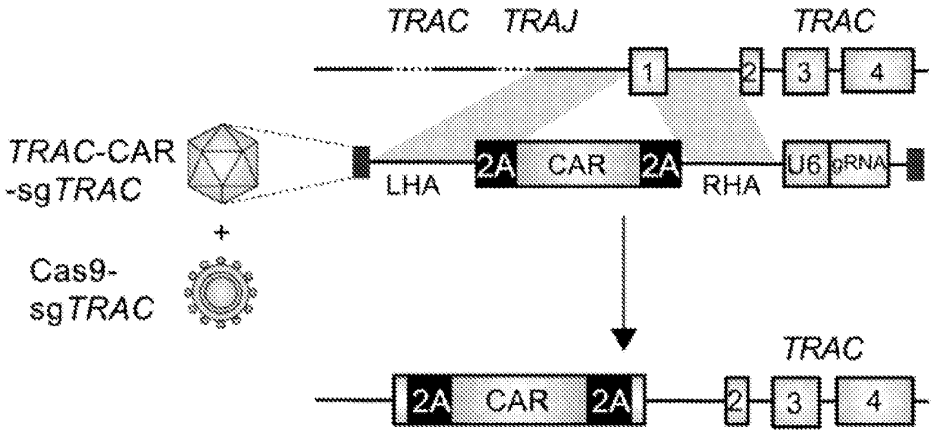


Figure 1A

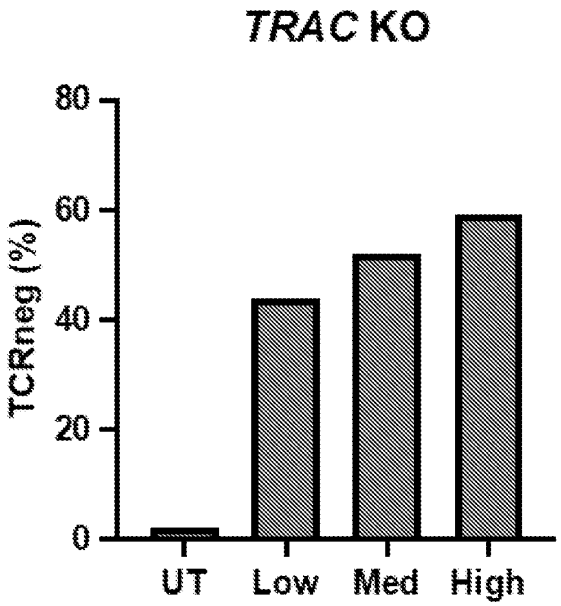


Figure 1B

Figure 1C

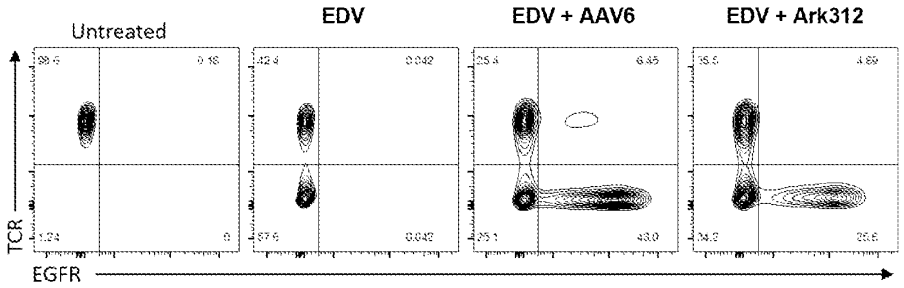
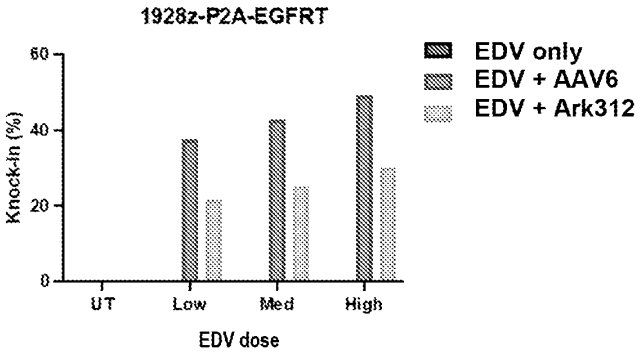


