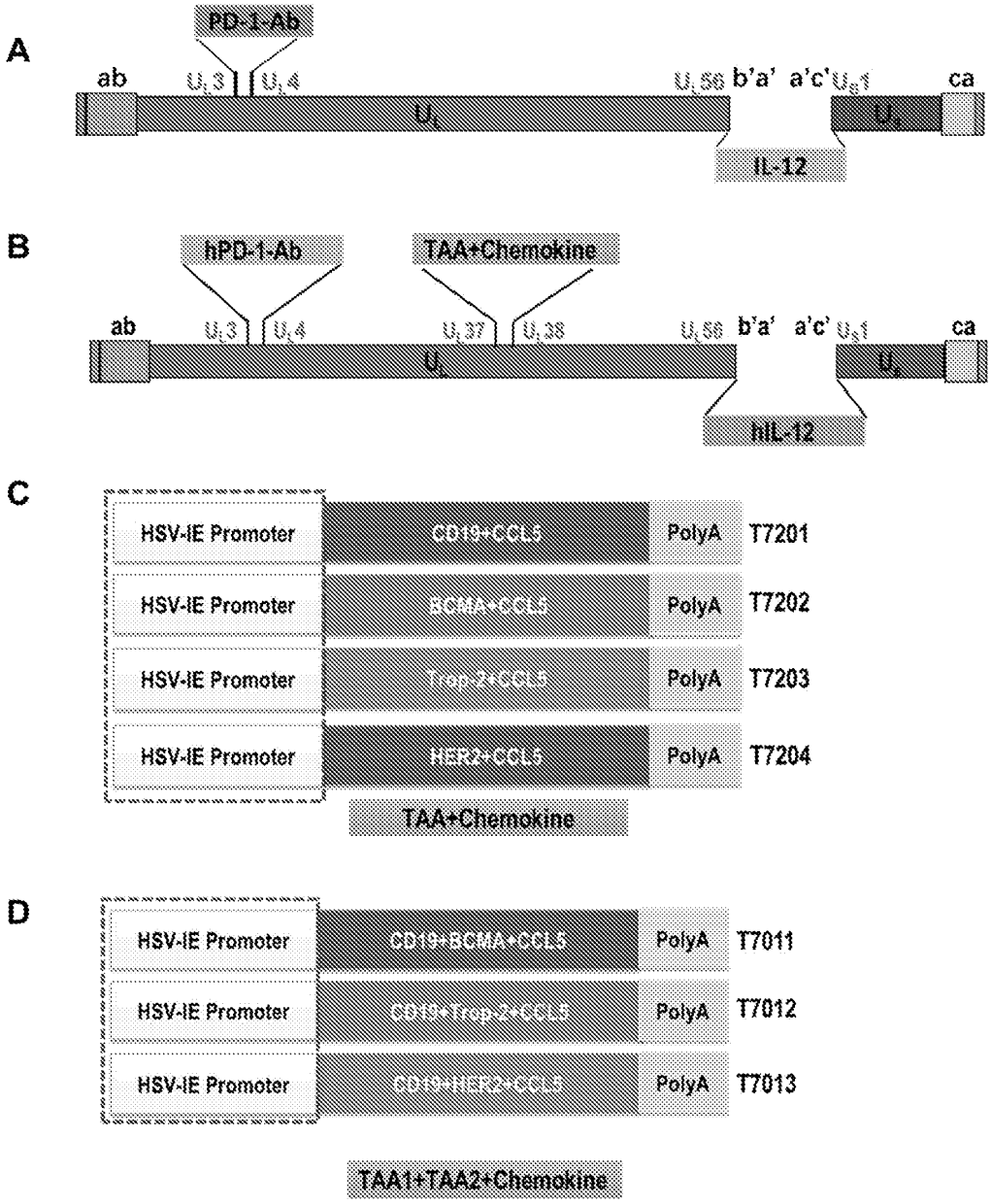

A
PD-1-Ab
ab
U_L3
U_L4
U_L
U_L56
b'a'
a'c'
U_S1
U_S
ca
IL-12
B
hPD-1-Ab
TAA+Chemokine
ab
U_L3
U_L4
U_L37
U_L38
U_L
U_L56
b'a'
a'c'
U_S1
U_S
ca
hIL-12
C
HSV-IE Promoter
CD19+CCL5
PolyA
T7201
HSV-IE Promoter
BCMA+CCL5
PolyA
T7202
HSV-IE Promoter
Trop-2+CCL5
PolyA
T7203
HSV-IE Promoter
HER2+CCL5
PolyA
T7204
TAA+Chemokine
D
HSV-IE Promoter
CD19+BCMA+CCL5
PolyA
T7011
HSV-IE Promoter
CD19+Trop-2+CCL5
PolyA
T7012
HSV-IE Promoter
CD19+HER2+CCL5
PolyA
T7013
TAA1+TAA2+Chemokine

