

FIG. 1

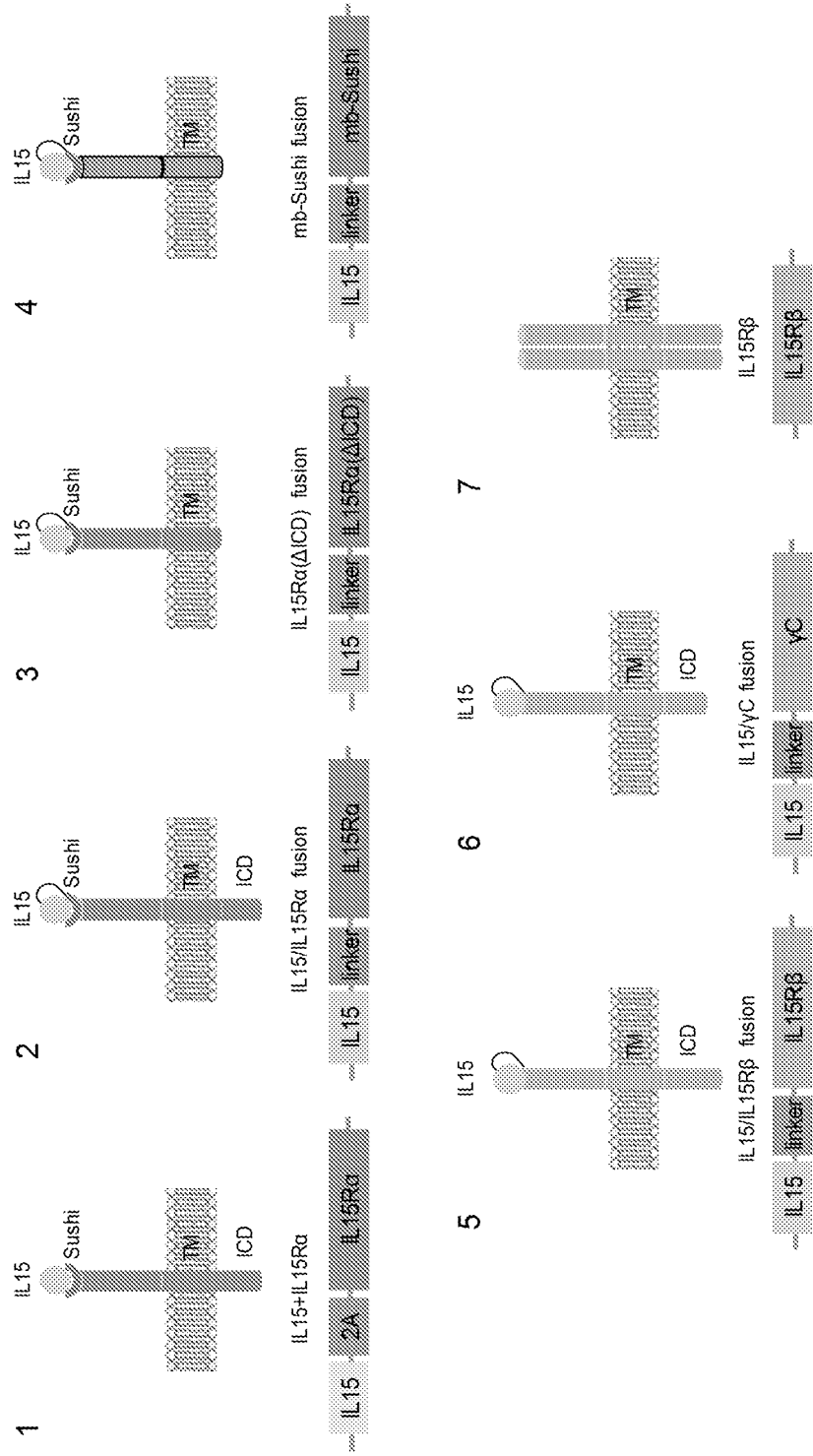


FIG. 2A



FIG. 2B

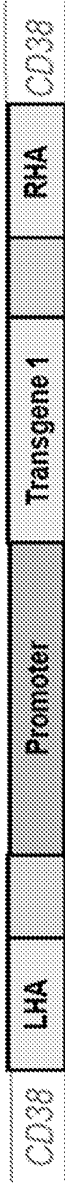


FIG. 2C



FIG. 2D



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

CAGAGGGCATTGTGTGCACACACGTATAGAAGCAGGCAGCCACCCTCATGCTTCCAGG SEQ ID NO: 22

AAGCAAATGTGGCTCAGGTGTAAAGTGCCCGGTTGATGAAGGGAGTTAGCGGAGGGAGTA
TAAGGATGTACTGTCTGCCCCCTTAGGACACCTGCAGAGGATTAAGGTGGCTGTTTCTCC
CTGGAGGTGGAGTGGGTGGGTCACTGCACAGGAGCCTATAGTTGTTGGTCTTTTAACTC
TTATTGGTGTAAACAGCCACGGAACCTCTGAGGCAAGGGGTTGGGGTGGGAAGGAAACA
GAGAAAAGGCAAGTGAAACAGAAGGGGAGGTGCAGTTTCAGAACCCAGCCAGCCTCTCTC
TTGCTGCCTAGCCTCCTGCCGGCCTCATCTTCGCCAGCCAACCCGCCTGGAGCCCTAT
GGCCAACTGCGAGTTCAGCCCGGTGTCCGGGGACAAACCTGCTGCCGGCTCTCTAGGAG
AGCCCAACTCTGTCTTGGCGTCAGTATCCTGGTCCTGATCCTCGTCGTGGTGCTCGCGGT
GGTCGTCCCGAGGTGGCGCCAGCAGTGGAGCGGTCCGGGCACCACCAAGCGCTTCCCGA

GTCAGCCTAAAGCTTTTTCCCGTATCCCCCAGGTGTCTGCAGGCTCAAAGAGCAGCGA SEQ ID NO: 23

GAAGCGTTCAGAGGAAAGCGATCCCGTGCCACCTTCCCGTGCCCGGGCTGTCCCGCAC
GCTGCCGGCTCGGGGATGCGGGGGGAGCGCCGGACCGAGCGGAGCCCCGGGCGGCTCGC
TGCTGCCCCCTAGCGGGGGAGGGACGTAATTACATCCCTGGGGGCTTTGGGGGGGGCTG

TCCCGTGAGCTCATCGATACTAGTGACAGTTAATGATGTTGACATTGATTATTGACT SEQ ID NO: 24

AGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCGCG
GTTACATAACTTACGGTAAATGGCCGCCTGGCTGACCGCCCAACGACCCCCGCCATTG
ACGTCATAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCATTGACGTCAA
TGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCA
AGTACGCCCCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCAGTAC
ATGACCTTATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACC
ATGGTCGAGGTGAGCCCCACGTTCTGCTTCACTCTCCCCATCTCCCCCCCCCTCCCCACCC
CCAATTTTGTATTTATTTATTTTAAATTATTTTGTGCAGCGATGGGGGCGGGGGGGGG
GGGGGGCGCGGCCAGGCGGGGCGGGGCGGGGCGAGGGGCGGGGCGGGGCGAGGCGGAGA
GGTGCGGGCGCAGCAATCAGAGCGGCGCGCTCCGAAAGTTTCCTTTATGGCGAGGCGG
CGGCGGCGGCGGCCCTATAAAAAGCGAAGCGCGCGGGCGGGGAGTCGCTGCGACGCT
GCCTTCGCCCCGTGCCCCGCTCCGCCCGCCCTCGCGCCGCCCGCCCCGGCTCTGACTGA

FIG. 3

CCGCGTTACTCCACAGGTGAGCGGGCGGGACGGCCCTTCTCCTCCGGGCTGTAATTAGC
GCTTGTTTAATGACGGCTTGTTTCTTTTCTGTGGCTGCGTGAAAGCCTTGAGGGGCTCC
GGGAGGGCCCTTTGTGCGGGGGAGCGGCTCGGGGGGTGCGTGCGTGTGTGTGCGTGG
GGAGCGCCGCTGCGGCTCCGCGCTGCCCGGCGGCTGTGAGCGCTGCGGGCGCGGCGCGG
GGCTTTGTGCGCTCCGCAAGTGTGCGGAGGGGAGCGCGGCCGGGGGCGGTGCCCCGCGGT
GCGGGGGGGGCTGCGAGGGGAACAAAGGCTGCGTGCGGGGTGTGTGCGTGGGGGGGTGAG
CAGGGGGTGTGGGCGCGTCGGTCGGGCTGCAACCCCCCTGCACCCCCCTCCCGAGTTG
CTGAGCACGGCCCGGCTTCGGGTGCGGGGCTCCGTACGGGGCGTGGCGCGGGGCTCGCCG
TGCCGGGCGGGGGGTGGCGGCAGGTGGGGGTGCCGGGCGGGGCGGGGCCGCTCGGGCCG
GGGAGGGCTCGGGGAGGGGCGCGGCGGCCCGGAGCGCCGGCGGCTGTGAGGCGCGG
CGAGCCGACAGCATTGCCTTTATGGTAATCGTGCGAGAGGGCGAGGACTTCCTTTGT
CCCAAATCTGTGCGGAGCCGAAATCTGGGAGGCGCCGCCGACCCCCCTAGCGGGCGCG
GGGCGAAGCGGTGCGGCGCCGGCAGGAAGGAAATGGGCGGGGAGGGCCTTCGTGCGTCGC
CGCGCCGCGTCCCCTTCTCCTCTCCAGCCTCGGGGTGTCCGCGGGGGGACGGGTGCC
TTCGGGGGGGACGGGGCAGGGCGGGGTTCTGGCTTCTGGCGTGTGACCGGCGGCTCTAGAG
CCTCTGCTAACCATGTTTCATGCCTTCTTTTCTTCTACAGCTCCTGGGCAACGTGCTGG
TTATTGTGCTGTCTCATCATTTTGGCAAAGAATTGCTAGCGCCACCATGGACTGGACCTG SEQ ID NO: 25
GATTCTGTTCTCTGGTCGCGGCTGCAACGCGAGTCCATAGCGGTATCCATGTTTTTATTCT
TGGGTGTTTTTCTGCTGGGCTGCCTAAGACCGAGGCCAACTGGGTAAATGTCATCAGTGA
CCTCAAGAAAATAGAAGACCTTATACAAAGCATGCACATTGATGCTACTCTCTACACTGA
GTCAGATGTACATCCCTCATGCAAAGTGACGGCCATGAAATGTTTCTCCTCGAACTTCA
AGTCATATCTCTGGAAAGTGGCGACGCGTCCATCCACGACACGGTCGAAAACCTGATAAT
ACTCGCTAATAATAGTCTCTTTCAAATGGTAACGTAACCGAGTCAGTTGCAAAGAGTG
CGAAGAGTTGGAAGAAAAAACATAAAGGAGTTCTTGCAAAGTTTCGTGCACATTGTGCA
GATGTTTATTAATACCTCTAGCGGCGGAGGATCAGGTGGCGGTGGAAGCGGAGGTGGAGG
CTCCGGTGGAGGAGGTAGTGGCGGAGGTTCTTTCAAATAACTTGTCTCCACCGATGTC
CGTAGAACATGCGGATATTTGGGTAAAATCCTATAGCTTGACAGCCGAGAGCGGTATAT

FIG. 3 con't.

