

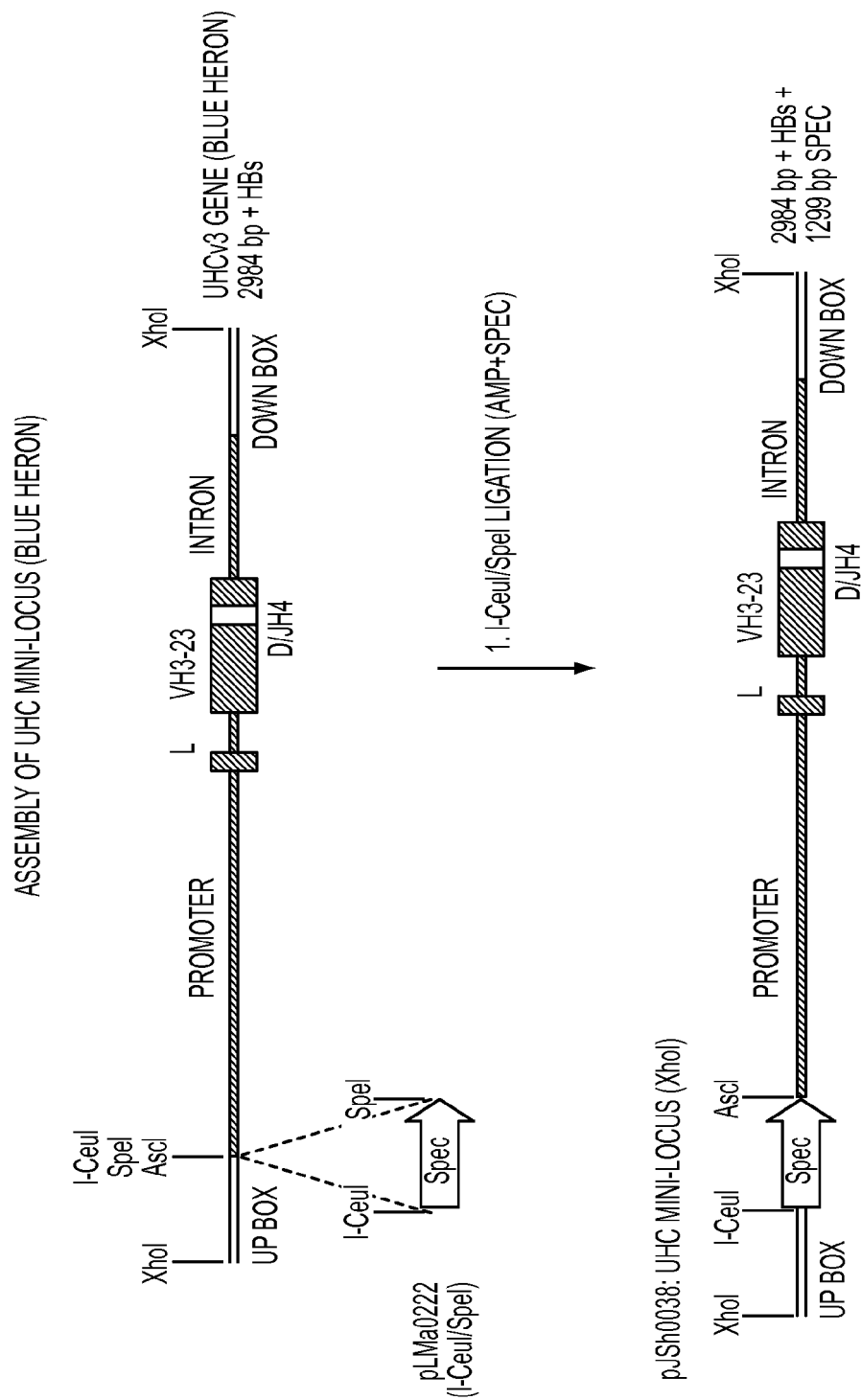


FIG. 1

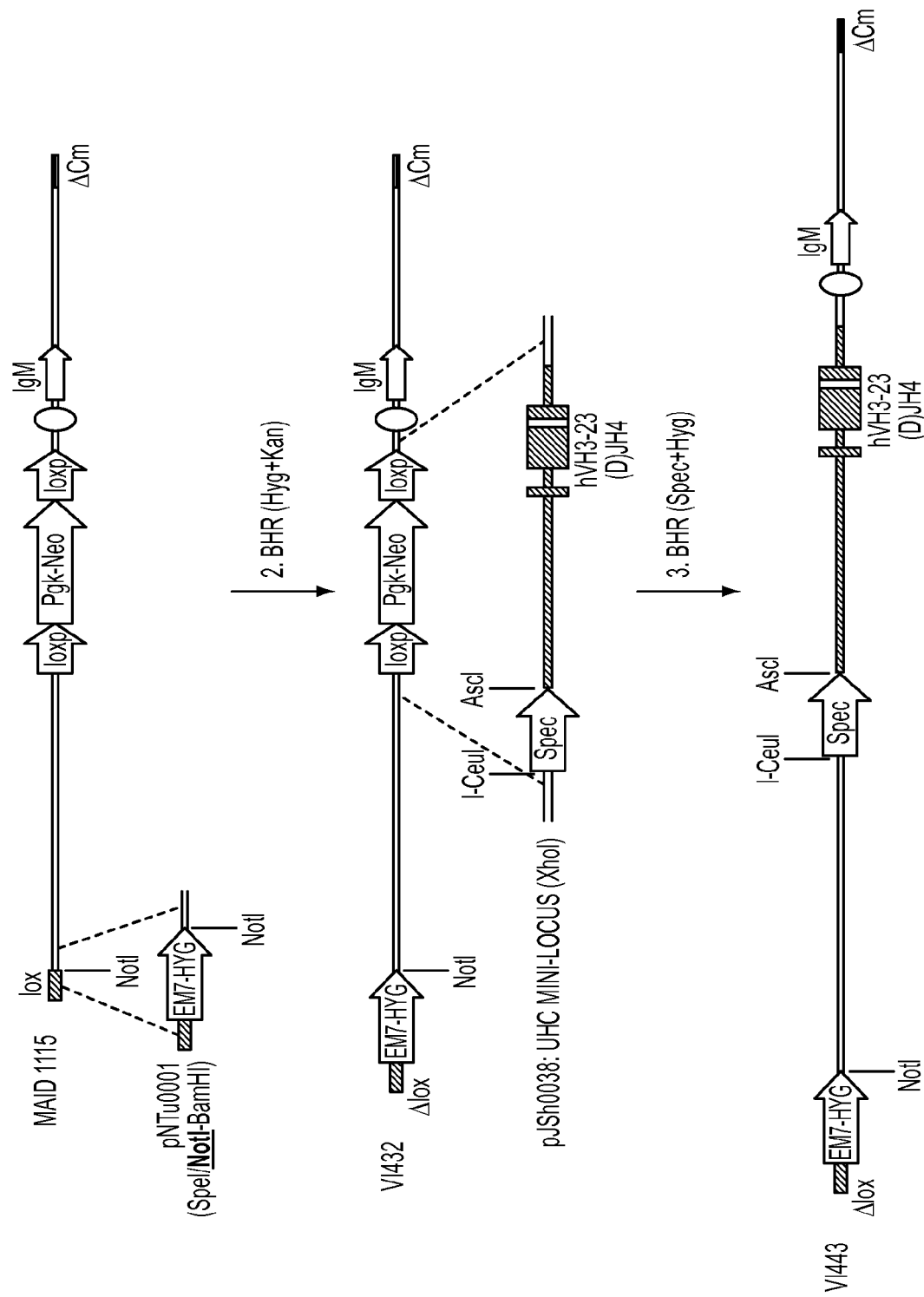


FIG. 2

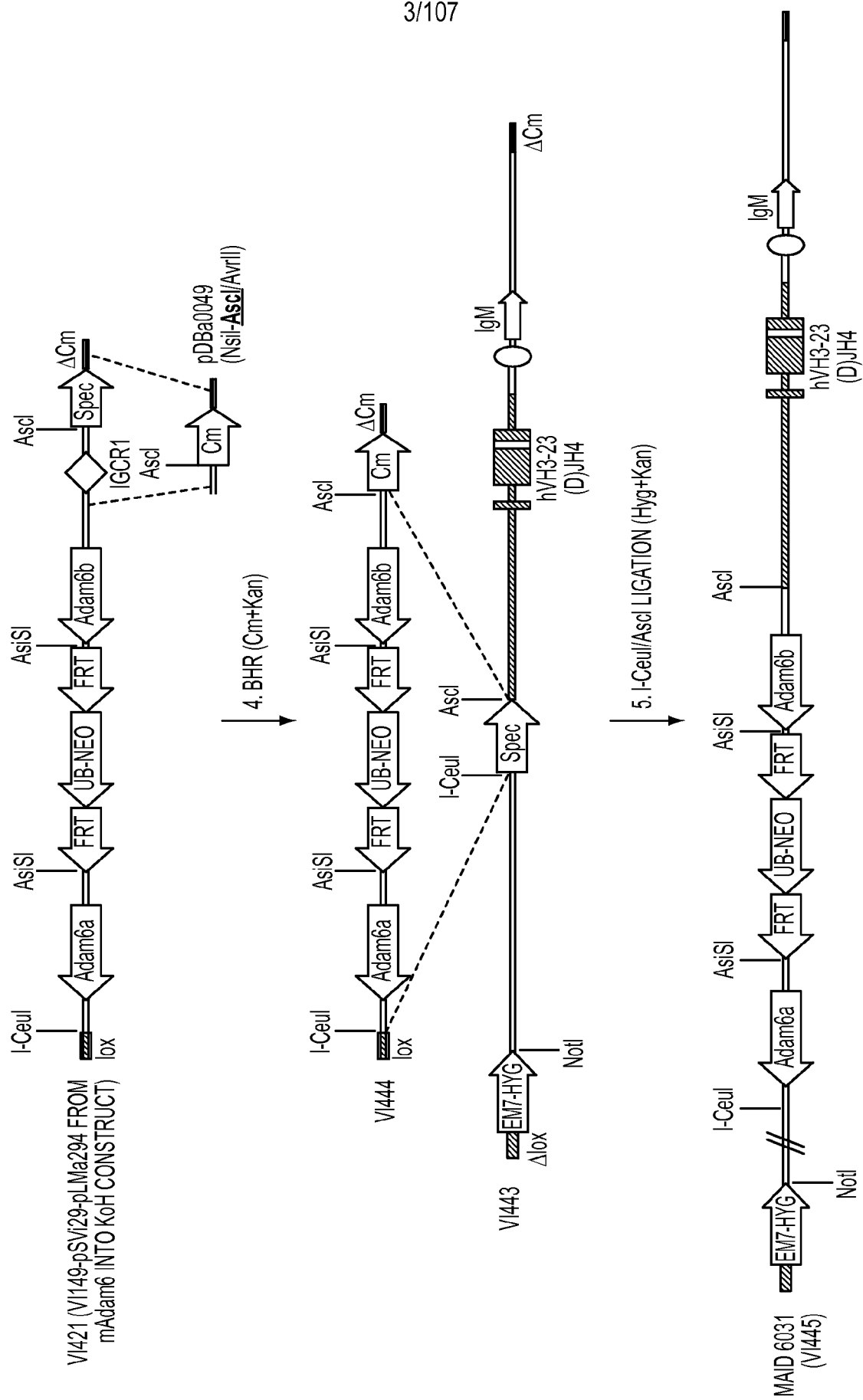
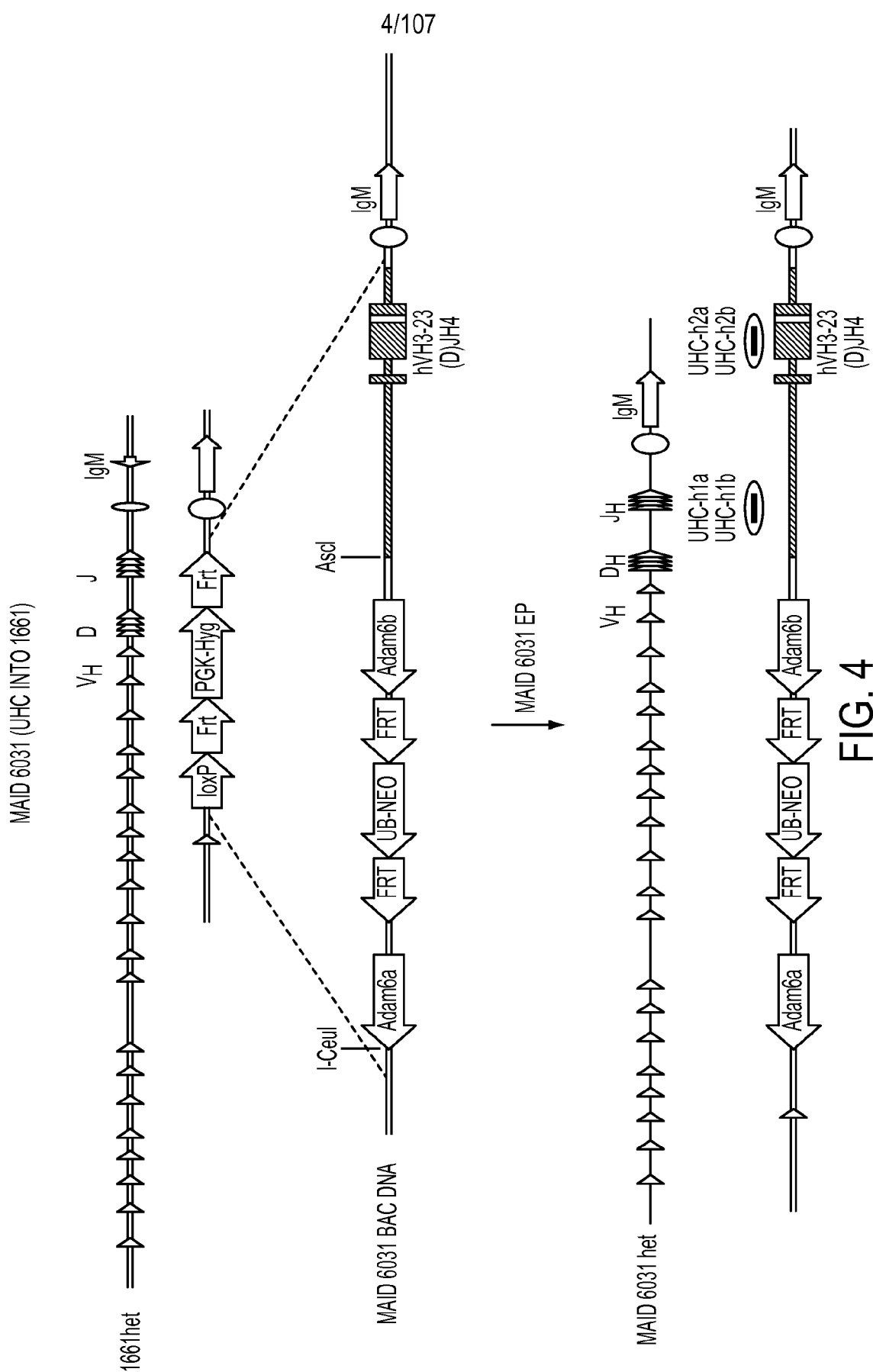


FIG. 3



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

ANTIBODY	ANTIGEN	GERMLINE VH	GERMLINE JH	CDR3
SEARCH WITH DYSN OR YSNY:				
H1H-136B	EGFR	3-23*04	J6*02	<u>AYDYSNYWDHYGMDV</u>
H4H1789B	CD48	3-23*04	J5*02	<u>AKYSNYDYFDP</u>
H1H962B	GDF8	3-33*04	J6*02	<u>AKYSNYGYYYNGLDV</u>
H2M744H	ANG2	1-18*01	J5*02	<u>ARDQDYSNFWLDP</u>
H1M1981	CA9	4-31*03	J6*02	<u>ARESHYSNYEDYYYGMDV</u>
SEARCH WITH AKDY:				
H4H381B	NAV1.7	3-23*04	J4*02	<u>AKDYYGPPDY</u>
H1H1058B	NAV1.7	3-23*04	J4*02	<u>AKDYCNSTYYYGED</u>
SEARCH WITH YYFDY:				
H1H2002B	CA9	3-23*01	J4*02	<u>AKGY~~Y~~FDY</u>
H1H2221B	CA9	3-23*04	J4*02	<u>AI~~G~~Y~~Y~~FDY</u>
H1H2225B	CA9	3-33*04	J4*02	<u>AKGY~~Y~~FDY</u>

FIG. 5

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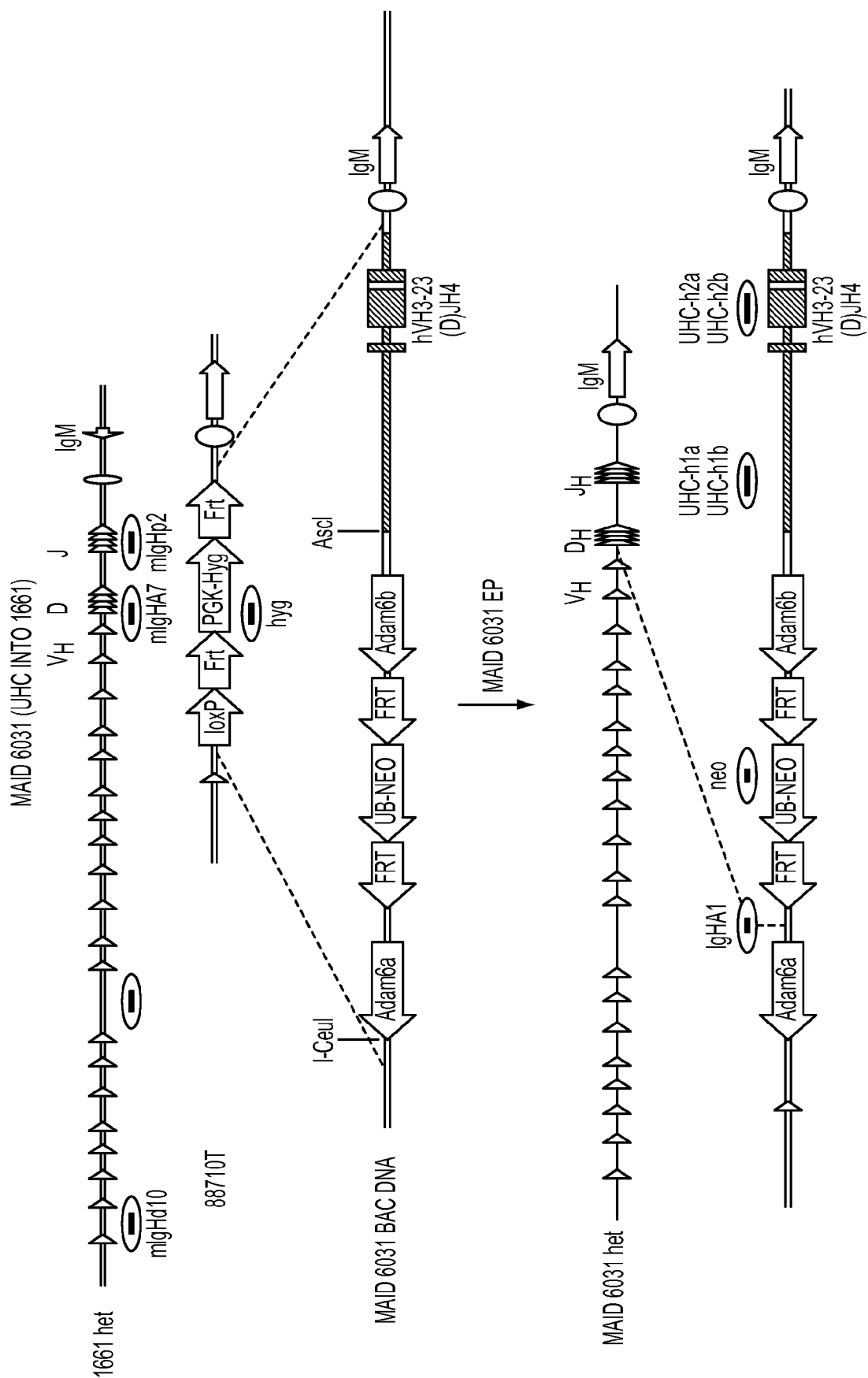


FIG. 6

MAID 6031 (JLC 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
GOA	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	TGCGGCGATCTTTAGCC (SEQ ID NO: 151)	ACGAGGGGGTTGGGCCAATTC (SEQ ID NO: 152)	TTGACCGATTCTTGCGG (SEQ ID NO: 153)	BHQ-1	LOA	
UHC-h1a	TCAGGTGTGATGCTGATCCA (SEQ ID NO: 154)	TGCATCTTCTCCCAATTCCTGGTA (SEQ ID NO: 155)	TGGCTGCTGGGAGAAGATTG (SEQ ID NO: 156)	BHQ-1	GOA	hVH3-23 PROMOTER (202-296)
UHC-h1b	CCCAGAGCCACTATGTC (SEQ ID NO: 157)	TCCCACTGATGCTTTCAGTTTCCTC (SEQ ID NO: 158)	CCCTCAGGAATAACAGACTCATC (SEQ ID NO: 159)	BHQ-1	GOA	hVH3-23 PROMOTER (368-474)
UHC-h2a	AAGGCGGGTTCACCATCT (SEQ ID NO: 160)	CCAGAGACAATTCCAAGAACAGCTG (SEQ ID NO: 161)	CGGCTCTCAGGCTGTTC (SEQ ID NO: 162)	BHQ-1	GOA	hVH3-23 EXON (2592-2664)
UHC-h2b	GCAGCCTCTGGATTACCTT (SEQ ID NO: 163)	ACCAACTCTCAATGAGCTGGGTC (SEQ ID NO: 164)	TCACGGAGTCTCCGTAGAATG (SEQ ID NO: 165)	BHQ-1	GOA	hVH3-23 EXON (2466-2592)
mIghA1	CTCAGTGATTCTGGCCCTGC (SEQ ID NO: 166)	TGCTCCACAGCTACAAACCCCTTCCTATAATG (SEQ ID NO: 167)	GGATGATGGCTCAGCACAGAG (SEQ ID NO: 168)		GOA	mAdam6a
neo	GGTGAGAGGCTATTGGC (SEQ ID NO: 169)	TGGGCACAACAGACAATCGGCTG (SEQ ID NO: 170)	GAACACGGCGGCATCAG (SEQ ID NO: 171)	BHQ-1	GOA	
mIghD10	GGTGTGCGATGTACCTCTGAAC (SEQ ID NO: 172)	CTAAATAATGCTACACCTGGGGCAAAACACCTG (SEQ ID NO: 173)	TGTGGCAGTTTAAATCCAGCTTTATC (SEQ ID NO: 174)		PARENTAL	mIgh D10AL V
887-10	GATGGGAAGAGACTGGTAACATTTGTAC (SEQ ID NO: 175)	CCTCCACTGTGTAAATGGCTGCCACAA (SEQ ID NO: 176)	TTCTCTATTTCACTCTTTGAGGCTC (SEQ ID NO: 177)		PARENTAL	mIgh V
mIghA7	TGGTCACTCCAGGAGGCTC (SEQ ID NO: 178)	AGTCTCTGCTTCCCCCTTGTGGCTATGAGC (SEQ ID NO: 179)	GCTGCAGGGTGTATCAGGTGC (SEQ ID NO: 180)	BHQ-1	PARENTAL	mAdam6b
mIghp2	GCCATGCAAGGCCAAGC (SEQ ID NO: 181)	CCAGGAAATGCTGCCAGAGCCTG (SEQ ID NO: 182)	AGTTCTTGAGCCTTAGGGTGTAG (SEQ ID NO: 183)	BHQ-1	PARENTAL	mIgh D-J

