

1/57

	Stop	SEQ ID NO.	Hydrophilic	SEQ ID NO.	Hydrophobic	SEQ ID NO.
D1-1	VQLER	8	YNWND	45	GTTGT	88
HD1-1	VPLAR	9	YHWH	46	GTTGT	88
D1-7	V*LEL	-	YNWNY	47	GTTGT	89
HD1-7	VSLAL	10	YHWHY	48	GTTGT	89
D1-20	V*LER	-	YNWND	45	GTTGT	89
HD1-20	VSLAR	11	YHWH	46	GTTGT	89
D1-26	V*WELL	12	YSGSY	49	GIVGAT	90
HD1-26	VSWEPL	13	YHGSY	50	GIMGAT	91
D2-2*02	RIL**YQLLY	14	GYCSSTSCYT	51	DIVVPAAI	92
HD2-2*02	RTL*SYQLPY	15	GHCSHTSOHT	52	DIVVPAAI	93
D2-8*01	RILY*WCMLY	16, 17	GYCTNGVCYT	53	DIVLMVYAI	94
HD2-8*01	RTLYSWCMPY	18	GHCTHGVCHT	54	DIVLMVYAI	94
D2-15	RIL*WW*LLL	-	GYCSGGSCYS	55	DIVVVAAT	95
HD2-15	RTL*SW*LPL	-	GHCSHGSCHS	56	DIVVVAAT	96
D2-21*02	SILWW*LLF	19	AYCGDCYS	57	HIVVTAI	97
HD2-21*02	STLWWSLPF	20	AHCGGHCHS	58	HIVVTAI	97
D3-3*01	VLRFLEWLLY	21	YYDFWSGYT	59	ITIFGVII	98
HD3-3*01	VSPFLEWSLY	22	YHFWWSGHYT	60	ITIFGVII	98
D3-9	VLRYFDWLL*	23	YYDILTGYN	61	ITIF*LVII	99, 100
HD3-9	VSPYFDWSL*	24	YHHILTGHYN	62	ITIF*LVII	99, 100
D3-10*01	VLLWFGELL*	25	YYYSGSYN	63	ITMVRGVII	101
HD3-10*01	VSPWFGESE*	26	YHGGSGSHYN	64	ITMVRGVII	101
D3-16*02	VL*LRLGELSLY	27	YYDYVWGSYRYT	65	IMITFGGVVI	102
HD3-16*02	VS*SRLGESSLY	28	YHDHVVWGSYRYT	66	IMITFGGVVI	102
D3-22	VLL***WLLI	29	YYDSSGYYY	67	ITMIVVIT	103
HD3-22	VSL***WLLI	30, 31	YHYHSSGHYY	68	ITIVVIT	104
D4-4	*LQ*L	-	DYSNY	69	TTVT	105
HD4-4	*PQSL	32	DHSY	70	TTVT	105
D4-11p	*LQ*L	-	DYSNY	69	TTVT	105

FIG. 1A

2/57

	Stop	SEQ ID NO.	Hydrophilic	SEQ ID NO.	Hydrophobic	SEQ ID NO.
HD4-11p	*PQSL	32	DHSY	70	TTVT	105
D4-17	*LR*L	-	DYGDY	71	TTVT	105
HD4-17	*PRSL	33	DHGHY	72	TTVT	105
D4-23p	*LRW*L	-	DYGGNS	73	TTVT	106
HD4-23p	*PRWSL	34	DHGGHS	74	TTVT	106
D5-5	WIQLWL	35	GYSGY	75	VDTAMV	107
HD5-5	WTQPWL	36	GSHGY	76	VDTAMV	107
D5-12	WI*WLRL	37	GYSGYDY	77	VDIVATI	108
HD5-12	WT*WPPL	38	GSHGHY	78	VDIVATI	108
D5-18	WIQLWL	35	GYSGY	75	VDTAMV	107
HD5-18	WTQPWL	36	GSHGY	76	VDTAMV	107
D5-24p	*RWLQL	39	RDGYNY	79	VEMAT	109
HD5-24p	*TWPL	40	RHGHY	80	VDMATI	110
D6-6	V*QLV	-	EYSSS	81	SIAAR	111
HD6-6	A*PLV	-	ESHSS	82	SIATR	112
D6-13	V*QQLV	41	GYSSSWY	83	GIAAG	113
HD6-13	A*PQLV	42	GSHSWY	84	GIATAG	114
D6-19	V*QWL	43	GYSSGWY	85	GIAVAG	115
HD6-19	A*PWL	44	GSHGWY	86	GIAMAG	116
D6-25	V*QRL	-	GYSSGY	87	GIAA	117
HD6-25	A*PRL	-	GSHGY	76	GIATA	118

FIG. 1B

3/57

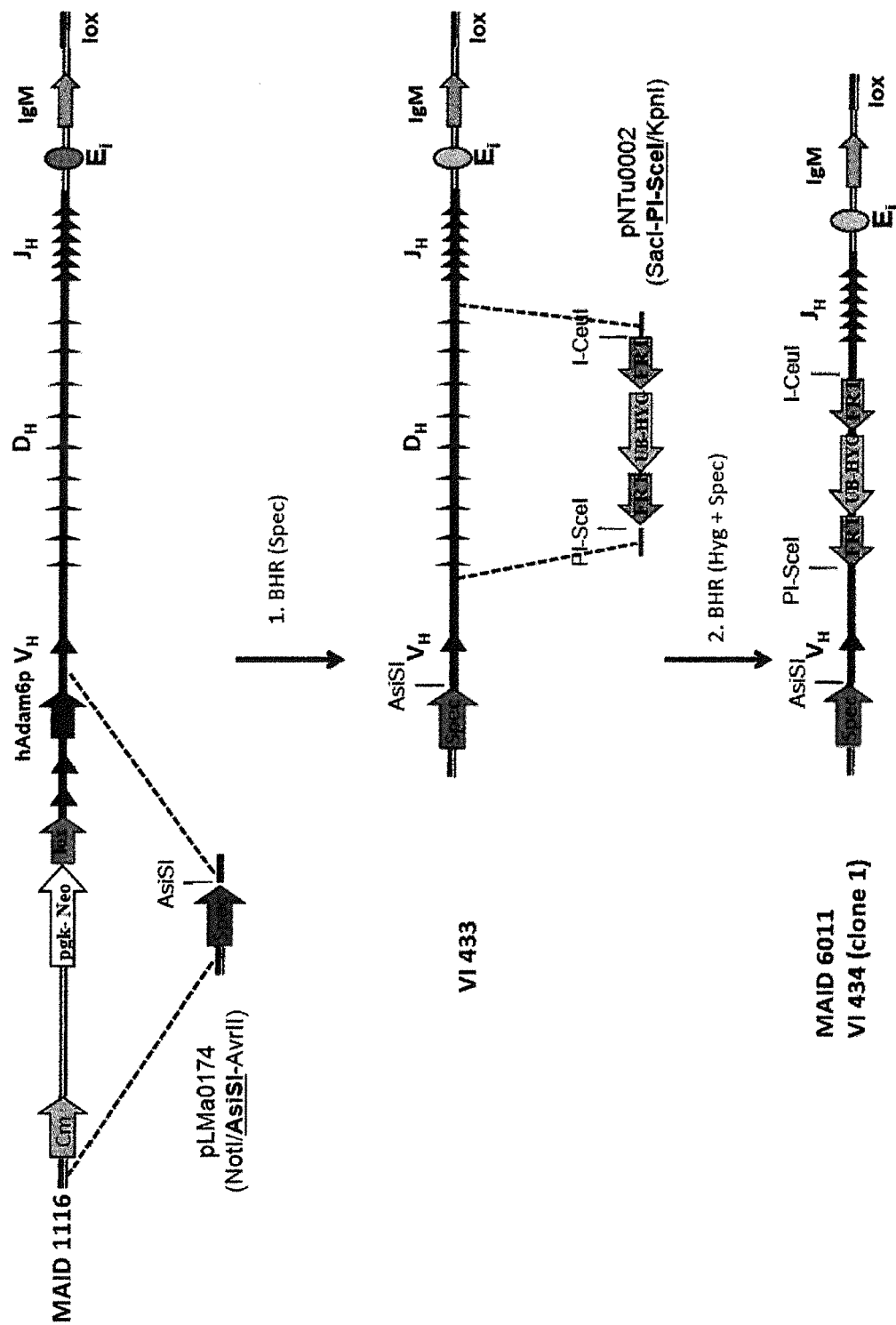
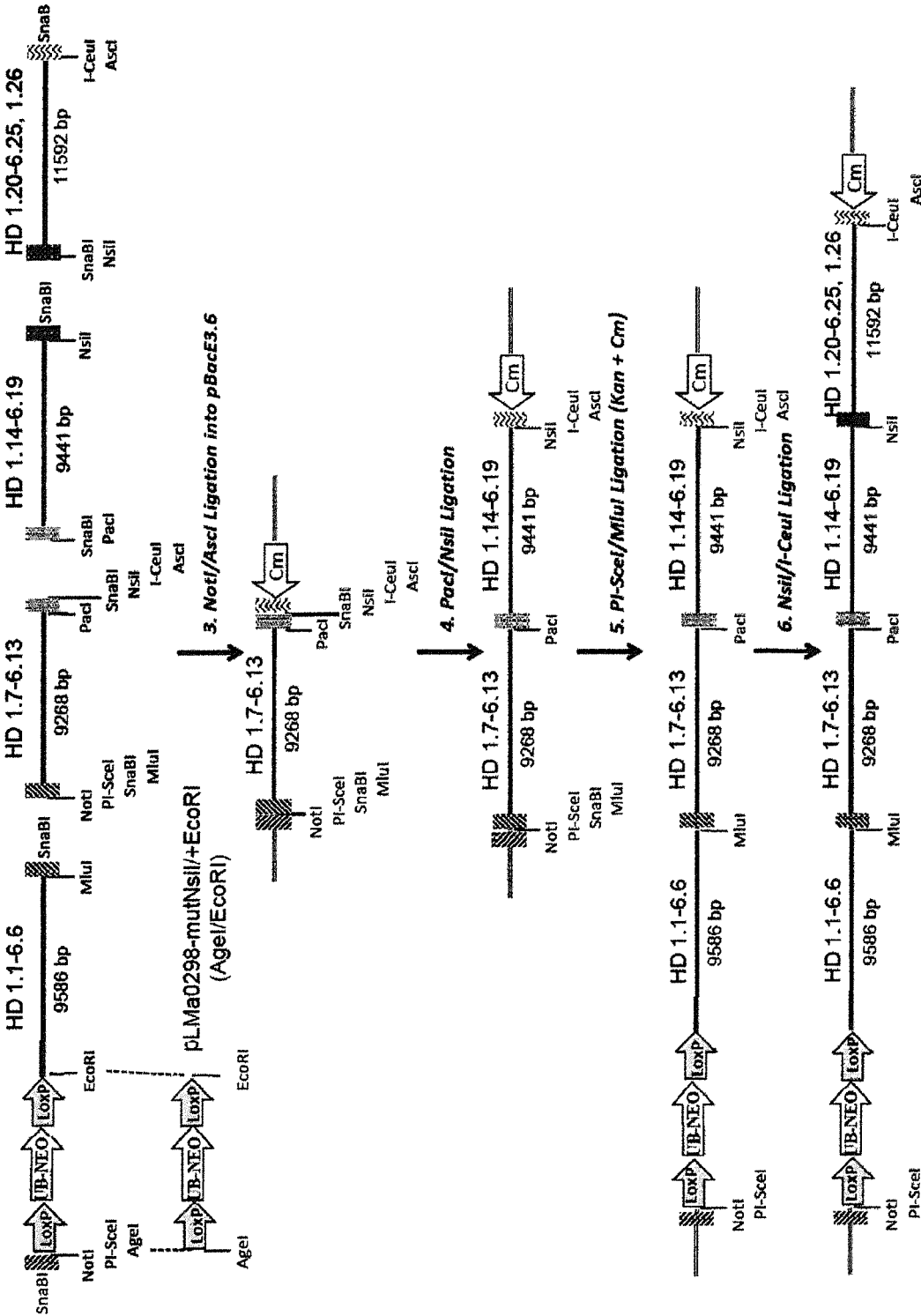


