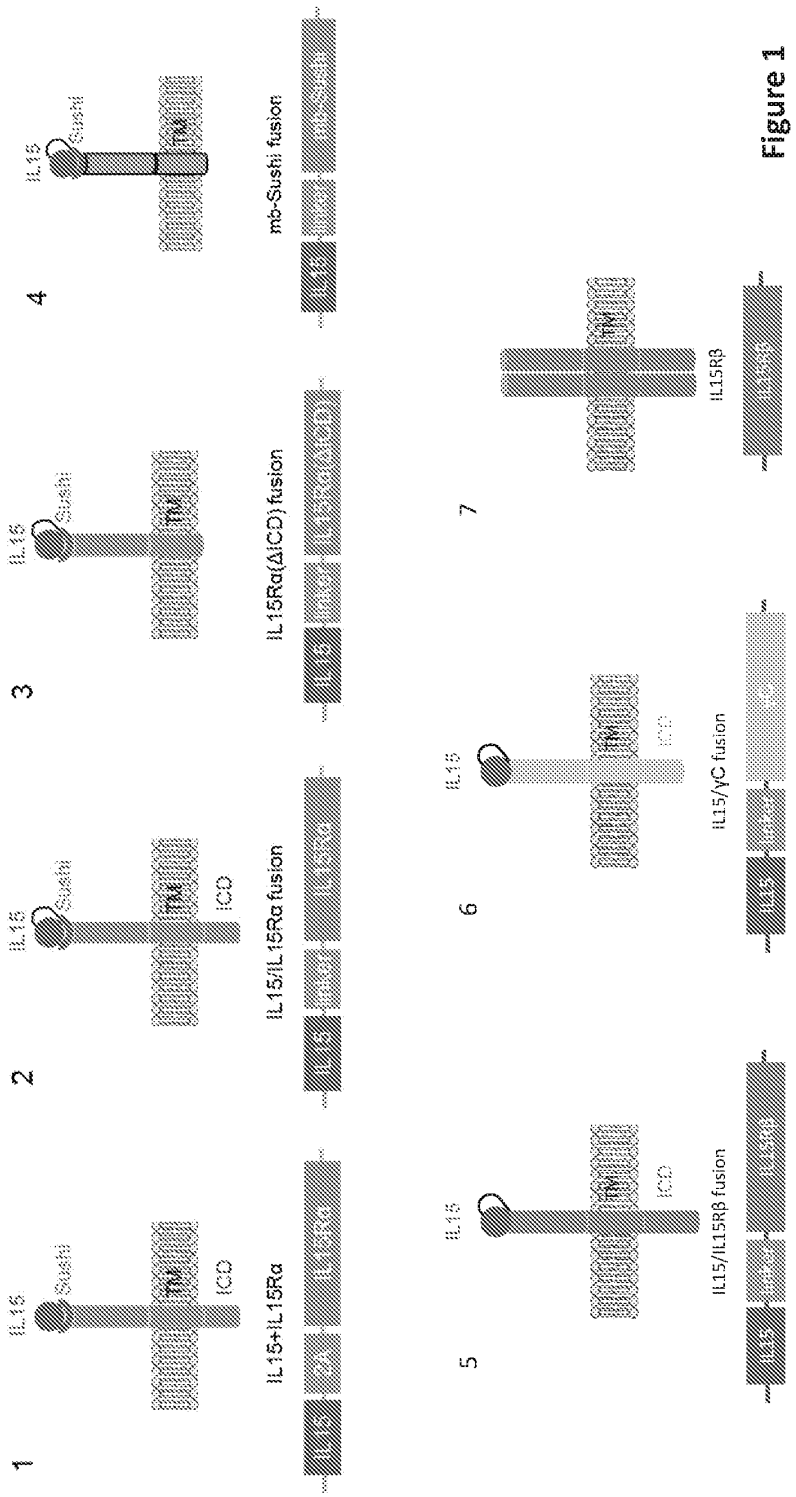

1
IL15
Sushi
TM
ICD
IL15+IL15Rα
2A
IL15Rα
2
IL15
Sushi
TM
ICD
IL15/IL15Rα fusion
IL15Rα
3
IL15
Sushi
TM
IL15/IL15Rα(ΔiCD) fusion
IL15Rα(ΔiCD)
4
IL15
Sushi
TM
mb-Sushi fusion
mb-Sushi
5
IL15
TM
ICD
IL15/IL15Rβ fusion
IL15Rβ
6
IL15
TM
ICD
IL15/γC fusion
γC
7
TM
IL15/IL15Rβ
IL15Rβ
γC