FIG. 8

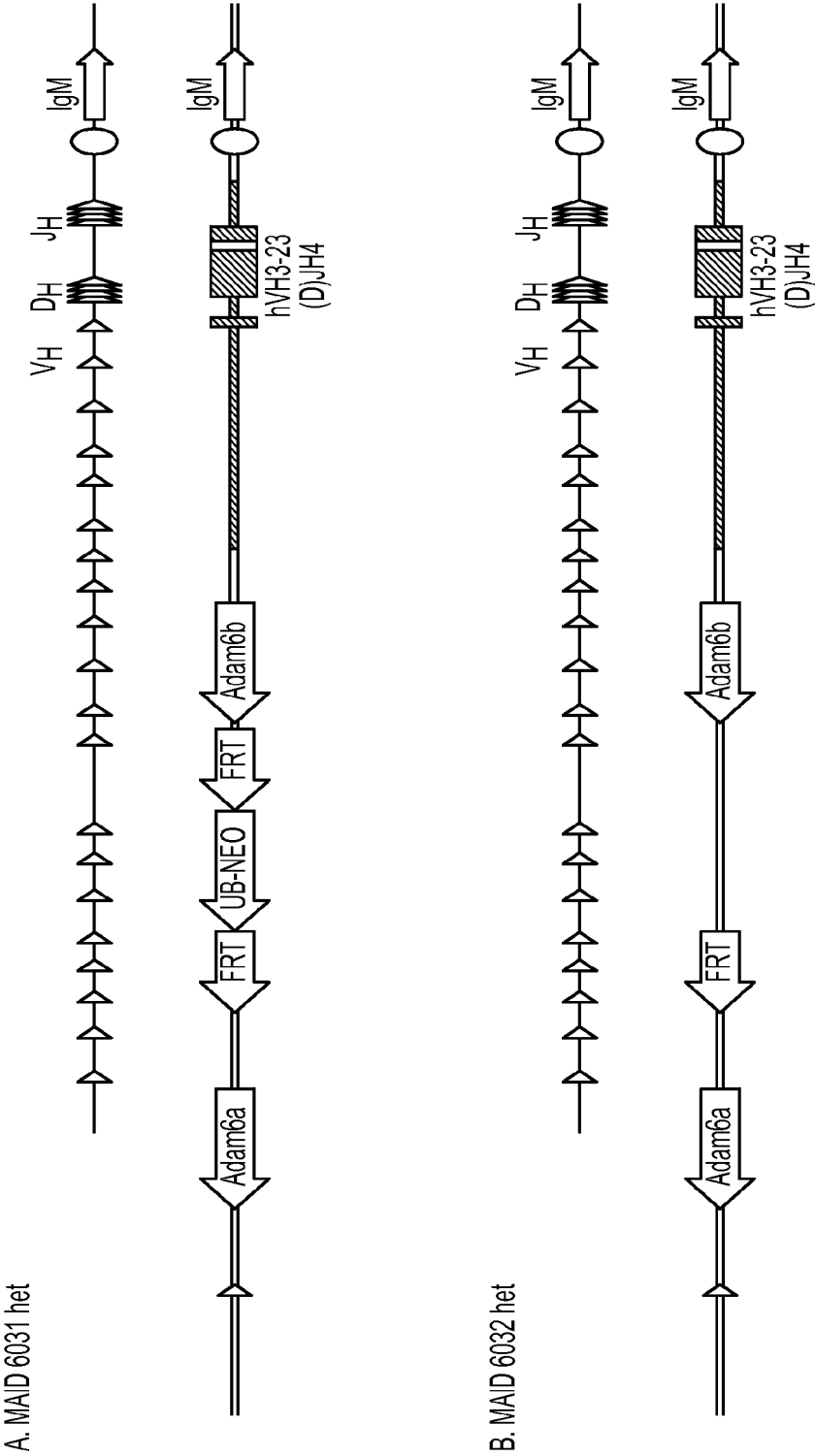


FIG. 9

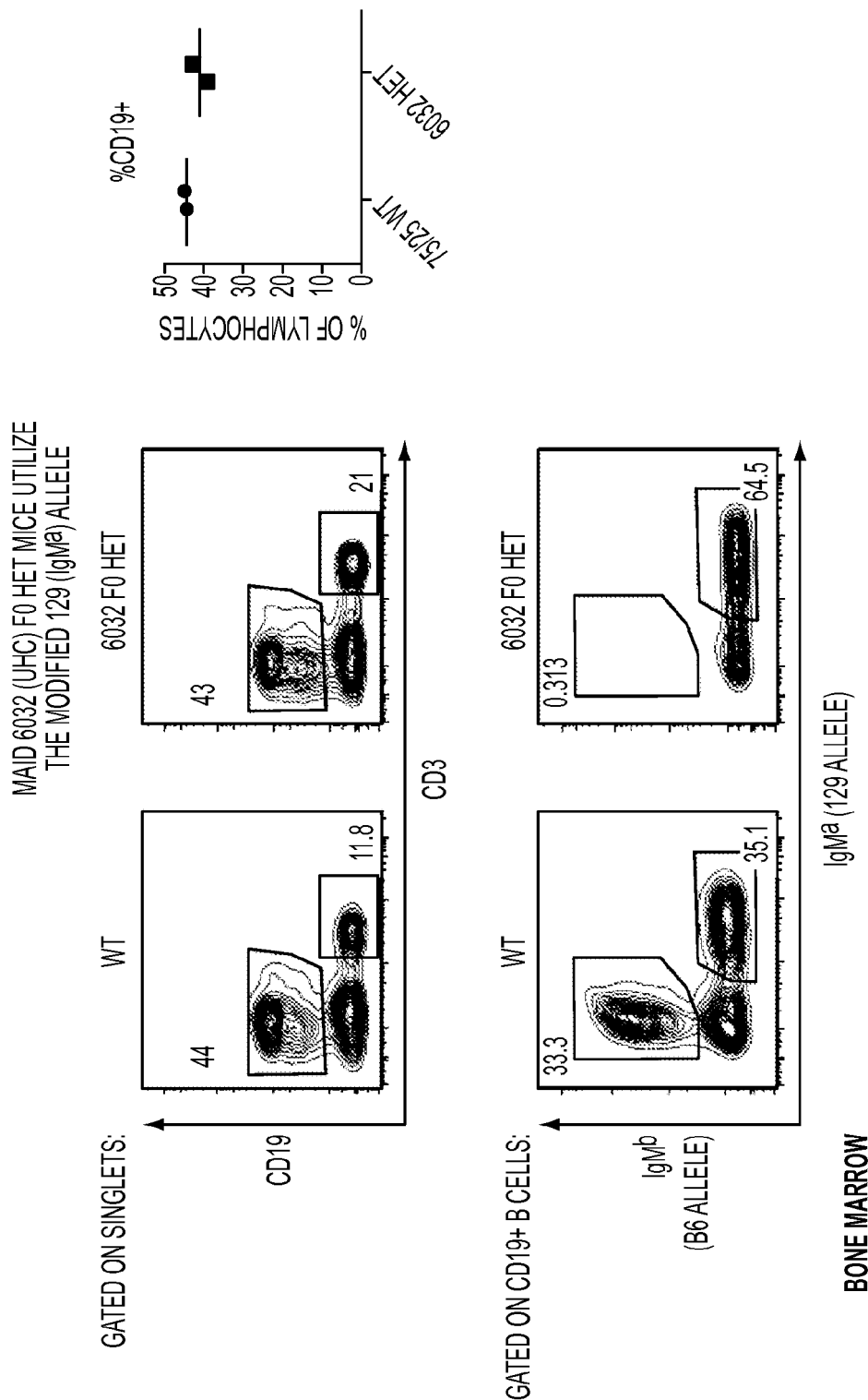


FIG. 10

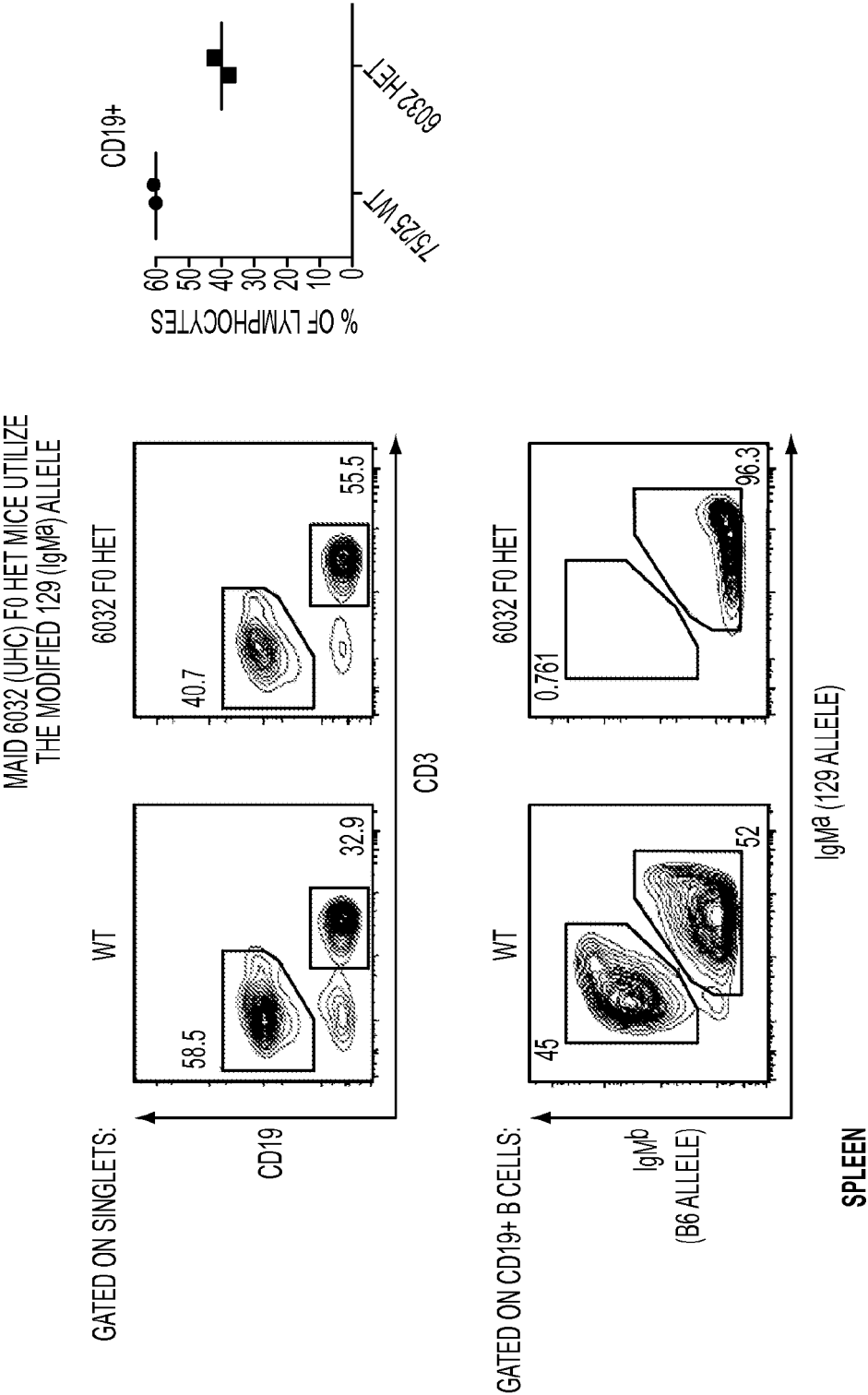


FIG. 11

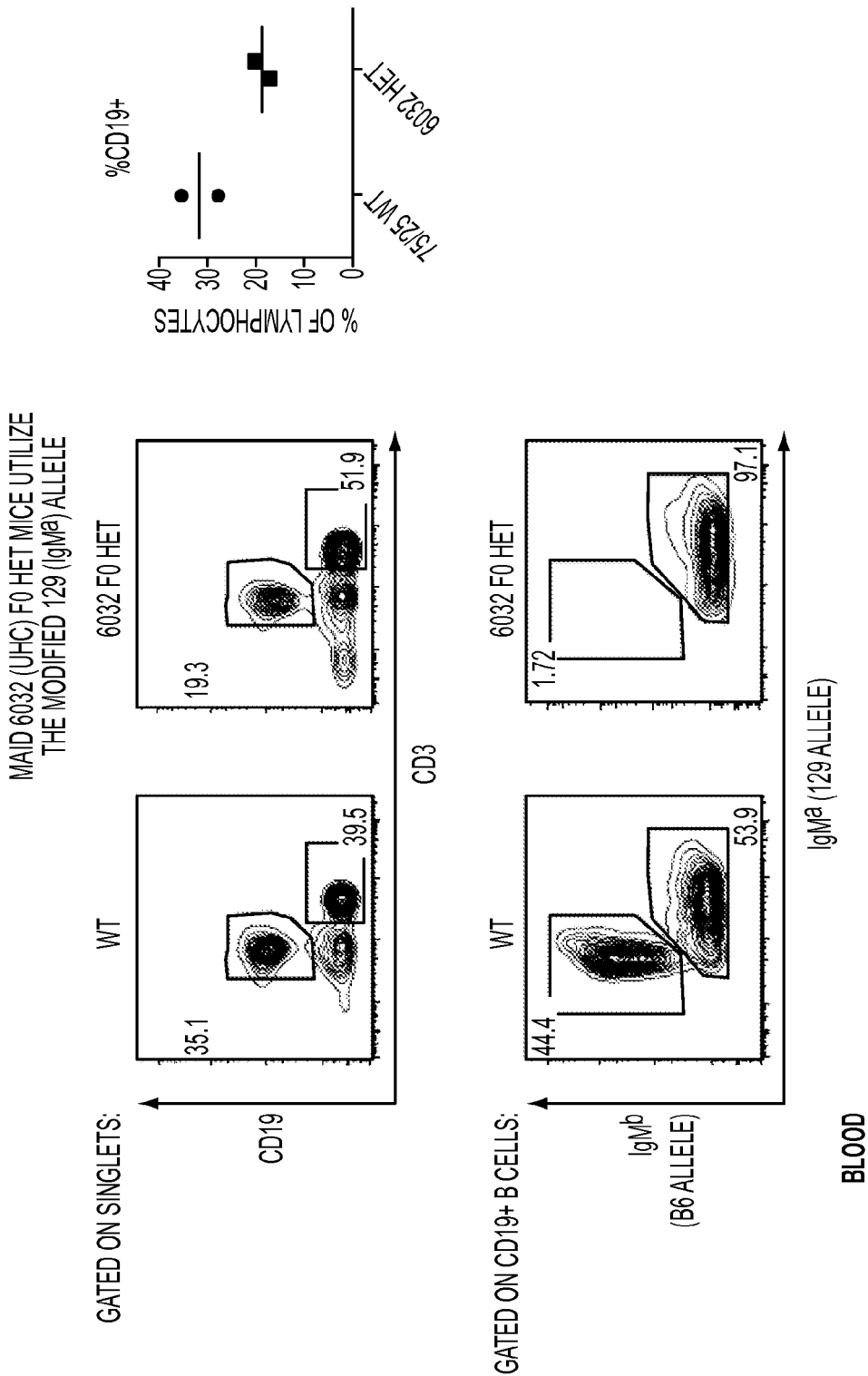


FIG. 12

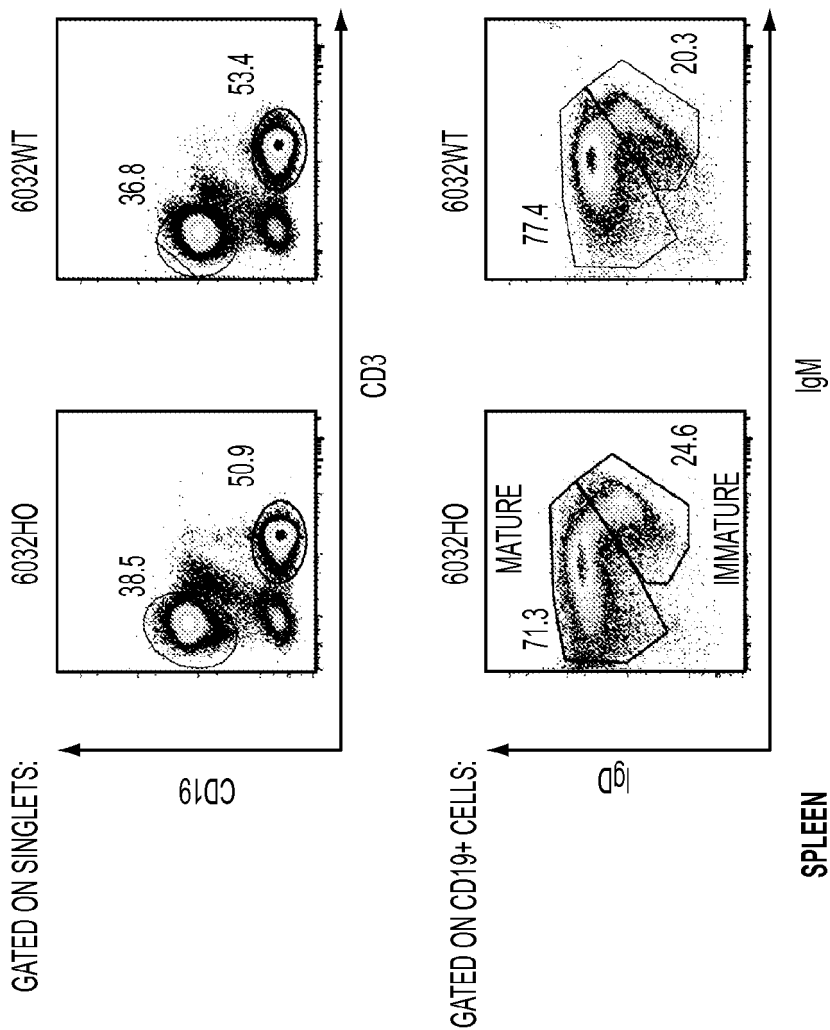


FIG. 13A

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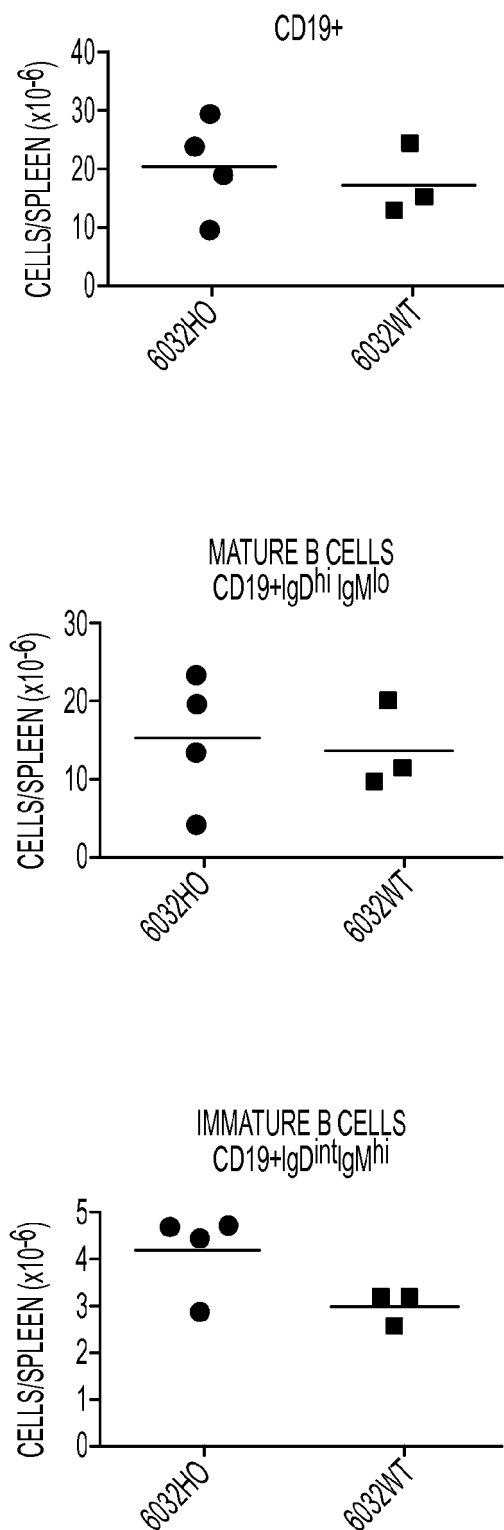


FIG. 13B

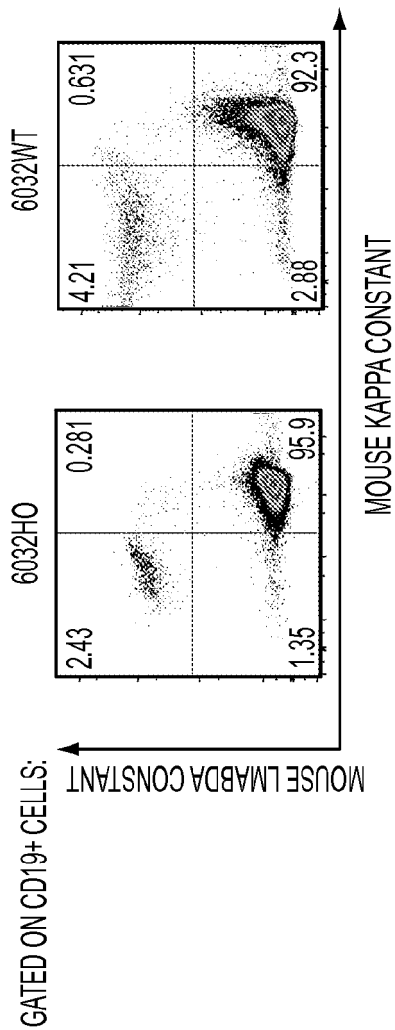


FIG. 13C

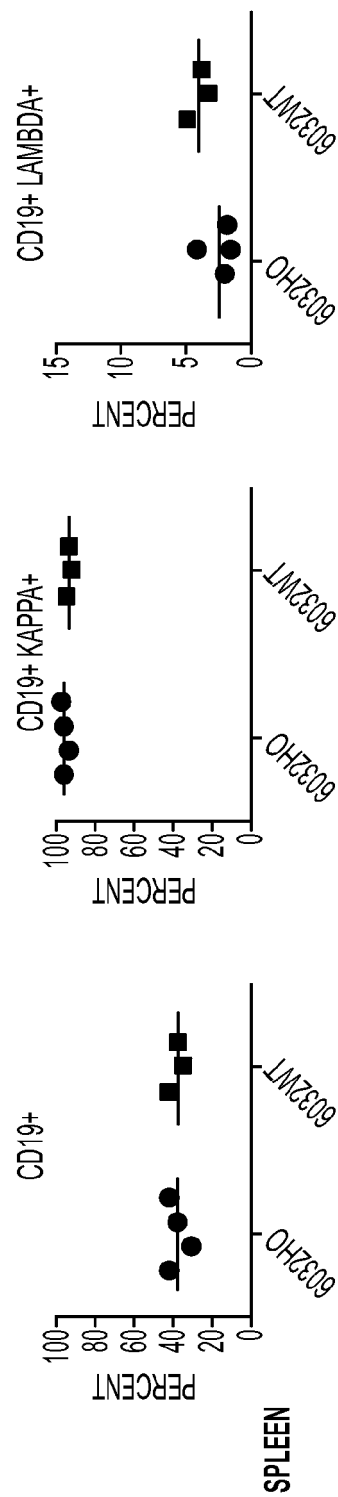


FIG. 13D

FIG. 13E

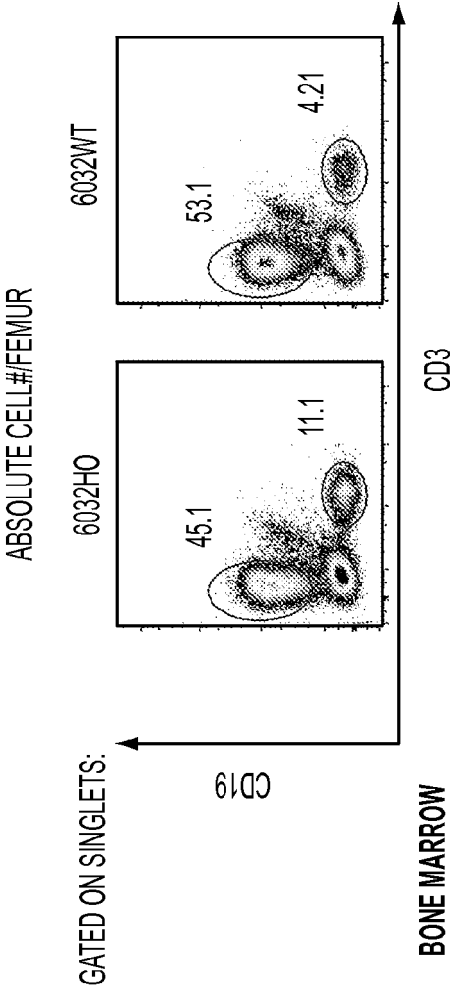


FIG. 14A

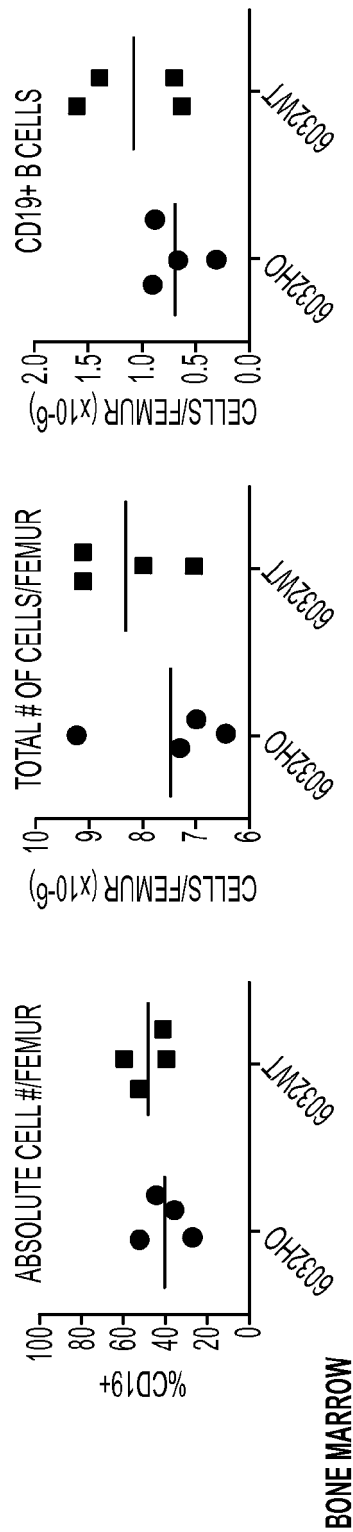


FIG. 14B

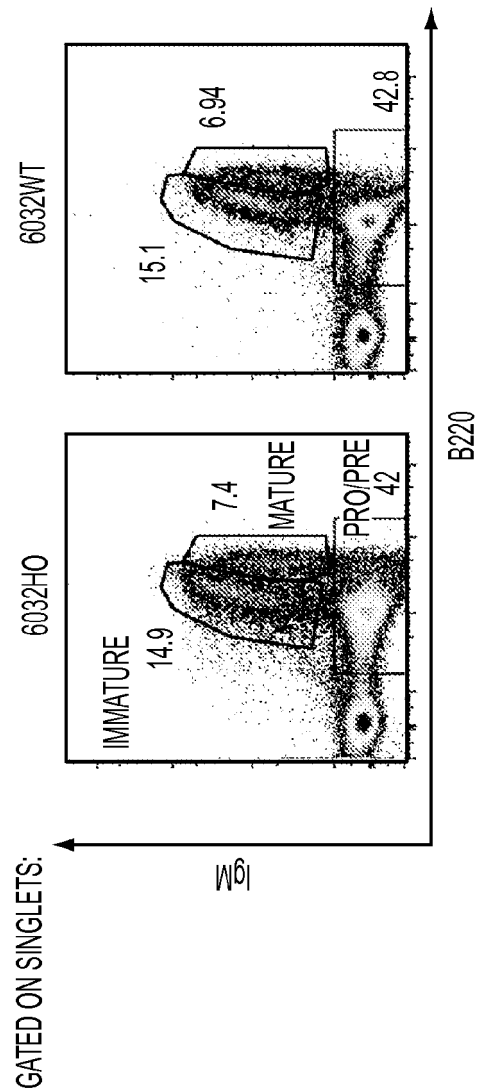


FIG. 14C

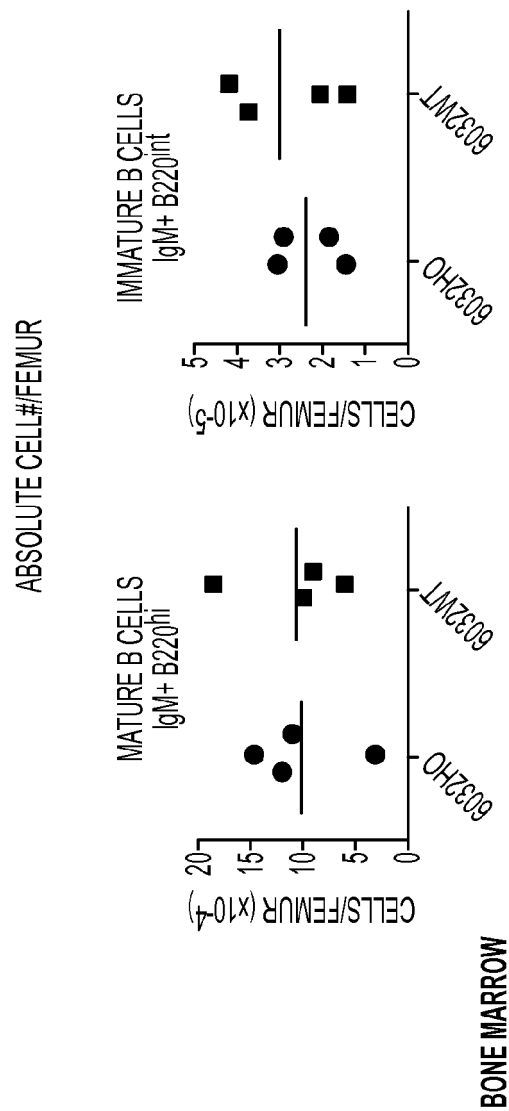


FIG. 14D

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GATED ON SINGLET:

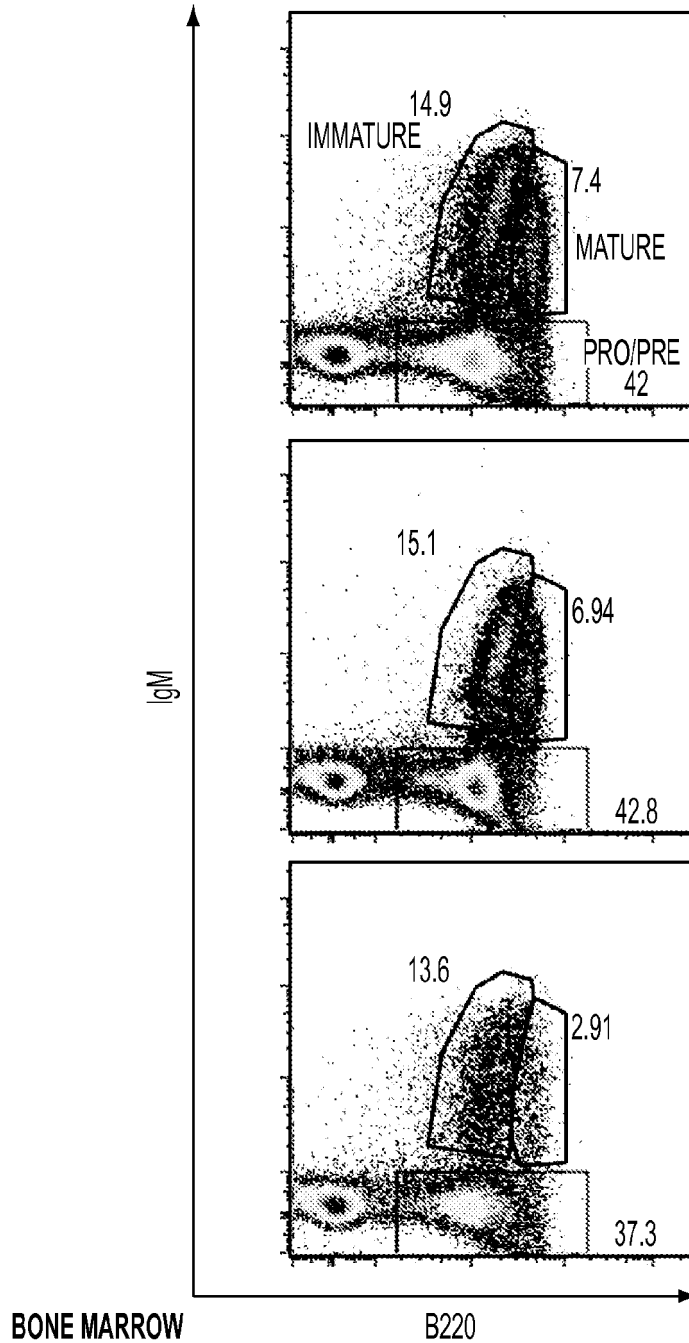


FIG. 14E

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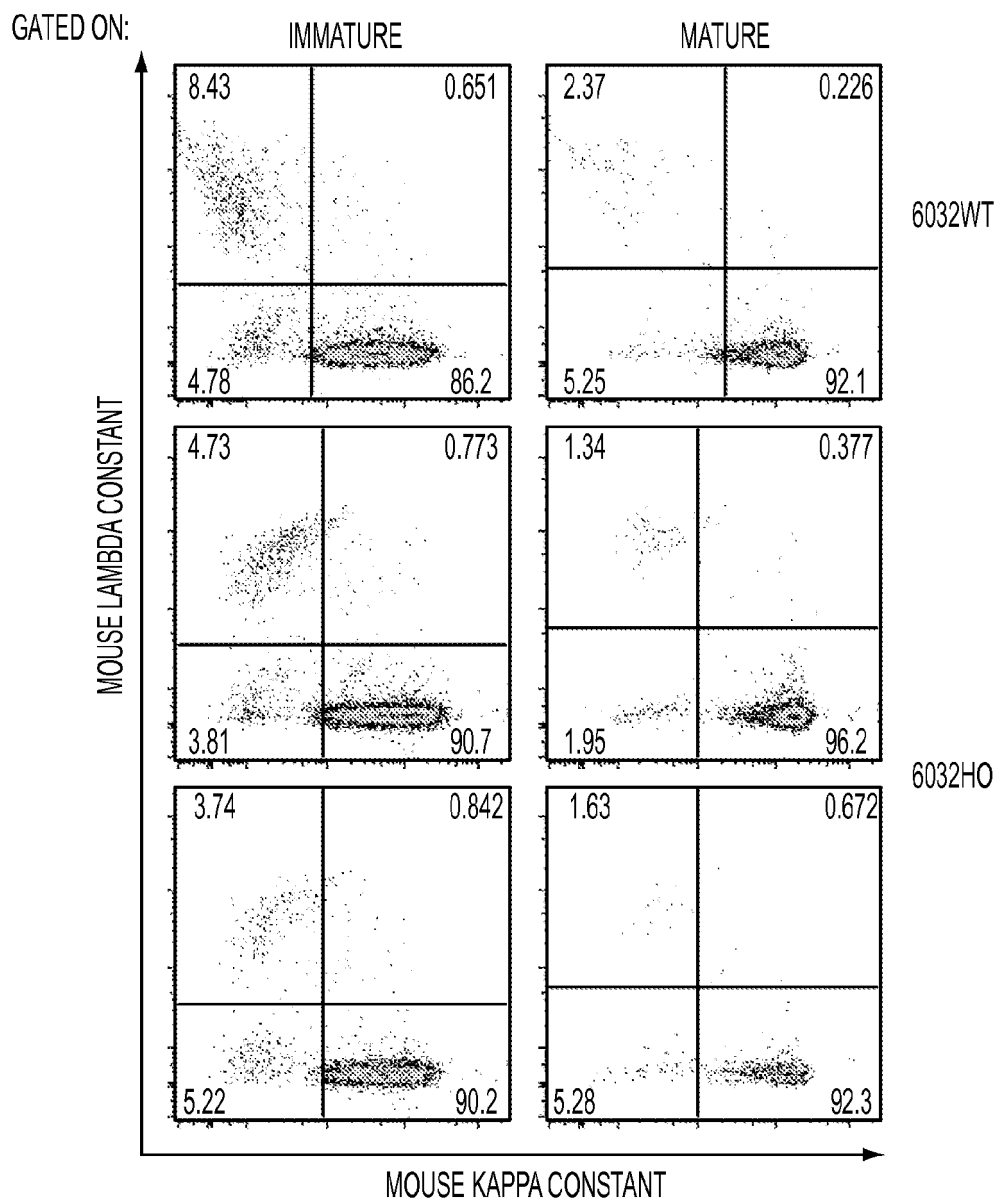


FIG. 14F

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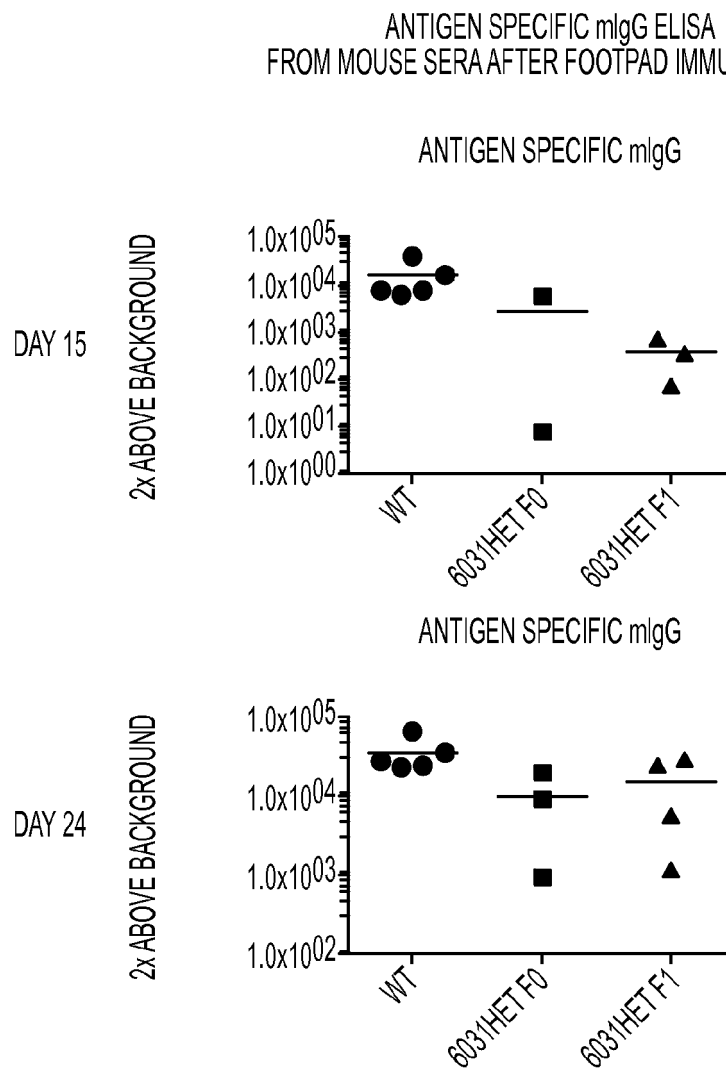
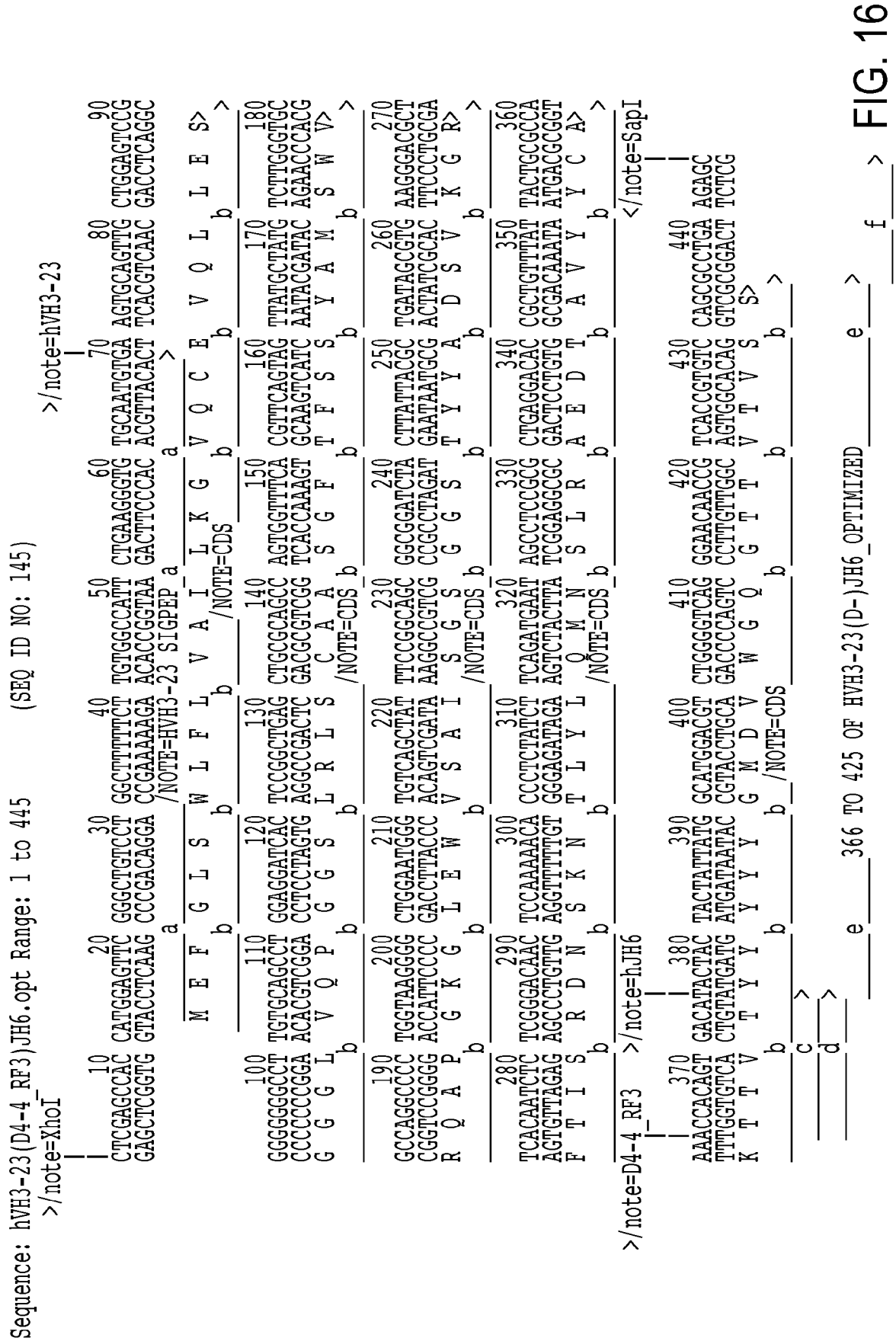


FIG. 15



>/note=hVH3-23

```
>/note=xhoI
```

10	20	30	40	50	60	70	80	90
CTCGAGGCAC	CATGAGTTC	GGGCTGTCT	GGCTTTTCT	TGTGGCCATT	CTGAAGGGTG	TGCAATGTGA	AGTGCAGTTG	CTGGAGTCCG
GAGCTCGGTG	GTACCTCAAG	CCGACAGGA	CCGAAAAGA	ACACCGGAA	GACITCCAC	ACGTTACACT	TCACTCAAC	GACCTCAGC
	a		/NOTE=HVH3-23	SIGPEP a		a		
M E F	G L S	W L F L	V A I	L K G	V Q C E	V Q L L	L E S	>
b	b	b	b	b	b	b	b	b
				/NOTE=CDS				
100	110	120	130	140	150	160	170	180
GGGGGGGCT	TGTGAGCCT	GGAGGATCAC	TCCGGCTGAG	CTGCGCAGCC	AGTGGTTTCA	CGTTGAGTAG	TTATGCTATG	TCTTGGGTGC
CCCCCGGGA	ACACGTGGA	CTTCTTAGTG	AGGCCGACTC	GACGCGTCGG	TCACCAAGT	GCAAGTCATC	AAATACGATAC	AGAACCCACG
G G G L	V Q P	G G S	L R L S	C A A S	G F T F S S	Y A M S	W V	>
b	b	b	b	/NOTE=CDS	b	b	b	b
190	200	210	220	230	240	250	260	270
GCCAGGCCCC	TGGTAAGGGG	CTGGAATGGG	TGTGAGCTAT	TTCCGGGCAGC	GGCGGATCTA	CTTATTTACGC	TGATAGCGTG	AAGGGACGCT
CGGTCCGGGG	ACCATTTCCC	GACCTTACCC	ACAGTCGATA	AAGGCCGTGC	CCGCCATGAT	GAATATGCG	ACTATCGCAC	TTCCCTGCGA
R Q A P	G K G	L E W	V S A I	S G S G	G S T Y Y A	D S V K	G R	>
b	b	b	b	/NOTE=CDS	b	b	b	b
280	290	300	310	320	330	340	350	360
TCACAAATTC	TCGGGACAAC	TCGAAAACA	CCCTCTATCT	TCAGATGAAT	AGCCTCCGG	CTGAGGACAC	CGTGTGTTTAT	TACTGCGCCA
AGTGTTAGAG	AGCCTGTGTG	AGTGTGTTGT	GGGAGATAGA	AGTCTACTTA	TCGGAGGCGC	GACTCTGTG	GCGACAAATA	ATGACGCGGT
F T I S	R D N	S K N	T L Y L	O M N S	L R A E D T	A V Y Y	C A	>
b	b	b	b	/NOTE=CDS	b	b	b	b
4-4 RF2	>/note=hJH6							</note=S
370	380	390	400	410	420	430	440	
AAGATTATTC	AAATTACTAC	TACTACTATT	ATGGCATGGA	CGTCTGGGGT	CAGGGAACAA	CCGTCACCGT	GTCACAGCGCC	TGAAGAGC
TTCTAATAAG	TTTAAATGATG	ATGATGATAA	TACCGTACCT	GCAGACCCCA	GTCCCTTGTT	GGCAGTGGCA	CAGGTCCGGG	ACTTCTCG
K D Y S	N Y Y	Y Y Y	Y G M D	V W G Q	G T T V T V	S S	S	>
b	b	b	b	b	b	b	b	b
			/NOTE=CDS					
c	366 TO 425 OF	HVH3-23(D-)	JH6 OPTIMIZED	c				>

