



Ace2 Knockout Mouse (Model # 18180) Technical Information

Gene isoforms

The Ensembl database shows two isoforms of mouse ACE2 protein, one starting from Exon 2 of the gene (805 aa) and the second starting from Exon 6 (521 aa). The modification in this model targets the second exon (first coding exon) of Ace2, which is expected to result in a loss-of-function allele for the full-length isoform. It is unknown whether the second isoform will be produced in this model and if produced whether it is functional or not and can compensate for the loss of the full-length isoform. Correct targeting of the allele was confirmed by Southern blot analysis. Several publications have described phenotypic differences between wild type and homozygous mutant animals for this modification, consistent with interference with Ace2 function. It is recommended that researchers confirm loss-of-function status of the allele in their experimental system or tissue of interest.

Genetic background

The genetic background of this line is mixed C57BL/6NTac, 129S5 and C57BL/6J (B6;129S5). C57BL/6NTac is the predominant background strain. Due to the urgency of the research response to the COVID-19 pandemic, there is not sufficient time to backcross the Ace2 knockout mutation to an inbred genetic background. Researchers should be aware that phenotypes such as hypertension may vary for specific Ace2 knockout alleles on different inbred genetic backgrounds (Gurley and Coffman, 2007). Thus, as the result of a mixed genetic background the Ace2 knockout mice may show considerable inter-animal variation in phenotypes. It is recommended to carefully consider the impact of the genetic background when planning and interpreting experiments. Taconic can advise on backcross strategies and provide testing for marker-assisted speed congenic breeding. Generation of a fully congenic line can take 12-18 months.

Murine Ace2 is X-linked

The murine Ace2 gene is located on the X chromosome. Female knockouts are homozygous (ko/ko). Male knockouts are hemizygous (ko/y). Other genotypes available for sale include female heterozygotes (ko/wt) and wild type littermates of both sexes (wt/wt females and wt/y males).

Possible mating formats and expected progeny are as below:

- Heterozygous female x hemizygous male: expected to produce homozygous and heterozygous females, hemizygous and wild type males.
- Heterozygous female x wild type male: expected to produce heterozygous and wild type females, hemizygous and wild type males.
- Homozygous female x hemizygous male: expected to produce homozygous females and hemizygous males. Will not provide a wild type control.



Reproductive data

Breeding performance of heterozygous female by C57BL/6NTac male setups is very good. 100% of heterozygous females (10 of 10) setup with C57BL/6NTac males produced a first litter within 4-5 weeks and ~90% of them produced a second litter within the next 4 weeks. Average litter size was 8.3 pups per litter (for the first 2 litters) and no pre-wean mortality was observed. These reproductive characteristics could differ for other mating formats. Genotype ratios in pups from heterozygous female x C57BL/6NTac male matings is so far as expected.

Genotyping protocol

The genotyping protocol for this line requires performance of two separate PCR reactions, one to detect the wild type allele and one to detect the knockout allele. Each reaction includes an internal control. Combine results from each PCR to determine genotype as follows:

Sex	Genotype	PCR 26784 result	PCR 27005 result
Female	Homozygous knockout	335 bp, 468 bp	335 bp
Female	Heterozygous knockout	335 bp, 468 bp	335 bp, 500 bp
Female	Wild type	335 bp	335 bp, 500 bp
Male	Hemizygous knockout	335 bp, 468 bp	335 bp
Male	Wild type	335 bp	335 bp, 500 bp

If the 335 bp control fragment is not present, that result cannot be used in determination of genotype. Note that assay performance may vary and you may need to adjust PCR conditions based on the specific equipment and enzymes available. Taconic is not able to troubleshoot assay performance in customer labs.

PCR SOP ID: 26784

Gene: *Ace2^{tm1Lex}*

Primers

26784_Neo3A: GCAGCGCATCGCCTTCTATC (forward primer), 25.0 uM

26784_37: GCTCAATAACGACTTAGAACAT (reverse primer), 25.0 uM

1281_1: GTGGCACGGAAGTTCTAGTC (control forward primer), 12.5 uM

1281_2: CTTGTCAAGTAGCAGGAAGA (control reverse primer), 12.5 uM

Reaction

0.50µl Oligo Mix L.26784

0.25µl Taq (5U/µl, QIAGEN)

5.0µl DNA

16.25µL water



2.5µL 10X buffer

0.5µL dNTP

Program

95°C 15:00'

94°C 0:45'

60°C 1:00'

72°C 1:00'

35 cycles

72°C 5:00'

Expected Fragments

335 bp – Cd79b wild type allele (control)

468 bp – knockout allele

PCR SOP ID: 27005

Gene: *Ace2^{tm1Lex}*

Primers

26784_3: GATGTCCAGCTCCTCCTGG (forward primer), 25.0 uM

26784_37: GCTCAATAACGACTTAGAACAT (reverse primer), 25.0 uM

1281_1: GTGGCACGGAACTTCTAGTC (control forward primer), 12.5 uM

1281_2: CTTGTCAAGTAGCAGGAAGA (control reverse primer), 12.5 uM

Reaction

0.50µl Oligo Mix L.27005

0.25µl Taq (5U/µl, QIAGEN)

5.0µl DNA

16.25µL water

2.5µL 10X buffer

0.5µL dNTP

Program



95°C 15:00'

94°C 0:45'

60°C 1:00'

72°C 1:00'

35 cycles

72°C 5:00'

Expected Fragments

335 bp - Cd79b wild type allele (control)

500 bp – wild type allele

Molecular Genetics Project Materials

Gene name and accession:	Ace2 (NM_001130513)	Date of Submission:	4/18/20
Mutation Type:	<input checked="" type="checkbox"/> Standard Knock out	Is this gene X-linked?	Yes
	<input type="checkbox"/> Conditional	Genetics background of target vector and ES cells:	129S5

Southern Blot Analysis:

External/Internal Probe Strategies

	<u>5' External</u>	<u>3' External</u>
Name of Probe:	28/27	29/30
Restriction Enzyme for Genomic Digest:	KpnI	HindIII
Predicted Wild-type Band (kb):	14.4	10.3
Predicted Mutant Band (kb):	7.9	11
Probe Size (bp):	403 bp	488 bp

PCR Strategies:

Wild type-specific (absent in targeted allele)		Mutation-specific product (absent in wt)	
5' Primer Name:	3	5' Primer Name:	Neo3A
3' Primer Name:	37	3' Primer Name:	37
Predicted Wild-type Band (bp):	500	Predicted Wild-type Band (bp):	none
Predicted mutant band (bp)	none	Predicted mutant band (bp)	468

