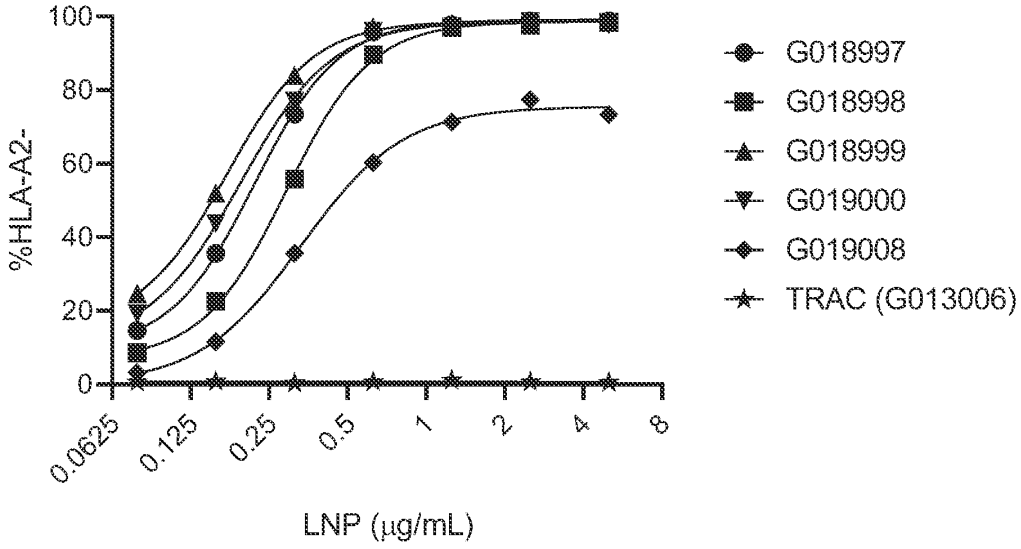
100
80
60
40
20
0
%HLA-A2-
0.0625
0.125
0.25
0.5
1
2
4
8
LNP (μg/mL)
G018997
G018998
G018999
G019000
G019008
TRAC (G013006)

FIG. 1A

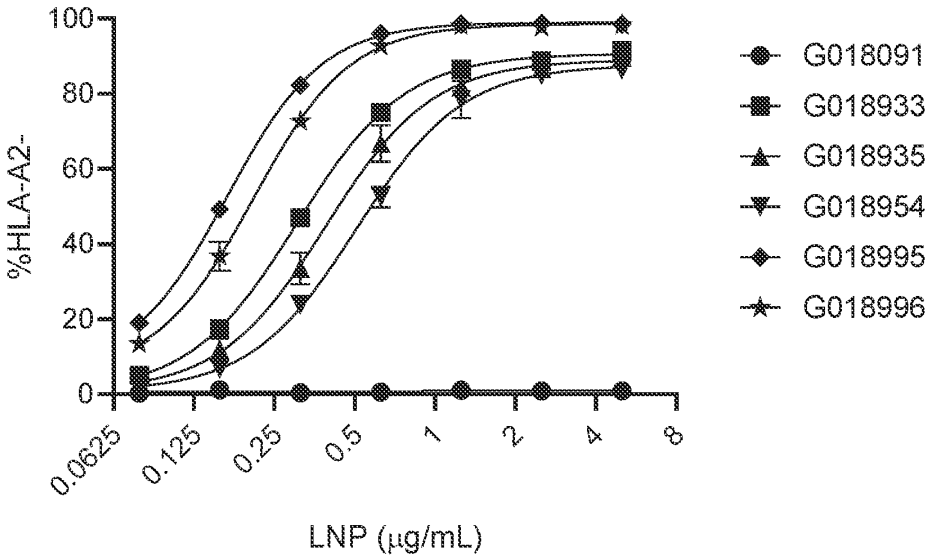
100
80
60
40
20
0
%HLA-A2-
0.0625
0.125
0.25
0.5
1
2
4
8
LNP (μg/mL)
G018091
G018933
G018935
G018954
G018995
G018996

FIG. 1B

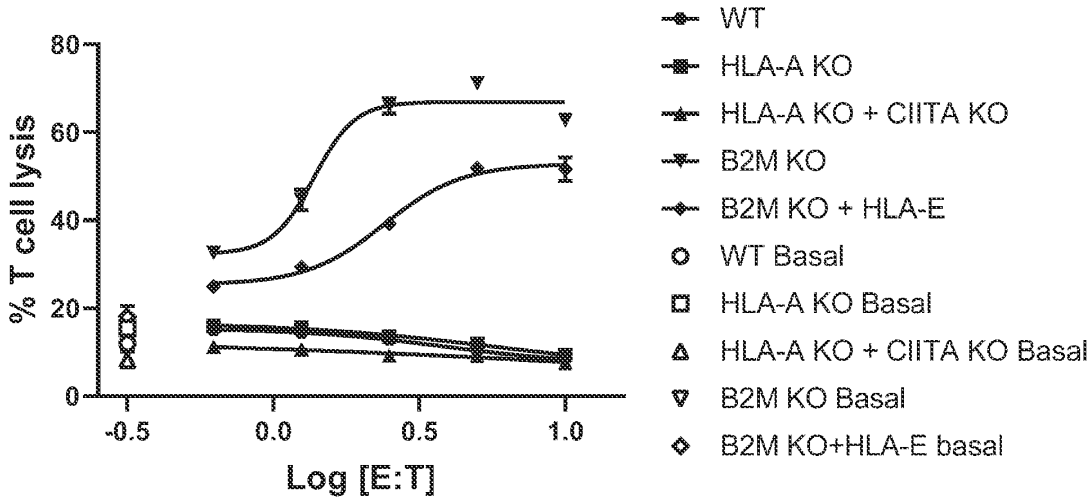
% T cell lysis
80
60
40
20
0
-0.5
0.0
0.5
1.0
Log [E:T]
WT
HLA-A KO
HLA-A KO + CIITA KO
B2M KO
B2M KO + HLA-E
WT Basal
HLA-A KO Basal
HLA-A KO + CIITA KO Basal
B2M KO Basal
B2M KO+HLA-E basal

FIG. 2

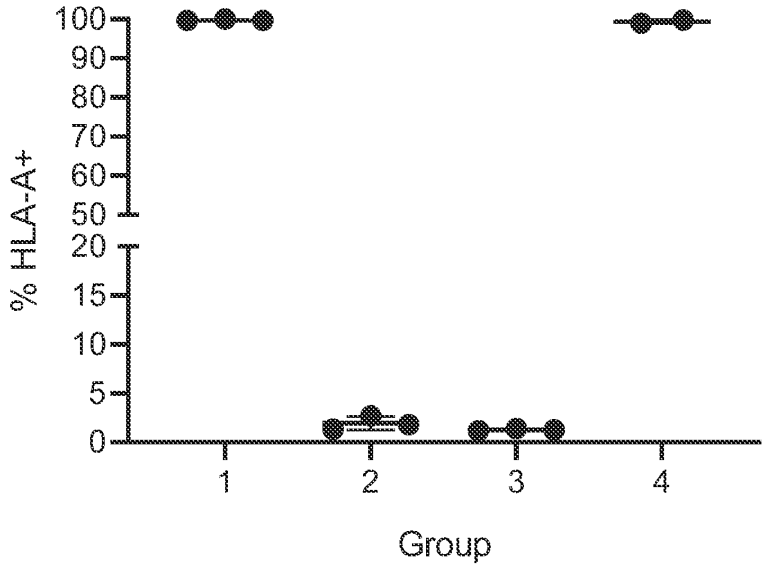
100
90
80
70
60
50
20
15
10
5
0
% HLA-A+
1
2
3
4
Group