FIG. 17

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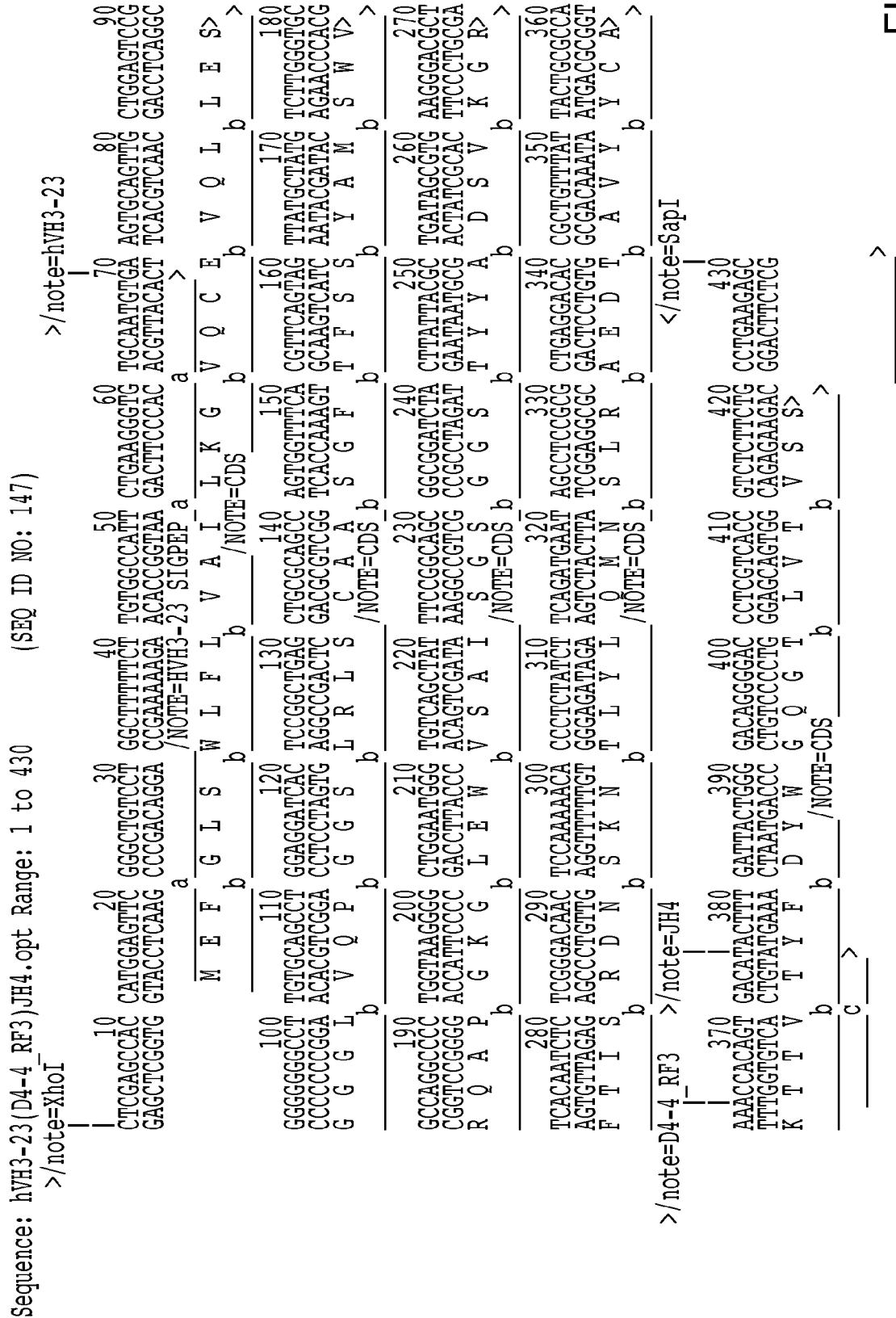


FIG. 18

Sequence: hVH3-23 (D4-4 RF2) JH4.opt Range: 1 to 433 (SEQ ID NO: 148)
 >/note=XhoI_>/note=hVH3-23
 10 20 30 40 50 60 70 80 90
 CTCGAGCCAC CATGGAGTTC GGGCTGTCCT GGCCTTTTCT TGTGGCCATT CTGAAGGGTG TGAATGTGA AGTCAGTTG CTGGAGTCCG
 GAGCTCGGTG GTACCTCAAG CCCGACAGGA CCAGAAAAGA ACACCGGTAA GACTTCCAC ACCTTACACT TCAGTCAAC GACCTCAGGC
 /NOTE=H3-23 SIGPEP a
 M E F G L S W L F L V A I L K G V Q C E V Q L L L E S>
 100 110 120 130 140 150 160 170 180
 GGGGGGCT TGTGAGCTT GGAGATCAC TCCGGCTGAG CTGCGCAGCC AGTGGTTTCA CGTTCAGTAG TTAATGCTATG TCTTGGGTGC
 CCCCCCGGA ACACGTGGA CCTCCTAGTG AGGCCGACTC GACGCGTCGG TCACCAAAGT GCAAGTCATC AATACGATAC AGAACCCACG
 G G L V Q P G G S L R L S C A A S G F T F S S Y A M S W V>
 /NOTE=CDS b
 190 200 210 220 230 240 250 260 270
 GCCAGGCC TGGTAAGGG CTGGAATGGG TGTGAGCTAT TTCCGGCAGC GCGGATCTA CTTATTTACGC TGATAGCGTG AAGGACGCT
 CCGTCCGGG ACCATTCCC GACCTTACCC ACATCTGATA AAGGCCGTCG CCGCTTAGAT GAATTAATGCG ACTATCGCAC TTCCCTGCGA
 R Q A P G K G L E W V S A I S G S G G S T Y Y A D S V K G R>
 /NOTE=CDS b
 280 290 300 310 320 330 340 350 360
 TCACAAATTC TCGGGACAC TCCAAAACA CCTCTATCT TCAGATGAAT AGCCTCCGG CTGAGGACAC CGCTGTTTAT TACTGCGCCA
 AGTGTTAGAG AGCCCTGTTG AGGTTTGT GCGAGATAGA AGTCTACTTA TCGGAGGCGC GACTCTGTG GCGACAAATA ATGACGCGGT
 F T I S R D N S K N T L Y L Q M N S L R A E D T A V Y Y C A>
 /NOTE=CDS b
 >/note=D4-4 RF2 >/note=JH4 >/note=SapI
 370 380 390 400 410 420 430
 AAGATTATTC AAATTACTAC TTTGATTACT GGGACAGGG GACCTCTGTC ACCGTCTCTT CTGCTGAAG AGC
 TTCTAATAAG TTTAATGATG AAATTAATGA CCGCTGTCCC CTGGAGCAG TGGCAGAGAA GACGGACTTC TCG
 K D Y S N Y Y F D Y W G Q G T L V T V S S>
 /NOTE=CDS b
 c >

FIG. 19

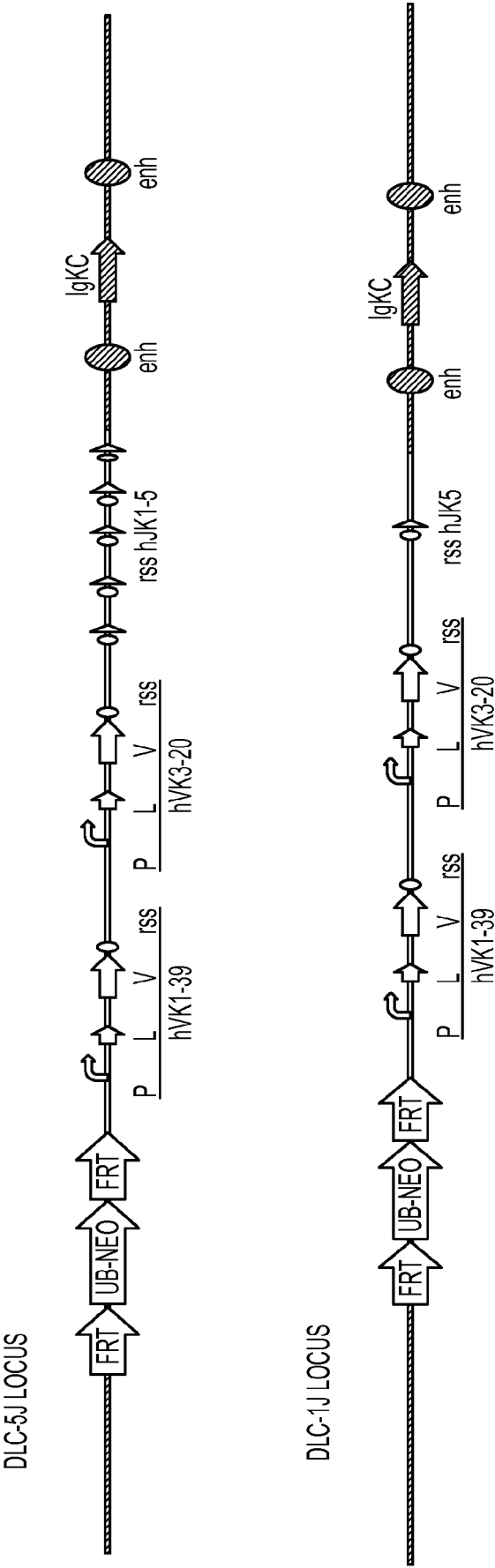
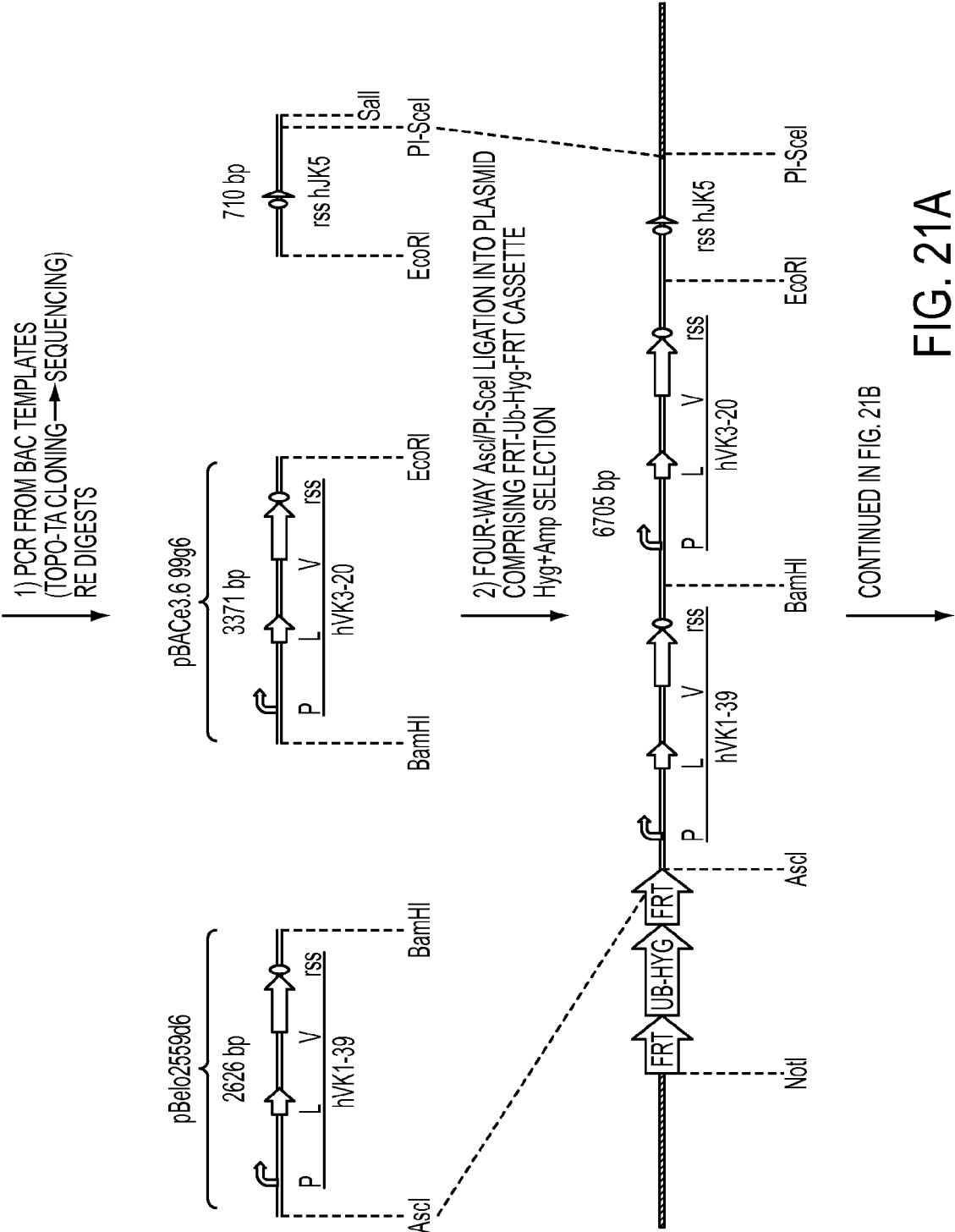


FIG. 20



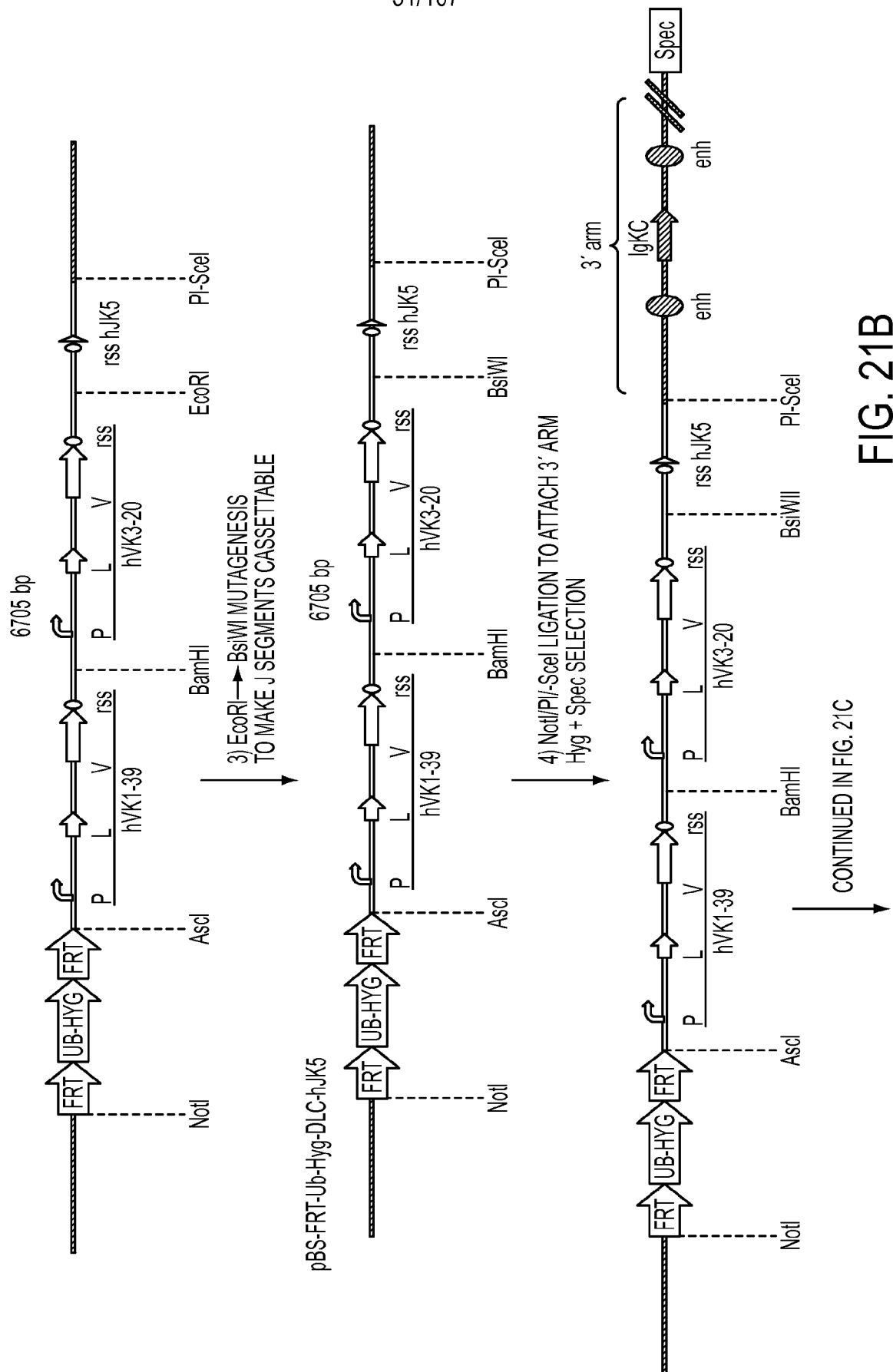


FIG. 21B

CONTINUED IN FIG. 21C

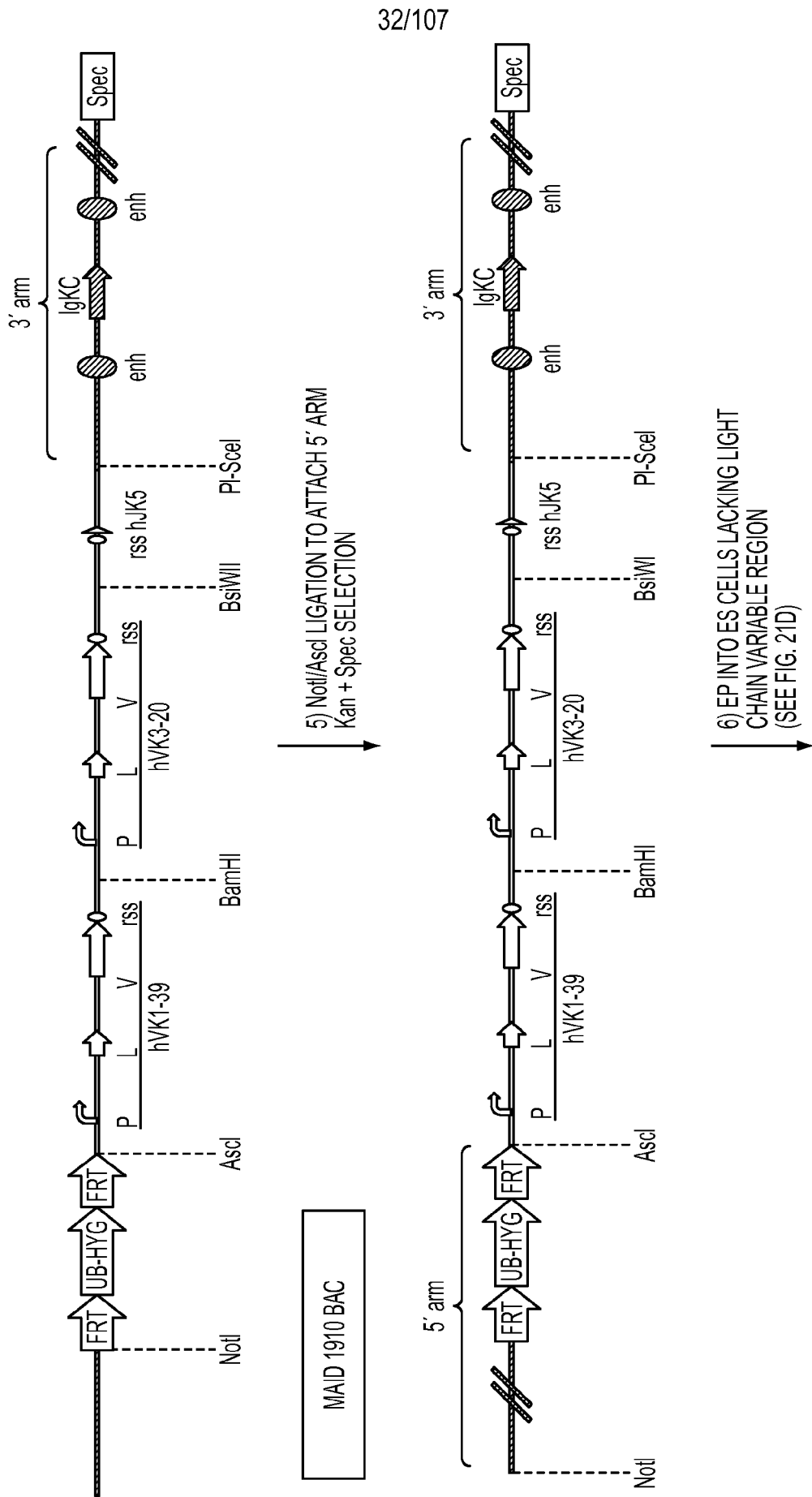


FIG. 21C

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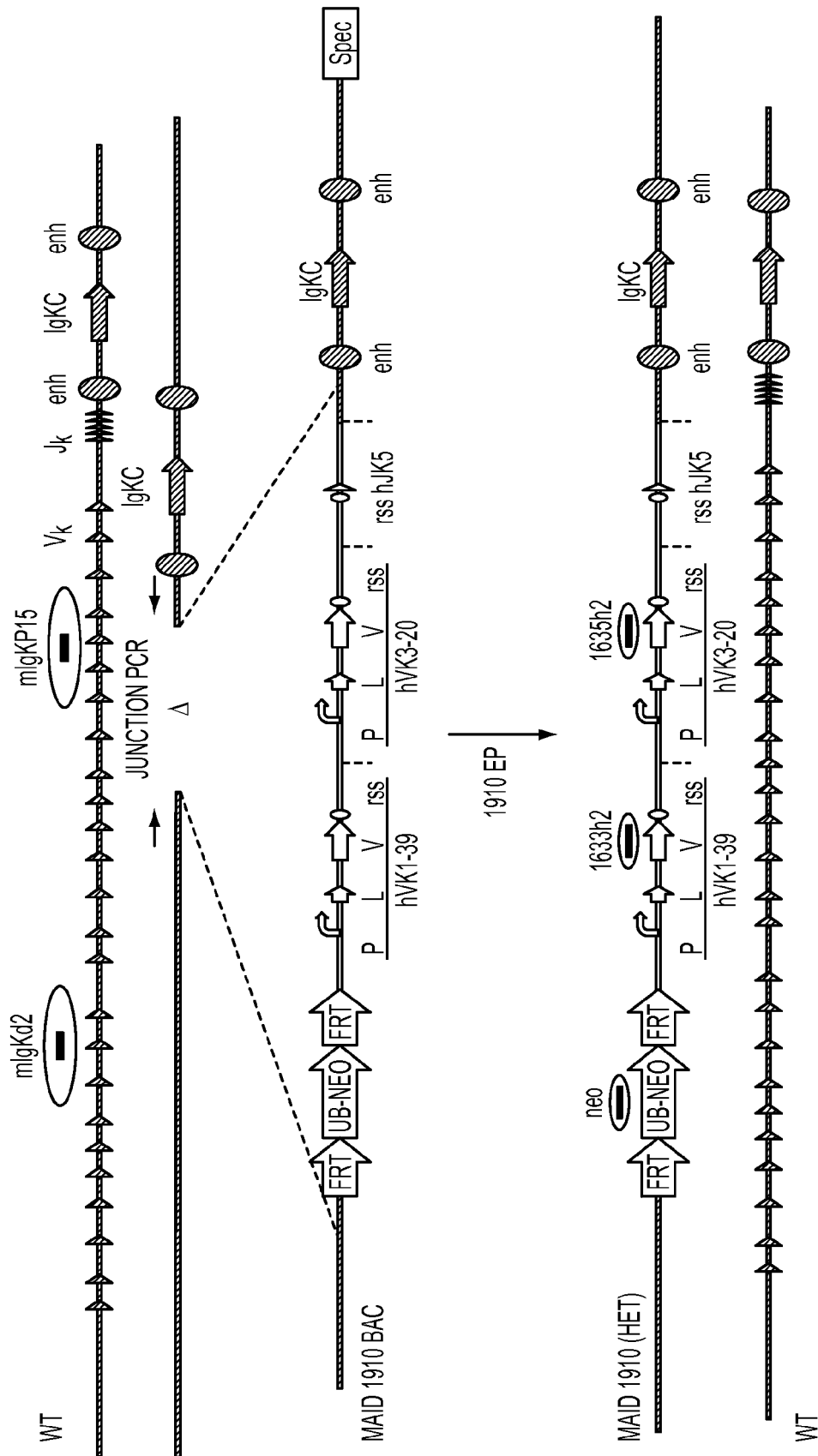


FIG. 21D

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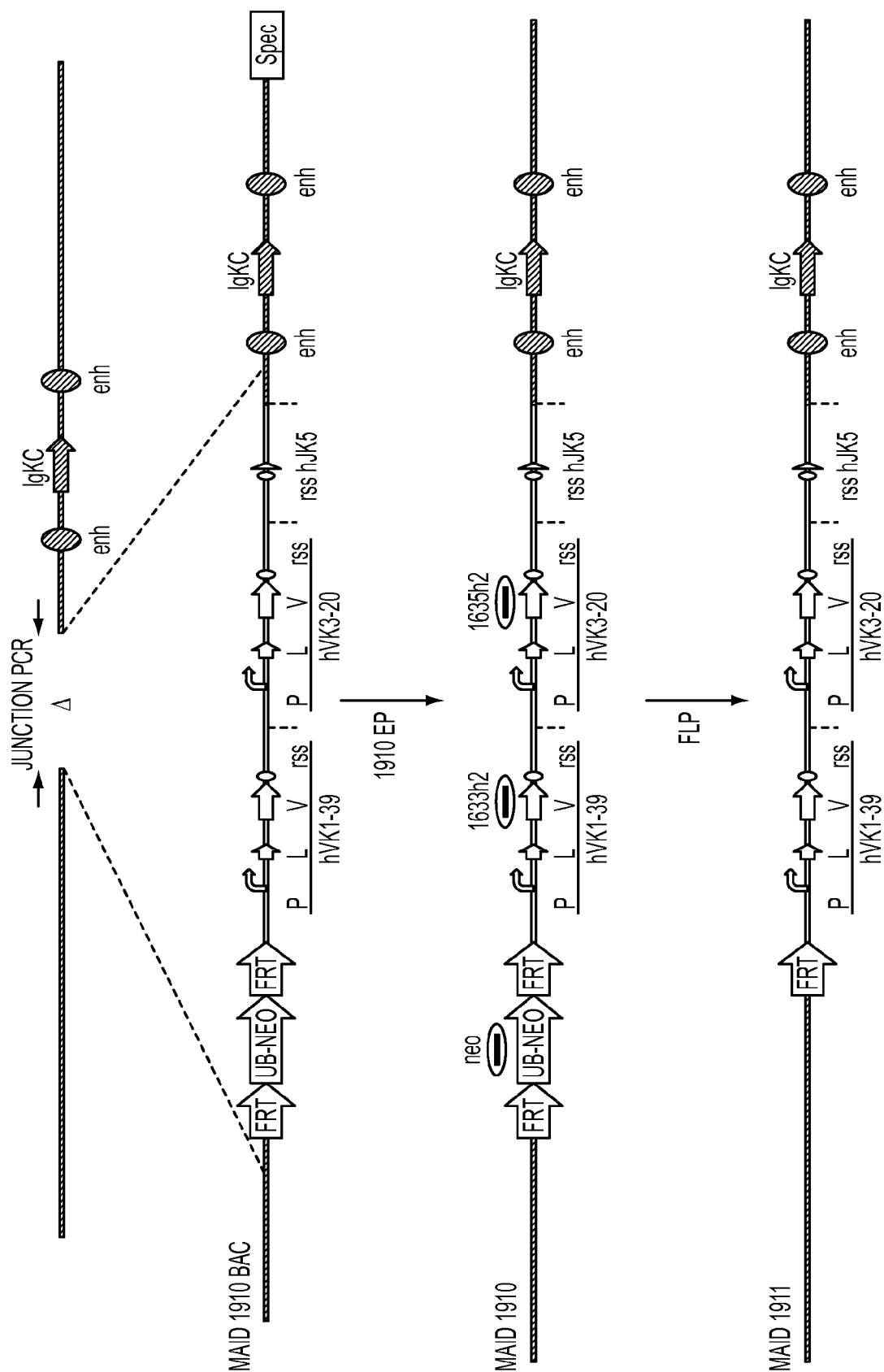


FIG. 21E

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DLC-1J SEQ ID NO:82

GCACCACTTCGTCGCAGCGCAGGCTTTGGTCTCCCTTGTCTCCCTTGTCTCCGTCGGCGGCACGCCACCGAGTTTACGCACACAGCACCCGAGGTCTGGTTGGTACCG
 AAGTTCCTATTCCGAAGTTCCCTATTCTCTAGAAAGTATAGGAACCTTCTCGCGCTCTGGCTCCGAGGCTCCGCGCGGTTTGGCGCTCCCGG
 GCGCCCCCTCCTCACCGCGAGCGCTGCCACCTCAGACGAAGCGCAGCGAGGCTCTGATCCTTCCGCGCGGACGCTCAGCACAGCGCGCGCTG
 CTCATAAGACTCGGCTTAGAACCCCAAGTATCAGCAGAAAGACATTTAGACGGGACTTGGGTGACTCTAGGGCACTGGTTTCTTCCAGAGCGG
 GAACAGCGAGGAAAGTAGTCCCTTCTCGCGGATCTCGCGAGGGAATCTCGTGGGCGGTGAACGCCGATGATATATAAGACCGCGCGGCTGTG
 GCACAGTAGTTCCGTCCGACGCCGGGATTTGGTTCGGCTTCTTGTGTGGATCGCTGTGATCGTCACTTGGTAGTAGCGGGCTGTGGGCTGGCC
 GGGGCTTCGTGGCCCGCGCGCGCTCGGTGGACGGAAGCGTGTGGAGAGACCGCAAGGCTGTAGTCTGGTCCGCGAGCAAGGTTGCCCTGAAC
 TGGGGTTGGGGGAGCGCAGCAAAATGGCGGCTGTCCGAGTCTTGAATGGAAGACGCTGTGAGGCGGGCTGTGAGGTCTGTGAAACAAAGGTGGG
 GGGCATGCTGGCGGCAAGAACCCCAAGTCTTGAGGCTCTCGCTAATGGGGAAGCTCTTATTCGGGTGAGATGGGCTGGGCGACCATCTGGGGACC
 CTGACGTGAAGTTTGTCACTGACTGAGAACTCGGTTCGTCTGTTCGGGGCGGCGAGTTATGGCGGTGCCGTGGGCGAGTGCACCCGTACCTTT
 GGGAGCGCGCGCTCGTCTGTCGTCGTCACCTCACCCGTTCTGTTCGCTTATAATGCAGGTGGGCGCACCTGCCGTAGGTGTCCGTAGGCTTTCT
 CCGTCGAGGACGCGAGGTTCCGGCTAGGTAGGCTCTCCTGAATCAGACGGCGCGGACCTCTGGTGGGAGGAGGATAAGTGAAGCTCAGTTTC
 TTTGGTCGGTTTATGTACCTATCTTCTTAAGTACCTCGGTTTGAACATAAGCTCGGCTCGGGTGGCGAGTGTGTGTGAAATTTTGTAG
 GCACCTTTTGAATGTAAATCATTTGGGTCAATATGTAATTTTCACTGTAGACTAGTAAATTTCTCCGCTAAATTTCTGGCGTTTTCGGCTTTTGTGT
 AGACGTCGAGCTCTAGATTGGAAACCCGGTCTCTCGAATTTGTGACAAATTAATCATCGGCATAGTATATCGGCATAGTATAACGACAAAGTGAAG
 AACTAAACCATCCACCATGATTGAACAAGATGGATTGCACCGAGTTCTCCGGCGCTTGGGTGGAGAGGCTATTTCGGCTATGACTGGGCAACAACAGA
 CAATCGGCTGTCATGATCCCGCTGTTCGGCTGTACGCGAGGGCGCGCGGTTCTTTTGTCAAGACCGACCTGTCCGCTGCCCTGAATGAACATG
 CAGGACGAGGACGCGGCTATCGTGGCTGGCCACGACGGGCTTCTTGGCGAGCTGTCTCGACCTGTCTCACTGAAGCGGGAAGGACTGGCTGCT
 ATTGGGCGAAAGTCCCGGGGACGATCTCCTGTCTCATCTCACCTTGTCTCTGCGGAGAAAGTATCCATCATGGCTGATGCAATGCGGCGGCTGCATACGC
 TTGATCCGGCTACCTGCCATTCCGACCCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGCTCTTGTCTGATCAGGATGATCTG
 GACGAAGACGATCAGGGGCTCGCGCCAGCCGAACTGTTCGCGAGGCTCAAGGCGCGCATGCCGACGGCGGAGGATCTCGTCTGTGACCCATGGCGGATGC
 CTGCTTGCGGAATATCATGGTGGAAATGGCCGCTTTCTGGATTTCATCGACTGTGGCGGCTGGGTGTGGCGGACCGCTATCAGGACATAGCGTTGG
 CTACCCGTGATATTGCTGAAGACTTGGGCGGAATGGGCTGACCGCTTCTCGTGTCTTACGGTATCGCGCTCCCGATTCGCAGCGCATCGCCCTTC
 TATCGCCTTCTTGACGAGTTCTTCTGAAGATCCGCTGAAGTCTGCAGAAATTTGATGATCTATTAACAATAAAGATGTCCACTAAATGGAAGTTT
 TCCTGTCTATCTTTGTTAAGAGGTGAGAACAGTACCTACATTTTGAATGGAAGGATGGAGCTACGGGGTGGGTGGGTGGGATAGATAA
 ATGCTGCTCTTTTACTGAAGCTCTTACTATTGCTTTATGATAATGTTTCATAGTTGGATATCATAAATTAACAAGCAAAACCAATTAAGGGCCA
 GCTCATTTCTCCCACTCATGATCTATAGATCTCTCGTGGGATCATTTGTTTTTCTTGTATCCCACTTTGTGGTTCTAAGTACTGTGGTT
 TCCAAATGTGTACGTTTCATAGCCCTGAAGACGAGATCAGCAGCTCTGTTCACATACACTTCATTTCTCAGTATTTGTTTTGCCAAGTTCTAATCCA
 TCAGACCTCGACCTGCAGCCCTTAGAGAAGTTCTATTCCGAAGTTCTATTCTCTAGAAAGTATAGGAACCTTCTTAGGGTTTACCGGTGGCGCGCC
 GAGAGAGAAAGAGAGCAGCGATACCGAAATGTCTCAGCGAGAAGTACACAGAGGATGAATGGAGATCAAGCCACGCTGGAACACATGGGAAAT
 GTCTCAGTATTTTCCACCTAAGAAGGAGGAGATGGGTATGTATACACCTCCCTGTCTCATCTGATTCAGGGCTTCCGAGAGGATGCTCATTTCC
 AGGTGCTGTGATAGGCCATGTGTACAGGACGGCTGCCCTTCTCAGCTTCAGATAGCAGTGAAGGAAAGATATGGCCATGGGGGTGAGCAGAAGT
 ACAGCAAAAGGGAAGGGGTAGCAAGTGAACAATATATTCACCCCGCCACACACACACACACGAAATTTGTGTATTGCAATCCAG
 AACTGCTTCTCTGAACCTAAATCTTAGCAAGCAGTTTACCAGTAACTTGCCCTTGAAATTCAGGCCCTTGGAAGGAGCAGGGGTGTGTGTACAGGC

FIG. 22A

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VK3-20

JK5

FIG. 22C

DLC-1J SEQ ID NO:82 CONTINUED

CCCTTTTGTGATAAAATTATTTTGTCTCAGACAACAATAAAAAATCAATAGCACGCCCTAAAGATCTAGATGCATGCTCGAGTGCCTTTCATTACCTCTTT
TCTCCGACCCGACATAGATAAGCTTTATCGATACCGTTCGACCTCGAGGGGGGGCCCCGGTACCCCGTGGCATACAGTGTCAGATTTTCTGTTTATCAAG
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