FIG. 2



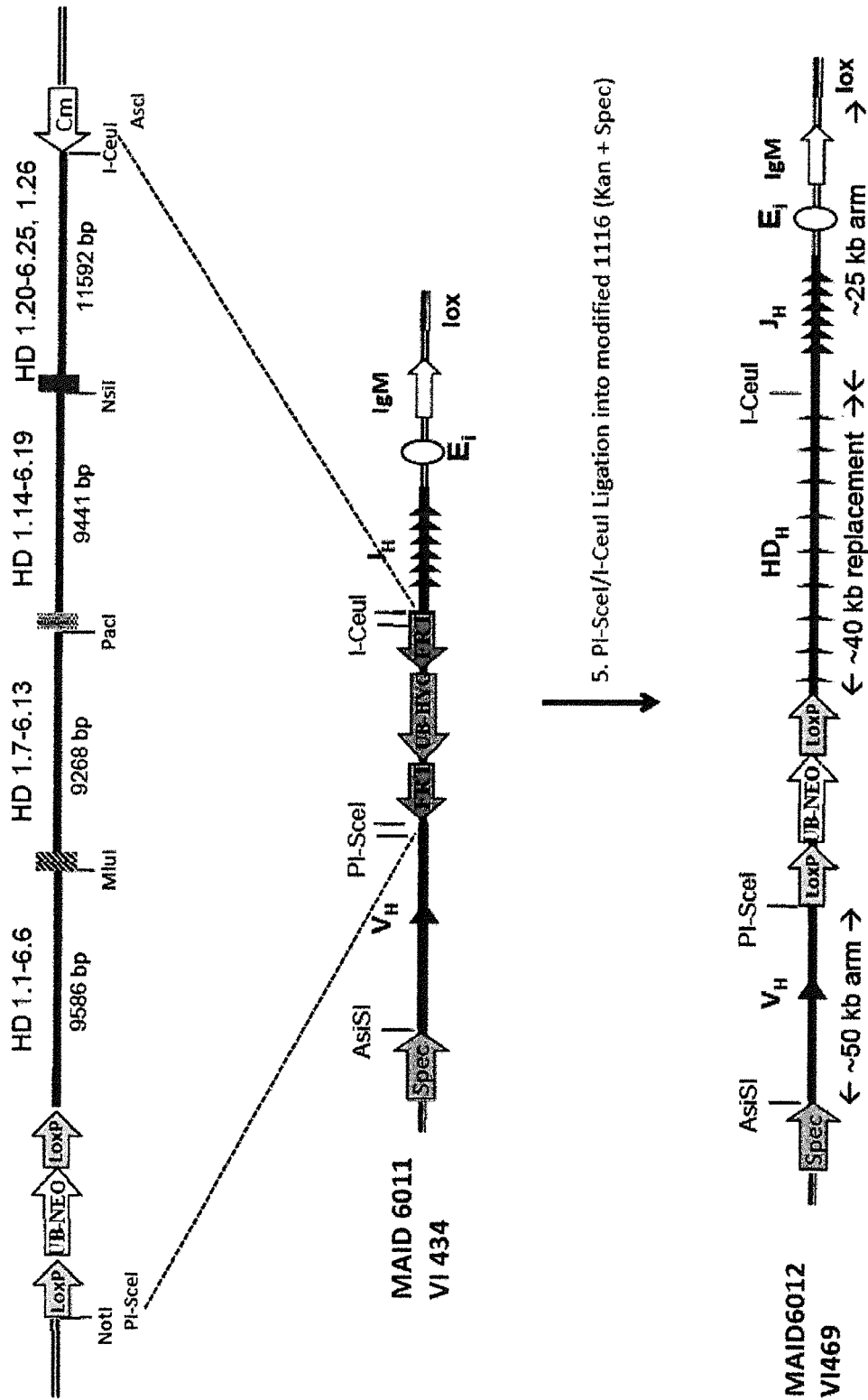


FIG. 4

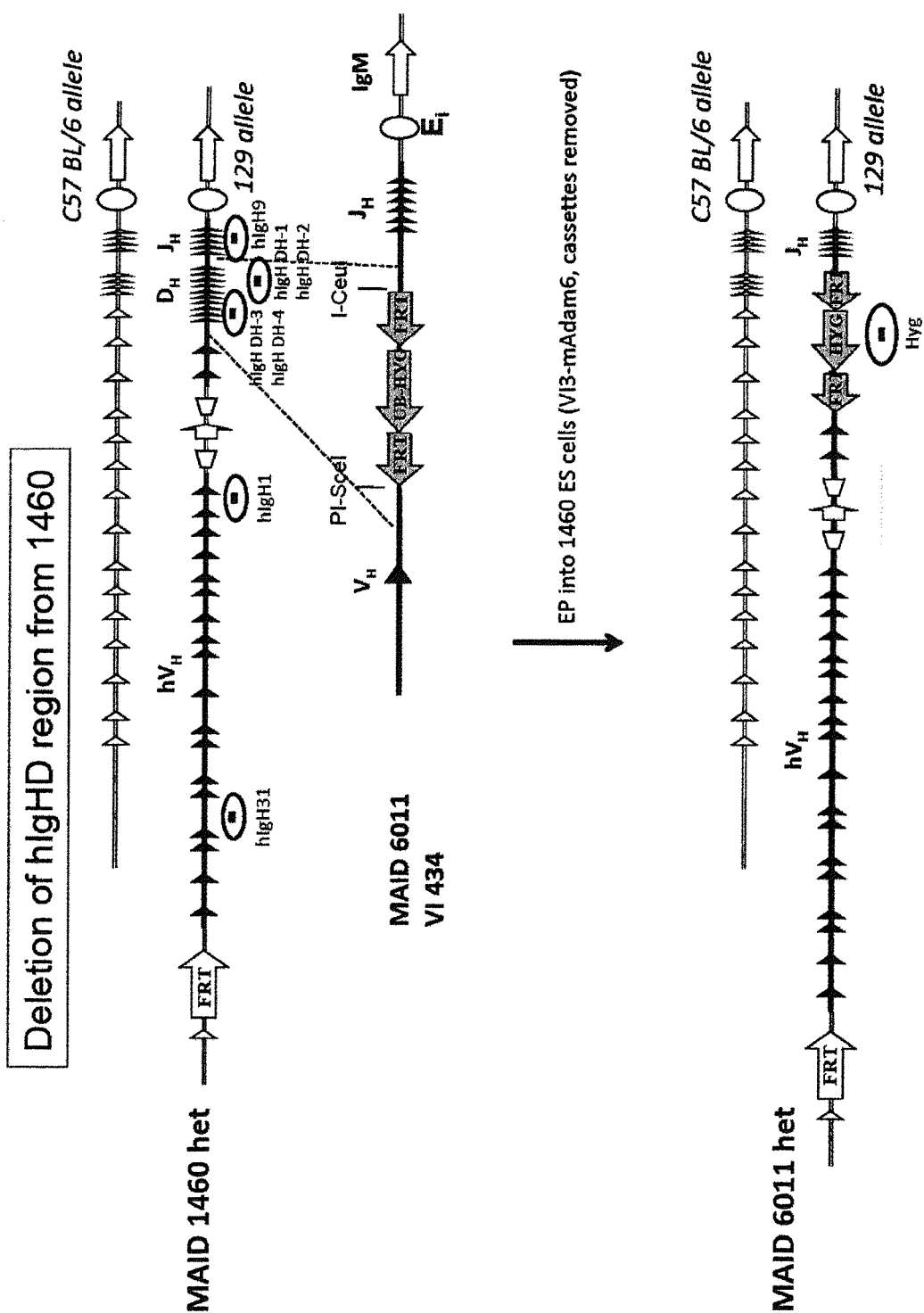


FIG. 5

7/57

Probes for MAID 6011 (deletion of hlgH DH segments in MAID1460)						
Name	Forward Primer	Probe	Reverse Primer	Type	Label	Location
hlgH DH-1	CGGGTCACTGCCATTCTG (SEQ ID NO: 119)	TCTGCATTGCTCCAGCGC (SEQ ID NO: 120)	TCTGGCGCATGAACCCAAT (SEQ ID NO: 121)	LOA	FAM- BHQ 1	hlgH D segments
hlgH DH-2	GTGCAGGGGAGGACCTTCT G (SEQ ID NO: 122)	AGTCACCAAGCACAGAGCCCTGAC (SEQ ID NO: 123)	GCCAGGGAGTTGCCTAGTG (SEQ ID NO: 124)	LOA	FAM- BHQ 1	hlgH D segments
hlgH DH-3	GTGGCCCACTTCCCTTCT (SEQ ID NO: 125)	CAGCTGGAACCCACCATGACCT (SEQ ID NO: 126)	GACCTGCCCTCGGATGACA (SEQ ID NO: 127)	LOA	FAM- BHQ 1	hlgH D segments
hlgH DH-4	TGGCCAGAACTGACCCCTAC (SEQ ID NO: 128)	ACCGACAAGAGTCCCTCAGG (SEQ ID NO: 129)	GGAGTCGGCTCTGGATGTG (SEQ ID NO: 130)	LOA	BHQ- plus	hlgH D segments
hyg	TGCGGCCGATCTTAGCC (SEQ ID NO: 131)	ACGAGCGGGTTCGGCCCATTC (SEQ ID NO: 132)	TTGACCGATTCTTGCGG (SEQ ID NO: 133)	GOA	FA- BHQ 1	
hlgH1	CAGTCCCGTTGATCCAGCC (SEQ ID NO: 134)	CCCATCAGGATTTGTATCTCTGT GGACG (SEQ ID NO: 135)	GGATATGCAGCACTGTGCCAC (SEQ ID NO: 136)	AR		hlgH
hlgH9	TCCTCCAACGACAGGTCCC (SEQ ID NO: 137)	TCCCTGGAACCTCTGCCCGACACA (SEQ ID NO: 138)	GATGAACTGACGGGCACAGG (SEQ ID NO: 139)	AR		hlgH
hlgH31	ATCACACTCATCCCATCCCC (SEQ ID NO: 140)	CCCTTCCCTAAGTACCACAGAGTGG GCTC (SEQ ID NO: 141)	CACAGGGAAGCAGGAACCTGC (SEQ ID NO: 142)	AR		hlgH

FIG. 6

Insertion of HD_H (His-substituted) hIgH D_H region

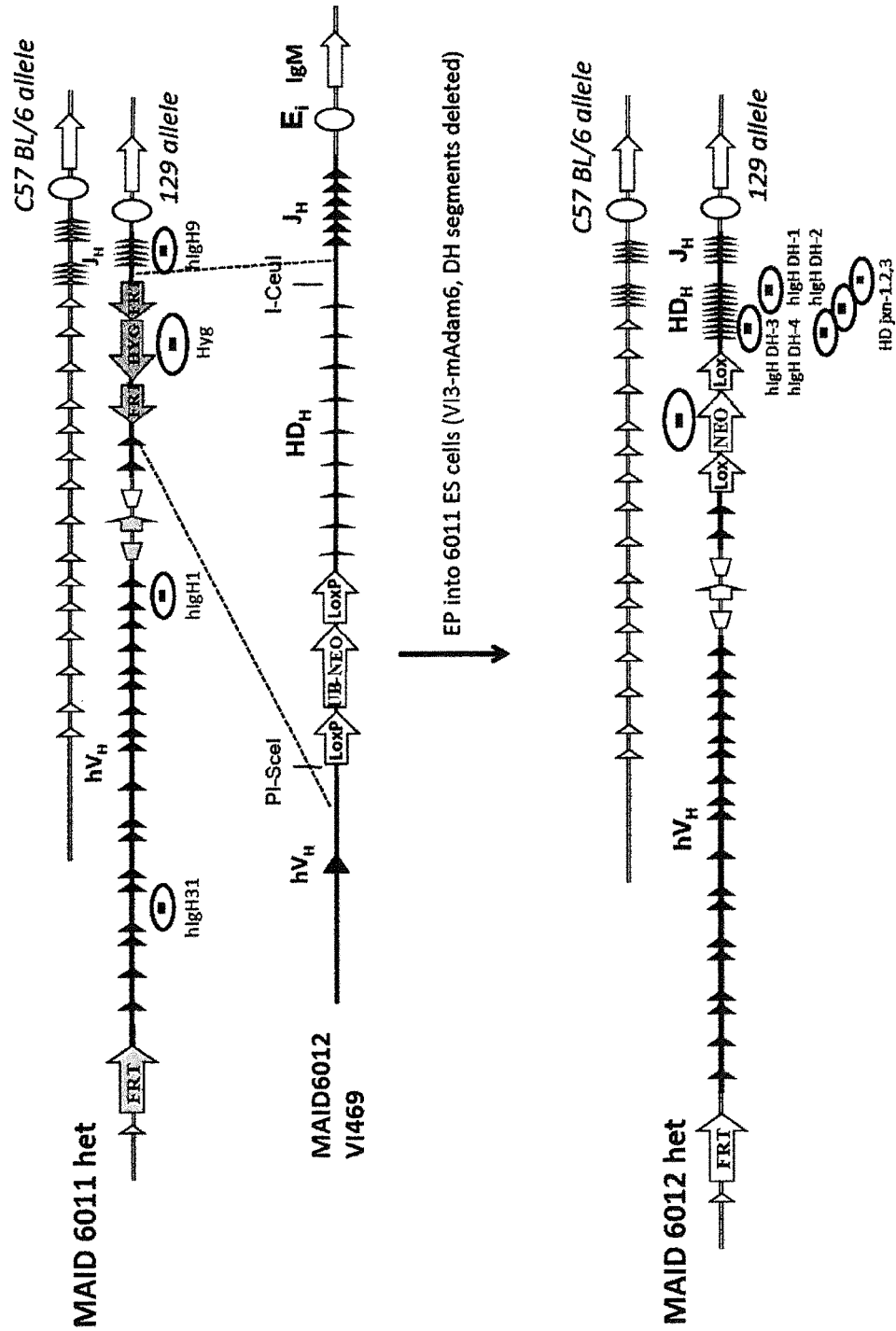


FIG. 7

9/19

Probes for MAID 6012 (insertion of HD, His-substituted high DH segments)						
Name	Forward Primer	Probe	Reverse Primer	Type	Label	Location
hyg	TGCGCCGATCTTAGCC (SEQ ID NO: 131)	ACGAGCGGTTCGGCCCATTC (SEQ ID NO: 132)	TTGACCGATTCTTGCGG (SEQ ID NO: 133)	LOA	FAM- BHQ1	
HD jxn-1	GGAGCCAGGCAGGACACA (SEQ ID NO: 143)	TGGGCTCGTAGTTTGACGT (SEQ ID NO: 144)	GGGACTTCTTACCCACA CTTCA (SEQ ID NO: 145)	GOA	MGB	Synthetic linker-1 in HD segments
HD jxn-2	GGTCCCGAGCACTCTTAATAAA C (SEQ ID NO: 146)	CCTCGAATGGAATAC (SEQ ID NO: 147)	GGGAGAGCAACCATTCG TTGT (SEQ ID NO: 148)	GOA	MGB	Synthetic linker-2 in HD segments
HD jxn-3	CCGAGCACCAGTCATCTA (SEQ ID NO: 149)	CGCAGTCATGTAATGC (SEQ ID NO: 150)	GGGAGGCGAATGACTG TCA (SEQ ID NO: 151)	GOA	MGB	Synthetic linker-3 in HD segments
high DH-1	CGGGTCACTGCCATTCTG (SEQ ID NO: 119)	TCTGCATTGCTCCAGCGC (SEQ ID NO: 120)	TCTGCGGCATGAACCCAA T (SEQ ID NO: 121)	GOA	FAM- BHQ1	high D segments
high DH-2	GTGAGGGAGGACCTTCTG (SEQ ID NO: 122)	AGTACCAAGCACAGAGCCCTGA C (SEQ ID NO: 123)	GCCAGGGAGTTGCCTAG TG (SEQ ID NO: 124)	GOA	FAM- BHQ1	high D segments
high DH-3	GTGGCCCACTCCCTTCCT (SEQ ID NO: 125)	CAGCTGGAACCCACCATGACCT (SEQ ID NO: 126)	GACCTGCTCGGATGACA (SEQ ID NO: 127)	GOA	FAM- BHQ1	high D segments
high DH-4	TGGCCAGAACTGACCCCTAC (SEQ ID NO: 128)	ACCGACAAGAGTCCCTCAGG (SEQ ID NO: 129)	GGAGTCGGCTCTGGATGTG (SEQ ID NO: 130)	GOA	BHQ- plus	high D segments
neo	GGTGGAGAGGCTATTGGC (SEQ ID NO: 152)	TGGGCACAACAGACAATCGGCTG (SEQ ID NO: 153)	GAACACGGCGGCATCAG (SEQ ID NO: 154)	GOA	FAM- BHQ1	
highH1	CAGTCCCGTTGATCCAGCC (SEQ ID NO: 134)	CCCATCAGGGATTTGTATCTC TGTGGACG (SEQ ID NO: 135)	GGATGCGAGCACTGTGCC AC (SEQ ID NO: 136)	AR		high
highH9	TCCTCCAACGACAGGTCCC (SEQ ID NO: 137)	TCCCTGGAACCTGCCCCGACACA (SEQ ID NO: 138)	GATGAACCTGACGGGCACA GG (SEQ ID NO: 139)	AR		high
highH31	ATCACACTCATCCCATCCCC (SEQ ID NO: 140)	CCCTTCCCTTAAGTACCACAGAGTG GGCTC (SEQ ID NO: 141)	CACAGGGAAGCAGGAAGT GC (SEQ ID NO: 142)	AR		high

FIG. 8

10/57

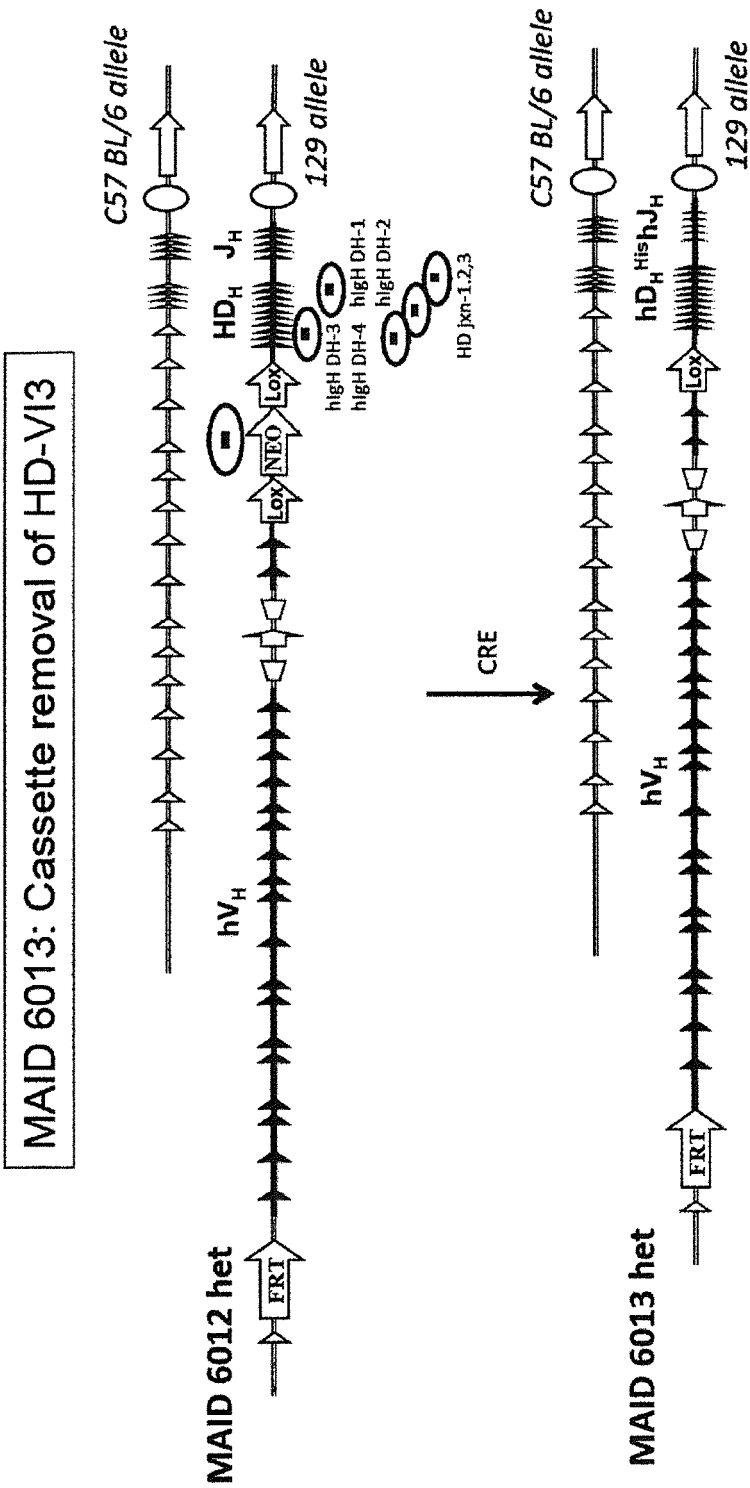


FIG. 9

11/57

Human D Gene Segment	Direct 5'-3' Orientation	SEQ ID NO.	Inverted Orientation	SEQ ID NO.
IGHD1-1 X97051, IGHD1-1*01	ggtaaacctggaacgac G T T G T V Q L E R Y N W N D	155 88 8 45	gtcgtccagttgtacc V V P V V S F Q L Y R S S C T	206 207 208 209
IGHD1-7 X13972, IGHD1-7*01	ggtaaacctggaacac G I T G T V * L E L Y N W N Y	156 89 - 47	gtagttccagttatacc V V P V I * F Q L Y S S S Y T	210 211 212 213
IGHD 1-20 X13972, IGHD1- 14*01	ggtaaacctggaacac G I T G T V * P E P Y N R N H	157 89 - 158	gtggtccggtatacc V V P V I W F R L Y G S G Y T	214 211 215 216
IGHD 1-20 X97501, IGHD1- 20*01	ggtaaacctggaacgac G I T G T V * L E R Y N W N D	159 89 - 45	gtcgtccagttatacc V V P V I S F Q L Y R S S Y T	217 211 208 218
IGHD1-26 X97501, IGHD1- 26*01	ggtagtagggagctactac G I V G A T V * W E L L Y S G S Y Y	160 90 12 49	gtagtagctccactatacc V V A P T I * * L P L Y S S S H Y T	219 220 221 222
IGHD2-2 J00232, IGHD2-2*01	aggatattgtagtagtaccagctgctatgcc R I L * * Y Q L L C G Y C S S T S C Y A D I V V V P A M	161 162 163 164	ggcatagcagctgtagtactactacaatcct G I A A G T T T I S A * Q L V L L Q Y P H S S W Y Y Y N I	223 224 225 226

FIG. 10A

12/57

Human D Gene Segment	Direct 5'-3' Orientation	SEQ ID NO.	Inverted Orientation	SEQ ID NO.
X97051, IGHD2-2*02	aggatattgtagtagtaccagctgctatacc	165	ggatagcagctggtagtactacaataatcct	227
	R I L * * Y Q L L Y	14	G I A A G T T T I S	224
	G Y C S S T S C Y T	51	V * Q L V L L Q Y P	225
	D I V V V P A A I	92	Y S S W Y Y Y N I	226
M35648, IGHD2-2*03	tggaattgtagtagtaccagctgctatgcc	166	ggatagcagctggtagtactacaataatcca	228
	W I L * * Y Q L L C	167	G I A A G T T T I S	224
	G Y C S S T S C Y A	168	A * Q L V L L Q Y P	225
	D I V V V P A A M	169	H S S W Y Y Y N I	226
X13972, IGHD2-8*01	aggatattgtagtagtaccagctgctatacc	170	ggatagcagctggtagtactacaataatcct	229
	R I L Y * W C M L Y	16, 17	G I A Y T I S T I S	230
	G Y C T N G V C Y T	53	V * H T P L V Q Y P	231
	D I V L M V Y A I	94	Y S I H H * Y N I	232
J000233, IGHD2-8*02	aagatattgtagtagtaccagctgctatacc	171	ggatagcagctggtagtactacaataatcct	233
	R I L Y W W C M L Y	172	G I A Y T T S T I S	234
	G Y C T G G V C Y T	173	V * H T P P V Q Y L	235
	D I V L V V Y A I	174	Y S I H H Q Y N I	236
J00234, IGHD2-15*01	aggatattgtagtagtaccagctgctatacc	175	ggatagcagctggtagtactacaataatcct	237
	R I L * W W * L L L	-	G V A A T T T T I S	238
	G Y C S G G S C Y S	55	E * Q L P P L Q Y P	239
	D I V V V V A A T	95	S S S Y H H Y N I	240
J00235, IGHD2-21*01	agcatattgtagtagtaccagctgctatcc	176	ggatagcagctggtagtactacaataatgct	241
	S I L W W * L L F	19	G I A I T T T I C	242
	A Y C G G D C Y S	57	E * Q S P P Q Y A	243
	H I V V V I A I	177	N S N H H H N M	244
X97051, IGHD2-21*02	agcatattgtagtagtaccagctgctatcc	178	ggatagcagctggtagtactacaataatgct	245
	S I L W W * L L F	19	G I A V T T T I C	246
	A Y C G G D C Y S	57	E * Q S P P Q Y A	247
	H I V V V T A I	97	N S S H H H N M	248

