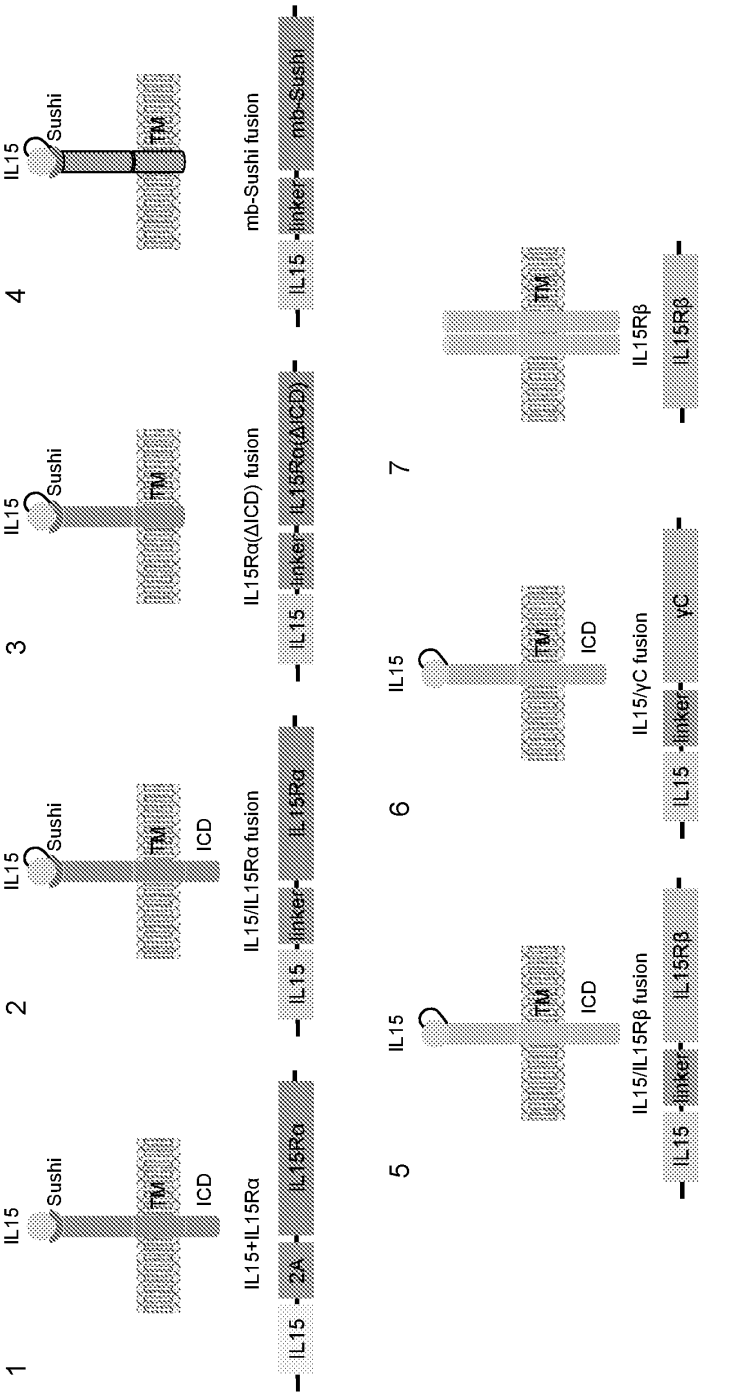

1
IL15
Sushi
TM
ICD
IL15+IL15Rα
IL15
2A
IL15Rα
2
IL15
Sushi
TM
ICD
IL15/IL15Rα fusion
IL15
linker
IL15Rα
3
IL15
Sushi
TM
IL15Rα(ΔICD) fusion
IL15
linker
IL15Rα(ΔICD)
4
IL15
Sushi
TM
mb-Sushi fusion
IL15
linker
mb-Sushi
5
IL15
TM
ICD
IL15/IL15Rβ fusion
IL15
linker
IL15Rβ
6
IL15
TM
ICD
IL15/γC fusion
IL15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

Figure 1

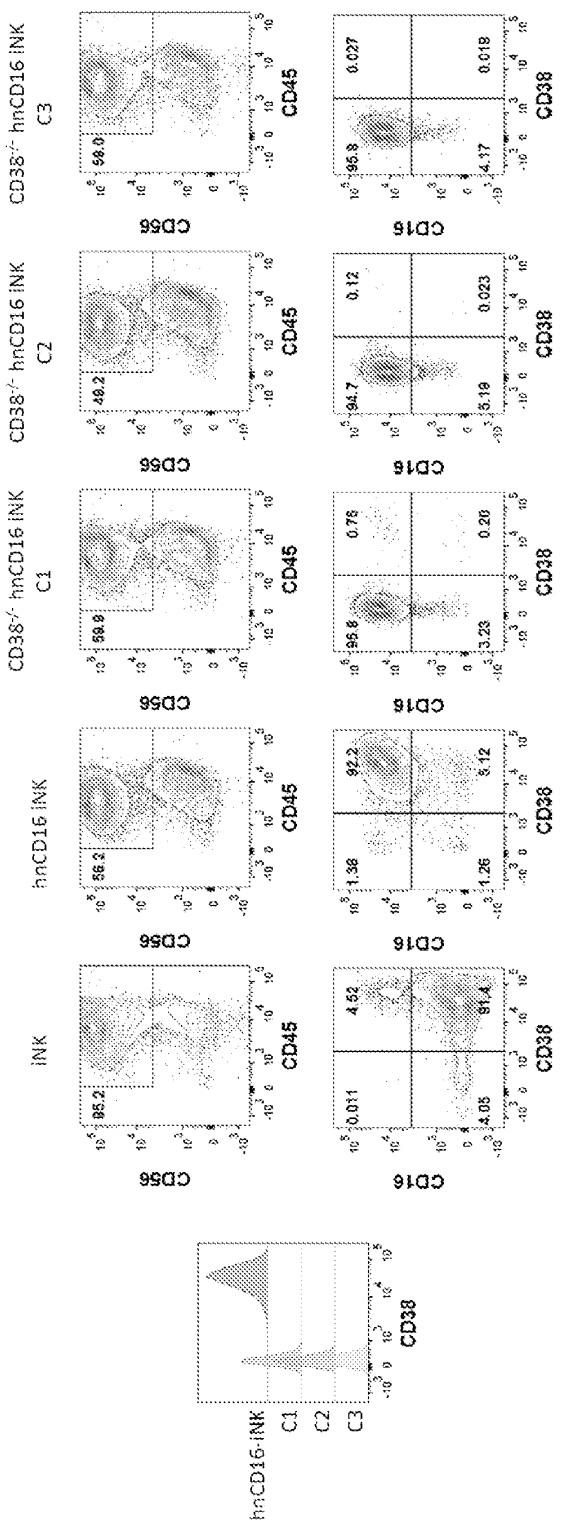

iNK
hnCD16 iNK
CD38-/- hnCD16 iNK C1
CD38-/- hnCD16 iNK C2
CD38-/- hnCD16 iNK C3
CD56
CD45
CD16
CD38
95.2
56.2
59.0
46.2
59.0
4.52
91.4
0.011
4.05
92.2
6.12
1.38
1.26
95.8
3.23
0.78
0.26
94.7
5.19
0.12
0.023
95.8
4.17
0.027
0.018
hnCD16-iNK
C1
C2
C3

Figure 2

Figure 3

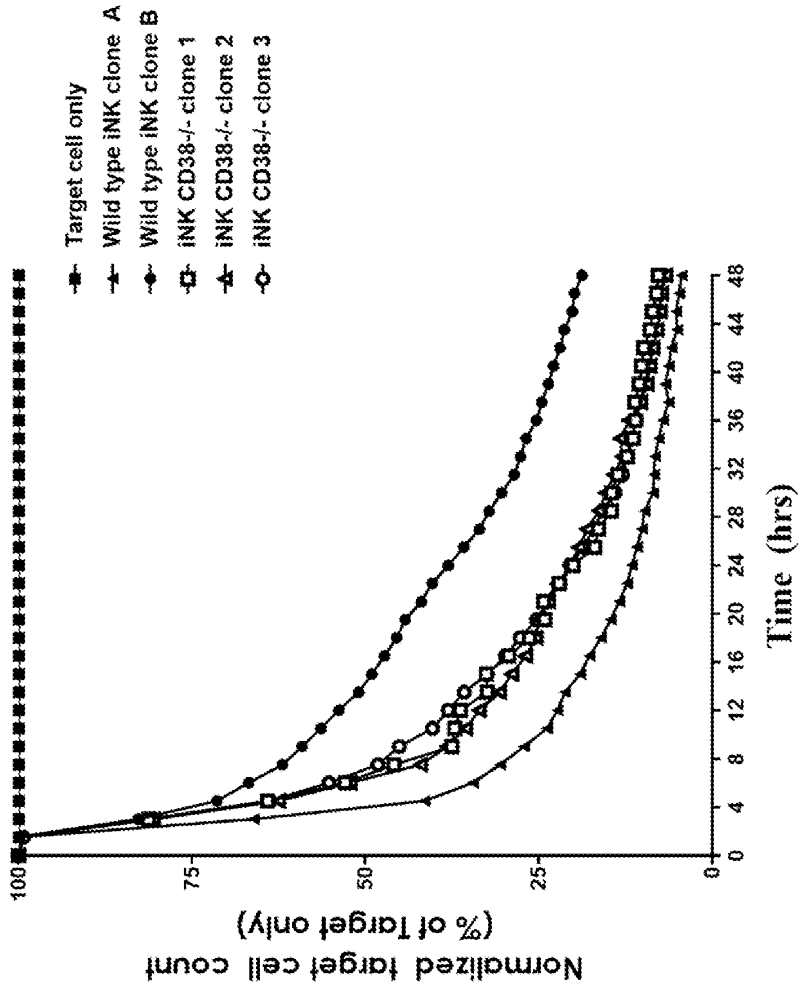
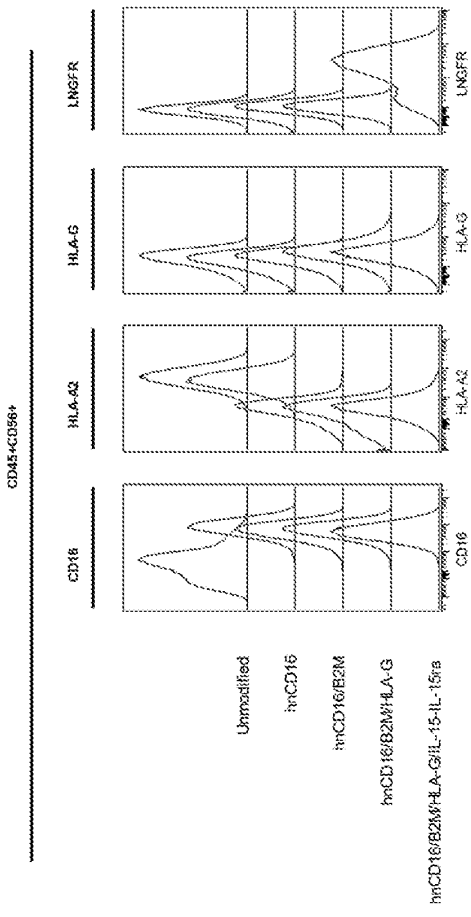

