**A gene-within-a-gene Cas9/sgRNA hybrid construct** **enables gene editing and gene replacement strategies in *Chlamydomonas reinhardtii***

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**Supplemental Data**

**Supplemental Data Tables**

**Table S1.** The 19-20nt sequences in sgRNA complementary to the 19-21nt sequence target sequence in mutant *GFP*, *PDS3*, mutant *Ble,* *FKB12*, *Ku 70*, *ALS* and *ARG* genes. The NGG PAM sequences of the target genes are shown in red.

|  |  |  |
| --- | --- | --- |
| **Target gene** | **19-21nt sgRNA sequence (5’-3’)** | **19-21nt target sequence in gene (5’-3’)** |
| *mGFP* | GCGCTTCAAGGTGCACATGG | GCGCTTCAAGGTGCACATGGAGG |
| Nb*PDS3*-1 | GCCGTTAATTTGAGAGTCCA | GCCGTTAATTTGAGAGTCCAAGG |
| Nb*PDS3*-2 | GTTTTGGTAGTAGCGACTCCA | GTTTTGGTAGTAGCGACTCCATGG |
| m*Ble* | GCGCTTCAAGGTGCACATGG | GCGCTTCAAGGTGCACATGGAGG |
| *FKB12* | GACCGTGTTTGTGCACTACA | GACCGTGTTTGTGCACTACACGG |
| *Ku70* | GTGGGGTCGCTGCCCGGGGG | GTGGGGTCGCTGCCCGGGGGCGG |
| *ALS* | GCTGCTGCTGGATGTCCTT | GCTGCTGCTGGATGTCCTTGGG |
| *ARG* | GGCATGAGCGAGGAGCTGG | GGCATGAGCGAGGAGCTGGTGG |

**Table S2.** Primer pairs used to exchange the target sequence in an intron-sgRNA gene by a two step overlapping PCR processes [Supplemental Data*,* Fig. S2 and Li et al., (33)]. The template for the first PCR reaction is a Cas9/intron-RNA gene (Supplemental Data*,* Fig. S2) designed either for use in tobacco or in Chlamydomonas, respectively. For the second round of PCR, a mix of the two products from first round PCR (i.e., PCR products produced with primer pairs F1/R1+ F2/R2) and the general primer pairs F1/R2 were used. Red underlined nucleotides are *ApaI* or *Bsp1407I* sites.

|  |  |
| --- | --- |
| **Primer** | **Sequence of primer** |
| Primer F1 for all genes | 5’-TTTTTGGGCCCACTTGCTAGAGGAAACTCTC-3’ |
| Primer R2 for all genes | 5’-TTTTTTGTACACGGTGAAGTACTCGTAAAG-3’ |
| Primer R1 for *NtPDS3-1* | 5’- TGGACTCTCAAATTAACGGCCTAATTAATGATAATTAT -3’ |
| Primer F2 for *NtPDS3-1* | 5’- GCCGTTAATTTGAGAGTCCAGTTTTAGAGCTAGAAATAG -3’ |
| Primer R1 for *NtPDS3-2* | 5’-TGGAGTCGCTACTACCAAAACCTAATTAATGATAATTAT-3’ |
| Primer F2 for *NtPDS3-2* | 5’-GTTTTGGTAGTAGCGACTCCAGTTTTAGAGCTAGAAATAG-3’ |
| Primer R1 for *FKB12* | 5’-TGTAGTGCACAAACACGGTCCTGATCCGCCGGGCTTG-3’ |
| Primer F2 for *FKB12* | 5’-GACCGTGTTTGTGCACTACAGTTTTAGAGCTAGAAATAG-3’ |
| Primer R1 for *Ble* | 5’-CCATGTGCACCTTGAAGCGCCTCGTCGACTCACCTCCTC-3’ |
| Primer F2 for *Ble* | 5’-GCGCTTCAAGGTGCACATGGGTTTTAGAGCTAGAAATAG-3’ |
| Primer R1 for *Ku70* | 5’-CCACCCGGGAGCGCAGCTGCCTCGTCGACTCACCTCCTC-3’ |
| Primer F2 for *Ku70* | 5’-GCAGCTGCGCTCCCGGGTGGGTTTTAGAGCTAGAAATAG-3’ |
| Primer R1 for *ALS* | 5’-AAGGACATCCAGCAGCAGCCTGATCCGCCGGGCTTGC-3’ |
| Primer F2 for *ALS* | 5’-GCTGCTGCTGGATGTCCTTGTTTTAGAGCTAGAAATAG-3’ |
| Primer R1 for *ARG* | 5’-CCAGCTCCTCGCTCATGCCCTCGTCGACTCACCTCCTCG-3’ |
| Primer F2 for *ARG* | 5’-GGCATGAGCGAGGAGCTGGGTTTTAGAGCTAGAAATAGC-3’ |

**Table S3.** Primers upstream and downstream of the target site in mutant *GFP, PDS3, Ble, FKB12, Ku70, ALS* and *ARG* genes used for PCR amplification of the target region.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Target gene** | **Upstream primer (5’-3’)** | **Downstream primer (5’-3’)** | **PCR Fragment (bp)** | **Restriction fragment**  **(bp)** |
| m*GFP* | TTTTTGAGCTCTCCACGGCAATGACGATGTGACCTGTG | TTTTTGGATCCTGCATCACCTTCACCCTCTC | 268 | 134,134 |
| Nb*PDS3*  Target 1 | TTTTTGAGCTCGCATAGTATTTAGGTTCACAAGTG | TTTTTGGATCCACATAACAAATTCCTTTGCAAGC | 243 | 149,94 |
| Nb*PDS3*  Target 2 | TTTTGAGCTCTATCTTTGGAGCTCGAGGTCTTCTTTG | TTTTGGATCCGGATTAAAGTCCTTTGTCAATCTTCG | 180 | 90,90 |
| m*Ble* | TTTTTGAGCTCAGGTGTTGCGCTCTTGACTCGTTGTG | TTTTTGGATCCGCGAAGTCGTCCTCCACGAAGTCC | 229 | 140,89 |
| *FKB12* | TTTTTGAGCTCCTTGACCCTGCACAGTGCCTTGCCAG | TTTTTGGATCCGGAGCTGTCGAACTTCTTGC | 164 | 106,58 |
| *Ku70* | CTGCCCTGCCTACGACTTCACTTC | CAGCTCCCTCAGCATGGTGAGGTCGTC | 259 | 69,190 |
| *ALS* | GCTGCTGCTGGATGTCCTTGG | CAGTGTTCACGTACTGATGCTGCAC | 243 | N/A |
| *ARG* | CAGCCTGCTGTGCGTGCACCTGTC | TACGCCTTCACTTCTTAACTAAC | 218 | N/A |

**Table S4.** Primers designed to check for the potential presence of 5' and 3' termini of the Cas9 gene in transformed Chlamydomonas colonies.

|  |  |  |  |
| --- | --- | --- | --- |
| **Target gene** | **Upstream primer (5’-3’)** | **Downstream primer (5’-3’)** | **PCR Fragment (bp)** |
| N termini Cas9 gene | ATGGACAAGAAGTACAGCATCG | GTTCAGGTCGCCCTCGATCAGGAAG | 525 |
| C termini Cas9 gene | AGCGCTACACCTCCACGAAAGAG | CACCTTGCGCTTCTTCTTCGGGT | 137 |

**Supplemental Data Figures**

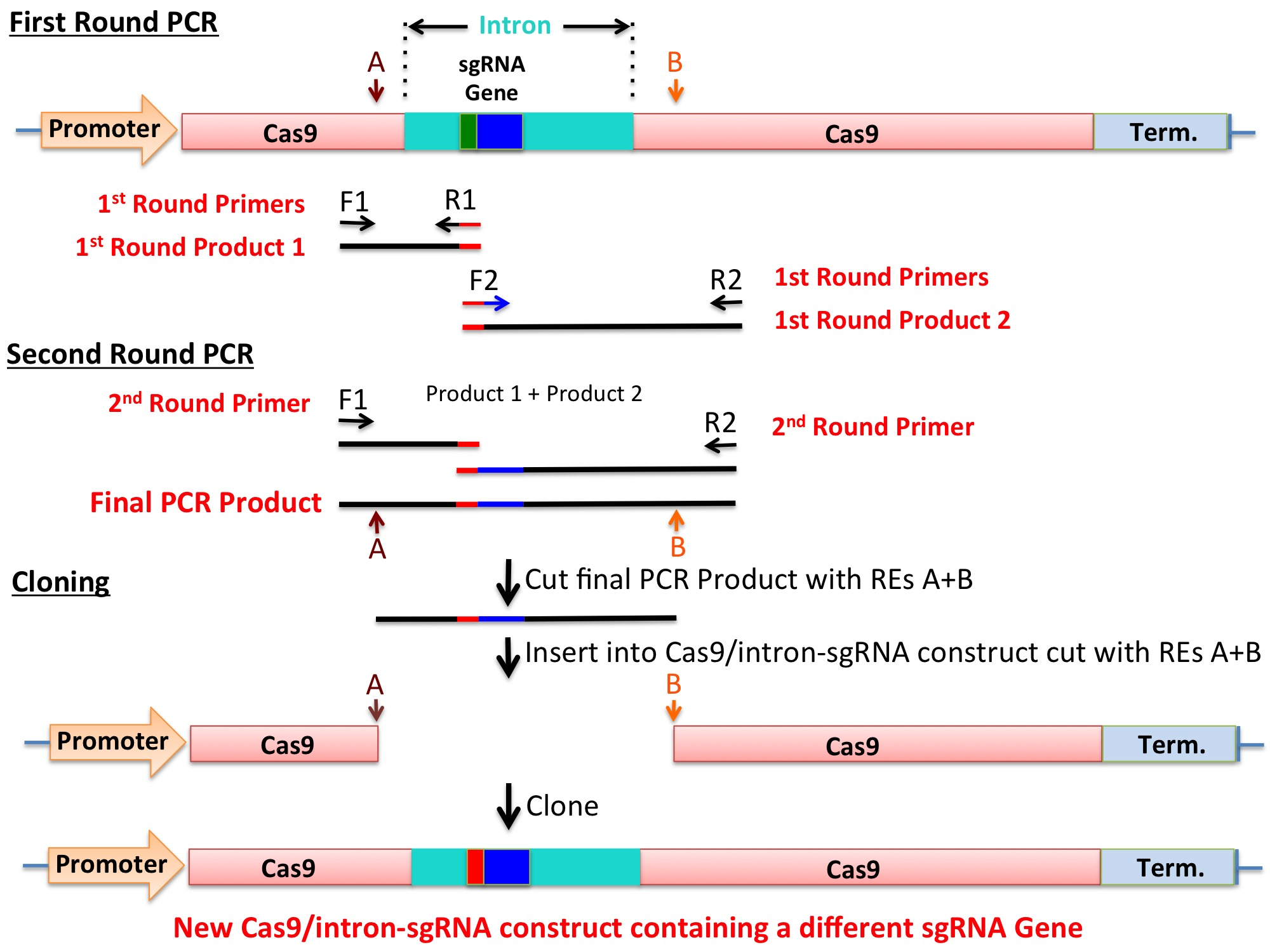
**A**

5’*GGGCCC*ACTTGCTAGAGGAAACTCTCGTTTCGCTTGGATGACCAGAAAGTCTGAGGAGACCATCACCCCTTGGAACTTCGAGGAGGTAAGTTTCTGCTTCTACCTTTGATATATATATAATAATTATCATTAATTAGGCGCTTCAAGGTGCACATGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAAC*TTGAA*AAAGTGGCACCGAGTCGGTGCTTTTTTTTAGTAATATAATATTTCAAATATTTTTTTCAAAATAAAAGAATGTAGTATATAGCAATTGCTTTTCTGTAG*TTTAT*AAGTGTGTATATTTTAA*TTTAT*AACTTTT*CTAAT*ATATGACCAAAATTTGTTGATGTGCAGGTTGTTGATAAGGGAGCTTCTGCTCAGTCTTTCATCGAGAGAATGACCAACTTCGATAAGAACCTTCCAAACGAGAAGGTTCTTCCAAAGCACTCTCTTCTTTACGAGTACTTCACCG*TGTACA*-3’

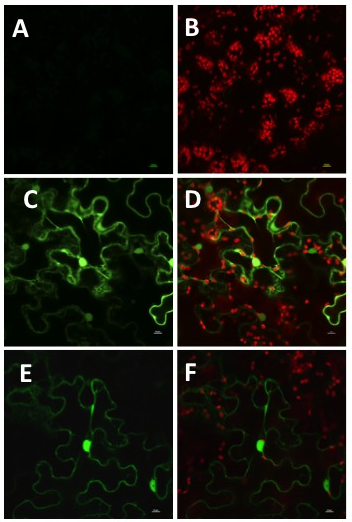
**B**

5’*GGGCCC*ACTTGCTAGAGGAAACTCTCGTTTCGCTTGGATGACCAGAAAGTCTGAGGAGACCATCACCCCTTGGAACTTCGAGGAGGTGAGTCGACGAGCAAGCCCGGCGGATCAGGACCGTGTTTGTGCACTACAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTTTTTGCAGCGTGCTTGCAGATTTGACTTGCAACGCCCGCATTGTGTCGACGAAGGCTTTTGGCTCCTCTGTCGCTGTCTCAAGCAGCATCTAACCCTGCGTCGCCGTTTCCATTTGCAGGTTGTTGATAAGGGAGCTTCTGCTCAGTCTTTCATCGAGAGAATGACCAACTTCGATAAGAACCTTCCAAACGAGAAGGTTCTTCCAAAGCACTCTCTTCTTTACGAGTACTTCACCG*TGTACA*-3’

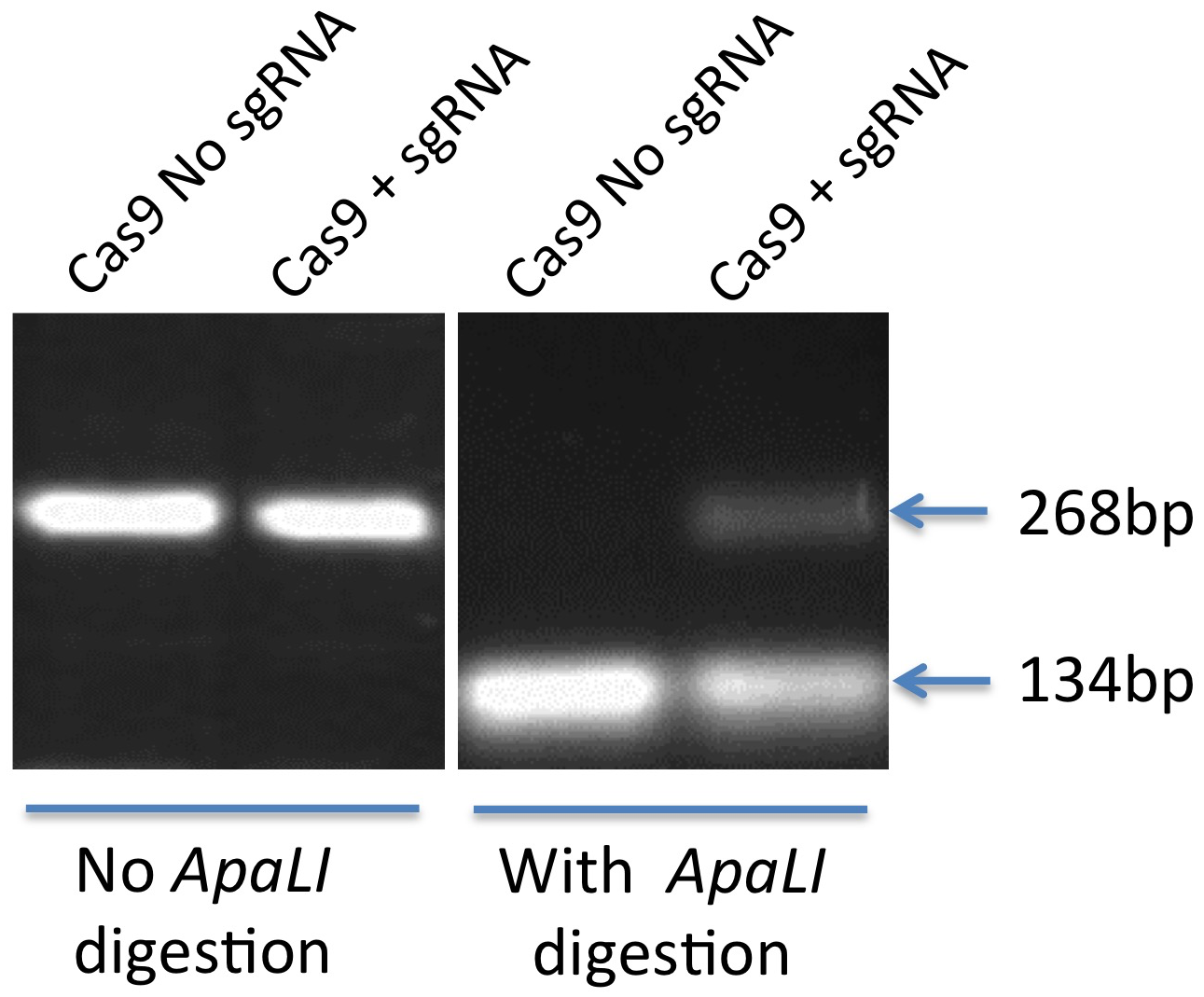
**Fig. S1.** *ApaI*- and *Bsp1407I*-flanked fragments of the Cas9 gene containing an artificial intron with an inserted sgRNA gene. **A)** DNA sequence of a Cas9 *ApaI-Basp1407I* gene fragment for use in tobacco and containing the potato IV2 intron with a sgRNA insert targeting the *mGFP* gene and **B)** the same Cas9 gene fragmentcontaining aChlamydomonas *RBCS2* gene intron with a sgRNA gene insertion targeting the *FKB12* gene. Color code: black: Cas9 gene fragments; Green: intron nucleotide sequences; red: 20 nucleotide (nt) sequence of the sgRNA gene used in targeting a specific gene (and which can be replaced by another 20 nt targeting sequence using the two-step PCR-based cloning procedure described in Figure S2); purple: hairpin region of the sgRNA gene; italic and underlined: potential intron branch points; italic, orange and underlined: *ApaI* and *Bsp1407I* restriction enzyme sites used for cloning the intron-sgRNA fragment into an *ApaI-* and *Bsp1407I-*digested Cas9 gene.



