FIGURE 1A

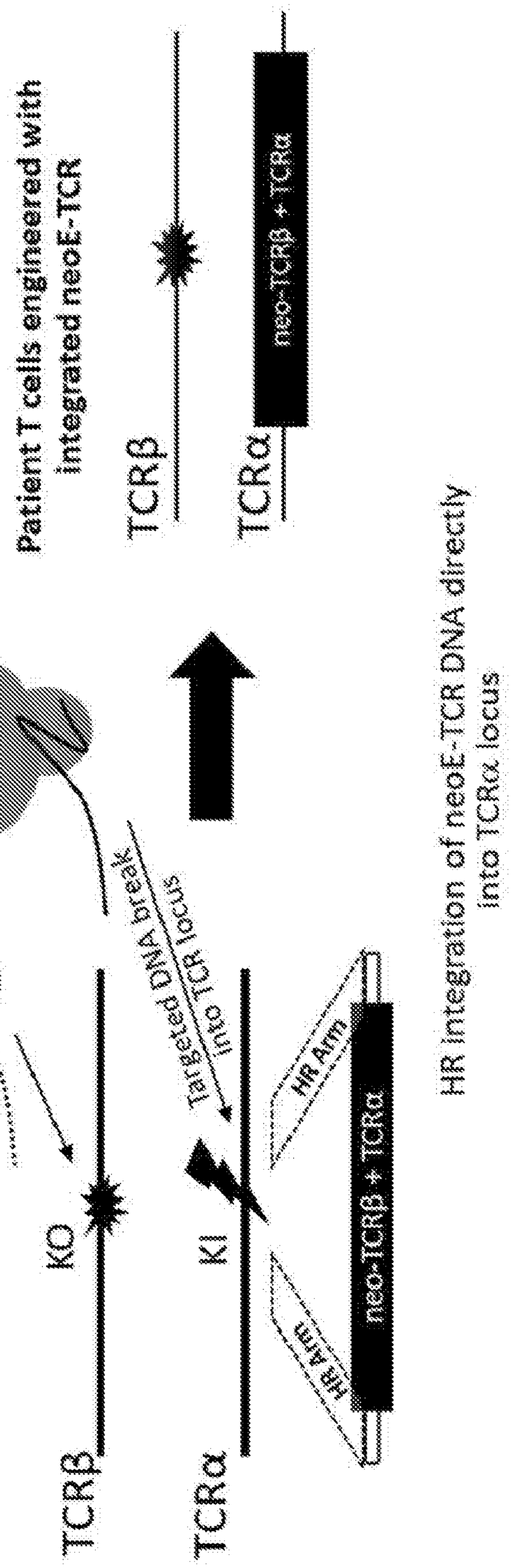

Patient T cells engineered with integrated neoE-TCR
TCRβ
TCRα
neoE-TCRβ + TCRα
RNP
KO
TCRβ
Targeted DNA break into TCRβ locus
KI
TCRα
HR Arm
HR integration of neoE-TCR DNA directly into TCRα locus
neoE-TCRβ + TCRα

FIGURE 1B

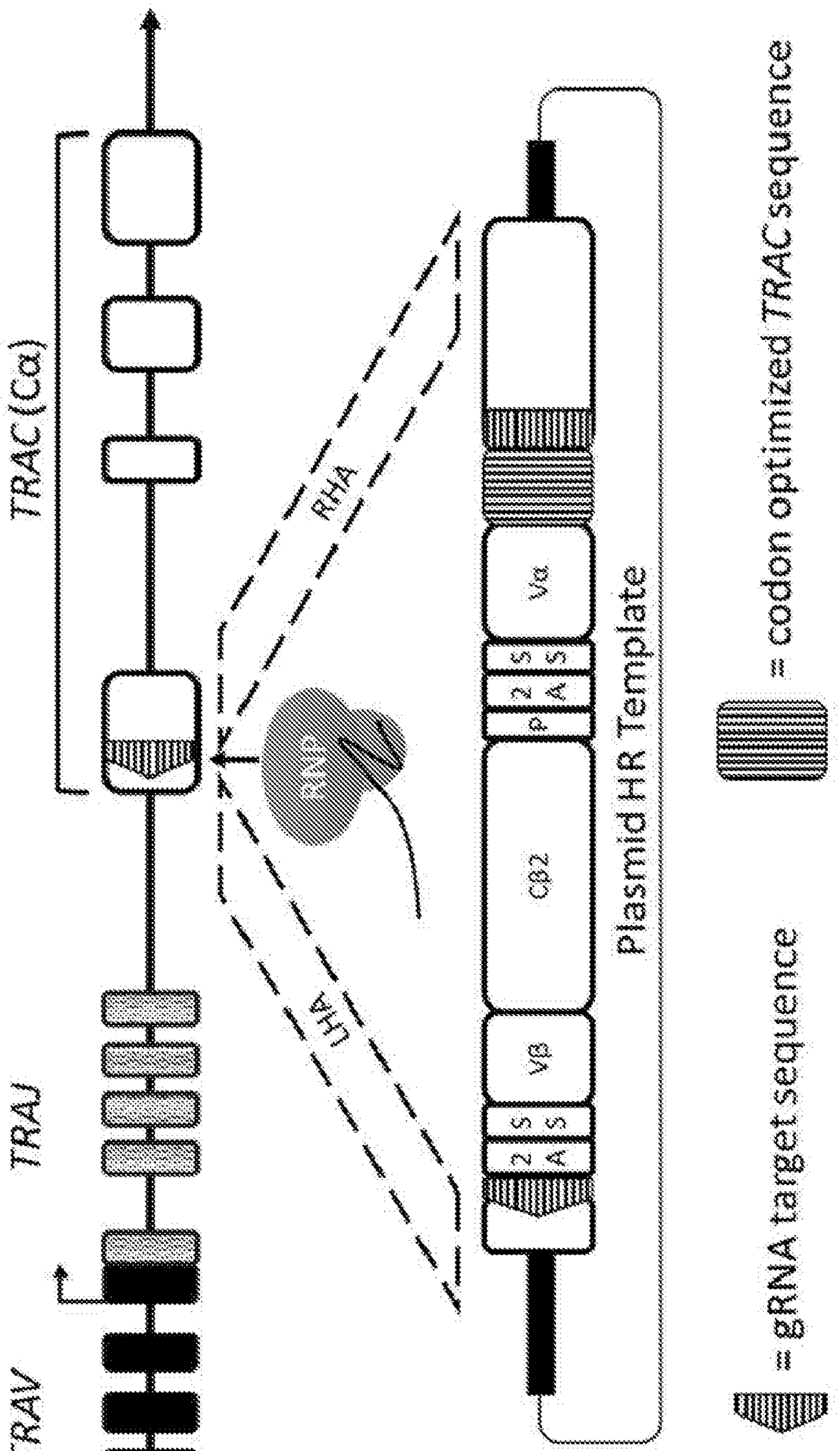

Rearranged TCRα Locus
TRAC (Cα)
TRAJ
TRAV
RHA
LHA
ELNB
Vα
Cβ2
Vβ
Plasmid HR Template
= codon optimized TRAC 4C sequence
= gRNA target sequence

FIGURE 1C

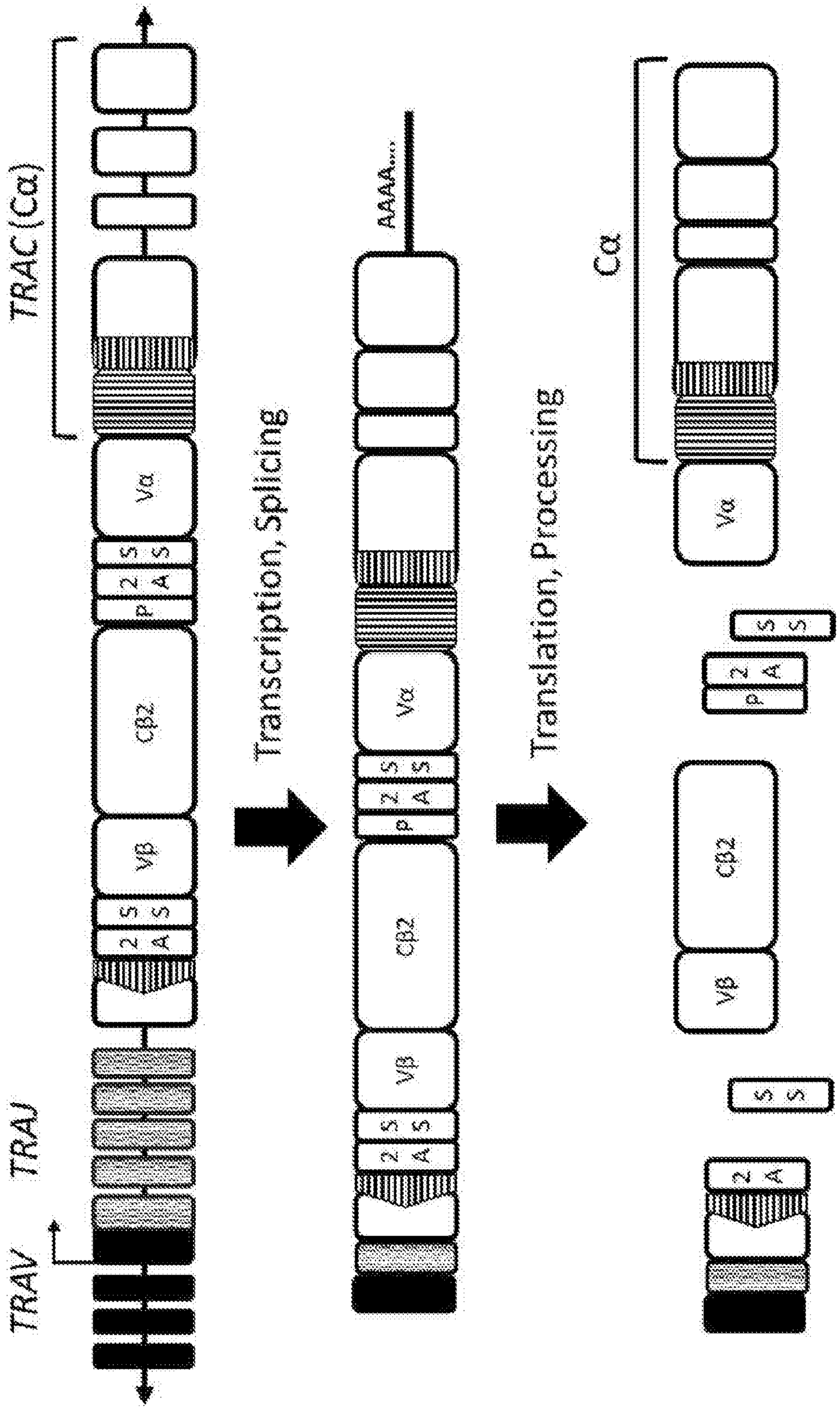

TRAV
TRAJ
TRAC (Cα)
AAAA...
Transcription, Splicing
Translation, Processing
Cα
Vα
Cβ2
Vβ
L
P
2
A
S

FIGURE 2A

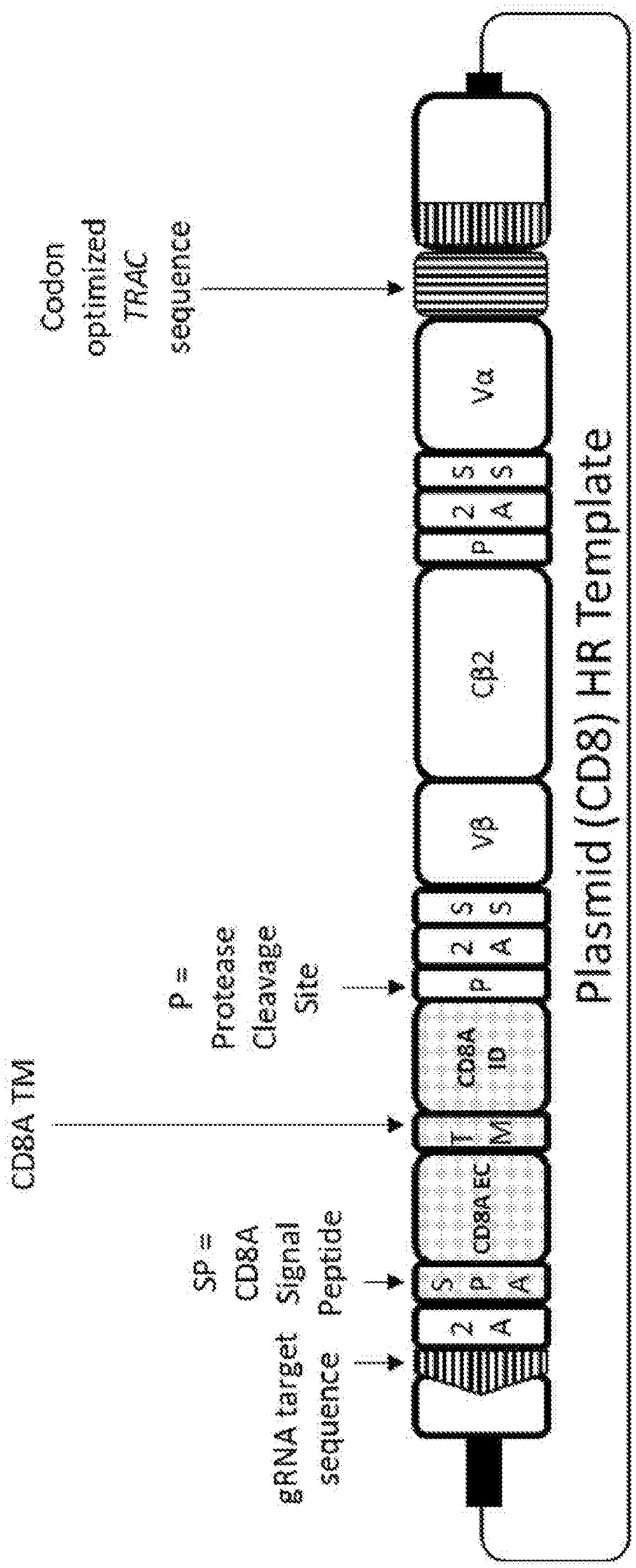
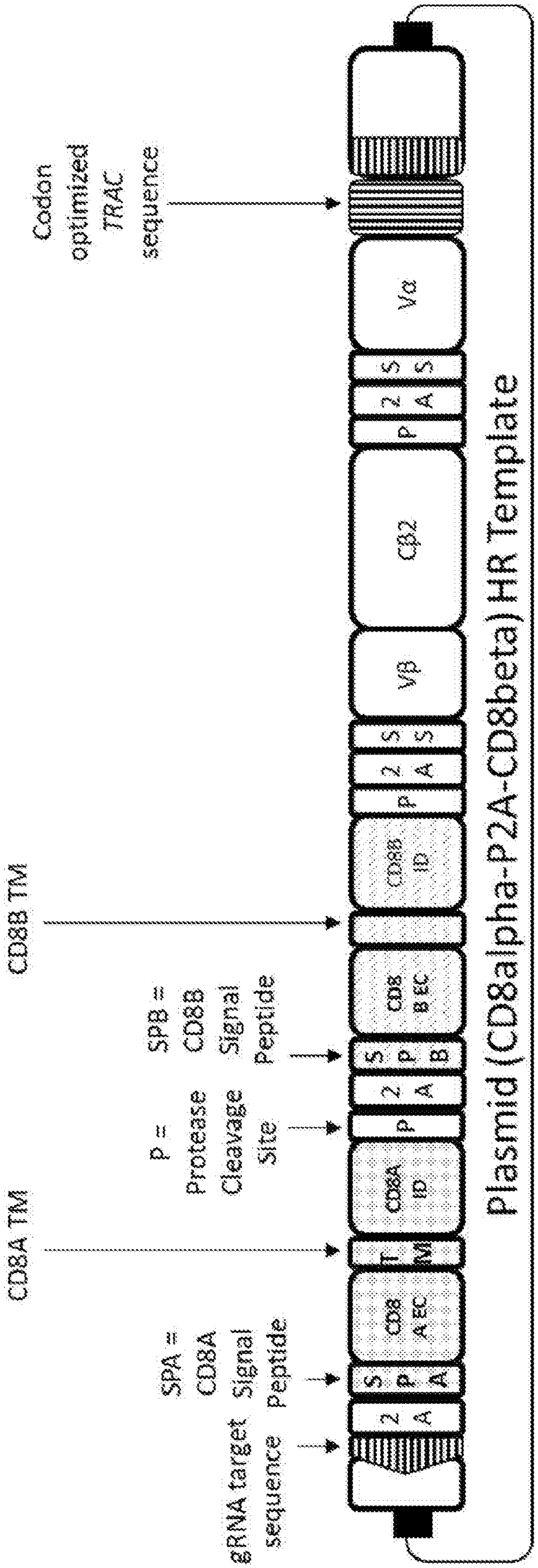

Codon optimized TRAC sequence
Plasmid (CD8) HR Template
CD8 Product 1
CD8A TM
P = Protease Cleavage Site
SP = CD8A Signal Peptide
gRNA target sequence
Vα
Vβ
Cβ2
P2A
SS
CD8A TM
CD8A EC
CD8A ID

FIGURE 2B


Codon optimized TRAC sequence
CD8B TM
CD8A TM
P = Protease Cleavage Site
SPB = CD8B Signal Peptide
SPA = CD8A Signal Peptide
gRNA target sequence
Vβ
Cβ2
P2A
Vα
CD8A ID
CD8 B EC
CD8B ID
CD8 A EC
Plasmid (CD8alpha-P2A-CD8beta) HR Template
CD8 Product 2

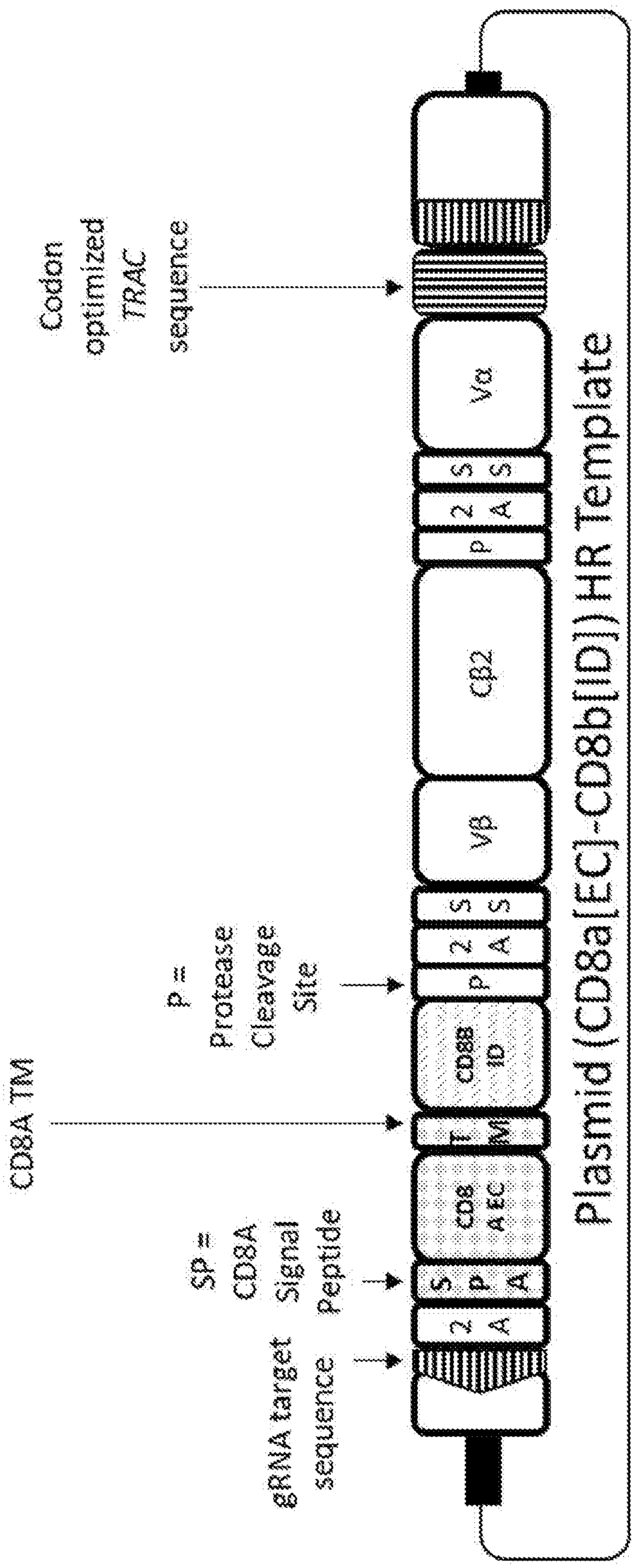

Codon optimized TRAC sequence
Va
P2A
SS
CB2
Plasmid (CD8a[EC]-CD8b[ID]) HR Template
CD8 Product 3
gRNA target sequence
SP = CD8A Signal Peptide
CD8A TM
P = Protease Cleavage Site
SS
P2A
Vb
CB2