Figure 1

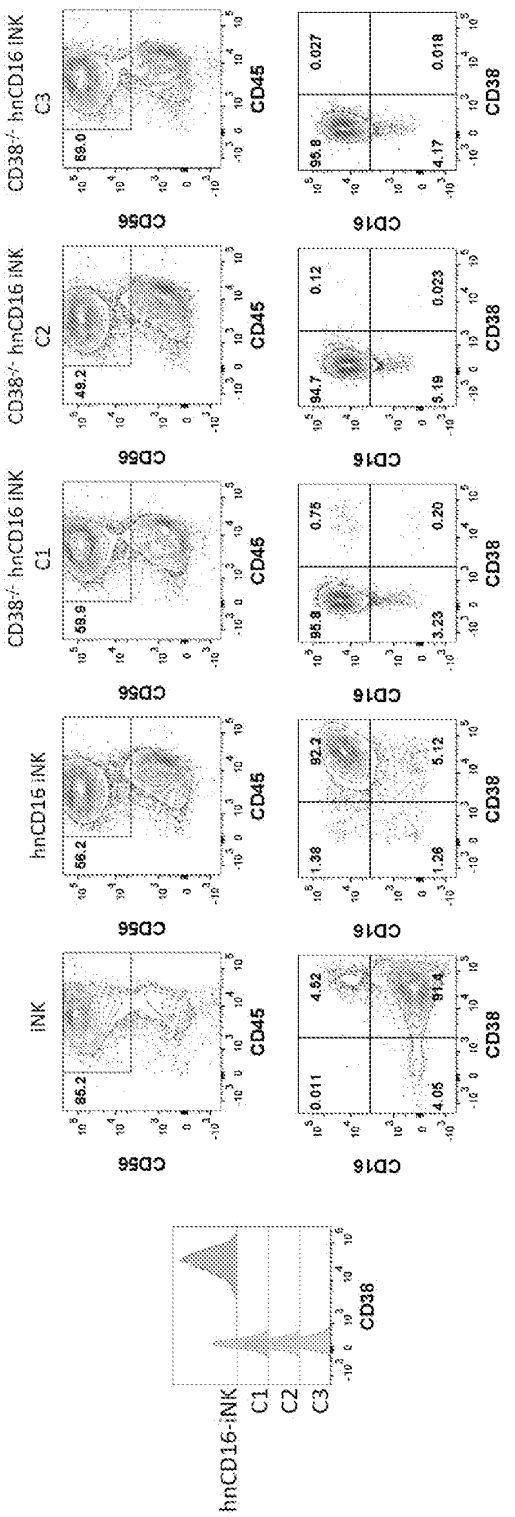

iNK
hnCD16 iNK
CD38-/- hnCD16 iNK C1
CD38-/- hnCD16 iNK C2
CD38-/- hnCD16 iNK C3
CD56
CD45
CD16
CD38
85.2
66.2
69.9
49.2
69.0
0.011
4.52
91.4
4.05
1.38
92.3
5.12
1.26
95.8
0.75
0.20
3.23
94.7
0.12
0.023
5.19
95.8
0.027
0.018
4.17
hnCD16-iNK
C1
C2
C3

Figure 2

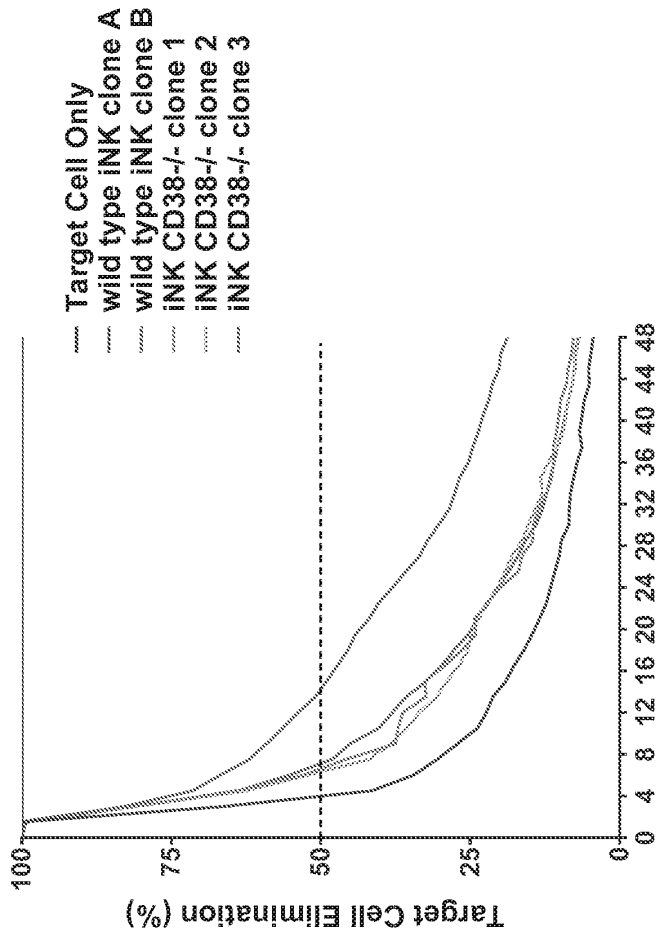

Target Cell Only
wild type iNK clone A
wild type iNK clone B
iNK CD38-/- clone 1
iNK CD38-/- clone 2
iNK CD38-/- clone 3
Target Cell Elimination (%)
100
75
50
25
0
0 4 8 12 16 20 24 28 32 36 40 44 48
Time, hrs