FIG. 3A

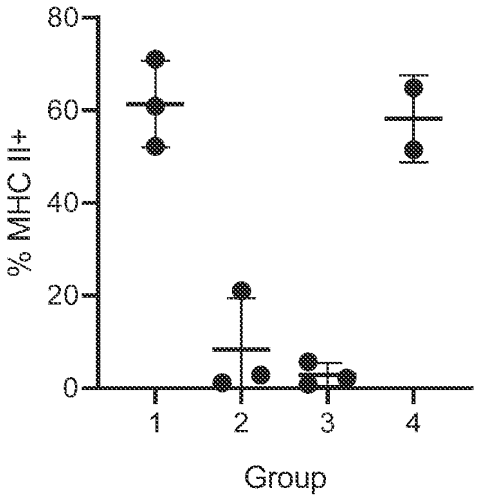
80
60
40
20
0
% MHC II+
1
2
3
4
Group

FIG. 3B

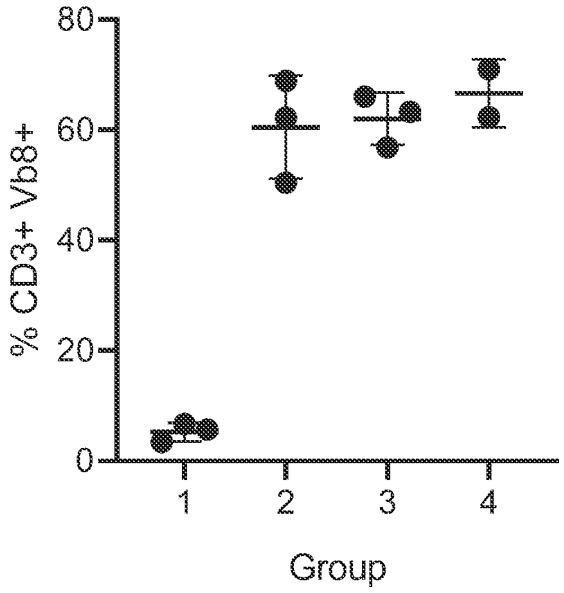
80
60
40
20
0
% CD3+ Vb8+
1
2
3
4
Group

FIG. 3C

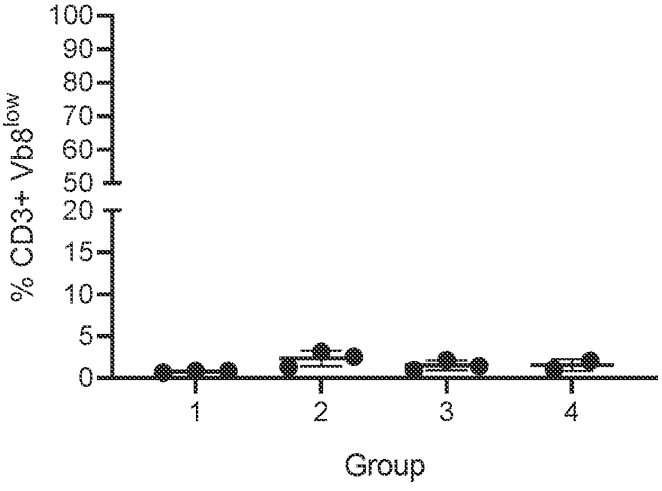
100
90
80
70
60
50
20
15
10
5
0
% CD3+ Vb8low
1
2
3
4
Group

FIG. 3D

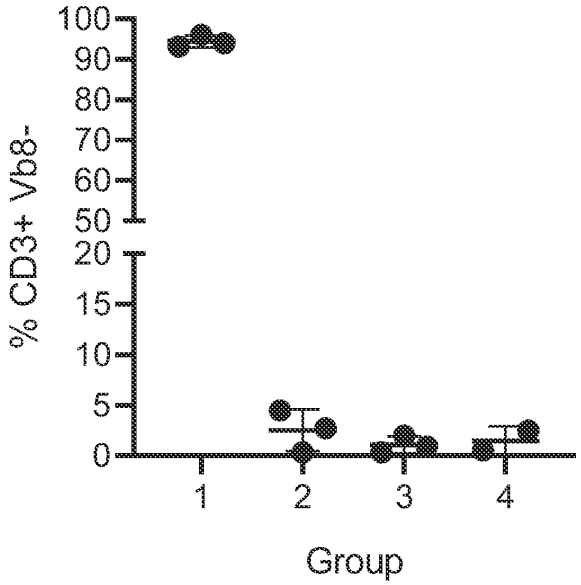
% CD3+ Vb8-
100
90
80
70
60
50
20
15
10
5
0
1
2
3
4
Group

FIG. 3E

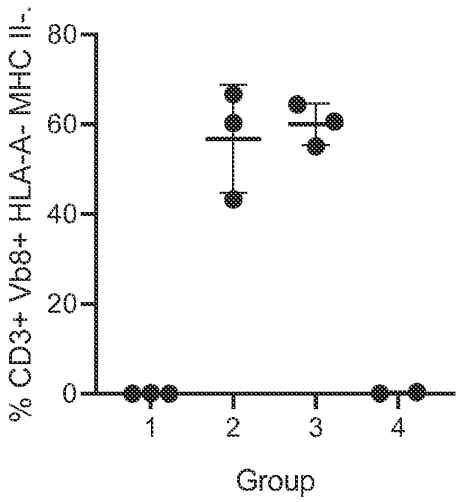
% CD3+ Vb8+ HLA-A- MHC II-
80
60
40
20
0
1
2
3
4
Group

FIG. 3F

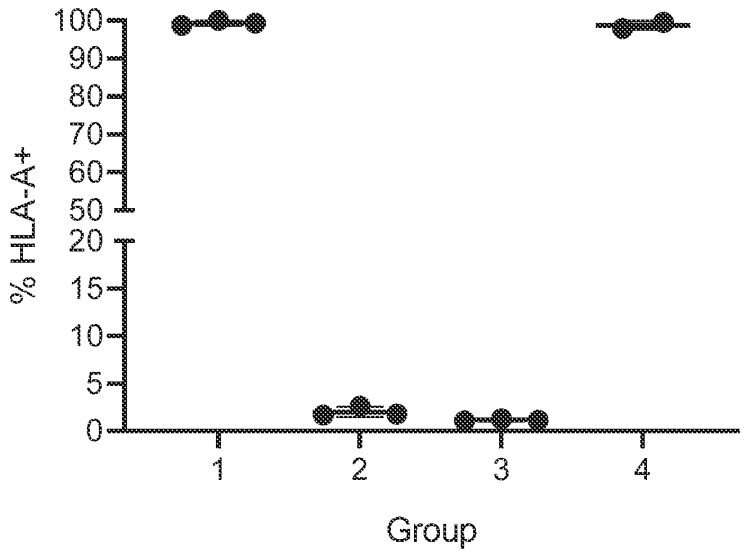
100
90
80
70
60
50
20
15
10
5
0
% HLA-A+
1
2
3
4
Group

FIG. 4A

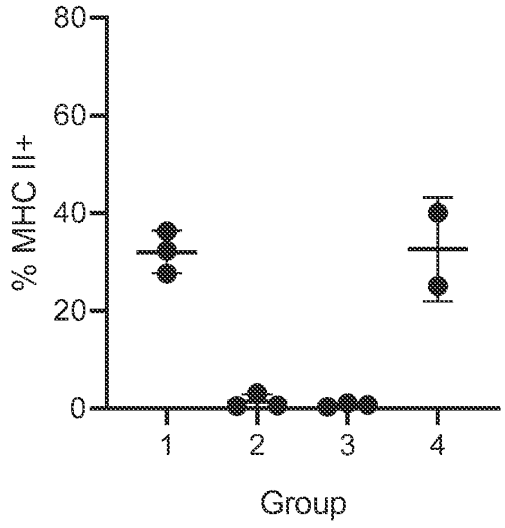
80
60
40
20
0
% MHC II+
1
2
3
4
Group

FIG. 4B

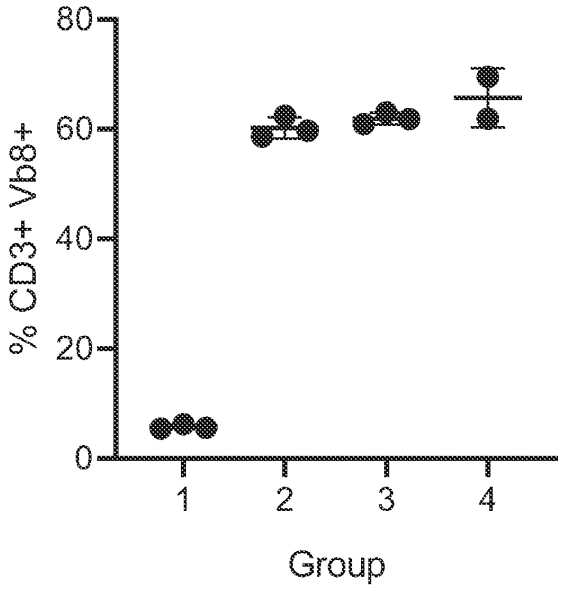
80
60
40
20
0
% CD3+ Vb8+
1
2
3
4
Group

FIG. 4C

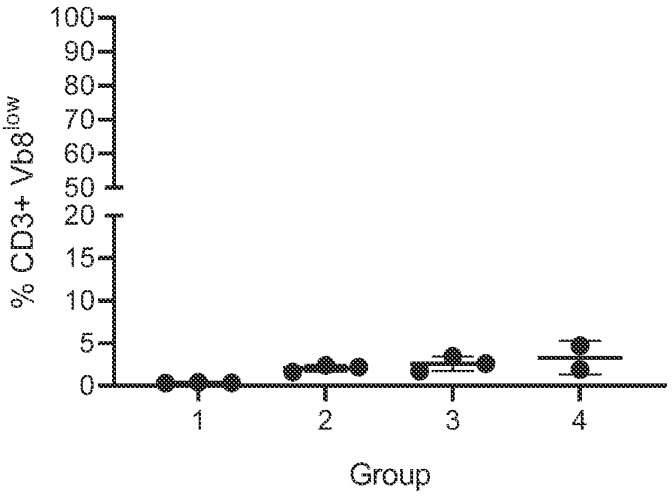
100
90
80
70
60
50
20
15
10
5
0
% CD3+ Vb8low
1
2
3
4
Group

