

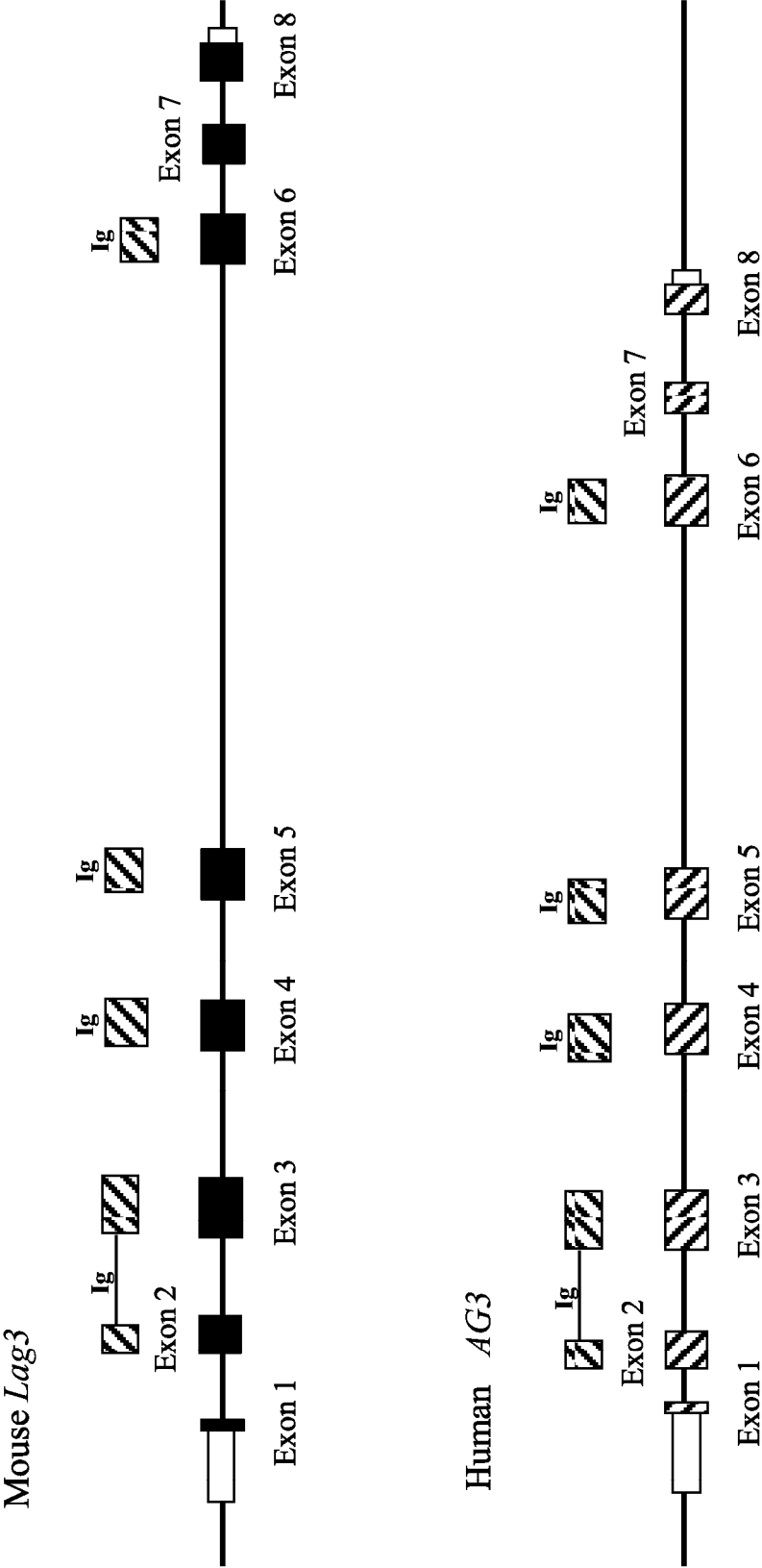


Figure 1

hLAG3	1	MWEAQFLGILLFLOPLWAPVKPLOPQGAEPVWVAQEGAPAOPLPCSPPTIPLQDLSLLRRAGVTWQHQPDSGPPAAAPGHPL	80
mLag3	1	MREDLILGFLILGLLWEAPVSSGPKELPVWVAQEGAPVHLPCSLKSPNLDPNFLRRGGVIWQHQPDSGQPTPIP----	76
HumLAG3	1	MREDLILGFLILGLLWEAPVKPLOPQGAEPVWVAQEGAPAOPLPCSPPTIPLQDLSLLRRAGVTWQHQPDSGPPAAAPGHPL	80

hLAG3	81	APGPHPAAPSSWGPRPRRYTVLSVPGGLRSGRLPLOPRVQLDERGRQGRDFSLWLRPARRADAGEYRAAVHLRDRALSC	160
mLag3	77	ALDLHQMPSPRQAPAGRYTVLSVAPGGLRSGRQPLHPHVQLEERGLQGRDFSLWLRPALRTDAGEYHATVRLPNRALSC	156
HumLAG3	81	APGPHPAAPSSWGPRPRRYTVLSVPGGLRSGRLPLOPRVQLDERGRQGRDFSLWLRPARRADAGEYRAAVHLRDRALSC	160

hLAG3	161	RLRLRGOASMTASPPGSLRASDWVILNCFSRPRDRPASVHWFRNRGQGRVPVRESPPHHHLAESFLFLPQVSPMDSGPWG	240
mLag3	157	SLRLRVGOASMIASPSGVLKLSDWVLLNCFSRPRDRPVSVHWFQ--GQNRVPVYNSPRHFLAETFLILLPQVSPLDSGTWG	234
HumLAG3	161	RLRLRGOASMTASPPGSLRASDWVILNCFSRPRDRPASVHWFRNRGQGRVPVRESPPHHHLAESFLFLPQVSPMDSGPWG	240
		*****/*****	
hLAG3	241	CILTYRDGFNVSIMYNLTVLGLEPPTPLTVYAGAGSRVGLPCRLPAGVGTFRSFLTAKWTPPGGGPDLVLVTGDNDFTLRL	320
mLag3	235	CVLTYRDGFNVSITYNLKVLGLEPVAPLTVYAAEGSRVELPCHLPPGVGTPSLLIAKWTPPGGPPELPVAGKSGNFTLHL	314
HumLAG3	241	CILTYRDGFNVSIMYNLTVLGLEPVAPLTVYAAEGSRVELPCHLPPGVGTPSLLIAKWTPPGGPPELPVAGKSGNFTLHL	320

hLAG3	321	EDVSAQAAGTYTCHIHLEQQLNATVTLAIITVTPKSFSGPSGLKLLCEVTPVSGQERFVWSSLDTPSQRSFSGPWLEA	400
mLag3	315	EAVGLAQAGTYTCSIHLQGGQLNATVTLAVITVTPKSGFLPGSRGKLLCEVTPASGKERFVWRPLNNLS-RSCP GPVLEI	393
HumLAG3	321	EAVGLAQAGTYTCSIHLQGGQLNATVTLAVITVTPKSGFLPGSRGKLLCEVTPASGKERFVWRPLNNLS-RSCP GPVLEI	399

hLAG3	401	QEAQLLSQPWQCQLYQGERLLGAAVYFTTELSSPGAQSRGRAPGALPAGHLLLLFLILGVLSLLLLVTGAFGFHLWRRQWRP	480
mLag3	394	QEARLLAERWQCQLYEGORLLGATVYAAESSS-GAHSARRISGDLKGGHLVLVLILGALSLFLLVAGAFGFHWRKQLLL	472
HumLAG3	400	QEARLLAERWQCQLYEGORLLGATVYAAESSS-GAHSARRISGDLKGGHLVLVLILGALSLFLLVAGAFGFHWRKQLLL	478