FIGURE 2C

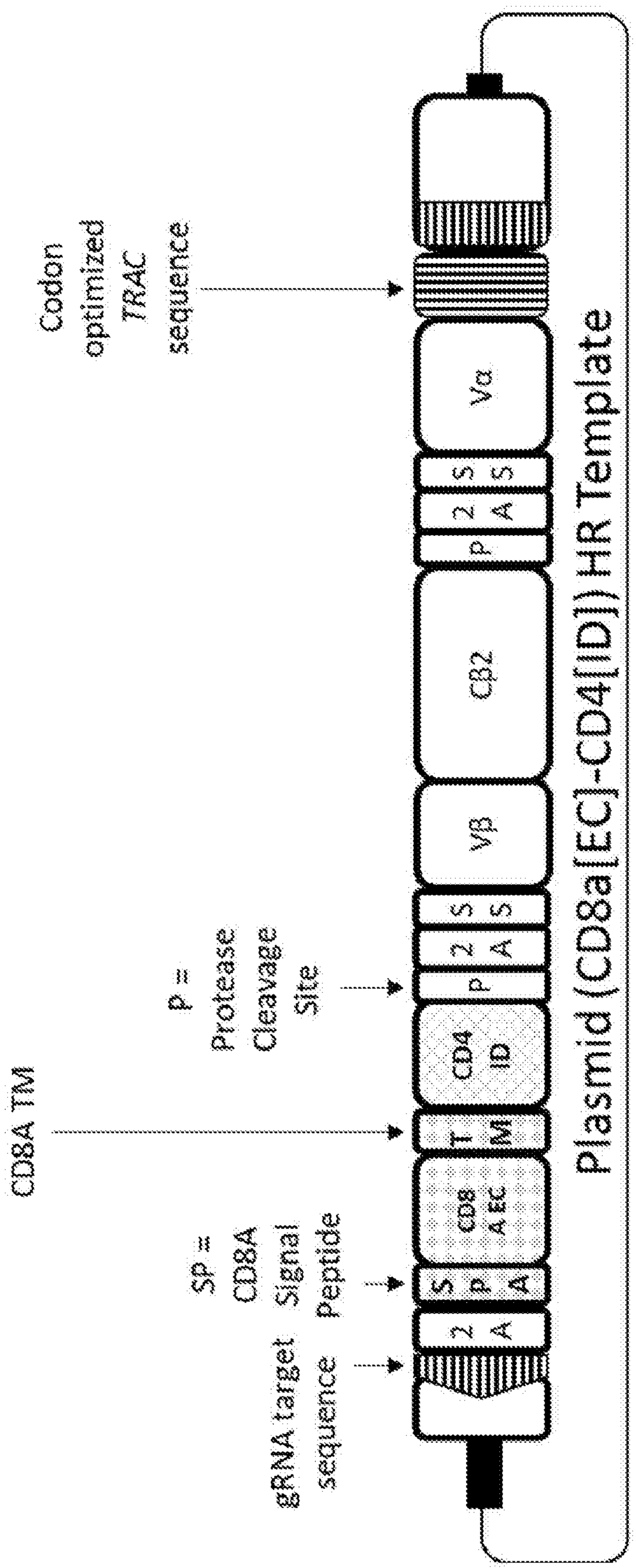

Codon optimized TRAC sequence
P = Protease Cleavage Site
CD8A TM
SP = CD8A Signal Peptide
gRNA target sequence
P
2A
SS
Vα
CD4 ID
TM
CD8 AEC
SS
P
2A
SS
Vβ
Cβ2
Plasmid (CD8a[EC]-CD4[ID]) HR Template
CD8 Product 4

FIGURE 2D

FIGURE 3A

(CD8A_CD8 Product 1)

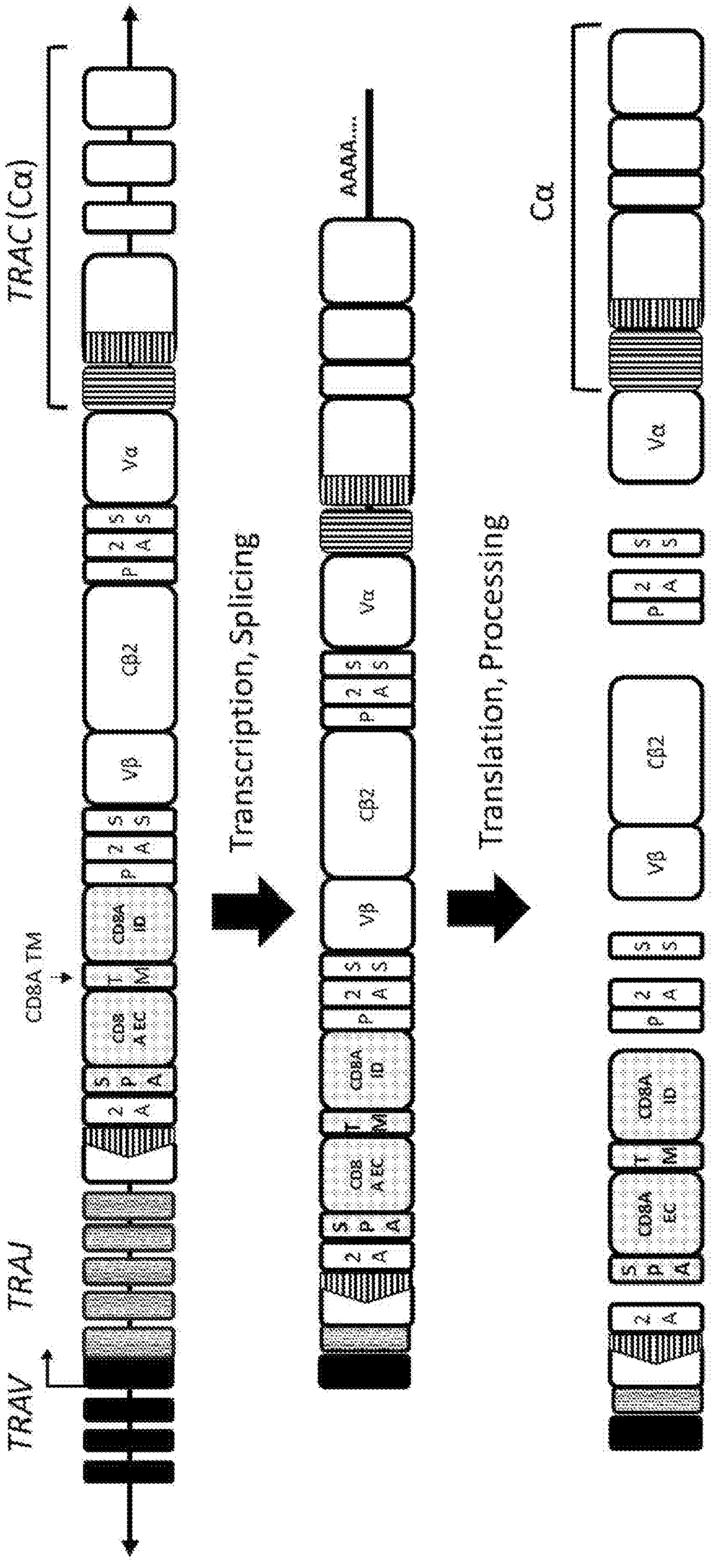


FIGURE 3B

(CD8alpha-P2A-CD8beta_CD8 Product 2)

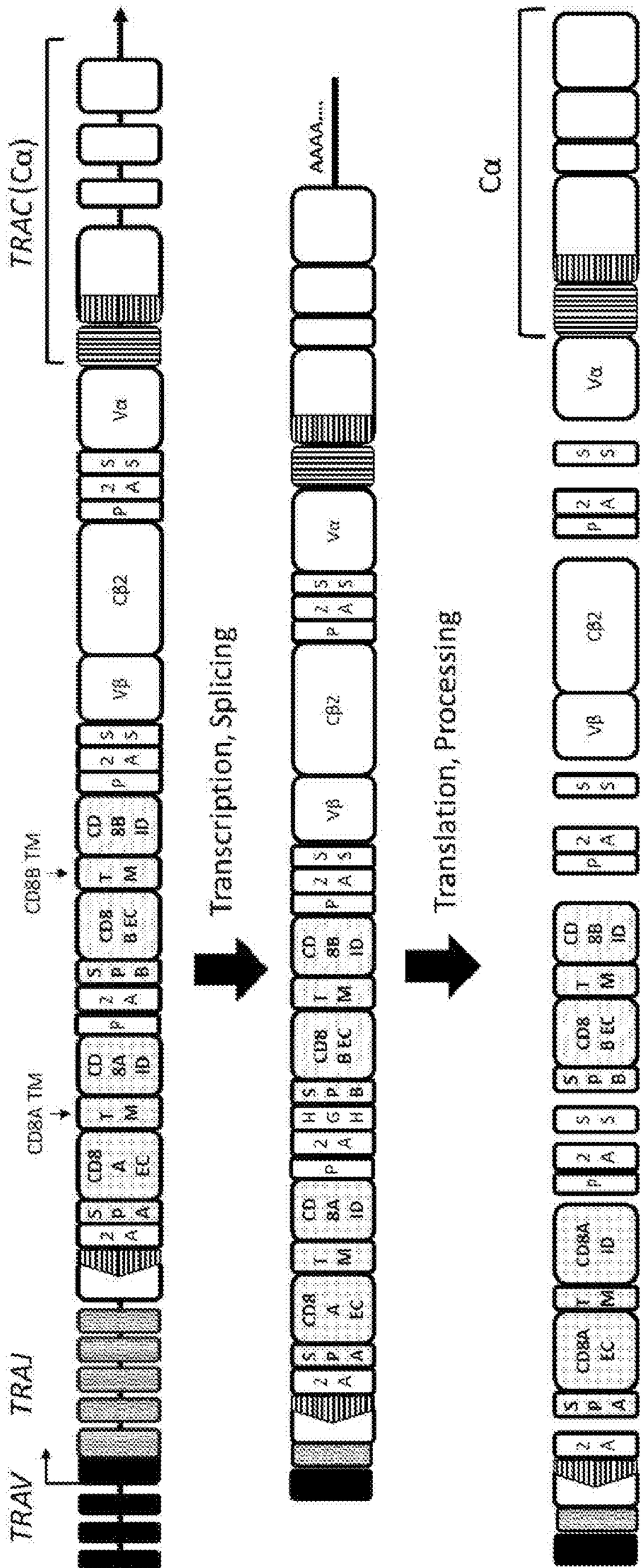


FIGURE 3C

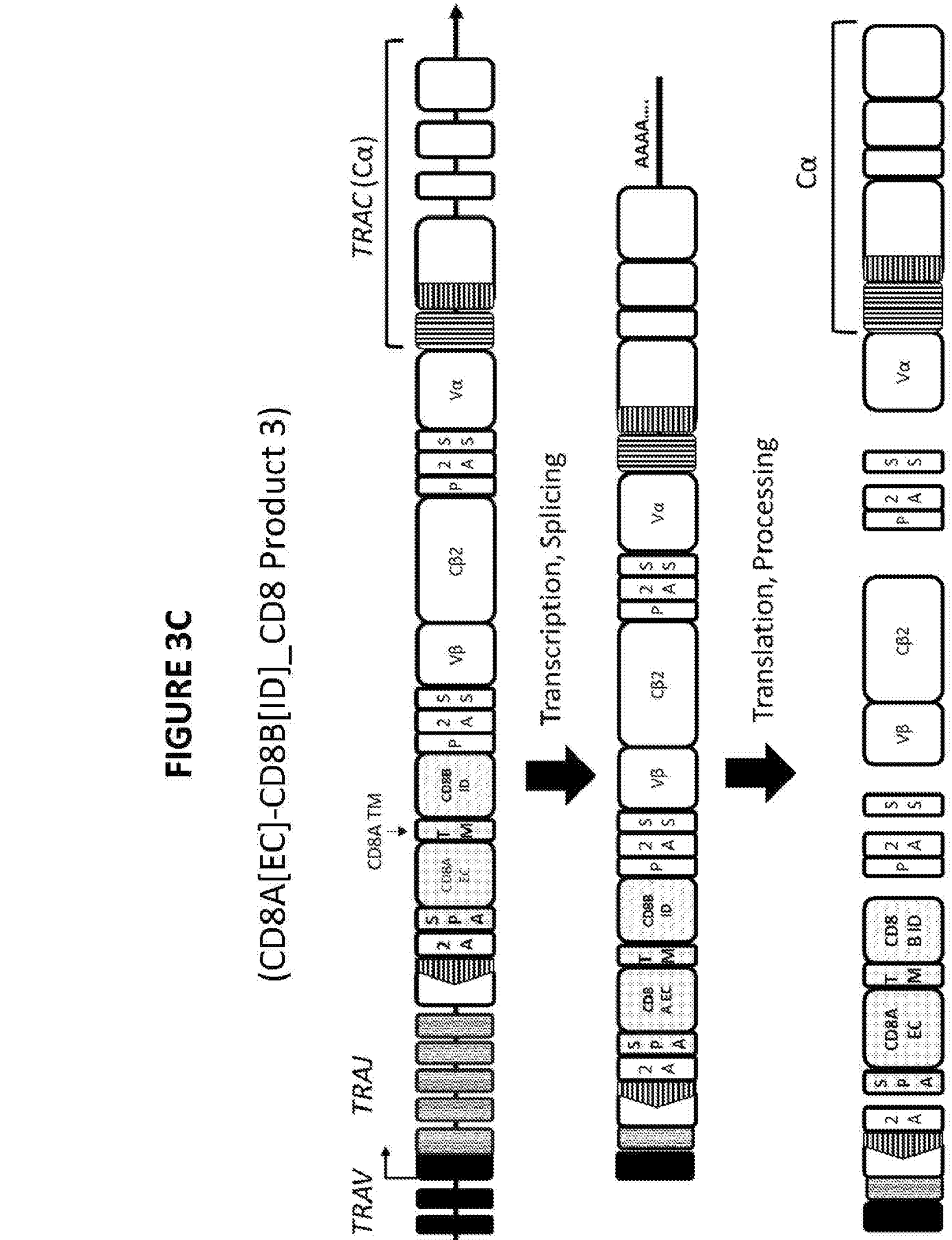

(CD8A[EC]-CD8B[ID]_CD8 Product 3)
CD8A TM
TRAV
TRAJ
Transcription, Splicing
Translation, Processing
AAAA....
Cα
Vα
Cβ2
Vβ
CD8A EC
CD8B ID
TM
T
S
P
A
2

FIGURE 3D

(CD8a[EC]-CD4[ID]_CD8 Product 4)

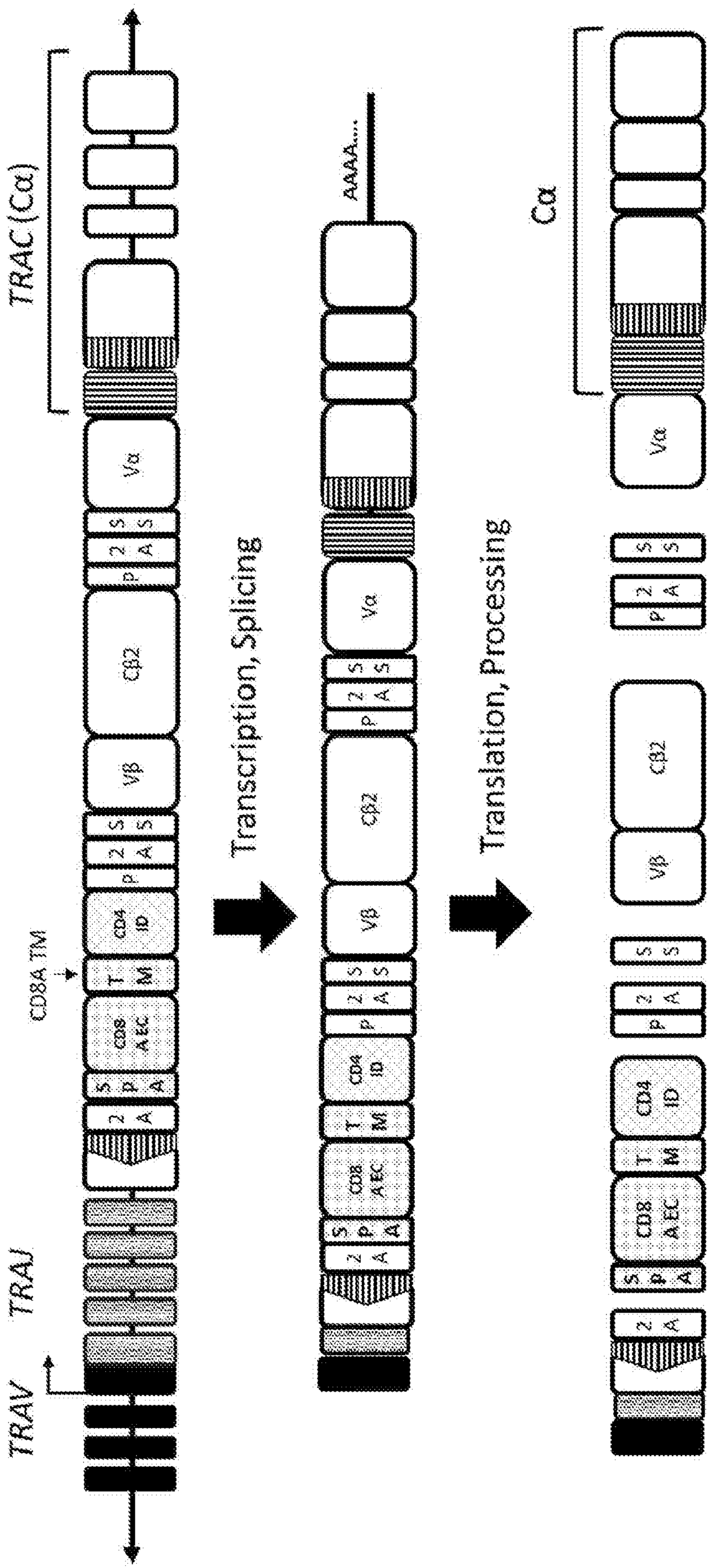


FIGURE 4A

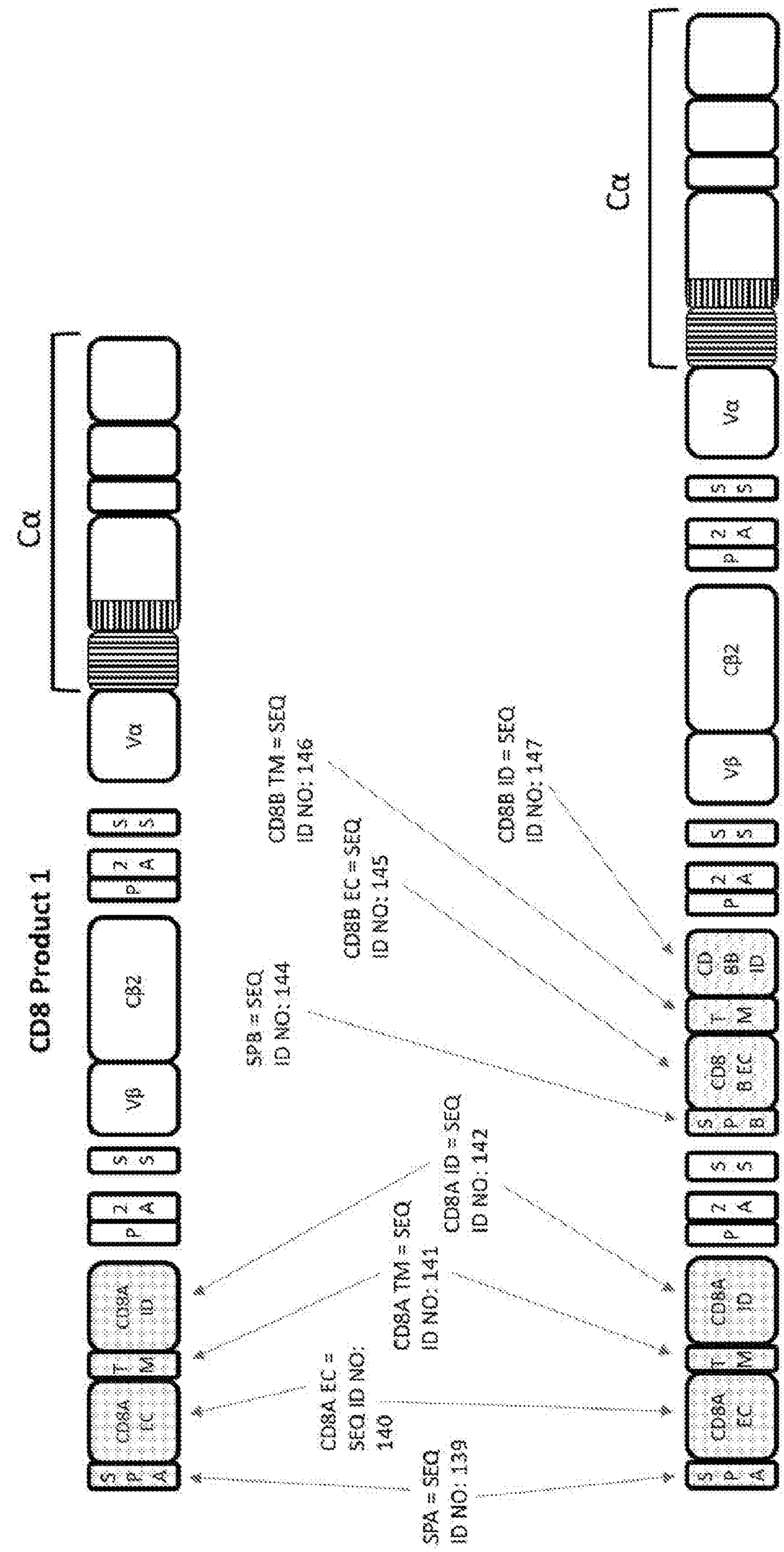

CD8 Product 1
Cα
Vβ
Cβ2
P 2 A
S S
Vα
SP8 = SEQ ID NO: 144
CD8B EC = SEQ ID NO: 145
CD8B TM = SEQ ID NO: 146
CD8B ID = SEQ ID NO: 147
SPA = SEQ ID NO: 139
CD8A EC = SEQ ID NO: 140
CD8A TM = SEQ ID NO: 141
CD8A ID = SEQ ID NO: 142
S P B
CD8 B EC
T M
CD 8B ID
CD8 A EC
CD8A ID
S P A
CD8 Product 2