FIG. 4D

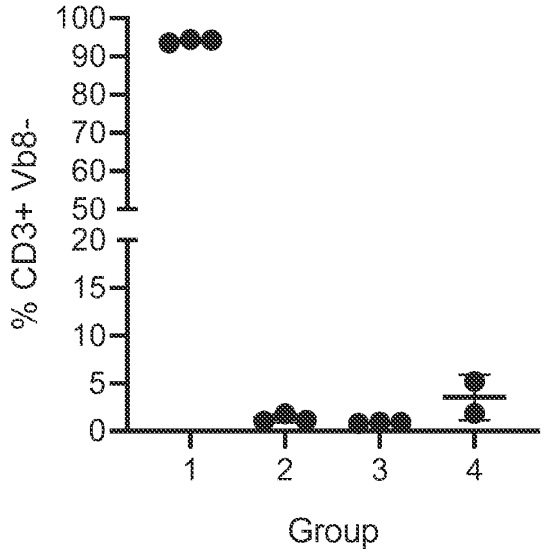
% CD3+ Vb8-
100
90
80
70
60
50
20
15
10
5
0
1
2
3
4
Group

FIG. 4E

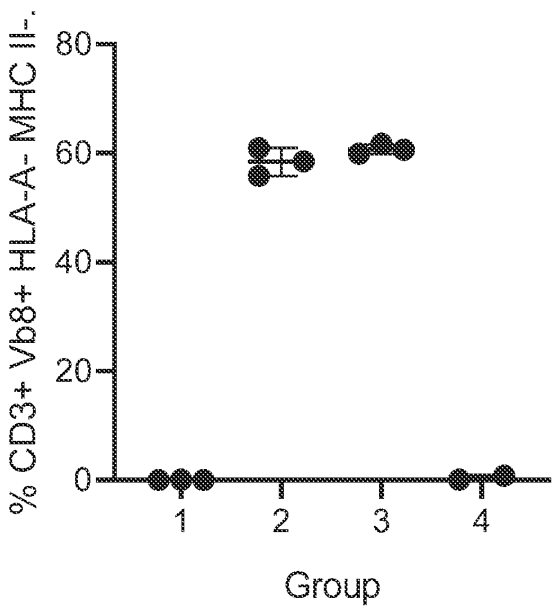
% CD3+ Vb8+ HLA-A- MHC II-.
80
60
40
20
0
1
2
3
4
Group

FIG. 4F

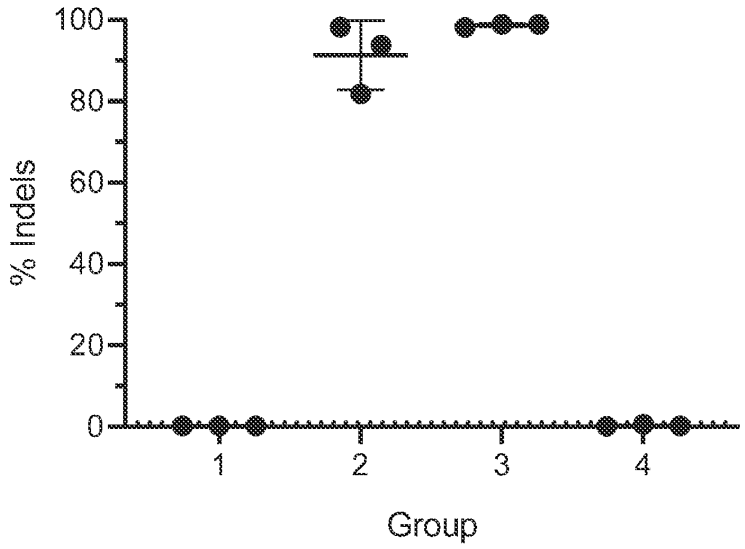
100
80
60
40
20
0
% Indels
1
2
3
4
Group

FIG. 5A

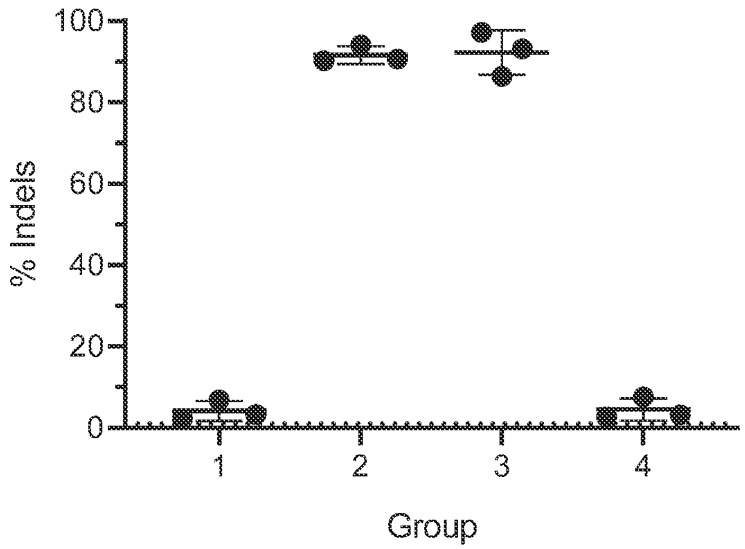
100
80
60
40
20
0
% Indels
1
2
3
4
Group

FIG. 5B

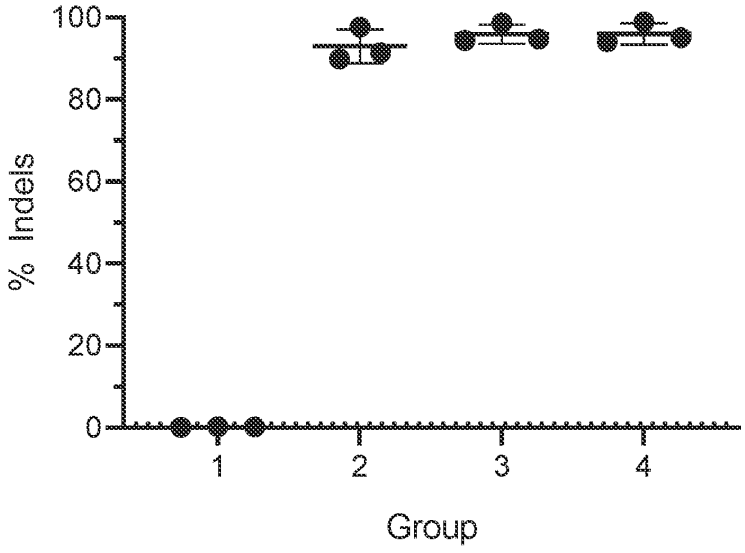
100
80
60
40
20
0
% Indels
1
2
3
4
Group

FIG. 5C

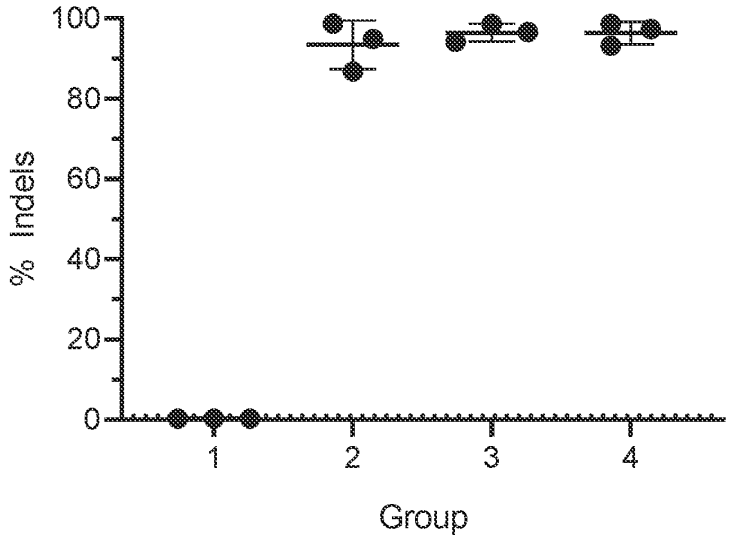
100
80
60
40
20
0
% Indels
1
2
3
4
Group

