Figure 1

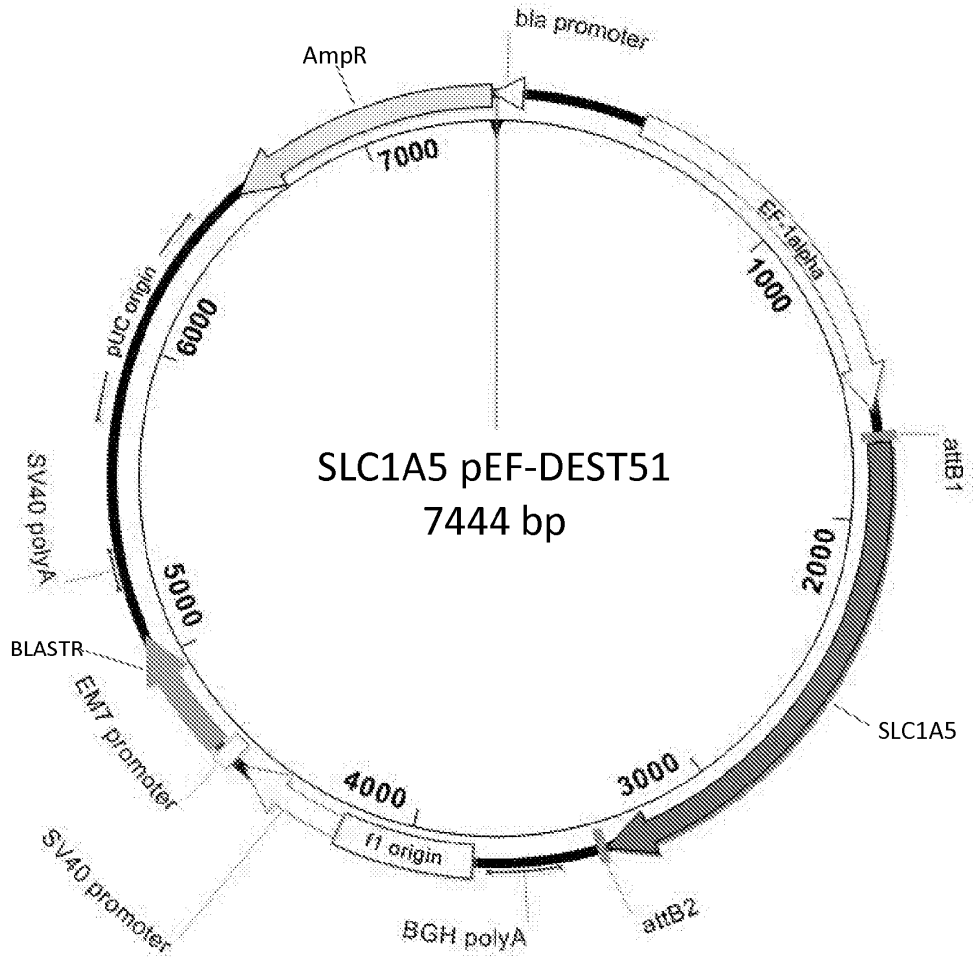

bla promoter
AmpR
7000
EF-1alpha
1000
attB1
pUC origin
6000
SV40 polyA
2000
SLC1A5 pEF-DEST51
7444 bp
5000
BLASTR
EM7 promoter
SLC1A5
4000
3000
f1 origin
SV40 promoter
BGH polyA
attB2