GGGTGGTGTGTTTCAGTAGTTTTTTCATTTTTGTCCGTTTGTGTTGGTGGTGGTTTTGGAGACAGGGTTCCTCTGGGTAAGTTTGGCTGTCTTG
TAGACCAGGCTGGTCTGAAGTCACTCAGAGCTCTACCTGCCTCGCTCCGGAGGACTGAGACTGAAGTGGACACCACCACACCTGAATCTTATTCGTGTA
TCTTATTTCTCTCAGTCTGAACAAAGTAATAATTTTCAGTACACTGGGATCACTTGGTCTTAATTGTCAAGGTAAGTTAATTTACCGTCTTAGTTGGC
AATTATCAGATTTAAATTCCTATCCCTGAACCTCTCTGCCAACTTCATATTTGTCTTCTCAGCATCTTCTTGGGTTTCCAACCTGATCTCACAAAGTCCAC
CAGACTCTTAATCATCCCTCCAAACCTGTTTACTAGCAATCTTCTCCTTCAAATGATTTCAACTTTGACCTTTTATTTGTTTAGCTTCCAAAGACTCAA
ATGATCTTTCAGCTTTGAGACTCTTTAAACAAAAACCAAGTGCATTCAGAATCTAAGCAGCTTTGGCAATACTCCGCCACCAAGCCCTATTATA
CCTTCTTGGATGACGGTGTCTTACTGATCTCTGCATATAGTCTTGGCTTATGTAGAGTGAAGTTCGAAATAGCAACCAAGTGGTTCCTCTCAACG
GTAAACAAGATCATGTCACATTTCTATTTACCTTTGCCACGAATCCTGTTTCATGTAGGATAAAGCCTACATGAAACAGGATTTTCATGAAACAGCCTT
GTTAAGTTCCTAGACATAAATTGATATTAGTGGTTCCCTGTTCCCGTGTCTGTGATATTTATAGTTTATATGTGAAAATATATCAGGATTACTGCAT
CAAGTAAGACAGAGTCATAAATTTCCAGGAACCTAATCGGTTTACTTCCAGGAACACACAGAGTATTCCTACAAATTTGACTTTTGTGAAAAAGATTT
GTCAAGTTGGTTAATGGAGATTATCTGTAGGAGCAACGGTCTACTGTGAAATTTGAATATGAAAAAGGAGAGAGTGGGCGAAACCAACTTGCTGTTT
TTTCTAAAGAACGTTTAAACTTACTGTATGTGATCAATGTGTAGCCAAAACCAATTGACTGCGTGTGATTCTTCTGGTTATGTAAACTTTAAATCTC
TCTCTCTCTCGTATTCTAATATCACCTTTTTGTTCCTGTGACAAGCATTAGTCAATTTAAGATAAAGTATTATCAGAAAATTTCTTTTCTTACACA
TATTTCCAGCCCGGGGAAGTAGAAGCTAGCTTTTTCTGAAAGTGTTTTGAACCTTACTGCTGTGACTCAGTTGGAAGTACATAAAAGTTGCTCAGTA
AGGAAACCTGGATCTAAAGTCTATGTACTTTGTTCTTGAAGACTGATGACCCACCCGAGGTATGAACTTATGCAAGGGGAGAAAGGAGATTATGA
TTATGCAGAACCTCATGATTATGCATTTCCACTGAAAGTCTTACAGCAGCAGATCAAAAAGCAGGGAGACTTACAGTGGGTGAGGCTACTAAGAGC
TGATACTCCAAGCAGCATTGGGAACCTCAGAGTTTTCAGAGACAGCAGAATTATTAGCAATAAAACTCCTTGGCGTCAATTTACTGCAGAGCCCTCAGGTC
CACCGTATAGACCAGCCAGTAAATAGAATGCAGGAAAAGAAAGCAACAACAAAATAATACAACACAAAGCAATACCCACGTAAATCGGGCTCAGTAT
GGAATCTGCCCTACGGCACTTCTCATTCAAAAAGGTTTAAAGCATAAAATTTGTTGATGCTAAACATCGCATTTCTGCTACGCTTGTGTGGCCCTGCTT
ATTCTGAGAACAATGGCAGATTATCTGTAGGACGTAAGTCTTGAAGTGTAGTATGACAGAGTTCGATGAAACAGAGAGTGGCTATCCATCTTCTT
AACAGCCTGAAACCCGTTCTGTGACGTTGTGGGAATTTAGATCAGAGAGTAGGACGTTGTTTCTTTATTGTAACAGGGTCTCTGGAGTCCAGTTATC
AGGGTTATGTTGGAAGATTTCTGTGACAGCCTGGTGCAAAAGCAAGTGTGACCCACAAAGATAGTATCTGGAATATCAGGAGGGGGGCCGTTATGTTT
ATGATTTTTTCCCTTCTTCTTAAAGACAGCATACTTCTTCTGTGTTGGGAAGCATACATCTGAGCCTGATTATTAGACTATTAGAGCACCTGGG
CATGGCTTTCGTGGCCAGCTTAAACAGACTTCTCTTCTTGAATCTTTCACAAAATAAACCTGCTTCTTCCACAGGTGTTTCCCTCCGATTTTAGCAT
AGGTCAGTTTAAAAAACAACCAACAAATCATGATCCTACAGTCCAAATGGACACTGGAATCAAGCCCTTAGCCAAAGTAAACGATGCATG
AATGTCCTGAAGGATTGTCTGACAGACAGGTTTCTTAAACATCTCAGTATGGAAGGTTACAAATGATTACACTGCCACTTTCATTATGAGTAGCTTTT
ATTACTACTCAGGTATGAATTCATAAAATGCACCTCTCCTAGACCCAGTAGCTTTGACAGTAAAGAAAGTATGTACAAAGTCTTAGTATACTGAAAG
CCTAAAGTCACACAGTCAATCTCTTACTAGTACTAAGCAGCCAAAGCCGTAAGACTCTGTATATACTTCTGTATATACTTCTGTGAGGCTTCCAACT
TCCATATGCCTAAGGATGAAAAATCAAAGTGGCATTCTTTTAAAGCCCTCCTGGTGTGAGACAAAGCTTTTCTTCTCAGCTTCTTAGCTAGTCAAT
AGGCCTCGATGTTTTGACACCTGCCTACACTCTGTGCACGGCTACCACCTTATCTGGAAGTTTTCTCCAGATGGCTTTCACACATCCTTTTAGA
CTTCTCACATTAACCTTTTCAGAGATAGCCCTTAAACAGAAAACCTCTCTCTACTTCTCATTCTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT
ATGTAAGCCATAGTATTTATCACAGAGTACTCAATGTGTCTTATACCCGAATACCATATAATACAACACCTATGGGAATCTTTGCTACCTTATGCATTA
GTGTTGTATACATAATCTAGAGTACTATAGAGCCACAGTAGGCATGAAATAAATACTAGTAAATCAAGATTTCTTGTGTCTGATGATAGGCAAC
TGCCCAATCCTGTGGTGTGTTTCAAGAACATTTAGCTTTACTCTCTCTCTCAATCTCTCTCTCTCTCACACACACACACACACACACACACACAC
ACACACACACATCCGTTATTGAGATGAAAGCTATGCTTTGTAATTTTTCTTATATGAAAAACAGATTGTATGCTTTCATTAGAGGAGTAGACAGGGA
GGCAGTACCTGATCTTGAATAATCCCTTATGACCAATAGACATTTTCAACTGCTTACTAGTACATAATAAAAAATTTATGTTTACAATTTTGTGTA
AGCATCAAGCTCAAACCTCTGTGTTTTTATCAGACACACCCCAACTTCAACGTTTTTCAAAGTTAGAATAGCTTTCTTGGCTGTCTAGCTACTCAACT
CTTTTTTTTTTTTTTCTGCTTCCCTTCTTAAAGATGATATGTTCTTGGAGCCAGTTGTTTTCTGGGTCACATGCTCTCCATCTCTAGAGGGTCTCTT
TAGTCTCAGAAATGGGACAAAGATAAATCTCCTAGGGAACAGAGTATCCCTATCTTCAATGAAGAGTGAACCCAAATCCCAGACTTTCAGTGCATA
CTTGTCTGTGGCCCTGCAGGCTAGTATCTGATGCTCACCATTGCTCCTGCTGCTCCTCAAGTTTTTGGTTTTCCGCAATTTCTCTCATCTTATTTT
AGTCTTCTGGTCTTCTACTTTAGCTTGGATTCTGTACTTGTCTTCTACGTTTTCTCTCAGTAAACTGAGTTGAACTGCTGTGTTCTCAGTCCCTAAC
CCAAGCAGTTCACTCAGGAAGTGTCTGAGCTACTAGAGGTTTCTTTCAGCTTTTTCTCACACATTGTTTATGTTTGGGGACTTACATGCTGTGCCCCAT
TGTTTGGCCGTTTCTCCCGCGCCCCCACCCCTTAAAGCTCGGAGAAGCAAGGAGATCACAGATTTCTGTGCTTGGAAAAGCATCATTGC
CACATCTACACAGCTTCTCTCTGCCATTTAATTAATTTATTTATTTAATTGAAAAATTTCTCCCTGCTTATCTTGATTCTCATTGATGTTGTAGAAG
CAAATCCATCTTACTTAGGGAAGTAAAGTCTTCTCTTAGCTATGATGGCTCAGCTGCTTCTACACTGTAACATACAACAGTACTAGGAG
CCTGACTCTAGAGCCAGACAGCTGGATCCAGGGCTGCTTCCACTCTTATAGCTTATGCTTACTGAGGTTTACTTTTCCCACTTTTTTATTAGGTAT
TTAGTCAATTTACATTTCCAATGCTATACCAAAAAGTCCCCATACCCACCCACCCCACTCCCTACCCACCACTCCCCTTTTTGGCCCTGGCTTTCC
CTGTACTGGGGCATATAAAGTTTGAAGTCCAATGGGTCTCTTGTTCAGTATGGCCGACTAGGCCATCTTTTGATACATATGCAAGCTAGAGACAAG
GCTCCAGGTTACTGCTTATGTTGTTTCCACTATAGGTTGCAAGTCTTCTGTTTACTGAGCTTCCCTTACTGCTTGGTGTGCTTCTTCTTCTTCTTCT
GTGGTCAATGCTGACTGTGAGCATCTCTGTGTTTACTGAGCCCTGGCATGGTCTCACAAAGAGACAGCTATAGAGGTTTACTACTTAAG
CTCAGTTTACACTCTGTAATAATGGTGTGATGTAATAATTTGCCACAGGTATATTGTGATGCTTAAATAAATGTTACAACACAAAGCACTTTGAGCAAT
TACTGCTTTTTCTTATTTCTACAATTTGCTGCCAGGTTTAGAATAAAGCGAAGTATGGAATTTATTTTTCAGGCTTGGTTATTAGCATTTCTTCTGAACCT
GGAAGACTGTTTTTCTGGATGGAGAAAAGGTTTGTCTGTGTGAAGTTTCAATAATCAATCAAGCAGGCCATGAGCCCTGCCATTTAAAGATGGCTC
CTCTTACACTTGGGAATGAGACAGGAGCCAGCTGCTGACTTCCAGTAAACCTAATAAATGCTTTGAGTTTCAATTTCCACAGTCCCTAT
GCCTATGGATGCCAAGGACTTGTATGGATGCGCTTTGGATTTCATAATGCAGAGTCAATTATTACTTCTTGGATTCTCAGCTGAGTTGTAAGCAGGTA
AGTAAAAGGAAAAGAGGCACCTGATAAAGTCAGCTGTAGGACTAGAGTTTAGCATGCTCCTGAGAAATAGAAAATGACTGCTTGAACCTTACCAA
GCCACACAGGAAGCATCAAACCTCCCTATGGAGTGGAGAAGAGTCTTATAATTTTTAAATGGGCAGAGAAATGAATTTATTTTAAATTTTAGAGACAG
GGTTCTTTGATAGCTCTAGCTGTCTTGTGATTGTAGACAAAGCTGCTCAAACCTCAGAGATCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT
GCATGGACCACCCTGCTTCCCTGCCCCATTCTCTCCATTAATTTAAGTGAATGCTTGCAAAAGCTCACTTCTTTGGTGAACAGCTTCTTTACAATAAGT
ACCTTTGCCCTTCGTTTTATAGGATTCTTAAAAAGAAAAAAGATTAGCCAGGTGGTGTGGTGCACACCTTAAATCCAGCAGTCAAGGAGGCAGAG
GAAAGCAGATCTTGTAGTTTGGAGTACCTAGTCTACAGAGGGAGTTCCAGGACAGCCAAAGGCTACAGAGAGGAACTGTCTAAAAACACCAAGAA
AGAGAGAAAGGAGAGGGAGAGGATGATAGTCTTATGATAGAATGTCAGAAAAGGCTATAAGTTCCAATATGTGTCCCATGATTTCTAAGTCTAG
CCCTTCTGTTATAGTAAATCATAGTACACCCTCTCTCCAGTGTACTTTAACAGCTTTAAGGAAACATATAACTAAATGTCCAGGTTTGTATTG
GCCATAAAATGTTAGCAAAGCTAAGGTTTTCTAGGATTAATGAATAACATGTCTTTATTTAGTTTACTTAAAAAATCATTCTAAAAATCTGTTTACAT
ATCTGTCTCTCCAGGATTAACCTCATATTTGGTCCAGCAGTGTGTTACTGTTCTCTTCTGTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT
CCCAAGTTCAAAGGCTGATGAGAGAAAAAATCATGAAGAGATTACTCTAGGAAAGTTGCTCAGTGGATGGGATCTTTGGCGACGGGAAAGA
TGTCAGCTCAACCTGCTTCTCAGCCTTGTGTTACTACTTCTCAGTCCCTACCCGAAAATGCCAAGACATTTTAAACAACTTTAACTAATCA
GGAAGCTGAAGACCTGTCTTATCAAAGTTCATTTGCTTCTTGGAAATATAATACTAACATTACTGAAGAAAATGCCAAAAGATGGTAAGTTCTTGGG
CTACAGGGGGTTATTGATTGCTTCTTAAAGATCAGAATTACTGCTTATAAAAACCTGGATAAGGAAATCATAGAGATCTTCAAGTGTGAGGATGAGT
GACTGCTCTGTAGCTCTGATCTTACTTCCAGATGGCTAAATTTCAATTTGACCTTACTGAGTTTCAATTTGTTATGAAATTTTGGCCAGA
TTCCAAAGATGAGTGAAGTTTAAATAAAGTTGCCATCAATTTCTTATTATTTGGTATGTAAGATTTCAAGCAATTTCAAGCAATTTCAAGCTGTTAG
CCAATAATTTTCTTATGCTTATAATGCCAACAGGTCTATCCGAGAATCAAAATGACATATTAAGTGAAGAAATGCAACTGGGGTTTACTGAAGGCAGCA
GCTTAGTAATTAAGGTAACCATGGCTTAGGTGAAACTGGACCTGGGAATTCCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT
GAAAAGCTATAATTAACCTAGTCCCAAAAAATCTCAGCTACTCTGGAAAGCAGCATATTTTGTGTTGACAAAGTCAAGGACTTAGAACTTTTTTTTT