FIG. 10B

13/57

Human D Gene Segment	Direct 5'-3' Orientation	SEQ ID NO.	Inverted Orientation	SEQ ID NO.
IGHD3-3	X13972, IGHD3-3*01 gtattacgattttggagtggtattataacc V L R F L E W L L Y Y Y D F W S G Y Y T I T I F G V V I I	179 21 59 98	ggataataaccacacccaataatcgtaataac G I I T T P K I V I V * * P L Q K S * Y Y N N H S K N R N	249 250 251 252
	X93618, IGHD3-3*02 gtattacgattttggagtggtattataacc V L A F L E W L L Y Y * H F W S G Y Y T I S I F G V V I I	180 181 182 183	ggataataaccacacccaataatcgtaataac G I I T T P K M L I V * * P L Q K C * Y Y N N H S K N A N	253 254 255 256
	X13972, IGHD3-9*01 gtattacgattttggagtggtattataacc V L R Y F D W L L * Y Y D I L T G Y Y N I T I F * L V I I	184 23 61 99, 100	gtataataaccagtcacaaataatcgtaataac V I I T S Q N I V I L * * P V K I S * Y Y N N Q S K Y R N	257 258 259 260
IGHD3-10	X13972, IGHD3-10*01 gtattactatgttcggggagtgattataacc V L L W F G E L L * Y Y Y G S G S Y Y N I T M V R G V I I	185 25 63 101	gtataataactcccgaaacataatcgtaataac V I I T P R T I V I L * * L P E P * * Y Y N N S P N H S N	261 262 263 264
	X93615, IGHD3-10*02 gtattactatgttcggggagtgattataacc V L L C S G S Y Y N Y Y Y V R G V I I I T M F G R L L *	186 187 188 189	gtataataactcccgaaacataatcgtaataac V I I T P R T * * Y L * * L P E H S N Y N N S P N I V I	265 266 267 268
	X93614, IGHD3-16*01 gtattatgattacgtttggggagtgattataacc V L * L R L G E L C L Y Y Y D Y V W G S Y A Y T I M I T F G G V M L I	190 191 192 193	ggataagcataactccccaacataatcgtaataac G I S I T P P N V I I I V * A * L P Q T * S * Y Y K H N S P K R N H N	269 270 271 272
IGHD3-22	X93616, IGHD3-22*01 gtattactatgattagtggtattataacc V L L * * * W L L L Y Y Y D S S G Y Y Y I T M I V V V I T	194 29 67 103	gtagtaataaccacacacacataatcgtaataac V V I T T T I I V I * * * P L L S * * Y S N N H Y Y H S N	273 274 275 276

FIG. 10C

14/57

Human D Gene Segment	Direct 5'-3' Orientation	SEQ ID NO.	Inverted Orientation	SEQ ID NO.
IGHD4-4	X13972, IGHD4-4*01	195	gtagtactgtagtca V V T V V * L L * S S Y C S	277
		-		278
		69		-
		105		279
IGHD4-11	X13972, IGHD4-11*01	195	gtagtactgtagtca V V T V V * L L * S S Y C S	277
		-		278
		69		-
		105		279
IGHD4-17	X97501, IGHD4-17*01	196	gtagtaccgtagtca V V T V V * S P * S S H R S	280
		-		278
		71		-
		105		281
IGHD4-23	X97051, IGHD4-23*01	197	ggagtaccaccgtagtca G V T T V V E L P P * S S Y H R S	282
		-		283
		73		284
		106		285
IGHD5-5	X13972, IGHD5-5*01	198	gtaaccatagctgtagtccac V T I A V S * P * L Y P N H S C I H	286
		107		287
		35		-
		75		288
IGHD5-12	X13972, IGHD5-12*01	199	gtaatcgtagccactatccac V I V A T I S * S * P L Y P N R S H Y I H	289
		108		290
		37		291
		77		292
IGHD5-18	X97051, IGHD5-18*01	198	gtaaccatagctgtagtccac V T I A V S * P * L Y P N H S C I H	286
		107		287
		35		-
		75		288

FIG. 10D

15/57

Human D Gene Segment	Direct 5'-3' Orientation	SEQ ID NO.	Inverted Orientation	SEQ ID NO.
IGHD5-24	X97051, IGHD5- 24*01 gtagataggctacaattac V E M A T I * R W L Q L R D G Y N Y	200	gtaattgtagccatctctac V I V A I S * L * P S L N C S H L Y	293
		110		294
		39		-
		79		295
IGHD6-6	X13972, IGHD6-6*01 gagatagcagctgtctcc E Y S S S S S I A A R V * Q L V	201	ggacgagctgtctatctc G R A A I L D E L L Y T S C Y T	296
		81		297
		112		298
		-		299
IGHD6-13	X13972, IGHD6- 13*01 ggatagcagcagctggtac G Y S S S W Y G I A A A G V * Q Q L V	202	glaccagctgtctatataccc V P A A A I P Y Q L L L Y T S C C Y T	300
		83		301
		114		302
		41		303
IGHD6-19	X97051, IGHD6- 19*01 ggatagcagctggtggtac G Y S S G W Y G I A V A G V * Q W L V	203	glaccagccacgtctataccc V P A T A I P Y Q P L L Y T S H C Y T	304
		85		305
		116		306
		44		307
IGHD6-25	X97051, IGHD6- 25*01 ggatagcagcagcggtac G Y S S G Y G I A A A V * Q R L	204	glagccgctgtctataccc V A A A I P * P L L Y S R C Y T	308
		87		309
		116		310
		-		311
IGHD7-27	J00256, IGHD7- 27*01 ctaactgggga L T G * L G N W G	205	tcccagttag S P V P Q L P S *	312
		-		-
		-		-
		-		-

FIG. 10E

Antibody Sequence 1

1c1|Query_1_reversed
IGHV4-34*01

<-----FWR1----->-----CDR1
Q V Q L Q Q W G A G L L K P S D T L S L T C A V Y G G S F S
CAGTGCACCTACACAGTGGGCGCAGGACTGTTGAGCCTTCGATACCTGTCCTCAGCTCTATGGTGGTCCCTTCAGT
.....G.....
Q V Q L Q Q W G A G L L K P S E T L S L T C A V Y G G S F S
-----FWR2----->-----CDR2
G Y Y W S W I R Q P P G K G L E W I G E I N H S G S T N Y N
GGTTACTGCGAGCTGGATCCGCCAGCCGCCAGGGAGGGCTGGAGTGGATGGGAAATCAATCATATGTGGAGCAACCACTACAC
.....
G Y Y W S W I R Q P P G K G L E W I G E I N H S G S T N Y N
-----FWR3-----
P S L K S R V T I S V D T S K N Q F S L K L S S V T A A D T
CCGTCCCTCAGAGTGGAGTCAACCATATCAGTAGACACGTCCTCCAGACCCAGTCTCTCCCTGAGCTCTGTGACCCGCCGGACACG
.....
P S L K S R V T I S V D T S K N Q F S L K L S S V T A A D T
----->-----
A V Y Y C A G H S H G W Y Y Y Y Y G M D V W G Q G T T V T V
CCTGTCTATTACTGTCCGGCGATAGCCATGGCTGGTACTACTACTACGCTATGGACGCTCTGGGGCCAGGGACCACTCCCGTC
.....
A V Y Y C A (SEQ ID NO:314)
----->-----

1c1|Query_1_reversed
IGHV4-34*01

S S (SEQ ID NO:313)
TCCTCA 473 (SEQ ID NO:312)
..... 62

1c1|Query_1_reversed
IGHV4-34*01
IGHVD6-19.RUC1
IGHJ6*02

----->-----
A V Y Y C A G H S H G W Y Y Y Y Y G M D V W G Q G T T V T V
CCTGTCTATTACTGTCCGGCGATAGCCATGGCTGGTACTACTACTACGCTATGGACGCTCTGGGGCCAGGGACCACTCCCGTC
.....
A V Y Y C A (SEQ ID NO:314)
----->-----

1c1|Query_1_reversed
IGHJ6*02

S S (SEQ ID NO:313)
TCCTCA 473 (SEQ ID NO:312)
..... 62

D gene segment	Hydrophilic	SEQ ID NO.
D6-19	GYSSGWY	85
HD6-19	GSHGWY	86

FIG. 11

17/57

D gene segment	Hydrophilic	SEQ ID NO.
D4-17	DYGDY	71
HD4-17	DHGHY	72

FIG. 12

D gene segment	Hydrophilic	SEQ ID NO.
D6-13	GYSSSWY	83
HD6-13	GHSHSWY	84

FIG. 13

19/57

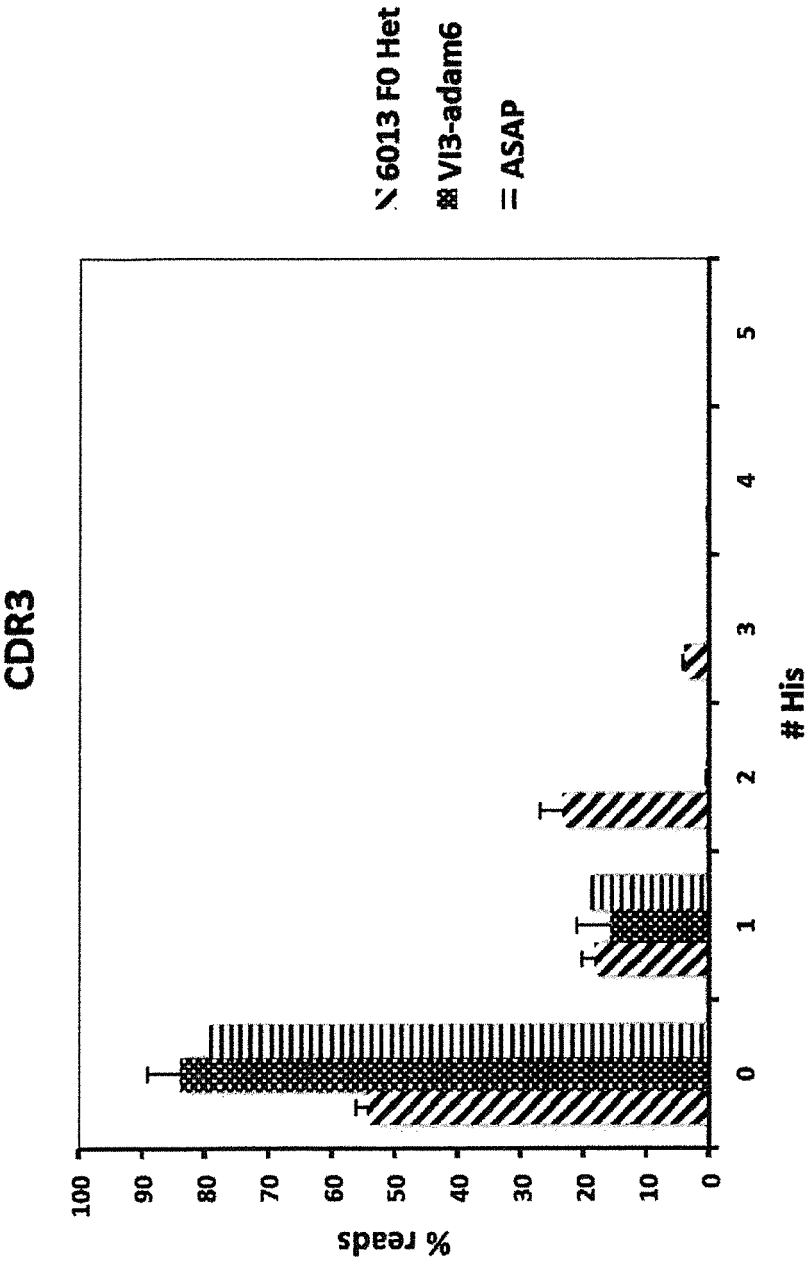


FIG. 14

20/57

IGKV1-39*01	-----FR1-IMGT----- CDR1 -----FR2-IMGT----- C -----	
A	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQKPGKAPKLLIYAASLQSGVPS	
B	F...T H I...V...YT....	
C	A.....I..NF.....G.YN.....	
D	 HN NN.....H.....N.....	
E	A.....T..N.....	
F	N.....D.....	
G	A..L.....N.N.....N..D.....	
H	A.....N.N.. H D..F.....	
I	A..L.....	
J	A.....	
K	A..L.....M.....	
IGKV1-39*01	-----FR3-IMGT----- CDR3-	SEQ ID NO:325
A	RFSGSGSGTDFTLTISIQPEDFATYYCQQSYST-P-----	
B	...A.....T....NI..FTFGPGTKVDIKR	
C	Y...T.H...GN.....SMYTFGQGTQLEIKR	
D	 H I..ITFGQGTRLEIKR	
E	 H ...I...ITFGQGTRLEIKR	
F	T..H..... H ...ITFGQGTRLEIKR	
G	T..... H ...ITFGQGTRLEIKR	
H	P.ITFGQGTRVEIKR	
I	...K..... I H.ITFGQGTKEIKR	
J	 H .IP.ITFGQGTRLEIK.	
K	T.....R..... H ..P.ITFGQGTKEIKR	

FIG. 15

21/57

FIG. 16

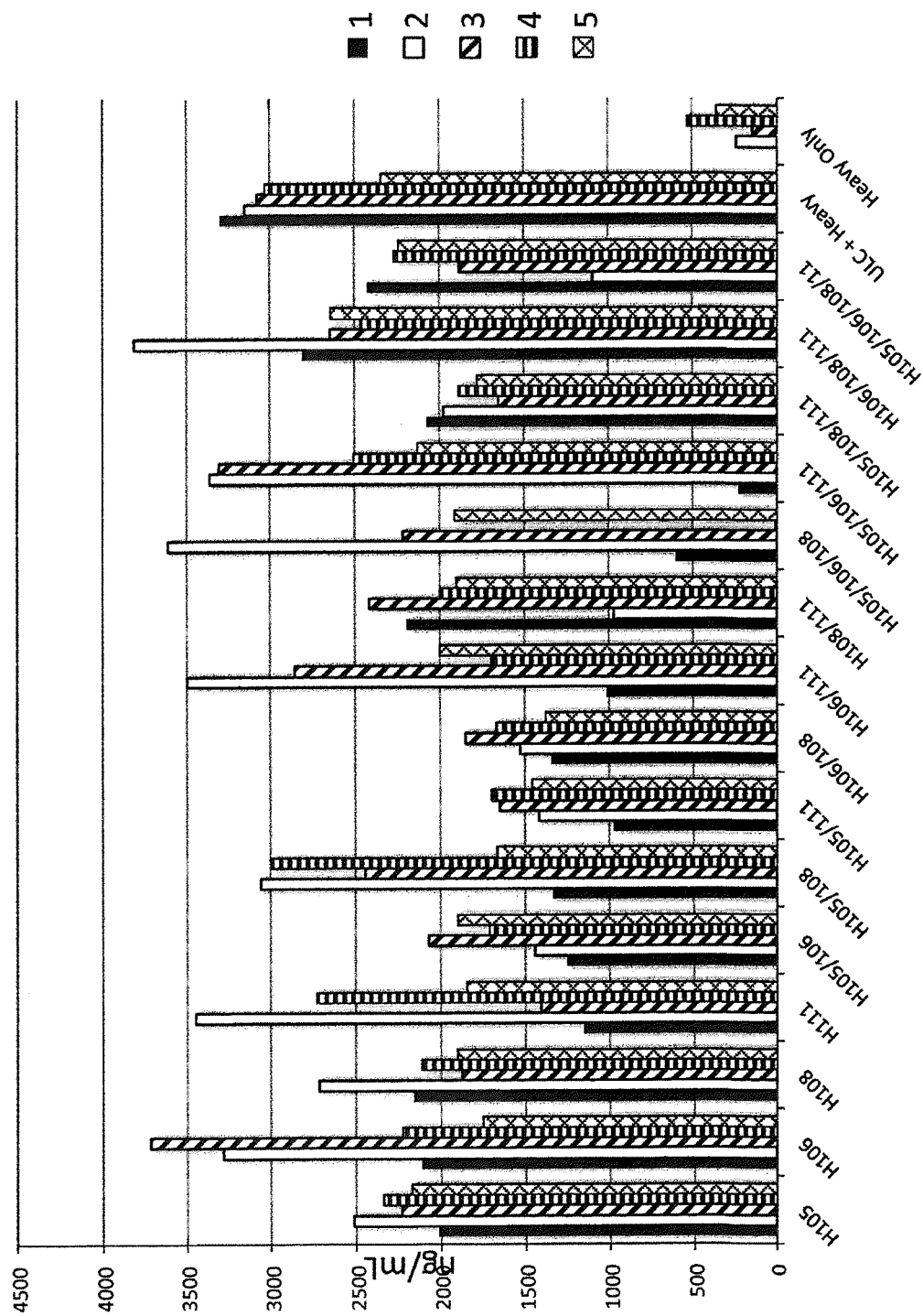


FIG. 17

23/57

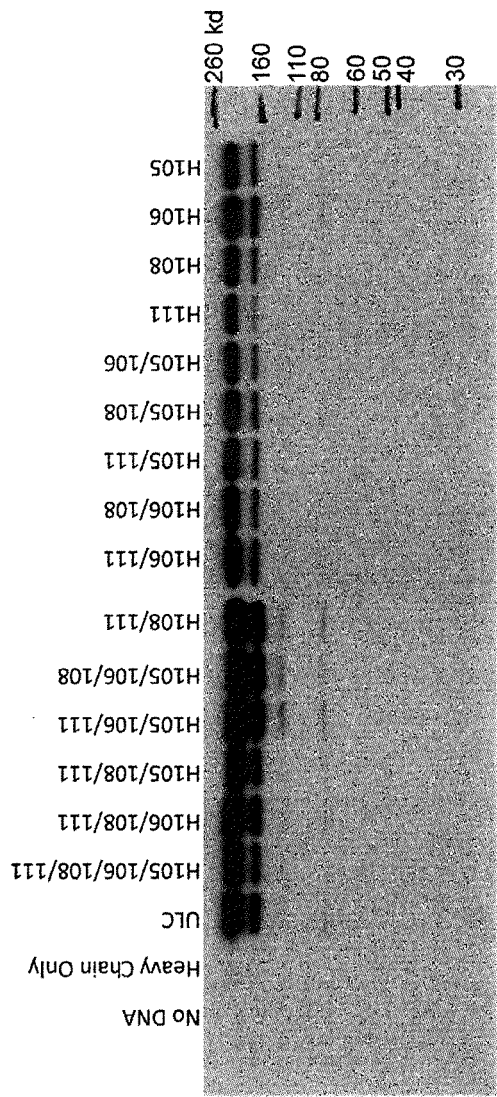


FIG. 18

24/57

HC	Vk mut	Kinetics at pH 7.2					Kinetics at pH 5.75					low/neutral pH				
		mAb capture level (RU)	100nM Antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	% (min)	mAb capture level (RU)	100nM antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	% (min)	ka	kd	KD
H4H6006	H105	44	11	4.25E+05	1.18E-03	2.77E-09	10	32	5	1.27E+06	2.03E-03	1.61E-09	6	3.0	1.7	0.6
	H106	46	12	4.42E+05	9.32E-04	2.11E-09	12	27	4	1.56E+06	1.72E-03	1.10E-09	7	3.5	1.8	0.5
	H108	46	12	4.51E+05	9.02E-04	2.00E-09	13	33	5	1.15E+06	1.47E-03	1.28E-09	8	2.5	1.6	0.6
	H111	47	13	3.86E+05	9.54E-04	2.47E-09	12	36	5	8.81E+05	1.52E-03	1.73E-09	8	2.3	1.6	0.7
	H105	16	1	NB	NB	NB	NB	6	-4	NB	NB	NB	NB			
	H105	40	11	4.83E+05	8.73E-04	1.81E-09	13	30	4	1.54E+06	1.26E-03	8.20E-10	9	3.2	1.4	0.5
	H105	22	4	3.81E+05	1.32E-03	3.45E-09	9	16	-2	NB	NB	NB	NB			
	H106	51	15	4.87E+05	7.60E-04	1.56E-09	15	40	8	1.16E+06	1.04E-03	8.96E-10	11	2.4	1.4	0.6
	H106	38	9	3.94E+05	9.00E-04	2.28E-09	13	29	2	1.55E+06	1.60E-03	1.03E-09	7	3.9	1.8	0.5
	H108	51	14	3.98E+05	8.29E-04	2.08E-09	14	40	6	8.42E+05	1.19E-03	1.42E-09	10	2.1	1.4	0.7
	H105	14	1	NB	NB	NB	NB	9	-5	NB	NB	NB	NB			
	H105	15	1	NB	NB	NB	NB	10	-5	NB	NB	NB	NB			
	H105	17	2	4.38E+05	9.60E-04	2.19E-09	12	12	-5	NB	NB	NB	NB			
	H10	40	10	3.72E+05	7.42E-04	2.00E-09	16	30	2	NB	NB	NB	NB			
	H105	15	1	NB	NB	NB	NB	9	-6	NB	NB	NB	NB			
	H106	72	22	3.90E+05	1.18E-03	3.03E-09	10	56	11	7.69E+05	1.84E-03	2.39E-09	6	2.0	1.6	0.8
	HC															