FIG. 1

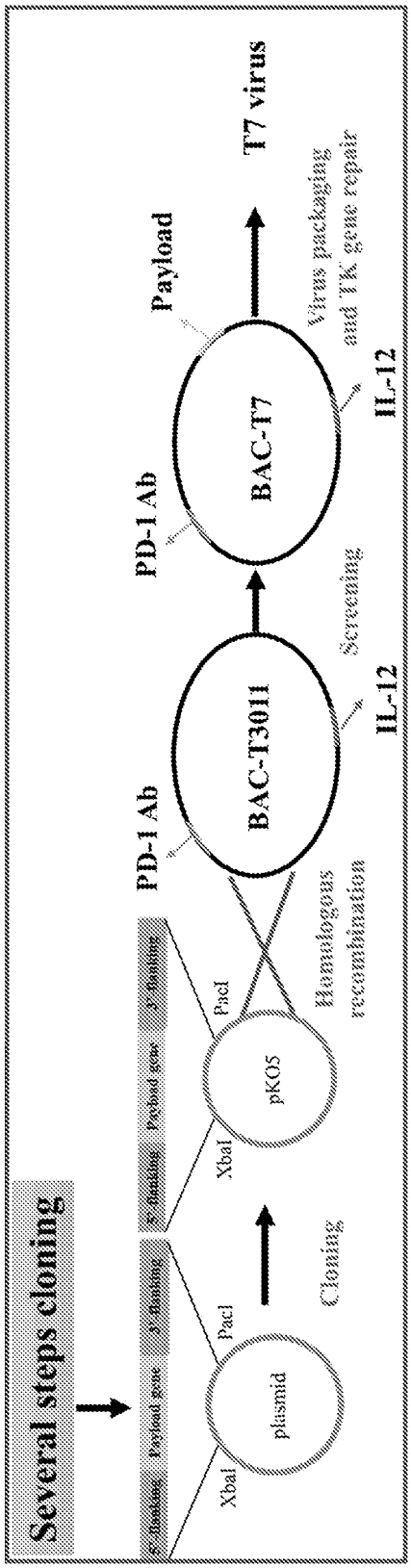

Several steps cloning
5' flanking
Payload gene
3' flanking
plasmid
XbaI
PacI
Cloning
5' flanking
Payload gene
3' flanking
pKO5
XbaI
PacI
Homologous recombination
PD-1 Ab
BAC-T3011
IL-12
Screening
PD-1 Ab
Payload
BAC-T7
IL-12
Virus packaging and TK gene repair
T7 virus

Fig. 2

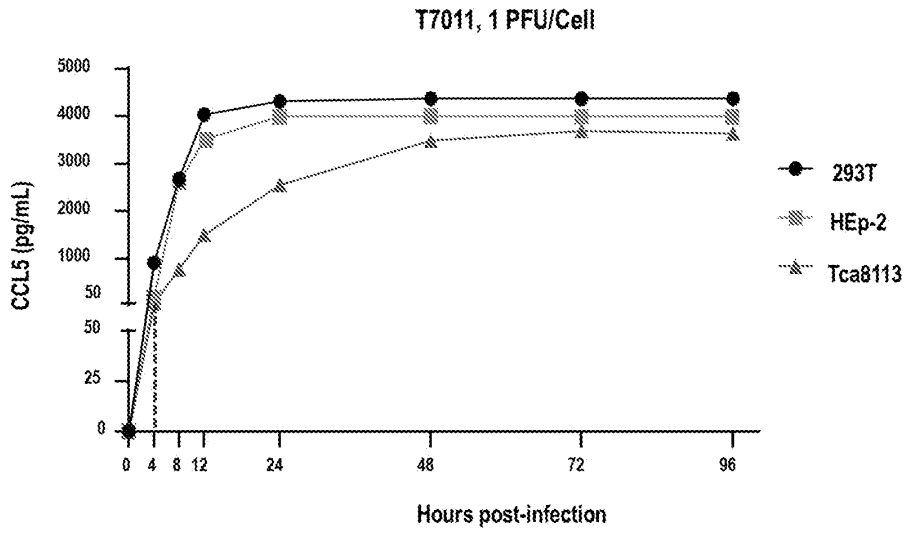

T7011, 1 PFU/Cell
CCL5 (pg/mL)
5000
4000
3000
2000
1000
50
50
25
0
0 4 8 12 24 48 72 96
Hours post-infection
293T
HEp-2
Tca8113

FIG. 3

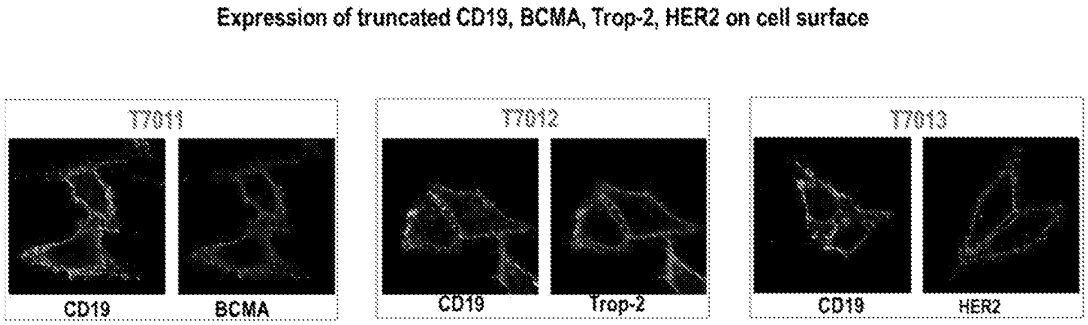

Expression of truncated CD19, BCMA, Trop-2, HER2 on cell surface
T7011
CD19
BCMA
T7012
CD19
Trop-2
T7013
CD19
HER2