hLAG3	481	RRFSALEQGIHPPQAQSKIEELEQEPE----PEPEPEPEPEPEPEQL	525
mLag3	473	RRFSALEHGIQPFPAQRKIEELERELETEMGQEPEPEPEPEPEPRQL	521
HumLAG3	479	RRFSALEHGIQPFPAQRKIEELERELETEMGQEPEPEPEPEPEPRQL	527

hLAG3 - SEQ ID NO:6
mLag3 - SEQ ID NO:4
HumLAG3 - SEQ ID NO:8

Figure 2

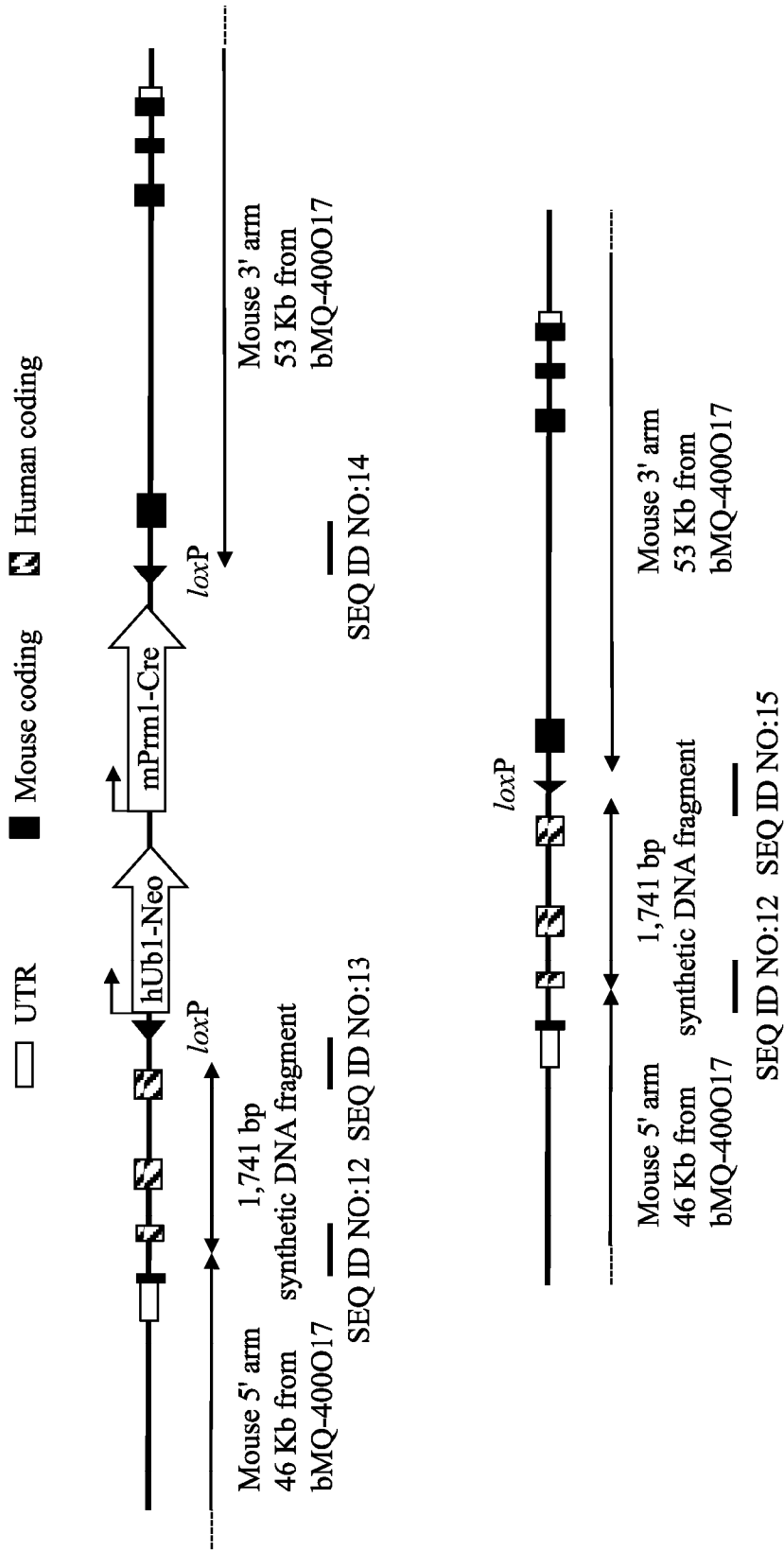


Figure 3

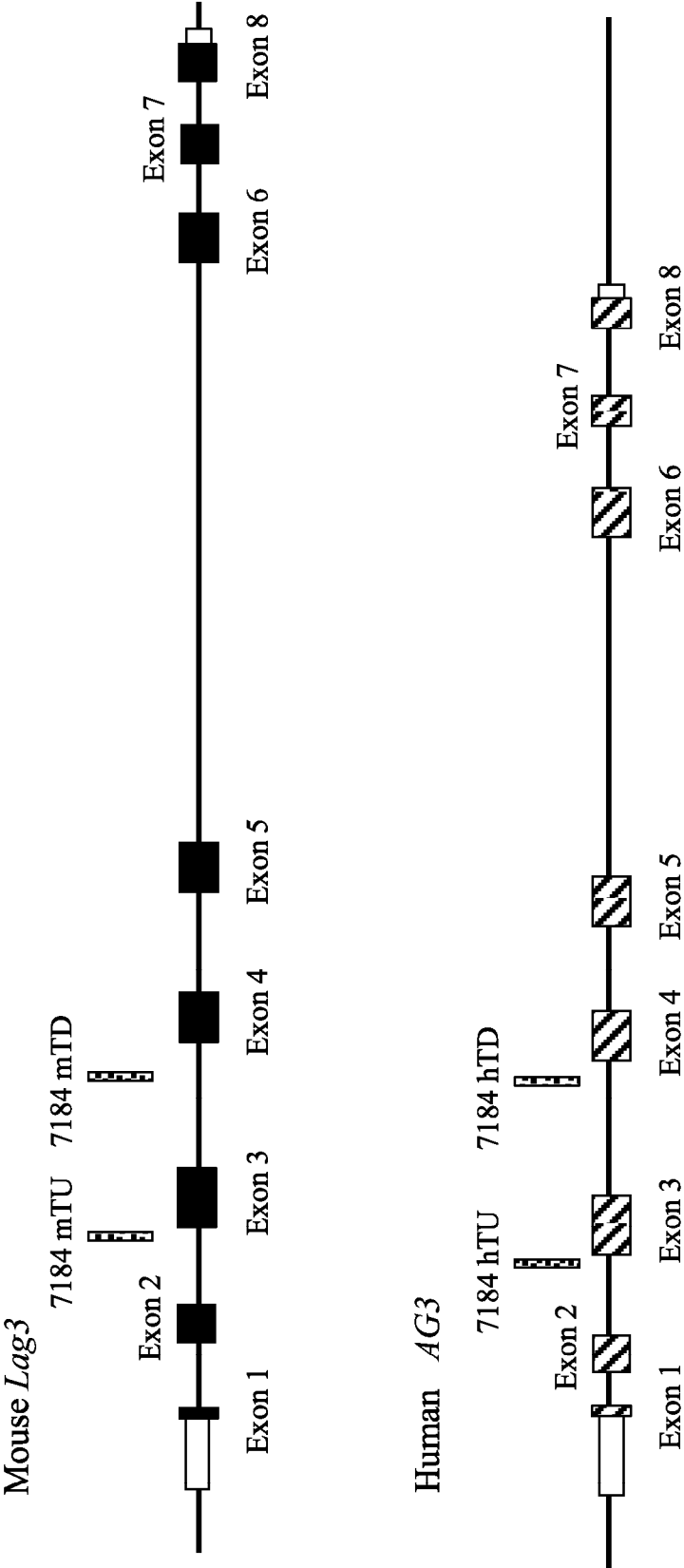


Figure 4

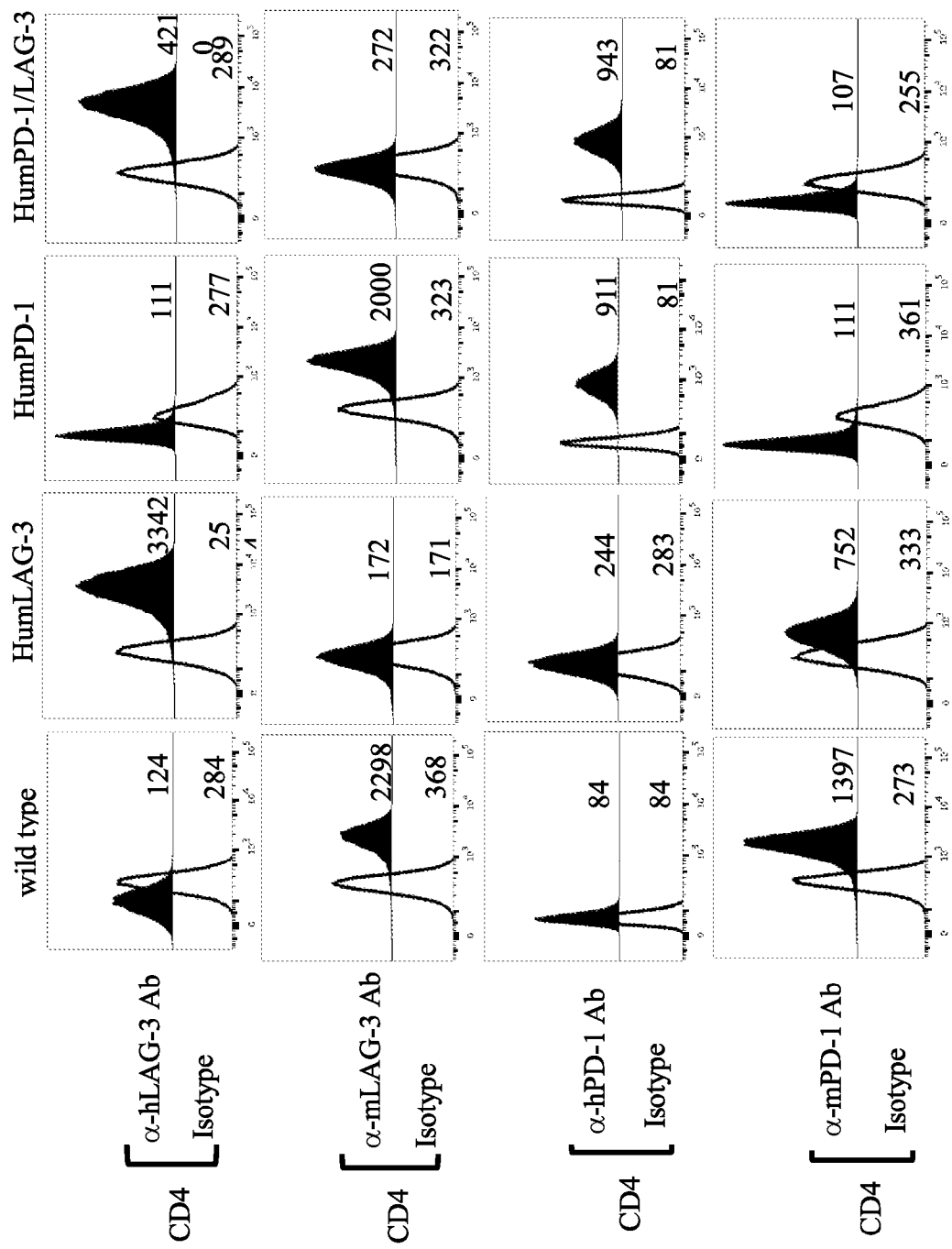


Figure 5

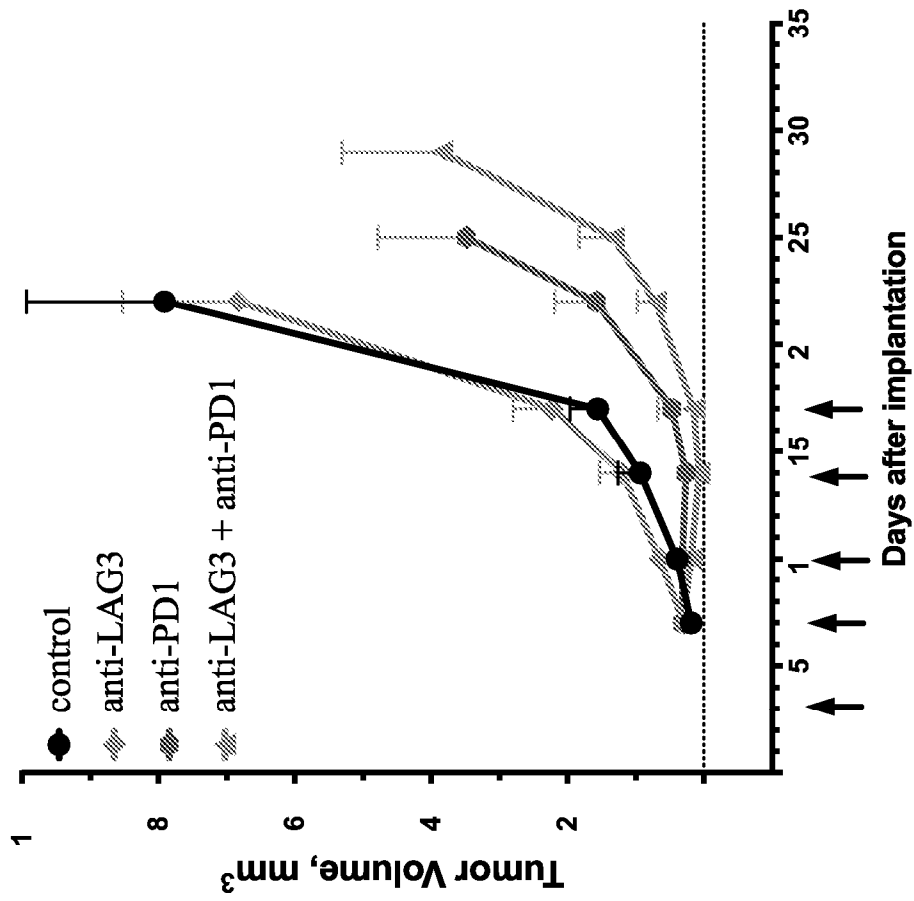
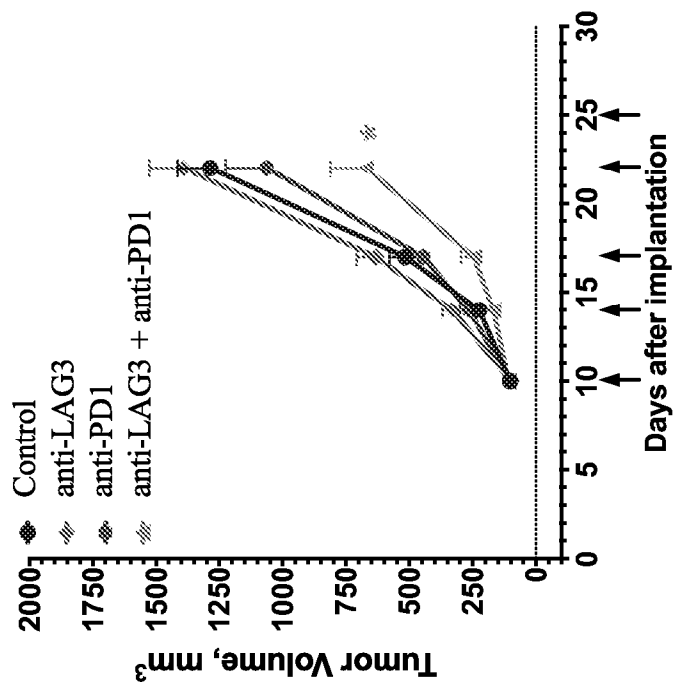