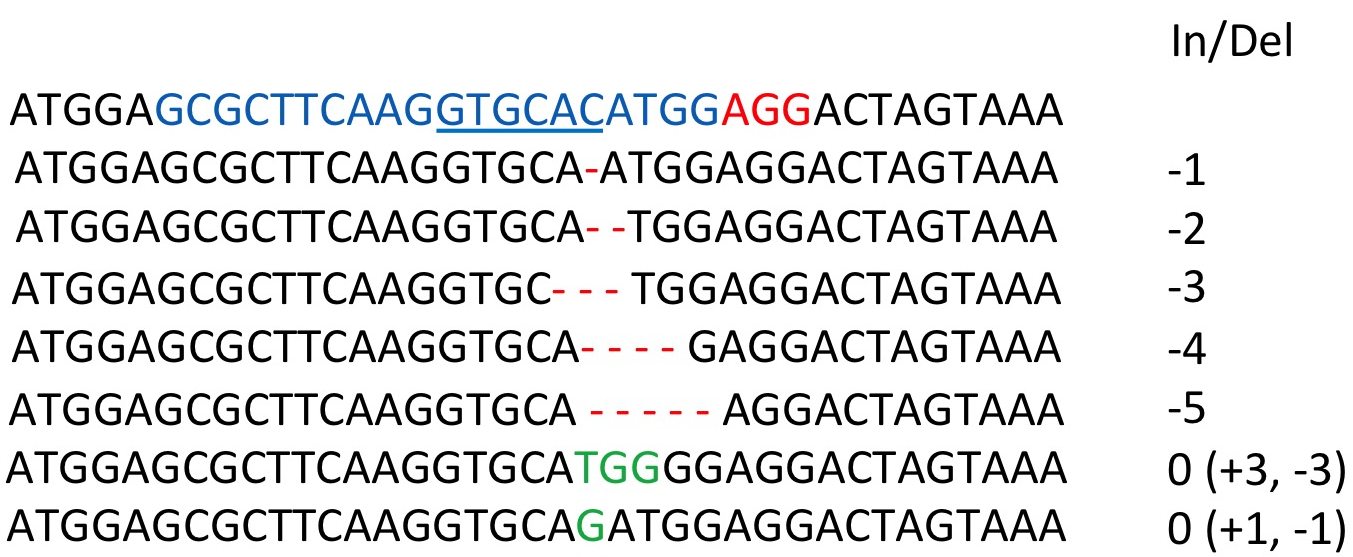
**Fig. S2.** Schematic of a two-step PCR approach for synthesis and insertion of a new sgRNA gene in place of a previous sgRNA gene in a Cas9/intron-sgRNA construct. In a first round PCR reaction, pairs of primers (sequences provided in Methods Table 4) are used to amplify two (soon-to-be overlapping) segments of an existing Cas9/intron-sgRNA construct. Primers R1 and F2 contain at their 5' end a new 20 nucleotide (nt) guide (targeting) sequence (red) that does not match the 20 nt guide sequence in the template construct (green). This ultimately allows creation, within the existing intron sequence, of a new sgRNA with specificity for the new genomic target site. Following the first PCR reaction, the two products of the reaction are purified and mixed into a second PCR reaction to become overlapping PCR mega-primers as a result of the pairing of their complementary 20nt 3' ends. Simultaneously, they also become PCR reaction templates for the PCR primers, F1 and R2. Both the Cas9/intron-sgRNA construct and the final PCR product have a restriction enzyme site for *ApaLI* (A) and *Bsp1407I* (B) that are used to allow cloning of the new sgRNA gene into an *ApaLI*- and *Bsp1407I*-cut Cas9/intron-sgRNA construct. Dark blue in the graphics represents the "hairpin region" of the sgRNA gene recognized by Cas9; Promoter, a suitable gene promoter region, Term., a suitable gene termination region; Cas9, Cas9 gene codon-optimized for the organism of choice.

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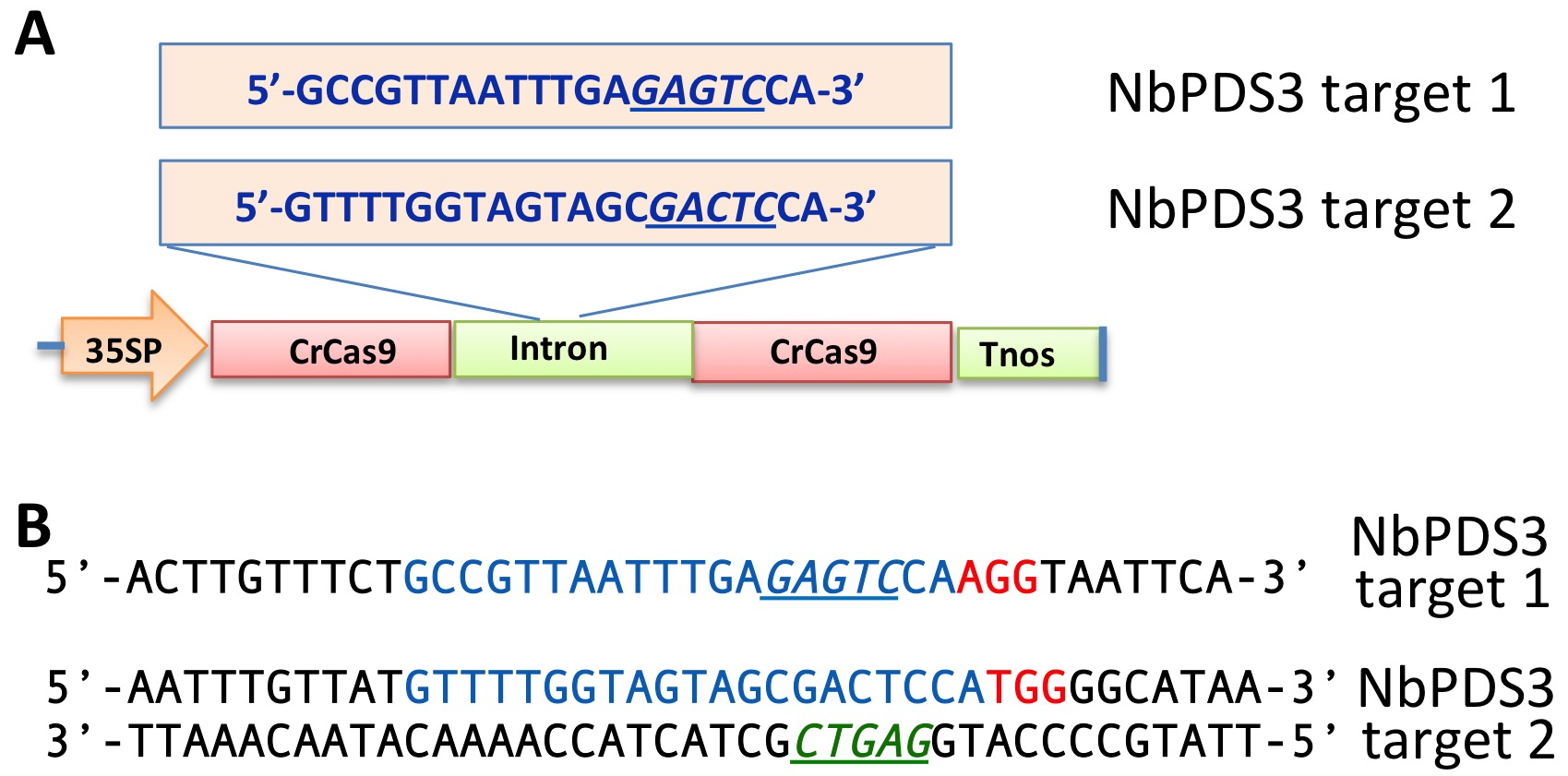
**Figure S3**. Tests for GFP expression in transiently transformed *Nicotiana benthamiana* leaf cells following leaf infiltration with *A. tumefaciens* carrying a vector containing a mutant GFP and a Cas9 gene, but lacking a sgRNA gene (images A and B) or with a vector containing a Cas9/intron-sgRNA gene and a mutant GFP gene (images C through F). The Cas9/intron-sgRNA gene contains an intron that can produce a sgRNA specific to the target sequence in the mutant GFP gene. Expression of GFP in these leaf cells can occur only if a DNA target site in the non-functional GFP is recognized and cleaved by a Cas9/sgRNA complex and if resulting error-prone DNA repair by NHEJ leads to deletion or insertion of nucleotides that restore a proper reading frame in the GFP gene coding region. Leaves were photographed at 600× magnification 48 h after *A. tumefaciens* infiltration. Cells were photographed using a GFP fluorescence channel (A, C and E) or as a merged image of green fluorescence and red fluorescence to detect chlorophyll fluorescence (B, D and F). Scale bar: 10μM



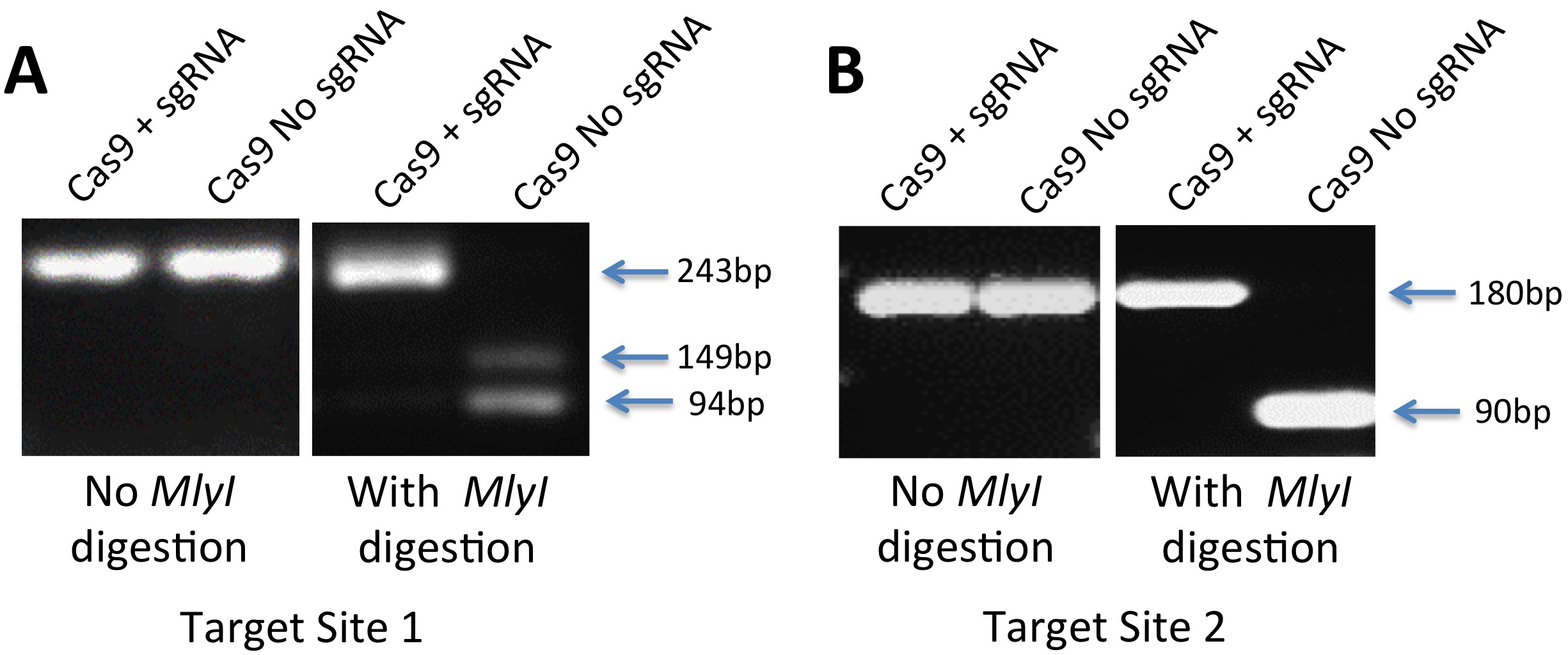
**Fig. S4**. PCR/Restriction Enzyme (PCR/RE) analysis of total DNA extracts from a Cas9/intron-sgRNA treated tobacco leaf showing the nonfunctional *GFP* genes mutagenized by Cas9/sgRNA activity. Bottom arrow indicates the expected ~134 bp DNA fragments resulting from *ApaLI* cleavage of the ~268 bp PCR product amplified from the nonfunctional, out-of-frame, nonmutagenized *GFP* genes that contain an intact *ApaLI* cleavage site in the sgRNA target region. Top arrow, right panel, also indicates the expected ~268 bp size of PCR products from *GFP* genes mutagenized by the Cas9/sgRNA system in a manner that destroys the *ApaLI* cleavage site. Lanes 1 and 3, DNA extracted from leaf segments receiving only the Cas9 gene construct; Lanes 2 and 4, DNA from segments receiving the Cas9/intron-sgRNA gene construct.



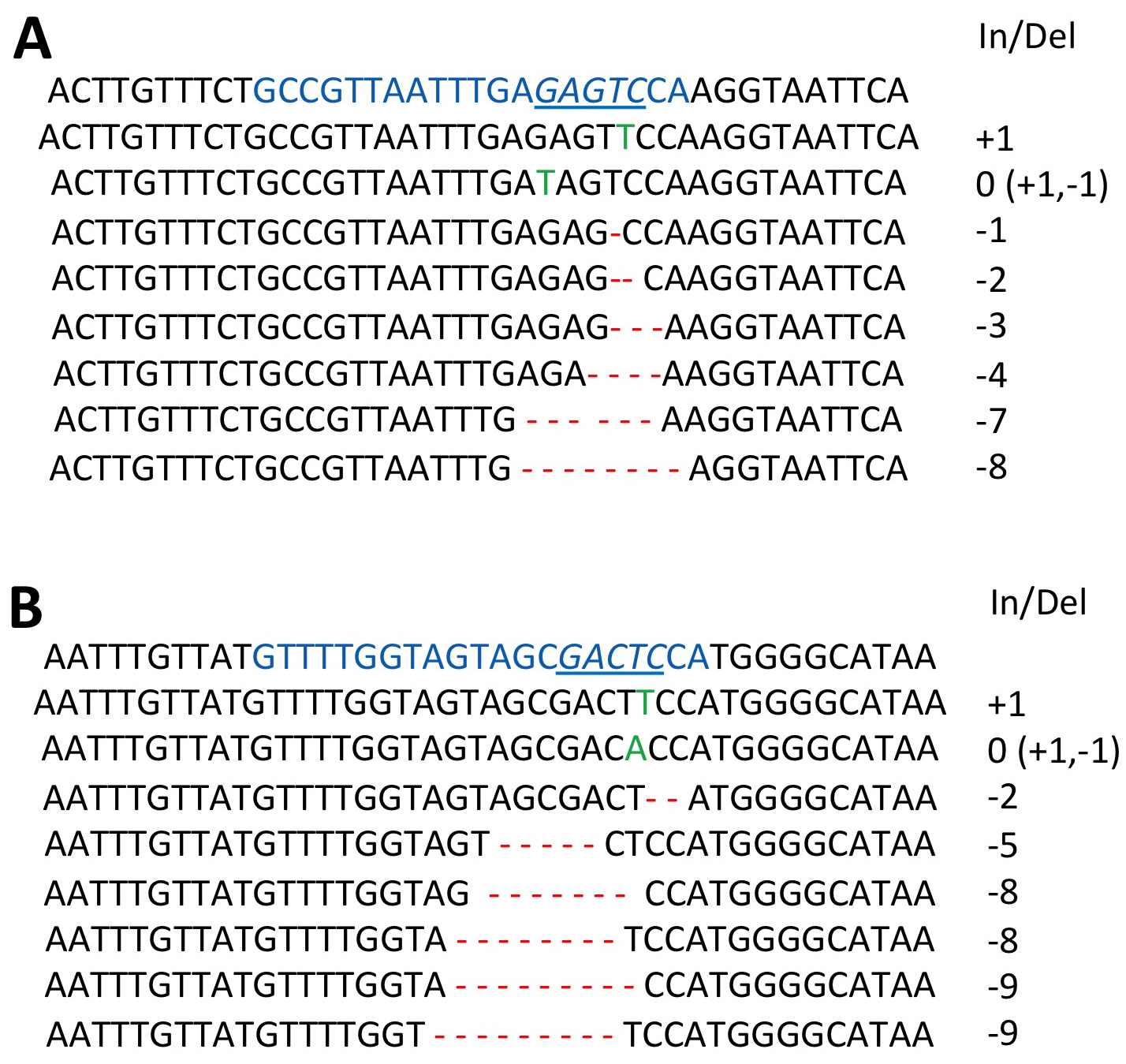
**Fig. S5.** DNA sequence confirmation of Cas9/intron-sgRNA-mediated mutagenesis of the sgRNA target site within the nonfunctional *GFP* gene in the leaf cells of Cas9/intron-sgRNA-treated tobacco plants. Cloned DNA fragments were PCR amplified target regions of mutagenized *GFP* genes that were obtained using genomic DNA from leaf cells infiltrated with *A. tumefaciens* carrying a vector containing the Cas9/intron sgRNA gene and the nonfunctional *GFP* gene. Top line shows the nonmutagenized DNA region surrounding the sgRNA target site while remaining lines display DNA sequences of clones of eight PCR-amplified *GFP* genes mutagenized by the Cas9/sgRNA complex.The PAM site is displayed in red, *ApaLI* recognition site is underlined and the 20 nucleotide target sequence for the Cas9/sgRNA complex is depicted in blue. Deleted nucleotides are denoted as red dots and inserted nucleotides are shown in green. Values in the column to the right indicate the net length of insertions and/or deletions (In/Del).



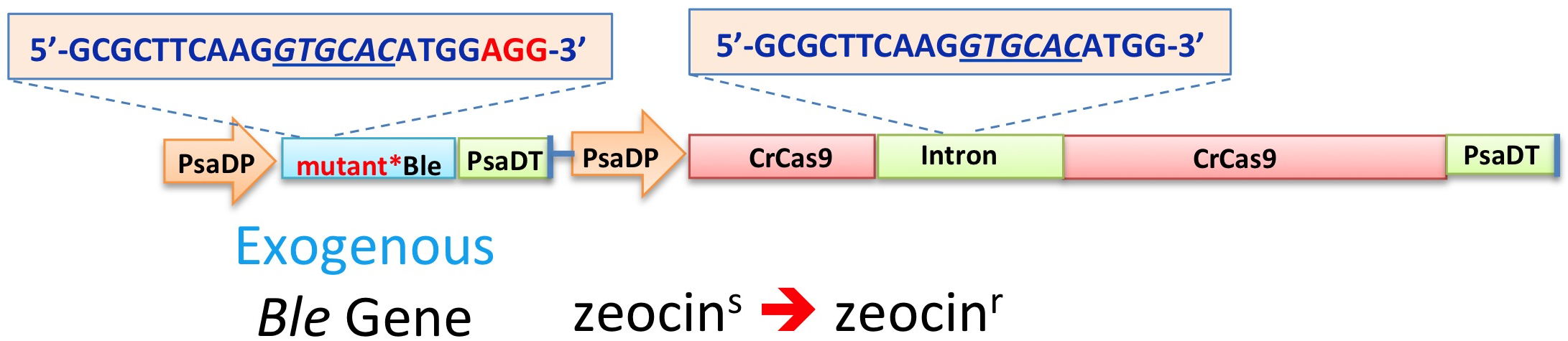
**Fig. S6.** Design of constructs used for testing transient expression of the Cas9/intron-sgRNA system targeting the endogenous phytoene desaturase tobacco gene. **(A)** Two constructs with a 20nt or a 21nt sequence in the sgRNAgenetargeting two different sites **(B)** in the endogenous phytoene desaturase gene (*NbPDS3*; GenBank EU1653551) of *Nicotiana benthamiana*. 35S: CaMV 35S promoter region; Tnos: termination region of the *Agrobacterium tumefaciens* T-DNA nopoline synthase gene; nucleotides in red: PAM site; nucleotides in blue: 20nt or 21nt target sequences containing the restriction site *MlyI* in italic. DNA sequence in green on opposite DNA strand in target 2 is a *MlyI* recognition site (5’ GAGTC 3’).