FIG. 4

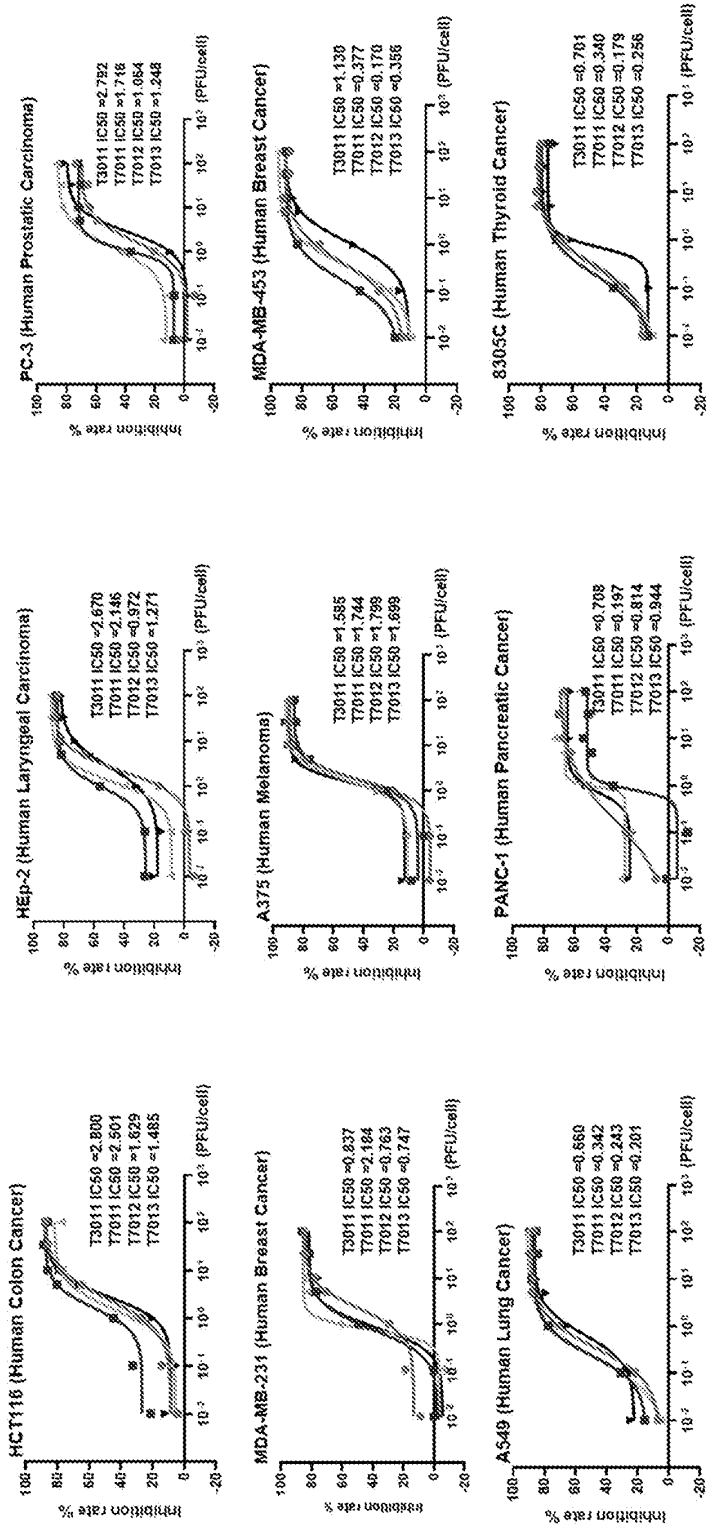

HCT116 (Human Colon Cancer)
T3011 IC50 =2.800
T7011 IC50 =2.501
T7012 IC50 =1.829
T7013 IC50 =1.485
HEp-2 (Human Laryngeal Carcinoma)
T3011 IC50 =2.670
T7011 IC50 =2.146
T7012 IC50 =0.972
T7013 IC50 =1.271
PC-3 (Human Prostatic Carcinoma)
T3011 IC50 =2.792
T7011 IC50 =1.718
T7012 IC50 =1.064
T7013 IC50 =1.248
MDA-MB-231 (Human Breast Cancer)
T3011 IC50 =0.837
T7011 IC50 =2.184
T7012 IC50 =0.763
T7013 IC50 =0.747
A375 (Human Melanoma)
T3011 IC50 =1.585
T7011 IC50 =1.744
T7012 IC50 =1.798
T7013 IC50 =1.698
MDA-MB-453 (Human Breast Cancer)
T3011 IC50 =1.139
T7011 IC50 =0.377
T7012 IC50 =0.170
T7013 IC50 =0.356
A549 (Human Lung Cancer)
T3011 IC50 =0.660
T7011 IC50 =0.342
T7012 IC50 =0.243
T7013 IC50 =0.201
PANC-1 (Human Pancreatic Cancer)
T3011 IC50 =0.708
T7011 IC50 =0.197
T7012 IC50 =0.814
T7013 IC50 =0.944
8305C (Human Thyroid Cancer)
T3011 IC50 =0.701
T7011 IC50 =0.340
T7012 IC50 =0.179
T7013 IC50 =0.256
Inhibition rate %
(PFU/cell)
T3011
T7011
T7012
T7013

