

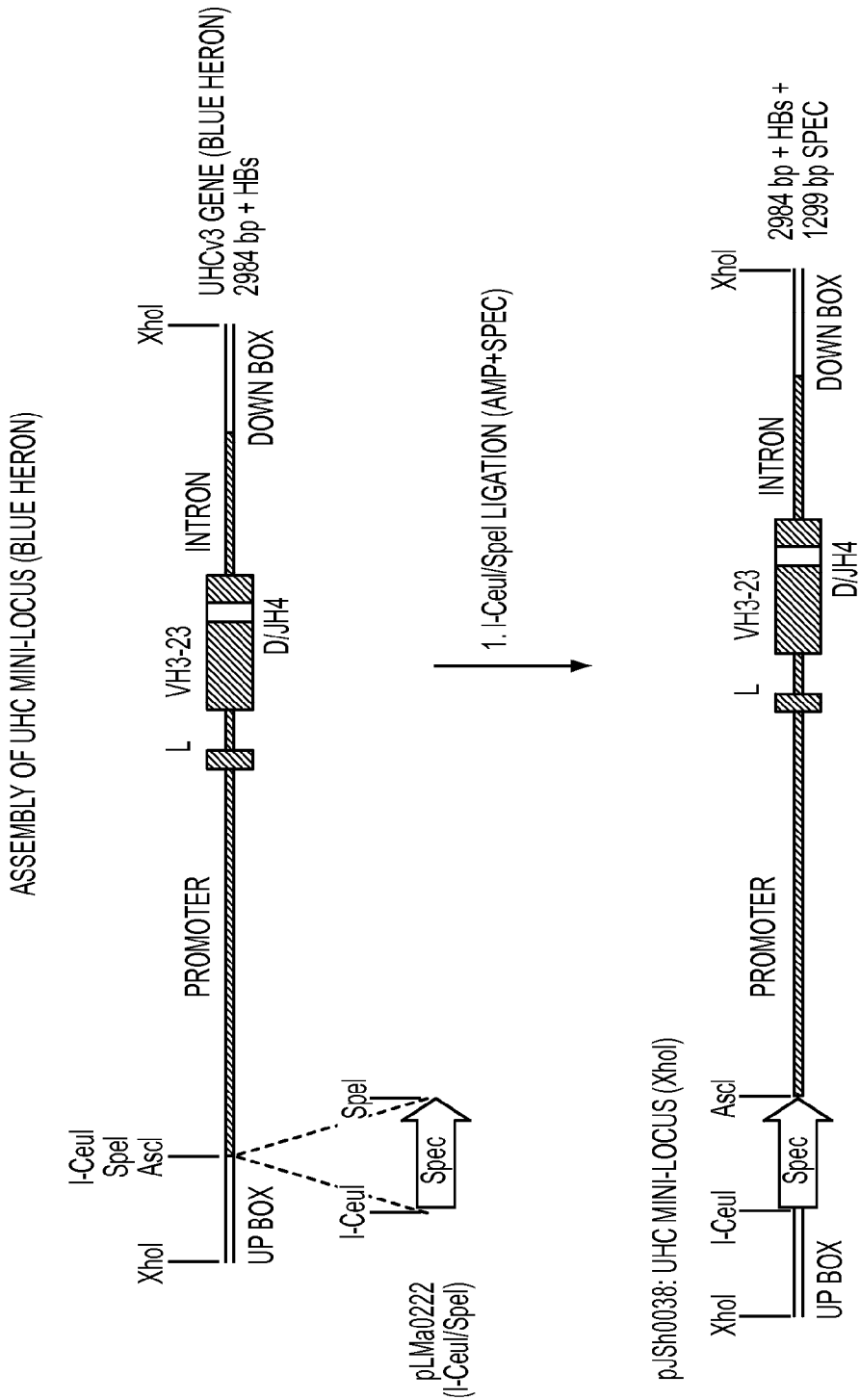


FIG. 1

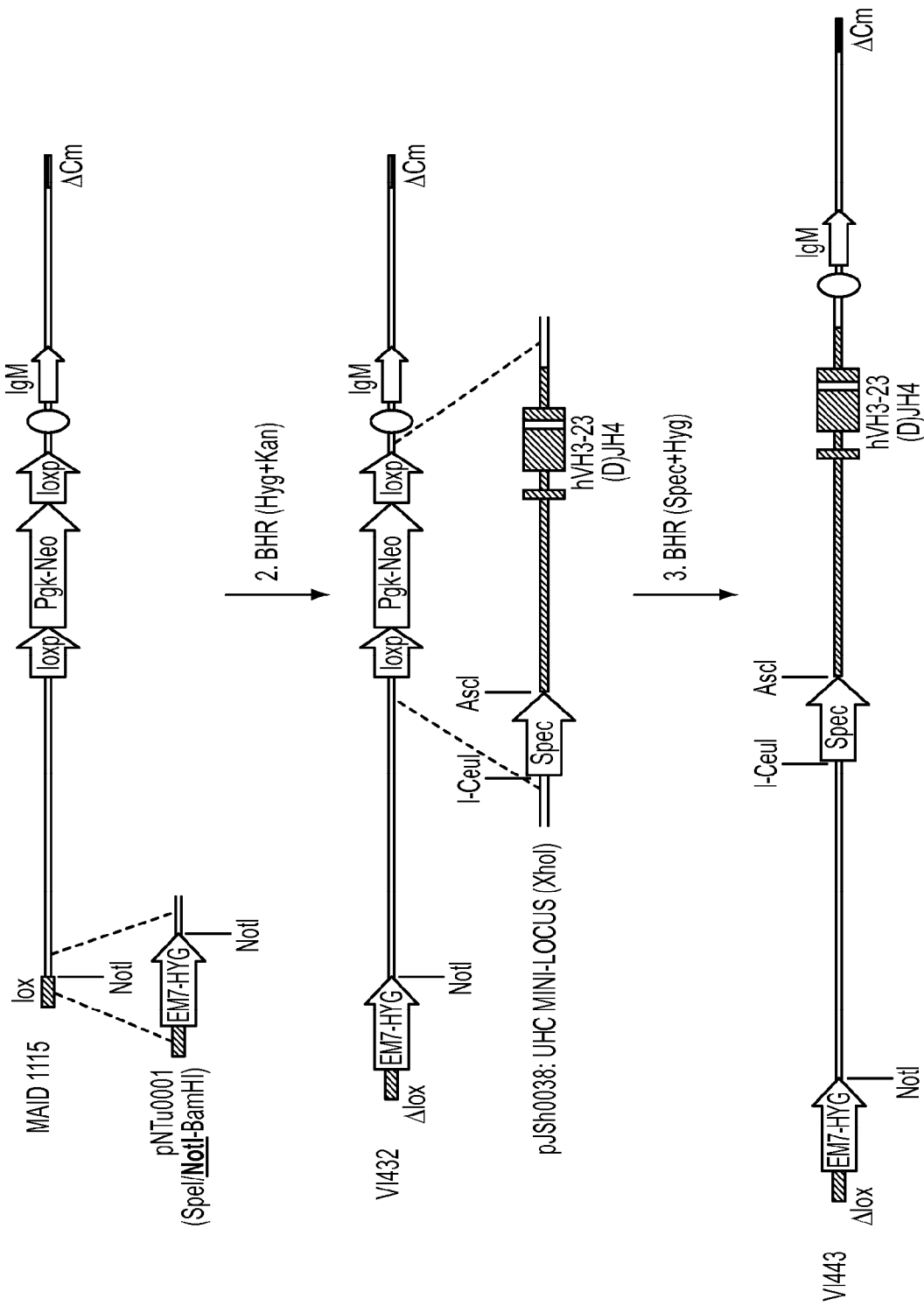


FIG. 2

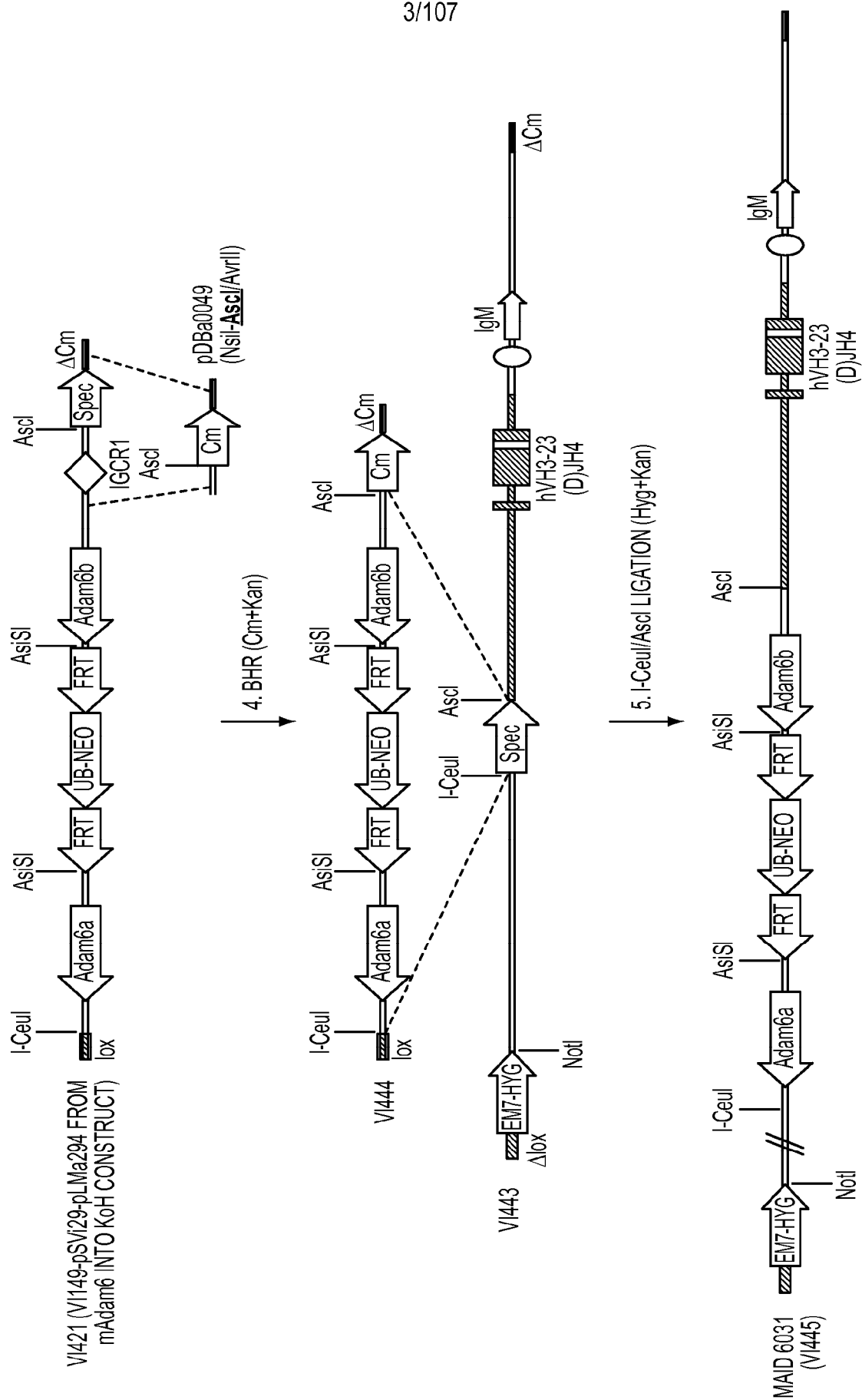
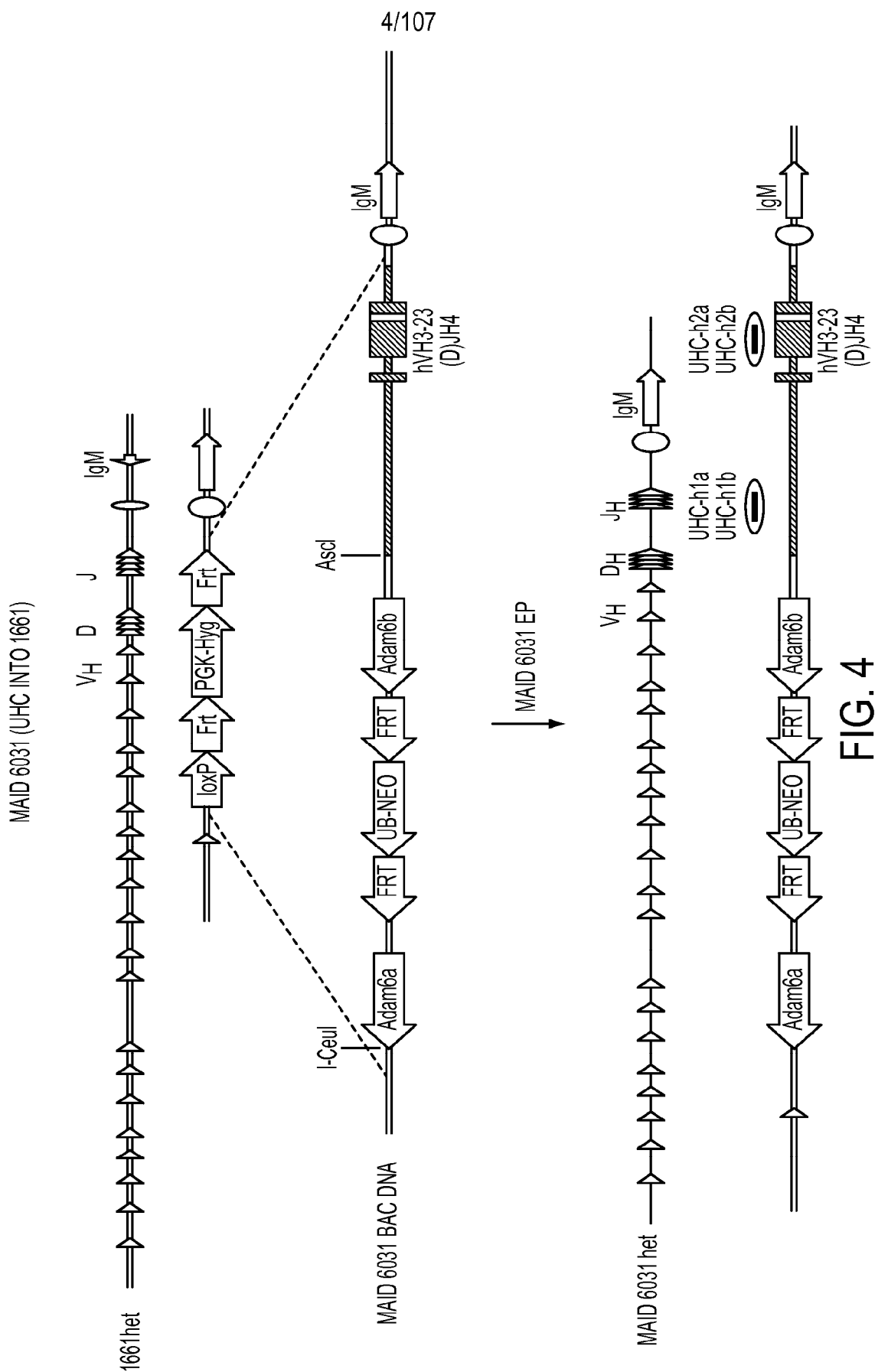


FIG. 3

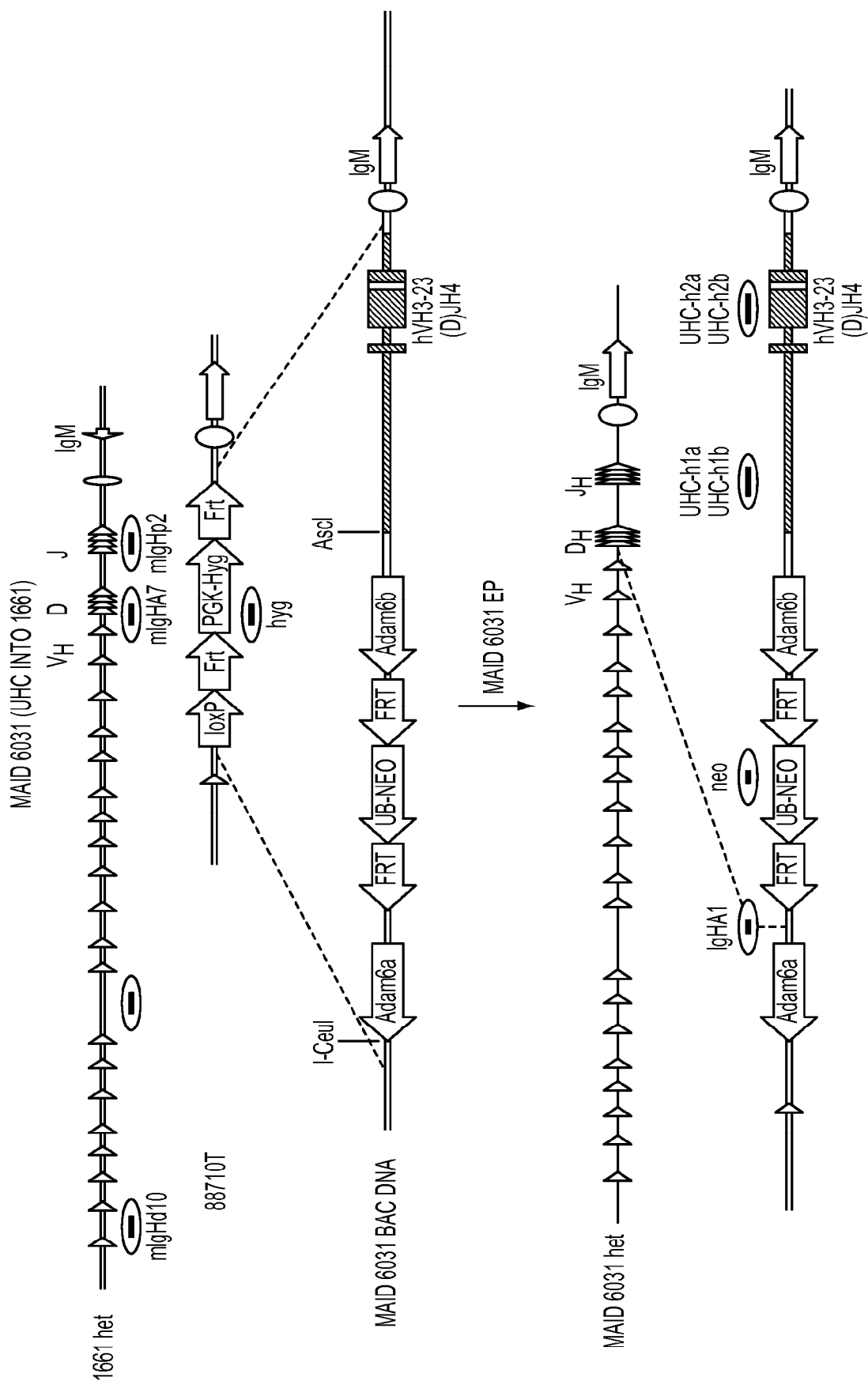


SEARCH OF ASAP DATABASE FOR REGN ANTIBODIES WITH UHC CDR3 SEQUENCE (AKDYSNYYFDY)

| ANTIBODY                         | ANTIGEN | GERMLINE VH | GERMLINE JH | CDR3                        |
|----------------------------------|---------|-------------|-------------|-----------------------------|
| <b>SEARCH WITH DYSN OR YSNY:</b> |         |             |             |                             |
| H1H-136B                         | EGFR    | 3-23*04     | J6*02       | <u>AYDYSNY</u> WDHYGMDV     |
| H4H1789B                         | CD48    | 3-23*04     | J5*02       | <u>AKYSNY</u> DYFDP         |
| H1H962B                          | GDF8    | 3-33*04     | J6*02       | <u>AKYSNY</u> GYYNGLDV      |
| H2M744H                          | ANG2    | 1-18*01     | J5*02       | <u>ARDQDYSN</u> FHWLDP      |
| H1M1981                          | CA9     | 4-31*03     | J6*02       | <u>ARESHYSN</u> YEDYYYIGMDV |
| <b>SEARCH WITH AKDY:</b>         |         |             |             |                             |
| H4H381B                          | NAV1.7  | 3-23*04     | J4*02       | <u>AKDY</u> YGPFDY          |
| H1H1058B                         | NAV1.7  | 3-23*04     | J4*02       | <u>AKDY</u> CNSTYYYGED      |
| <b>SEARCH WITH YYFDY:</b>        |         |             |             |                             |
| H1H2002B                         | CA9     | 3-23*01     | J4*02       | <u>AKGY</u> YFDY            |
| H1H2221B                         | CA9     | 3-23*04     | J4*02       | <u>AI</u> GYFDY             |
| H1H2225B                         | CA9     | 3-33*04     | J4*02       | <u>AKGY</u> YFDY            |

FIG. 5

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MAID 6031 (ULC INTO 1661)

| ASSAY    | PROBE NAME     | 1° | CONFIRMATION | RECONFIRMATION | PARENTAL (1661het) | F1H4 | COPY# MODIF ALLELE | COPY# WT ALLELE |
|----------|----------------|----|--------------|----------------|--------------------|------|--------------------|-----------------|
| LOA      | hyg            | 0  | 0            | 0              | 1                  | 0    | 0                  | 0               |
|          | UHC-h1a OR h1b | 1  | 1            | 1              | 0                  | 0    | 1                  | 0               |
|          | UHC-h2a OR h2b | 1  | 1            | 1              | 0                  | 0    | 1                  | 0               |
|          | mlgHA1         | 2  | 2            | 2              | 1                  | 2    | 1                  | 1               |
|          | neo            |    |              | 1              | 0                  | 0    | 1                  | 0               |
| PARENTAL | mlgHd10        |    |              | 1              | 1                  | 2    | 0                  | 1               |
|          | 88710T         |    |              | 1              | 1                  | 2    | 0                  | 1               |
|          | mlgHA7         |    |              | 1              | 1                  | 2    | 0                  | 1               |
|          | mlgHp2         |    |              | 1              | 1                  | 2    | 0                  | 1               |

GENOTYPE 6031het

FIG. 7

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PROBES FOR MAID 6031 (UHC INTO 1661)

| NAME    | FORWARD PRIMER                                   | PROBE                                                 | REVERSE PRIMER                                 | TYPE OF PROBE | ASSAY    | LOCATION (bp POSITION IN UHC) |
|---------|--------------------------------------------------|-------------------------------------------------------|------------------------------------------------|---------------|----------|-------------------------------|
| hyg     | TGCGGCGGATCTTTAGCC<br>(SEQ ID NO: 151)           | ACGAGCGGGTTGGGCCCAATTC<br>(SEQ ID NO: 152)            | TTGACCGATTCTTGGCG<br>(SEQ ID NO: 153)          | BHQ-1         | LOA      |                               |
| UHC-h1a | TCAGGTGTGATGCTGATCCA<br>(SEQ ID NO: 154)         | TGCATCTTCTCCCAATTCCTGGTA<br>(SEQ ID NO: 155)          | TGGCTGCTGGGAGAAGATTG<br>(SEQ ID NO: 156)       | BHQ-1         | GOA      | hVH3-23 PROMOTER<br>(202-296) |
| UHC-h1b | CCGAGCAGCCACTATGTC<br>(SEQ ID NO: 157)           | TCCCACTGATGTCTTTCAGCTTCCTC<br>(SEQ ID NO: 158)        | CCCTCAGGAATAACAGACTCATC<br>(SEQ ID NO: 159)    | BHQ-1         | GOA      | hVH3-23 PROMOTER<br>(368-474) |
| UHC-h2a | AAGGCGGGTTCACCATCT<br>(SEQ ID NO: 160)           | CCAGAGACAATTCCAAGACACGCTG<br>(SEQ ID NO: 161)         | CGGCTCTCAGGCTGTTC<br>(SEQ ID NO: 162)          | BHQ-1         | GOA      | hVH3-23 EXON<br>(2592-2664)   |
| UHC-h2b | GCAGCCTCTGGATTCACCTT<br>(SEQ ID NO: 163)         | AGCAACTCTCCAATGAGCTGGGTC<br>(SEQ ID NO: 164)          | TCACGGAGTCTCGTAGAATG<br>(SEQ ID NO: 165)       | BHQ-1         | GOA      | hVH3-23 EXON<br>(2466-2592)   |
| mighA1  | CTCAGTGATTTCTGGCCCTGC<br>(SEQ ID NO: 166)        | TGCTCCACAGCTACAAACCCCTTCCCTATAATG<br>(SEQ ID NO: 167) | GGATGATGGCTCAGCACAGAG<br>(SEQ ID NO: 168)      |               | GOA      | mAdan6a                       |
| neo     | GGTGGAGAGGCTATTGGC<br>(SEQ ID NO: 169)           | TGGGCACAACAGACAATCGGCTG<br>(SEQ ID NO: 170)           | GAACACGGCGGCATCAG<br>(SEQ ID NO: 171)          | BHQ-1         | GOA      |                               |
| mighD10 | GGTGTGCGATGTACCCCTCTGAAC<br>(SEQ ID NO: 172)     | CTAAAAATGCTACACCTGGGGCAAAACACCTG<br>(SEQ ID NO: 173)  | TGTGGCAGTTTAAATCCAGCTTTATC<br>(SEQ ID NO: 174) |               | PARENTAL | mighDISTAL V                  |
| 887-10  | GATGGGAAGAGACTGGTAACATTTGTAC<br>(SEQ ID NO: 175) | CCTCCACTGTGTAAATGGCTGCCACAA<br>(SEQ ID NO: 176)       | TTCTCTATTTCACTCTTTGAGGCTC<br>(SEQ ID NO: 177)  |               | PARENTAL | mighV                         |
| mighA7  | TGGTCACCTCCAGGAGGCTC<br>(SEQ ID NO: 178)         | AGTCTCTGCTTCCCCCTTGTGGCTATGAGC<br>(SEQ ID NO: 179)    | GCTGCAGGGTGTATCAGGTGC<br>(SEQ ID NO: 180)      | BHQ-1         | PARENTAL | mAdan6b                       |
| mighr2  | GCCATGCAAGGCCAAGC<br>(SEQ ID NO: 181)            | CCAGGAAATGCTGCCAGAGCCTG<br>(SEQ ID NO: 182)           | AGTTCTTGAGCCTTAGGGTGCTAG<br>(SEQ ID NO: 183)   | BHQ-1         | PARENTAL | mighD-J                       |

FIG. 8

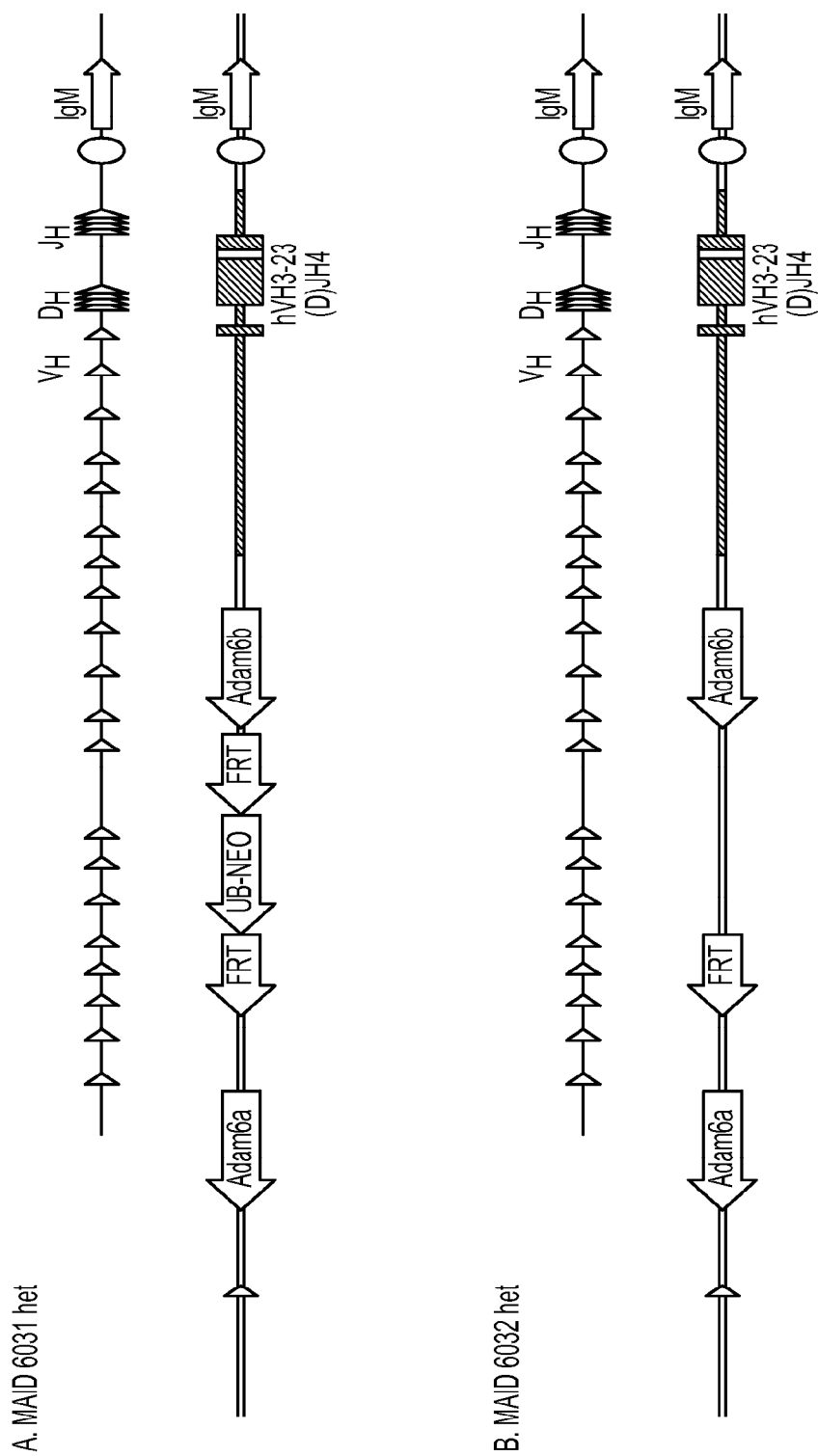


FIG. 9

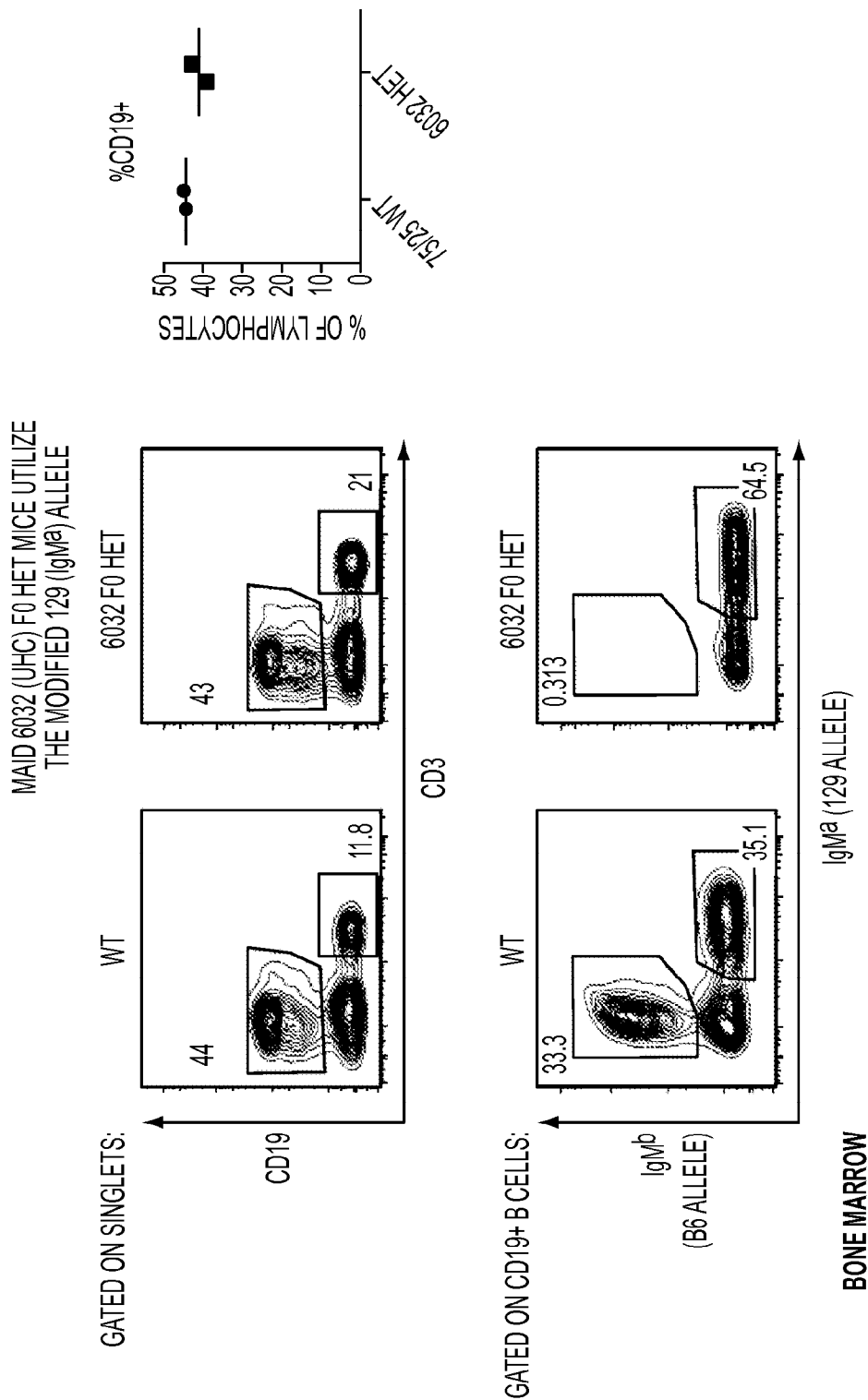


FIG. 10

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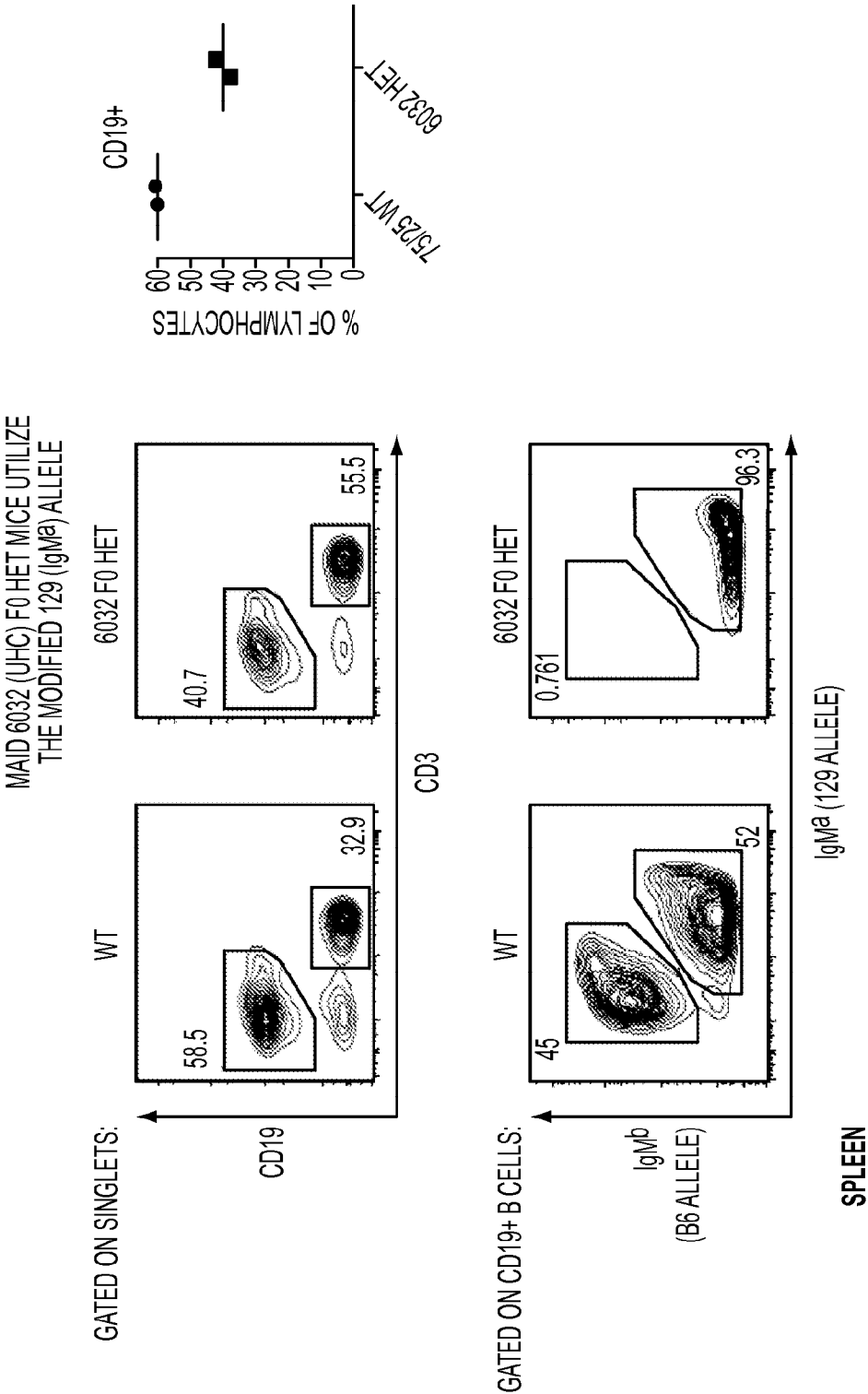