Figure 3

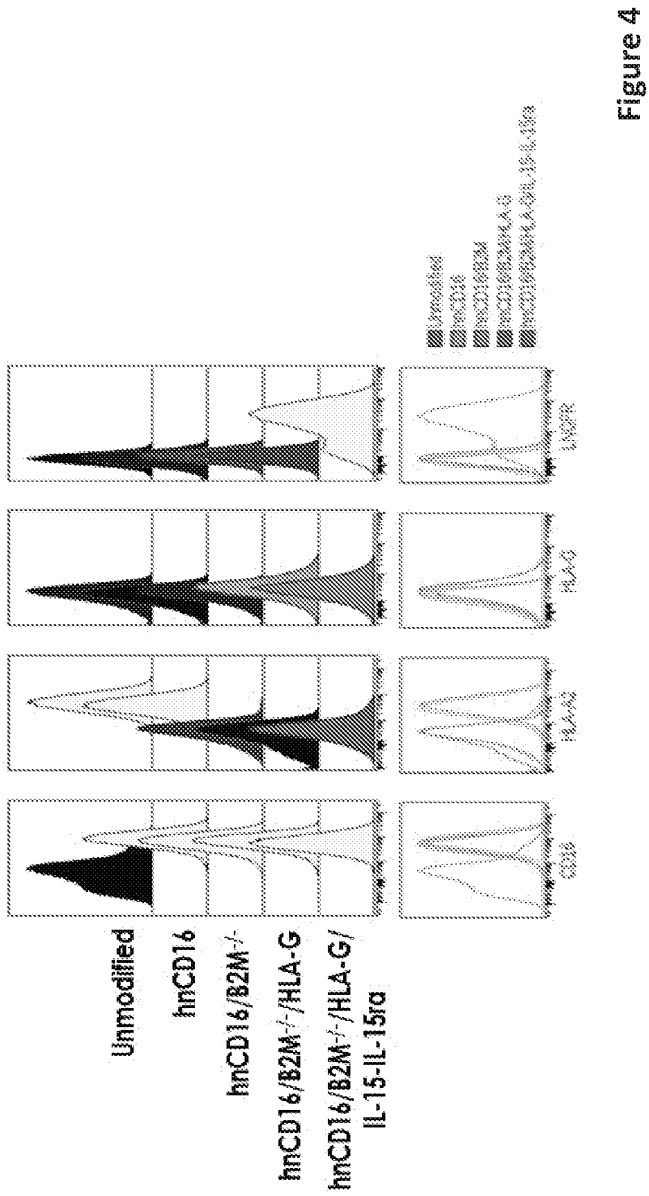

Unmodified
hnCD16
hnCD16/B2M-/-
hnCD16/B2M-/-/HLA-G
hnCD16/B2M-/-/HLA-G/
IL-15-IL-15ra
CD16
HLA-G
LNGFR

Figure 4

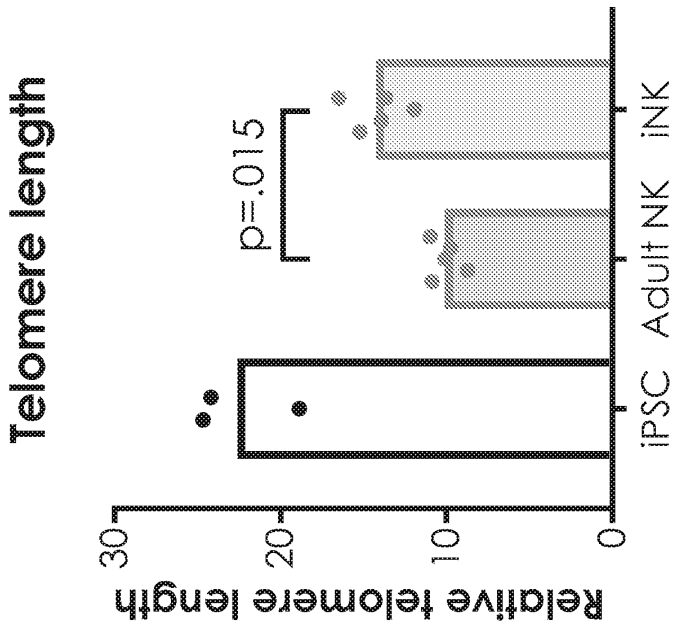

Telomere length
Relative telomere length
30
20
10
0
p=.015
iPSC
Adult NK
iNK

Figure 5

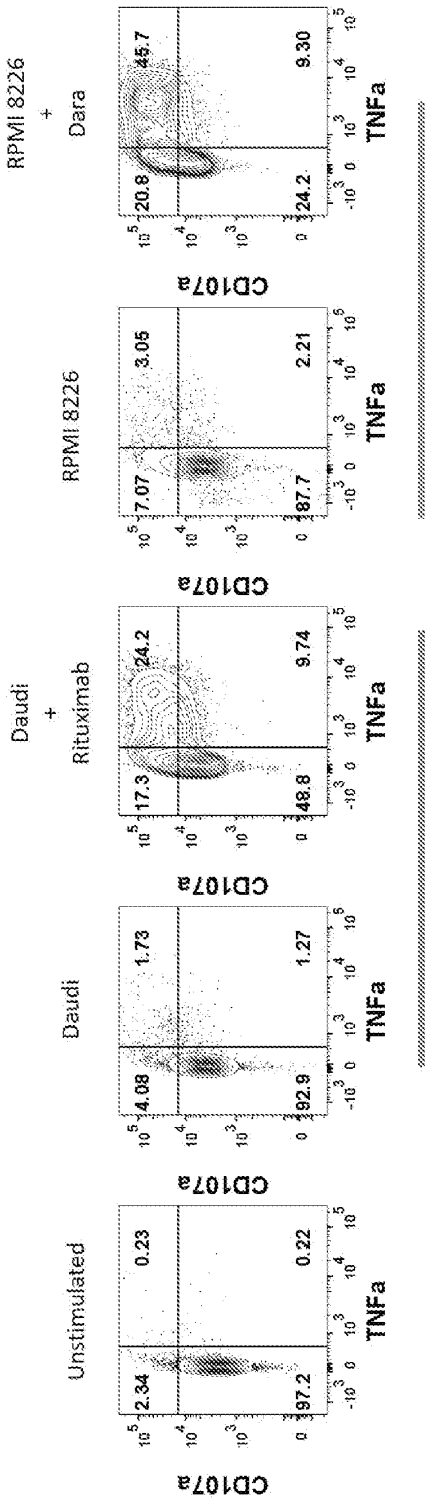

Unstimulated
Daudi
Daudi
+
Rituximab
RPMI 8226
RPMI 8226
+
Dara
CD107a
TNFa
2.34
0.23
97.2
0.22
4.08
1.73
92.9
1.27
17.3
24.2
48.8
9.74
7.07
3.05
87.7
2.21
20.8
45.7
24.2
9.30