FIG. 5D

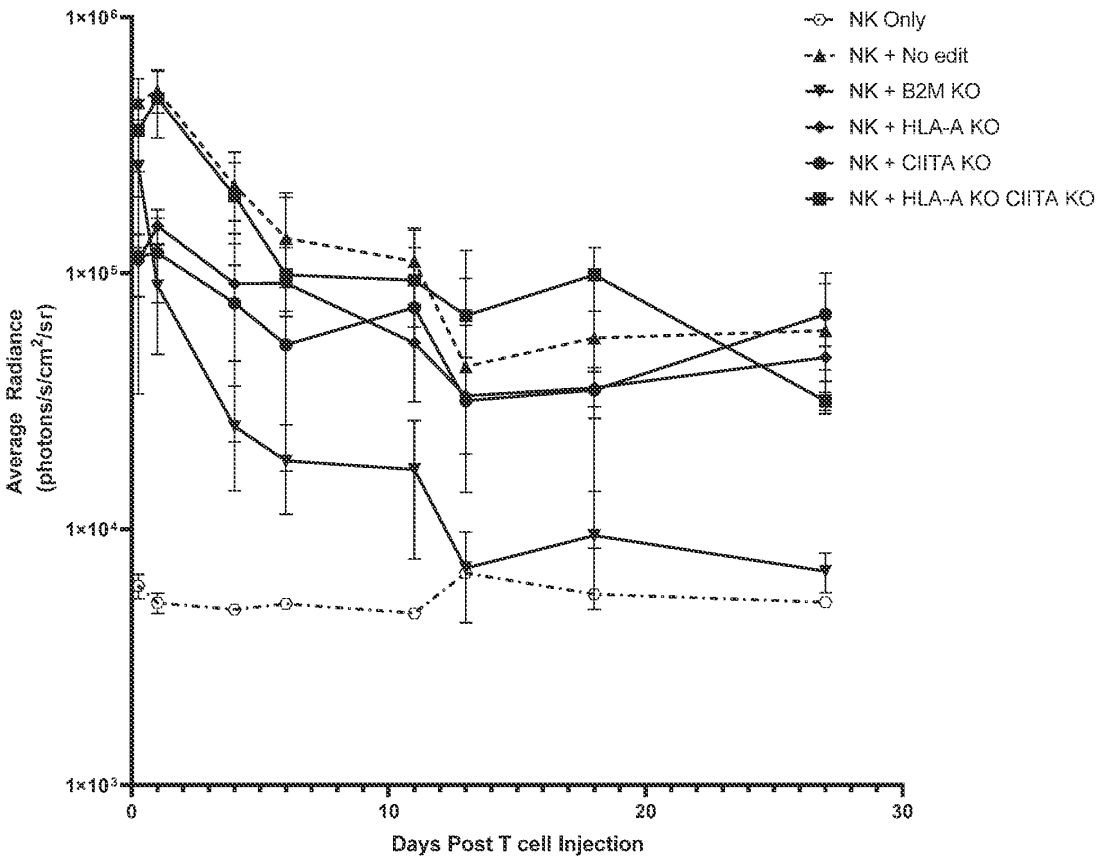
NK Only
NK + No edit
NK + B2M KO
NK + HLA-A KO
NK + CIITA KO
NK + HLA-A KO CIITA KO
1×10⁶
1×10⁵
1×10⁴
1×10³
Average Radiance (photons/s/cm²/sr)
0
10
20
30
Days Post T cell Injection

FIG. 6A

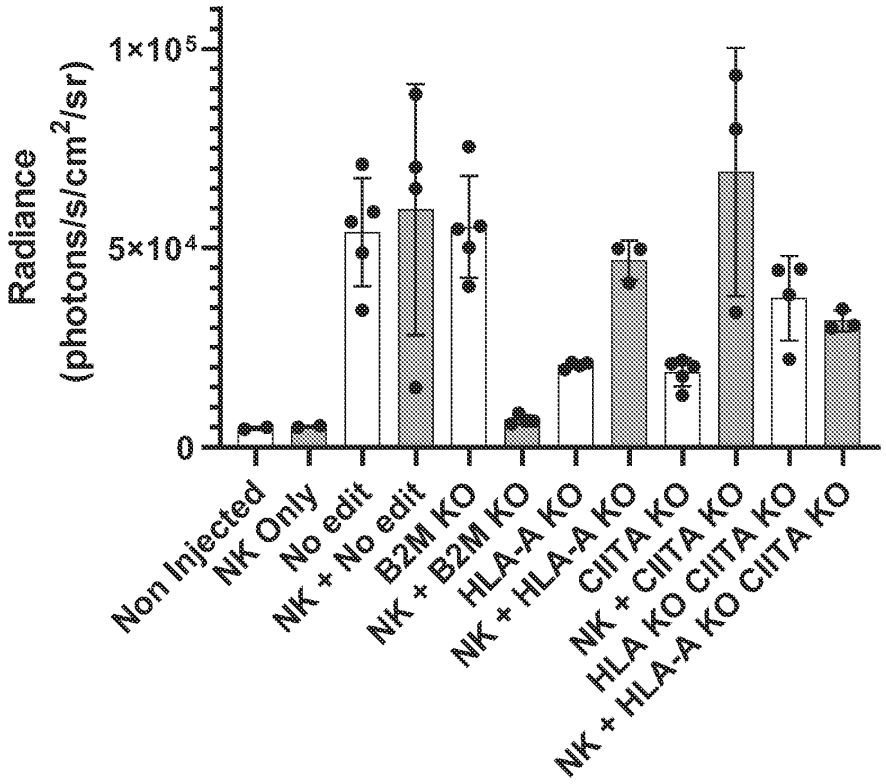
Radiance (photons/s/cm^2/sr)
1×10^5
5×10^4
0
Non Injected
NK Only
No edit
NK + No edit
B2M KO
NK + B2M KO
HLA-A KO
NK + HLA-A KO
CIITA KO
NK + CIITA KO
HLA KO CIITA KO
NK + HLA-A KO CIITA KO

FIG. 6B

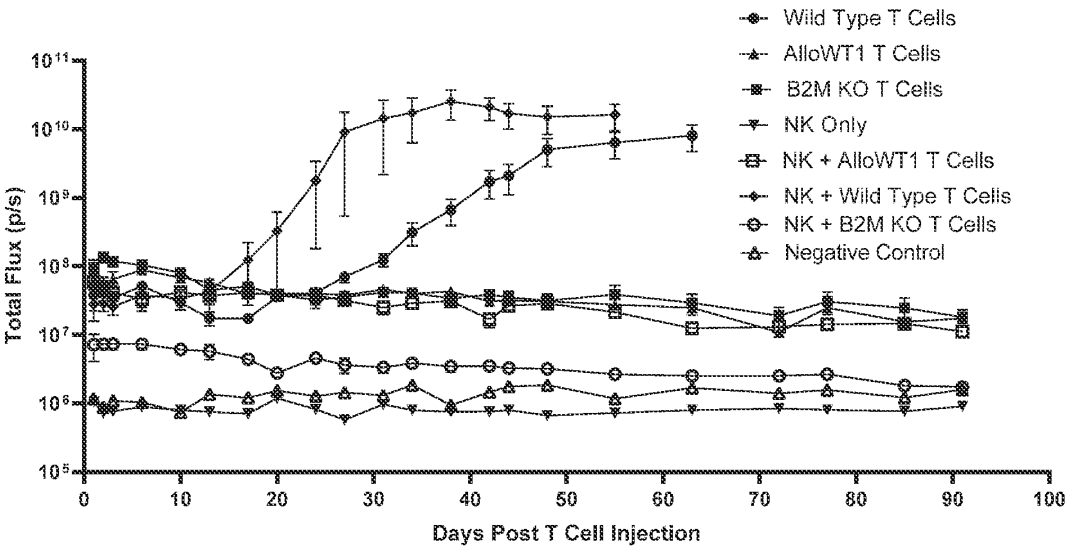
Wild Type T Cells
AlloWT1 T Cells
B2M KO T Cells
NK Only
NK + AlloWT1 T Cells
NK + Wild Type T Cells
NK + B2M KO T Cells
Negative Control
Total Flux (p/s)
Days Post T Cell Injection