Figure 1D



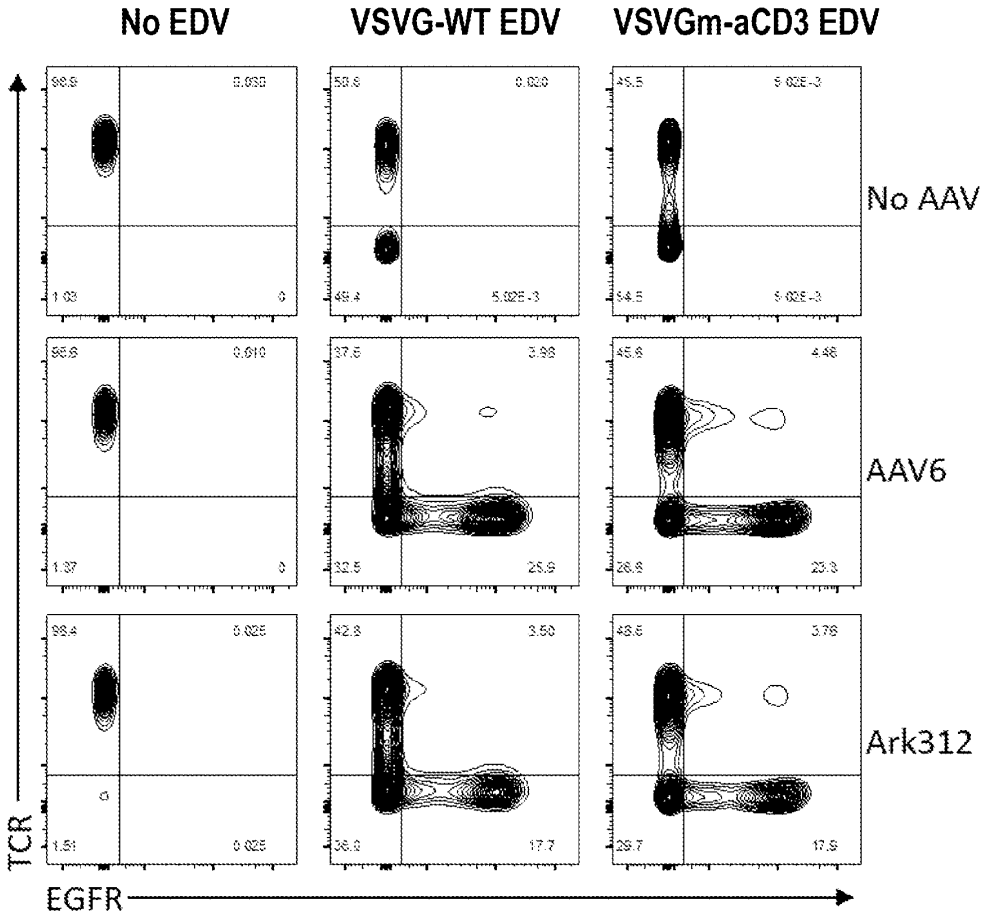


Figure 2A

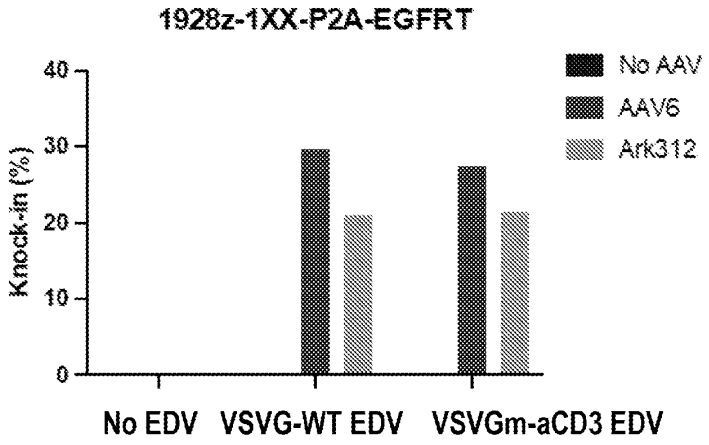


Figure 2B

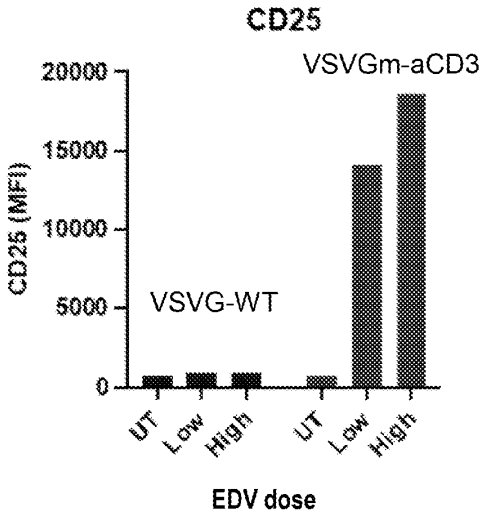


Figure 2C

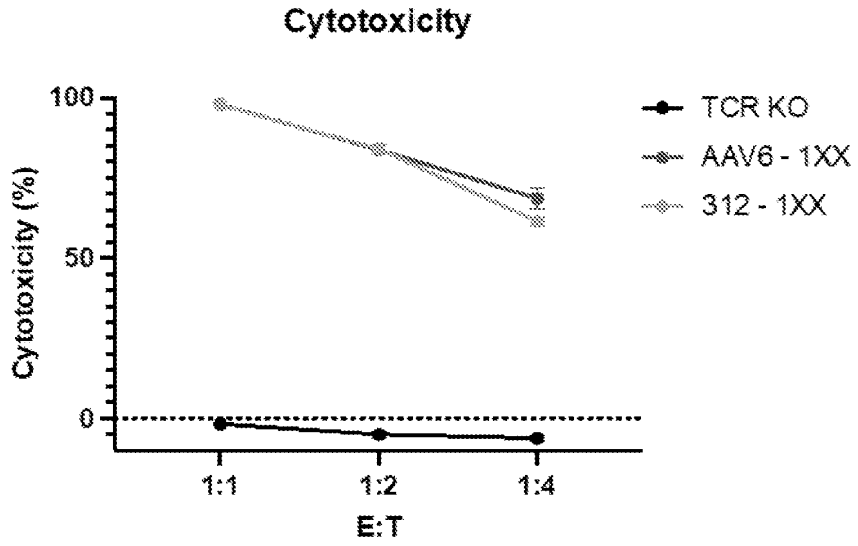


Figure 2D

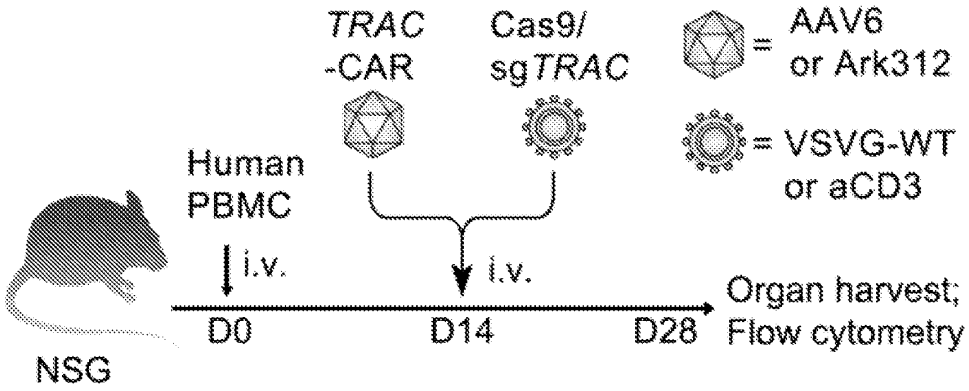


Figure 3A

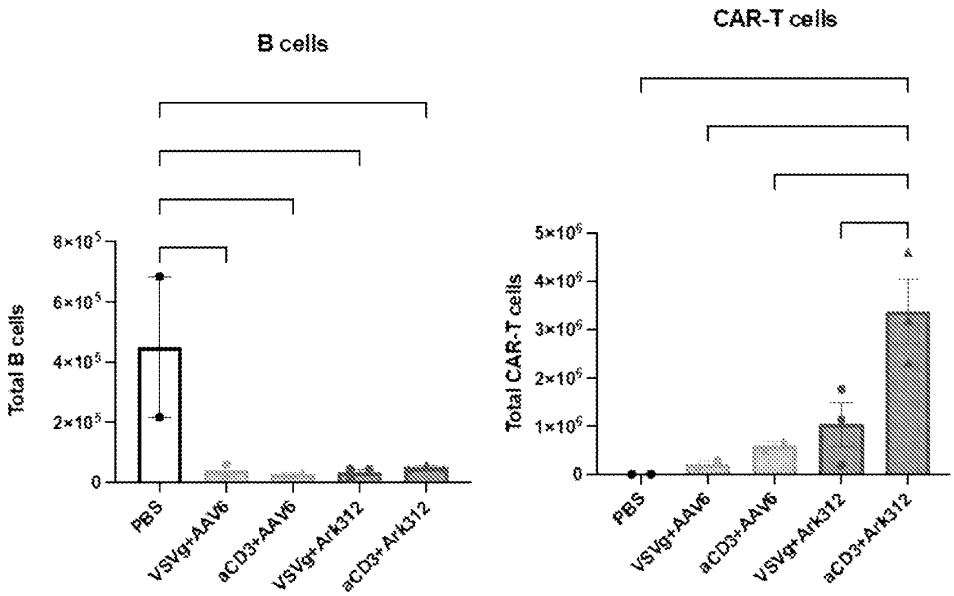