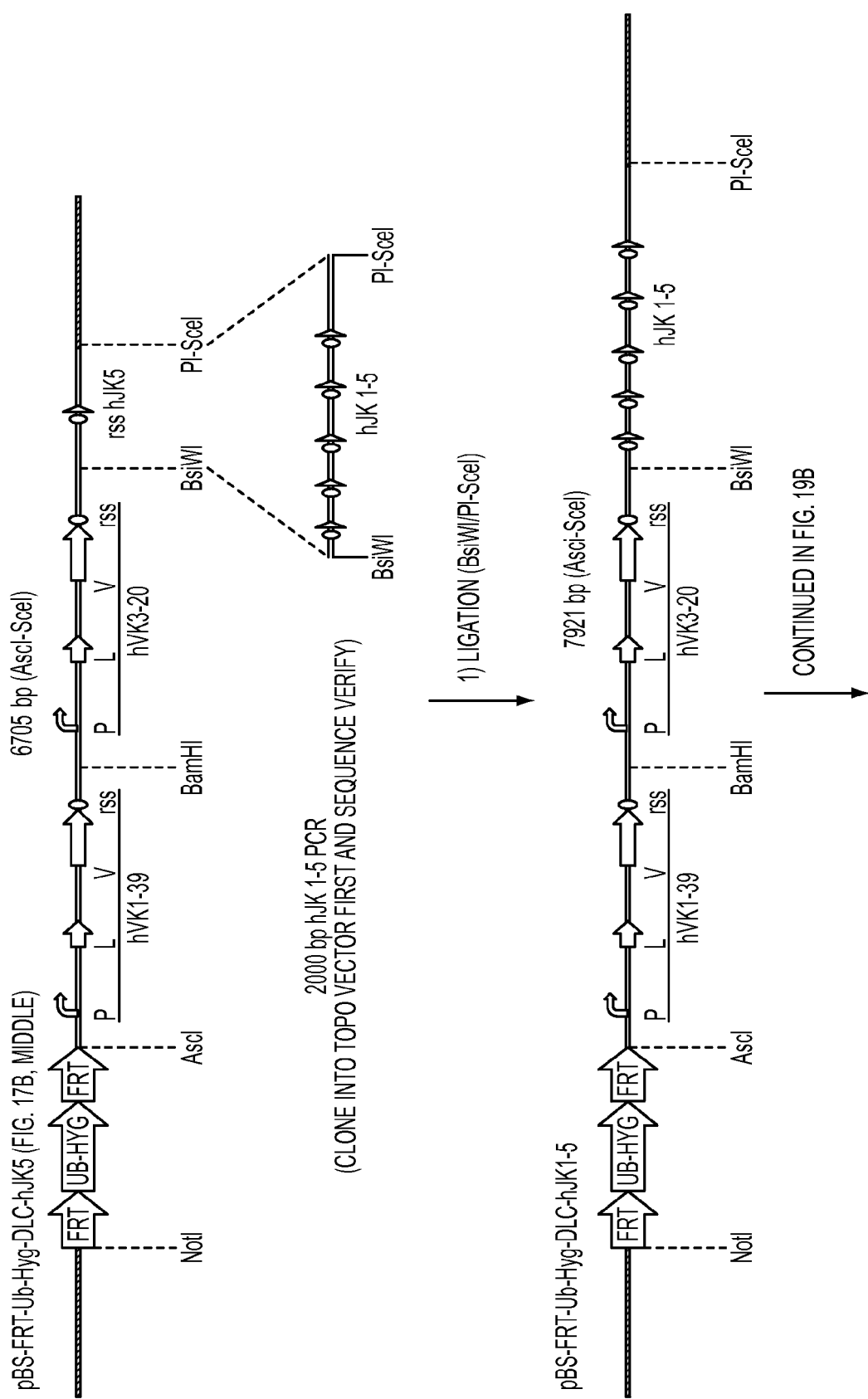


FIG. 23A

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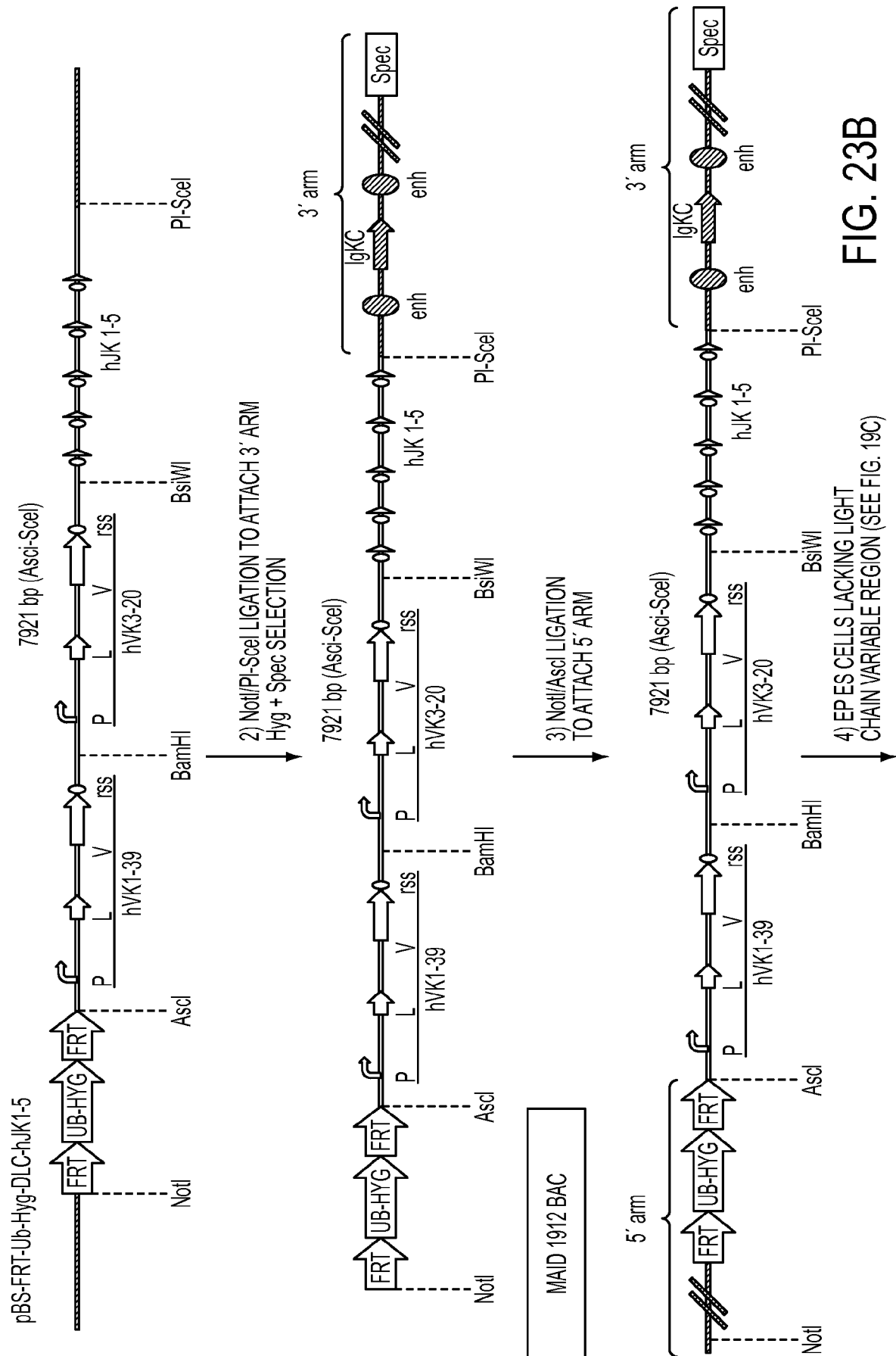


FIG. 23B

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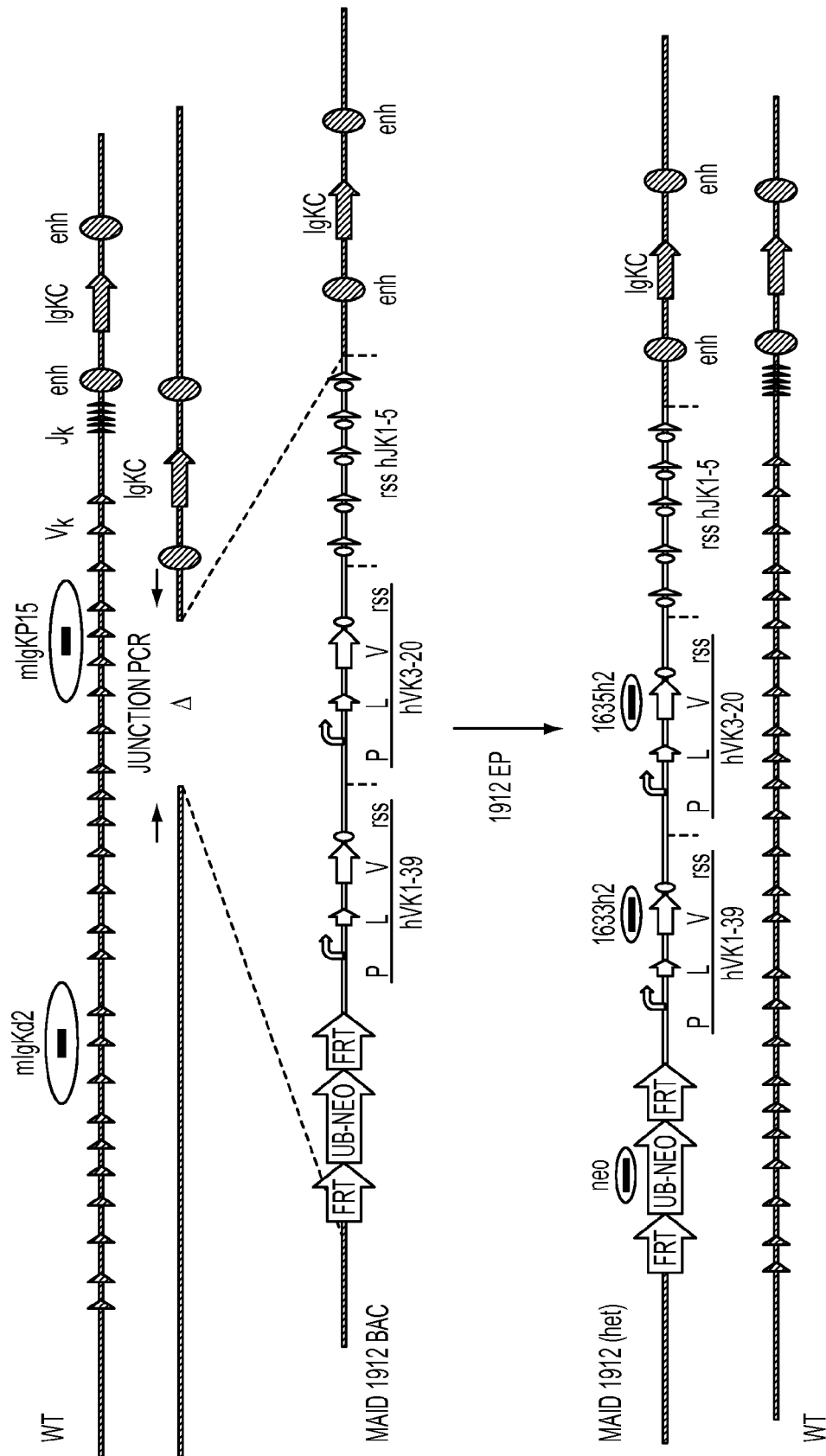
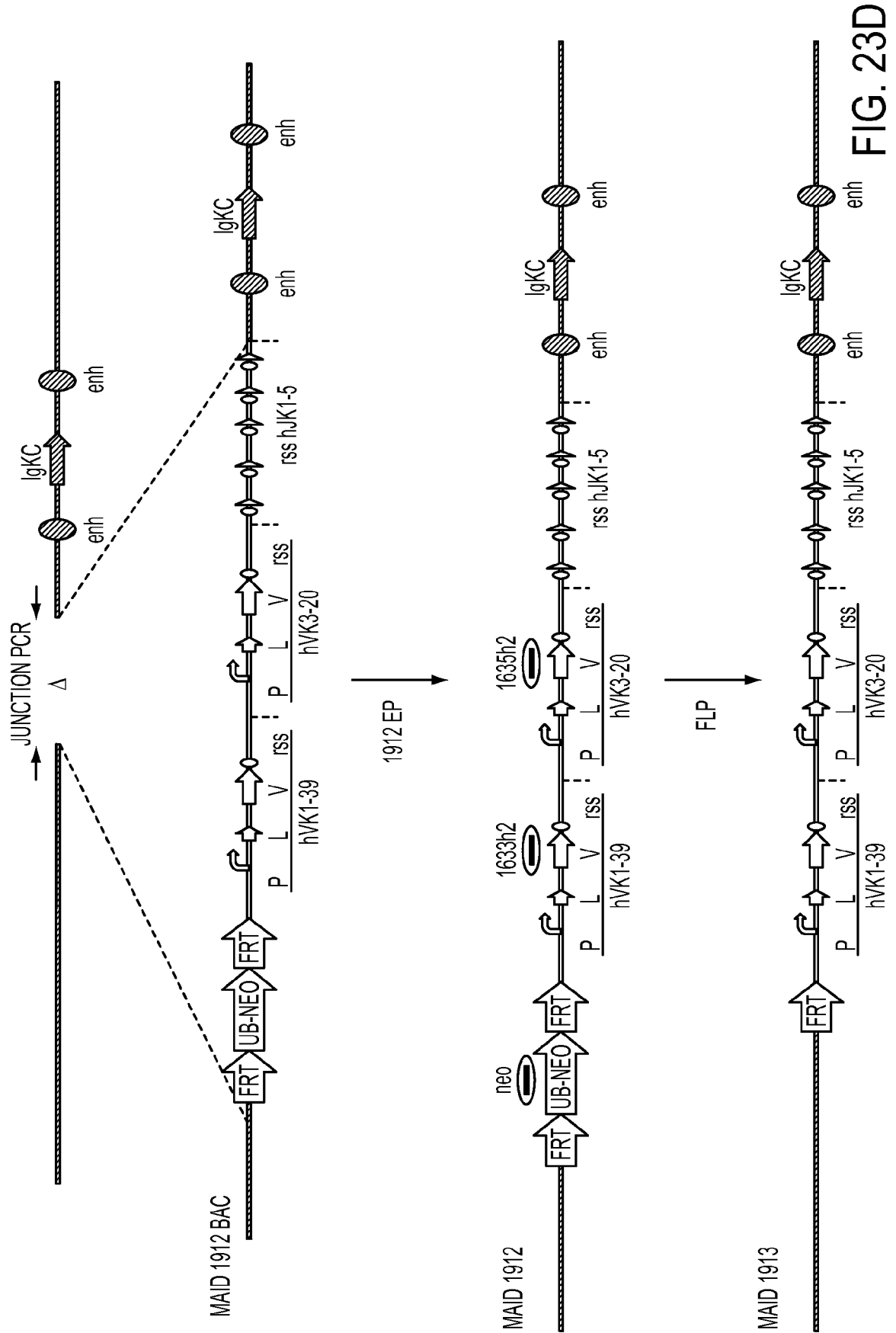


FIG. 23C

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DLC-5J SEQ ID NO:83

GCACCACTTCGTCCGACGGCAGGCTTTGGTCTCCCTTGTCCGTGGGGCGCACGCCACCGAGTTTACGCACACGACACCGAGGCTTGGTTGGTACCG
 AAGTTCCTATTCCGAAGTTCTCTAGAAAGTATAGGAACCTTCTCGCGCTCTGGCTCCGAGGCTCCGCGCGGTTTGGCGCTCCCGCG
 GCGCGCGCTTCTCAGCGGAGGCTGCCAGCTCAGACCAAGGGCGAGGAGGCTCTGATCCTTCCGCGCGGACGCTCAGGACAGCGGCGCGCTG
 CTCATAAGACTCGGCTTAGAACCCAGTATCAGCAGAAGACATTTAGGACGGGACTTTGGGTGACTCTAGGCACTGGTTTCTTCCAGAGAGCG
 GAACAGGAGGAAAGTAGTCCCTTCTCGCGGATTTCTCGGAGGATCTCCGTGGGGGAGTAAACCGCATGATATATAAGGACGCGCGGGGTGTG
 GCACAGTAGTTCGTCGACGCGGGATTTGGGTCCGGTTCTTGTGTGGATCGCTGTGATCGTCACTTGGTAGTAGCGGGCTGTGGGTGGCC
 GGGGCTTTCGTGGCGCGCGCGCTCGGTGGACGGAAGCGTGTGGAGAGACCGCAAGGCTGTAGTCTGGTCCGCGAGCAAGGTTGCCCTGAAC
 TGGGGTTGGGGGAGCGCAGCAAAATGGCGCTGTCCGAGTCTTGAATGGAAGACGCTGTGAGGCGGGCTGTGAGGTCTGTGAACAAGGTGGG
 GGGCATGTTGGGCGGCAAGAACCCAGGCTCTGAGGCTTCTGCTAATGGGAAAGCTCTTATTCGGGTGAGATGGGCTGGGCAACATCTGGGGACC
 CTGACGTGAAGTTGTCACTGACTGAGAACTCGGTCTGTCTGTGGGGGCGGAGTTATGGGGTGCGGTGGGCACTGCACCGTACCTTTT
 GGGAGCGCGCGCTCGTCTGTGAGCTACCGCTCTGTGGCTTATATGCAAGGTGGGCGCACCTGCCGTAGGTGTCCGTAGGCTTTCT
 CCGTCGAGGACGCGAGGTTCCGGCTAGGTAGCTCTCTGAATCGACAGGCGCGGACCTCTGGTGAGGGAGGATAGTGAAGCTCAGTTTC
 TTTGGTCGGTTTATGTACCTATCTTTAAGTAGCTGAAGTCCGTTTGAACATACGCTCGGTTGGGTGGCGAGTGTGTGTGAAGTTTTTAG
 GCACCTTTTGAATGTAACTATTTGGGTCAATATGTAAATTTTCACTGTAGACTAGTAAATTTGTCGGCTAAATTTCTGGCGTTTGGCTTTTGT
 AGACCTCGAGCTTAGATTGGAAACCGGCTCTCTGAATTTGTGACAAATATCATCGGCATAGTATATCGGCATAGTATATACGACAAGGTGAGG
 AACTAAACCATCCACCATGATTGAACAAGATGGATTGCACCGAGTTCTCCGGCGGCTTGGGTGGAGAGGCTATTCGGCTATGACTGGGCAACAAG
 CAATCGGCTGCTGATCCCGCTGTCCGGCTGTACGCGAGGGCGCGGTTCTTTTGTCAAGACCGACCTGTCCGGTCCCTGAATGAACGTG
 CAGGACGAGGACGCGGCTATCGTGGCTGGCCACGACGGGCTTCTTGGCGAGCTGTGCTCGACGTTGTCACTGAAGCGGGAAGGACGTGGCTGCT
 ATTGGGCGAAGTGCCTGGGCGAGGATCTCTGTCTCATCTCACCTTGTCTGCTGCGGAGAAAGTATCCATCATGGCTGATGCAATGCGGCGGCTGCATACGC
 TTGATCCGGCTACCTGCCATTCGACCCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGGTCTTGTCTGATCAGGATGATCTG
 GACGAAGAGCATCAGGGCTCGCGCGAGCCGAACTGTTCGCGAGGCTCAAGCGCGCATGCCGACGCGGAGGATCTCGTCTGACCCATGGCGGATGC
 CTGCTTGCAGATATCATGGTGGAAATGGCGCTTCTTGGATTTCATCGACTGTGGCGGCTGGGTGTGGCGGACCGCTATCAGGACATAGCGGTGG
 CTACCGCTGATATTGCTGAAGACTTGGGCGGATGGGCTGACCGCTTCTCTGCTGCTTACGGTATCGCGCTCCGATTCGCAGCGCATCGGCTTC
 TATCGCTTCTTGACGAGTTCTTCTGAAGATCCGCTGTAAGTCTGCAGAAATTTGATGATCTATTAACAATAAAGATGTCCACTAAATGGAAAGTTTT
 TCCTGTCACTATTTTGAAGAGGTGAGAACAGTACATTTTGAATGGAAGGATGGAGCTACGGGGTGGGGTGGGATAGATAA
 ATGCTGCTCTTTTACTGAAGCTCTTTACTATTGCTTTATGATAATGTTTCATAGTTGGATATCATAAATTAACAAGCAAAACCAATTAAGGGCCA
 GCTCATTCCTCCACTCATGATCTATAGATCTCTCGTGGATCATTTGTTTTCTCTTGTATCCCACTTTGTGGTTCTAAGTACTGTGGTT
 TCCAAATGTCTCAGTTTCAATAGCTGAAGACGAGATCAGACGCTCTGTTCACATACACTTCATTTCTCAGTATTTGTTTTGCCAAGTTCTAATCCA
 TCAGACCTCGACCTGCAGCCCTTAGAAGTTCTTATTCGAAAGTTCTTATTCCTAGAAAGTATAGGAACCTTCTAGGGTTTACCGGTGGCGCGGCG
 GAGAGGAAAGAGAGCAGCGATACCGAAATGTCTCAGCGAGAAAGTACACAGAGGATGAATGGAGATCAAGCCACGCTGGAACAACATGGGAAAT
 GTCTCAGTATTTTCCACCTAAGAAGGAGGAGATGGGTATGTATACACCTCCCTGTCTCATCTGATTTGAGGGCTTTCCGAGAGGATGCTCATTC
 AGGTGCTGTATAGGCCATGTGTACAGGACGGCTGCCCTTCTCCAGCTTCAGATAGAGCAGTGAAGGAAAGATATGGCCATGGGGGTGAGCAGAAGT
 ACAGCAAGGGGAAAGGGTAGCAAGAGTGACAACTATATTCACCCCGCCACACACACACACACAAATTTGTGTATTGCAAT

FIG. 24A

DLC-5J SEQ ID NO:83 CONTINUED

GGGTGGATGACGTTATCAGACATGTCAATTTTCTACAGTACTTGACCTGCCCTTCTAGAACTGGACAACCGAGGGTGAAAGGACTGGATCAAGCAACAATGGCAATGGTGCCCAAGAGGTTAGTCTCAGAACAGGGAGAGACAGACTGAGTCCCTCCACTAACTCAGCCCAACACCTGTGGATGAGTAGGGGATGGCTGAGATCCCTGGGTGGATGGGAGTGGGCACTGATCTGTCAATCTGCTTTTCTTCAAGGATCAGGCAGCAGAGACCCAGAAGCTTCATGTCTTTGTAAGGCTCTTCCAAAGCCAACACAGATAATTTGACAAAACACTGTATCTGCATCCAGACCTCAACCCTGCACAGACTGAAGTGGTTGTTTCATCCCTACTAAAGGTAAACTATACCAGCTATACAGAAATAAAAAGACTGGATAGTTTAGAGGATCACCCAGAAATAGTCTTTTGCCTGCATGGACAAAAACCATCTTCTGTCTTTAGGGAAATGGTATCACTACCTGAGGATTTGGAGCCCAAGTCTCACTTATCTGTGCAGTTGTGAAAGTCTTCACACCCACAGTGTCTAGGTAAATGGAATGTTACTCTTTTAAATTTCTGCAAGAATGAGACAGCTTCTGGACCTTCAGGAAAGATCACTAACAGTAAATACAAGTATATCCGGAAAGATAAAGTTGTAATAGACTCTTCTCTTCAACCTGATCCCATCATGCTTTAGGGAGCTGACTGGGCACAAGTTGGAGCAGAAAGAGAAAAATGAACACACAGCCTTCTAATTTGTCTTAAACAGACTTGTACAAAACATTTCTGTGGCTCAATCTAGGTGATGTGTGAGACAAGAGGACACAGGGGTTTAAATTTCTGTGGCCGAGGGAGAGTTTACCCCTCAGACTGAGCCCAACGGCCTTTTCTGGCCTGATCACCTGGCATGGGCTGCTGAGAGCAGAAAGGGAGGCAGATTGTGTTCTGCAGCTGAAGCCAGCACCCGCCCTCAGCTGCTTTGCATGTCCCTCCAGCCGCCCTGCAGTCCAGAGCCCATATCAATGCTTGGTTCAGAGCTCTGGAGAAGAGCTGCTCAGTTAGGACCCAGAGGGAACCATGGAAACCCAGCGCAGCTTCTCTTCTCTGCTACTCTGGCTCCCAAGGTGAGGGGGAACATGGATGGTTTTGCATGTCAGTGAAACCTCTTCAAGTCTCTTTTACCTGGCAACTCTGCTCAGTCAATACAATAATTAAGCTCAATATATAAGCAATAATCTGGCTCTTCTGGGAAGACAATGGGTTTGATTTAGATTACATGGGTGACTTTTTCTGTTTTTATTTTCCAAATCTCAGATACCCACCGGCAAAAG

ATTGTGTTGACGCAGTCTCCAGGCACCTGCTTTGTCTCCAGGGAAAGAGCCACCCTCTCTGCAGGGCCAGTCA
GAGTGTTAGCAGCAGCTACTTAGCTGGTACCAGCAGAAACCTGGCCAGGCTCCAGGCTCCTCATCTATGGTGCAT
CCAGCAGGGCCACTGGCATCCCAGACAGGTTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGA

CTGGAGCCTGAAGATTTTGCAGTGTTATTACTGTCAGCAGTATGGTAGCTCACCTCC CACAGTGATTACAGTTCAGCTTGAAAACAAAAA
CCCTCTGCAAGACCTTCATTGTTTTACTAGATTATACCAGTGTCTCTTTTACAGATAGCTGTGCAATGACAACTCAATTTTTCATCTCTCTGCT
TGGGCAATTTGGGGATCTTAAAAAGTAATCCCTTGATATATTTTTGACTGCTGATTCCTGCAATTTCTCAGACCAAGATGGACAGCCAGGTTTAAAG
CACAGTTTACAGTAATGGCCACTGGATCAGATTACATCAGTGGATGTCAGTAAGGTCCCAACACAGAGCCATAAGGCAACAACAATAGCAACAAT
AAATCAAAAATTGGAAAAAGAAGAAATTAAGCTGTCTAAATTCACTGTATGAAGGATTTGTGTGCAGATAAAAATTCAAATTTGTCTACAGAGAACTACTAAA
AATTGACATGAGAAAATAGAAAATCAATTAGATTCAAGATCAATTTATTAATTCAATGATTCAAAAAATCAATTTTCATTTCTGCATAATAAAAAATTCGCTAAA
AAATTAACATTTATAAAACAACACACACCATTTTACAAAAACATCAAAAGTATCAATTTATTTAAAAAAAATAGACTAAATACACTGACGTCTTCAGAAATATTA
TTTTTGAAAAATATAAAGAAACCTAAGTAAATAGAAATTCAGTTCAAAGACTGAATGTCTCAGTACTATAAAAAATGTCAATTCCTTCAAAAGATTAAAAATA
TTTGATTACATATAAGAAAAATCAAAAATCTTAAAGTATACCTCCAATTTAAATTAAGAAAGTAAATCTAAAATATTATATGCGAATGTCAAGGATGTAGAAAT
AGCCACAGTGAACCTGAAGAAACACCAAATAGAACTTCCAGTGCCTGAATACCTGGAAATATAGTGTGGGTGGCAGTATGGTGATGGTGAGATCAGATCAGA
AGTTTAAAAATTTGCAACCGTGTCTATTTTTTGAAAAATAATCACTACGCAGATGAGCCAAACCTCTTCAACTGTGGCGTACGCACCTGCTCGAAAAAG
GGAGTTGAGCTTCAGCAGCTGACCCAGGACTGTGTCCCTTTGGTGAGAAAGGTTTTTTGTTCAGCAAGACAATGGAGAGCTCTCACTGTG **GTGGA**

CGTTCCGCCAAGGACCAAGTGGAATCAAACTGAGTAGAATTTAAACTTTTCTCTCCTCAGTTGCTGTGCTCTTCTGTTCCCTGTGTCTATGAAGTGATCTATAAGCTGACTCTGCAATCAGCCTCTGATATCCTTCAGGAAAAGATAAGATAAGTCTGTAGTCAAACTCGAGAATTGATTGC

A

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VK3-20

JK1

FIG. 24C

SEQUENCES OF V_k1-39, V_k3-20, J_k1, J_k2, J_k3, J_k4, AND J_k5 ARE IN LARGE FONT AND BOXED

MOUSE SEQUENCES ITALICIZED

HUMAN SEQUENCES IN REGULAR FONT

RESTRICTION ENZYME SITES IN BOLD

NEO CASSETTE SEQUENCES UNDERLINED

NEW GAGGLES & SENSES AND
FRT SITES DOUBLE UNDERLINED

FIG. 24D

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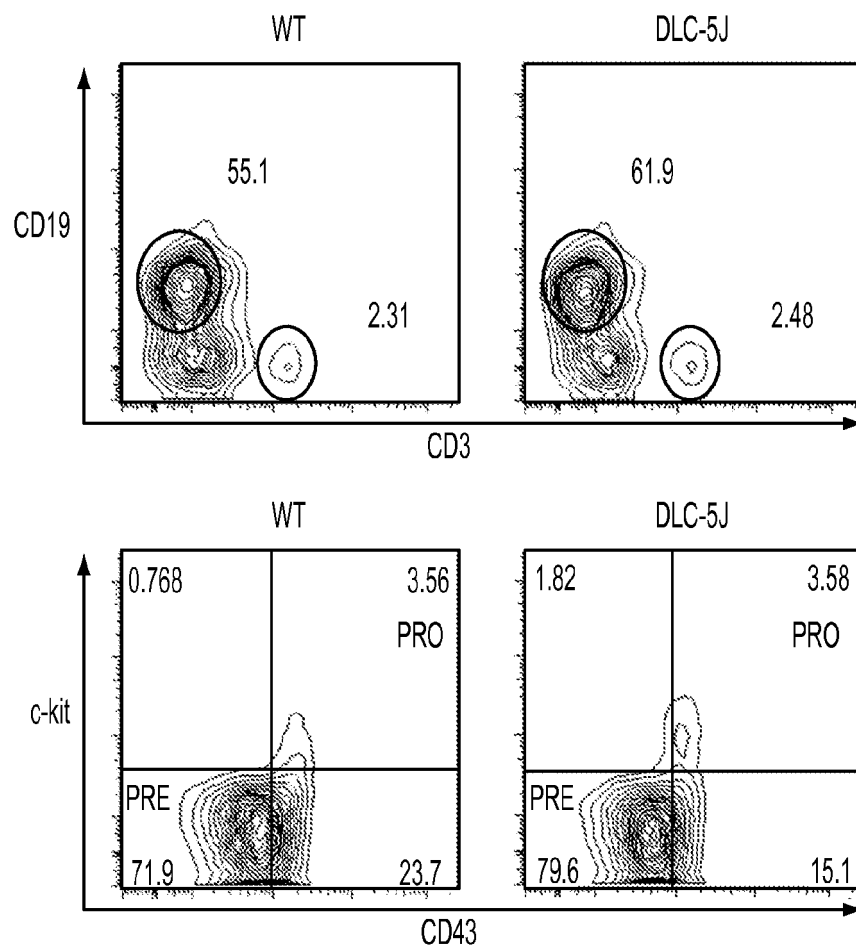


FIG. 25A

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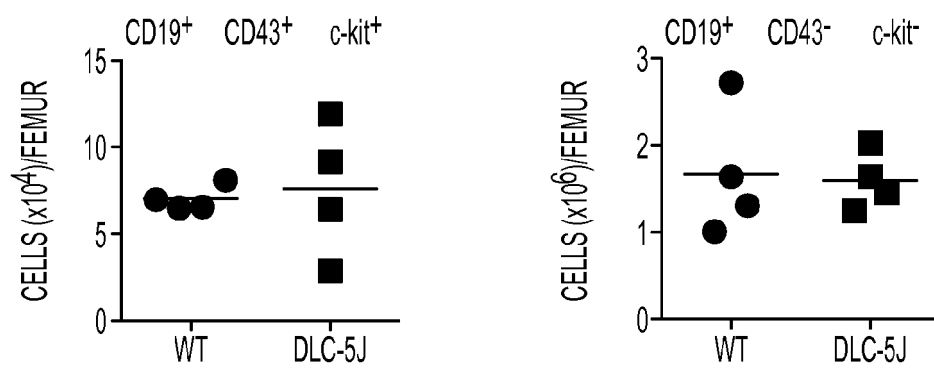


FIG. 25B

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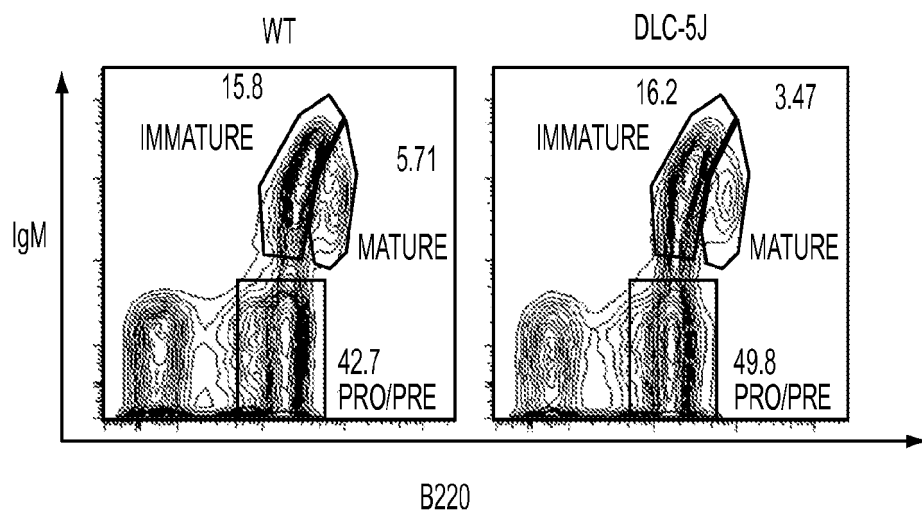