FIG. 7A

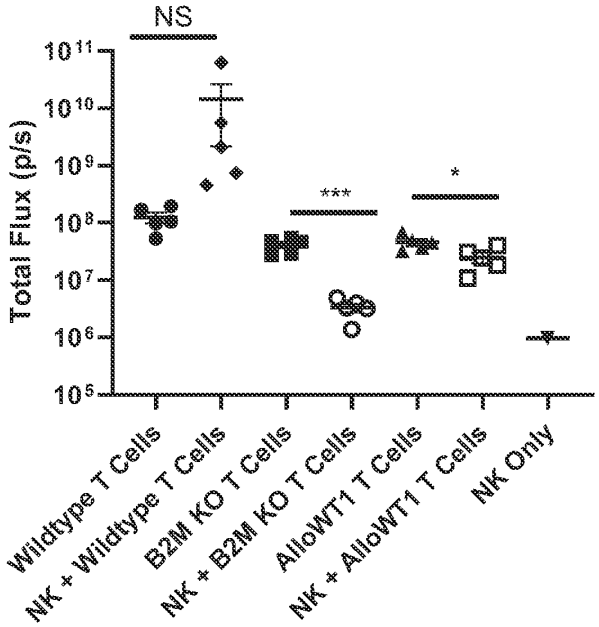
NS
***
*
Total Flux (p/s)
Wildtype T Cells
NK + Wildtype T Cells
B2M KO T Cells
NK + B2M KO T Cells
AlloWT1 T Cells
NK + AlloWT1 T Cells
NK Only

FIG. 7B

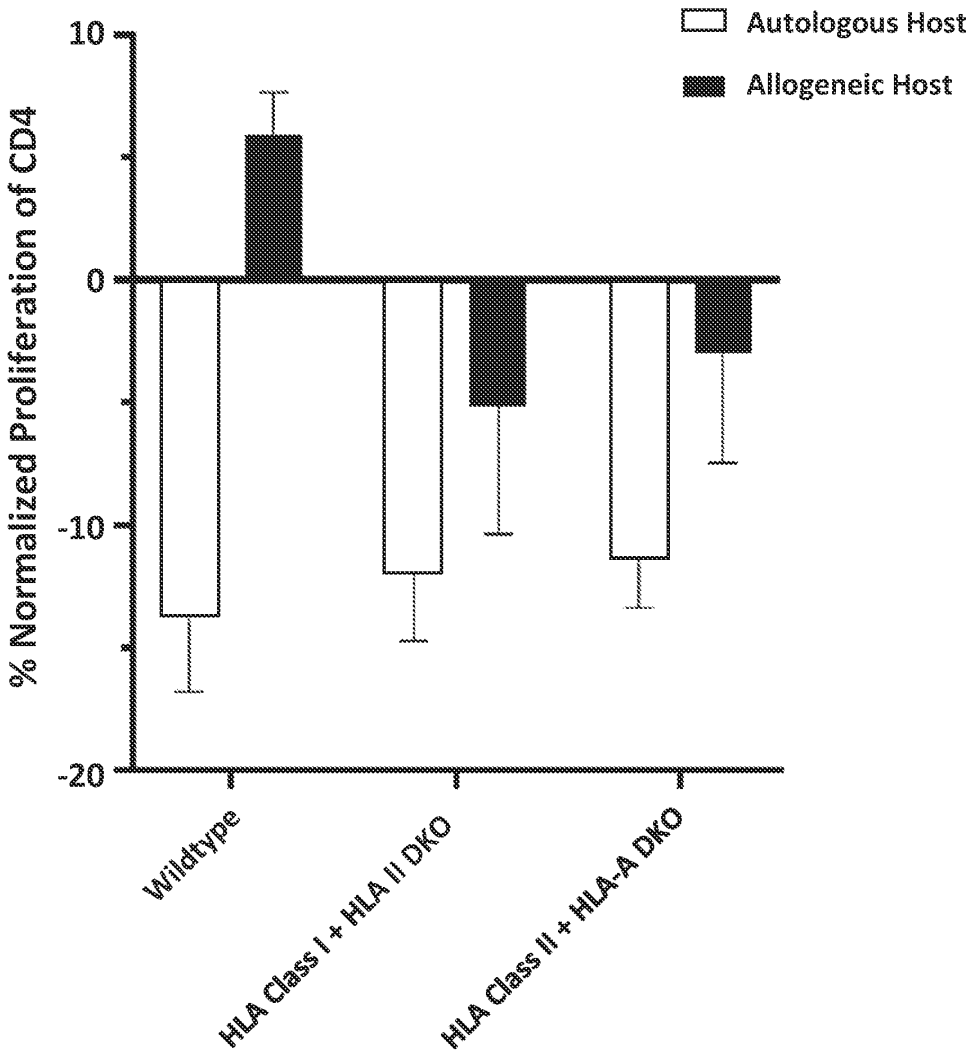
Autologous Host
Allogeneic Host
% Normalized Proliferation of CD4
10
0
-10
-20
Wildtype
HLA Class I + HLA II DKO
HLA Class II + HLA-A DKO

FIG. 8A

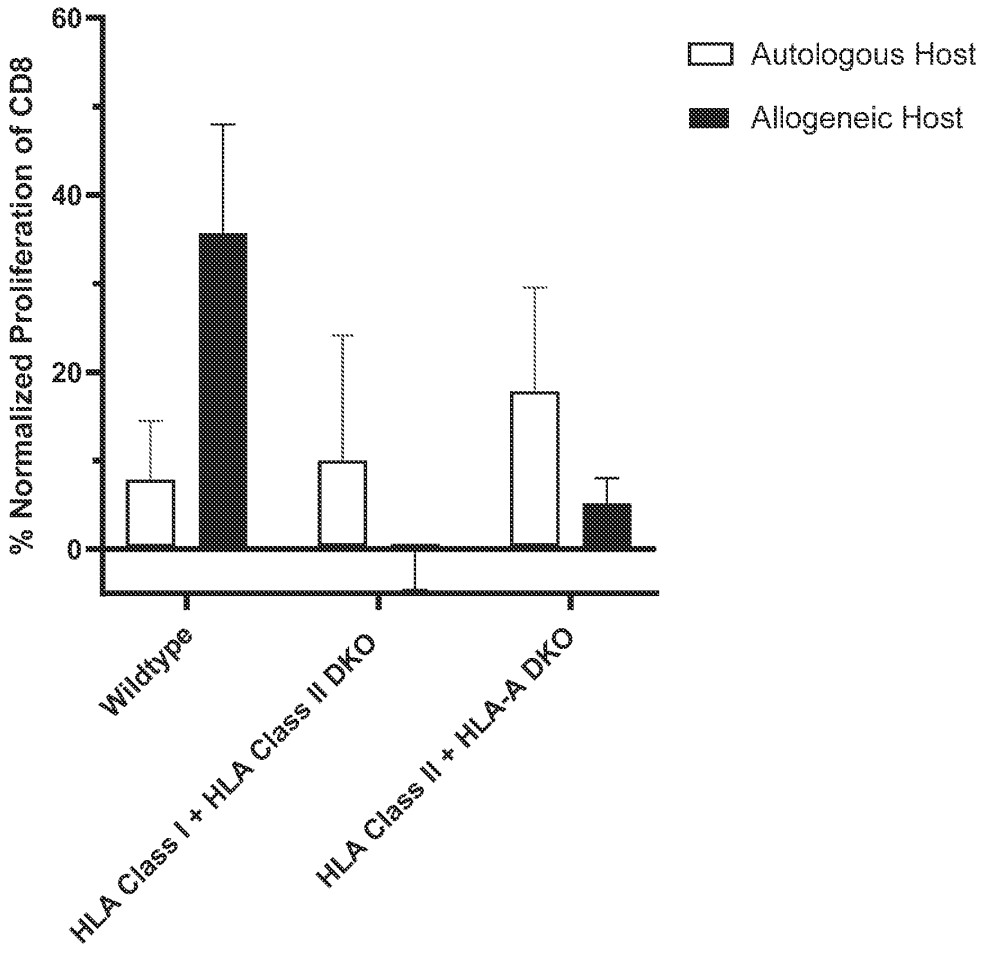
60
40
20
0
% Normalized Proliferation of CD8
Autologous Host
Allogeneic Host
Wildtype
HLA Class I + HLA Class II DKO
HLA Class II + HLA-A DKO

FIG. 8B

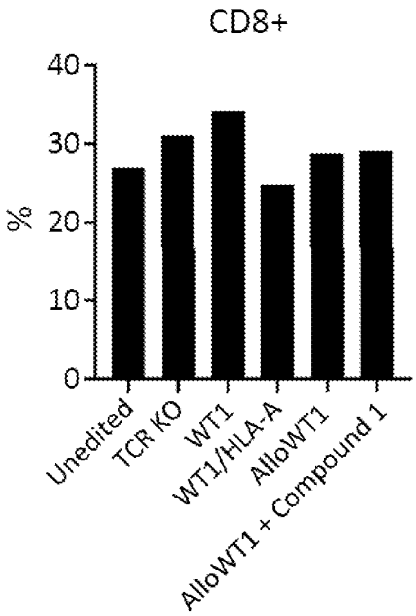
CD8+
40
30
20
10
0
%
Unedited
TCR KO
WT1
WT1/HLA-A
AlloWT1
AlloWT1 + Compound 1

