

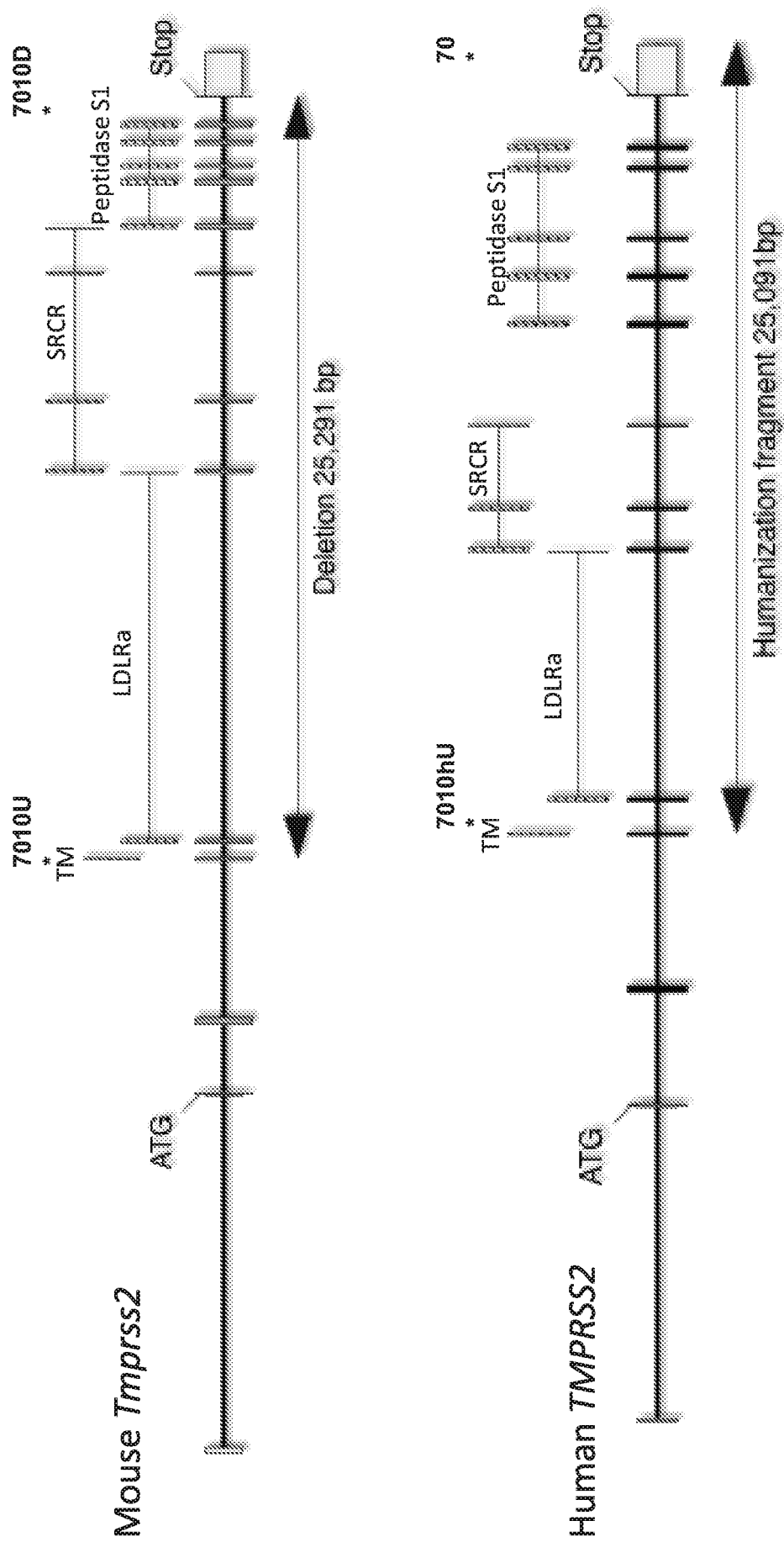
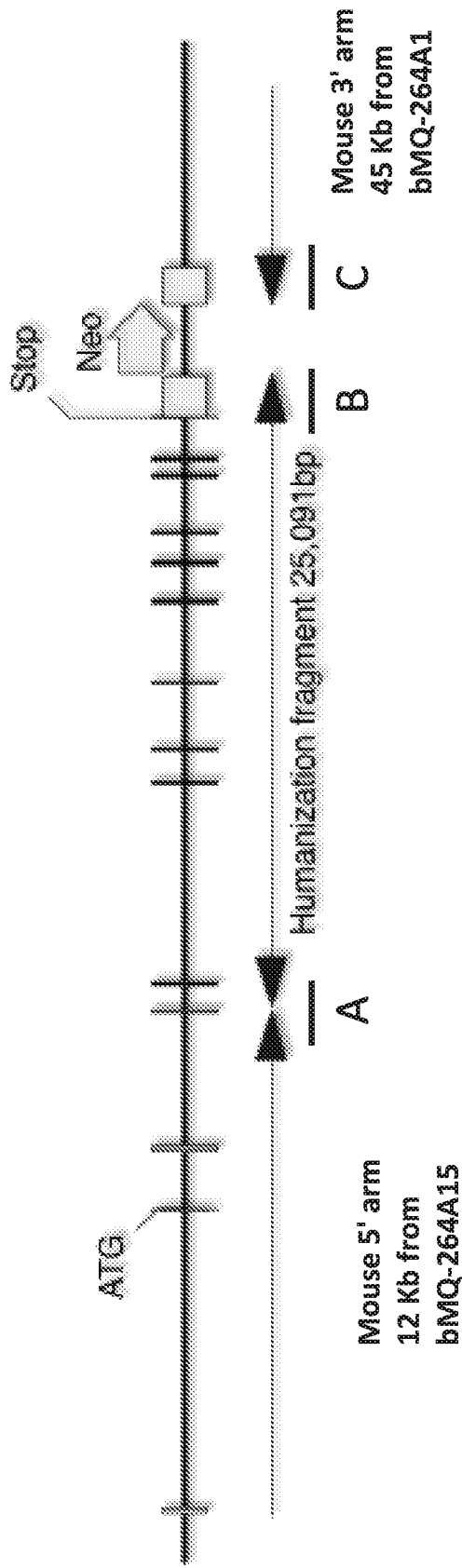
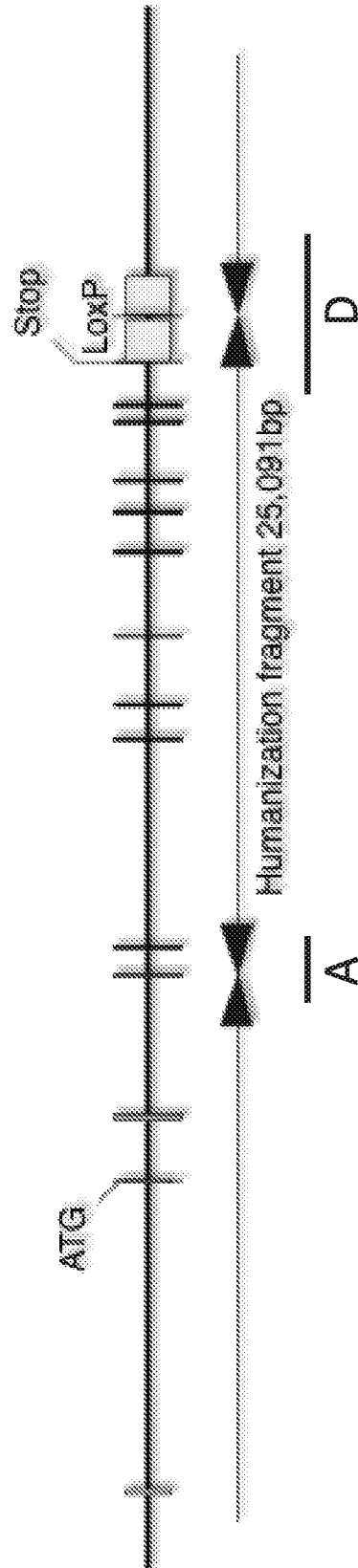