FIG. 26A

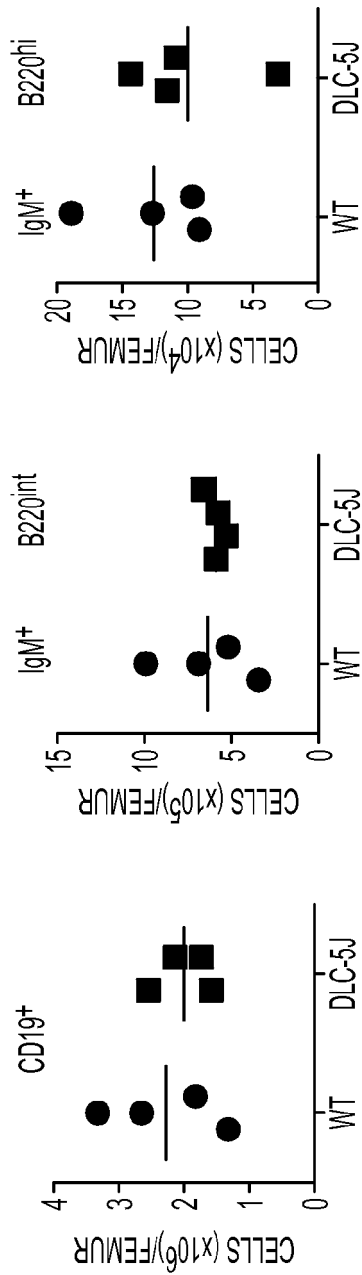


FIG. 26B

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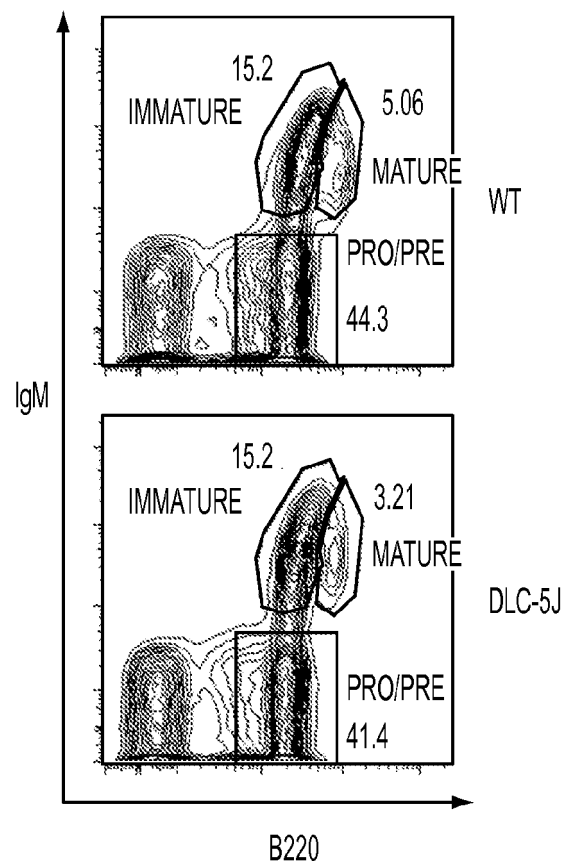


FIG. 27A

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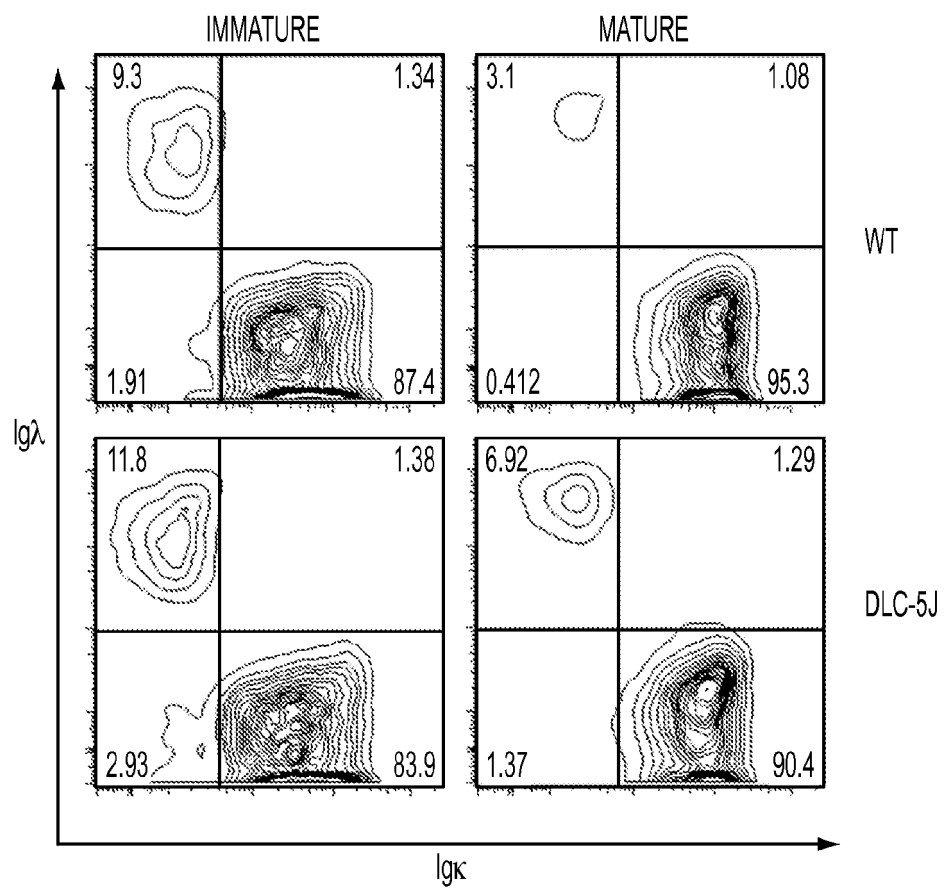


FIG. 27B

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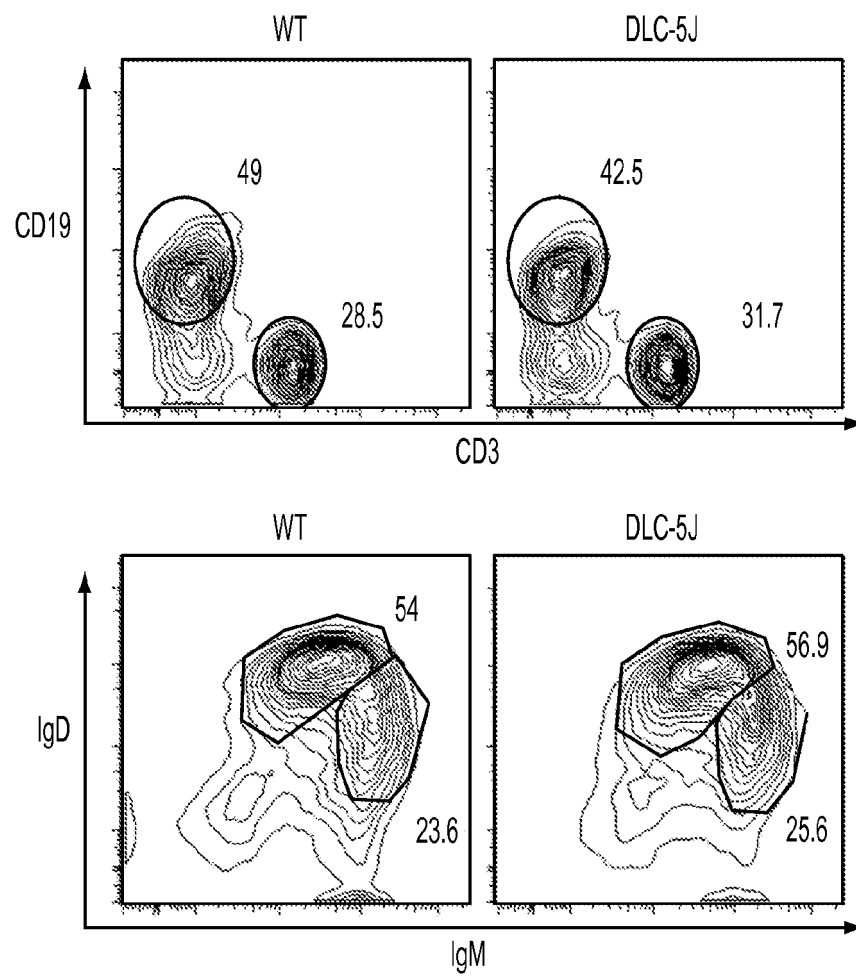


FIG. 28A

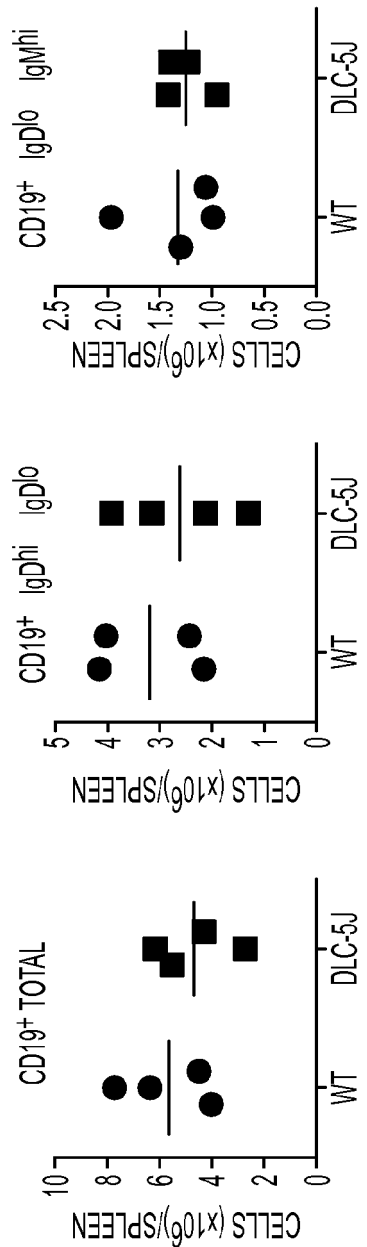


FIG. 28B

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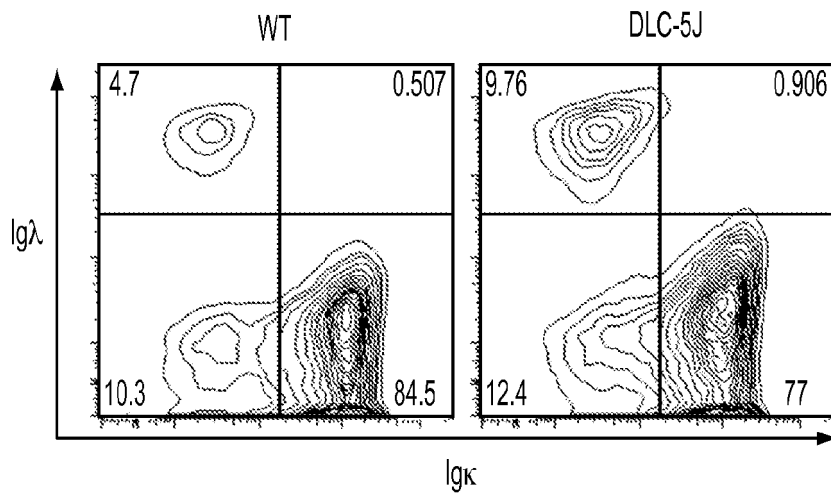


FIG. 29A

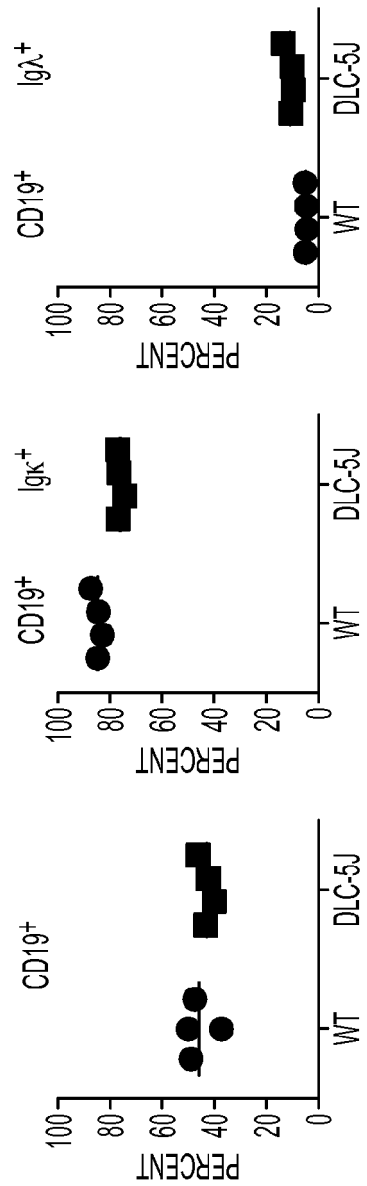


FIG. 29B

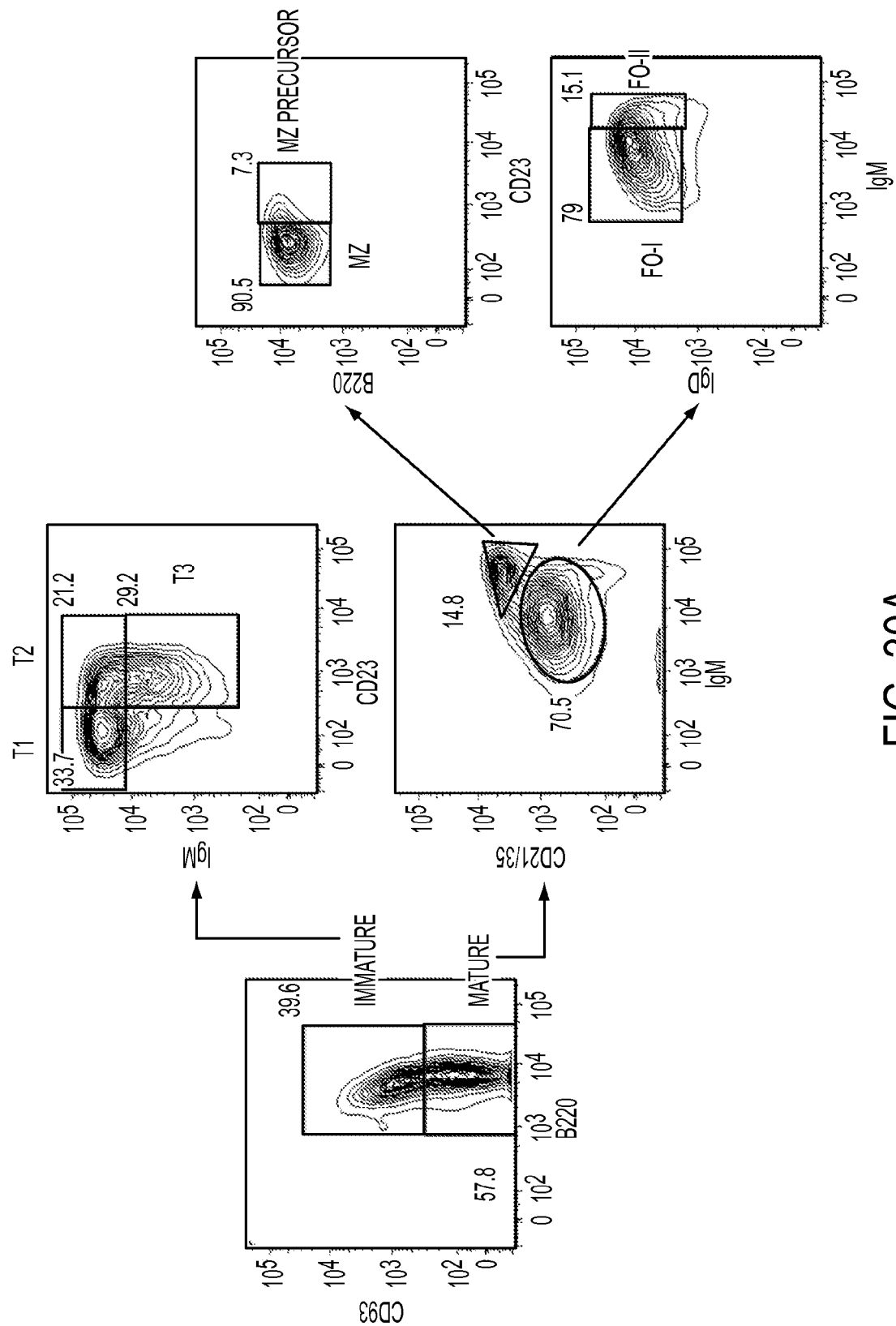


FIG. 30A

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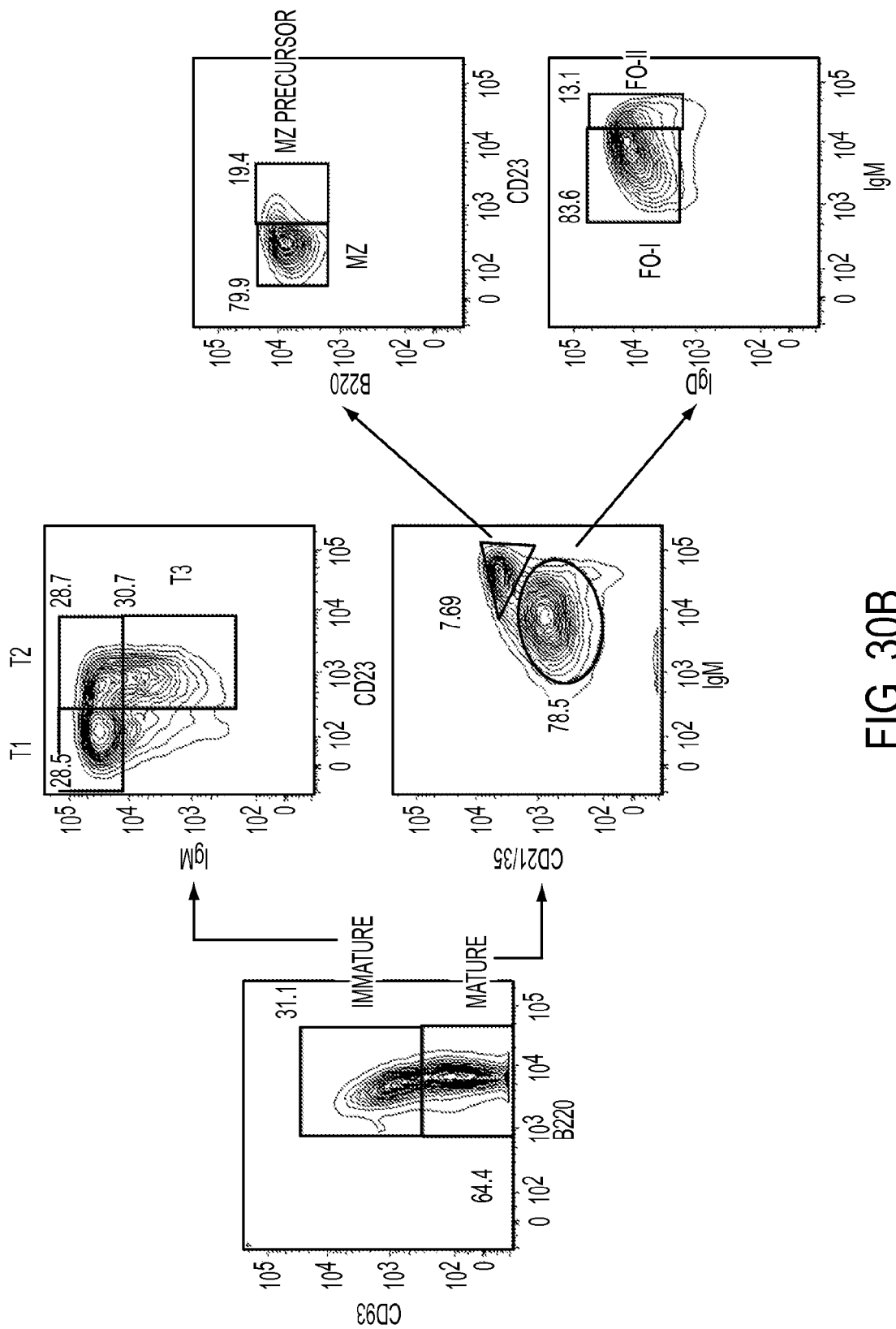


FIG. 30B

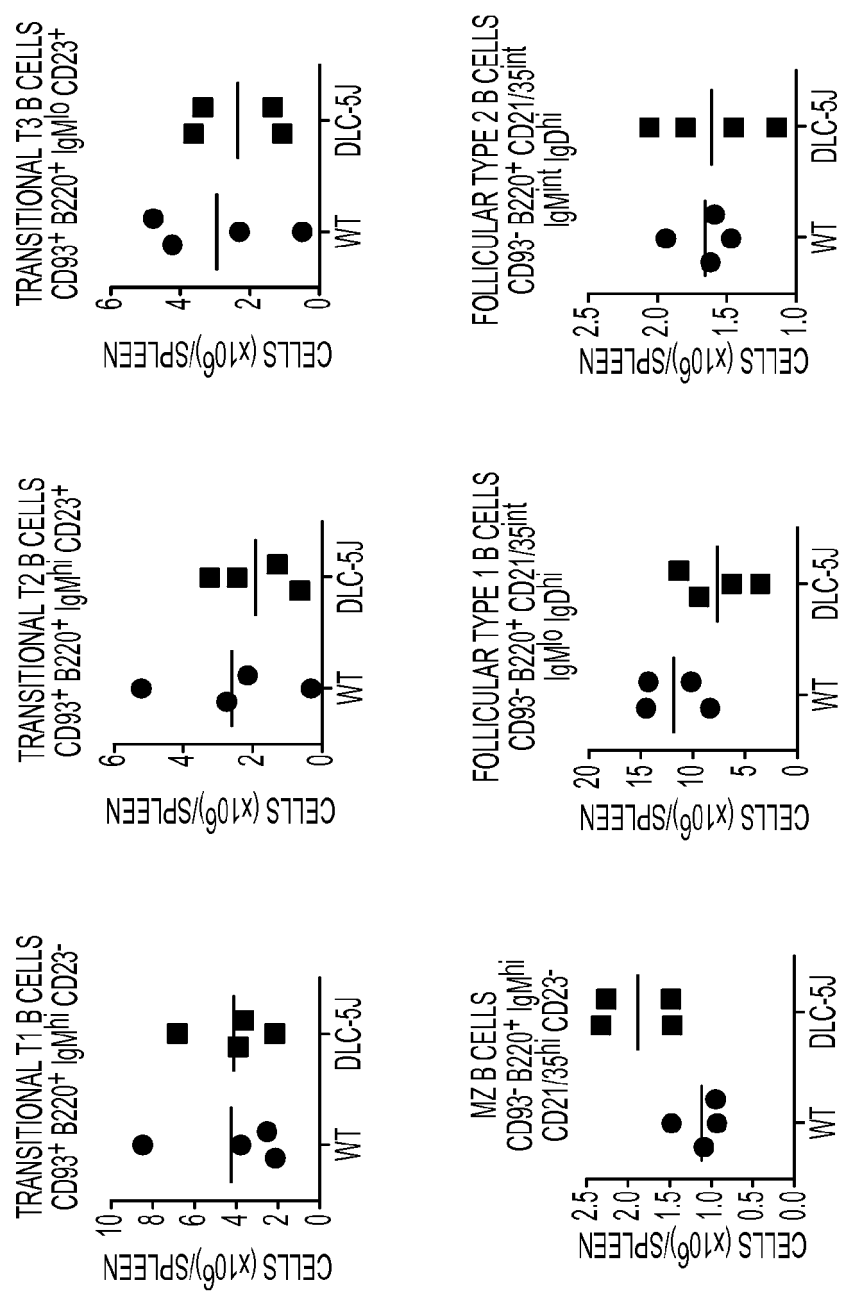


FIG. 31

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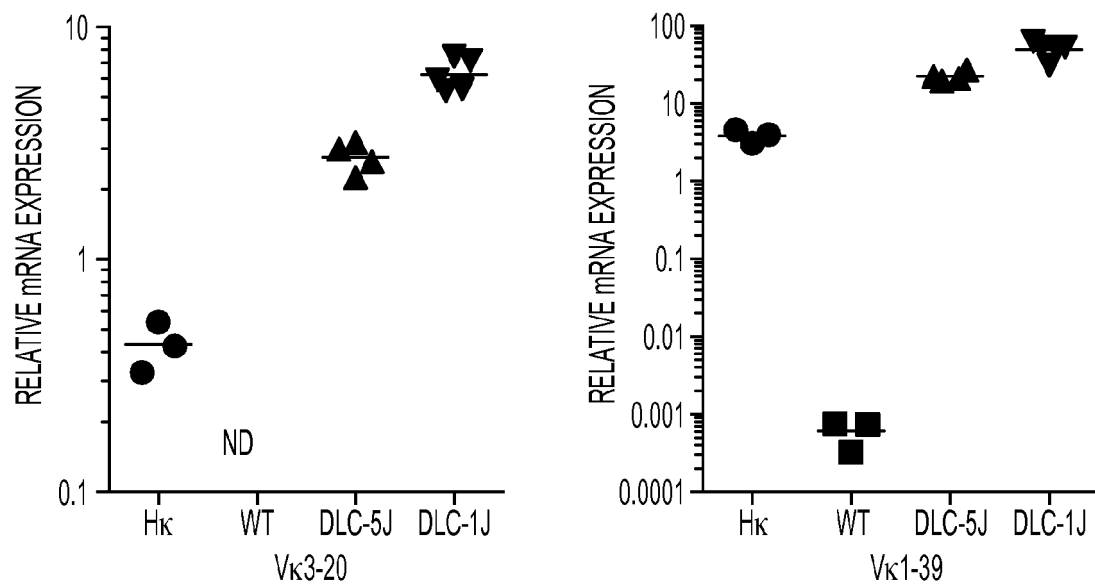


FIG. 32

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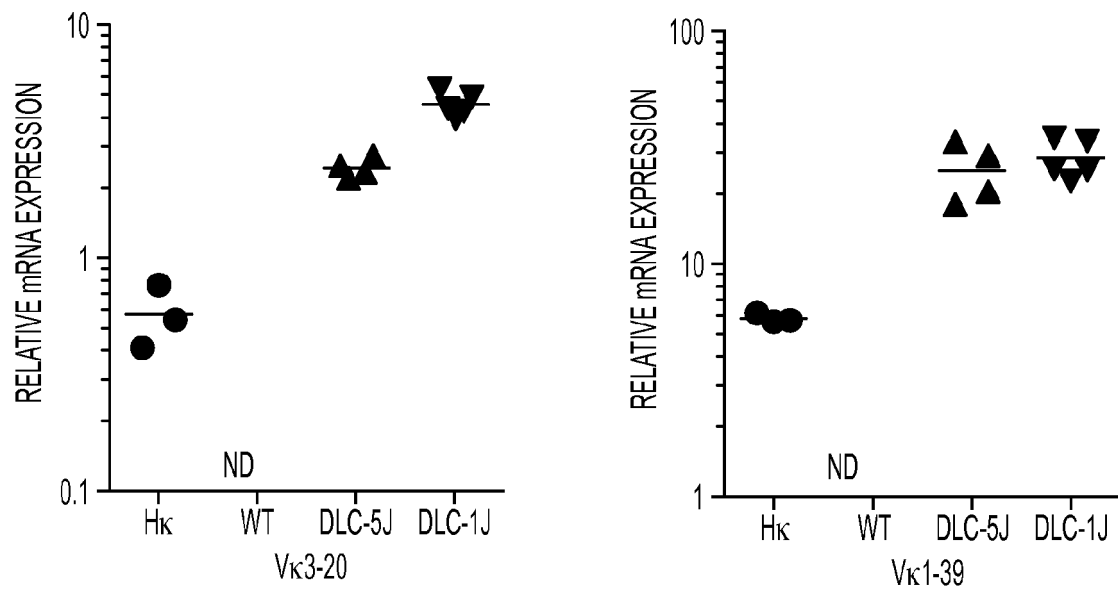


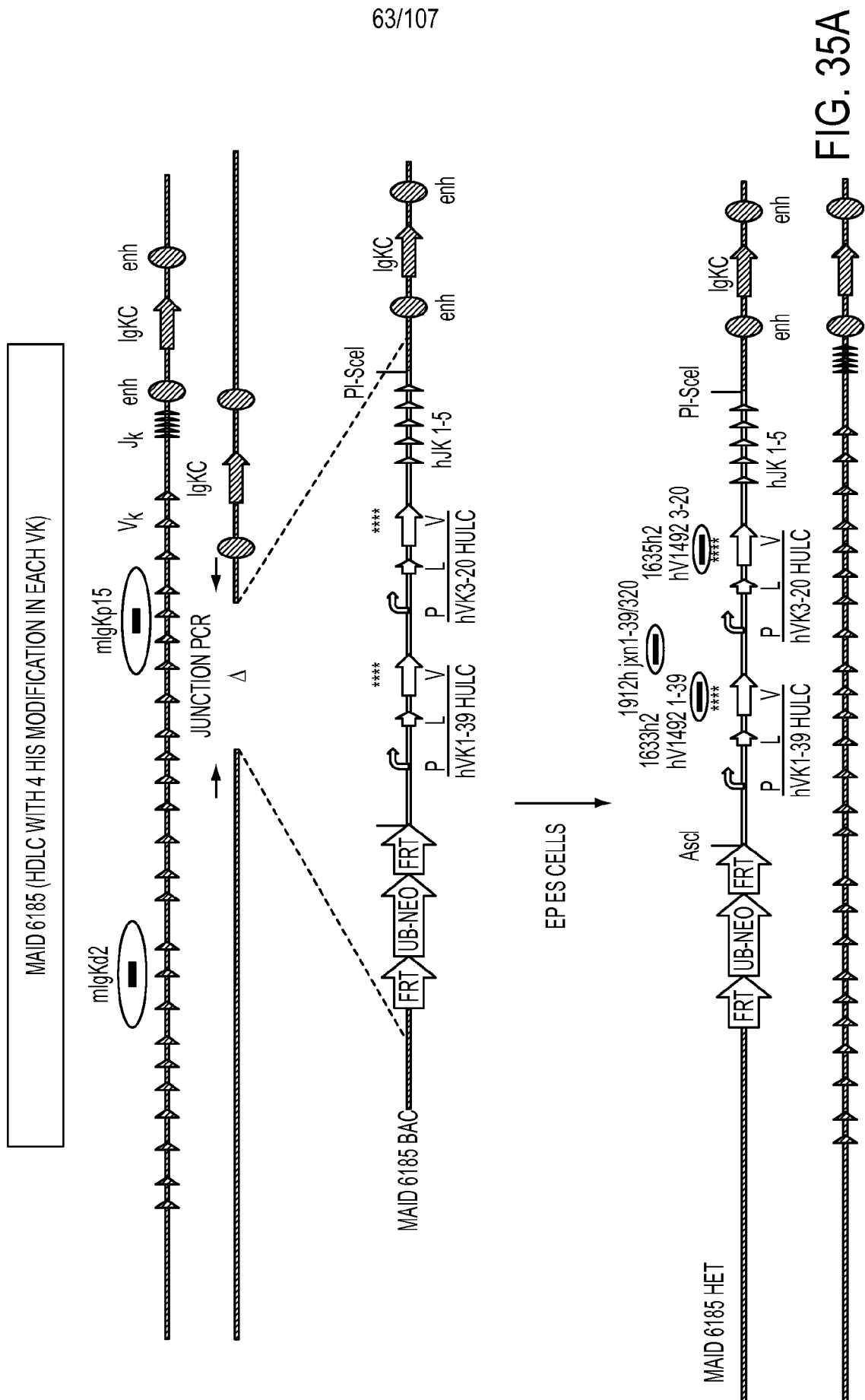
FIG. 33

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 ACA GAGT TACAGTACCC CT CCACAGTGT TACAAG				
hVK1-39 HDLC(Q105H/Q106H/Y108H/P111H) F	CAACTTACTACTGTCA CCA TAGT CAC AGTACCC AT CCACAGTGT TACAAG	45	51	4	79
hVK1-39 HDLC(Q105H/Q106H/Y108H/P111H) R	CTTGTAACACTGTGGG AT GGGTACTGT GACT ATGGT GC ACAGTAGT AA GT TG	45	51	4	79
GERMLINE hVK3-20	GCAGTGTATTACTGTCA GCA GTATGGT AG CTCACCTCC CAC				
hVK3-20 HDLC(Q105H/Q106H/Y107H/S109H) F	AGATTTTGCAGTGTATTACTGTCA CCA TCTATGGT CACT CACTCCACAGT GAT TCAGCT	45	60	5	82
hVK3-20 HDLC(Q105H/Q106H/Y107H/S109H) R	AGCTGAATCACTGTGGGAGGT GAGT CA CC AT GA TGGT GC ACAGTAATACACT GCA AAATCT	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