Figure 6

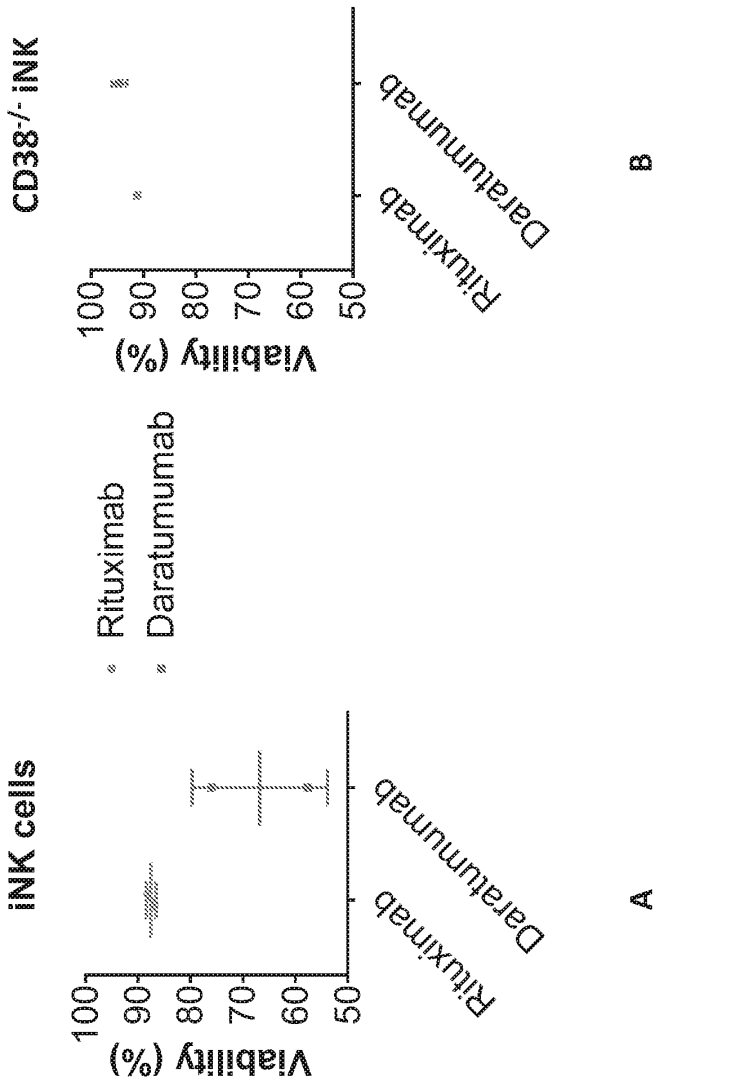

iNK cells
Viability (%)
100
90
80
70
60
50
Rituximab
Daratumumab
A
Rituximab
Daratumumab
CD38-/- iNK
Viability (%)
100
90
80
70
60
50
Rituximab
Daratumumab
B

Figure 7

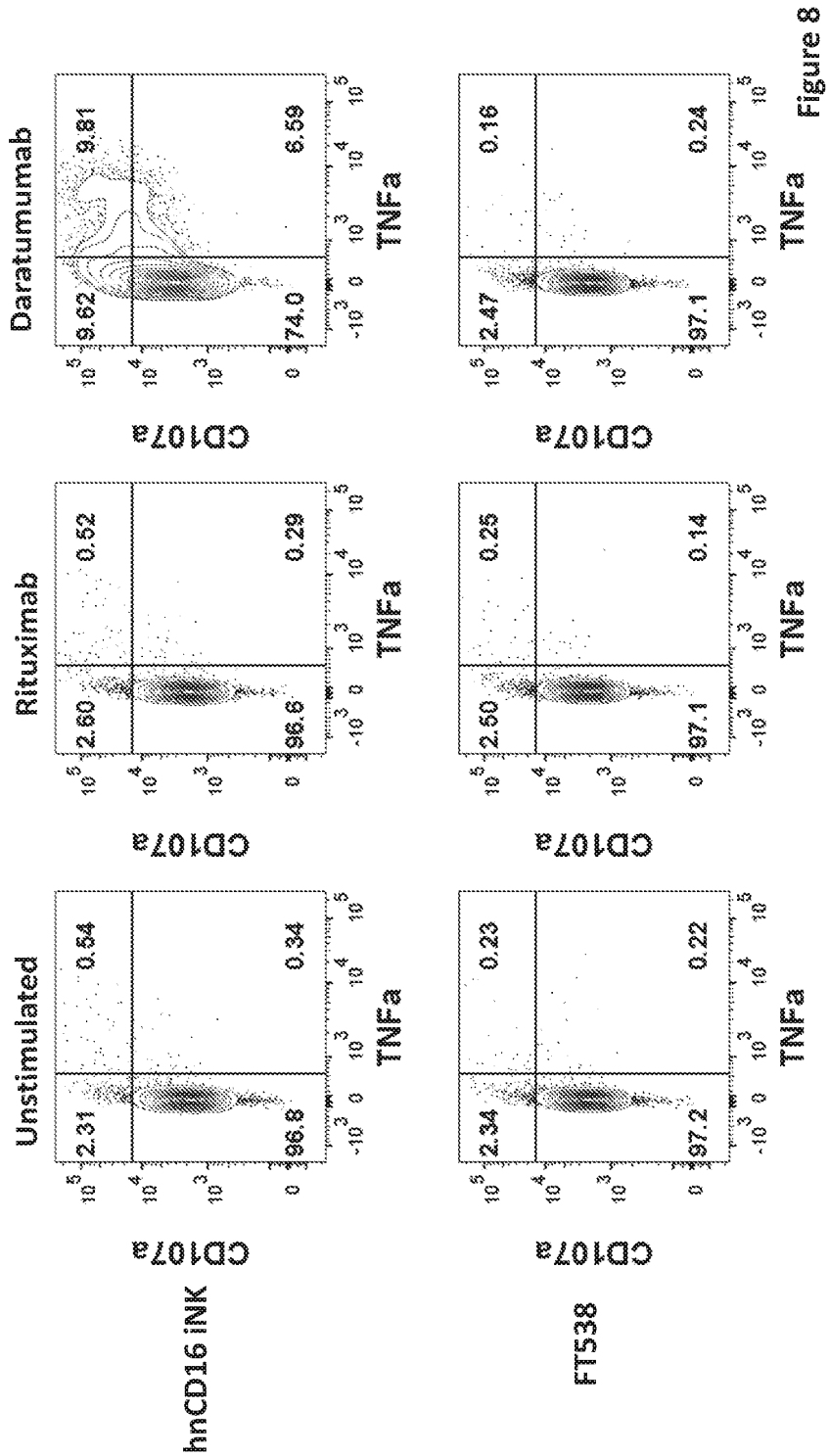

Unstimulated
Rituximab
Daratumumab
hnCD16 iNK
FT538
CD107a
TNFa
2.31
0.54
96.8
0.34
2.60
0.52
96.6
0.29
9.62
9.81
74.0
6.59
2.34
0.23
97.2
0.22
2.60
0.25
97.1
0.14
2.47
0.16
97.1
0.24