FIGURE 4B

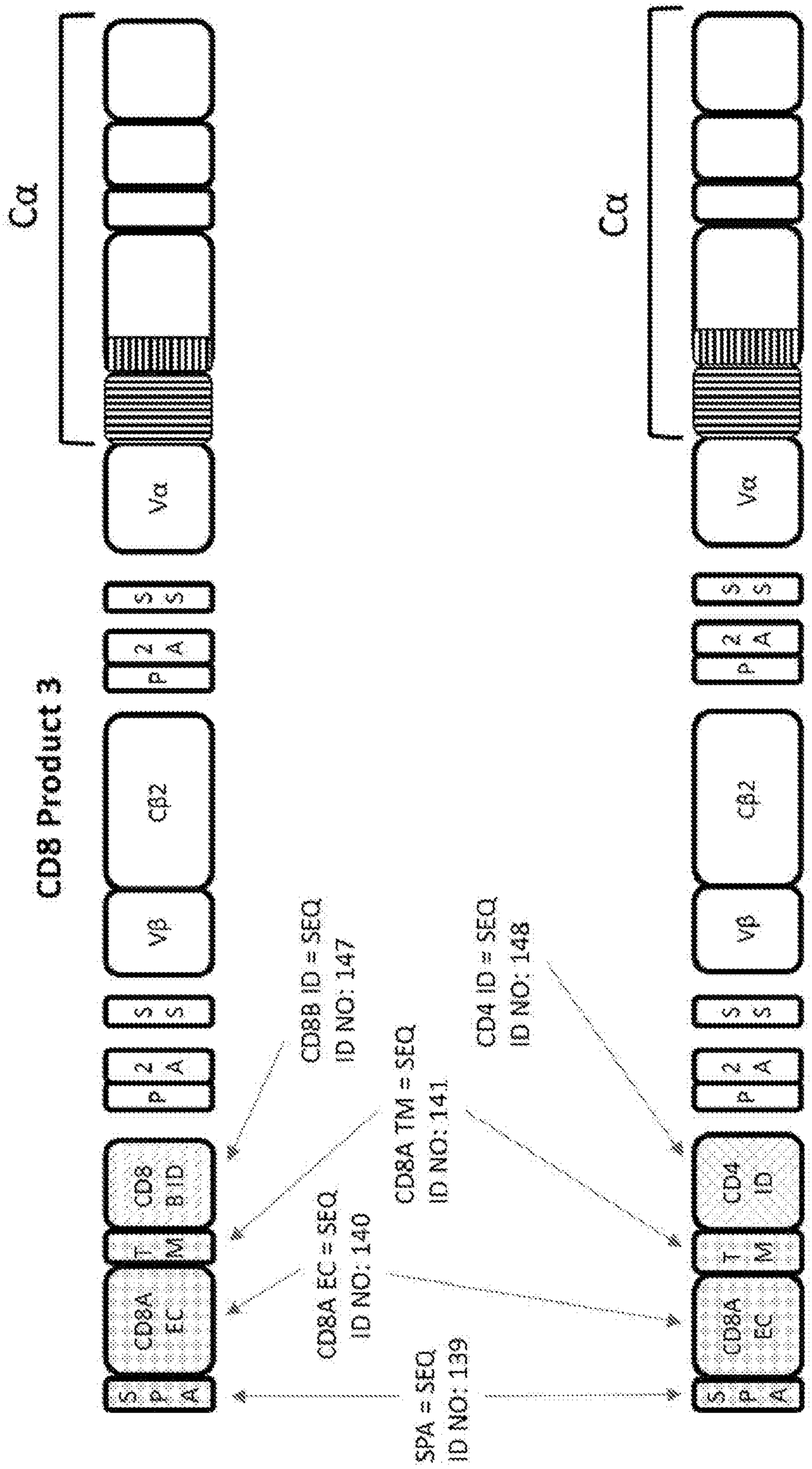

CD8 Product 3
CD8 α:ID
CD8A EC
CD8A TM
CD8A IP
CD8B ID
Vβ
Cβ2
CD8 Product 4
CD4 ID
CD4 EC
CD4 TM
CD4 IP
Vα
Cα2
SPA = SEQ ID NO: 139
CD8A EC = SEQ ID NO: 140
CD8A TM = SEQ ID NO: 141
CD8B ID = SEQ ID NO: 147
CD4 ID = SEQ ID NO: 148

FIGURE 5

NeoTCR Product Nucleic Acid Sequence

ACATTAAAAACACAAAATCCTACGGAAATACTGAAGAATGAGTCTCAGCACTAAGGAAAAGC
CTCCAGCAGCTCCTGCTTTCTGAGGGTGAAGGATAGACGCTGTGGCTCTGCATGACTCACTA
GCACTCTATCACGGCCATATTCTGGCAGGGTCAGTGGCTCCAACTAACATTTGTTTGGTACTT
TACAGTTTATTAAATAGATGTTTATATGGAGAAGCTCTCATTTCTTTCTCAGAAGAGCCTGGCT
AGGAAGGTGGATGAGGCACCATATTCATTTTGCAGGTGAAATTCCTGAGATGTAAGGAGCT
GCTGTGACTTGCTCAAGGCCTTATATCGAGTAAACGGTAGTGCTGGGGCTTAGACGCAGGTG
TTCTGATTTATAGTTCAAAACCTCTATCAATGAGAGAGCAATCTCCTGGTAATGTGATAGATTT
CCCAACTTAATGCCAACATACCATAAACCTCCCATTCTGCTAATGCCCAGCCTAAGTTGGGGA
GACCACTCCAGATTCCAAGATGTACAGTTTGCTTTGCTGGGCCTTTTTCCCATGCCTGCCTTTA
CTCTGCCAGAGTTATATTGCTGGGGTTTTGAAGAAGATCCTATTAAATAAAAGAATAAGCAGT
ATTATTAAGTAGCCCTGCATTTCAGGTTTCCTTGAGTGGCAGGCCAGGCCTGGCCGTGAACG
TTCACTGAAATCATGGCCTCTTGGCCAAGATTGATAGCTTGTGCCTGTCCCTGAGTCCCAGTC
CATCACGAGCAGCTGGTTTCTAAGATGCTATTTCCCGTATAAAGCATGAGACCGTGACTTGCC
AGCCCCACAGAGCCCCGCCCTTGTCCATCACTGGCATCTGGACTCCAGCCTGGGTTGGGGCA
AAGAGGGAAATGAGATCATGTCCTAACCCTGATCCTCTTGTCCCACAG

Left HR Arm (SEQ ID NO:1)

ATATCCAGAACCCTGACCCTGCCGTGTACCAGCTGAGAGACTCTAAATCCAGTG
ACAAGTCTGTCTGCCTATTC

TRAC CDS (SEQ ID NO:2)

GAATTCGGCTCCGGA

GSG Linker 1 (SEQ ID NO:3)

GCCACTAACTTCTCCCTGTTGAAACAGGCTGGCGATGTTGAAGAAAACCCCGG
TCCT

P2A (SEQ ID NO:4)

FIGURE 5 Cont.

ATGGCCACCGGCTCTAGAACAAGCCTGCTGCTCGCTTTTGGCCTGCTCTGCCTCCCATGGCTC
CAAGAAGGATCTGCT

HGH/SS/2 (SEQ ID NO:5)

[[TRB_VDJ Sequence, specific for the NeoTCR]]

Insertion site for neoTCR TRB_VDJ sequence

CTGAAAAACGTGTTCCCTCCAAAAGTGGCCGTGTTCGAGCCTTCTGAGGCCGAGATCAGCC
ACACACAGAAAGCCACACTCGTGTGTCTGGCTACCGGCTTCTACCCCGATCACGTGGAACTG
TCTTGGTGGGTCAACGGCAAAGAGGTGCACAGCGGCGTCAGCACAGATCCCCAGCCTCTGA
AAGAACAGCCCGCTCTGAACGACAGCCGCTACTGCCTGTCTAGCAGACTGAGAGTGTCCGC
CACCTTCTGGCAGAACCCCAGAAACCACTTCAGATGCCAGGTCCAGTTCTACGGCCTGAGCG
AGAACGATGAGTGGACCCAGGACAGAGCCAAGCCTGTGACACAGATCGTGTCTGCCGAAG
CCTGGGGCAGAGCCGATTGTGGCTTTACCAGCGAGTCATACCAGCAGGGCGTGCTGTCTGC
CACCATCCTGTATGAGATCCTGCTCGGCAAGGCCACACTGTACGCTGTGCTGGTGTCTGCTCT
GGTGCTGATGGCTATGGTCTCCCGGGAGCGCATCCCCGAGGCC

TCR-beta/constant (SEQ ID NO:7)

CGGGCCAAGCGG

Furin Cleavage Site (SEQ ID NO: 8)

GGCAGCGGC

GSG Linker (SEQ ID NO:9)

GCCACCAACTTCAGCCTGCTGAAGCAGGCCGGCGACGTGGAGGAGAACCCCGGCCCT

P2A (SEQ ID NO:10)

ATGGCCACAGGCAGCAGAACATCTCTGCTGCTGGCCTTCGGACTGCTGTGTCTGCCTTGGCT
GCAAGAGGGTTCCGCC

HGH SS (SEQ ID NO:11)

FIGURE 5 Cont.

[[TRA_VDJ Sequence, specific for the NeoTCR]]

Insertion site for neoTCR TRA_VDJ sequence

ATATTCAGAACCCCGATCCTGCTGTGTATCAGCTGCGCGACAGCAAGAGCAGCGACAAGAGC
GTGTGTTTGTTC

TCR-alpha/constant (SEQ ID NO:13)

ACCGATTTTGATTCTCAAACAAATGTGTCACAAAGTAAGGATTCTGATGTGTATATCACAGAC
AAAACTGTGCTAGACATGAGGTCTATGGACTTCAAGAGCAACAGTGCTGTGGCCTGGAGCA
ACAAATCTGACTTTGCATGTGCAAACGCCTTCAACAACAGCATTATTCCAGAAGACACCTTCT
TCCCCAGCCCAGG

TRAC CDS/right HR arm(SEQ ID NO: 14)

TAAGGGCAGCTTTGGTGCCTTCGCAGGCTGTTTCCTTGCTTCAGGAATGGCCAGGTTCTGCC
CAGAGCTCTGGTCAATGATGTCTAAAACTCCTCTGATTGGTGGTCTCGGCCTTATCCATTGCC
ACCAAAACCCTCTTTTTACTAAGAAACAGTGAGCCTTGTTCTGGCAGTCCAGAGAATGACAC
GGGAAAAAAGCAGATGAAGAGAAGGTGGCAGGAGAGGGCACGTGGCCCAGCCTCAGTCT
CTCCAACTGAGTTCCTGCCTGCCTGCCTTTGCTCAGACTGTTTGCCCCTTACTGCTCTTCTAGG
CCTCATTCTAAGCCCCTTCTCCAAGTTGCCTCTCCTTATTTCTCCCTGTCTGCCAAAAAATCTTT
CCCAGCTCACTAAGTCAGTCTCACGCAGTCACTCATTAACCCACCAATCACTGATTGTGCCGG
CACATGAATGCACCAGGTGTTGAAGTGGAGGAATTAAAAAGTCAGATGAGGGGTGTGCCCA
GAGGAAGCACCATTCTAGTTGGGGGAGCCCATCTGTCAGCTGGGAAAAGTCCAAATAACTT
CAGATTGGAATGTGTTTTAACTCAGGGTTGAGAAAACAGCTACCTTCAGGACAAAAGTCAG
GGAAGGGCTCTCTGAAGAAATGCTACTTGAAGATACCAGCCCTACCAAGGGCAGGGAGAG
GACCCTATAGAGGCCTGGGACAGGAGCTCAATGAGAAAGGAGAAGAGCAGCAGGCATGA
GTTGAATGAAGGAGGCAGGGCCGGGTCACAGGGCCTTCTAGGCCATGAGAGGGTAGACAG

Right HR arm (SEQ ID NO:15)

GCTAGC

(SEQ ID NO:16)

FIGURE 5 Cont.

CGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCT
CAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAG
CTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCT
TCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTT
CGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGG
TAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTG
GTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCC
TAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTT
CGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTT
TTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAGGATCTCAAGAAGATCCTTTGATCT
TTAGAAAAACTCATCGAGCATCAAATGAAACTGCAATTTATTCATATCAGGATTATCAATACCA
TATTTTTGAAAAAGCCGTTTCTGTAATGAAGGAGAAAACTCACCGAGGCAGTTCCATAGGAT
GGCAAGATCCTGGTATCGGTCTGCGATTCCGACTCGTCCAACATCAATACAACCTATTAATTTC
CCCTCGTCAAAAATAAGGTTATCAAGTGAGAAATCACCATGAGTGACGACTGAATCCGGTGA
GAATGGCAAAAGTTTATGCATTTCTTTCCAGACTTGTTCAACAGGCCAGCCATTACGCTCGTC
ATCAAAATCACTCGCATCAACCAAACCGTTATTCATTCGTGATTGCGCCTGAGCCAGACGAAA
TACGCGATCGCTGTTAAAAGGACAATTACAAACAGGAATCGAATGCAACCGGCGCAGGAAC
ACTGCCAGCGCATCAACAATATTTTCACCTGAATCAGGATATTCTTCTAATACCTGGAATGCTG
TTTTTCCGGGGATCGCAGTGGTGAGTAACCATGCATCATCAGGAGTACGGATAAAATGCTTG
ATGGTCGGAAGAGGCATAAATTCCGTCAGCCAGTTTAGTCTGACCATCTCATCTGTAACATCA
TTGGCAACGCTACCTTTGCCATGTTTCAGAAACAACTCTGGCGCATCGGGCTTCCCATACAAG
CGATAGATTGTCGCACCTGATTGCCCGACATTATCGCGAGCCCATTTATACCCATATAAATCAG
CATCCATGTTGGAATTTAATCGCGGCCTCGACGTTTCCCGTTGAATATGGCTCAT

AACACCCCTTGTATTACTGTTTATGTAAGCAGACAGTTTTATTGTTCATGATGATATATTTTTATC
TTGTGCAATGTAACATCAGAGATTTTGAGACAC

pBR322_origin (SEQ ID NO:17)

Kanamycin resistant gene (KanR2) (SEQ ID NO:18)

Kanamycin Promoter (SEQ ID NO:19)

FIGURE 6

CD8 Product 1 Product Nucleic Acid Sequence

ACATTAAAAACACAAAATCCTACGGAAATACTGAAGAATGAGTCTCAGCACTAAGGAAAAGC
CTCCAGCAGCTCCTGCTTTCTGAGGGTGAAGGATAGACGCTGTGGCTCTGCATGACTCACTA
GCACTCTATCACGGCCATATTCTGGCAGGGTCAGTGGCTCCAACTAACATTTGTTTGGTACTT
TACAGTTTATTAAATAGATGTTTATATGGAGAAGCTCTCATTTCTTTCTCAGAAGAGCCTGGCT
AGGAAGGTGGATGAGGCACCATATTCATTTTGCAGGTGAAATTCCTGAGATGTAAGGAGCT
GCTGTGACTTGCTCAAGGCCTTATATCGAGTAAACGGTAGTGCTGGGGCTTAGACGCAGGTG
TTCTGATTTATAGTTCAAAACCTCTATCAATGAGAGAGCAATCTCCTGGTAATGTGATAGATTT
CCCAACTTAATGCCAACATACCATAAACCTCCCATTCTGCTAATGCCCAGCCTAAGTTGGGGA
GACCACTCCAGATTCCAAGATGTACAGTTTGCTTTGCTGGGCCTTTTTCCCATGCCTGCCTTTA
CTCTGCCAGAGTTATATTGCTGGGGTTTTGAAGAAGATCCTATTAAATAAAAGAATAAGCAGT
ATTATTAAGTAGCCCTGCATTTCAGGTTTCCTTGAGTGGCAGGCCAGGCCTGGCCGTGAACG
TTCACTGAAATCATGGCCTCTTGGCCAAGATTGATAGCTTGTGCCTGTCCCTGAGTCCCAGTC
CATCACGAGCAGCTGGTTTCTAAGATGCTATTTCCCGTATAAAGCATGAGACCGTGACTTGCC
AGCCCCACAGAGCCCCGCCCTTGTCCATCACTGGCATCTGGACTCCAGCCTGGGTTGGGGCA
AAGAGGGAAATGAGATCATGTCCTAACCCTGATCCTCTTGTCCCACAG

Left HR Arm (SEQ ID NO:22)

ATATCCAGAACCCTGACCCTGCCGTGTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTCTG
TCTGCCTATTC

TRAC CDS (SEQ ID NO:23)

GAATTCGGCTCCGGA

GSG Linker 1 (SEQ ID NO:24)

GCCACTAACTTCAGCCTGTTGAAGCAGGCCGGCGACGTTGAGGAAAACCCCGGTCCT

P2A (SEQ ID NO:25)

FIGURE 6 Cont.

ATGGCCTTACCAGTGACCGCCTTGCTCCTGCCGCTGGCCTTGCTGCTCCACGCCGCCAGGCC G	**CD8A Signal peptide (SEQ ID NO:26)**
AGCCAGTTCCGGGTGTCGCCGCTGGATCGGACCTGGAACCTGGGCGAGACAGTGGAGCTG AAGTGCCAGGTGCTGCTGTCCAACCCGACGTCGGGCTGCTCGTGGCTCTTCCAGCCGCGCG GCGCCGCCGCCAGTCCCACCTTCCTCCTATACCTCTCCCAAAACAAGCCCAAGGCGGCCGAG GGGCTGGACACCCAGCGGTTCTCGGGCAAGAGGTTGGGGGACACCTTCGTCCTCACCCTG AGCGACTTCCGCCGAGAGAACGAGGGCTACTATTTCTGCTCGGCCCTGAGCAACTCCATCAT GTACTTCAGCCACTTCGTGCCGGTCTTCCTGCCAGCGAAGCCCACCACGACGCCAGCGCCGC GACCACCAACACCGGCGCCCACCATCGCGTCGCAGCCCCTGTCCCTGCGCCCAGAGGCGTG CCGGCCAGCGGCGGGGGGCGCAGTGCACACGAGGGGGCTGGACTTCGCCTGTGAT	**CD8A Extracellular domain (SEQ ID NO:27)**
ATCTACATCTGGGCGCCCTTGGCCGGGACTTGTGGGGTCCTTCTCCTGTCACTGGTTATCACC	**CD8A transmembrane domain (SEQ ID NO:28)**
CTTTACTGCAACCACAGGAACCGAAGACGTGTTTGCAAATGTCCCCGGCCTGTGGTCAAATC GGGAGACAAGCCCAGCCTTTCGGCGAGATACGTC	**CD8A Intracellular domain (SEQ ID NO:29)**
AGGGCTAAACGG	**Furin cleavage site (SEQ ID NO:30)**
GAATTCGGCTCCGGA	**GSG Linker (SEQ ID NO:31)**
GCCACTAACTTCTCCCTGTTGAAACAGGCTGGCGATGTTGAAGAAAACCCCGGTCCT	**P2A (SEQ ID NO:32)**
ATGGCCACCGGCTCTAGAACAAGCCTGCTGCTCGCTTTTGGCCTGCTCTGCCTCCCATGGCTC CAAGAAGGATCTGCT	**HGH/SS/2 (SEQ ID NO:33)**

FIGURE 6 Cont.