Target cell only
Wild type iNK clone A
Wild type iNK clone B
iNK CD38-/- clone 1
iNK CD38-/- clone 2
iNK CD38-/- clone 3
Normalized target cell count
(% of Target only)
100
75
50
25
0
0
4
8
12
16
20
24
28
32
36
40
44
48
Time (hrs)

Figure 4



	CD16	HLA-A2	HLA-G	LNGFR
Unmodified	1	19.41	1.17	1
hnCD16	12.14	15.63	1	1.11
hnCD16/B2M	9.41	1.52	1.25	1.64
hnCD16/B2M/HLA-G	9.34	1	2.33	1.58
hnCD16/B2M/HLA-G/IL-15-IL-15ra	8.66	1.9	2.13	48.13
Calculated Fold of Means by Column's Minimum using X-Axis channel(s): Panel/Channel Values				

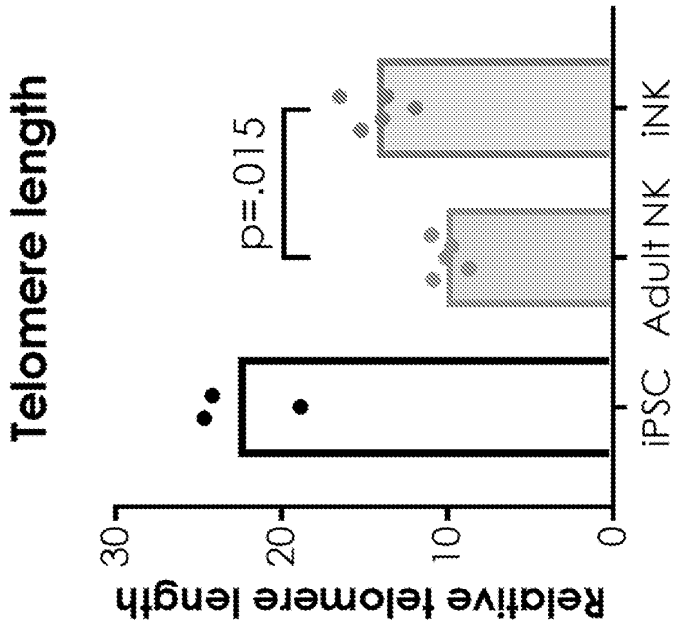

Telomere length
Relative telomere length
30
20
10
0
p=.015
iPSC
Adult NK
iNK

Figure 5

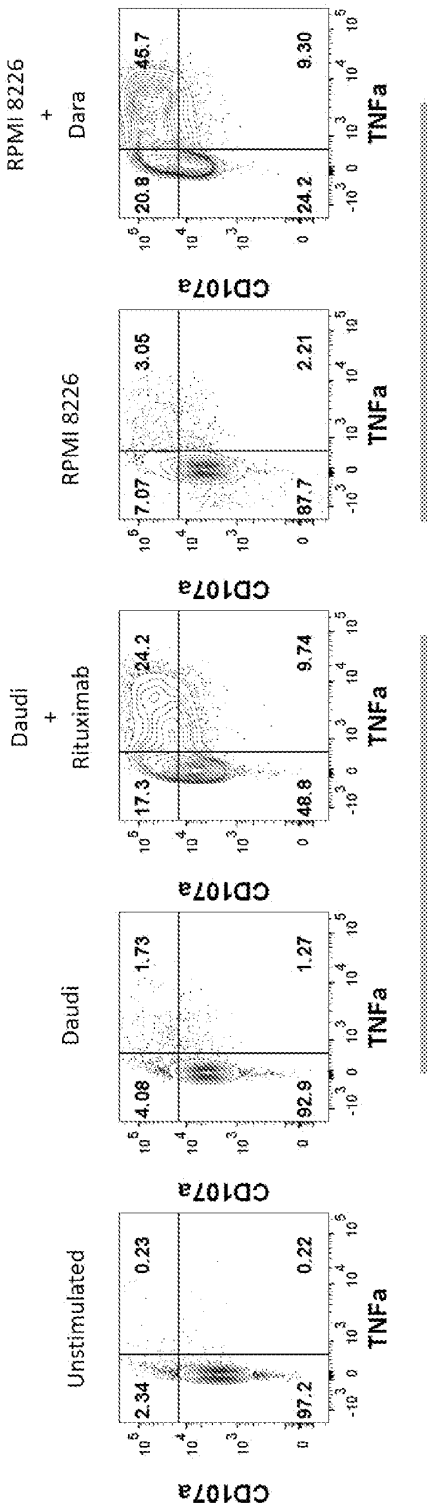

Unstimulated
Daudi
Daudi
+
Rituximab
RPMI 8226
RPMI 8226
+
Dara
CD107a
TNFa
2.34
0.23
97.2
0.22
4.08
1.73
92.9
1.27
17.3
24.2
48.8
9.74
7.07
3.05
87.7
2.21
20.8
45.7
24.2
9.30

Figure 6

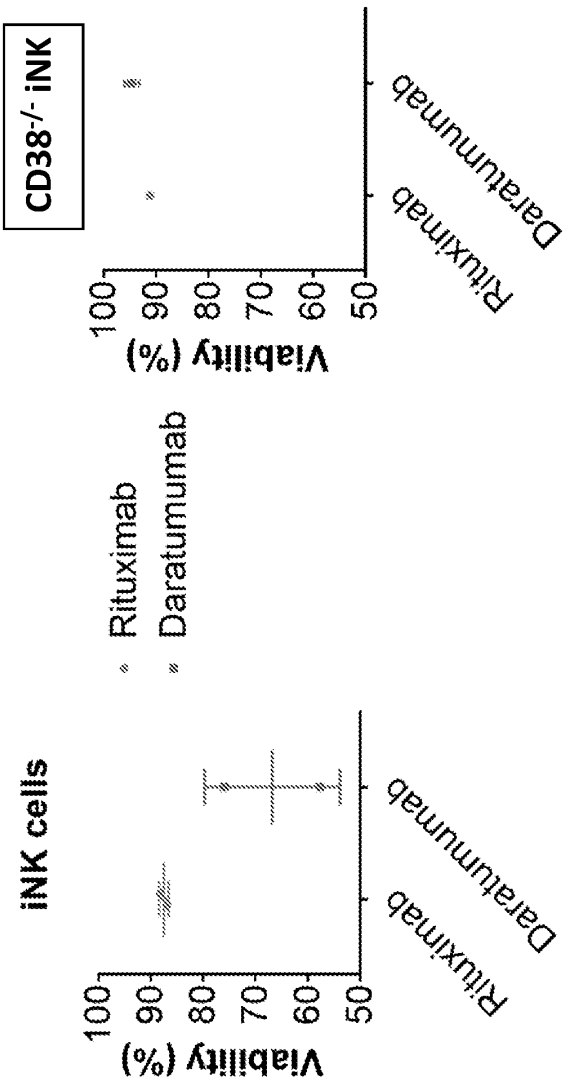

iNK cells
Viability (%)
100
90
80
70
60
50
Rituximab
Daratumumab
Rituximab
Daratumumab
A
Rituximab
Daratumumab
CD38-/- iNK
Viability (%)
100
90
80
70
60
50
Rituximab
Daratumumab
B

