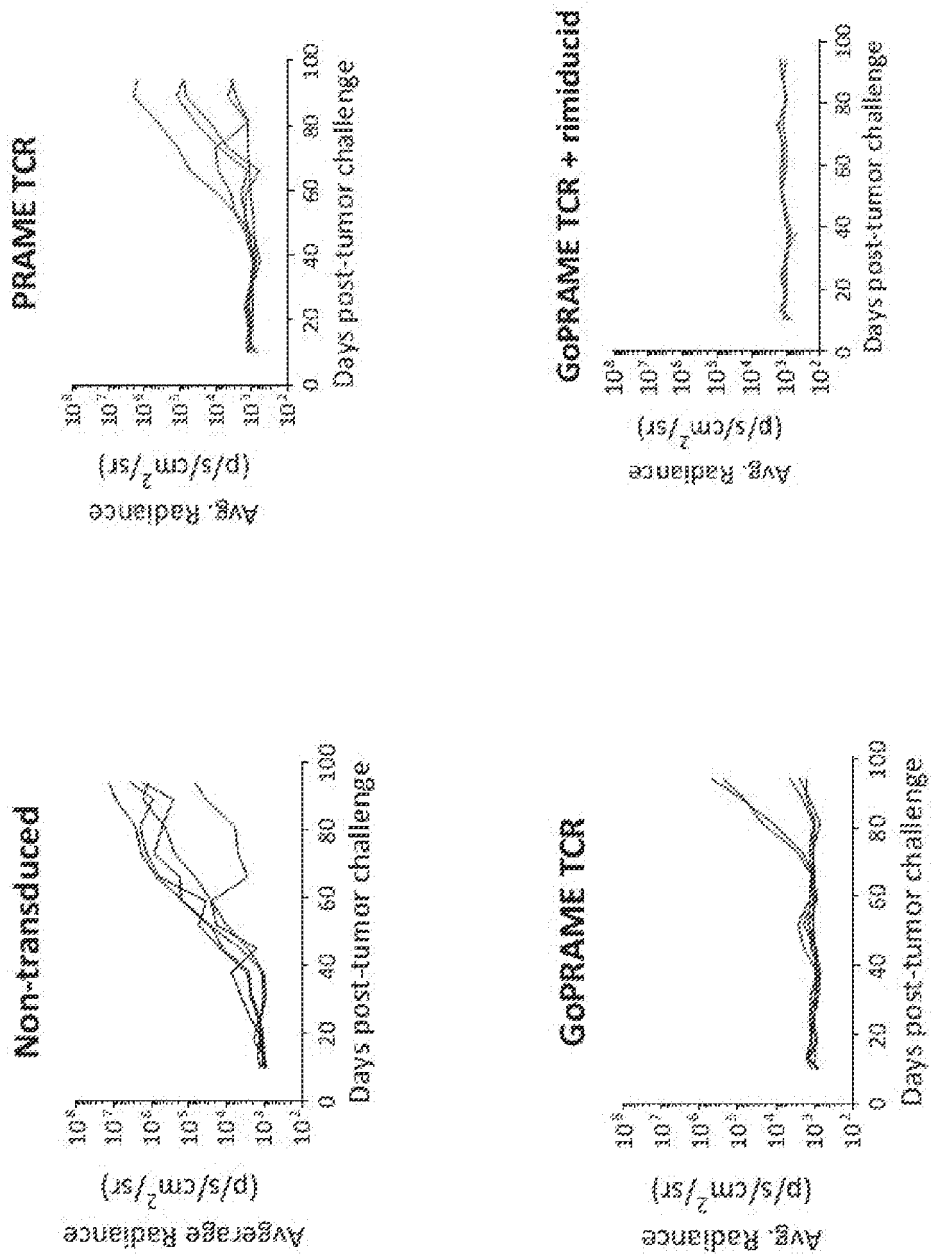

Non-transduced
PRAME TCR
GoPRAME TCR
GoPRAME TCR + rimiducid
Average Radiance (p/s/cm²/sr)
Avg. Radiance (p/s/cm²/sr)
Days post-tumor challenge
0
20
40
60
80
100

Fig. 121B

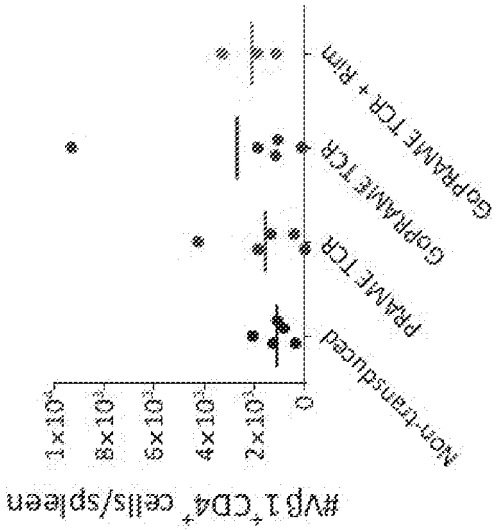


Fig. 121D

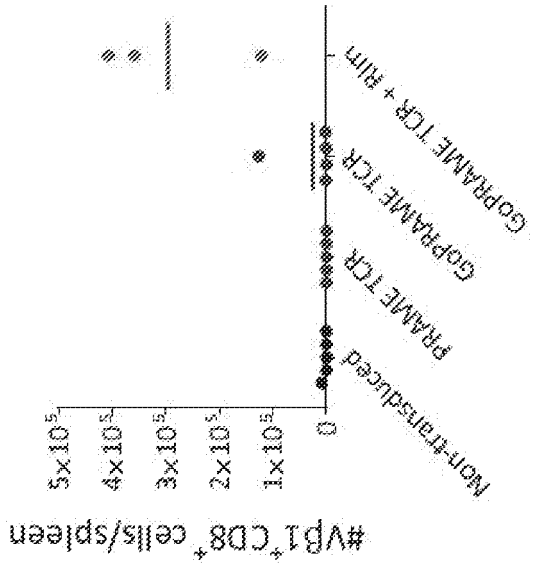


Fig. 121C