Figure 1A



A. 5' mouse // 5' human (SEQ ID NO:22)	AGACCCCTC TCCTCCGAG AGCTAAGAA ATCGTGTGT TTAGCCCTCG CCCTGGGCAC TGTCCTCACG GGAGCTGCTG TGGCTGCTGT CTTGCTTTGG // AAGTTCAGTA AGTGCAGGGA GCCTCGATCC CACCATGTGC TCCTGCAGTC CCCAGTGCTC TGAGCCAGAC CCTGCTCTCT GGGCTATTGA GACCTCTGGA GGCCCTCCGT GAGGTTCCCTC TCTTACATAA CGAGGCTGTC TCTCTCCCT TCTCTTG
B. human// <u>XhoI</u> //(<u>loxP</u>) Cassette (SEQ ID NO:23)	GGTCAGAGGA CCAAAGGTGA GGCAAGGCCA GACTTGGTGC TCCTGTGGTT// <u>CTCGAG</u> // <u>ATAACTTCG</u> <u>TATAATGTAT</u> <u>GCTATACGAA</u> <u>GTAT</u> ATGCATGGCC TCCGCGCCGG GTTTTGGCGC CTCGCCGGG CGCCCCCCTC CTCACGGCGA GCGCTGCCAC GTCAGACGAA GGGCGCAGCG AGCGTCTCTGA
C. Cassette (<u>loxP</u>)/ICEU1// <u>NheI</u> // mouse (SEQ ID NO:24)	ATTGTTTTGC CAAGTTCTAA TTCCATCAGA CCTCGACCTG CAGCCCCCTAG <u>ATAACTTCGT</u> <u>ATAATGTATG</u> <u>CTATACGAAG</u> <u>TTAT</u> / GCTAGTAACATAACGGTCCTAAGGTAGCGA // <u>GCTAGC</u> // TCCACGTGGC TTTGTGCCAG ACTTCCCTTG TCTTCAACAA CCTTCTGCAA

Figure 1B



A. 5' mouse // 5' human (SEQ ID NO:22)	AGCACCCCTC TCCTCCGCAG AGCTAAGAA ATCGCTGTGT TTAGCCCTCG CCCTGGGCAC TGTCCTCACG GGAGCTGCTG TGGCTGCTGT CTTCCTTTGG // AAGTTCAGTA AGTGCAGGGA GCCTCGATCC CACCATGTGC TCCTGCAGTC CCCAGTGCTC TGAGCCAGAC CCTGCTCTCT GGGCTATTGA GACCTCTGGA GGCCCTCCGT GAGGTTCCCTC TCTTACATAA CGAGGCTGTC TCTCTTCCCT TCCTTG
D. human// <u>XhoI</u> //(<u>loxP</u>) /ICEUI// <u>NheI</u> // mouse (SEQ ID NO:25)	GGTCAGAGGA CCAAAGGTGA GGCAAGGCCA GACTTGGTGC TCCTGTGGTT// CTCGAG //ATAACTTCG TATAATGTAT GCTATACGAA GTTAT /GCTAGTAACTATAACGGTCTAAGGTAGCGA // GCTAGC // TCCACGTGGC TTTGTCCCAG ACTTCCTTTG TCTTCAACAA CCTTCTGCAA