Figure 7

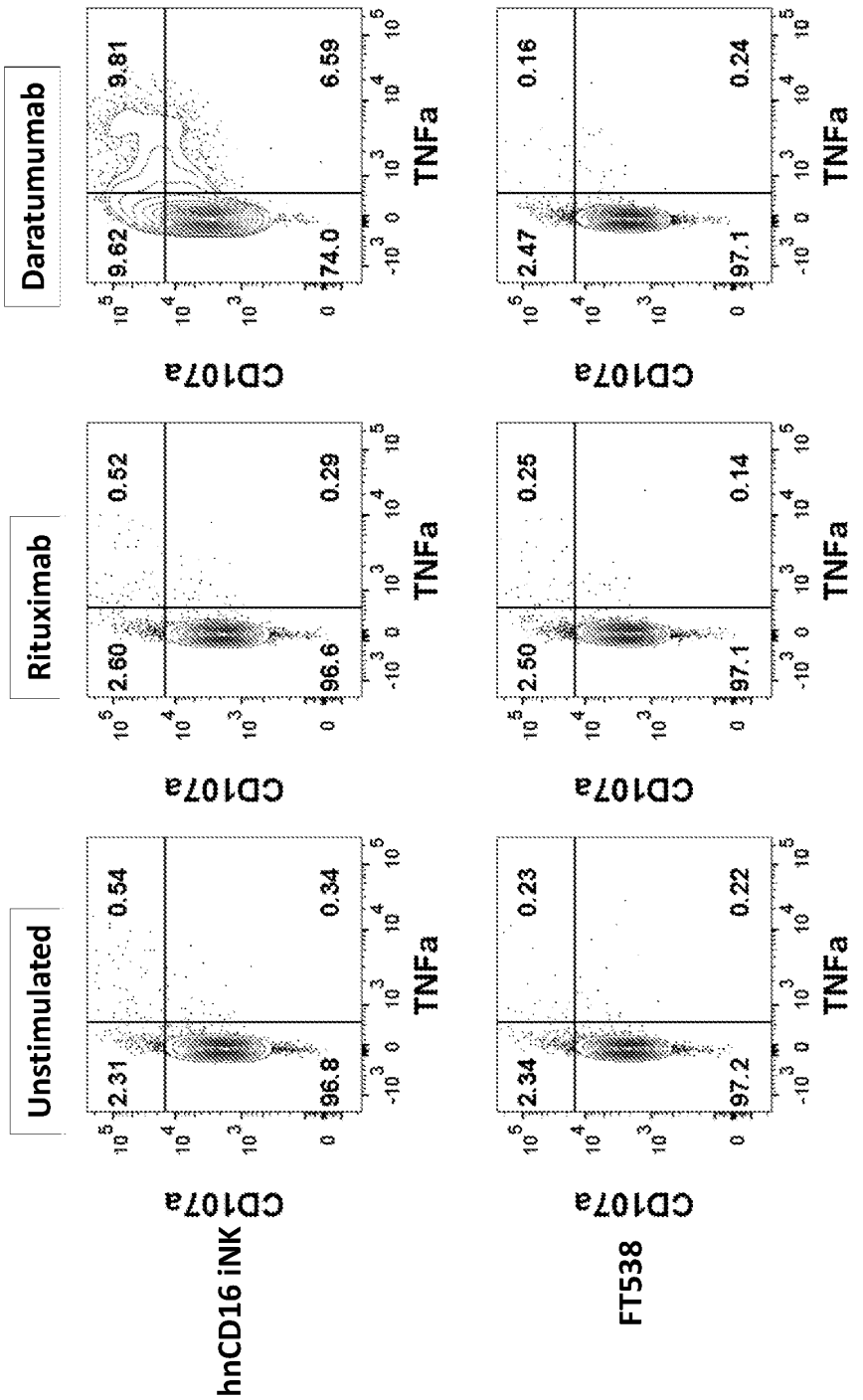

Unstimulated
Rituximab
Daratumumab
hnCD16 iNK
FT538
CD107a
TNFa
2.31
0.54
96.8
0.34
2.60
0.52
96.6
0.29
9.62
9.81
74.0
6.59
2.34
0.23
97.2
0.22
2.50
0.25
97.1
0.14
2.47
0.16
97.1
0.24

Figure 8

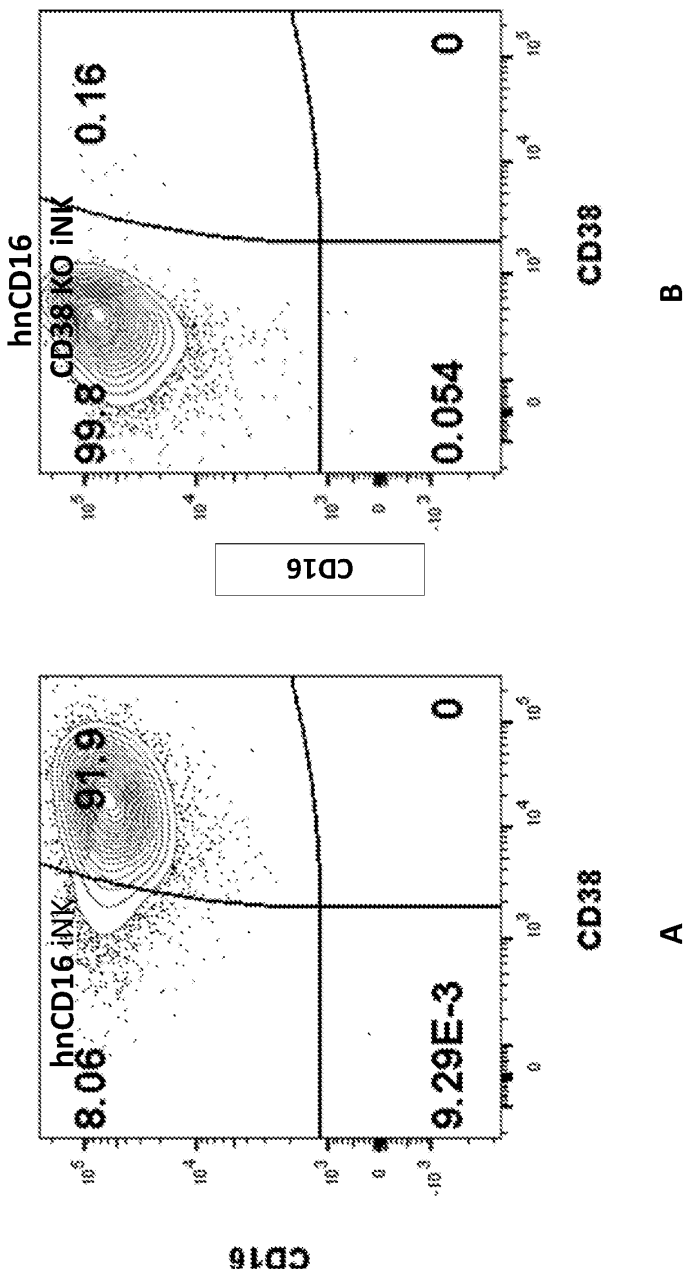

hnCD16
CD38 KO iNK
99.8
0.16
0.054
0
CD38
B
CD16
hnCD16 iNK
8.06
91.9
9.29E-3
0
CD38
A
CD16

Figure 9

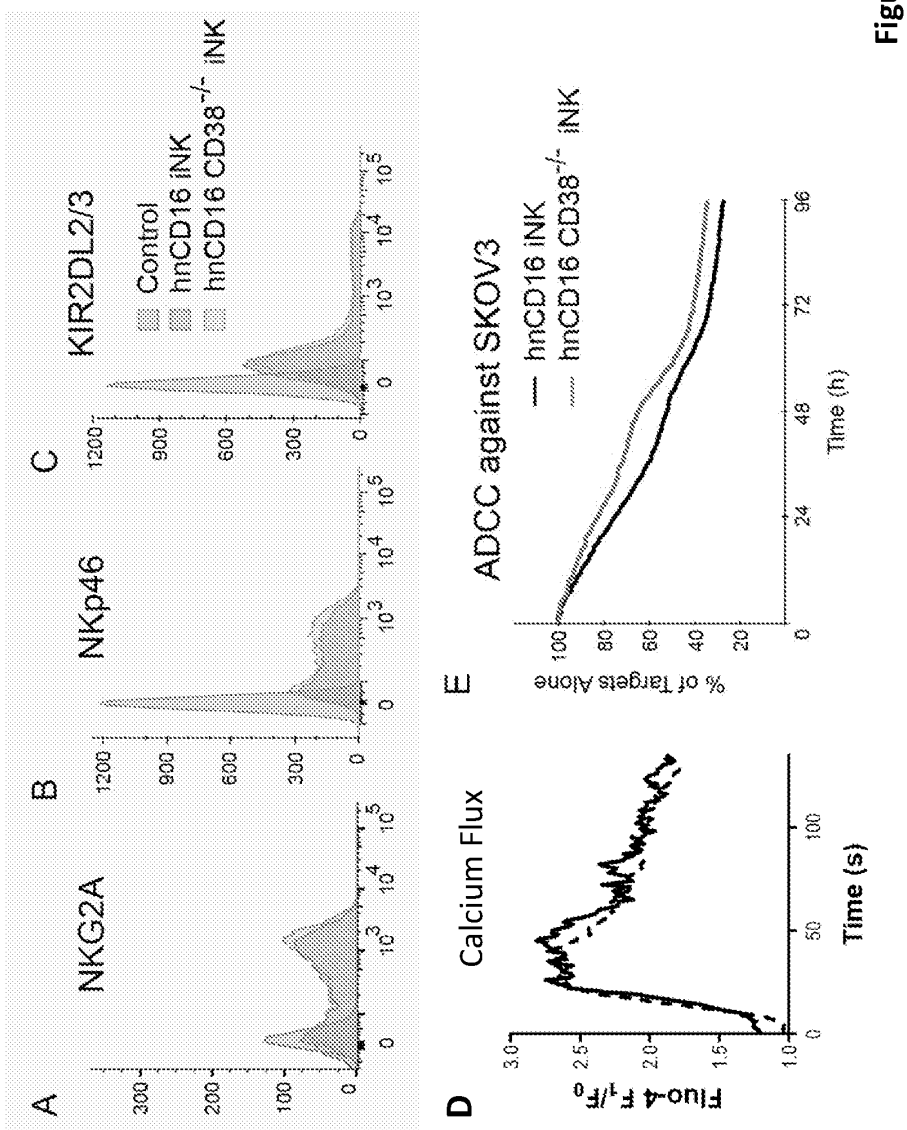

A
NKG2A
B
NKp46
C
KIR2DL2/3
Control
hnCD16 iNK
hnCD16 CD38-/- iNK
D
Calcium Flux
Fluo-4 F1/F0
Time (s)
E
ADCC against SKOV3
hnCD16 iNK
hnCD16 CD38-/- iNK
% of Targets Alone
Time (h)