[[TRB_VDJ Sequence, specific for the NeoTCR]]

Insertion site for neoTCR TRB_VDJ sequence

CTGAAAAACGTGTTCCCTCCAAAAGTGGCCGTGTTCGAGCCTTCTGAGGCCGAGATCAGCC
ACACACAGAAAGCCACACTCGTGTGTCTGGCTACCGGCTTCTACCCCGATCACGTGGAACTG
TCTTGGTGGGTCAACGGCAAAGAGGTGCACAGCGGCGTCAGCACAGATCCCCAGCCTCTGA
AAGAACAGCCCGCTCTGAACGACAGCCGCTACTGCCTGTCTAGCAGACTGAGAGTGTCCGC
CACCTTCTGGCAGAACCCCAGAAACCACTTCAGATGCCAGGTCCAGTTCTACGGCCTGAGCG
AGAACGATGAGTGGACCCAGGACAGAGCCAAGCCTGTGACACAGATCGTGTCTGCCGAAG
CCTGGGGCAGAGCCGATTGTGGCTTTACCAGCGAGTCATACCAGCAGGGCGTGCTGTCTGC
CACCATCCTGTATGAGATCCTGCTCGGCAAGGCCACACTGTACGCTGTGCTGGTGTCTGCTCT
GGTGCTGATGGCTATGGTCTCCCGGGAGCGCATCCCCGAGGCC

TCR-beta/constant (SEQ ID NO:35)

CGGGCCAAGCGG

Furin cleavage site (SEQ ID NO:36)

GGCAGCGGC

GSG linker (SEQ ID NO:37)

GCCACCAACTTCAGCCTGCTGAAGCAGGCCGGCGACGTGGAGGAGAACCCCGGCCCT

P2A (SEQ ID NO:38)

ATGGCCACAGGCAGCAGAACATCTCTGCTGCTGGCCTTCGGACTGCTGTGTCTGCCTTGGCT
GCAAGAGGGTTCCGCC

HGH/SS (SEQ ID NO:39)

[[TRA_VDJ Sequence, specific for the NeoTCR]]

Insertion site for neoTCR TRA_VDJ sequence

ATATTCAGAACCCCGATCCTGCTGTGTATCAGCTGCGCGACAGCAAGAGCAGCGACAAGAGC
GTGTGTTTGTTC

TCR-alpha/constant (SEQ ID NO:41)

SUBSTITUTE SHEET (RULE 26)

FIGURE 6 Cont.

ACCGATTTTGATTCTCAAACAAATGTGTCACAAAGTAAGGATTCTGATGTGTATATCACAGAC
AAAACTGTGCTAGACATGAGGTCTATGGACTTCAAGAGCAACAGTGCTGTGGCCTGGAGCA
ACAAATCTGACTTTGCATGTGCAAACGCCTTCAACAACAGCATTATTCCAGAAGACACCTTCT
TCCCCAGCCCAGG

TRAC CDS/right HR arm (SEQ ID NO:42)

TAAGGGCAGCTTTGGTGCCTTCGCAGGCTGTTTCCTTGCTTCAGGAATGGCCAGGTTCTGCC
CAGAGCTCTGGTCAATGATGTCTAAAACTCCTCTGATTGGTGGTCTCGGCCTTATCCATTGCC
ACCAAAACCCTCTTTTTACTAAGAAACAGTGAGCCTTGTTCTGGCAGTCCAGAGAATGACAC
GGGAAAAAAGCAGATGAAGAGAAGGTGGCAGGAGAGGGCACGTGGCCCAGCCTCAGTCT
CTCCAACTGAGTTCCTGCCTGCCTGCCTTTGCTCAGACTGTTTGCCCCTTACTGCTCTTCTAGG
CCTCATTCTAAGCCCCTTCTCCAAGTTGCCTCTCCTTATTTCTCCCTGTCTGCCAAAAAATCTTT
CCCAGCTCACTAAGTCAGTCTCACGCAGTCACTCATTAACCCACCAATCACTGATTGTGCCGG
CACATGAATGCACCAGGTGTTGAAGTGGAGGAATTAAAAAGTCAGATGAGGGGTGTGCCCA
GAGGAAGCACCATTCTAGTTGGGGGAGCCCATCTGTCAGCTGGGAAAAGTCCAAATAACTT
CAGATTGGAATGTGTTTTAACTCAGGGTTGAGAAAACAGCTACCTTCAGGACAAAAGTCAG
GGAAGGGCTCTCTGAAGAAATGCTACTTGAAGATACCAGCCCTACCAAGGGCAGGGAGAG
GACCCTATAGAGGCCTGGGACAGGAGCTCAATGAGAAAGGAGAAGAGCAGCAGGCATGA
GTTGAATGAAGGAGGCAGGGCCGGGTCACAGGGCCTTCTAGGCCATGAGAGGGTAGACAG

Right HR arm (SEQ ID NO:43)

GCTAGC

(SEQ ID NO:44)

SUBSTITUTE SHEET (RULE 26)

FIGURE 6 Cont.

CGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCT
CAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAG
CTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCT
TCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTT
CGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGG
TAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTG
GTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCC
TAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTT
CGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTT
TTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAGGATCTCAAGAAGATCCTTTGATCT

pBR322_origin (SEQ ID NO:45)

TTAGAAAAACTCATCGAGCATCAAATGAAACTGCAATTTATTCATATCAGGATTATCAATACCA
TATTTTTGAAAAAGCCGTTTCTGTAATGAAGGAGAAAACTCACCGAGGCAGTTCCATAGGAT
GGCAAGATCCTGGTATCGGTCTGCGATTCCGACTCGTCCAACATCAATACAACCTATTAATTTC
CCCTCGTCAAAAATAAGGTTATCAAGTGAGAAATCACCATGAGTGACGACTGAATCCGGTGA
GAATGGCAAAAGTTTATGCATTTCTTTCCAGACTTGTTCAACAGGCCAGCCATTACGCTCGTC
ATCAAAATCACTCGCATCAACCAAACCGTTATTCATTCGTGATTGCGCCTGAGCCAGACGAAA
TACGCGATCGCTGTTAAAAGGACAATTACAAACAGGAATCGAATGCAACCGGCGCAGGAAC
ACTGCCAGCGCATCAACAATATTTTCACCTGAATCAGGATATTCTTCTAATACCTGGAATGCTG
TTTTTCCGGGGATCGCAGTGGTGAGTAACCATGCATCATCAGGAGTACGGATAAAATGCTTG
ATGGTCGGAAGAGGCATAAATTCCGTCAGCCAGTTTAGTCTGACCATCTCATCTGTAACATCA
TTGGCAACGCTACCTTTGCCATGTTTCAGAAACAACTCTGGCGCATCGGGCTTCCCATACAAG
CGATAGATTGTCGCACCTGATTGCCCGACATTATCGCGAGCCCATTTATACCCATATAAATCAG
CATCCATGTTGGAATTTAATCGCGGCCTCGACGTTTCCCGTTGAATATGGCTCAT

Kanamycin resistance (KanR2) (SEQ ID NO:46)

AACACCCCTTGTATTACTGTTTATGTAAGCAGACAGTTTTATTGTTCATGATGATATATTTTTATC
TTGTGCAATGTAACATCAGAGATTTTGAGACAC

Kanamycin promoter (SEQ ID NO:47)

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FIGURE 7

CD8 Product 2 Product Nucleic Acid Sequence

ACATTAAAAACACAAAATCCTACGGAAATACTGAAGAATGAGTCTCAGCACTAAGGAAAAGC
CTCCAGCAGCTCCTGCTTTCTGAGGGTGAAGGATAGACGCTGTGGCTCTGCATGACTCACTA
GCACTCTATCACGGCCATATTCTGGCAGGGTCAGTGGCTCCAACTAACATTTGTTTGGTACTT
TACAGTTTATTAAATAGATGTTTATATGGAGAAGCTCTCATTTCTTTCTCAGAAGAGCCTGGCT
AGGAAGGTGGATGAGGCACCATATTCATTTTGCAGGTGAAATTCCTGAGATGTAAGGAGCT
GCTGTGACTTGCTCAAGGCCTTATATCGAGTAAACGGTAGTGCTGGGGCTTAGACGCAGGTG
TTCTGATTTATAGTTCAAAACCTCTATCAATGAGAGAGCAATCTCCTGGTAATGTGATAGATTT
CCCAACTTAATGCCAACATACCATAAACCTCCCATTCTGCTAATGCCCAGCCTAAGTTGGGGA
GACCACTCCAGATTCCAAGATGTACAGTTTGCTTTGCTGGGCCTTTTTCCCATGCCTGCCTTTA
CTCTGCCAGAGTTATATTGCTGGGGTTTTGAAGAAGATCCTATTAAATAAAAGAATAAGCAGT
ATTATTAAGTAGCCCTGCATTTCAGGTTTCCTTGAGTGGCAGGCCAGGCCTGGCCGTGAACG
TTCACTGAAATCATGGCCTCTTGGCCAAGATTGATAGCTTGTGCCTGTCCCTGAGTCCCAGTC
CATCACGAGCAGCTGGTTTCTAAGATGCTATTTCCCGTATAAAGCATGAGACCGTGACTTGCC
AGCCCCACAGAGCCCCGCCCTTGTCCATCACTGGCATCTGGACTCCAGCCTGGGTTGGGGCA
AAGAGGGAAATGAGATCATGTCCTAACCCTGATCCTCTTGTCCCACAG

Left HR Arm (SEQ ID NO:49)

ATATCCAGAACCCTGACCCTGCCGTGTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTCTG
TCTGCCTATTC

TRAC CDS (SEQ ID NO:50)

GAATTCGGCTCCGGA

GSG Linker 1 (SEQ ID NO:51)

GCCACTAACTTCAGCCTGTTGAAGCAGGCCGGCGACGTTGAGGAAAACCCCGGTCCT

P2A (SEQ ID NO:52)

FIGURE 7 Cont.

ATGGCCTTACCAGTGACCGCCTTGCTCCTGCCGCTGGCCTTGCTGCTCCACGCCGCCAGGCC G	**CD8A Signal peptide (SEQ ID NO:53)**
AGCCAGTTCCGGGTGTCGCCGCTGGATCGGACCTGGAACCTGGGCGAGACAGTGGAGCTG AAGTGCCAGGTGCTGCTGTCCAACCCGACGTCGGGCTGCTCGTGGCTCTTCCAGCCGCGCG GCGCCGCCGCCAGTCCCACCTTCCTCCTATACCTCTCCCAAAACAAGCCCAAGGCGGCCGAG GGGCTGGACACCCAGCGGTTCTCGGGCAAGAGGTTGGGGGACACCTTCGTCCTCACCCTG AGCGACTTCCGCCGAGAGAACGAGGGCTACTATTTCTGCTCGGCCCTGAGCAACTCCATCAT GTACTTCAGCCACTTCGTGCCGGTCTTCCTGCCAGCGAAGCCCACCACGACGCCAGCGCCGC GACCACCAACACCGGCGCCCACCATCGCGTCGCAGCCCCTGTCCCTGCGCCCAGAGGCGTG CCGGCCAGCGGCGGGGGGCGCAGTGCACACGAGGGGGCTGGACTTCGCCTGTGAT	**CD8A Extracellular domain (SEQ ID NO:54)**
ATCTACATCTGGGCGCCCTTGGCCGGGACTTGTGGGGTCCTTCTCCTGTCACTGGTTATCACC	**CD8A transmembrane domain (SEQ ID NO:55)**
CTTTACTGCAACCACAGGAACCGAAGACGTGTTTGCAAATGTCCCCGGCCTGTGGTCAAATC GGGAGACAAGCCCAGCCTTTCGGCGAGATACGTC	**CD8A Intracellular domain (SEQ ID NO:56)**
AGAGCAAAGCGG	**Furin cleavage site (SEQ ID NO:57)**
GGCTCCGGA	**GSG Linker (SEQ ID NO:58)**
GCTACCAATTTTAGCCTCCTGAAGCAGGCTGGCGATGTTGAGGAAAACCCTGGTCCC	**P2A (SEQ ID NO:59)**
ATGCGGCCGCGGCTGTGGCTCCTCTTGGCCGCGCAGCTGACAGTTCTCCATGGCAACTCAGT C	**CD8B Signal Peptide (SEQ ID NO:60)**

FIGURE 7 Cont.

CTCCAGCAGACCCCTGCATACATAAAGGTGCAAACCAACAAGATGGTGATGCTGTCCTGCGA
GGCTAAAATCTCCCTCAGTAACATGCGCATCTACTGGCTGAGACAGCGCCAGGCACCGAGCA
GTGACAGTCACCACGAGTTCCTGGCCCTCTGGGATTCCGCAAAAGGGACTATCCACGGTGA
AGAGGTGGAACAGGAGAAGATAGCTGTGTTTCGGGATGCAAGCCGGTTCATTCTCAATCTC
ACAAGCGTGAAGCCGGAAGACAGTGGCATCTACTTCTGCATGATCGTCGGGAGCCCCGAGC
TGACCTTCGGGAAGGGAACTCAGCTGAGTGTGGTTGATTTCCTTCCCACCACTGCCCAGCCC
ACCAAGAAGTCCACCCTCAAGAAGAGAGTGTGCCGGTTACCCAGGCCAGAGACCCAGAAG
GGCCCACTTTGTAGCCCC

CD8B Extracellular domain (SEQ ID NO:61)

ATCACCCTTGGCCTGCTGGTGGCTGGCGTCCTGGTTCTGCTGGTTTCCCTGGGAGTGGCCAT
C

CD8B Transmembrane domain (SEQ ID NO:62)

CACCTGTGCTGCCGGCGGAGGAGAGCCCGGCTTCGTTTCATGAAACAATTTTACAAA

CD8B Intracellular domain (SEQ ID NO:63)

AGGGCTAAACGG

Furin cleavage site (SEQ ID NO:64)

GAATTCGGCTCCGGA

GSG Linker (SEQ ID NO:65)

GCCACTAACTTCTCCCTGTTGAAACAGGCTGGCGATGTTGAAGAAAACCCCGGTCCT

P2A (SEQ ID NO:66)

ATGGCCACCGGCTCTAGAACAAGCCTGCTGCTCGCTTTTGGCCTGCTCTGCCTCCCATGGCTC
CAAGAAGGATCTGCT

HGH/SS/2 (SEQ ID NO:67)

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FIGURE 7 Cont.

[[TRB_VDJ Sequence, specific for the NeoTCR]]

Insertion site for neoTCR TRB_VDJ sequence

CTGAAAAACGTGTTCCCTCCAAAAGTGGCCGTGTTCGAGCCTTCTGAGGCCGAGATCAGCC
ACACACAGAAAGCCACACTCGTGTGTCTGGCTACCGGCTTCTACCCCGATCACGTGGAACTG
TCTTGGTGGGTCAACGGCAAAGAGGTGCACAGCGGCGTCAGCACAGATCCCCAGCCTCTGA
AAGAACAGCCCGCTCTGAACGACAGCCGCTACTGCCTGTCTAGCAGACTGAGAGTGTCCGC
CACCTTCTGGCAGAACCCCAGAAACCACTTCAGATGCCAGGTCCAGTTCTACGGCCTGAGCG
AGAACGATGAGTGGACCCAGGACAGAGCCAAGCCTGTGACACAGATCGTGTCTGCCGAAG
CCTGGGGCAGAGCCGATTGTGGCTTTACCAGCGAGTCATACCAGCAGGGCGTGCTGTCTGC
CACCATCCTGTATGAGATCCTGCTCGGCAAGGCCACACTGTACGCTGTGCTGGTGTCTGCTCT
GGTGCTGATGGCTATGGTCTCCCGGGAGCGCATCCCCGAGGCC

TCR-beta/constant (SEQ ID NO:69)

CGGGCCAAGCGG

Furin cleavage site (SEQ ID NO:70)

GGCAGCGGC

GSG Linker (SEQ ID NO:71)

GCCACCAACTTCAGCCTGCTGAAGCAGGCCGGCGACGTGGAGGAGAACCCCGGCCCT

P2A (SEQ ID NO:72)

ATGGCCACAGGCAGCAGAACATCTCTGCTGCTGGCCTTCGGACTGCTGTGTCTGCCTTGGCT
GCAAGAGGGTTCCGCC

HGH/SS/2 (SEQ ID NO:73)

[[TRA_VDJ Sequence, specific for the NeoTCR]]

Insertion site for neoTCR TRA_VDJ sequence

ATATTCAGAACCCCGATCCTGCTGTGTATCAGCTGCGCGACAGCAAGAGCAGCGACAAGAGC
GTGTGTTTGTTC

TCR-alpha/constant (SEQ ID NO:75)

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FIGURE 7 Cont.

ACCGATTTTGATTCTCAAACAAATGTGTCACAAAGTAAGGATTCTGATGTGTATATCACAGAC
AAAACTGTGCTAGACATGAGGTCTATGGACTTCAAGAGCAACAGTGCTGTGGCCTGGAGCA
ACAAATCTGACTTTGCATGTGCAAACGCCTTCAACAACAGCATTATTCCAGAAGACACCTTCT
TCCCCAGCCCAGG

TRAC CDS/right HR arm (SEQ ID NO:76)

TAAGGGCAGCTTTGGTGCCTTCGCAGGCTGTTTCCTTGCTTCAGGAATGGCCAGGTTCTGCC
CAGAGCTCTGGTCAATGATGTCTAAAACTCCTCTGATTGGTGGTCTCGGCCTTATCCATTGCC
ACCAAAACCCTCTTTTTACTAAGAAACAGTGAGCCTTGTTCTGGCAGTCCAGAGAATGACAC
GGGAAAAAAGCAGATGAAGAGAAGGTGGCAGGAGAGGGCACGTGGCCCAGCCTCAGTCT
CTCCAACTGAGTTCCTGCCTGCCTGCCTTTGCTCAGACTGTTTGCCCCTTACTGCTCTTCTAGG
CCTCATTCTAAGCCCCTTCTCCAAGTTGCCTCTCCTTATTTCTCCCTGTCTGCCAAAAAATCTTT
CCCAGCTCACTAAGTCAGTCTCACGCAGTCACTCATTAACCCACCAATCACTGATTGTGCCGG
CACATGAATGCACCAGGTGTTGAAGTGGAGGAATTAAAAAGTCAGATGAGGGGTGTGCCCA
GAGGAAGCACCATTCTAGTTGGGGGAGCCCATCTGTCAGCTGGGAAAAGTCCAAATAACTT
CAGATTGGAATGTGTTTTAACTCAGGGTTGAGAAAACAGCTACCTTCAGGACAAAAGTCAG
GGAAGGGCTCTCTGAAGAAATGCTACTTGAAGATACCAGCCCTACCAAGGGCAGGGAGAG
GACCCTATAGAGGCCTGGGACAGGAGCTCAATGAGAAAGGAGAAGAGCAGCAGGCATGA
GTTGAATGAAGGAGGCAGGGCCGGGTCACAGGGCCTTCTAGGCCATGAGAGGGTAGACAG

Right HR arm (SEQ ID NO:77)

GCTAGC

(SEQ ID NO:78)

FIGURE 7 Cont.

CGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCT
CAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAG
CTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCT
TCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTT
CGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGG
TAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTG
GTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCC
TAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTT
CGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTT
TTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAGGATCTCAAGAAGATCCTTTGATCT

pBR322_origin (SEQ ID NO:79)

TTAGAAAAACTCATCGAGCATCAAATGAAACTGCAATTTATTCATATCAGGATTATCAATACCA
TATTTTTGAAAAAGCCGTTTCTGTAATGAAGGAGAAAACTCACCGAGGCAGTTCCATAGGAT
GGCAAGATCCTGGTATCGGTCTGCGATTCCGACTCGTCCAACATCAATACAACCTATTAATTTC
CCCTCGTCAAAAATAAGGTTATCAAGTGAGAAATCACCATGAGTGACGACTGAATCCGGTGA
GAATGGCAAAAGTTTATGCATTTCTTTCCAGACTTGTTCAACAGGCCAGCCATTACGCTCGTC
ATCAAAATCACTCGCATCAACCAAACCGTTATTCATTCGTGATTGCGCCTGAGCCAGACGAAA
TACGCGATCGCTGTTAAAAGGACAATTACAAACAGGAATCGAATGCAACCGGCGCAGGAAC
ACTGCCAGCGCATCAACAATATTTTCACCTGAATCAGGATATTCTTCTAATACCTGGAATGCTG
TTTTTCCGGGGATCGCAGTGGTGAGTAACCATGCATCATCAGGAGTACGGATAAAATGCTTG
ATGGTCGGAAGAGGCATAAATTCCGTCAGCCAGTTTAGTCTGACCATCTCATCTGTAACATCA
TTGGCAACGCTACCTTTGCCATGTTTCAGAAACAACTCTGGCGCATCGGGCTTCCCATACAAG
CGATAGATTGTCGCACCTGATTGCCCGACATTATCGCGAGCCCATTTATACCCATATAAATCAG
CATCCATGTTGGAATTTAATCGCGGCCTCGACGTTTCCCGTTGAATATGGCTCAT

Kanamycin resistance (KanR2) (SEQ ID NO:80)

AACACCCCTTGTATTACTGTTTATGTAAGCAGACAGTTTTATTGTTCATGATGATATATTTTTATC
TTGTGCAATGTAACATCAGAGATTTTGAGACAC

Kanamycin promoter (SEQ ID NO:81)

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FIGURE 8

CD8 Product 3 Product Nucleic Acid Sequence

ACATTAAAAACACAAAATCCTACGGAAATACTGAAGAATGAGTCTCAGCACTAAGGAAAAGC
CTCCAGCAGCTCCTGCTTTCTGAGGGTGAAGGATAGACGCTGTGGCTCTGCATGACTCACTA
GCACTCTATCACGGCCATATTCTGGCAGGGTCAGTGGCTCCAACTAACATTTGTTTGGTACTT
TACAGTTTATTAAATAGATGTTTATATGGAGAAGCTCTCATTTCTTTCTCAGAAGAGCCTGGCT
AGGAAGGTGGATGAGGCACCATATTCATTTTGCAGGTGAAATTCCTGAGATGTAAGGAGCT
GCTGTGACTTGCTCAAGGCCTTATATCGAGTAAACGGTAGTGCTGGGGCTTAGACGCAGGTG
TTCTGATTTATAGTTCAAAACCTCTATCAATGAGAGAGCAATCTCCTGGTAATGTGATAGATTT
CCCAACTTAATGCCAACATACCATAAACCTCCCATTCTGCTAATGCCCAGCCTAAGTTGGGGA
GACCACTCCAGATTCCAAGATGTACAGTTTGCTTTGCTGGGCCTTTTTCCCATGCCTGCCTTTA
CTCTGCCAGAGTTATATTGCTGGGGTTTTGAAGAAGATCCTATTAAATAAAAGAATAAGCAGT
ATTATTAAGTAGCCCTGCATTTCAGGTTTCCTTGAGTGGCAGGCCAGGCCTGGCCGTGAACG
TTCACTGAAATCATGGCCTCTTGGCCAAGATTGATAGCTTGTGCCTGTCCCTGAGTCCCAGTC
CATCACGAGCAGCTGGTTTCTAAGATGCTATTTCCCGTATAAAGCATGAGACCGTGACTTGCC
AGCCCCACAGAGCCCCGCCCTTGTCCATCACTGGCATCTGGACTCCAGCCTGGGTTGGGGCA
AAGAGGGAAATGAGATCATGTCCTAACCCTGATCCTCTTGTCCCACAG

Left HR Arm (SEQ ID NO:83)

ATATCCAGAACCCTGACCCTGCCGTGTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTCTG
TCTGCCTATTC

TRAC CDS (SEQ ID NO:84)

GAATTCGGCTCCGGA

GSG Linker 1 (SEQ ID NO:85)

GCCACTAACTTCAGCCTGTTGAAGCAGGCCGGCGACGTTGAGGAAAACCCCGGTCCT

P2A (SEQ ID NO:86)

FIGURE 8 Cont.

ATGGCCTTACCAGTGACCGCCTTGCTCCTGCCGCTGGCCTTGCTGCTCCACGCCGCCAGGCC
G

CD8A Signal peptide (SEQ ID NO:87)

AGCCAGTTCCGGGTGTCGCCGCTGGATCGGACCTGGAACCTGGGCGAGACAGTGGAGCTG
AAGTGCCAGGTGCTGCTGTCCAACCCGACGTCGGGCTGCTCGTGGCTCTTCCAGCCGCGCG
GCGCCGCCGCCAGTCCCACCTTCCTCCTATACCTCTCCCAAAACAAGCCCAAGGCGGCCGAG
GGGCTGGACACCCAGCGGTTCTCGGGCAAGAGGTTGGGGGACACCTTCGTCCTCACCCTG
AGCGACTTCCGCCGAGAGAACGAGGGCTACTATTTCTGCTCGGCCCTGAGCAACTCCATCAT
GTACTTCAGCCACTTCGTGCCGGTCTTCCTGCCAGCGAAGCCCACCACGACGCCAGCGCCGC
GACCACCAACACCGGCGCCCACCATCGCGTCGCAGCCCCTGTCCCTGCGCCCAGAGGCGTG

CD8A Extracellular domain (SEQ ID NO:88)

CCGGCCAGCGGCGGGGGGCGCAGTGCACACGAGGGGGCTGGACTTCGCCTGTGAT

ATCTACATCTGGGCGCCCTTGGCCGGGACTTGTGGGGTCCTTCTCCTGTCACTGGTTATCACC

CD8A transmembrane domain (SEQ ID NO:89)

CACCTGTGCTGCCGGCGGAGGAGAGCCCGGCTTCGTTTCATGAAACAATTTTACAAA

CD8B Intracellular domain (SEQ ID NO:90)

AGGGCTAAACGG

Furin cleavage site (SEQ ID NO:91)

GAATTCGGCTCCGGA

GSG Linker (SEQ ID NO:92)

GCCACTAACTTCTCCCTGTTGAAACAGGCTGGCGATGTTGAAGAAAACCCCGGTCCT

P2A (SEQ ID NO:93)

ATGGCCACCGGCTCTAGAACAAGCCTGCTGCTCGCTTTTGGCCTGCTCTGCCTCCCATGGCTC
CAAGAAGGATCTGCT

HGH/SS/2 (SEQ ID NO:94)

FIGURE 8 Cont.

[[TRB_VDJ Sequence, specific for the NeoTCR]]

Insertion site for neoTCR TRB_VDJ sequence

CTGAAAAACGTGTTCCCTCCAAAAGTGGCCGTGTTCGAGCCTTCTGAGGCCGAGATCAGCC
ACACACAGAAAGCCACACTCGTGTGTCTGGCTACCGGCTTCTACCCCGATCACGTGGAACTG
TCTTGGTGGGTCAACGGCAAAGAGGTGCACAGCGGCGTCAGCACAGATCCCCAGCCTCTGA
AAGAACAGCCCGCTCTGAACGACAGCCGCTACTGCCTGTCTAGCAGACTGAGAGTGTCCGC
CACCTTCTGGCAGAACCCCAGAAACCACTTCAGATGCCAGGTCCAGTTCTACGGCCTGAGCG
AGAACGATGAGTGGACCCAGGACAGAGCCAAGCCTGTGACACAGATCGTGTCTGCCGAAG
CCTGGGGCAGAGCCGATTGTGGCTTTACCAGCGAGTCATACCAGCAGGGCGTGCTGTCTGC
CACCATCCTGTATGAGATCCTGCTCGGCAAGGCCACACTGTACGCTGTGCTGGTGTCTGCTCT
GGTGCTGATGGCTATGGTCTCCCGGGAGCGCATCCCCGAGGCC

TCR-beta/constant (SEQ ID NO:96)

CGGGCCAAGCGG

Furin cleavage site (SEQ ID NO:97)

GGCAGCGGC

GSG Linker (SEQ ID NO:98)

GCCACCAACTTCAGCCTGCTGAAGCAGGCCGGCGACGTGGAGGAGAACCCCGGCCCT

P2A (SEQ ID NO:99)

ATGGCCACAGGCAGCAGAACATCTCTGCTGCTGGCCTTCGGACTGCTGTGTCTGCCTTGGCT
GCAAGAGGGTTCCGCC

HGH/SS/2 (SEQ ID NO:100)

[[TRA_VDJ Sequence, specific for the NeoTCR]]

Insertion site for neoTCR TRA_VDJ sequence

ATATTCAGAACCCCGATCCTGCTGTGTATCAGCTGCGCGACAGCAAGAGCAGCGACAAGAGC
GTGTGTTTGTTC

TCR-alpha/constant (SEQ ID NO:102)

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FIGURE 8 Cont.

TRAC CDS/right HR arm (SEQ ID NO:103)

ACCGATTTTGATTCTCAAACAAATGTGTCACAAAGTAAGGATTCTGATGTGTATATCACAGAC
AAAACTGTGCTAGACATGAGGTCTATGGACTTCAAGAGCAACAGTGCTGTGGCCTGGAGCA
ACAAATCTGACTTTGCATGTGCAAACGCCTTCAACAACAGCATTATTCCAGAAGACACCTTCT
TCCCCAGCCCAGG

Right HR arm (SEQ ID NO:104)

TAAGGGCAGCTTTGGTGCCTTCGCAGGCTGTTTCCTTGCTTCAGGAATGGCCAGGTTCTGCC
CAGAGCTCTGGTCAATGATGTCTAAAACTCCTCTGATTGGTGGTCTCGGCCTTATCCATTGCC
ACCAAAACCCTCTTTTTACTAAGAAACAGTGAGCCTTGTTCTGGCAGTCCAGAGAATGACAC
GGGAAAAAAGCAGATGAAGAGAAGGTGGCAGGAGAGGGCACGTGGCCCAGCCTCAGTCT
CTCCAACTGAGTTCCTGCCTGCCTGCCTTTGCTCAGACTGTTTGCCCCTTACTGCTCTTCTAGG
CCTCATTCTAAGCCCCTTCTCCAAGTTGCCTCTCCTTATTTCTCCCTGTCTGCCAAAAAATCTTT
CCCAGCTCACTAAGTCAGTCTCACGCAGTCACTCATTAACCCACCAATCACTGATTGTGCCGG
CACATGAATGCACCAGGTGTTGAAGTGGAGGAATTAAAAAGTCAGATGAGGGGTGTGCCCA
GAGGAAGCACCATTCTAGTTGGGGGAGCCCATCTGTCAGCTGGGAAAAGTCCAAATAACTT
CAGATTGGAATGTGTTTTAACTCAGGGTTGAGAAAACAGCTACCTTCAGGACAAAAGTCAG
GGAAGGGCTCTCTGAAGAAATGCTACTTGAAGATACCAGCCCTACCAAGGGCAGGGAGAG
GACCCTATAGAGGCCTGGGACAGGAGCTCAATGAGAAAGGAGAAGAGCAGCAGGCATGA
GTTGAATGAAGGAGGCAGGGCCGGGTCACAGGGCCTTCTAGGCCATGAGAGGGTAGACAG

(SEQ ID NO:105)

GCTAGC

FIGURE 8 Cont.

CGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCT
CAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAG
CTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCT
TCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTT
CGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGG
TAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTG
GTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCC
TAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTT
CGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTT
TTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCT

pBR322_origin (SEQ ID NO:106)

TTAGAAAAACTCATCGAGCATCAAATGAAACTGCAATTTATTCATATCAGGATTATCAATACCA
TATTTTTGAAAAAGCCGTTTCTGTAATGAAGGAGAAAACTCACCGAGGCAGTTCCATAGGAT
GGCAAGATCCTGGTATCGGTCTGCGATTCCGACTCGTCCAACATCAATACAACCTATTAATTTC
CCCTCGTCAAAAATAAGGTTATCAAGTGAGAAATCACCATGAGTGACGACTGAATCCGGTGA
GAATGGCAAAAGTTTATGCATTTCTTTCCAGACTTGTTCAACAGGCCAGCCATTACGCTCGTC
ATCAAAATCACTCGCATCAACCAAACCGTTATTCATTCGTGATTGCGCCTGAGCCAGACGAAA
TACGCGATCGCTGTTAAAAGGACAATTACAAACAGGAATCGAATGCAACCGGCGCAGGAAC
ACTGCCAGCGCATCAACAATATTTTCACCTGAATCAGGATATTCTTCTAATACCTGGAATGCTG
TTTTTCCGGGGATCGCAGTGGTGAGTAACCATGCATCATCAGGAGTACGGATAAAATGCTTG
ATGGTCGGAAGAGGCATAAATTCCGTCAGCCAGTTTAGTCTGACCATCTCATCTGTAACATCA
TTGGCAACGCTACCTTTGCCATGTTTCAGAAACAACTCTGGCGCATCGGGCTTCCCATACAAG
CGATAGATTGTCGCACCTGATTGCCCGACATTATCGCGAGCCCATTTATACCCATATAAATCAG
CATCCATGTTGGAATTTAATCGCGGCCTCGACGTTTCCCGTTGAATATGGCTCAT

Kanamycin resistance (KanR2) (SEQ ID NO:107)

AACACCCCTTGTATTACTGTTTATGTAAGCAGACAGTTTTATTGTTCATGATGATATATTTTTATC
TTGTGCAATGTAACATCAGAGATTTTGAGACAC

Kanamycin promoter (SEQ ID NO:108)

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FIGURE 9

CD8 Product 4 Product Nucleic Acid Sequence

ACATTAAAAACACAAAATCCTACGGAAATACTGAAGAATGAGTCTCAGCACTAAGGAAAAGC
CTCCAGCAGCTCCTGCTTTCTGAGGGTGAAGGATAGACGCTGTGGCTCTGCATGACTCACTA
GCACTCTATCACGGCCATATTCTGGCAGGGTCAGTGGCTCCAACTAACATTTGTTTGGTACTT
TACAGTTTATTAAATAGATGTTTATATGGAGAAGCTCTCATTTCTTTCTCAGAAGAGCCTGGCT
AGGAAGGTGGATGAGGCACCATATTCATTTTGCAGGTGAAATTCCTGAGATGTAAGGAGCT
GCTGTGACTTGCTCAAGGCCTTATATCGAGTAAACGGTAGTGCTGGGGCTTAGACGCAGGTG
TTCTGATTTATAGTTCAAAACCTCTATCAATGAGAGAGCAATCTCCTGGTAATGTGATAGATTT
CCCAACTTAATGCCAACATACCATAAACCTCCCATTCTGCTAATGCCCAGCCTAAGTTGGGGA
GACCACTCCAGATTCCAAGATGTACAGTTTGCTTTGCTGGGCCTTTTTCCCATGCCTGCCTTTA
CTCTGCCAGAGTTATATTGCTGGGGTTTTGAAGAAGATCCTATTAAATAAAAGAATAAGCAGT
ATTATTAAGTAGCCCTGCATTTCAGGTTTCCTTGAGTGGCAGGCCAGGCCTGGCCGTGAACG
TTCACTGAAATCATGGCCTCTTGGCCAAGATTGATAGCTTGTGCCTGTCCCTGAGTCCCAGTC
CATCACGAGCAGCTGGTTTCTAAGATGCTATTTCCCGTATAAAGCATGAGACCGTGACTTGCC
AGCCCCACAGAGCCCCGCCCTTGTCCATCACTGGCATCTGGACTCCAGCCTGGGTTGGGGCA
AAGAGGGAAATGAGATCATGTCCTAACCCTGATCCTCTTGTCCCACAG

Left HR Arm (SEQ ID NO:110)

ATATCCAGAACCCTGACCCTGCCGTGTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTCTG
TCTGCCTATTC

TRAC CDS (SEQ ID NO:111)

GAATTCGGCTCCGGA

GSG Linker 1 (SEQ ID NO:112)

GCCACTAACTTCAGCCTGTTGAAGCAGGCCGGCGACGTTGAGGAAAACCCCGGTCCT

P2A (SEQ ID NO:113)

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FIGURE 9 Cont.

ATGGCCTTACCAGTGACCGCCTTGCTCCTGCCGCTGGCCTTGCTGCTCCACGCCGCCAGGCC
G

CD8A Signal peptide (SEQ ID NO:114)

AGCCAGTTCCGGGTGTCGCCGCTGGATCGGACCTGGAACCTGGGCGAGACAGTGGAGCTG
AAGTGCCAGGTGCTGCTGTCCAACCCGACGTCGGGCTGCTCGTGGCTCTTCCAGCCGCGCG
GCGCCGCCGCCAGTCCCACCTTCCTCCTATACCTCTCCCAAAACAAGCCCAAGGCGGCCGAG
GGGCTGGACACCCAGCGGTTCTCGGGCAAGAGGTTGGGGGACACCTTCGTCCTCACCCTG
AGCGACTTCCGCCGAGAGAACGAGGGCTACTATTTCTGCTCGGCCCTGAGCAACTCCATCAT
GTACTTCAGCCACTTCGTGCCGGTCTTCCTGCCAGCGAAGCCCACCACGACGCCAGCGCCGC
GACCACCAACACCGGCGCCCACCATCGCGTCGCAGCCCCTGTCCCTGCGCCCAGAGGCGTG
CCGGCCAGCGGCGGGGGGCGCAGTGCACACGAGGGGGCTGGACTTCGCCTGTGAT

CD8A Extracellular domain (SEQ ID NO:115)

ATCTACATCTGGGCGCCCTTGGCCGGGACTTGTGGGGTCCTTCTCCTGTCACTGGTTATCACC

CD8A transmembrane domain (SEQ ID NO:116)

TGTGTCAGGTGCCGGCACCGAAGGCGCCAAGCAGAGCGGATGTCTCAGATCAAGAGACTCC
TCAGTGAGAAGAAGACCTGCCAGTGTCCTCACCGGTTTCAGAAGACATGTAGCCCCATT

CD4 Intracellular domain (SEQ ID NO:117)

AGGGCTAAACGG

Furin cleavage site (SEQ ID NO:118)

GAATTCGGCTCCGGA

GSG Linker (SEQ ID NO:119)

GCCACTAACTTCTCCCTGTTGAAACAGGCTGGCGATGTTGAAGAAAACCCCGGTCCT

P2A (SEQ ID NO:120)

ATGGCCACCGGCTCTAGAACAAGCCTGCTGCTCGCTTTTGGCCTGCTCTGCCTCCCATGGCTC
CAAGAAGGATCTGCT

HGH/SS/2 (SEQ ID NO:121)

FIGURE 9 Cont.

[[TRB_VDJ Sequence, specific for the NeoTCR]]

Insertion site for neoTCR TRB_VDJ sequence

CTGAAAAACGTGTTCCCTCCAAAAGTGGCCGTGTTCGAGCCTTCTGAGGCCGAGATCAGCC
ACACACAGAAAGCCACACTCGTGTGTCTGGCTACCGGCTTCTACCCCGATCACGTGGAACTG
TCTTGGTGGGTCAACGGCAAAGAGGTGCACAGCGGCGTCAGCACAGATCCCCAGCCTCTGA
AAGAACAGCCCGCTCTGAACGACAGCCGCTACTGCCTGTCTAGCAGACTGAGAGTGTCCGC
CACCTTCTGGCAGAACCCCAGAAACCACTTCAGATGCCAGGTCCAGTTCTACGGCCTGAGCG
AGAACGATGAGTGGACCCAGGACAGAGCCAAGCCTGTGACACAGATCGTGTCTGCCGAAG
CCTGGGGCAGAGCCGATTGTGGCTTTACCAGCGAGTCATACCAGCAGGGCGTGCTGTCTGC
CACCATCCTGTATGAGATCCTGCTCGGCAAGGCCACACTGTACGCTGTGCTGGTGTCTGCTCT
GGTGCTGATGGCTATGGTCTCCCGGGAGCGCATCCCCGAGGCC

TCR-beta/constant (SEQ ID NO:123)

CGGGCCAAGCGG

Furin cleavage site (SEQ ID NO:124)

GGCAGCGGC

GSG Linker (SEQ ID NO:125)

GCCACCAACTTCAGCCTGCTGAAGCAGGCCGGCGACGTGGAGGAGAACCCCGGCCCT

P2A (SEQ ID NO:126)

ATGGCCACAGGCAGCAGAACATCTCTGCTGCTGGCCTTCGGACTGCTGTGTCTGCCTTGGCT
GCAAGAGGGTTCCGCC

HGH/SS/2 (SEQ ID NO:127)

[[TRA_VDJ Sequence, specific for the NeoTCR]]

Insertion site for neoTCR TRA_VDJ sequence

ATATTCAGAACCCCGATCCTGCTGTGTATCAGCTGCGCGACAGCAAGAGCAGCGACAAGAGC
GTGTGTTTGTTC

TCR-alpha/constant (SEQ ID NO:129)

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FIGURE 9 Cont.