Figure 6



two-way ANOVA (Dunnett's multiple comparison test),
 *p<0.05

Figure 7

FIGURE 8

Rattus norvegicus Lag-3 mRNA (SEQ ID NO:1, NCBI Reference Sequence NM_212513.2):

ACATTCTTTGCCTCACCTCCCTCCTTGTGGAATTTCTCTCTCTCTCTCTCTTTTTTTTTTTCT
 CCCAGGACCTTTTTCTGAACTCCCTTGCAGGGCCTGTGAAGCCCGGGGGGCCACAGAGGA
 GATGAGGCAGGATCTGTTCTTGACCTTTTGCTTCTGCAGCTGCTTTGGGAAGCTC
 CAGTTGTGTCTTCAGGGCCTGGGAAAGAGCTCTCCGTGGTGTGGGCCCAGGAGGG
 AGCTCCTGTCCATCTTCCCTGCAGCCTCGAATTTCCCCACCTGGATCCCAACTTTC
 TGCGAAGAGGATGGGTACCTGGCAACATCGACCAGACAGTGACCAACCCGCTTC
 CATCCCGGCCCTTGACCTTCTCCAGGGAATGCCCTCGACTAGGAGACACCCACCCC
 ATCGCTACACGGTGCTGAGTGTGGCTCCAGGAGGCCTGCGCAGCGGGAGGCAGCC
 CCTGCTATCCACAGTGCAGCTGGAGAAGCGTGGCCCCCAGCGCGGGGACTTCTCT
 CTGTGGTTGCGCCCAGCTACGCGCAAAGATGCGGGCGAGTACCACGCCTTCGTGC
 GCCTCCCGGACCGCGACTTCTCCTGCAGCCTCCGCCTGCGCGTCTGGCCAGGCCTC
 GATGATTGCCAGTCCCCCAGGAACCTCAAGCCGTCTGATTGGGTCAATTTGAACT
 GCTCCTTCAGTCGTCCTGACCGCCAGTCTCTGTGCACTGGTTCCAGGGCCAAAGC
 CGAGTGCCCGTCCACAATTCACCCCGTCATTATCTAGCTGAAAGTTTCTCTTACT
 GCCCCAAGTCAGCCCACTGGATTCCGGGACCTGGGGCTGTGTCTCACCTACAGA
 GATGGCTTCAATGTCTCCATCACGTACAACCTCAAGGTTTCAGGGTCTGGAACCTGT
 AGCCCCCTTTGACAGTGTACGCTGCTGAAGGTTCTAGGGTGGAGCTGCCCTGTCACT
 TGCTTCCCGTTGTGGGGACCCCTTCTTTGCTCATTGCCAAGTGGACTCCTCCTGGG
 GGAGGTCTTGAGCTCCCGGTGACTGGAAAAGAGTGGCAATTTTACCCTTCAACTTGA
 GAATGTGGGTCTGGGCACAGGCTGGGACCTACACCTGCAGCATCCATCTGCAGGGG
 CGGCAGCTCAGTGCGGCTGTGACGTTGGCAGTCATCACAGTGAATCCTAAATCCTT
 CGGGTTACCTGGCTCCCCGCAGAAGCTGTTATGTGAGGTAGTCCCGGCATCTGGA
 GAAGGAAGATTTGTGTGGCGCCCCCTCAGCGATCTGTCCAGGAGTTCCCTGGGCC
 CTGTGCTGGAGTTGCAGGAGGCCAAGCTTCTGGCTGAGCAATGGCAGTGTACAGCT
 GTATGAGGGCCAGAACTTCTTGGAGCAACAGTGTACACCGCAGAGTCTAGCTCA
 GGCGCCTGGAGTGCTAAGAGAATCTCAGGTGACCTTAAAGGAGGCCATCTCTTCC
 TCTCTCTCATCCTTGGTGCCCTTGCCCTTGTCTCTTGGTGACCGGGGCCCTTTGGC
 TTTCACCTGTGGAGAAGACAGTTGCTACGGAGAAGATTTTCTGCCTTAGAGCATGG
 GATTTCGCCACCTCCGGTTCAGAGTAAGATAGAGGAGCTGGAGCGAGAACC GGAG
 ACCGAGATGGAACCAGAGACAGAGCCCGATCCGGAGCCTCAGCCGGAGCCCGAGC
 TGGAACCAGAGTCCAGGCAGCTCTGACCAGGAGCTGAGACAGCCAGCAGCAGGTCTC
 AGCAGCTCTGCCCCGCCGCCCGCTGCCCGCCCCGCGGAATAAACTCCCTGTCAGCAGC
 AAAAAAAAAAAAAAAAAAAAAAAAAA

Rattus norvegicus Lag-3 amino acid (SEQ ID NO:2, NCBI Reference Sequence: NP_997678.2):

MRQDLFLDLLLQLLWEAPVVSSGPGKELSVVWAQEGAPVHLPCSLEFPHLDPNFLRRGW
 VTWQHRPDSQPASIPALDLLQGMPSTRRHPPHRYTVLSVAPGGLRSGRQPLL SHVQLEKR
 GPQRGDFSLWLRPATRKDAGEYHAFVRLPDRDFSCSLRLRVGQASMIASPPGTLKPSDWVIL
 NCSFSRPDRPVSVHWFQGGQSRVPVHNSPRHYLAESFLLLPQVSPLDSGTWGCVLTYRDGFN
 VSITYNLKVQGLEPVAPLTVYAAEGSRVELPCHLPPVVGTPSLIAKWTPPGGGPELPVTGK
 SGNFTLQLENVGRAQAGTYTCSIHLQGRQLSAAVTLAVITVTPKSFGLPSPQKLLCEV VPA
 SGEGRFVWRPLSDLSRSSLGPVLELQEAKLLAEQWQCQLYEGQKLLGATVYTAESSSGAWS
 AKRISGDLKGGHLFSLILGALALFLLVTGAFGFHLWRRQLLRRRFSALEHGIRPPPVSQKIE
 ELEREPETEMEPETEPDPEPQPEPELEPESRQL

FIGURE 8 (Continued)

Mus musculus Lag-3 amino acid (SEQ ID NO:4, NCBI Reference Sequence: NP_032505.1):

MREDLLLGFLLLGLLWEAPVVSSGPGKELPVVWAQEGAPVHLPCSLKSPNLDPNFLRRGGV
IWQHQPDSGQPTPIPALDLHQGMPSRQPAPGRYTVLSVAPGGLRSGRQPLHPHVQLEERGL
QRGDFSLWLRPALRTDAGEYHATVRLPNRALSCSLRLRVGQASMIASPSGVKLSDWVLLN
CSFSRPDRPVSVHWFQGNRVVPVYNSPRHFLAETFLLLPQVSPLDSGTWGCVLTYRDGFNV
SITYNLKVLGLEPVAPLTVYAAEGSRVELPCHLPPGVGTGPSLLIAKWTPPGGGPELPVAGKS
GNFTLHLEAVGLAQAGTYTCSIHLQGGQLNATVTLAVITVTPKSFGLPGSRGKLLCEVTPAS
GKERFVWRPLNNLSRSCPGPVLEIQEARLLAERWQCQLYEGQRLLGATVYAAESSSGAHS
ARRISGDLKGGHLVLVLILGALSFLLVAGAFGFHWWRKQLLLRRFSALEHGIQPFPAQRKIE
ELERELETEMGQEPEPEPEPQLEPEPRQL

Homo sapiens LAG-3 mRNA (SEQ ID NO:5, NCBI Reference Sequence: NM_002286.5):