Figure 2

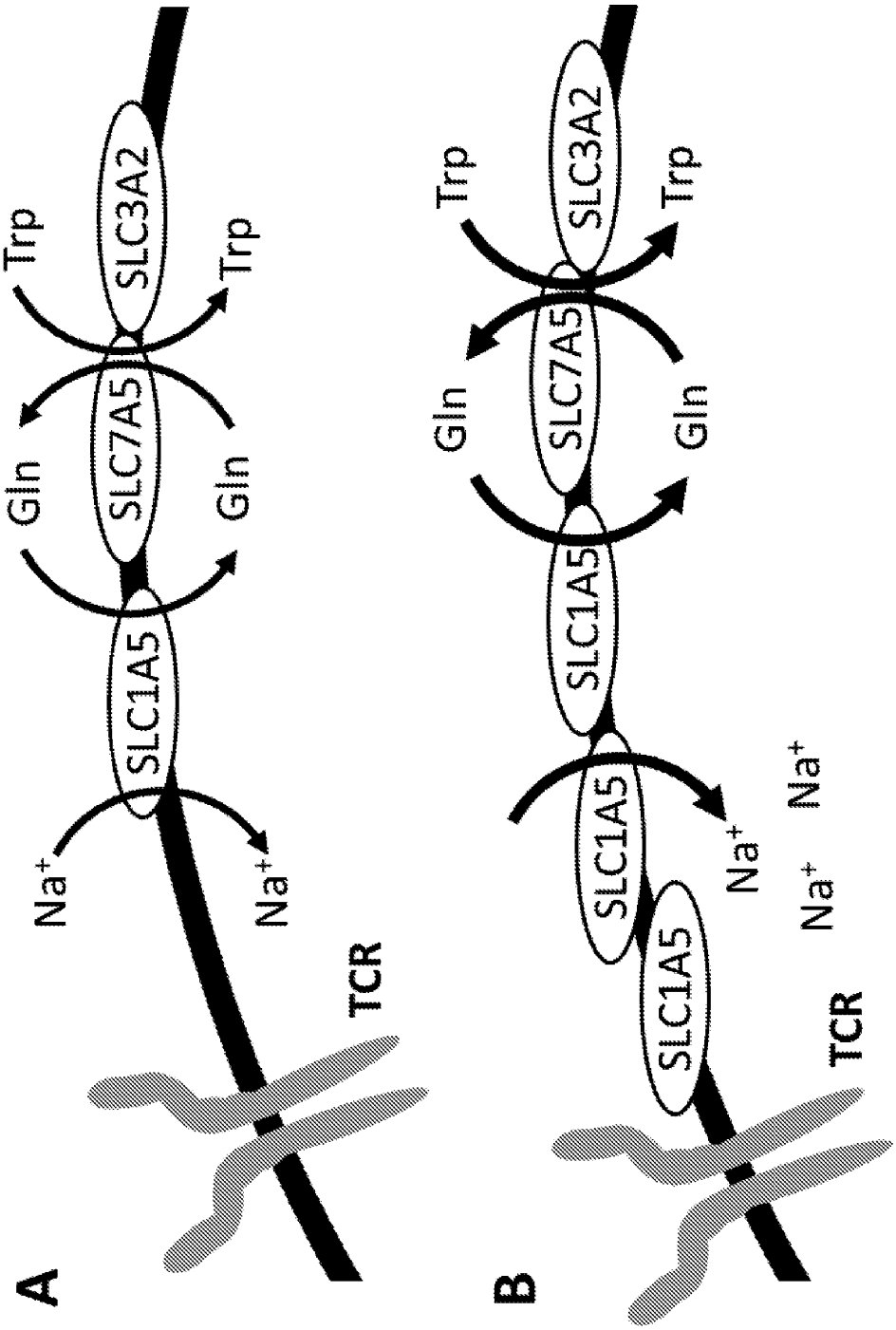

A
Trp
SLC3A2
Trp
Gln
SLC7A5
Gln
SLC1A5
Na+
Na+
TCR
B
Trp
SLC3A2
Trp
Gln
SLC7A5
Gln
SLC1A5
SLC1A5
Na+
Na+
Na+
TCR