FIG. 19A

25/57

HC	V _k mut	Kinetics at pH 7.2						Kinetics at pH 5.75						low/neutral pH		
		mAb capture level (RU)	100nM Antigen bound (RU)	k _a (1/Ms)	k _d (1/s)	KD (M)	% (min)	mAb capture level (RU)	100nM antigen bound (RU)	k _a (1/Ms)	k _d (1/s)	KD (M)	t _{1/2} (min)	k _a	k _d	KD
HA6008	H105	79	21	3.47E+05	1.09E-03	3.15E-09	11	62	8	5.15E+05	3.54E-03	6.87E-09	3	1.5	3.2	2.2
	H106	60	13	3.19E+05	1.92E-03	6.02E-09	6	48	2	1.92E+06	2.48E-02	1.29E-08	0	6.0	12.9	2.1
	H108	84	20	2.89E+05	2.66E-03	9.17E-09	4	1	-5	NB	NB	NB	NB			
	H111	77	19	3.28E+05	1.54E-03	4.69E-09	8	60	5	4.96E+05	7.85E-03	1.58E-08	1	1.5	5.1	3.4
	H105	30	4	3.39E+05	9.91E-04	2.92E-09	12	-1	-7	NB	NB	NB	NB			
	H105	77	20	3.16E+05	1.40E-03	4.45E-09	8	62	6	4.76E+05	5.41E-03	1.14E-08	2	1.5	3.9	2.6
	H105	44	11	3.51E+05	4.10E-04	1.17E-09	28	34	0	NB	NB	NB	NB			
	H106	81	18	2.99E+05	2.20E-03	7.34E-09	5	66	4	3.87E+05	1.16E-02	3.01E-08	1	1.3	5.3	4.1
	H106	87	19	3.05E+05	1.64E-03	5.38E-09	7	73	5	4.34E+05	6.96E-03	1.60E-08	2	1.4	4.2	3.0
	H108	85	22	3.42E+05	1.63E-03	4.76E-09	7	70	5	3.94E+05	8.00E-03	2.03E-08	1	1.2	4.9	4.3
	H105	29	4	3.53E+05	9.63E-04	2.73E-09	12	24	-5	NB	NB	NB	NB			
	H105	32	5	2.87E+05	9.83E-04	3.43E-09	12	26	-5	NB	NB	NB	NB			
	H105	39	9	3.47E+05	3.26E-04	9.38E-10	35	32	-2	NB	NB	NB	NB			
	H106	57	11	2.72E+05	1.63E-03	5.99E-09	7	46	-1	NB	NB	NB	NB			
	H105	36	6	2.93E+05	1.05E-03	3.58E-09	11	29	-5	NB	NB	NB	NB			
	1-39	128	33	3.02E+05	1.86E-03	6.15E-09	6	103	13	3.24E+05	5.67E-03	1.75E-08	2	1.1	3.1	2.8
	UIC															

FIG. 19B

26/57

HC	Vk mut	Kinetics at pH 7.2						Kinetics at pH 5.75						low/neutral pH		
		mAb capture level (RU)	100nM Antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t½ (min)	mAb capture level (RU)	100nM antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t½ (min)	ka	kd	KD
H4H30A6	H105	73	0	NB	NB	NB	NB	62	-8	NB	NB	NB	NB			
	H106	64	0	NB	NB	NB	NB	54	-9	NB	NB	NB	NB			
	H108	75	1	NB	NB	NB	NB	64	-8	NB	NB	NB	NB			
	H111	73	0	NB	NB	NB	NB	62	-9	NB	NB	NB	NB			
	H105	45	0	NB	NB	NB	NB	38	-9	NB	NB	NB	NB			
	H106															
	H105	65	0	NB	NB	NB	NB	56	-9	NB	NB	NB	NB			
	H108															
	H105	34	0	NB	NB	NB	NB	27	-9	NB	NB	NB	NB			
	H111															
	H106	77	0	NB	NB	NB	NB	67	-9	NB	NB	NB	NB			
	H108															
	H106	75	0	NB	NB	NB	NB	67	-9	NB	NB	NB	NB			
	H111															
	H108	66	0	NB	NB	NB	NB	56	-9	NB	NB	NB	NB			
	H105	54	0	NB	NB	NB	NB	46	-9	NB	NB	NB	NB			
	H106															
	H105	47	0	NB	NB	NB	NB	41	-9	NB	NB	NB	NB			
	H111															
	H105	37	0	NB	NB	NB	NB	31	-9	NB	NB	NB	NB			
	H108															
	H106	69	0	NB	NB	NB	NB	59	-9	NB	NB	NB	NB			
	H111															
	H105	54	0	NB	NB	NB	NB	49	-9	NB	NB	NB	NB			
	H108															
	H111															
	1-39 ULC	97	0	NB	NB	NB	NB	88	-9	NB	NB	NB	NB			

FIG. 19C

27/57

HC	Vk mut	Kinetics at pH 7.2						Kinetics at pH 5.75						low/neutral pH		
		mAb capture level (RU)	100nM Antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t½ (min)	mAb capture level (RU)	100nM antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t½ (min)	ka	kd	KD
H4H2964	H105	327	23	1.43E+05	8.40E-03	5.89E-08	1	318	2	IC	IC	IC	IC			
	H106	303	26	9.67E+04	3.40E-03	3.52E-08	3	289	11	9.46E+04	2.08E-02	2.20E-07	1	1.0	6.1	6.3
	H108	287	29	1.37E+05	2.46E-03	1.80E-08	5	268	12	7.69E+04	1.32E-02	1.71E-07	1	0.6	5.4	9.5
	H111	311	21	1.31E+05	6.83E-03	5.20E-08	2	292	0	NB	NB	NB	NB			
	H105	285	17	9.65E+04	6.20E-03	6.43E-08	2	262	-3	NB	NB	NB	NB			
	H106															
	H108	271	21	1.23E+05	9.82E-03	7.99E-08	1	262	-3	NB	NB	NB	NB			
	H105	221	11	2.37E+05	2.11E-02	8.88E-08	1	216	-6	NB	NB	NB	NB			
	H106	344	28	1.04E+05	6.66E-03	6.38E-08	2	316	3	IC	IC	IC	IC			
	H108	341	25	1.16E+05	9.09E-03	7.81E-08	1	321	2	IC	IC	IC	IC			
	H111	300	20	9.64E+04	1.01E-02	1.05E-07	1	274	-4	NB	NB	NB	NB			
	H105	269	10	1.31E+05	2.52E-02	1.93E-07	0	243	-8	NB	NB	NB	NB			
	H106	286	5	6.34E+04	5.06E-02	7.99E-07	0	265	-9	NB	NB	NB	NB			
	H108	315	9	1.55E+05	5.89E-02	3.81E-07	0	279	-8	NB	NB	NB	NB			
	H111															
	H105	260	0	NB	NB	NB	NB	238	-10	NB	NB	NB	NB			
	H106															
	H108															
	H111															
	1-39 ULC	386	32	1.30E+05	2.05E-03	1.58E-08	6	362	17	7.58E+04	7.97E-03	1.05E-07	1	0.6	3.9	6.6

FIG. 19D

28/57

HC	Vk mut	Kinetics at pH 7.2						Kinetics at pH 5.75						low/neutral pH		
		mAb capture level (RU)	100nM Antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t½ (min)	mAb capture level (RU)	100nM antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t½ (min)	ka	kd	KD
H43010	H105	52	8	1.06E+05	7.43E-04	7.04E-09	16	43	-1	NB	NB	NB	NB			
	H106	50	9	1.26E+05	3.54E-04	2.82E-09	33	40	0	NB	NB	NB	NB			
	H108	50	8	9.29E+04	2.43E-04	2.62E-09	48	42	-1	NB	NB	NB	NB			
	H111	55	11	1.53E+05	1.66E-04	1.09E-09	69	48	2	IC	IC	IC	IC			
	H105	55	10	1.31E+05	5.18E-04	3.94E-09	22	45	1	NB	NB	NB	NB			
	H106	48	8	8.96E+04	4.58E-04	5.12E-09	25	41	-1	NB	NB	NB	NB			
	H108	38	6	8.85E+04	1.64E-04	1.85E-09	70	32	-3	NB	NB	NB	NB			
	H105	59	11	1.06E+05	1.61E-04	1.52E-09	72	52	2	4.79E+05	1.00E-06	2.09E-12	11550	4.5	0.0	0.0
	H106	76	7	6.81E+04	5.23E-04	7.68E-09	22	72	0	NB	NB	NB	NB			
	H108	58	11	1.17E+05	9.26E-05	7.92E-10	125	52	2	IC	IC	IC	IC			
	H105	67	13	1.11E+05	3.17E-04	2.86E-09	36	58	4	IC	IC	IC	IC			
	H106	70	8	6.45E+04	9.94E-04	1.54E-08	12	57	-1	NB	NB	NB	NB			
	H108	49	8	8.52E+04	1.10E-04	1.29E-09	105	44	-1	NB	NB	NB	NB			
	H111	54	3	1.02E+04	1.46E-03	1.44E-07	8	46	-5	NB	NB	NB	NB			
	H105	70	6	7.28E+04	5.55E-03	7.61E-08	2	62	-5	NB	NB	NB	NB			
	H106	83	15	1.02E+05	1.79E-04	1.77E-09	64	77	7	2.11E+05	1.00E-06	4.74E-12	11550	2.1	0.0	0.0
	1-39 ULC															

FIG. 19E

29/57

HC	Vk mut	Kinetics at pH 7.2						Kinetics at pH 5.75						low/neutral pH		
		mAb capture level (RU)	100nM Antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t½ (min)	mAb capture level (RU)	100nM antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t½ (min)	ka	kd	KD
H4H3029	H105	71	8	1.41E+05	2.96E-04	2.10E-09	39	60	-3	NB	NB	NB	NB			
	H106	72	8	1.50E+05	2.39E-04	1.59E-09	48	64	-2	NB	NB	NB	NB			
	H108	68	7	1.19E+05	7.97E-05	6.70E-10	145	61	-2	NB	NB	NB	NB			
	H111	69	8	1.50E+05	1.78E-04	1.19E-09	65	63	-2	NB	NB	NB	NB			
	H105	88	10	1.60E+05	2.45E-04	1.53E-09	47	77	0	NB	NB	NB	NB			
	H106															
	H105	67	8	1.45E+05	1.14E-04	7.84E-10	102	59	-3	NB	NB	NB	NB			
	H108															
	H105	13	0	NB	NB	NB	NB	14	-11	NB	NB	NB	NB			
	H106															
	H108	92	10	1.34E+05	1.34E-04	9.98E-10	86	82	0	NB	NB	NB	NB			
	H106															
	H108	85	5	5.82E+04	1.10E-03	1.89E-08	10	78	-4	NB	NB	NB	NB			
	H105	62	7	1.48E+05	1.73E-04	1.17E-09	67	55	-4	NB	NB	NB	NB			
	H106															
	H108	85	10	1.36E+05	1.97E-04	1.46E-09	59	75	0	NB	NB	NB	NB			
	H105															
	H106	78	6	1.35E+05	2.18E-03	1.61E-08	5	70	-4	NB	NB	NB	NB			
	H108															
	H105	55	6	1.50E+05	2.48E-04	1.65E-09	47	48	-5	NB	NB	NB	NB			
	H106															
	H108	73	4	8.60E+04	1.59E-03	1.85E-08	7	66	-6	NB	NB	NB	NB			
	H105															
	H106	95	7	1.19E+05	6.71E-03	5.66E-08	2	86	-6	NB	NB	NB	NB			
	H108															
	H111															
	1-39 ULC	108	12	1.34E+05	1.65E-04	1.23E-09	70	98	2	IC	IC	IC	IC			

FIG. 19F

30/57

HC	Vk mut	Kinetics at pH 7.2						Kinetics at pH 5.75						low/neutral pH		
		mAb capture level (RU)	100nM Antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t% (min)	mAb capture level (RU)	100nM antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t% (min)	ka	kd	KD
H4HS978	H105	44	7	3.88E+05	5.73E-03	1.48E-08	2	41	-5	NB	NB	NB	NB			
	H106	36	7	3.15E+05	3.03E-03	9.62E-09	4	34	-5	NB	NB	NB	NB			
	H108	38	8	3.18E+05	9.61E-04	3.02E-09	12	32	-4	NB	NB	NB	NB			
	H111	43	8	3.13E+05	2.32E-03	7.40E-09	5	40	-5	NB	NB	NB	NB			
	H105	33	4	2.69E+05	5.41E-03	2.01E-08	2	29	-9	NB	NB	NB	NB			
	H105	34	7	2.13E+05	2.15E-03	1.01E-08	5	30	-7	NB	NB	NB	NB			
	H105	32	5	3.47E+05	6.27E-03	1.81E-08	2	30	-8	NB	NB	NB	NB			
	H106	50	10	3.67E+05	3.09E-03	8.42E-09	4	46	-4	NB	NB	NB	NB			
	H106	62	12	2.88E+05	4.47E-03	1.55E-08	3	56	-2	NB	NB	NB	NB			
	H108	45	9	3.22E+05	2.05E-03	6.37E-09	6	43	-4	NB	NB	NB	NB			
	H105	36	5	3.57E+05	7.48E-03	2.10E-08	2	35	-8	NB	NB	NB	NB			
	H105	39	7	3.37E+05	8.35E-03	2.48E-08	1	35	-6	NB	NB	NB	NB			
	H105	29	4	2.94E+05	4.52E-03	1.54E-08	3	28	-8	NB	NB	NB	NB			
	H106	41	7	3.12E+05	6.37E-03	2.04E-08	2	39	-6	NB	NB	NB	NB			
	H105	50	9	2.97E+05	6.83E-03	2.30E-08	2	45	-5	NB	NB	NB	NB			
	1-39	74	16	2.92E+05	1.73E-03	5.91E-09	7	67	3	1.20E+06	9.67E-03	8.05E-09	1	4.1	5.6	1.4
	UIC															

FIG. 19G

31/57

HC	Vk mut	Kinetics at pH 7.2						Kinetics at pH 5.75						low/neutral pH		
		mAb capture level (RU)	100nM Antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	% (min)	mAb capture level (RU)	100nM antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	% (min)	ka	kd	KD
H4H5981	H105	121	24	3.04E+05	8.81E-03	2.90E-08	1	112	7	4.47E+05	6.21E-02	1.39E-07	0	1.5	7.1	4.8
	H106	113	29	2.41E+05	2.99E-03	1.24E-08	4	103	10	6.84E+05	1.89E-02	2.76E-08	1	2.8	6.3	2.2
	H108	114	31	3.09E+05	2.83E-03	9.16E-09	4	104	11	5.06E+05	1.33E-02	2.63E-08	1	1.6	4.7	2.9
	H111	104	26	3.45E+05	3.98E-03	1.15E-08	3	96	4	4.54E+05	6.26E-02	1.38E-07	0	1.3	15.8	12.0
	H105	109	26	2.39E+05	3.10E-03	1.29E-08	4	103	9	5.00E+05	1.77E-02	3.53E-08	1	2.1	5.7	2.7
	H105	109	27	2.91E+05	4.48E-03	1.54E-08	3	97	7	1.00E+06	9.77E-02	9.76E-08	0	3.4	21.8	6.3
	H105	85	16	2.62E+05	7.59E-03	2.90E-08	2	80	-1	NB	NB	NB	NB			
	H106	121	33	2.33E+05	2.71E-03	1.16E-08	4	115	14	3.88E+05	1.19E-02	3.07E-08	1	1.7	4.4	2.6
	H106	117	32	2.29E+05	2.28E-03	9.97E-09	5	113	13	3.71E+05	8.88E-03	2.40E-08	1	1.6	3.9	2.4
	H108	93	24	3.39E+05	4.04E-03	1.19E-08	3	87	3	4.54E+05	5.11E-02	1.12E-07	0	1.3	12.7	9.4
	H105	94	25	2.24E+05	1.23E-03	5.47E-09	9	85	8	4.94E+05	3.02E-03	6.12E-09	4	2.2	2.5	1.1
	H105	111	24	2.31E+05	4.65E-03	2.01E-08	2	100	4	1.94E+05	8.05E-02	4.15E-07	0	0.8	17.3	20.6
	H105	83	21	2.60E+05	5.20E-03	2.00E-08	2	79	1	NB	NB	NB	NB			
	H106	100	28	2.11E+05	2.23E-03	1.05E-08	5	93	6	4.26E+05	1.83E-02	4.29E-08	1	2.0	8.2	4.1
	H105	104	24	2.46E+05	5.05E-03	2.05E-08	2	98	2	IC	IC	IC	IC			
	H105	133	34	2.80E+05	3.40E-03	1.22E-08	3	124	13	4.29E+05	1.42E-02	3.30E-08	1	1.5	4.2	2.7
	1-39 ULC															