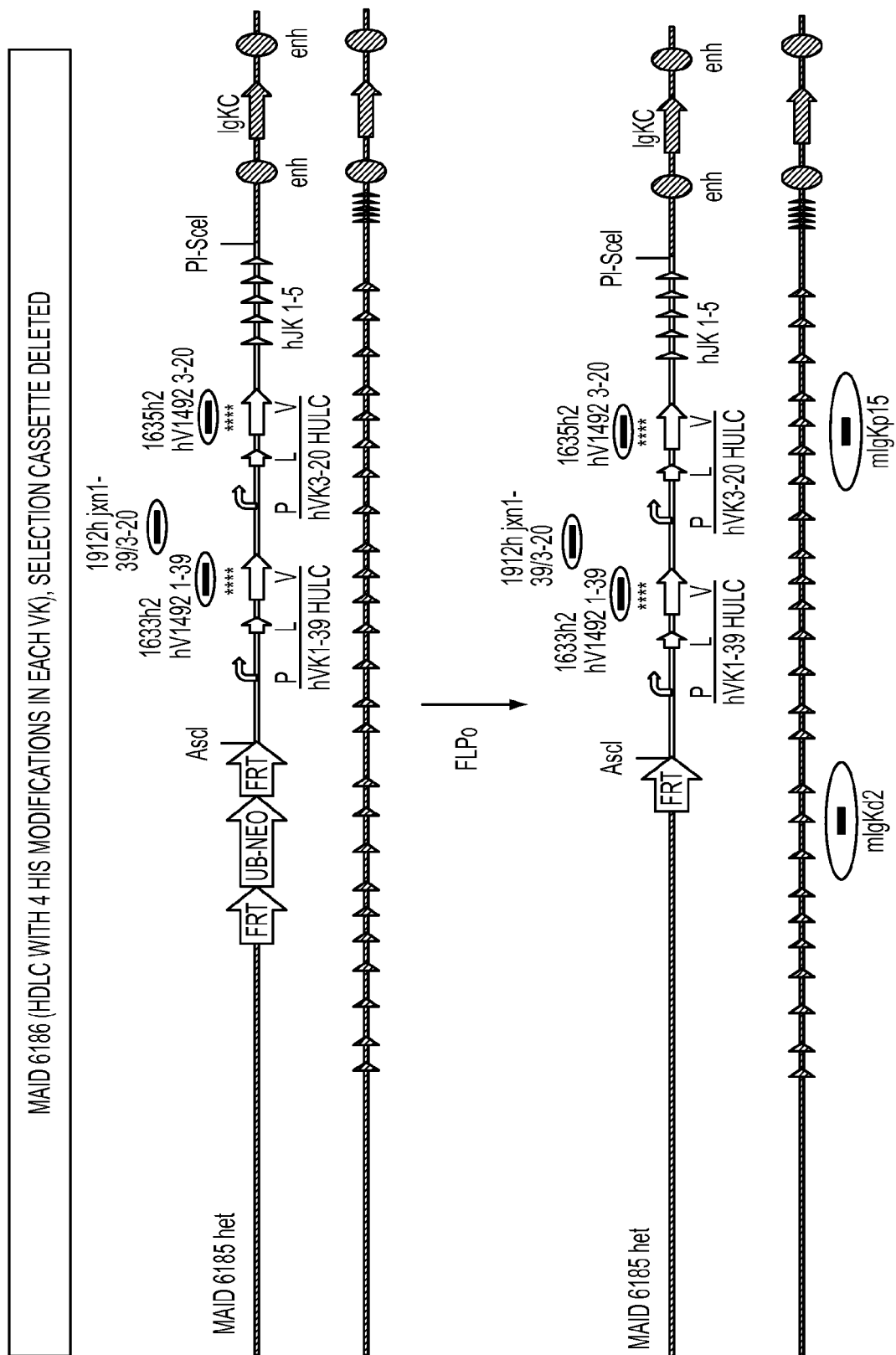


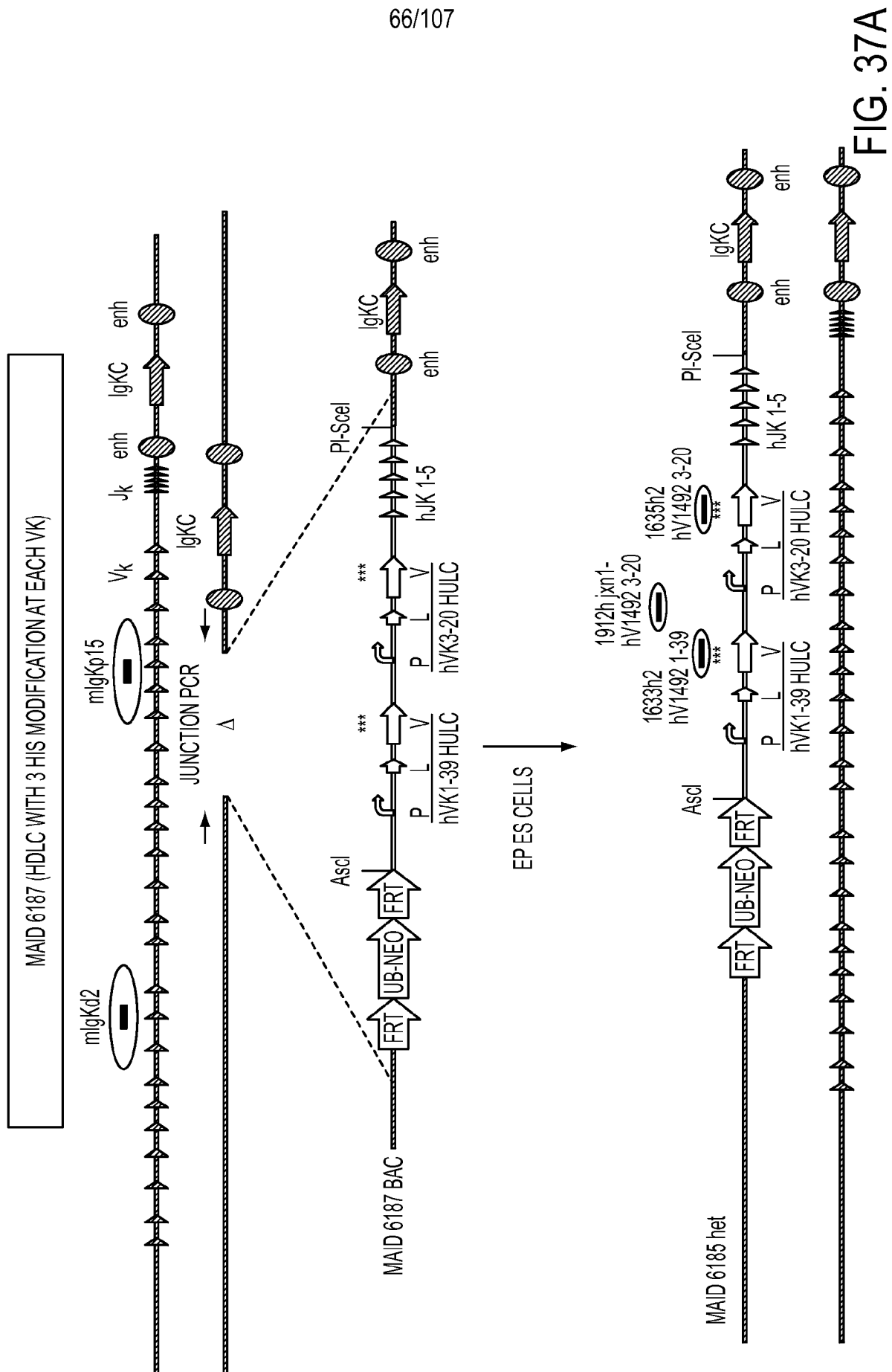
FIG. 35B

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	CAACTTACTACTGTCAACAGAGTTACAGTACCCCTCCACAGTGTACAAG				
hVK1-39 HDLC(Q105H/Q106H/Y108H/P111H) F	ATTTTGCAACTTACTACTGTCAACATAAGTCACAGTACCCATCCCACAGTGTTCAC	40.7	54	3	73
hVK1-39 HDLC(Q105H/Q106H/Y108H/P111H) R	GTAACACTGTGGGATGGGTACTGTGACTATGTGTGACAGTAGTAAGTTGCCAAAT	40.7	54	3	73
GERMLINE hVK3-20	GCAGTGTATTACTGTGACGAGTATGGTAGCTCACCTCCAC				
hVK3-20 HDLC(Q105H/Q106H/Y107H/S109H) F	ATTTTGCAGTGTATTACTGTGACCAATATGGTCACTCACCTCCACAGTGTTCAG	42.9	56	4	75
hVK3-20 HDLC(Q105H/Q106H/Y107H/S109H) R	CTGAATCACTGTGGGAGGTGAGTGACCAATAATGGTGACAGTAATACACTGCCAAAT	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



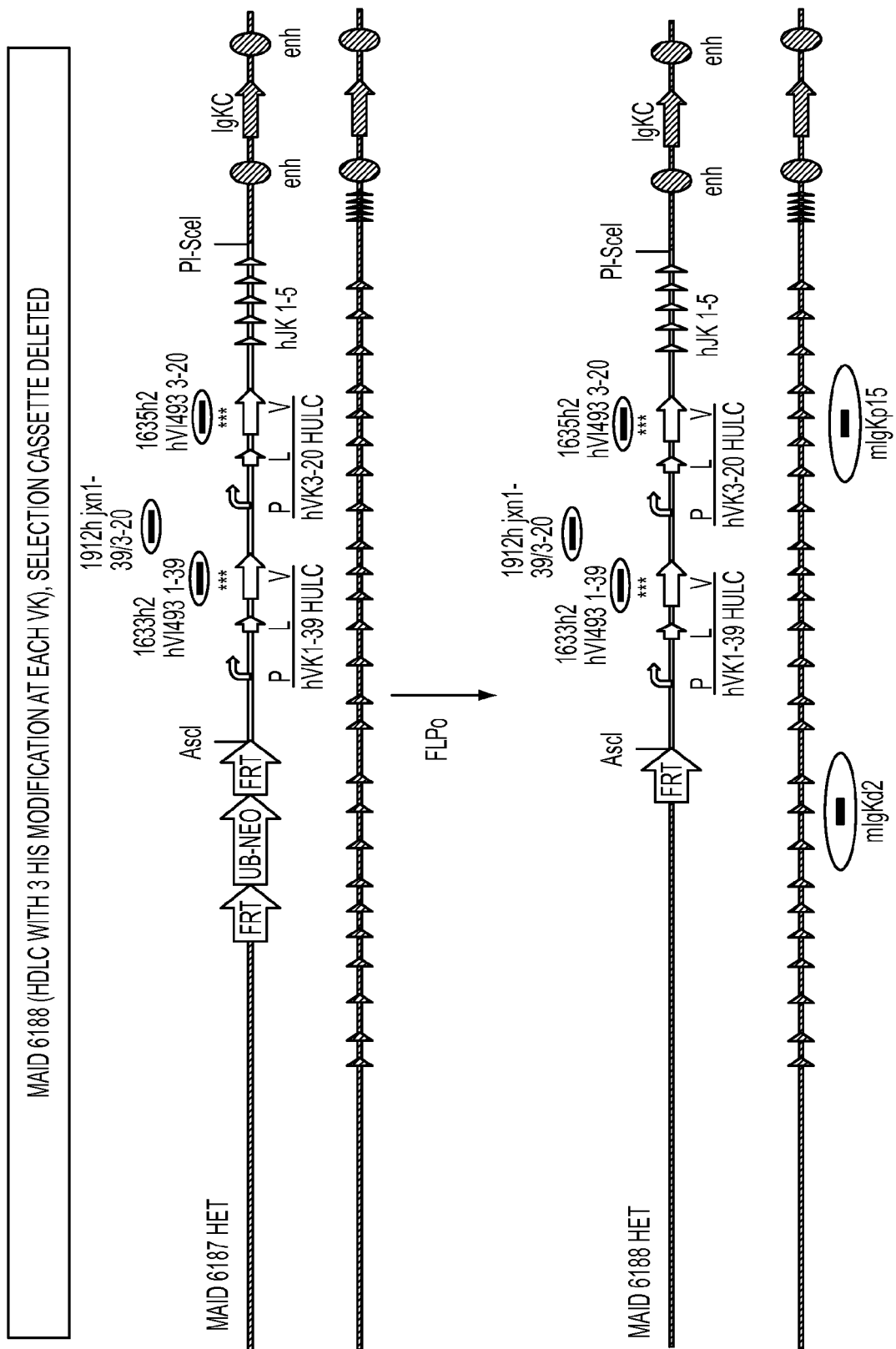


FIG. 37B

IGKV3-20*01 F	FR1	CDR1	FR2	CDR2
	<u>EIVLTQSPGTL~~S~~SPGERATL~~S~~CRAS</u> EIVLTQSPGTL ~~S~~ SPGERATL ~~S~~ CRAS	<u>QSVSSSY</u> QSVSSSY	<u>LAWYQQKPGQAPRLIIY</u> LAWYQQKPGQAPRLIIY	<u>GAS</u> GAS
IGKV3-20*01 F	FR3	CDR3		
	<u>SRATGIPDRFSGSGGTDF~~T~~LTISRLEPEDFAVYYC</u> SRATGIPDRFSGSGGTDF ~~T~~ LTISRLEPEDFAVYYC	<u>HHYCHS</u> QQYGSSP HH H		SEQ ID NO:131 SEQ ID NO:132

FIG. 38A

IGKV1-39*01 F	FR1		FR2		CDR2	
	<u>DIQMTQSPSSLSASVGDRTITCRAS</u>		<u>QSISSY LNWYQQKPGKAPKLLIY</u>		<u>AAS</u>	
	DIQMTQSPSSLSASVGDRTITCRAS		QSISSY LNWYQQKPGKAPKLLIY		AAS	
IGKV1-39*01 F	FR3		CDR3		SEQ ID NO:133	
	<u>SLQSGVPSRFSGSGGTFTLTISSLQPEDFATYYC</u>		<u>QHSSTH</u>		SEQ ID NO:134	
	SLQSGVPSRFSGSGGTFTLTISSLQPEDFATYYC		QHSSTP			
			H H H			
IGKV1-39*01 F	FR1		FR2		CDR2	
	<u>DIQMTQSPSSLSASVGDRTITCRAS</u>		<u>QSISSY LNWYQQKPGKAPKLLIY</u>		<u>AAS</u>	
	DIQMTQSPSSLSASVGDRTITCRAS		QSISSY LNWYQQKPGKAPKLLIY		AAS	
IGKV1-39*01 F	FR3		CDR3		SEQ ID NO:135	
	<u>SLQSGVPSRFSGSGGTFTLTISSLQPEDFATYYC</u>		<u>QHSSTK</u>		SEQ ID NO:134	
	SLQSGVPSRFSGSGGTFTLTISSLQPEDFATYYC		QHSSTP			
			H H H			

FIG. 38B

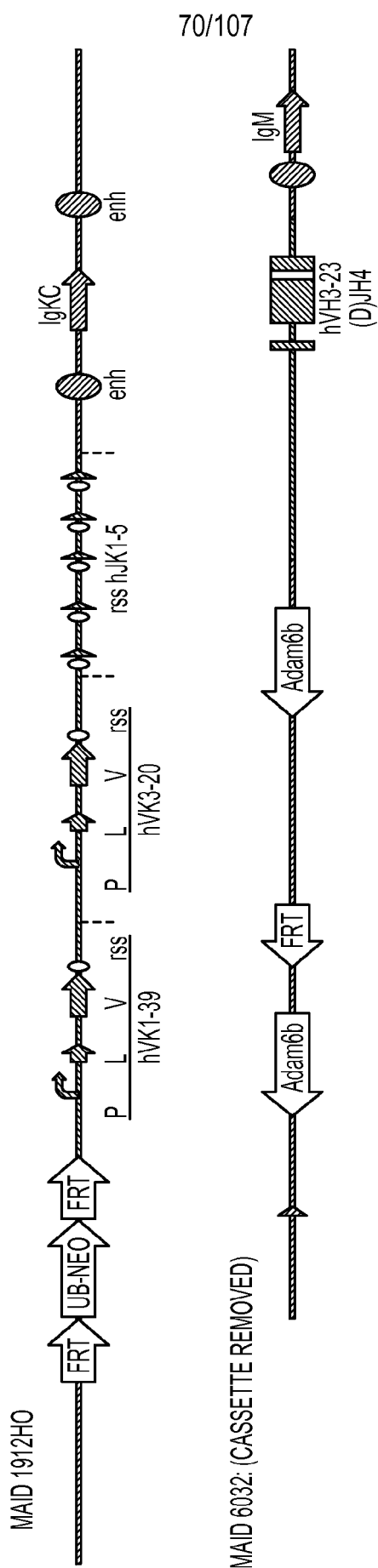


FIG. 39

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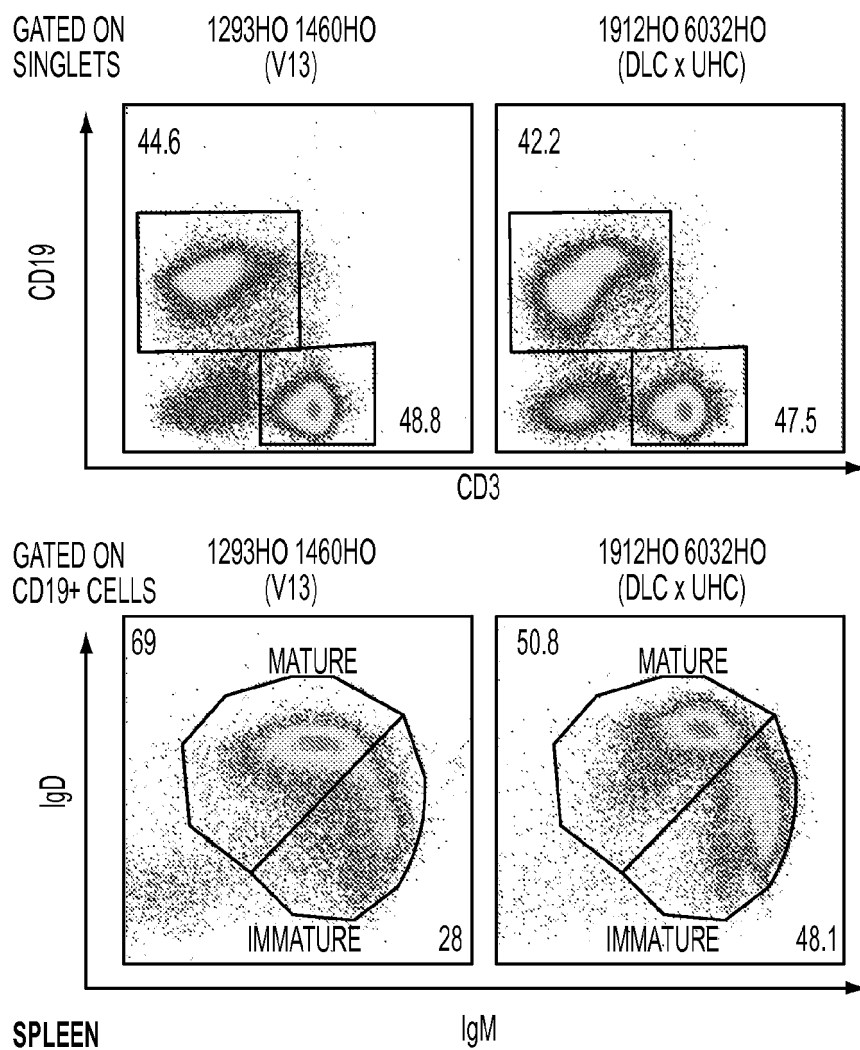


FIG. 40A

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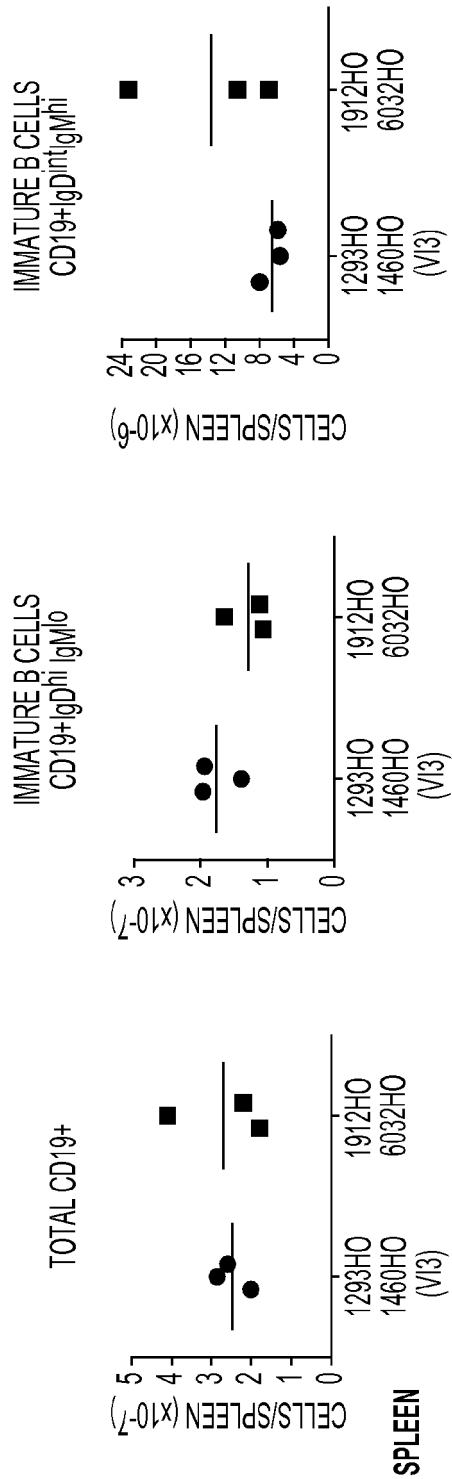


FIG. 40B

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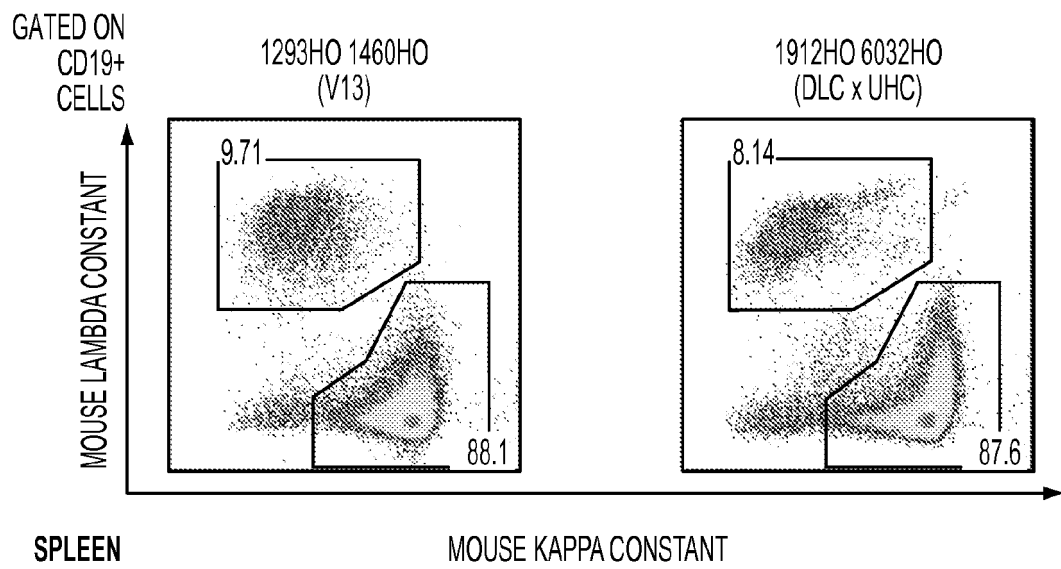


FIG. 41A

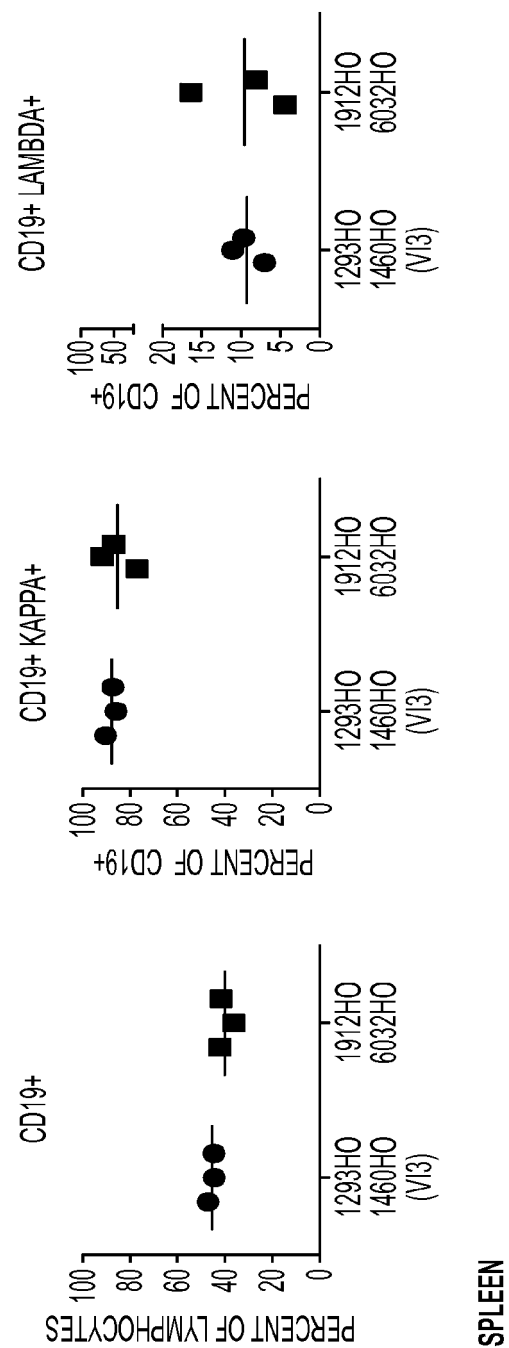


FIG. 41B

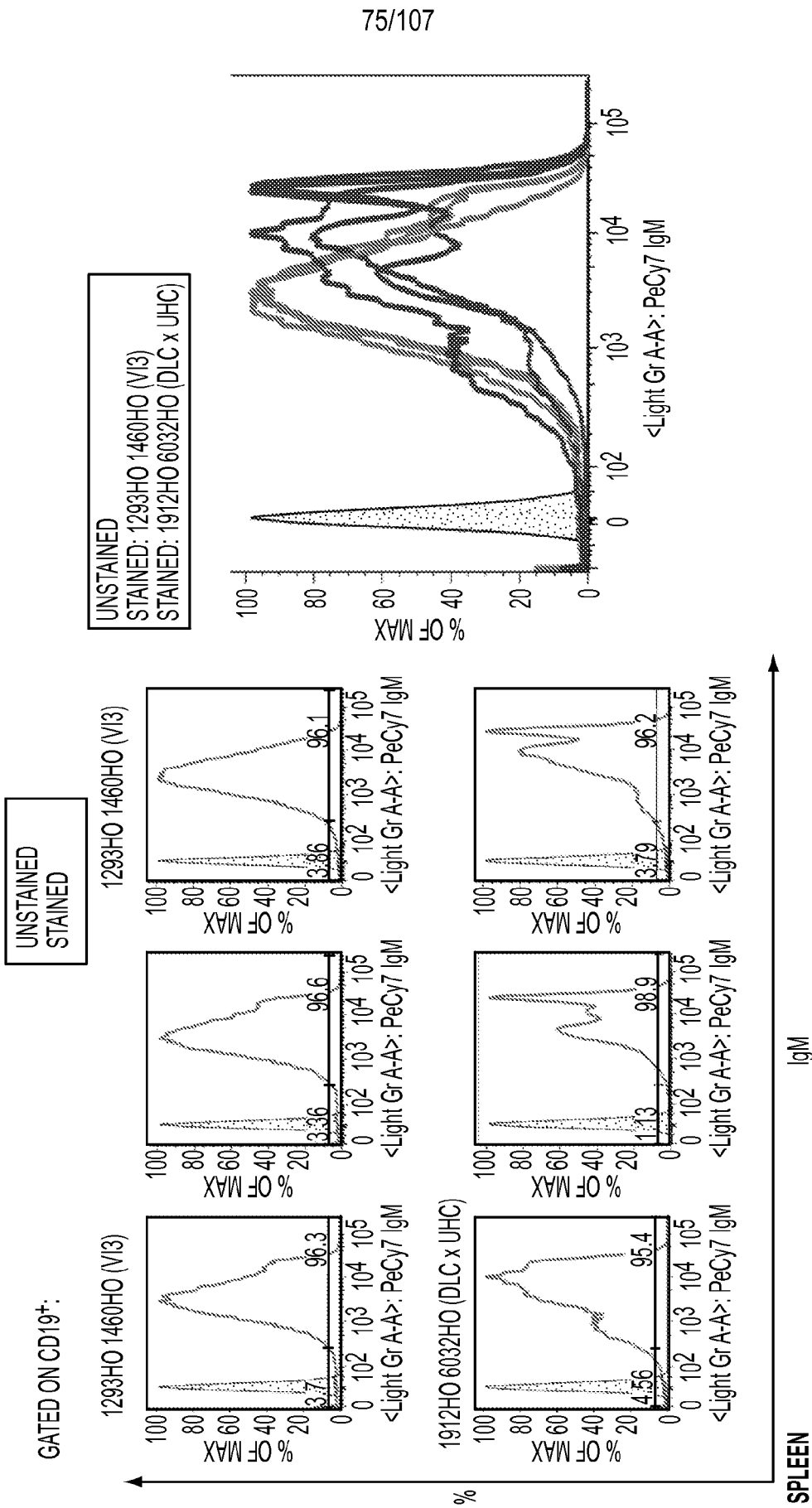


FIG. 42

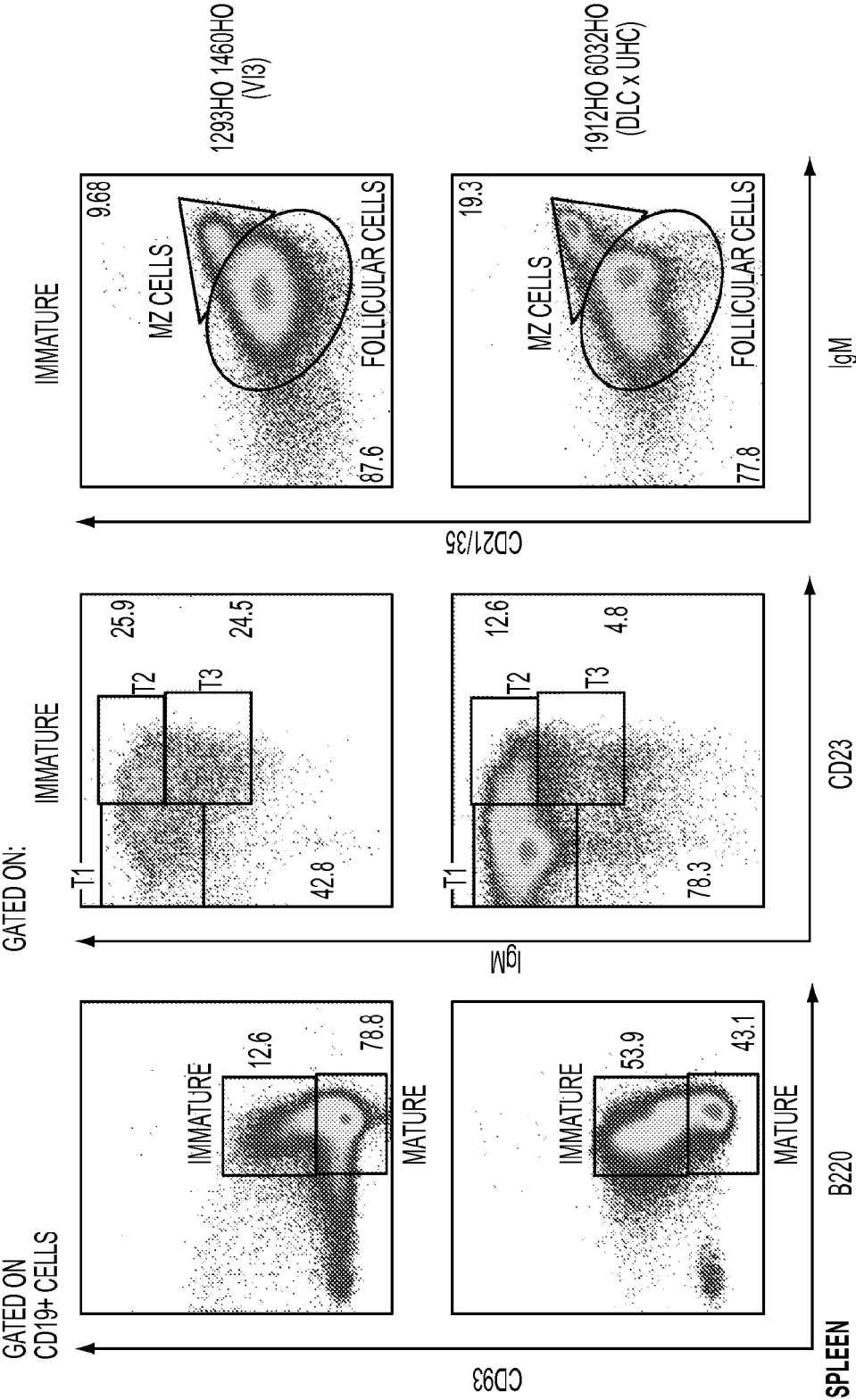


FIG. 43A

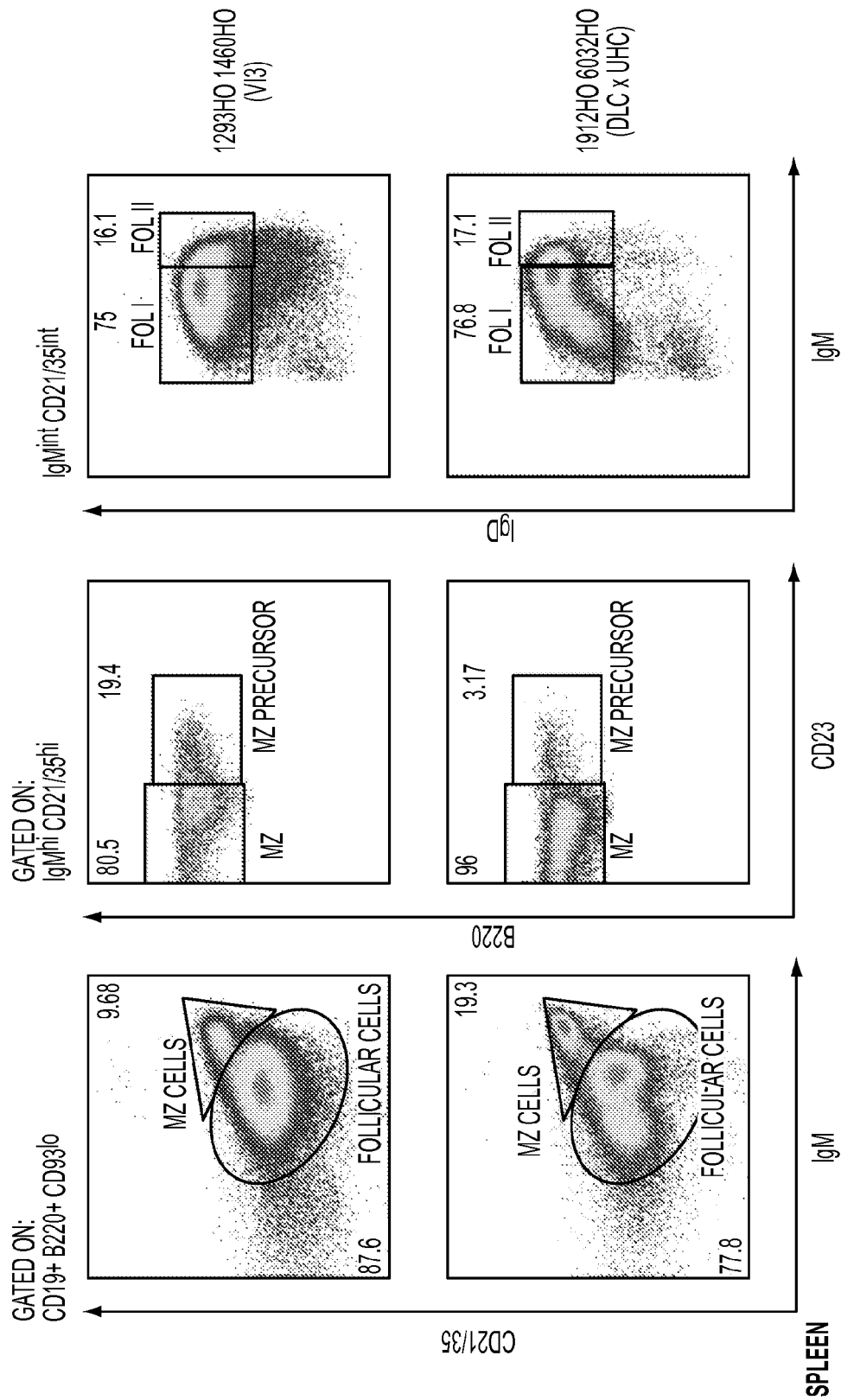


FIG. 43B

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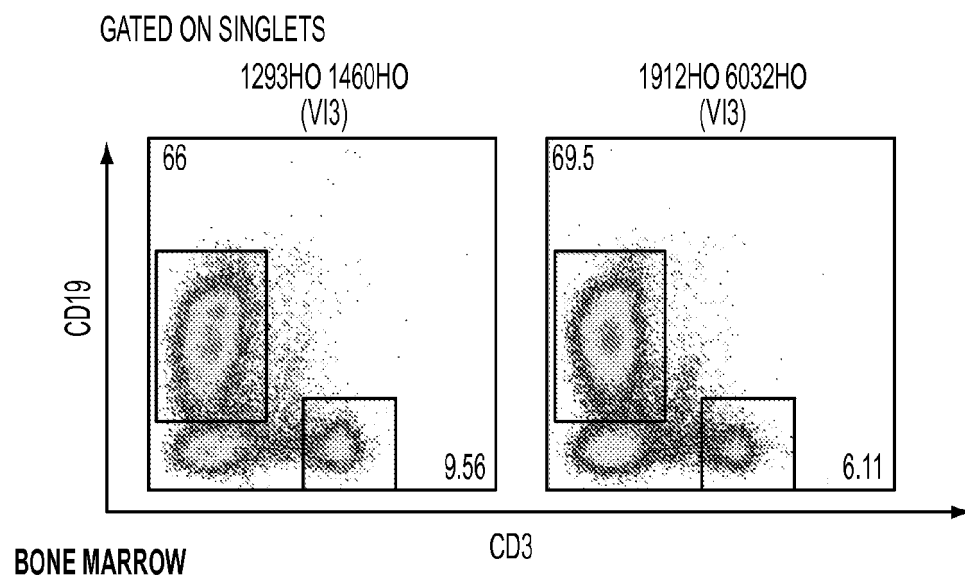