CTGCAACAGCGGCTTCAAGCGGAAGGCCGGCACAAAGCAGCCTGACCGAGTGCGTGCTGAA
CAAGGCCACCAACGTGGCCCACTGGACCACCCCTAGCCTGAAGTGCATCAGAGATCCCCGC
CCTGGTGCATCAGCGGCTGCCCCCTCCAAGCACAGTGACAACAGCTGGCGTGACCCCCCA
GCCTGAGAGCCTGAGCCCTTCTGGAAAAGAGCCTGCCGCCAGCAGCCCCAGCAGCAACAA
TACTGCCGCCACCACAGCCGCCATCGTGCCTGGATCTCAGCTGATGCCAGCAAGAGCCC
TAGCACCGGCACACCGAGATCAGCAGCCACGAGTCTAGCCACGGCACCCCATCTCAGAC
CACCGCCAAGAACTGGGAGCTGACAGCCAGCGCCTCTCACCAGCCTCCAGGCGTGATCCC
TCAGGGCCACAGCGATACCACAGTGGCCATCAGCACCTCCACCGTGCTGCTGTGTGGACT
GAGCGCCGTGTCACTGCTGGCCTGCTACCTGAAGTCCAGACAGGGATCCGGAGCTACTAA SEQ ID NO: 26
CTTCAGCCTGCTGAAGCAGGCTGGAGACGTGGAGGAGAACCCTGGACCTATGTGGCAGCT SEQ ID NO: 27
GCTGCTGCCTACAGCTCTCCTGCTGCTGGTGTCCGCCGGCATGAGAACCAGGATCTGCC
TAAGGCCGTGGTGTTCTTGGAACCCCAGTGGTACAGAGTGCTGGAAAAGGACAGCGTGAC
CCTGAAGTGCCAGGGCGCCTACAGCCCTGAGGACAATTCCACACAGTGGTTTCACAATGA
GAGCCTCATCTCAAGCCAGGCCTCGAGCTACTTCATCGACGCCGCCACCGTGGACGACAG
CGGCGAGTATAGATGCCAGACCAACCTGAGCACCTGAGCGACCCCGTGCAGCTGGAAGT
GCACATCGGATGGCTGCTGCTGCAGGCCCCAGATGGGTGTTCAAAGAAGAGGACCCCAT
CCACCTGAGATGCCACTCTTGGAAGAACACCGCCCTGCACAAAGTGACCTACCTGCAGAA
CGGCAAGGGCAGAAAGTACTTCCACCACAACAGCGACTTCTACATCCCCAAGGCCACCCT
GAAGGACTCCGGCTCCTACTTCTGCAGAGGCCTCGTGGGAGCAAGAACGTGTCCAGCGA
GACAGTGAACATCACCATCACCCAGGGCCTGGCCGTGCCTACCATCAGCAGCTTTTTCCC
ACCCGGCTACCAGGTGTCTTCTGCCTCGTGATGGTGCTGCTGTTCCCGTGGACACCGG
CCTGTACTTCAGCGTGAAAACAAACATCAGAAGCAGCACCCGGGACTGGAAGGACCACAA
GTTCAAGTGGCGGAAGGACCCCAAGGACAAGTGAACGCGTGGGGGAGGCTAACTGAAACA SEQ ID NO: 28
CGGAAGGAGACAATACCGGAAGGAACCCGCGCTATGACGGCAATAAAAAGACAGAATAAA
ACGCACGGGTGTTGGGTCGTTTGTTCATAAACGCGGGGTTCCGTCCCAGGGCTGGCACTC
TGTCGATACCCACCGAGACCCATTGGGGCCAATACGCCCCGTTTTCTTCTTTTCCCC

FIG. 3 con't.

ACCCCACCCCCAAGTTCGGGTGAAGGCCAGGGCTCGCAGCCAACGTCGGGGCGGCAGG
 CCCTGCCATAGCAGGTACCTCAGCCTAAAGCTTTTTCCCGTATCCCCCAGGTGTCTGC SEQ ID NO: 23
 AGGCTCAAAGAGCAGCGAGAAGCGTTCAGAGGAAAGCGATCCCGTGCCACCTTCCCGTG
 CCCGGGCTGTCCCGCACGCTGCCGGCTCGGGGATGCGGGGGAGCGCCGGACCGGAGCG
 GAGCCCCGGGCGGCTCGCTGCTGCCCCCTAGCGGGGAGGGACGTAATTACATCCCTGGG
 GGCTTTGGGGGGGGGCTGTCCCGTGAGCTCGATGCGTCAAGTACACTGAAATTCATCCT SEQ ID NO: 29
 GAGATGAGGTGGGTTGGCGACTAAGGCGCACCGGTGGGCACTGCGGGGACAGCAGGGCCC
 CGCGCGCAGGGAAGCCGCCCGGATCGCCCGGAACCGGGCATCTTCCGTGGCGGGTCAGCC
 GAGAGCCCCCGGGTGGTGTGAGTAGGGAGTCCCGGGCTCGGGGCTCCGCGGGCCGCTT
 TCAGGAGCAGCTGGCCTTGGCACCGAGCGTGCCCGCGGGAGGCGGGGGGGGCGCTGCTC
 GGTGGCTCTGCTGCGTAGCCGGTGAACACTTGGCACCGATGCCGCCTTCTGGGCAAGGT
 GCCCTGAGCCCAGCCCCTCGCCGGGCTGCAGCCACCCTCGGCGCGCTCAGCCGCTTCA
 CCGCTTCAGGGACGGAATAGAACTCGCAGATGCAGGGTGTGCTGACATTTTCAACTTTT
 TCTGCGGTTTCCGCCGCTGTCTCTGACCCGAAAGTGCCCCGGACGTTACAGAGGACA
 CTTAAGTGGTTTGCAAAGCCTGTGGTAGGGGAGGAGGGGTAGAGAAGGGCCAAACCACGGA
 ACTTAGTTTTATTCAATTTATATAAAGCAGCA

- **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
- **TKpA**: 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. 3 con't.

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

AGAGGGCATTGTGTGCACACACGTATAGAAGCAGGCAGCCCACCCTCATGCTTTCCAGGA SEQ ID NO: 30

AGCAAATGTGGCTCAGGTGTAAAGTGCCCGGTTGATGAAGGGAGTTAGCGGAGGGAGTAT

AAGGATGTACTGTCTGCCCCCTTAGGACACCTGCAGAGGATTAAGGTGGCTGTTTCTCCC

TGGAGGTGGAGTGGGTGGGTCACTGCACAGGAGCCTATAGTTGTTGGTCTTTTAACTCT

TATTGGTGTAAACCAGCCACGGAACCTCTGAGGCAAGGGGTTGGGGTGGGAAGGGAACAG

AGAAAAGGCAAGTGAAACAGAAGGGGAGGTGCAGTTTCAGAACCCAGCCAGCCTCTCTCT

TGCTGCCTAGCCTCTGCCGGCCTCATCTTCGCCAGCCAACCCGCCTGGAGCCCTATG

GCCAACTGCGAGTTCAGCCCGGTGTCCGGGGACAAACCCTGCTGCCGGCTCTCTAGGAGA

GCCCAACTCTGTCTTGGCGTCAGTATCCTGGTCCTGATCCTCGTCGTGGTGCTCGCGGTG

GTCGTCCCAGGTTGGCGCCAGCAGTGGAGCGGTCCGGGCACCAAGCGCTTTCCCGAG

GGCAGCGGAGAGGGCAGAGGAAGTCTTCTAACATGCGGTGACGTGGAGGAGAATCCCGGC SEQ ID NO: 31CCTATGGACTGGACCTGGATTCTGTTCTGGTCGCGGCTGCAACGCGAGTCCATAGCGGT SEQ ID NO: 25