FIG. 19H

32/57

HC	Vk mut	Kinetics at pH 7.2						Kinetics at pH 5.75						low/neutral pH		
		mAb capture level (RU)	100nM Antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t% (min)	mAb capture level (RU)	100nM antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t% (min)	ka	kd	KD
H4HS999	H105	87	8	5.04E+04	1.18E-03	2.34E-08	10	78	-5	NB	NB	NB	NB			
	H106	72	7	1.04E+05	6.40E-04	6.17E-09	18	66	-7	NB	NB	NB	NB			
	H108	77	6	3.47E+04	1.47E-03	4.23E-08	8	72	-8	NB	NB	NB	NB			
	H111	77	6	1.39E+05	4.59E-03	3.31E-08	3	71	-8	NB	NB	NB	NB			
	H105	85	8	9.95E+04	3.69E-04	3.71E-09	31	77	-6	NB	NB	NB	NB			
	H106															
	H108	71	6	2.60E+03	8.63E-04	3.32E-07	13	63	-7	NB	NB	NB	NB			
	H105	51	3	9.81E+03	7.03E-03	7.16E-07	2	47	-10	NB	NB	NB	NB			
	H111															
	H106	80	6	4.81E+04	4.78E-04	9.94E-09	24	71	-10	NB	NB	NB	NB			
	H108	91	9	3.28E+04	6.44E-04	1.96E-08	18	85	-6	NB	NB	NB	NB			
	H111	70	6	3.98E+04	2.01E-03	5.05E-08	6	65	-9	NB	NB	NB	NB			
	H105	79	5	4.95E+04	5.53E-04	1.12E-08	21	74	-10	NB	NB	NB	NB			
	H106															
	H108	74	8	1.92E+04	4.59E-04	2.39E-08	25	68	-6	NB	NB	NB	NB			
	H111															
	H105	56	4	1.03E+03	4.18E-03	4.04E-06	3	52	-10	NB	NB	NB	NB			
	H106															
	H108	74	5	8.96E+03	1.66E-03	1.86E-07	7	66	-9	NB	NB	NB	NB			
	H111															
	H105	79	7	1.73E+04	9.49E-04	5.50E-08	12	75	-9	NB	NB	NB	NB			
	H106															
	H108	110	10	5.01E+05	4.02E-03	8.02E-09	3	100	-5	NB	NB	NB	NB			
	H111															
	1-39 ULC															

FIG. 19I

33/57

HC	Vk mut	Kinetics at pH 7.2						Kinetics at pH 5.75						low/neutral pH		
		mAb capture level (RU)	100nM Antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t½ (min)	mAb capture level (RU)	100nM antigen bound (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t½ (min)	ka	kd	KD
H4H6011	H105	150	22	1.15E+05	3.17E-04	2.77E-09	36	147	6	7.61E+04	1.00E-06	1.31E-11	11550	0.7	0.0	0.0
	H106	127	17	8.73E+04	3.46E-04	3.96E-09	33	119	2	4.89E+04	1.00E-06	2.05E-11	11550	0.6	0.0	0.0
	H108	124	15	7.56E+04	5.90E-04	7.80E-09	20	112	-4	NB	NB	NB	NB			
	H111	135	17	1.08E+05	5.59E-04	5.19E-09	21	128	0	NB	NB	NB	NB			
	H105	130	18	1.03E+05	3.91E-04	3.81E-09	30	123	3	1.89E+05	2.33E-04	1.23E-09	49	1.8	0.6	0.3
	H106	117	16	9.29E+04	5.24E-04	5.64E-09	22	110	-2	NB	NB	NB	NB			
	H108	109	16	1.06E+05	4.39E-04	4.15E-09	26	105	0	NB	NB	NB	NB			
	H111	105	8	6.95E+04	4.86E-04	7.00E-09	24	100	-8	NB	NB	NB	NB			
	H106	171	16	3.07E+05	1.44E-03	4.69E-09	8	163	0	NB	NB	NB	NB			
	H108	133	16	9.17E+04	6.20E-04	6.76E-09	19	126	-3	NB	NB	NB	NB			
	H111	135	10	6.11E+04	6.93E-04	1.13E-08	17	132	-8	NB	NB	NB	NB			
	H105	117	12	6.52E+04	8.99E-04	1.38E-08	13	111	-3	NB	NB	NB	NB			
	H108	129	16	9.95E+04	5.82E-04	5.85E-09	20	121	-3	NB	NB	NB	NB			
	H111	124	11	2.36E+04	8.53E-04	3.62E-08	14	118	-6	NB	NB	NB	NB			
	H105	144	14	3.65E+04	9.51E-04	2.60E-08	12	140	-6	NB	NB	NB	NB			
	H106	198	25	1.13E+05	4.36E-04	3.85E-09	27	181	6	6.02E+04	2.02E-04	3.36E-09	57	0.5	0.5	0.9
	1-39 ULC	2	1	NB	NB	NB	NB	-2	-11	NB	NB	NB	NB			
	Buffer	3	1	NB	NB	NB	NB	0	-10	NB	NB	NB	NB			

FIG. 19J

34/57

Heavy Chain	Light Chain Mutant	Kinetics at pH 7.4						Kinetics at pH 5.75						Ratio of low pH / neutral pH		
		mAb captured (RU)	50nM Antigen Binding (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t _{1/2} (min)	mAb captured (RU)	50nM Antigen Binding (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t _{1/2} (min)	ka	kd	KD
1	H105	488	47.2	3.52E+05	9.30E-03	2.64E-08	1.2	378	37.8	4.24E+05	1.38E-02	3.24E-08	0.8	1.2	1.5	1.2
	H106	620	73.7	3.22E+05	3.67E-03	1.14E-08	3.1	505	65.4	3.66E+05	4.86E-03	1.33E-08	2.4	1.1	1.3	1.2
	H108	648	99.0	3.17E+05	2.07E-03	6.54E-09	5.6	496	80.7	3.59E+05	3.02E-03	8.41E-09	3.8	1.1	1.5	1.3
	H111	669	81.0	3.01E+05	3.81E-03	1.27E-08	3.0	536	62.8	3.32E+05	5.41E-03	1.63E-08	2.1	1.1	1.4	1.3
	H105/106	492	55.6	3.74E+05	6.44E-03	1.72E-08	1.8	404	45.7	4.30E+05	1.01E-02	2.34E-08	1.1	1.2	1.6	1.4
	H105/108	538	75.2	3.28E+05	4.17E-03	1.27E-08	2.8	416	56.3	3.87E+05	7.43E-03	1.92E-08	1.6	1.2	1.8	1.5
	H105/111	501	44.6	3.44E+05	9.77E-03	2.84E-08	1.2	402	31.9	4.06E+05	1.70E-02	4.19E-08	0.7	1.2	1.7	1.5
	H106/108	494	64.9	3.36E+05	4.14E-03	1.23E-08	2.8	407	43.0	4.07E+05	1.17E-02	2.86E-08	1.0	1.2	2.8	2.3
	H106/111	536	78.2	3.09E+05	3.10E-03	1.00E-08	3.7	423	61.4	3.62E+05	4.68E-03	1.29E-08	2.5	1.2	1.5	1.3
	H108/111	584	78.5	3.11E+05	3.80E-03	1.22E-08	3.0	473	59.0	3.50E+05	6.13E-03	1.75E-08	1.9	1.1	1.6	1.4
	H105/106/108	442	51.2	3.72E+05	6.38E-03	1.71E-08	1.8	370	28.4	4.26E+05	2.13E-02	5.00E-08	0.5	1.1	3.3	2.9
	H105/106/111	473	62.8	3.40E+05	4.55E-03	1.34E-08	2.5	378	47.6	4.07E+05	7.42E-03	1.82E-08	1.6	1.2	1.6	1.4
	H105/108/111	433	49.5	3.57E+05	7.42E-03	2.08E-08	1.6	354	31.3	4.09E+05	1.73E-02	4.23E-08	0.7	1.1	2.3	2.0
	H106/108/111	491	66.6	3.44E+05	3.82E-03	1.11E-08	3.0	415	43.3	3.91E+05	1.06E-02	2.72E-08	1.1	1.1	2.8	2.5
	H105/106/108/111	454	57.9	3.51E+05	5.77E-03	1.64E-08	2.0	368	36.8	4.06E+05	1.35E-02	3.32E-08	0.9	1.2	2.3	2.0
	ULC + Heavy	586	76.0	3.16E+05	3.85E-03	1.22E-08	3.0	483	66.5	3.45E+05	4.58E-03	1.33E-08	2.5	1.1	1.2	1.1
Heavy only		141	-1.3	NB	NB	NB	NB	107	-6.7	NB	NB	NB	NB	Negative Control		
No DNA		60	-1.5	NB	NB	NB	NB	26	-7.2	NB	NB	NB	NB			

FIG. 20A

35/57

Heavy Chain	Light Chain Mutant	Kinetics at pH 7.4						Kinetics at pH 5.75						Ratio of low pH / neutral pH		
		mAb capture d (RU)	50nM Antigen Binding (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t _{1/2} (min)	mAb capture d (RU)	50nM Antigen Binding (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t _{1/2} (min)	ka	kd	KD
	H105	720	33.7	1.02E+05	9.10E-04	8.89E-09	12.7	595	0.3	NB	NB	NB	NB	No binding at Low pH		
	H106	735	32.9	9.11E+04	4.47E-04	4.91E-09	25.8	623	4.3	2.27E+04	6.41E-03	2.82E-07	1.8	0.2	14.3	57.4
	H108	728	32.2	8.48E+04	2.67E-04	3.14E-09	43.3	598	3.6	1.16E+03	3.41E-03	2.93E-06	3.4	0.0	12.8	933.1
	H111	802	42.4	1.17E+05	1.15E-04	9.88E-10	100.3	670	14.1	3.01E+04	7.08E-04	2.35E-08	16.3	0.3	6.1	23.8
	H105/106	570	24.9	8.51E+04	2.92E-04	3.43E-09	39.5	484	2.4	1.14E+04	6.47E-03	5.69E-07	1.8	0.1	22.1	165.9
	H105/108	723	28.4	8.73E+04	1.30E-03	1.49E-08	8.9	603	-2.6	NB	NB	NB	NB	No binding at Low pH		
	H105/111	627	28.5	8.82E+04	3.60E-04	4.08E-09	32.1	519	2.3	1.02E+04	1.30E-02	1.27E-06	0.9	0.1	36.2	311.3
	H106/108	550	21.1	6.75E+04	9.12E-04	1.35E-08	12.7	470	-1.9	NB	NB	NB	NB	No binding at Low pH		
	H106/111	808	32.7	9.01E+04	6.78E-04	7.52E-09	17.0	678	0.9	NB	NB	NB	NB	No binding at Low pH		
	H108/111	801	40.5	1.17E+05	9.80E-05	8.40E-10	117.8	676	10.6	1.87E+04	5.84E-04	3.12E-08	19.8	0.2	6.0	37.1
	H105/106/108	409	13.0	8.21E+04	4.29E-04	5.22E-09	26.9	345	-4.4	NB	NB	NB	NB	No binding at Low pH		
	H105/106/111	767	9.3	4.84E+04	1.25E-03	2.58E-08	9.3	645	-6.1	NB	NB	NB	NB	No binding at Low pH		
	H105/108/111	578	24.5	8.99E+04	2.87E-04	3.19E-09	40.2	479	-0.7	NB	NB	NB	NB	No binding at Low pH		
	H106/108/111	765	15.1	5.04E+04	1.65E-03	3.27E-08	7.0	661	-5.9	NB	NB	NB	NB	No binding at Low pH		
	H105/106/108/111	723	0.3	NB	NB	NB	NB	611	-7.0	NB	NB	NB	NB	No binding at either pH tested		
	ULC + Heavy	781	39.8	1.13E+05	1.78E-04	1.57E-09	64.9	665	11.7	2.04E+04	1.22E-03	6.00E-08	9.4	0.2	6.9	38.2
	Heavy only	143	-1.8	NB	NB	NB	NB	115	-6.1	NB	NB	NB	NB	Negative Control		
	No DNA	63	-2.1	NB	NB	NB	NB	35	-6.4	NB	NB	NB	NB			

FIG. 20B

36/57

Heavy Chain	Light Chain Mutant	Kinetics at pH 7.4						Kinetics at pH 5.75						Ratio of low pH / neutral pH		
		mAb captured (RU)	50nM Antigen Binding (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t _{1/2} (min)	mAb captured (RU)	50nM Antigen Binding (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t _{1/2} (min)	ka	kd	KD
3	H105	574	12.4	5.64E+04	1.21E-03	2.15E-08	9.5	496	0.1	NB	NB	NB	NB	No binding at Low pH		
	H106	662	16.1	7.37E+04	5.36E-04	7.27E-09	21.5	584	3.0	3.00E+04	4.79E-03	1.58E-07	2.4	0.4	8.9	21.7
	H108	518	12.3	4.82E+04	2.15E-04	4.46E-09	53.7	440	2.2	3.70E+04	1.25E-03	3.40E-08	9.3	0.8	5.8	7.6
	H111	480	9.1	1.82E+04	4.16E-04	2.28E-08	27.7	406	0.4	NB	NB	NB	NB	No binding at Low pH		
	H105/106	487	7.4	1.82E+04	7.45E-03	4.10E-07	1.6	423	-4.1	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H105/108	548	11.8	3.25E+04	5.25E-04	1.62E-08	22.0	468	0.0	NB	NB	NB	NB	No binding at Low pH		
	H105/111	504	7.9	1.06E+04	1.66E-03	1.57E-07	7.0	430	-1.6	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H106/108	487	10.7	6.64E+04	2.91E-04	4.38E-09	39.7	424	-4.2	NB	NB	NB	NB	No binding at Low pH		
	H106/111	563	10.5	2.75E+04	3.71E-04	1.35E-08	31.2	482	-1.9	NB	NB	NB	NB	No binding at Low pH		
	H108/111	528	10.1	1.10E+04	8.01E-05	7.27E-09	144.2	449	-0.5	NB	NB	NB	NB	No binding at Low pH		
	H105/106/108	470	6.4	2.64E+04	5.40E-03	2.04E-07	2.1	412	-5.3	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H105/106/111	539	0.8	NB	NB	NB	NB	462	-5.6	NB	NB	NB	NB	No binding at either pH tested		
	H105/108/111	419	6.5	1.76E+04	4.01E-04	2.27E-08	28.8	354	-3.8	NB	NB	NB	NB	No binding at Low pH		
	H106/108/111	509	3.3	5.47E+04	9.07E-04	1.66E-08	12.7	443	-5.9	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H105/106/108/111	450	-1.1	NB	NB	NB	NB	382	-6.4	NB	NB	NB	NB	No binding at either pH tested		
	ULC + Heavy	688	16.9	3.54E+04	3.57E-04	1.01E-08	32.3	598	5.0	1.19E+04	1.76E-03	1.52E-07	6.6	0.3	4.9	15.0
	Heavy only	152	-1.6	NB	NB	NB	NB	127	-5.4	NB	NB	NB	NB	Negative Control		
	No DNA	54	-1.7	NB	NB	NB	NB	30	-5.6	NB	NB	NB	NB			

FIG. 20C

37/57

Heavy Chain	Light Chain Mutant	Kinetics at pH 7.4						Kinetics at pH 5.75						Ratio of low pH / neutral pH		
		mAb captured (RU)	50nM Antigen Binding (RU)	ka (1/MS)	kd (1/s)	KD (M)	t _{1/2} (min)	mAb captured (RU)	50nM Antigen Binding (RU)	ka (1/MS)	kd (1/s)	KD (M)	t _{1/2} (min)	ka	kd	KD
4	H105	598	4.9	2.80E+04	1.38E-03	4.91E-08	8.4	512	-0.2	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H106	569	7.1	1.49E+04	9.67E-04	6.49E-08	11.9	494	1.2	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H108	587	6.3	2.25E+04	2.02E-03	8.96E-08	5.7	500	-0.9	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H111	606	5.6	3.46E+04	2.19E-03	6.33E-08	5.3	521	-0.9	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H105/106	517	3.1	2.00E+04	2.05E-03	1.03E-07	5.6	460	-1.1	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H105/108	581	2.5	1.61E+05	2.30E-03	1.43E-08	5.0	506	-2.7	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H105/111	575	3.8	1.01E+04	1.70E-03	1.68E-07	6.8	504	-2.0	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H106/108	498	2.5	4.01E+04	6.07E-04	1.51E-08	19.0	447	-3.9	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H106/111	587	3.0	7.85E+04	9.20E-04	1.17E-08	12.6	509	-2.6	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H108/111	599	4.0	9.68E+04	2.02E-03	2.09E-08	5.7	528	-2.6	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H105/106/108	64	-1.7	NB	NB	NB	NB	46	-5.4	NB	NB	NB	NB	No binding at either pH tested		
	H105/106/111	561	1.1	NB	NB	NB	NB	493	-2.8	NB	NB	NB	NB	No binding at either pH tested		
	H105/108/111	521	2.7	7.66E+04	1.29E-03	1.68E-08	9.0	461	-3.2	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H106/108/111	577	1.3	NB	NB	NB	NB	514	-4.2	NB	NB	NB	NB	No binding at either pH tested		
	H105/106/108/111	554	0.6	NB	NB	NB	NB	495	-4.8	NB	NB	NB	NB	No binding at either pH tested		
	ULC + Heavy	585	7.4	5.69E+04	2.01E-03	3.53E-08	5.7	527	1.9	NB	NB	NB	NB	No binding at Low pH		
	Heavy only	187	-2.4	NB	NB	NB	NB	161	-5.4	NB	NB	NB	NB	No binding at Low pH		
	No DNA	49	-2.6	NB	NB	NB	NB	25	-5.6	NB	NB	NB	NB	Negative Control		

FIG. 20D

38/57

Heavy Chain	Light Chain Mutant	Kinetics at pH 7.4						Kinetics at pH 5.75						Ratio of low pH / neutral pH		
		mAb captured (RU)	50nM Antigen Binding (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t _{1/2} (min)	mAb captured (RU)	50nM Antigen Binding (RU)	ka (1/Ms)	kd (1/s)	KD (M)	t _{1/2} (min)	ka	kd	KD
5	H105	522	3.2	5.05E+04	9.48E-03	1.88E-07	1.2	463	-4.3	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H106	496	0.3	NB	NB	NB	NB	437	-5.2	NB	NB	NB	NB	No binding at either pH tested		
	H108	475	-0.1	NB	NB	NB	NB	415	-5.7	NB	NB	NB	NB	No binding at either pH tested		
	H111	523	1.6	NB	NB	NB	NB	463	-4.7	NB	NB	NB	NB	No binding at either pH tested		
	H105/106	534	-0.6	NB	NB	NB	NB	472	-5.5	NB	NB	NB	NB	No binding at either pH tested		
	H105/108	499	2.0	5.80E+04	1.16E-02	1.99E-07	1.0	433	-5.5	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H105/111	489	0.1	NB	NB	NB	NB	426	-4.7	NB	NB	NB	NB	No binding at either pH tested		
	H106/108	441	-0.5	NB	NB	NB	NB	386	-4.2	NB	NB	NB	NB	No binding at either pH tested		
	H106/111	529	-0.8	NB	NB	NB	NB	461	-6.3	NB	NB	NB	NB	No binding at either pH tested		
	H108/111	495	4.1	1.73E+05	1.06E-02	6.11E-08	1.1	435	-4.0	NB	NB	NB	NB	Poor binding at Neutral, No binding at Low pH		
	H105/106/108	505	-1.1	NB	NB	NB	NB	444	-5.5	NB	NB	NB	NB	No binding at either pH tested		
	H105/106/111	499	-1.7	NB	NB	NB	NB	438	-5.8	NB	NB	NB	NB	No binding at either pH tested		
	H105/108/111	436	0.8	NB	NB	NB	NB	388	-3.7	NB	NB	NB	NB	No binding at either pH tested		
	H106/108/111	539	-1.4	NB	NB	NB	NB	477	-4.0	NB	NB	NB	NB	No binding at either pH tested		
	H105/106/108/111	556	-1.6	NB	NB	NB	NB	490	-4.4	NB	NB	NB	NB	No binding at either pH tested		
	ULC + Heavy	516	0.6	NB	NB	NB	NB	451	-5.0	NB	NB	NB	NB	No binding at either pH tested		
	Heavy only	144	-1.3	NB	NB	NB	NB	122	-5.7	NB	NB	NB	NB	No binding at either pH tested		
	No DNA	47	-1.4	NB	NB	NB	NB	25	-5.8	NB	NB	NB	NB	Negative Control		