Figure 3

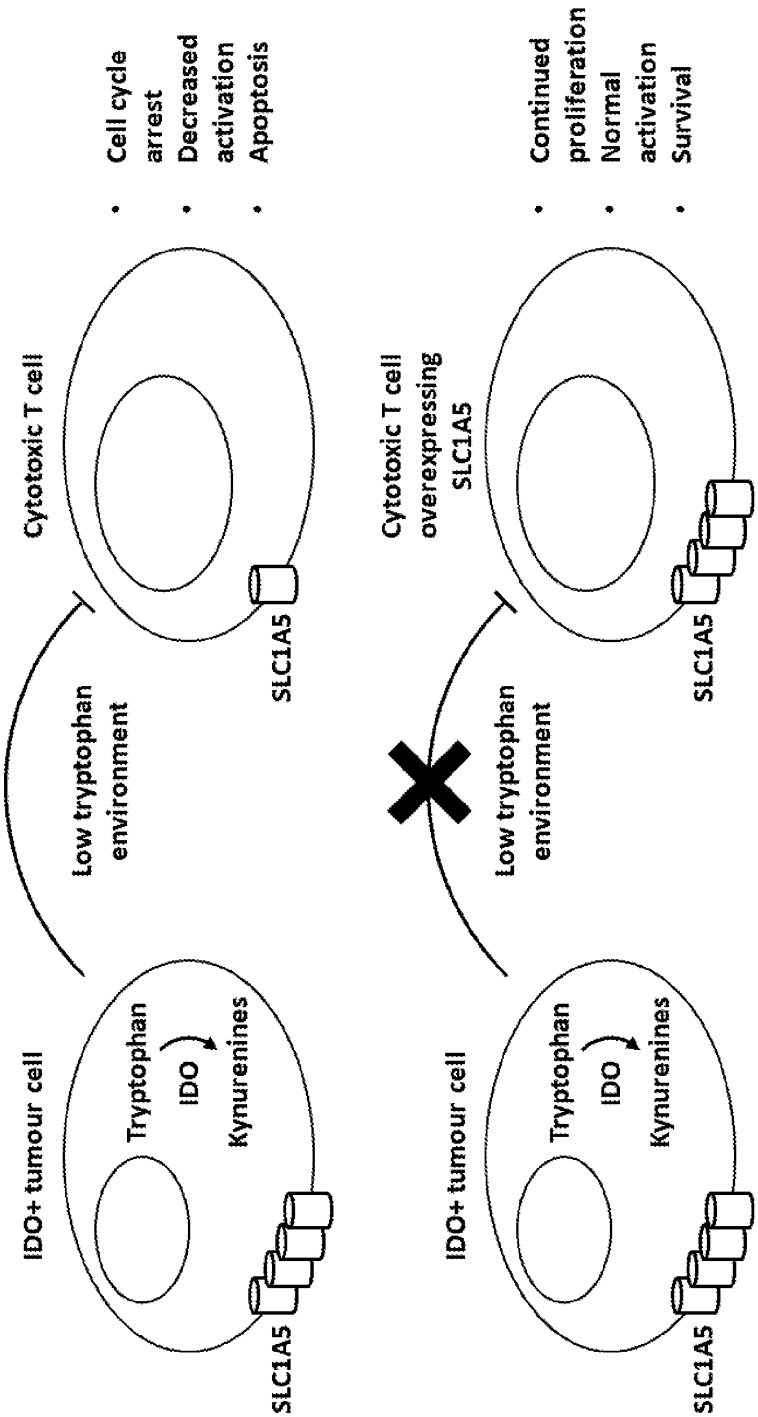

IDO+ tumour cell
Tryptophan
IDO
Kynurenines
SLC1A5
Low tryptophan environment
Cytotoxic T cell
SLC1A5
• Cell cycle arrest
• Decreased activation
• Apoptosis
IDO+ tumour cell
Tryptophan
IDO
Kynurenines
SLC1A5
Low tryptophan environment
Cytotoxic T cell overexpressing SLC1A5
SLC1A5
• Continued proliferation
• Normal activation
• Survival