Figure 1C

	70	80	90	100	110	120
hTmPrSS2	SNPVVCTQPKSPSGTVCTSKTKKALCITLTGLTFLVGAALAAAGLLWKFMG	SKCSNSGIEC				
mTmprss2	STSVIHThPKS-SGALCTSKSKSLCLALALGTVLTGAAVAALLWRFWD	SNCSSTSEMEC				
7010 mutant pro	STSVIHThPKS-SGALCTSKSKSLCLALALGTVLTGAAVAALLWKFMG	SKCSNSGIEC				

	130	140	150	160	170	180
hTmPrSS2	DSSGTCINPSNWC	DGVSHCPGG	EDENRCVRL	YGPNFILQ	VYSSQ	RKSWHPVCQDDWN
hTmTmPrss2	GSSGTCISSSLWC	DGVAHCPNG	EDENRCVRL	YGQSFILQ	VYSSQ	RKAWYPVCQDDWSESY
hTm7010 mutant	DSSGTCINPSNWC	DGVSHCPGG	EDENRCVRL	YGPNFILQ	VYSSQ	RKSWHPVCQDDWN

	190	200	210	220	230	240
hTMPRSS2	GRAACRDMGYKNNFYSSQGI	VDDSGST	FMKINTS	AGNVDI	YKKLYHSD	ACSSKAVVSLR
mTmprss2	GRAACKDMGYKNNFYSSQGI	PDQSGAT	FMKLNVS	SGNVDLY	KKLYHSD	SCSSRMVVSLR
77010 mutant pro	GRAACRDMGYKNNFYSSQGI	VDDSGST	FMKINTS	AGNVDI	YKKLYHSD	ACSSKAVVSLR

	250	260	270	280	290	300
hhTMRSS2	CIACGVNLSSRQSRIVGGESALPGAWPQVSLHVQNVHVC	CGSIITPEWIVTAAHCVEK				
Tmprss2	CIIEGVRSLVKRQSRIVGGLNASPGDWPQVSLHVQGVHVC	CGSIITPEWIVTAAHCVEE				
TmTmprss2	CIACGVNLSSRQSRIVGGESALPGAWPQVSLHVQNVHVC	CGSIITPEWIVTAAHCVEK				
7010 mutant pro	CIACGVNLSSRQSRIVGGESALPGAWPQVSLHVQNVHVC	CGSIITPEWIVTAAHCVEK				

Turn 1D

[illegible]

Figure 1D (Continued)