ACAGGGGTGAAGGCCAGAGACCAGCAGAACGGCATCCCAGCCACGACGGCCACTTTG
CTCTGTCTGCTCTCCGCCACGGCCCTGCTCTGTTCCCTGGGACACCCCCGCCCCACCTC
CTCAGGCTGCCTGATCTGCCAGCTTTCAGCTTTCCTCTGGATTCCGGCCTCTGGTCAT
CCCTCCCCACCCTCTCTCCAAGGCCCTCTCCTGGTCTCCCTTCTTCTAGAACCCTTCTCT
CACCTCCCTCTCTGCAGAACTTCTCCTTTACCCCCACCCCCACCACTGCCCCCTTTCCT
TTTCTGACCTCCTTTTGGAGGGCTCAGCGCTGCCAGACCATAGGAGAGATGTGGGAG
GCTCAGTTCCTGGGCTTGCTGTTTCTGCAGCCGCTTTGGGTGGCTCCAGTGAAGCC
TCTCCAGCCAGGGGCTGAGGTCCCGGTGGTGTGGGCCAGGAGGGGGCTCCTGCC
CAGTCCCCTGCAGCCCCACAATCCCCCTCCAGGATCTCAGCCTTCTGCGAAGAGC
AGGGGTCACTTGGCAGCATCAGCCAGACAGTGGCCCCGCCGCTGCCGCCCCCGGC
CATCCCCTGGCCCCCGGCCCTACCCGGCGGCGCCCTCCTCCTGGGGGCCAGGC
CCCGCCGCTACACGGTGCTGAGCGTGGGTCCCGGAGGCCTGCGCAGCGGGAGGC
TGCCCCCTGCAGCCCCGCGTCCAGCTGGATGAGCGCGGCCGGCAGCGCGGGGACTT
CTCGCTATGGCTGCGCCCAGCCCCGGCGCGCGGACGCCGGCGAGTACCGCGCCGC
GGTGACCTCAGGGACCGCGCCCTCTCCTGCCGCTCCGTCTGCGCCTGGGCCAG
GCCTCGATGACTGCCAGCCCCCAGGATCTCTCAGAGCCTCCGACTGGGTCAATTT
GAAGTGTCTCTTCAGCCGCCCTGACCGCCCAGCCTCTGTGCATTGGTTCCGGAACC
GGGGCCAGGGCCGAGTCCCTGTCCGGGAGTCCCCCATCACCCTTAGCGGAAAG
CTTCCTCTTCTGCCCCAAGTCAGCCCCATGGACTCTGGGCCCTGGGGCTGCATCC
TCACCTACAGAGATGGCTTCAACGTCTCCATCATGTATAACCTCACTGTTCTGGGT
CTGGAGCCCCCACTCCCTTGACAGTGTACGCTGGAGCAGGTTCCAGGGTGGGGC
TGCCCTGCCGCTGCCTGCTGGTGTGGGGACCCGGTCTTTCCTCACTGCCAAGTG
GACTCCTCCTGGGGGAGGCCCTGACCTCCTGGTGACTGGAGACAATGGCGACTTT
ACCCTTCGACTAGAGGATGTGAGCCAGGCCAGGCTGGGACCTACACCTGCCATA
TCCATCTGCAGGAACAGCAGCTCAATGCCACTGTACATTGGCAATCATCACAGTG
ACTCCCAAATCCTTTGGGTACCTGGATCCCTGGGGAAGCTGCTTTGTGAGGTGAC
TCCAGTATCTGGACAAGAACGCTTTGTGTGGAGCTCTCTGGACACCCCATCCCAGA
GGAGTTTCTCAGGACCTTGGCTGGAGGCACAGGAGGCCAGCTCCTTTCCCAGCC
TTGGCAATGCCAGCTGTACCAGGGGGAGAGGCTTCTTGGAGCAGCAGTGTACTTC
ACAGAGCTGTCTAGCCCAGGTGCCCAACGCTCTGGGAGAGCCCCAGGTGCCCTCC
CAGCAGGCCACCTCCTGCTGTTTCTCATCCTTGGTGTCTTCTCTGCTCCTTTTG
TGACTGGAGCCTTTGGCTTTCACCTTTGGAGAAGACAGTGGCGACCAAGACGATT
TCTGCCTTAGAGCAAGGGATTCACCCTCCGCAGGCTCAGAGCAAGATAGAGGAGC
TGGAGCAAGAACCGGAGCCGGAGCCGGAGCCGGAACCGGAGCCCCGAGCCCCGAGC

FIGURE 8 (Continued)

GGTGGCCCGGGCCCTTTGGCTTTCACTGGTGGAGAAAACAGTTGCTACTGAGAAGA
TTTTCTGCCTTAGAACATGGGATTTCAGCCATTTCGGCTCAGAGGAAGATAGAGGA
GCTGGAGCGAGAACTGGAGACGGAGATGGGACAGGAGCCGGAGCCCGAGCCGGA
GCCACAGCTGGAGCCAGAGCCCAGGCAGCTCTGA)CCTGGAGCCGAGGCAGCCAGC
AGGTCTCAGCAGCTCCGCCCCGCCGCCGCCGCCGAATAAACTCCCTGTCAGCAGCA
TCAAAAAAAAAAAAAAAAAAAAA

Exemplary Humanized Lag-3 amino acid (SEQ ID NO:8):

MREDLLLGLLLLGLLWEAPV(KPLQPGAIEVPVWVAQEGAPAQLPCSPTIPLQDLSLLRRA
 GVTWQHQPDSGPPAAAPGHPLAPGPHPAAPSSWGPRPRRYTVLSVGPGLRSGRLPL
 QPRVQLDERGRQRGDFSLWLRPARRADAGEYRAAVHLRDRALSCRLRLRLGQASMT
 ASPPGSLRASDWILNCSFSRPDRPASVHWFRNRGQGRVPVRESPPHHHLAESFLFLPQV
 SPMDSGPWGCILTYRDGFNVSIMYNLTVL)GLEPVAPLTVYAAEGSRVELPCHLPPGVGTP
 SLLIAKWTPPGGPELPVAGKSGNFTLHLEAVGLAQAGTYTCSIHLQGGQLNATVTLAVITV
 TPKSFGLPGRGKLLCEVTPASGKERFVWRPLNNLSRSCPGPVLEIQEARLLAERWQCQLYE
 GQRLLGATVYAAESSGAHSARRISGDLKGGHLVLVLILGALSFLLVAGAFGFHWWRKQL
 LLRRFSALEHGIQPFPAQRKIEELERELETEMGQEPPEPEPEPQLEPEPRQL

Exemplary synthetic DNA fragment for humanization (SEQ ID NO:9; 1,741 bp including exons 2-4
 and part of intron 4 of a human *LAG3* gene):