FIG. 20E

39/57

V_H	V_K	K_D at pH7.4 (nM)	K_D at pH5.75 (nM)	$T_{1/2}$ at pH7.4 (min)	$T_{1/2}$ at pH5.75 (min)
2	Parental ULC	1.6	60	65	9.4
2	ULC (His105,106)	3.4	570	39	1.8
2	ULC (His105,111)	4.1	1270	32	0.9
2	ULC (His105,108,111)	3.2	NB	40	NB
2	ULC (His105,106,108)	5.2	NB	27	NB
3	Parental ULC	10.1	152	32	6.6
3	ULC (His106,108)	4.4	NB	40	NB
3	ULC (His108,111)	7.3	NB	144	NB
6	Parental ULC	3.0	2.4	10	6
6	ULC (His105,111)	3.5	NB	9	NB
6	ULC (His106, 108,111)	2.0	NB	16	NB

FIG. 21

Site-directed mutagenesis primers for Histidine substitutions in CDR3 of Universal Light Chain of hVK1-39JK5

Primer name	Sequence	%GC	N	%mismatch	Tm
GERMLINE hVH1-39/JK5	CAACTTACTACTGTCAACAGAGT TACAGTACCCCTCCGATCACCTTCGGC				
1633-H106/108/111 F	CTTACTACTGTCAACA T AGT C ACAGTACCC A TCCGATCACCTTCG	47.0	45	6.7	79.0
1633-H105/106/108/111 F	CAACTTACTACTGTCA CCA TAGT C ACAGTACCC A TCCGATCACCTTCGGC	50.0	50	8.0	80.5
1633-H106/108/111 R	CGAAGGTGATCGGATGGGTACTGT G ACT A TGTTGACAGTAGTAAG	47.0	45	6.7	79.0
1633-H105/106/108/111 R	GCCGAAGGTGATCGGATGGGTACTGT G ACT A TGTTGACAGTAGTAAGTTG	50.0	50	8.0	80.5

Primer	SEQ ID NO
GERMLINE hVK1-39/JK5	405
1633-H106/108/111 F	358
1633-H105/106/108/111 F	359
1633-H106/108/111 R	360
1633-H105/106/108/111 R	361

FIG. 22

Construction of VK1-39 HULC LTVECs

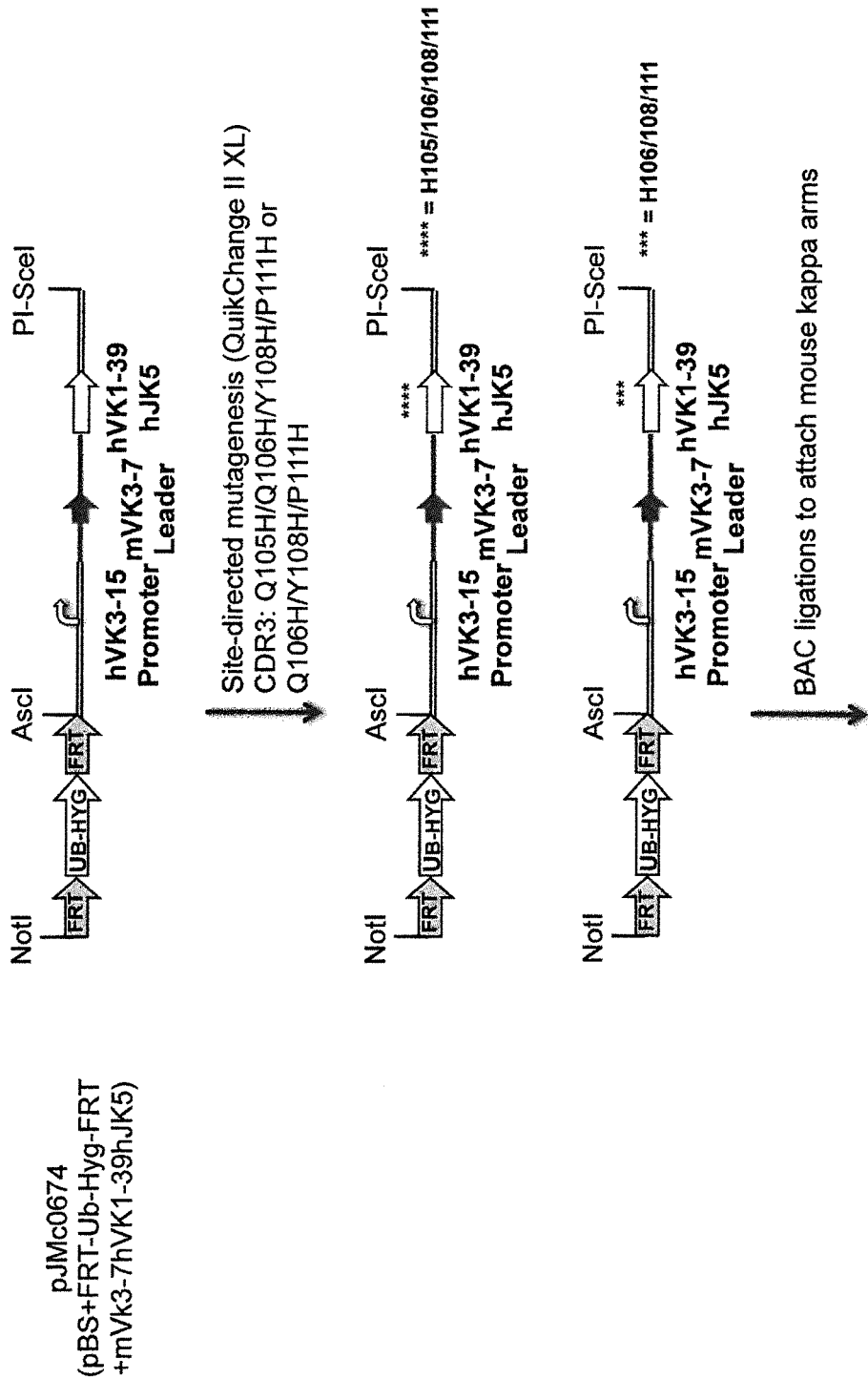
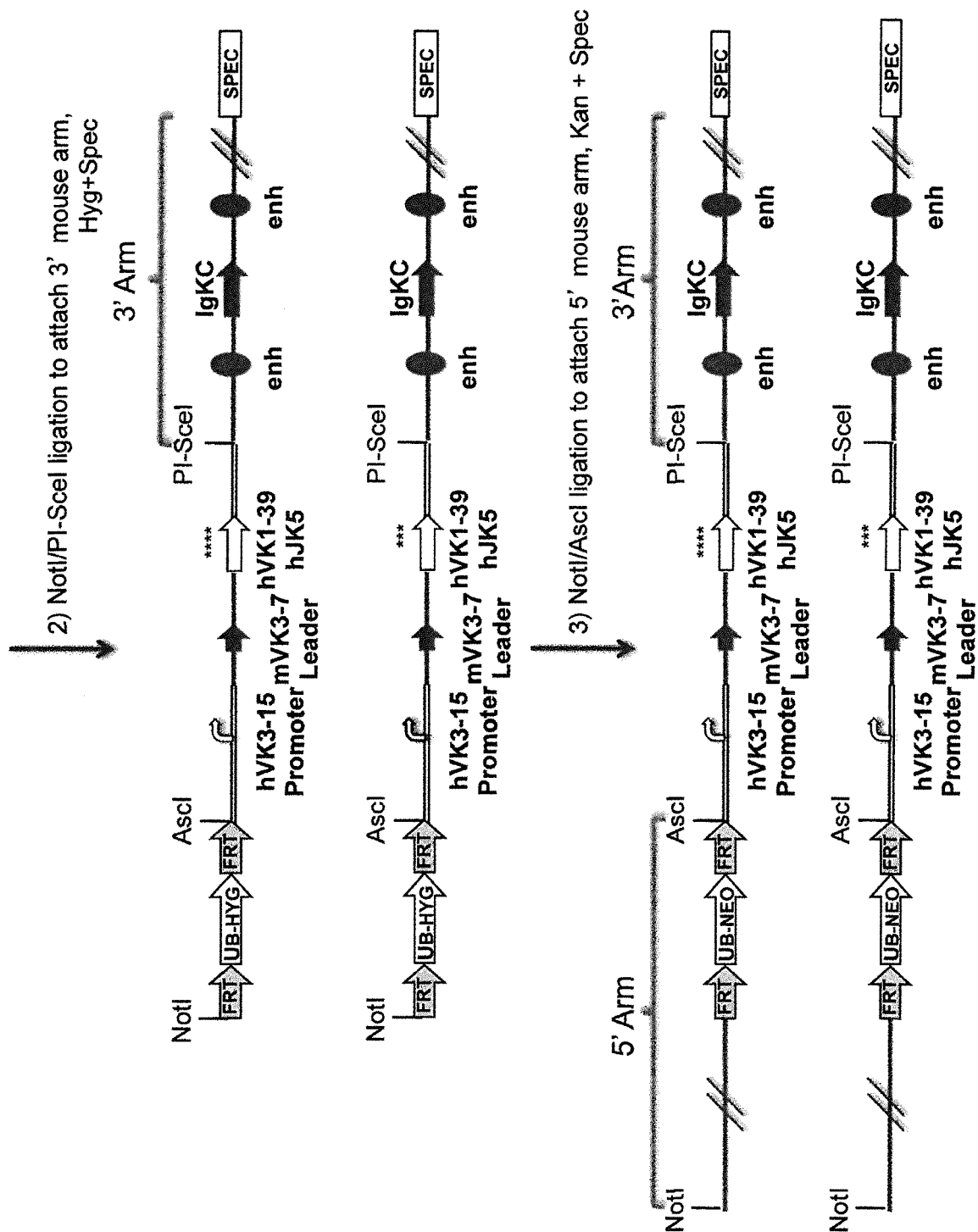


FIG. 23A

42/57



(ULC-H105/106/108/111)

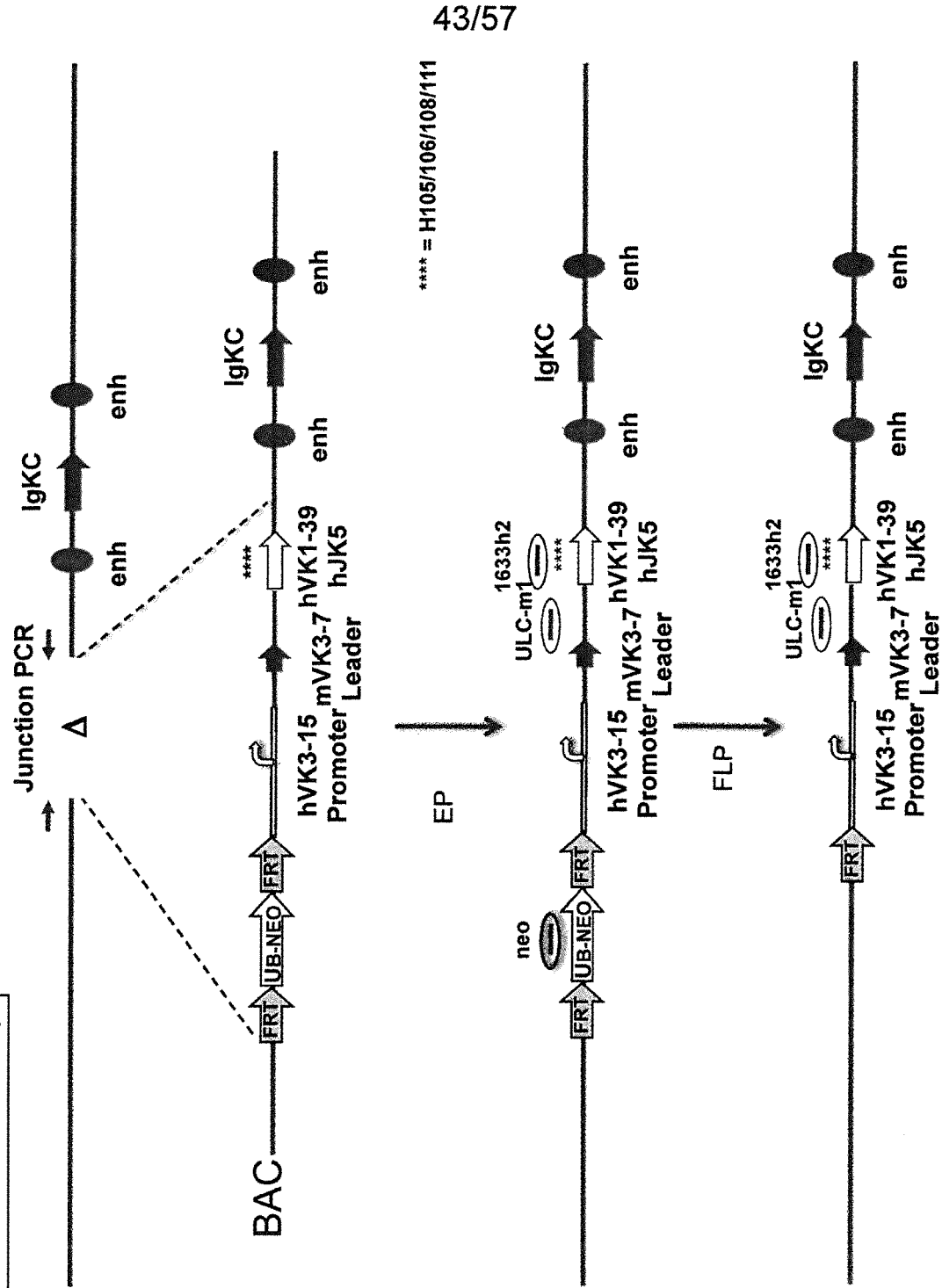


FIG. 23C

(ULC-H105/106/108/111)