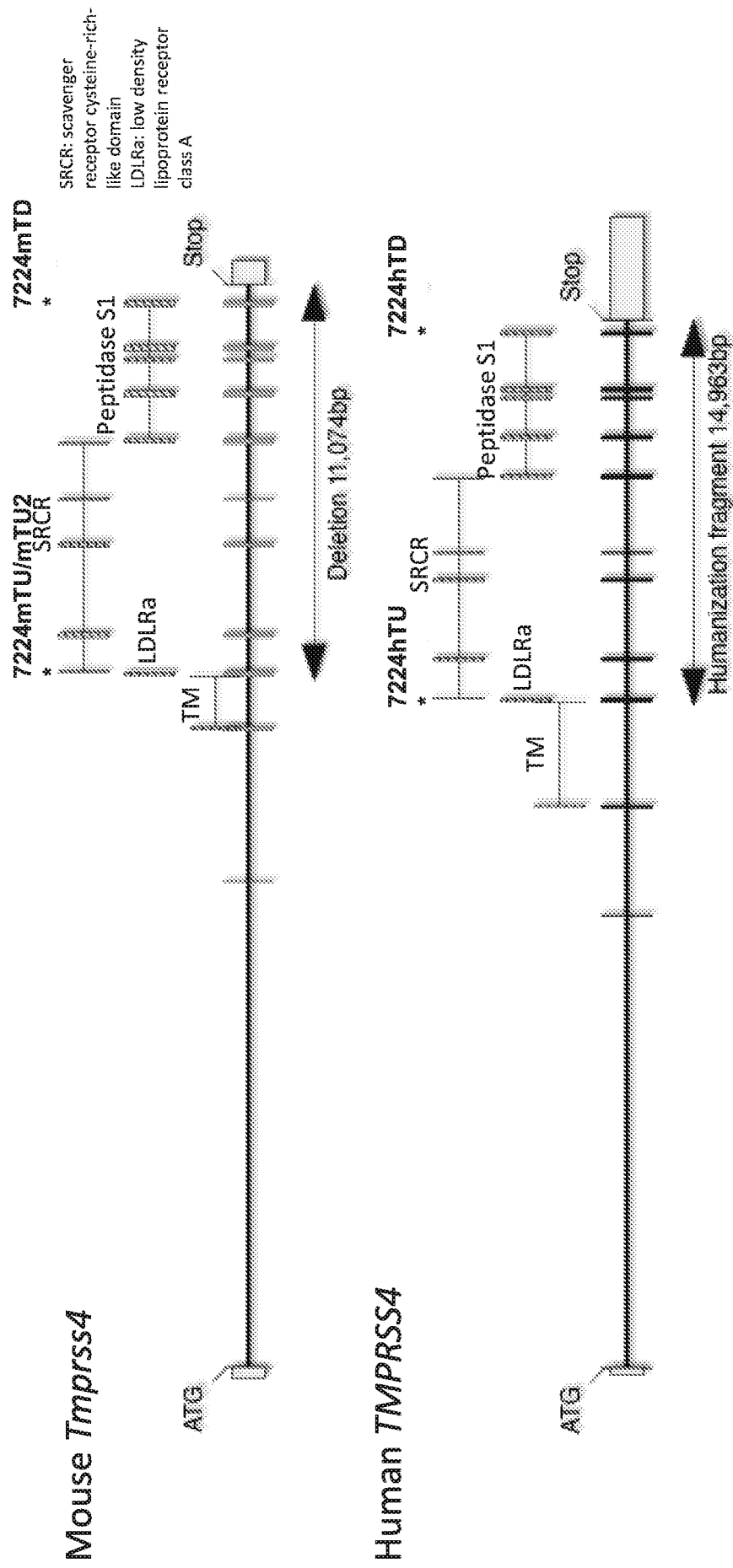
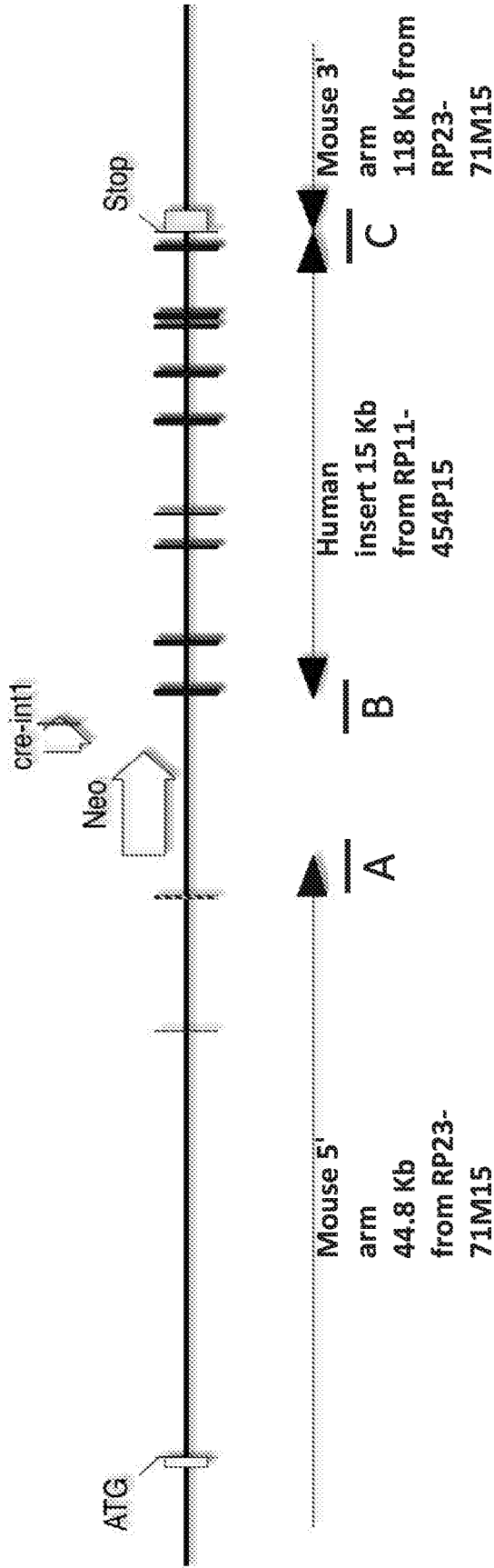
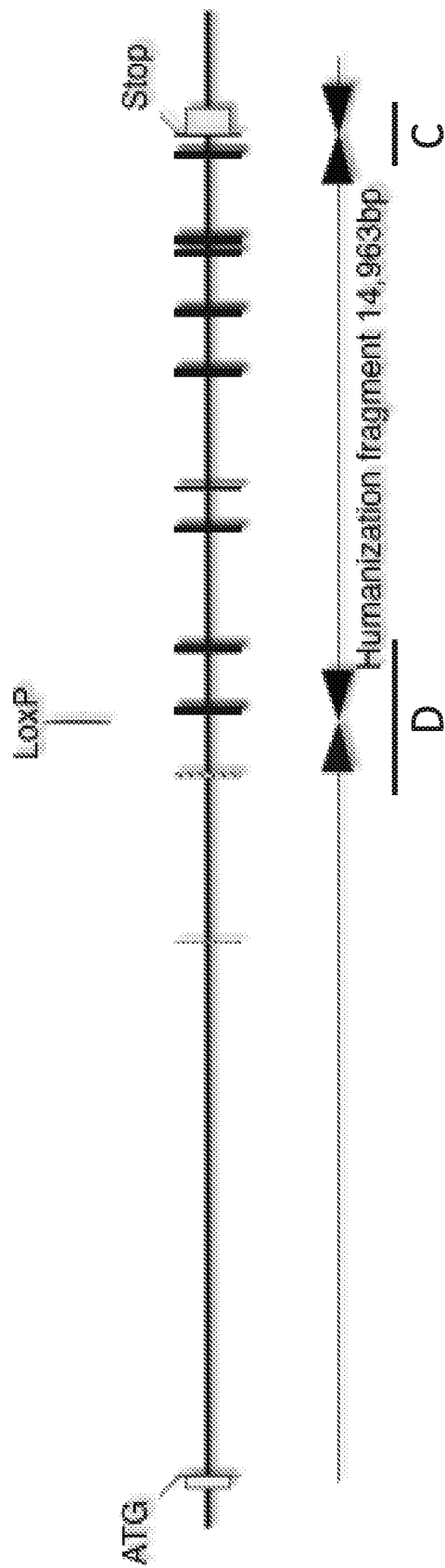