Figure 4

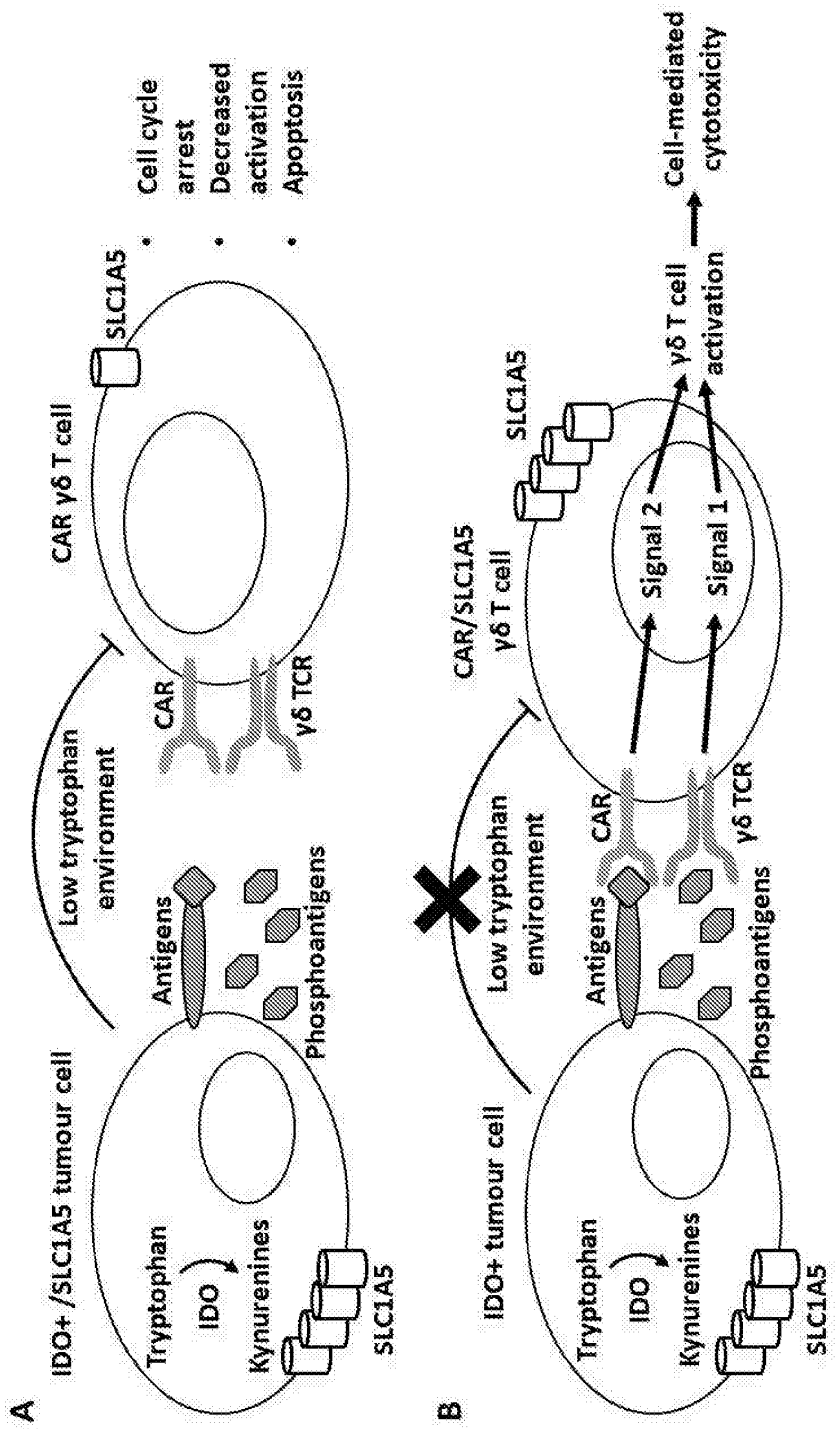

A
IDO+ /SLC1A5 tumour cell
Tryptophan
IDO
Kynurenines
SLC1A5
Antigens
Phosphoantigens
Low tryptophan environment
CAR γδ T cell
SLC1A5
CAR
γδ TCR
Cell cycle arrest
Decreased activation
Apoptosis
B
IDO+ tumour cell
Tryptophan
IDO
Kynurenines
SLC1A5
Antigens
Phosphoantigens
Low tryptophan environment
CAR/SLC1A5 γδ T cell
SLC1A5
CAR
γδ TCR
Signal 2
Signal 1
γδ T cell activation
Cell-mediated cytotoxicity