Figure 3B

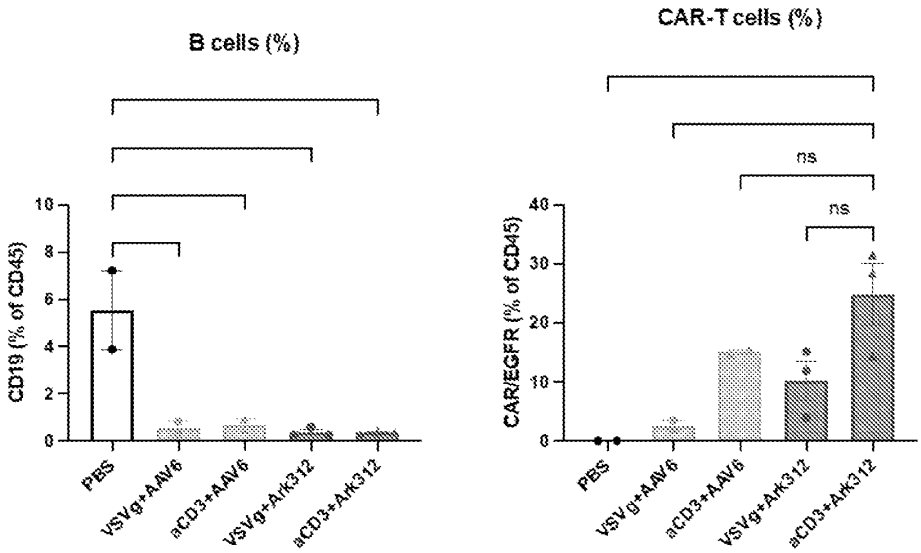


Figure 3C

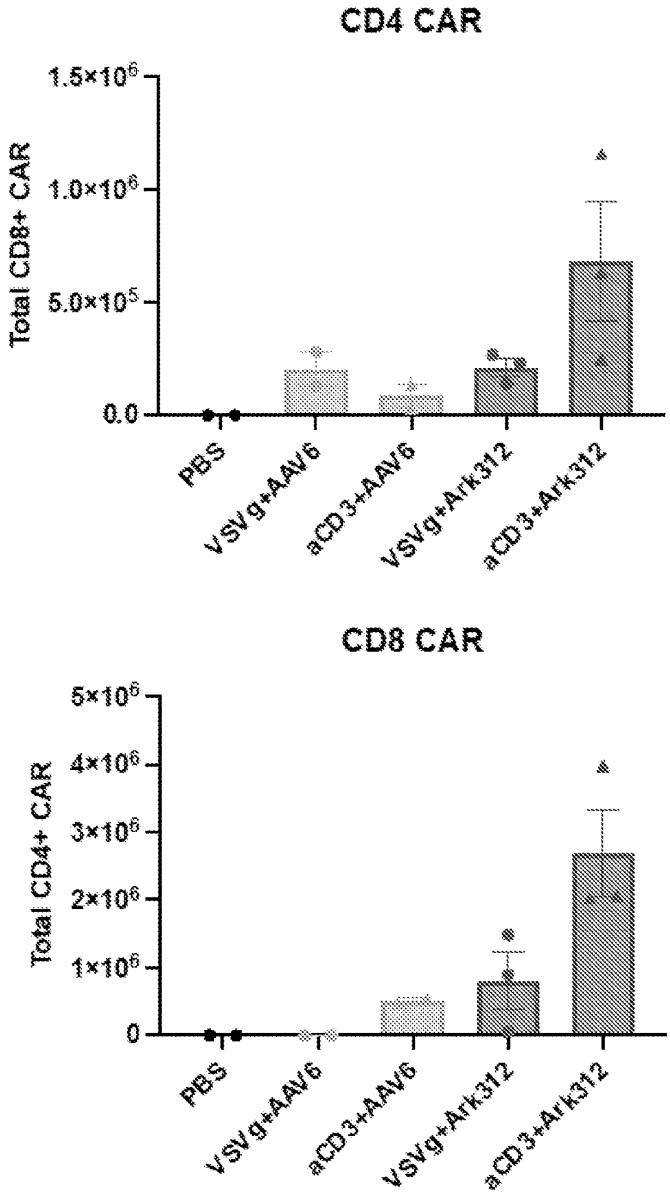

CD4 CAR
Total CD8+ CAR
1.5×10^6
1.0×10^6
5.0×10^5
0.0
PBS
VSVg+AAV6
aCD3+AAV6
VSVg+Ark312
aCD3+Ark312
CD8 CAR
Total CD4+ CAR
5×10^6
4×10^6
3×10^6
2×10^6
1×10^6
0
PBS
VSVg+AAV6
aCD3+AAV6
VSVg+Ark312
aCD3+Ark312