Figure 2A



A. mouse// SaII-XhoI //(<i>loxP</i>) Cassette (SEQ ID NO:38)	CCAGTCAGGG ACACACATGC TCACAGGCC GCCACCCGC ACACACTACA //GTGAG //ATAACTTCGT ATAAIGTATG CTATACGAAG TTAI ATGCATGGCC TCCGGCCGG GTTTTGCGC
B. Cassette (<i>loxP</i>)/ICEUI// NheI //human (SEQ ID NO:39)	ATTCTAGTTG TGGTTTGTC AACATCATCA ATGTAICTTA TCATGCTGG AATAACTTCGTATAATGTAATGCTATACGAAGTTAT/GCTAG / TAACTATAACGGTCCTAAGGTAGCGA //GCTAGC// CAAGTCTGTG TGCTACCAAG TAGCAAACT GAGCCTGGAA CTCACACATG CGTGTCTGAG AGCCCAGCAC TATCGC
C. human//mouse (SEQ ID NO:40)	TAATCTGACT TTCTCTTCAT CGGTCTCTCT TATTCTAGGC TGAGCTGTAA //CGCTGCCGTC CCCCACATCC AGAAGCTGCT TCCCTTCAGA CCTACCTACG

Figure 2B



D. mouse// Sall /Xh oI//(<i>loxP</i>) /ICEUI// NheI // human (SEQ ID NO:41)	CCAGTCAGGG ACACACATGC TCACACGCCG GCCACCCGC ACACACTACA // GTCGAG //ATAACTTCG TATAATGIAT GCTATACGAA GTTAT /GCTAGTAACTATAACGGTCCTAAGGTAGCGA// GCTAGC // CAAGTCTGTG TGCTACCAAG TAGCAAAACT GAGCCTGGAA CTCACACATG
C. human//mouse (SEQ ID NO:40)	TAATCTGACT TTCTCTTCAT CCGTCTCTCT TATTCTAGGC TGAGCTGTAA // CGCTGCCGTC CCCCACATCC AGAAGCTGCT TCCCTTCAGA CCTACCTACG

Figure 2C

Tmprs4 protein alignment

	10	20	30	40	50	60
hTMPRSS4	MLQDPDS	DQPLNSLDV	KPLRKPRIP	MTETFRKVG	IIPIIA	LLSLASIIIVVVLK
mTmprs4	MESDSGQ	PLNNRDI	VPFRKPRRP	QETFKVGI	PIIAVLLS	LIALLIKVILDKY
7224 mutant pro	MESDSGQ	PLNNRDI	VPFRKPRRP	QETFKVGI	PIIAVLLS	LIALLIKVILDKY
	..	****	*. *	****	* ****	*****
	70	80	90	100	110	120
hTMPRSS4	YFLCGQPLH	FIPRKQLCD	GELDCPL	GEDEEHCV	KSFPEGPA	VAVRLSKDRSTLQV
mTmprs4	YFICGSPLT	FIQRGQLCD	GHLDCA	SGEDEEHCV	KDFPEKPG	VAVRLSKDRSTLQV
7224 mutant pro	YFLCGQPLH	FIPRKQLCD	GELDCPL	GEDEEHCV	KSFPEGPA	VAVRLSKDRSTLQV
	***	***	***	***	***	***
	130	140	150	160	170	180
hTMPRSS4	GNWFSACF	DNFTEALAE	TACRQMG	YSKKPTF	RAVEIGPD	QDLDVVEITENSQEL
mTmprs4	GTWASVCF	DNFTEALAK	TACRQMG	YDSQPA	RAVEIRPD	QNLPPVAQVTGNSQEL
7224 mutant pro	GNWFSACF	DNFTEALAE	TACRQMG	YSKKPTF	RAVEIGPD	QDLDVVEITENSQEL
	***	***	***	***	***	***
	190	200	210	220	230	240
hTMPRSS4	GPCLSGSLV	SLHCLACG	KS	SLKTPRV	VVGGEAS	VDSWPWQVSIQYDKQHVCGGSILDP
mTmprs4	RSCLSGSLV	SLRCLDCG	KS	SLKTPRV	VVGVEAP	VDSWPWQVSIQYNKQHVCGGSILDP
7224 mutant pro	GPCLSGSLV	SLHCLACG	KS	SLKTPRV	VVGVEAS	VDSWPWQVSIQYDKQHVCGGSILDP
	*****	*****	*****	*****	*****	*****
	250	260	270	280	290	300
hTMPRSS4	LTAAHCFER	KHTDVF	NWKVRAGS	DKLGSE	FP	SLAVAKIIIEFNPMYPKDN
mTmprs4	LTAAHCFER	KYLDV	SSWKVRAGS	NI	LGNSP	SLPVAKIFIAEPNPLYPKEDIALVKLQ
7224 mutant pro	LTAAHCFER	KHTDVF	NWKVRAGS	DKLGSE	FP	SLAVAKIIIEFNPMYPKDN
	*****	*****	*****	*****	*****	*****