CTCACTGATCTGGAAGTGCCTTTAAGTATAGTTAAAGTGGTGGAAAAATTGAGCAACTATTTAAGAAAAGACTCTTTTTTTTCTTCTCCAGCAATGCTTT
CCTTCAAACCGTAGCTTCAAACCTCTGTCTTTAAATGATCAGGGGGCTGTGTGTTAAATATTGCCATTCATAGAACAGAGTGGGTCTGAGGAT
GCCTGTTTCCTTTGAAATCTATGCCCCCTCCAGTTTTCTAAAATTTAAGAAAACCAGAGACTTTGACAAATGTAGTTGCCAAAATGAGTTGCTTTTTAAC
TGCTCTAATAGTTTGGTCTTACCGGTGTTGTTTTAGTGTAACTTTTTTCCCCTCAGTTTTATTTTTATTTCTGTTGGAGATCACCACCGTGTACTGTAGA
TTTTCTGAGCTGAATGGTTCAAGGTGAGACTAATATTATACCTGAAAAGCCTAGCCTGGAGCTGACATCCAGATCCCTGGCTGTACCACTTTTAGCTGGG
TAAACTTGAATTCATTAATGGACAGCTGGGTCTAGTTACTTTTTGTTTTAAGATGTATTTAAATTTAAAACTATGTGTATGTGTGTGCTCCCGAA
TATAAGTATAGATGCCATGAAGGTGACAGATATTGAAACCCAGGAGTGGTGCAGAGCTATTGTGTGCCACCAGACTAGATGTGGCAACTTG
CAACCTCTGCAAGGGAAGTACATATCCCTAACCATCGAGCCACCTTTCTACCCAGTCTTAGTTGAAAAATAACACTCACATATACTTCATCGAGTATA
CAAAGATACCAGAAGAATGTGTGATGCTTGTAGGGTTAGGAGAAAATGAAGATATCATCTTTATTAGTGTGAAAAGGAGTTAGGGTTTTGAAAAGGT
ACATAATAGCTCTTTAAAGGACCTACATATACAGAAGTCCATTATAGAGTGTAGATGTAATGCTGTTTGTGAAAACCATCTCTGAGATTATTATGATGT
TGGGTTTTGGCTTAGTGAACAAAAAAGAGAGAGAGAGAGAAAATGTTACCATTTTTTAAACAGATTATTATTATTATTATTATTATTATATGTAA
GTACATTGTAGCTGTCTTCCAGACTCCAGAAGAGAGCATCAGATTTGTTACGGATGGTTGTGAGCCACCATGTGGTTGCTGGGATTTGAACTCAGGA
CCTTTGGAAGAGCAGTCGGTGTCTTAAACCGCTGAGCCATCTCACCAGTCCGAATGTTATCATTTTTTAATTATACAGGTTGATTAGAGCAAAACTAGAA
ATGGGAGAGATGAATGATCAGCTGTTTTAAACCGGAAAAAAGTGTGCTAGCCTTTAAAGTGAAAAAAGAAACATTTAAGTGAAAAGAAAA
TGACAAGGGCTCCATAGCCCTCCACCAGAGTGGTCAATGGTGCATAAAGCGCTTAGTGAACCTGGTGTGAGCGTAAAGAGGGAGGCACCT
GTGGGGAGGAAGATGGTCCCTTCCCTCTCTCTGATTTTTATGTTGTTGCAATTTCTTATATGTAGTCCAGCATTGGCCAGCCAGCATTAGAGGAGTTACT
GAAATATGCTGTGCTATAAGGGCAACGAATTGACACGGAATGTGACCATCACATAGTGAAGTAAAGTTGGGACAAACAACCTGGGTTCCAGACCCTCC
TTTGAATGTTAGAAGCTGAAGGTCTTGATTAAGTGCCTTATTGACATCGATTTTTTATTGTCTCACATACTATATCTGATTGCAGTTTGGCCCTCCACT
CTCCCAGTCTCTCCATCTCTCTCATCCGGATCCACCCCTTTCTGTCTCGTTAGAAAAACAACAGACTTCTGAAAGATAATAATAAATGAAA
TGTAATAAGATAGAACAAAAAATTAACGTATCAGATTAGGACAAAAACAACAAAAAGAAAGGCCAAAGAAAAAGGCAAAACCCAGATACAGCCGC
AGAGACAGTCAATCATACTCAGCAATCTCATAAAAAACTAACCTGGAAGCTGTAATATATACGCAAAGGACCTTTAGGAGGGAGGAGGATGTATA
TAAAAAAGAAAGAAAGTAAATTAATAAATGCAACAAACAAGCAAAACAACAAAAAGTTATCCCTGCAAAAGATGTATAGAGGTTTTGTTTTT
GTTTTTGTTTTTTCTTTGGTCTACTGTGAATGTGGCCCTACCCCTAAAGAGTGTATTTTCCCAAGTGTCTCTTTGGGAAAGTAAAT
TTTCACTGCAAGTGGTTATCAATTTGGAGATGGTGTAGGGATGGGGCATGCGTCCACTTCTTTCATCTAGGACCTTGGCCCTGGTGGCAGAGCTGT
GCAGGCCCTGTGCTTGTGCTCAGTCTGTGTGAGTTGCTGTGAGCTTTGCTTGTGTTCAATTCATTGGGCCCTGTTCCTAGGTGTCTCCACCCTCTCTG
GCTCTTACTCTTCTGCATCTCTCCACAGGGTTCCTTGGGCCCTGGTGGGGAGGGGTTGATGGAGACAGCTCAACTAGGGCTGAGTGTCCAAGT
CTCTCATTTCGACAGTGTCTGGCTGTGGGTCTGTATTTGTTCCATCTTCAGACCCATTTAECTCAGATGTAACCTGAATAAAATTTATGATCACGG
TATTAATAGTAGACTGTACTATATGGAATGTGGAAATGTAGAAAATAACTCTGTGTGTGTGAATTTGGTACTGTACTGTCCTGACTTGTGACT
TCATCAAGATTATTATTAGTGGGTTTACATTTTGAATTTCAACTGTCTACTGGTGTCTCCAGTATGGGGTTTTGTTTTTAGACTTTTTTGGTGTGTGG
TACAGGGATGTAGCCAGAACCTTGAGAGTGCCAGCTAAGTGTGAGCATTGAGTCCCTGTGAGCCAGGTGCTTTTGAATACAGATTTCCCTGTGA
AAGGTGAGTTTGAAGGAGCTCTCAGGCTCTTCTGATTTACAGAAAGCTGTGGGAAAGTAAAGTTTCTGGGAAAAAGCCATCGTGTCTCTCTT
GCCTGCCTCTTGGCTTGTGAGTGAAGTTCAGGGTCAAGAAATGAAATAATCAACTTGTCTGTATTTTTACAGTAAAGCTTACTGGGCAAA
GGGGAAATGTGTCCCTCAAAAATTTGCAATATAGTACCTTACTAGTTTTTATTGTGCATCAACTTGTCTTAGATGTACTGAGTTGCAAGAAATAG
ACTGTGAGTTGCTTGAATAAGATTATCTGAGGATCCAGTTTATCTTTTCCGGAGTTAATGGAAAATGAACTTCTTGAATAGATAAAAGAAATAGTTCT
GGAATTTCCAGAGTTAATATGTGCTCAGCAGTAACTGGCCCGTAACTGAAAACAAGTGAAGACTTGAATACCATGATGCATTTGAGGTCGTTA
GGTTTTTCTGATCTTAGTTTATGATGCATTTATTTGCTTTAGGGAGAGTATAACAAGTTTTGAAAAAAGTTCTCCCATGAAATAAATTTACAAGATGCC
CAAAGAAAAGTTTATAGATCACTAGCAGCATTGGCAAGTATTGTATAAGACTAACTCTAAGTGAACAAAAACATTTACCACCAAAAGTTGTCATATATTA
TGGAAAGACATAAAATGAAATTAGGCTGGAAAATACAAAATGAGTATAAGTTAGTTCTTCTAGGGAGCAACTGAGGCATAAGAAAATAGTTTCTGATCA
GAAGAGAGCCTAGACGTCAGTTTGGATTGTCTCCTGAAGAGATTAACATAAATACATTTTTCTGATGACAGTGTAGTCCGTTGTTCCAGAGACAGTTTGG
GCGATAAAATGAGAACATTTTCTAAGCCTTAAAAAACAATAATGCGGAGTAAAGATGTAAGAAAGAAAAGAAAGAAAATACCAAGAAAATGGATTCT
TTGCTCCCAACCCCAACCCCAACCAAGTAACTAGAAATGAGTTAAGGGGTGAGAGAGGTTGGGAAAAGTGTGACCTGGAACAAGAAAGGAGGGA
TGTTGACAGTTGGGTTGGCTCAGTCTTTTTCCACCTGAAAGGCAATACAGCCAAAAGCACAGCAGAGATAAAATTCAGAGTAAATAGAGGGAAAGCACTC
TTTGCAGTGCAGGTGTTGAAGCTGATAAGACCTGTA AAACTTTAATCTAAAAAATGTGAGACATTGACAACCTCAAGTAGGCTTTCAAAGCATTAAA
CAAACATGTGGCTTGGCCTCTACTGTGGGTAAGGAAAGTATGGTCAATTTGCATTGATGGACTGTAGACTTCATCCTTTCCCTAGGATGATATCTAAGGT
CATGTACCCGTCAGTGCACCTCCAGTGCAGGTTCTGGGAGTGTGCTCTGATCAATTTGCTGATTTCTGTGAAGCAAGGCTGCTGACAATGACTTA
GTGGCTTGAACAATAGGTTTACTCTCCACTTCCAGTTTGGAAATGCAAAAGCAACCTGCTCAGGTTAGCCAATTTGAAGGAGTGTGCGAGAGGAC
TTGGAGTGTGGCCAAAGCAGAAGCCAACTTTCAGAGTTGCATGCAAAATGCAGCCAAAGATCAACAGAGGTGTCTGCCAACTCCAAGCTATTTAGGCA
CATAACAATAAACACTATGCTATTTGACGCTTTTCTGTTGTTCTTAGATAGTATTATTTAATGTAATAGATAAATTGATACAGGACAGGAAATAGACTGT
ATGACATTTCTGTGTTCTATCTATCCTGTTGACATTTCTGAGGTAACTATTGAGGAGTCAAGGAGTGTGGGGTTACCAGCTACAGATCTAGCATAGTA
TGGTTTACTTAAAGTTGTGGAACATGCTGCAAAAATAAGAAAGCCACAACCTTTTCCATATGATGTCTCAAAAGGTTACTCCAAAAGGAGGCG
AGAAACCAGGAAAAGGGATAAGAAAAAAGAAACTTGGCTCAAAAACAGCTTTTTAAAGCTCTCTACTTTTTCTGTCTATGGTGGTGTGTTGGGCTA
ACTCCAGCTAAACTCTTGTCTCTTATGAGACTTTTGTAGATTATATTATTCTGGCCAAAGAAATAAAATCTAGAATCACTTTATTCCCTAGTGGATTGG
ATGAAAATCGTGGTAAAAAAGAAAGTTTCAGCTATAATTTCAATGGGAGGCAATTTGGAGAATAACCAAGCTGGGATGCTGGTCTGTGAGTATCTTG
ATTTCTGGCTATGATAAAAAAGTACCAAAATCAACTGGGAGGAAAGGTTATTCTGACTGTTTTGGGTAAACAGTCCATCAGTCAAGGGGAA
GTCAGGGCAGAGGAAACTCAAGGGAGGAAAGCTGGAAGCAGGAACTGAAGCAGAAGTCAACAAGGTATGTTGTTTACTGGCTTGTCTCCCGGTGACTTGC
TAAGGTGTCTTCTTAGACACCTCAAGACCCTACCCCGAGACAGGACAACAGCACCCACGGACTTACTATAGGCCAGTCTGATGGAGGCATTTAC
TCAGTTGATCTTCTTATCTTAGATGGCCCTAGCTTCTATCAAGTTGACAAAAGTCAACCAAGGACAATAATTGATGACACACACCGTGTGATGCTATATT
CAGTCACTACTACTTAACTTCTAGCTGAAAAGGTGAACTACTGTACTGTACAATTTGAAAATGCTTCCAGAAAAGGCAATTTTTCTATTTCCATTTATG
CCTCTATACTGATAGTTAGTTCAACAGTTGATATGTAAAAGCTTTGGTTAAAAAAGAAAGCCGGGCGTGGTGGCGTACGCCCTTAAATCCAGCACT
TGGGAGGCAGAGGCAGGTGGATTTCTGAGTTCTAGGCCAGCCTGGTCTACAGAGTTCAGGACAGCCGGAGGTACACAGAGAAAACCTGTCTCGGTGT
CTGGGGGGGGGGGGGGGAGGTTTGAAGTGTGCAAGAAATTCAGTGAATACTTTCAAACTCATGTAATAGACTGCAACAACAAATTTCAACAAGAA
ATGTAGACTGAGTTTCCAGAGCTCAAGTGAAGAAATCTCAGGAAAATGGCCCTACTTTTTTAAAGGCATTACCCATTCTCGTAGTTTATGGTG
GTTTTTGAATTTTGAATAAGATTCTTTGTAATCTTCTCAAGGGCACAAAGTATAGTTAGAGTGTGCATATGCTTGTGTGAGTGTGTGTTTTGTTG
CCGAGAGGTTAAACCTGGGTACCATTGCCAGGGTCTAGCCAGTTATTTTTGAGACAGGATCTTCTTCTGAACCTAGAGCTCACTATTTGATTAGACT
ACTTGACTAAAAAGCCAAAGGAGCTTCCCTGGCTTCTCTCCCTCTTCTGAAATTTACAGATGAGTCTCACTATACTGACTCCCCCAACCACCCTTTT
ATTGGATTTTTCTTTTATTTACATTTCAAATGTTATCCCTTTTGGAGGGCTCCCTCTATCCCATCCCCCTACTCTCTGCTTCTAAGA
GGGACTTCCCACCCATCCACTCCCTCTGCTCTGCTCCCTGGCAATCCCTACTCTGGAGCATCAACACCCTAGGCCAACCCTCCCTCCCA
TTGATGTCAACAAGGCCATTCTCTGCCACATATGTGGCCGGAGCCATTGGTCTCTCCATATGTACTCTTTGGTTGGTGGTCCAGTCCCAAGGAGCTCTGG
GGGGGGGGTGTCTAGCCTGTTGACACTGTTGCTCCCACTATGGGGCTGCAAAACCCTCAGCTCCTCAGTCCCTCTCTCCAACTCCCACTCCCACTGGGACC
CTGTGCTCAGTCCAAATGGTGGCTGCAAGCATCTGCCTCTGTATGCTGACTTTTTAATGTGGTTCTGGGGATTACGCCAGGCTCATGCTGTGCATG
GCAAGCTAGTCTTTCTAAGTCATCTCTGGCCCTTAAAAATCTTTTTATTTTTCCACACAAAGATGTTTTAGGGAAAAATGGGCGCCT
CCTAACAACAATTTCAAAAACAGTCAATGGTTGGTTTTTAAATAAAAAGGTTGGTAGCTCTCCAGCAGTATAGAATGTCTCTGGATCATTGAAATCCTAG
AGAGAGCAAGAGGACCCAGTATTTAGCAATAACTATGGCAACCCTCTACTCCGGTCCATGTCCCTGAAAAGCACTTTGAAGATTGTCTTGAACCT
ATTTTATTTAAATCAGAAGTTGTTGGAGAGAGTGAAGAGCTGGTGTGATTCTCTGGTGTCTCTGGGGCCCTCAGCGTTTCTGCTGGGTCTTTAG