Figure 10

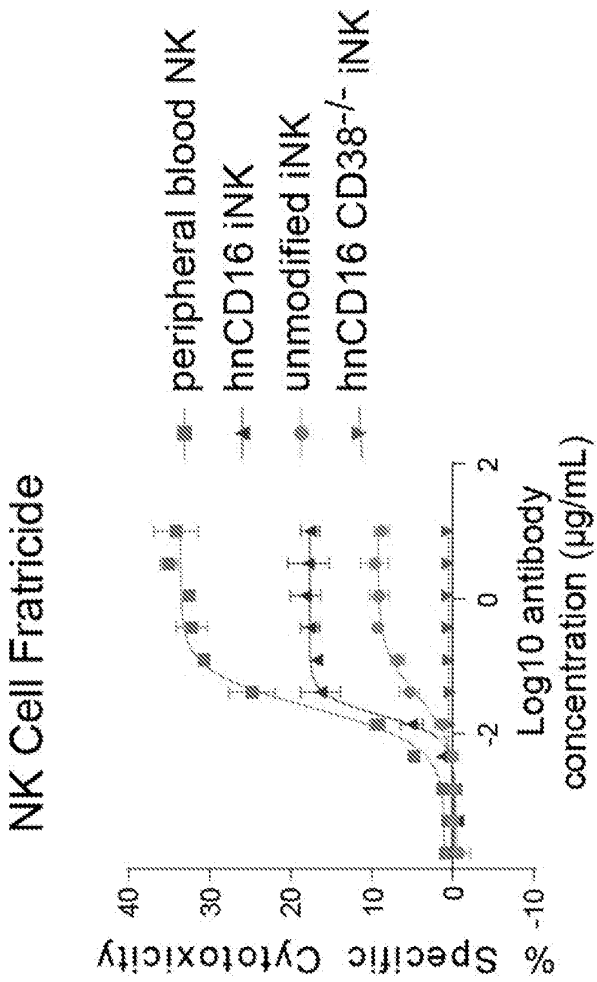

NK Cell Fratricide
peripheral blood NK
hnCD16 iNK
unmodified iNK
hnCD16 CD38-/- iNK
% Specific Cytotoxicity
40
30
20
10
0
-10
-2
0
2
Log10 antibody concentration (µg/mL)

Figure 11

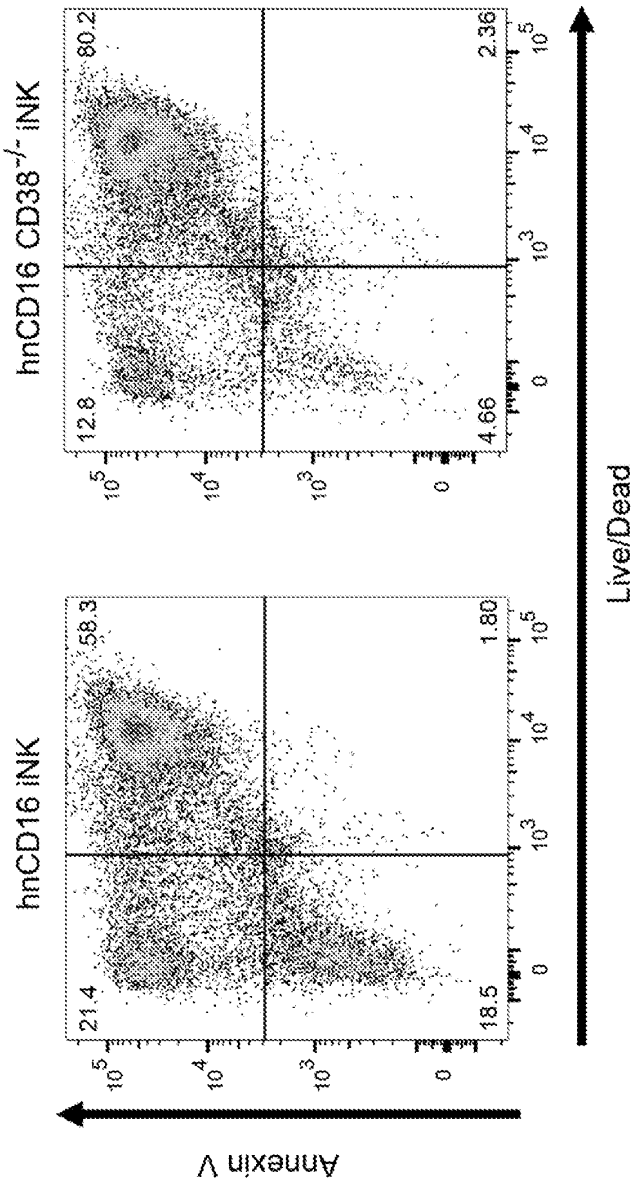

hnCD16 CD38-/- iNK
hnCD16 iNK
80.2
2.36
12.8
4.66
58.3
1.80
21.4
18.5
Annexin V
Live/Dead

Figure 12

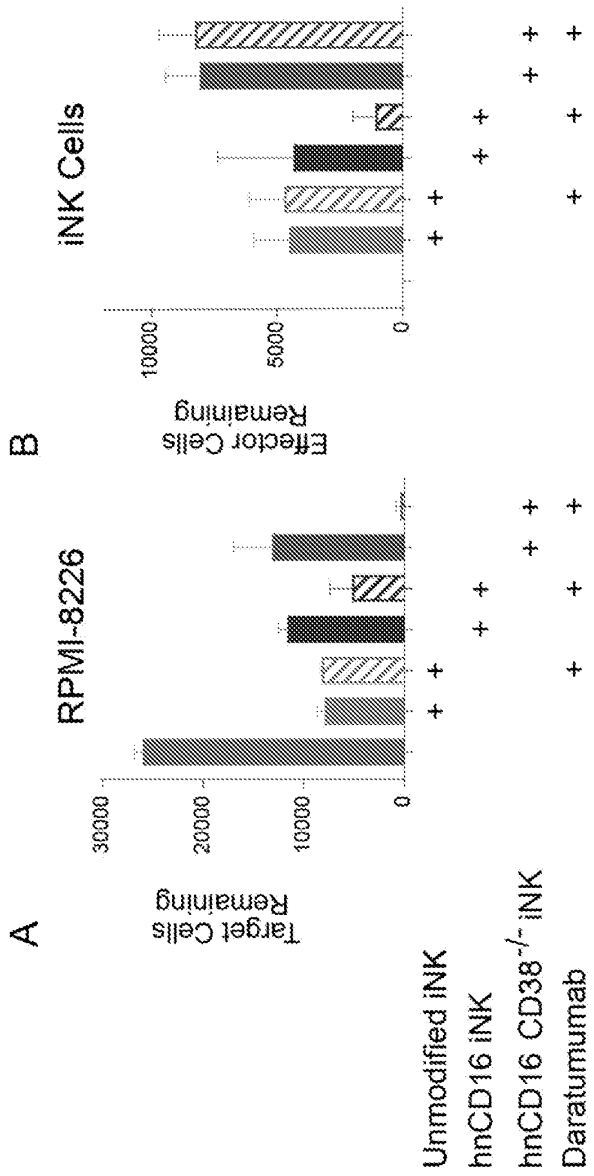

A
RPMI-8226
Target Cells Remaining
30000
20000
10000
0
B
iNK Cells
Effector Cells Remaining
10000
5000
0
Unmodified iNK
hnCD16 iNK
hnCD16 CD38-/- iNK
Daratumumab

Figure 13

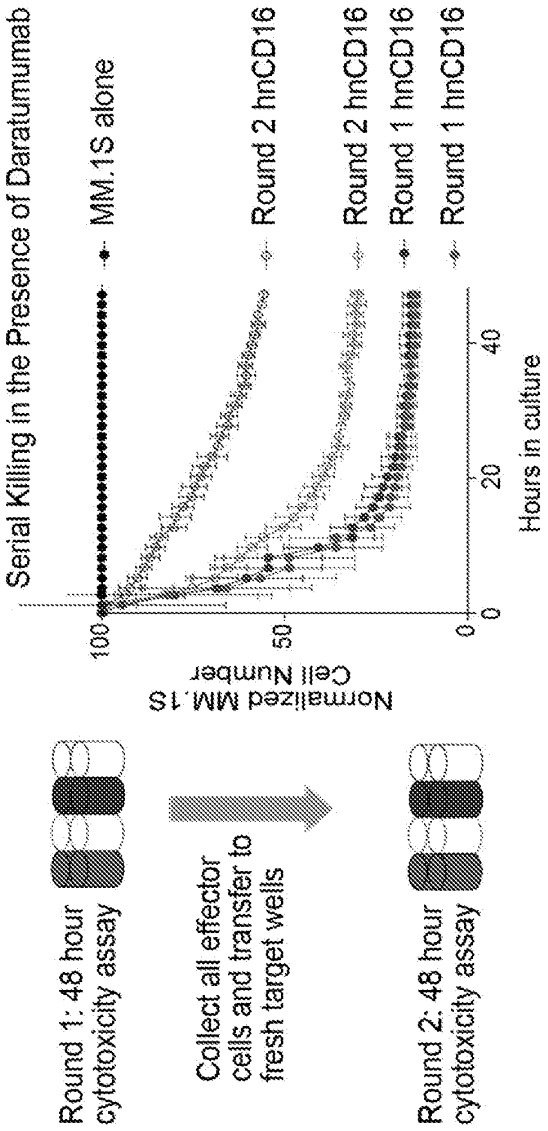

Serial Killing in the Presence of Daratumumab
MM.1S alone
Round 2 hnCD16
Round 2 hnCD16 CD38 -/-
Round 1 hnCD16
Round 1 hnCD16 CD38 -/-
Normalized MM.1S Cell Number
100
50
0
0
20
40
Hours in culture
Round 1: 48 hour cytotoxicity assay
Collect all effector cells and transfer to fresh target wells
Round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