Figure 3D

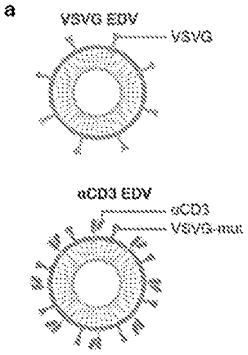


Figure 4A

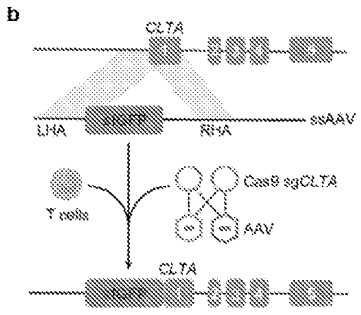


Figure 4B

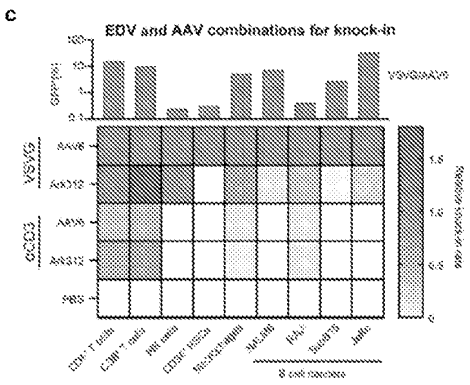


Figure 4C

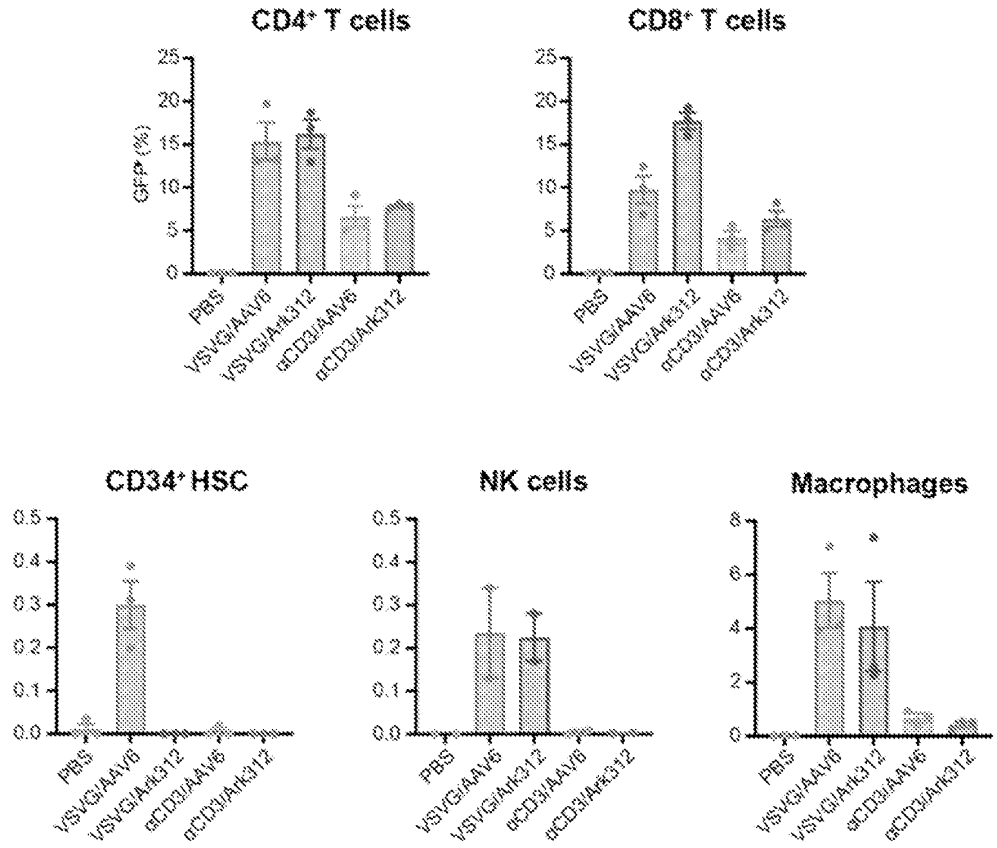

CD4+ T cells
CD8+ T cells
CD34+ HSC
NK cells
Macrophages
GFP (%)
PBS
VSVG/AAV6
VSVG/AAV312
αCD3/AAV6
αCD3/AAV312

Figure 5A

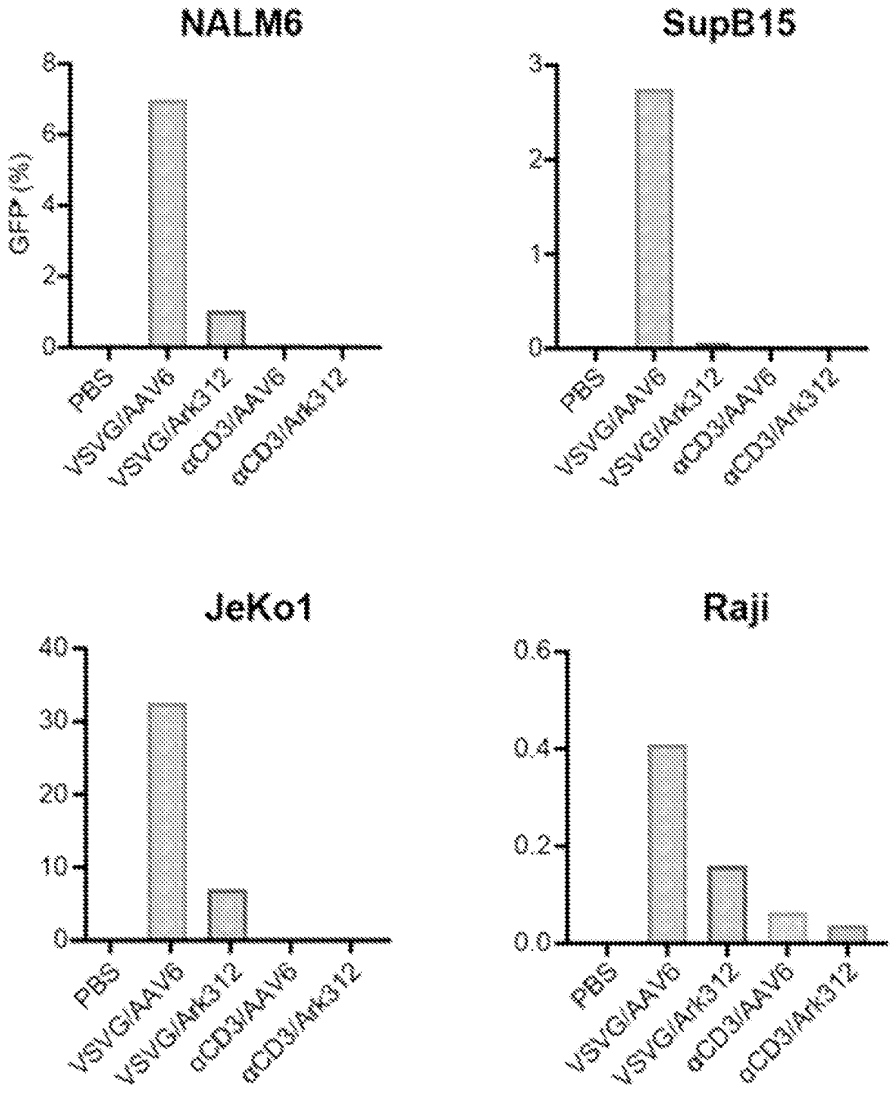

NALM6
SupB15
JeKo1
Raji
GFP (%)
PBS
VSVG/AAV6
VSVG/ArK312
αCD3/AAV6
αCD3/ArK312

Figure 5B

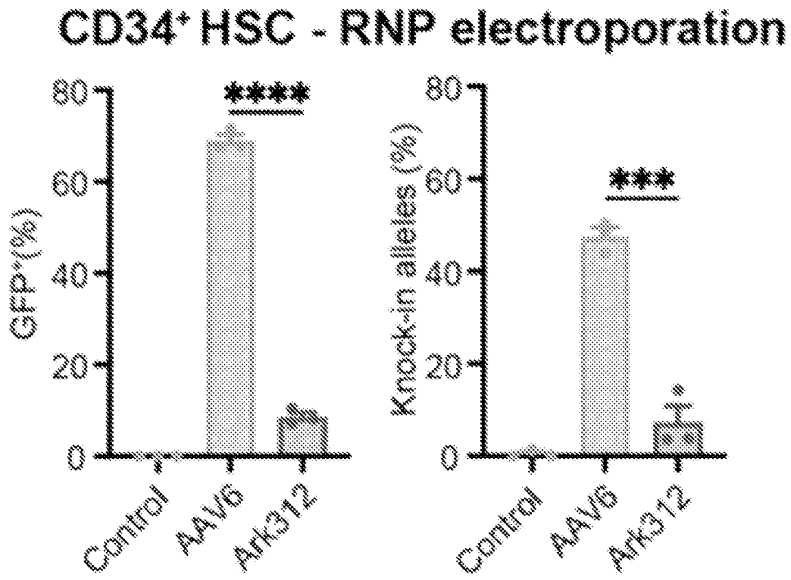

CD34+ HSC - RNP electroporation
GFP+(%)
80
60
40
20
0
****
Control
AAV6
Ark312
Knock-in alleles (%)
80
60
40
20
0
***
*
Control
AAV6
Ark312