Figure 8

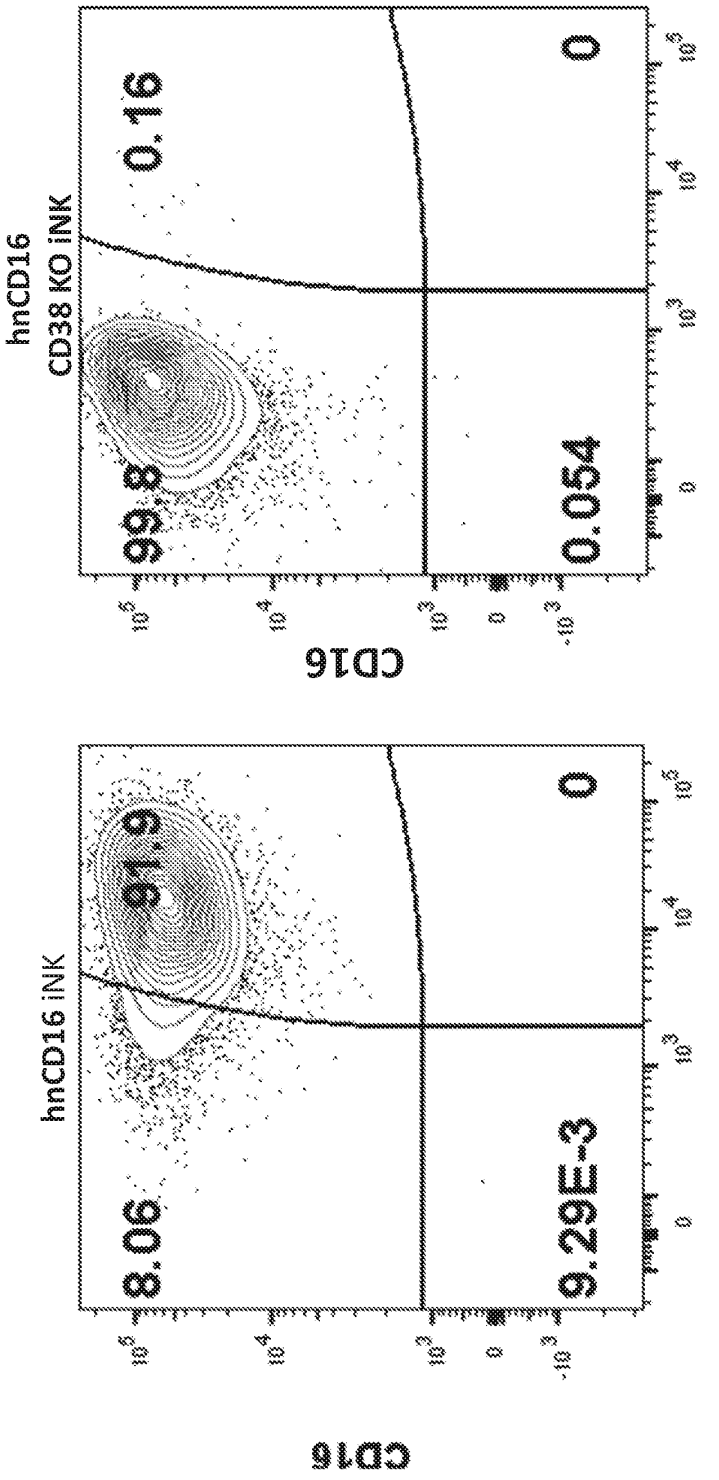

hnCD16 iNK
91.9
8.06
9.29E-3
0
CD16
CD38
A
hnCD16
CD38 KO iNK
0.16
99.8
0.054
0
CD16
CD38
B