FIG. 44A

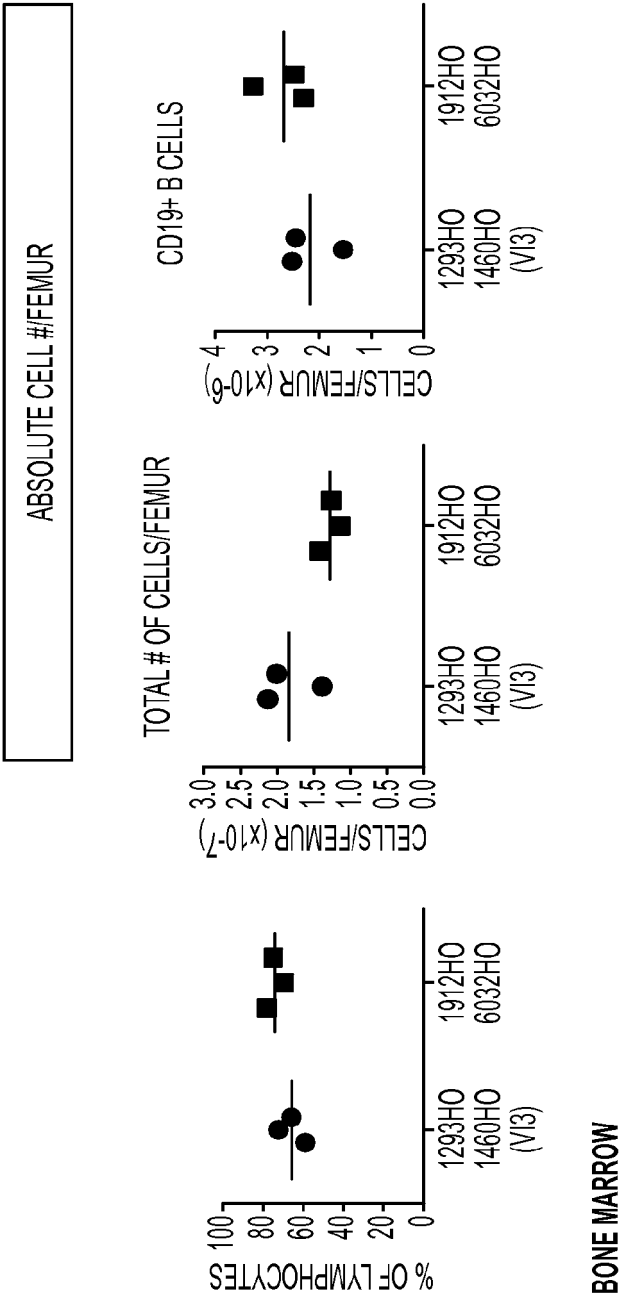


FIG. 44B

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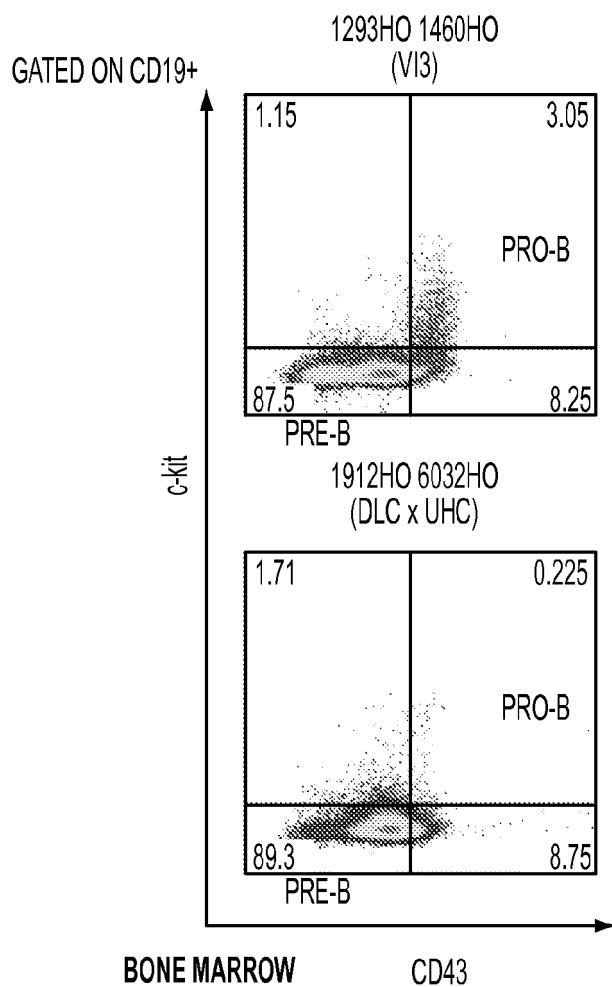


FIG. 45A

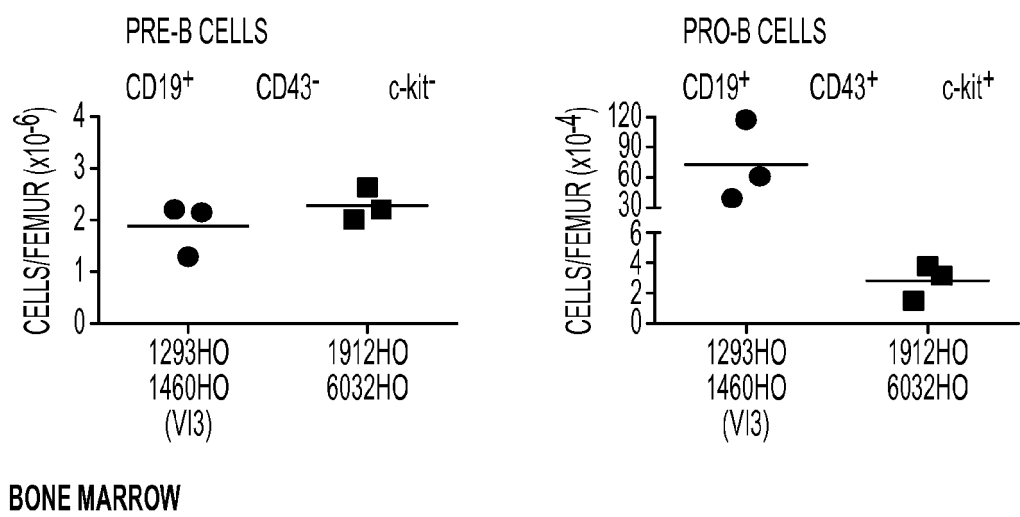


FIG. 45B

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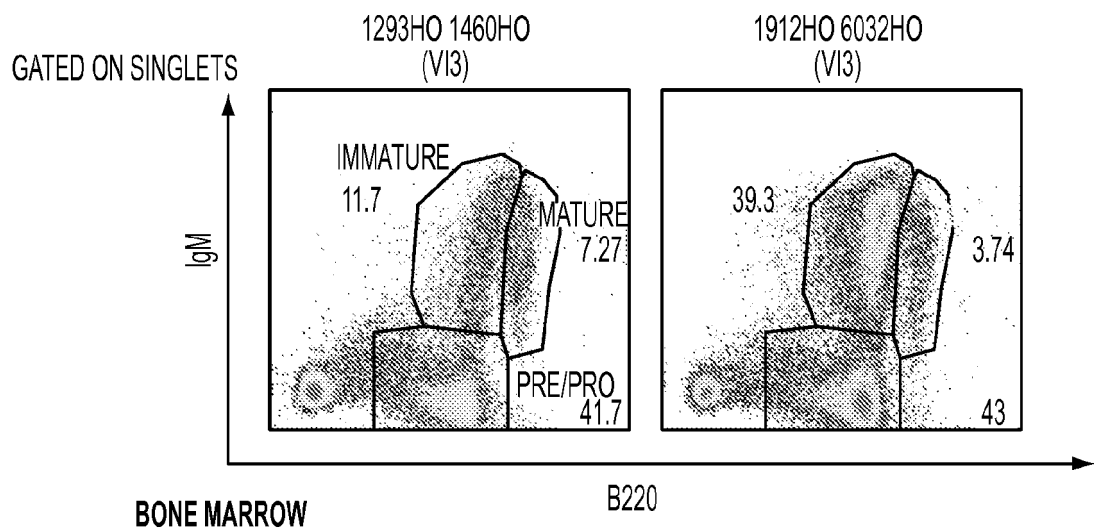


FIG. 46A

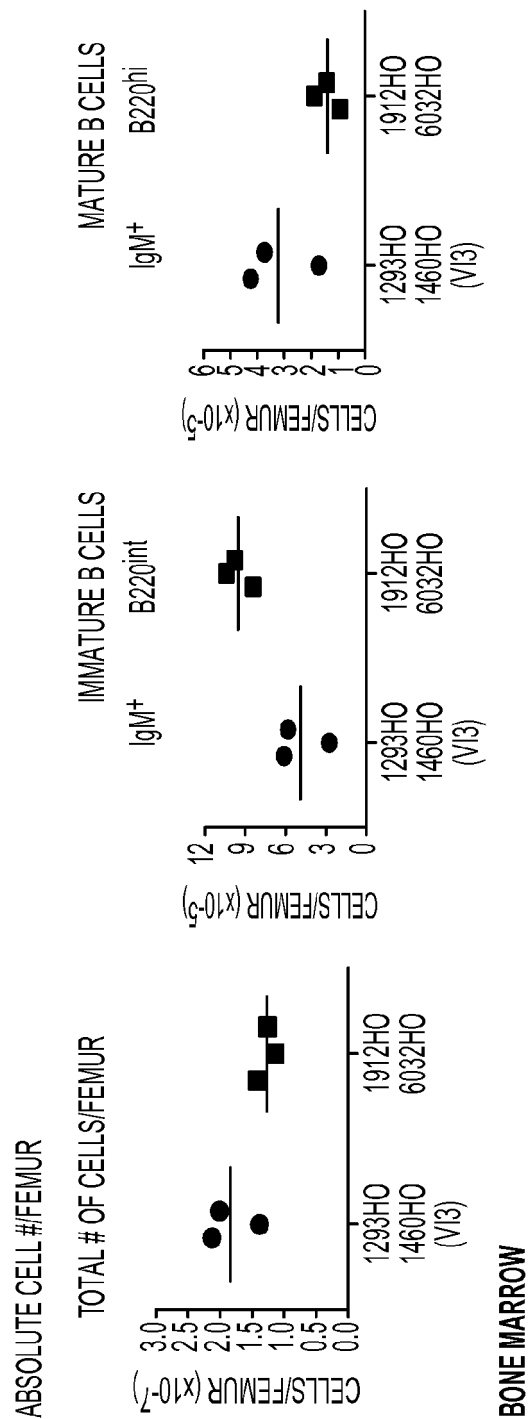


FIG. 46B

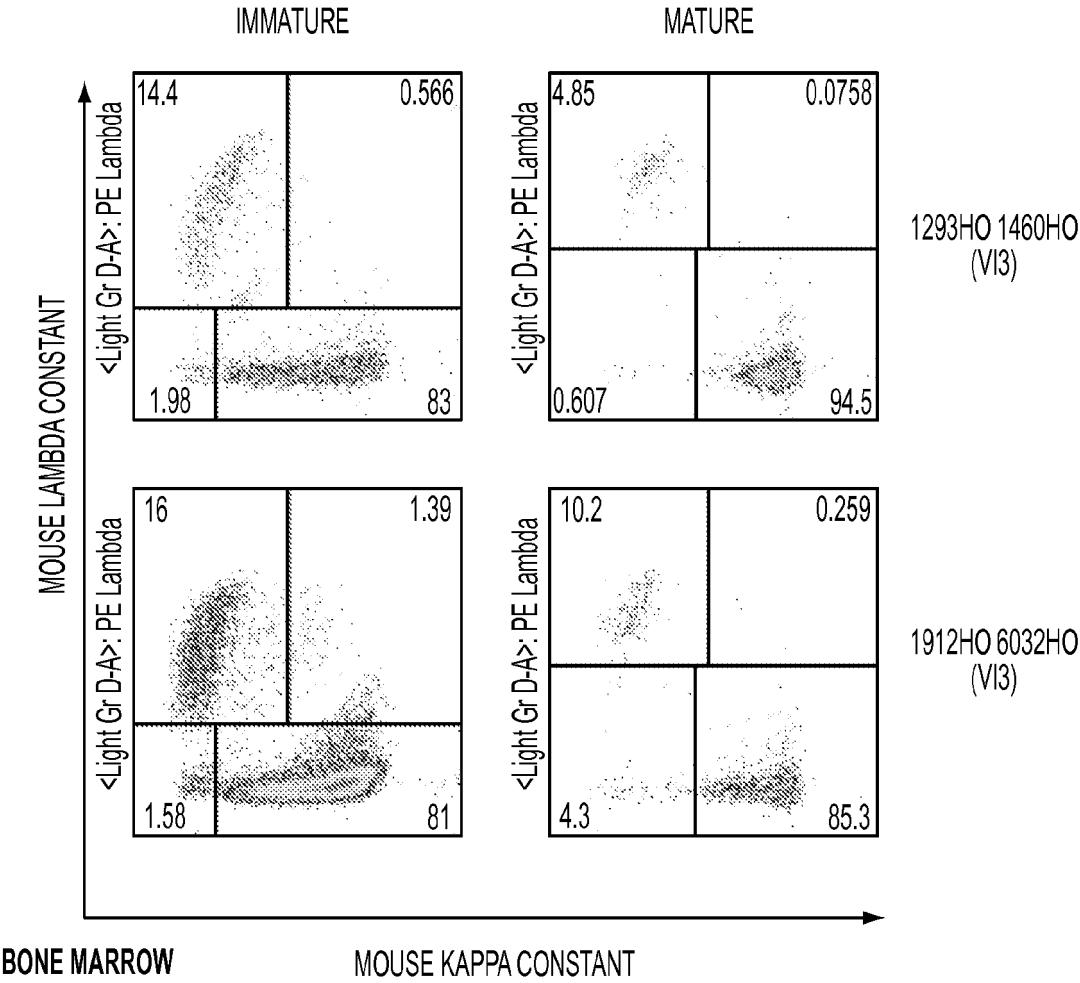


FIG. 47

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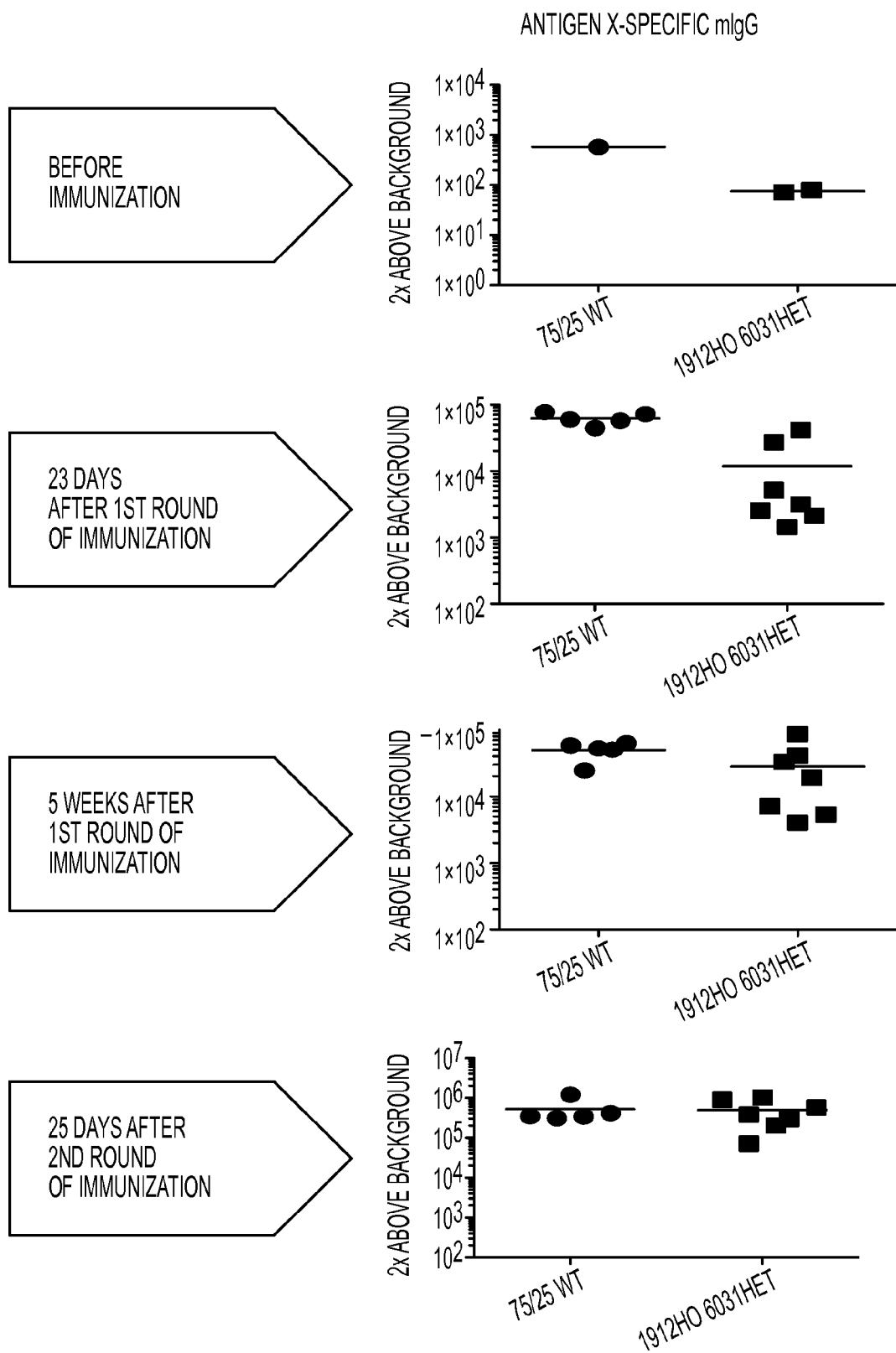


FIG. 48

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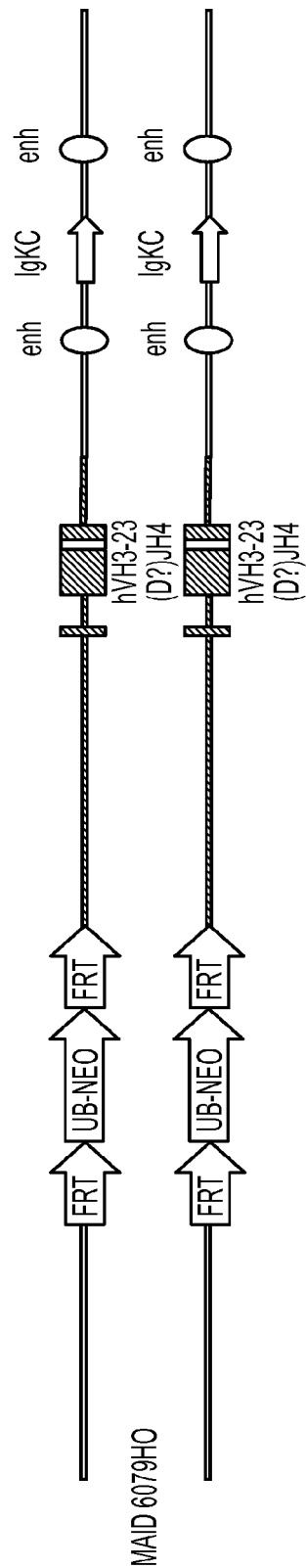


FIG. 49

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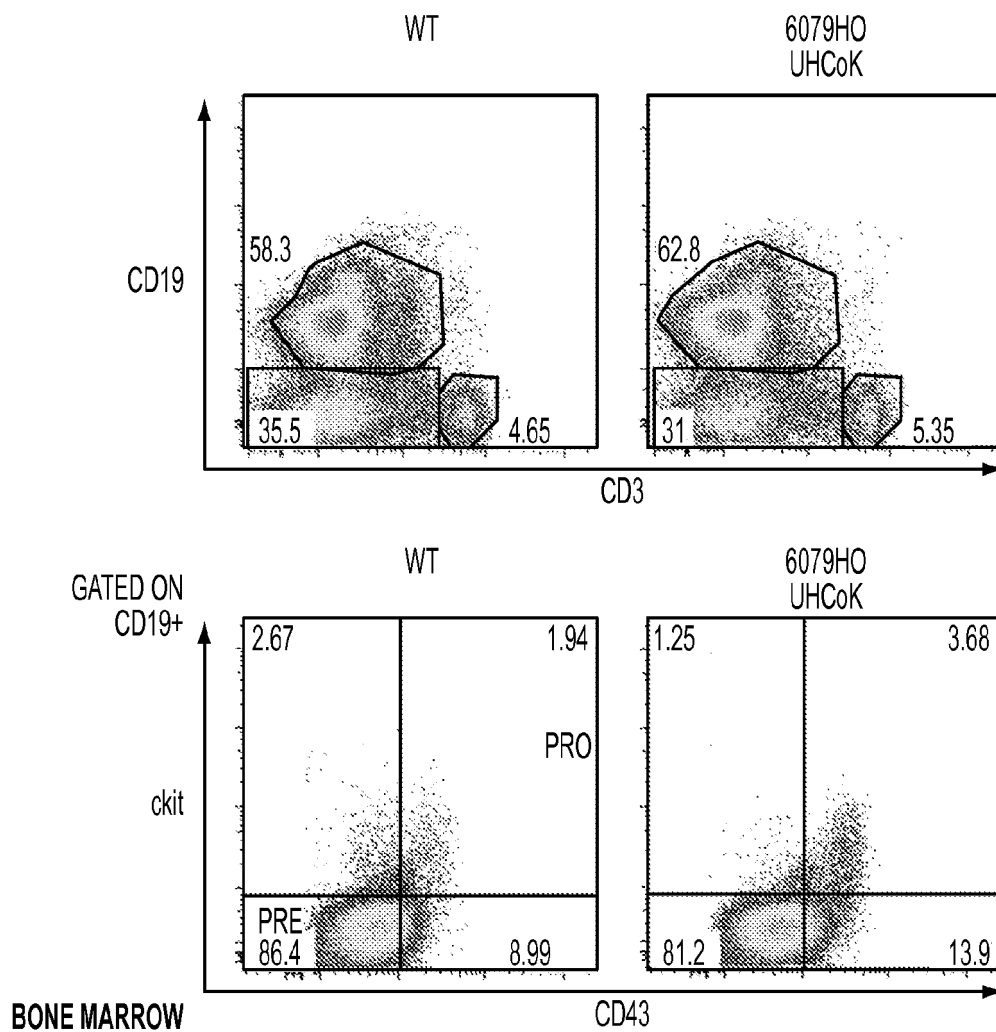


FIG. 50A

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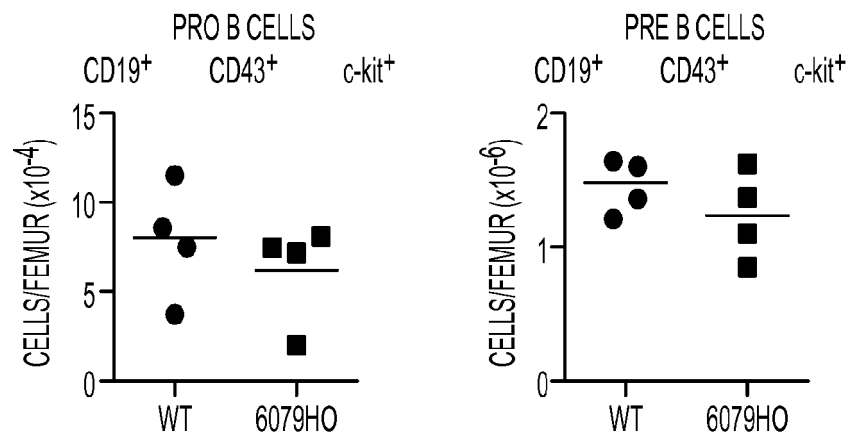


FIG. 50B

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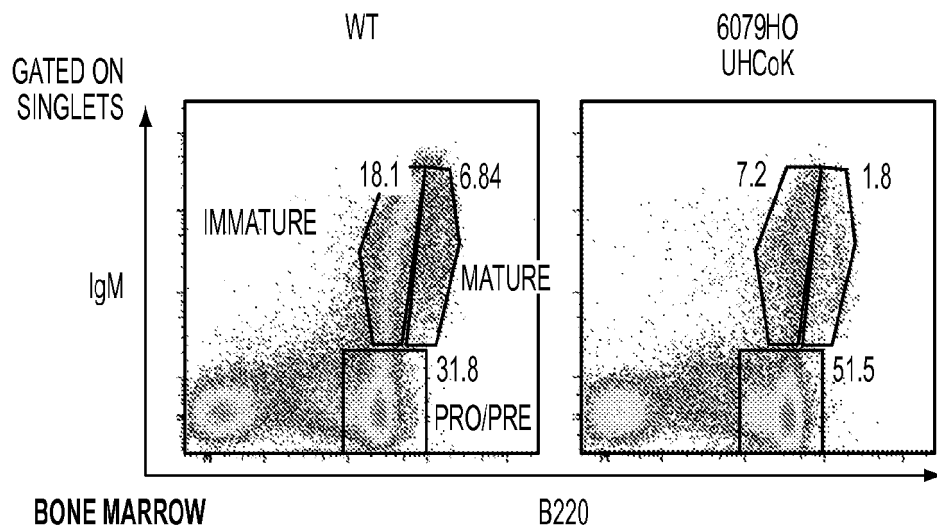


FIG. 51A

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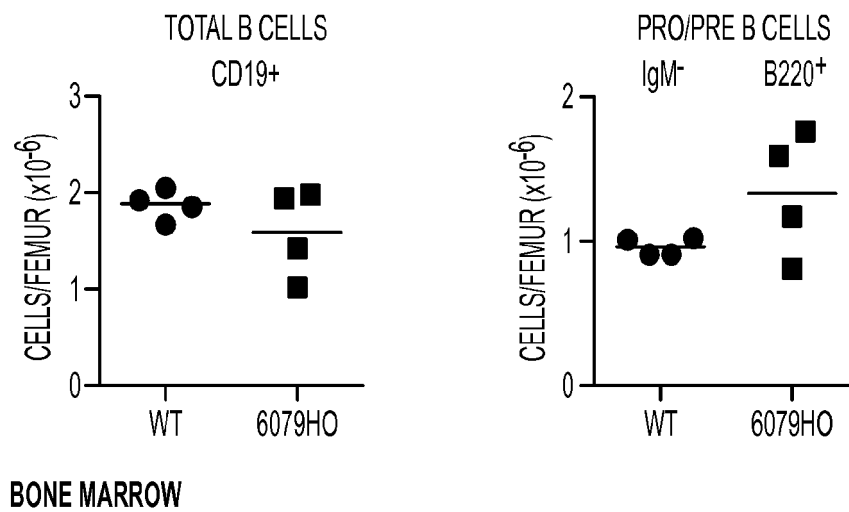


FIG. 51B

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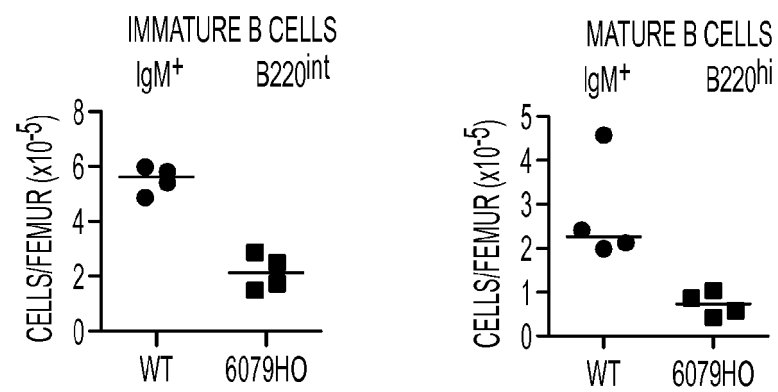


FIG. 51C

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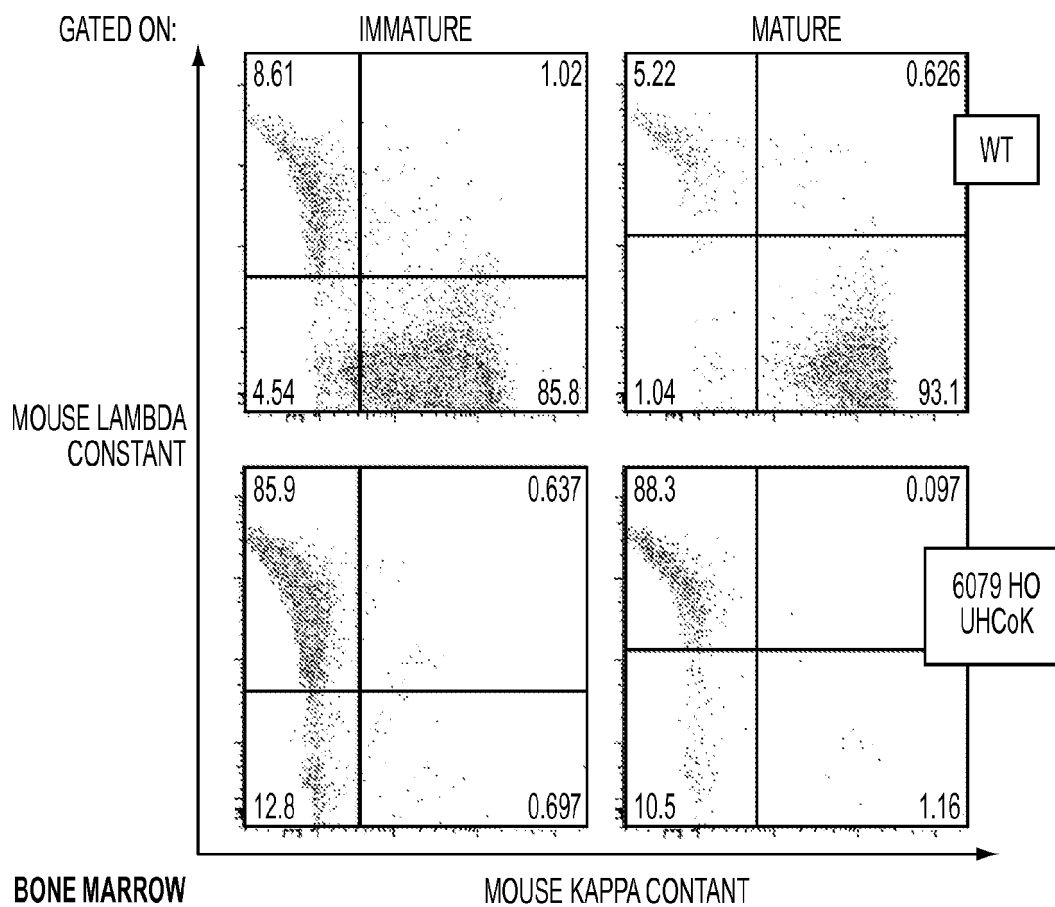


FIG. 52

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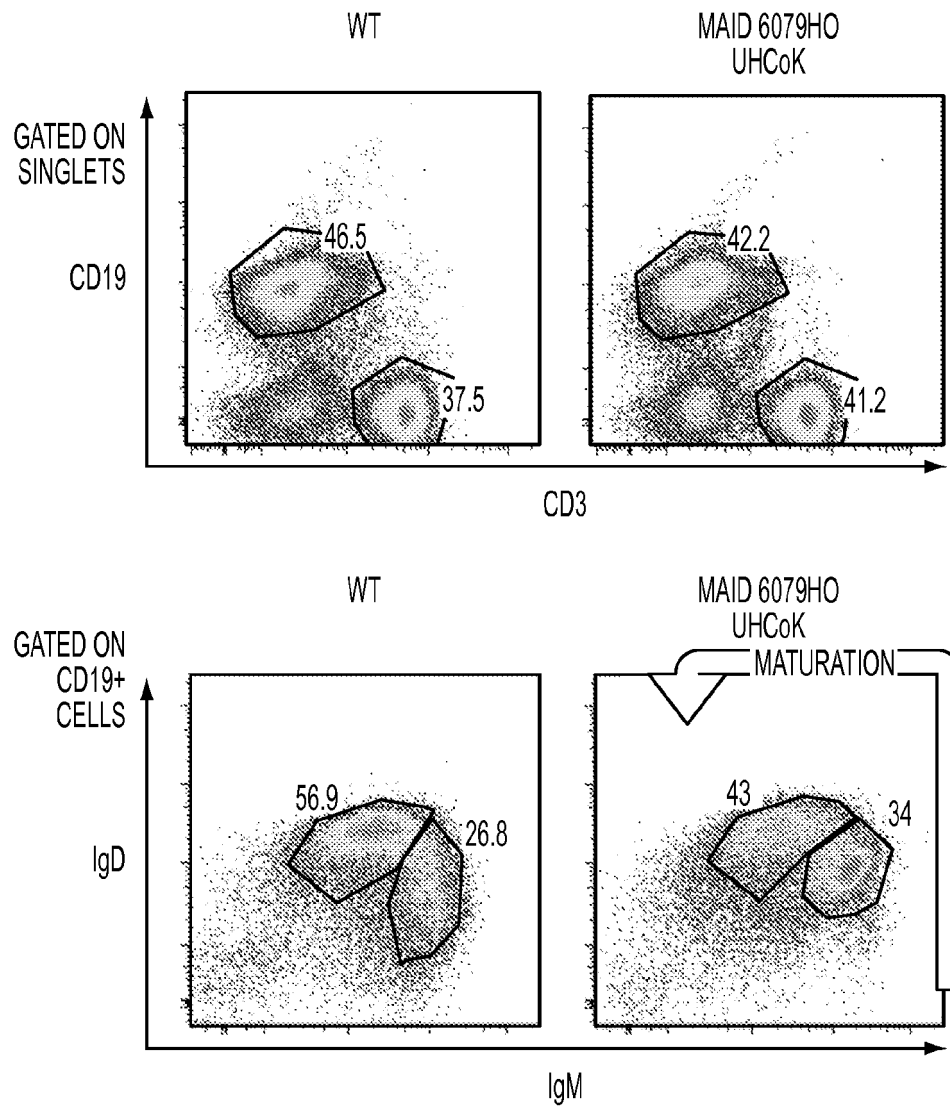