FIG. 11

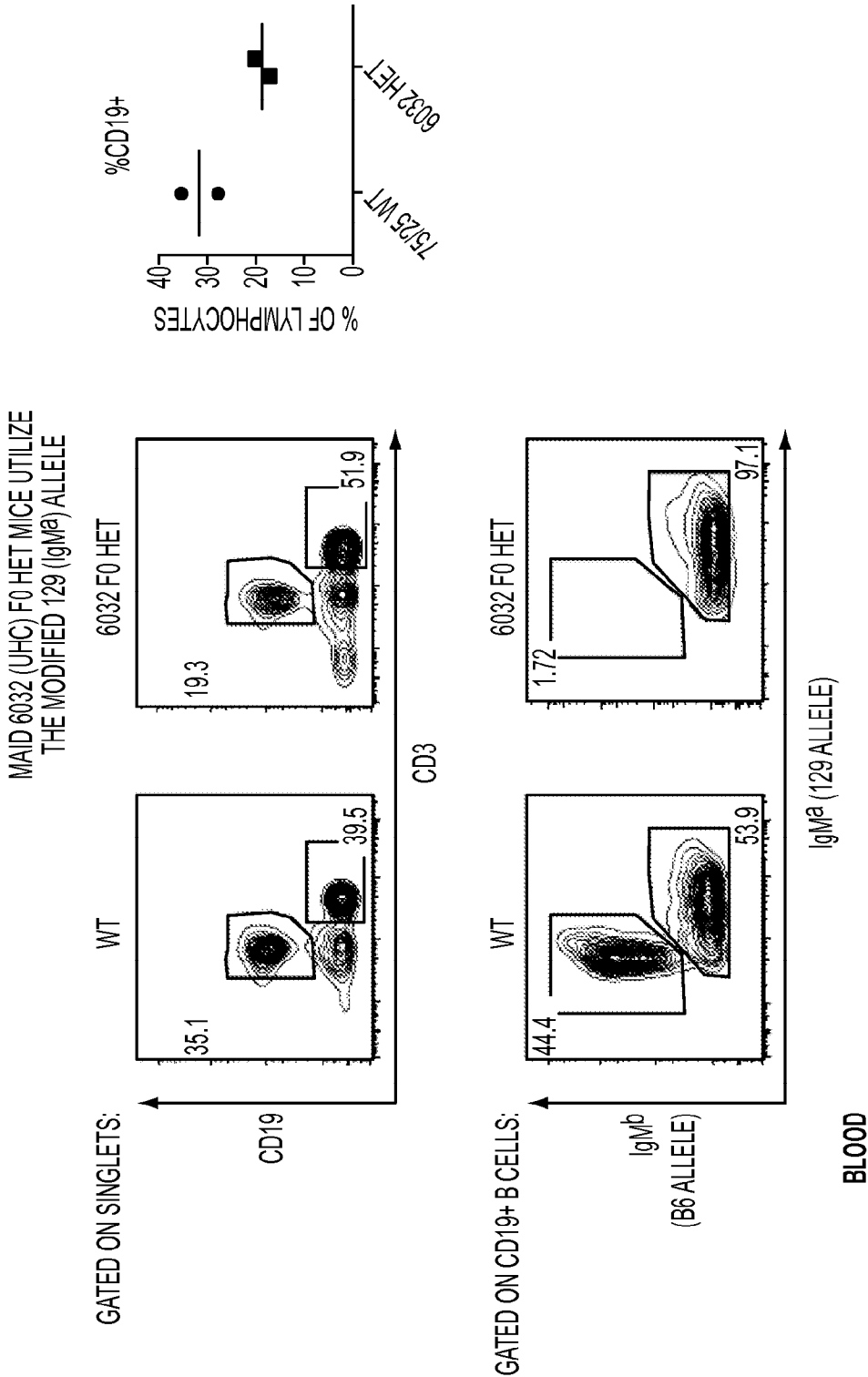


FIG. 12

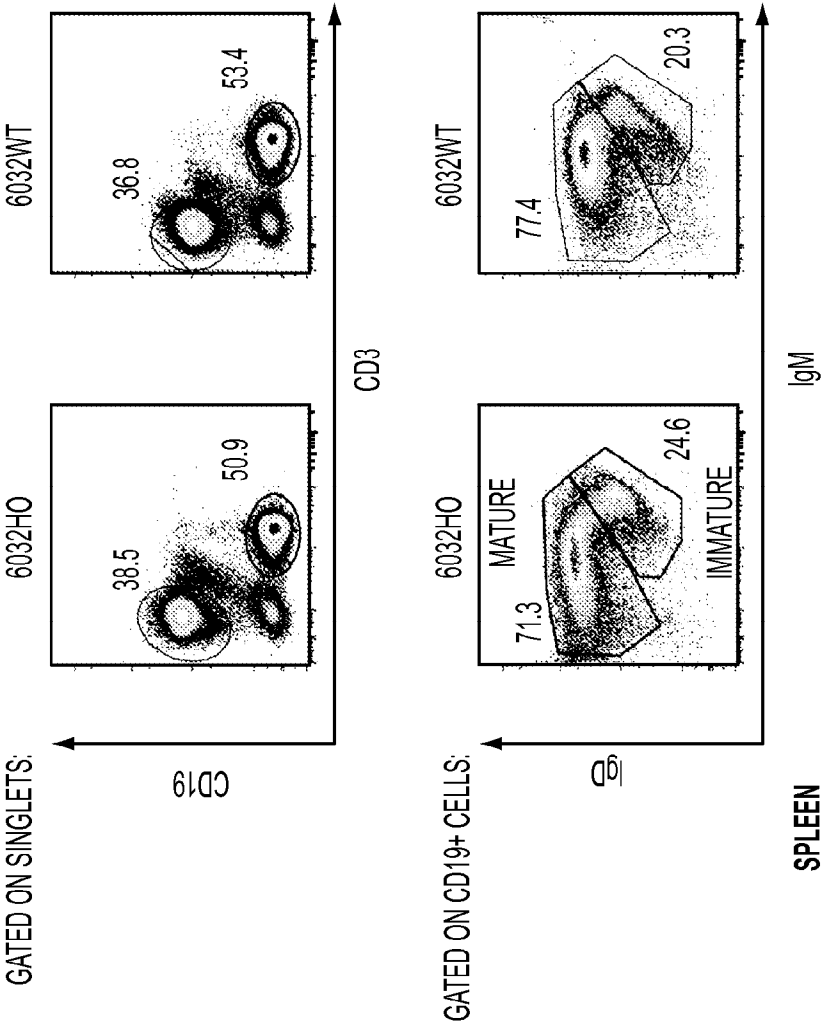


FIG. 13A

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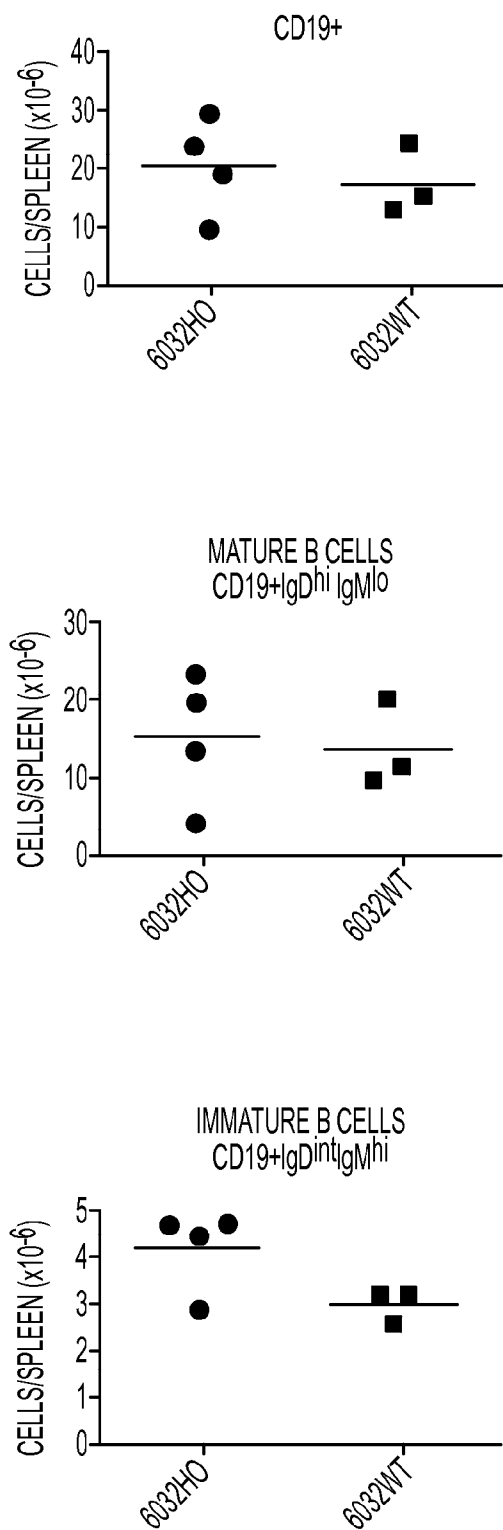


FIG. 13B

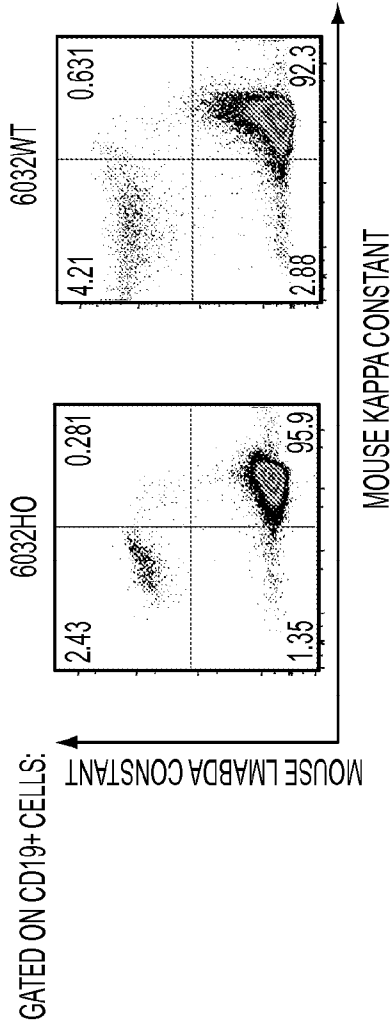


FIG. 13C

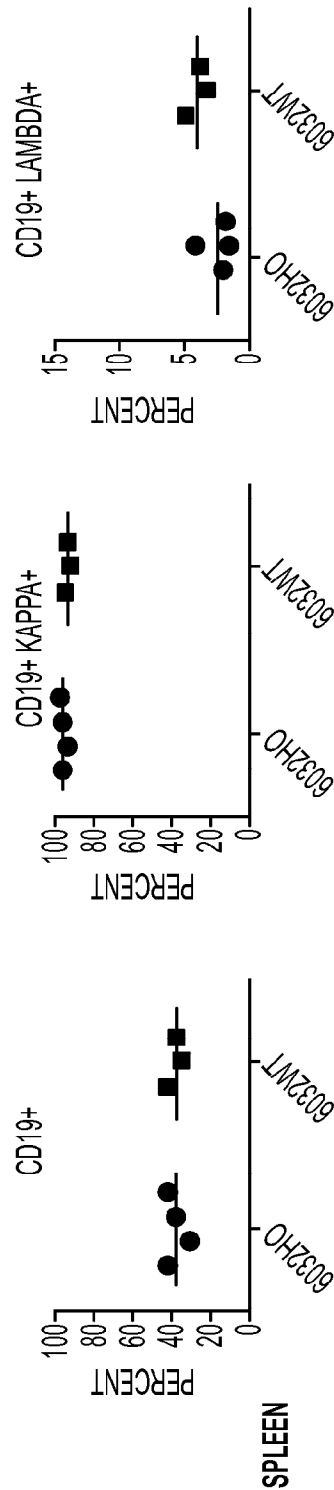


FIG. 13D

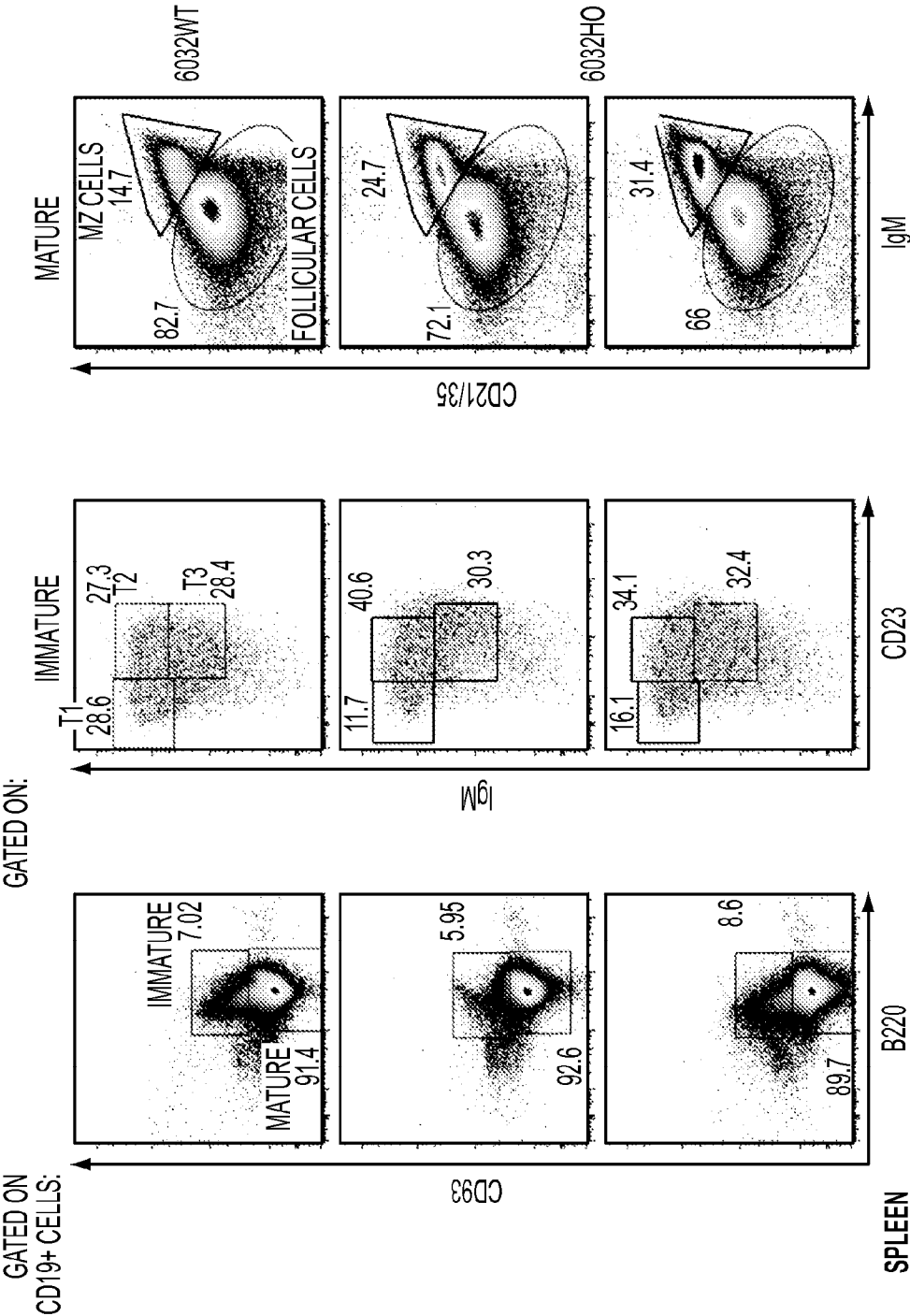


FIG. 13E

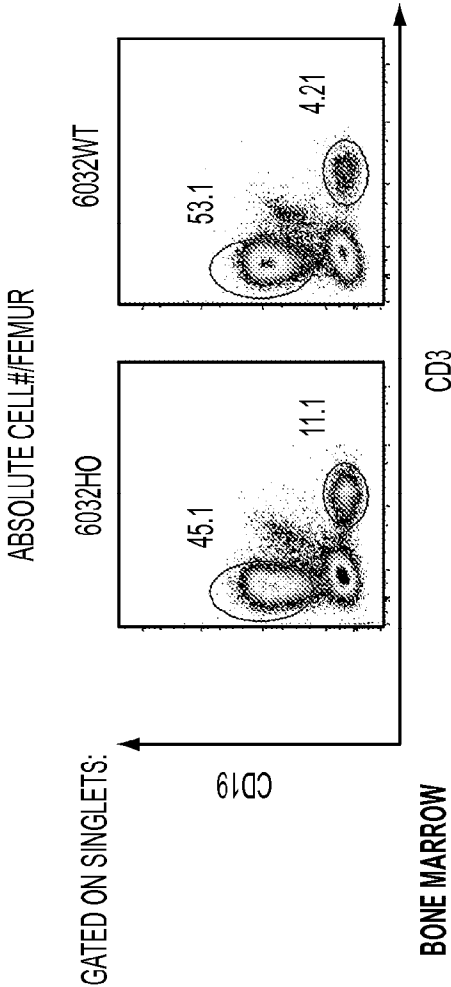


FIG. 14A

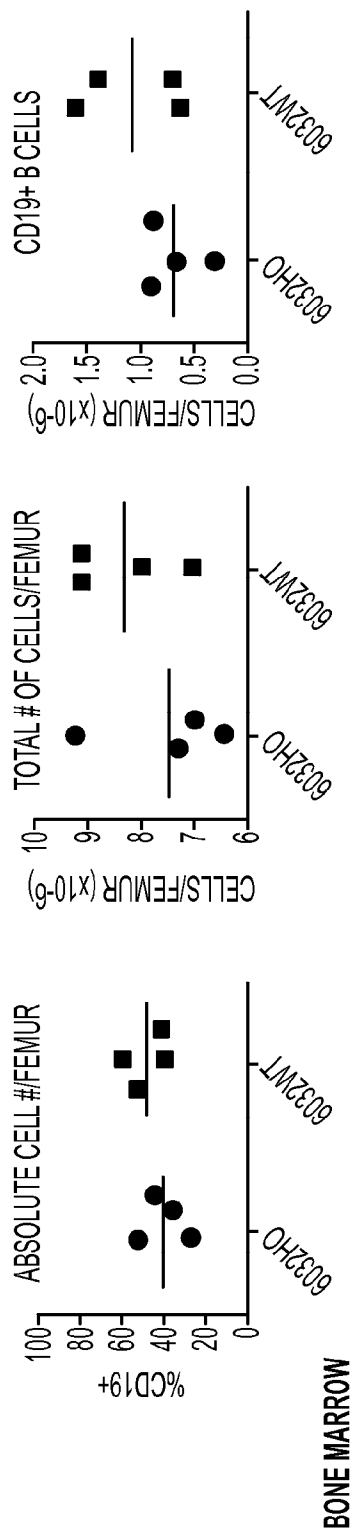


FIG. 14B

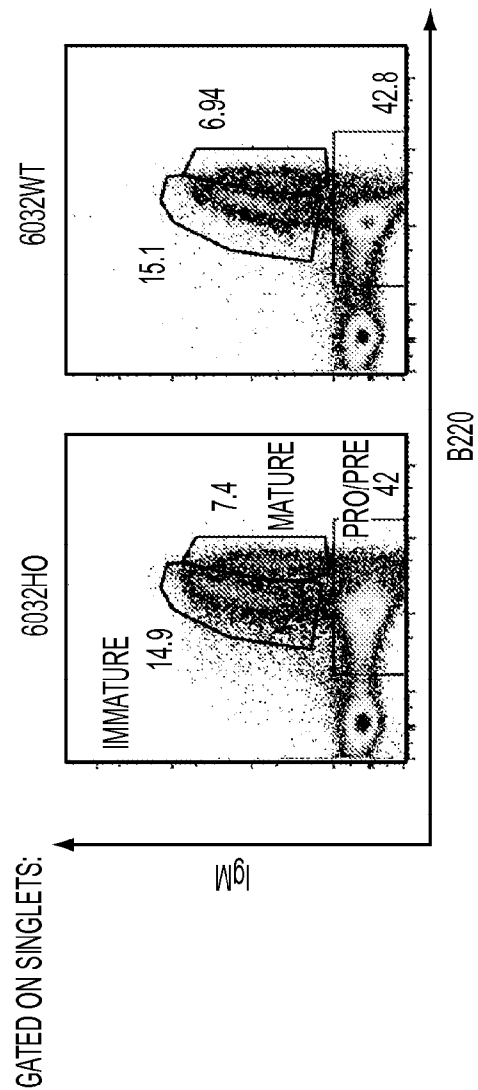


FIG. 14C

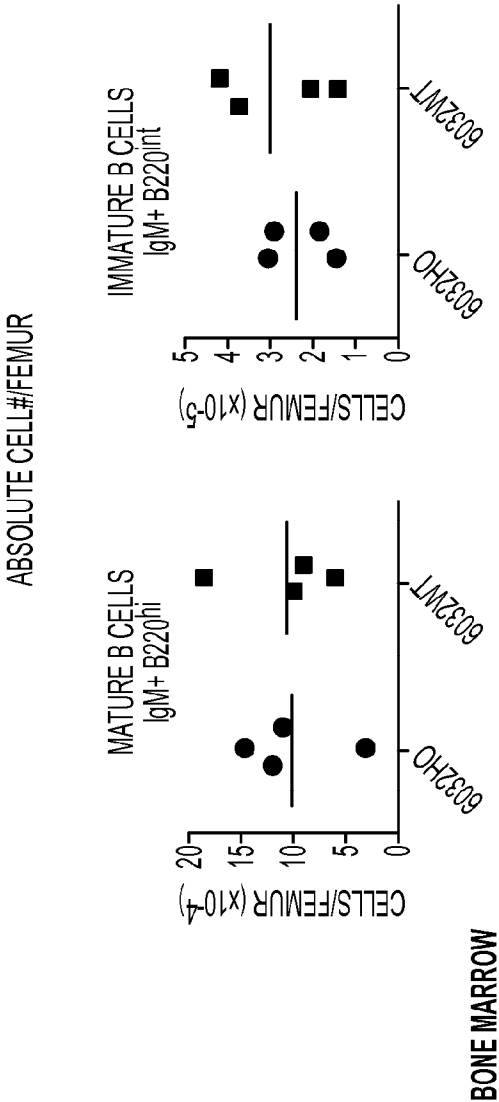


FIG. 14D

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GATED ON SINGLET:

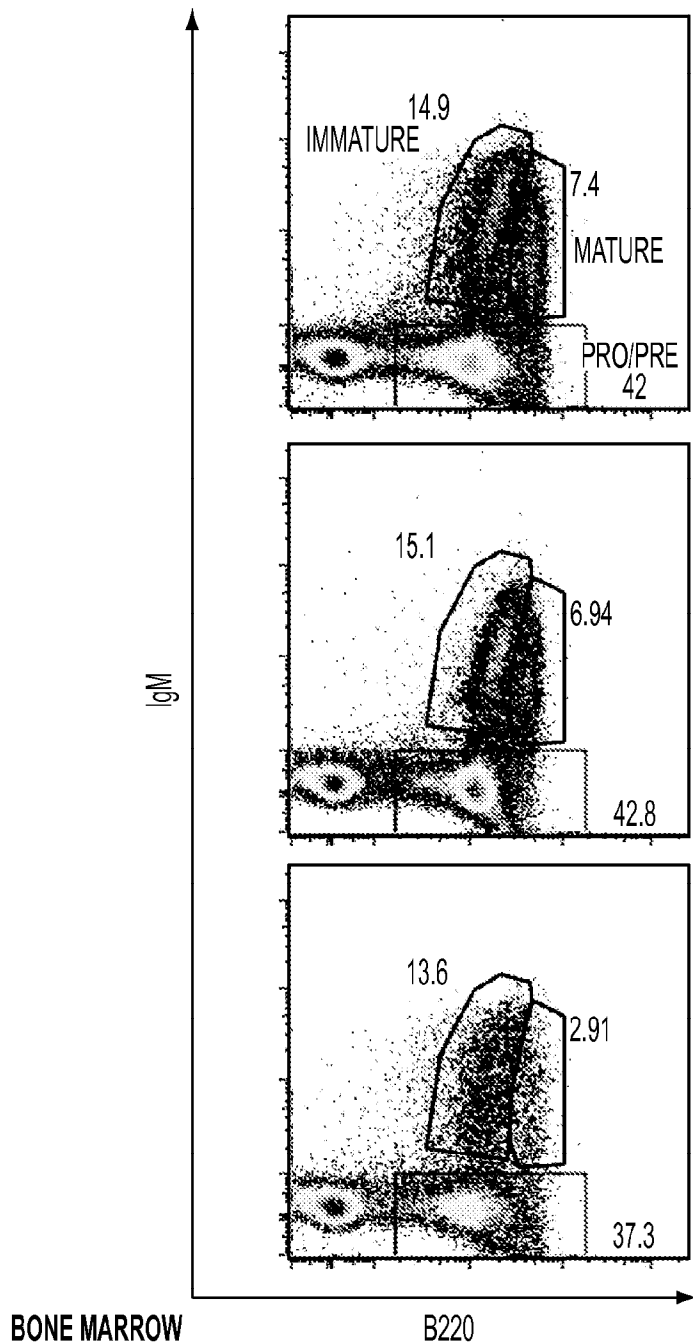


FIG. 14E

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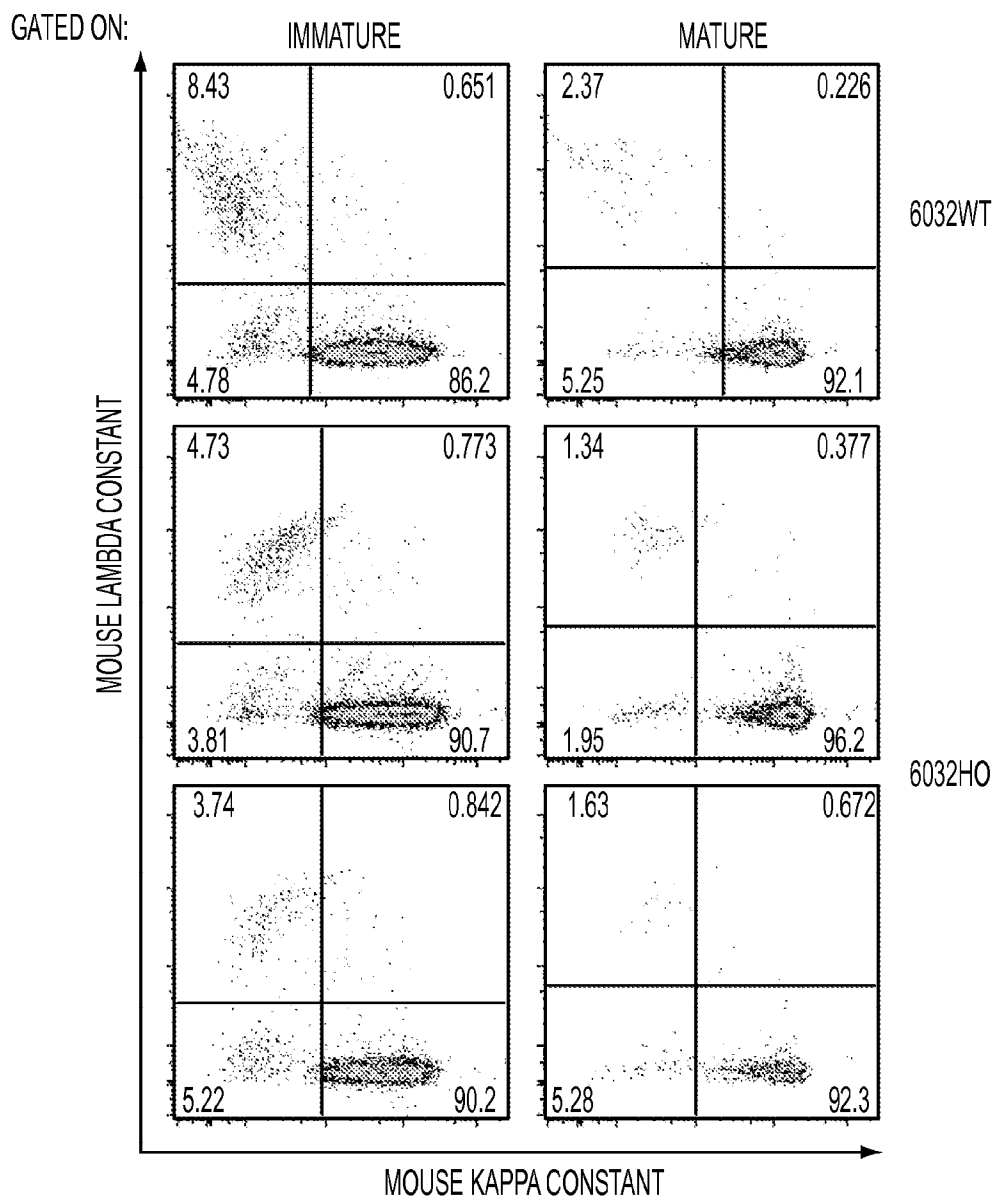


FIG. 14F

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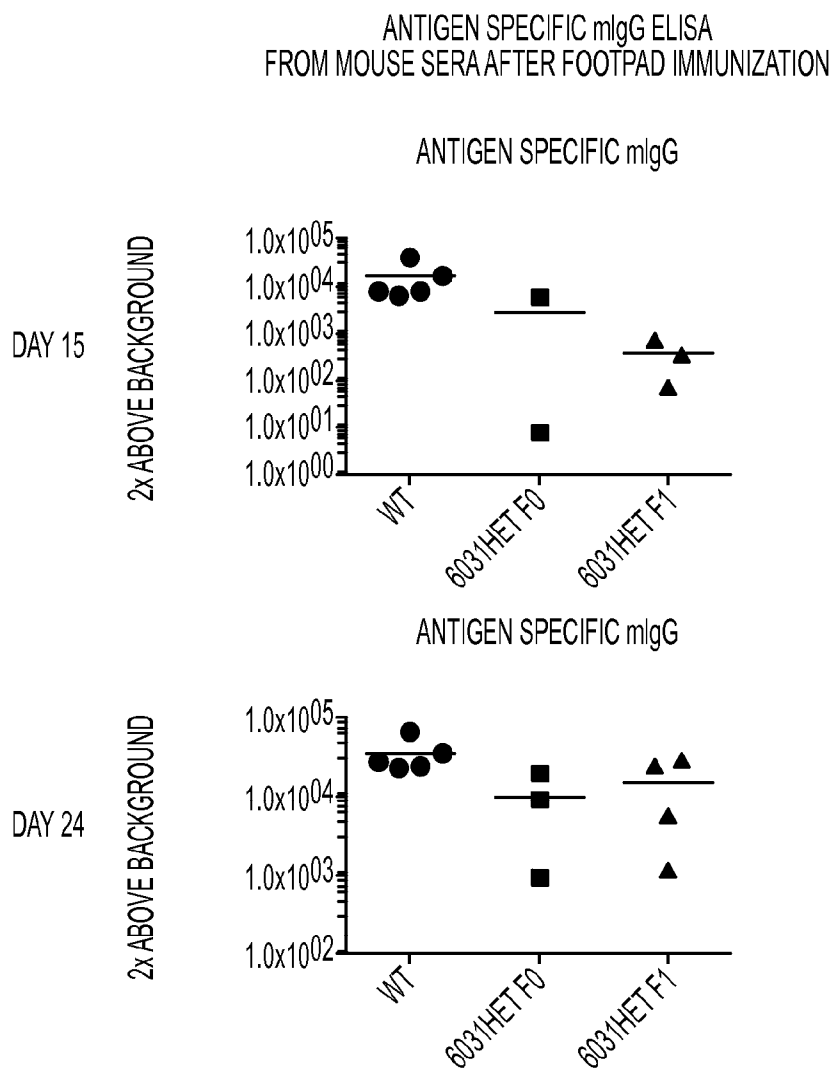


FIG. 15

[illegible]

SUBSTITUTE SHEET (RULE 26)

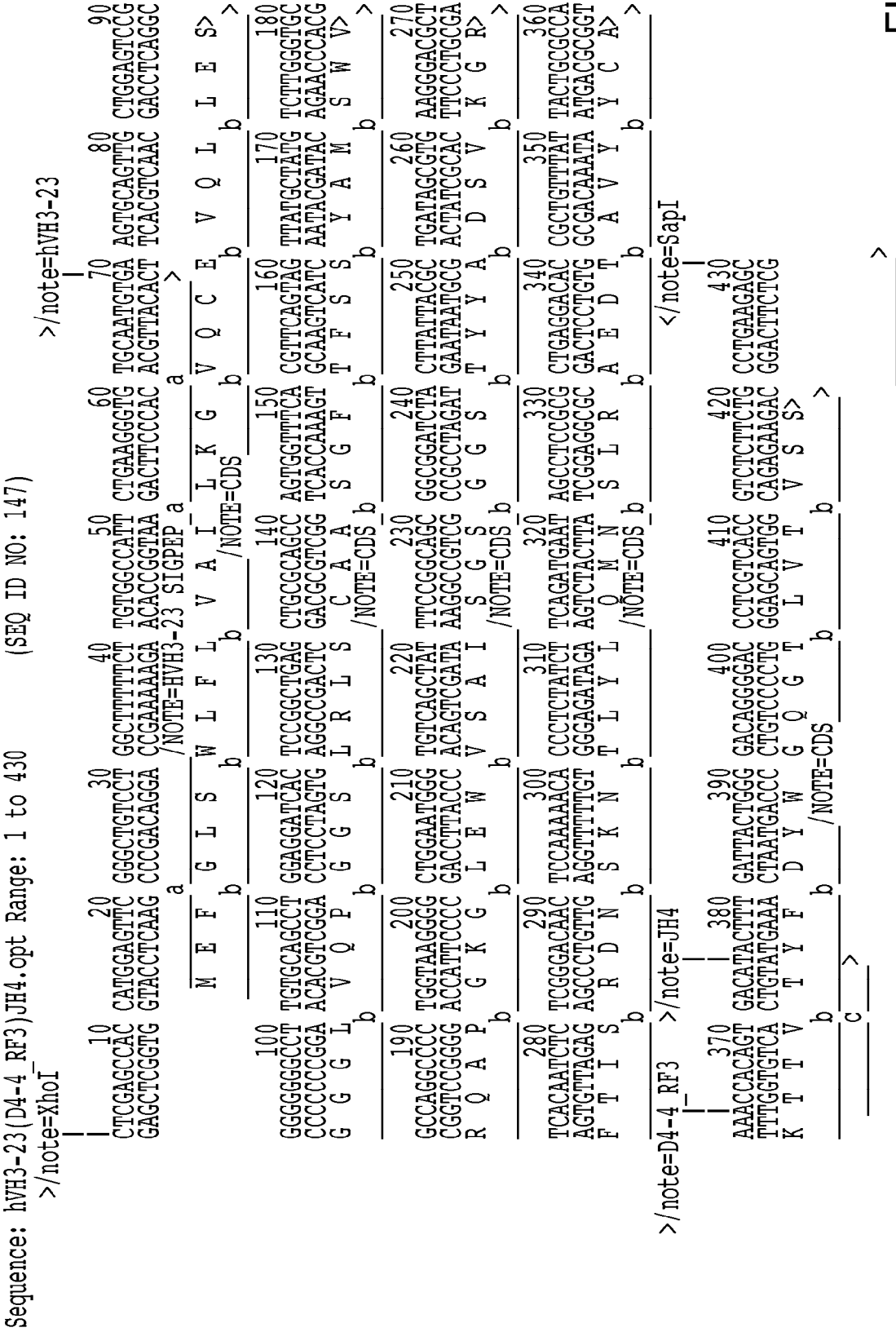


FIG. 18

SUBSTITUTE SHEET (RULE 26)