AGGATCTAGCCATACCCTTTACCTTTCTGCCCCAGGGAACTCAGGACCTGATAATGCATAAATAAGCTGCGATCCTCCATCCAAGAAAAGA
ATGTTGAGCGTCCTCTAATGGTTCCACACAGGCTTACGACATGTGTAATAAAATACCTTATCTGAGAGCATGAGTAGGGGAGCATCAGCATGGTA
CAAGGATACCAGAATTCAGGGCTGAGTATTTTTTCCAAAAAGATAAGAGACAGGAAAATAAAAAATGTTTTTCAGGAGTCGAAAAGCTTAAAAATGTCAAC
AATCTCATGCAAAAATATAGAAAAGGTTTTGGAGTTCTAGGATGGAGTGACAGGATTCATATAAAGTTGTTACGTAATAGATAAAATTTCT
TTTTCTAAAATCTCTGGATGTGTGAAAAGTGATCAAGGACGCTTTGCTCTGAGCATGCAGCCTTGAGGGTCGCATCTGAAAACCCAGAG
CAGCCTATGGGGCTTGAGGGTAGAGCTTTGCCGAGGAGTGGTTCAAGTGCCAGTCCCAGATGGATGCTCAGGTTTTCAGTTTTTTCAGAAA
ATTGCCACAGGCTTAGGCTAGGAGGTTGCAGATGGTTTTAGCTCAATCAGGGATGATGCTCTAGAAAAAGAAAATAAAGTGTCCAGCATTTA
TATCTCAAGCAAAATATCAGAAGGAGAACTGGCCTCTTTGTTGGCCAATGTGTTTTCAATAGATAAGTTGCATATTTTAGCATATAAAATCTTACA
GGCATAAAAAGTATGATAGTTATCTATCAAAAAGCAGGGATCAACAACCTTTCTAGTTAAGTGTGAGCTGTGGGCTTCTTGGCTTCGAAGGTTTTAT
GGTTCTTCAAGACTCCGAGCCCTGCAGTTGTGTGGCAGAAGCAGCCATAATCAGTGTGGTATAAATGGATGTGTGGTGACCAATAAAAAGTAAAT
AAGAAAAGAGCAGTGATATCTAAGCTTGGCCAAAGGGCTATAAATTTATCAGCCCTGATTAAGGAAGAAAGCCCTGATTTATAAATTTTGAAAAGAAAATA
AATATAGGTCATAAAGAGTTGCCTAGGAAAATAAGAAAGTTTATATAGCACTAATCTATATAAATTTATGTTAATGACATGGATAGCTAGATTTGTTTTCA
TCACTACAGAATATAGTGGGTTTTTTTTTCTTCACTATCTTTAAATTTGTTAAATGATAACATGCAAGCAAGGAGATTCATTGTAGTGTTCATGTACA
CTTTGCTTATAATCAGTGGCCACTTTCTTACCTGTCTCTGCTCTCTTGTCTAGTGTCTGCTTACCCCCCTCCCCCATGGCAGCTTTCTGCCCTTTGTG
TCATACCTTTCTCTTTTCACTTCTCTTTTGCCTCTTTTTAAAAATGGTTTTCTTTGTCATGATCCCTTTTTAGTTTTTCAACAACACAGAGAGAGAG
ACAGAGACAGAGACAGACAGAGACAGATAGAGAGAAAATAGACAGAGACAGATAGAGAAAACACACACAGATCGAAAAGATCTAAGG
TCTACAAAAAGAAAATATGTGATTTTATCAATATTTGTTTAAAAATAAACCAATTTGGGTAGGGCCGCTAGACCTAAGGTCTAAGACAAG
CTCTCATGAAGACGTTAAGACGATAAGACATACTACACAGATAGTTAGAATTTTGTGTTTGAACATTTAAAAGTAGAATTTACTAGTTTACTTGATG
TACTTGGATTTGCCAGGAAGTCTACGGGTTGACAAATACAGATTTCTGCAGTTATAGATGGAAGTACAGAGATGAATTTCTTCCGTTGTGTTTTAA
AAAATATGTGCTCTTGTCCCAAACTCTACGGATGGCTGTAATAAAAATTTGGCTGTTTTAGTTGCTACTTGTCTGCCTTTGCAAAAAGGAGTGTGGAAA
GCTACTTACTTCACTGAGCTTGCTCTTTAAGATGAGGAGCTATCTAAGCTTCTGTCTAAGCTTTACTTCAACATTAGCCAAGTCCGTAATT

Selection Cassette:

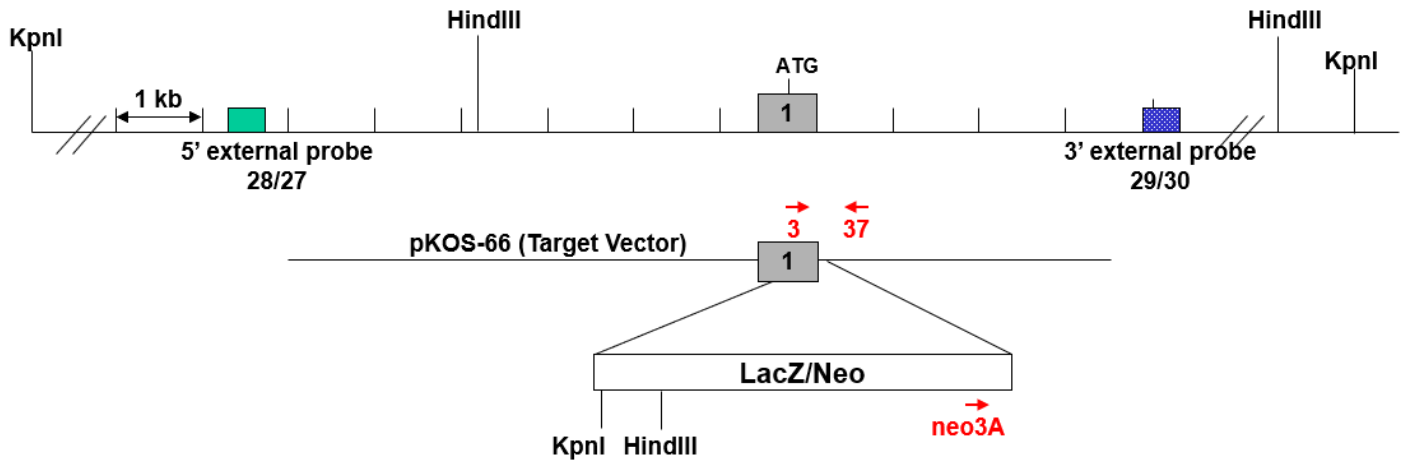
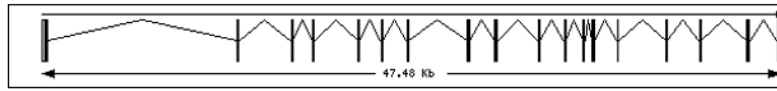
GGCCATAGCGGCCATTTAAATGGCGCGCGGATCCCGGGCCGCTCTAGCTAGACTAGTCTAGCTAGAGGAATTCGGCCCCCTCCTCCCTCCCCCCCCCTAACGTTACTGGCCG
AAGCCGCTTGGAAATAAGGCGCGTGTGCGTTTTGCTATATGTTATTTCCACCATATTGGCGCTTTTGGCAATGTTGAGGGCCGGAAACCTGGCCCTGTCTTTGAGCAGC
ATTCCTAGGGGTCTTTCCCTCTCGCCAAAGGAATGCAAGGCTCTGTTGAATGTCGTGAAGGAAGCAGTTCTCTGGAAGCTTCTTGAAGACAAAACAGCTCTGTAGCGACCC
TTTGCAGGACGCGGAACCCCTTGGCAGAGGTGCTCTGCGGCCAAAAGCCAGGTGTATAAGATACACCTGCAAGGGCGGCACAACCCAGTGCCACGTTGTGAGTTG
GATAGTTGTGAAAGAGTCAAAATGGCTCTCTCAAGCGTATTCAACAAGGGGCTGAAGGATGCCAGAAAGTACCCCATTTGTTATGGGATCTGATCTGGGGCCCTCGGTGCACA
TGCTTTACATGTGTTTAGTCAGGTTAAAAAAGCTTAGGCCCCCGAACCCAGGGGACGTGGTTTTCTTTGAAAACACAGATGATAAGCTTGCCACAACCATGGAAGAT
CCCGTCTGTTTTCAACCGTCTGACTGGGAAAACCTTGGCGTTTACCACCTTAATCGCTTGCAGCACATCCCTCTTTCGCGAGCTGGCGTAATAGCGAAGAGGCCCGCACCC
ATCGCCTTCCCAACAGTTGCGCAGCCTGAATGGCGAATGGCGTTTTGCTGTTTTCCGGCACCAAGCGGTCGGTGGAGTGCATCTTCTGAGGCCGA
TACTGCTCTCGTCCGCTTGGCAGATGCAGGTTACGATGCGCGCATCTACCAACGTAACCTTACGCTTACGCTTACGCTTACGCTTACGCTTACGCTTACGCTTACGCT
ACGGTTGTACTCGCTCACATTTAATGTTGATGAAAGCTGGTACAGGAAGGCCAGACGCAATTTTGTGATGGCGTTAACTCGCGCTTTCATCTGTGGTGCACCGGGC
GCTGGGTGCGTTACGGCCAGGACAGTCGTTTGCCTGTGAATTTGACCTGAGCGCATTTTTACGCGCGGAGAAAACCCGCTCGCGGTGATGGTGTCTGCGCTGGAGTACGG
CAGTTATCTGGAAGATCAGGATATGTGGCGGATGAGCGGCATTTCCGTGACGCTCTGTTGCTGCATAAACCGACTACACAATCAGCGATTTCCATGTTGCCACTCGCTTT
AATGATGATTTTCAGCCCGCTACTGGCAGGCTGAAAGTTGAGTTGCGCGGTTTCGCTGAAATACCTAGCGGTAACAGTTTTCTTTATGGCAGGTTGAAACCGCGCTCGCC
CGGCACCGCGCTTTCCGGCGTGAATATCGATGAGCGTGTGTTATGCCGATCGCGTCACTACTGCTGAACGTCGAAAACCCGAAACTGTGGAGCGCGGAAATCCC
GAATCTCTATCGTGGCGTGGTTGAAGTGCACACCGCGCACGCTGATTGAAGCAAGAGCCTGCGATGTCCGTTTTCCGCGAGGTGGCGATGAAAATGGTCTGTCTGTG
CTGAACGGCAAGCCGTGCTGATTCGAGGCGTTAACCGTCAAGGATCATCTCTGATGTTGAGTTCAGGTTCAGTATGATGAGCAGAGATGGTGCAGGATATCTCTGTGATGAGC
AGAACAACCTTTAACCGCTGCGCTGTTCGCATTATCCGAACCTATCGCGTGTGTTACACGCTGTGCGCAGCCTACGCGCTGATGGTGGTGGATGAAAGCAATATTGAAACCC
CGCATGTTGCCAATGAATCGCTGACCAGTATCCGCGTGGCTACCGCGATGAGCGAACCGTAACCGCAATGGTGCAGCGCATCGTAATACCCGAGTGTGATCATC
TGGTCTGGGGAATGAATCAGGCCACGGCGCTAATCAGACCGCGCTGATCGCTGGATCAAACTCTGTCGATCCTTCCCAGCGGTGAGTATGAAAGCGCGGGAGCGCACA
CCACGGCCACCGATATTTATGCCCCGATGACGCGCGGCTGGATGAAGACAGCCCTTCCCGCTGTGCCAAATGGTCCATCAAAAAATGGCTTTTCGCTACTTGGAGAGAC
GCGCCGATTTTCAGCTTCCGTAACCGCAGCGGATGGGTAACGCTCTGCGCGGTTGCGTAAATACCTAGCGGTAACAGTTTTCTTTATGGCAGGTTGAAACCGCGCTCGTC
TGGACTGGGTTGATCAGTCTGATTTAATATGATGAAAACGGCAACCCGTTGGTGGCTTACGGCGTGTATTTGGCGATACGCCGAACGATCGCCAGTTCTGTATGAAG
GTCGCTGCTTTTCCGACCGCACCGCGCATCCAGCGCTGACGGAGCAAAAACCCAGAGCAGTTTTTCAGTTCCGTTTATCCGGGCAAAACATCGAAGTACCGACCGCAATA
CCTTGTGATGCTGGTGTGATACAGCCGCTCAGCGTGGCAGCTCAGCGGAAAACCTTATTTATCAGCGGAAAACCTACCGGATGATGGTGAATGTTGCAATGGCGAT
TACCGTTGATGTTGAAGTGGCGAGGATACACCGCATCCGGCGCGGATTTGGCTGAACTGCCAGTGGCGCAGGTAGCAGAGCGGGTAAACTGGCTCGGATTAGGGCCGCAA
GAAAACATCCCGACCGCTTACTGCGCGCTGTTTTGACCCTGCGGATCTGCCATTTGTCAGACATGTATACCCCGTACGTTCTCCCGAGCGAAAACCGTCTGCGCTGGGGGA
CGCGCAATGAATATGCCCCACACCAGTGGCGCGCGACTTCCAGTTCAACATCAGCCGCTACAGTCAACAGCAACTGATGAAAACCGCATCGCCATCTGTGCACGC
GGAAGAGGCACATGGCTGAATATCGAGGTTTCCATATGGGATTTGGTGCCGAGCTCTGAGGACCGCTCAGTATCGCGGAATTTCCAGCTGAGCCGCGCTGCCATC
TACCAGTTGGTCTGGTGTCAAAAATAAATAAACCAGGCGAGCCATGCTGCGCGTATTTCCGCGTAAAGAAAATCCATTATGTACTATTTAAAAACACAAAACCTTTGGATGT
TCGGTTTATCTTTTTCTTTACTTTTTTATCATGGGAGCCTACTTCCGTTTTTCCCGATTTGGCTACATGACATCAACCATTACGAAAAAGTGATACGGTATTATTTT
TGCCGCTATTTCTCTGTTCTGCTATTTATTTCAACCGCTGTTTGGCTGCTTTTCTGCAAAACTCGGAATTTTATTGACAGTTATAATGGTTACAAAATAAGCAATAGCA
TCAACAAATTTCAAAAATTTAAGGCTGCGGATCCGCTCGAGCAGTGTGGTTTTCAAGGAAAGCAAAAAGCCCTTCCACCCAGGCTGGAATGTTTTCCACCAATGTCGAGCAACCCCGCCAGCGTCTGTCTATTGGCGAAT
TGTGAGCAGTGTGGTTTTGCAAGAGGAAGCAAAAAGCCCTTCCACCCAGGCTGGAATGTTTTCCACCAATGTCGAGCAACCCCGCCAGCGTCTGTCTATTGGCGAAT
CGAACACGAGATGACAGTGGGGCGGCGGCTCCAGGTCCACTTTCGATATTAAGGTTGACCGGTGTGGCCTCGAACCCGAGCGACCTGACAGCAATATGGGATCGGCCA
TTGAACAGAGTGGATGCAAGCAGGTTCTCCGGCGCTGGGTGGAGAGGCTATTCCGCTATGACTGGGCAACAGACAACTCGGCTGCTGATGCGCCGCTGTCCGGCT
GTCAAGAGGCGCGCTTTTTTGTCAAAGACGACGATCTCCGCTGCTGCTGAACTGAATGAACTGACAGGACAGGCGCGCTATCGTGGTGGAGGACAGCGCGCTTCTT
TGCAGCTGTGCTCGACGTTGTCACTGAAGCGGGAAGGACTGGCTGCTATTGGGCGAAGTGCAGGCGGAGGATCTCCTGTCATCTCACCTTGTCTCCTGCCGAAAAGTAT
CCATCATGGCTGATGCAATGCGCGCGCTGCATACGCTTGTATCCGGCTACCTGCCATTCGACACCAAGCGAAAACATCGCATCGAGCGAGCAGTACTCGGATGGAAGCCGG
TCTTGTGATCAGGATGACTGGACGAAGAGATCAGGGGCTCGGCCAGCGCAACTGTTCCGCGAGCTCAAGGCGCGCATCCCCGAGCGAGGATCTCGTCTGTGCCAT
GGCGAGCTGCTTGGCAATATCATGGTGGAAAATGGCCGCTTTCTGAGATTCAGTGTGGCGGCTGGGTTGGGCGGAGCCTATCAGGATGAGGATGAGCGTTGGCTACCC
GTGATATTGCTGAAGAGCTTGGCGCGAATGGGCTGACCGCTTCTCTGTGCTTTACGGTATCGCGCTCCCGATTCGAGCGCATCGCTTCTATCGCTTCTTACGAGTT
CTTCTGAGGGATCGCAATAAAAAGACAGAATAAAACGACCGGTTGTTGGTCTTGTTCGGATCCGAATCTCAGAGGCGCGCATTTAAATGGCCAGCGAGGCC