Figure 5

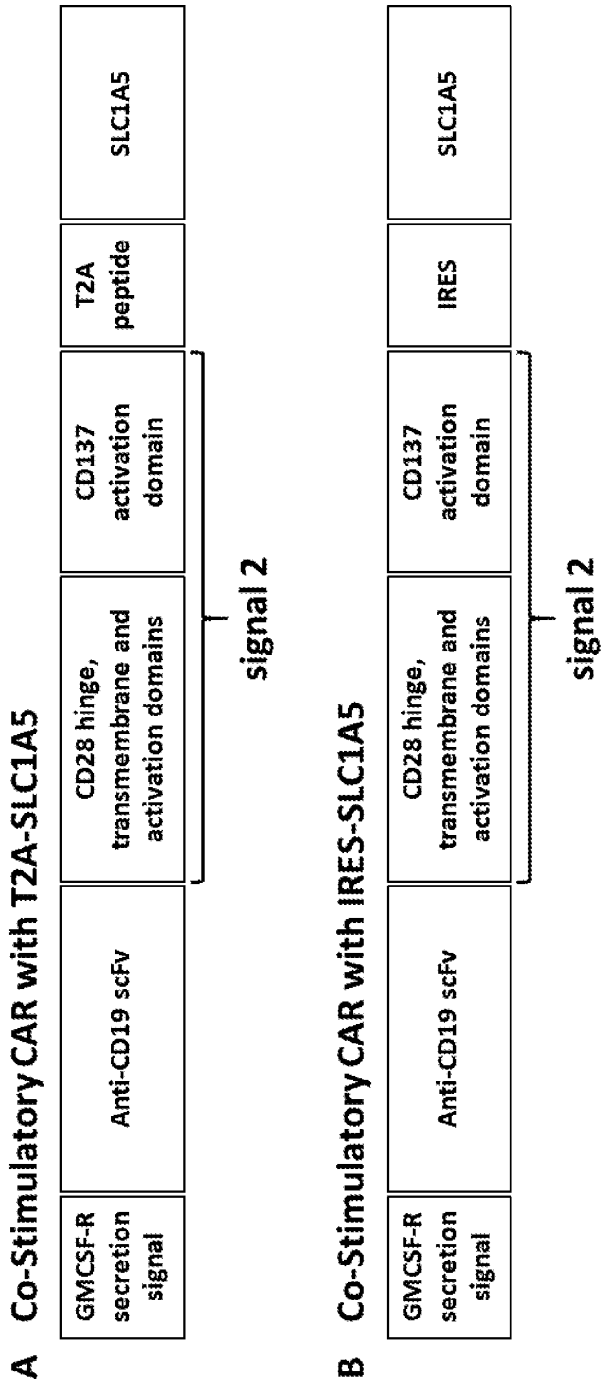