TGAAGCCTCTCCAGCCAGGGGCTGAGGTCCCGGTGGTGTGGGCCAGGAGGGGGCTCCT
 GCCCAGCTCCCCTGCAGCCCCACAATCCCCCTCCAGGATCTCAGCCTTCTGCGAAGAGC
 AGGGGTCACTTGGCAGCATCAGCCAGACAGGTATGCACCCCAAACCTTGGGCAACAGGA
 CCTCCGAATCCAGCACTCAACCCACACCCGTGCCGGTCTCTGTCCCCTGCCCTGAGGT
 GTCCTCCCTCTGAAGCCAGTGACCCAGTCTCCCTGCCCTCGCTTGACCCGTTCTGCCC
 TTGCTCTGCAATCAGCGACCCCTACGCCAGCATCCCTTCTCTCCAGAAGTGATGCGGC
 CAGTCCAACAGAGGGGTGCGGCGTGAGGGGACGGTTGGTGGTCAAGAGAACTCTTGGG
 GCGGGCTTTCTCATCTCAACGGGTGGCTGCCTGCATCCTCCCGGGCTTCTACCCCTGG
 AGCTTCTCAACTCCATTCTCTTTCCCGCCAGTGCCCCGCCCCGCTGCCGCCCCCGGCCAT
 CCCCTGGCCCCCGGCCCTCACCCGGCGGCGCCCTCCTCCTGGGGGCCAGGCCCCGCG
 CTACACGGTGCTGAGCGTGGGTCCCGGAGGCCTGCGCAGCGGGAGGCTGCCCTGCAG
 CCCCCTGCTCCAGCTGGATGAGCGCGGCGGCGAGCGCGGGGACTTCTCGCTATGGCTGCG
 CCCAGCCCCGGCGCGCGGACGCCGGCGAGTACCGCGCCGCGGTGCACCTCAGGGACCGC
 GCCCTCTCCTGCCGCCTCCGTCTGCGCCTGGGCCAGGCCTCGAGTATGTGGGGCGGGAC
 GATGGGAGAAGGGCTGGGAGGTGGGTCCCCATCCCCTGCCTCCCGGGACGCAGGAAGG
 GCTGGGGCAGAGGCTGCGCCCTAGGCCCTGTCGGAGAGCTCCAGAAAGAGTAGAGGAA
 GGGGGTGGGCGGCTGCTGGAGTGGAAGGTGCCCCGAAGCACGTGTATGGGGGGCCC
 TGTGGAGAGATTGTGTACCCCCGAGCTCCCCTTCTCCACCCACGCGGGAGTGCCAG
 AGGGAGGGGGAGGGGGGGAGAGCATGGGGCTAAAGTGATTCAATTCAGATATCTGTAG
 CTCAGGGGGTGGGCTTCGCGGGGTTCAGGCCAGGAAAACGGCAAGGGTGGCTGATGC
 CAAGTAACTCCAGGCCAGGGACGGGGAAAGTGGTCCTGGGGAGTCTTGGGGATCCAC
 TTTATGCACCTCCAGGTGCTGGAAGCTGAGATGGGGAGAGGGTGTGTGGGAGAGGAG
 AAGACAAGTCTAAAGCCAGGTGCCTGTTTCCAGGAGCTTCCGGCTTGGCAGCCCTGCTG
 TGTTGGGAAATTGTTTCCAGTGGGCTGATGAAGTCTTCTTTATCCTTGACAGTGACTGC
 CAGCCCCCAGGATCTCTCAGAGCCTCCGACTGGGTCAATTTGAACTGCTCCTTCAGCCG

FIGURE 8 (Continued)

CCCTGACCGCCCAGCCTCTGTGCATTGGTTCCGGAACCGGGGCCAGGGCCGAGTCCCTG
 TCCGGGAGTCCCCCATCACCCTTAGCGGAAAGCTTCCTCTTCTGCCCCAAGTCAGCC
 CCATGGACTCTGGGCCCTGGGGCTGCATCCTCACCTACAGAGATGGCTTCAACGTCTCC
 ATCATGTATAACCTCACTGTTCTGGGTAACCTCCCCACTCTGCTTCACATTTGACCACAA
 CTCCTTCTGCCCCCTTGTACCTCCCCTAAC

Exemplary humanized Lag3 allele including a selection cassette (SEQ ID NO:10; human sequence indicated in bold uppercase font, selection cassette sequence indicated in lowercase font, and mouse sequence indicated by regular uppercase font):

TGAAGCCTCTCCAGCCAGGGGCTGAGGTCCCGGTGGTGTGGGCCCAGGAGGGGG
 CTCCTGCCCAGCTCCCCTGCAGCCCCACAATCCCCCTCCAGGATCTCAGCCTTCTG
 CGAAGAGCAGGGGTCACCTTGGCAGCATCAGCCAGACAGGTATGCACCCCAAACCTT
 GGGCAACAGGACCTCCGAATCCAGCACTCAACCCACACCCGTGCCGGTCTCTG
 TCCCCTGCCCTGAGGTGTCACTCCCTCTGAAGCCAGTGACCCAGTCTCCCTGCCCT
 CGCTTGACCGTTTCTGCCCCTTGCTCTGCAATCAGCGACCCCTCACGCCAGCATCCC
 TTCTCTCCAGAAGTGGATGCGGCCAGTCCAACAGAGGGGTGCGGGCGTGAGGGGAC
 GGTGGTGGTCAAGAGAACTCTTGGGGCGGGCTTTCTCATCCTCAACGGGTGGCT
 GCCTGCATCCTCCCGGGCTTCTTACCCCTGGAGCTTCTCAACTCCATTCTCTTTCC
 CGCCAGTGGCCCGCCCGCTGCCGCCCGGGCCATCCCCTGGCCCCCGGCCCTCA
 CCCGGCGGCGCCCTCCTCCTGGGGGCCAGGCCCCGCGCTACACGGTGCTGAGC
 GTGGGTCCCGGAGGCCTGCGCAGCGGGAGGCTGCCCTGCAGCCCCGCGTCCAG
 CTGGATGAGCGCGGCCGCGCAGCGCGGGGACTTCTCGCTATGGCTGCGCCCAGCCC
 GGCGCGCGGACGCCGCGCAGTACCGCGCCGCGGTGCACCTCAGGGACCGCGCCC
 TCTCCTGCCGCTCCGTCTGCGCCTGGGCCAGGCCTCGAGTATGTGGGGCGGGAC
 GATGGGAGAAGGGCTGGGAGGTGGGTCCCCATCCCCTGCCTCCCGGGACGCAGG
 AAGGGCTGGGGCAGAGGCTGCGCCCTAGGCCCTGTGCGAGAGCTCCCAGAAGAGT
 AGAGGAAGGGGGTGGGCGGCCTGCTGGAGTGGAAGGTGCCCCGAAGCACGTGT
 ATGGGGGGCCCTGTGGAGAGATTGTGTACCCCCGAGCTCCCCTTCTCCACCCA
 CGCGGGAGTGCCCAGAGGGAGGGGGAGGGGGGAGAGCATGGGGCTAAAGTGAT
 TCATTTAGATATCTGTAGCTCAGGGGGTGGGCTTCGCGGGGTTCCAGGCCAGGA
 AAACGGCAAGGGTGGCTGATGCCAAGTAACTCCAGGCCAGGGACGGGGAAAGTG
 GTCCTGGGGAGTCTTGGGGATCCACTTTATGCACCTCCAGGTGCTGGAAGCTGAG
 ATGGGGAGAGGGTGATGTGGGAGAGGAGAAGACAAGTCTAAAGCCAGGTGCCTGT
 TTCCAGGAGCTTCCGGCTTGGCAGCCCTGCTGTGTTGGGAAATTGTTTCCAGTGGG
 CTGATGAAGTCTTCTTTATCCTTGACAGTGAAGTCCAGCCCCCAGGATCTCTCA
 GAGCCTCCGACTGGGTCATTTTGAAGTGTCTCTTACGCCGCCCTGACCGCCCAGCC
 TCTGTGCATTGGTTCCGGAACCGGGGCCAGGGCCGAGTCCCTGTCCGGGAGTCCC
 CCCATCACCCTTAGCGGAAAGCTTCCTCTTCTGCCCCAAGTCAGCCCCATGGAC
 TCTGGGCCCTGGGGCTGCATCCTCACCTACAGAGATGGCTTCAACGTCTCCATCAT
 GTATAACCTCACTGTTCTGGGTAACCTCCCCACTCTGCTTCACATTTGACCACAA
 TCCTTCTGCCCCCTTGTACCTCCCCTAACgtcagataaactcgataatgtatgctatacgaagtatatgc
 atggcctccgcgcgggttttggcgctcccgccggcgccccctcctcacggcgagcgctgccacgtcagacgaaggcgagcgagcg
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 ccgtggggcggtgaacccgatgattatataaggacgcgcgggtgtggcacagtagttccgtcgagccgggatttgggtcgcggttctgtt
 tgtggatcgctgtatcgctcacttggtgagtagcgggctgctgggctggccggggcttctgtggccgcccggcgctcggtgggacggaagcg