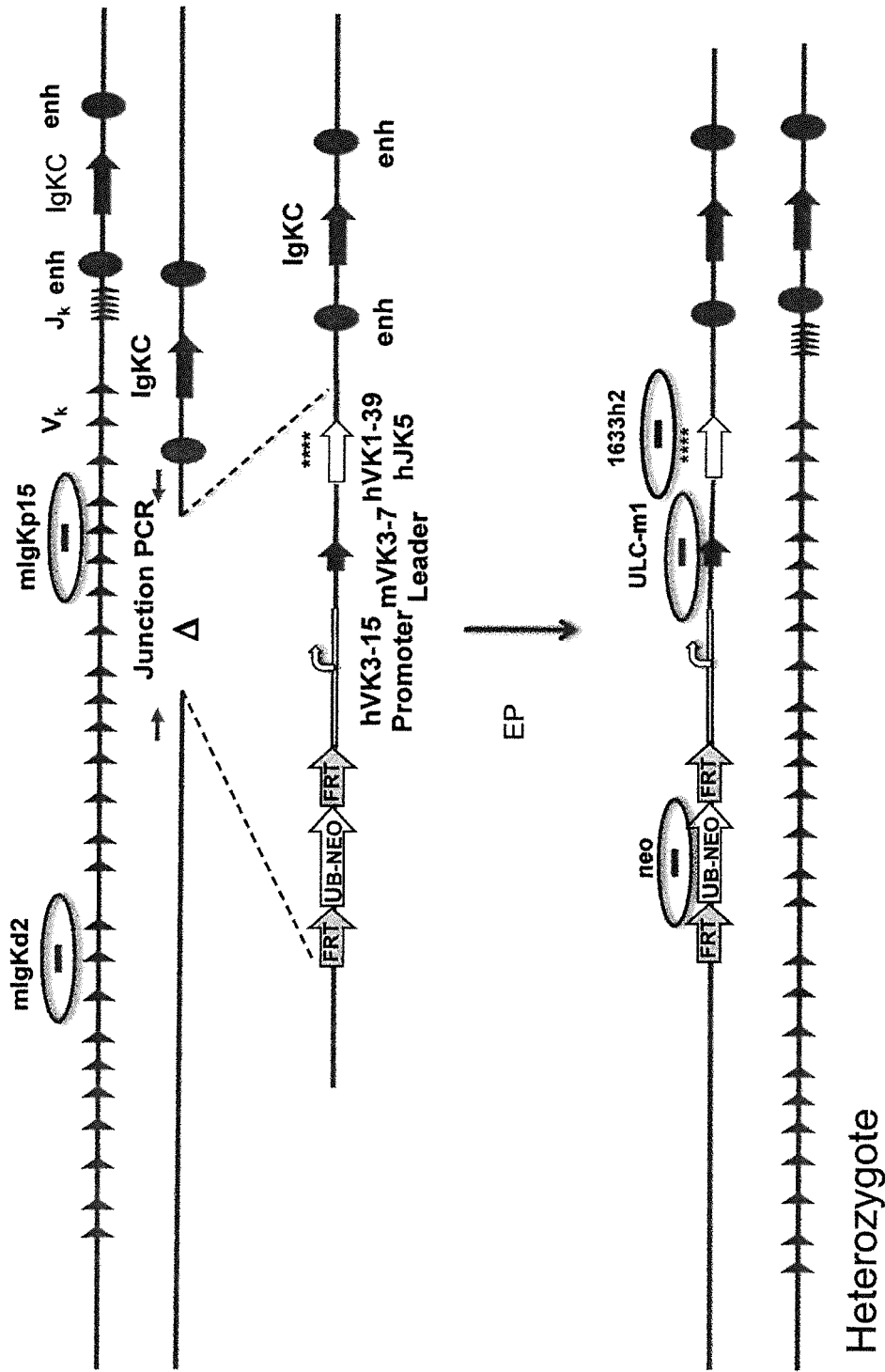


FIG. 23D

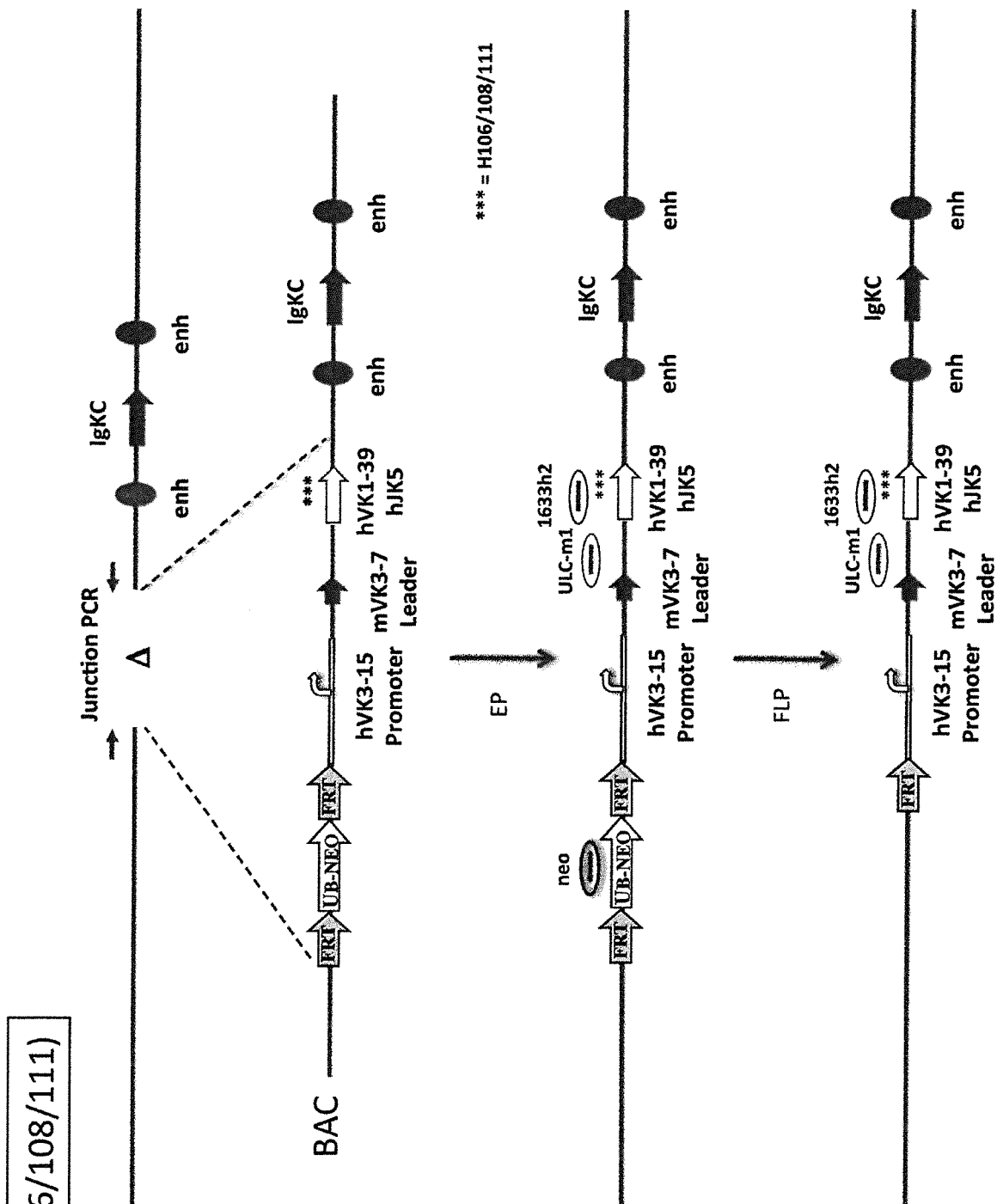


FIG. 23E

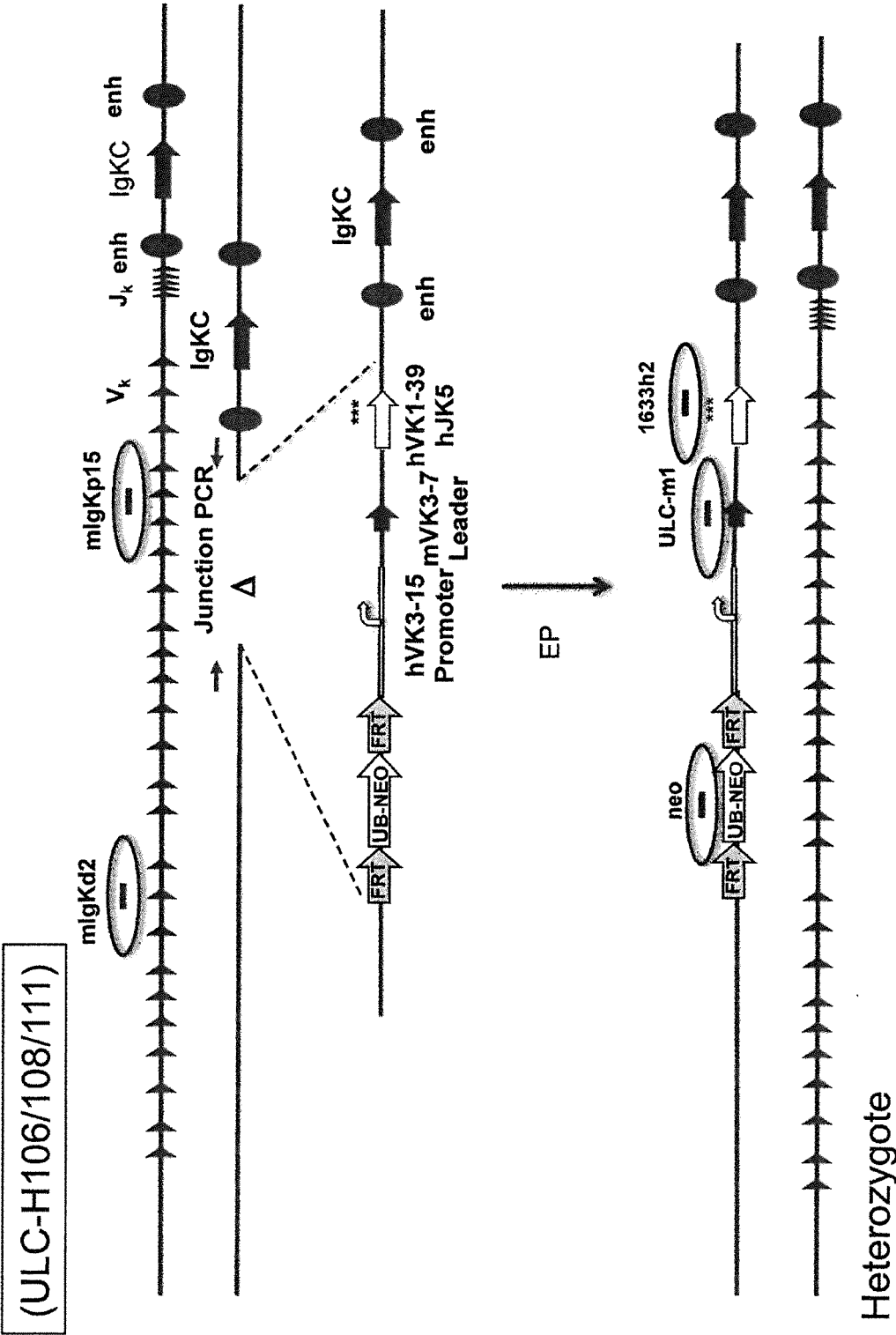


FIG. 23F

47/57

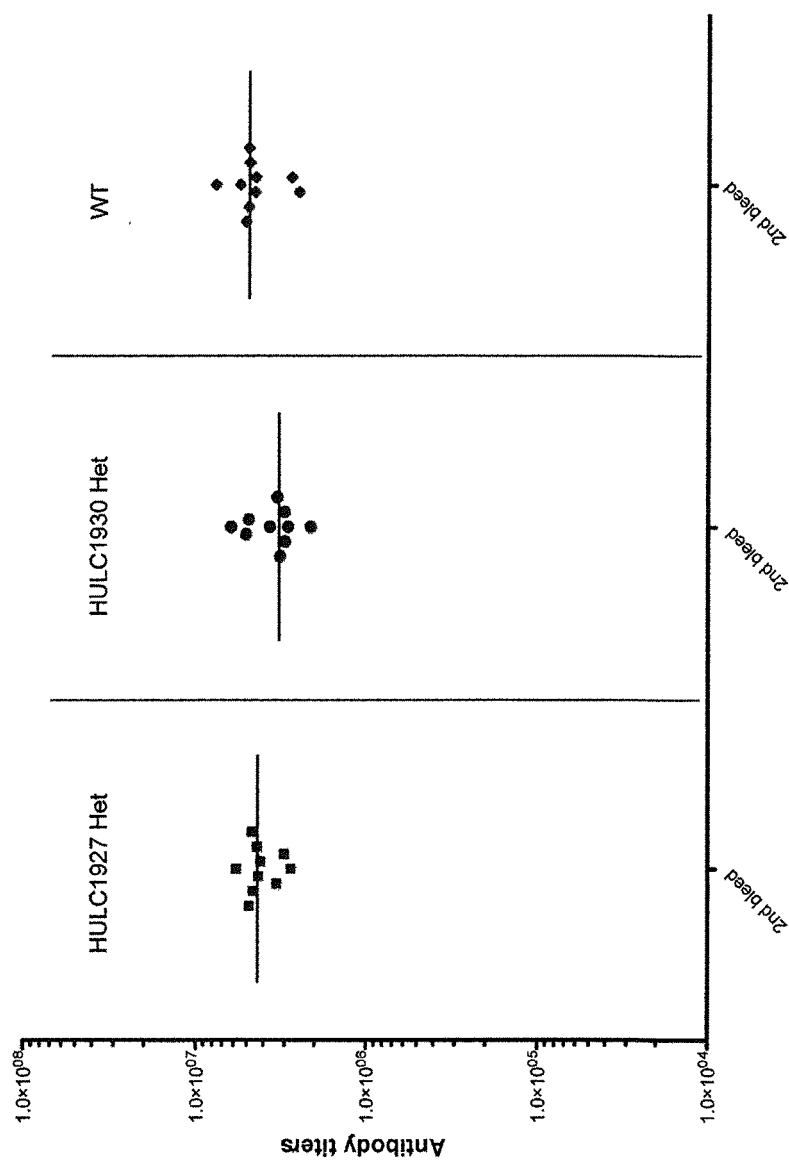


FIG. 24

48/57

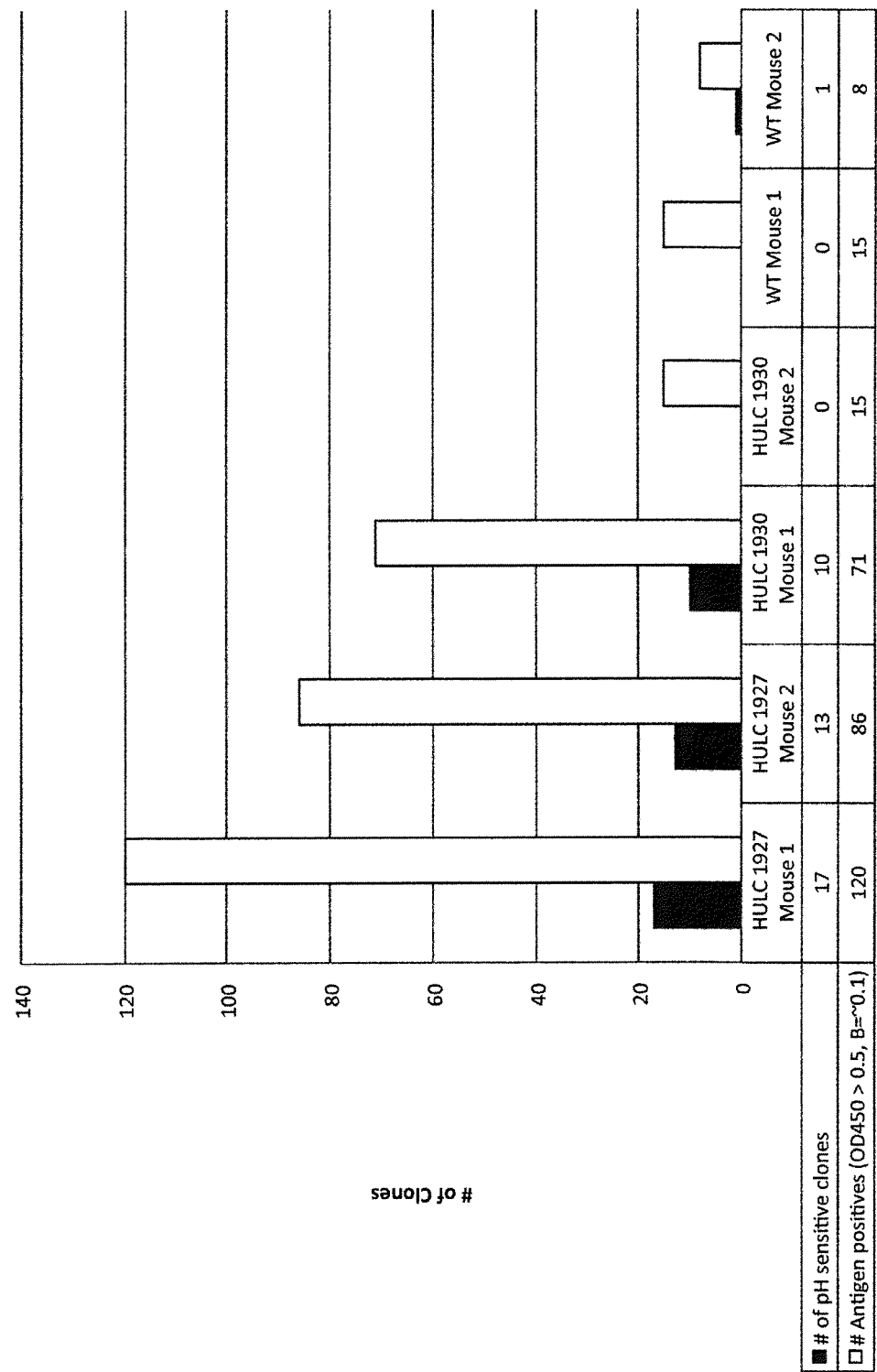


FIG. 25

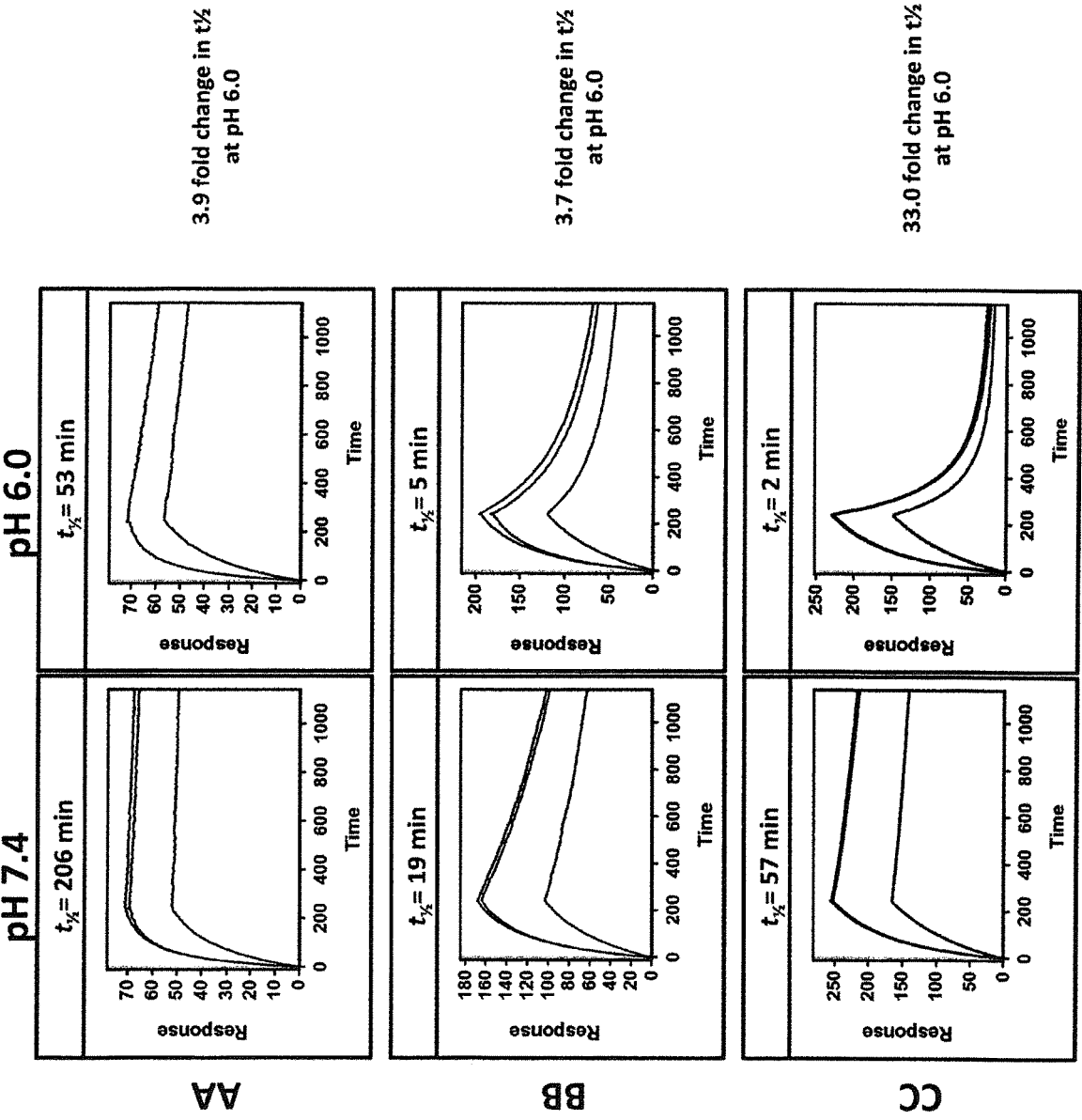


FIG. 26A

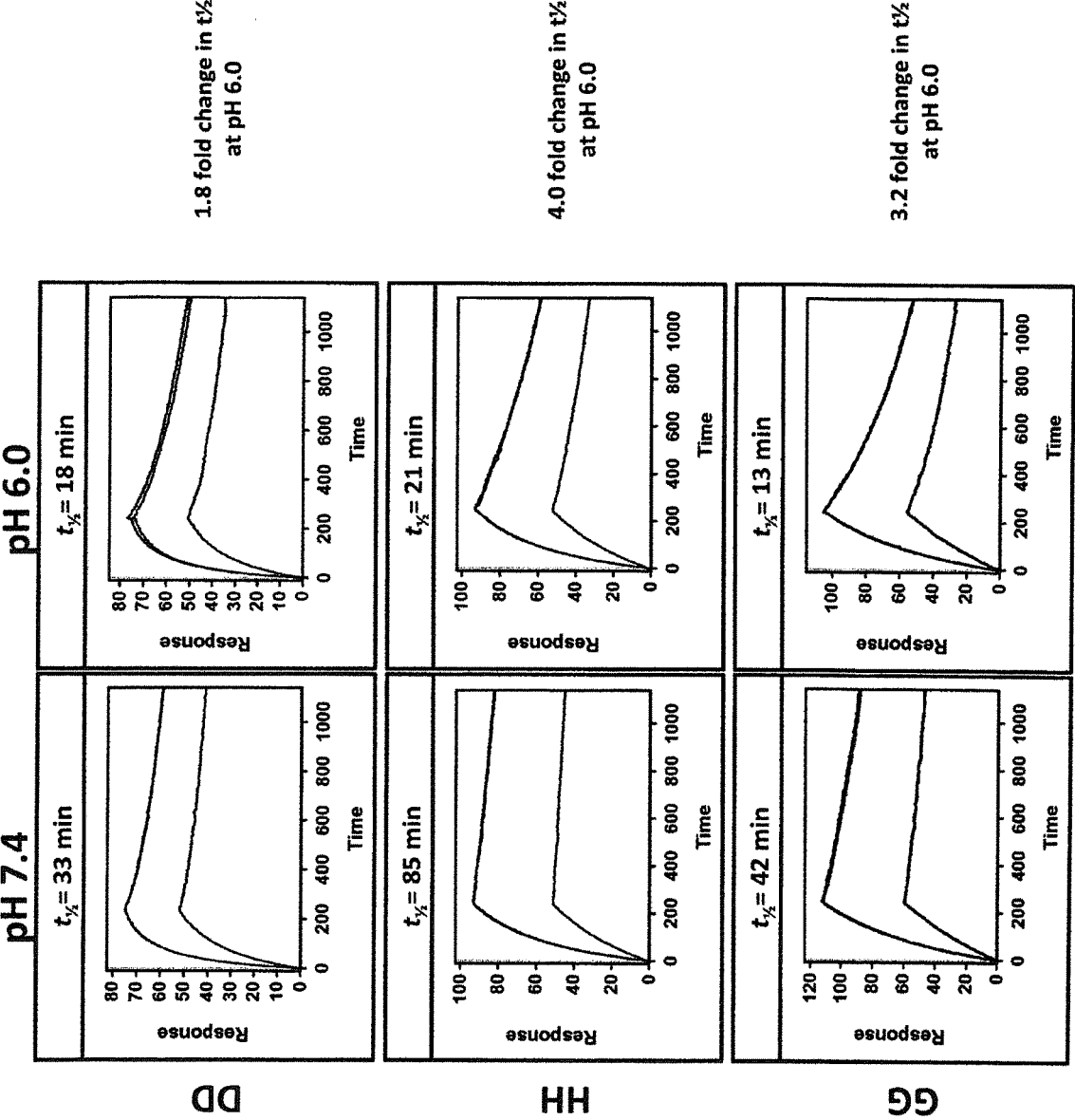


FIG. 26B

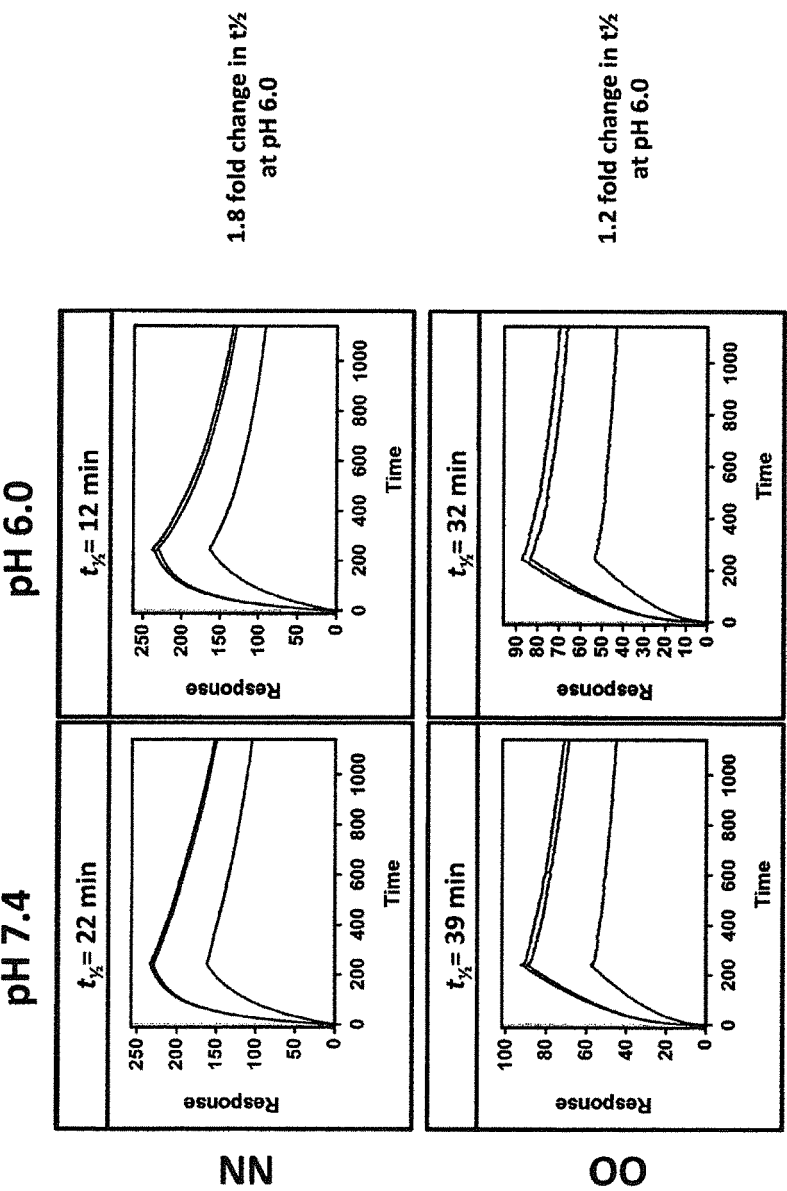


FIG. 26C

WT	105	106	107	108	109	110	111	
	Q	Q	Y	G	S	S	P	SEQ ID NO:399
	CAG	CAG	TAT	GGT	AGC	TCA	CCT	SEQ ID NO:398
H105/106/107/109	H	H	H	G	H	S	P	SEQ ID NO:401
	CAT	CAC	CAT	GGT	CAC	TCA	CCT	SEQ ID NO:400
H105/106/109	H	H	Y	G	H	S	P	SEQ ID NO:403
	CAT	CAC	TAT	GGT	CAC	TCA	CCT	SEQ ID NO:402

FIG. 27

Site-directed mutagenesis primers for Histidine substitutions in CDR3 of VK3-20JK1 ULC plasmid