FIG. 9A

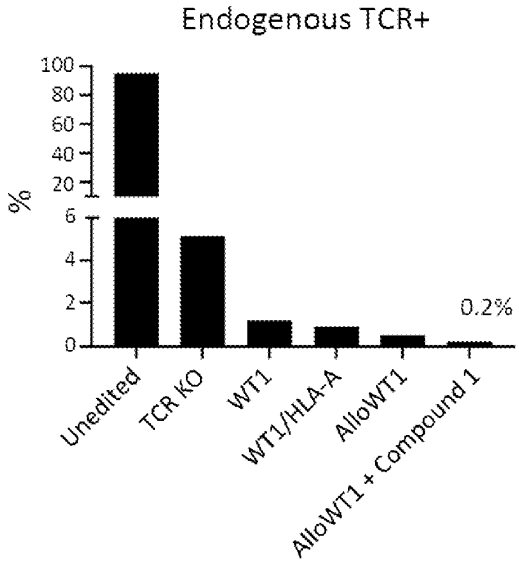
Endogenous TCR+
100
80
60
40
20
6
4
2
0
%
0.2%
Unedited
TCR KO
WT1
WT1/HLA-A
AlloWT1
AlloWT1 + Compound 1

FIG. 9B

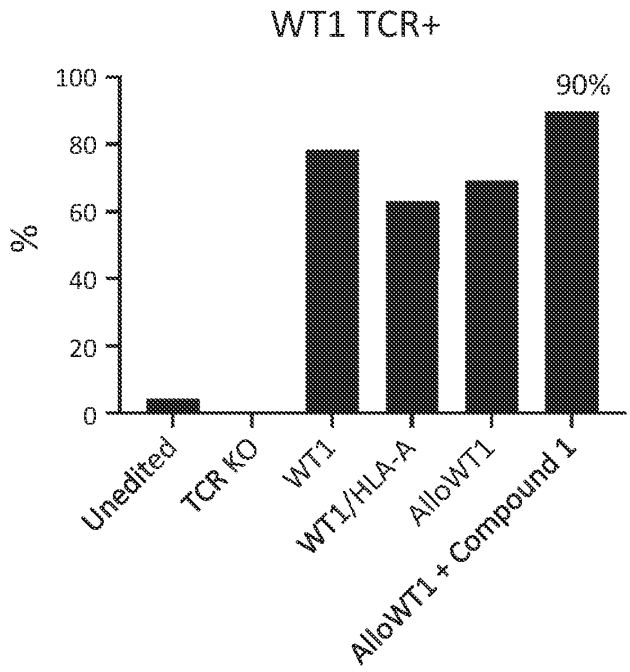
WT1 TCR+
100
80
60
40
20
0
%
90%
Unedited
TCR KO
WT1
WT1/HLA-A
AlloWT1
AlloWT1 + Compound 1

FIG. 9C

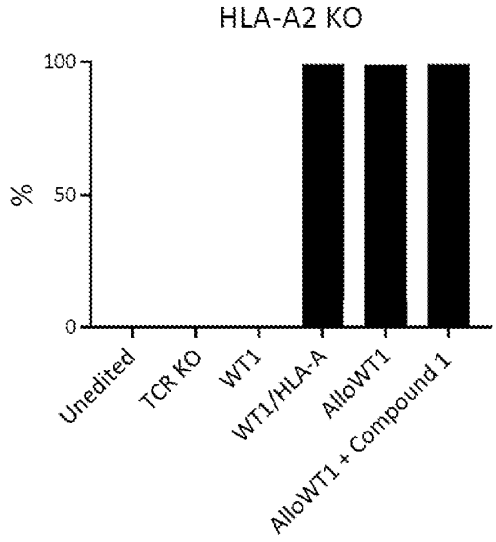
HLA-A2 KO
100
50
0
%
Unedited
TCR KO
WT1
WT1/HLA-A
AlloWT1
AlloWT1 + Compound 1

FIG. 9D

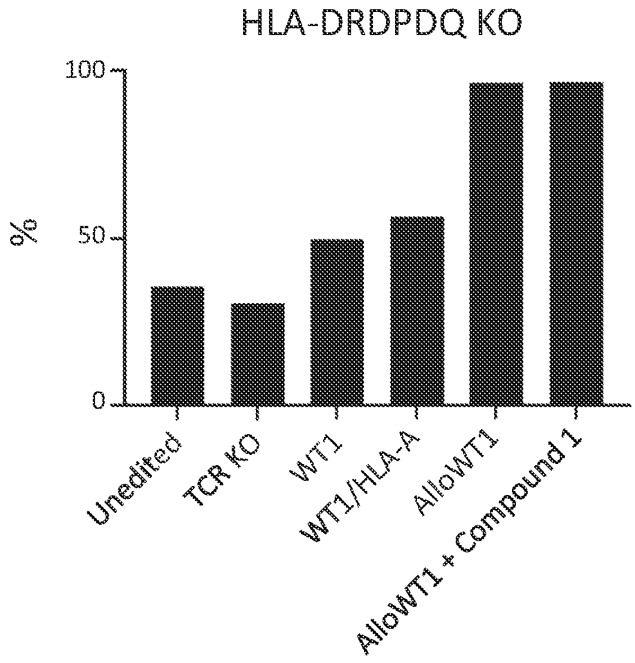
HLA-DRDPDQ KO
100
50
0
%
Unedited
TCR KO
WT1
WT1/HLA-A
AlloWT1
AlloWT1 + Compound 1

FIG. 9E

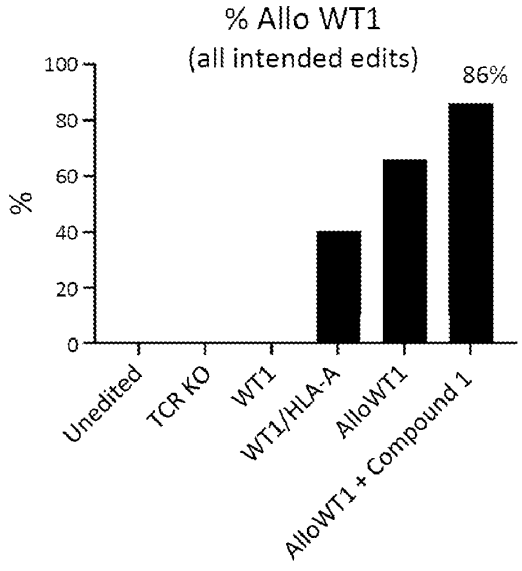
% Allo WT1
(all intended edits)
86%
100
80
60
40
20
0
%
Unedited
TCR KO
WT1
WT1/HLA-A
AlloWT1
AlloWT1 + Compound 1

FIG. 9F

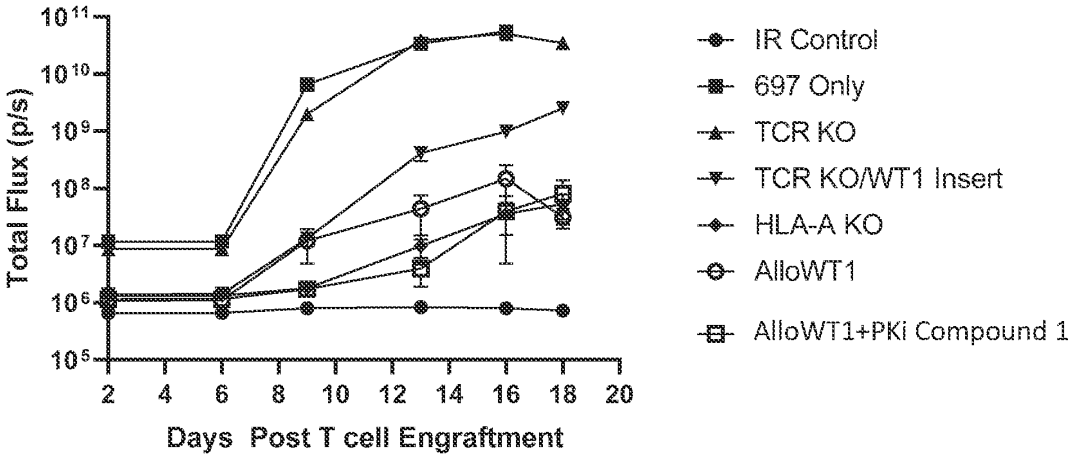
Total Flux (p/s)
10^{11}
10^{10}
10^{9}
10^{8}
10^{7}
10^{6}
10^{5}
2
4
6
8
10
12
14
16
18
20
Days Post T cell Engraftment
IR Control
697 Only
TCR KO
TCR KO/WT1 Insert
HLA-A KO
AlloWT1
AlloWT1+PKi Compound 1