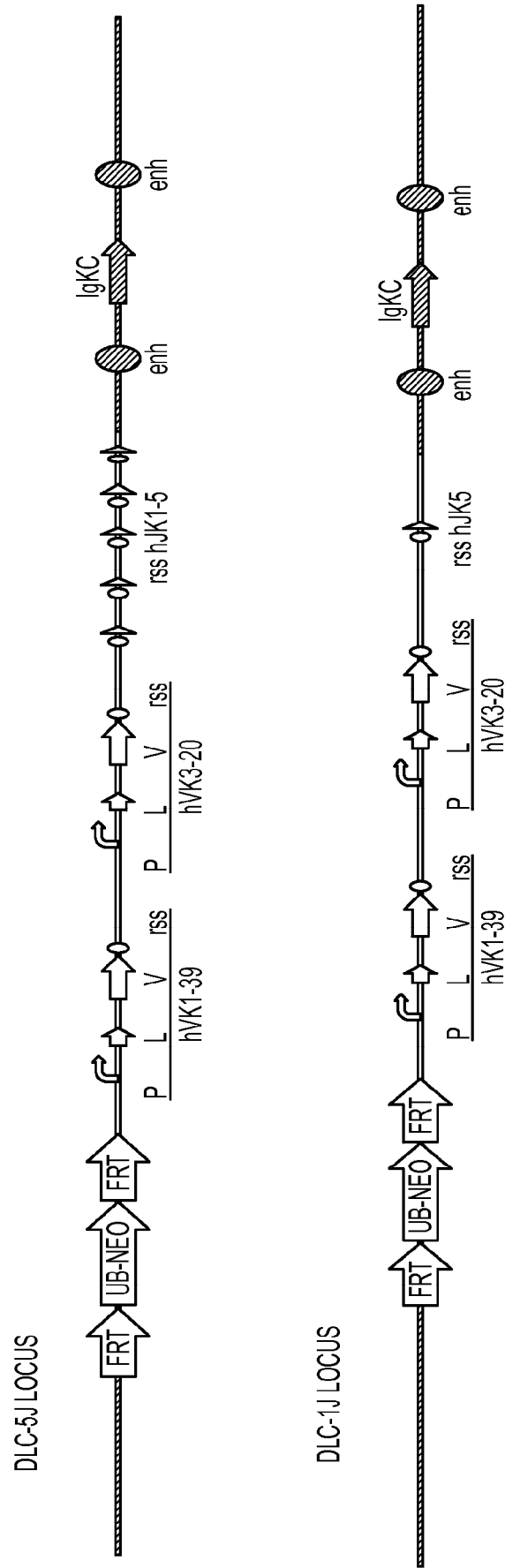
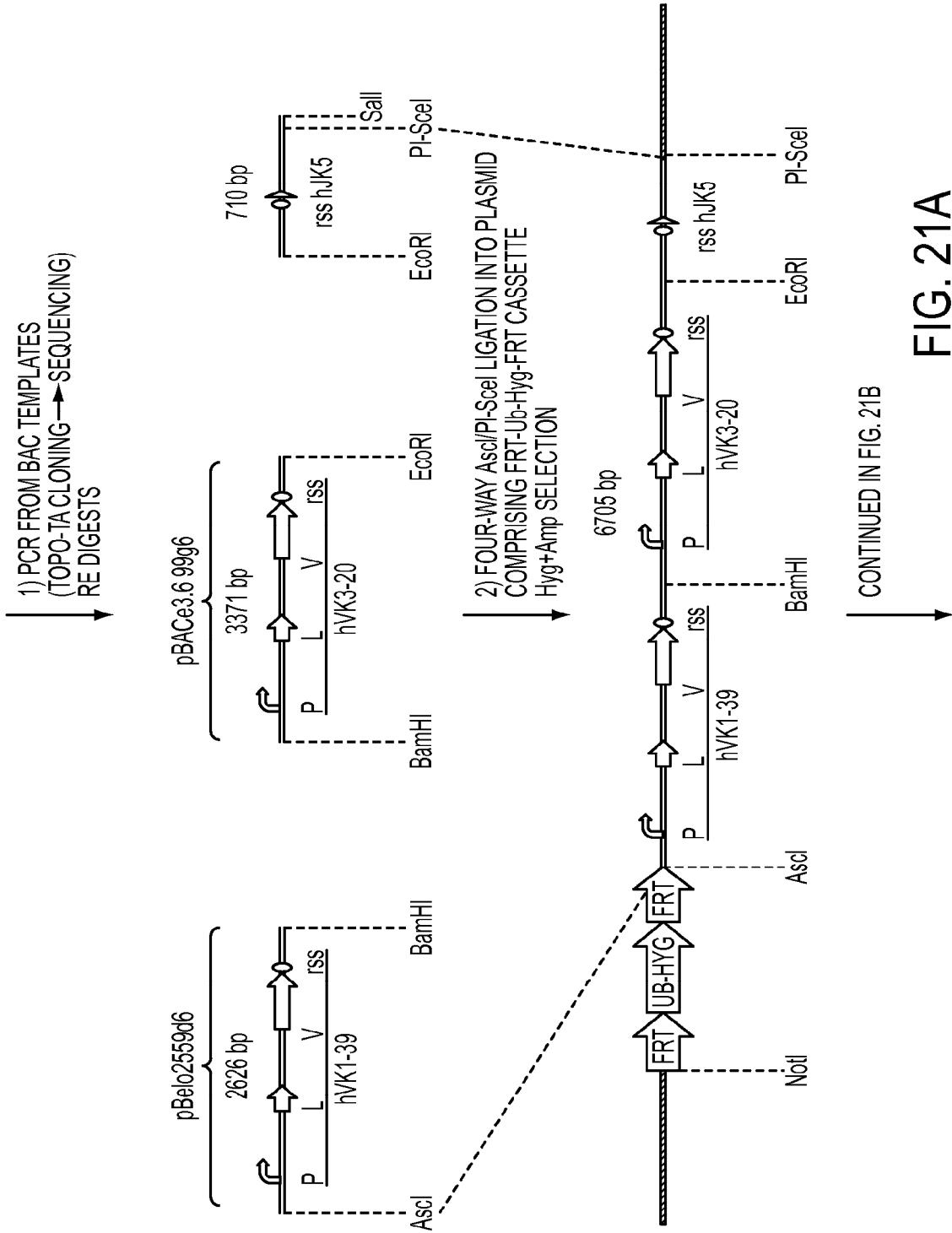


FIG. 20



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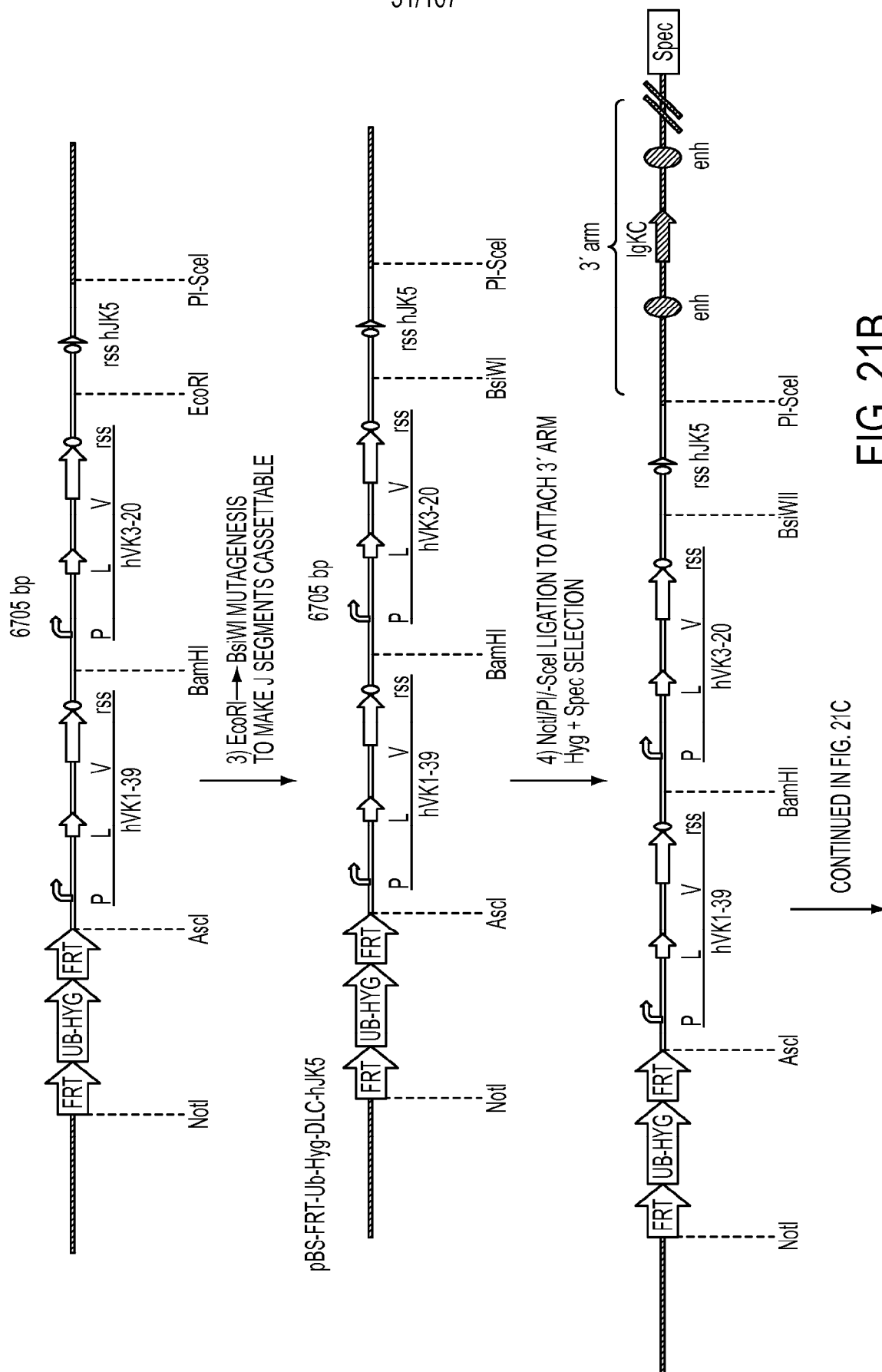


FIG. 21B

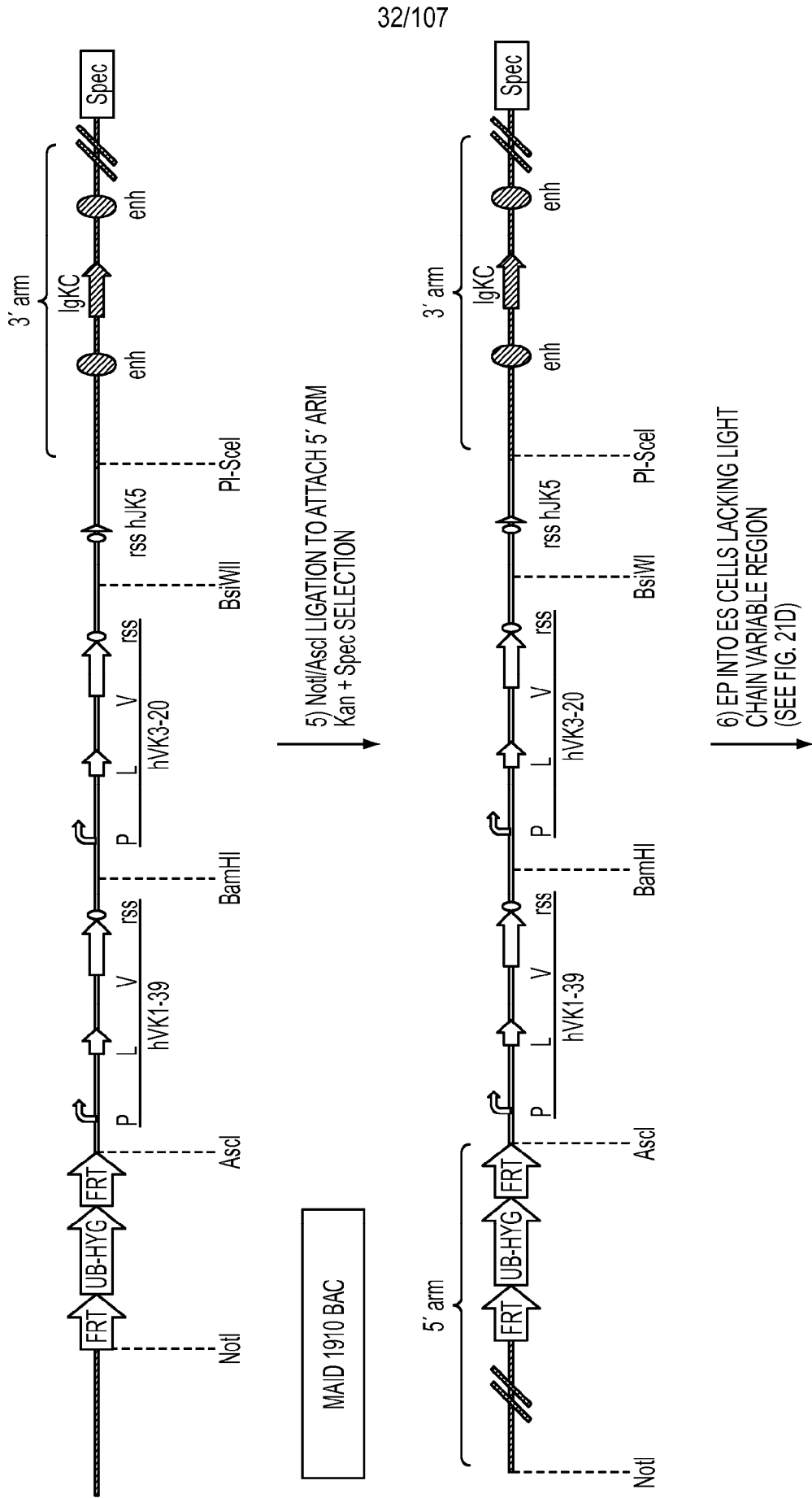


FIG. 21C

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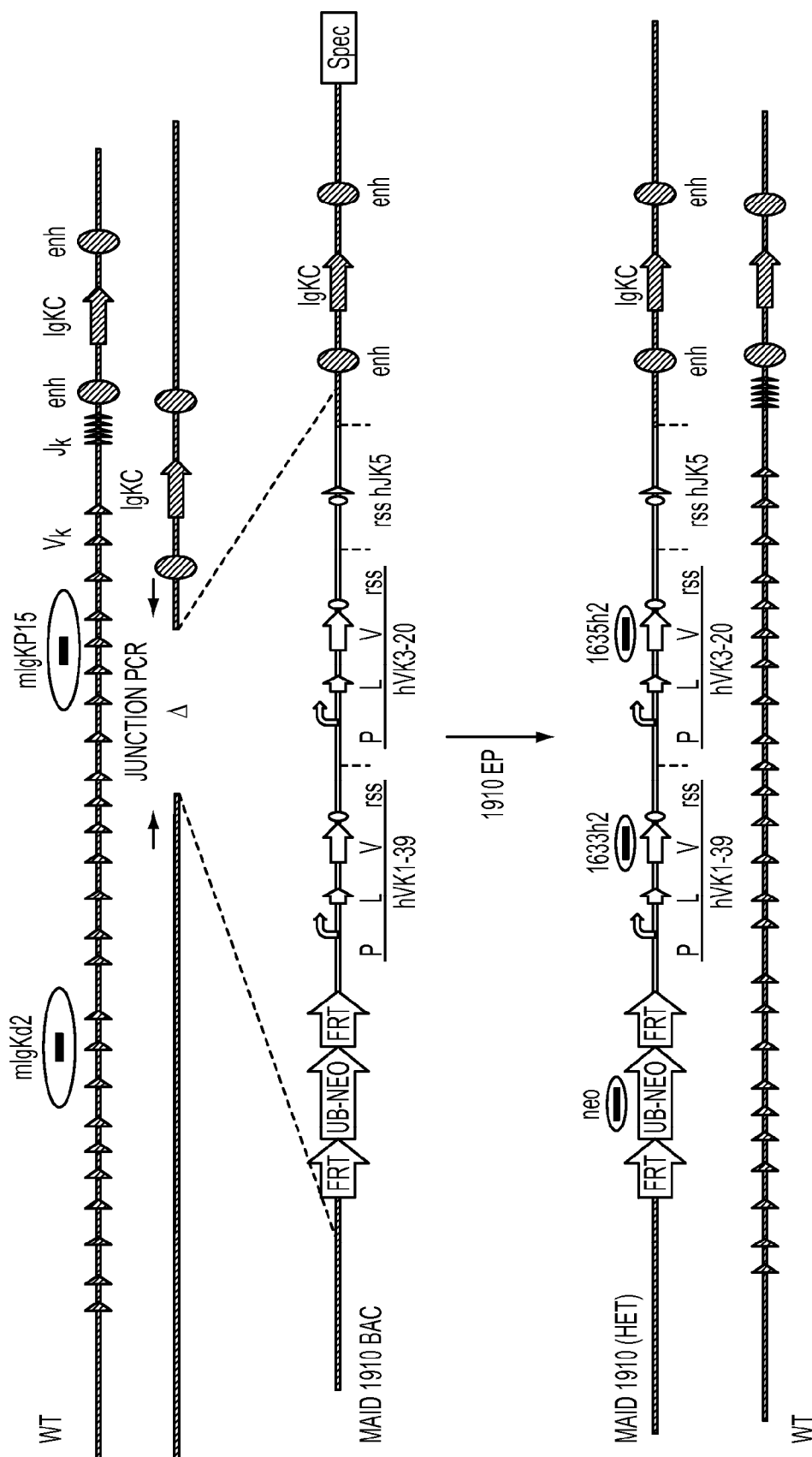


FIG. 21D

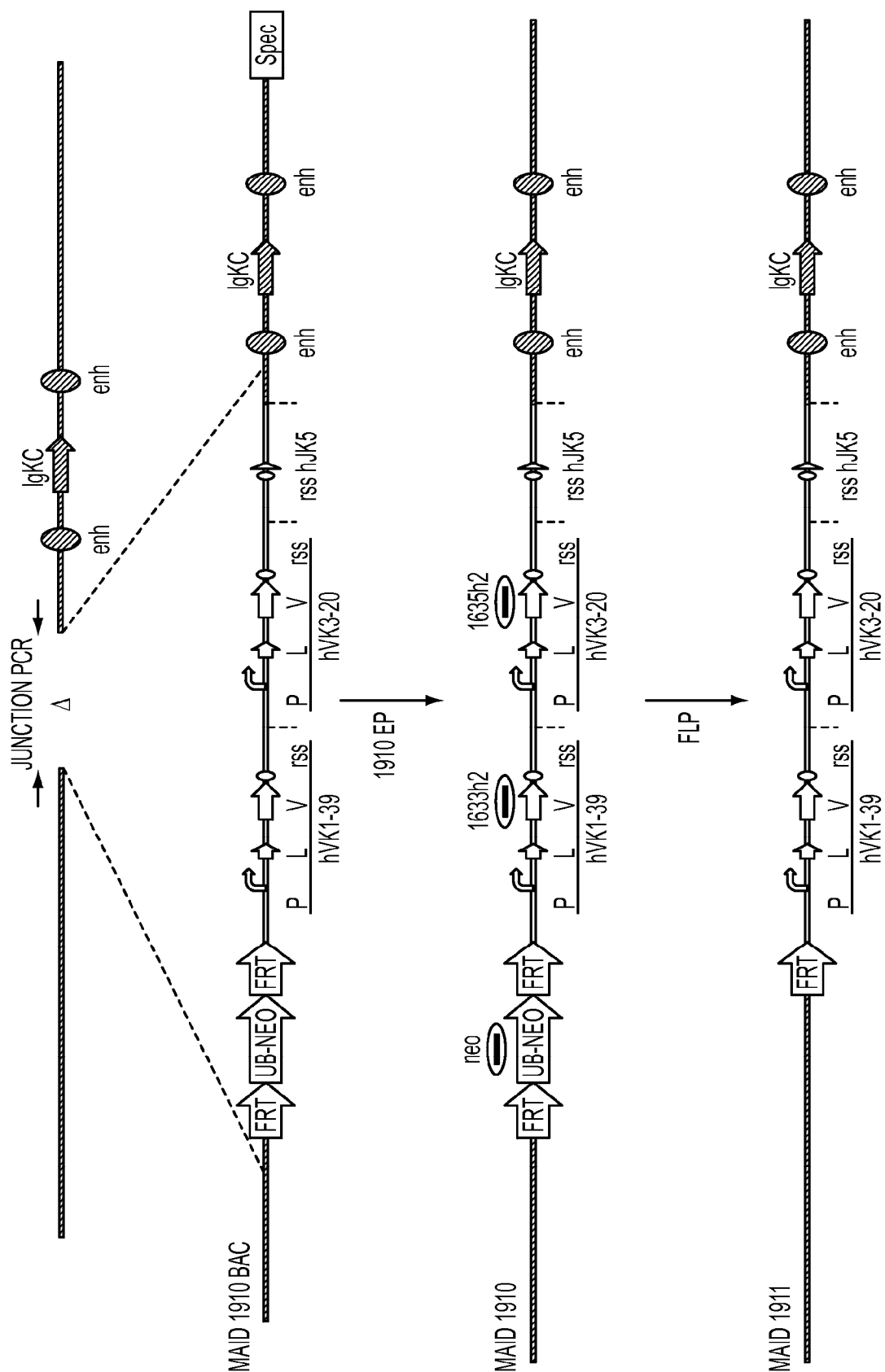


FIG. 21E

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DLC-1J SEQ ID NO:82

GCACCACTTCGTCGCGCAGCGGCTTTGGTCTCCCTTGTCTCGTGGCGGCACGCCACCCAGTTTACGCACACAGCACCCGAGGTCTGGTTGGTACCG  
 AAGTTCCTATTCCGAAGTTCCCTATTCTCTAGAAAAGTATAGGAACCTTCTCGCGCTCTGGCTCCGAGGCCCTCCGCGCGGGTTTTCGCGCCCTCCCGC  
 GCGCCCCCTCTCACCAGCGAGCGCTGCCACCTCAGACGAAGCGCGCAGAGGCTCTGATCTCTCCGCCCCGACCGCTCAGGACACAGCGCCCCGCTG  
 CTCTAAGACTCGGCTTTAGAACCCCAAGTATCAGCAGAAGGACATTTAGGACGGGACTTGGGTGACTCTAGGGCACTGGTTTCTTTCCAGAGAGCG  
 GAACAGCGAGGAAAAGTAGTCCCTTCTCCGGCGATTCTCGGAGGGATCTCCGTGGGGCGGTGAACGCCGATGATTAATAAGGACGCGCGCGGTGTG  
 GCACAGTAGTTCGTCGACGCCGGGATTTGGGTCTGGGTCTGATCTGCTCACTTGGTGAAGTAGCGGGCTGCTGGGCTGGCC  
 GGGCTTTCTGTGGCCCGCGCGCGCTCGGTGGACGGAAGCGTGTGGAGAGACCGCCAAAGGCTGTAGTCTGGTCCGCGAGCAAGGTTGCCCTGAAC  
 TGGGGTTGGGGGAGCGCAGCAAAATGGCGGCTGTTCGAGTCTTTGAATGGAAAGACGCTTATTCGGGTGAGATGGGTGGGCACCATCTTGGGAC  
 GGGCATGGTGGCGGCAAGAACCCCAAGTCTTGAGGCTCTCGCTAATGGGGAAGCTTATTCGGGTGAGATGGGTGGGCACCATCTTGGGAC  
 CTGACGTGAAGTTTGTCACTGACTGGAGAACTCGGTCTGTCTGTTCGGGGCGGCGAGTTATGGCGGTGCGGTGGGCAGTGCACCCGTACCTTT  
 GGGAGCGCGCCCTCGTCTGCTGACGTCACCCGTTCTGTGGCTTATAATGCAGGGTGGGCCACCTGCCGCTAGGTGTGGGTAGGCTTTCT  
 CCGTCGAGGACGCGAGGTTCCGGCTAGGTAGGCTCTCTGAATCAGACGGCGCGGACCTCTGGTGGGGAGGGATAAGTGAAGCTCAGTTTC  
 TTTGGTCCGTTTATGTAACCTATCTTTAAGTAGCTGAAGTCCGTTTGAACCTATGCGCTCGGGTGGCGAGTGTGTGTGAAGTTTTTAG  
 GCACCTTTTGAATGTAATCATTTGGGTCAATATGTAATTTTCACTAGTAAATTTGTCGCTAAATTTCTGGCCGTTTTTGGCTTTTTTGT  
 AGACGTCGAGCTTAGATTGGAAACCCGGTCTCTCGAATTTGTGACAAATATCATCGGCATAGTATATCGGCATAGTATAACGACAAAGGTGAGG  
 AACTAAACCATCCACCATGATTGAACAAGATGGATTGCACCGAGTTCTCCGGCGCTTGGGTGGAGAGGCTATTCGGCTATGACTGGGCAACAAGA  
 CAATCGGCTGTCTGATCCCGCTGTTCGGCTGTTCAGCGCAGGGCGCGCGGTTCTTTTGTCAAGACCGACCTGTCCGGTCCCTGAAATGAAC  
 CAGGACGAGGACGCGGCTATCGTGGCTGGCCACGACGGCGTTCTTGGCAGCTGTGCTCGACGTTGTCACTGAAGCGGGAAGGCACTGGCTGCT  
 ATTGGGCGAAAGTGGCGGGGCGAGGATCTCTGCTCATCTCACCTTGTCTCTGCGCAGAAAAGTATCCATCATGGCTGATGCAATGCGGCGGCTGCATAGCG  
 TTGATCCGGCTACCTGCCATTCGACCCCAAGCAACATCGCATCGAGCGAGACGTAATCCGATGGAAGCGCGTCTTGTGATCAGGATGATCTG  
 GACGAAGAGCATCAGGGGCTCGCGCCAGCCGAACCTGTTCGCGAGGCTCAAGGGCGGCTATGCCGCGGAGGATCTCGTCTGACCCATGGCGATGC  
 CTGCTTGGCGAATATCATGGTGGAAAATGGCGGCTTTCTGGATTCATCGACTGTGGCGGCTGGGTGGCGGACCGCTATCAGGACATAGCGTTGG  
 CTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCTCTGCTTACGGTATCGCGGCTCCCGATTCGCGCGCATCGCGCTTC  
 TATCGCTTCTTGACGAGTTCTCTGAAGATCCGCTGTAAAGTCTGCAGAAAATGATGATCTATTAACAATAAAGATGTCCACTAAAATGCAAGTTTT  
 TCCTGTCACTTTTGAAGGTTGAGAACAGAGTACCTACATTTGAATGGAAGGATGGAGCTACGGGTGGGGTGGGTGGGATAGATAA  
 ATGCTGTCTTTTACTGAAGGCTTTTACTATTGCTTTATGATAATGTTTCATAGTTGGATATCATATAATTTAAACAAGCAAAACCAAAATTAAGGCCA  
 GCTCATTCCTCCACTCATGATCTATAGATCTCTCGTGGATCATTTGTTTTCTCTGATTTCCCACTTTTGTGTTCTAAGTACTGTGGTT  
 TCCAAATGTGTGATTTTCAAGCTGAAGACGAGATCAGACGCTCTGTTCACATACACTTCTATCTCAGTATGTTTTGCCAAGTTCTAATCCA  
 TCAGACCTCGACCTGACGCTTACAGAGTTCTTATTCGAAAGTTCTTATCTAGAAAAGTATAGGAACCTTCTAGGGTTTACCGGTGGCGCGC  
 GAGAGGAAAAGAGAGCAGGATACCGAAAATGTCTCAGCGAGAAGCTACACAGAGGATGAATGGAGATCAAGCCACCGTGGAAAACATGGGAAAAT  
 GTCTCAGTATTTTCCACCTAAGAGGGAGGAGATGGGTATGTATACACTCCCTGTCTCATCTGATTTGAGGGCTTTCGAGAGGATGCTCATTC  
 AGGTGCTGTGATAGGCCATGTGTACAGCAGGCTGCCCTTCTCCAGCTTCAGATAGAGCAGTGAAGAAAAGATATGGCCATGGGGGTGAGCAGAAAT  
 ACAGCAAGGGGAAAAGGGTAGCAAGATGACAACTATATTCACCCCCCACACACACACACACGAAATTTGTGATTTGCAATCCAG  
 AACTGCTTCTCTGAAACCTAAATCTTAGCAAGCAGTTTACCAGTAACCTGCCCCTTGAAATTCAGGCCCTTGAAAGGAGCAGGGGTTGTGTACAGGC

FIG. 22A

DLC-1J SEQ ID NO:82 CONTINUED

TATATACACACAGCAGTCTGCCCACCCCTTAGTGATGCAATGAGTAATGCTCCCTGGACTCCCACAGGTTCTAGTCTTCTCATGTGCGATGTGATTTCCACTTATATCCCTTGTCGACAAACAGGCTGGGATGCCCTGGGCAGAGGCAGACATGTGAGGTATAGGGGTTCAAATCTGTTTCCAAAGTTTATCCAGCTTCAAAGCTTCCCTCCGTTACATGAGCGGTGGCTTGACAGGAGATGGAGACTCTCTTTCTGGATGTAGGCAAGGAGCGCTGAGTCAGGATGATGTCCCTACTACTCTATAAGAGAAAAGTGGCTTTGATGGTCAGGGCAGGGAATGCACGTAGTGGTCGCCACCTCACAGAAGAGAAAAGTGTTCACTGACC

TGGCCCTTTCCCAGGGCTCTCCCTCCCATGCTTTCCAGAAAAGCCATGATTTTTTGAGAGCCACACTGAACACTCACAAACATATATGGTGGGAAAAGCAGATCAGAGCATAGGCCAAGTTGCATTACCTTGGCTTCTTCTTTGGAGACAAATTGATGTGGGTTCTAGATTGACCCAGAGTTTCAAAGTTTATCC

TGATTCAGGCTTCAACAGCTGGAGGAAGAAACAGAGATGTTTTTGAAGTAAACAGATCTAGCATTAATCAACCCCTTCATCTGATGACCTATGGTGAATAAATACCAAGGCAGAAAAATGGGCAGAAATAAGGGAGCCCAACCAAGACGAAGCTGCTGCCCATTGAGACCCCTGGGTATTAACAGAGACCTATATAGCTCTGGATAATGGAAGATCTATGAGTGGCACAGGCGCTGAGGAATCACAGCATCATATTGTCGCATCTGCAGGGAATTGCTTGTAAATATACTGTGTAAGGTCACTACAAATACTTTTGGAGTGTAATTAATATGCTTCTGTATAAAGACTGTTTTTCTCACATGAAACAAATGGGAACCCATGTGTACAAATCACAGAGGTGTTGTTACTATAGCAAAAAGGGATGTTTACTCTCCACATCCCTTTAAAGTAACTTGAAGGCTGTATAGACCCACCCCTCTAAAGACTTTCATTAGACATCCCTACGAATGGTTATACTCTCTGTATATCCCAATACAACTCTAAAAATATATTAATTCATATAGTCTTAGGTTTGTATTAA

ATAGTTTGACTTTTTTCCCTCAAATATCTCTTGTACAAACAGCGGCTCTAGAGAGAAAATAGATTCCTCCAGGCAAACTATGCTGCGCTGGTCTGACC

TTGGGACCCCTGGGGACATTTGCCCTGTGCTGAGTTACTAAGATGAGCCAGCCCTGCAGCTGTGCTCAGCCTGCCCATGCCCTGCTGATTTGATTTGCAT

TTCCAGACACAGCCCCCTGCCCTGAAGACTTTTTTATGGCTGGTCGCAACCTGTGCAGGAGTCAGTCTCAGTCAGGACACAGCATGGACATGAGG

GTCCCCGTCACTCTCCTGGGGCTCCTGCTACTCTGGCTCCGAGGTAAGGATGGAGAACACTAGGAAATTTACTCAGCCAGTGTGCTCAGTACTGACTGG

TAACACTTCAGGGAAGTTCTCTGATAACATGATTAATAGTAAGAAATATTTGTTTTTTTATGTTTTTCCAAATCTCAGGTGCCAGATGTTGACATCCAGATGAC

CCAGTCTCCATCCCTCCCTGTCTGCAATCTGTAGGAGACAGAGTCACCATCATCTTGCCGGCAAAGTCAGAGCATTAGCA

TTTTTGCAACTTACTGTCAACAGAGTTACAGTACCCCTCC

FIG. 22B

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DLC-1J SEQ ID NO:82 CONTINUED

TGAGATCCTGGGGTGGATGGGAGGTGGGGCACTGATCTGTCAATCTGCTTTTCTTCAAGGATCAGGCAGCAGAGACCCAGAAAGCTTCATGTCCTTTGT  
 AAGGCTCTTCCAAGCCAACACAGATAAATTTGACAAAACACTGTATCTGCATCCAGACCTCACCTGTACAGACTGAAGTGGTGTGTTTTCATCCTACT  
 AAGGTTAAACTATACCAGCTATACAGAAATAAAAAGACTGGATAGTTTAGAGGATCACCCAAAGAAATAGTTCTTTGCCCTGCATGGACAAAACCATCTTC  
 TGCTTTAGGGAATGGTATCACTACCTGAGGATTTGGAGCCAGGTCCTACTTATCTGTGCAGTTGTGAAGTCTTCCACCCACAGTGTGAGGT  
 TAAATTGAATGTTACTCTTTTAAATTTCTGCAAGAAATGAGACAGCTTCTGGACCTTCAGGAAAGATCACTAACTAAGTAAATACAGTATATCCGGAAGA  
 TAAAGTTGTAATAGACTCTTCTTCACTGATCCATCATGCAATTTAGGGAGCTGACTGGGCACAAAGTTGGAGCAGAAAGAGAAAAATGAAACCCACA  
 GCTTCTATTTTGTCTAAACAGACTTGTACCAACATTTCTGTGGCTCAATCTAGGTGATGGTGAGACAAAGGACACAGAGGTTAAATTTCTGTGGCC  
 GCAGGGAGAAGTTCTACCTCAGACTGAGCCAAAGGCTTTTCTGGCCCTGATCACCTGGGCATGGCTGCTGAGAGCAGAAAGGGAGGCAGATTGT  
 CTCTGAGCTGCAAGCCAGCACCCGCCCTGAGTCTTGTGATGTCCTCCAGCCGCTTCCAGTCCAGAGCCCATATCAATGCTTGGGTGAGAGCT  
 CTGGAGAAGAGCTGCTCAGTTAGGACCCAGAGGGAACCATGGAAACCCAGCGCAGCTTCTCTTCTCTCTGCTACTCTGGCTCCAGGTGAGGGGAAC  
 ATGGGATGGTTTGGCATGTTCAGTGAAACCCCTCTCAAGTCTCTGTTACCTGGCAACTCTGCTCAGTCAATAAATAAAGTCAATAAAGCAAT  
 AATCTGGCTCTTCTGGGAAGACAAATGGGTTTGAATTAGATTACATGGGTGACTTTTCTGTTTTTATTTTCCAATCTCAGATACCACCGGA**GAAATTG**  
**TGTTGACGCAGTCTCCAGGCACCCCTGTCTTTGTCTCTCCAGGGAAAGAGCCACCCCTCTCTCTGAGGGCCAGTCAGAGT**  
**GTTAGCAGCAGCTACTTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCAGGCTCCTCATCTATGTTGGTGCATCCAG**  
**CAGGGCCACTGGCATCCACAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCAACCATCAGCAGACTGG**  
**AGCCTGAAGATTTTGCAGTGTATTACTGTGTCAGCAGTATGGTAGCTCACCTCC** **CACAGTGATTCAGCTTGAAACAAAACCTCT**  
 GCAAGACCTTCTATTTTACTAGATTATACCAGCTGCTTCTTACAGATAGTGTGCAATGACAACTCAATTTTAGCATCTCTTCTGCTGCTGGGC  
 ATTTTGGGGATCTTAAAGTAATCCCTTGATATATTTTGAATCTGATTTCTGATTTTCTCAGACCAAGATGGACAGCCAGGTTTAAAGCACAG  
 TTTTACAGATAATGGCCACTGGATCAGATTACATCAGTGGATGTCAGTAAAGTCCCAACCAGAGCCATAAGGCAACAATAAGCAACAAATAATCA  
 AAATTGGAAAAGAAATTAAGCTGTCTAATTTCTGTAAGGATTTGTGTCAGATAAAATTTCAAAATTTGTCTACAGAGAAACTACTAAAAATTGA  
 CATGAGAAATAGAAAAATCATTAGATTCAAGATCAATTTATTAATTCATAGATTCAAAAAATAGACTAAATACTGACGTCTCCAGAAATATATTTTG  
 ACATATATAAACAAACACACCATTTACAAAACATCAAGATCAATTTATTAATTTAAAAAATAAGACTAAATACTGACGTCTCCAGAAATATATTTTG  
 AAAAAATAAAGAAAAACCTAAGTAAATAGAAATTCAGTTCAAGTCAAAAGTGAATGTCAATTTCTCAAGATTAATAATATTTGAT  
 TACATATAAGAAAAATCAAAATCCTAAGTATACCTCAATTTAAATTAAGAACTAATCTAAATATATATGGAATGTCAAGGATGTAGAAATAGCCA  
 CAGTGAACCTGAAGAAACACCAAAATGAGAACTTCCAGTGCTTGAATACCTGGAATATAGTGGTGGCAGTATGGTGTGATGGTGTGAGATCAGAAAGTTT  
 AAAAAATTTGCAACCGTCTTATTTTGGAAATAATCACTACGCAGATGTAGCCAAACCTCTTCAACTGTGGCTAGGCTCAGGTCAATTTCCAAAGAG  
 TACCAGATTCTTCAAAAAGTCAAGTGAAGGATAGAAAAATAGTTTCATCTTAAGGAACAGCCAGCGCTAGCCAGTTAAGTGAGGCACTCTCAAT  
 TGCAAGATTTTCTCTGATCGGTGAGTTAGTGATATTAACAGCAAAAGAGATTTTGTAAAGGGAAGTAAATAAGTTAACTGCTG**GATCAC**  
**CTTCGGCCAAAGGACACGACTGGAGATTAAAC** **GTAAGTAAATTTTTCATATTGTCTTCTTGAATTTTGGTCTGATGGCCAGTATTGACT**  
 TTTAGAGGCTTAAATAGGAGTTTGGTAAAGATTGGTAAATGAGGGCAATTAAAGATTTGCCATGGGTGCAAAAGTTAACTCAGCTTCAAAAATGGAT  
 TTGGAGAAAAAAGATTAAATTTGCTCTAACTGAATGACACAAAGTAAAAAAAAGTGAACCTAAAGGAACCTTGTATTTCTAAGGAGCAAAA  
 GTAAATTTATTTTGTCTCACTCTTGGCCAAATATTTGATTTGGTTGTGCTGATTATGCATGATACAGAAAAAGTGGAAAAATACATTTTGTAGTCTTCT