Figure 14

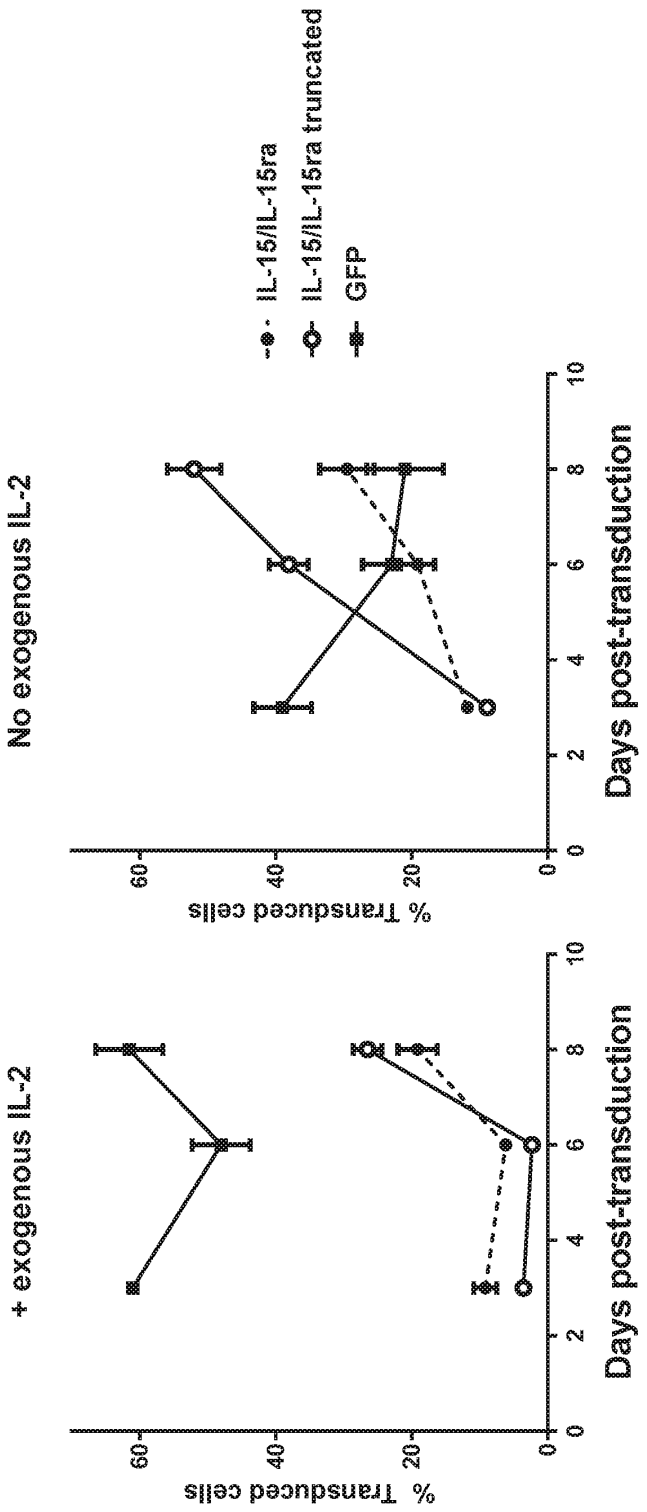
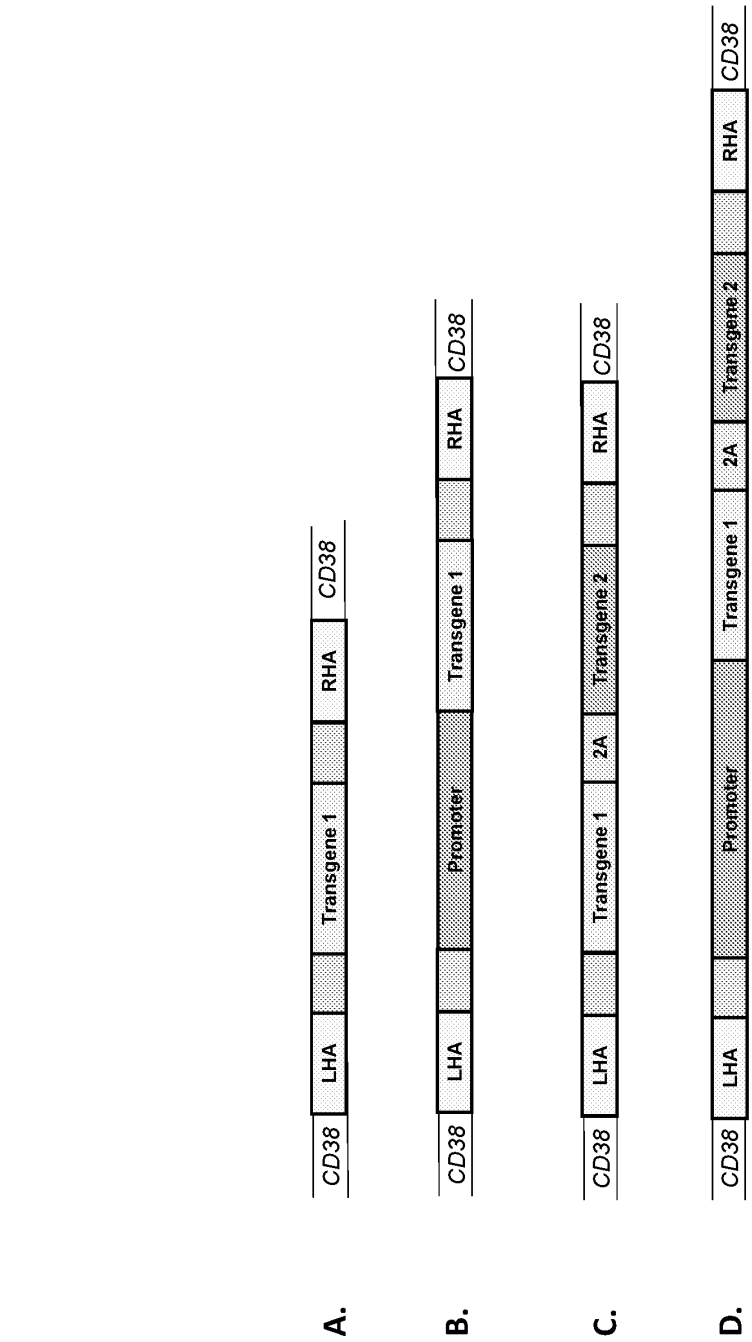

IL-15/IL-15ra
IL-15/IL-15ra truncated
GFP
No exogenous IL-2
+ exogenous IL-2
% Transduced cells
Days post-transduction
0
20
40
60
0
2
4
6
8
10

Figure 15

FIG. 16


A.
CD38
LHA
Transgene 1
RHA
CD38
B.
CD38
LHA
Promoter
Transgene 1
RHA
CD38
C.
CD38
LHA
Transgene 1
2A
Transgene 2
RHA
CD38
D.
CD38
LHA
Promoter
Transgene 1
2A
Transgene 2
RHA
CD38

LHA/CD38-insol-CAG-IL15RF(tr)-P2A-hnCD16-TKpA-insol-RHA/CD38:

CAGAGGGCATTGTGTGCACACACGTATAGAAGCAGGCAGCCCACCCTCATGCTTTCCAGG SEQ ID NO: 22
AAGCAAATGTGGCTCAGGTGTAAAGTGCCCGGTTGATGAAGGGAGTTAGCGGAGGGAGTA
TAAGGATGTACTGTCTGCCCCCTTAGGACACCTGCAGAGGATTAAGGTGGCTGTTTCTCC
CTGGAGGTGGAGTGGGTGGGTCACTGCACAGGAGCCTATAGTTGTTGGTCTTTTAAACTC
TTATTGGTGTAACCAGCCACGGAACTCTGAGGCAAGGGGTTGGGGGTGGGAAGGGAAACA
GAGAAAAGGCAAGTGAAACAGAAGGGGAGGTGCAGTTTCAGAACCCAGCCAGCCTCTCTC
TTGCTGCCTAGCCTCCTGCCGGCCTCATCTTCGCCCAGCCAACCCCGCCTGGAGCCCTAT
GGCCAACTGCGAGTTCAGCCCGGTGTCCGGGGACAAACCCTGCTGCCGGCTCTCTAGGAG
AGCCCAACTCTGTCTTGGCGTCAGTATCCTGGTCCTGATCCTCGTCGTGGTGCTCGCGGT
GGTCGTCCCGAGGTGGCGCCAGCAGTGGAGCGGTCCGGGCACCACCAAGCGCTTTCCCGA
GTCAGCCTAAAGCTTTTTCCCCGTATCCCCCCAGGTGTCTGCAGGCTCAAAGAGCAGCGA SEQ ID NO: 23
GAAGCGTTCAGAGGAAAGCGATCCCGTGCCACCTTCCCCGTGCCCGGGCTGTCCCCGCAC
GCTGCCGGCTCGGGGATGCGGGGGGAGCGCCGGACCGGAGCGGAGCCCCGGGCGGCTCGC
TGCTGCCCCCTAGCGGGGGAGGGACGTAATTACATCCCTGGGGGCTTTGGGGGGGGGCTG
TCCCCGTGAGCTCATCGATACTAGTGTACAGGTTAATGATGTTGACATTGATTATTGACT SEQ ID NO: 24
AGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGC
GTTACATAACTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTG
ACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAA
TGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCA
AGTACGCCCCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTAC
ATGACCTTATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACC
ATGGTCGAGGTGAGCCCCACGTTCTGCTTCACTCTCCCCATCTCCCCCCCCTCCCCACCC
CCAATTTTGTATTTATTTATTTTTTAATTATTTTGTGCAGCGATGGGGGCGGGGGGGGGG
GGGGGGCGCGCGCCAGGCGGGGCGGGGCGGGGCGAGGGGCGGGGCGGGGCGAGGCGGAGA
GGTGCGGCGGCAGCCAATCAGAGCGGCGCGCTCCGAAAGTTTCCTTTTATGGCGAGGCGG
CGGCGGCGGCGGCCCTATAAAAAGCGAAGCGCGCGGCGGGCGGGGAGTCGCTGCGACGCT
GCCTTCGCCCCGTGCCCCGCTCCGCCGCCGCCTCGCGCCGCCCGCCCCGGCTCTGACTGA FIG. 17