Fig. 5

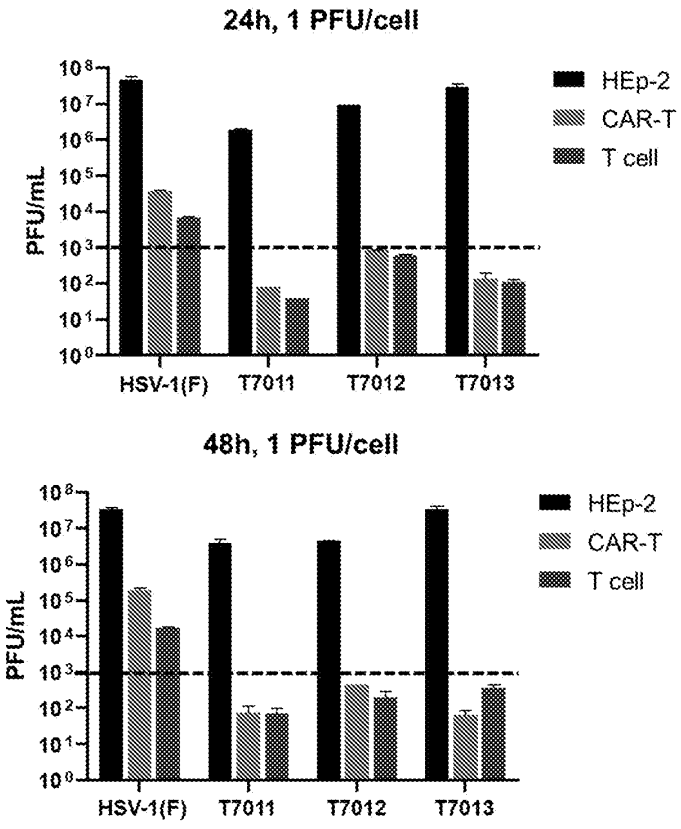

24h, 1 PFU/cell
PFU/mL
HEp-2
CAR-T
T cell
HSV-1(F)
T7011
T7012
T7013
48h, 1 PFU/cell
PFU/mL
HEp-2
CAR-T
T cell
HSV-1(F)
T7011
T7012
T7013

FIG. 6

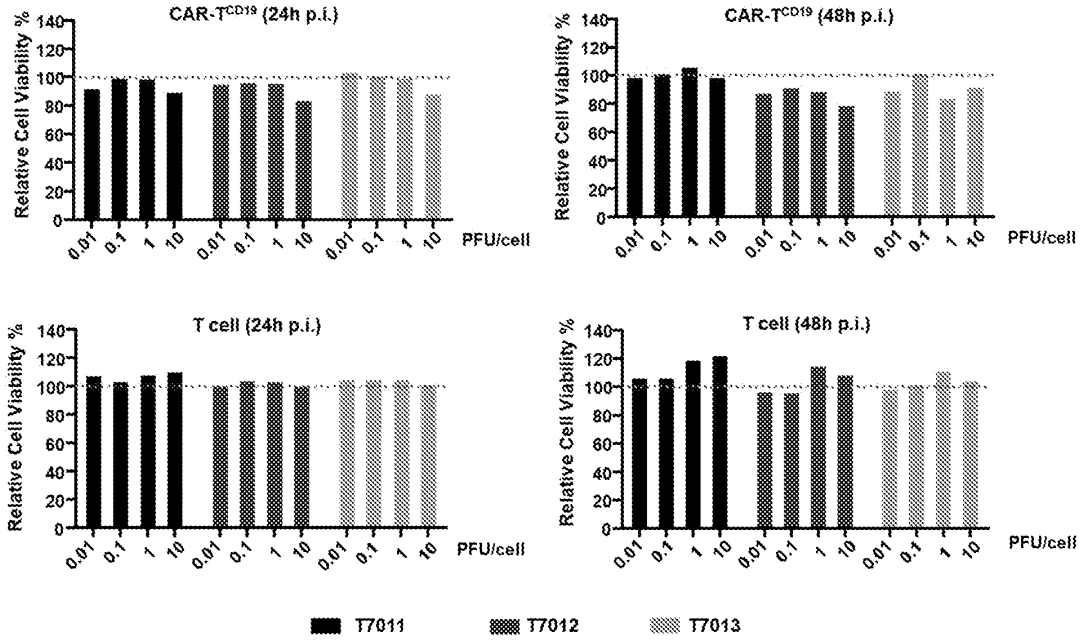

CAR-T^{CD19} (24h p.i.)
CAR-T^{CD19} (48h p.i.)
T cell (24h p.i.)
T cell (48h p.i.)
Relative Cell Viability %
PFU/cell
T7011
T7012
T7013