GGCAGTACCTGATCTCTAGAAAATCCCTTATGGACCAAAATAGACATTTTCCAACCTGCTTACTAGTCACATAATAAAAAATATGTTTACAATTTTGTTA
AGCATCAAGGTCAAACCTGTGTGTTTTATCAGACACACCCCAACTCCAACGTTTTTCAAAGTTAGAATAGCTTCTTGCCGTGCTAGTCATCTCAATC
CTTTTTTTTTTTTTCTGCTTCCCTTTCTTAAAGATGATATGTTCTTGAGGCCAGTTGTTTTCTGGGTCACATGCTCTCCATCTCTAGAGGGTCTTTTC
TAGTCTCAGAATGGGCACAAAGATAATACTCCTAGGGAACAGAGTATCCCTATCTTCTCAATGAAGAGTGAACCCAAATCCCAGCAGTTTCAAGTGCATA
CTTGCTGTTGGCCGTCGCAGGCTAGTATCGTAGTAGCTCACCATTCCCTTGCTGCTCCAAAGTTTTTGGTTTTCCGCCATTTTCTGCCTCATCTCTATTTT
AGTCTTCTGGTCTTCTACTTTTAGCTTGGATTCTGTATCTTGTCTTACGTTTTCTCTCAGTAACTGAGTTTGAAGTGTCTGTTCTCAGTCTAACCC
CCAAGAGTTCACTAGGAAGTGTCTGAGCTACTAGAGGTTTCTTTACGTTTTTCTCACACATTGTTTCATGTTCCGGGACTTACATGTGTGCCCAT
TGTGTTGGCCGTTTTCTCCCGCGCCCCACCCCAACCTTTAAGCTCGCGAGAAGCAAGGAGATCACAGATTTCTGTGCTTGGAAAAGCATCATTGC
CACATCTACACCAGCTTCTCTCCTGCCATTTAATTAATTTATTTATTTGAAAATTTCCCTCCCTGCTTATCTTGTATTCTCATTTGATGTGTAGAAC
CAAATCCATCATCTTACATAGGGAAGTAAAGTCTTCTCTTTAGCTATGTATGGCTCCAGTCTGCTTCTTACACTGTAACATAACAACGTAGCTAGGAG
CCTGTACTAGAGCCAGACAGCCTGGATGCCAGGCTTCCACTCTTATAGCTTAGTGAGGTTTAGCTACTTTTTCCCCCATTTTTATTAGGTAT
TTAGCTCATTTACATTTCCAAATGCTATACCAAAAAGTCCCCATACCCACCCACCCCACTCCCTACCCACCCACTCCCTTTTTGGCCCTGGCTTTCC
CTGTACTGGGGCATATAAAGTTGCAAGTCCAATGGGTCTCTTTGCAAGTGTAGGCCGACTAGGCCATTTTTGATACATATGCAGCTAGAGACAAGA
GTCCTCAGGCTACTGCTTAGTTTCAATTTGTTTCCACCTAATAGGGTTCAGTTCCCTTTAGTTCTTGGGTGCTTCTCTAGTTCTCCATTGGGGCCCT
GTGGTTTCAATAGCTGACTGTGAGCATCCACTCTGTGTTACTAGGCCCTGGCATGGTCTACAAGAGACAGCTATAGAGGTTTAGCTACTTAAG
CTCAGTTTACACTGTGATAAATGGTGTAAATTTGCCACAGTATTTGTGTAGTCTAAAATAAAATGTTTACAACAAAAGCATTGAGCAAT
TACTGCTTTTTCTTATTTACAATTTGCTGCCAGGTTTAGAATAAAGCGAAGTGTGGAATTTTTCAGGCTTGGTTATTAGCATTTCTTCTGAACCT
GGAAGACTGTTTTTCTGGATGGAGAAAGGTTTGTCTGTGTGAAGGTTTTCATAATCATAATCAAGCAGGCCCATGAGCCCTGCCATTTAAAGTGGCTC
CTCTTTACACTCTGGGAATGAGGACCGGAGCTGCTGAACCTTACCAGGATAACCTAAAATTTGGAGTTCATATTTCCACGATCCCT
GCCTATGGATGCCAAGGACTTGTCTATGGATGCGCTTTGGATTTCATAATTCAGAGTCAATATTACTTCTTGGATTCTCAGTGTGATAAGCAGGTA
AGTGAAGGGAAAAGAGGCACCTGATAAAGTCAAGCTGTAGGACTAGAGTTTAGCATGTCTCTGAGAAATAGAAAATGACTGCTTGAACCTTACAAA
GCCACACAGGAAGCATCAAATCCCTATGGAGTGGAGAAAGTCTTATAAATTTTTAAATGGGCGAGAGAAATGAATTTAATTTTATAGAGACAG
GGTTTTTGTATAGCTCTAGTCTTTGATTGGTAGACAAGGCTGTCTCAAACCTAGAGATCTTCTTCTTGTCTGAGTGTGGGATTTAAAG
GCATGGACCACTGCCTGCCCTTCTCTCAATTTAAGTGAATGCTTGAAGGCTCACTTCTTGGTGAACAGTCTTCTTGAACAAATAAGT
ACCTTTGCCTTCGTTTTATAGGATTCTTAAAAAGAAAAAAGATTTCAGCCAGGTGGTTGTGGTGCACACCTTAAATCCAGCAGTCAGGAGGCAGAG
GAAAGCAGATCTCTTGGTGTGAGGCTAGCTTACAGAGGGAGTTCCAGGACAGCCAAGGCTACAGAGAGGAAGTCTAAAAACACCAAGAA
AGAGAGAAAAGGAGAGGAGAGGATGGATAGCTTATTGATAGAATTTGAGAAAAGGCTATAAGTTCCAATATGTGTCCATGATTTCTAAGTCTAG
CCCTTCTGTTATAGTAAAGCTAAGGTTTTCTAGGATTAATGAATAACATCTTTTATTTAGTTTACTTAAAAAATACTAATTAAGATTTGATTG
GCCATAAAAGTTAGCAAAGCTAAGGTTTTCTAGGATTAATGAATAACATCTTTTATTTAGTTTACTTAAAAAATACTAATTAAGATTTGATTG
ATCTGTCTCTCCAGGATTAACCTCATATTTGGTCCAGCAGCTGTTTACTGTTCTTCTTCTTCTGCTTTTTTTTTCTTCTTCTCAGTGCCCAA
CCCAAGTTCAAGGCTGATGAGAGAGAAAAAAGCTCGGCCGCTTAGAGCCATAGCGCCAAATTAAGTGGCGCGCCGGATCCCGGCCCTGCTAG
ACTAGTCTAGAGAAATTCGCCCCCTCTCCCTCCCCCCCCCTAACGTTACTGGCCGAAAGCCGTTGGAATAAGCCGGTGTGCGTTTGTCTATAT
GTTATTTTCCACCATATTGCGCTTTTTGGCAATGTGAGGGCCCGAAACCTGGCCCTGTCTTCTTGGACGAGCATCTTCAAGGCTTCTTCCCTCTCGCC
AAAGGAATGCAAGGTCTGTTGAATGTCGTGAAGGAAGCAGTTCCTCTGGAAGCTTCTTGAAGACAAAACAAGCTCTGTAGCGACCTTTGCAGGCAGCG
GAACCCCCACCTGGCGACAGGTGCCTCTGCGGCCAAAAGCCAGTGTATAAGATACACCTGCAAAGGCGGCACAACCCAGTCCACGTTGTGAGTT
GGATAGTTGTGGAAGAGTCAAATGGCTCTCTCAAGCGTATTCAACAAGGGGCTGAAGGATGCCAGAAGGTACCCCATTTGATGGGATCTGATCTG
GGGCTCGGTGCACATGCTTACATGTGTTAGTCAAGGTTAAAAAAGCTGTAGGCCCCCGAACCACGGGGACGTGGTTTTCTTTGAAAAACACGA
TGATAAGCTTGGCACAACCATGGAAGATCCCGTCTGTTTTACAACGTCGTGACTGGGAAAACCTGGCGTTACCCAATTAATCGCTTGCAGCACATCC
CCCTTTCGCCAGCTGGCGTAATAGGGAAGAGGCCCGCACGATCGCCCTTCCCAACAGTTGCGCAGCCTGAATGGCGAATGGCGCTTTGCCTGGTTTTCC
GGCACAGAACGGGTGGCCGAAAGCTGGCTGGATGCGCATCTTCTGAGGCCATCTGCTGCTGCTTCCCTCAAACCTGGCAGATGCACGGTTACGAT
CGCCACTAGACCAACCTGAACCTATCCCAATACGGTCAATCCCGTTTTGTTTCCCGAGAGAACCCGAGGTTGTTACTCGCTCACATTTAATGTTGA
TGAAAGCTGGCTACAGGAAGGCCAGACGCGAATTTATTTTGTAGGCGTTAACTCGGCGTTTCTGTTGTTGCAACGGGGCGTGGGTGGTTACGGCC
AGGACAGTCTGTTGCCGTCTGAATTTGACCTGAGCGCATTTTTACGCGCCGGAGAAAACCGCTCGCGGTGATGGTGTGCTGCGCTGGAGTGACGGCAGTT
ATCTGGAAGATCAGGATATGTGGCGGATGAGCGGCATTTCCGCTGACGCTCTGTTGCTGCATAAAACCGACTACACAAATCAGCGATTTCCATGTGCCA
CTCGCTTAAATGATGATTTACGCGCGCTGTACTGGAGGCTGAAGTTAGATGTCGCGGAGTTGCGTACTACCTACGGGTAACAGTTTCTTTATGCG
AGGTTGAAACGCAGCTCGCCAGCGGCACCGCCCTTTCGGCGGTGAAATATCTGATGAGCTGGTGGTTATGCCGATTCGCTCACACTACGCTGTAAC
GTCGAAAACCCGAAACTGTGAGCGCCGAAATCCGAATCTCTATCTGTCGGTGGTTGAACTGCACACCGCCGACGGCACGCTGATTGAAGCAGAAGC
CTGCGATGTCGGTTTTCCGCGAGGTGCGGATTGAAAATGGTCTGTCTGTCTGAACGGCAAGCCGTTGCTGATTTCGAGGCGTTAACCCGTCACGAGCATCA
TCCTCTGCATGGTCAAGTCAAGTATGAGCAGACGATGGTGCAGGATCTCTGTATGAGCAGAACAACCTTAAACGCGTGGCTGTTCGCTATTACCC
GAACCTCCGCTGTACAGCTGTGCGACCGCTACCGGCTGATGTGGTGTGATGAAAGCAATATTGAAACCCACCGCATCGCTGCAACGAAATGAACTGTC
TGACCGATGATCCGCGCTGGCTACCGGCGATGAGCGAACGCGTAACCGGAATGGTGCAGCGCATCTAATACCCGAGTGTGATCATCTGGTCTGCTG
GGGAATGAATCAGGCCACGGCGTAATCACGACGCGCTGTATCGCTGGATCAAATCTGTCGATCTTCCCGCCGGTGCAGTATGAAGGCGGGCGGAGC
CGACACCACGGCCAGCATATTTTGGCCGATGACCGCGCGTGGATGAAGACCGCTTCCCGGCTGTGCCGAAATGGTCCATCAAAAAATGGC
TTTTCTACCTGGAGAGCAGCGCCGCTGATCCTTTGCGAATGACCGCCACGATGGTAAACAGTCTTGGCGGTTTTGCTGAAATCAGCTGAGCGGCTTTC
GTCAGTATCCCCGTTTACAGGGCGGCTTCTGCTGGGACTGGGTGGATCAGTCTGCTGATTAAATATGATGAAAACGGCAACCCGTTGGTGGCTTACGGC
GGTGAATTTGGCGATACGCCGAACGATGCCAGTCTGTATGAACGGTCTGGTCTTTGCCGACCGCACGCCGATCCAGCGCTGACGGAAGCAAAAACA
CCAGCAGCAGTTTTTCCAGTTCCGTTTATCCGGGCAAAACCTGAAGTGACCGCAATAACCTGTTCCGTCATAGCGATAACGAGCTCTGCACTGGAT
GGTGGCGTGGATGGTAAGCCGCTGGCAAGCGTGAAGTGCCTTGGATGCTGCCCAAGTAAACAGTTGATTTGAACTGGCTGAACCTACCGCAGC
CGGAGAGCGCCGGCAACTCTGGCTCACAGTACGCGTAGTGCAACCGAACCGCACCGCATGGTTCAGAAAGCCGGGACATCAGCGCTGGCAGCAGTG
GCGTCTGGCGGAAAACCTCAGTGTGACGCTCCCCGCGCGTCCCACGCCATCCCGCATCTGACCACCAGCGAAATGGATTTTTGCATCGAGCTGGGTA
ATAAGCGTTGGCAATTTAACCGCAGCTCAGGCTTTCTTTACAGATGTGGATTGGCGATAAAAAACAACCTGCTGACCGCGCTGCGCGATCAGTTCACCC
GTGACCGCTGGATAACGACATTTGGCGTAAGTGAAGCAGCCGATGACCTAACGCTGGTTCGAACGCTGGAAGGCGCGGGCCATTACAGGC
CGAAGCAGCGTTGTTGCAAGTGCACGGCAGATACACTGCTGATGCGTGTGATTACGACCGCTACCGCTGGCAGCATCAGGGGAAAACCTTATTA
TCAGCCGAAAACCTACCGGATTGATGGTGTGTTCAATGGCGATTACCGTTGATGTTGAAGTGGCGAGCGATAACCCGATCCGGCGCGGATTGGC
CTGAACTGCCAGTGGCGCAGGATAGCAGAGCGGGTAAACTGGCTCGGATAGGGCCCAAGAAAACCTATCCCGACCGCTTACTGCCGCTGTTTTGA
CCGCTGGGATCTGCCATTTGTCAGACATGTATACCCGCTACGCTTCCCGAGCGAAAACCGTCTGCGTGGCGGACCGCGAATTTGAATTAAGCCAC
ACCAGTGGCGCGGACATTTCCAGTTCAACATCAGCCGCTACAGTCAACAGCAAGTATGAAACCCAGCCATCGCCATCGCCAGCGGAAGAGGC
ACATGGCTGAATATCGACGGTTTTCCATATGGGGATTGGTGGCGACGACTCTGGAGCCCGTCAAGTATCGGGGAAATTCAGCTGAGCGCGGTCGCTA
CCATTACAGTTGGTCTGGTGTCAAAAAATAATAAACCGGGCAGGCCATGCTGCGCCGATTTTCGCGTAAGGAAATCCATTATGACTATTTAAAAA
CACAAACTTTGGATGTTCCGTTTACTTTTTCTTTTATCTTTTATCTTTTATCTAGGAGCTACTTCCCGTTTTTCCGATTTGGCTACATGACATCAACCAT
CAGCAAAAGTATAGGTTATTTTTTGGCCTATTTCTCTGCTTATTATTTCAACACTGCTGTTGGTCTGTTTGGTCTGTTTGAACAACTCGGAATGTT
TATTGACGTTATAATGGTTACAAATAAAGCAATAGCATCACAAAATTTACAAAATTTAATTAAGGCGCGGGATCGATCCCGTGCAGCAGTGTGGTTTT
CAAGAGGAAGCAAAAAGCCTCTCCACCCAGGCTGGAATGTTTCCACCAATGTCGAGCAGTGTGGTTTTGCAAGAGGAAGCAAAAAGCCTCTCCACC
CAGGCTTGAATGTTTCCACCAATGTCGAGCAAAACCCGACGCTTGTGCTATTGGCGAATTCGAACACGAGATGAGTCTGGGCGGGCGGGTCT