FIG. 10

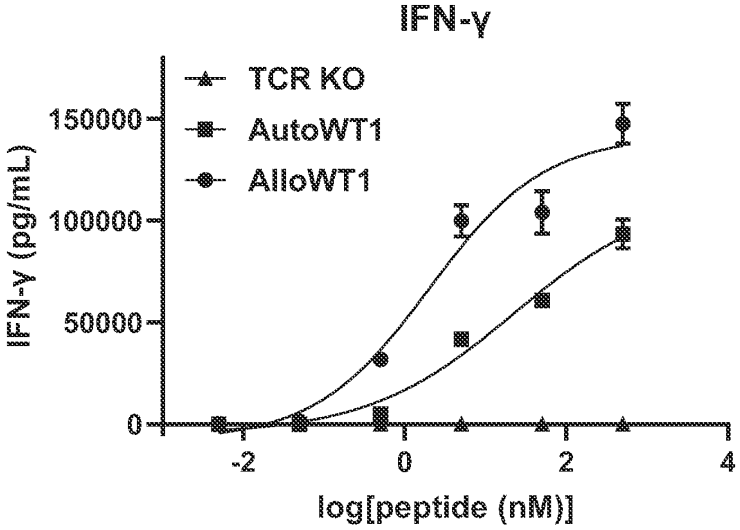

FIG. 11A

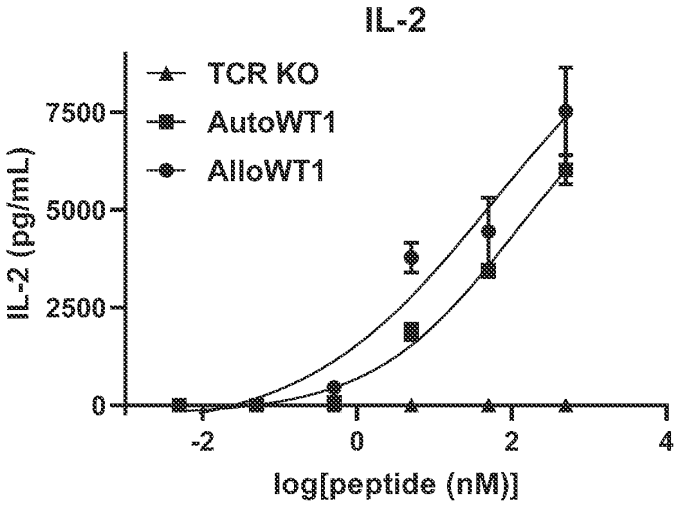

FIG. 11B

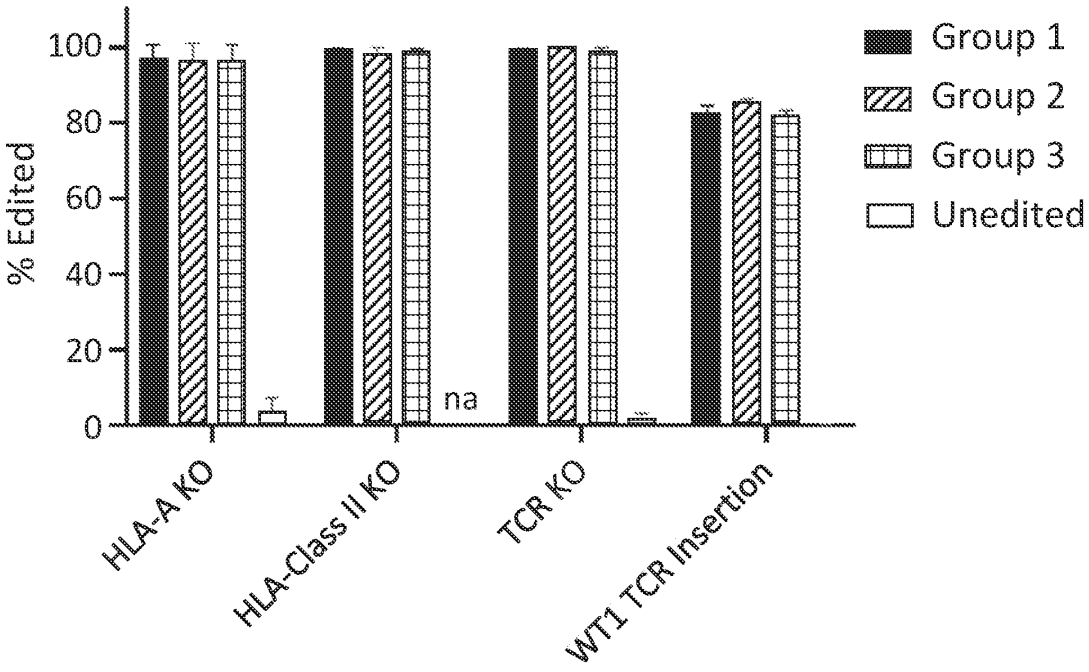
% Edited
100
80
60
40
20
0
na
HLA-A KO
HLA-Class II KO
TCR KO
WT1 TCR Insertion
Group 1
Group 2
Group 3
Unedited

FIG. 12A

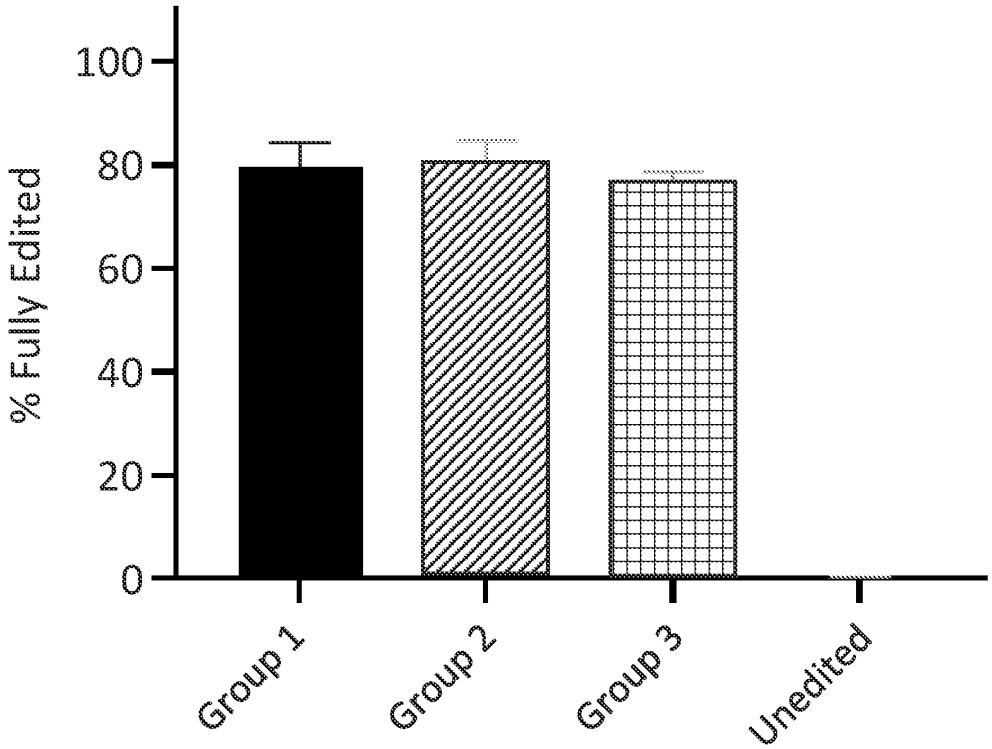

FIG. 12B

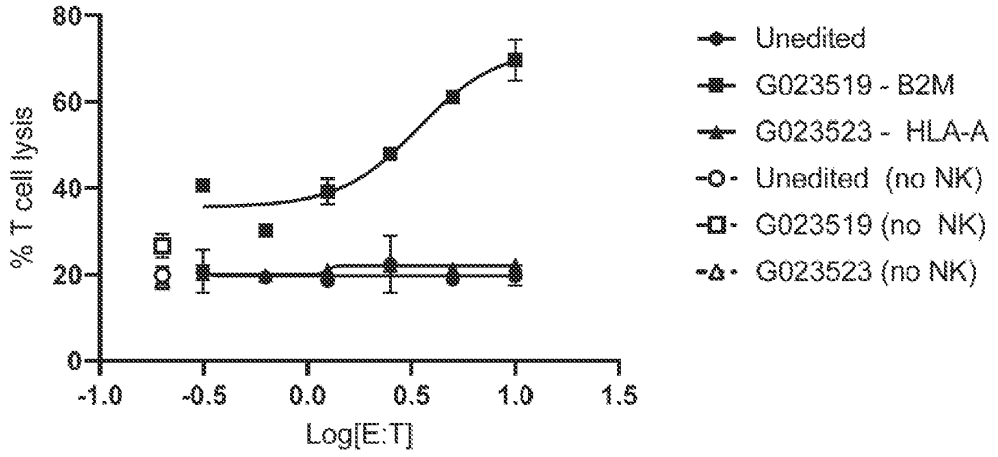
80
60
40
20
0
% T cell lysis
-1.0
-0.5
0.0
0.5
1.0
1.5
Log[E:T]
Unedited
G023519 - B2M
G023523 - HLA-A
Unedited (no NK)
G023519 (no NK)
G023523 (no NK)