Vk3-20

Jk5

FIG. 22C

DLC-1J SEQ ID NO:82 CONTINUED

CCCTTTTGTGATAAATTATTTTGTGACAGACAACAATAAAAAATCAATAGCACGCCCTAAAGATCTAGATGCAATGCTCGAGTGCCATTTCATTACCTCTTT  
**TCTCCGACCCGACATAGATAAGCTTATCGATACCGTCCGACCTCGAGGGGGGGCCCGGTACCCCGTGGCATACAGTGTCAGATTTTCTGTGTTTATCAAG**  
CTAGTGAGATTAGGGGCAAAA

SEQUENCES OF VK1-39, VK3-20, AND JK5 ARE IN LARGE FONT AND BOXED  
MOUSE SEQUENCES ITALICIZED  
HUMAN SEQUENCES IN REGULAR FONT  
RESTRICTION ENZYME SITES IN BOLD  
NEO CASSETTE SEQUENCES UNDERLINED  
FRT SITES DOUBLE UNDERLINED

FIG. 22D

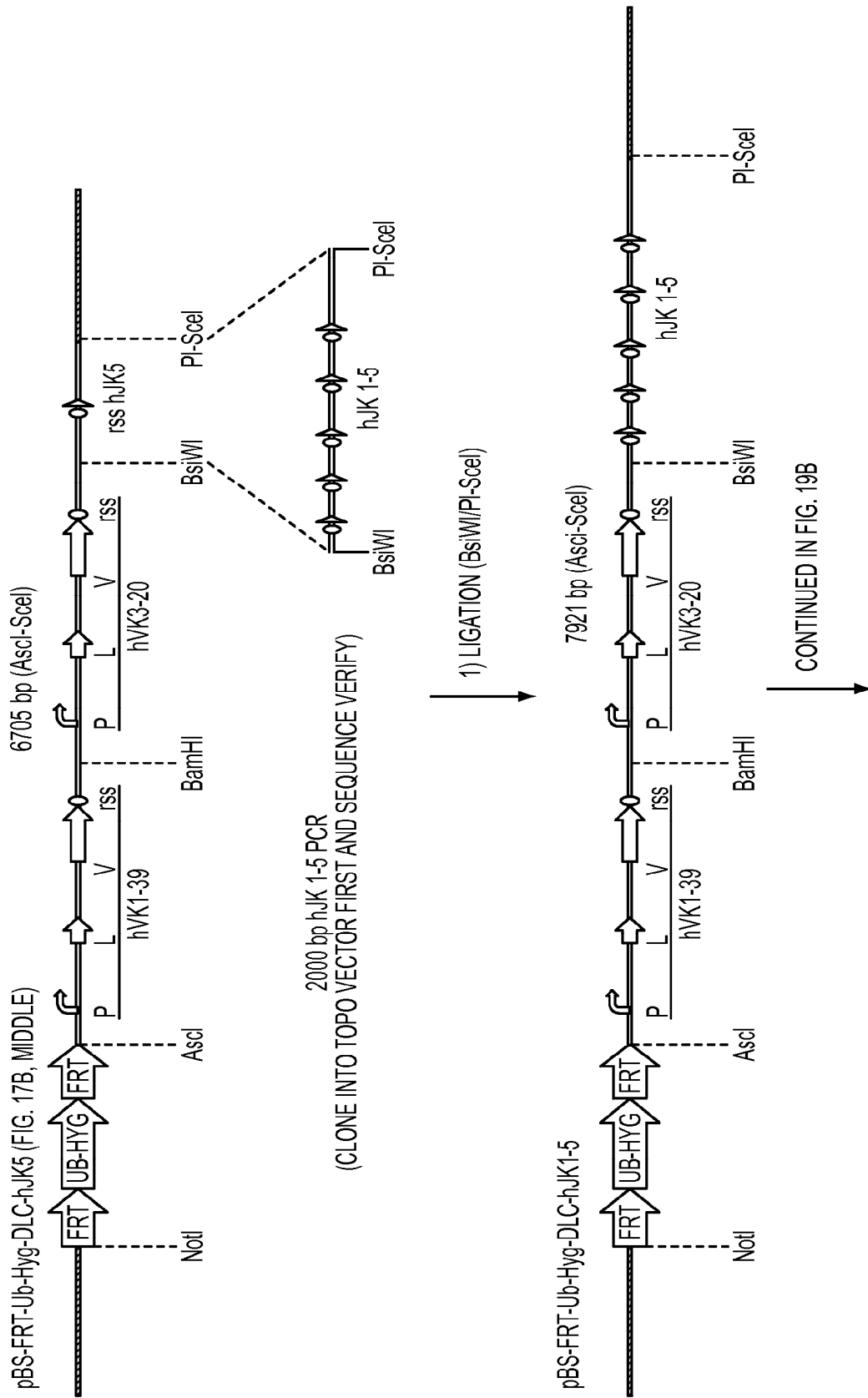


FIG. 23A

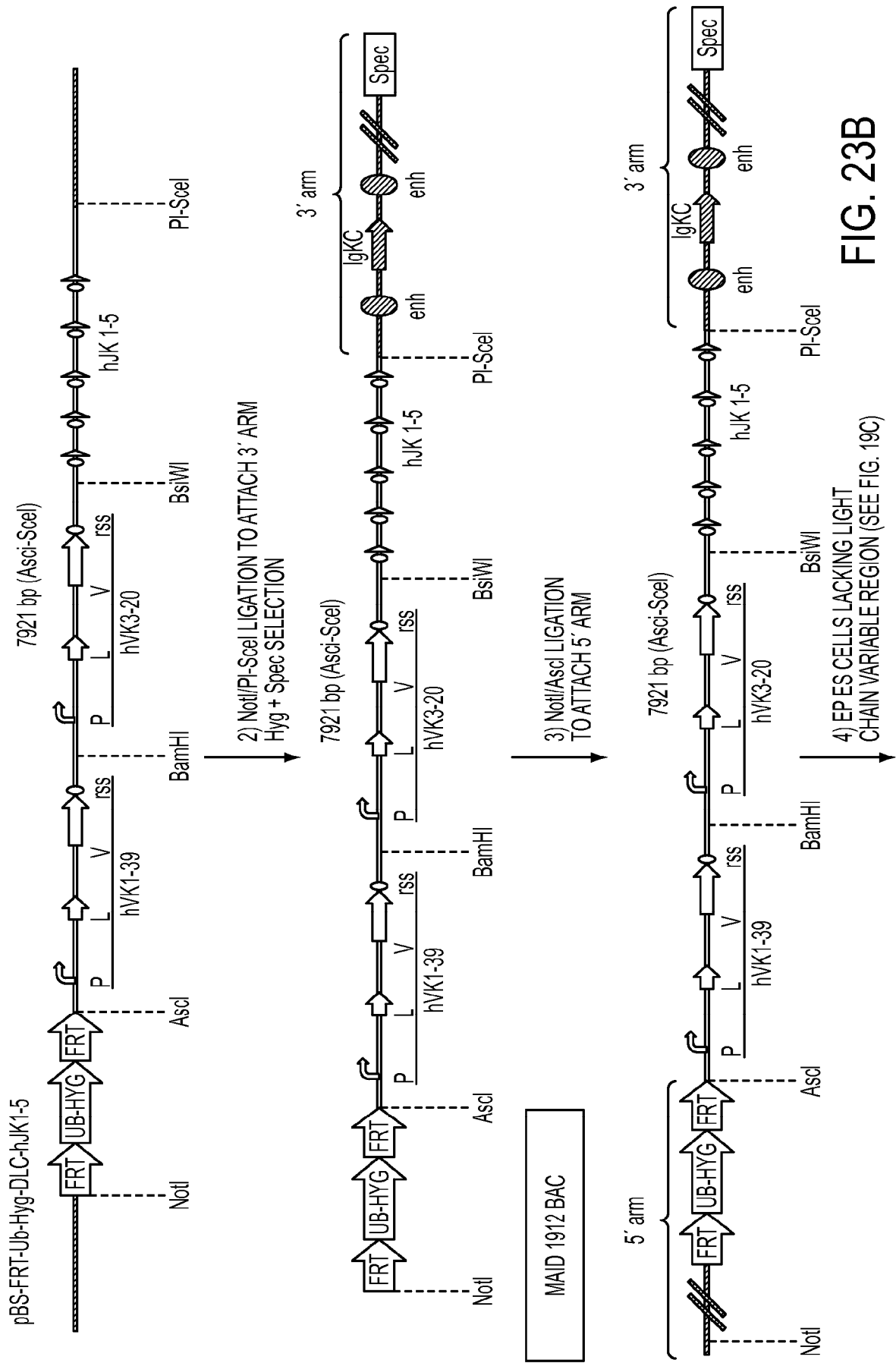


FIG. 23B

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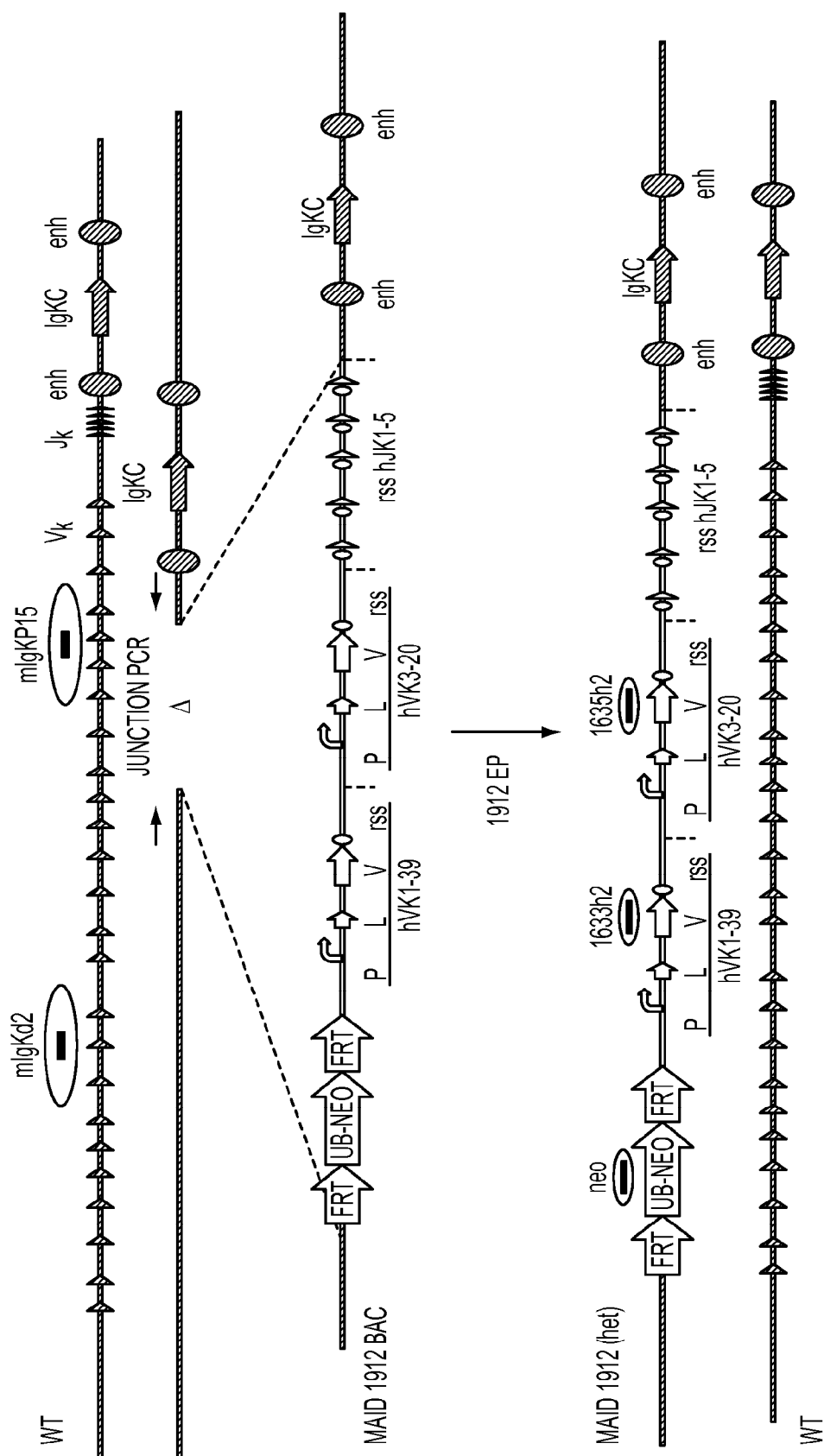
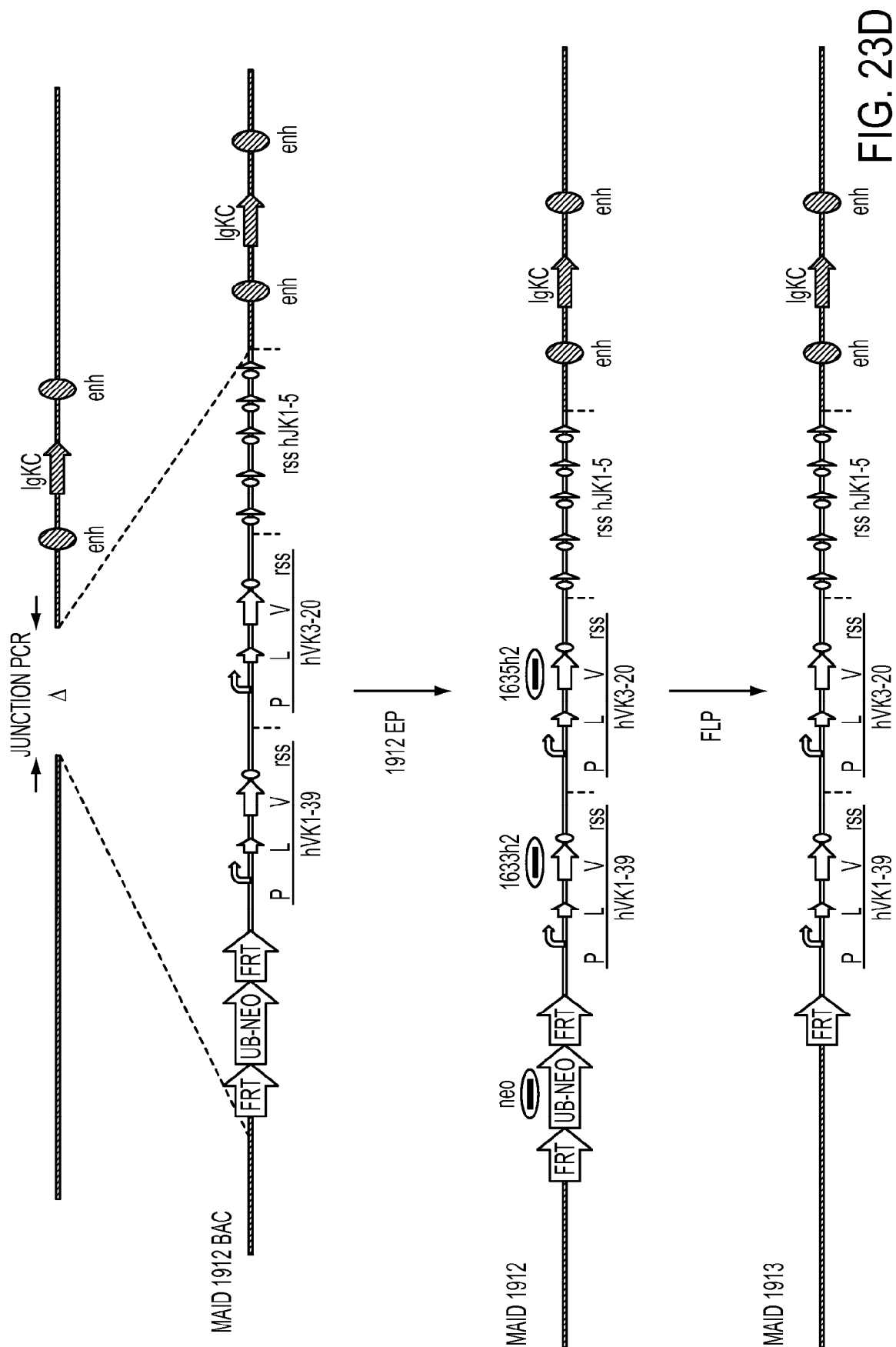


FIG. 23C

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DLC-5J SEQ ID NO:83

GCACCACTTCGTCCGACGGCCTTTGGTCTCCCTTTGTCTCCCTTGTCTCCGTCGGCGGCACGCCCAACCGAGTTTACGCACACACCGAGGTCCTGGTTGGTACCG  
 AAGTTCCTATTCCGAAGTTCCCTATTCTCTAGAAAGTATAGGAACCTTCTCGCGCTCTGGCTCCGAGGCTCCGCGCGGTTTGGCGCTCCCGC  
 GCGCCCCCTCTCTCACCGCGAGCGCTGCCACCTCAGACCAAGCGCCAGCGAGGCTCTGATCTCTCCGCGCGGACCGTTCAGCACACGCGCGCGCTG  
 CTCATAAGACTCGGCTTAGAACCCCAAGTATCAGCAGAAGACATTTAGGACGGGACTTTGGGTGACTCTAGGGCACTGGTTTCTTTCCAGAGCGG  
 GAACAGCGGAGGAAGTATGTCCTTCTCGGCGGATTTCTCGGAGGGAATCTCCGTGGGCGGTGAACGCCGATGATATATAAGACGCGCGCGGTGTG  
 GCACAGCTAGTTCCGTCCGACCGCGGATTTGGGTCCGCTGTGATCGTCACTTGGTGAGTAGCGGGCTGCTGGGCTGGC  
 GGGCTTTCTGTGCGCGCGCGCGCTCGGTGGACCGCAAGCGTGTGGAGACCGCCAAAGGCTGTAGTCTGGTCCGCGAGCAAGGTTGCCCTGAAC  
 TGGGGTTGGGGGAGCGCAGCAAAATGGCGCTGTCTCCGAGTCTTTGAAATGGAAGACGCTTGTAGGGCGGCTGTAGGTCTGTGAAACAAAGGTGGG  
 GGGCATGGTGGCGGCAAGAACCCCAAGGTCTTGAGGCTCTTGGTAAATGGGGAAGCTCTTATTCGGGTGAGATGGGCTGGGCAACCATCTGGGAC  
 CTGACGTGAAGTTTGTCACTGACTGGAGAACTCGGTCTGTCTGTCTGGGGGCGGCGAGTTATGGCGGTGCCGTGGGCGAGTGCACCCGTACCTTT  
 GGGAGCGCGCGCTCGTCTGTGAGCTACCCGTTCTGTGGCTTATAATGCAGGGTGGGCAACCTGCCGCTAGGTGTGGGTAGGCTTTCT  
 CCGTCGACGAGCGCAGGTTCCGGCTAGGCTAGGCTCTCTGAATCGACAGGCGCGGACCTCTGGTGGGAGGGGATAGTGAGCGCTCAGTTTC  
 TTTGGTCCGTTTATGTACCTATCTTTAAGTAGCTGAAGTCCGTTTGAACCTATCGGCTCGGTTGGCGAGTGTGTCTGAAATTTTGTAG  
 GCACCTTTTGAATGTAACTATTTGGTCAATATGTAAATTTTCACTGTAGACTAGTAAATTTGTCGCTAAATTTCTGGCGTTTGGCTTTTGT  
 AGACCTCGACTAGATTGGAAACCGGCTCTCTGAATTTGTGACAAATATCATCGGCATAGTATATCGGCATAGTATATACGACAAAGTGAGG  
 AACTAAACCATCACCATGATTGAACAAGATTGCACCGAGTTCTCGGCGCTTGGGTGGAGAGGCTATTCGGCTATGACTGGGCAACAACAGA  
 CAATCGGCTGTCTGATCCCGCTGTTCGGCTGTACGCGCAGGGCGCGCGGTTCTTTTGTCAAGACCGACCTGTCCGGTCCCTGAAATGAACGTG  
 CAGGACGAGGAGCGCGCTATCGTGGCTGGCCACGACGGCGTTCTTGGGAGCTGTGCTCGACCTGTCACTGAAGCGGGAAGGCACTGGCTGCT  
 ATTGGGCGAAGTGGCGGGGCGAGGATCTCTGTCTCATCTCACCTTGTCTCTGCCAGAAAGTATCCATCATGGCTGATGCAATGGCGCGGCTGCATACGC  
 TTGATCCGGCTACCTGCCATTCGACCCCAAGCGAACAATCGCATCGAGCGAGCACGTACTCGGATGGAAGCGCGTCTTGTCCATCAGGATGATCTG  
 GACGAAGAGCATCAGGGCTCGCGCCAGCCGAACGTGTTCGCCAGGCTCAAGGGCGCATGCCCGAGCGGAGGATCTCGTCTGACCCCATGGCGATGC  
 CTGCTTGGCGAATATCATGGTGGAAATGGCGCTTTCTGGATTCATCGACTGTGGCGGCTGGGTGTGGCGGACCGCTATCAGGACATAGCGTTGG  
 CTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCTCTCGTGTCTACGGTATCGCGCTCCCGATTCGCAGCGCATCGGCTTC  
 TATCGCTTCTTGACGAGTTCTCTGAAGATCCGCTGTAAAGTCTGCAGAAATGATGATCTATTAACAATAAAGATGTCCACTAAAATGGAAGTTT  
 TCCTGTCACTTTTGAAGGTTGAGAACAGAGTACCTACATTTGAATGGAAGGATGGAGCTACGGGGTGGGGTGGGTTGGGATAGATAA  
 ATGCTGTCTCTTACTGAAGCTCTTACTATTGATTAATGTTTCAATGTTGGATATCATAAATTTAAACAAGCAAAACCAAAATTAAGGGCCA  
 GCTCATTCCTCCACTCATGATCTATAGATCTCTCGTGGATCATTTGTTTCTCTGTATTCCTCATTTCCCACTTTGTGTTCTAAGTACTGTGTT  
 TCCAAATGTGTGAGTTTCAAGCTGAAGACGAGATCAGCGCTCTGTTCACATACACTTCTATCTCAGTATTTGTTTGGCAAGTTCTAATCCA  
 TCAGACCTCGACCTGCAGCCCTAGAGAAGTTCTTATTCGAAGTTCTTATTCCTAGAAAGTATAGGAACCTTCTAGGGTTTACCGGTGGGCGGCGC  
 GAGAGGAAGAAGAGCAGCGATACCGAAAATGTCTCAGCGAGAAGCTACCAAGAGGATGAATGGAGATCAAGCCACCGTGGAAACATGGGAAAT  
 GTCTCAGTATTTTCCACCTAAGAAGGAGGAGATGGGTATGTATACACCTCCCTGTCTCACTGATTTGAGGGCTTTCGAGAGGATGCTCATTC  
 AGGTGCTGTGATAGGCCATGTGTACAGGACGGCTGCTTCTCCAGCTTCAGATAGAGCAGTGAAGAAAGATATGGCCATGGGGGTGAGCAGAAAT  
 ACAGCAAAAGGGAAGAAGGGTAGCAAGTGTGACAACCTATATTACCCCCCCCCCACACACACACACACAAATTTGTGTATTGCAAT

FIG. 24A



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DLC-5J SEQ ID NO:83 CONTINUED

GGGTGGATGACGTTATCAGACATGTCAATTTTCTACAGTACTTGACCTGCCCTCTAGAACTGGACAACCGAGGGTGAAGGACTGGATCAAGCAACAA  
 TGGCAATGGGTGCCAAAGAGGTAGTAGTCTCAGAACAGGGAGAGACAGACTGAGTCCCTCCACTAACTCAGCCCAACACCTGTGGATGAGTAGGGGA  
 TGCTGAGATCCTGGGTGGATGGGAGGTGGGCACTGATCTGTCAATCTGCTTTTCTTCAAGGATCAGGCAGCAGAGACCCAGAAGCTTCATGTCT  
 TTGTAAGGCTCTTCCAAAGCCAAACACAGATAATTTGACAAAACACTGTATCTGCTATCCAGACCTCACCTGTACAGACTGAAGTGGTTTTCATCC  
 TACTAAGGGTAAACTATACCAGCTATACAGAAATAAAAGACTGGATAGTTTAGAGGATCACCCCAAGAAATAGTTCTTTCCCTGCATGGACAAAACCCAT  
 CTTCTGTCCTTAGGAAAATGGTATCACTACCTGAGGATTTGGAGCCCAAGTCTCACTTATCTGTGCAGTTGTGAAAGTCTTCACACCCACAGTGTG  
 AGGTAAATTGAATGTTACTCTTTTAAATTTCTGCAAGAATGAGACAGCTTCTGGACCTCAGGAAGATCACTAACAGTAAATACAGTATATCCGG  
 AAGATAAGTTGTAATAGACTCTTCTTCAACCTGATCCATGCTATTTAGGGAGCTGACTGGGCACAAAGTTGGAGCAGAAAGAAAAATGAAAC  
 CACAGCCTTCTATTTTGTCTTAAACAGACTTGTACCAACATTTCTGTGGCTCAATCTAGGTGATGGTGAGACAAGAGGACACAGGGTTAAATTTCTGT  
 GCGCAGGGGAGAAGTTCTACCTCAGACTGAGCCCAACGGCTTTTCTGTGGCTGATCACCTGGGCATGGGTGCTGAGAGCAGAAAGGGGAGGCAGA  
 TTGTCTCTGACGTGCAAGCCAGCACCCGCCAGCTGCTTTGCAATGTCCCTCCAGCCGCCCTGCAGTCCAGAGCCCATATCAATGCCCTGGGTGAG  
 AGCTCTGGAGAAGAGCTGCTCAGTTAGGACCCAGAGGGAAACCATGGAAACCCAGCGCAGCTTCTCTTCTCTCTGCTACTCTGTGGTCCCAGGTGAGGG  
 GAACATGGGATGGTTTGTGATGTGAGTGAACCCCTCTCAAGTCCCTGTTACCTGGCAACTCTGCTCAGTCAATACAATAAATTAAGGCTCAATATAAAG  
 CAATAAATCTGGCTCTCTGGAAGACAAATGGGTTTGATTTAGATTACATGGGTGACTTTTCTGTTTATTTTCCAATCTCAGATACCACCGGA**GAAA**  
**ATTGTGTTGACGCAGTCTCCAGGCACCCCTGTCTTTGTCTCTCAGGGGAAAGAGCCACCCCTCTCTCTGCGAGGGCCAGTCA**  
**GAGTGTAGCAGCAGCTACTTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCAGGCTCCTCATCTATGGTGCAT**  
**CCAGCAGGGCCACTGGCATCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGA**  
**CTGGAGCCCTGAAGATTTTGCAGTGTATTACTGTACAGCAGTATGGTAGCTCACCTCC** CACAGTGAATTCAGCTTGAAACAAAA  
 CCTCTGCAAGACCTTCATTTGTTTACTAGATTATACAGCTGCTTCTTTACAGATAGCTGCTGCAATGACAACTCAATTTTAGCATCTCTTCTCTGCT  
 TGGGCATTTTGGGGATCTTAAAAAGTAATCCCTTGATATATTTTGAATCTGATTCCTGCAATTTTCTCAGACCAAGATGGACAGCCAGGTTTAAAG  
 CACAGTTTCACAGTAAATGGCCACTGGATCAGATTTACATCAGTGGATGTGAGTAAAGTCCCAACCCAGAGCCATAAGGCAACAAATAGCAACAAAT  
 AATCAAAATTTGGAAGAAATTAAGCTGTCAATAATCACTGATGAAGGATTTGTGTGAGATAAAATTTCAAAATTTGTCTACAGAGAAACTACTAAA  
 ATTGACATGAGAAATAGAAAATCAATTAGATTCAAGATCAATTTATTAATTCATAGATTCAAAAATCAATTTTCAATTTCTGCATAATAAAAAATGCTAAA  
 AATTAAATTAATAAACAAAAACACACCACTTTACAAAAACATCAAAAGTATCAATTTATTTAAAAAAAATAGACTAAATACACTGACGCTCTCCAGAAATATTA  
 TTTTGAATAAATAAAGAAAAACCTAAGTAAATAGAAATTCAGTTCAAGAGACTGAATGTCTCAGTACTATAAAAAATGTCAATTTCTCAAGAGATTTAAAAATA  
 TTGATTTACATATAAGAAAAATCAAAATCTTAAAGTATATCTCAATTTAAATTAAGAGCTAATCTAAATATATATATGGGAATGTCAAGGATGTAGAAT  
 AGCCACAGTGAACCTGAAGAAACACCAAAATGAGAACTTCAGTGCCTGAATACCTGGAATATAGTGTGGTGGCAGTATGTTGATGGTGCAGATCAGA  
 AGTTTAAAAATTTGCAACCGTGTCTTATTTTGGAAATAATCACTACGAGATGTAGCCAAACCTCTTCAACTGTGGCT**AGC**CACCTGCTCGAAAAG  
 GGAGTTGAGCTTCAGCAGCTGACCCAGGACTCTGTCTCCCTTTGGTGAAGAGGTTTGTTCAGCAAGACAAATGGAGAGCTCTCACTGTG**GTGGA**  
**CGTTCCGCCCAAGGACCAAGGTGGAATCAAACT**GTGAGTAGAAATTTAAACCTTTGCTTCCCTCAGTTGTCTGTGTCTTCTGTTCCTCTGT  
 CTATGAAGTATATAAGCTGACTCTGCAATCAGCCTCTGATATCTCTTCAGGGGAAAAAGATAAAGATAAGTCTGTAGTCAAACCTCGAGAAATTGATTGC

Vk3-20

Jk1

FIG. 24C

A

CATTTTCTTTGAAGAGCAAGCAAGATTCAATTCATTTGGGTGAGAAATAACTTTGTCTAAAGTAATAGCTTTCAGAAATGTCTGGGGAACATAAACAATGTT  
 CTGGACAGAGCCTTGGTCAATTTGTCAAAAAGGGAGTTTTTGTATAGGAGGAAGTTAAGAGGAACCAATTTGTG**TGTACACTTTTGGCCAGG**  
 {  
**GGACCAAGCTGGAGATCAAAAC**GTAAAGTACTTTTTTCCACTGATTTCTTCACTGTTTGTCTAAATTAGTTTACTTTTGTGTTTCTTTTGTGTGGAT  
 TTTTCATTAGTCCGATGCCAGGGATCTAAACAACTTCAATCCCAGGTTAGGTACAGAGGAGGGGAAAATTGTTCCACAGGAAGCTAGCTTTGTGGCTA  
 ATTTTTAAGATTTCTAAATCAAAATAACTTCAATTTGGGGAAAGAGGCTTGTGAGCTTTTTCAGGAGGTTTTTGTAAAGGGAAGTTAAGACGAA  
 TCACTGT**CAATTCACTTTCCGGCCCTGGGACCAAAAGTGGATATCAAAAC**GTAAGTACATCTGTCTCAATTATTTCGTGAGATTTTTAGT  
 GCCATTGTATCATTTTGTGCAAGTTTTTGTGATATTTTTTGGTTGAATAAAACCTGGTGACCCAGAACTAAATAGCAGGACACCCAGAAAAATGAACCTTAA  
 AAGCTGAGCAAAATAGACGAATCATTTGGTTTTGAGAGGAGAATAGGATTCATGGGGGAAATGGGGAAGAAATAGCTAGATTTTTTCTCTGAACAAAGC  
 AGCCTATCTCATATGATTGGCTTCAAGAGAGGTTTTTGTGAGGGGAAAAGGGTGAGATCCCTCACTGT**GCTCACTTTCCGGCCGGAGGGA**  
 {  
**CCAAGTGGAGATCAAAAC**CTAAAGTGCACCTTTCCCTAATGCTTTTTTCTTATAAGGTTTTTAAATTTGGAGCGTTTTTGTGTTTGAGATATTAG  
 CTCAGGTCAATTTCCAAAGAGTACCAGATTCTTTTCAAAAAGTCAGATGAGTAAGGGATAGAAAAATTAGTTCATCTTAAGGAACACAGCCAAGCGCTAG  
 CCAGTTAAGTGAGGCATCTCAATTGCAAGATTTTCTCTGCATCCGTCAGGTTAGTGATATTAAACAGCGAAAAGAGATTTTTTTGTTAAGGGGAAAAGT  
 AATTAAAGTTAACACTGTG**GATCACCTTCCGGCCAAAGGGACACGACTGGAGATTAAAC**GTAAGTAATTTTTTTCACATAATTGTCTTCTC  
 AAAATTTGGGTCTGATGGCCAGTATTGACTTTTAGAGGCTTTAAATAGGAGTTTTTGGTAAAGATTGGTAAATGAGGGCATTTTAAAGATTTGCCATGGGT  
 TGCAAAAGTTAAACTCAGCTTCAAAAAATGGATTTGGAGAAAAAAAGATTAAATTGCTCTAAACTGAATGACACAAAAGTAAAAAAAAGTGTAAAC  
 TAAAAAGGAACCCCTTGATTTCTAAGGAGCAAAAAGTAAATTTATTTTTTGTTCACCTCTGCCAAATATTGTTATTTGGTTGTTGCTGATTATGCATGA  
 TACAGAAAAGTGGAAAAATACATTTTTTATGTCCTTCTCCCTTTTGTGATAAAATATTATTGTGACACAACATATAAAAAATCAATAGCACGCCCTA  
 AGATCTAGATGCTCGAGTGCCATTTTCATTACCTCTTTCTCCGCCACCCGACATAGATA**AAAGCTTATCGGATACCCGTGACCTCGAGGGGGGGG**  
 CCGGTA**CCA**CGTGGCATACAGTGTTCAGATTTTTCTGTTTTATCAAGCTAGTGAGATTAGGGGCAAAA

SEQUENCES OF V<sub>k</sub>1-39, V<sub>k</sub>3-20, J<sub>k</sub>1, J<sub>k</sub>2, J<sub>k</sub>3, J<sub>k</sub>4, AND J<sub>k</sub>5 ARE IN LARGE FONT AND BOXED  
 MOUSE SEQUENCES ITALICIZED  
 HUMAN SEQUENCES IN REGULAR FONT  
 RESTRICTION ENZYME SITES IN BOLD  
 NEO CASSETTE SEQUENCES UNDERLINED  
 FERT SITES DOUBLE UNDERLINED

FIG. 24D

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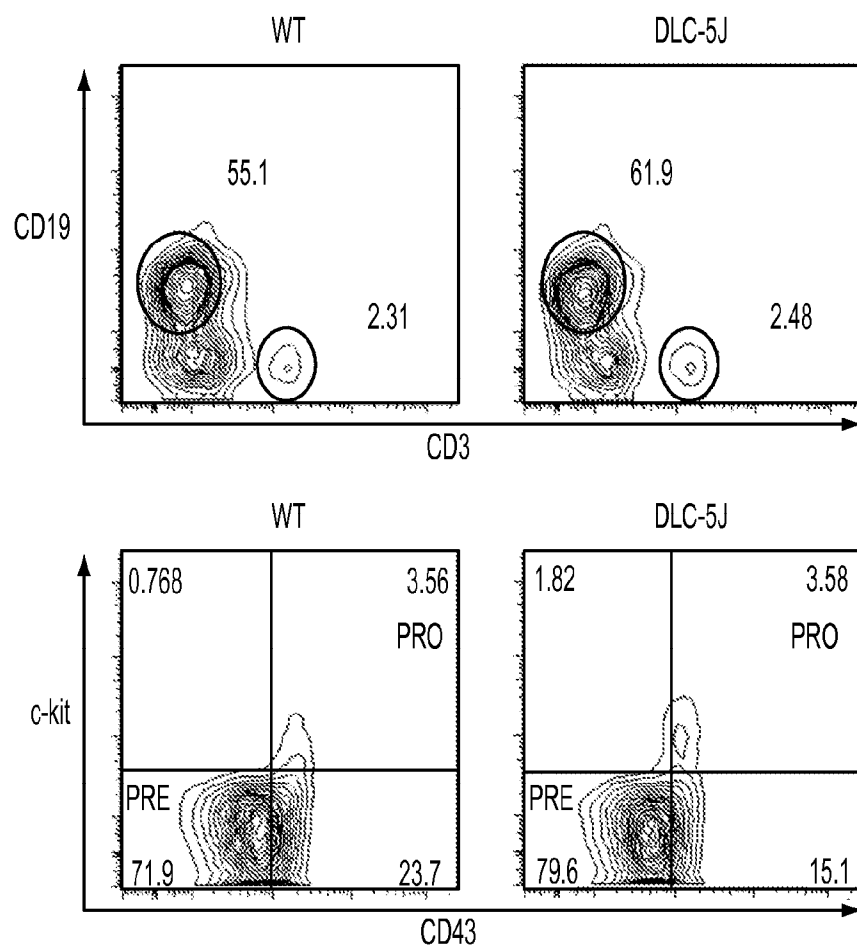