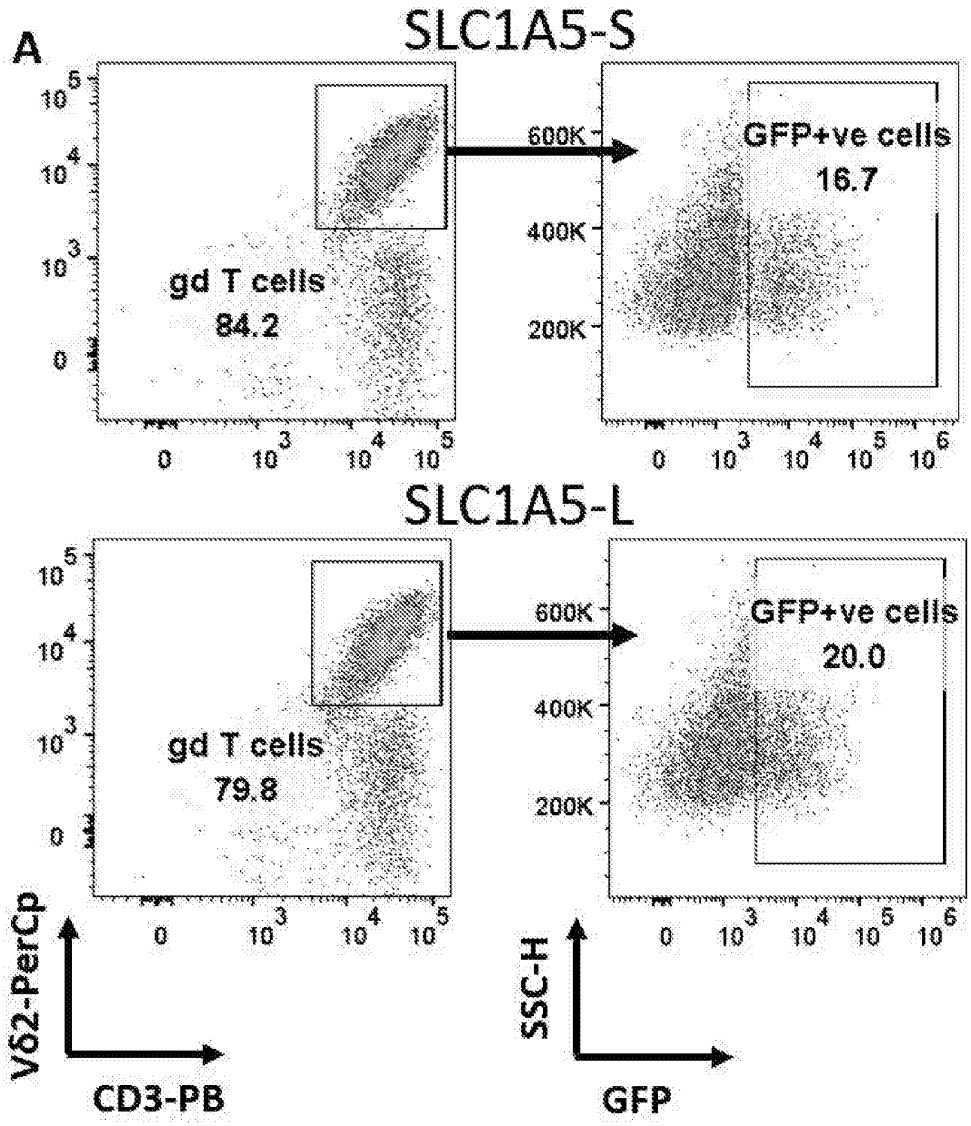