FIG. 13

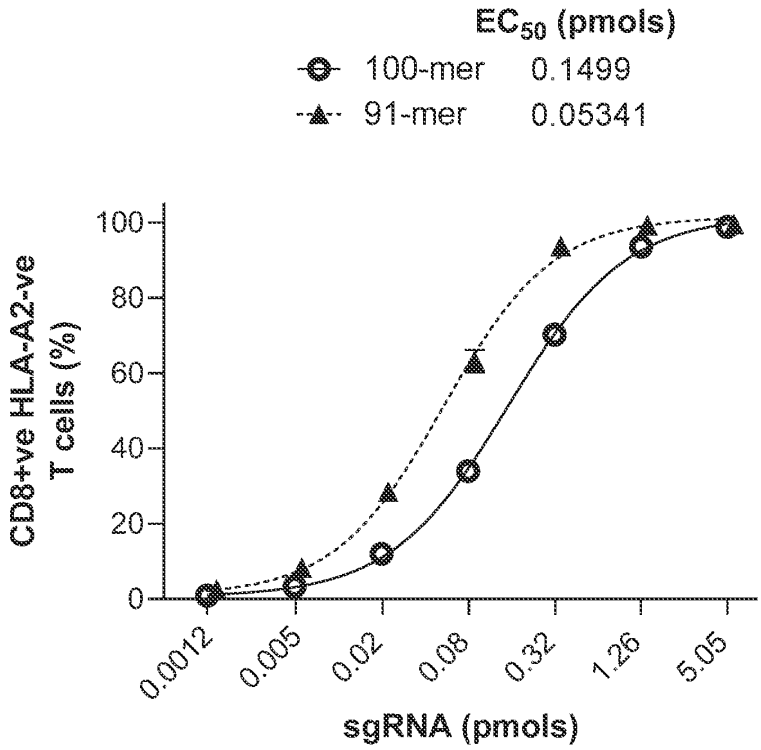
EC50 (pmols)
100-mer 0.1499
91-mer 0.05341
CD8+ve HLA-A2-ve T cells (%)
100
80
60
40
20
0
0.0012
0.005
0.02
0.08
0.32
1.26
5.05
sgRNA (pmols)

FIG. 14

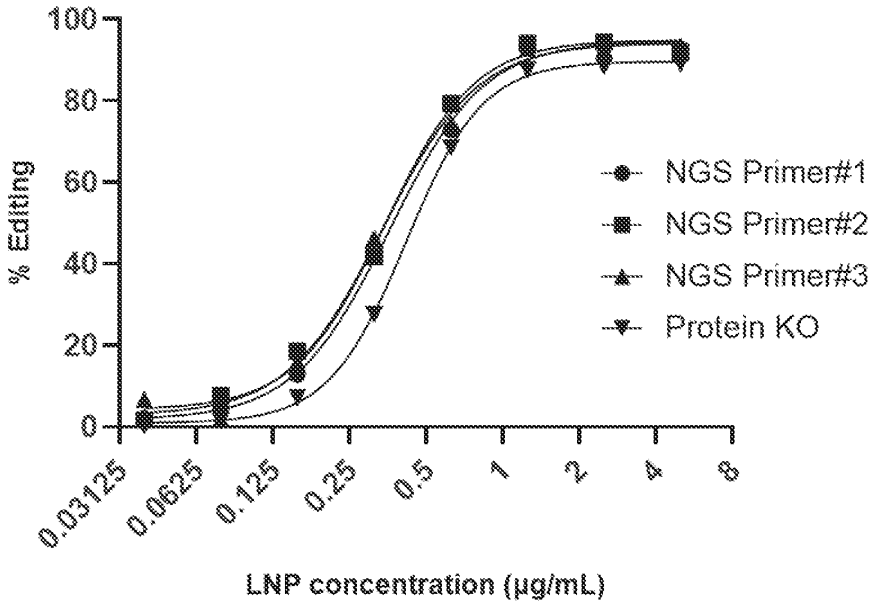

FIG. 15A

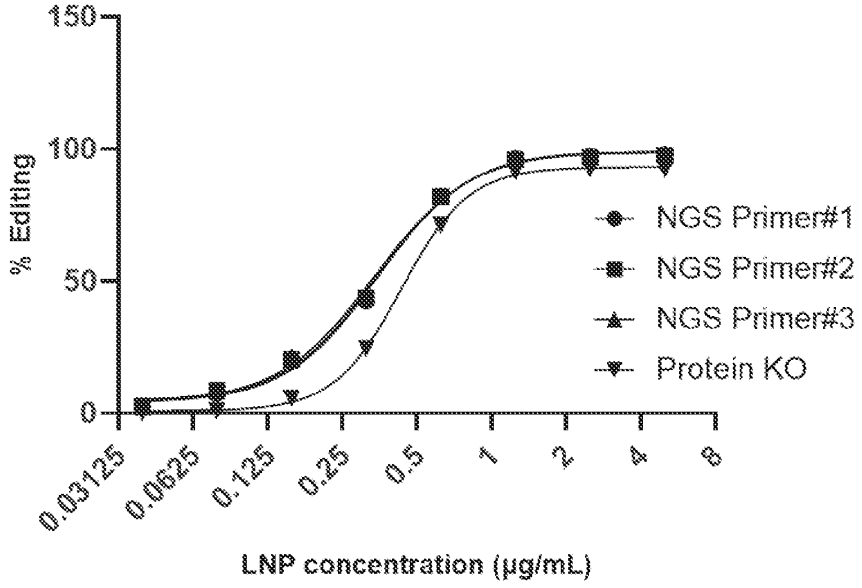

FIG. 15B

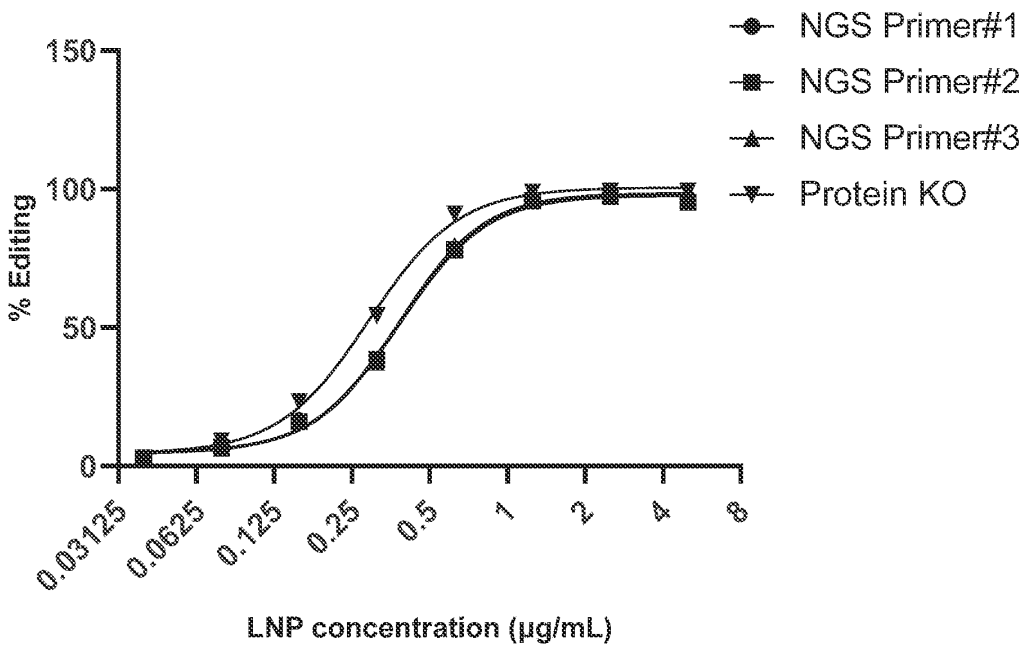
NGS Primer#1
NGS Primer#2
NGS Primer#3
Protein KO
% Editing
150
100
50
0
0.03125
0.0625
0.125
0.25
0.5
1
2
4
8
LNP concentration (µg/mL)

FIG. 15C