CCAGGTCCACTTCGCATATTAAGGTGACGGCTGTGGCCGCAACACCGAGCGACCCTGCAGCCAATATGGGATCGGCCATTGAACAAGATGGATTGCA
CGCAGGTTCTCCGGCCGCTTGGGTGGAGGCTATTCCGGCTATGACTGGGCAACAACAGACAATCGGCTGCTGTATGCCGCCGTTTCCGGCTGTCCAG
GCAGGGGCGCCCGGTTCTTTTTGTCAAGACCGACCTGTCCGGTGGCCGTAATGAACTGCAGGACGAGGCGCCGCTATCGTGGCTGGCCACGACGG
GCGTTCTTGGCGAGCTGTGCTCGACGTTGCTACTGAAGCGGGAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGGCAGGATCTCTGTATCTCACC
TTGCTCTCGCCGAGAAAGTATCCATCATGGCTGATGCAATGCGGGCGGCTGCATACGCTTGATCCGGCTACCTGCCATTTCGACCACCAAGCGAAACATC
GCATCGAGCGAGCAGCTACTCGGATGGAAGCCGGTCTTGTGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCCAGCCGAAGCTGTTCGGC
AGGCTCAAGGCGCGCATGCCCGGAGCGGAGGATCTGCTGTGACCCATGGCGATGCTTGGCCGAATATCATGGTGAAATATGCGCCGCTTTTCTGG
ATTCATCGACTGTGGCCGGCTGGGTGTGGCGGACCGCTATCAGGACATAGCGTTGGCTACCCGTTGATATTGCTGAAGAGCTTGGCGGGAATGGGCTG
ACCGTTCCTCGTCTTACGGTATCGCCGCTCCCGATTGCGAGCGCATCGCTTCTATCGCTTCTTGACGAGTTCCTTCTGAGGGGATCGGCAATAAAA
AGACAGAATAAAAACCGACGGGTGTTGGGTGCTTGTTCGGATCCGAATTCCTCGAGGGGCGGCCATTTAAATGGCCAGCGAGGGCCGATCCCAATTCG
CCCTATAGAGCTACCCAGGGGTTATTGATTGCTTCTTAAAGATCAGAATTACTGCCTATAAAAACCTGGATAAGGAAATCATAGAGATCTCTCAAGTGT
GAGGATGAGTGACTGCCTCTGTAGCTCTGATCCTAGTCTCCAGATGGCTAAATTCATTTGACCTTAGAGTTCATCTGGAAAATTGTTATGAATGAATT
ATTTGCCAGATCCAAAGATGAGTGAATGTTTAAATAAAGTTGCCATCACTATTCTCATTATATTGGTATGTAAGCATTTCATGGAAATGTTCTAA
GTCGTTATTGAGCAATAAATTTCTTTAGCTTATAATGCCAACAGGTTACTCCGAGAATAACAAATGACATATTAATGAAAATGCAACTGGGGTTTA
CTGAAGGCAGCAGCTTAGTAATTAAGTAAACCATGGCTTAGTGAACCTGGACCTGGGAATTCCTTCTTTCATTGACAGAGCTGTGAGAAATTTCA
AAGGTCACAGAAGAAAAGCTATAATTAACCTAGTCCCAAAAATCTCAGCTACTCTGGGAAAGCAGCATATTTTGTGGTGAAGTGAAGCAAGCTTAG
AACTTTTTTTTTTCTACTGATCCTGAAGTGCCTTTAAGTATAGTTAAGTGGTGGAAAATGAGCAACTATTTAAGAAAAGACTTTTTTTTTTCTTCTC
CAGCAATGGCTTTCTTCAAAAACGGTAGCTTCAAAACTCTCTGCTTTTAAATGATCAGGGGGCTGTGTGTTAAATATTGCCATTTCATAGAACAGAGTG
GGTCTGAGGATGCCTGTTTCTTTGAAATTTCTACCCCTCCAGTTTCTAAAATTTAAGAAAACACAGAGACTTTGACAATGTAGTTGCCAAATGA
GTTGCTTTTAACTGCTCTAATAGTTGGTCTAACGGTCTTACCGTGTGTTTTAGTGAACCTTTTTTCCCCTAGTTTTTATTTTCTGTGGACACCAAC
GTGACTGTAGATTTTTCTGAGCTGAATGGTTCAAGGTGAGACTAATATTACTTGAAAGCCTAGCCTGGAGCTGACATCCAGATCCTGGCTGTACCAC
TTTTAGCTGGGTAACCTGAAATTCATTAATGGACAGTCTGGGTCTTAGTTACTTTTTGTTTTAAAGATGATTTTTAAATTTAAAACATGTGTATGTGTG
TGTGCTCCGAAATAAAGTATAGATGCCATGAAGTCCAGATATTGGAACCCCGAGGAGTGGTGCAGCAGGCTATTGTGTGCCACCAGACCTAGAT
GCTGGCAACTTGAACCTCTGCAAGGGAAGTACATCTTAACCATGAGCCACTTTTACTCCCAAGTCTTAGTTGAAAATAAACACTCACATATACT
TCATCGAGTATACAAAGATACCAGAAGAATGTGTGATGCTTGTAGGGTTAGGAGAAAATGAAGATATCATCTTTATTAGTGTGAAAAGGAGTTAGGGT
TTTTGAAAAGGTACATAATAGCTCTTAAAGGACCTACATATACAGAAGTCTATTATAGAGTGAGATGTAATGCTGTTTGTGAAACCATCTCTGAGA
TTATTATGATGTTGGGGTTGGCTTAGTGCAAAAAAGAGAGAGAGAGAGAAATGTTACCATTTTTTAAACAGATTTTATTTATTTATTTATT
TATTATGTAAAGTACATTGTGCTTCCAGACACTCCAGAGAGAGACTAGTTTCTGTTACGGATGGTTGTGAGCCACCATTGGTTGTCTGGGAT
TTGAACTCAGGACCTTTGGAAGAGCAGTCCGTTGCTTCTAACCGCTGAGCCATCTCACCAGTCCGAATGTATCATTTTTAATATACAGGTTGATTAGA
GCAAACTAGAAAATGGGAGAGTATGAATGATCAGCTGTTTTAAACCGGAAAAAAGTGTGCAGCCTTTAAAGTAAAAAAGAACATTTAA
GTGAAAGAAAAATGACAAGGGCTCCATAGCCCTTACCAGAGATGGTCAATGGTGCATAAAGCGCTTAGGTGAACCTGGTGTGAGCGTGCCTAAAG
AGGGAGCCTTGTGGGGGAGGAAGATGGTCCCTTCCCATCTCTCCTAGTTTATGTGTTGCAATTCTTATATGTAGTCCAGGAGTGGCCAGGCATTA
GAGGAGTCTGAAATATGCTGTGCTATAAGGGCAACGAATTTGACACGGAATTTGACATCCAGTCAATAGTGAGTACAAAGTTGGGCAAAAACACTGG
GTTACAGACCTCTTTGAATGTTAGAAGCTGAAGGCTTTGATTAAGTGCCTTATTGACATCGATTTTTTATTGTCTCACATACTATATCCTGATTGCAGT
TTGCCCTCCACTTCTCCAGTTCTCTCCATTCTCTCTCATCCGAGTCCACCCCTTCTGTCTCTCGTTAGAAAACAAAACAGACTTCTGAAAAGATAAT
AATAAATGAAATGTAATAAGATAGAACAATAAATCAACGTATCAGATTAGGACAAAACAAAAGAAAAGAGCCCAAGAAAAGGACAAAACCCC
AGATAACGCCGAGAGAGTATTACATACACTCAGCAATCTCAAAAAAACTAACTGAAAGCTGTAATATATACGCAAAAGGACCTTTAGGAGGGA
GGAGGATGTATATAAAATAAAAAAGAAATGAAATTAATAATGCAAAACAAACAGCAAAACAAAACACAAAAGTTATCCCTGCAAAGATGCTATAGA
GGTTTTGTTTTGTTTTGTTTTTCTTCTTGGTCACTACTGCTGAATGTGCCGCTACCCTTAAAGAGTAGTTTATTTCCCAAGTGTCTCCTTTGG
AGGAAGTAAATTTTACTCTGCAAGTGGTTATCAATTTGAGATGGATGGTTAGGATGGGGGATGCGTCCACTTCTTCTATCTAGGACCCCGTCTG
GTGACAGCTGTGAGCCGCTGTGCTGCTGCCTAGTCTCTGTGAGTTCGTGTGAGCTTTGCTGTGTTCACTTATGGGCTGTTTTCTGAGGTTCTCT
CCACCCTCTCTGGCTTTACTCTTCTGCTCCTCTCCACAGGGTCCCTGGGCCCTGGTGGGGAGGGGTTTGTGAGGACAGCTCAACTAGGGCTGA
GTGTTCAAGGTCTCTCATTCTGCACACTGTCTGGCTGTGGGTCTCTGTATTGTTCCCATCCTCAGACCCATTAACTCAGATGTAACCTGAATAAAA
TTATGATCAGGATTAATAGTAGAGTATGACTATATGGAATGCTGGATTTAGAAAATATACTCTGTGTGTGTGTAATTTGATACTGTACCTGGC
ATTAGTTGAGCTTCATCAAGATTATTACAGTGGTTACATTTTGAATACTCAACTGTCTACTGTTGCTCCAGTATGGGTTTTGTTTTTAGACT
TTTTGGTGTGGTACAGGATGTAGCCAGAACCTTGAGAGTCCAGCTAAGTCTCAGACTTGAGCTCCCTGCTGAGCCAGGTTGTTTTGAATACA
GATTTCCCTGTAAAGGTCAGGTTTGAAGGAAGCTCTCAGGCTCTCTGATATTCACAGAACAGCTGCTGGGAAGTAAGTTTCTGGGAAAAAGCCATCG
TGTTCTCTCTTTGCTGCTCTTGGCTTGTGCTAGTGAAGATTCAGGTCAGGAATTAAGAAATATCAACCTTTGTCTGTATATTTTCACAGTAGGCT
TTACTGGGCAAGGGGAGATGTGTCCCAATAAATTTGATTAAGTCACTTACTCAGTTTATTGTTGATCAACACTGTTCTTAGATATGCATGAGT
TTGCAAGATAGCTGTAGATTTTTGCTTGAATAAGATTACTGAGGATCCAGTTTACTTTTTCGGGAGTAAATGGAAAATGAACTTCTGAATAGATAAA
AGAAATAGTTCTGGAATTTCCAGAGTTAATATGTGCTCAGCAGTAACTGGCCGTAAGTGAACAAGTGAAGACTTGAATTTACCAGTGTGCAT
TTGAGGTCGTTAGTTTTCTGTATCTTAGTTTCATGATGCATTTATTGCTTTAGGGAGAGTATACAAGTTTTGAAAAAAGTTCTCCCATGAAATAAATAT
TTACAAGATGCCAAAGAAAGTTTATAGATCACTAGCATTGGCAAGTATTTGATAAGACTAATCTAAGTGAACAAAACATTTACCACAAAAG
TTGCTATATATTAAGAAAGACTAAAATGAAATTTAGCTGGAATAACAAATTTGAGTATAAGTTCTTAGGGAGCAACTGAGGCAATAAGAAA
TAGTTTTCTGATCAGAAGAGAGCCTAGACGTCAGTTTGGATTGTCTCCTGAAGAGATTAACATAAATATCTTTCTGATGACAGTATTGCCGTTGTTCA
GAGACAGTTTTGGGCGATAAAATGAGAACATTATTCTAAGCTTAAAAAACATAATGCCGGAGTAAAGATGTAAGAAGAAAAGAAAGAGAAAATACC
AAGAAATGGATTCTTGCTCCCAACCCCAACCCCAACGAATAATCAGAATGAGTTAAGGGGGTTCAGAGAGGGGCTGGGAAAAGTGTGACTCGGAAACA
AGAAAAGGAGGATGTTGACAGTTGGGTGGCTAGTCTTTTCCACTGAAAGGTAAGTAAAGCAACAGCAAAAAGCAGCAAGATAAATTCAGAGTAAAT
AGAGGGAAGCCTCTTTGCACTGCAGGTGGTGAAGCTGATAAGACTGTAAGAACTTAACTTAAAAAATGTGAGACATTGACAATCCAAAGTAGGCTT
TCAAAGCATTAAACAACATGTGGCTTGGCGCTCTACTGTGGGCTAAGGAAGTATGGTCAATTGCATTGATGGACTGTAGACTTCATCTTCTCCTAGG
ATGATATCTAAGGTCATGTACCCTGACAGTCCATCCAGTGCAGGTTCTGGGAGTGTGCTCTTGTATCTTTGCTGATTCTGTGAAGCAAGGCTGTG
GACAATGACTTAGTGGGCTTGAACAATGAGGTTATCCTTCCACTTAGGATTTGCAAGCAACCTGCTCAGGTTAGCCAATTTGTAAGCAGTGTGAG
TGGAGAGAGACTGGAGTAGTTGCCAAGCAGAAGCCAACTTTAGAGTTGATGCAAAATGCAAGCAAGATCAACAGAGGTTGTTGTTACTGCTTGCCTCAAG
CTATTTTAGGCACATAAACAATAAACACTCATGCTATTGACGCTTTTCTGTTGTTTCTTAGATAGTATTATTATTGTAATAGATAATTGATACAGGACAGG
AAATTAGACTGTATGACATTTCTGTGTTTCATGTCTATCATGTTGACATTTCTGAGGTAACATTCAGGAGTCCAGATGTTGGGGTTACCAGCTACAGA
TCTAGCATAGTATGGTGTACTTAAAGTTGTGAGAACATGCCTGAAAATAAAAAGAAAGCCACAACCCCTTTCCATATGATGTTCTAAAAGGTGCTTACC
CAAAGGAGAGCAGAAACAGGAAGGATAAGAAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAA
GTTTGTGGCTAACTCCAGCTAAACTCTTGTCTTCTTATGAGACTTTTGTAGATTATATTATTCTGGCCAAGAAAATAAATACTAGAATCACTTTATCCCT
AGTGGATTTGGATGAAAACCTGGTAAAAAAGTTTCAGCTATAATTCCAATGGGAGGCAATTGGAGAATAACCAAGCTGGGATGCTGGGTCT
CTGAGTACTTGTCTGGCTAGTATAAAAACCTGACCAAACTCAACATGGGAGGAAAGGTTTATTCTACTGACTGTTTGGGTAAACAGTCCATC
ACTGAGGGGAGTCAAGGACAGGAACTCAAGGAGGAAAGTGGAAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAG
CGGTGACTTGTAAAGTTGCTTCTTAGACACCTCAAGACCACCTACCCGAGACAGGACAACAGCACCCACGGACTTGACTATAGGCCAGTCTGATG
GAGGCATTTACTCAGTTGATCTTCTTCTCATCTAGATGGCCCTAGCTTCTATCAAGTTGACAAAAGTCTAACAGGACAATAATTGATGACACACAGT
GTTAGCTATATTAGCTCACTATCACTTAACTTCTTAGCTGAAAAGGATGACTACTATCTGTACAATTGGAAAATGCTCCAGAAAAGGCAATTTTCTA