FIGURE 8 (Continued)

tgtggagagaccgccaagggtgtagtctgggtccgcgagcaaggttgcctgaactgggggttggggggagcgcagcaaaatggcggtgt
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 tgaggccttcgtaaatcggggaaagtcttattcgggtgagatgggtggggcaccatctggggaccctgacgtgaagttgtcactgactggag
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 gtggagaggctattcggctatgactgggcacaacagacaatcggtcgtctgtatgccgccgtgttcgggtgtcagcgcagggggcgcccggttc
 ttttgcgaagaccgacctgtccggtgccctgaatgaactgcaggacgagggcagcgcggctatcgtggctggccacgacggggcgttcttgcgc
 agctgtgtcgcaggtgtcactgaagcggggaagggtggtgtgttggcgaaagtccggggcaggtatcctgtcatctcaccctgtcctg
 ccgagaagatcatcatggctgatcaatcgggcggtgcatacgttgatccggctacctgccattcgaccaccaagcgaacatcgcatc
 gagcgagcagctactcggatggaagccggtctgtcgtacaggtatgttgacgaagagcatcaggggctcgcgccagccgaactgttcgcc
 aggtcaaggcgcatgccgacggcgatgatctcgtgtgacctatggcgatgctgttgcgaatatcatggtggaaaatggccgttttc
 tggattcatcactgtggccggtgtgtggcgaccgctatcaggacatagcgttggctaccgtgatattgtgaagagcttggcgcggaat
 ggggtgaccgcttctcgtgttctacggtatcgccgctcccgattcgagcgcacatcgcttctatcgcttctgacgagttctctgaggggatccg
 ctgtaagtctgcagaaattgatgatctattaaacaataaagatgtccactaaaatggaaagttttctgtcatactttgttaagaagggtgagaacaga
 gtacctacatttgaatggaaggattggagctacgggggtgggggtgggggtgggattagataaatgcctgctcttactgaaggctcttactattgc
 ttatgataatgtttcatagttggatatcataatttaacaagcaaaaccaaataaaggccagctcattcctccactcatgatctatagatctatagatc
 tctcgtgggatcattgttttcttctgattcccactttgtgttctaagtactgtgttccaatgtgtcagtttcatagcctgaagaacgagatcagcag
 cctctgttccacatacacttcattctcagttattgtttgccaagtctaatccatcagacctgcacctgcagccccctagccccggcgccagtagcagc
 acccagctccacttctgtctagtaatgtccaacacctccctcagtcacaacactgctctgcattcatgttggtcctcatttatactgaagcactgtat
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 ggtatctatcaggacctagcctagaagcaggtgtgtggcacttaacacctaagctgagtgactaactgaacactcaagtggatgccattttgtca
 ctcttgactgtgacacaagcaactcctgatgccaaagccctgccacccccctctcatgcccatattggacatggtacaggtcctcactggccatggt
 ctgtgaggctcctggtcctcttctgacttcataattcctaggggcccactagtatctataagagggaagggtgctggtcctccaggccacagcccaca
 aattccacctgctcacaggttggctggctcgaccaggtggtgtccctgctctgagccagctcccgccaagccagcaccatgggtaccccca
 agaagaagagggaagggtgctaccgatttaaatccaatttactgacctacacaaaatttgctgcattaccggctgatcaacgagtgatgagg
 ttcgaagaacctgatggacatgttcagggtatgccaggcggtttctgagcatacctggaaaatgttctgtccgtttgccggtcgtggcgcgcatg
 gtgcaagtgaataaccggaaatggttccgcgagaacctgaagatgttcgcgattatcttatacttcaggcgcgcggtctggcagtaaaaacta
 tccagcaacatttgggccagctaaacatgcttcacgtcgggtccgggtgccacgaccaagtgacagcaatgctgttccactggttatggcgcgga
 tccgaaaagaaaacgttgatgccggtgaacgtgcaaaacaggctctagcgttcgaacgactgatttcgaccaggttcgttactcatggaaaata
 gtgatcgtgccaggatatactgaatctggcatttctggggttcttataacacctgttacgtatagccgaaattgccaggatcagggttaaagat
 atctcacgtactgacgggtgggagaatgttaatccatattggcagaacgaaaacgctggttagcaccgcaggtgtagaagggcacttagcctggg
 ggtaactaaactggtcgagcagtgatttccgtctctggtgtagctgatgatccgaataactacctgtttgccgggtcagaaaaaatggtgttgcg
 cgccatctgccaccagccagctatcaactcgccctggaagggaattttgaagcaactcatcgattgatttacggcgctaaggtaaatataaaattt
 ttaagtgtataatgtgttaactactgattctaattgttgtgtattttaggatgactctggctcagagatacctggcctggtctggacacagtgcccgtgc
 ggagccgcgagatatggcccgctggagttcaataccggagatcatgcaagctggtggctggaccaatgtaaatattgtcatgaactatac
 cgtaacctggatagtgaaacaggggcaatggtgcgctgctggaagatggcgattgatctagataagtaatgatcataatcagccatcacatct
 gtgaggttttactgttttaaaaaacctcccacacctcccctgaacctgaaacataaaatgaatgcaattgttgtttaaacctgcccagtgtgcg
 ccaattccagctgagcgtgctccgcaccattaccagttggtctggtgtcaaaaaataataaaccgggcaggggggatcaagctctagataagt
 aatgatcataatcagccatcacatctgtagaggttttactgtttaaataaaacctcccacacctcccctgaacctgaaacataaaatgaatgcaatt
 gttgttgaactgtttattgcagcttataatggttacaaataaagcaatagcatcacaatttcacaataaagcatttttactgcattctagtgtgg
 tttgtccaaactcatcaatgtatcttatcatgtctggaataactctgtataatgtatgtctacgaagttatgctagtaactataacgggtcctaaggtagcg
 agctagcGACCCCCAAAACCTTTCTCAGCTGCGTGTGGTCTCACTCCACATCACTTTGTTTCAG
 TGTCCAAACCATTTTCTCTCTGGGCATCTTTTAGCTGCTGTCTCTCTTACTTTTATTTATTT

FIGURE 8 (Continued)

ATTTGTGTGTTTATTTATTTATTTTCATTTTAGCGTGCGTTGGTGTTTTGCCTGCATAGAT
 GTCTGTGTCAGGGTATTGGATTCCCTGGAACCTTGACCTACAGACAGTCATGAGATACCA
 TATGGGTGCTGGGAATTGAACCCAGCTCCTCTGGAAGGACAGCCAGTGTTCTAATCTGC
 CATCTCTCACTGTTTATCCCTTGGCTGTTTCAGCCTCCTGAGCCTTTGGTCTCTTGCTGCCT
 CAGTTTCCCTAGTTTCTCTGCTTTGCTCTGTTTCTTTCTGTGTTACAGCCAAATGCCTCCT
 TCCCCCTTCTGCCTTACTTCTTGTATGTCTCCACCCTCTGGCCCACTGCTTACCCTTGGTA
 ACGGCTTGGCTTTTCTTCTCTCTCCAGGTCTGGAGCCCGTAGCCCTCTGACAGTGTA
 CGCTGCTGAAGGTTCTAGGGTGGAGCTGCCCTGTCAATTTGCCCCCAGGAGTGGGGACCC
 CTTCTTTGCTCATTGCCAAGTGGACTCCTCCTGGAGGAGGTCTGAGCTCCCCGTGGCTG
 GAAAGAGTGGCAATTTTACCCTTACCTTGAGGCTGTGGGTCTGGCACAGGCTGGGACC
 TACACCTGTAGCATCCATCTGCAGGGACAGCAGCTCAATGCCACTGTCACGTTGGCGGT
 CATCACAG