ATCCATGTTTTATTCTTGGGTGTTTTCTGCTGGGCTGCCTAAGACCGAGGCCAACTGG

GTAAATGTCATCAGTGACCTCAAGAAAATAGAAGACCTTATACAAAGCATGCACATTGAT

GCTACTCTCTACACTGAGTCAGATGTACATCCCTCATGCAAAGTGACGGCCATGAAATGT

TTCCTCCTCGAACTTCAAGTCATATCTCTGGAAGTGGCGACGCTCCATCCACGACACG

GTCGAAAACCTGATAATACTCGCTAATAATAGTCTCTCTTCAAATGGTAACGTAACCGAG

TCAGGTTGCAAAGAGTGCGAAGAGTTGGAAGAAAAAACATAAAGGAGTTCCTGCAAAGT

TTCGTGCACATTGTGCAGATGTTCAATTAACCTCTAGCGGCGGAGGATCAGGTGGCGGT

GGAAGCGGAGGTGGAGGCTCCGGTGGAGGAGGTAGTGGCGGAGGTTCTCTTCAAATAACT

TGTCTCCACCGATGTCCGTAGAACATGCGGATATTTGGGTAAAATCCTATAGCTTGTAC

AGCCGAGAGCGGTATATCTGCAACAGCGGCTTCAAGCGGAAGGCCGGCACAAGCAGCCTG

ACCGAGTGCGTGCTGAACAAGGCCACCAACGTGGCCCACTGGACCACCCCTAGCCTGAAG

TGCATCAGAGATCCCGCCCTGGTGCATCAGCGGCCTGCCCTCCAAGCACAGTGACAACA

GCTGGCGTGACCCCCAGCCTGAGAGCCTGAGCCCTTCTGGAAAAGAGCCTGCCGCCAGC

AGCCCCAGCAGCAACAATACTGCCGCCACCACAGCCGCCATCGTGCCTGGATCTCAGCTG

FIG. 4

ATGCCCAGCAAGAGCCCTAGCACCGGCACCACCGAGATCAGCAGCCACGAGTCTAGCCAC
GGCACCCCATCTCAGACCACCGCCAAGAACTGGGAGCTGACAGCCAGCGCCTCTCACCAG
CCTCCAGGCGTGTAACCTCAGGGCCACAGCGATACCACAGTGGCCATCAGCACCTCCACC
GTGCTGCTGTGTGGACTGAGCGCCGTGTCACTGCTGGCCTGCTACCTGAAGTCCAGACAG
GGATCCGGAGCTACTAACTTCAGCCTGCTGAAGCAGGCTGGAGACGTGGAGGAGAACCT SEQ ID NO: 26
GGACCTATGTGGCAGCTGCTGCTGCCTACAGCTCTCCTGCTGCTGGTGTCCGCCGGCATG SEQ ID NO: 27
AGAACCGAGGATCTGCCTAAGGCCGTGGTGTTCCTGGAACCCAGTGGTACAGAGTGCTG
GAAAAGGACAGCGTGACCCTGAAGTGCCAGGGCGCCTACAGCCCTGAGGACAATTCCACA
CAGTGGTTTACAATGAGAGCCTCATCTCAAGCCAGGCCTCGAGCTACTTCATCGACGCC
GCCACCGTGGACGACAGCGGCGAGTATAGATGCCAGACCAACCTGAGCACCTGAGCGAC
CCCGTGAGCTGGAAGTGACATCGGATGGCTGCTGCTGCAGGCCCCCAGATGGGTGTTC
AAAGAAGAGGACCCCATCCACCTGAGATGCCACTCTTGAAGAACACCGCCCTGCACAAA
GTGACCTACCTGCAGAACGGCAAGGGCAGAAAGTACTTCCACCACAACAGCGACTTCTAC
ATCCCCAAGGCCACCCTGAAGGACTCCGGCTCCTACTTCTGCAGAGGCCTCGTGGGCAGC
AAGAACGTGTCCAGCGAGACAGTGAACATCACCATCACCAGGGCCTGGCCGTGCCTACC
ATCAGCAGCTTTTTCCACCCGGCTACCAGGTGTCCTTCTGCCTCGTGATGGTGCTGCTG
TTCGCCGTGGACACCGGCCTGTACTTCAGCGTGAAAACAAACATCAGAAGCAGCACCCGG
GACTGGAAGGACCACAAGTTCAAGTGGCGGAAGGACCCCAAGGACAAGTGAACGCGTGGG SEQ ID NO: 28
GGAGGCTAACTGAAACACGGAAGGAGACAATACCGGAAGGAACCCGCGCTATGACGGCAA
TAAAAAGACAGAATAAAACGCACGGGTGTTGGGTCGTTTGTTCATAAACCGGGGTTCGG
TCCCAGGGCTGGCACTCTGTCGATACCCACCGAGACCCATTGGGGCCAATACGCCCGC
GTTTCTTCCTTTTCCCCACCCACCCCAAGTTCGGGTGAAGGCCAGGGCTCGCAGCC
AACGTCGGGGCGGCAGGCCCTGCCATAGCAGGTACCGATGCGTCAAGTACACTGAAATTC SEQ ID NO: 32
ATCCTGAGATGAGGTGGGTGGCGACTAAGGCGCACCGGTGGGCACTGCGGGGACAGCAG
GGCCCCGCGCGCAGGGAAGCCGCCCGGATCGCCGGAACCGGGCATCTTCCGTGGCGGGT
CAGCCGAGAGCCCGCGGGTGGTGCTGAGTAGGGAGTCCCGGGCTCGGGGCTCCGCGGGC
CGCTTTCAGGAGCAGCTGGCCTTGGCACCGAGCGTGCCCGGGGAGGCGGGGGGGGGCGC

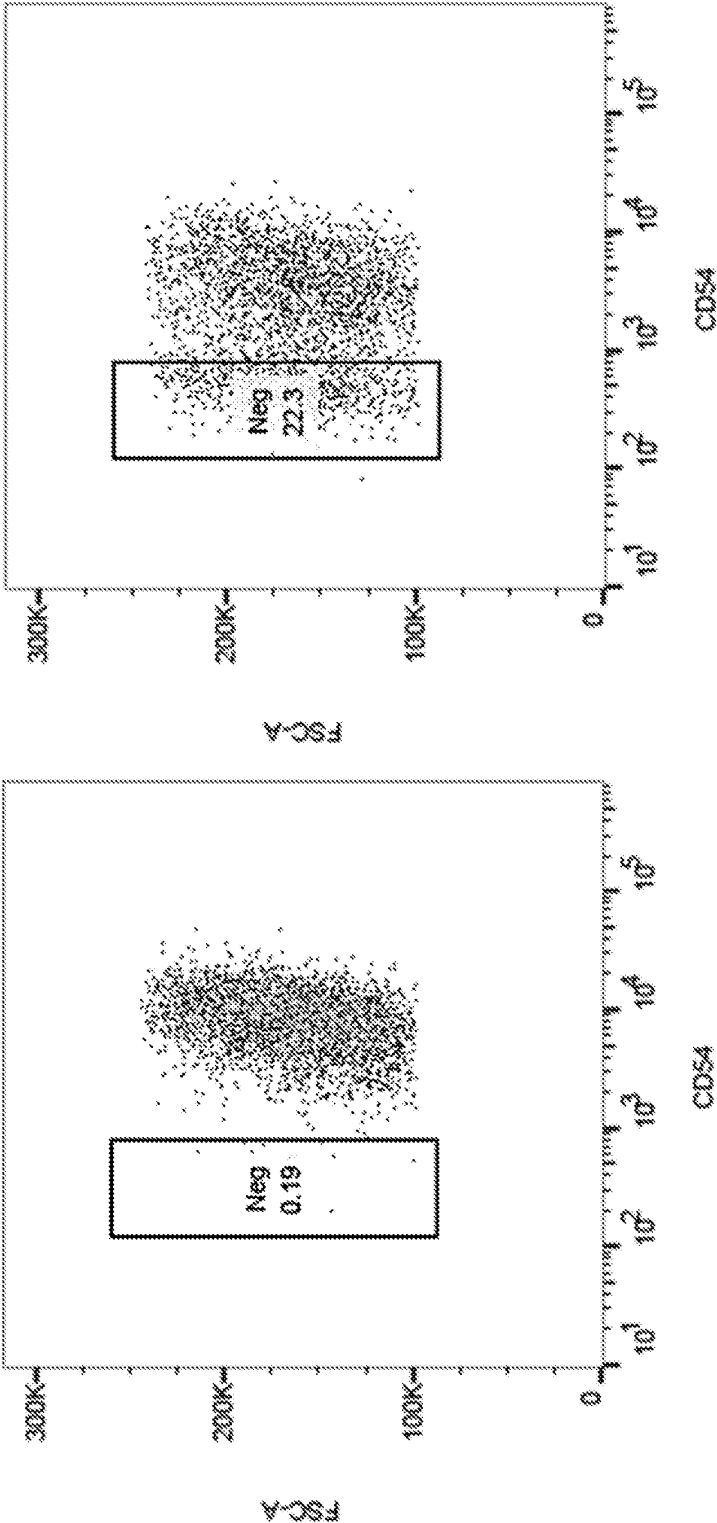
FIG. 4 con't.

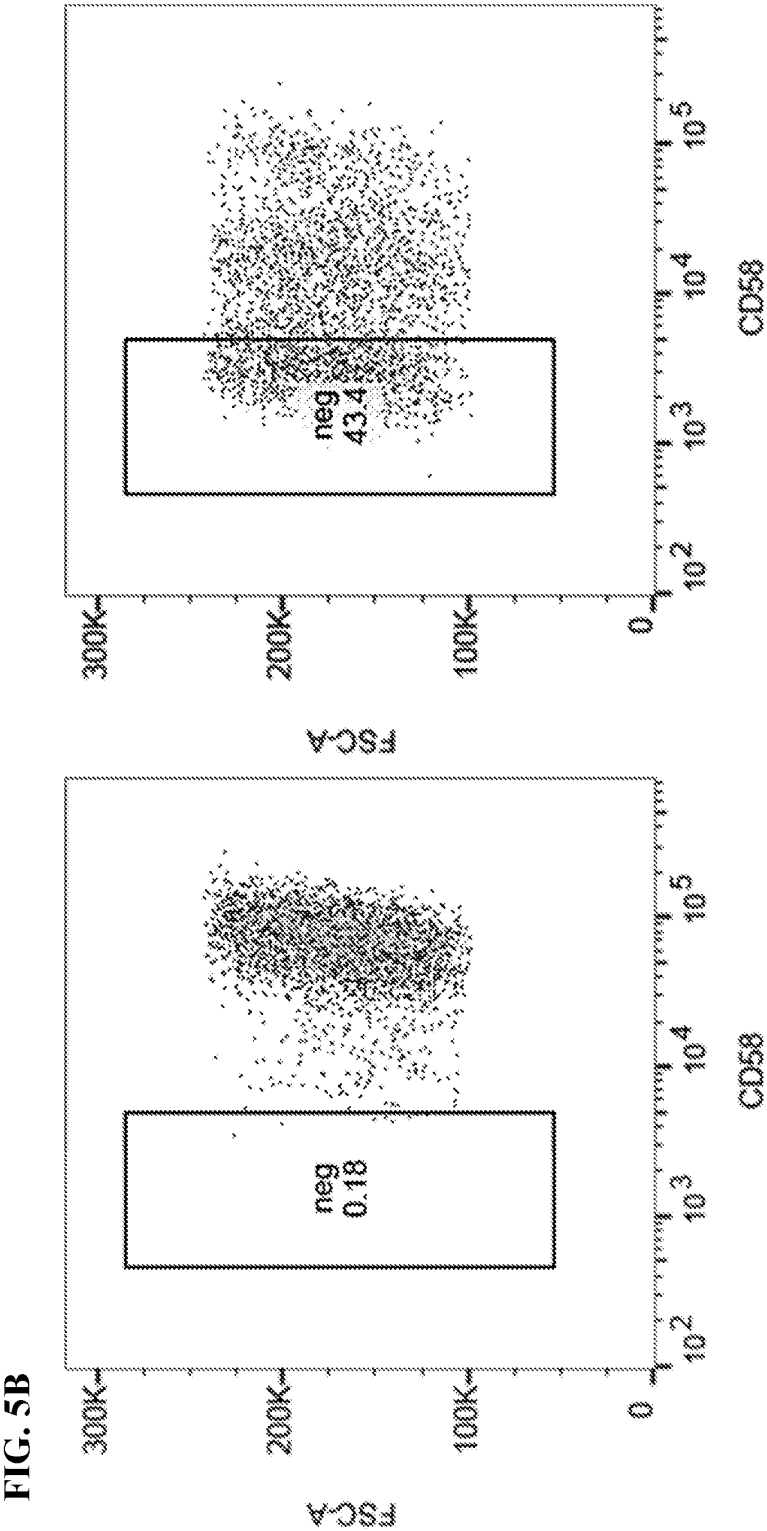
TGCTCGGTGGCTCTGCTGCGTAGCCGGTGAACACTTGGCACCGATGCCCCGCTTCTGGGC
 AAGGTGCCCTGAGCCCAGCCCCTCGCCGGGCTGCAGCCCACCCTCGGCGCGCTCAGCCCG
 CTTACCGCTTCAGGGACGGAATAGAACTCGCAGATGCAGGGTGTGCTGACATTTTCAA
 CTTTTTCTGCGGTTTCCGCCCGCTGTCTCTGACCCGAAAGTGCCCCGGACGGTTACAGA
 GGACACTTAAGTGGTTTGCAAAGCCTGTGGTAGGGGAGGAGGGTGTAGAAGGGCCAAACC
 ACGGAACCTAGTTTTATTCAATTTATATAAAGCAGCA