Figure 9

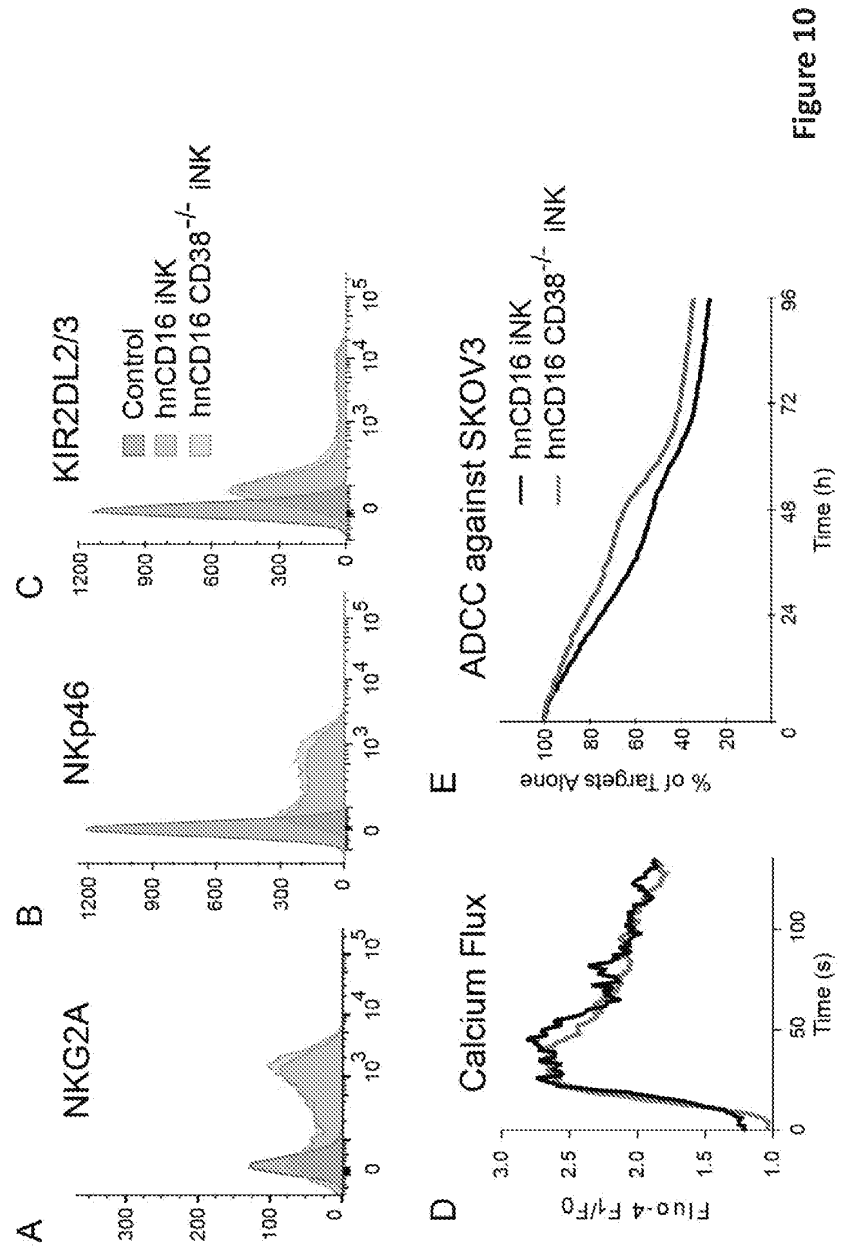

A
NKG2A
B
NKp46
C
KIR2DL2/3
Control
hnCD16 iNK
hnCD16 CD38-/- iNK
D
Calcium Flux
Fluo-4 F1/F0
Time (s)
E
ADCC against SKOV3
hnCD16 iNK
hnCD16 CD38-/- iNK
% of Targets Alone
Time (h)

Figure 10

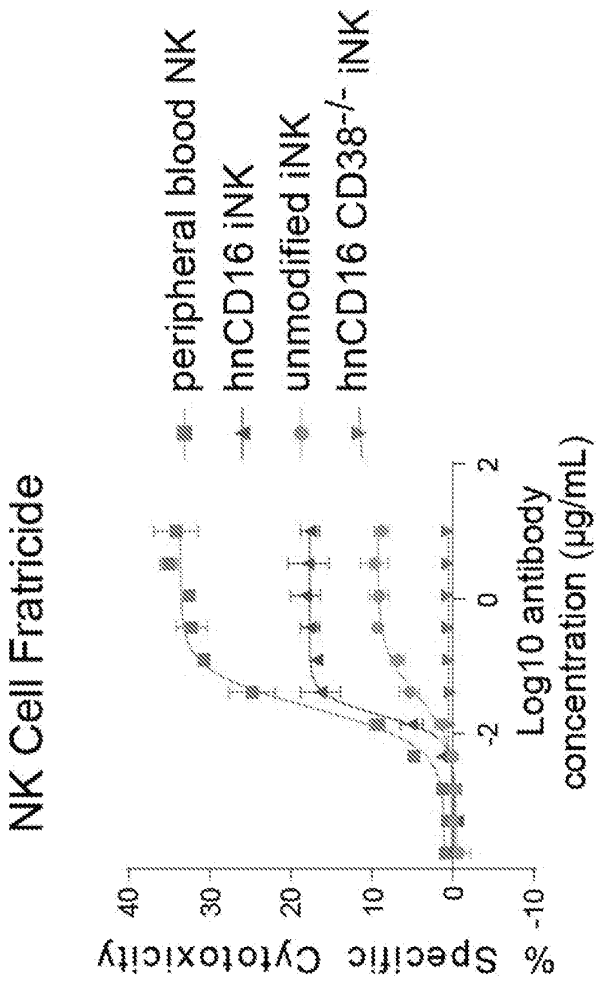

NK Cell Fratricide
peripheral blood NK
hnCD16 iNK
unmodified iNK
hnCD16 CD38-/- iNK
% Specific Cytotoxicity
40
30
20
10
0
-10
-2
0
2
Log10 antibody concentration (µg/mL)