TRAC CDS/right HR arm (SEQ ID NO:130)

ACCGATTTTGATTCTCAAACAAATGTGTCACAAAGTAAGGATTCTGATGTGTATATCACAGAC
AAAACTGTGCTAGACATGAGGTCTATGGACTTCAAGAGCAACAGTGCTGTGGCCTGGAGCA
ACAAATCTGACTTTGCATGTGCAAACGCCTTCAACAACAGCATTATTCCAGAAGACACCTTCT
TCCCCAGCCCAGG

Right HR arm (SEQ ID NO:131)

TAAGGGCAGCTTTGGTGCCTTCGCAGGCTGTTTCCTTGCTTCAGGAATGGCCAGGTTCTGCC
CAGAGCTCTGGTCAATGATGTCTAAAACTCCTCTGATTGGTGGTCTCGGCCTTATCCATTGCC
ACCAAAACCCTCTTTTTACTAAGAAACAGTGAGCCTTGTTCTGGCAGTCCAGAGAATGACAC
GGGAAAAAAGCAGATGAAGAGAAGGTGGCAGGAGAGGGCACGTGGCCCAGCCTCAGTCT
CTCCAACTGAGTTCCTGCCTGCCTGCCTTTGCTCAGACTGTTTGCCCCTTACTGCTCTTCTAGG
CCTCATTCTAAGCCCCTTCTCCAAGTTGCCTCTCCTTATTTCTCCCTGTCTGCCAAAAAATCTTT
CCCAGCTCACTAAGTCAGTCTCACGCAGTCACTCATTAACCCACCAATCACTGATTGTGCCGG
CACATGAATGCACCAGGTGTTGAAGTGGAGGAATTAAAAAGTCAGATGAGGGGTGTGCCCA
GAGGAAGCACCATTCTAGTTGGGGGAGCCCATCTGTCAGCTGGGAAAAGTCCAAATAACTT
CAGATTGGAATGTGTTTTAACTCAGGGTTGAGAAAACAGCTACCTTCAGGACAAAAGTCAG
GGAAGGGCTCTCTGAAGAAATGCTACTTGAAGATACCAGCCCTACCAAGGGCAGGGAGAG
GACCCTATAGAGGCCTGGGACAGGAGCTCAATGAGAAAGGAGAAGAGCAGCAGGCATGA
GTTGAATGAAGGAGGCAGGGCCGGGTCACAGGGCCTTCTAGGCCATGAGAGGGTAGACAG

GCTAGC **(SEQ ID NO:132)**

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FIGURE 9 Cont.

CGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCT
CAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAG
CTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCT
TCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTT
CGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGG
TAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTG
GTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCC
TAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTT
CGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTT
TTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAGGATCTCAAGAAGATCCTTTGATCT

pBR322_origin (SEQ ID NO:133)

TTAGAAAAACTCATCGAGCATCAAATGAAACTGCAATTTATTCATATCAGGATTATCAATACCA
TATTTTTGAAAAAGCCGTTTCTGTAATGAAGGAGAAAACTCACCGAGGCAGTTCCATAGGAT
GGCAAGATCCTGGTATCGGTCTGCGATTCCGACTCGTCCAACATCAATACAACCTATTAATTTC
CCCTCGTCAAAAATAAGGTTATCAAGTGAGAAATCACCATGAGTGACGACTGAATCCGGTGA
GAATGGCAAAAGTTTATGCATTTCTTTCCAGACTTGTTCAACAGGCCAGCCATTACGCTCGTC
ATCAAAATCACTCGCATCAACCAAACCGTTATTCATTCGTGATTGCGCCTGAGCCAGACGAAA
TACGCGATCGCTGTTAAAAGGACAATTACAAACAGGAATCGAATGCAACCGGCGCAGGAAC
ACTGCCAGCGCATCAACAATATTTTCACCTGAATCAGGATATTCTTCTAATACCTGGAATGCTG
TTTTTCCGGGGATCGCAGTGGTGAGTAACCATGCATCATCAGGAGTACGGATAAAATGCTTG
ATGGTCGGAAGAGGCATAAATTCCGTCAGCCAGTTTAGTCTGACCATCTCATCTGTAACATCA
TTGGCAACGCTACCTTTGCCATGTTTCAGAAACAACTCTGGCGCATCGGGCTTCCCATACAAG
CGATAGATTGTCGCACCTGATTGCCCGACATTATCGCGAGCCCATTTATACCCATATAAATCAG
CATCCATGTTGGAATTTAATCGCGGCCTCGACGTTTCCCGTTGAATATGGCTCAT

Kanamycin resistance (KanR2) (SEQ ID NO:134)

AACACCCCTTGTATTACTGTTTATGTAAGCAGACAGTTTTATTGTTCATGATGATATATTTTTATC
TTGTGCAATGTAACATCAGAGATTTTGAGACAC

Kanamycin promoter (SEQ ID NO:135)

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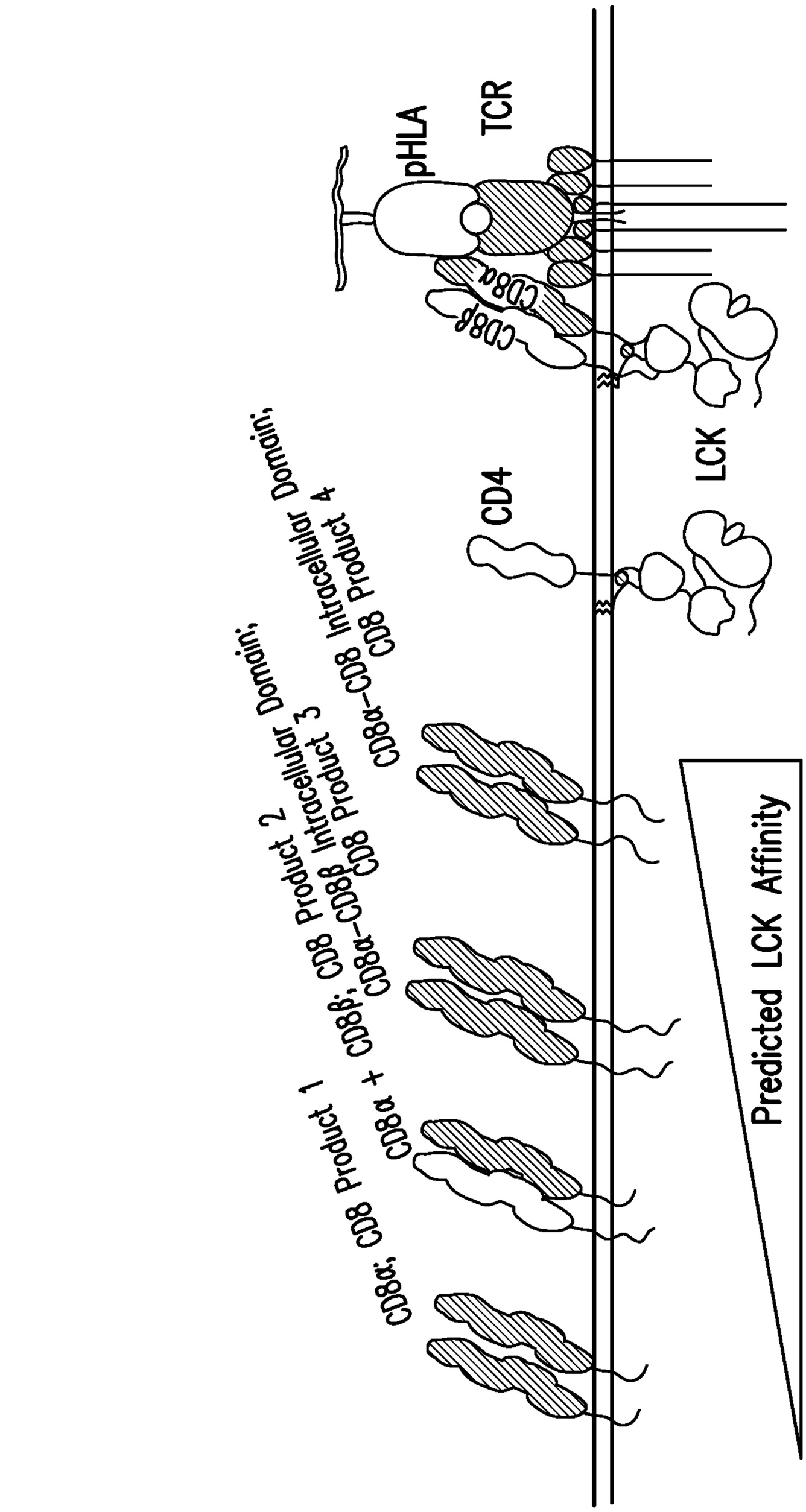

pHLA
TCR
CD8α
CD8β
CD4
LCK
CD8α + CD8β; CD8 Product 1
CD8α–CD8β CD8 Product 2
CD8α–CD8β CD8 Product 3
CD8α; CD8 Intracellular Domain;
CD8 Intracellular Domain;
CD8 Product 4
Predicted LCK Affinity

FIGURE 10

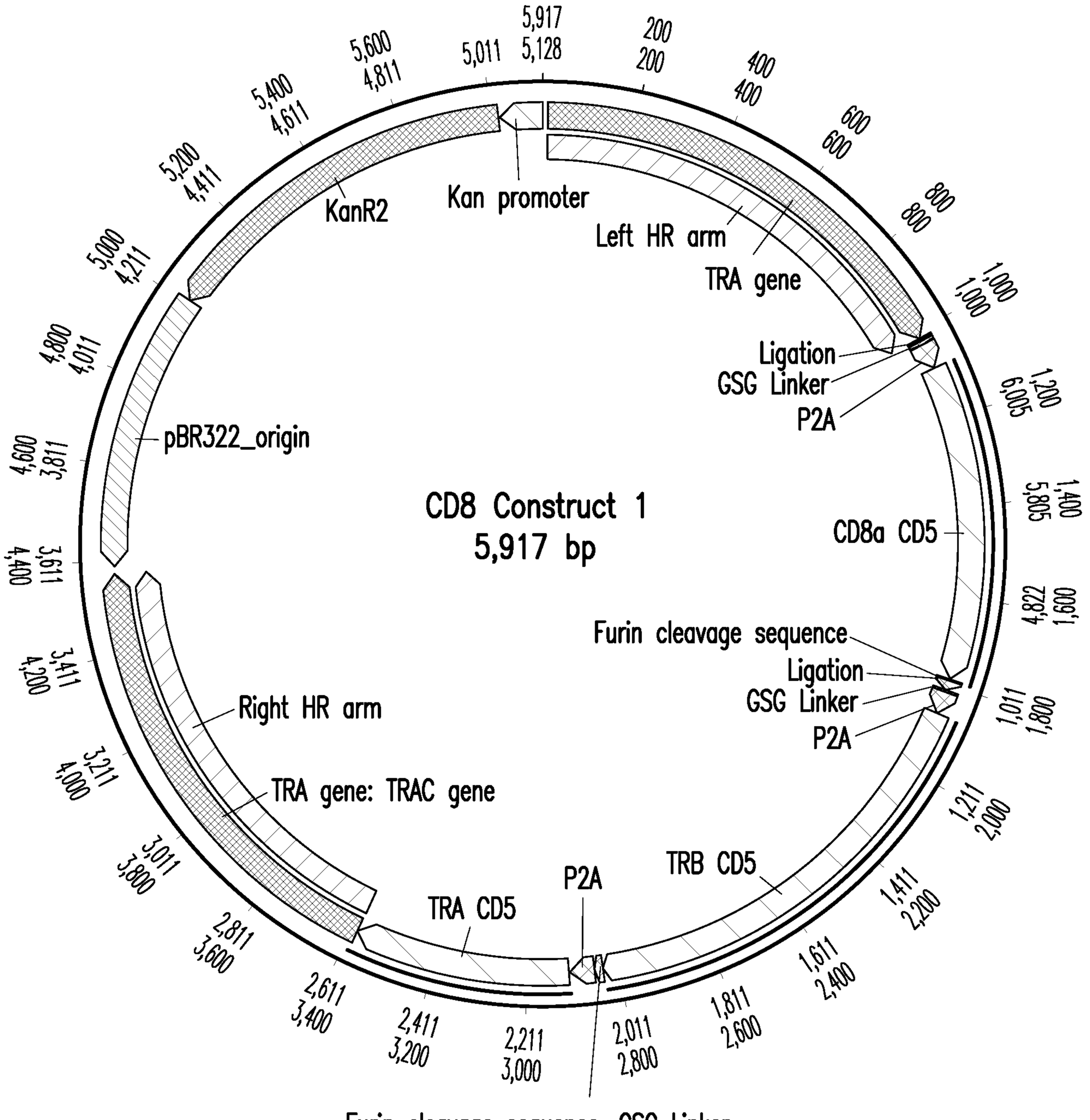
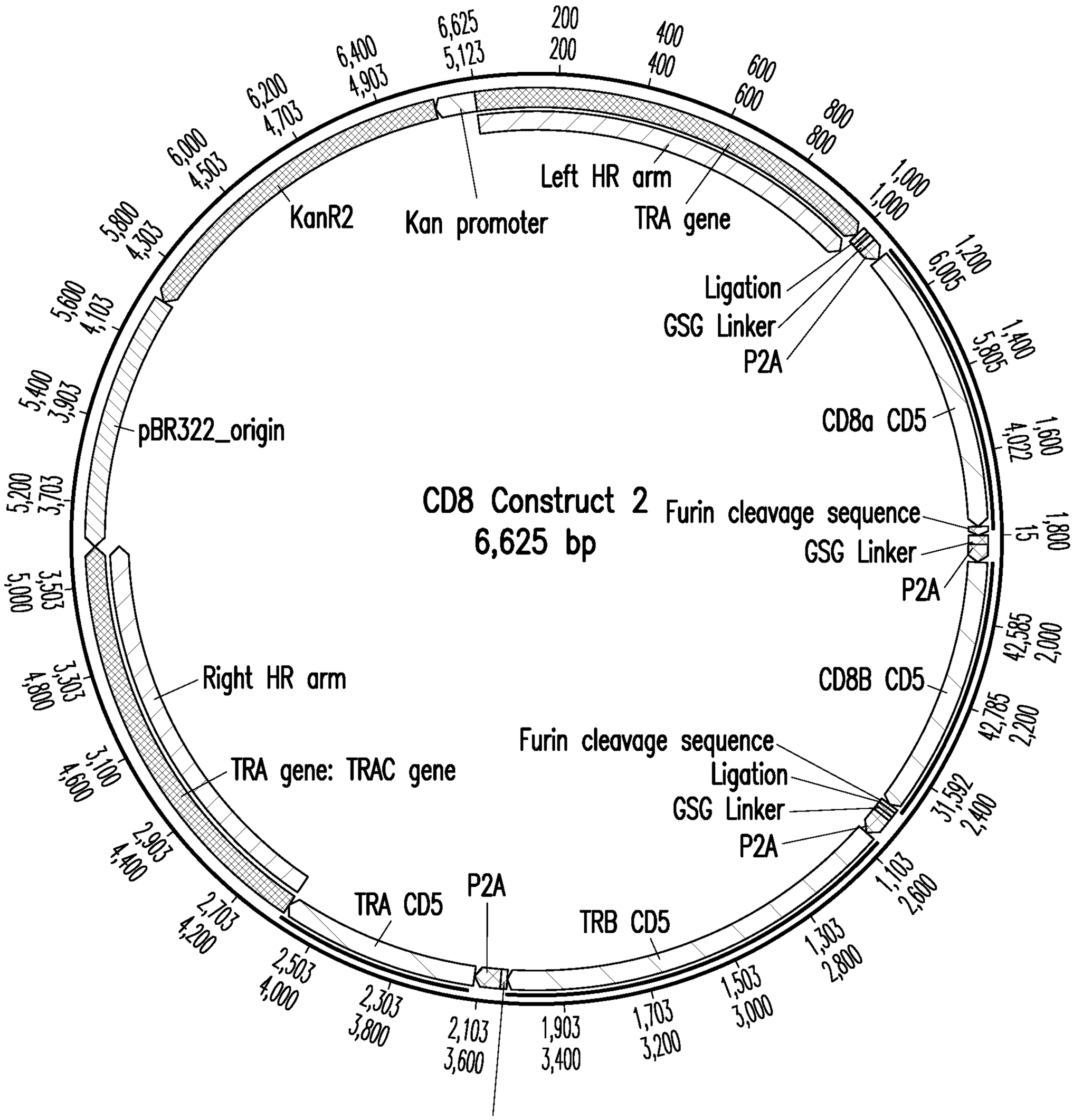

CD8 Construct 1
5,917 bp
KanR2
Kan promoter
Left HR arm
TRA gene
Ligation
GSG Linker
P2A
CD8a CD5
Furin cleavage sequence
Ligation
GSG Linker
P2A
TRB CD5
P2A
TRA CD5
TRA gene: TRAC gene
Right HR arm
pBR322_origin
Furin cleavage sequence, GSG Linker