Fig. 7

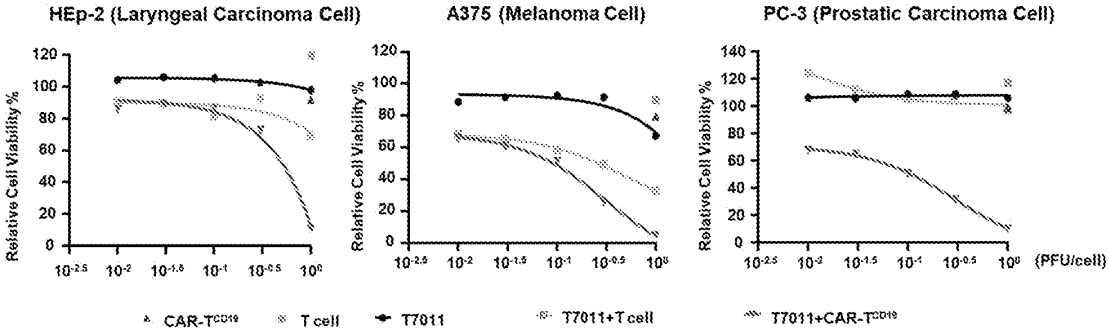


Fig. 8

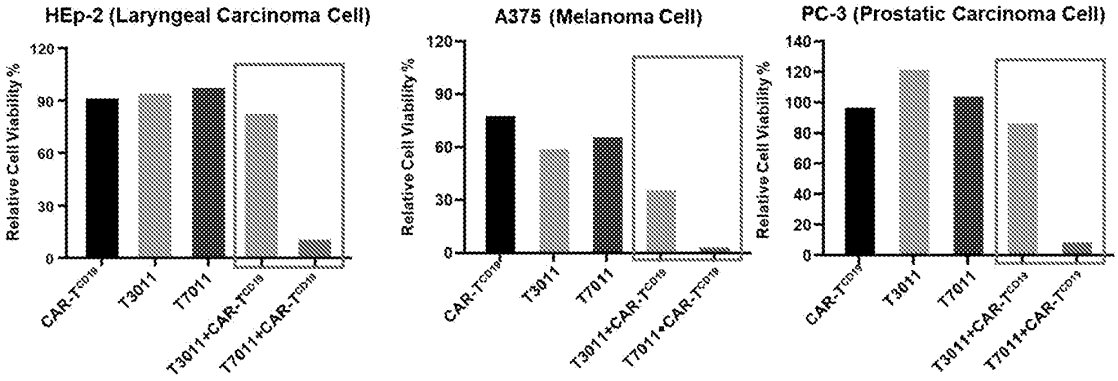


Fig. 9

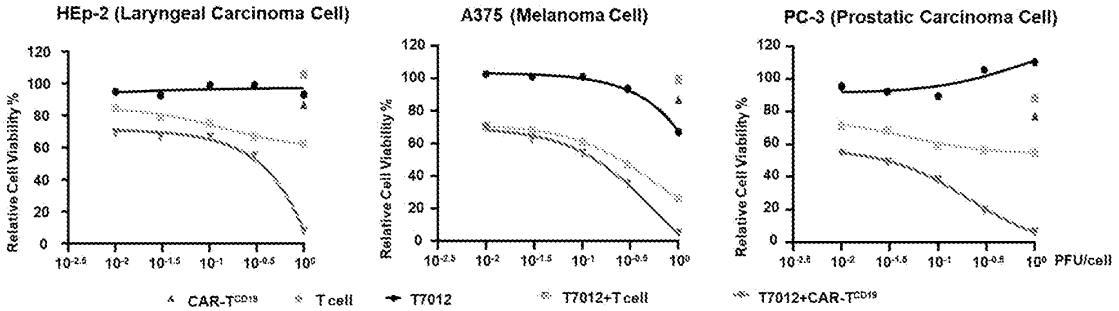


Fig. 10

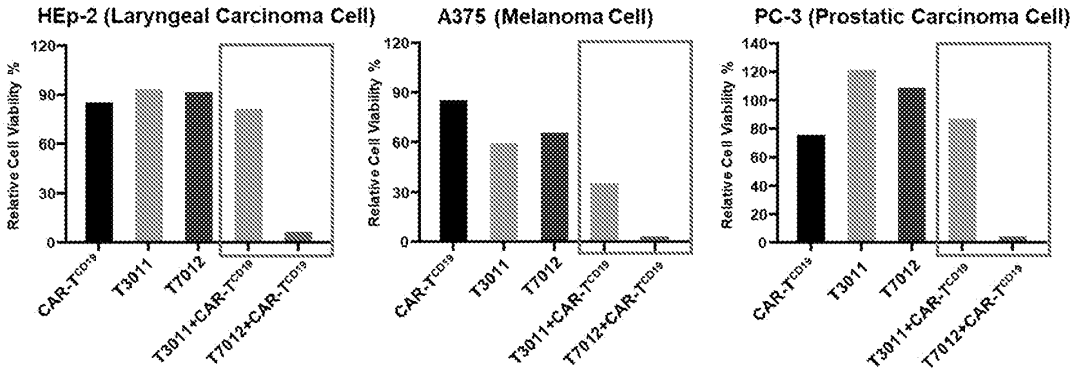


Fig. 11

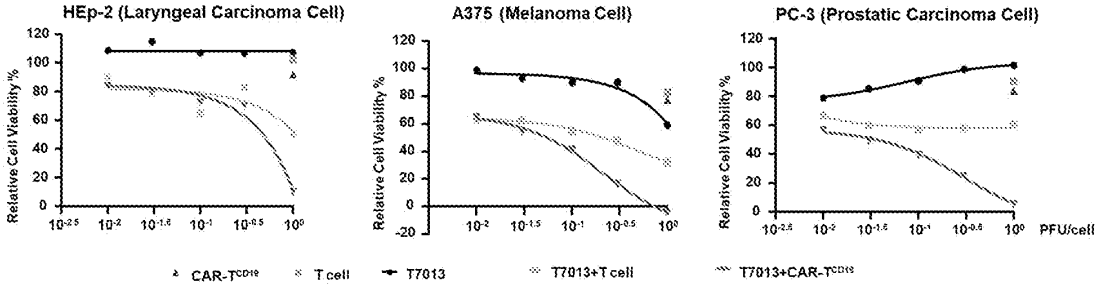


Fig. 12