TTTCCATTTATGCCTCTATACTGATAGGTTAGTTC AACAGTTGATATGTAAAAAGCTTTGGTTAAAAAAGCCGGGCGTGGTGGCGTACGCCTTT
AATCCCAGCACTTGGGAGGCAGAGGCAGGTGGATTTCTGAGTTCTAGGCCAGCCTGGTCTACAGAGTTCCAGGACAGCCGGAGGTACACAGAGAAAC
CCTGTCTCGGTGTCTGGGGGGGGGGGGGGAGGTTTGC AAGTAGCTCAGAAATTCAGTGAAAAATTCCTTACAAAACCTCATGTAATAGACTGCACAACAA
ATCTTACAAGAAATGTAGACTGAGTTCCAGCAGCTCAAGTGTAAAGAACTTCTCAGGAAAATGGCCCTACTTCTTTTTTAAGGCATTACCCATTCTTC
GTAGTTTATGGTGGTTTTGATTTTTGAAAATAAGATTCTTTGTAATCTTCTCAAGGGCACAAAGTATAGTTATGAGTGTGCATATGCTTGTGTGAGTGT
GTGTGTTTGTGTGCCGAGAGGTTAACCTGGGTACCATTGCCAGGGTCTAGCCACGTTATTTTTGAGACAGGATCTTCTTGAACCTAGAGCTACTA
TTGATTAGACTACTTGACTAAAAAGCCCAAGGAGCTTCTGGCTTCATCTCCCTCTTCTGAAAATTACAGATGAGTCTCACTATACCTGACTCCCCCA
CCACCACCTTTTATGGATATTTCTTTATTTACATTTCAAATGTTATCCCTCTTTCAGGGCTCCCCCTTCGGAGCCCTCTATCCCATTCCCCCTACTCC
TGCTTCTAAGAGGGTACTCCCCACCCATCCATCCACTCCTGTCTTCCCTGCCCTGGCATTCCCCCTACTCTGGAGCATCGAACACCCTCAGGCCCAAGGGC
CTCTCCTCCCATTGATGTCAACAAGGCCATTCTGCCACATATGTGGCCGGAGCCATTGGTCTCTCCATATGTACTCTTTGGTTGGTGGTCCAGTCCCC
AGGAGCTCTGGGGGGGGGGTGTCTAGCCTGTTGACACTGTTGCTCCCACTATGGGGCTGCAAAACCACCTCAGCTCCTCAGTCTCTCTCCAACCTCCC
CATCTGGGACCCTGTGCTCAGTCCAATGGTTGGCTGCAAGCATCTGCCTCTGTATGCCTGACTTTTTAATGTGGTTTTCTGGGGATTACAGCCAGGTCTG
ATGCTTGCATGGCAAGCAGTTGCTTCTAAGTCATATCCTGGGCCCTTAAAAATCCTTTTTATTTTTATTCCCACACAAAAGATGTTTTAGGGAAAA
ATTGGGGCCCTCTAACAACAATTTCAAAAACAGTCAATGGTTGGTTTTTAAATAAAAAAGGTTGGTAGCTCTCCAGCAGTATAGAATGTCTCTGGATCAT
TTGAATCCTAGAGAGAGCAAGAGGACCCAGTATTTAGCAATAACTATGGCAACCCTCCTACTCCGTTCCATGTCCCTGAAAAGCACTTTGAAGATT
GTCTTGCAACTATTTTTATTTAAATCAGAAGTTGTTGGAGAGAGTAGGAAGCTGGTGTATTCTCTTGGTGATCTCTGGGGCCCTCAGCGTTTTCTGCT
GGGTCTTTAGAGGATCTAGGCATACCCATTACCTTTCTATTTCTGCCCCAGGGAACTCAGGACCTGATAATGCTAAATAAGCTGCGATCCTCCAT
CCAAGAAAAGAAATGTTGACCCTGCCTCTAATGGTTCCACACCAGGCTTCACGACATGTGTAATAAATACCCTTATCTGAGAGCATGAGTAGGGGAGC
ATCAGCATGGTACAAGGATACCAGAATTCAGGGCTGAGTATTTTTCCCAAAAAGATAAGAGACAGGAAAATAAAAAATGTTTTCAGGAGTCGAAAAGCT
TAAAAATGTCAACAATCTCATGCAAAAATATAGAAAAGTTTTGGAGTTCTAGGATGGAGTGACAGGATTCATATAACTTGTGTACGTACTTCGTTGAATA
GAATAAATTTCTTTTTCTTTAAAAAATCTCTGGATGTGTGAAAAAGTGATCAAGGCAGCTTTGCTCTGAGCATCATGCAGCCTTGAGGGTTCGCATCT
GGAAACCAGAGCAGCCTATGGGGCTTGAGGGTAGAGCTTTGCCGAGGAGGTGGTACAAGTGTACAGTCCAGATGGATGCTCAGGTTCTTGCAGTTTT
ATTTTTCAGAAAATTGCCACAGGCTTAGGGCTAGGAGGTTGCAGATGGTTAGCTTCAATTCAGGGGATGATGATCTCTAGAAAAAGAGAAAATAAAGT
GCCAGCACTTTATATCTCAAGCAAATATCAGAAGGAGAAGTGGCACTCCTTGTGGCCAATGTGTTTTCAATAGAATAGTTGCATATTTTAGCATAT
AAATACTTACAGGCATTA AAAAAGTATGATAGTTATCTATCAAAAAGCAGGGATCAACAACCTTTCTAGTTAAGTGTGAGCTGTGGCCTTCTTGGCTT
CGAAGGTTTTATGGTTTCTTCAAGACTACCGAGCCTGCAGTTGTGTGGCAGAAGCAGCCATAATCAGTGTGGTATAAATGGATGTGTGGCTGACCAAT
AAAAGTGAATTTAAGAAAGAGCAGGTGATATCTAAGCTTGGCCCAAGGGCTATAAATTTATCAGCCCTGATTAAGGAAGAAGCCCTGATTTATAATTT
TGAAAAGAAAATAAATATAGGTATATAAGAGTTGCCTAGGAAATAAGAAAGTTATATAGCACTAATTCATATAAATTATGTTAATGACATGGATAGCTA
GATTTGTTTTTCACTACTACAGAATATAGTGGGTTTTTTTTCTTCACTATCTTTTAAATGTTAAATGATAACATGCAAAGCAAGGAGATTCATTGTAGT
GTTTTCATGTACACTTTGCTTATAATCAGTGGCCACTTTCTTACCTGTTCTCCTGCTCCTTCTTGTAGTGTCTGTCTTACCCCCCTCCCCCATGGCAGCT
TTCTGCCTTTGTGTACATACCTTTCTTTTTCACTTTCTCTTTTTGCCCTTTTTTAAATGGTTTTTCTTTTGTATGATCCCTTTTTTAGTTTTACAAAAC
ACAGAGAGAGAGACAGAGAGACAGAGACAGAGACAGAAAGACAGATAGAGAGAGAAATAGACAGAGACAGAGATAGAGAAAACACACACACAGATC
GAAAGATCTAGGTCTACAAAAAGAAAATATGTGATTTATCAATATTATTGTTTTAAATAAAAAAACCACAATTTGGGTAGGGCCGCTAGACCTAAGG
TCTAAGACAAAAGCTCTCATGAAGACGTTTAAAGACGATAAGACATACTACACACATAGTTAGAATTTTGTTTTTGAACATTTAAAAGTAGAATTTACTAG
TTTATACTTGTAGTACTTGGATTTGCCAGGAAGTCTCATGGGTGGACAATACAGTATTCTCTGCAGTTATAGATGGAAGTCAGAGAGTGAATGTCTTC
CTGGTTGTTTTAAAAAATATGTGTCTTGTCCCCAAACCTCTACGGATGGCTGTAAAAAATGGCTGTTTTTAGTTGCTACTTGTCTGCCTTTGCACAAAAG
GGAGTGTGGAAAGCTACTTACTTCACTGAGCTTGCTCCTTAAAGATGAGGAGCTATCTAAGCTTCTGTCTAAGCTTTACTTCATACATTAGCCAAGTCC
GTAATT