FIGURE 11A



Furin cleavage sequence, GSG Linker

FIGURE 11B

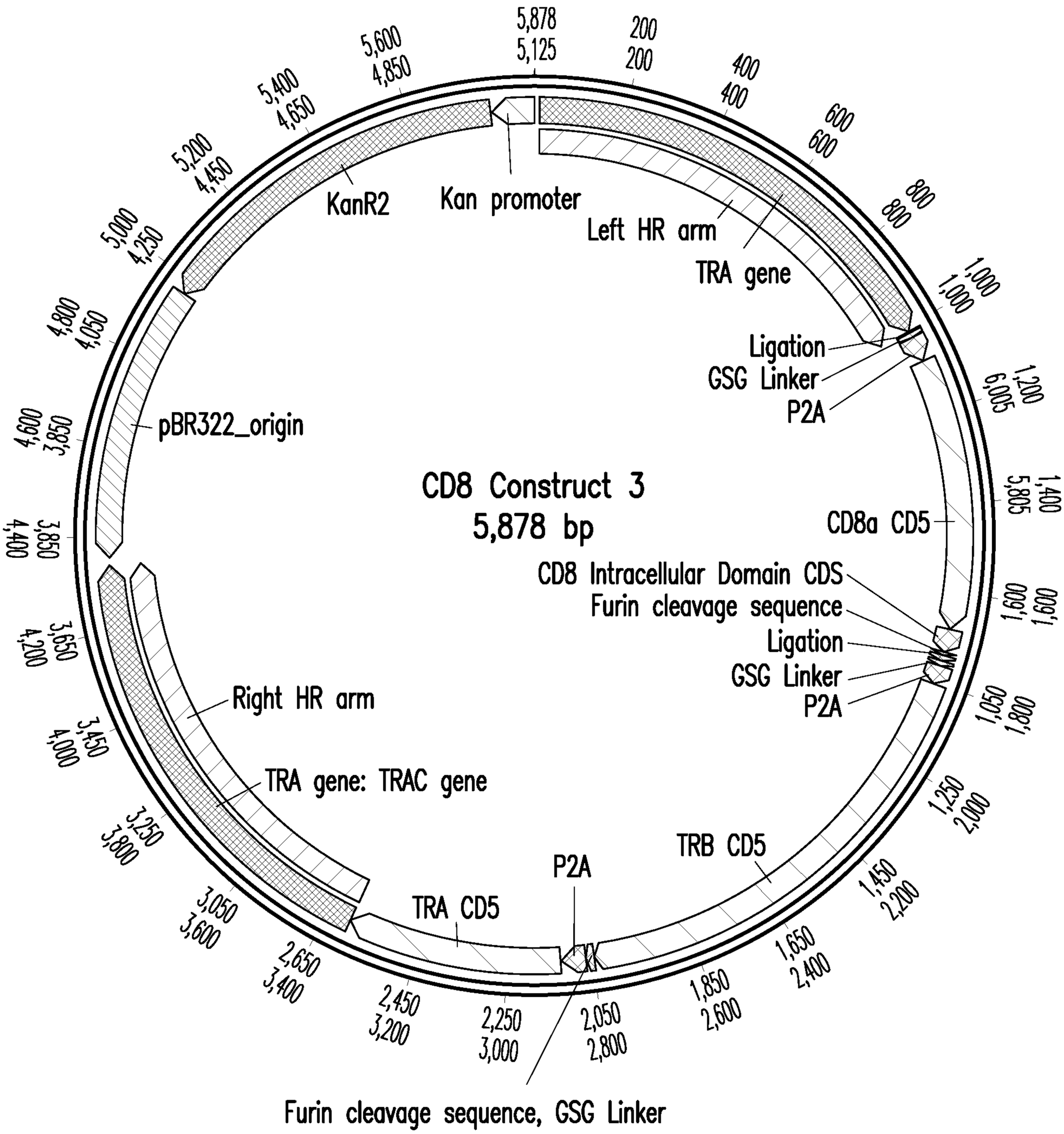
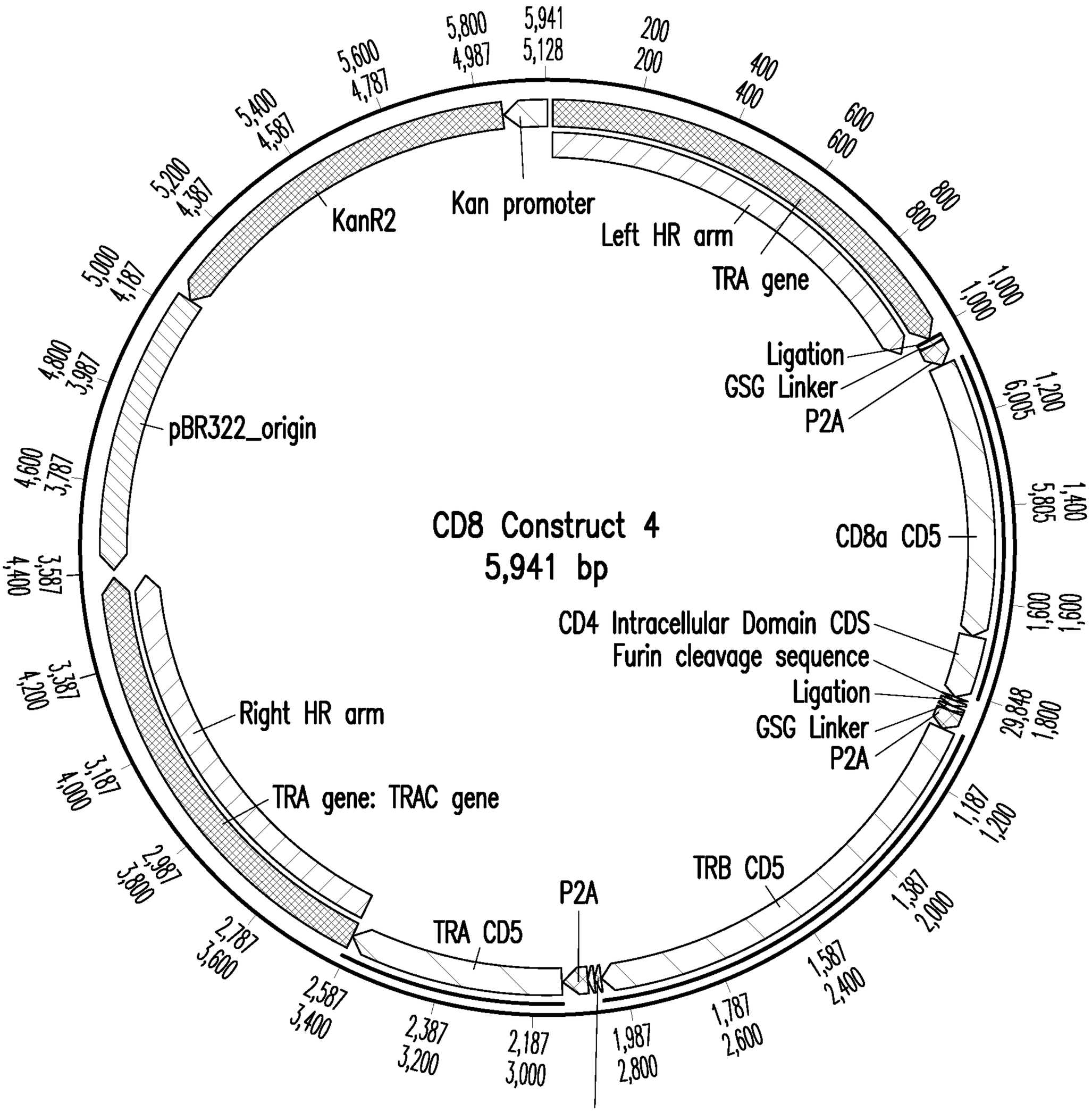

CD8 Construct 3
5,878 bp
KanR2
Kan promoter
Left HR arm
TRA gene
Ligation
GSG Linker
P2A
CD8a CD5
CD8 Intracellular Domain CDS
Furin cleavage sequence
Ligation
GSG Linker
P2A
TRB CD5
P2A
TRA CD5
TRA gene: TRAC gene
Right HR arm
pBR322_origin
Furin cleavage sequence, GSG Linker

FIGURE 11C



Furin cleavage sequence, GSG Linker

FIGURE 11D

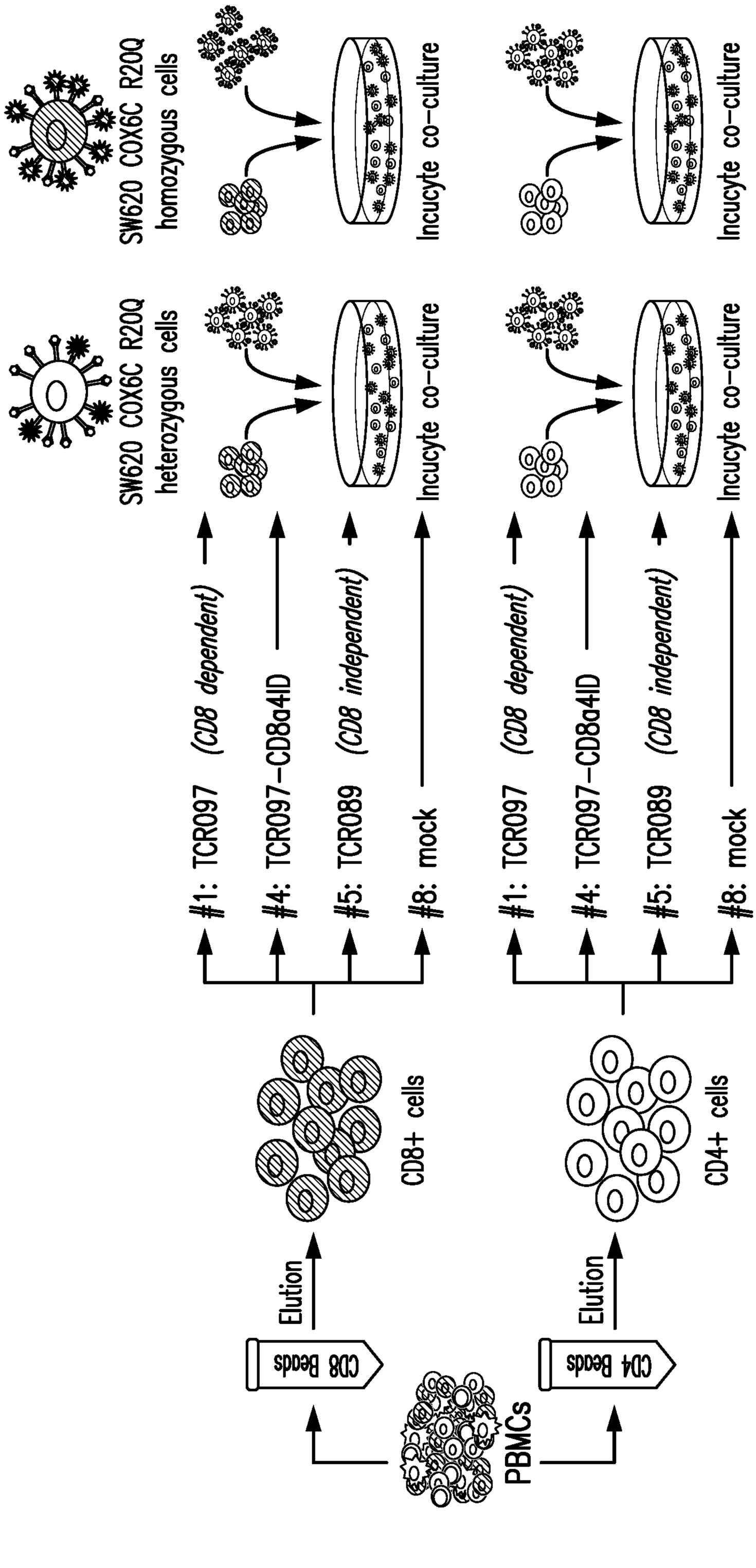

SW620 COX6C R20Q homozygous cells
SW620 COX6C R20Q heterozygous cells
Incucyte co-culture
Incucyte co-culture
Incucyte co-culture
Incucyte co-culture
#1: TCR097 (CD8 dependent)
#4: TCR097-CD8a4ID
#5: TCR089 (CD8 independent)
#8: mock
#1: TCR097 (CD8 dependent)
#4: TCR097-CD8a4ID
#5: TCR089 (CD8 independent)
#8: mock
CD8+ cells
CD4+ cells
Elution
Elution
CD8 Beads
CD4 Beads
PBMCs

FIGURE 12

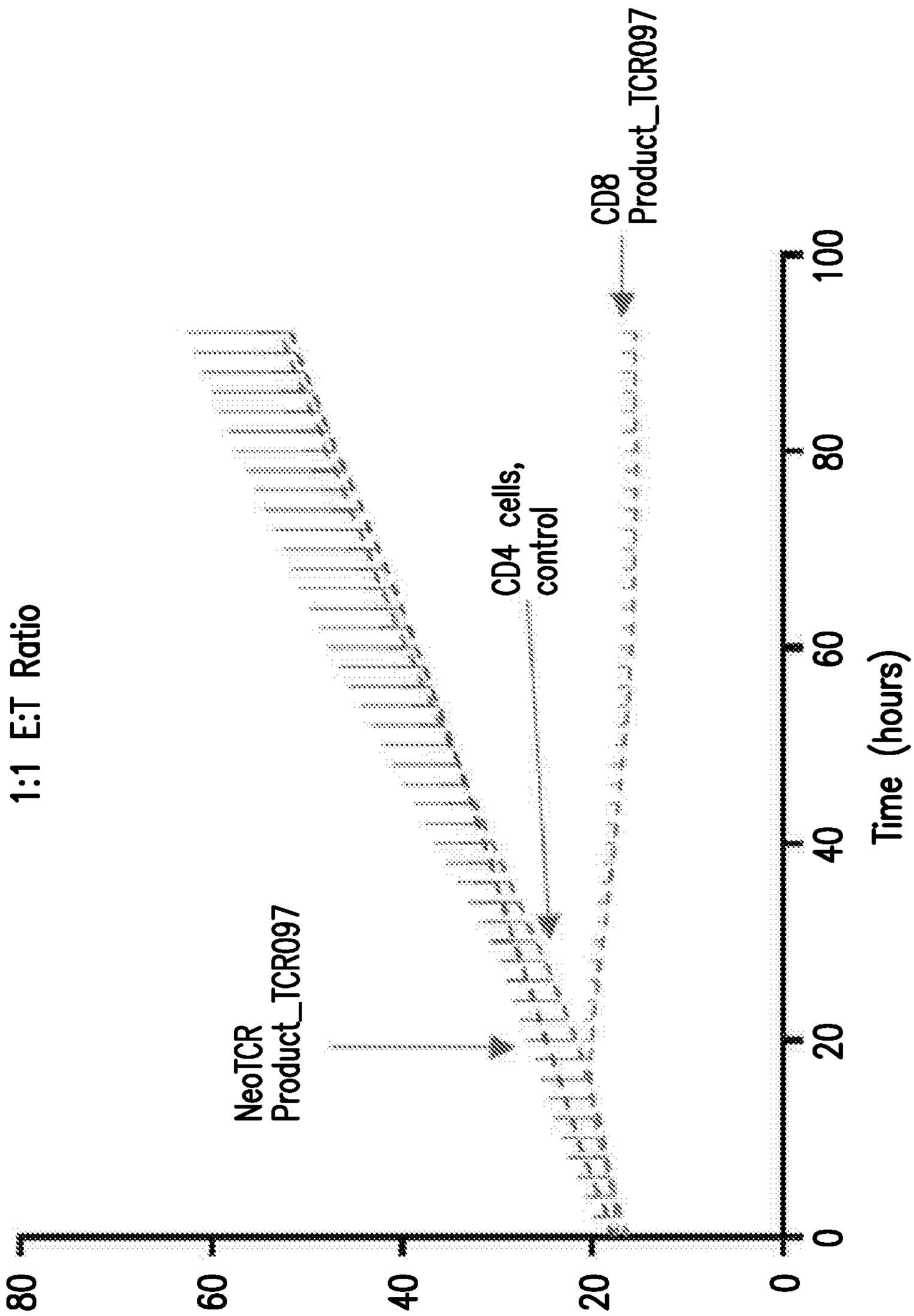

Percent SW620 het. R200Q Confluence
0
20
40
60
80
Time (hours)
0
20
40
60
80
100
1:1 E:T Ratio
NeoTCR Product_TCR097
CD4 cells, control
CD8 Product_TCR097

FIGURE 13A

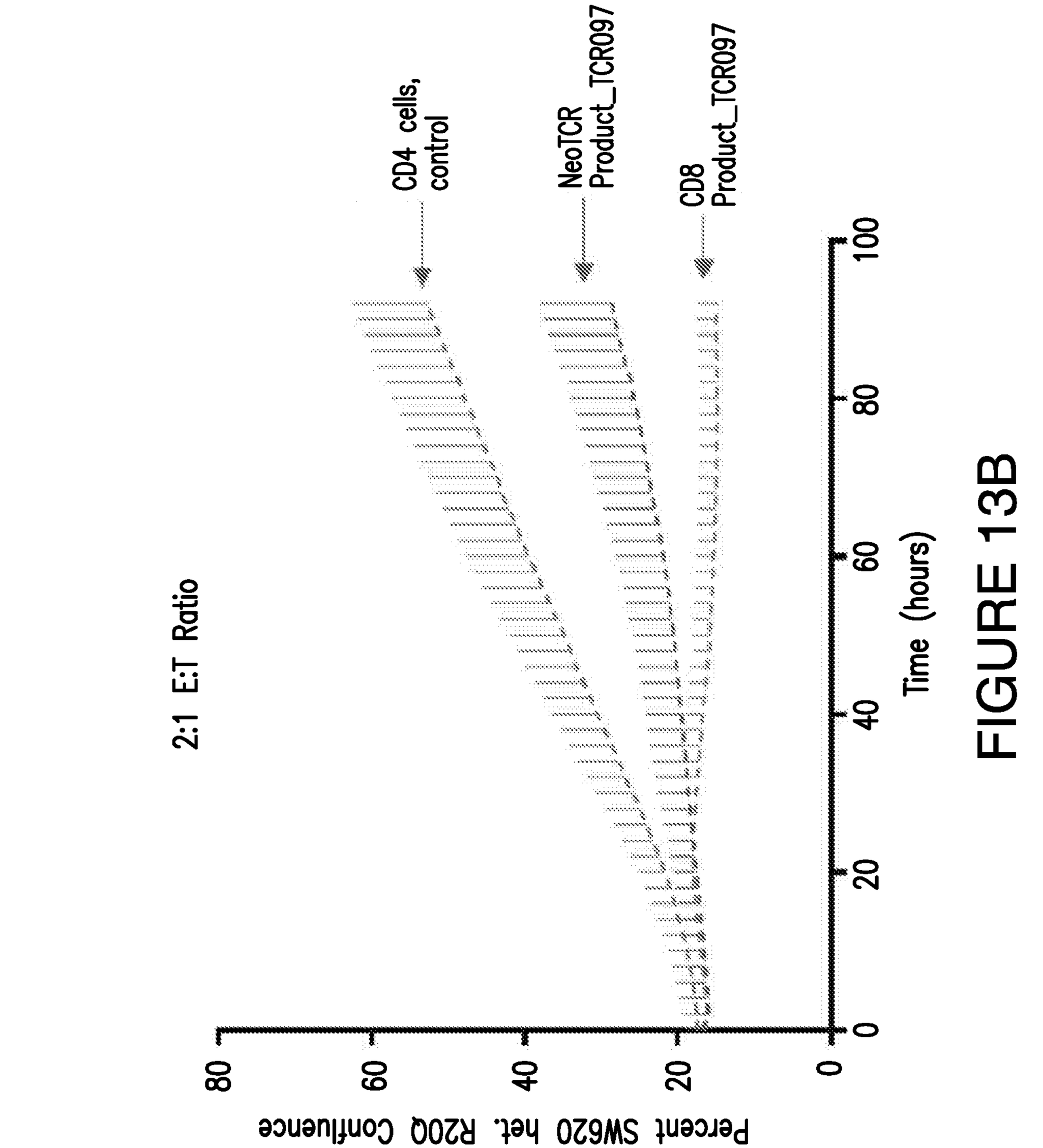

Percent SW620 het. R200Q Confluence
0
20
40
60
80
2:1 E:T Ratio
Time (hours)
0
20
40
60
80
100
CD4 cells, control
NeoTCR Product_TCR097
CD8 Product_TCR097

FIGURE 13B

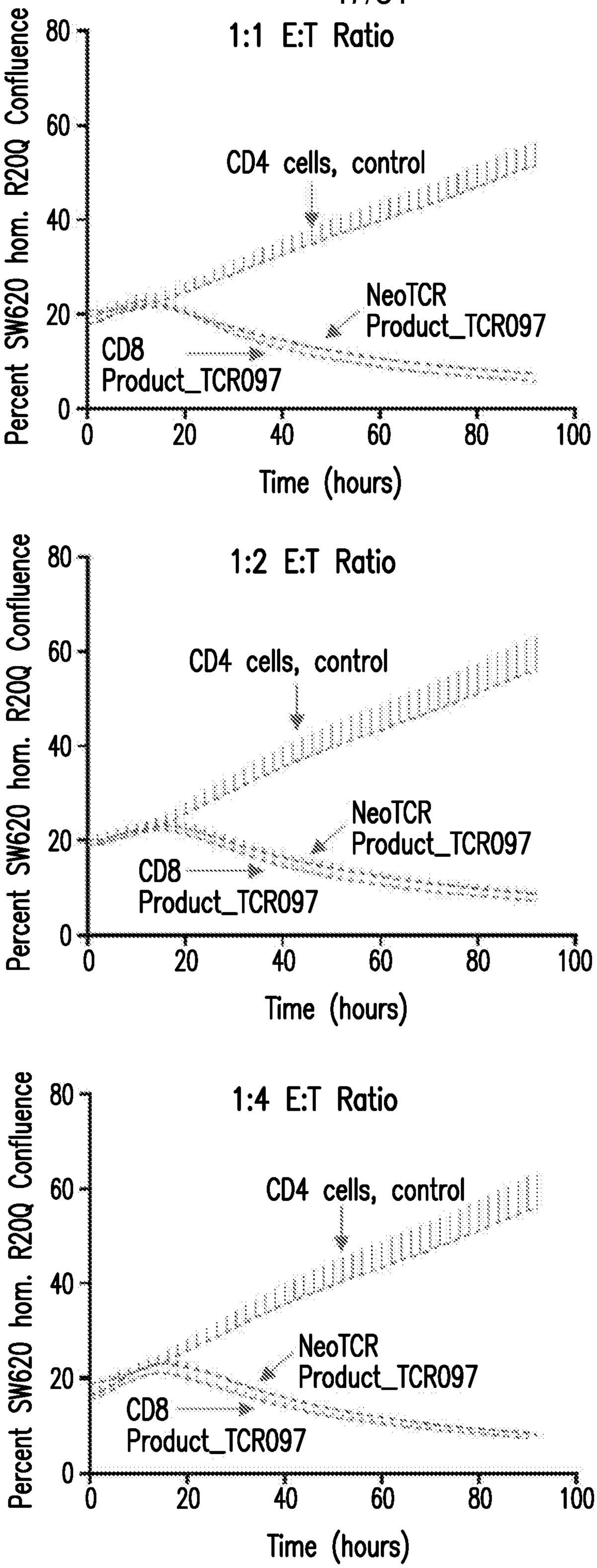

1:1 E:T Ratio
CD4 cells, control
NeoTCR
Product_TCR097
CD8
Product_TCR097
Percent SW620 hom. R20Q Confluence
Time (hours)
1:2 E:T Ratio
CD4 cells, control
NeoTCR
Product_TCR097
CD8
Product_TCR097
Percent SW620 hom. R20Q Confluence
Time (hours)
1:4 E:T Ratio
CD4 cells, control
NeoTCR
Product_TCR097
CD8
Product_TCR097
Percent SW620 hom. R20Q Confluence
Time (hours)
0
20
40
60
80
100