CCGCGTTACTCCCACAGGTGAGCGGGCGGGACGGCCCTTCTCCTCCGGGCTGTAATTAGC

GCTTGGTTTAATGACGGCTTGTTTCTTTTCTGTGGCTGCGTGAAAGCCTTGAGGGGCTCC

GGGAGGGCCCTTTGTGCGGGGGGAGCGGCTCGGGGGGTGCGTGCGTGTGTGTGTGCGTGG

GGAGCGCCGCGTGCGGCTCCGCGCTGCCCGGCGGCTGTGAGCGCTGCGGGCGCGGCGCGG

GGCTTTGTGCGCTCCGCAGTGTGCGCGAGGGGAGCGCGGCCGGGGGCGGTGCCCCGCGGT

GCGGGGGGGGCTGCGAGGGGAACAAAGGCTGCGTGCGGGGTGTGTGCGTGGGGGGGTGAG

CAGGGGGTGTGGGCGCGTCGGTCGGGCTGCAACCCCCCCTGCACCCCCCTCCCCGAGTTG

CTGAGCACGGCCCGGCTTCGGGTGCGGGGCTCCGTACGGGGCGTGGCGCGGGGCTCGCCG

TGCCGGGCGGGGGGTGGCGGCAGGTGGGGGTGCCGGGCGGGGCGGGGCCGCCTCGGGCCG

GGGAGGGCTCGGGGGAGGGGCGCGGCGGCCCCCGGAGCGCCGGCGGCTGTCGAGGCGCGG

CGAGCCGCAGCCATTGCCTTTTATGGTAATCGTGCGAGAGGGCGCAGGGACTTCCTTTGT

CCCAAATCTGTGCGGAGCCGAAATCTGGGAGGCGCCGCCGCACCCCCTCTAGCGGGCGCG

GGGCGAAGCGGTGCGGCGCCGGCAGGAAGGAAATGGGCGGGGAGGGCCTTCGTGCGTCGC

CGCGCCGCCGTCCCCTTCTCCCTCTCCAGCCTCGGGGCTGTCCGCGGGGGGACGGCTGCC

TTCGGGGGGGACGGGGCAGGGCGGGGTTCGGCTTCTGGCGTGTGACCGGCGGCTCTAGAG

CCTCTGCTAACCATGTTCATGCCTTCTTCTTTTTCCTACAGCTCCTGGGCAACGTGCTGG

TTATTGTGCTGTCTCATCATTTTGGCAAAGAATTGCTAGCGCCACCATGGACTGGACCTG SEQ ID NO: 25

GATTCTGTTCCTGGTCGCGGCTGCAACGCGAGTCCATAGCGGTATCCATGTTTTTATTCT

TGGGTGTTTTTCTGCTGGGCTGCCTAAGACCGAGGCCAACTGGGTAAATGTCATCAGTGA

CCTCAAGAAAATAGAAGACCTTATACAAAGCATGCACATTGATGCTACTCTCTACACTGA

GTCAGATGTACATCCCTCATGCAAAGTGACGGCCATGAAATGTTTCCTCCTCGAACTTCA

AGTCATATCTCTGGAAAGTGGCGACGCGTCCATCCACGACACGGTCGAAAACCTGATAAT

ACTCGCTAATAATAGTCTCTCTTCAAATGGTAACGTAACCGAGTCAGGTTGCAAAGAGTG

CGAAGAGTTGGAAGAAAAAAACATAAAGGAGTTCCTGCAAAGTTTCGTGCACATTGTGCA

GATGTTCATTAATACCTCTAGCGGCGGAGGATCAGGTGGCGGTGGAAGCGGAGGTGGAGG

CTCCGGTGGAGGAGGTAGTGGCGGAGGTTCTCTTCAAATAACTTGTCCTCCACCGATGTC

CGTAGAACATGCGGATATTTGGGTAAAATCCTATAGCTTGTACAGCCGAGAGCGGTATAT

FIG. 17 Con't

CTGCAACAGCGGCTTCAAGCGGAAGGCCGGCACAAGCAGCCTGACCGAGTGCGTGCTGAA

CAAGGCCACCAACGTGGCCCACTGGACCACCCCTAGCCTGAAGTGCATCAGAGATCCCGC

CCTGGTGCATCAGCGGCCTGCCCCTCCAAGCACAGTGACAACAGCTGGCGTGACCCCCCA

GCCTGAGAGCCTGAGCCCTTCTGGAAAAGAGCCTGCCGCCAGCAGCCCCAGCAGCAACAA

TACTGCCGCCACCACAGCCGCCATCGTGCCTGGATCTCAGCTGATGCCCAGCAAGAGCCC

TAGCACCGGCACCACCGAGATCAGCAGCCACGAGTCTAGCCACGGCACCCCATCTCAGAC

CACCGCCAAGAACTGGGAGCTGACAGCCAGCGCCTCTCACCAGCCTCCAGGCGTGTACCC

TCAGGGCCACAGCGATACCACAGTGGCCATCAGCACCTCCACCGTGCTGCTGTGTGGACT

GAGCGCCGTGTCACTGCTGGCCTGCTACCTGAAGTCCAGACAGGGATCCGGAGCTACTAA SEQ ID NO: 26

CTTCAGCCTGCTGAAGCAGGCTGGAGACGTGGAGGAGAACCCTGGACCTATGTGGCAGCT SEQ ID NO: 27

GCTGCTGCCTACAGCTCTCCTGCTGCTGGTGTCCGCCGGCATGAGAACCGAGGATCTGCC

TAAGGCCGTGGTGTTCCTGGAACCCCAGTGGTACAGAGTGCTGGAAAAGGACAGCGTGAC

CCTGAAGTGCCAGGGCGCCTACAGCCCTGAGGACAATTCCACACAGTGGTTTCACAATGA

GAGCCTCATCTCAAGCCAGGCCTCGAGCTACTTCATCGACGCCGCCACCGTGGACGACAG

CGGCGAGTATAGATGCCAGACCAACCTGAGCACCCTGAGCGACCCCGTGCAGCTGGAAGT

GCACATCGGATGGCTGCTGCTGCAGGCCCCCAGATGGGTGTTCAAAGAAGAGGACCCCAT

CCACCTGAGATGCCACTCTTGGAAGAACACCGCCCTGCACAAAGTGACCTACCTGCAGAA

CGGCAAGGGCAGAAAGTACTTCCACCACAACAGCGACTTCTACATCCCCAAGGCCACCCT

GAAGGACTCCGGCTCCTACTTCTGCAGAGGCCTCGTGGGCAGCAAGAACGTGTCCAGCGA

GACAGTGAACATCACCATCACCCAGGGCCTGGCCGTGCCTACCATCAGCAGCTTTTTCCC

ACCCGGCTACCAGGTGTCCTTCTGCCTCGTGATGGTGCTGCTGTTCGCCGTGGACACCGG

CCTGTACTTCAGCGTGAAAACAAACATCAGAAGCAGCACCCGGGACTGGAAGGACCACAA

GTTCAAGTGGCGGAAGGACCCCCAGGACAAGTGAACGCGTGGGGGAGGCTAACTGAAACA SEQ ID NO: 28

CGGAAGGAGACAATACCGGAAGGAACCCGCGCTATGACGGCAATAAAAAGACAGAATAAA

ACGCACGGGTGTTGGGTCGTTTGTTCATAAACGCGGGGTTCGGTCCCAGGGCTGGCACTC

TGTCGATACCCCACCGAGACCCCATTGGGGCCAATACGCCCGCGTTTCTTCCTTTTCCCC

FIG. 17 Con't

ACCCCACCCCCCAAGTTCGGGTGAAGGCCCAGGGCTCGCAGCCAACGTCGGGGCGGCAGG

CCCTGCCATAGCAGGTACCTCAGCCTAAAGCTTTTTCCCCGTATCCCCCCAGGTGTCTGC SEQ ID NO: 23

AGGCTCAAAGAGCAGCGAGAAGCGTTCAGAGGAAAGCGATCCCGTGCCACCTTCCCCGTG

CCCGGGCTGTCCCCGCACGCTGCCGGCTCGGGGATGCGGGGGGAGCGCCGGACCGGAGCG

GAGCCCCGGGCGGCTCGCTGCTGCCCCCTAGCGGGGGAGGGACGTAATTACATCCCTGGG

GGCTTTGGGGGGGGGCTGTCCCCGTGAGCTCGATGCGTCAAGTACACTGAAATTCATCCT SEQ ID NO: 29

GAGATGAGGTGGGTTGGCGACTAAGGCGCACCGGTGGGCACTGCGGGGACAGCAGGGCCC

CGCGCGCAGGGAAGCCGCCCGGATCGCCCGGAACCGGGCATCTTCCGTGGCGGGTCAGCC

GAGAGCCCGCCGGGTGGTGCTGAGTAGGGAGTCCCGGGCTCGGGGCTCCGCGGGCCGCTT

TCAGGAGCAGCTGGCCTTGGCACCGAGCGTGCCCGCGGGAGGCGGGGGGGGGCGCTGCTC

GGTGGCTCTGCTGCGTAGCCGGTGAACACTTGGCACCGATGCCCGCCTTCTGGGCAAGGT

GCCCTGAGCCCAGCCCCTCGCCGGGCTGCAGCCCACCCTCGGCGCGCTCAGCCCGCTTCA

CCGCTTCAGGGACGGAATAGAACTCGCAGATGCAGGGTGTCGCTGACATTTTCAACTTTT

TCTGCGGTTTCCGCCCGCTGTCTCTGACCCGAAAGTGCCCCCGGACGGTTACAGAGGACA

CTTAAGTGGTTTGCAAAGCCTGTGGTAGGGGAGGAGGGTGTAGAAGGGCCAAACCACGGA

ACTTAGTTTTATTCATTTATATAAAGCAGCA

- LHA/CD38: can have variable length and sequence depending on the targeting site; exemplary sequence--SEQ ID NO: 22
- insol: not required, sequence can vary; exemplary sequence-- SEQ ID NO: 23
- CAG: can be any exogenous promoters; exemplary sequence-- SEQ ID NO: 24
- IL15RF(tr)-P2A-hnCD16: can be any transgenes
- IL15RF(tr): can be any versions of IL15/R fusion protein; exemplary sequence--SEQ ID NO: 25
- P2A: can be any 2A variants; exemplary sequence-- SEQ ID NO: 26
- hnCD16: can be any Fc receptors; exemplary sequence-- SEQ ID NO: 27
- IKpA: can be any poly A signals; exemplary sequence-- SEQ ID NO: 28
- insol: not required, sequence can vary; exemplary sequence-- SEQ ID NO: 23
- RHA/CD38: can have variable length and sequence depending on the targeting site exemplary sequence-- SEQ ID NO: 29

FIG. 17 Con't

LHA/CD38-T2A-IL15RF(tr)-P2A-hnCD16-TKpA-RHA/CD38:

AGAGGGCATTGTGTGCACACACGTATAGAAGCAGGCAGCCCACCCTCATGCTTTCCAGGA SEQ ID NO: 30

AGCAAATGTGGCTCAGGTGTAAAGTGCCCGGTTGATGAAGGGAGTTAGCGGAGGGAGTAT

AAGGATGTACTGTCTGCCCCCTTAGGACACCTGCAGAGGATTAAGGTGGCTGTTTCTCCC

TGGAGGTGGAGTGGGTGGGTCACTGCACAGGAGCCTATAGTTGTTGGTCTTTTAAACTCT

TATTGGTGTAACCAGCCACGGAACTCTGAGGCAAGGGGTTGGGGGTGGGAAGGGAAACAG

AGAAAAGGCAAGTGAAACAGAAGGGGAGGTGCAGTTTCAGAACCCAGCCAGCCTCTCTCT

TGCTGCCTAGCCTCCTGCCGGCCTCATCTTCGCCCAGCCAACCCCGCCTGGAGCCCTATG

GCCAACTGCGAGTTCAGCCCGGTGTCCGGGGACAAACCCTGCTGCCGGCTCTCTAGGAGA

GCCCAACTCTGTCTTGGCGTCAGTATCCTGGTCCTGATCCTCGTCGTGGTGCTCGCGGTG

GTCGTCCCGAGGTGGCGCCAGCAGTGGAGCGGTCCGGGCACCACCAAGCGCTTTCCCGAG

GGCAGCGGAGAGGGCAGAGGAAGTCTTCTAACATGCGGTGACGTGGAGGAGAATCCCGGC SEQ ID NO: 31

CCTATGGACTGGACCTGGATTCTGTTCCTGGTCGCGGCTGCAACGCGAGTCCATAGCGGT SEQ ID NO: 25

ATCCATGTTTTTATTCTTGGGTGTTTTTCTGCTGGGCTGCCTAAGACCGAGGCCAACTGG

GTAAATGTCATCAGTGACCTCAAGAAAATAGAAGACCTTATACAAAGCATGCACATTGAT

GCTACTCTCTACACTGAGTCAGATGTACATCCCTCATGCAAAGTGACGGCCATGAAATGT

TTCCTCCTCGAACTTCAAGTCATATCTCTGGAAAGTGGCGACGCGTCCATCCACGACACG

GTCGAAAACCTGATAATACTCGCTAATAATAGTCTCTCTTCAAATGGTAACGTAACCGAG

TCAGGTTGCAAAGAGTGCGAAGAGTTGGAAGAAAAAAACATAAAGGAGTTCCTGCAAAGT

TTCGTGCACATTGTGCAGATGTTCATTAATACCTCTAGCGGCGGAGGATCAGGTGGCGGT

GGAAGCGGAGGTGGAGGCTCCGGTGGAGGAGGTAGTGGCGGAGGTTCTCTTCAAATAACT

TGTCCTCCACCGATGTCCGTAGAACATGCGGATATTTGGGTAAAATCCTATAGCTTGTAC

AGCCGAGAGCGGTATATCTGCAACAGCGGCTTCAAGCGGAAGGCCGGCACAAGCAGCCTG

ACCGAGTGCGTGCTGAACAAGGCCACCAACGTGGCCCACTGGACCACCCCTAGCCTGAAG

TGCATCAGAGATCCCGCCCTGGTGCATCAGCGGCCTGCCCCTCCAAGCACAGTGACAACA

GCTGGCGTGACCCCCCAGCCTGAGAGCCTGAGCCCTTCTGGAAAAGAGCCTGCCGCCAGC

AGCCCCAGCAGCAACAATACTGCCGCCACCACAGCCGCCATCGTGCCTGGATCTCAGCTG

FIG. 18

ATGCCCAGCAAGAGCCCTAGCACCGGCACCACCGAGATCAGCAGCCACGAGTCTAGCCAC

GGCACCCCATCTCAGACCACCGCCAAGAACTGGGAGCTGACAGCCAGCGCCTCTCACCAG

CCTCCAGGCGTGTACCCTCAGGGCCACAGCGATACCACAGTGGCCATCAGCACCTCCACC

GTGCTGCTGTGTGGACTGAGCGCCGTGTCACTGCTGGCCTGCTACCTGAAGTCCAGACAG

GGATCCGGAGCTACTAACTTCAGCCTGCTGAAGCAGGCTGGAGACGTGGAGGAGAACCCT SEQ ID NO: 26

GGACCTATGTGGCAGCTGCTGCTGCCTACAGCTCTCCTGCTGCTGGTGTCCGCCGGCATG SEQ ID NO: 27

AGAACCGAGGATCTGCCTAAGGCCGTGGTGTTCCTGGAACCCCAGTGGTACAGAGTGCTG

GAAAAGGACAGCGTGACCCTGAAGTGCCAGGGCGCCTACAGCCCTGAGGACAATTCCACA

CAGTGGTTTCACAATGAGAGCCTCATCTCAAGCCAGGCCTCGAGCTACTTCATCGACGCC

GCCACCGTGGACGACAGCGGCGAGTATAGATGCCAGACCAACCTGAGCACCCTGAGCGAC

CCCGTGCAGCTGGAAGTGCACATCGGATGGCTGCTGCTGCAGGCCCCCAGATGGGTGTTC

AAAGAAGAGGACCCCATCCACCTGAGATGCCACTCTTGGAAGAACACCGCCCTGCACAAA

GTGACCTACCTGCAGAACGGCAAGGGCAGAAAGTACTTCCACCACAACAGCGACTTCTAC

ATCCCCAAGGCCACCCTGAAGGACTCCGGCTCCTACTTCTGCAGAGGCCTCGTGGGCAGC

AAGAACGTGTCCAGCGAGACAGTGAACATCACCATCACCCAGGGCCTGGCCGTGCCTACC

ATCAGCAGCTTTTTCCCACCCGGCTACCAGGTGTCCTTCTGCCTCGTGATGGTGCTGCTG

TTCGCCGTGGACACCGGCCTGTACTTCAGCGTGAAAACAAACATCAGAAGCAGCACCCGG

GACTGGAAGGACCACAAGTTCAAGTGGCGGAAGGACCCCCAGGACAAGTGAACGCGTGGG SEQ ID NO:28

GGAGGCTAACTGAAACACGGAAGGAGACAATACCGGAAGGAACCCGCGCTATGACGGCAA

TAAAAAGACAGAATAAAACGCACGGGTGTTGGGTCGTTTGTTCATAAACGCGGGGTTCGG

TCCCAGGGCTGGCACTCTGTCGATACCCCACCGAGACCCCATTGGGGCCAATACGCCCGC

GTTTCTTCCTTTTCCCCACCCCACCCCCCAAGTTCGGGTGAAGGCCCAGGGCTCGCAGCC

AACGTCGGGGCGGCAGGCCCTGCCATAGCAGGTACCGATGCGTCAAGTACACTGAAATTC SEQ ID NO: 32

ATCCTGAGATGAGGTGGGTTGGCGACTAAGGCGCACCGGTGGGCACTGCGGGGACAGCAG

GGCCCCGCGCGCAGGGAAGCCGCCCGGATCGCCCGGAACCGGGCATCTTCCGTGGCGGGT

CAGCCGAGAGCCCGCCGGGTGGTGCTGAGTAGGGAGTCCCGGGCTCGGGGCTCCGCGGGC

CGCTTTCAGGAGCAGCTGGCCTTGGCACCGAGCGTGCCCGCGGGAGGCGGGGGGGGGCGC

FIG. 18 Con't

TGCTCGGTGGCTCTGCTGCGTAGCCGGTGAACACTTGGCACCGATGCCCGCCTTCTGGGC

AAGGTGCCCTGAGCCCAGCCCCTCGCCGGGCTGCAGCCCACCCTCGGCGCGCTCAGCCCG

CTTCACCGCTTCAGGGACGGAATAGAACTCGCAGATGCAGGGTGTCGCTGACATTTTCAA

CTTTTTCTGCGGTTTCCGCCCGCTGTCTCTGACCCGAAAGTGCCCCCGGACGGTTACAGA

GGACACTTAAGTGGTTTGCAAAGCCTGTGGTAGGGGAGGAGGGTGTAGAAGGGCCAAACC

ACGGAACTTAGTTTTATTCATTTATATAAAGCAGCA

- LHA/CD38: can have variable length and sequence depending on the targeting site; exemplary sequence--SEQ ID NO: 30
- T2A: can be any 2A variants; exemplary sequence-- SEQ ID NO: 31
- IL15RF(tr)-P2A-hnCD16: can be any transgenes
- IL15RF(tr): can be any versions of IL15/R fusion protein; exemplary sequence-- SEQ ID NO: 25
- P2A: can be any 2A variants; exemplary sequence-- SEQ ID NO: 26
- hnCD16: can be any Fc receptors; exemplary sequence-- SEQ ID NO: 27
- IKpA: can be any poly A signals; exemplary sequence-- SEQ ID NO: 28
- RHA/CD38: can have variable length and sequence depending on the targeting site; exemplary sequence-- SEQ ID NO: 32