Figure 11

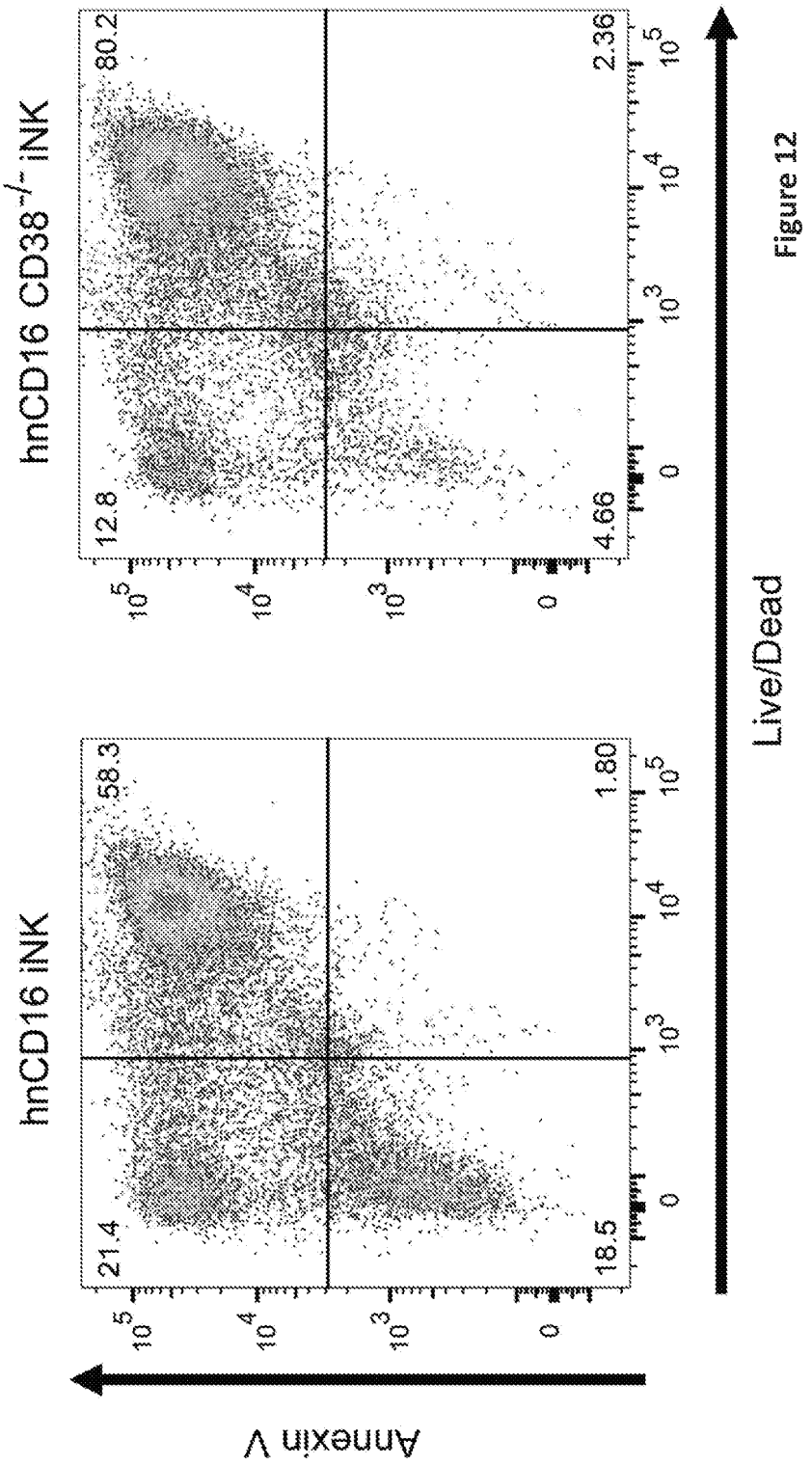

hnCD16 CD38-/- iNK
hnCD16 iNK
80.2
2.36
12.8
4.66
58.3
1.80
21.4
18.5
Annexin V
Live/Dead
0
10^3
10^4
10^5

Figure 12

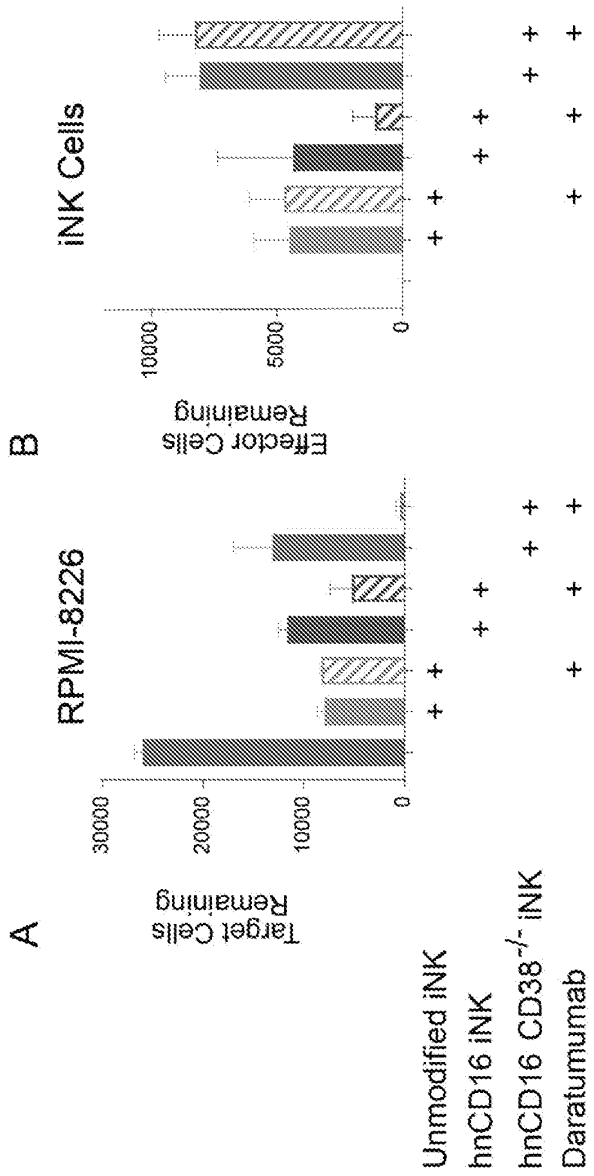

A
RPMI-8226
Target Cells Remaining
30000
20000
10000
0
B
iNK Cells
Effector Cells Remaining
10000
5000
0
Unmodified iNK
hnCD16 iNK
hnCD16 CD38-/- iNK
Daratumumab