Figure 2D

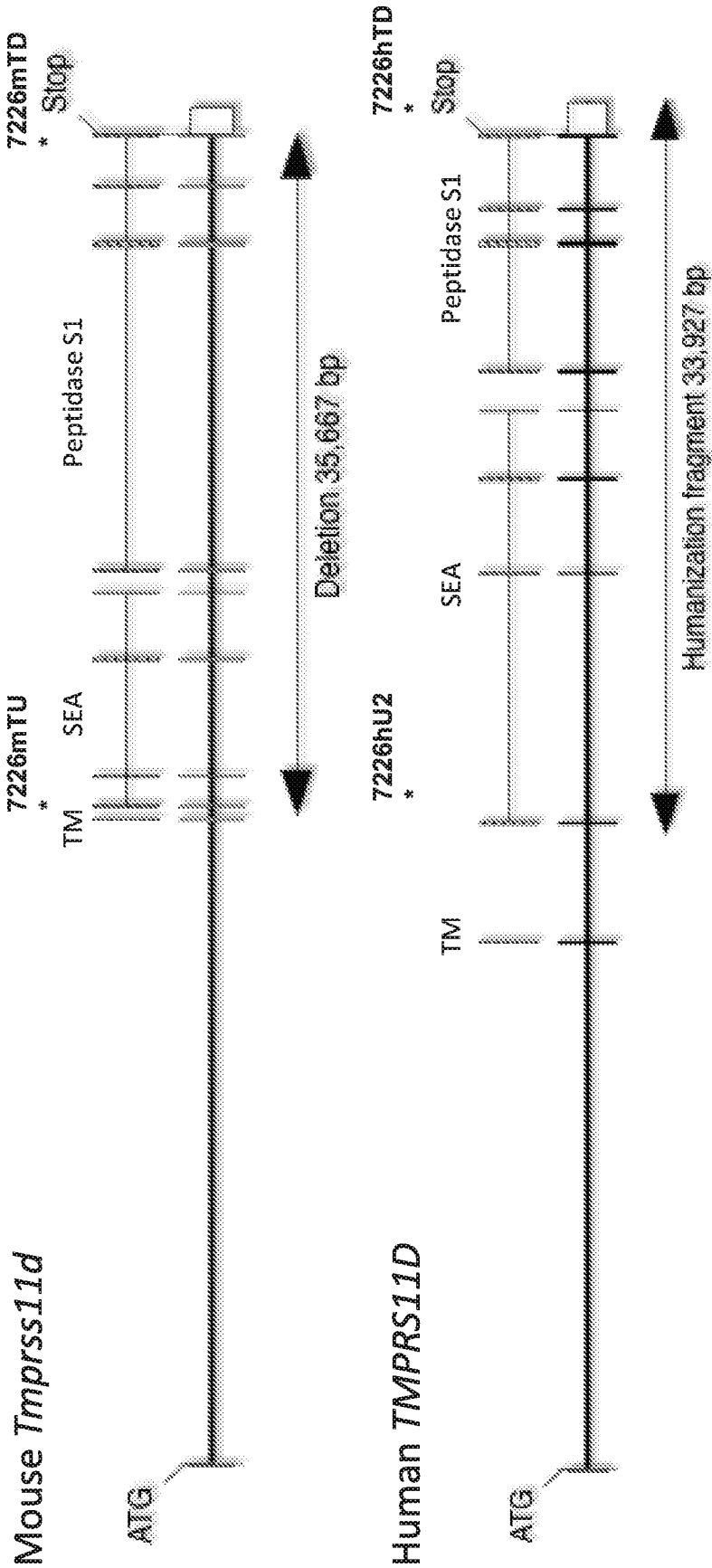
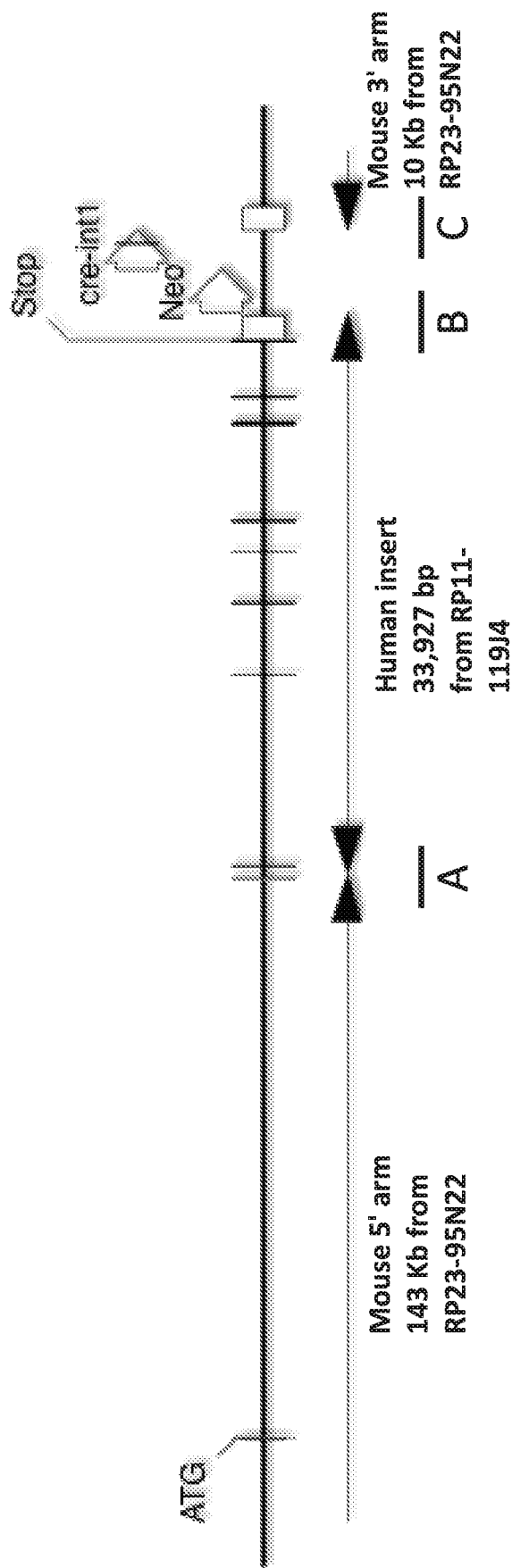
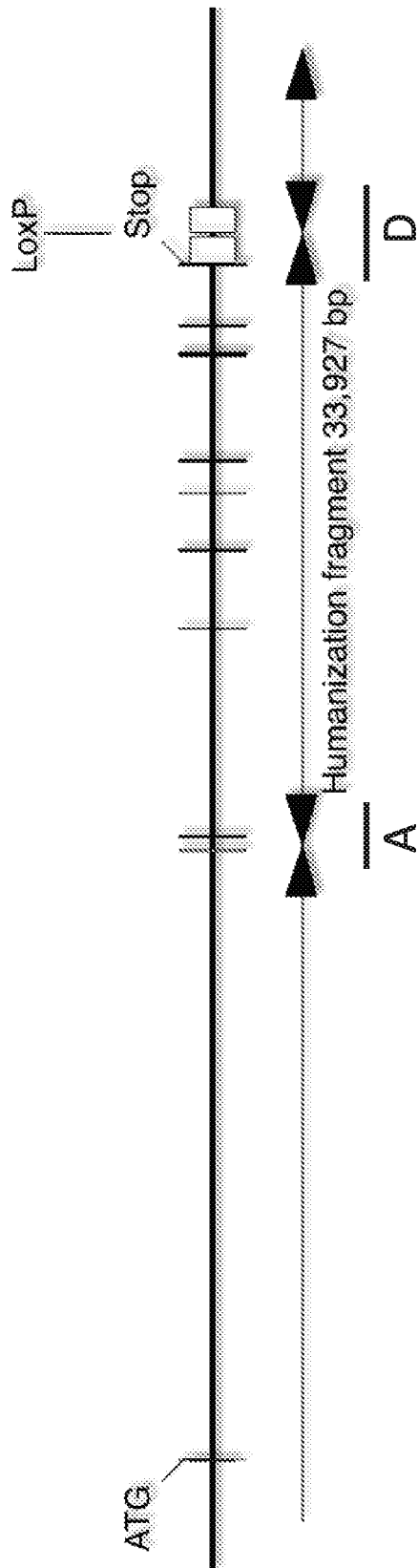