FIG. 18 Con't

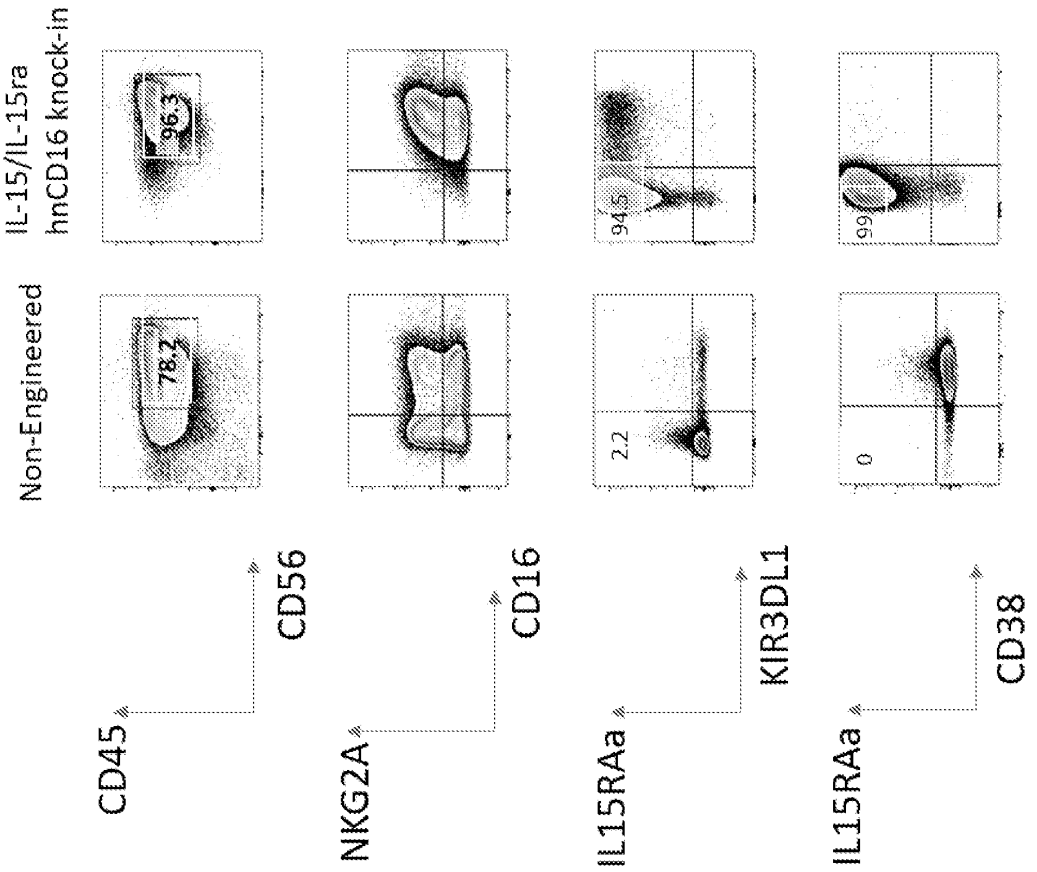
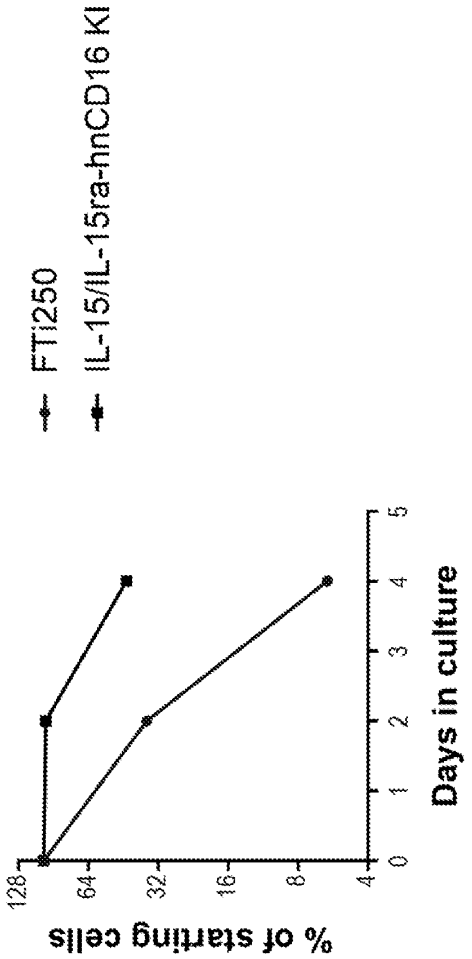

Non-Engineered
IL-15/IL-15ra hnCD16 knock-in
78.2
96.3
2.2
94.5
0
99
CD45
CD56
NKG2A
CD16
IL15RAa
KIR3DL1
IL15RAa
CD38

FIG. 19

FIG. 20


FTi250
IL-15/IL-15ra-hnCD16 KI
% of starting cells
128
64
32
16
8
4
0
1
2
3
4
5
Days in culture

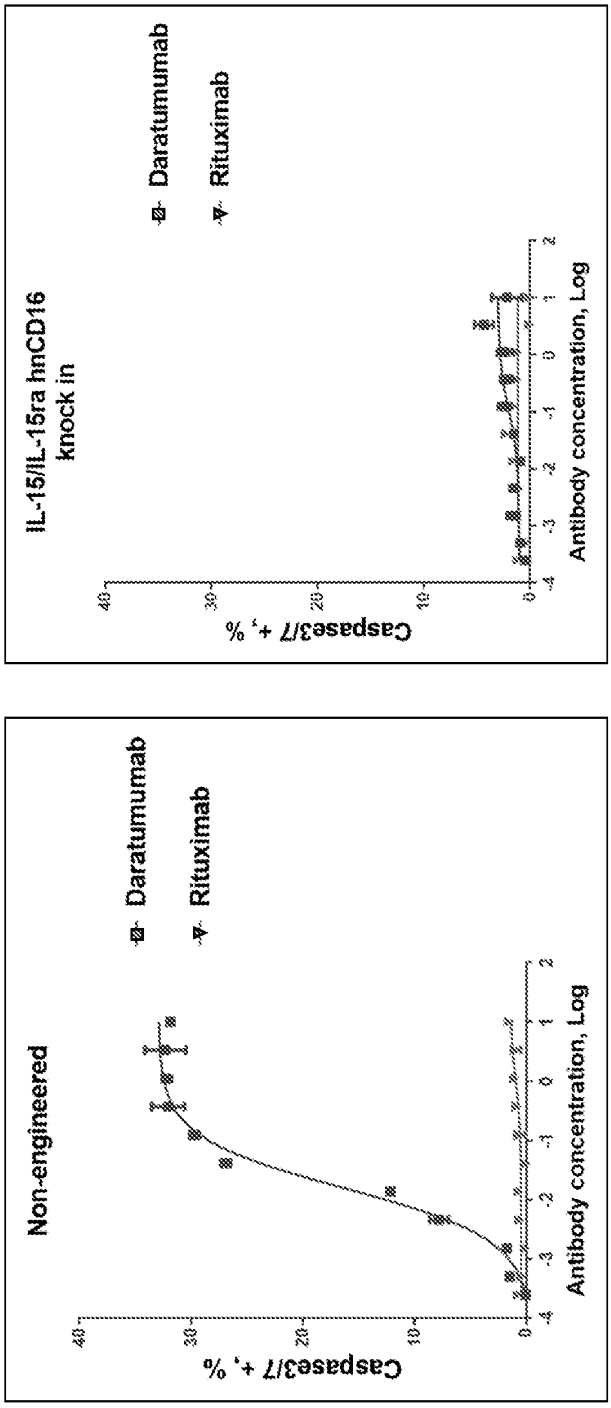

Non-engineered
Daratumumab
Rituximab
Caspase3/7 +, %
Antibody concentration, Log
IL-15/IL-15ra hnCD16
knock in
Daratumumab
Rituximab
Caspase3/7 +, %
Antibody concentration, Log

FIG. 21

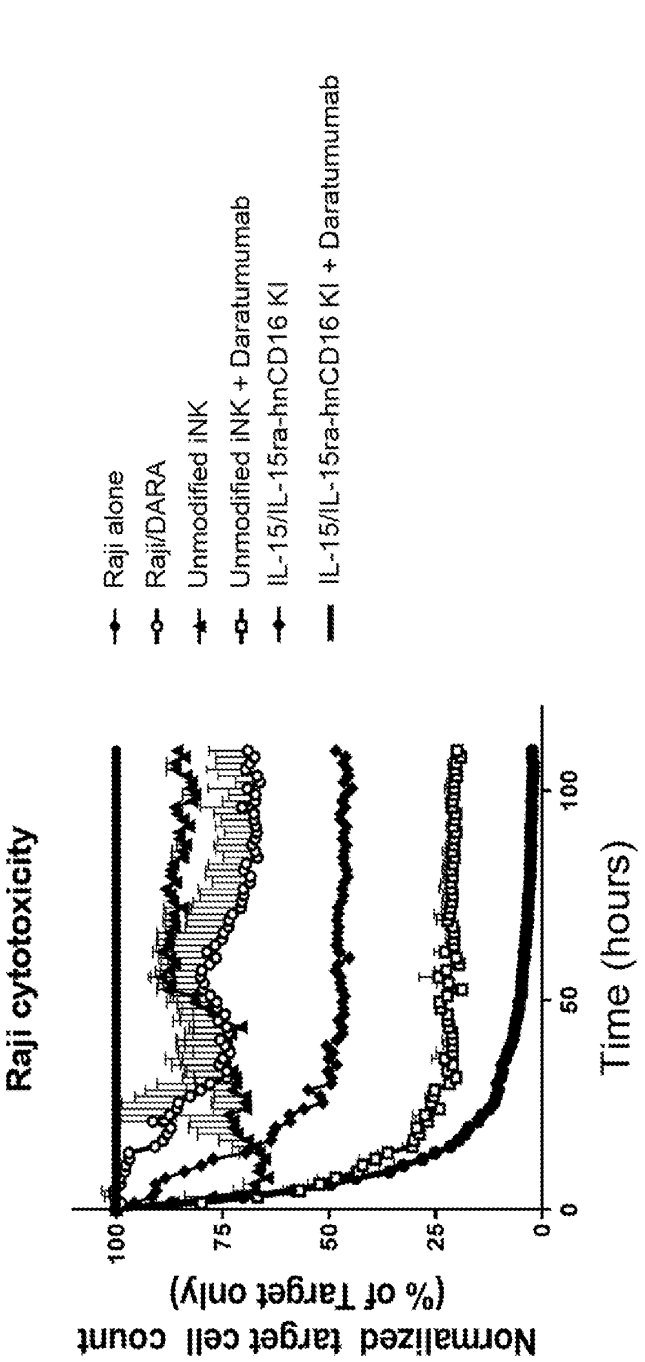

Raji cytotoxicity
Raji alone
Raji/DARA
Unmodified iNK
Unmodified iNK + Daratumumab
IL-15/IL-15ra-hnCD16 KI
IL-15/IL-15ra-hnCD16 KI + Daratumumab
Normalized target cell count
(% of Target only)
100
75
50
25
0
0
50
100
Time (hours)

FIG. 22