Figure 13

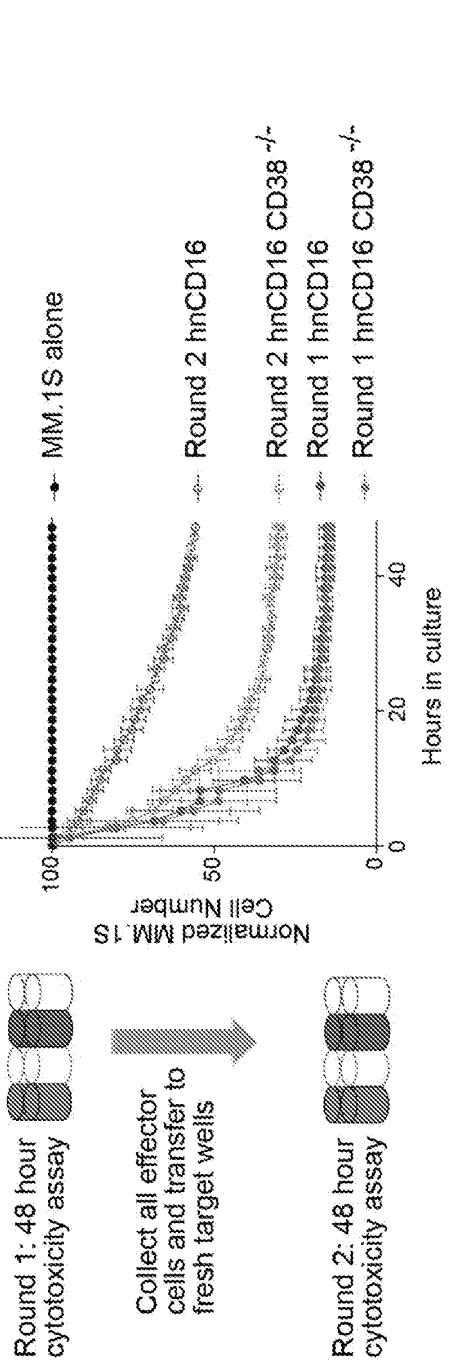

Serial Killing in the Presence of Daratumumab
MM.1S alone
Round 2 hnCD16
Round 2 hnCD16 CD38 -/-
Round 1 hnCD16
Round 1 hnCD16 CD38 -/-
Normalized MM.1S Cell Number
100
50
0
0
20
40
Hours in culture
Round 1: 48 hour cytotoxicity assay
Collect all effector cells and transfer to fresh target wells
Round 2: 48 hour cytotoxicity assay

Figure 14

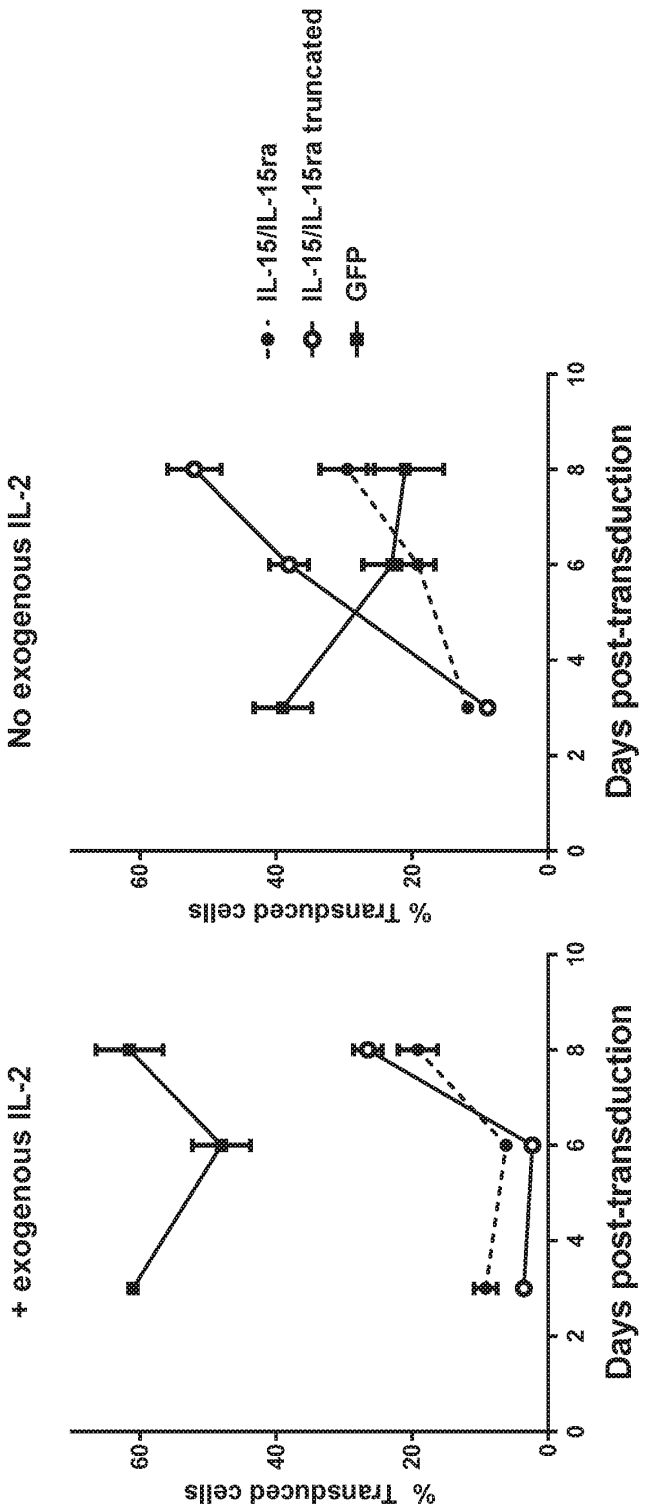

IL-15/IL-15ra
IL-15/IL-15ra truncated
GFP
No exogenous IL-2
+ exogenous IL-2
% Transduced cells
Days post-transduction
0
20
40
60
0
2
4
6
8
10

Figure 15