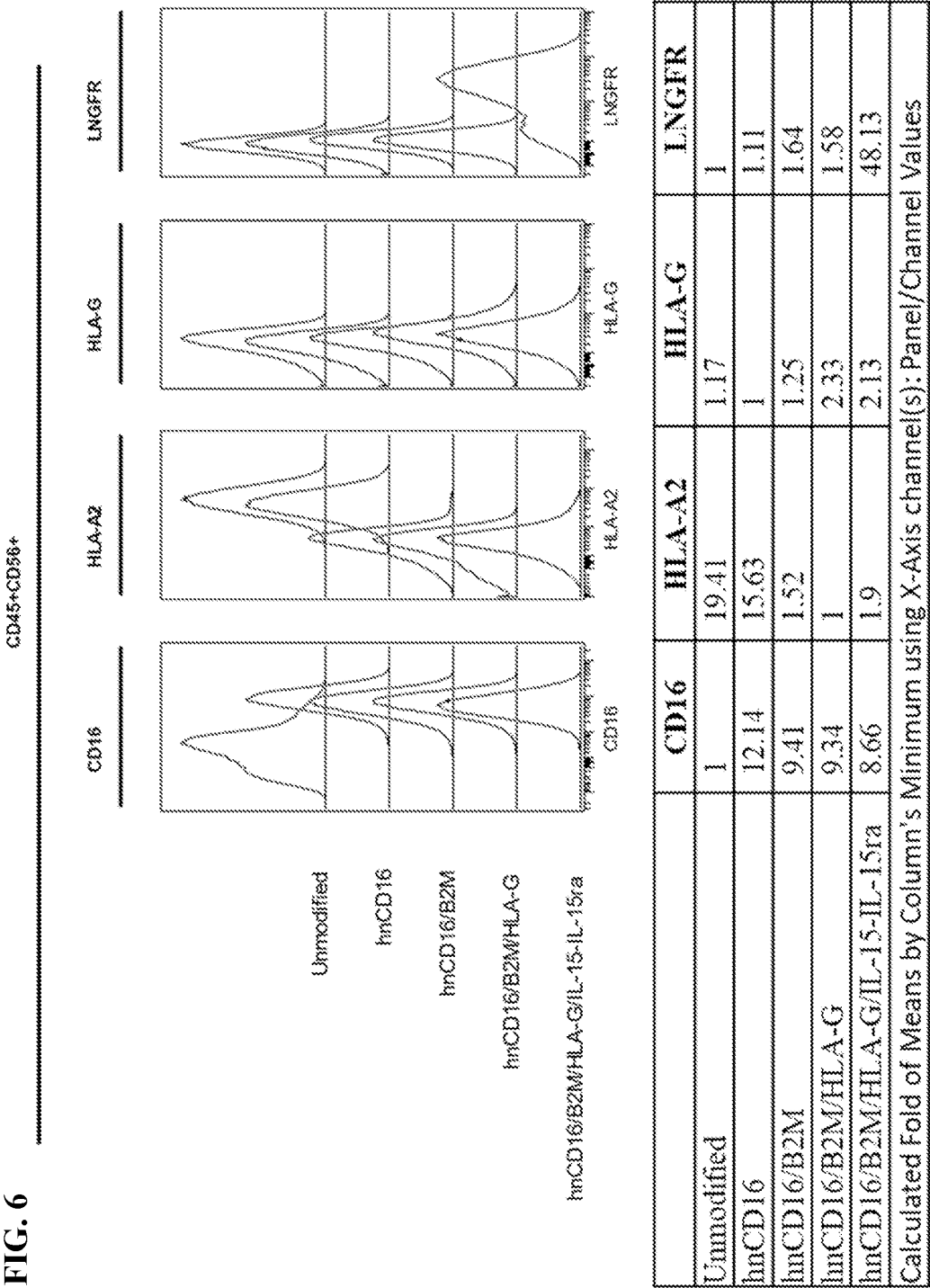
- **LHA/CD38**: can have variable length and sequence depending on the targeting site; exemplary sequence--SEQ ID NO: 30
- **T2A**: can be any 2A variants; exemplary sequence-- SEQ ID NO: 31
- **IL15RF(tr)-P2A-hnCD16**: can be any transgenes
- **IL15RF(tr)**: can be any versions of IL15/R fusion protein; 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
- **TKpA**: 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. 4 con't.