FIG. 25A

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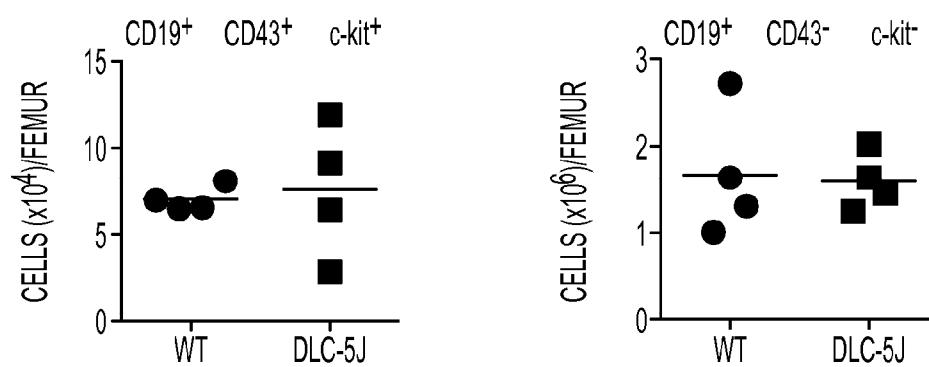


FIG. 25B

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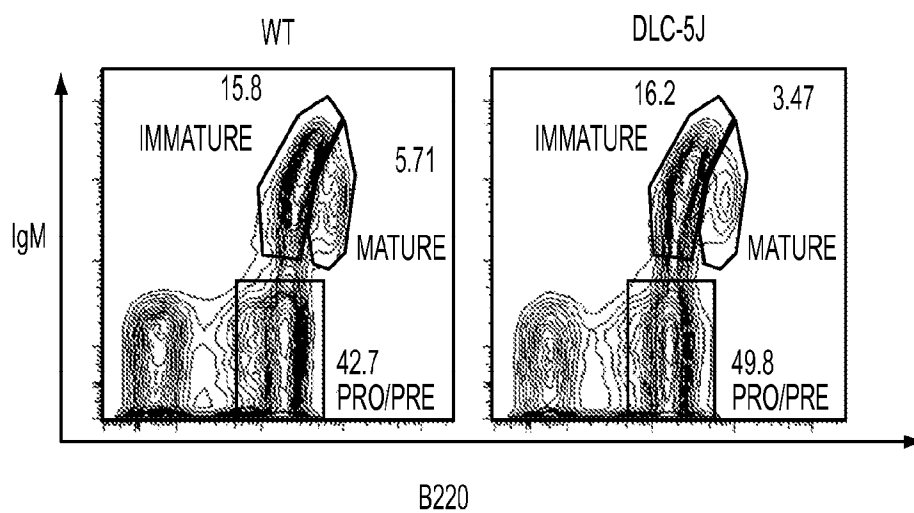


FIG. 26A

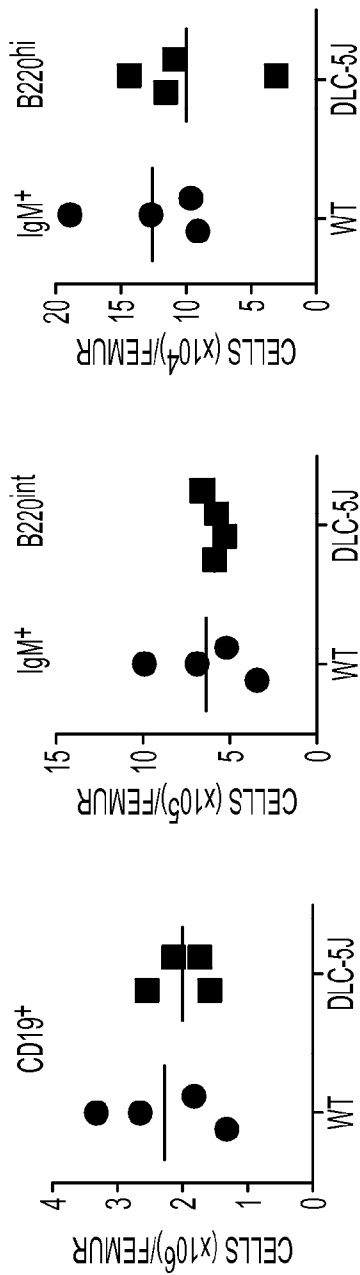


FIG. 26B

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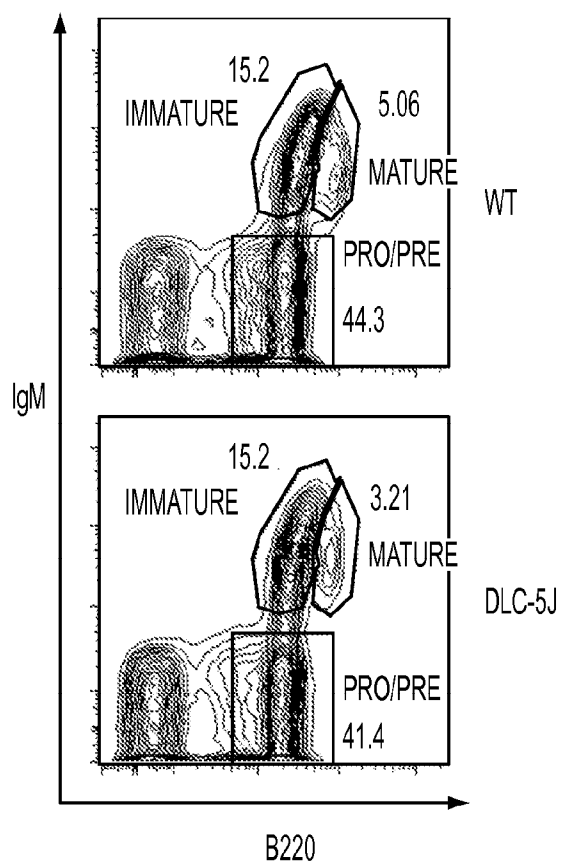


FIG. 27A

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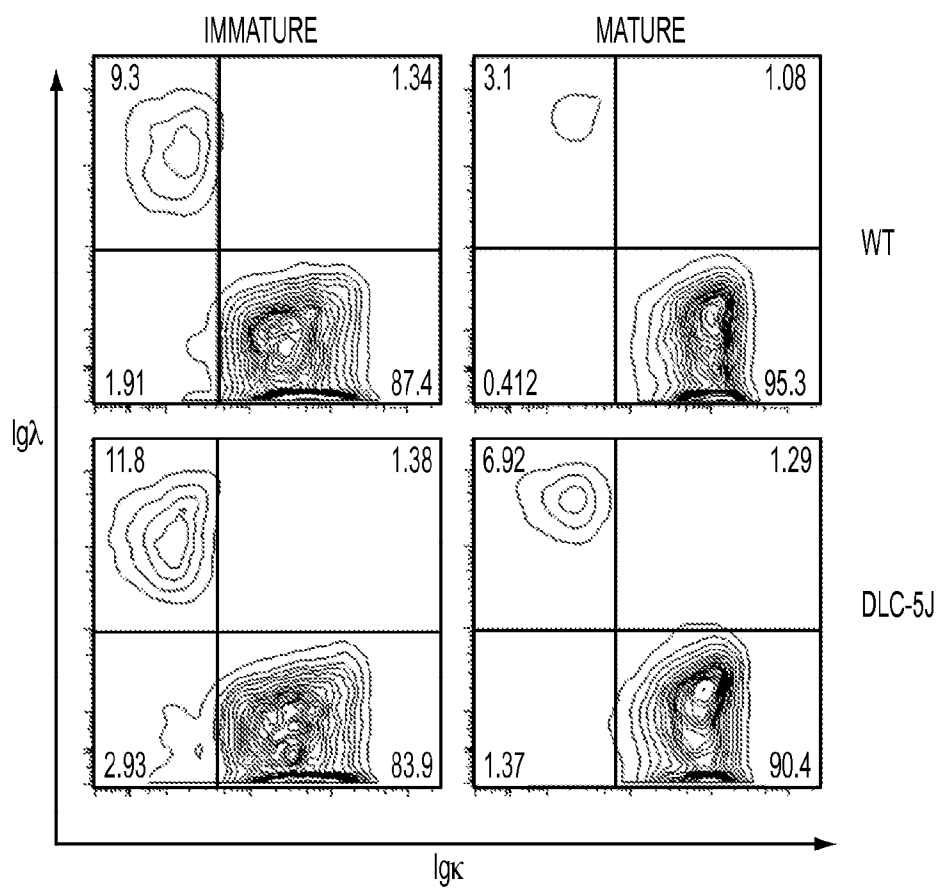


FIG. 27B

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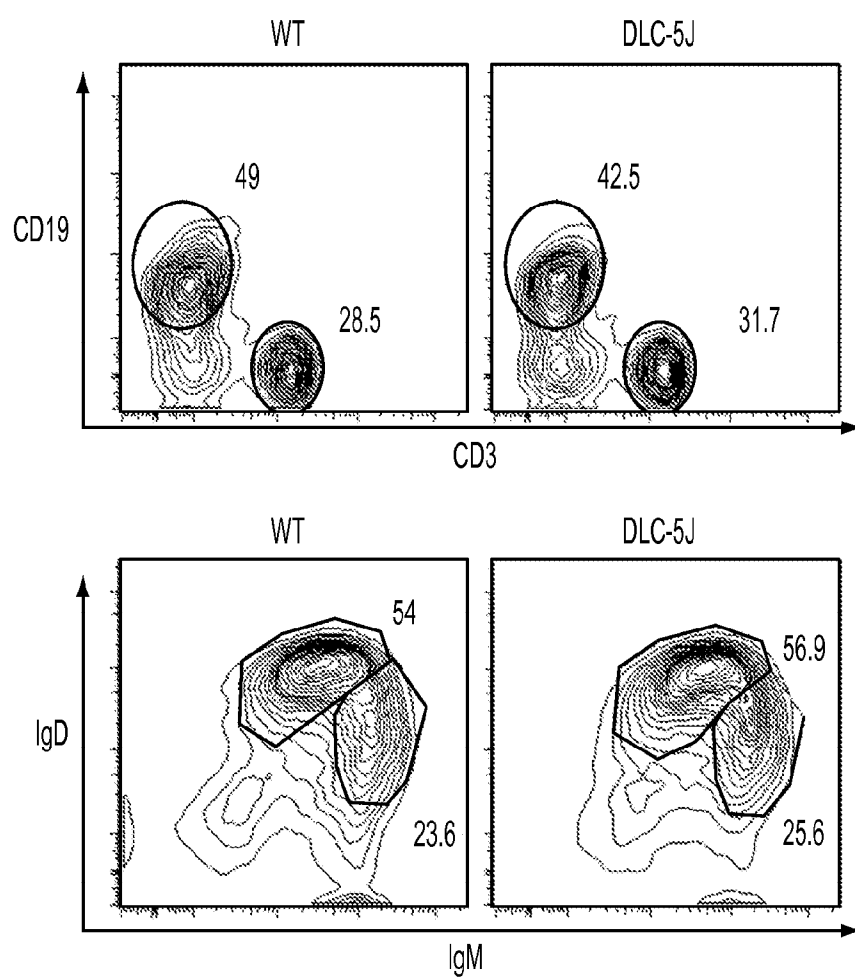


FIG. 28A

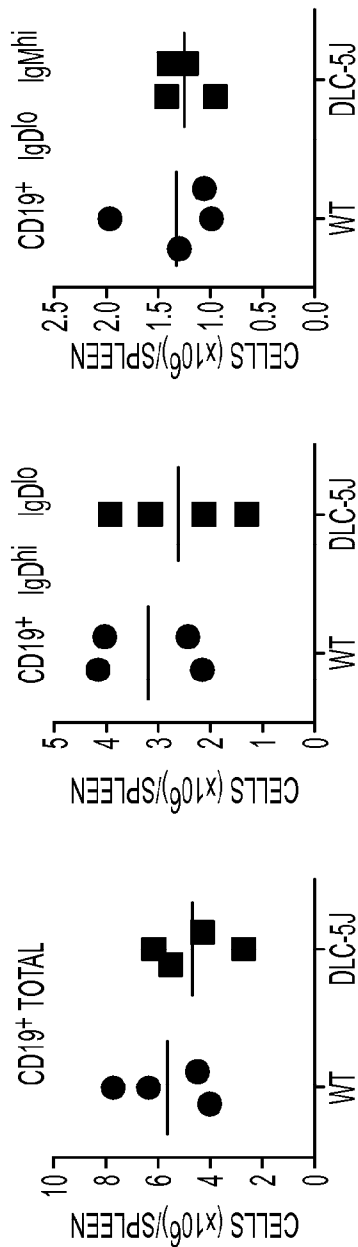


FIG. 28B

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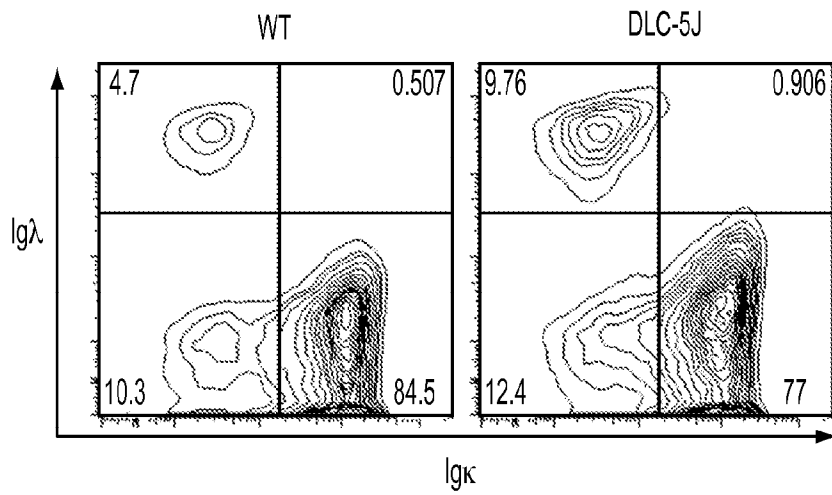


FIG. 29A

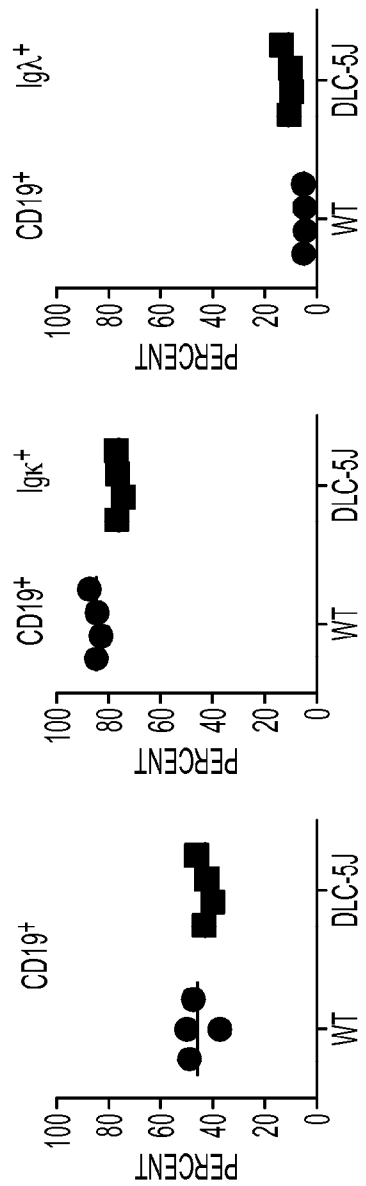


FIG. 29B

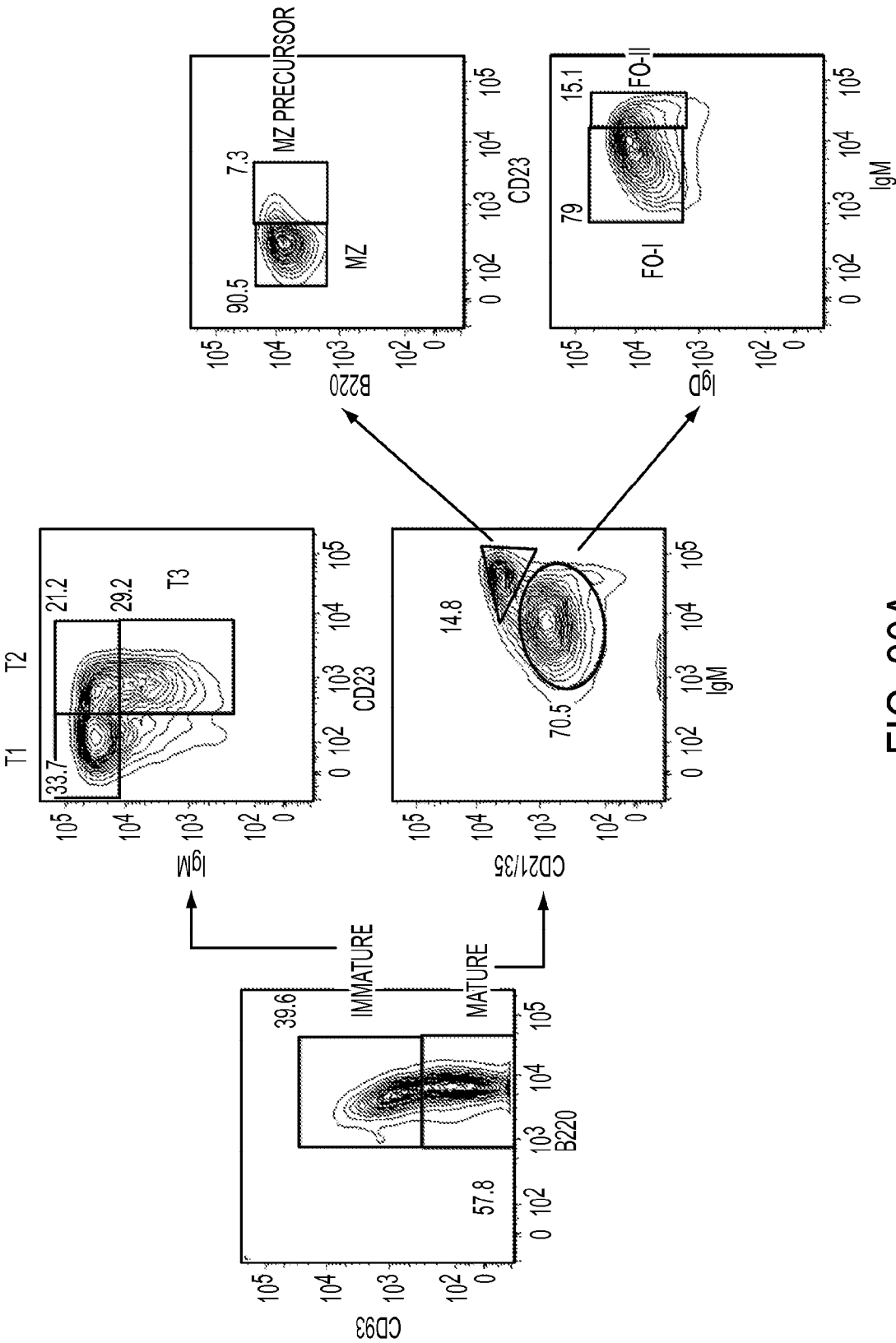


FIG. 30A

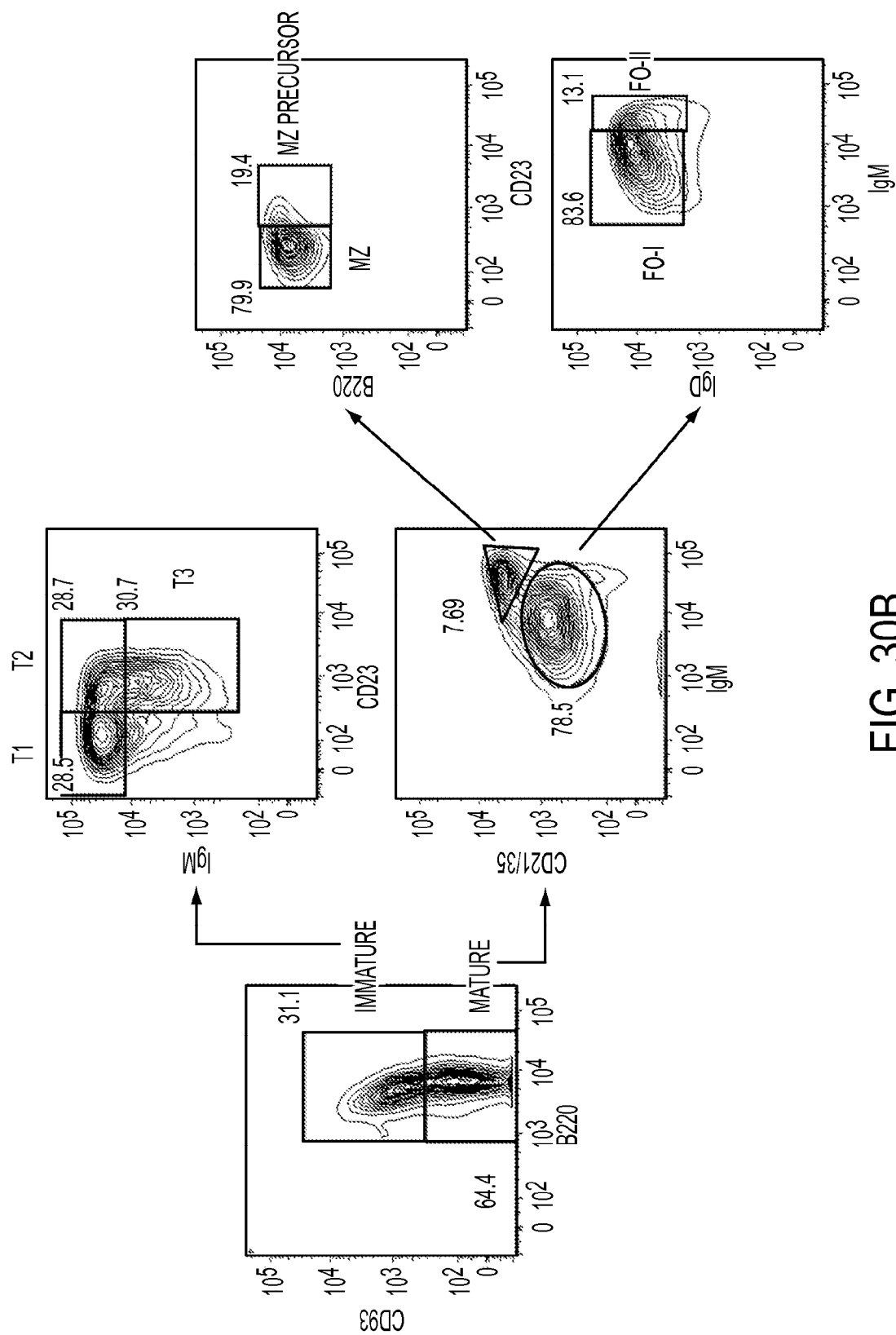


FIG. 30B

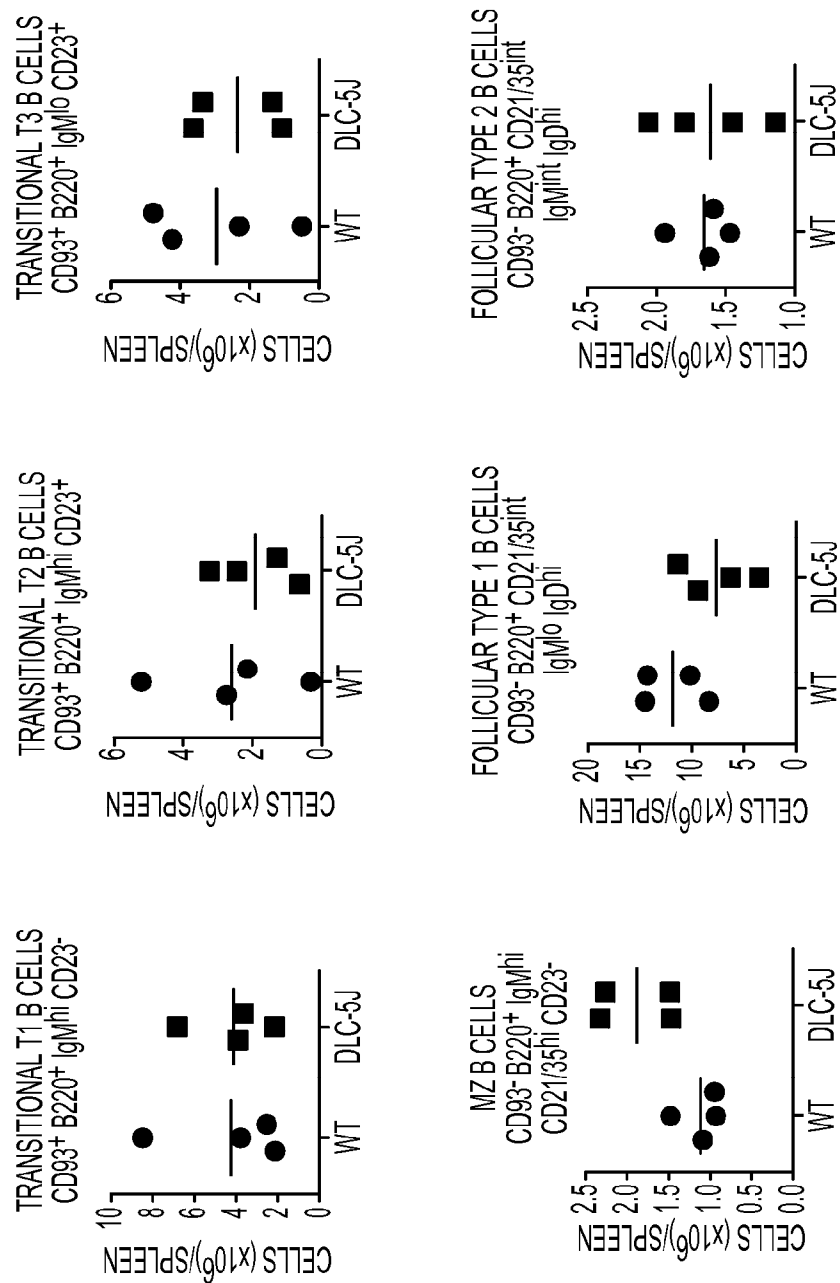


FIG. 31

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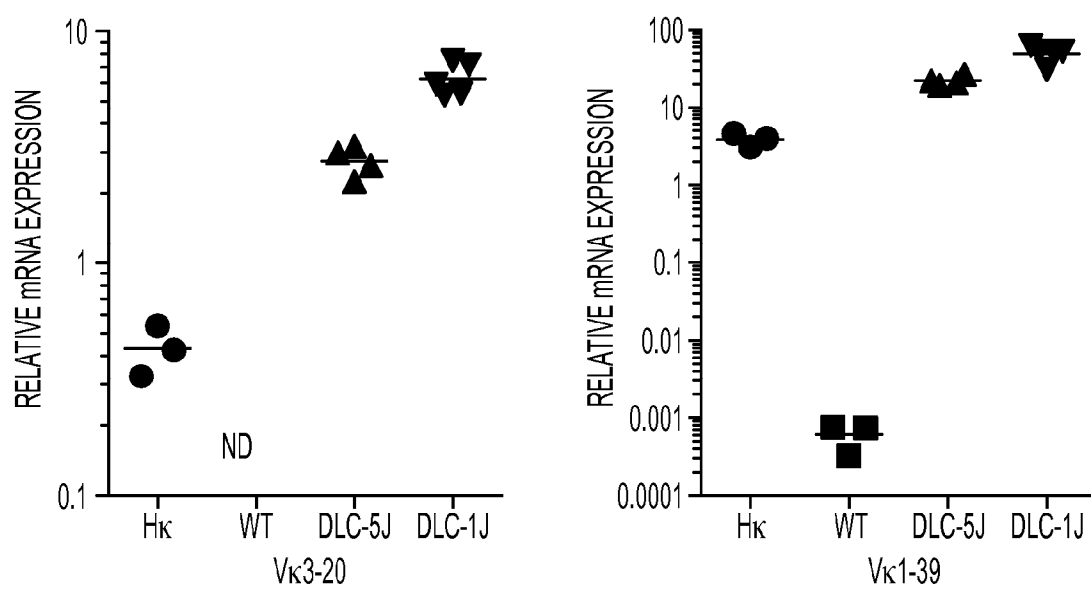


FIG. 32

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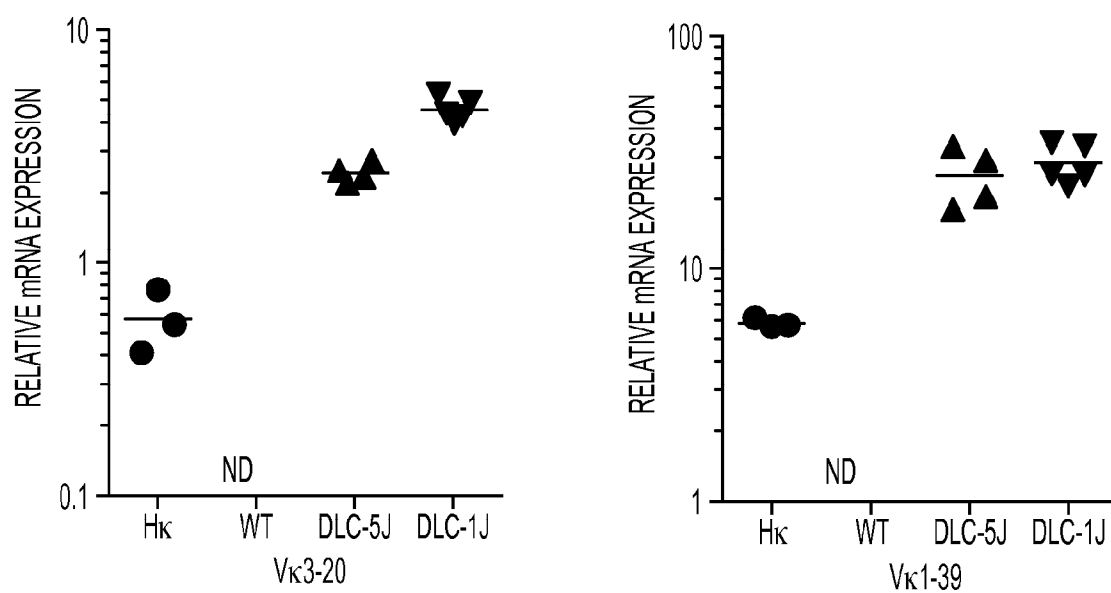
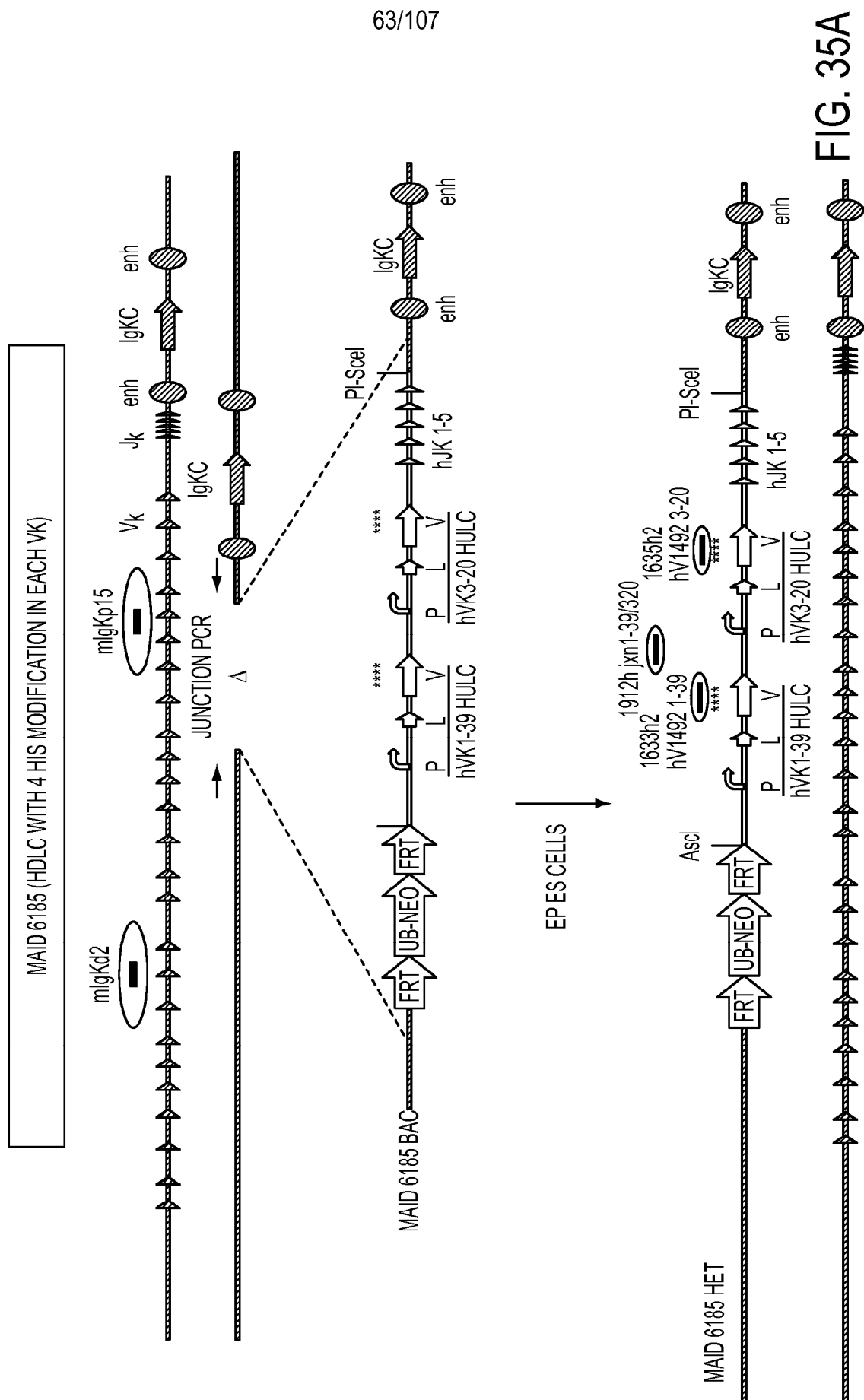


FIG. 33

| SITE-DIRECTED MUTAGENESIS PRIMERS FOR 4 HISTIDINE SUBSTITUTIONS IN CDR3s OF EACH VK OF DLC-JK1-5 PLASMID |                                                                                 |     |    |            |    |
|----------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------|-----|----|------------|----|
| PRIMER NAME                                                                                              | SEQUENCE                                                                        | %GC | N  | MISMATCHES | Tm |
| GERMLINE hVK1-39                                                                                         | CAACTTACTACTGTCA <b>ACA GAGT</b> TACAGTACCCCTCCACAGTGTACAAG                     |     |    |            |    |
| hVK1-39 HDLC(Q105H/Q106H/Y108H/P111H) F                                                                  | CAACTTACTACTGTCA <b>CCA TAGT</b> CACAGTACCCATCCACAGTGTACAAG                     | 45  | 51 | 4          | 79 |
| hVK1-39 HDLC(Q105H/Q106H/Y108H/P111H) R                                                                  | CTTGTAACACTGTGTGGG <b>AT</b> GGGTACTGT <b>GACTAT</b> GGTGACAGTAGTAAGTTG         | 45  | 51 | 4          | 79 |
| GERMLINE hVK3-20                                                                                         | GCAGTGTATTACTGTCA <b>GCAGTAT</b> GGT <b>AGCT</b> CACCTCCAC                      |     |    |            |    |
| hVK3-20 HDLC(Q105H/Q106H/Y107H/S109H) F                                                                  | AGATTTTGCAGTGTATTACTGT <b>CACCATCAT</b> GGT <b>CACT</b> CACCTCCACAGTTCAGCT      | 45  | 60 | 5          | 82 |
| hVK3-20 HDLC(Q105H/Q106H/Y107H/S109H) R                                                                  | AGCTGAATCACTGTGTGGAGGT <b>GAGT</b> GA <b>CCATGAT</b> GGTGACAGTAATACACTGCAAAATCT | 45  | 60 | 5          | 82 |

| PRIMER                                  | SEQ ID NO |
|-----------------------------------------|-----------|
| GERMLINE hVK1-39                        | 105       |
| hVK1-39 HDLC(Q105H/Q106H/Y108H/P111H) F | 106       |
| hVK1-39 HDLC(Q105H/Q106H/Y108H/P111H) R | 107       |
| GERMLINE hVK3-20                        | 108       |
| hVK3-20 HDLC(Q105H/Q106H/Y107H/S109H) F | 109       |
| hVK3-20 HDLC(Q105H/Q106H/Y107H/S109H) R | 110       |