Figure 5C

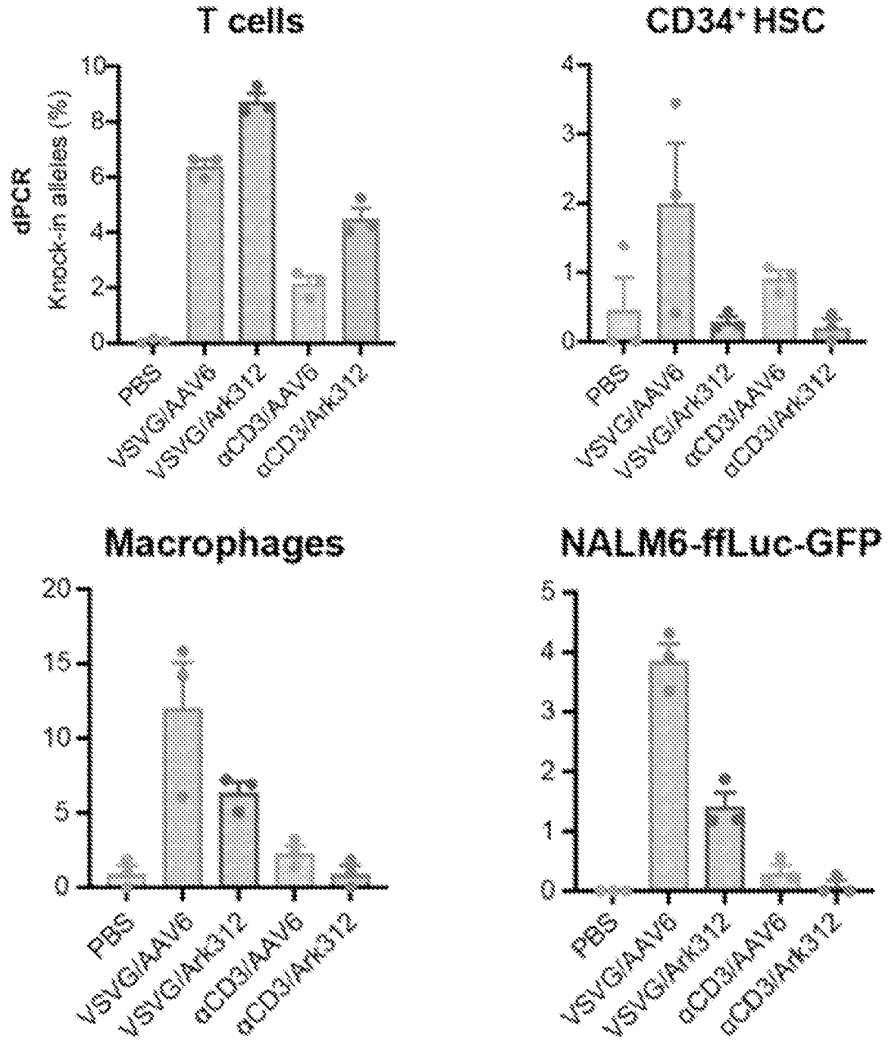

T cells
CD34+ HSC
Macrophages
NALM6-ffLuc-GFP
dPCR
Knock-in alleles (%)
PBS
VSVG/AAV6
VSVG/Ark312
αCD3/AAV6
αCD3/Ark312

Figure 5D

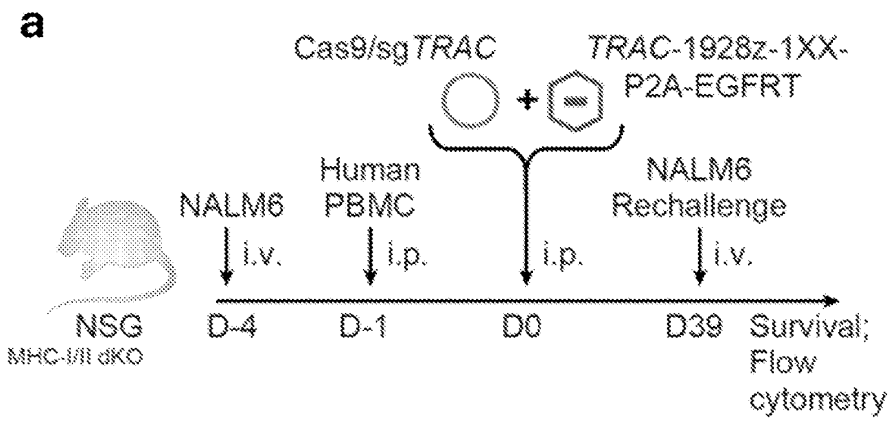

a
Cas9/sgTRAC
TRAC-1928z-1XX-
P2A-EGFRT
Human
PBMC
NALM6
Rechallenge
NALM6
i.v.
i.p.
i.p.
i.v.
NSG
MHC-I/II dKO
D-4
D-1
D0
D39
Survival;
Flow
cytometry

Figure 6A

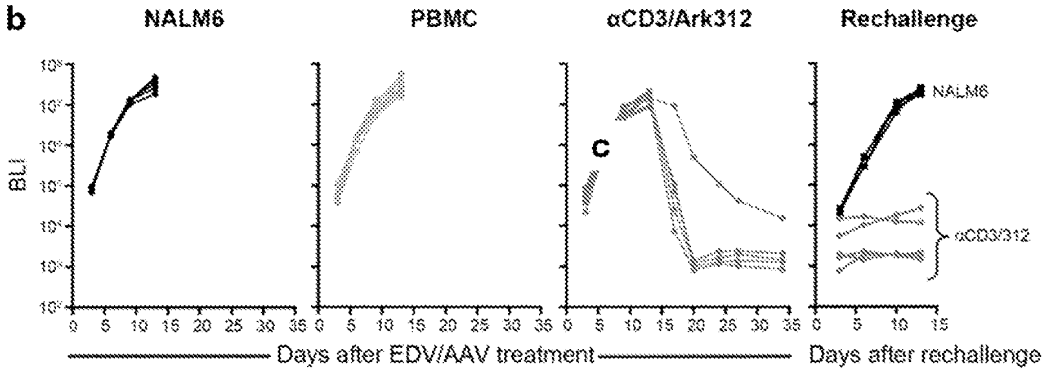

b
NALM6
PBMC
αCD3/Ark312
Rechallenge
BLI
c
NALM6
αCD3/312
Days after EDV/AAV treatment
Days after rechallenge