**Fig. S7**. PCR/Restriction Enzyme (PCR/RE) analysis of total DNA extracts from a leaf of Cas9/intron-sgRNA-treated *Nicotiana benthamiana* plants containing two different target sites in the *NbPDS3* gene mutagenized by Cas9/sgRNA activity. **(A)**  Bottom arrows indicates the expected ~149bp and 94 bp DNA fragments resulting from *MlyI* cleavage of the ~243bp PCR product amplified from target site 1. Lanes 2 and 4, DNA extracted from leaf segments receiving only the Cas9 gene construct; Lanes 1 and 3, DNA from leaf segments receiving both the Cas9 gene and sgRNA constructs. **(B)** Bottom arrow indicates the expected ~90bp DNA fragments resulting from MlyI cleavage of the ~180bp PCR product amplified from target site 2. Top arrows indicate the expected ~243 bp and 180bp size of PCR products from target sites 1 and 2, respectively, of the *NbPDS3* gene mutagenized by the Cas9/sgRNA system in such a manner that they are no longer are susceptible to cleavage by *MlyI*. Lanes 1 and 3, DNA from segments receiving the Cas9/intron-sgRNA gene construct. Lanes 2 and 4, DNA extracted from leaf segments receiving only the Cas9 gene construct.



**Fig. S8.** DNA sequence confirmation of Cas9/intron-sgRNA-mediated mutagenesis of the sgRNA target site 1 **(A)** and site 2 **(B)** within the *PDS3* gene in the cells of tobacco leaves infiltrated with *Agrobacterium tumefaciens* carrying Cas9/intron-sgRNA genes. Cloned DNA fragments were PCR amplified target regions of the two targeted *NbPDS3* gene regions. Top lines show the DNA region surrounding the sgRNA target sites while remaining lines display DNA sequences of clones of eight PCR-amplified *GFP* genes mutagenized by the Cas9/sgRNA complex. The PAM site is in red, the *MlyI* recognition site is underlined in blue and the 20-21 nucleotide target sequence for the Cas9/intron-sgRNA complex is depicted in blue. Deleted nucleotides are depicted as red dots and inserted nucleotides are shown in green. Values in the column to the right indicate the net length of insertions and/or deletions (In/Del).



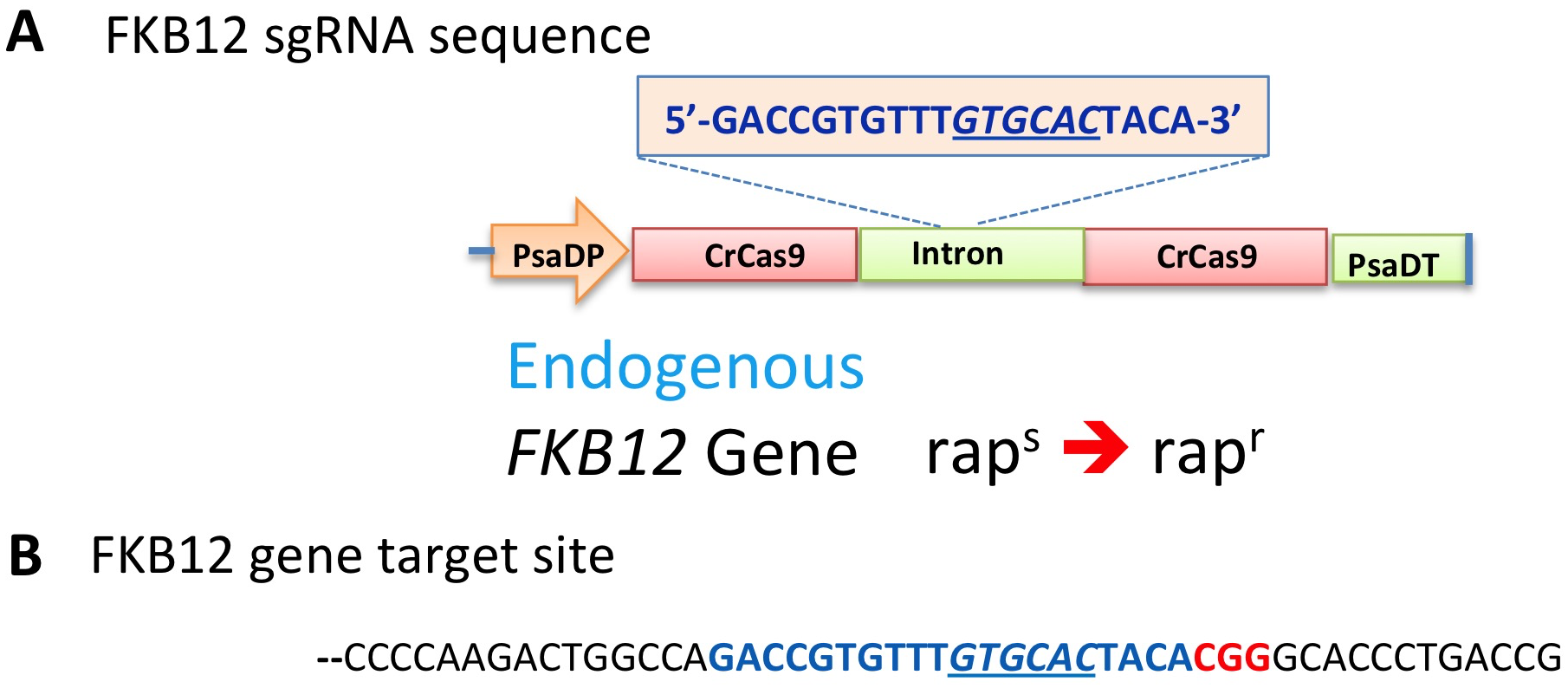
**Fig. S9.** Design of construct for testing transient expression in *C. reinhardtii* of the Cas9/intron-sgRNA system targeting an exogenously supplied, nonfuctional, *Ble* gene containing an insertion upstream of the sgRNA target site putting the coding region out of its proper reading frame*.* The Cas9 gene has a RbcS2 intron in the coding region and the intron is embedded with a sgRNA gene targeting the exogenous, nonfuctional *Ble* gene. PsaDP, Chlamydomonas *PsaD* gene promoter region; PsaDT, termination region of the Chlamydomonas *PsaD* gene ; nucleotides in blue, 20nt target sequence containing a restriction site for *ApaLI* (in italic); nucleotides in red, PAM site.



**Fig. S10.** DNA sequence confirmation of Cas9/intron-sgRNA mutagenesis of the sgRNA target site within the mutant *Ble* gene in Cas9/intron-sgRNA-transformed cells. Cloned DNA fragments were PCR amplified target regions of the mutagenized *Ble* gene using genomic DNA isolated from single colonies resistant to zeocin. Top line shows the DNA sequence of the DNA region surrounding the sgRNA target site while DNA sequences of individual mutant clones are shown below. The PAM site is in red, the *ApaLI* recognition site is underlined and the 20 nucleotide target sequence is depicted in blue. Inserted nucleotides are shown in green. Values indicating the net length of insertions and the number of each mutant clones examined are listed to the right in the first and second columns, respectively. The 7 mutated sequence were obtained in 4 experiments employing a total of 4x108 cells (i.e., a rate of one site-specific mutation in ~6x107 initial cells).



**Fig. S11**. Dual targeting to restore a mutant selectable marker gene and simultaneously disrupt a non-selectable target gene. **A:** Design of Cas9/intron-sgRNA targeting a 20nt genomic sequence present both in exon 7 of the putative Chlamydomonas *Ku70* gene (Cre13.g607500.t1.2) and in a co-transformed nonfuntional *Ble* gene containing the same 20nt sequence near its 5' terminus so as to create an out-of-reading-frame mutant *Ble* gene. **B:** DNA sequences of PCR-amplified regions of target areas of *Ble* genes in zeocin resistant colonies resulting from the co-transformation of *Chlamydomonas reinhardtii*, cc503, with the mutant *Ble* gene and the Cas9/intron-sgRNA gene shown in A. Top line is the DNA target sequence within the designed mutant *Ble* DNA sequence. **C:** A seven bp deletion in *Ku70* gene of the zeocin resistant mutant depicted in B as the first transformant containing an in-frame *Ble* gene restoration. Red AGG, PAM site; blue nucleotides, sgRNA target sites; green letters, inserted nucleotides; red dashes, deleted nucleotides.



**Fig. S12.** Design of constructs used for testing transient expression of the Cas9/intron-sgRNA system for targeting the *C. reinhardtii* peptidyl-prolyl cis-trans isomerase gene (i.e., the *FKB12* gene; phytozome Cre13.g586300.t1.2)with a 20nt target sequence in sgRNA**(A)** and in genomic DNA **(B)**. Nucleotides in blue: 20nt target sequence with restriction site *ApaLI* underlined and in italic; in red: PAM site.