FIGURE 14

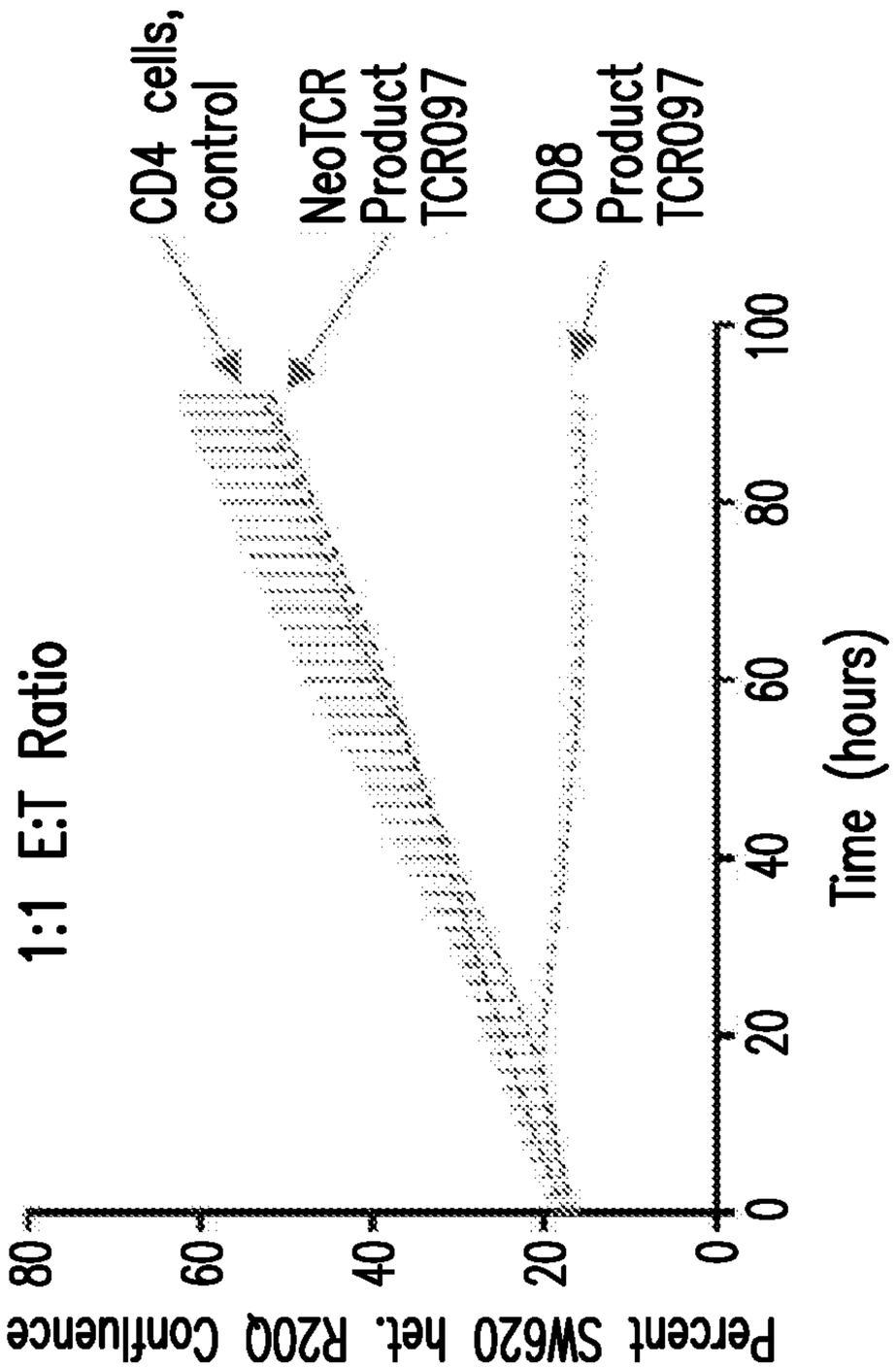


FIGURE 15B

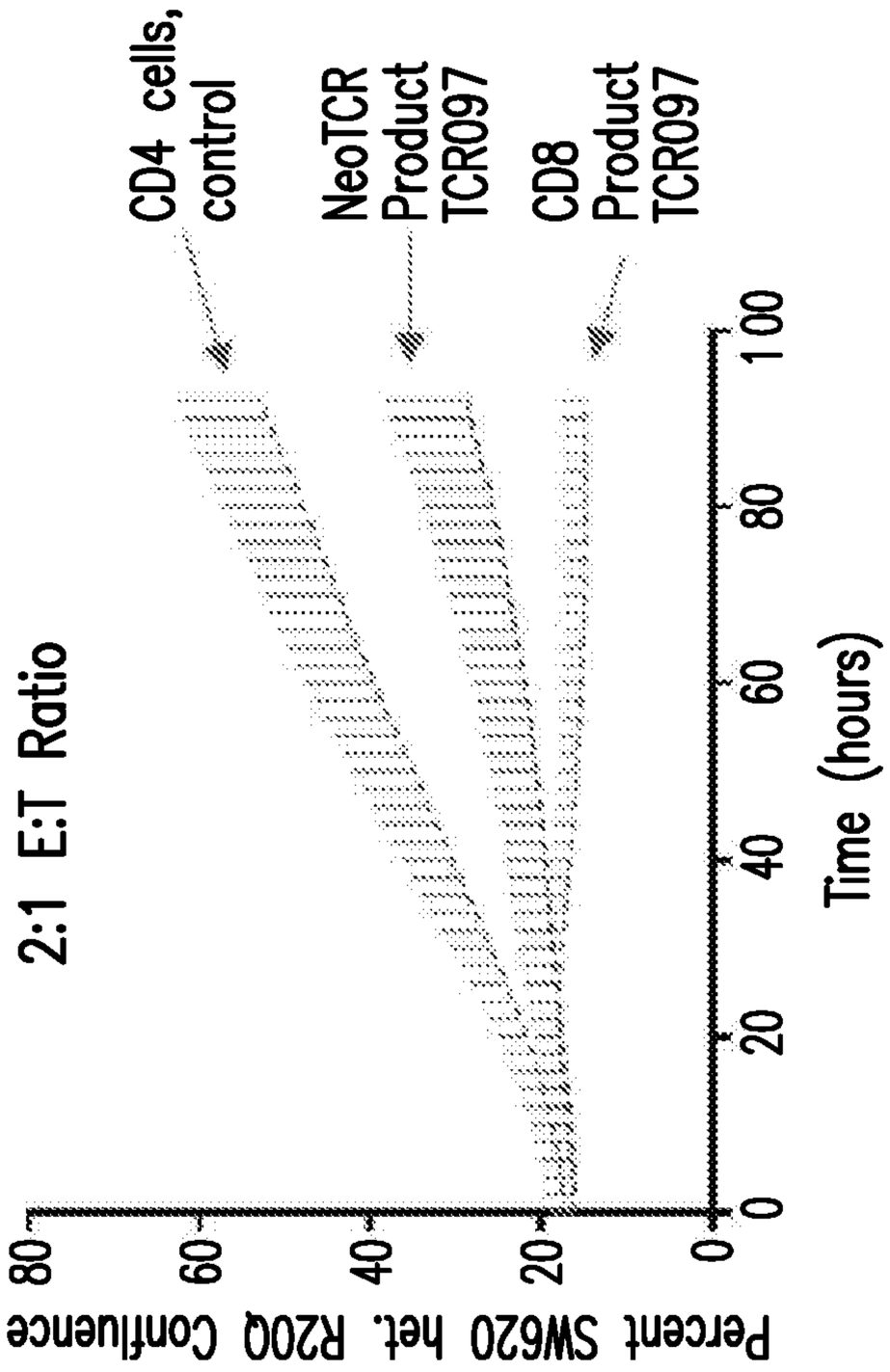


FIGURE 15A

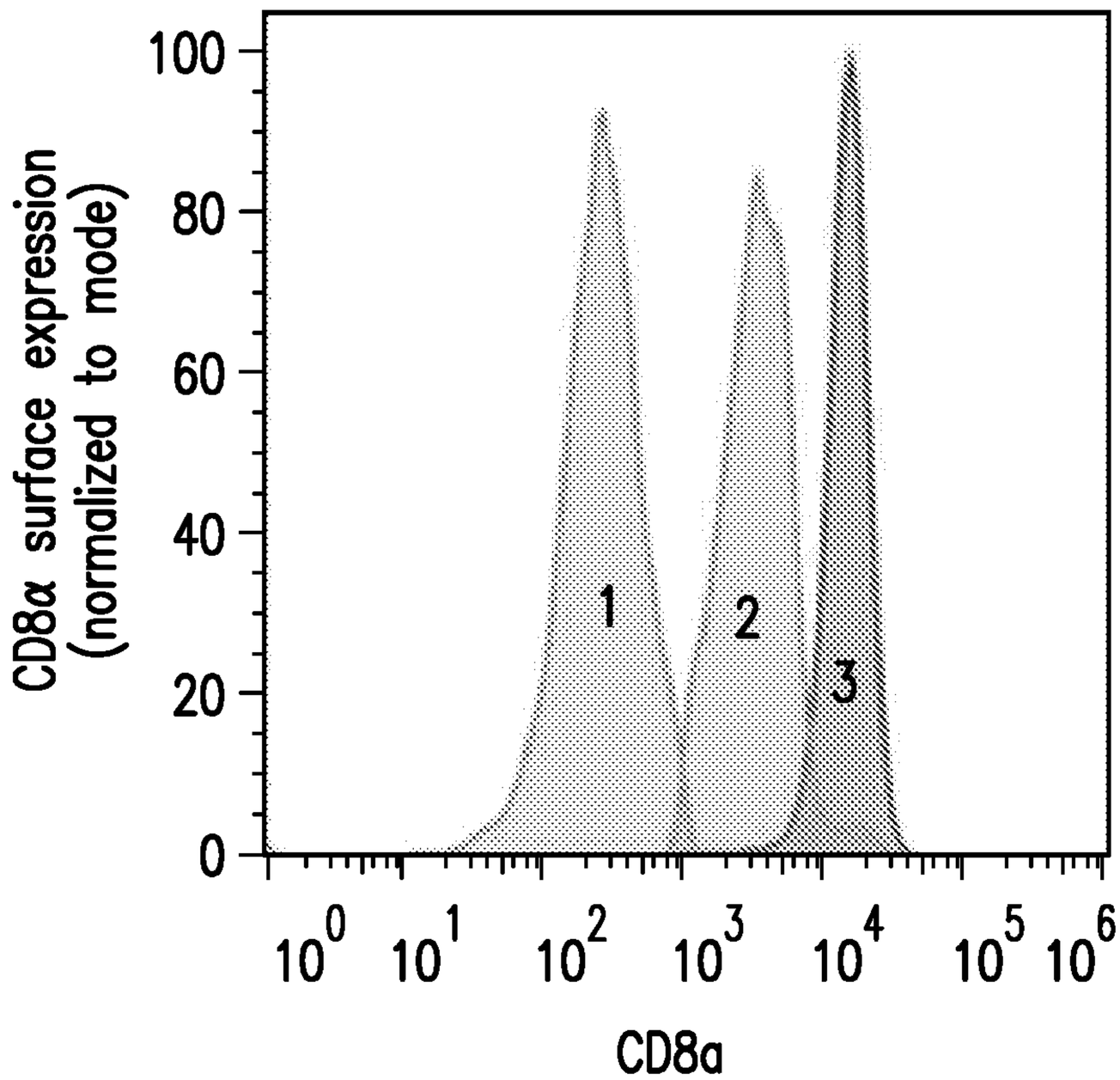

CD8α surface expression
(normalized to mode)
100
80
60
40
20
0
1
2
3
10^0 10^1 10^2 10^3 10^4 10^5 10^6
CD8α

FIGURE 16

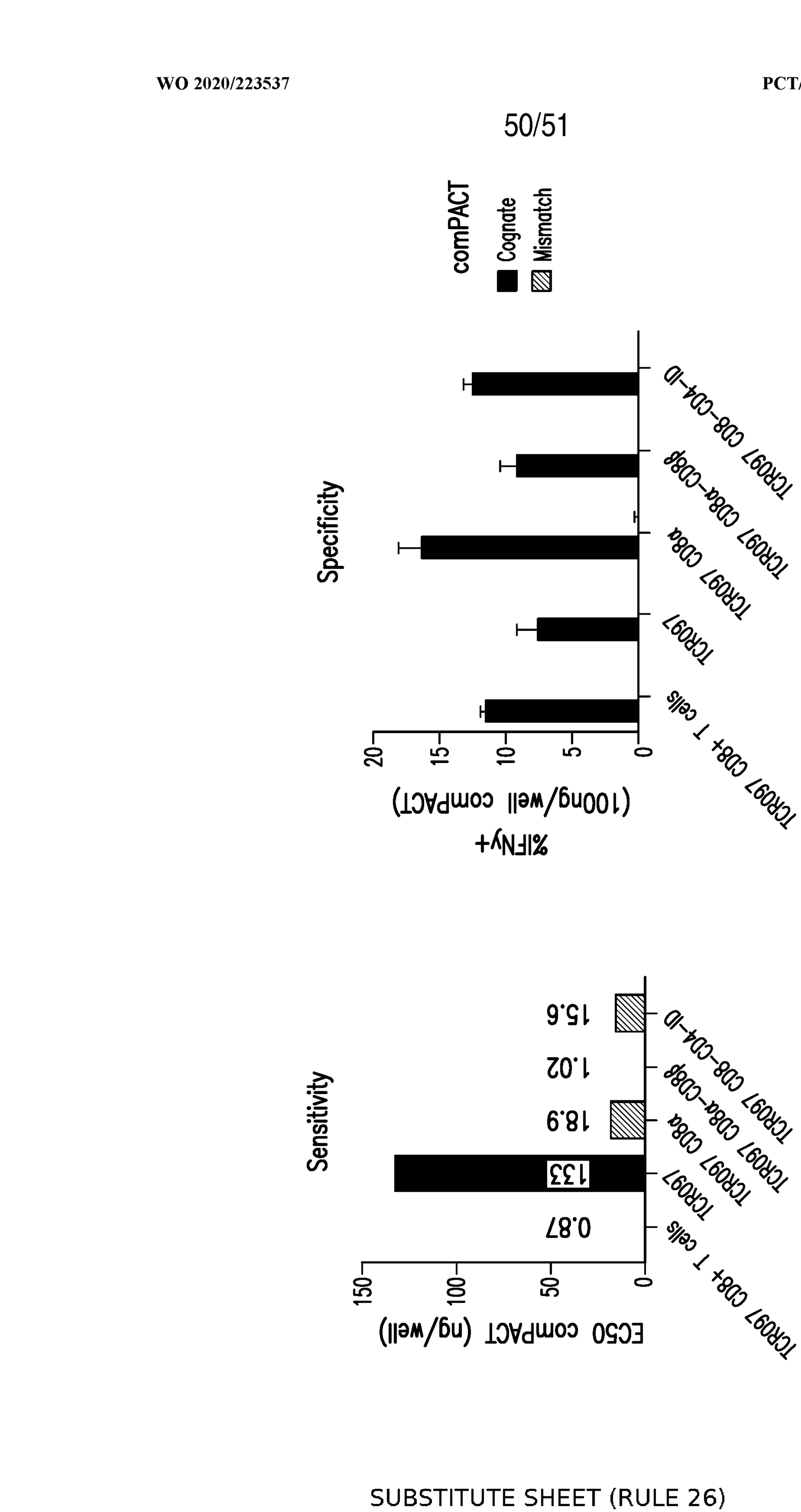


FIGURE 17B

FIGURE 17A

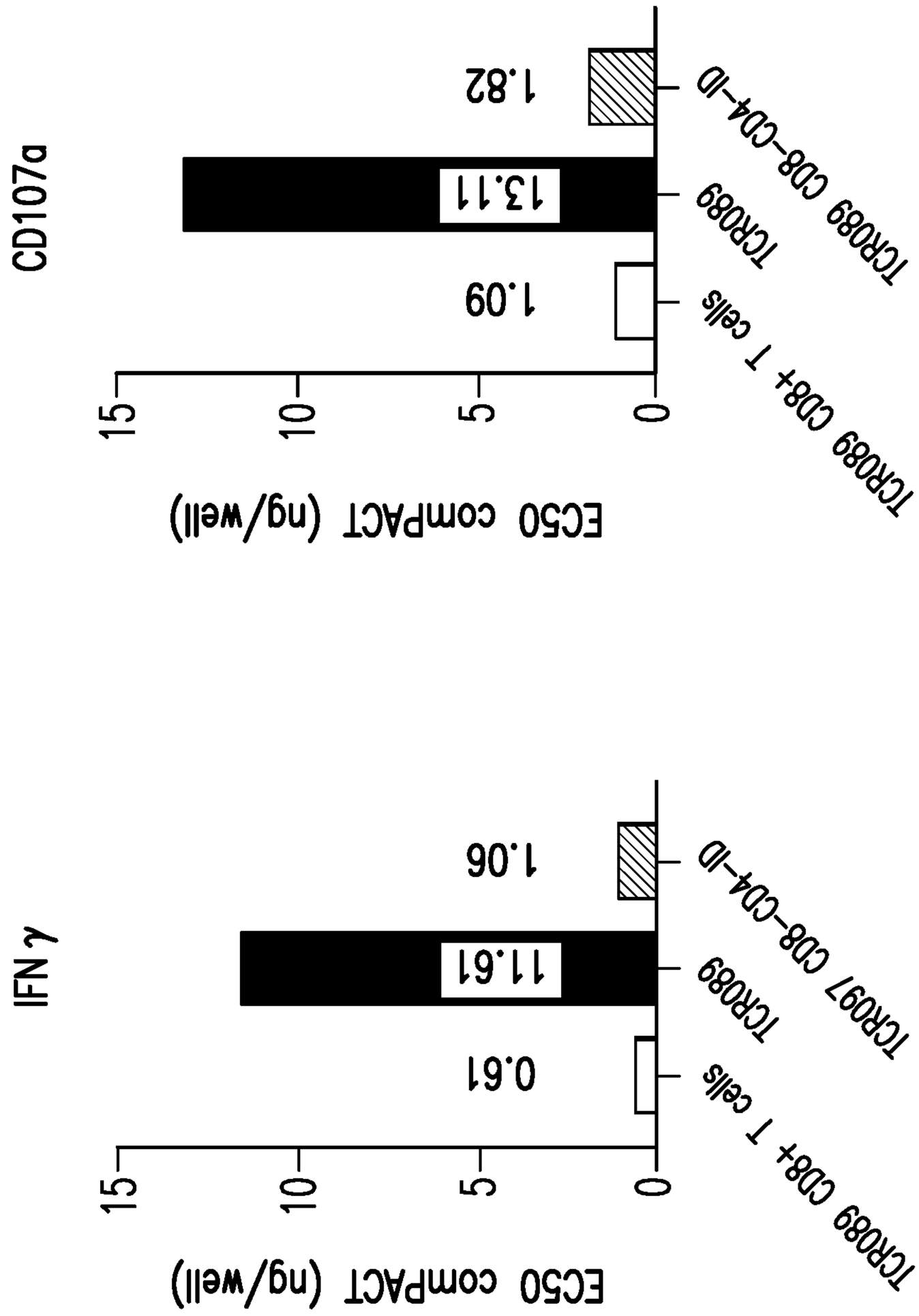

CD107a
1.82
13.11
1.09
TCR089 CD8-CD4-ID
TCR089
TCR089 CD8+ T cells
0
5
10
15
EC50 comPACT (ng/well)
IFN γ
1.06
11.61
0.61
TCR097 CD8-CD4-ID
TCR089
TCR089 CD8+ T cells
0
5
10
15
EC50 comPACT (ng/well)

FIGURE 18