FIG. 34



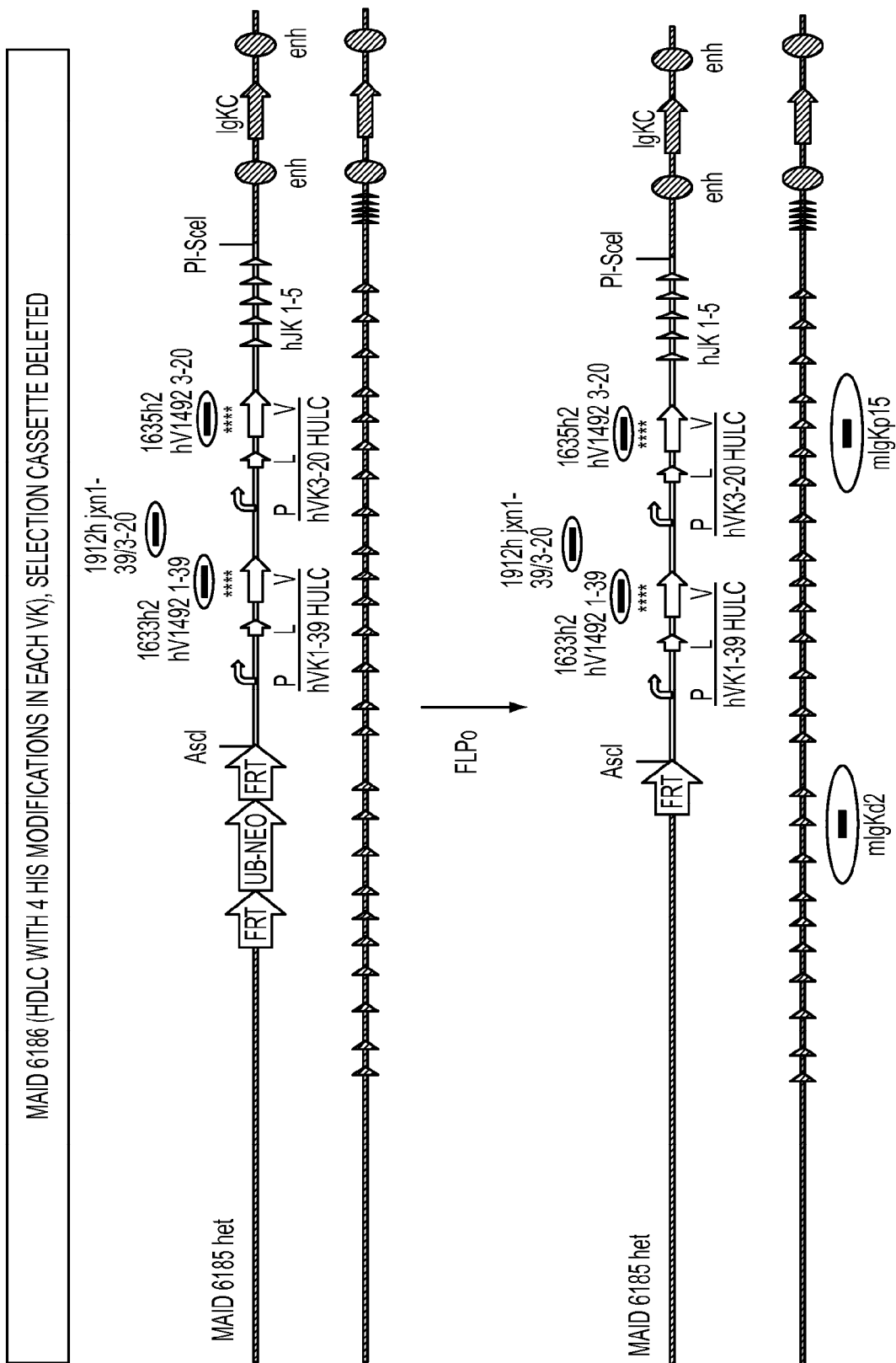


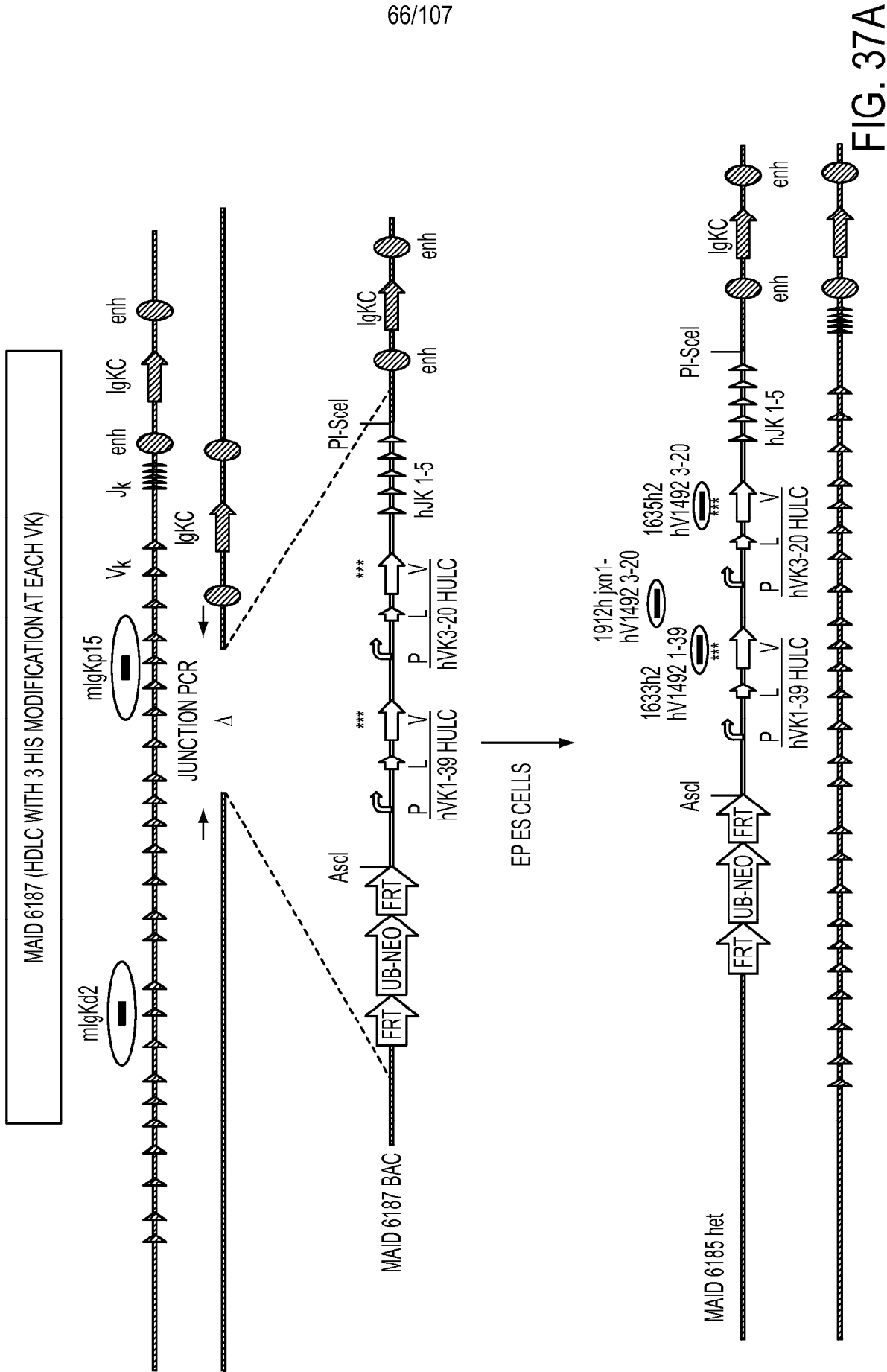
FIG. 35B

SITE-DIRECTED MUTAGENESIS PRIMERS FOR 3 HISTIDINE SUBSTITUTIONS IN CDR3s OF EACH VK OF DLC-JK1-5 PLASMID

| PRIMER NAME                             | SEQUENCE                                                                        | %GC  | N  | MISMATCHES | Tm |
|-----------------------------------------|---------------------------------------------------------------------------------|------|----|------------|----|
| GERMLINE hVK1-39                        | CAACTTACTACTGTCAACAGAGT <b>T</b> CAGTACCC <b>CT</b> CCACAGTGTACAAG              |      |    |            |    |
| hVK1-39 HDLC(Q105H/Q106H/Y108H/P111H) F | ATTTTGCAACTTACTACTGTCAACATAGT <b>C</b> ACAGTACCC <b>AT</b> CCACAGTGTAC          | 40.7 | 54 | 3          | 73 |
| hVK1-39 HDLC(Q105H/Q106H/Y108H/P111H) R | GTAACACTGTGGGATGGGTACTGT <b>G</b> ACTATGT <b>T</b> GACAGTAGTAAGTTGCCAAAT        | 40.7 | 54 | 3          | 73 |
| GERMLINE hVK3-20                        | GCAGTGTTACTGTGCAGCAGTATGGT <b>AG</b> CTCACCTCCAC                                |      |    |            |    |
| hVK3-20 HDLC(Q105H/Q106H/Y107H/S109H) F | ATTTTGCAGTGTTACTGTGCACCA <b>TT</b> ATGGT <b>CA</b> CTCACCTCCACAGTGT <b>C</b> AG | 42.9 | 56 | 4          | 75 |
| hVK3-20 HDLC(Q105H/Q106H/Y107H/S109H) R | CTGAATCACTGTGGGAGGTGAGT <b>G</b> ACCATA <b>AT</b> TGGTGACAGTAATACACTGCCAAAT     | 42.9 | 56 | 4          | 75 |

| PRIMER                                  | SEQ ID NO |
|-----------------------------------------|-----------|
| GERMLINE hVK1-39                        | 117       |
| hVK1-39 HDLC(Q105H/Q106H/Y108H/P111H) F | 118       |
| hVK1-39 HDLC(Q105H/Q106H/Y108H/P111H) R | 119       |
| GERMLINE hVK3-20                        | 120       |
| hVK3-20 HDLC(Q105H/Q106H/Y107H/S109H) F | 121       |
| hVK3-20 HDLC(Q105H/Q106H/Y107H/S109H) R | 122       |

FIG. 36



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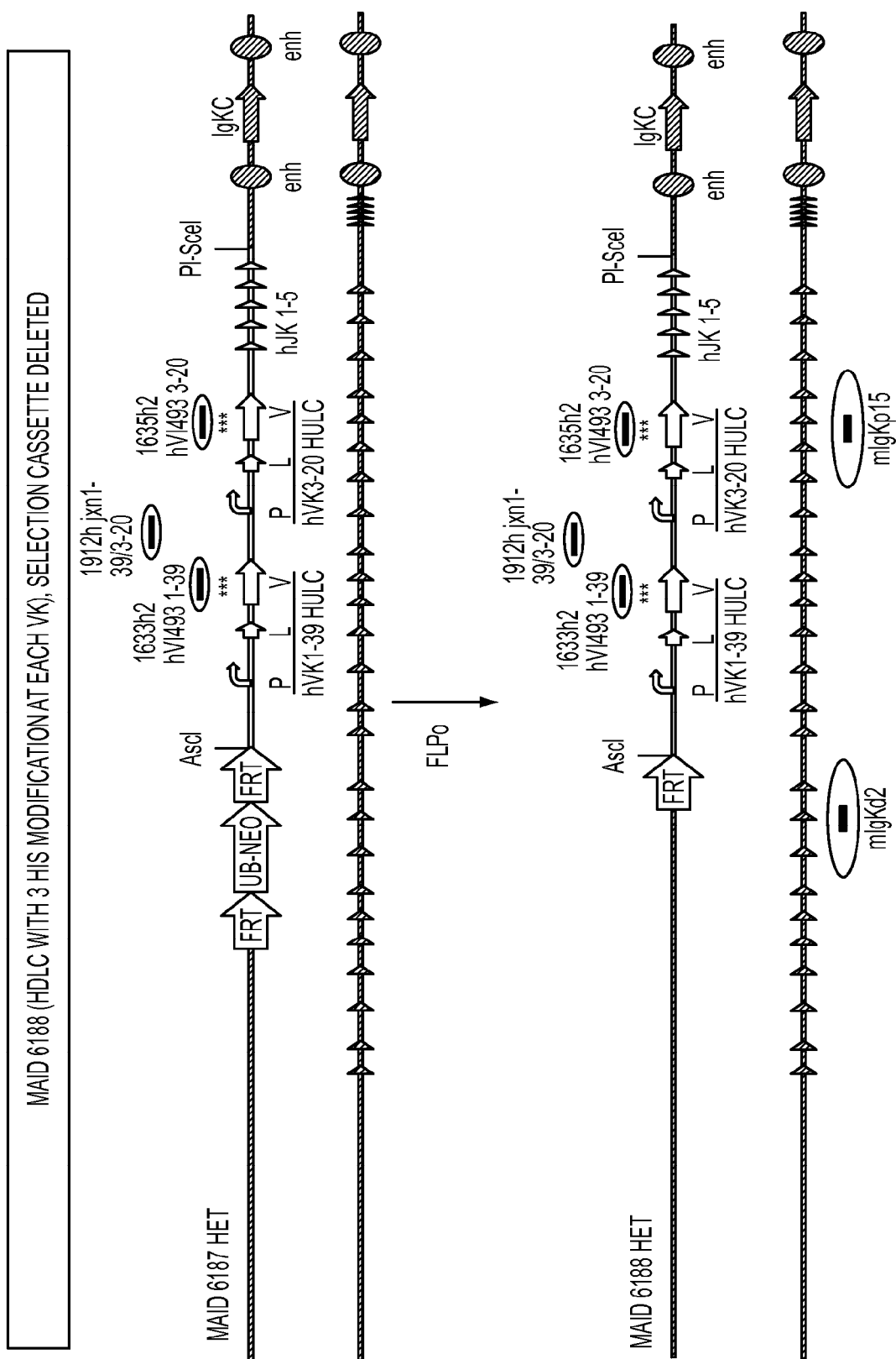


FIG. 37B

|               |                                             |                   |                          |               |
|---------------|---------------------------------------------|-------------------|--------------------------|---------------|
| IGKV3-20*01 F | FR1                                         | CDR1              | FR2                      | CDR2          |
|               | <u>EIVLTQSPGTL</u> SLSPGERATLSCRAS          | <u>QSVSSSY</u>    | <u>LAWYQQKPGQAPRLLIY</u> | <u>GAS</u>    |
|               | EIVLTQSPGTL                                 | SLSPGERATLSCRAS   | LAWYQQKPGQAPRLLIY        | GAS           |
|               |                                             |                   |                          |               |
| IGKV3-20*01 F | FR3                                         | CDR3              |                          |               |
|               | <u>SRATGIPDRFSGSGGTDF</u> TLTISRLEPEDFAVYYC | <u>HHYGH</u> S    |                          | SEQ ID NO:131 |
|               | SRATGIPDRFSGSGGTDF                          | TLTISRLEPEDFAVYYC | QQYGSSP                  | SEQ ID NO:132 |
|               |                                             |                   | <b>HH H</b>              |               |

FIG. 38A

|               |                                    |                          |               |      |
|---------------|------------------------------------|--------------------------|---------------|------|
| IGKV1-39*01 F | FR1                                | CDR1                     | FR2           | CDR2 |
|               | DIQMTQSPSSLSASVGDRTITCRAS          | QSISSY LNWYQQKPGKAPKLLIY | AAS           |      |
|               | DIQMTQSPSSLSASVGDRTITCRAS          | QSISSY LNWYQQKPGKAPKLLIY | AAS           |      |
| IGKV1-39*01 F | FR3                                | CDR3                     |               |      |
|               | SLQSGVPSRFSGSGTDFTLTISSLQPEDFATYYC | QHSSTH                   | SEQ ID NO:133 |      |
|               | SLQSGVPSRFSGSGTDFTLTISSLQPEDFATYYC | QQSYSTP                  | SEQ ID NO:134 |      |
|               |                                    | H H H                    |               |      |

|               |                                    |                          |               |      |
|---------------|------------------------------------|--------------------------|---------------|------|
| IGKV1-39*01 F | FR1                                | CDR1                     | FR2           | CDR2 |
|               | DIQMTQSPSSLSASVGDRTITCRAS          | QSISSY LNWYQQKPGKAPKLLIY | AAS           |      |
|               | DIQMTQSPSSLSASVGDRTITCRAS          | QSISSY LNWYQQKPGKAPKLLIY | AAS           |      |
| IGKV1-39*01 F | FR3                                | CDR3                     |               |      |
|               | SLQSGVPSRFSGSGTDFTLTISSLQPEDFATYYC | QHSSTK                   | SEQ ID NO:135 |      |
|               | SLQSGVPSRFSGSGTDFTLTISSLQPEDFATYYC | QQSYSTP                  | SEQ ID NO:134 |      |
|               |                                    | H H H                    |               |      |

FIG. 38B

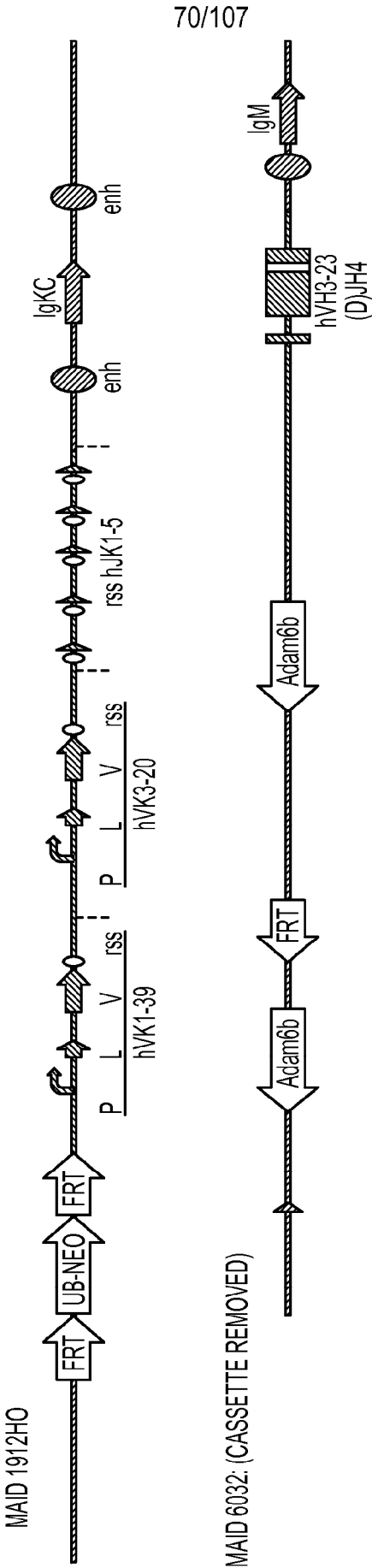


FIG. 39

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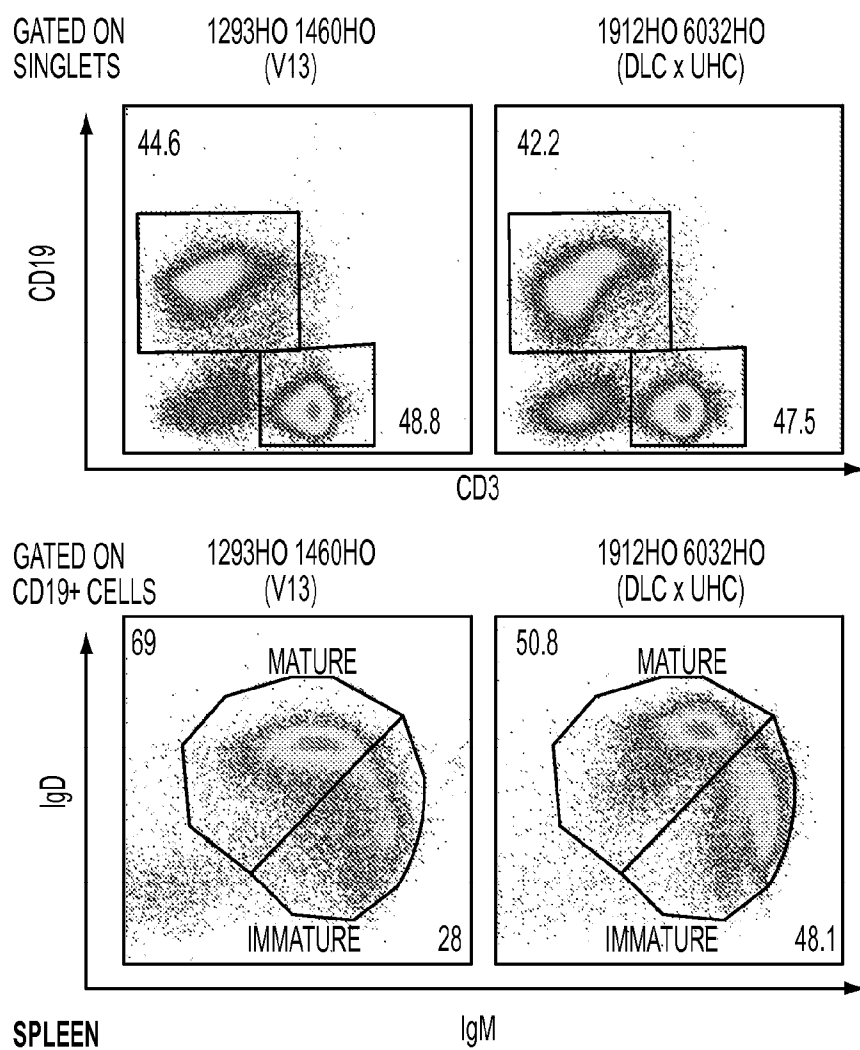


FIG. 40A

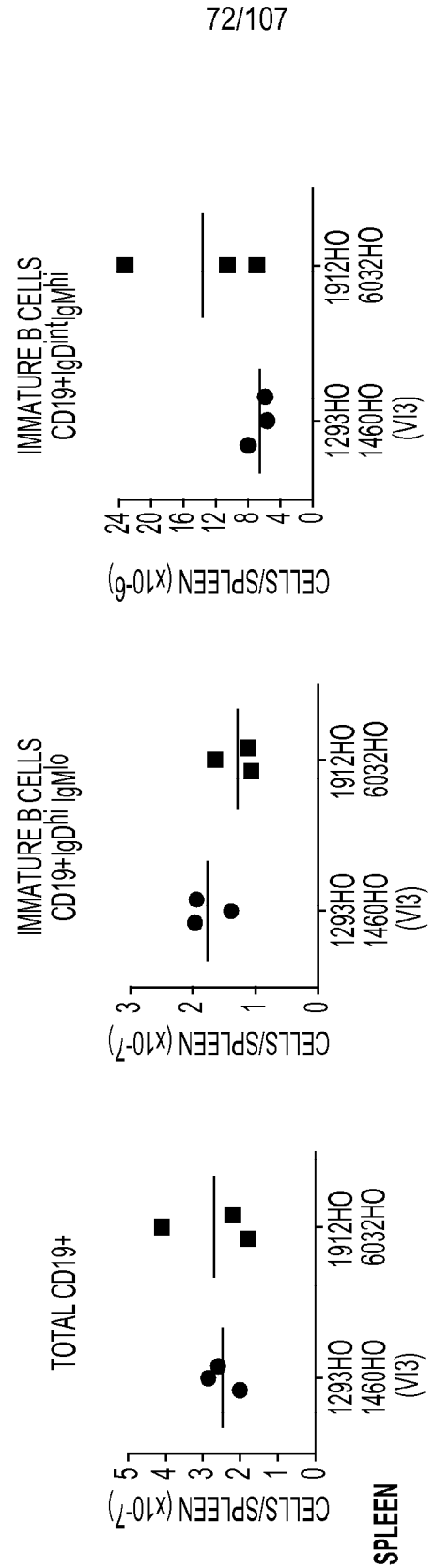


FIG. 40B

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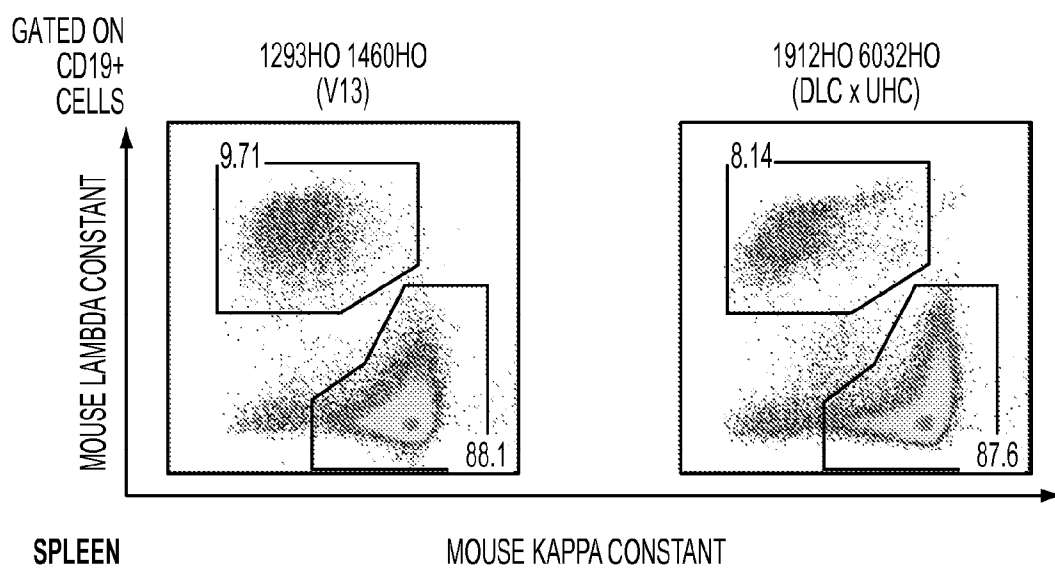
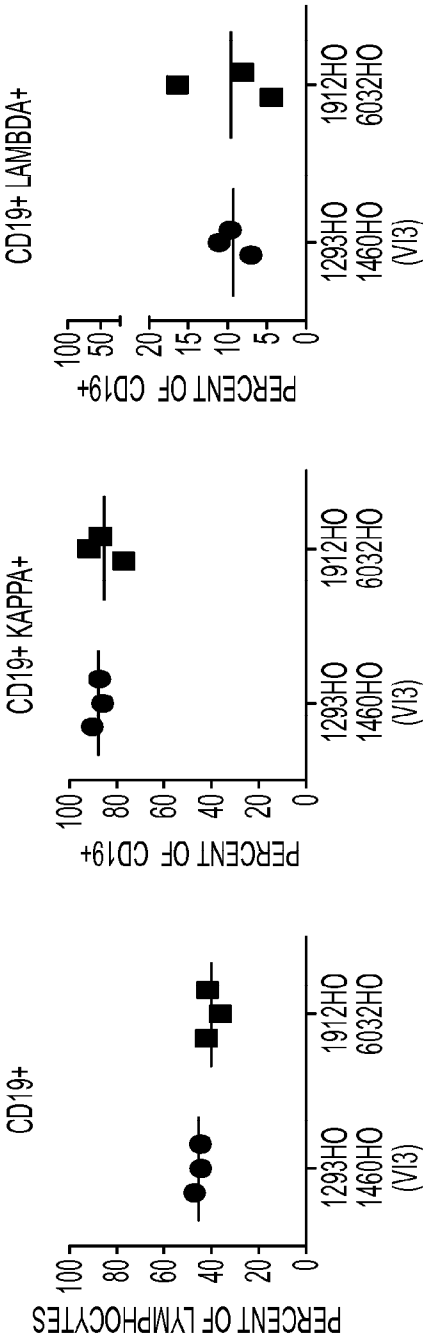


FIG. 41A



SPLEEN

FIG. 41B

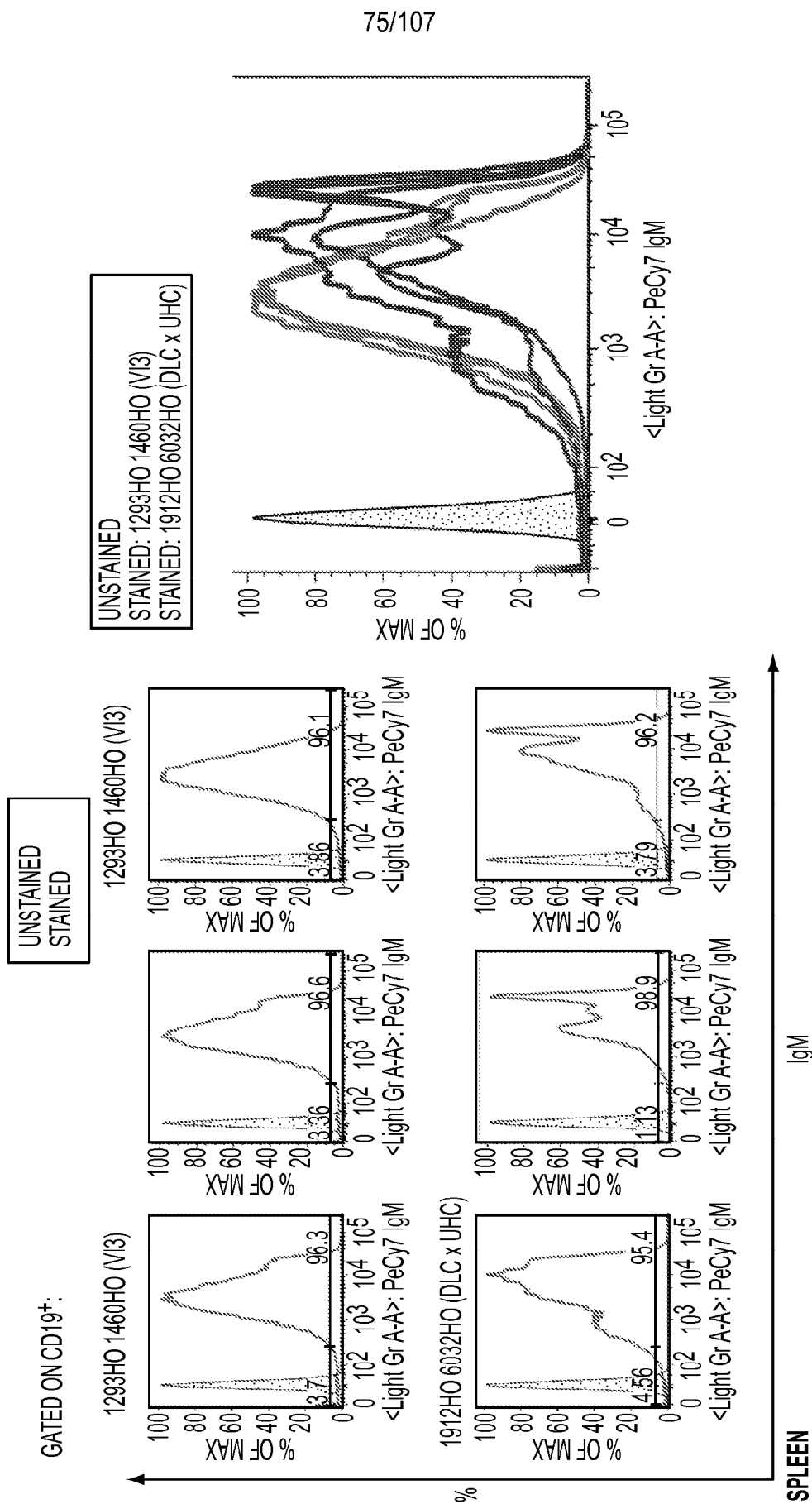


FIG. 42

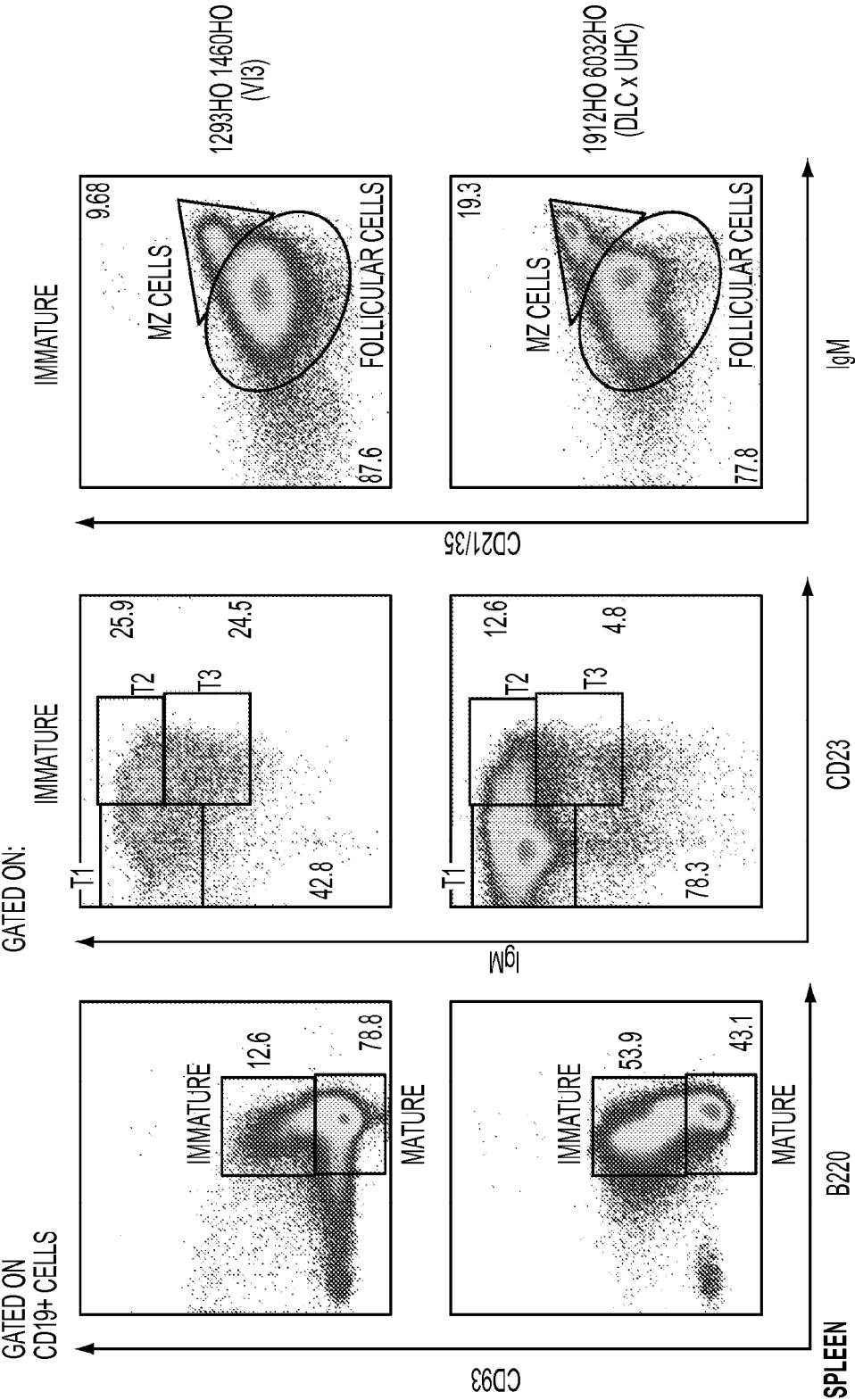


FIG. 43A

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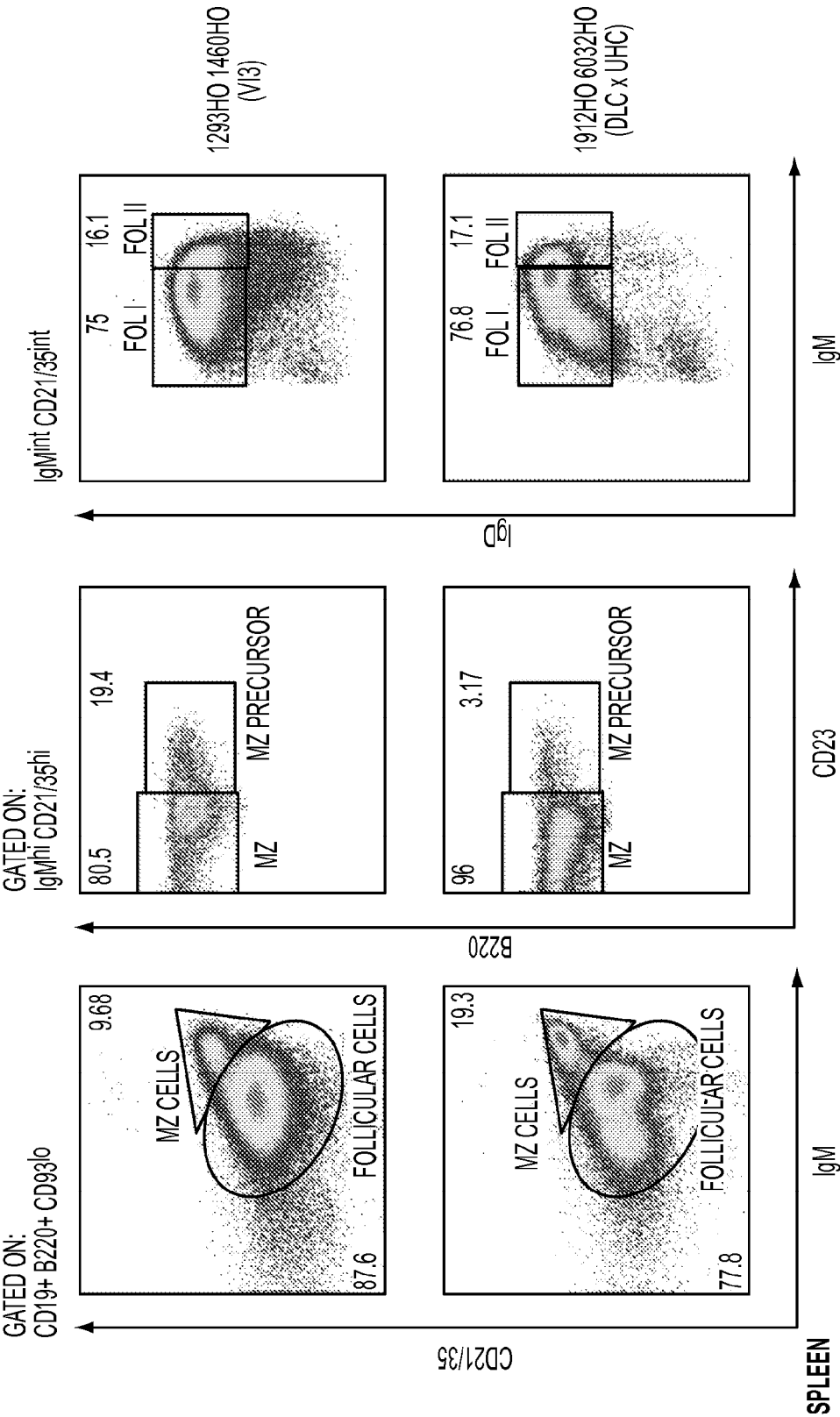