FIG. 53A

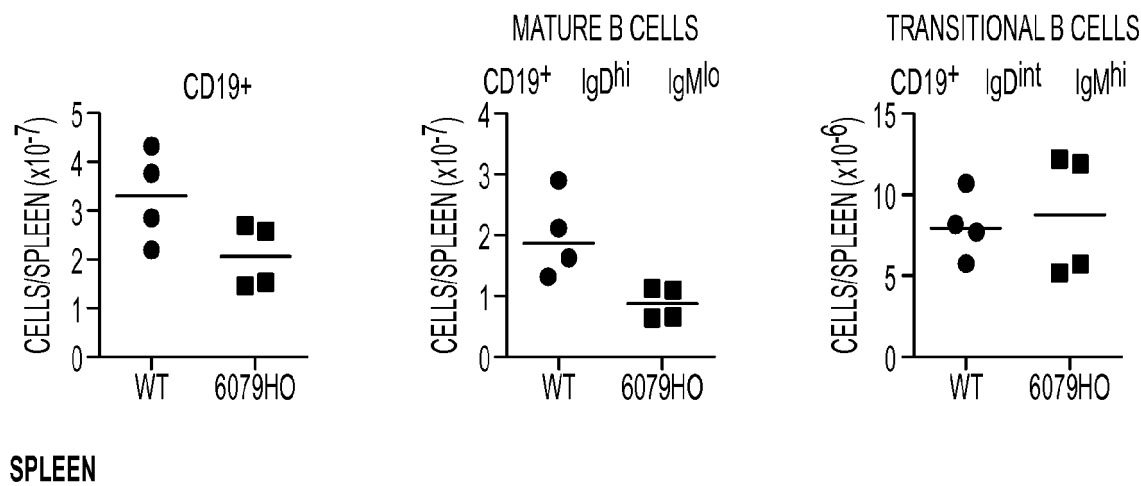


FIG. 53B

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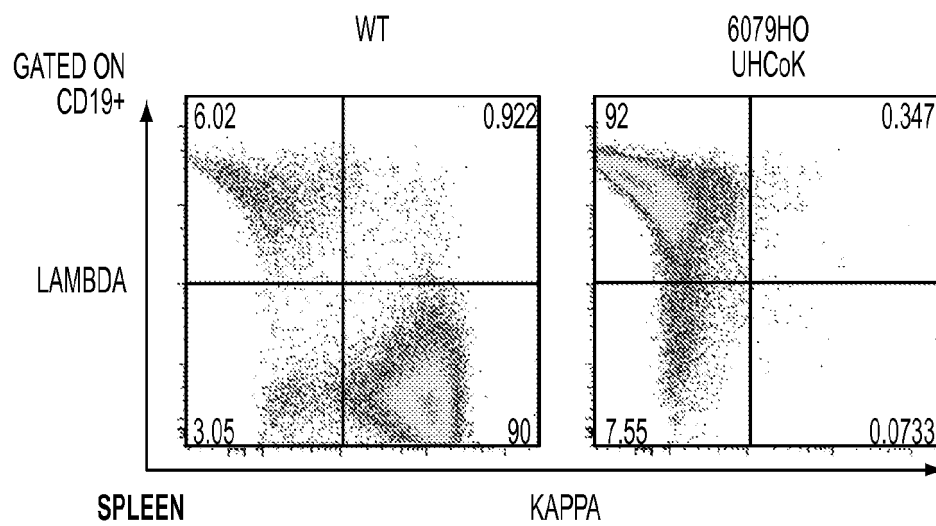


FIG. 54A

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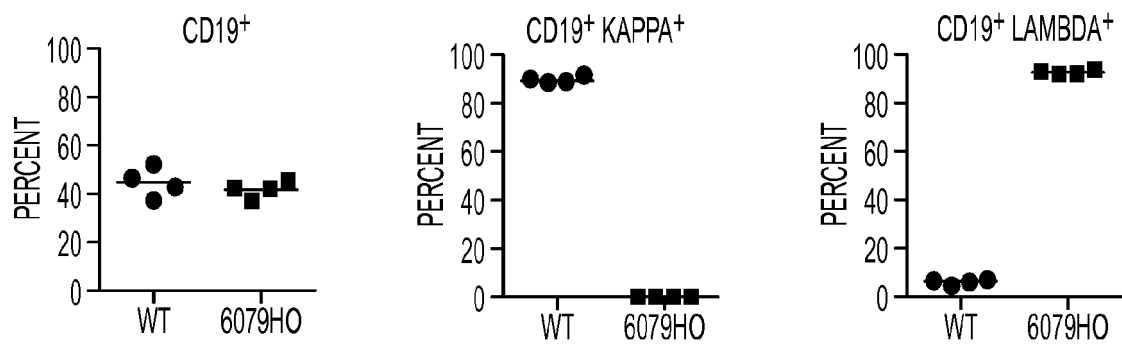


FIG. 54B

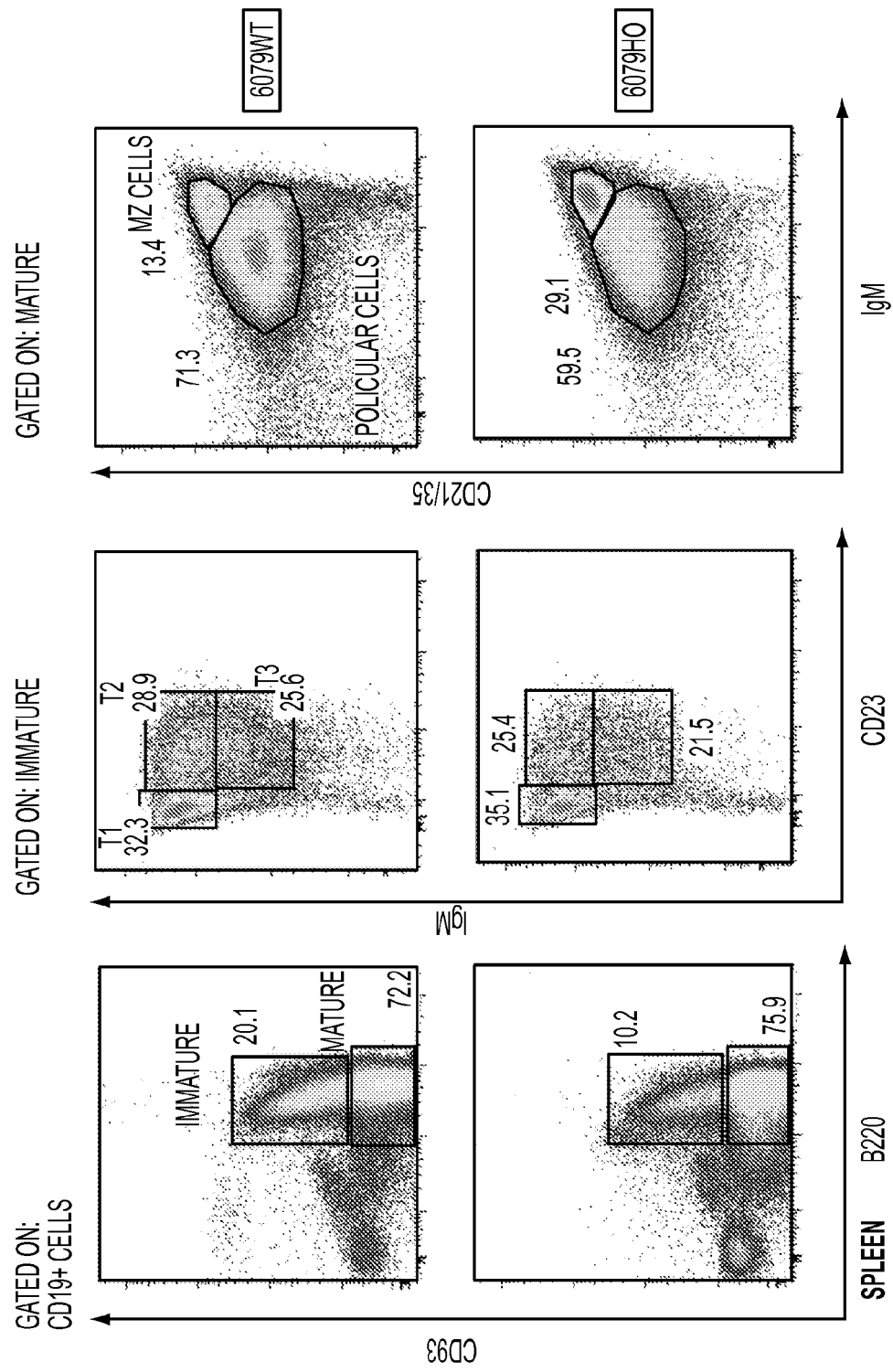


FIG. 55

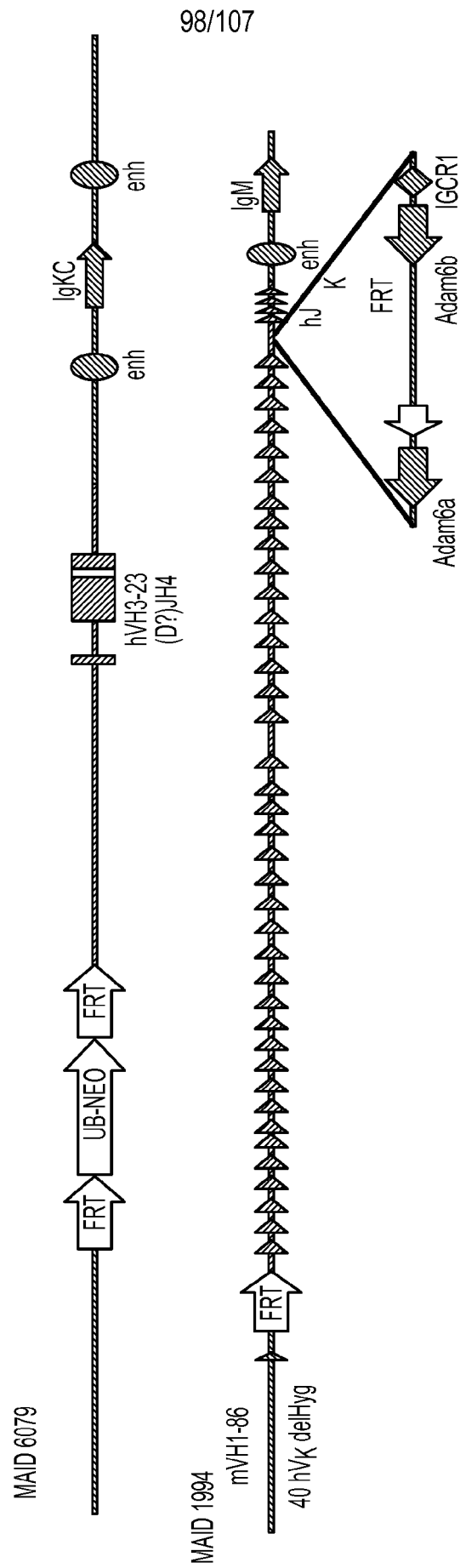


FIG. 56

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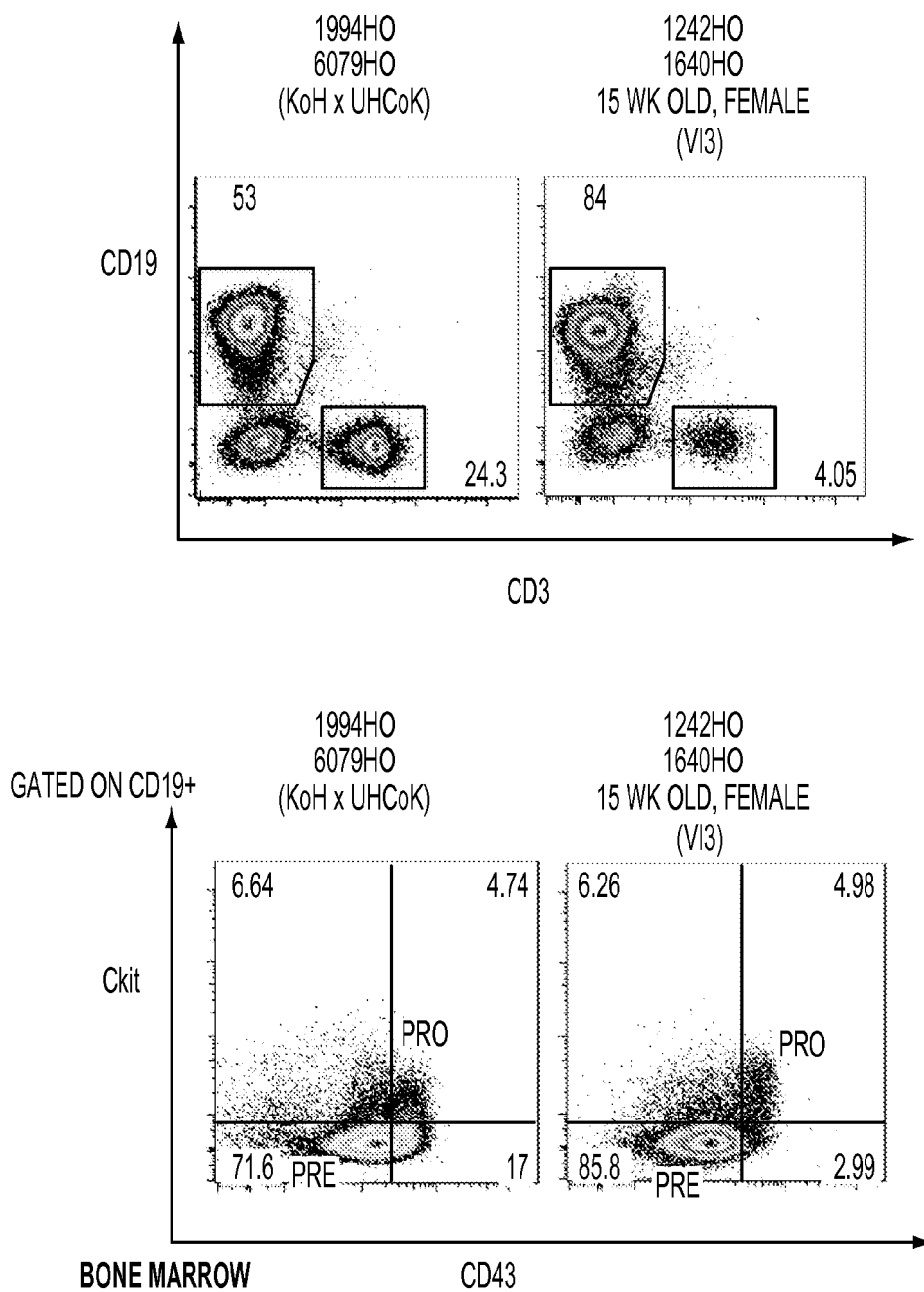


FIG. 57A

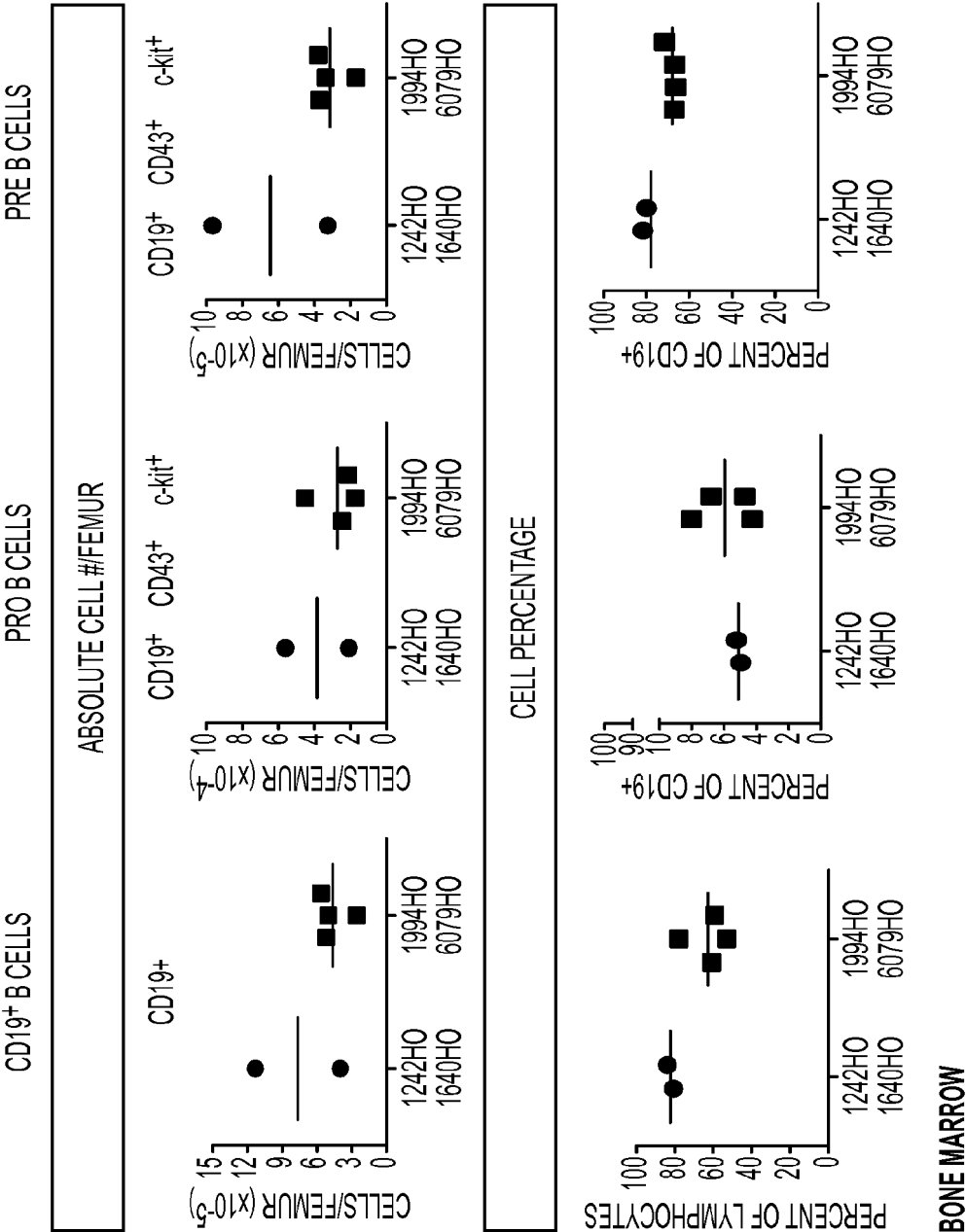


FIG. 57B

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GATED ON SINGLET:

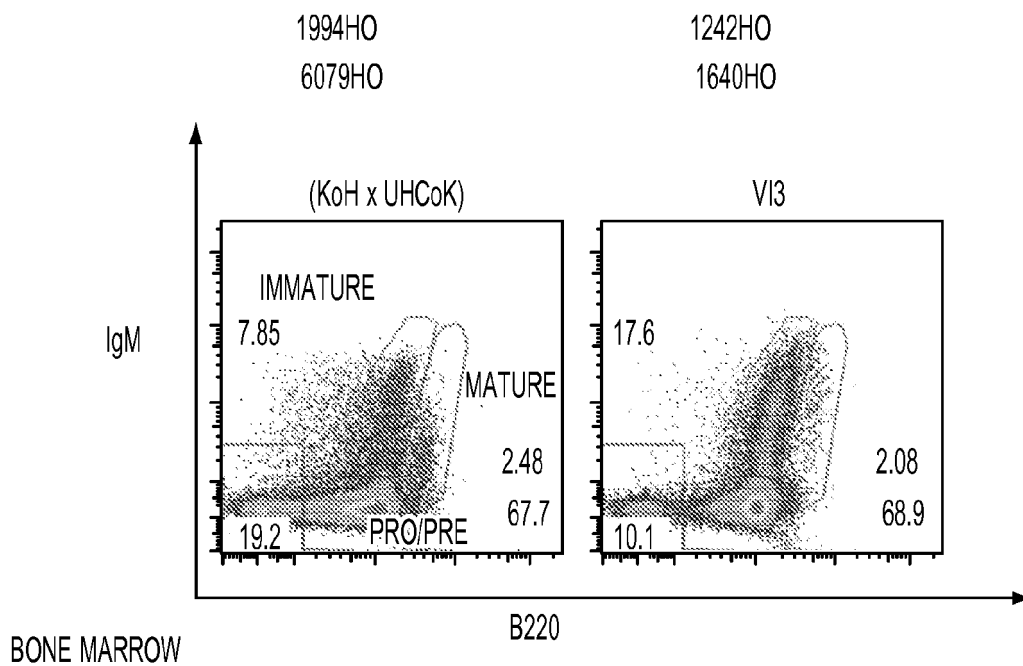


FIG. 58A

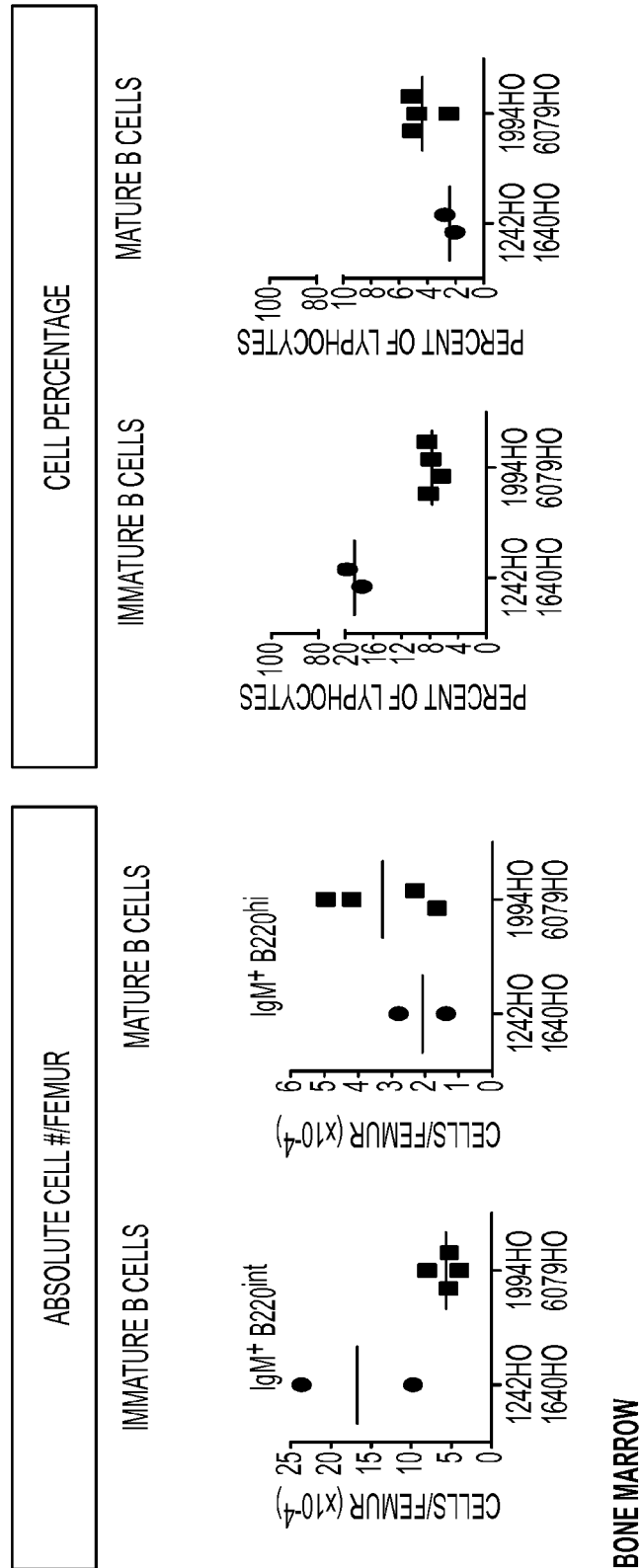


FIG. 58B

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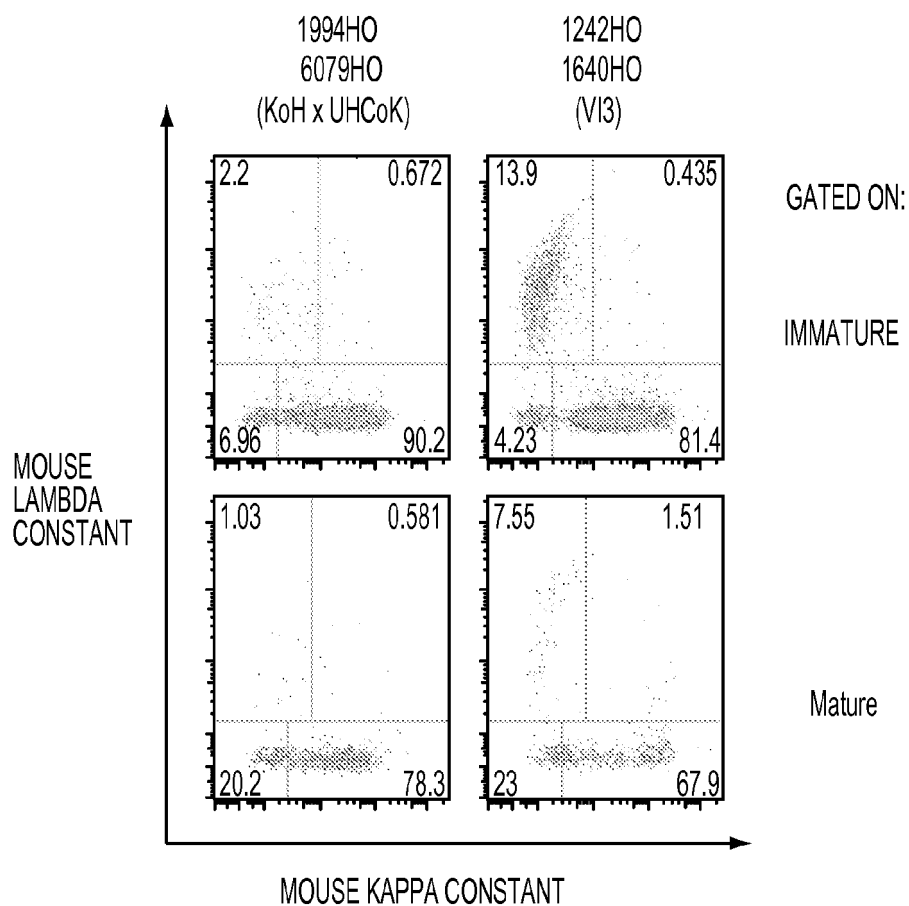
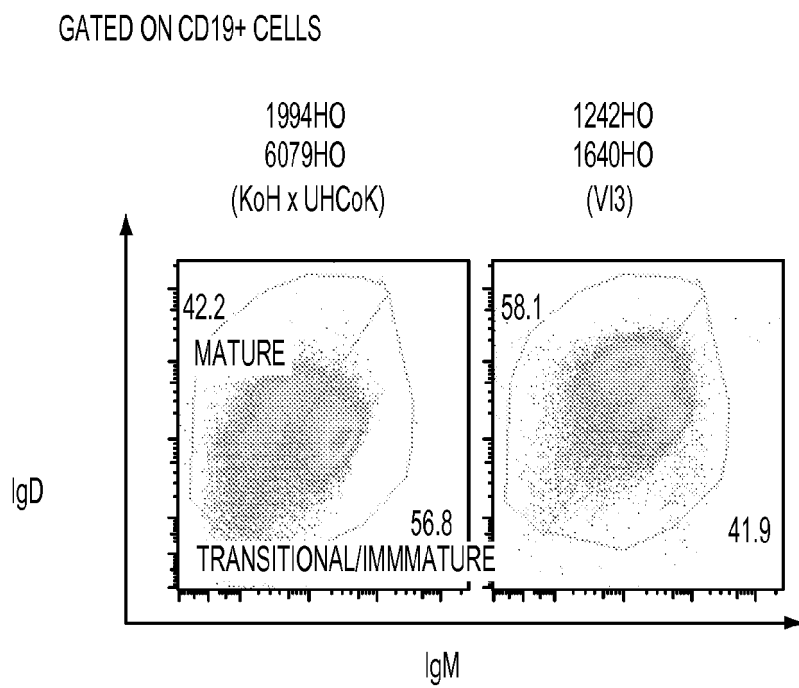


FIG. 59

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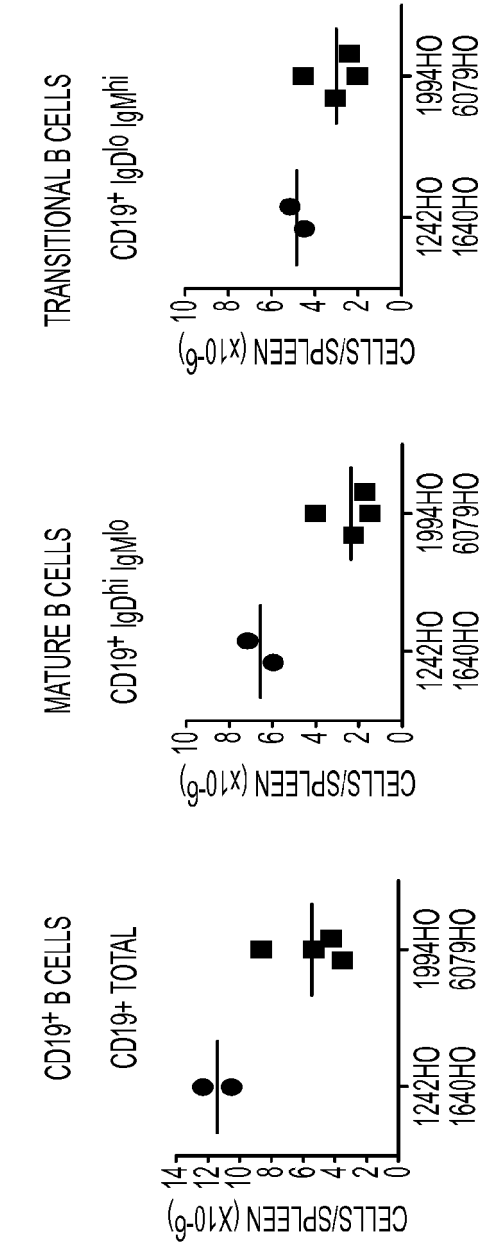


FIG. 60B

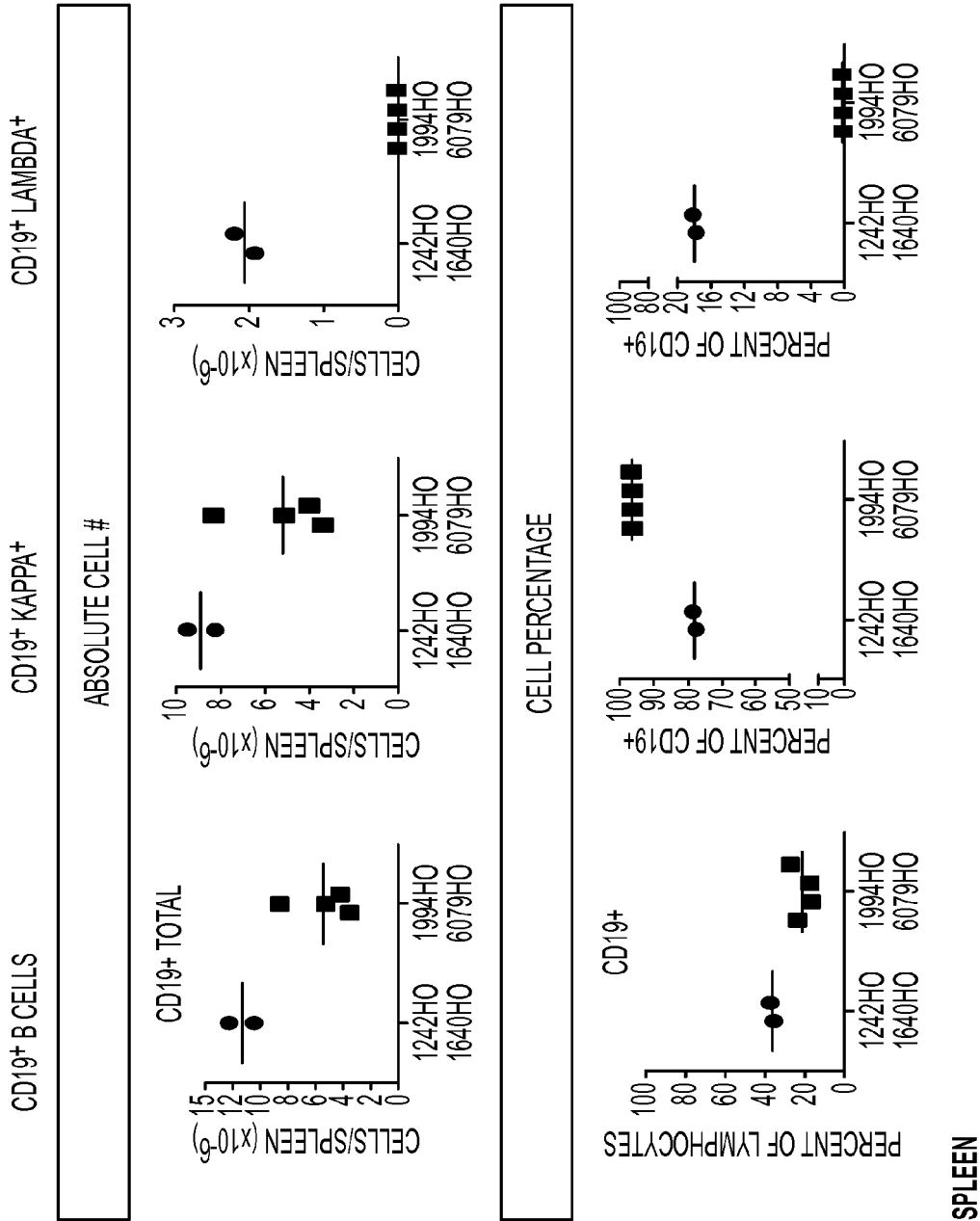


FIG. 61

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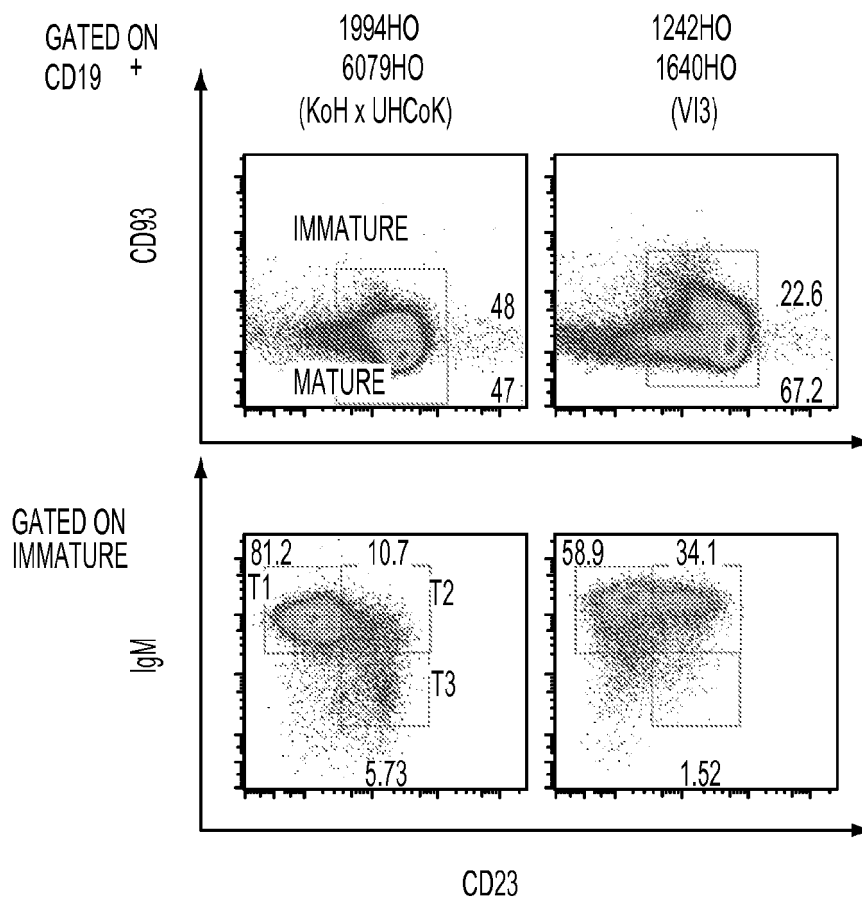


FIG. 62