**Fig. S13.** The complete DNA sequence of the Cas9/intron-sgRNA gene targeting the exogenous mutant *GFP* gene.

AATTCCATGGAGTCAAAGATTCAAATAGAGGACCTAACAGAACTCGCCGTAAAGACTGGCGAACAGTTCATACAGAGTCTCTTACGACTCAATGACAAGAAGAAAATCTTCGTCAACATGGTGGAGCACGACACACTTGTCTACTCCAAAAATATCAAAGATACAGTCTCAGAAGACCAAAGGGCAATTGAGACTTTTCAACAAAGGGTAATATCCGGAAACCTCCTCGGATTCCATTGCCCAGCTATCTGTCACTTTATTGTGAAGATAGTGGAAAAGGAAGGTGGCTCCTACAAATGCCATCATTGCGATAAAGGAAAGGCCATCGTTGAAGATGCCTCTGCCGACAGTGGTCCCAAAGATGGACCCCCACCCACGAGGAGCATCGTGGAAAAAGAAGACGTTCCAACCACGTCTTCAAAGCAAGTGGATTGATGTGATATCTCCACTGACGTAAGGGATGACGCACAATCCCACTATCCTTCGCAAGACCCTTCCTCTATATAAGGAAGTTCATTTCATTTGGAGAGAACACGGGGGACTCTTGACCATGGTAGATCTGACTAGTGATTACAAGGACGATGATGACAAGAAAGACTATAAAGATGACGATGATAAGCATATGGACAAGAAGTACAGCATCGGCCTGGACATCGGCACGAACTCGGTGGGCTGGGCGGTGATCACGGACGAGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGCCACTCGATCAAGAAGAACCTGATCGGCGCCCTGCTGTTCGACTCCGGCGAGACCGCCGAGGCGACGCGCCTGAAGCGCACCGCGCGTCGCCGCTACACGCGTCGCAAGAACCGCATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACTCGTTCTTCCACCGCCTGGAGGAGTCCTTCCTGGTGGAGGAAGACAAGAAGCACGAGCGCCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCCGACGATCTACCACCTGCGCAAGAAGCTGGTGGACAGCACCGACAAGGCGGACCTGCGCCTGATCTACCTGGCCCTGGCGCACATGATCAAGTTCCGCGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACTCGGACGTGGACAAGCTGTTCATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCGATCAACGCCTCCGGCGTGGACGCCAAGGCGATCCTGAGCGCGCGCCTGTCCAAGAGCCGTCGCCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGTTCGGCAACCTGATCGCGCTGTCGCTGGGCCTGACGCCGAACTTCAAGTCCAACTTCGACCTGGCCGAGGACGCGAAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCGGACCTGTTCCTGGCCGCGAAGAACCTGTCGGACGCCATCCTGCTGTCCGACATCCTGCGCGTGAACACCGAGATCACGAAGGCCCCCCTGTCGGCGTCCATGATCAAGCGCTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCGCTGGTGCGCCAGCAGCTGCCGGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCGTCGCAAGAGGAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACGGAGGAGCTGCTGGTGAAGCTGAACCGCGAGGACCTGCTGCGCAAGCAGCGCACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGCACGCCATCCTGCGTCGCCAAGAGGACTTCTACCCGTTCCTGAAGGACAACCGCGAGAAGATCGAGAAGATCCTGACGTTCCGCATCCCCTACTACGTGGGCCCACTTGCTAGAGGAAACTCTCGTTTCGCTTGGATGACCAGAAAGTCTGAGGAGACCATCACCCCTTGGAACTTCGAGGAGGTAAGTTTCTGCTTCTACCTTTGATATATATATAATAATTATCATTAATTAGGCGCTTCAAGGTGCACATGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTTTTTTAGTAATATAATATTTCAAATATTTTTTTCAAAATAAAAGAATGTAGTATATAGCAATTGCTTTTCTGTAGTTTATAAGTGTGTATATTTTAATTTATAACTTTTCTAATATATGACCAAAATTTGTTGATGTGCAGGTTGTTGATAAGGGAGCTTCTGCTCAGTCTTTCATCGAGAGAATGACCAACTTCGATAAGAACCTTCCAAACGAGAAGGTTCTTCCAAAGCACTCTCTTCTTTACGAGTACTTCACCGTGTACAACGAGCTGACGAAGGTGAAGTACGTGACCGAGGGCATGCGCAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCGATCGTGGACCTGCTGTTCAAGACCAACCGCAAGGTGACGGTGAAGCAGCTGAAAGAGGACTACTTCAAGAAGATCGAGTGCTTCGACAGCGTGGAGATCTCGGGCGTGGAGGACCGCTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACGCTGTTCGAGGACCGCGAGATGATCGAGGAGCGCCTGAAGACGTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGTCGCCGCTACACCGGCTGGGGCCGCCTGAGCCGCAAGCTGATCAACGGCATCCGCGACAAGCAGTCCGGCAAGACCATCCTGGACTTCCTGAAGAGCGACGGCTTCGCGAACCGCAACTTCATGCAGCTGATCCACGACGACTCGCTGACCTTCAAAGAGGACATCCAGAAGGCCCAGGTGTCGGGCCAGGGCGACTCCCTGCACGAGCACATCGCCAACCTGGCGGGCTCCCCCGCGATCAAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGCCACAAGCCGGAGAACATCGTGATCGAGATGGCCCGCGAGAACCAGACCACGCAGAAGGGCCAGAAGAACAGCCGCGAGCGCATGAAGCGCATCGAGGAAGGCATCAAGGAGCTGGGCTCGCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTACTACCTGCAGAACGGCCGCGACATGTACGTGGACCAGGAGCTGGACATCAACCGCCTGTCCGACTACGACGTGGACCACATCGTGCCCCAGAGCTTCCTGAAGGACGACTCGATCGACAACAAGGTGCTGACCCGCAGCGACAAGAACCGCGGCAAGAGCGACAACGTGCCGTCGGAGGAAGTGGTGAAGAAGATGAAGAACTACTGGCGCCAGCTGCTGAACGCCAAGCTGATCACGCAGCGCAAGTTCGACAACCTGACCAAGGCCGAGCGCGGTGGCCTGTCGGAGCTGGACAAGGCGGGCTTCATCAAGCGCCAGCTGGTGGAGACCCGCCAGATCACGAAGCACGTGGCGCAGATCCTGGACTCCCGCATGAACACGAAGTACGACGAGAACGACAAGCTGATCCGCGAGGTGAAGGTGATCACCCTGAAGTCCAAGCTGGTCAGCGACTTCCGCAAGGACTTCCAGTTCTACAAGGTGCGCGAGATCAACAACTACCACCACGCCCACGACGCGTACCTGAACGCCGTGGTGGGCACCGCGCTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGCAAGATGATCGCCAAGTCGGAGCAGGAGATCGGCAAGGCCACCGCGAAGTACTTCTTCTACTCCAACATCATGAACTTCTTCAAGACCGAGATCACGCTGGCCAACGGCGAGATCCGCAAGCGCCCGCTGATCGAGACCAACGGCGAGACGGGCGAGATCGTGTGGGACAAGGGCCGCGACTTCGCGACCGTGCGCAAGGTGCTGAGCATGCCCCAGGTGAACATCGTGAAGAAGACCGAGGTGCAGACGGGCGGCTTCTCCAAGGAGAGCATCCTGCCGAAGCGCAACTCGGACAAGCTGATCGCCCGCAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACTCCCCGACCGTGGCCTACAGCGTGCTGGTGGTGGCGAAGGTGGAGAAGGGCAAGTCCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGCAGCTCGTTCGAGAAGAACCCCATCGACTTCCTGGAGGCCAAGGGCTACAAAGAGGTGAAGAAGGACCTGATCATCAAGCTGCCGAAGTACTCGCTGTTCGAGCTGGAGAACGGCCGCAAGCGCATGCTGGCCTCCGCGGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCCCAGCAAGTACGTGAACTTCCTGTACCTGGCGTCCCACTACGAGAAGCTGAAGGGCTCGCCGGAGGACAACGAGCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCTCGGAGTTCTCCAAGCGCGTGATCCTGGCCGACGCGAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCGCGACAAGCCCATCCGCGAGCAGGCGGAGAACATCATCCACCTGTTCACCCTGACGAACCTGGGCGCCCCGGCCGCGTTCAAGTACTTCGACACCACGATCGACCGCAAGCGCTACACCTCCACGAAAGAGGTGCTGGACGCGACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGACGCGCATCGACCTGAGCCAGCTGGGCGGCGACTCCCGCGCGGACCCGAAGAAGAAGCGCAAGGTGTAAGAATTAATTCGGATCGATCCATTGGTGACCAGCTCGAATTTCCCCGATCGTTCAAACATTTGGCAATAAAGTTTCTTAAGATTGAATCCTGTTGCCGGTCTTGCGATGATTATCATATAATTTCTGTTGAATTACGTTAAGCATGTAATAATTAACATGTAATGCATGACGTTATTTATGAGATGGGTTTTTATGATTAGAGTCCCGCAATTATACATTTAATACGCGATAGAAAACAAAATATAGCGCGCAAACTAGGATAAATTATCGCGCGCGGTGTCATCTATGTTACTAGATCGGGGGTACCGATTACGAATTGAATCGtCAACGAGATCTTGAGCCAATCAAAGAGGAGTGATGTAGACCTAAAGCAATAATGGAGCCATGACGTAAGGGCTTACgCCCATACGAAATAATTAAAGGCTGATGTGACCTGTCGGTCTCTCAGAACCTTTACTTTTTATGTTTGGCGTGTATTTTTAAATTTCCACGGCAATGACGATGTGACCCAACGAGATCTTGAGCCAATCAAAGAGGAGTGATGTAGACCTAAAGCAATAATGGAGCCATGACGTAAGGGCTTACGCCCATACGAAATAATTAAAGGCTGATGTGACCTGTCGGTCTCTCAGAACCTTTACTTTTTATATTTGGCGTGTATTTTTAAATTTCCACGGcAATGACgATGTGACCTGtGCATcCGCTTTGCCTATAAATAAGtTTTaagTTTGTaTTGATCGACACGGTcGAGAAGACACGGcCATAAGCTTGTTCACCATGGAGCGCTTCAAGGTGCACATGGAGGACTAGTAAAGGAGAAGAACTTTTCACTGGAGTTGTCCCAATTCTTGTTGAATTAGATGGTGATGTTAATGGGCACAAATTTTCTGTCAGTGGAGAGGGTGAAGGTGATGCAACATACGGAAAACTTACCCTTAAATTTATTTGCACTACTGGAAAACTACCTGTTCCGTGGCCAACACTTGTCACTACTTTCTCTTATGGTGTTCAATGCTTTTCAAGATACCCAGATCATATGAAGCGGCACGACTTCTTCAAGAGCGCCATGCCTGAGGGATACGTGCAGGAGAGGACCATCTTCTTCAAGGACGACGGGAACTACAAGACACGTGCTGAAGTCAAGTTTGAGGGAGACACCCTCGTCAACAGGATCGAGCTTAAGGGAATCGATTTCAAGGAGGACGGAAACATCCTCGGCCACAAGTTGGAATACAACTACAACTCCCACAACGTATACATCATGGCCGACAAGCAAAAGAACGGCATCAAAGCCAACTTCAAGACCCGCCACAACATCGAAGACGGCGGCGTGCAACTCGCTGATCATTATCAACAAAATACTCCAATTGGCGATGGCCCTGTCCTTTTACCAGACAACCATTACCTGTCCACACAATCTGCCCTTTCGAAAGATCCCAACGAAAAGAGAGACCACATGGTCCTTCTTGAGTTTGTAACAGCTGCTGGGATTACACATGGCATGGATGAACTATACAAAGCTAGCTAATCTAGAGCTTTCGgTTCGtATCATCGGTTTCGaCAACGTTCGTCcAAGTtCAATGCATCAGTTTCATTGCGCACACACCAGAATCCTACTGAGTTTGAGTATTATGGCATTGGGAAAACTGTTTTTCTTGtACCATTTGTTGTGCTTGTAATTTACTGTGTTTTTTATTCGGTTTTCGCTATCGAACTGTGAAATGGAAATGGATGGAGAAGAGTTAATGAATGATATGGTCCTTTTGTTCATTCTCAAATTAATATTATTTGTTTTTTCTCTTATTTGTTGTGTGTTGAATTTGAAATTATAAGAGATATGCAAACATTTTGTTTTGAGTAAAAATGTGTCAAATCGTGGCCTCTAATGACCGAAGTTAATATGAGGAGTAAAACACTTGTAGTTGTACCATTATGCTTATTCACTAGGCAACAAATATATTTTCAGACCTAGAAAAGCTGCAAATGTTACTGAATACAAGTATGTCCTCTTGTGTTTTAGACATTTATGAACTTTCCTTTATGTAATTTTCCAGAATCCTTGTCAGATTCTAATCATTGCTTTATAATTATAGTTATACTCATGGATTTGTAGTTGAGTATGAAAATATTTTTTAATGCATTTTATGACTTGCCAATTGATTGaCAACATGCATCAATCGcTAGGATCCTCTAGAGTCGACCTGCAGGCATGCAAGCTTGGCACTGGCCGTCGTTTTACAACGTCGTGACTGGGAAAACCCTGGCGTTACCCAACTTAATCGCCTTGCAGCACATCCCCCTTTCGCCAGCTGGCGTAATAGCGAAGAGGCCCGCACCGATCGCCCTTCCCAACAGTTGCGCAGCCTGAATGGCGAATGCTAGAGCAGCTTGAGCTTGGATCAGATTGTCGTTTCCCGCCTTCAGTTTAAACTATCAGTGTTTGACAGGATATATTGGCGGGTAAACCTAAGAGAAAAGAGCGTTTATTAGAATAACGGATATTTAAAAGGGCGTGAAAAGGTTTATCCGTTCGTCCATTTGTATGTGCATGCCAACCACAGGGTTCCCCTCGGGATCAAAGTACTTTGATCCAACCCCTCCGCTGCTATAGTGCAGTCGGCTTCTGACGTTCAGTGCAGCCGTCTTCTGAAAACGACATGTCGCACAAGTCCTAAGTTACGCGACAGGCTGCCGCCCTGCCCTTTTCCTGGCGTTTTCTTGTCGCGTGTTTTAGTCGCATAAAGTAGAATACTTGCGACTAGAACCGGAGACATTACGCCATGAACAAGAGCGCCGCCGCTGGCCTGCTGGGCTATGCCCGCGTCAGCACCGACGACCAGGACTTGACCAACCAACGGGCCGAACTGCACGCGGCCGGCTGCACCAAGCTGTTTTCCGAGAAGATCACCGGCACCAGGCGCGACCGCCCGGAGCTGGCCAGGATGCTTGACCACCTACGCCCTGGCGACGTTGTGACAGTGACCAGGCTAGACCGCCTGGCCCGCAGCACCCGCGACCTACTGGACATTGCCGAGCGCATCCAGGAGGCCGGCGCGGGCCTGCGTAGCCTGGCAGAGCCGTGGGCCGACACCACCACGCCGGCCGGCCGCATGGTGTTGACCGTGTTCGCCGGCATTGCCGAGTTCGAGCGTTCCCTAATCATCGACCGCACCCGGAGCGGGCGCGAGGCCGCCAAGGCCCGAGGCGTGAAGTTTGGCCCCCGCCCTACCCTCACCCCGGCACAGATCGCGCACGCCCGCGAGCTGATCGACCAGGAAGGCCGCACCGTGAAAGAGGCGGCTGCACTGCTTGGCGTGCATCGCTCGACCCTGTACCGCGCACTTGAGCGCAGCGAGGAAGTGACGCCCACCGAGGCCAGGCGGCGCGGTGCCTTCCGTGAGGACGCATTGACCGAGGCCGACGCCCTGGCGGCCGCCGAGAATGAACGCCAAGAGGAACAAGCATGAAACCGCACCAGGACGGCCAGGACGAACCGTTTTTCATTACCGAAGAGATCGAGGCGGAGATGATCGCGGCCGGGTACGTGTTCGAGCCGCCCGCGCACGTCTCAACCGTGCGGCTGCATGAAATCCTGGCCGGTTTGTCTGATGCCAAGCTGGCGGCCTGGCCGGCCAGCTTGGCCGCTGAAGAAACCGAGCGCCGCCGTCTAAAAAGGTGATGTGTATTTGAGTAAAACAGCTTGCGTCATGCGGTCGCTGCGTATATGATGCGATGAGTAAATAAACAAATACGCAAGGGGAACGCATGAAGGTTATCGCTGTACTTAACCAGAAAGGCGGGTCAGGCAAGACGACCATCGCAACCCATCTAGCCCGCGCCCTGCAACTCGCCGGGGCCGATGTTCTGTTAGTCGATTCCGATCCCCAGGGCAGTGCCCGCGATTGGGCGGCCGTGCGGGAAGATCAACCGCTAACCGTTGTCGGCATCGACCGCCCGACGATTGACCGCGACGTGAAGGCCATCGGCCGGCGCGACTTCGTAGTGATCGACGGAGCGCCCCAGGCGGCGGACTTGGCTGTGTCCGCGATCAAGGCAGCCGACTTCGTGCTGATTCCGGTGCAGCCAAGCCCTTACGACATATGGGCCACCGCCGACCTGGTGGAGCTGGTTAAGCAGCGCATTGAGGTCACGGATGGAAGGCTACAAGCGGCCTTTGTCGTGTCGCGGGCGATCAAAGGCACGCGCATCGGCGGTGAGGTTGCCGAGGCGCTGGCCGGGTACGAGCTGCCCATTCTTGAGTCCCGTATCACGCAGCGCGTGAGCTACCCAGGCACTGCCGCCGCCGGCACAACCGTTCTTGAATCAGAACCCGAGGGCGACGCTGCCCGCGAGGTCCAGGCGCTGGCCGCTGAAATTAAATCAAAACTCATTTGAGTTAATGAGGTAAAGAGAAAATGAGCAAAAGCACAAACACGCTAAGTGCCGGCCGTCCGAGCGCACGCAGCAGCAAGGCTGCAACGTTGGCCAGCCTGGCAGACACGCCAGCCATGAAGCGGGTCAACTTTCAGTTGCCGGCGGAGGATCACACCAAGCTGAAGATGTACGCGGTACGCCAAGGCAAGACCATTACCGAGCTGCTATCTGAATACATCGCGCAGCTACCAGAGTAAATGAGCAAATGAATAAATGAGTAGATGAATTTTAGCGGCTAAAGGAGGCGGCATGGAAAATCAAGAACAACCAGGCACCGACGCCGTGGAATGCCCCATGTGTGGAGGAACGGGCGGTTGGCCAGGCGTAAGCGGCTGGGTTGTCTGCCGGCCCTGCAATGGCACTGGAACCCCCAAGCCCGAGGAATCGGCGTGACGGTCGCAAACCATCCGGCCCGGTACAAATCGGCGCGGCGCTGGGTGATGACCTGGTGGAGAAGTTGAAGGCCGCGCAGGCCGCCCAGCGGCAACGCATCGAGGCAGAAGCACGCCCCGGTGAATCGTGGCAAGCGGCCGCTGATCGAATCCGCAAAGAATCCCGGCAACCGCCGGCAGCCGGTGCGCCGTCGATTAGGAAGCCGCCCAAGGGCGACGAGCAACCAGATTTTTTCGTTCCGATGCTCTATGACGTGGGCACCCGCGATAGTCGCAGCATCATGGACGTGGCCGTTTTCCGTCTGTCGAAGCGTGACCGACGAGCTGGCGAGGTGATCCGCTACGAGCTTCCAGACGGGCACGTAGAGGTTTCCGCAGGGCCGGCCGGCATGGCCAGTGTGTGGGATTACGACCTGGTACTGATGGCGGTTTCCCATCTAACCGAATCCATGAACCGATACCGGGAAGGGAAGGGAGACAAGCCCGGCCGCGTGTTCCGTCCACACGTTGCGGACGTACTCAAGTTCTGCCGGCGAGCCGATGGCGGAAAGCAGAAAGACGACCTGGTAGAAACCTGCATTCGGTTAAACACCACGCACGTTGCCATGCAGCGTACGAAGAAGGCCAAGAACGGCCGCCTGGTGACGGTATCCGAGGGTGAAGCCTTGATTAGCCGCTACAAGATCGTAAAGAGCGAAACCGGGCGGCCGGAGTACATCGAGATCGAGCTAGCTGATTGGATGTACCGCGAGATCACAGAAGGCAAGAACCCGGACGTGCTGACGGTTCACCCCGATTACTTTTTGATCGATCCCGGCATCGGCCGTTTTCTCTACCGCCTGGCACGCCGCGCCGCAGGCAAGGCAGAAGCCAGATGGTTGTTCAAGACGATCTACGAACGCAGTGGCAGCGCCGGAGAGTTCAAGAAGTTCTGTTTCACCGTGCGCAAGCTGATCGGGTCAAATGACCTGCCGGAGTACGATTTGAAGGAGGAGGCGGGGCAGGCTGGCCCGATCCTAGTCATGCGCTACCGCAACCTGATCGAGGGCGAAGCATCCGCCGGTTCCTAATGTACGGAGCAGATGCTAGGGCAAATTGCCCTAGCAGGGGAAAAAGGTCGAAAAGGTCTCTTTCCTGTGGATAGCACGTACATTGGGAACCCAAAGCCGTACATTGGGAACCGGAACCCGTACATTGGGAACCCAAAGCCGTACATTGGGAACCGGTCACACATGTAAGTGACTGATATAAAAGAGAAAAAAGGCGATTTTTCCGCCTAAAACTCTTTAAAACTTATTAAAACTCTTAAAACCCGCCTGGCCTGTGCATAACTGTCTGGCCAGCGCACAGCCGAAGAGCTGCAAAAAGCGCCTACCCTTCGGTCGCTGCGCTCCCTACGCCCCGCCGCTTCGCGTCGGCCTATCGCGGCCGCTGGCCGCTCAAAAATGGCTGGCCTACGGCCAGGCAATCTACCAGGGCGCGGACAAGCCGCGCCGTCGCCACTCGACCGCCGGCGCCCACATCAAGGCACCCTGCCTCGCGCGTTTCGGTGATGACGGTGAAAACCTCTGACACATGCAGCTCCCGGAGACGGTCACAGCTTGTCTGTAAGCGGATGCCGGGAGCAGACAAGCCCGTCAGGGCGCGTCAGCGGGTGTTGGCGGGTGTCGGGGCGCAGCCATGACCCAGTCACGTAGCGATAGCGGAGTGTATACTGGCTTAACTATGCGGCATCAGAGCAGATTGTACTGAGAGTGCACCATATGCGGTGTGAAATACCGCACAGATGCGTAAGGAGAAAATACCGCATCAGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGCATTCTAGGTACTAAAACAATTCATCCAGTAAAATATAATATTTTATTTTCTCCCAATCAGGCTTGATCCCCAGTAAGTCAAAAAATAGCTCGACATACTGTTCTTCCCCGATATCCTCCCTGATCGACCGGACGCAGAAGGCAATGTCATACCACTTGTCCGCCCTGCCGCTTCTCCCAAGATCAATAAAGCCACTTACTTTGCCATCTTTCACAAAGATGTTGCTGTCTCCCAGGTCGCCGTGGGAAAAGACAAGTTCCTCTTCGGGCTTTTCCGTCTTTAAAAAATCATACAGCTCGCGCGGATCTTTAAATGGAGTGTCTTCTTCCCAGTTTTCGCAATCCACATCGGCCAGATCGTTATTCAGTAAGTAATCCAATTCGGCTAAGCGGCTGTCTAAGCTATTCGTATAGGGACAATCCGATATGTCGATGGAGTGAAAGAGCCTGATGCACTCCGCATACAGCTCGATAATCTTTTCAGGGCTTTGTTCATCTTCATACTCTTCCGAGCAAAGGACGCCATCGGCCTCACTCATGAGCAGATTGCTCCAGCCATCATGCCGTTCAAAGTGCAGGACCTTTGGAACAGGCAGCTTTCCTTCCAGCCATAGCATCATGTCCTTTTCCCGTTCCACATCATAGGTGGTCCCTTTATACCGGCTGTCCGTCATTTTTAAATATAGGTTTTCATTTTCTCCCACCAGCTTATATACCTTAGCAGGAGACATTCCTTCCGTATCTTTTACGCAGCGGTATTTTTCGATCAGTTTTTTCAATTCCGGTGATATTCTCATTTTAGCCATTTATTATTTCCTTCCTCTTTTCTACAGTATTTAAAGATACCCCAAGAAGCTAATTATAACAAGACGAACTCCAATTCACTGTTCCTTGCATTCTAAAACCTTAAATACCAGAAAACAGCTTTTTCAAAGTTGTTTTCAAAGTTGGCGTATAACATAGTATCGACGGAGCCGATTTTGAAACCGCGGTGATCACAGGCAGCAACGCTCTGTCATCGTTACAATCAACATGCTACCCTCCGCGAGATCATCCGTGTTTCAAACCCGGCAGCTTAGTTGCCGTTCTTCCGAATAGCATCGGTAACATGAGCAAAGTCTGCCGCCTTACAACGGCTCTCCCGCTGACGCCGTCCCGGACTGATGGGCTGCCTGTATCGAGTGGTGATTTTGTGCCGAGCTGCCGGTCGGGGAGCTGTTGGCTGGCTGGTGGCAGGATATATTGTGGTGTAAACAAATTGACGCTTAGACAACTTAATAACACATTGCGGACGTTTTTAATGTACTGAATTAACGCCGAATTAATTCGGGGGATCTGGATTTTAGTACTGGATTTTGGTTTTAGGAATTAGAAATTTTATTGATAGAAGTATTTTACAAATACAAATACATACTAAGGGTTTCTTATATGCTCAACACATGAGCGAAACCCTATAGGAACCCTAATTCCCTTATCTGGGAACTACTCACACATTATTATGGAGAAACTCGAGCTTGTCGATCGACAGATCCGGTCGGCATCTACTCTATTTCTTTGCCCTCGGACGAGTGCTGGGGCGTCGGTTTCCACTATCGGCGAGTACTTCTACACAGCCATCGGTCCAGACGGCCGCGCTTCTGCGGGCGATTTGTGTACGCCCGACAGTCCCGGCTCCGGATCGGACGATTGCGTCGCATCGACCCTGCGCCCAAGCTGCATCATCGAAATTGCCGTCAACCAAGCTCTGATAGAGTTGGTCAAGACCAATGCGGAGCATATACGCCCGGAGTCGTGGCGATCCTGCAAGCTCCGGATGCCTCCGCTCGAAGTAGCGCGTCTGCTGCTCCATACAAGCCAACCACGGCCTCCAGAAGAAGATGTTGGCGACCTCGTATTGGGAATCCCCGAACATCGCCTCGCTCCAGTCAATGACCGCTGTTATGCGGCCATTGTCCGTCAGGACATTGTTGGAGCCGAAATCCGCGTGCACGAGGTGCCGGACTTCGGGGCAGTCCTCGGCCCAAAGCATCAGCTCATCGAGAGCCTGCGCGACGGACGCACTGACGGTGTCGTCCATCACAGTTTGCCAGTGATACACATGGGGATCAGCAATCGCGCATATGAAATCACGCCATGTAGTGTATTGACCGATTCCTTGCGGTCCGAATGGGCCGAACCCGCTCGTCTGGCTAAGATCGGCCGCAGCGATCGCATCCATAGCCTCCGCGACCGGTTGTAGAACAGCGGGCAGTTCGGTTTCAGGCAGGTCTTGCAACGTGACACCCTGTGCACGGCGGGAGATGCAATAGGTCAGGCTCTCGCTAAACTCCCCAATGTCAAGCACTTCCGGAATCGGGAGCGCGGCCGATGCAAAGTGCCGATAAACATAACGATCTTTGTAGAAACCATCGGCGCAGCTATTTACCCGCAGGACATATCCACGCCCTCCTACATCGAAGCTGAAAGCACGAGATTCTTCGCCCTCCGAGAGCTGCATCAGGTCGGAGACGCTGTCGAACTTTTCGATCAGAAACTTCTCGACAGACGTCGCGGTGAGTTCAGGCTTTTTCATATCTCATTGCCCCCCGGGATCTGCGAAAGCTCGAGAGAGATAGATTTGTAGAGAGAGACTGGTGATTTCAGCGTGTCCTCTCCAAATGAAATGAACTTCCTTATATAGAGGAAGGTCTTGCGAAGGATAGTGGGATTGTGCGTCATCCCTTACGTCAGTGGAGATATCACATCAATCCACTTGCTTTGAAGACGTGGTTGGAACGTCTTCTTTTTCCACGATGCTCCTCGTGGGTGGGGGTCCATCTTTGGGACCACTGTCGGCAGAGGCATCTTGAACGATAGCCTTTCCTTTATCGCAATGATGGCATTTGTAGGTGCCACCTTCCTTTTCTACTGTCCTTTTGATGAAGTGACAGATAGCTGGGCAATGGAATCCGAGGAGGTTTCCCGATATTACCCTTTGTTGAAAAGTCTCAATAGCCCTTTGGTCTTCTGAGACTGTATCTTTGATATTCTTGGAGTAGACGAGAGTGTCGTGCTCCACCATGTTATCACATCAATCCACTTGCTTTGAAGACGTGGTTGGAACGTCTTCTTTTTCCACGATGCTCCTCGTGGGTGGGGGTCCATCTTTGGGACCACTGTCGGCAGAGGCATCTTGAACGATAGCCTTTCCTTTATCGCAATGATGGCATTTGTAGGTGCCACCTTCCTTTTCTACTGTCCTTTTGATGAAGTGACAGATAGCTGGGCAATGGAATCCGAGGAGGTTTCCCGATATTACCCTTTGTTGAAAAGTCTCAATAGCCCTTTGGTCTTCTGAGACTGTATCTTTGATATTCTTGGAGTAGACGAGAGTGTCGTGCTCCACCATGTTGGCAAGCTGCTCTAGCCAATACGCAAACCGCCTCTCCCCGCGCGTTGGCCGATTCATTAATGCAGCTGGCACGACAGGTTTCCCGACTGGAAAGCGGGCAGTGAGCGCAACGCAATTAATGTGAGTTAGCTCACTCATTAGGCACCCCAGGCTTTACACTTTATGCTTCCGGCTCGTATGTTGTGTGGAATTGTGAGCGGATAACAATTTCACACAGGAAACAGCTATGACCATGATTACG