Figure 6B

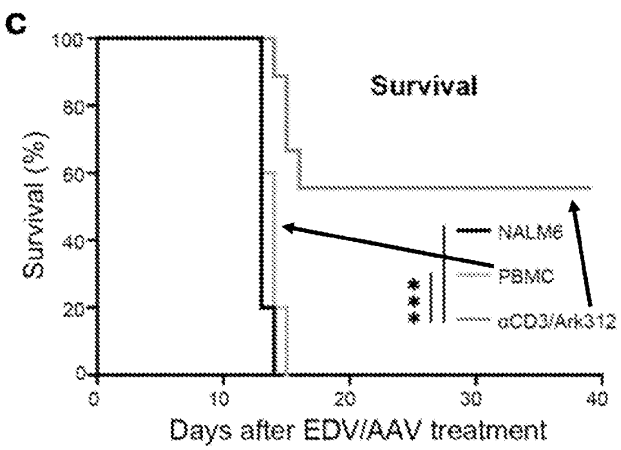


Figure 6C

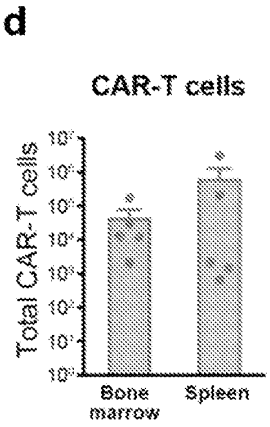


Figure 6D

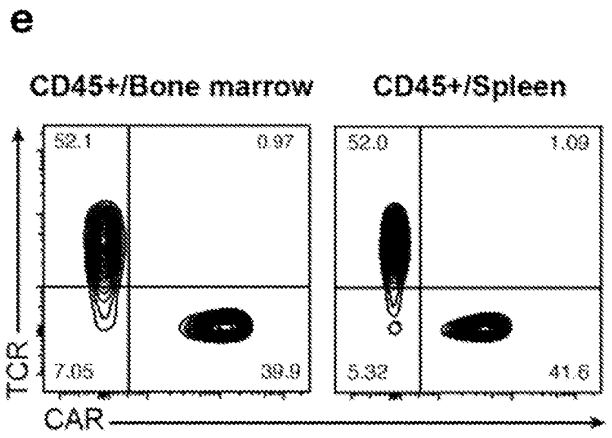


Figure 6E

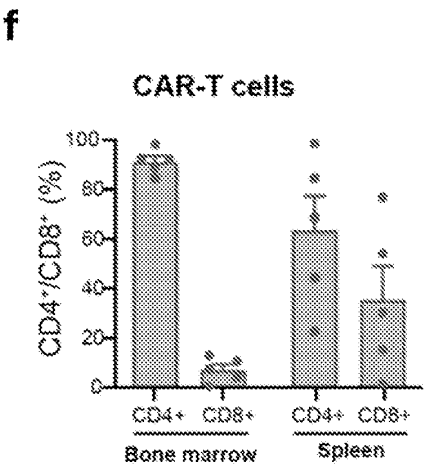


Figure 6F

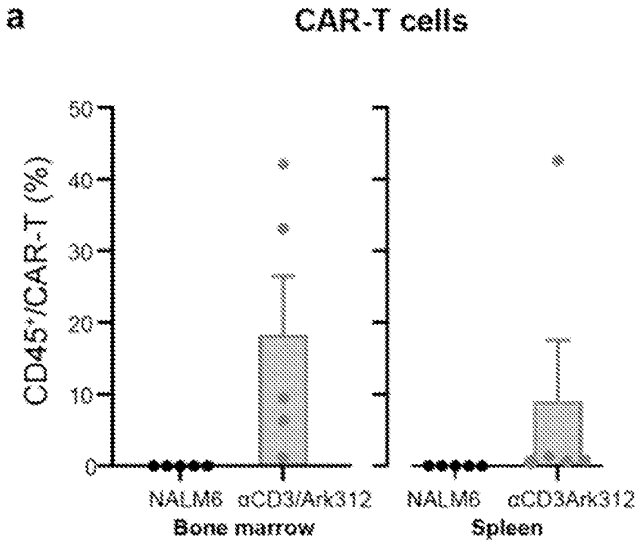


Figure 7A

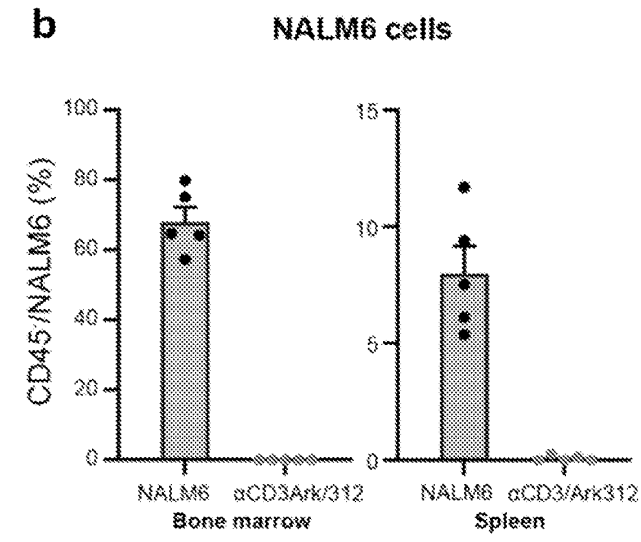


Figure 7B

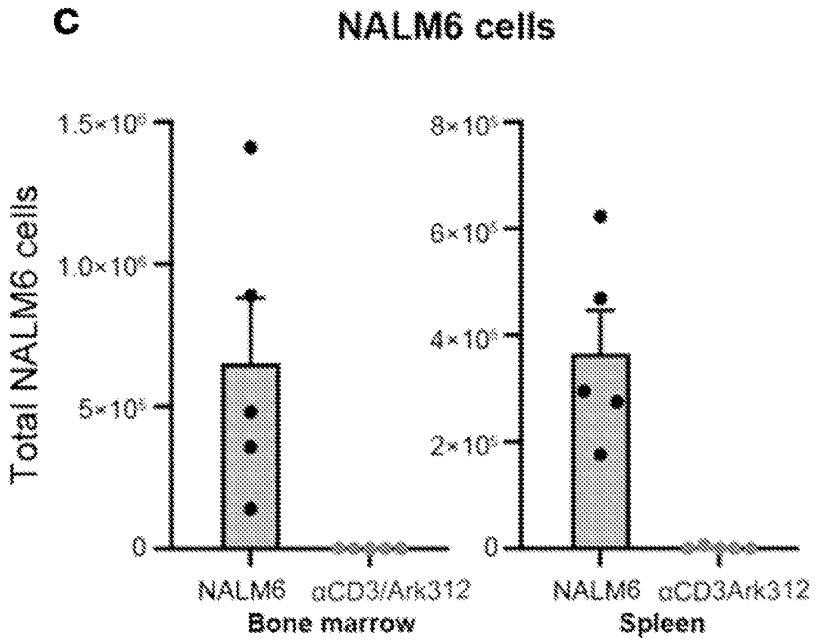
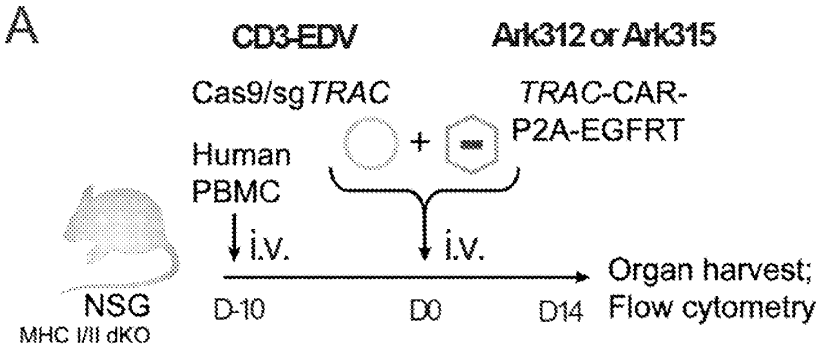