TF3738 Targeting



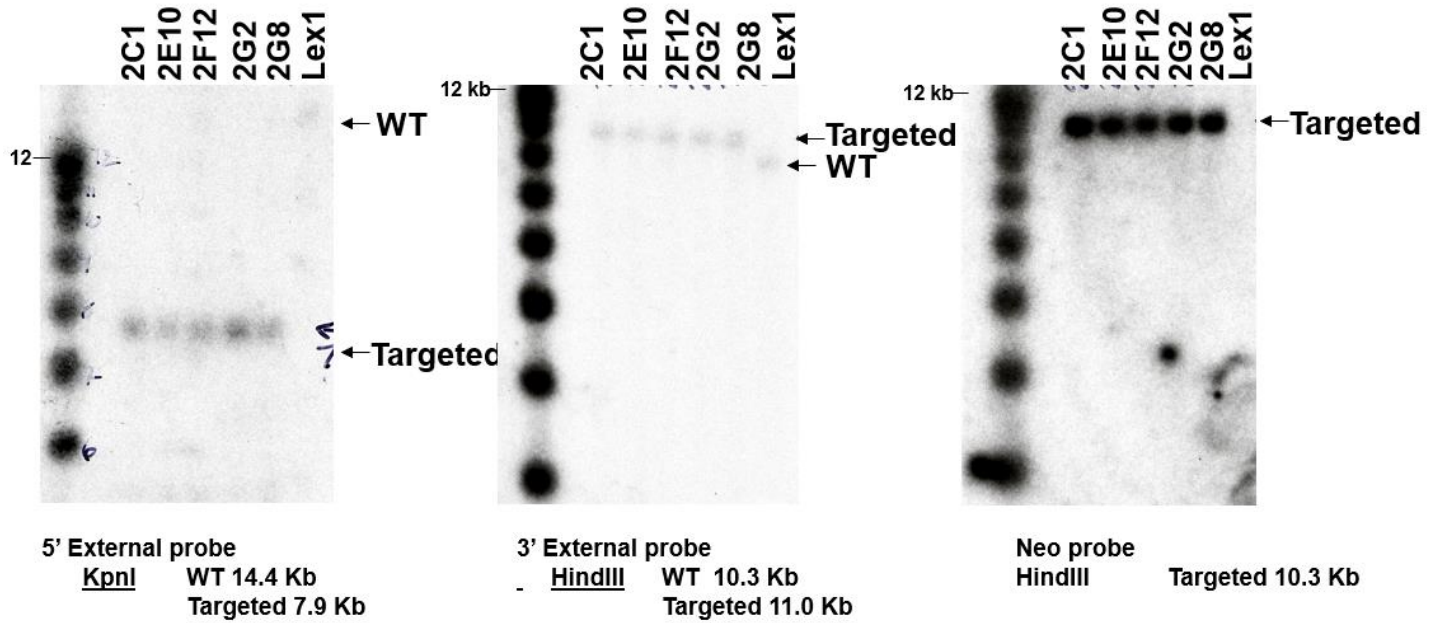
Southern Strategies (note: X-linked gene)

Probe	5' external ■	3' external ■
Enzyme	KpnI	HindIII
Wildtype	14.4 Kb	10.3 Kb
Targeted	7.9 Kb	11 Kb

PCR Strategies

Strategy	Wildtype	Targeted
Primers	3+37 bp	Neo3A+37
Wildtype	500 bp	-----
Targeted	-----	468 bp

TF3738 Southern Data



NOTE: The TF3738 gene is X-linked