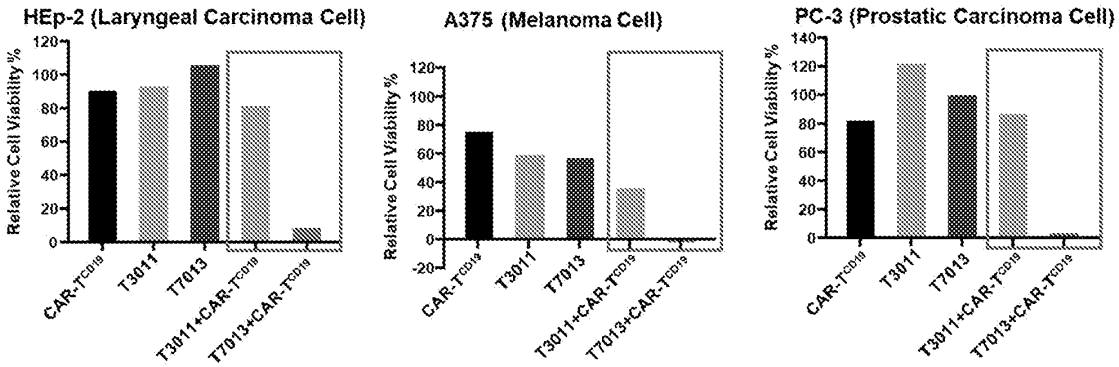


Fig. 13

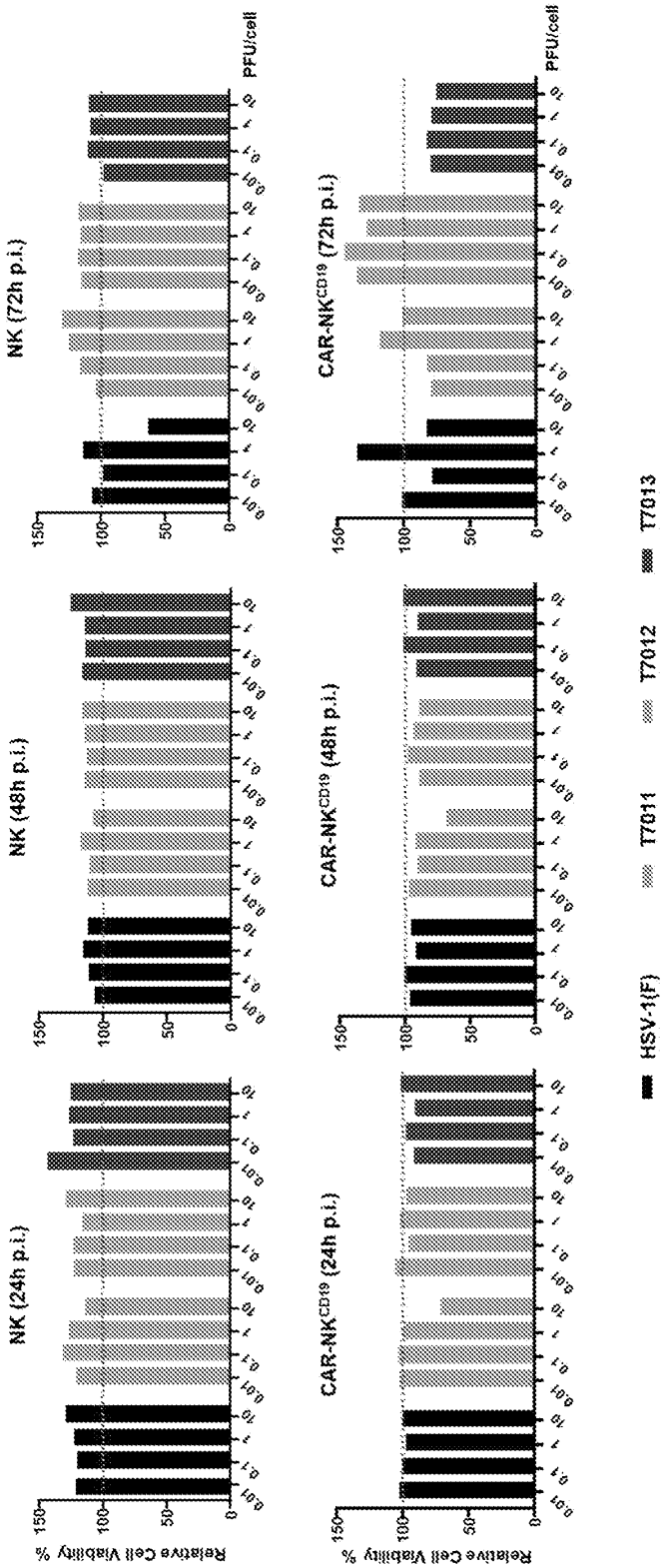

NK (24h p.i.)
NK (48h p.i.)
NK (72h p.i.)
CAR-NK^{CD19} (24h p.i.)
CAR-NK^{CD19} (48h p.i.)
CAR-NK^{CD19} (72h p.i.)
Relative Cell Viability %
PFU/cell
HSV-1(F)
T7011
T7012
T7013