**Fig. S14.** The complete DNA sequence of the Cas9/intron-sgRNA gene targeting the native *PDS3-1* gene.

AATTCCATGGAGTCAAAGATTCAAATAGAGGACCTAACAGAACTCGCCGTAAAGACTGGCGAACAGTTCATACAGAGTCTCTTACGACTCAATGACAAGAAGAAAATCTTCGTCAACATGGTGGAGCACGACACACTTGTCTACTCCAAAAATATCAAAGATACAGTCTCAGAAGACCAAAGGGCAATTGAGACTTTTCAACAAAGGGTAATATCCGGAAACCTCCTCGGATTCCATTGCCCAGCTATCTGTCACTTTATTGTGAAGATAGTGGAAAAGGAAGGTGGCTCCTACAAATGCCATCATTGCGATAAAGGAAAGGCCATCGTTGAAGATGCCTCTGCCGACAGTGGTCCCAAAGATGGACCCCCACCCACGAGGAGCATCGTGGAAAAAGAAGACGTTCCAACCACGTCTTCAAAGCAAGTGGATTGATGTGATATCTCCACTGACGTAAGGGATGACGCACAATCCCACTATCCTTCGCAAGACCCTTCCTCTATATAAGGAAGTTCATTTCATTTGGAGAGAACACGGGGGACTCTTGACCATGGTAGATCTGACTAGTGATTACAAGGACGATGATGACAAGAAAGACTATAAAGATGACGATGATAAGCATATGGACAAGAAGTACAGCATCGGCCTGGACATCGGCACGAACTCGGTGGGCTGGGCGGTGATCACGGACGAGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGCCACTCGATCAAGAAGAACCTGATCGGCGCCCTGCTGTTCGACTCCGGCGAGACCGCCGAGGCGACGCGCCTGAAGCGCACCGCGCGTCGCCGCTACACGCGTCGCAAGAACCGCATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACTCGTTCTTCCACCGCCTGGAGGAGTCCTTCCTGGTGGAGGAAGACAAGAAGCACGAGCGCCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCCGACGATCTACCACCTGCGCAAGAAGCTGGTGGACAGCACCGACAAGGCGGACCTGCGCCTGATCTACCTGGCCCTGGCGCACATGATCAAGTTCCGCGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACTCGGACGTGGACAAGCTGTTCATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCGATCAACGCCTCCGGCGTGGACGCCAAGGCGATCCTGAGCGCGCGCCTGTCCAAGAGCCGTCGCCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGTTCGGCAACCTGATCGCGCTGTCGCTGGGCCTGACGCCGAACTTCAAGTCCAACTTCGACCTGGCCGAGGACGCGAAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCGGACCTGTTCCTGGCCGCGAAGAACCTGTCGGACGCCATCCTGCTGTCCGACATCCTGCGCGTGAACACCGAGATCACGAAGGCCCCCCTGTCGGCGTCCATGATCAAGCGCTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCGCTGGTGCGCCAGCAGCTGCCGGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCGTCGCAAGAGGAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACGGAGGAGCTGCTGGTGAAGCTGAACCGCGAGGACCTGCTGCGCAAGCAGCGCACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGCACGCCATCCTGCGTCGCCAAGAGGACTTCTACCCGTTCCTGAAGGACAACCGCGAGAAGATCGAGAAGATCCTGACGTTCCGCATCCCCTACTACGTGGGCCCACTTGCTAGAGGAAACTCTCGTTTCGCTTGGATGACCAGAAAGTCTGAGGAGACCATCACCCCTTGGAACTTCGAGGAGGTAAGTTTCTGCTTCTACCTTTGATATATATATAATAATTATCATTAATTAGGCCGTTAATTTGAGAGTCCAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTTTTTTAGTAATATAATATTTCAAATATTTTTTTCAAAATAAAAGAATGTAGTATATAGCAATTGCTTTTCTGTAGTTTATAAGTGTGTATATTTTAATTTATAACTTTTCTAATATATGACCAAAATTTGTTGATGTGCAGGTTGTTGATAAGGGAGCTTCTGCTCAGTCTTTCATCGAGAGAATGACCAACTTCGATAAGAACCTTCCAAACGAGAAGGTTCTTCCAAAGCACTCTCTTCTTTACGAGTACTTCACCGTGTACAACGAGCTGACGAAGGTGAAGTACGTGACCGAGGGCATGCGCAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCGATCGTGGACCTGCTGTTCAAGACCAACCGCAAGGTGACGGTGAAGCAGCTGAAAGAGGACTACTTCAAGAAGATCGAGTGCTTCGACAGCGTGGAGATCTCGGGCGTGGAGGACCGCTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACGCTGTTCGAGGACCGCGAGATGATCGAGGAGCGCCTGAAGACGTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGTCGCCGCTACACCGGCTGGGGCCGCCTGAGCCGCAAGCTGATCAACGGCATCCGCGACAAGCAGTCCGGCAAGACCATCCTGGACTTCCTGAAGAGCGACGGCTTCGCGAACCGCAACTTCATGCAGCTGATCCACGACGACTCGCTGACCTTCAAAGAGGACATCCAGAAGGCCCAGGTGTCGGGCCAGGGCGACTCCCTGCACGAGCACATCGCCAACCTGGCGGGCTCCCCCGCGATCAAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGCCACAAGCCGGAGAACATCGTGATCGAGATGGCCCGCGAGAACCAGACCACGCAGAAGGGCCAGAAGAACAGCCGCGAGCGCATGAAGCGCATCGAGGAAGGCATCAAGGAGCTGGGCTCGCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTACTACCTGCAGAACGGCCGCGACATGTACGTGGACCAGGAGCTGGACATCAACCGCCTGTCCGACTACGACGTGGACCACATCGTGCCCCAGAGCTTCCTGAAGGACGACTCGATCGACAACAAGGTGCTGACCCGCAGCGACAAGAACCGCGGCAAGAGCGACAACGTGCCGTCGGAGGAAGTGGTGAAGAAGATGAAGAACTACTGGCGCCAGCTGCTGAACGCCAAGCTGATCACGCAGCGCAAGTTCGACAACCTGACCAAGGCCGAGCGCGGTGGCCTGTCGGAGCTGGACAAGGCGGGCTTCATCAAGCGCCAGCTGGTGGAGACCCGCCAGATCACGAAGCACGTGGCGCAGATCCTGGACTCCCGCATGAACACGAAGTACGACGAGAACGACAAGCTGATCCGCGAGGTGAAGGTGATCACCCTGAAGTCCAAGCTGGTCAGCGACTTCCGCAAGGACTTCCAGTTCTACAAGGTGCGCGAGATCAACAACTACCACCACGCCCACGACGCGTACCTGAACGCCGTGGTGGGCACCGCGCTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGCAAGATGATCGCCAAGTCGGAGCAGGAGATCGGCAAGGCCACCGCGAAGTACTTCTTCTACTCCAACATCATGAACTTCTTCAAGACCGAGATCACGCTGGCCAACGGCGAGATCCGCAAGCGCCCGCTGATCGAGACCAACGGCGAGACGGGCGAGATCGTGTGGGACAAGGGCCGCGACTTCGCGACCGTGCGCAAGGTGCTGAGCATGCCCCAGGTGAACATCGTGAAGAAGACCGAGGTGCAGACGGGCGGCTTCTCCAAGGAGAGCATCCTGCCGAAGCGCAACTCGGACAAGCTGATCGCCCGCAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACTCCCCGACCGTGGCCTACAGCGTGCTGGTGGTGGCGAAGGTGGAGAAGGGCAAGTCCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGCAGCTCGTTCGAGAAGAACCCCATCGACTTCCTGGAGGCCAAGGGCTACAAAGAGGTGAAGAAGGACCTGATCATCAAGCTGCCGAAGTACTCGCTGTTCGAGCTGGAGAACGGCCGCAAGCGCATGCTGGCCTCCGCGGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCCCAGCAAGTACGTGAACTTCCTGTACCTGGCGTCCCACTACGAGAAGCTGAAGGGCTCGCCGGAGGACAACGAGCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCTCGGAGTTCTCCAAGCGCGTGATCCTGGCCGACGCGAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCGCGACAAGCCCATCCGCGAGCAGGCGGAGAACATCATCCACCTGTTCACCCTGACGAACCTGGGCGCCCCGGCCGCGTTCAAGTACTTCGACACCACGATCGACCGCAAGCGCTACACCTCCACGAAAGAGGTGCTGGACGCGACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGACGCGCATCGACCTGAGCCAGCTGGGCGGCGACTCCCGCGCGGACCCGAAGAAGAAGCGCAAGGTGTAAGAATTAATTCGGATCGATCCATTGGTGACCAGCTCGAATTTCCCCGATCGTTCAAACATTTGGCAATAAAGTTTCTTAAGATTGAATCCTGTTGCCGGTCTTGCGATGATTATCATATAATTTCTGTTGAATTACGTTAAGCATGTAATAATTAACATGTAATGCATGACGTTATTTATGAGATGGGTTTTTATGATTAGAGTCCCGCAATTATACATTTAATACGCGATAGAAAACAAAATATAGCGCGCAAACTAGGATAAATTATCGCGCGCGGTGTCATCTATGTTACTAGATCGGGGGTACCCGGGGATCCTCTAGAGTCGACCTGCAGGCATGCAAGCTTGGCACTGGCCGTCGTTTTACAACGTCGTGACTGGGAAAACCCTGGCGTTACCCAACTTAATCGCCTTGCAGCACATCCCCCTTTCGCCAGCTGGCGTAATAGCGAAGAGGCCCGCACCGATCGCCCTTCCCAACAGTTGCGCAGCCTGAATGGCGAATGCTAGAGCAGCTTGAGCTTGGATCAGATTGTCGTTTCCCGCCTTCAGTTTAAACTATCAGTGTTTGACAGGATATATTGGCGGGTAAACCTAAGAGAAAAGAGCGTTTATTAGAATAACGGATATTTAAAAGGGCGTGAAAAGGTTTATCCGTTCGTCCATTTGTATGTGCATGCCAACCACAGGGTTCCCCTCGGGATCAAAGTACTTTGATCCAACCCCTCCGCTGCTATAGTGCAGTCGGCTTCTGACGTTCAGTGCAGCCGTCTTCTGAAAACGACATGTCGCACAAGTCCTAAGTTACGCGACAGGCTGCCGCCCTGCCCTTTTCCTGGCGTTTTCTTGTCGCGTGTTTTAGTCGCATAAAGTAGAATACTTGCGACTAGAACCGGAGACATTACGCCATGAACAAGAGCGCCGCCGCTGGCCTGCTGGGCTATGCCCGCGTCAGCACCGACGACCAGGACTTGACCAACCAACGGGCCGAACTGCACGCGGCCGGCTGCACCAAGCTGTTTTCCGAGAAGATCACCGGCACCAGGCGCGACCGCCCGGAGCTGGCCAGGATGCTTGACCACCTACGCCCTGGCGACGTTGTGACAGTGACCAGGCTAGACCGCCTGGCCCGCAGCACCCGCGACCTACTGGACATTGCCGAGCGCATCCAGGAGGCCGGCGCGGGCCTGCGTAGCCTGGCAGAGCCGTGGGCCGACACCACCACGCCGGCCGGCCGCATGGTGTTGACCGTGTTCGCCGGCATTGCCGAGTTCGAGCGTTCCCTAATCATCGACCGCACCCGGAGCGGGCGCGAGGCCGCCAAGGCCCGAGGCGTGAAGTTTGGCCCCCGCCCTACCCTCACCCCGGCACAGATCGCGCACGCCCGCGAGCTGATCGACCAGGAAGGCCGCACCGTGAAAGAGGCGGCTGCACTGCTTGGCGTGCATCGCTCGACCCTGTACCGCGCACTTGAGCGCAGCGAGGAAGTGACGCCCACCGAGGCCAGGCGGCGCGGTGCCTTCCGTGAGGACGCATTGACCGAGGCCGACGCCCTGGCGGCCGCCGAGAATGAACGCCAAGAGGAACAAGCATGAAACCGCACCAGGACGGCCAGGACGAACCGTTTTTCATTACCGAAGAGATCGAGGCGGAGATGATCGCGGCCGGGTACGTGTTCGAGCCGCCCGCGCACGTCTCAACCGTGCGGCTGCATGAAATCCTGGCCGGTTTGTCTGATGCCAAGCTGGCGGCCTGGCCGGCCAGCTTGGCCGCTGAAGAAACCGAGCGCCGCCGTCTAAAAAGGTGATGTGTATTTGAGTAAAACAGCTTGCGTCATGCGGTCGCTGCGTATATGATGCGATGAGTAAATAAACAAATACGCAAGGGGAACGCATGAAGGTTATCGCTGTACTTAACCAGAAAGGCGGGTCAGGCAAGACGACCATCGCAACCCATCTAGCCCGCGCCCTGCAACTCGCCGGGGCCGATGTTCTGTTAGTCGATTCCGATCCCCAGGGCAGTGCCCGCGATTGGGCGGCCGTGCGGGAAGATCAACCGCTAACCGTTGTCGGCATCGACCGCCCGACGATTGACCGCGACGTGAAGGCCATCGGCCGGCGCGACTTCGTAGTGATCGACGGAGCGCCCCAGGCGGCGGACTTGGCTGTGTCCGCGATCAAGGCAGCCGACTTCGTGCTGATTCCGGTGCAGCCAAGCCCTTACGACATATGGGCCACCGCCGACCTGGTGGAGCTGGTTAAGCAGCGCATTGAGGTCACGGATGGAAGGCTACAAGCGGCCTTTGTCGTGTCGCGGGCGATCAAAGGCACGCGCATCGGCGGTGAGGTTGCCGAGGCGCTGGCCGGGTACGAGCTGCCCATTCTTGAGTCCCGTATCACGCAGCGCGTGAGCTACCCAGGCACTGCCGCCGCCGGCACAACCGTTCTTGAATCAGAACCCGAGGGCGACGCTGCCCGCGAGGTCCAGGCGCTGGCCGCTGAAATTAAATCAAAACTCATTTGAGTTAATGAGGTAAAGAGAAAATGAGCAAAAGCACAAACACGCTAAGTGCCGGCCGTCCGAGCGCACGCAGCAGCAAGGCTGCAACGTTGGCCAGCCTGGCAGACACGCCAGCCATGAAGCGGGTCAACTTTCAGTTGCCGGCGGAGGATCACACCAAGCTGAAGATGTACGCGGTACGCCAAGGCAAGACCATTACCGAGCTGCTATCTGAATACATCGCGCAGCTACCAGAGTAAATGAGCAAATGAATAAATGAGTAGATGAATTTTAGCGGCTAAAGGAGGCGGCATGGAAAATCAAGAACAACCAGGCACCGACGCCGTGGAATGCCCCATGTGTGGAGGAACGGGCGGTTGGCCAGGCGTAAGCGGCTGGGTTGTCTGCCGGCCCTGCAATGGCACTGGAACCCCCAAGCCCGAGGAATCGGCGTGACGGTCGCAAACCATCCGGCCCGGTACAAATCGGCGCGGCGCTGGGTGATGACCTGGTGGAGAAGTTGAAGGCCGCGCAGGCCGCCCAGCGGCAACGCATCGAGGCAGAAGCACGCCCCGGTGAATCGTGGCAAGCGGCCGCTGATCGAATCCGCAAAGAATCCCGGCAACCGCCGGCAGCCGGTGCGCCGTCGATTAGGAAGCCGCCCAAGGGCGACGAGCAACCAGATTTTTTCGTTCCGATGCTCTATGACGTGGGCACCCGCGATAGTCGCAGCATCATGGACGTGGCCGTTTTCCGTCTGTCGAAGCGTGACCGACGAGCTGGCGAGGTGATCCGCTACGAGCTTCCAGACGGGCACGTAGAGGTTTCCGCAGGGCCGGCCGGCATGGCCAGTGTGTGGGATTACGACCTGGTACTGATGGCGGTTTCCCATCTAACCGAATCCATGAACCGATACCGGGAAGGGAAGGGAGACAAGCCCGGCCGCGTGTTCCGTCCACACGTTGCGGACGTACTCAAGTTCTGCCGGCGAGCCGATGGCGGAAAGCAGAAAGACGACCTGGTAGAAACCTGCATTCGGTTAAACACCACGCACGTTGCCATGCAGCGTACGAAGAAGGCCAAGAACGGCCGCCTGGTGACGGTATCCGAGGGTGAAGCCTTGATTAGCCGCTACAAGATCGTAAAGAGCGAAACCGGGCGGCCGGAGTACATCGAGATCGAGCTAGCTGATTGGATGTACCGCGAGATCACAGAAGGCAAGAACCCGGACGTGCTGACGGTTCACCCCGATTACTTTTTGATCGATCCCGGCATCGGCCGTTTTCTCTACCGCCTGGCACGCCGCGCCGCAGGCAAGGCAGAAGCCAGATGGTTGTTCAAGACGATCTACGAACGCAGTGGCAGCGCCGGAGAGTTCAAGAAGTTCTGTTTCACCGTGCGCAAGCTGATCGGGTCAAATGACCTGCCGGAGTACGATTTGAAGGAGGAGGCGGGGCAGGCTGGCCCGATCCTAGTCATGCGCTACCGCAACCTGATCGAGGGCGAAGCATCCGCCGGTTCCTAATGTACGGAGCAGATGCTAGGGCAAATTGCCCTAGCAGGGGAAAAAGGTCGAAAAGGTCTCTTTCCTGTGGATAGCACGTACATTGGGAACCCAAAGCCGTACATTGGGAACCGGAACCCGTACATTGGGAACCCAAAGCCGTACATTGGGAACCGGTCACACATGTAAGTGACTGATATAAAAGAGAAAAAAGGCGATTTTTCCGCCTAAAACTCTTTAAAACTTATTAAAACTCTTAAAACCCGCCTGGCCTGTGCATAACTGTCTGGCCAGCGCACAGCCGAAGAGCTGCAAAAAGCGCCTACCCTTCGGTCGCTGCGCTCCCTACGCCCCGCCGCTTCGCGTCGGCCTATCGCGGCCGCTGGCCGCTCAAAAATGGCTGGCCTACGGCCAGGCAATCTACCAGGGCGCGGACAAGCCGCGCCGTCGCCACTCGACCGCCGGCGCCCACATCAAGGCACCCTGCCTCGCGCGTTTCGGTGATGACGGTGAAAACCTCTGACACATGCAGCTCCCGGAGACGGTCACAGCTTGTCTGTAAGCGGATGCCGGGAGCAGACAAGCCCGTCAGGGCGCGTCAGCGGGTGTTGGCGGGTGTCGGGGCGCAGCCATGACCCAGTCACGTAGCGATAGCGGAGTGTATACTGGCTTAACTATGCGGCATCAGAGCAGATTGTACTGAGAGTGCACCATATGCGGTGTGAAATACCGCACAGATGCGTAAGGAGAAAATACCGCATCAGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGCATTCTAGGTACTAAAACAATTCATCCAGTAAAATATAATATTTTATTTTCTCCCAATCAGGCTTGATCCCCAGTAAGTCAAAAAATAGCTCGACATACTGTTCTTCCCCGATATCCTCCCTGATCGACCGGACGCAGAAGGCAATGTCATACCACTTGTCCGCCCTGCCGCTTCTCCCAAGATCAATAAAGCCACTTACTTTGCCATCTTTCACAAAGATGTTGCTGTCTCCCAGGTCGCCGTGGGAAAAGACAAGTTCCTCTTCGGGCTTTTCCGTCTTTAAAAAATCATACAGCTCGCGCGGATCTTTAAATGGAGTGTCTTCTTCCCAGTTTTCGCAATCCACATCGGCCAGATCGTTATTCAGTAAGTAATCCAATTCGGCTAAGCGGCTGTCTAAGCTATTCGTATAGGGACAATCCGATATGTCGATGGAGTGAAAGAGCCTGATGCACTCCGCATACAGCTCGATAATCTTTTCAGGGCTTTGTTCATCTTCATACTCTTCCGAGCAAAGGACGCCATCGGCCTCACTCATGAGCAGATTGCTCCAGCCATCATGCCGTTCAAAGTGCAGGACCTTTGGAACAGGCAGCTTTCCTTCCAGCCATAGCATCATGTCCTTTTCCCGTTCCACATCATAGGTGGTCCCTTTATACCGGCTGTCCGTCATTTTTAAATATAGGTTTTCATTTTCTCCCACCAGCTTATATACCTTAGCAGGAGACATTCCTTCCGTATCTTTTACGCAGCGGTATTTTTCGATCAGTTTTTTCAATTCCGGTGATATTCTCATTTTAGCCATTTATTATTTCCTTCCTCTTTTCTACAGTATTTAAAGATACCCCAAGAAGCTAATTATAACAAGACGAACTCCAATTCACTGTTCCTTGCATTCTAAAACCTTAAATACCAGAAAACAGCTTTTTCAAAGTTGTTTTCAAAGTTGGCGTATAACATAGTATCGACGGAGCCGATTTTGAAACCGCGGTGATCACAGGCAGCAACGCTCTGTCATCGTTACAATCAACATGCTACCCTCCGCGAGATCATCCGTGTTTCAAACCCGGCAGCTTAGTTGCCGTTCTTCCGAATAGCATCGGTAACATGAGCAAAGTCTGCCGCCTTACAACGGCTCTCCCGCTGACGCCGTCCCGGACTGATGGGCTGCCTGTATCGAGTGGTGATTTTGTGCCGAGCTGCCGGTCGGGGAGCTGTTGGCTGGCTGGTGGCAGGATATATTGTGGTGTAAACAAATTGACGCTTAGACAACTTAATAACACATTGCGGACGTTTTTAATGTACTGAATTAACGCCGAATTAATTCGGGGGATCTGGATTTTAGTACTGGATTTTGGTTTTAGGAATTAGAAATTTTATTGATAGAAGTATTTTACAAATACAAATACATACTAAGGGTTTCTTATATGCTCAACACATGAGCGAAACCCTATAGGAACCCTAATTCCCTTATCTGGGAACTACTCACACATTATTATGGAGAAACTCGAGCTTGTCGATCGACAGATCCGGTCGGCATCTACTCTATTTCTTTGCCCTCGGACGAGTGCTGGGGCGTCGGTTTCCACTATCGGCGAGTACTTCTACACAGCCATCGGTCCAGACGGCCGCGCTTCTGCGGGCGATTTGTGTACGCCCGACAGTCCCGGCTCCGGATCGGACGATTGCGTCGCATCGACCCTGCGCCCAAGCTGCATCATCGAAATTGCCGTCAACCAAGCTCTGATAGAGTTGGTCAAGACCAATGCGGAGCATATACGCCCGGAGTCGTGGCGATCCTGCAAGCTCCGGATGCCTCCGCTCGAAGTAGCGCGTCTGCTGCTCCATACAAGCCAACCACGGCCTCCAGAAGAAGATGTTGGCGACCTCGTATTGGGAATCCCCGAACATCGCCTCGCTCCAGTCAATGACCGCTGTTATGCGGCCATTGTCCGTCAGGACATTGTTGGAGCCGAAATCCGCGTGCACGAGGTGCCGGACTTCGGGGCAGTCCTCGGCCCAAAGCATCAGCTCATCGAGAGCCTGCGCGACGGACGCACTGACGGTGTCGTCCATCACAGTTTGCCAGTGATACACATGGGGATCAGCAATCGCGCATATGAAATCACGCCATGTAGTGTATTGACCGATTCCTTGCGGTCCGAATGGGCCGAACCCGCTCGTCTGGCTAAGATCGGCCGCAGCGATCGCATCCATAGCCTCCGCGACCGGTTGTAGAACAGCGGGCAGTTCGGTTTCAGGCAGGTCTTGCAACGTGACACCCTGTGCACGGCGGGAGATGCAATAGGTCAGGCTCTCGCTAAACTCCCCAATGTCAAGCACTTCCGGAATCGGGAGCGCGGCCGATGCAAAGTGCCGATAAACATAACGATCTTTGTAGAAACCATCGGCGCAGCTATTTACCCGCAGGACATATCCACGCCCTCCTACATCGAAGCTGAAAGCACGAGATTCTTCGCCCTCCGAGAGCTGCATCAGGTCGGAGACGCTGTCGAACTTTTCGATCAGAAACTTCTCGACAGACGTCGCGGTGAGTTCAGGCTTTTTCATATCTCATTGCCCCCCGGGATCTGCGAAAGCTCGAGAGAGATAGATTTGTAGAGAGAGACTGGTGATTTCAGCGTGTCCTCTCCAAATGAAATGAACTTCCTTATATAGAGGAAGGTCTTGCGAAGGATAGTGGGATTGTGCGTCATCCCTTACGTCAGTGGAGATATCACATCAATCCACTTGCTTTGAAGACGTGGTTGGAACGTCTTCTTTTTCCACGATGCTCCTCGTGGGTGGGGGTCCATCTTTGGGACCACTGTCGGCAGAGGCATCTTGAACGATAGCCTTTCCTTTATCGCAATGATGGCATTTGTAGGTGCCACCTTCCTTTTCTACTGTCCTTTTGATGAAGTGACAGATAGCTGGGCAATGGAATCCGAGGAGGTTTCCCGATATTACCCTTTGTTGAAAAGTCTCAATAGCCCTTTGGTCTTCTGAGACTGTATCTTTGATATTCTTGGAGTAGACGAGAGTGTCGTGCTCCACCATGTTATCACATCAATCCACTTGCTTTGAAGACGTGGTTGGAACGTCTTCTTTTTCCACGATGCTCCTCGTGGGTGGGGGTCCATCTTTGGGACCACTGTCGGCAGAGGCATCTTGAACGATAGCCTTTCCTTTATCGCAATGATGGCATTTGTAGGTGCCACCTTCCTTTTCTACTGTCCTTTTGATGAAGTGACAGATAGCTGGGCAATGGAATCCGAGGAGGTTTCCCGATATTACCCTTTGTTGAAAAGTCTCAATAGCCCTTTGGTCTTCTGAGACTGTATCTTTGATATTCTTGGAGTAGACGAGAGTGTCGTGCTCCACCATGTTGGCAAGCTGCTCTAGCCAATACGCAAACCGCCTCTCCCCGCGCGTTGGCCGATTCATTAATGCAGCTGGCACGACAGGTTTCCCGACTGGAAAGCGGGCAGTGAGCGCAACGCAATTAATGTGAGTTAGCTCACTCATTAGGCACCCCAGGCTTTACACTTTATGCTTCCGGCTCGTATGTTGTGTGGAATTGTGAGCGGATAACAATTTCACACAGGAAACAGCTATGACCATGATTACG