FIG. 5A







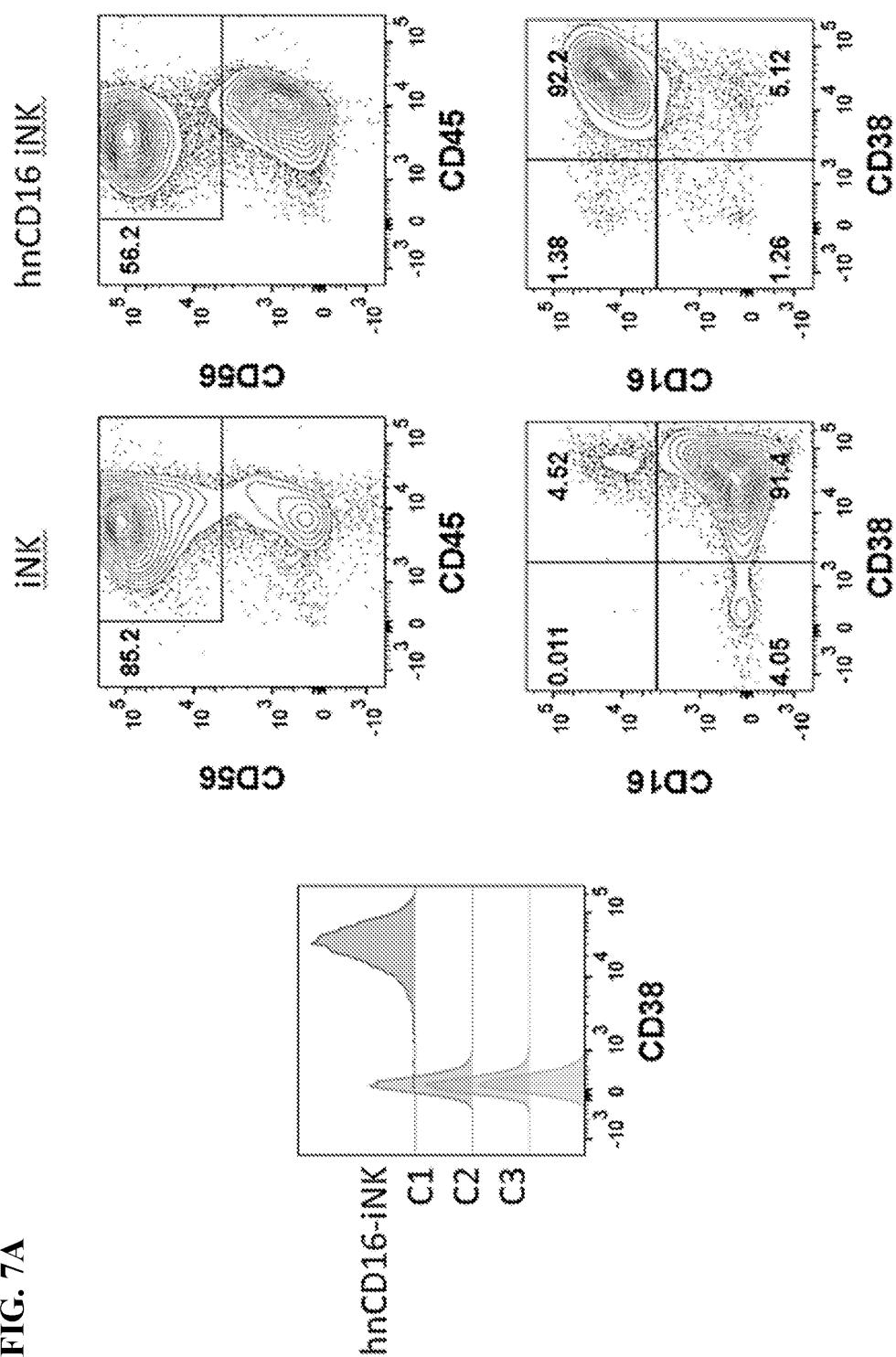


FIG. 7A

FIG. 7B

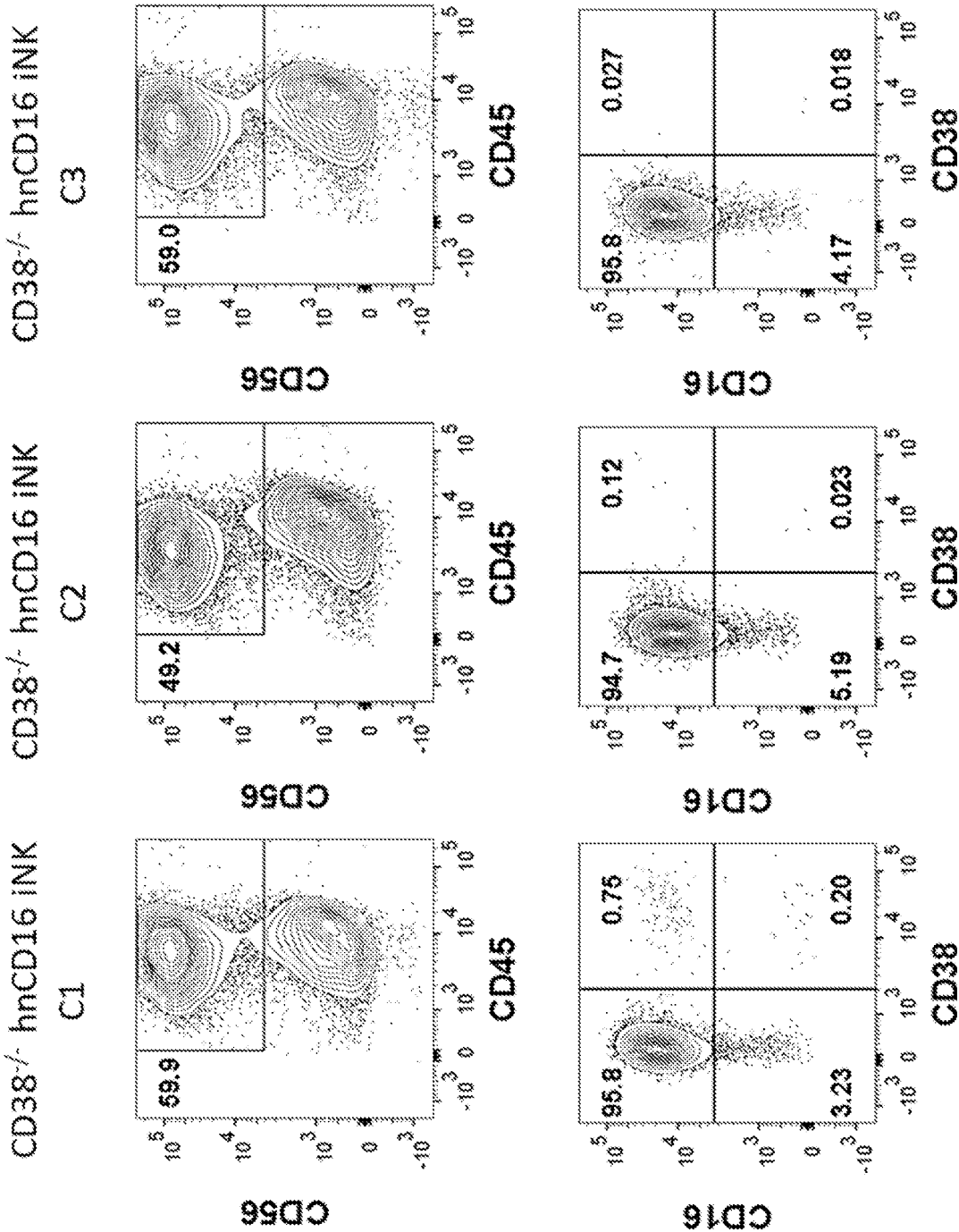


FIG. 8

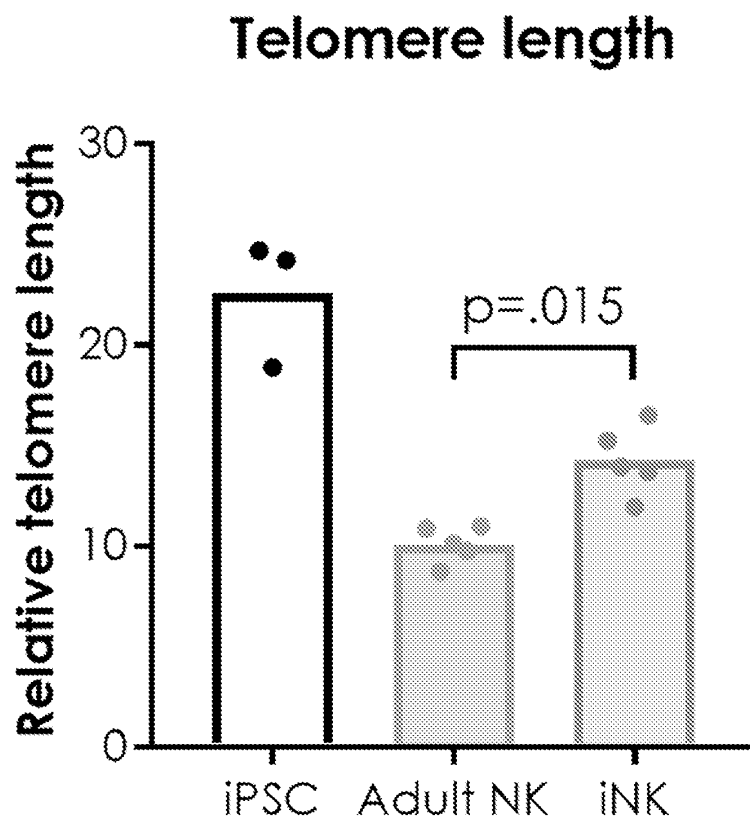


FIG. 9A