Figure 3A



A. mouse // human (SEQ ID NO:57)	GACCATTTTA AGGTTTGTGCT TGGTTGTTTT GGAGGGAGGG TGGTGCTTTG // CTAATGGTGA ATTACTAACT CCTCAATAAA GAATATTATT TGAATAAATT
B. human// <u>XhoI</u> // (<u>loxP</u>) Cassette (SEQ ID NO:58)	GCTGCTTTT AATCCAGCGC TATAATTGAG GCAAGCGTCC AGCTTGACAC// CTCGAG // <u>ATAACITTCG TATAATGTA</u> T <u>GCTATACGAA GTTA</u> T ATGCATGGCC TCCGCGCCGG GTTTGGCGC CTCGCGCGG CGCCCCCTC CTCACGGCGA GCGCTGCCAC GTCAGACGAA GGGCGCAGCG AGCGTCCTGA
C. Cassette (<u>loxP</u>)/ICEUI// NheI //mouse (SEQ ID NO:59)	ATTGTTTTGC CAAGTTCTAA TTCCATCAGA CCTCGACCTG CAGCCCCCTAG <u>ATAACITTCGT ATAATGTATG CTATACGAAG TTA</u> T/ <u>GCTAGTA</u> CTATAACGGTCCTAAGGTAGCGA // GCTAGC //TGCAACCGAG GAAAAACGT GCCATGAGGT CTCTGTATCC AAGTGTGACT

Figure 3B



A. mouse // human (SEQ ID NO:57)	GACCAATTTTA AGGTTTTTGCT TGGTTGTTTT GGAGGGAGGG TGGTGCTTTG // CTAATGGTGA ATTACTAACT CCTCAATAAA GAATATTATT TGAATAATT
D. human// <u>XhoI</u> //(<i>oxP</i>)// <u>NheI</u> //mouse (SEQ ID NO:60)	CCAGTCAGGG ACACACATGC TCACACGCCC GCCACCCGC ACACACTACA //CTCGAG//ATAACTTCG TATAATGTAT GCTATACGAA GTTAT /GCTAGTAACTATAACGGTCCCTAAGGTAGCGA // GCTAGC // TGCAACCCGAG GAAAAACGT GCCATGAGGT CTCTGTATCC AAGTGTGACT

Figure 3C

	10	20	30	40	50	60
hTMPRSS11D	MYRPARVTST	REFLNPYV	CFVVAGV	ILAVTIAL	VYFLAFDQ	KSYFYRSFQ
hTMPRSS11D	MYRPRMLSP	RFETPF	FAVAFV	IITVGL	AMAGLLIH	ELAFDQKAYFYHSFQ
hTMPRSS11D	MYRPRMLSP	RFETPF	FAVAFV	IITVGL	AMAGLLIH	ELAFDQKSYFYRSFQ