Fig. 14

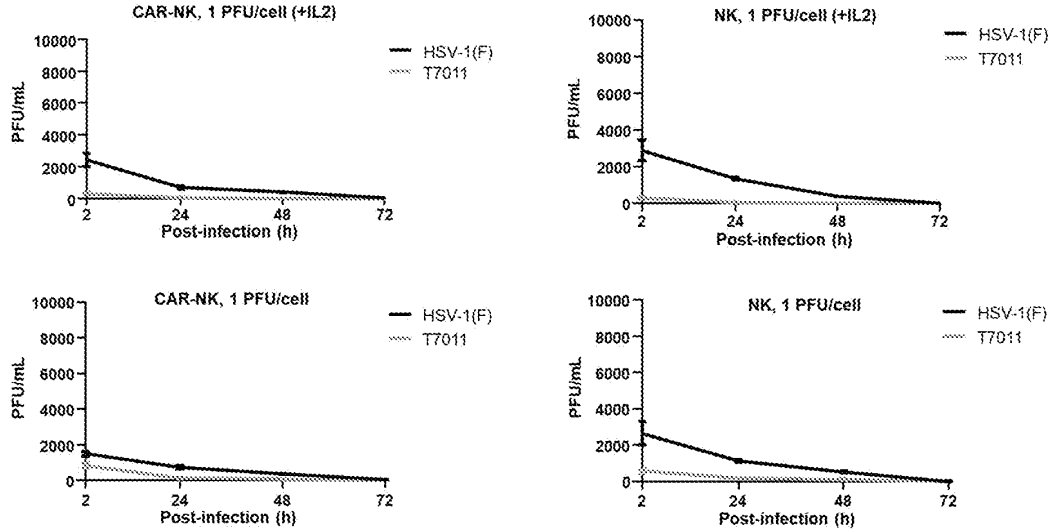

CAR-NK, 1 PFU/cell (+IL2)
NK, 1 PFU/cell (+IL2)
CAR-NK, 1 PFU/cell
NK, 1 PFU/cell
HSV-1(F)
T7011
PFU/mL
Post-infection (h)

Fig. 15

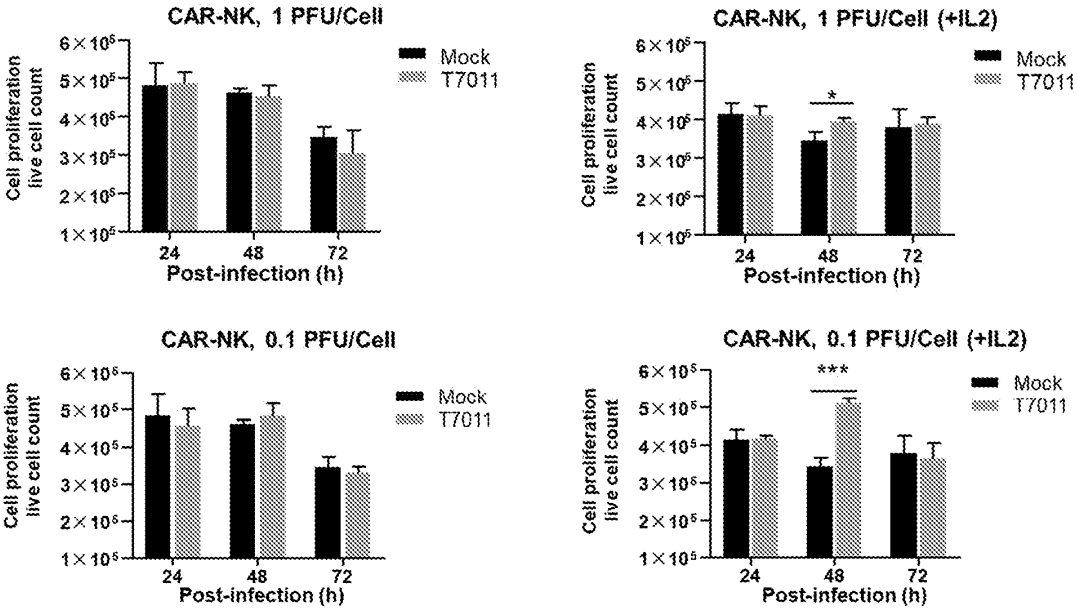

CAR-NK, 1 PFU/Cell
CAR-NK, 1 PFU/Cell (+IL2)
CAR-NK, 0.1 PFU/Cell
CAR-NK, 0.1 PFU/Cell (+IL2)
Mock
T7011
Cell proliferation
live cell count
Post-infection (h)