C
NALM6 cells
Total NALM6 cells
1.5×10⁶
1.0×10⁶
5×10⁵
0
8×10⁵
6×10⁵
4×10⁵
2×10⁵
0
NALM6
αCD3/Ark312
Bone marrow
NALM6
αCD3Ark312
Spleen

Figure 7C

Figure 8A



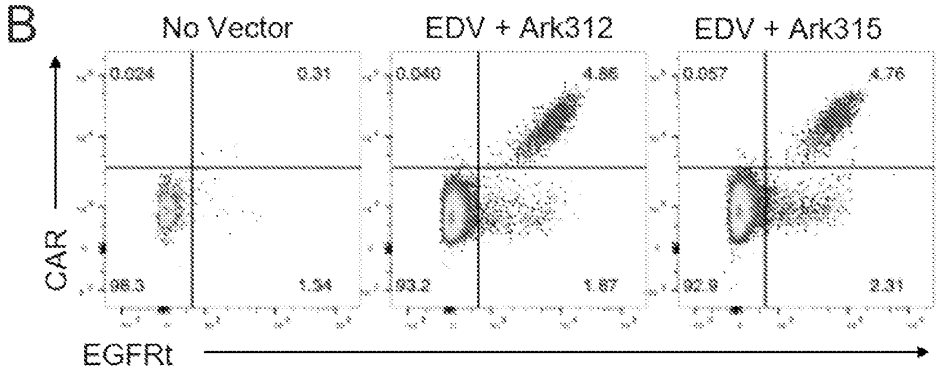


Figure 8B

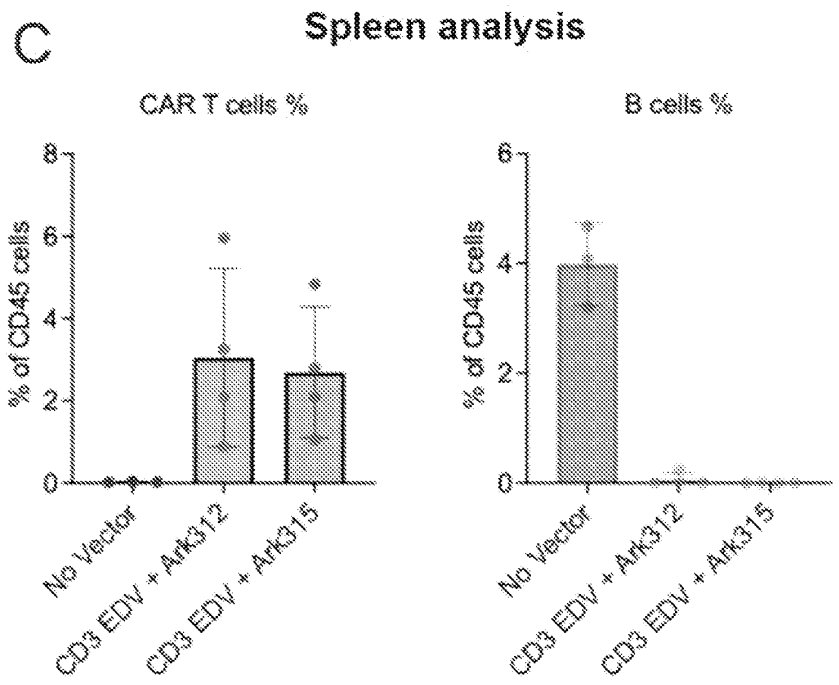

C
Spleen analysis
CAR T cells %
% of CD45 cells
0
2
4
6
8
No Vector
CD3 EDV + ArK312
CD3 EDV + ArK315
B cells %
% of CD45 cells
0
2
4
6
No Vector
CD3 EDV + ArK312
CD3 EDV + ArK315