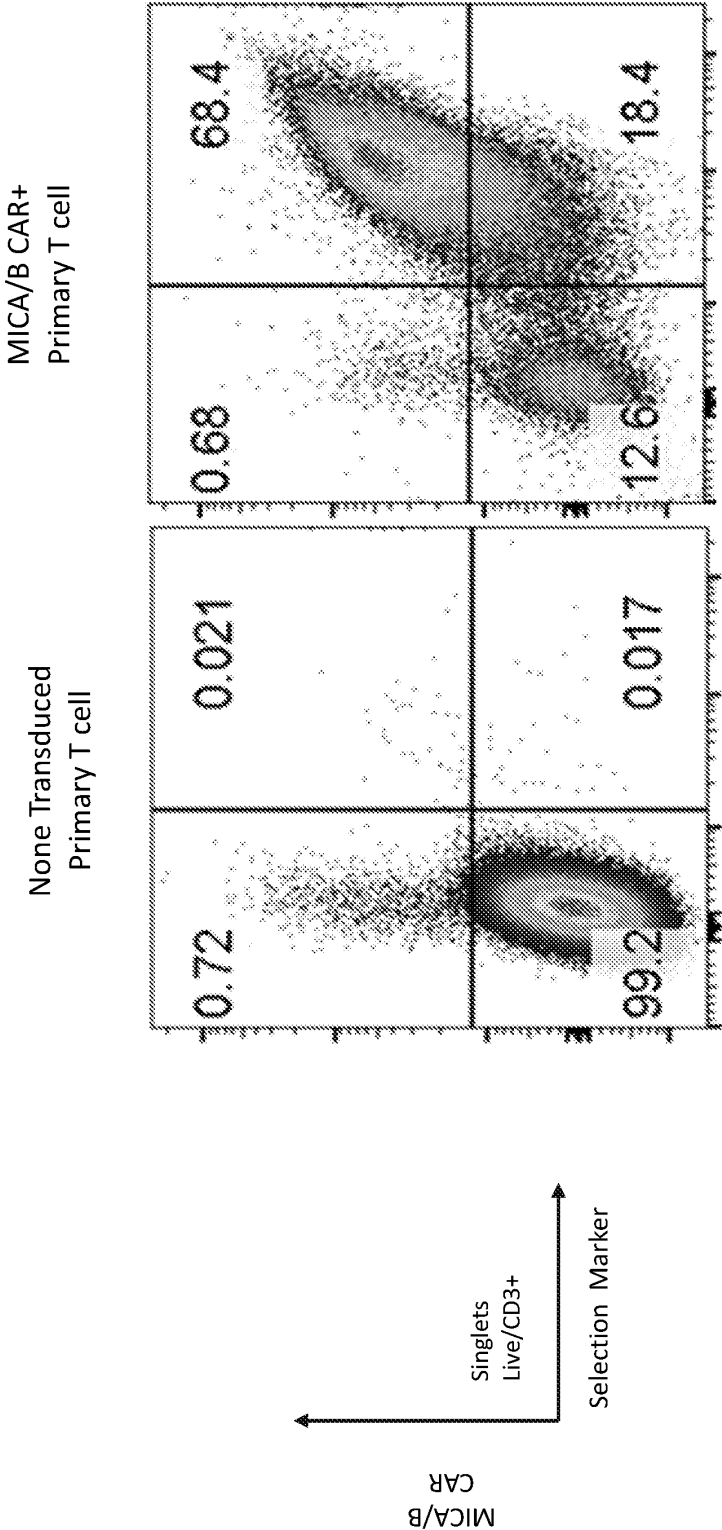


FIG. 9B

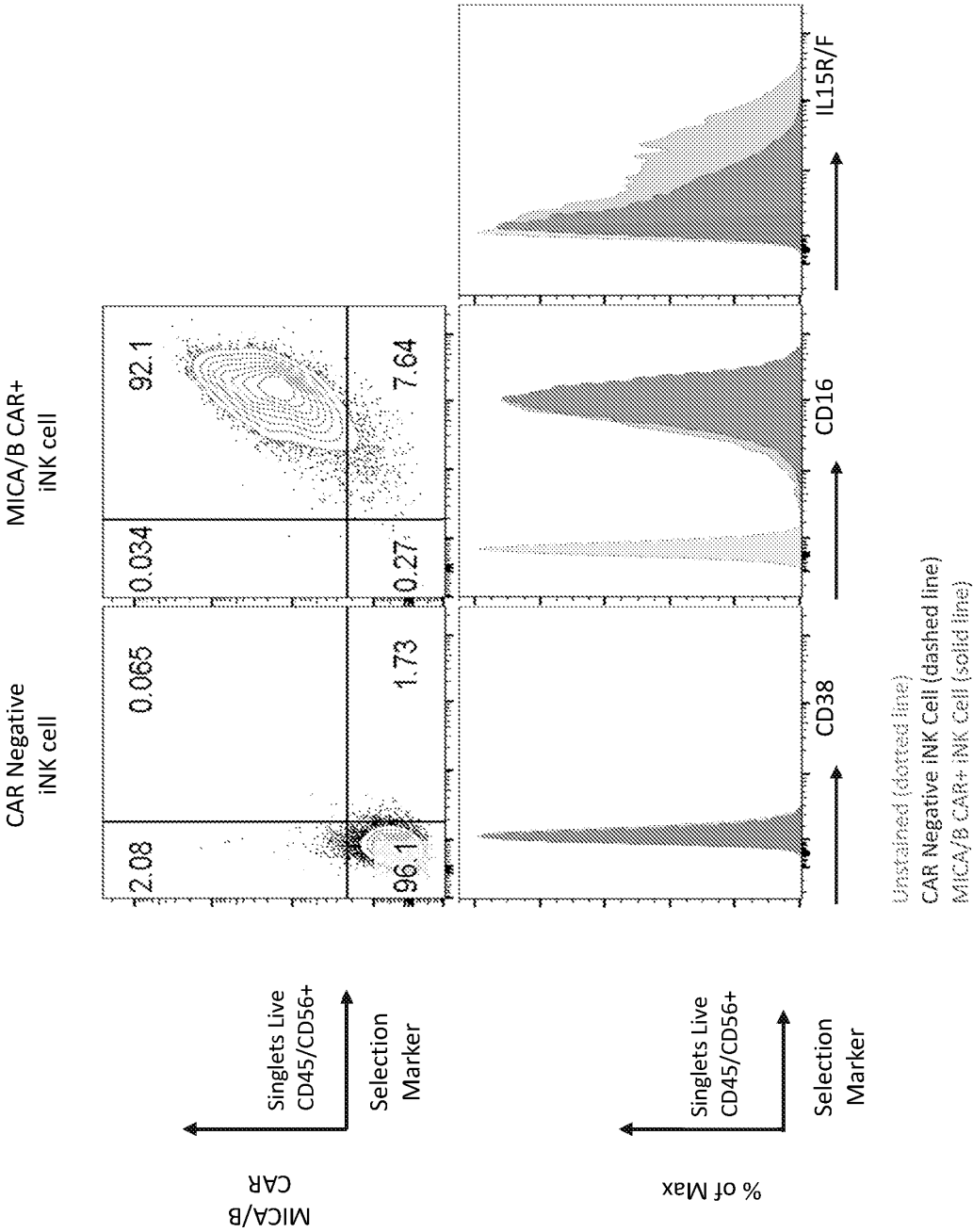


FIG. 10A

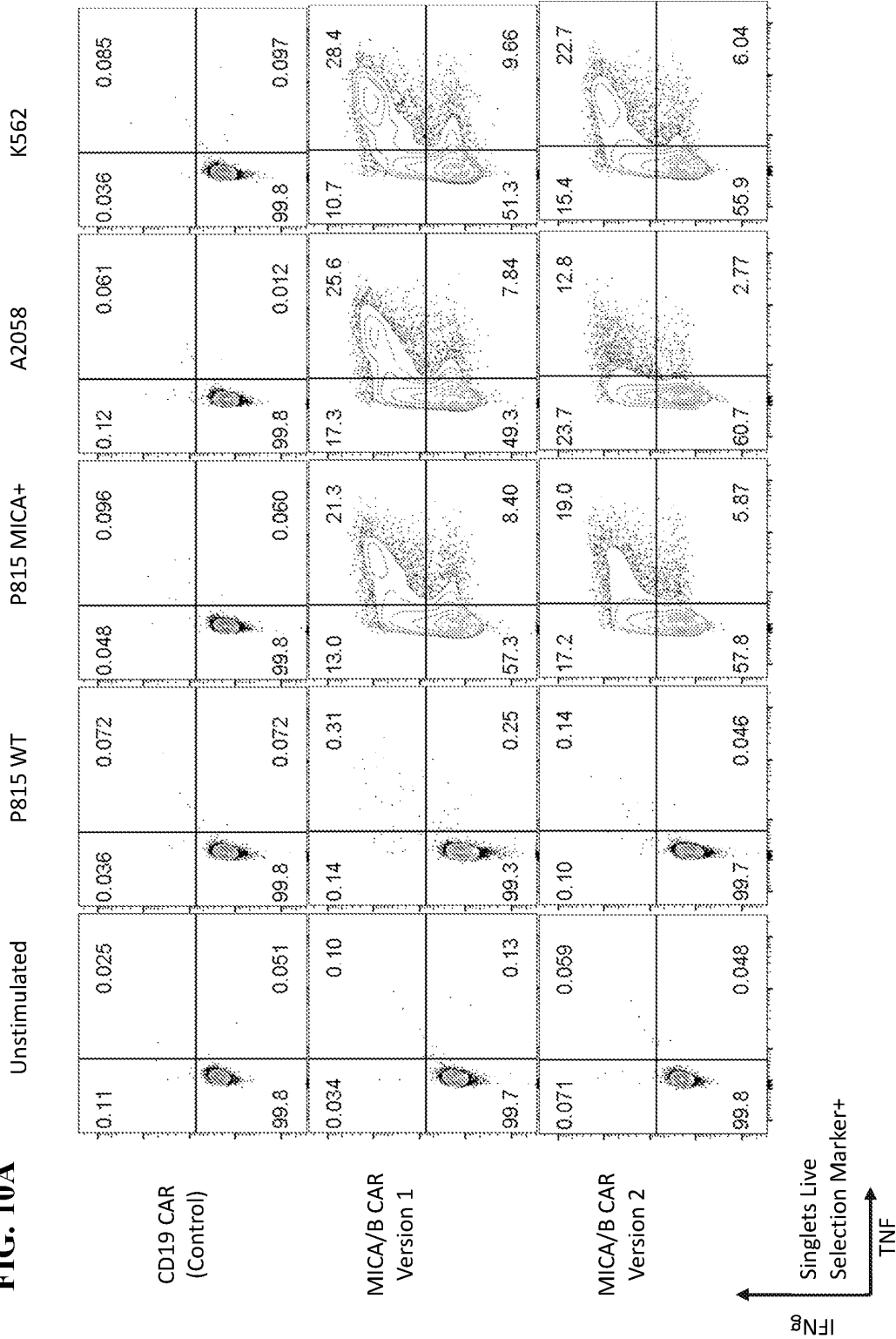


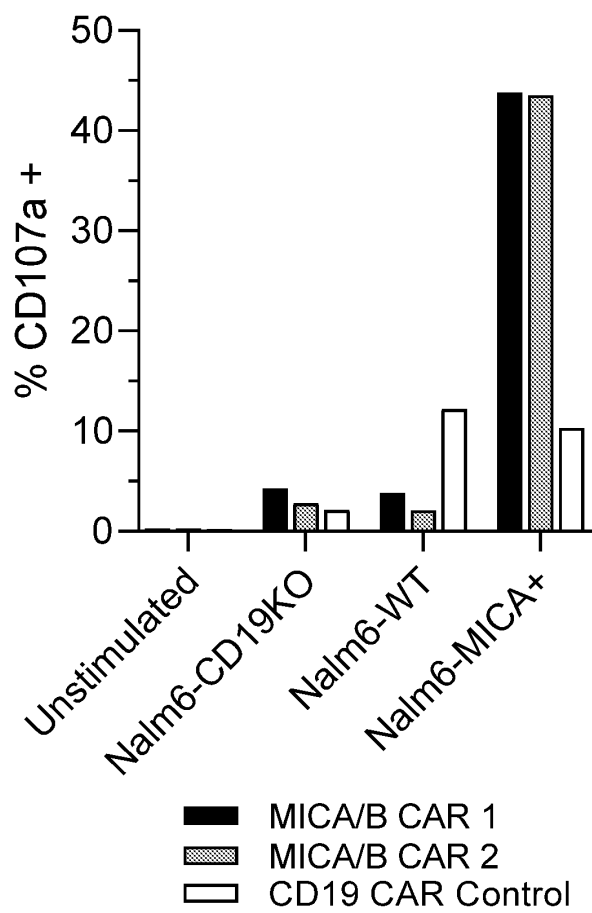
FIG. 10B

FIG. 10C