**Fig. S15.** The complete DNA sequence of the Cas9/intron-sgRNA gene targeting the native *PDS3-2* gene

AATTCCATGGAGTCAAAGATTCAAATAGAGGACCTAACAGAACTCGCCGTAAAGACTGGCGAACAGTTCATACAGAGTCTCTTACGACTCAATGACAAGAAGAAAATCTTCGTCAACATGGTGGAGCACGACACACTTGTCTACTCCAAAAATATCAAAGATACAGTCTCAGAAGACCAAAGGGCAATTGAGACTTTTCAACAAAGGGTAATATCCGGAAACCTCCTCGGATTCCATTGCCCAGCTATCTGTCACTTTATTGTGAAGATAGTGGAAAAGGAAGGTGGCTCCTACAAATGCCATCATTGCGATAAAGGAAAGGCCATCGTTGAAGATGCCTCTGCCGACAGTGGTCCCAAAGATGGACCCCCACCCACGAGGAGCATCGTGGAAAAAGAAGACGTTCCAACCACGTCTTCAAAGCAAGTGGATTGATGTGATATCTCCACTGACGTAAGGGATGACGCACAATCCCACTATCCTTCGCAAGACCCTTCCTCTATATAAGGAAGTTCATTTCATTTGGAGAGAACACGGGGGACTCTTGACCATGGTAGATCTGACTAGTGATTACAAGGACGATGATGACAAGAAAGACTATAAAGATGACGATGATAAGCATATGGACAAGAAGTACAGCATCGGCCTGGACATCGGCACGAACTCGGTGGGCTGGGCGGTGATCACGGACGAGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGCCACTCGATCAAGAAGAACCTGATCGGCGCCCTGCTGTTCGACTCCGGCGAGACCGCCGAGGCGACGCGCCTGAAGCGCACCGCGCGTCGCCGCTACACGCGTCGCAAGAACCGCATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACTCGTTCTTCCACCGCCTGGAGGAGTCCTTCCTGGTGGAGGAAGACAAGAAGCACGAGCGCCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCCGACGATCTACCACCTGCGCAAGAAGCTGGTGGACAGCACCGACAAGGCGGACCTGCGCCTGATCTACCTGGCCCTGGCGCACATGATCAAGTTCCGCGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACTCGGACGTGGACAAGCTGTTCATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCGATCAACGCCTCCGGCGTGGACGCCAAGGCGATCCTGAGCGCGCGCCTGTCCAAGAGCCGTCGCCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGTTCGGCAACCTGATCGCGCTGTCGCTGGGCCTGACGCCGAACTTCAAGTCCAACTTCGACCTGGCCGAGGACGCGAAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCGGACCTGTTCCTGGCCGCGAAGAACCTGTCGGACGCCATCCTGCTGTCCGACATCCTGCGCGTGAACACCGAGATCACGAAGGCCCCCCTGTCGGCGTCCATGATCAAGCGCTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCGCTGGTGCGCCAGCAGCTGCCGGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCGTCGCAAGAGGAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACGGAGGAGCTGCTGGTGAAGCTGAACCGCGAGGACCTGCTGCGCAAGCAGCGCACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGCACGCCATCCTGCGTCGCCAAGAGGACTTCTACCCGTTCCTGAAGGACAACCGCGAGAAGATCGAGAAGATCCTGACGTTCCGCATCCCCTACTACGTGGGCCCACTTGCTAGAGGAAACTCTCGTTTCGCTTGGATGACCAGAAAGTCTGAGGAGACCATCACCCCTTGGAACTTCGAGGAGGTAAGTTTCTGCTTCTACCTTTGATATATATATAATAATTATCATTAATTAGGTTTTGGTAGTAGCGACTCCAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTTTTTTAGTAATATAATATTTCAAATATTTTTTTCAAAATAAAAGAATGTAGTATATAGCAATTGCTTTTCTGTAGTTTATAAGTGTGTATATTTTAATTTATAACTTTTCTAATATATGACCAAAATTTGTTGATGTGCAGGTTGTTGATAAGGGAGCTTCTGCTCAGTCTTTCATCGAGAGAATGACCAACTTCGATAAGAACCTTCCAAACGAGAAGGTTCTTCCAAAGCACTCTCTTCTTTACGAGTACTTCACCGTGTACAACGAGCTGACGAAGGTGAAGTACGTGACCGAGGGCATGCGCAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCGATCGTGGACCTGCTGTTCAAGACCAACCGCAAGGTGACGGTGAAGCAGCTGAAAGAGGACTACTTCAAGAAGATCGAGTGCTTCGACAGCGTGGAGATCTCGGGCGTGGAGGACCGCTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACGCTGTTCGAGGACCGCGAGATGATCGAGGAGCGCCTGAAGACGTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGTCGCCGCTACACCGGCTGGGGCCGCCTGAGCCGCAAGCTGATCAACGGCATCCGCGACAAGCAGTCCGGCAAGACCATCCTGGACTTCCTGAAGAGCGACGGCTTCGCGAACCGCAACTTCATGCAGCTGATCCACGACGACTCGCTGACCTTCAAAGAGGACATCCAGAAGGCCCAGGTGTCGGGCCAGGGCGACTCCCTGCACGAGCACATCGCCAACCTGGCGGGCTCCCCCGCGATCAAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGCCACAAGCCGGAGAACATCGTGATCGAGATGGCCCGCGAGAACCAGACCACGCAGAAGGGCCAGAAGAACAGCCGCGAGCGCATGAAGCGCATCGAGGAAGGCATCAAGGAGCTGGGCTCGCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTACTACCTGCAGAACGGCCGCGACATGTACGTGGACCAGGAGCTGGACATCAACCGCCTGTCCGACTACGACGTGGACCACATCGTGCCCCAGAGCTTCCTGAAGGACGACTCGATCGACAACAAGGTGCTGACCCGCAGCGACAAGAACCGCGGCAAGAGCGACAACGTGCCGTCGGAGGAAGTGGTGAAGAAGATGAAGAACTACTGGCGCCAGCTGCTGAACGCCAAGCTGATCACGCAGCGCAAGTTCGACAACCTGACCAAGGCCGAGCGCGGTGGCCTGTCGGAGCTGGACAAGGCGGGCTTCATCAAGCGCCAGCTGGTGGAGACCCGCCAGATCACGAAGCACGTGGCGCAGATCCTGGACTCCCGCATGAACACGAAGTACGACGAGAACGACAAGCTGATCCGCGAGGTGAAGGTGATCACCCTGAAGTCCAAGCTGGTCAGCGACTTCCGCAAGGACTTCCAGTTCTACAAGGTGCGCGAGATCAACAACTACCACCACGCCCACGACGCGTACCTGAACGCCGTGGTGGGCACCGCGCTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGCAAGATGATCGCCAAGTCGGAGCAGGAGATCGGCAAGGCCACCGCGAAGTACTTCTTCTACTCCAACATCATGAACTTCTTCAAGACCGAGATCACGCTGGCCAACGGCGAGATCCGCAAGCGCCCGCTGATCGAGACCAACGGCGAGACGGGCGAGATCGTGTGGGACAAGGGCCGCGACTTCGCGACCGTGCGCAAGGTGCTGAGCATGCCCCAGGTGAACATCGTGAAGAAGACCGAGGTGCAGACGGGCGGCTTCTCCAAGGAGAGCATCCTGCCGAAGCGCAACTCGGACAAGCTGATCGCCCGCAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACTCCCCGACCGTGGCCTACAGCGTGCTGGTGGTGGCGAAGGTGGAGAAGGGCAAGTCCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGCAGCTCGTTCGAGAAGAACCCCATCGACTTCCTGGAGGCCAAGGGCTACAAAGAGGTGAAGAAGGACCTGATCATCAAGCTGCCGAAGTACTCGCTGTTCGAGCTGGAGAACGGCCGCAAGCGCATGCTGGCCTCCGCGGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCCCAGCAAGTACGTGAACTTCCTGTACCTGGCGTCCCACTACGAGAAGCTGAAGGGCTCGCCGGAGGACAACGAGCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCTCGGAGTTCTCCAAGCGCGTGATCCTGGCCGACGCGAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCGCGACAAGCCCATCCGCGAGCAGGCGGAGAACATCATCCACCTGTTCACCCTGACGAACCTGGGCGCCCCGGCCGCGTTCAAGTACTTCGACACCACGATCGACCGCAAGCGCTACACCTCCACGAAAGAGGTGCTGGACGCGACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGACGCGCATCGACCTGAGCCAGCTGGGCGGCGACTCCCGCGCGGACCCGAAGAAGAAGCGCAAGGTGTAAGAATTAATTCGGATCGATCCATTGGTGACCAGCTCGAATTTCCCCGATCGTTCAAACATTTGGCAATAAAGTTTCTTAAGATTGAATCCTGTTGCCGGTCTTGCGATGATTATCATATAATTTCTGTTGAATTACGTTAAGCATGTAATAATTAACATGTAATGCATGACGTTATTTATGAGATGGGTTTTTATGATTAGAGTCCCGCAATTATACATTTAATACGCGATAGAAAACAAAATATAGCGCGCAAACTAGGATAAATTATCGCGCGCGGTGTCATCTATGTTACTAGATCGGGGGTACCCGGGGATCCTCTAGAGTCGACCTGCAGGCATGCAAGCTTGGCACTGGCCGTCGTTTTACAACGTCGTGACTGGGAAAACCCTGGCGTTACCCAACTTAATCGCCTTGCAGCACATCCCCCTTTCGCCAGCTGGCGTAATAGCGAAGAGGCCCGCACCGATCGCCCTTCCCAACAGTTGCGCAGCCTGAATGGCGAATGCTAGAGCAGCTTGAGCTTGGATCAGATTGTCGTTTCCCGCCTTCAGTTTAAACTATCAGTGTTTGACAGGATATATTGGCGGGTAAACCTAAGAGAAAAGAGCGTTTATTAGAATAACGGATATTTAAAAGGGCGTGAAAAGGTTTATCCGTTCGTCCATTTGTATGTGCATGCCAACCACAGGGTTCCCCTCGGGATCAAAGTACTTTGATCCAACCCCTCCGCTGCTATAGTGCAGTCGGCTTCTGACGTTCAGTGCAGCCGTCTTCTGAAAACGACATGTCGCACAAGTCCTAAGTTACGCGACAGGCTGCCGCCCTGCCCTTTTCCTGGCGTTTTCTTGTCGCGTGTTTTAGTCGCATAAAGTAGAATACTTGCGACTAGAACCGGAGACATTACGCCATGAACAAGAGCGCCGCCGCTGGCCTGCTGGGCTATGCCCGCGTCAGCACCGACGACCAGGACTTGACCAACCAACGGGCCGAACTGCACGCGGCCGGCTGCACCAAGCTGTTTTCCGAGAAGATCACCGGCACCAGGCGCGACCGCCCGGAGCTGGCCAGGATGCTTGACCACCTACGCCCTGGCGACGTTGTGACAGTGACCAGGCTAGACCGCCTGGCCCGCAGCACCCGCGACCTACTGGACATTGCCGAGCGCATCCAGGAGGCCGGCGCGGGCCTGCGTAGCCTGGCAGAGCCGTGGGCCGACACCACCACGCCGGCCGGCCGCATGGTGTTGACCGTGTTCGCCGGCATTGCCGAGTTCGAGCGTTCCCTAATCATCGACCGCACCCGGAGCGGGCGCGAGGCCGCCAAGGCCCGAGGCGTGAAGTTTGGCCCCCGCCCTACCCTCACCCCGGCACAGATCGCGCACGCCCGCGAGCTGATCGACCAGGAAGGCCGCACCGTGAAAGAGGCGGCTGCACTGCTTGGCGTGCATCGCTCGACCCTGTACCGCGCACTTGAGCGCAGCGAGGAAGTGACGCCCACCGAGGCCAGGCGGCGCGGTGCCTTCCGTGAGGACGCATTGACCGAGGCCGACGCCCTGGCGGCCGCCGAGAATGAACGCCAAGAGGAACAAGCATGAAACCGCACCAGGACGGCCAGGACGAACCGTTTTTCATTACCGAAGAGATCGAGGCGGAGATGATCGCGGCCGGGTACGTGTTCGAGCCGCCCGCGCACGTCTCAACCGTGCGGCTGCATGAAATCCTGGCCGGTTTGTCTGATGCCAAGCTGGCGGCCTGGCCGGCCAGCTTGGCCGCTGAAGAAACCGAGCGCCGCCGTCTAAAAAGGTGATGTGTATTTGAGTAAAACAGCTTGCGTCATGCGGTCGCTGCGTATATGATGCGATGAGTAAATAAACAAATACGCAAGGGGAACGCATGAAGGTTATCGCTGTACTTAACCAGAAAGGCGGGTCAGGCAAGACGACCATCGCAACCCATCTAGCCCGCGCCCTGCAACTCGCCGGGGCCGATGTTCTGTTAGTCGATTCCGATCCCCAGGGCAGTGCCCGCGATTGGGCGGCCGTGCGGGAAGATCAACCGCTAACCGTTGTCGGCATCGACCGCCCGACGATTGACCGCGACGTGAAGGCCATCGGCCGGCGCGACTTCGTAGTGATCGACGGAGCGCCCCAGGCGGCGGACTTGGCTGTGTCCGCGATCAAGGCAGCCGACTTCGTGCTGATTCCGGTGCAGCCAAGCCCTTACGACATATGGGCCACCGCCGACCTGGTGGAGCTGGTTAAGCAGCGCATTGAGGTCACGGATGGAAGGCTACAAGCGGCCTTTGTCGTGTCGCGGGCGATCAAAGGCACGCGCATCGGCGGTGAGGTTGCCGAGGCGCTGGCCGGGTACGAGCTGCCCATTCTTGAGTCCCGTATCACGCAGCGCGTGAGCTACCCAGGCACTGCCGCCGCCGGCACAACCGTTCTTGAATCAGAACCCGAGGGCGACGCTGCCCGCGAGGTCCAGGCGCTGGCCGCTGAAATTAAATCAAAACTCATTTGAGTTAATGAGGTAAAGAGAAAATGAGCAAAAGCACAAACACGCTAAGTGCCGGCCGTCCGAGCGCACGCAGCAGCAAGGCTGCAACGTTGGCCAGCCTGGCAGACACGCCAGCCATGAAGCGGGTCAACTTTCAGTTGCCGGCGGAGGATCACACCAAGCTGAAGATGTACGCGGTACGCCAAGGCAAGACCATTACCGAGCTGCTATCTGAATACATCGCGCAGCTACCAGAGTAAATGAGCAAATGAATAAATGAGTAGATGAATTTTAGCGGCTAAAGGAGGCGGCATGGAAAATCAAGAACAACCAGGCACCGACGCCGTGGAATGCCCCATGTGTGGAGGAACGGGCGGTTGGCCAGGCGTAAGCGGCTGGGTTGTCTGCCGGCCCTGCAATGGCACTGGAACCCCCAAGCCCGAGGAATCGGCGTGACGGTCGCAAACCATCCGGCCCGGTACAAATCGGCGCGGCGCTGGGTGATGACCTGGTGGAGAAGTTGAAGGCCGCGCAGGCCGCCCAGCGGCAACGCATCGAGGCAGAAGCACGCCCCGGTGAATCGTGGCAAGCGGCCGCTGATCGAATCCGCAAAGAATCCCGGCAACCGCCGGCAGCCGGTGCGCCGTCGATTAGGAAGCCGCCCAAGGGCGACGAGCAACCAGATTTTTTCGTTCCGATGCTCTATGACGTGGGCACCCGCGATAGTCGCAGCATCATGGACGTGGCCGTTTTCCGTCTGTCGAAGCGTGACCGACGAGCTGGCGAGGTGATCCGCTACGAGCTTCCAGACGGGCACGTAGAGGTTTCCGCAGGGCCGGCCGGCATGGCCAGTGTGTGGGATTACGACCTGGTACTGATGGCGGTTTCCCATCTAACCGAATCCATGAACCGATACCGGGAAGGGAAGGGAGACAAGCCCGGCCGCGTGTTCCGTCCACACGTTGCGGACGTACTCAAGTTCTGCCGGCGAGCCGATGGCGGAAAGCAGAAAGACGACCTGGTAGAAACCTGCATTCGGTTAAACACCACGCACGTTGCCATGCAGCGTACGAAGAAGGCCAAGAACGGCCGCCTGGTGACGGTATCCGAGGGTGAAGCCTTGATTAGCCGCTACAAGATCGTAAAGAGCGAAACCGGGCGGCCGGAGTACATCGAGATCGAGCTAGCTGATTGGATGTACCGCGAGATCACAGAAGGCAAGAACCCGGACGTGCTGACGGTTCACCCCGATTACTTTTTGATCGATCCCGGCATCGGCCGTTTTCTCTACCGCCTGGCACGCCGCGCCGCAGGCAAGGCAGAAGCCAGATGGTTGTTCAAGACGATCTACGAACGCAGTGGCAGCGCCGGAGAGTTCAAGAAGTTCTGTTTCACCGTGCGCAAGCTGATCGGGTCAAATGACCTGCCGGAGTACGATTTGAAGGAGGAGGCGGGGCAGGCTGGCCCGATCCTAGTCATGCGCTACCGCAACCTGATCGAGGGCGAAGCATCCGCCGGTTCCTAATGTACGGAGCAGATGCTAGGGCAAATTGCCCTAGCAGGGGAAAAAGGTCGAAAAGGTCTCTTTCCTGTGGATAGCACGTACATTGGGAACCCAAAGCCGTACATTGGGAACCGGAACCCGTACATTGGGAACCCAAAGCCGTACATTGGGAACCGGTCACACATGTAAGTGACTGATATAAAAGAGAAAAAAGGCGATTTTTCCGCCTAAAACTCTTTAAAACTTATTAAAACTCTTAAAACCCGCCTGGCCTGTGCATAACTGTCTGGCCAGCGCACAGCCGAAGAGCTGCAAAAAGCGCCTACCCTTCGGTCGCTGCGCTCCCTACGCCCCGCCGCTTCGCGTCGGCCTATCGCGGCCGCTGGCCGCTCAAAAATGGCTGGCCTACGGCCAGGCAATCTACCAGGGCGCGGACAAGCCGCGCCGTCGCCACTCGACCGCCGGCGCCCACATCAAGGCACCCTGCCTCGCGCGTTTCGGTGATGACGGTGAAAACCTCTGACACATGCAGCTCCCGGAGACGGTCACAGCTTGTCTGTAAGCGGATGCCGGGAGCAGACAAGCCCGTCAGGGCGCGTCAGCGGGTGTTGGCGGGTGTCGGGGCGCAGCCATGACCCAGTCACGTAGCGATAGCGGAGTGTATACTGGCTTAACTATGCGGCATCAGAGCAGATTGTACTGAGAGTGCACCATATGCGGTGTGAAATACCGCACAGATGCGTAAGGAGAAAATACCGCATCAGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGCATTCTAGGTACTAAAACAATTCATCCAGTAAAATATAATATTTTATTTTCTCCCAATCAGGCTTGATCCCCAGTAAGTCAAAAAATAGCTCGACATACTGTTCTTCCCCGATATCCTCCCTGATCGACCGGACGCAGAAGGCAATGTCATACCACTTGTCCGCCCTGCCGCTTCTCCCAAGATCAATAAAGCCACTTACTTTGCCATCTTTCACAAAGATGTTGCTGTCTCCCAGGTCGCCGTGGGAAAAGACAAGTTCCTCTTCGGGCTTTTCCGTCTTTAAAAAATCATACAGCTCGCGCGGATCTTTAAATGGAGTGTCTTCTTCCCAGTTTTCGCAATCCACATCGGCCAGATCGTTATTCAGTAAGTAATCCAATTCGGCTAAGCGGCTGTCTAAGCTATTCGTATAGGGACAATCCGATATGTCGATGGAGTGAAAGAGCCTGATGCACTCCGCATACAGCTCGATAATCTTTTCAGGGCTTTGTTCATCTTCATACTCTTCCGAGCAAAGGACGCCATCGGCCTCACTCATGAGCAGATTGCTCCAGCCATCATGCCGTTCAAAGTGCAGGACCTTTGGAACAGGCAGCTTTCCTTCCAGCCATAGCATCATGTCCTTTTCCCGTTCCACATCATAGGTGGTCCCTTTATACCGGCTGTCCGTCATTTTTAAATATAGGTTTTCATTTTCTCCCACCAGCTTATATACCTTAGCAGGAGACATTCCTTCCGTATCTTTTACGCAGCGGTATTTTTCGATCAGTTTTTTCAATTCCGGTGATATTCTCATTTTAGCCATTTATTATTTCCTTCCTCTTTTCTACAGTATTTAAAGATACCCCAAGAAGCTAATTATAACAAGACGAACTCCAATTCACTGTTCCTTGCATTCTAAAACCTTAAATACCAGAAAACAGCTTTTTCAAAGTTGTTTTCAAAGTTGGCGTATAACATAGTATCGACGGAGCCGATTTTGAAACCGCGGTGATCACAGGCAGCAACGCTCTGTCATCGTTACAATCAACATGCTACCCTCCGCGAGATCATCCGTGTTTCAAACCCGGCAGCTTAGTTGCCGTTCTTCCGAATAGCATCGGTAACATGAGCAAAGTCTGCCGCCTTACAACGGCTCTCCCGCTGACGCCGTCCCGGACTGATGGGCTGCCTGTATCGAGTGGTGATTTTGTGCCGAGCTGCCGGTCGGGGAGCTGTTGGCTGGCTGGTGGCAGGATATATTGTGGTGTAAACAAATTGACGCTTAGACAACTTAATAACACATTGCGGACGTTTTTAATGTACTGAATTAACGCCGAATTAATTCGGGGGATCTGGATTTTAGTACTGGATTTTGGTTTTAGGAATTAGAAATTTTATTGATAGAAGTATTTTACAAATACAAATACATACTAAGGGTTTCTTATATGCTCAACACATGAGCGAAACCCTATAGGAACCCTAATTCCCTTATCTGGGAACTACTCACACATTATTATGGAGAAACTCGAGCTTGTCGATCGACAGATCCGGTCGGCATCTACTCTATTTCTTTGCCCTCGGACGAGTGCTGGGGCGTCGGTTTCCACTATCGGCGAGTACTTCTACACAGCCATCGGTCCAGACGGCCGCGCTTCTGCGGGCGATTTGTGTACGCCCGACAGTCCCGGCTCCGGATCGGACGATTGCGTCGCATCGACCCTGCGCCCAAGCTGCATCATCGAAATTGCCGTCAACCAAGCTCTGATAGAGTTGGTCAAGACCAATGCGGAGCATATACGCCCGGAGTCGTGGCGATCCTGCAAGCTCCGGATGCCTCCGCTCGAAGTAGCGCGTCTGCTGCTCCATACAAGCCAACCACGGCCTCCAGAAGAAGATGTTGGCGACCTCGTATTGGGAATCCCCGAACATCGCCTCGCTCCAGTCAATGACCGCTGTTATGCGGCCATTGTCCGTCAGGACATTGTTGGAGCCGAAATCCGCGTGCACGAGGTGCCGGACTTCGGGGCAGTCCTCGGCCCAAAGCATCAGCTCATCGAGAGCCTGCGCGACGGACGCACTGACGGTGTCGTCCATCACAGTTTGCCAGTGATACACATGGGGATCAGCAATCGCGCATATGAAATCACGCCATGTAGTGTATTGACCGATTCCTTGCGGTCCGAATGGGCCGAACCCGCTCGTCTGGCTAAGATCGGCCGCAGCGATCGCATCCATAGCCTCCGCGACCGGTTGTAGAACAGCGGGCAGTTCGGTTTCAGGCAGGTCTTGCAACGTGACACCCTGTGCACGGCGGGAGATGCAATAGGTCAGGCTCTCGCTAAACTCCCCAATGTCAAGCACTTCCGGAATCGGGAGCGCGGCCGATGCAAAGTGCCGATAAACATAACGATCTTTGTAGAAACCATCGGCGCAGCTATTTACCCGCAGGACATATCCACGCCCTCCTACATCGAAGCTGAAAGCACGAGATTCTTCGCCCTCCGAGAGCTGCATCAGGTCGGAGACGCTGTCGAACTTTTCGATCAGAAACTTCTCGACAGACGTCGCGGTGAGTTCAGGCTTTTTCATATCTCATTGCCCCCCGGGATCTGCGAAAGCTCGAGAGAGATAGATTTGTAGAGAGAGACTGGTGATTTCAGCGTGTCCTCTCCAAATGAAATGAACTTCCTTATATAGAGGAAGGTCTTGCGAAGGATAGTGGGATTGTGCGTCATCCCTTACGTCAGTGGAGATATCACATCAATCCACTTGCTTTGAAGACGTGGTTGGAACGTCTTCTTTTTCCACGATGCTCCTCGTGGGTGGGGGTCCATCTTTGGGACCACTGTCGGCAGAGGCATCTTGAACGATAGCCTTTCCTTTATCGCAATGATGGCATTTGTAGGTGCCACCTTCCTTTTCTACTGTCCTTTTGATGAAGTGACAGATAGCTGGGCAATGGAATCCGAGGAGGTTTCCCGATATTACCCTTTGTTGAAAAGTCTCAATAGCCCTTTGGTCTTCTGAGACTGTATCTTTGATATTCTTGGAGTAGACGAGAGTGTCGTGCTCCACCATGTTATCACATCAATCCACTTGCTTTGAAGACGTGGTTGGAACGTCTTCTTTTTCCACGATGCTCCTCGTGGGTGGGGGTCCATCTTTGGGACCACTGTCGGCAGAGGCATCTTGAACGATAGCCTTTCCTTTATCGCAATGATGGCATTTGTAGGTGCCACCTTCCTTTTCTACTGTCCTTTTGATGAAGTGACAGATAGCTGGGCAATGGAATCCGAGGAGGTTTCCCGATATTACCCTTTGTTGAAAAGTCTCAATAGCCCTTTGGTCTTCTGAGACTGTATCTTTGATATTCTTGGAGTAGACGAGAGTGTCGTGCTCCACCATGTTGGCAAGCTGCTCTAGCCAATACGCAAACCGCCTCTCCCCGCGCGTTGGCCGATTCATTAATGCAGCTGGCACGACAGGTTTCCCGACTGGAAAGCGGGCAGTGAGCGCAACGCAATTAATGTGAGTTAGCTCACTCATTAGGCACCCCAGGCTTTACACTTTATGCTTCCGGCTCGTATGTTGTGTGGAATTGTGAGCGGATAACAATTTCACACAGGAAACAGCTATGACCATGATTACG