Humanized Lag3 allele after recombinase-mediated excision of a selection cassette (SEQ ID NO:11; human sequence indicated in bold uppercase font, remaining sequence after recombinase-mediated deletion of a selection cassette indicated in lowercase font, and mouse sequence indicated by regular uppercase font):

CCATCACTTTGTATAAGGGCAGATCCCAAAGCTGCCTCAGCCTCCCTTCAACAGGG
 AGGCATGATGTTTCTTTCTTAGGAAAGCCAGGGCATTCTCTATTCTCCAATCTCTT
 GGCTCAATGCCCTTGGCCTCTCTTTTGTTCCTAGTGAAGCCTCTCCAGCCAGGG
 GCTGAGGTCCCGGTGGTGTGGGCCCAGGAGGGGGCTCCTGCCAGCTCCCTTGCA
 GCCCCACAATCCCCCTCCAGGATCTCAGCCTTCTGCGAAGAGCAGGGGTCACTTG
 GCAGCATCAGCCAGACAGGTATGCACCCCAAACCTTGGGCAACAGGACCTCCGAAT
 CCAGCACTCAACCCACACCCGTGCCGGTCTCTGTCCCCTGCCCTGAGGTGTCAC
 TCCCTCTGAAGCCAGTGACCCAGTCTCCCTGCCCTCGCTTGACCGTTCTGCCCCT
 TGCTCTGCAATCAGCGACCCTCACGCCAGCATCCCTTCTCTCCAGAAGTGGATGCG
 GCCAGTCCAACAGAGGGGTGCGGGCGTGAGGGGACGGTTGGTGGTCAAGAGAACT
 CTTGGGGCGGGCTTTCTCATCCTCAACGGGTGGCTGCCTGCATCCTCCCGGGCTTC
 CTACCCCTGGAGCTTCTCAACTCCATTCTCTTTCCCGCCAGTGGCCCGCCCGCTG
 CCGCCCCCGGCCATCCCTGGCCCCCGGCCCTCACCCGGCGGGCGCCCTCCTCCTG
 GGGGCCAGGCCCGCCGCTACACGGTGCTGAGCGTGGGTCCCGGAGGCCTGCG
 CAGCGGGAGGCTGCCCTGCAGCCCCGCGTCCAGCTGGATGAGCGCGGCCGGCA
 GCGCGGGGACTTCTCGCTATGGCTGCGCCCAGCCCGGCGCGCGGACGCCGGCGA
 GTACCGCGCCGCGGTGCACCTCAGGGACCGCGCCCTCTCCTGCCGCCTCCGTCTG
 CGCCTGGGCCAGGCCTCGAGTATGTGGGGCGGGACGATGGGAGAAGGGCTGGGA
 GGTGGGTCCCCATCCCTGCCTCCCGGGACGCAGGAAGGGCTGGGGCAGAGGCT
 GCGCCCTAGGCCCTGTCCGAGAGCTCCAGAAAGAGTAGAGGAAGGGGGTGGGCG
 GCCTGCTGGAGTGGAAGGTGCCCCCGAAGCACGTGTATGGGGGGCCCTGTGGAGA
 GATTGTGTCACCCCGAGCTCCCTTCTCCACCCACGCGGGAGTGCCAGAGGG
 AGGGGGAGGGGGGGAGAGCATGGGGCTAAAGTGATTCAATTCAGATATCTGTAGC
 TCAGGGGGTGGGCTTCGCGGGGTTCAGGCCAGGAAAACGGCAAGGGTGGCTGA
 TGCCAAGTAACTCCAGGCCAGGGACGGGGAAAGTGGTCTGGGGAGTCTTGGGG
 ATCCACTTTATGCACCTCCAGGTGCTGGAAGCTGAGATGGGGAGAGGGTGATGTG
 GGAGAGGAGAAGACAAGTCTAAAGCCAGGTGCCTGTTTCCAGGAGCTTCCGGCTT
 GGCAGCCCTGCTGTGTTGGGAAATTGTTTCCAGTGGGCTGATGAAGTCTTCTTTAT
 CCTTGACAGTGACTGCCAGCCCCCAGGATCTCTCAGAGCCTCCGACTGGGTCAT

FIGURE 8 (Continued)

TTTGAACTGCTCCTTCAGCCGCCCTGACCGCCCAGCCTCTGTGCATTGGTTCCGGA
ACCGGGGCCAGGGCCGAGTCCCTGTCCGGGAGTCCCCCATCACCACCTTAGCGGA
AAGCTTCCTCTTCCTGCCCCAAGTCAGCCCCATGGACTCTGGGCCCTGGGGCTGCA
TCCTCACCTACAGAGATGGCTTCAACGTCTCCATCATGTATAACCTCACTGTTCTG
GGTAACTCCCCCACTCTGCTTCACATTTGACCACAACCTCCTTCCTGCCCCCCTTGT
CACCTCCCCTAACgctcgagataacttcgtataatgtatgctatacgaagttatgctagtaactataacggtcctaaggtagcgagctag
cGACCCCCAAAACCTTTCTCAGCTGCGTGTGGTCTCACTCCACATCACTTTGTTTCAGTGTC
CAAACCATTTTCTCTCTGGGCATCTTTTAGCTGCTGTCTCTTACTTTTATTTATTTATTT
GTGTGTTTATTTATTTATTTTCATTTTAGCGTGCGTTGGTGTGTTTGCCTGCATAGATGTCT
GTGTCAGGGTATTGGATTCCCTGGAACCTTGACCTACAGACAGTCATGAGATAACCATATG
GGTGCTGGGAATTGAACCCAGCTCCTCTGGAAGGACAGCCAGTGTTCTAATCTGCCATC
TCTCACTGTTTATCCCTTGGCTGT

FIGURE 9A

(CATGATGTTT CTTTCTTAGG AAAGCCAGGG CATTCTCTA TTCTCCAATC TCTTGGCTCA ATGCCCTTGG CCTCTCTTT GTTCCACTAG) TGAAGCCTCT CCAGCCAGGG GCTGAGGTC CCGGTGGTG TGGGCCCAG GAGGGGGCTC CTGCCCAGCT CCC (SEQ ID NO:12)

FIGURE 9B

TTCACATTG ACCACAATC CTTCTGCCC CCTTGTAC CTCCCCTAAC (*GTCGAG* **ATAACTTCG TATAATGTAT GCTATACGAA GTTAT** ATGCATGGC TCCGCGCCGG GTTTTGGCGC CTCCC GCGG) CGCCCCCTC CTCACGGCGA GCGCTGCCAC GTCAGACGAA GGGCGCAGCG AGCGTCTGA) (SEQ ID NO:13)

FIGURE 9C

(TTTCACTGCAT TCTAGTTGTG GTTTGTCCAA ACTCATCAAT GTATCTTATC ATGTCTGGA **ATAACTTCGT ATAATGTATG CTATACGAAG TTAT** GCTAGTAACT ATAACGGTCC TAAGTAGCG A GCTAGC) GACCCCCAAA ACTTTCTCAG CTGCGTGTGG TCTCACTCCA CATCACTTTG TTTCAGTGTC CAAACCATTT TCTCTCTGGG CATCTTTTAG (SEQ ID NO:14)

FIGURE 9D

ACGTCTCCAT CATGTATAAC CTCACTGTTT TGGTAACT CCCCACCTCT GCTTCACATT TGACCACAAC TCCTTCTCTG CCCCCTTGTC ACCTCCCCT AAC (*GTCGAG* **ATAACTTCGTA TAATGTATGC TATACGAAGT TAT GCTAGTA ACTATAACGG TCCTAAGGTA GCGA GCTAGC) GACCCCCAAA ACTTTCTCAG CTGCGTGTGG TCTCACTCCA CATCACTTTG TTTCAGTGTC CAAACCATTT TCTCTCTGG GCATCTTTA GCTGCTGTCTC (SEQ ID NO:15)**