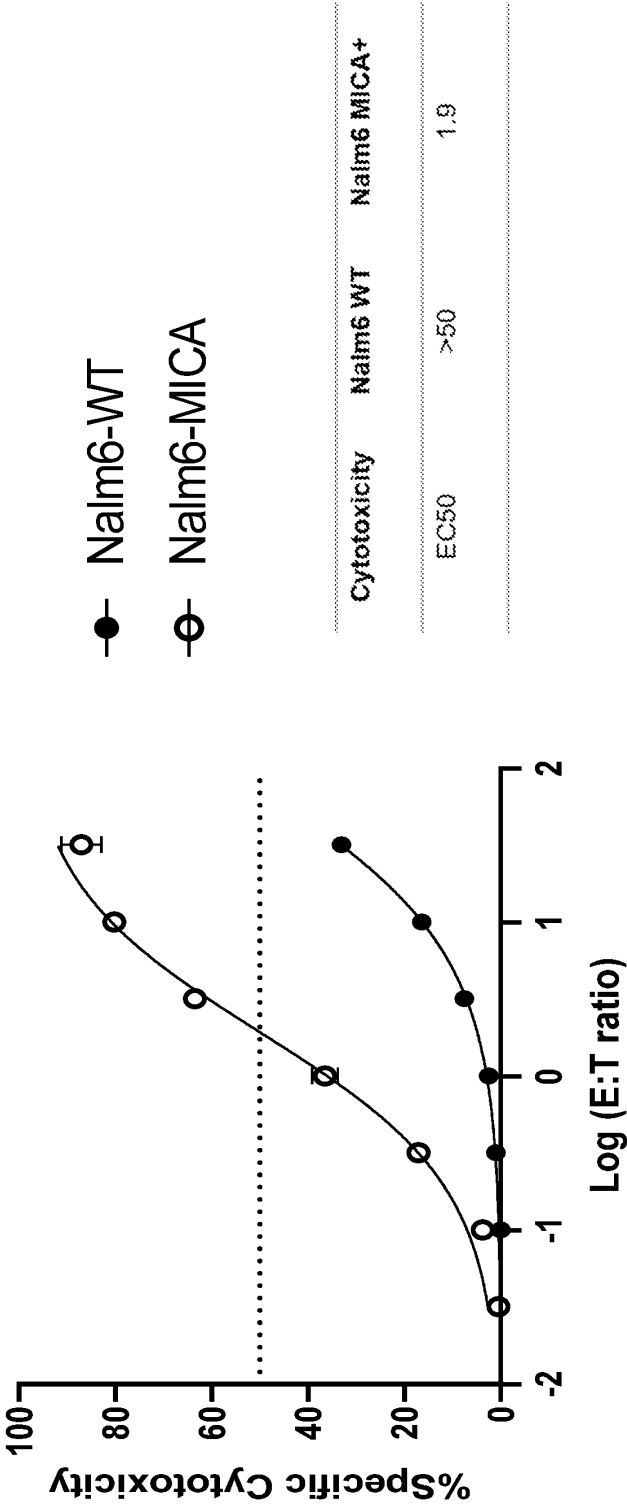


FIG. 11A

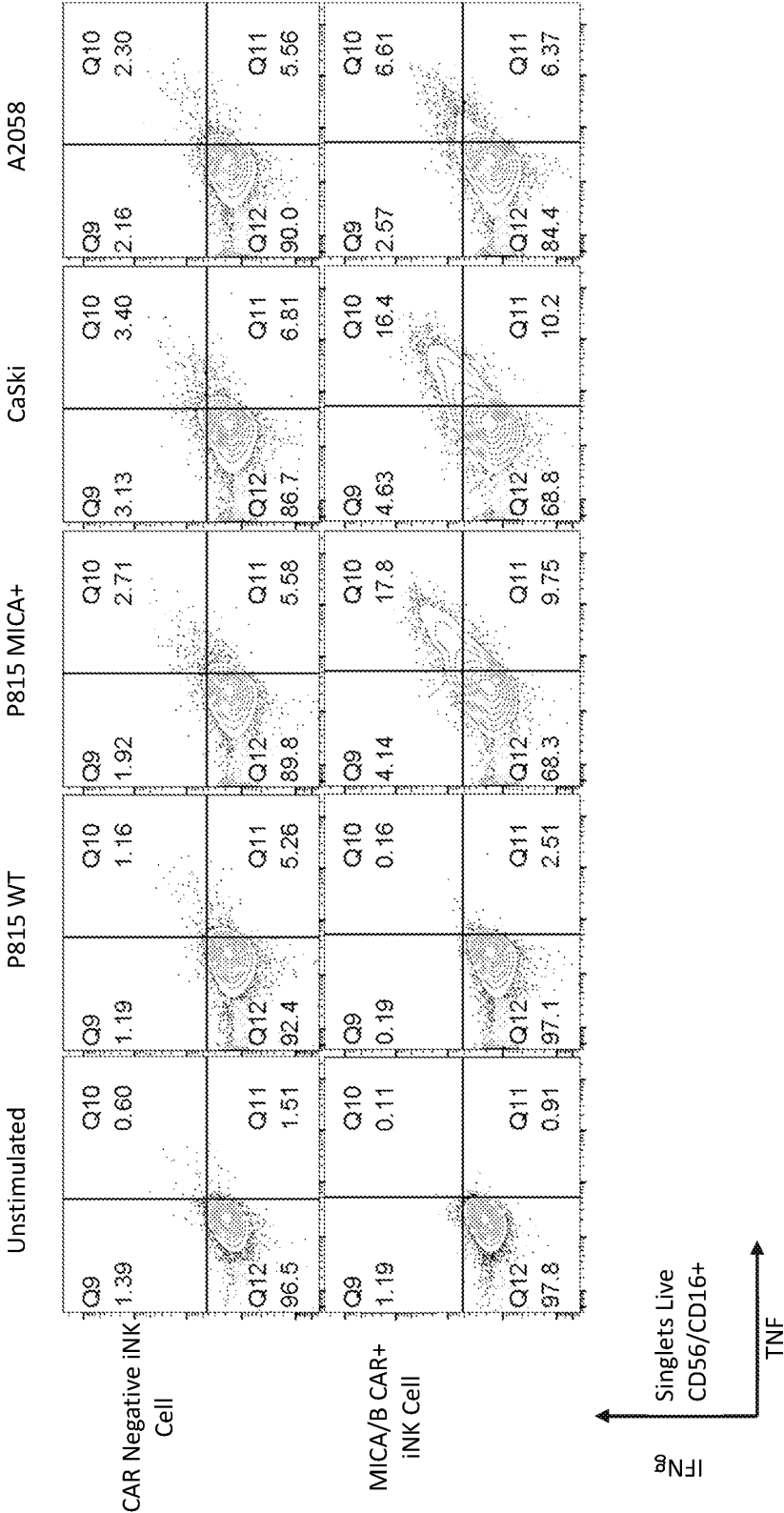


FIG. 11B

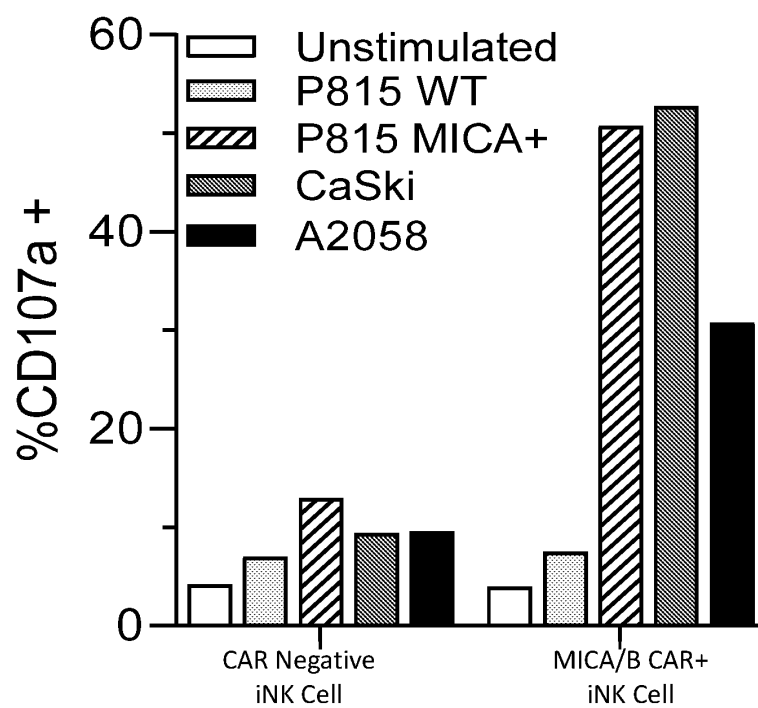
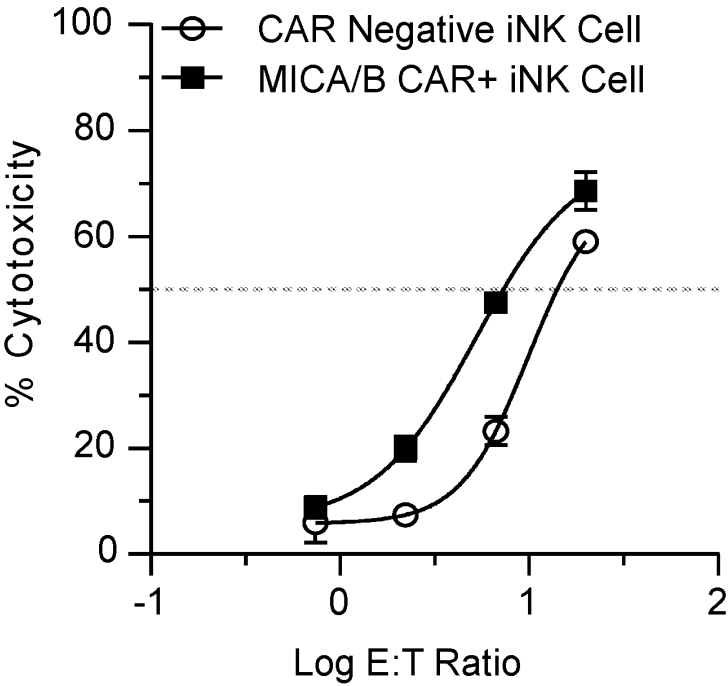