A Co-Stimulatory CAR with T2A-SLC1A5
GMCSF-R secretion signal
Anti-CD19 scFv
CD28 hinge, transmembrane and activation domains
CD137 activation domain
T2A peptide
SLC1A5
signal 2
B Co-Stimulatory CAR with IRES-SLC1A5
GMCSF-R secretion signal
Anti-CD19 scFv
CD28 hinge, transmembrane and activation domains
CD137 activation domain
IRES
SLC1A5
signal 2

Figure 6


A
SLC1A5-S
gd T cells
84.2
GFP+ve cells
16.7
SLC1A5-L
gd T cells
79.8
GFP+ve cells
20.0
Vδ2-PerCp
CD3-PB
SSC-H
GFP

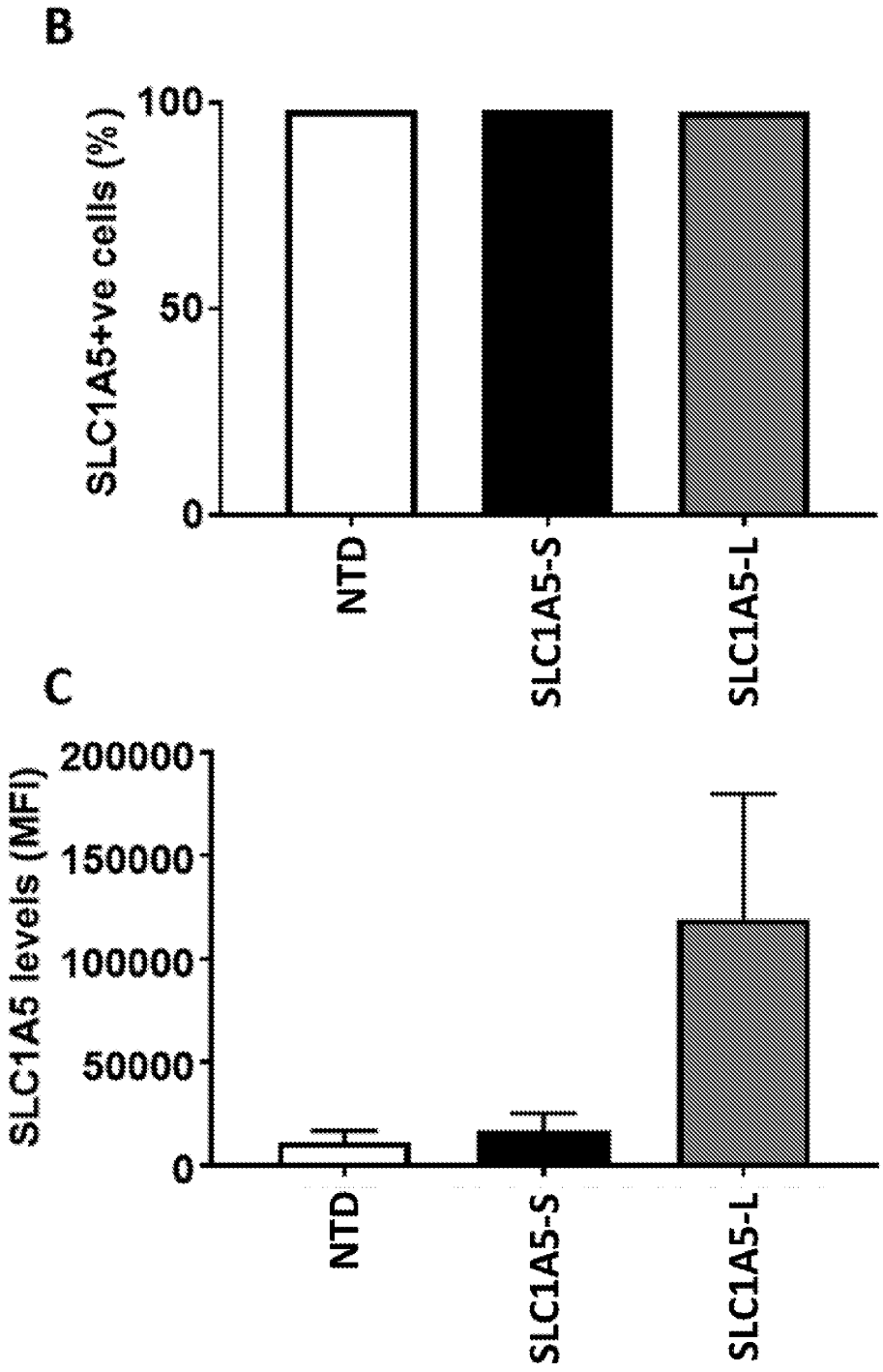
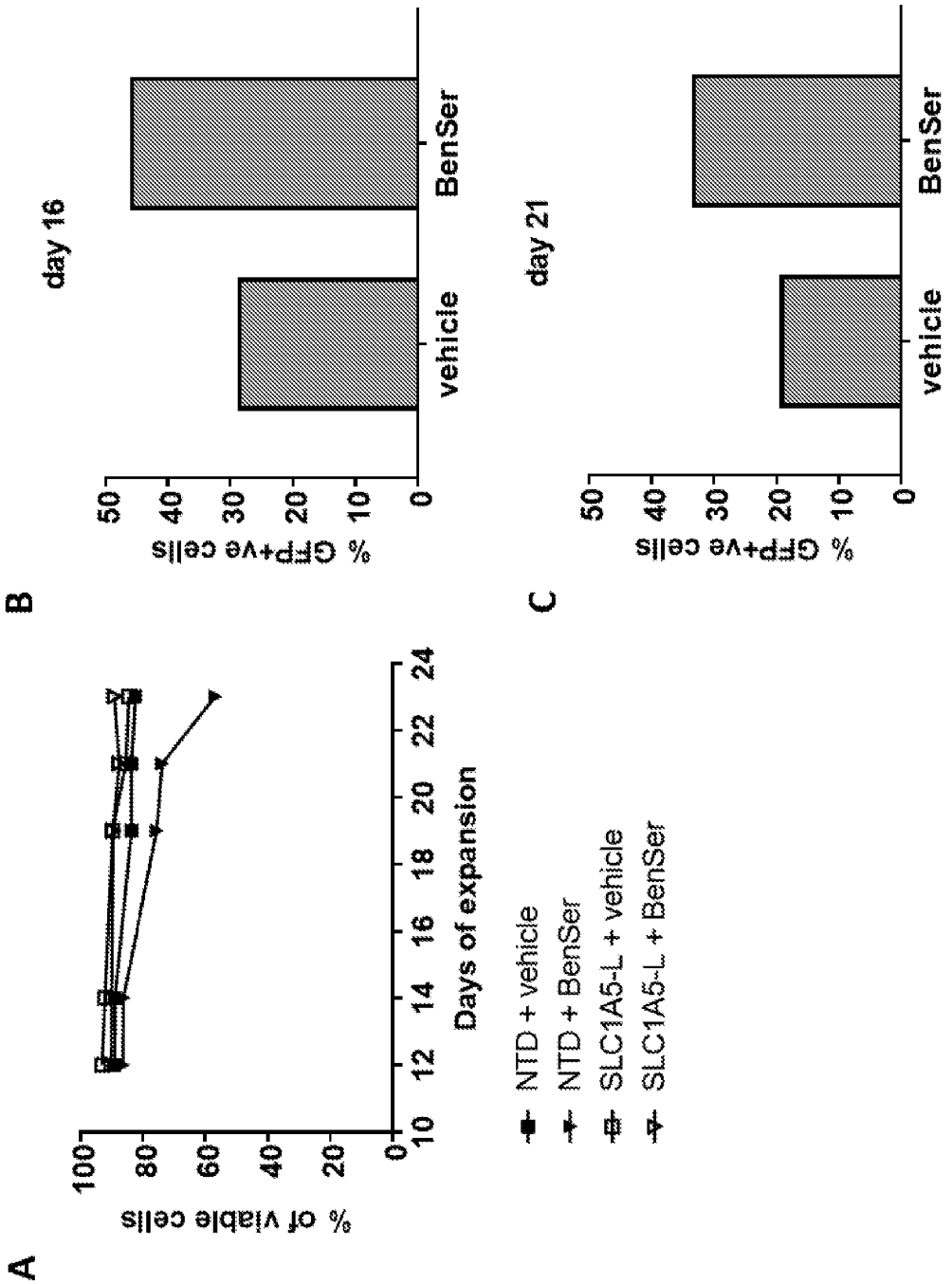

B
SLC1A5+ve cells (%)
100
50
0
NTD
SLC1A5-S
SLC1A5-L
C
SLC1A5 levels (MFI)
200000
150000
100000
50000
0
NTD
SLC1A5-S
SLC1A5-L

Figure 6

Figure 7


A
% of viable cells
100
80
60
40
20
0
10
12
14
16
18
20
22
24
Days of expansion
NTD + vehicle
NTD + BenSer
SLC1A5-L + vehicle
SLC1A5-L + BenSer
B
day 16
% GFP+ve cells
50
40
30
20
10
0
vehicle
BenSer
C
day 21
% GFP+ve cells
50
40
30
20
10
0
vehicle
BenSer