FIG. 43B

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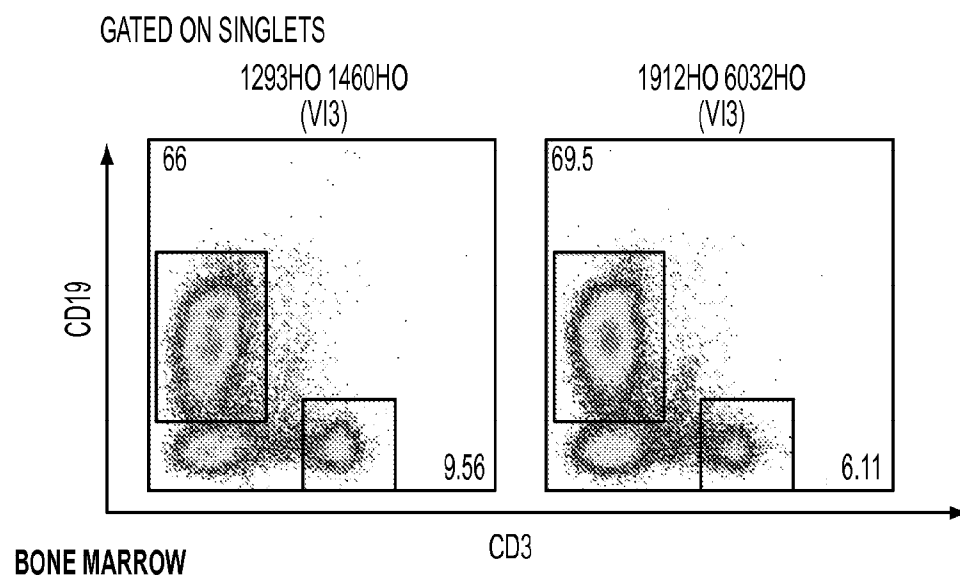


FIG. 44A

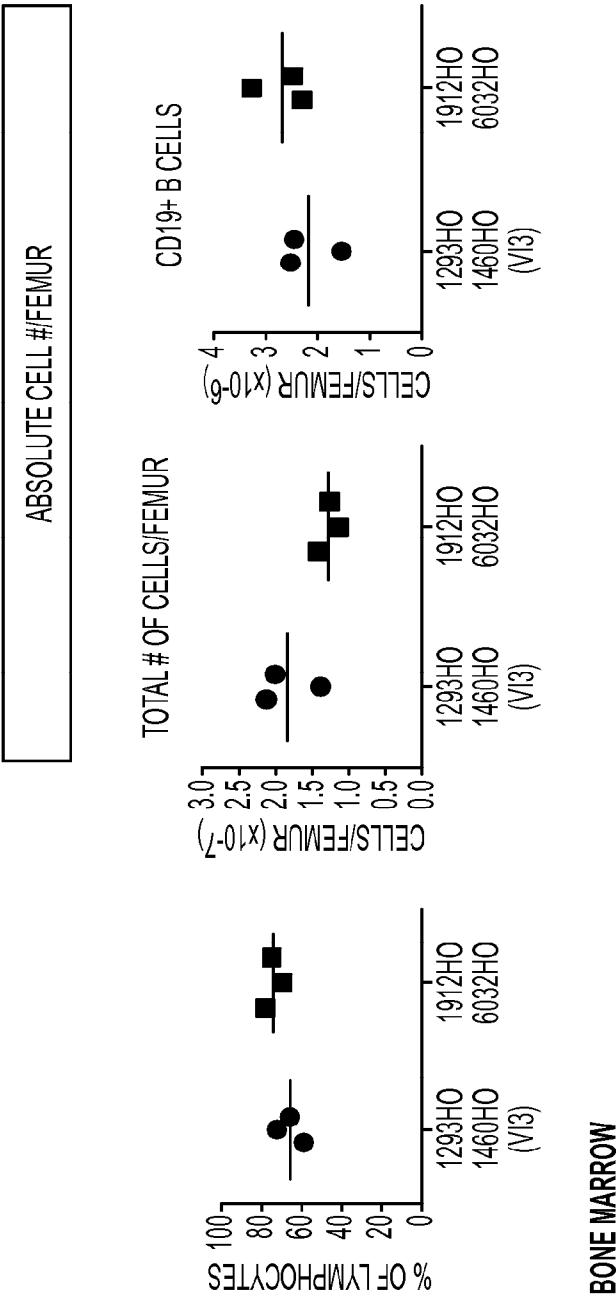


FIG. 44B

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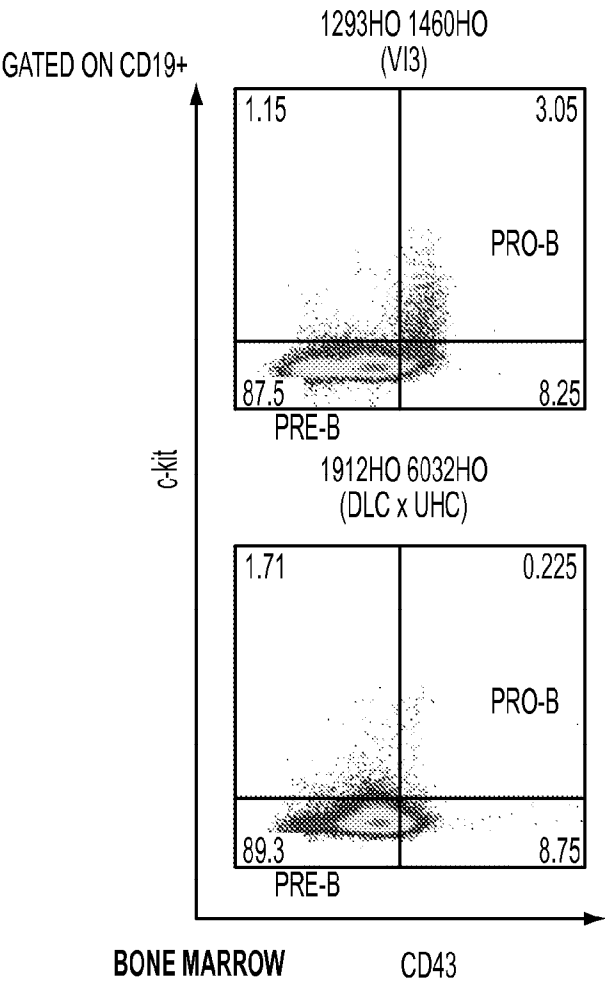


FIG. 45A

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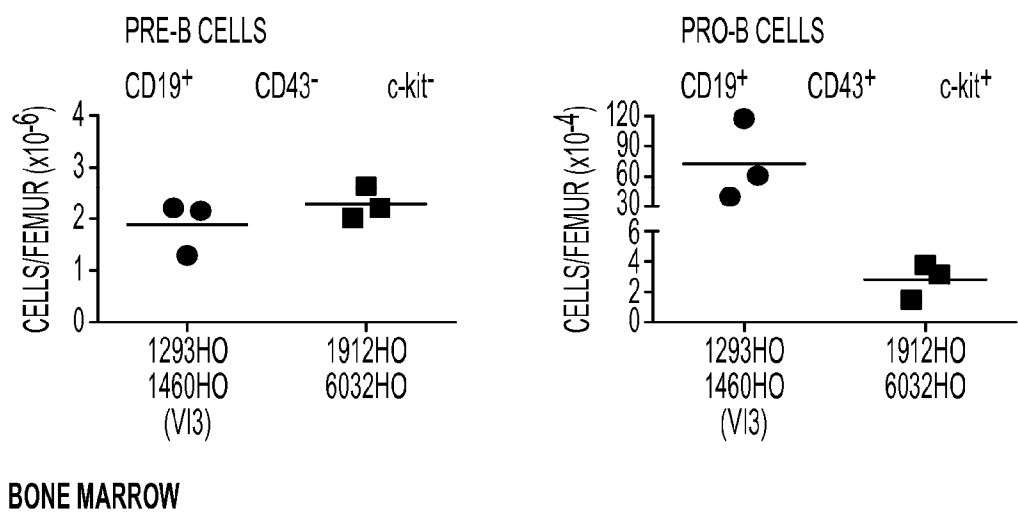


FIG. 45B

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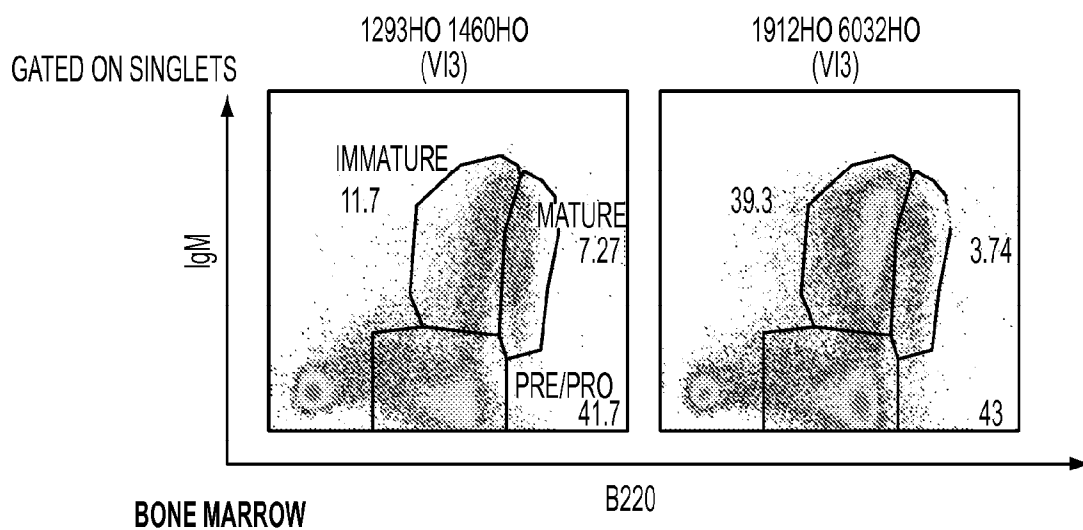


FIG. 46A

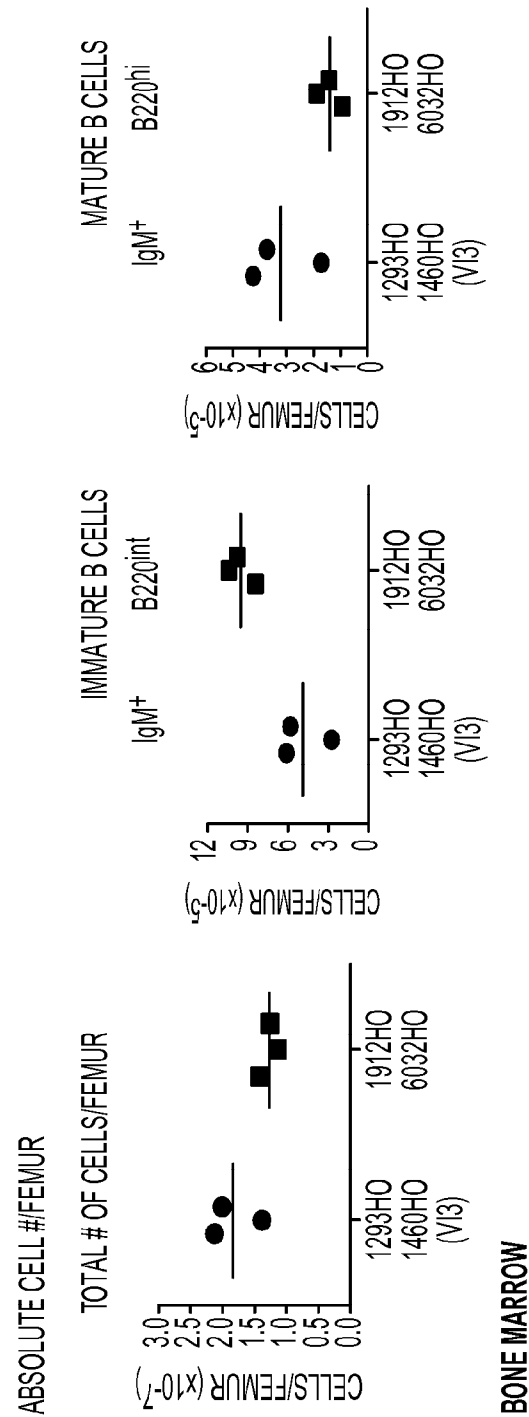


FIG. 46B

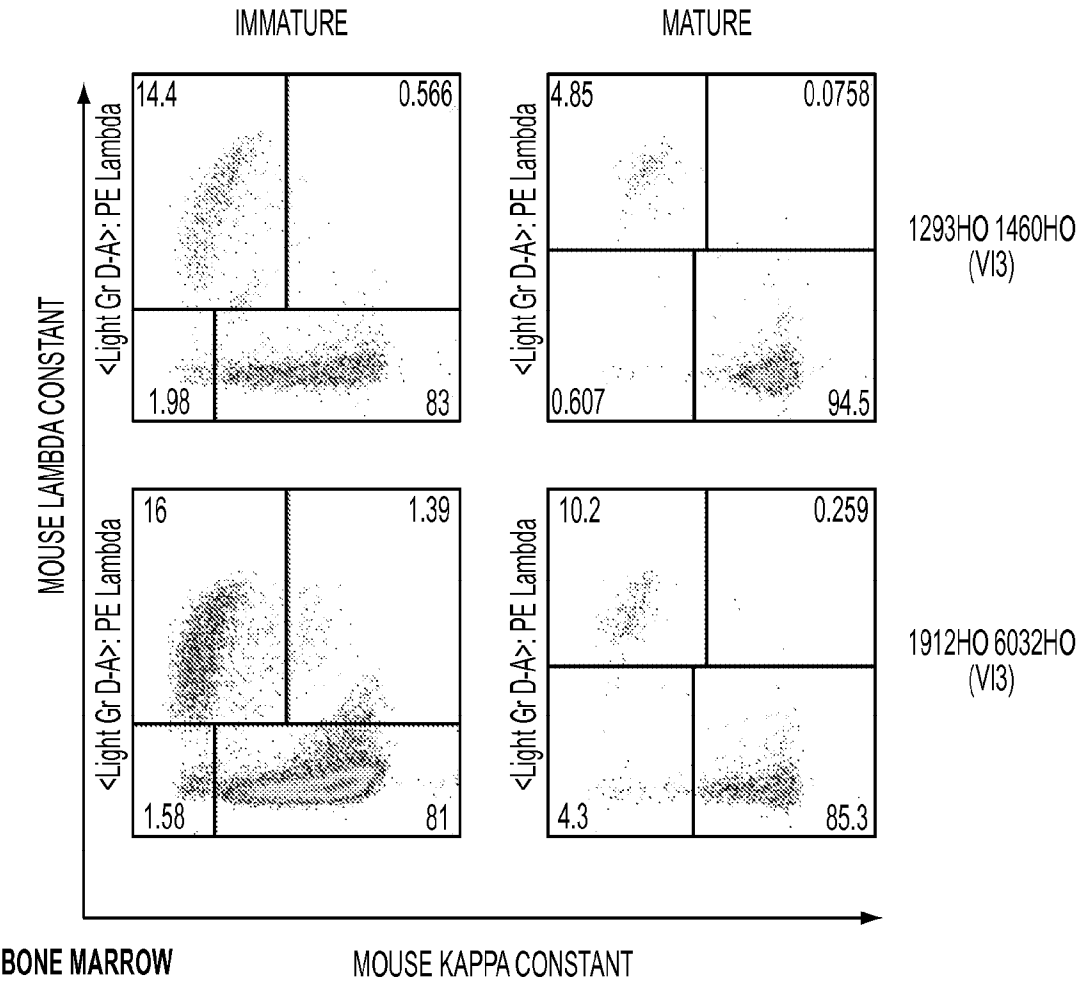


FIG. 47

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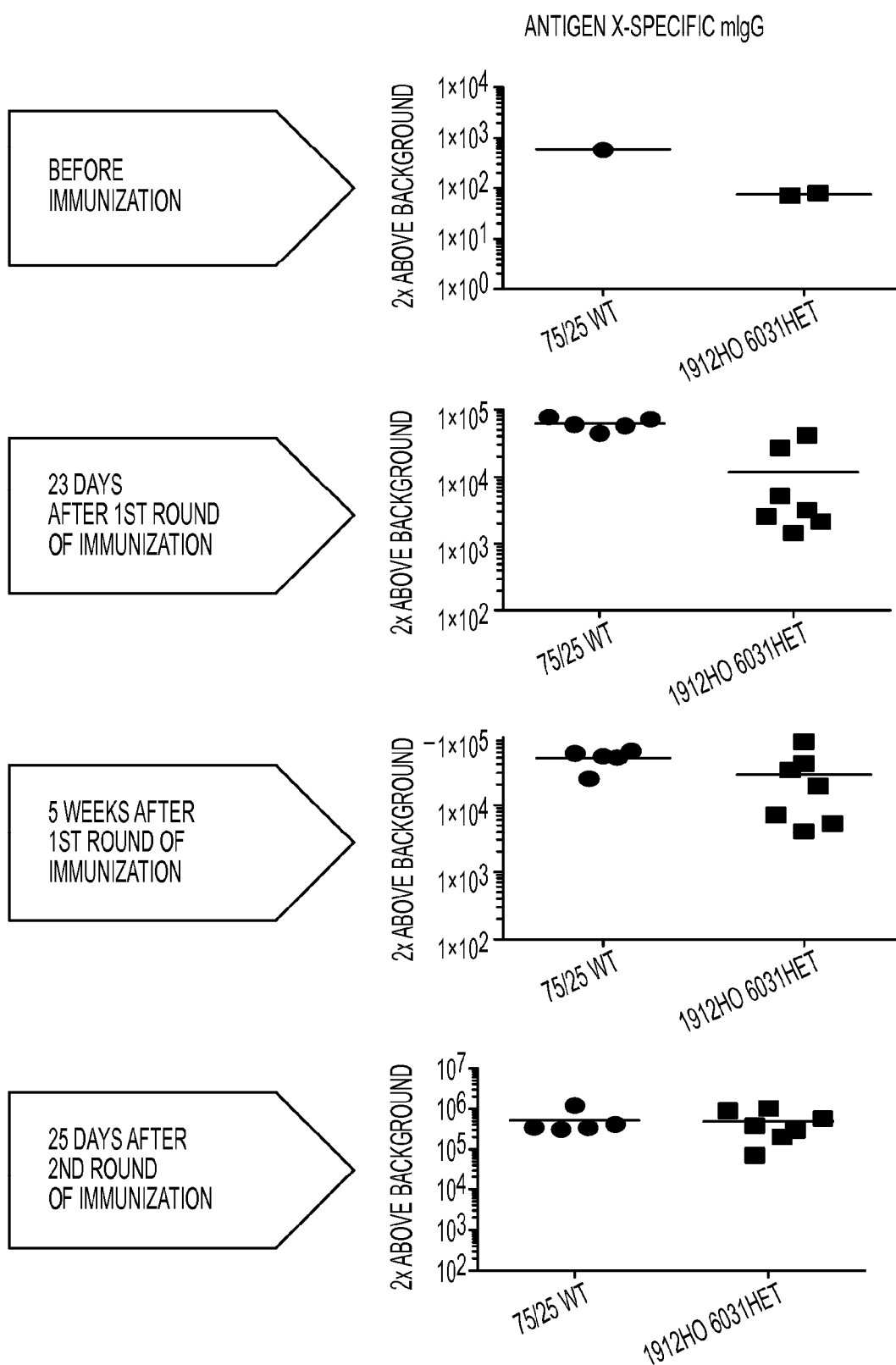


FIG. 48

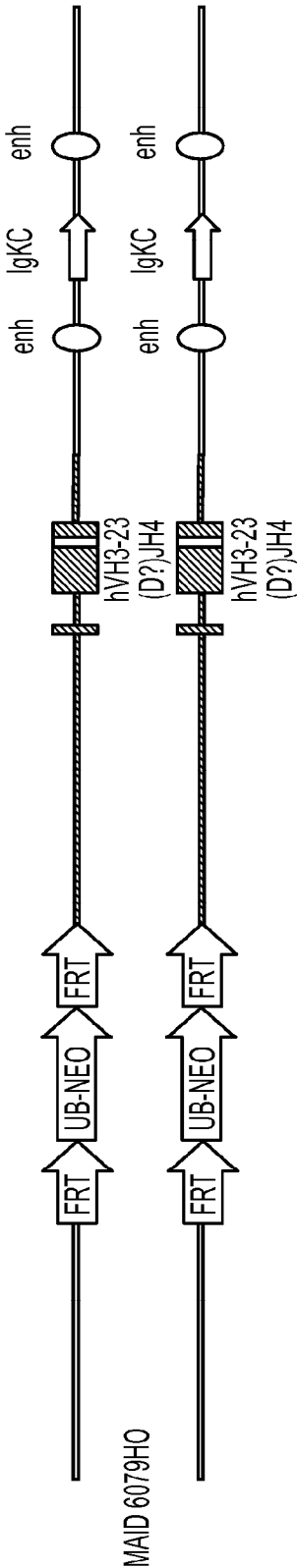


FIG. 49

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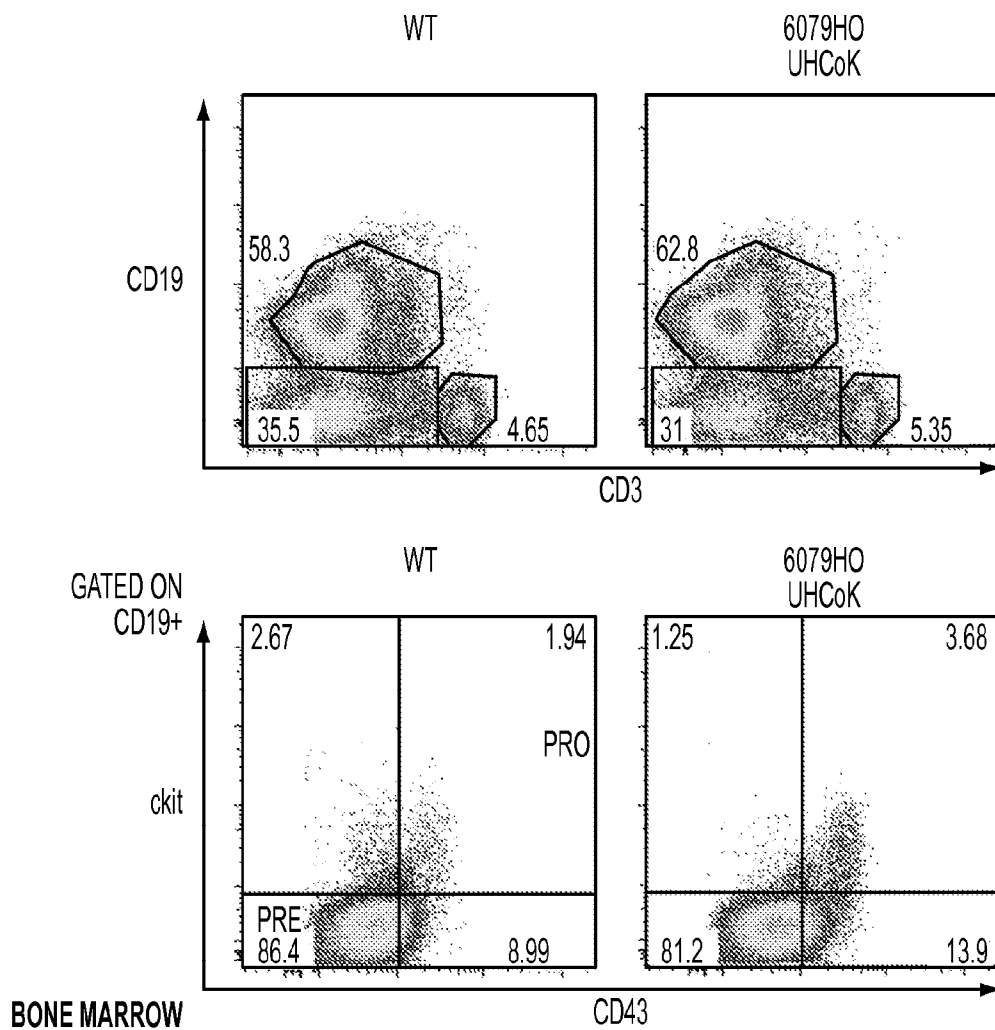


FIG. 50A

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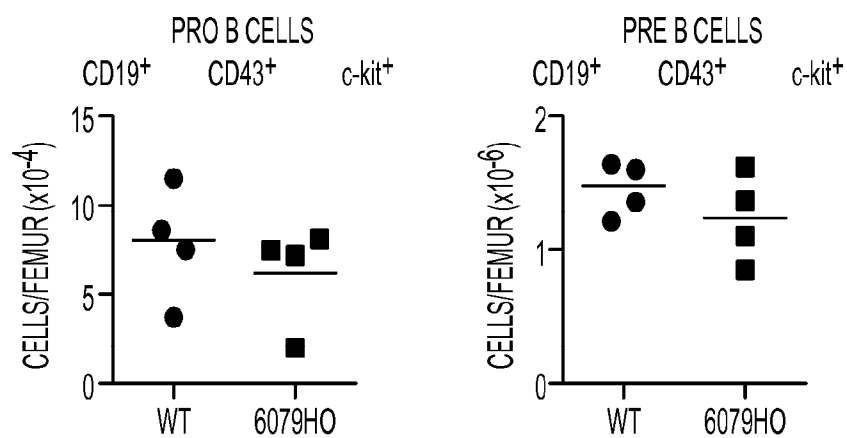


FIG. 50B

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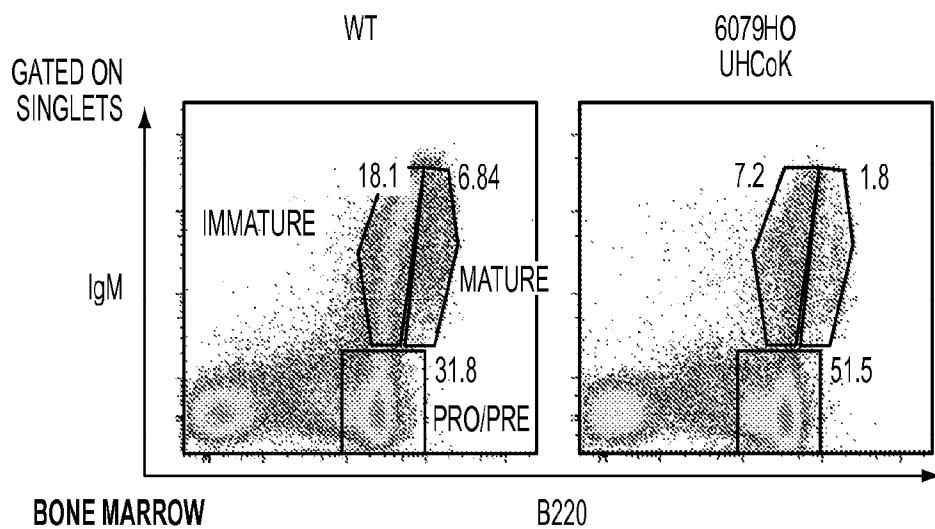


FIG. 51A

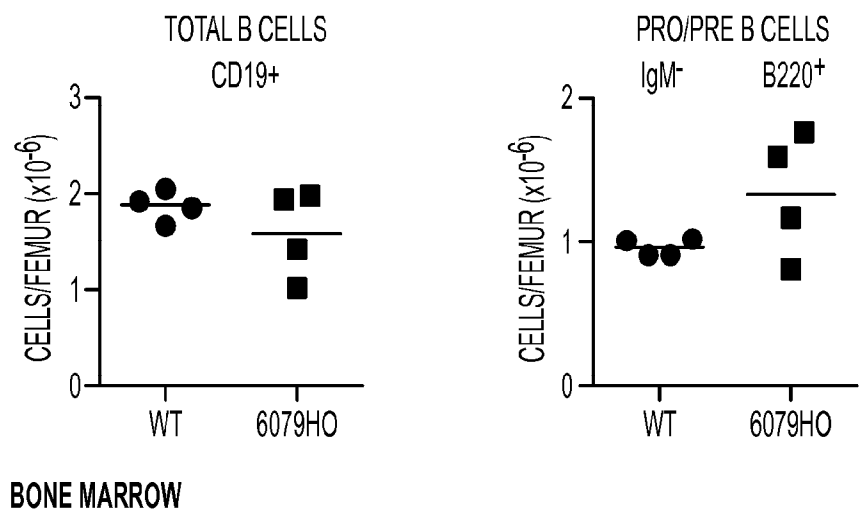


FIG. 51B

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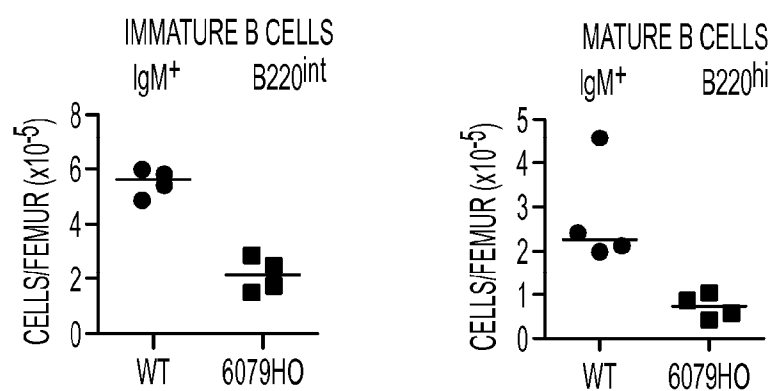


FIG. 51C

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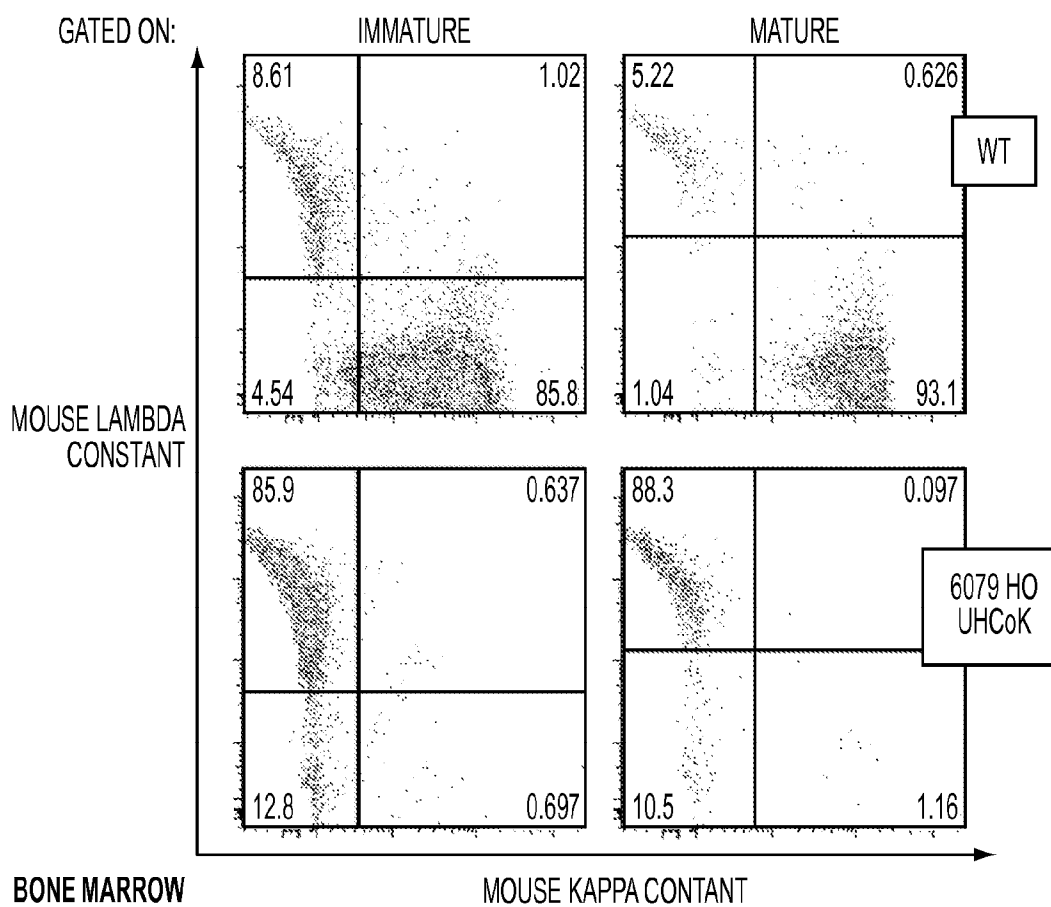