FIG. 11C



Cytotoxicity	CAR Negative iNK Cell	MICA/B CAR+ iNK Cell
EC50	9.9	5.2

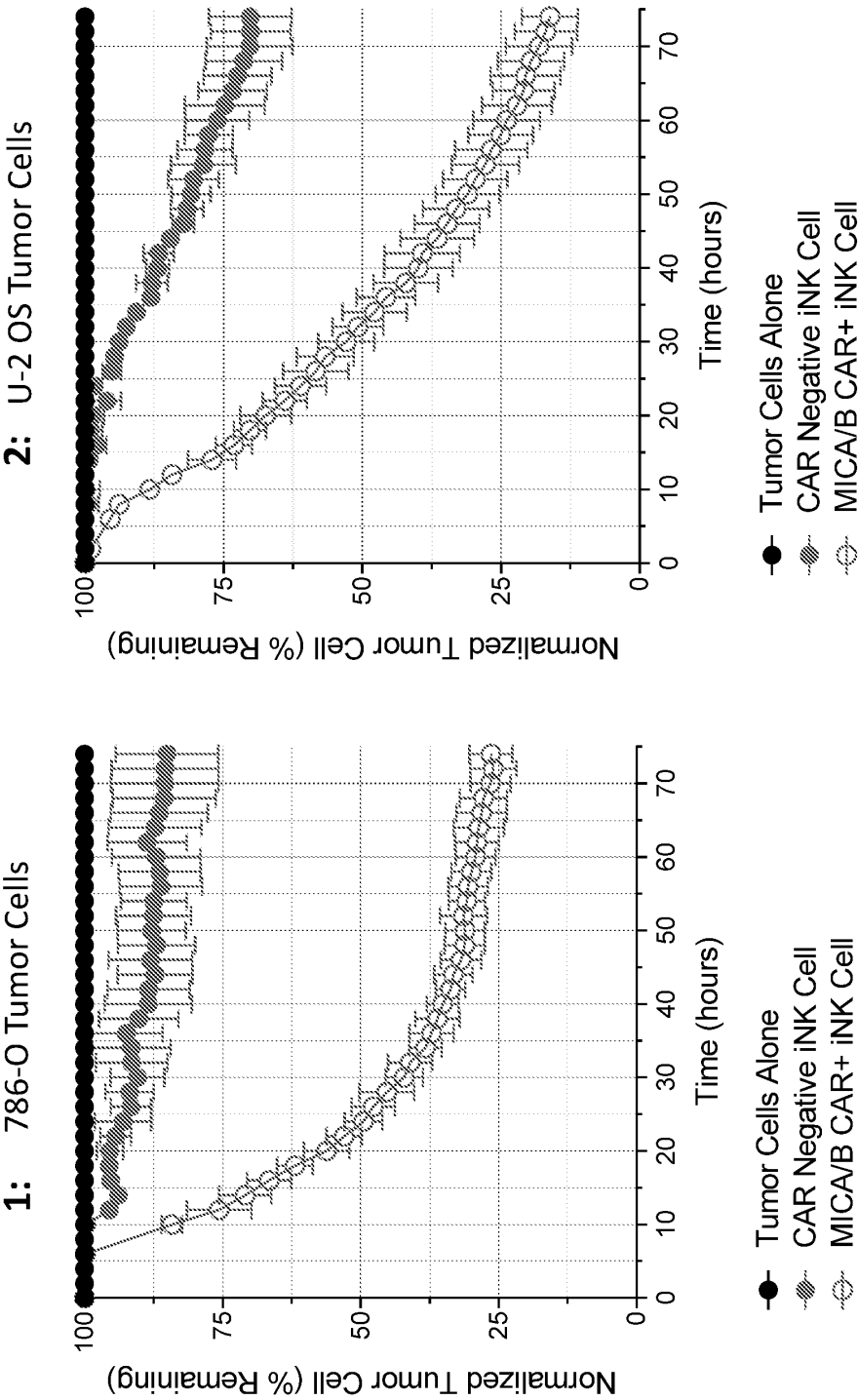


FIG. 12A

FIG. 12B

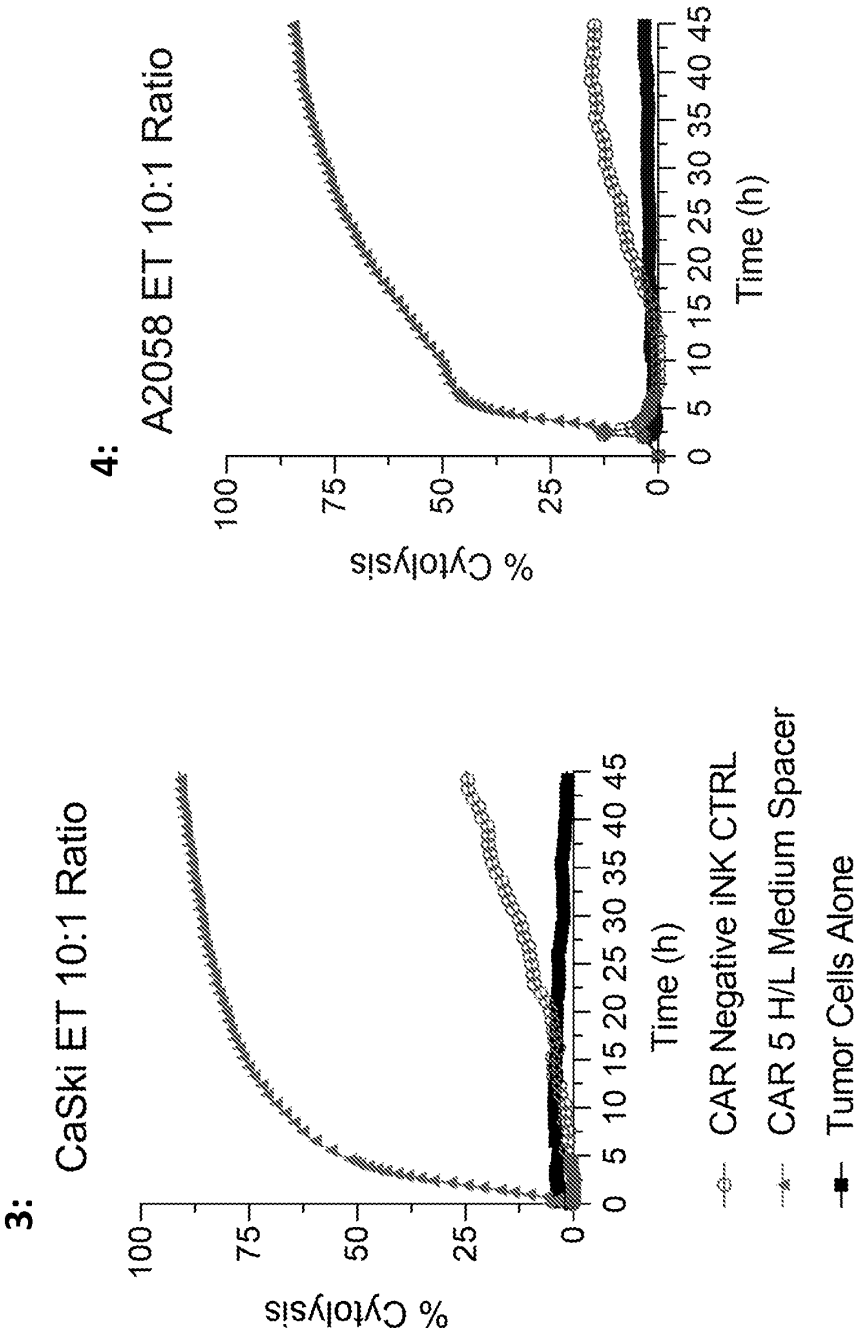


FIG. 13

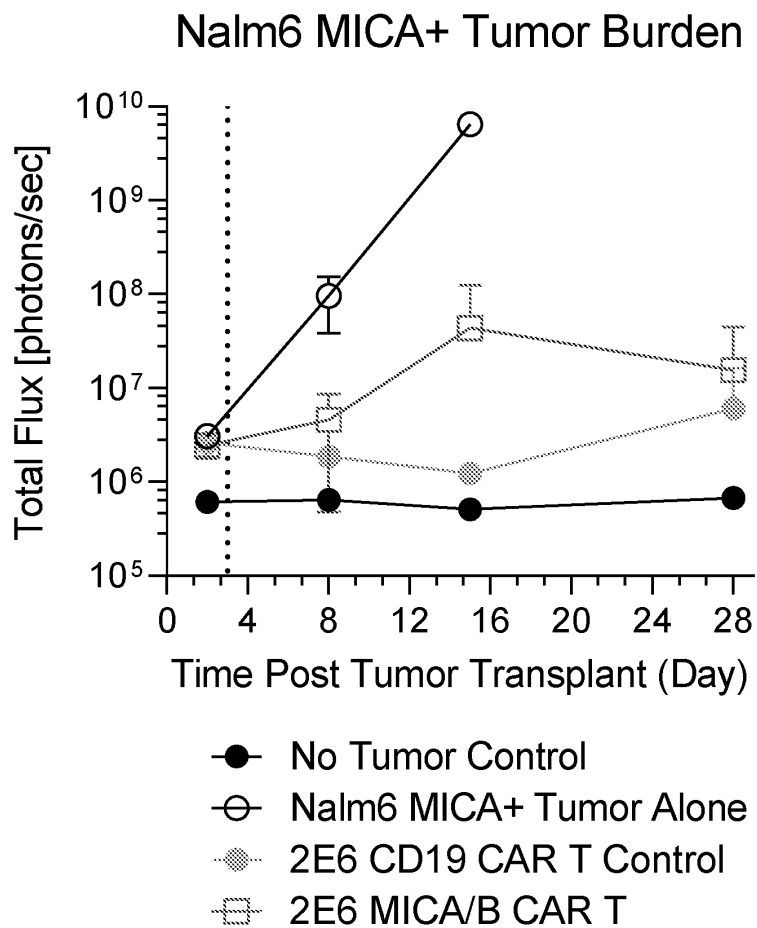


FIG. 14

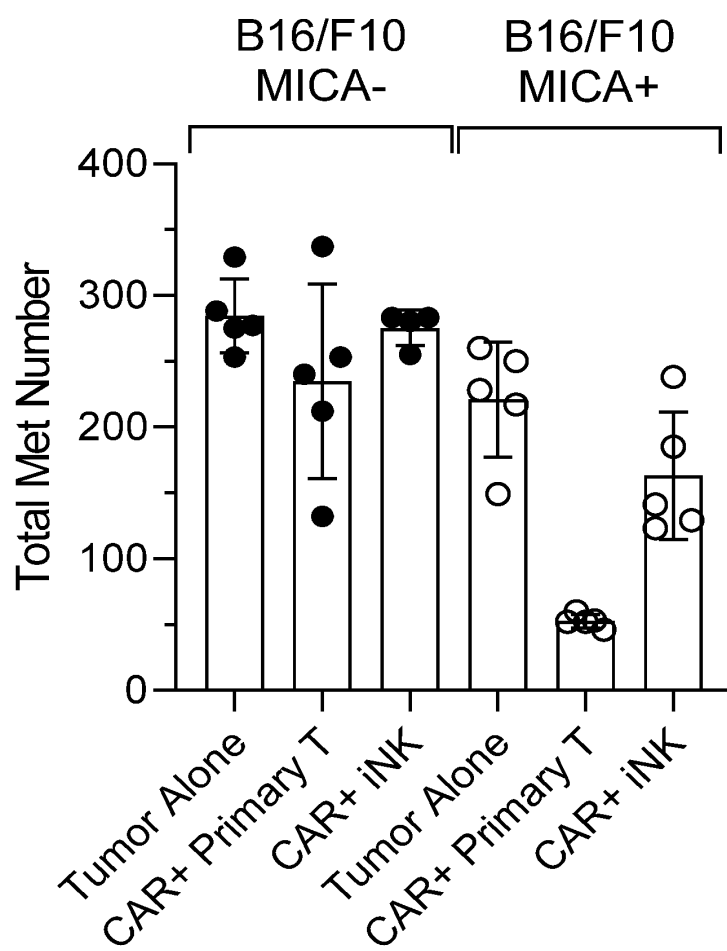


FIG. 15A

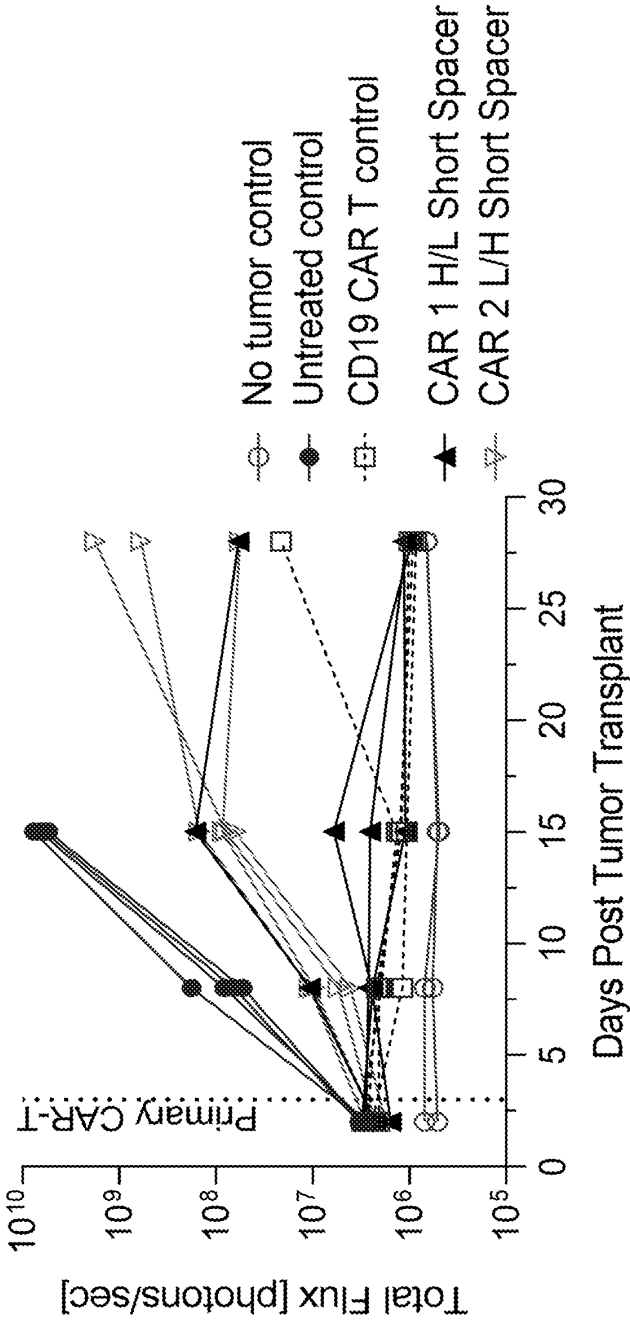


FIG. 15B