Fig. 16

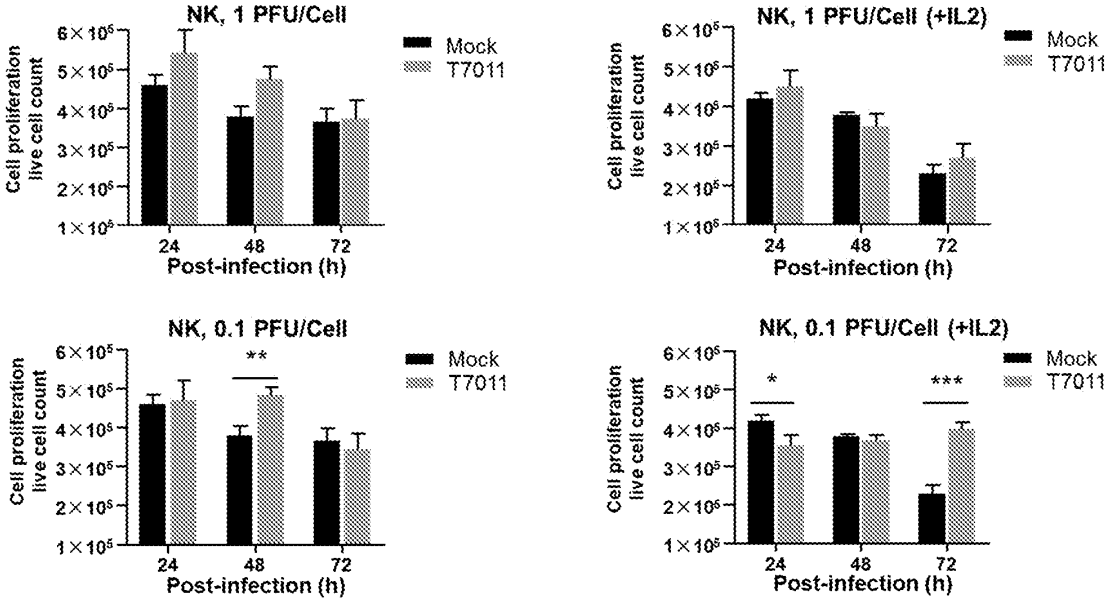

NK, 1 PFU/Cell
NK, 1 PFU/Cell (+IL2)
NK, 0.1 PFU/Cell
NK, 0.1 PFU/Cell (+IL2)
Cell proliferation live cell count
Post-infection (h)
Mock
T7011
**
*
***

Fig. 17

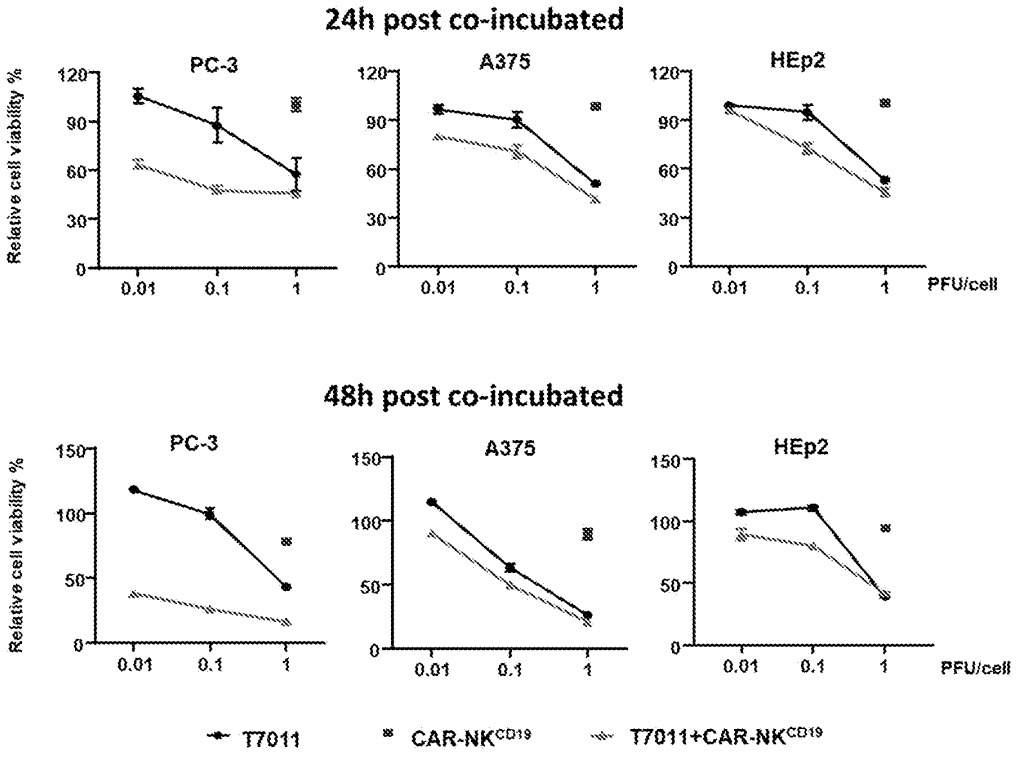

24h post co-incubated
48h post co-incubated
PC-3
A375
HEp2
Relative cell viability %
PFU/cell
T7011
CAR-NKCD19
T7011+CAR-NKCD19

Fig. 18

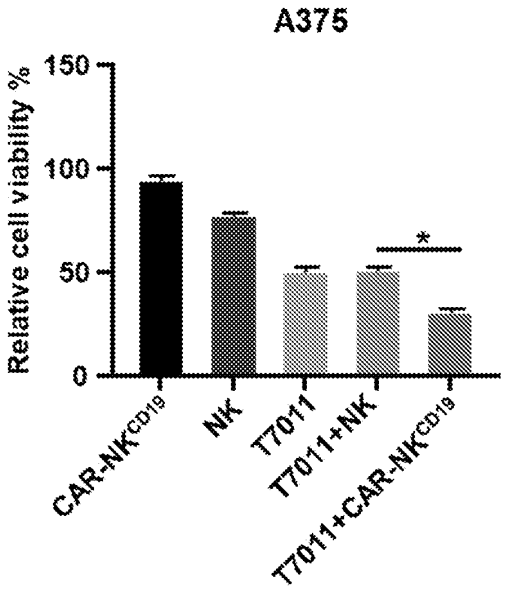

A375
Relative cell viability %
150
100
50
0
*
CAR-NKCD19
NK
T7011
T7011+NK
T7011+CAR-NKCD19

Fig. 19