Primer name	Sequence	%GC	N	mismatches	Tm
GERMLINE hVK3-20	GATTTTCAGTGTATTACTGTCAAGCAGTATGGTAGCTCACCTTGGACGTTTCGGC				
hVK3-20 (H105/106/107/109) F	GATTTTCAGTGTATTACTGTCAATCAACCATGGTCACTCACCTTGGACGTTTCGGC	48	54	5	79.5
hVK3-20 (H105/106/107/109) R	GCCGAACGTCCAAGGTGAGTCAACCATGGTATGACAGTAATACACTGCAAAATC	48	54	5	79.5
hVK3-20 (H105/106/109) F	GCAGTGTATTACTGTCAATCACTATGGTCACTCACCTTGGACGTTTCGG	49	47	4	78.7
hVK3-20 (H105/106/109) R	CCGAACGTCCAAGGTGAGTCAACCATAGTATGACAGTAATACACTGC	49	47	4	79.7

53/57

Primer	SEQ ID NO
GERMLINE hVK3-20/JK1	384
hVK3-20 H105/106/107/109 F	385
hVK3-20 H105/106/107/109 R	386
hVK3-20 H105/106/109 F	387
hVK3-20 H105/106/109 R	388

FIG. 28

Construction of VK3-20 HULC LTVECs

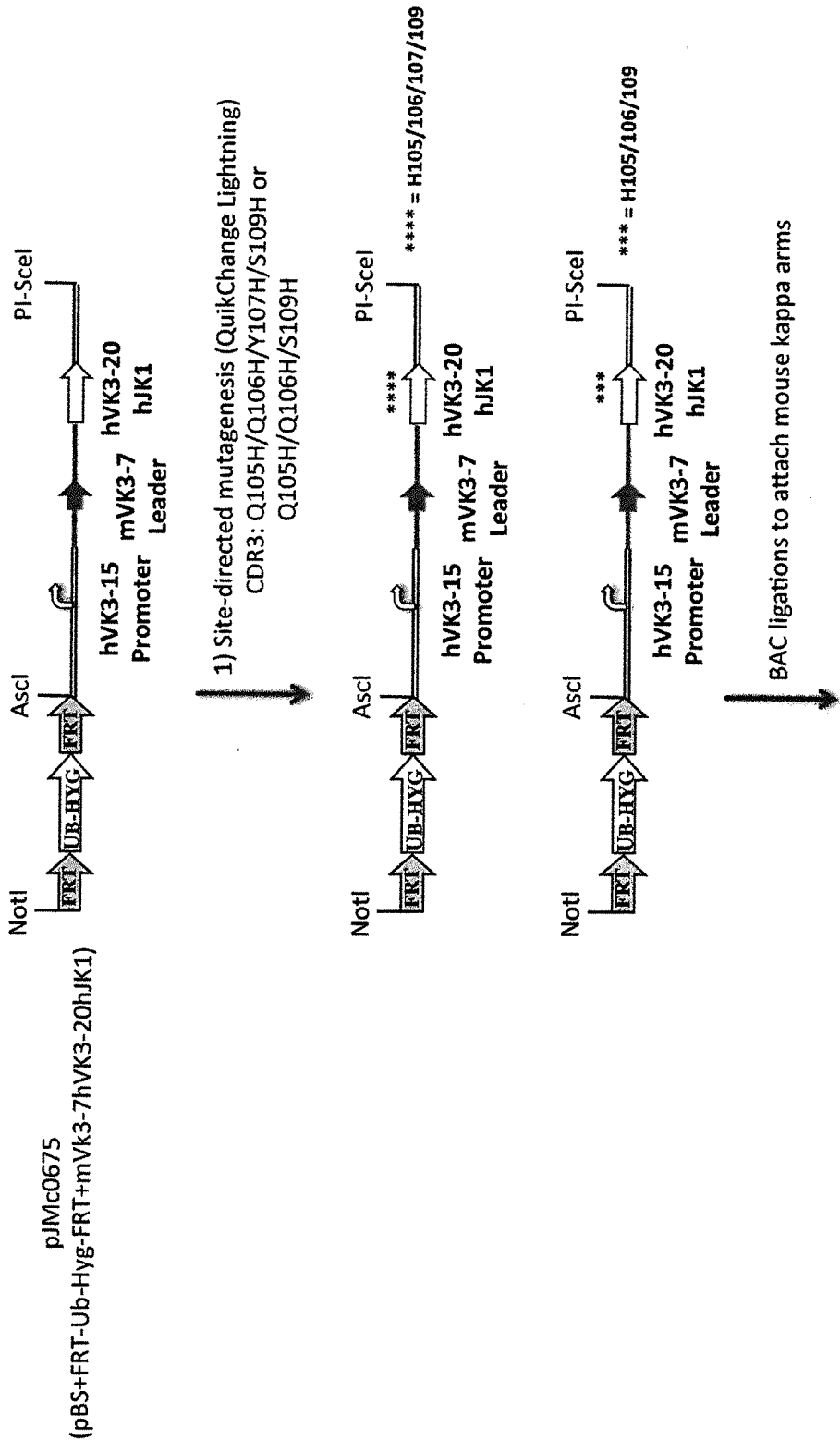
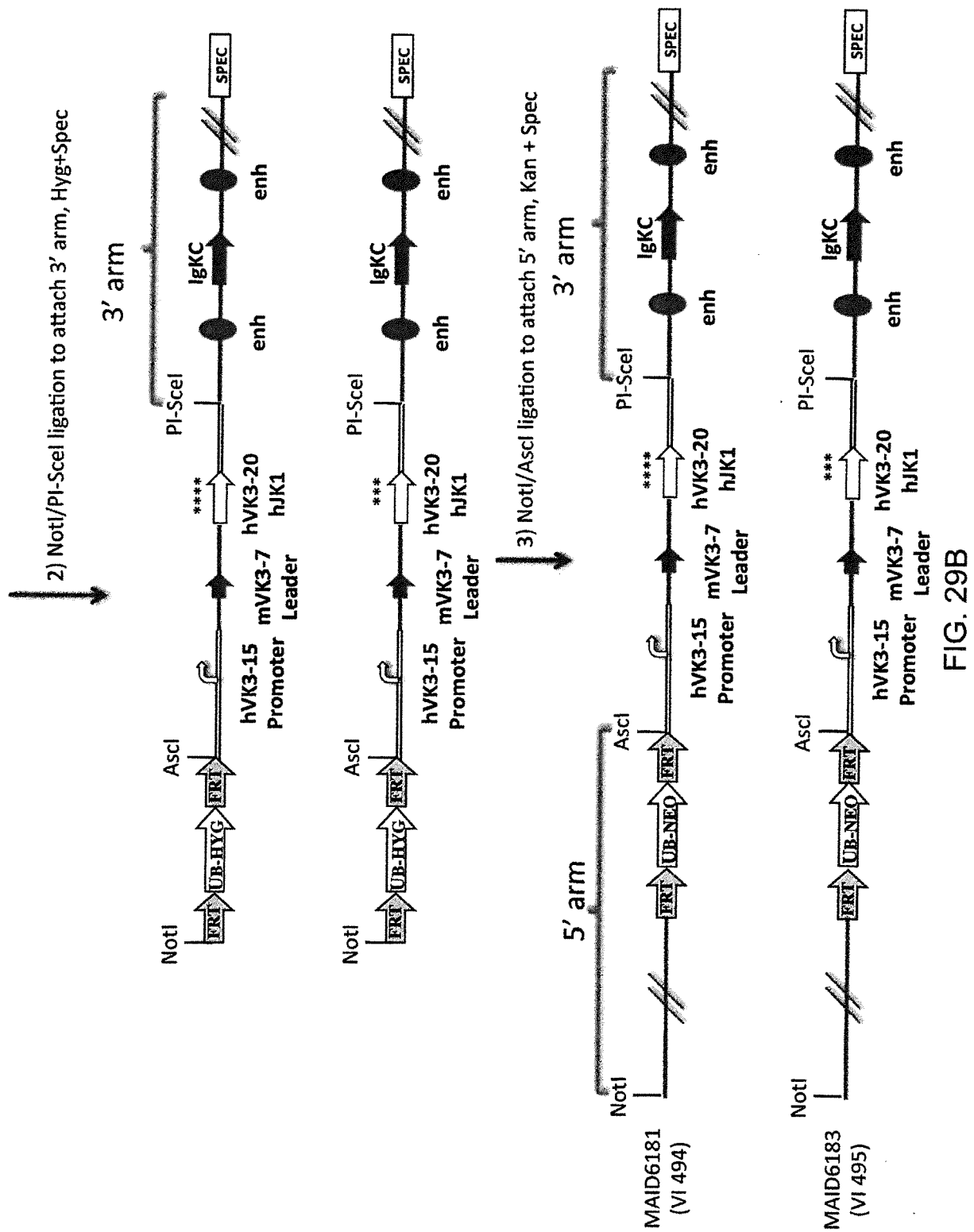
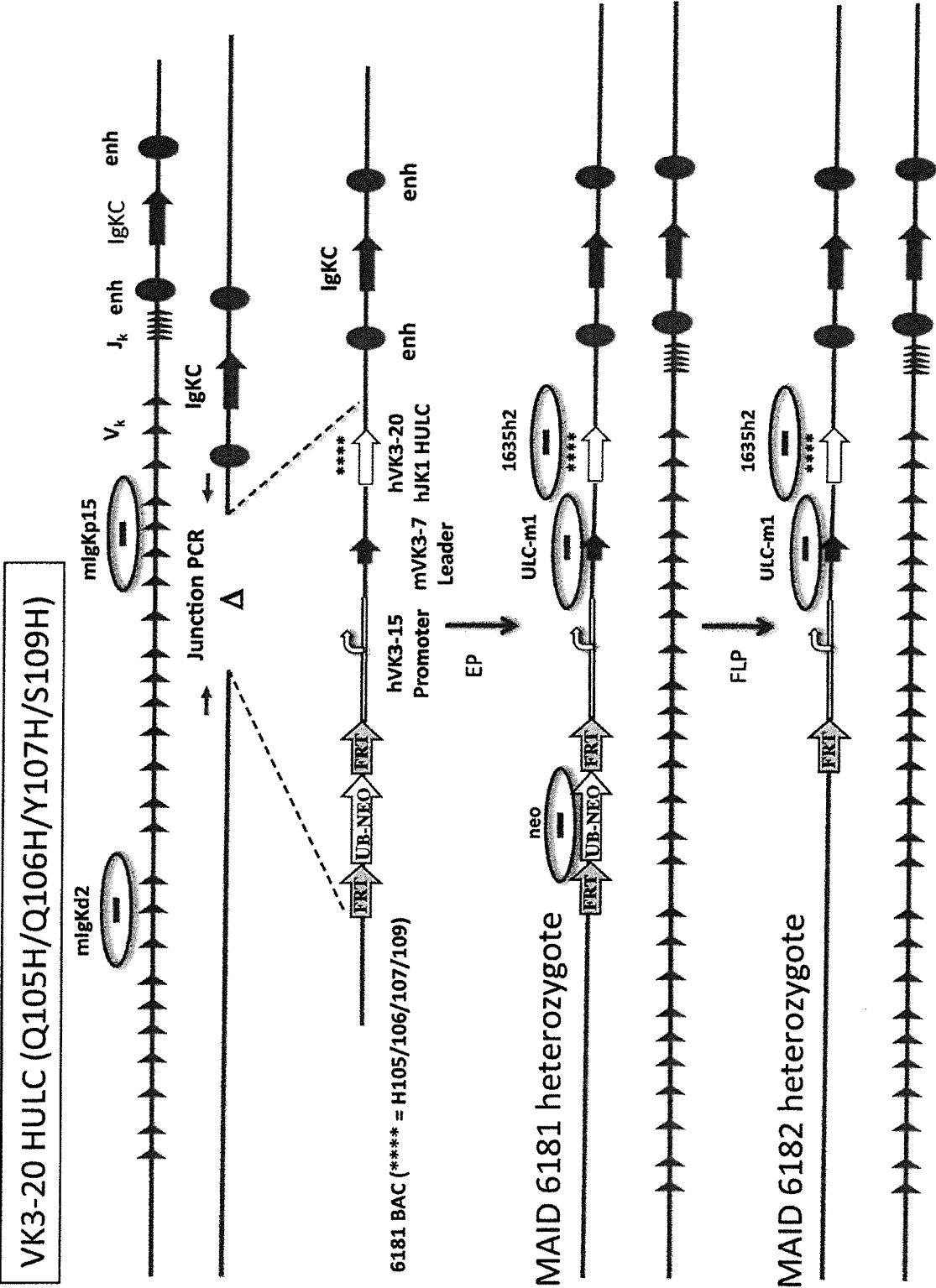


FIG. 29A





57/57