	70	80	90	100	110	120
hTMPRSS11D	YNSQLNSPATQ	EYRTL	SGRIESLIT	TKTKESNL	RNQFIRAH	VAKLRQD
mTmprs11d	YTEALNSPAT	HEYRTL	SERIEAMIT	DEFRGSS	LKSEFIR	THVVKLR
7226 mutant	YNSQLNSPAT	QEYRTL	SGRIESLIT	TKTKESNL	RNQFIRAH	VAKLRQD

	130	140	150	160	170	180
hTMPRSS11D	QFTRNNNGASMKSR	IESVLRQMLNNSG	LEINPSTEITSLTDQ	AAANWL	INECGAPD	LI
mTmprss11d	RSSKRNNRKVMKTR	IQSVLRR-LSSSGN	LEIAPSNEITSLTDQ	DTENVLTQ	ECGARPD	LI
7226 mutant	QFTRNNNGASMKSR	IESVLRQMLNNSG	LEINPSTEITSLTDQ	AAANWL	INECGAPD	LI

	190	200	210	220	230	240
hTMPRSS11D	TLSEQRILGGTEAE	EEGSGWPQVSLRL	NAHHCGGSLINN	MWILTA	AHCFRSNSN	PRDWIA
mTmprss11d	TLSEERIIGMQAEP	GDWPQVSLQLNN	VHHC	GALISNMWVLT	AAHCFKSY	PNPQYWTA
7226 mutant	pro TLSEQRILGGTEAE	EEGSGWPQVSLRL	NAHHCGGSLINN	MWILTA	AHCFRSNSN	PRDWIA

	250	260	270	280	290	300
hTMPRSS11D	TSGISTTFPKLRMRVRN	ILIHNNYKSATHENDI	ALVRL	ENSVTF	TKDIH	SVCLPAATQNI
hTMPRSS11d	TFGVSTMSPLRVRVR	RAILAH	DGYSSVTRDNDIA	VVQLDR	SVAFSRNI	HRVCLPAATQNI
hTMPRSS11d mutant	TSGISTTFPKLRMRVRN	ILIHNNYKSATHENDI	ALVRL	ENSVTF	TKDIH	SVCLPAATQNI

14/16

	370	380	390	400	410
hTMPRSS11D	VDACQD	SGGPLVQEDSRRLWFIVGIVSWG	QCGLPKPGVYTRVTAYLDWIRQQTG		
mTmprss11d	VDACQD	SGGPLVQEDSRRLWFVVGIVSWG	YQCGLPNKPGVYTRVTAYRNWIRQQTG		
7226 mutant	pro VDACQD	SGGPLVQEDSRRLWFIVGIVSWG	QCGLPKPGVYTRVTAYLDWIRQQTG		

solid line: TM
solid box: SEA domain
dotted line: peptidase S1

Figure 3D (Continued)

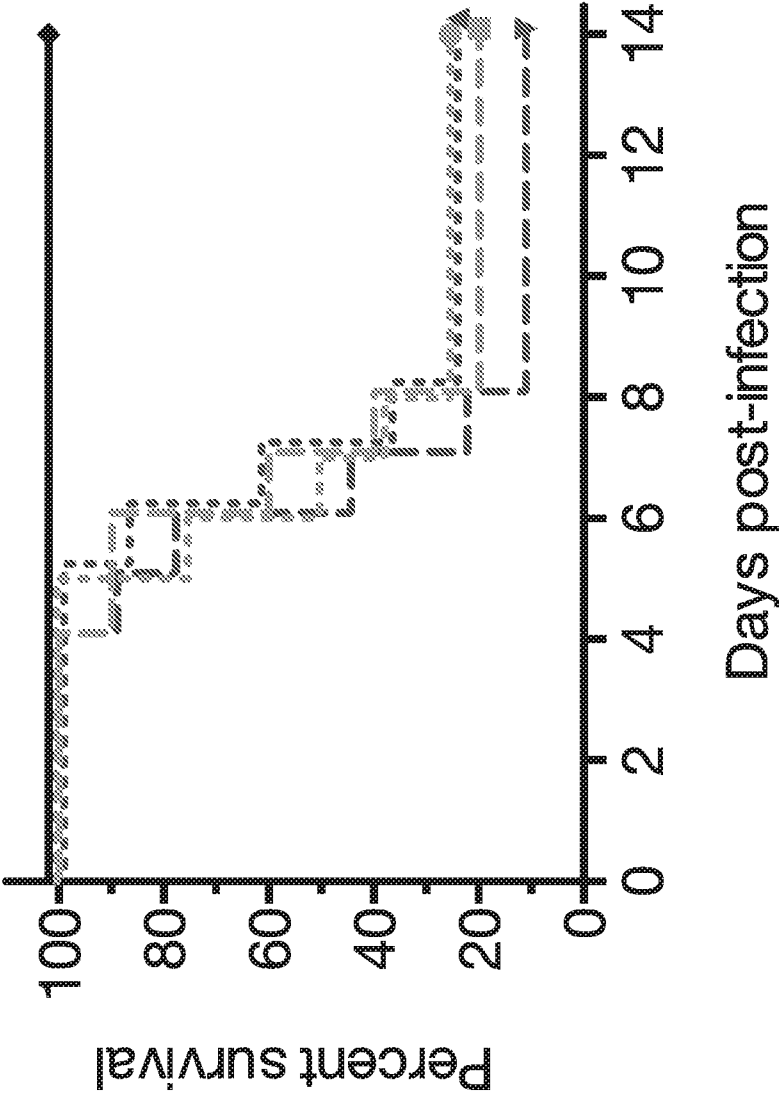


Figure 4