FIG. 52

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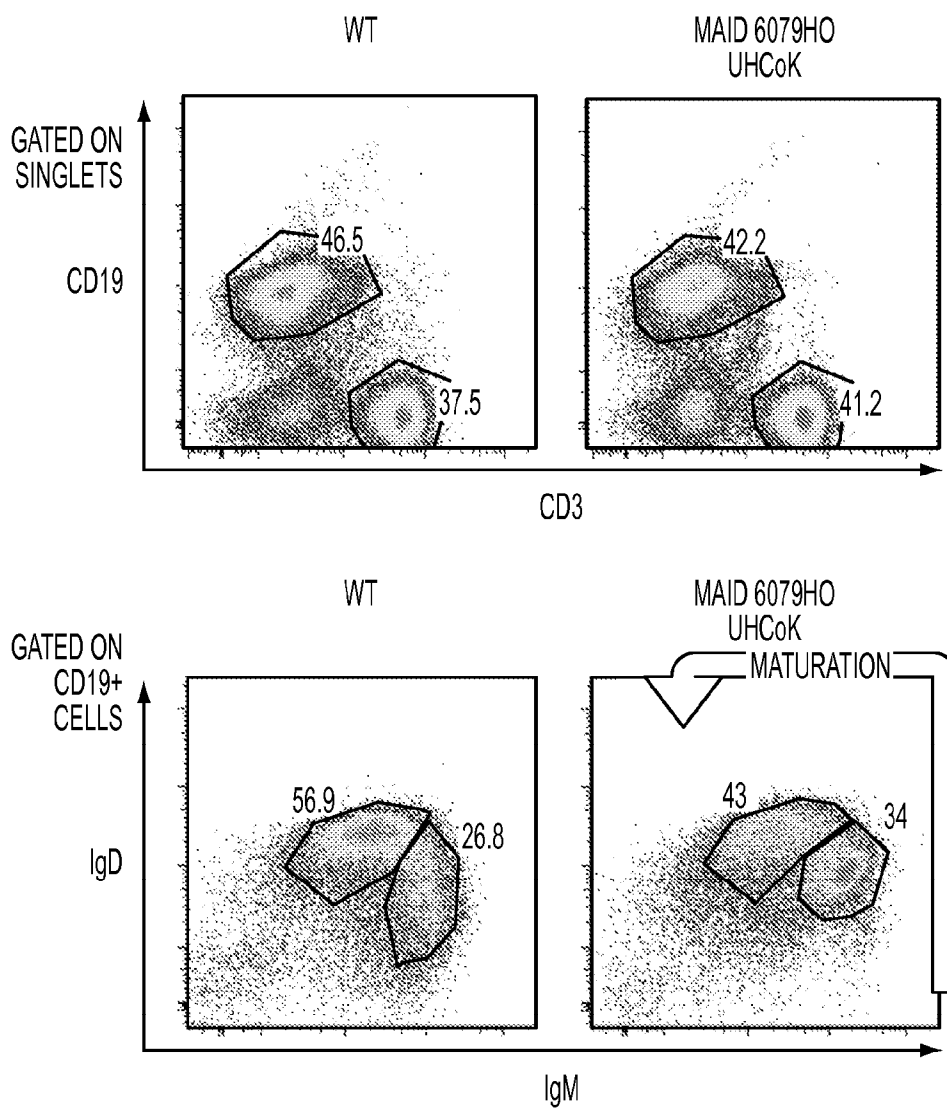
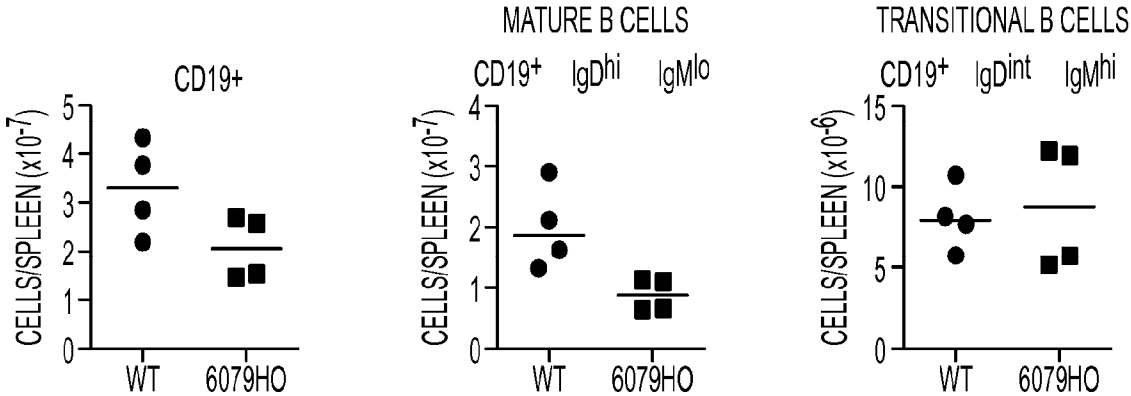


FIG. 53A



SPLEEN

FIG. 53B

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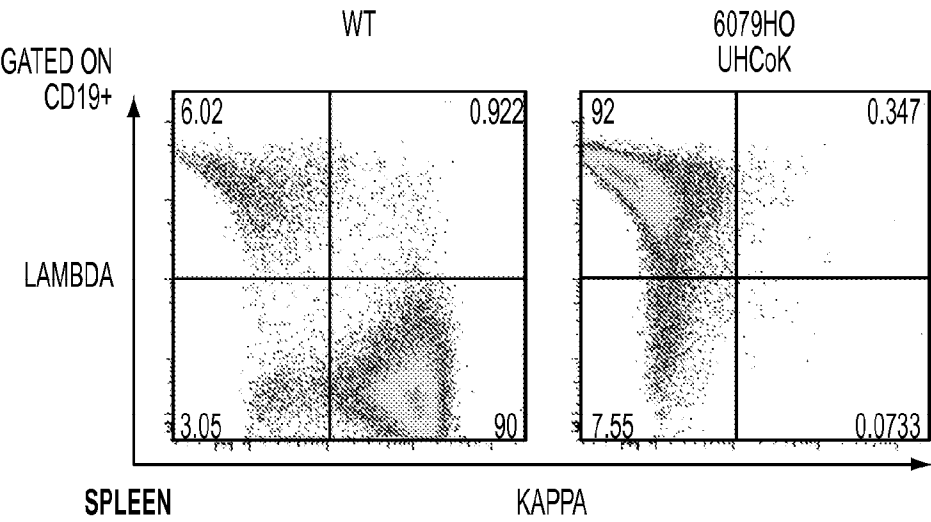


FIG. 54A

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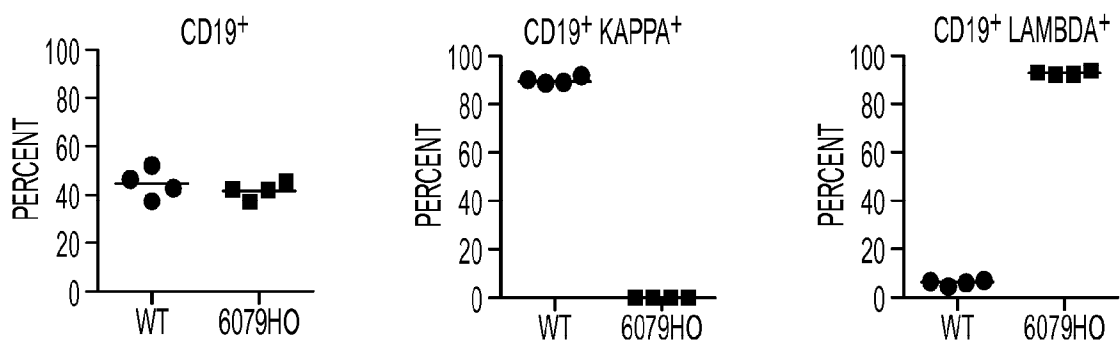


FIG. 54B

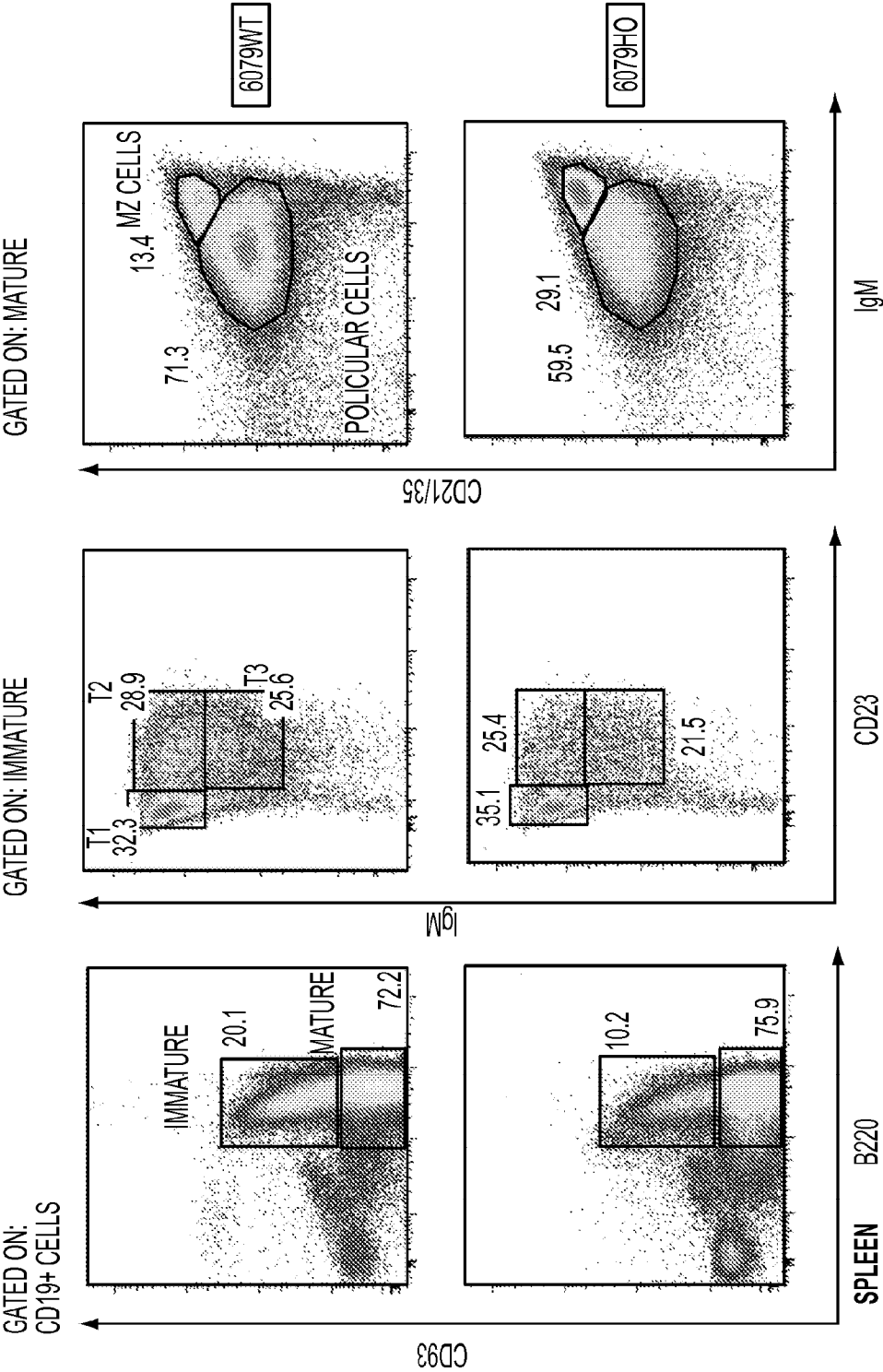


FIG. 55

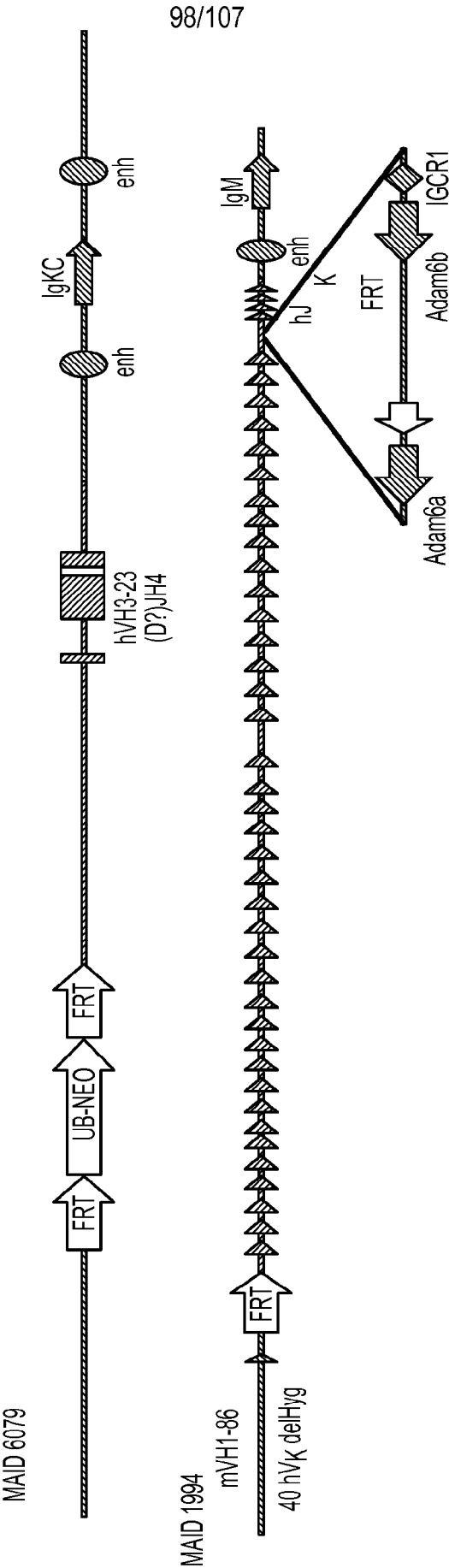


FIG. 56

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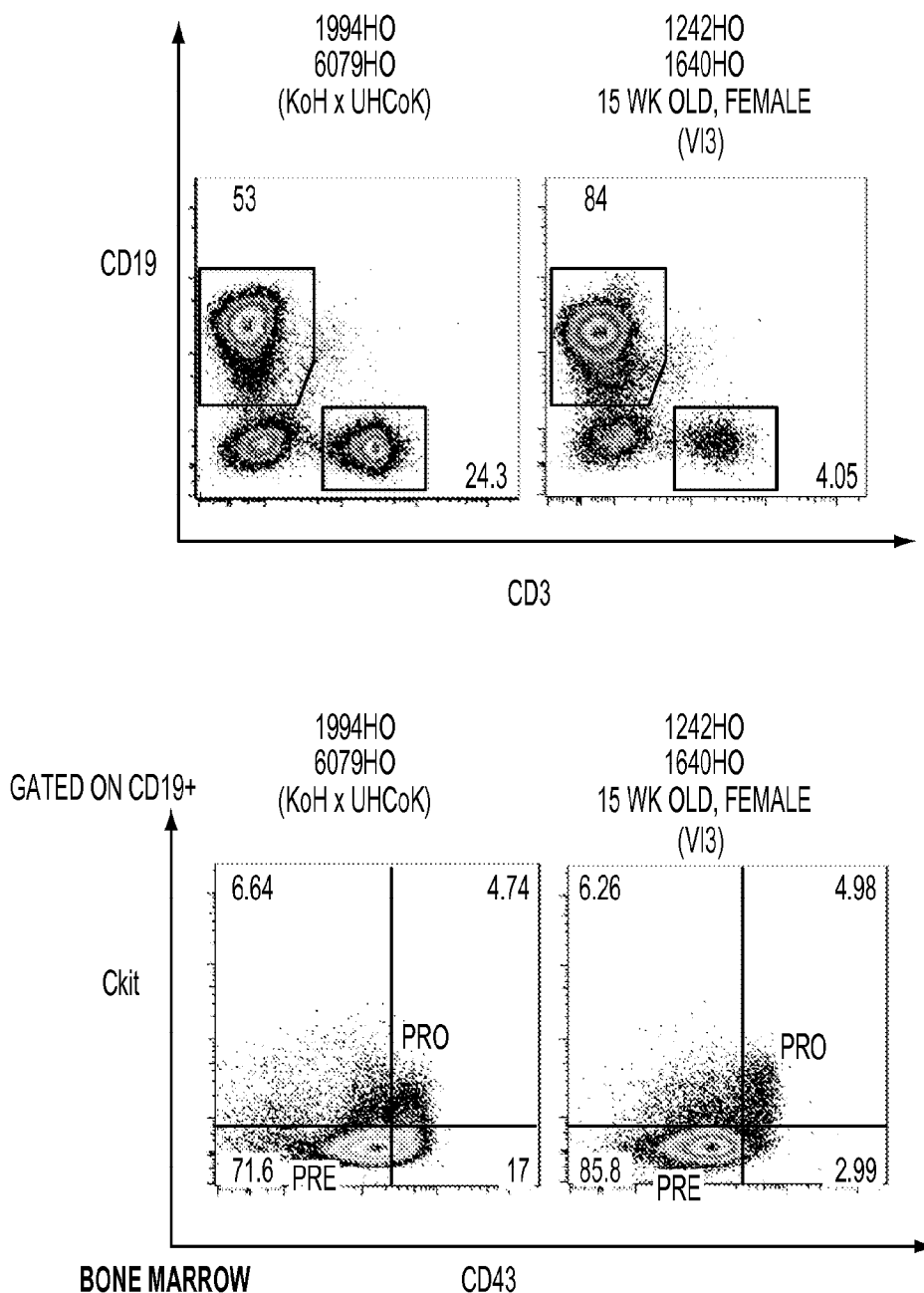


FIG. 57A

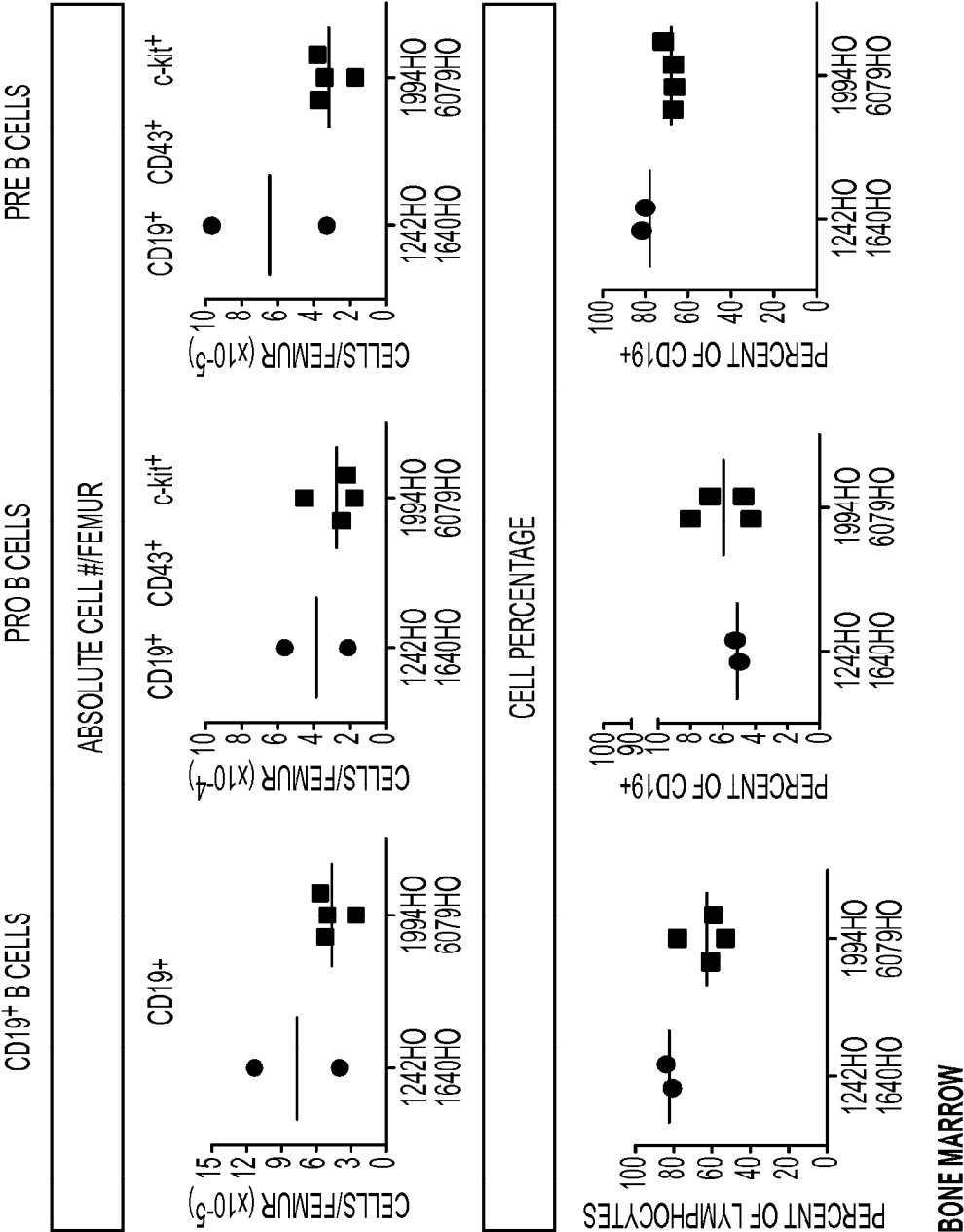


FIG. 57B

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GATED ON SINGLET:

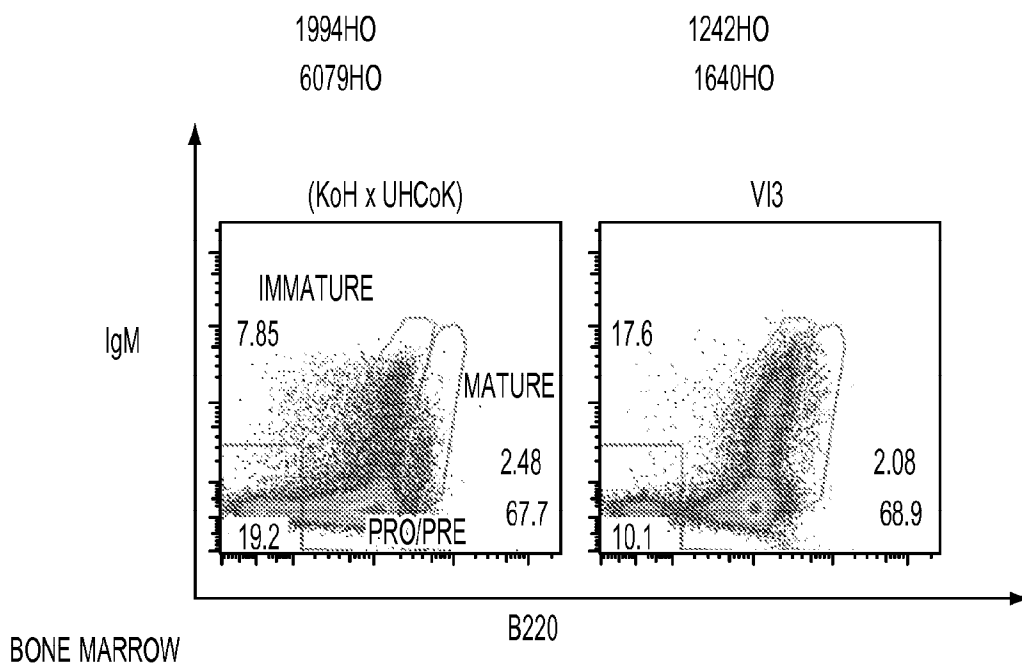


FIG. 58A

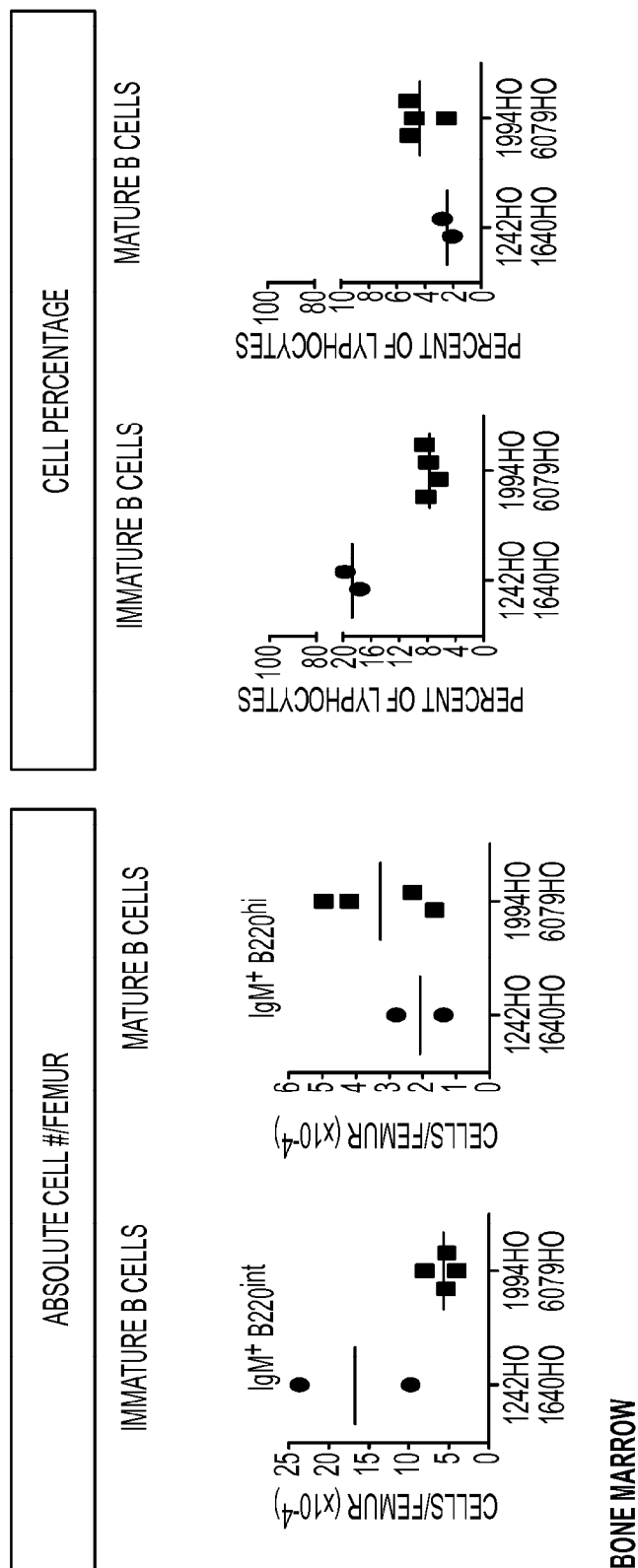
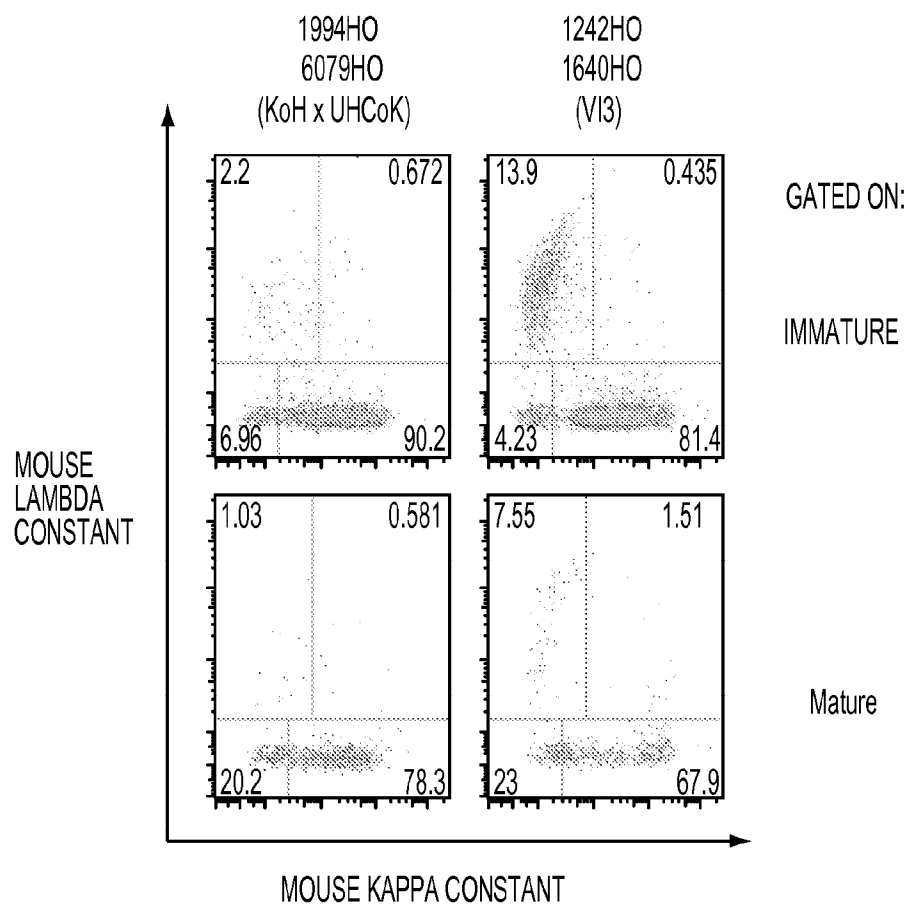


FIG. 58B

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BONEMARROW

FIG. 59

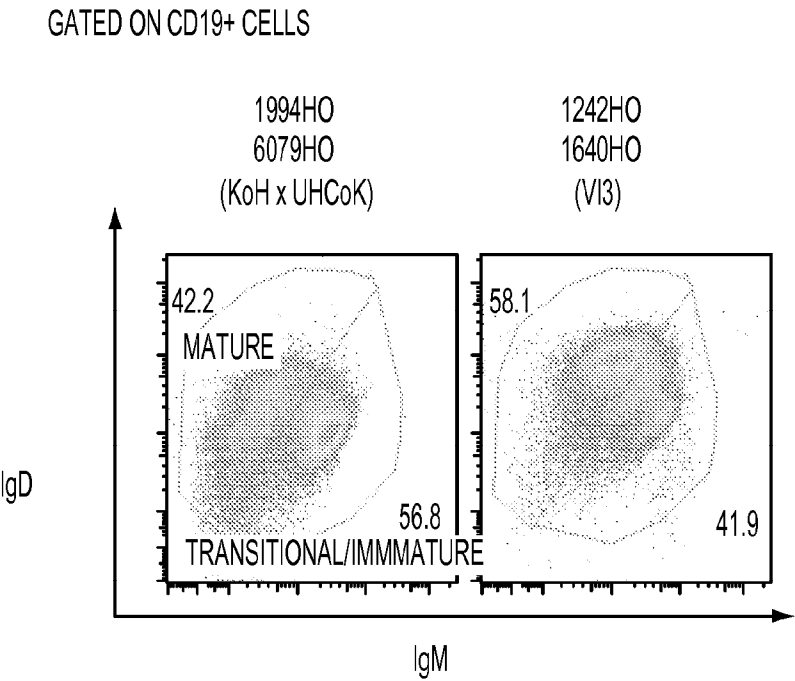


FIG. 60A

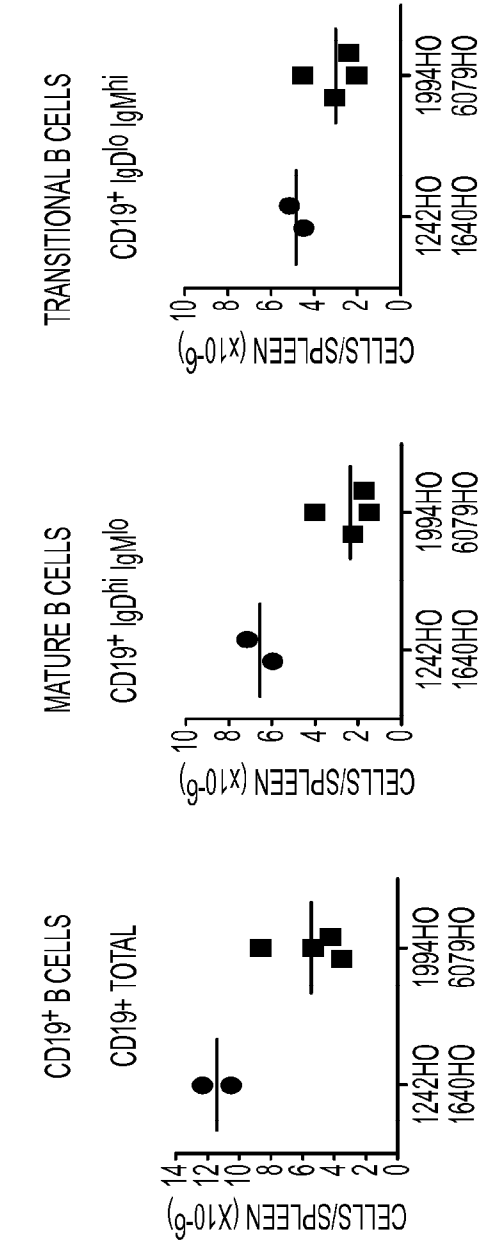


FIG. 60B

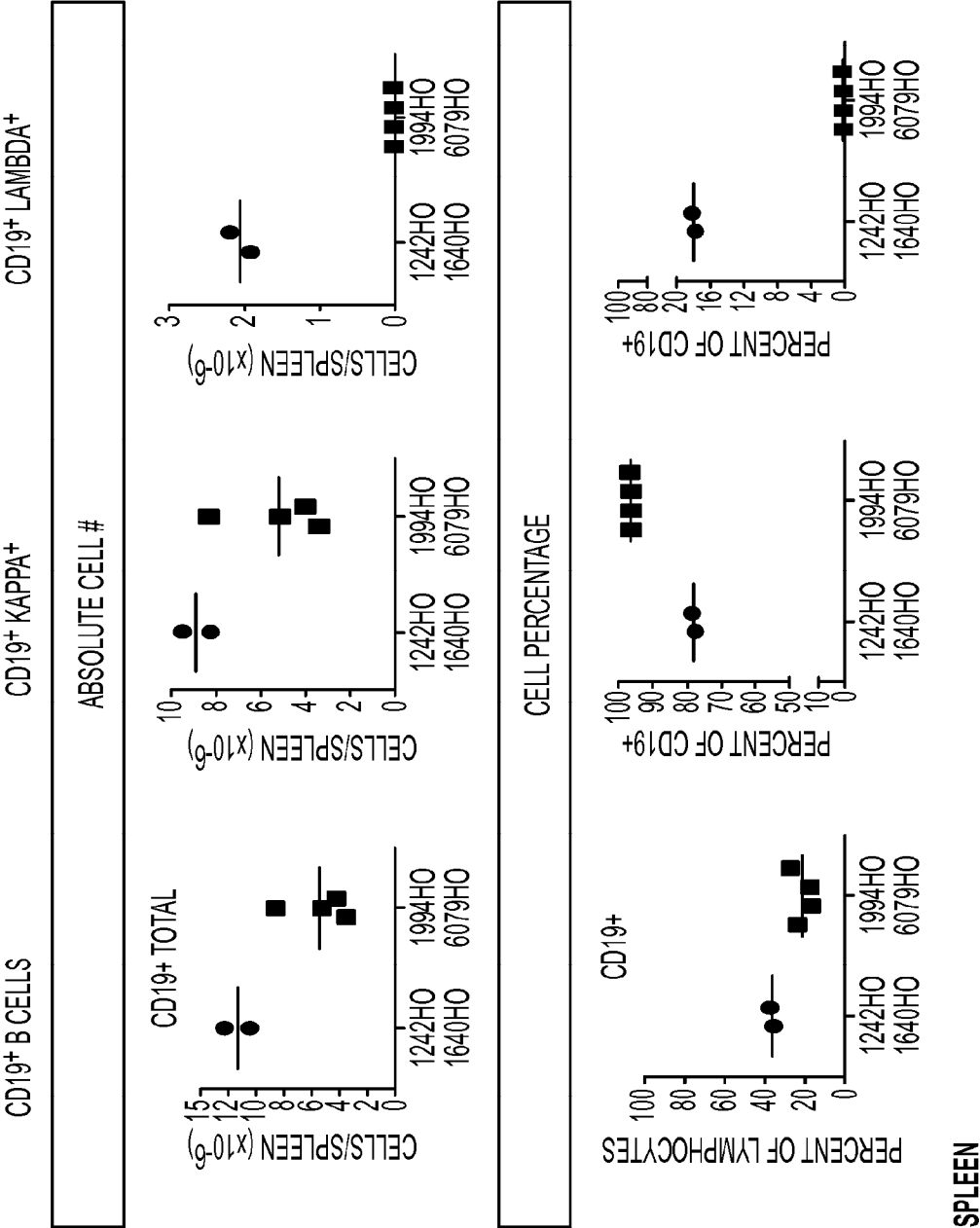


FIG. 61

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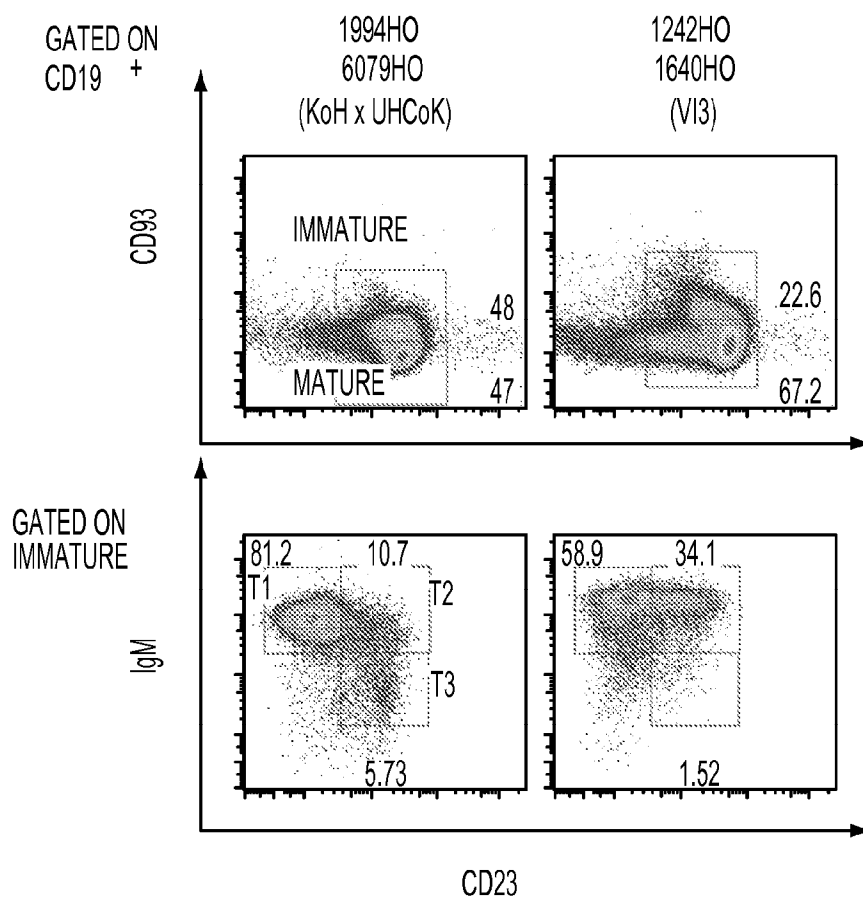


FIG. 62