Figure 8C

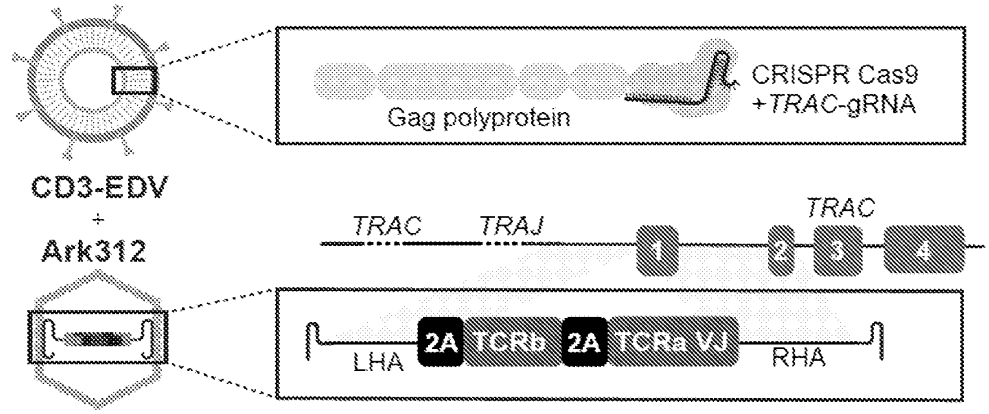


Figure 9A

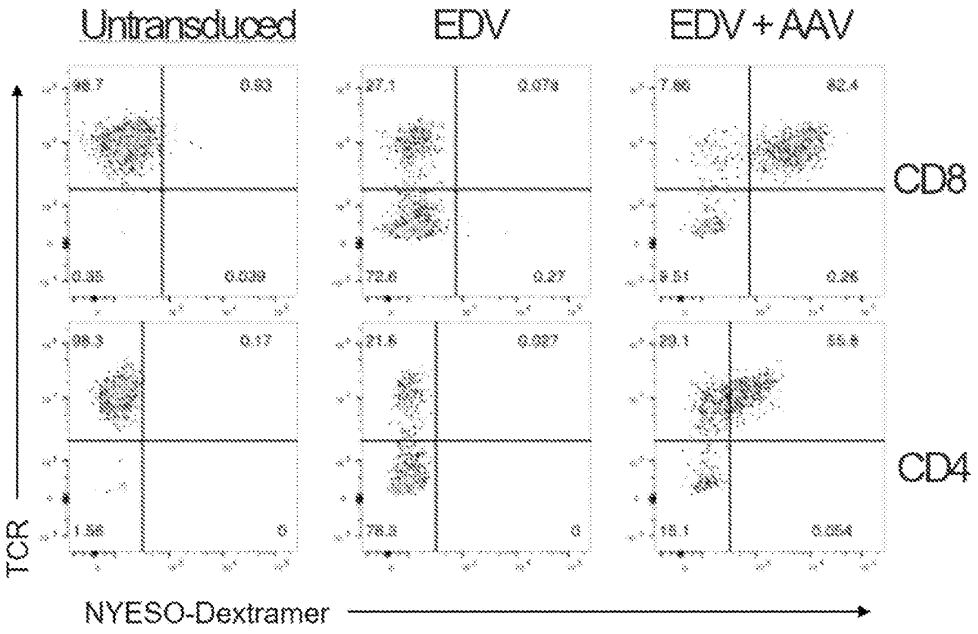


Figure 9B

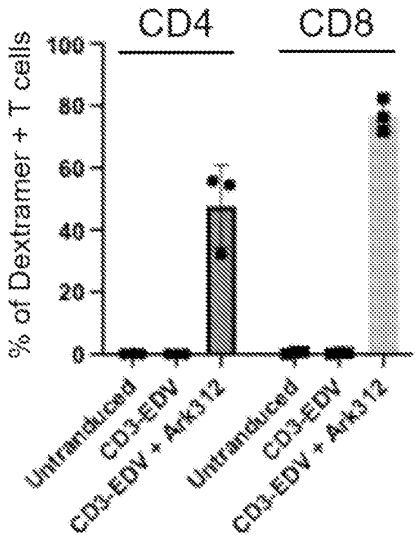


Figure 9C

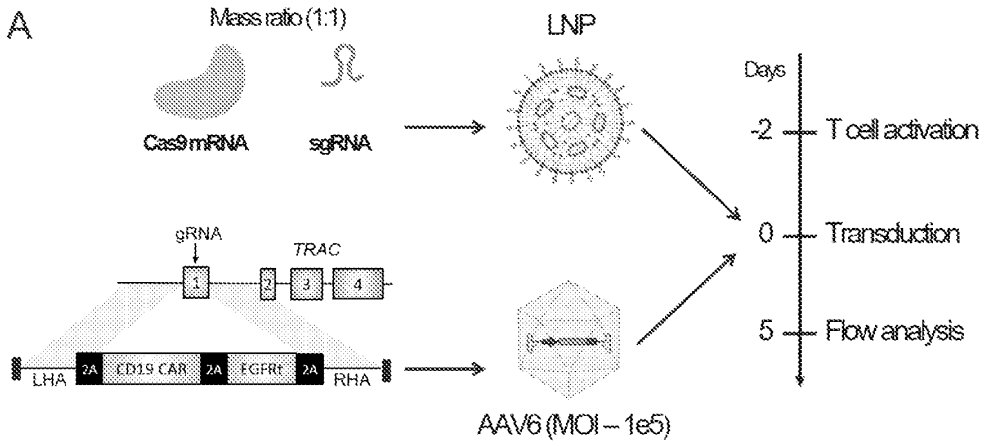


Figure 10A

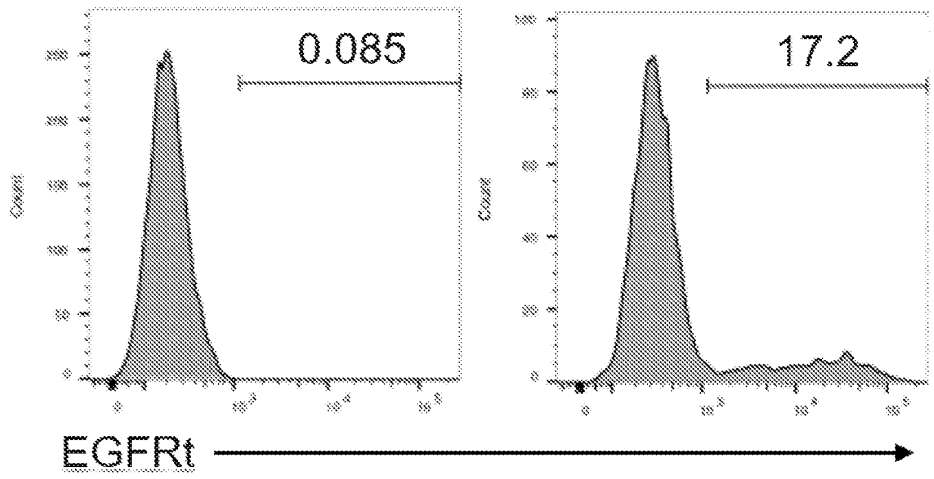


Figure 10B

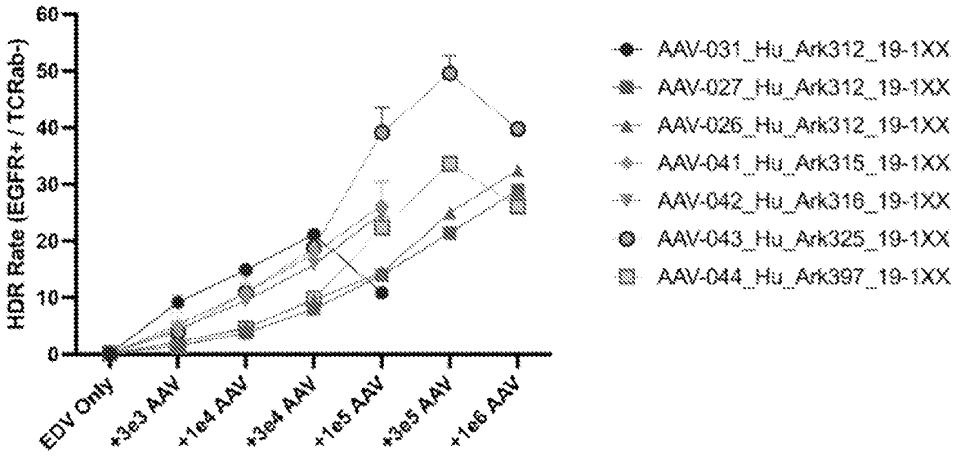

HDR Rate (EGFR+ / TCRab-)
60
50
40
30
20
10
0
EDV Only
+3e3 AAV
+1e4 AAV
+3e4 AAV
+1e5 AAV
+3e5 AAV
+1e6 AAV
AAV-031_Hu_Ark312_19-1XX
AAV-027_Hu_Ark312_19-1XX
AAV-026_Hu_Ark312_19-1XX
AAV-041_Hu_Ark315_19-1XX
AAV-042_Hu_Ark316_19-1XX
AAV-043_Hu_Ark325_19-1XX
AAV-044_Hu_Ark397_19-1XX

Figure 11