**Fig. S16.** The targeted exogenous mutant *Ble* gene placed in a plasmid containing the Cas9/intron-sgRNA gene

CGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCTAAATTGTAAGCGTTAATATTTTGTTAAAATTCGCGTTAAATTTTTGTTAAATCAGCTCATTTTTTAACCAATAGGCCGAAATCGGCAAAATCCCTTATAAATCAAAAGAATAGACCGAGATAGGGTTGAGTGTTGTTCCAGTTTGGAACAAGAGTCCACTATTAAAGAACGTGGACTCCAACGTCAAAGGGCGAAAAACCGTCTATCAGGGCGATGGCCCACTACGTGAACCATCACCCTAATCAAGTTTTTTGGGGTCGAGGTGCCGTAAAGCACTAAATCGGAACCCTAAAGGGAGCCCCCGATTTAGAGCTTGACGGGGAAAGCCGGCGAACGTGGCGAGAAAGGAAGGGAAGAAAGCGAAAGGAGCGGGCGCTAGGGCGCTGGCAAGTGTAGCGGTCACGCTGCGCGTAACCACCACACCCGCCGCGCTTAATGCGCCGCTACAGGGCGCGTCCCATTCGCCATTCAGGCTGCGCAACTGTTGGGAAGGGCGATCGGTGCGGGCCTCTTCGCTATTACGCCAGCTGGCGAAAGGGGGATGTGCTGCAAGGCGATTAAGTTGGGTAACGCCAGGGTTTTCCCAGTCACGACGTTGTAAAACGACGGCCAGTGAATTGTAATACGACTCACTATAGGGCGAATTGGAGCTCCACCGCGGTGGCGGCCGCGATCCCACACACCTGCCCGTCTGCCTGACAGGAAGTGAACGCATGTCGAGGGAGGCCTCACCAATCGTCACACGAGCCCTCGTCAGAAACACGTCTCCGCCACGCTCTCCCTCTCACGGCCGACCCCGCAGCCCTTTTGCCCTTTCCTAGGCCACCGACAGGACCCAGGCGCTCTCAGCATGCCTCAACAACCCGTACTCGTGCCAGCGGTGCCCTTGTGCTGGTGATCGCTTGGAAGCGCATGCGAAGACGAAGGGGCGGAGCAGGCGGCCTGGCTGTTCGAAGGGCTCGCCGCCAGTTCGGGTGCCTTTCTCCACGCGCGCCTCCACACCTACCGATGCGTGAAGGCAGGCAAATGCTCATGTTTGCCCGAACTCGGAGTCCTTAAAAAGCCGCTTCTTGTCGTCGTTCCGAGACATGTTAGCAGATCGCAGTGCCACCTTTCCTGACGCGCTCGGCCCCATATTCGGACGCAATTGTCATTTGTAGCACAATTGGAGCAAATCTGGCGAGGCAGTAGGCTTTTAAGTTGCAAGGCGAGAGAGCAAAGTGGGACGCGGCGTGATTATTGGTATTTACGCGACGGCCCGGCGCGTTAGCGGCCCTTCCCCCAGGCCAGGGACGATTATGTATCAATATTGTTGCGTTCGGGCACTCGTGCGAGGGCTCCTGCGGGCTGGGGAGGGGGATCTGGGAATTGGAGGTACGACCGAGATGGCTTGCTCGGGGGGAGGTTTCCTCGCCGAGCAAGCCAGGGTTAGGTGTTGCGCTCTTGACTCGTTGTGCATTCTAGGACCCCACTGCTACTCACAACAAGCCCATATGAGCGCTTCAAGGTGCACATGGAGGTATGGCCAAGCTGACCAGCGCCGTTCCGGTGCTCACCGCGCGCGACGTCGCCGGAGCGGTCGAGTTCTGGACCGACCGGCTCGGGTTCTCCCGGGACTTCGTGGAGGACGACTTCGCCGGTGTGGTCCGGGACGACGTGACCCTGTTCATCAGCGCGGTCCAGGACCAGGTGAGTCGACGAGCAAGCCCGGCGGATCAGGCAGCGTGCTTGCAGATTTGACTTGCAACGCCCGCATTGTGTCGACGAAGGCTTTTGGCTCCTCTGTCGCTGTCTCAAGCAGCATCTAACCCTGCGTCGCCGTTTCCATTTGCAGGACCAGGTGGTGCCGGACAACACCCTGGCCTGGGTGTGGGTGCGCGGCCTGGACGAGCTGTACGCCGAGTGGTCGGAGGTCGTGTCCACGAACTTCCGGGACGCCTCCGGGCCGGCCATGACCGAGATCGGCGAGCAGCCGTGGGGGCGGGAGTTCGCCCTGCGCGACCCGGCCGGCAACTGCGTGCACTTCGTGGCCGAGGAGCAGGACTGAGAATTCTGGCAGCAGCTGGACCGCCTGTACCATGGAGAAGAGCTTTACTTGCCGGGATGGCCGATTTCGCTGATTGATACGGGATCGGAGCTCGGAGGCTTTCGCGCTAGGGGCTAGGCGAAGGGCAGTGGTGACCAGGGTCGGTGTGGGGTCGGCCCACGGTCAATTAGCCACAGGAGGATCAGGGGGAGGTAGGCACGTCGACTTGGTTTGCGACCCCGCAGTTTTGGCGGACGTGCTGTTGTAGATGTTAGCGTGTGCGTGAGCCAGTGGCCAACGTGCCACACCCATTGAGAAGACCAACCAACTTACTGGCAATATCTGCCAATGCCATACTGCATGTAATGGCCAGGCCATGTGAGAGTTTGCCGTGCCTGCGCGCGCCCCGGGGGCGCAGTTTAGCTGACCAGCCGTGGGATGATGCACGCATTTGCAAGGACAGGGTAATCACAGCAGCAACATGGTGGGCTTAGGACAGCTGTGGGTCAGTGGACGGACGGCAGGGGAGGGACGGCGCAGCTCGGGAGACAGGGGGAGACAGCGTGACTGTGCAATCACTAGTGGATCCCACACACCTGCCCGTCTGCCTGACAGGAAGTGAACGCATGTCGAGGGAGGCCTCACCAATCGTCACACGAGCCCTCGTCAGAAACACGTCTCCGCCACGCTCTCCCTCTCACGGCCGACCCCGCAGCCCTTTTGCCCTTTCCTAGGCCACCGACAGGACCCAGGCGCTCTCAGCATGCCTCAACAACCCGTACTCGTGCCAGCGGTGCCCTTGTGCTGGTGATCGCTTGGAAGCGCATGCGAAGACGAAGGGGCGGAGCAGGCGGCCTGGCTGTTCGAAGGGCTCGCCGCCAGTTCGGGTGCCTTTCTCCACGCGCGCCTCCACACCTACCGATGCGTGAAGGCAGGCAAATGCTCATGTTTGCCCGAACTCGGAGTCCTTAAAAAGCCGCTTCTTGTCGTCGTTCCGAGACATGTTAGCAGATCGCAGTGCCACCTTTCCTGACGCGCTCGGCCCCATATTCGGACGCAATTGTCATTTGTAGCACAATTGGAGCAAATCTGGCGAGGCAGTAGGCTTTTAAGTTGCAAGGCGAGAGAGCAAAGTGGGACGCGGCGTGATTATTGGTATTTACGCGACGGCCCGGCGCGTTAGCGGCCCTTCCCCCAGGCCAGGGACGATTATGTATCAATATTGTTGCGTTCGGGCACTCGTGCGAGGGCTCCTGCGGGCTGGGGAGGGGGATCTGGGAATTGGAGGTACGACCGAGATGGCTTGCTCGGGGGGAGGTTTCCTCGCCGAGCAAGCCAGGGTTAGGTGTTGCGCTCTTGACTCGTTGTGCATTCTAGGACCCCACTGCTACTCACAACAAGCCCATATGGACAAGAAGTACAGCATCGGCCTGGACATCGGCACGAACTCGGTGGGCTGGGCGGTGATCACGGACGAGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGCCACTCGATCAAGAAGAACCTGATCGGCGCCCTGCTGTTCGACTCCGGCGAGACCGCCGAGGCGACGCGCCTGAAGCGCACCGCGCGTCGCCGCTACACGCGTCGCAAGAACCGCATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACTCGTTCTTCCACCGCCTGGAGGAGTCCTTCCTGGTGGAGGAAGACAAGAAGCACGAGCGCCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCCGACGATCTACCACCTGCGCAAGAAGCTGGTGGACAGCACCGACAAGGCGGACCTGCGCCTGATCTACCTGGCCCTGGCGCACATGATCAAGTTCCGCGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACTCGGACGTGGACAAGCTGTTCATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCGATCAACGCCTCCGGCGTGGACGCCAAGGCGATCCTGAGCGCGCGCCTGTCCAAGAGCCGTCGCCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGTTCGGCAACCTGATCGCGCTGTCGCTGGGCCTGACGCCGAACTTCAAGTCCAACTTCGACCTGGCCGAGGACGCGAAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCGGACCTGTTCCTGGCCGCGAAGAACCTGTCGGACGCCATCCTGCTGTCCGACATCCTGCGCGTGAACACCGAGATCACGAAGGCCCCCCTGTCGGCGTCCATGATCAAGCGCTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCGCTGGTGCGCCAGCAGCTGCCGGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCGTCGCAAGAGGAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACGGAGGAGCTGCTGGTGAAGCTGAACCGCGAGGACCTGCTGCGCAAGCAGCGCACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGCACGCCATCCTGCGTCGCCAAGAGGACTTCTACCCGTTCCTGAAGGACAACCGCGAGAAGATCGAGAAGATCCTGACGTTCCGCATCCCCTACTACGTGGGCCCACTTGCTAGAGGAAACTCTCGTTTCGCTTGGATGACCAGAAAGTCTGAGGAGACCATCACCCCTTGGAACTTCGAGGAGGTGAGTCGACGAGGCGCTTCAAGGTGCACATGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTTTTTGCAGCGTGCTTGCAGATTTGACTTGCAACGCCCGCATTGTGTCGACGAAGGCTTTTGGCTCCTCTGTCGCTGTCTCAAGCAGCATCTAACCCTGCGTCGCCGTTTCCATTTGCAGGTTGTTGATAAGGGAGCTTCTGCTCAGTCTTTCATCGAGAGAATGACCAACTTCGATAAGAACCTTCCAAACGAGAAGGTTCTTCCAAAGCACTCTCTTCTTTACGAGTACTTCACCGTGTACAACGAGCTGACGAAGGTGAAGTACGTGACCGAGGGCATGCGCAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCGATCGTGGACCTGCTGTTCAAGACCAACCGCAAGGTGACGGTGAAGCAGCTGAAAGAGGACTACTTCAAGAAGATCGAGTGCTTCGACAGCGTGGAGATCTCGGGCGTGGAGGACCGCTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACGCTGTTCGAGGACCGCGAGATGATCGAGGAGCGCCTGAAGACGTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGTCGCCGCTACACCGGCTGGGGCCGCCTGAGCCGCAAGCTGATCAACGGCATCCGCGACAAGCAGTCCGGCAAGACCATCCTGGACTTCCTGAAGAGCGACGGCTTCGCGAACCGCAACTTCATGCAGCTGATCCACGACGACTCGCTGACCTTCAAAGAGGACATCCAGAAGGCCCAGGTGTCGGGCCAGGGCGACTCCCTGCACGAGCACATCGCCAACCTGGCGGGCTCCCCCGCGATCAAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGCCACAAGCCGGAGAACATCGTGATCGAGATGGCCCGCGAGAACCAGACCACGCAGAAGGGCCAGAAGAACAGCCGCGAGCGCATGAAGCGCATCGAGGAAGGCATCAAGGAGCTGGGCTCGCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTACTACCTGCAGAACGGCCGCGACATGTACGTGGACCAGGAGCTGGACATCAACCGCCTGTCCGACTACGACGTGGACCACATCGTGCCCCAGAGCTTCCTGAAGGACGACTCGATCGACAACAAGGTGCTGACCCGCAGCGACAAGAACCGCGGCAAGAGCGACAACGTGCCGTCGGAGGAAGTGGTGAAGAAGATGAAGAACTACTGGCGCCAGCTGCTGAACGCCAAGCTGATCACGCAGCGCAAGTTCGACAACCTGACCAAGGCCGAGCGCGGTGGCCTGTCGGAGCTGGACAAGGCGGGCTTCATCAAGCGCCAGCTGGTGGAGACCCGCCAGATCACGAAGCACGTGGCGCAGATCCTGGACTCCCGCATGAACACGAAGTACGACGAGAACGACAAGCTGATCCGCGAGGTGAAGGTGATCACCCTGAAGTCCAAGCTGGTCAGCGACTTCCGCAAGGACTTCCAGTTCTACAAGGTGCGCGAGATCAACAACTACCACCACGCCCACGACGCGTACCTGAACGCCGTGGTGGGCACCGCGCTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGCAAGATGATCGCCAAGTCGGAGCAGGAGATCGGCAAGGCCACCGCGAAGTACTTCTTCTACTCCAACATCATGAACTTCTTCAAGACCGAGATCACGCTGGCCAACGGCGAGATCCGCAAGCGCCCGCTGATCGAGACCAACGGCGAGACGGGCGAGATCGTGTGGGACAAGGGCCGCGACTTCGCGACCGTGCGCAAGGTGCTGAGCATGCCCCAGGTGAACATCGTGAAGAAGACCGAGGTGCAGACGGGCGGCTTCTCCAAGGAGAGCATCCTGCCGAAGCGCAACTCGGACAAGCTGATCGCCCGCAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACTCCCCGACCGTGGCCTACAGCGTGCTGGTGGTGGCGAAGGTGGAGAAGGGCAAGTCCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGCAGCTCGTTCGAGAAGAACCCCATCGACTTCCTGGAGGCCAAGGGCTACAAAGAGGTGAAGAAGGACCTGATCATCAAGCTGCCGAAGTACTCGCTGTTCGAGCTGGAGAACGGCCGCAAGCGCATGCTGGCCTCCGCGGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCCCAGCAAGTACGTGAACTTCCTGTACCTGGCGTCCCACTACGAGAAGCTGAAGGGCTCGCCGGAGGACAACGAGCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCTCGGAGTTCTCCAAGCGCGTGATCCTGGCCGACGCGAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCGCGACAAGCCCATCCGCGAGCAGGCGGAGAACATCATCCACCTGTTCACCCTGACGAACCTGGGCGCCCCGGCCGCGTTCAAGTACTTCGACACCACGATCGACCGCAAGCGCTACACCTCCACGAAAGAGGTGCTGGACGCGACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGACGCGCATCGACCTGAGCCAGCTGGGCGGCGACTCCCGCGCGGACCCGAAGAAGAAGCGCAAGGTGTAAGAATTCTGGCAGCAGCTGGACCGCCTGTACCATGGAGAAGAGCTTTACTTGCCGGGATGGCCGATTTCGCTGATTGATACGGGATCGGAGCTCGGAGGCTTTCGCGCTAGGGGCTAGGCGAAGGGCAGTGGTGACCAGGGTCGGTGTGGGGTCGGCCCACGGTCAATTAGCCACAGGAGGATCAGGGGGAGGTAGGCACGTCGACTTGGTTTGCGACCCCGCAGTTTTGGCGGACGTGCTGTTGTAGATGTTAGCGTGTGCGTGAGCCAGTGGCCAACGTGCCACACCCATTGAGAAGACCAACCAACTTACTGGCAATATCTGCCAATGCCATACTGCATGTAATGGCCAGGCCATGTGAGAGTTTGCCGTGCCTGCGCGCGCCCCGGGGGCGCAGTTTAGCTGACCAGCCGTGGGATGATGCACGCATTTGCAAGGACAGGGTAATCACAGCAGCAACATGGTGGGCTTAGGACAGCTGTGGGTCAGTGGACGGACGGCAGGGGAGGGACGGCGCAGCTCGGGAGACAGGGGGAGACAGCGTGACTGTGCAATCAAGCTGGCGCGCCGGTACCAAGCTTATCGATACCGTCGACCTCGACAGCTTTTGTTCCCTTTAGTGAGGGTTAATTTCGAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGA

**Fig. S17.** The complete DNA sequences of the mutant *Ble* gene containing a Cas9/intron-sgRNA target site identical to the target site in the *KU70* gene.

GGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCTAAATTGTAAGCGTTAATATTTTGTTAAAATTCGCGTTAAATTTTTGTTAAATCAGCTCATTTTTTAACCAATAGGCCGAAATCGGCAAAATCCCTTATAAATCAAAAGAATAGACCGAGATAGGGTTGAGTGTTGTTCCAGTTTGGAACAAGAGTCCACTATTAAAGAACGTGGACTCCAACGTCAAAGGGCGAAAAACCGTCTATCAGGGCGATGGCCCACTACGTGAACCATCACCCTAATCAAGTTTTTTGGGGTCGAGGTGCCGTAAAGCACTAAATCGGAACCCTAAAGGGAGCCCCCGATTTAGAGCTTGACGGGGAAAGCCGGCGAACGTGGCGAGAAAGGAAGGGAAGAAAGCGAAAGGAGCGGGCGCTAGGGCGCTGGCAAGTGTAGCGGTCACGCTGCGCGTAACCACCACACCCGCCGCGCTTAATGCGCCGCTACAGGGCGCGTCCCATTCGCCATTCAGGCTGCGCAACTGTTGGGAAGGGCGATCGGTGCGGGCCTCTTCGCTATTACGCCAGCTGGCGAAAGGGGGATGTGCTGCAAGGCGATTAAGTTGGGTAACGCCAGGGTTTTCCCAGTCACGACGTTGTAAAACGACGGCCAGTGAATTGTAATACGACTCACTATAGGGCGAATTGGAGCTCCACCGCGGTGGCGGCCGCTCTAGAACTAGTGGATCCCACACACCTGCCCGTCTGCCTGACAGGAAGTGAACGCATGTCGAGGGAGGCCTCACCAATCGTCACACGAGCCCTCGTCAGAAACACGTCTCCGCCACGCTCTCCCTCTCACGGCCGACCCCGCAGCCCTTTTGCCCTTTCCTAGGCCACCGACAGGACCCAGGCGCTCTCAGCATGCCTCAACAACCCGTACTCGTGCCAGCGGTGCCCTTGTGCTGGTGATCGCTTGGAAGCGCATGCGAAGACGAAGGGGCGGAGCAGGCGGCCTGGCTGTTCGAAGGGCTCGCCGCCAGTTCGGGTGCCTTTCTCCACGCGCGCCTCCACACCTACCGATGCGTGAAGGCAGGCAAATGCTCATGTTTGCCCGAACTCGGAGTCCTTAAAAAGCCGCTTCTTGTCGTCGTTCCGAGACATGTTAGCAGATCGCAGTGCCACCTTTCCTGACGCGCTCGGCCCCATATTCGGACGCAATTGTCATTTGTAGCACAATTGGAGCAAATCTGGCGAGGCAGTAGGCTTTTAAGTTGCAAGGCGAGAGAGCAAAGTGGGACGCGGCGTGATTATTGGTATTTACGCGACGGCCCGGCGCGTTAGCGGCCCTTCCCCCAGGCCAGGGACGATTATGTATCAATATTGTTGCGTTCGGGCACTCGTGCGAGGGCTCCTGCGGGCTGGGGAGGGGGATCTGGGAATTGGAGGTACGACCGAGATGGCTTGCTCGGGGGGAGGTTTCCTCGCCGAGCAAGCCAGGGTTAGGTGTTGCGCTCTTGACTCGTTGTGCATTCTAGGACCCCACTGCTACTCACAACAAGCCCATATGAGCAGCTGCGCTCCCGGGTGGAGGTATGGCCAAGCTGACCAGCGCCGTTCCGGTGCTCACCGCGCGCGACGTCGCCGGAGCGGTCGAGTTCTGGACCGACCGGCTCGGGTTCTCCCGGGACTTCGTGGAGGACGACTTCGCCGGTGTGGTCCGGGACGACGTGACCCTGTTCATCAGCGCGGTCCAGGACCAGGTGAGTCGACGAGCAAGCCCGGCGGATCAGGCAGCGTGCTTGCAGATTTGACTTGCAACGCCCGCATTGTGTCGACGAAGGCTTTTGGCTCCTCTGTCGCTGTCTCAAGCAGCATCTAACCCTGCGTCGCCGTTTCCATTTGCAGGACCAGGTGGTGCCGGACAACACCCTGGCCTGGGTGTGGGTGCGCGGCCTGGACGAGCTGTACGCCGAGTGGTCGGAGGTCGTGTCCACGAACTTCCGGGACGCCTCCGGGCCGGCCATGACCGAGATCGGCGAGCAGCCGTGGGGGCGGGAGTTCGCCCTGCGCGACCCGGCCGGCAACTGCGTGCACTTCGTGGCCGAGGAGCAGGACTGAGAATTCTGGCAGCAGCTGGACCGCCTGTACCATGGAGAAGAGCTTTACTTGCCGGGATGGCCGATTTCGCTGATTGATACGGGATCGGAGCTCGGAGGCTTTCGCGCTAGGGGCTAGGCGAAGGGCAGTGGTGACCAGGGTCGGTGTGGGGTCGGCCCACGGTCAATTAGCCACAGGAGGATCAGGGGGAGGTAGGCACGTCGACTTGGTTTGCGACCCCGCAGTTTTGGCGGACGTGCTGTTGTAGATGTTAGCGTGTGCGTGAGCCAGTGGCCAACGTGCCACACCCATTGAGAAGACCAACCAACTTACTGGCAATATCTGCCAATGCCATACTGCATGTAATGGCCAGGCCATGTGAGAGTTTGCCGTGCCTGCGCGCGCCCCGGGGGCGCAGTTTAGCTGACCAGCCGTGGGATGATGCACGCATTTGCAAGGACAGGGTAATCACAGCAGCAACATGGTGGGCTTAGGACAGCTGTGGGTCAGTGGACGGACGGCAGGGGAGGGACGGCGCAGCTCGGGAGACAGGGGGAGACAGCGTGACTGTGCAATCAAGCTTATCGATACCGTCGACCTCGAGGGGGGGCCCGGTACCCAGCTTTTGTTCCCTTTAGTGAGGGTTAATTTCGAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCC

**Fig. S18.** The complete DNA sequences of the Cas9/intron-sgRNA gene targeting the *KU70* gene.

CGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCTAAATTGTAAGCGTTAATATTTTGTTAAAATTCGCGTTAAATTTTTGTTAAATCAGCTCATTTTTTAACCAATAGGCCGAAATCGGCAAAATCCCTTATAAATCAAAAGAATAGACCGAGATAGGGTTGAGTGTTGTTCCAGTTTGGAACAAGAGTCCACTATTAAAGAACGTGGACTCCAACGTCAAAGGGCGAAAAACCGTCTATCAGGGCGATGGCCCACTACGTGAACCATCACCCTAATCAAGTTTTTTGGGGTCGAGGTGCCGTAAAGCACTAAATCGGAACCCTAAAGGGAGCCCCCGATTTAGAGCTTGACGGGGAAAGCCGGCGAACGTGGCGAGAAAGGAAGGGAAGAAAGCGAAAGGAGCGGGCGCTAGGGCGCTGGCAAGTGTAGCGGTCACGCTGCGCGTAACCACCACACCCGCCGCGCTTAATGCGCCGCTACAGGGCGCGTCCCATTCGCCATTCAGGCTGCGCAACTGTTGGGAAGGGCGATCGGTGCGGGCCTCTTCGCTATTACGCCAGCTGGCGAAAGGGGGATGTGCTGCAAGGCGATTAAGTTGGGTAACGCCAGGGTTTTCCCAGTCACGACGTTGTAAAACGACGGCCAGTGAATTGTAATACGACTCACTATAGGGCGAATTGGAGCTCCACCGCGGTGGCGGCCGCTCTAGAACTAGTGGATCCCACACACCTGCCCGTCTGCCTGACAGGAAGTGAACGCATGTCGAGGGAGGCCTCACCAATCGTCACACGAGCCCTCGTCAGAAACACGTCTCCGCCACGCTCTCCCTCTCACGGCCGACCCCGCAGCCCTTTTGCCCTTTCCTAGGCCACCGACAGGACCCAGGCGCTCTCAGCATGCCTCAACAACCCGTACTCGTGCCAGCGGTGCCCTTGTGCTGGTGATCGCTTGGAAGCGCATGCGAAGACGAAGGGGCGGAGCAGGCGGCCTGGCTGTTCGAAGGGCTCGCCGCCAGTTCGGGTGCCTTTCTCCACGCGCGCCTCCACACCTACCGATGCGTGAAGGCAGGCAAATGCTCATGTTTGCCCGAACTCGGAGTCCTTAAAAAGCCGCTTCTTGTCGTCGTTCCGAGACATGTTAGCAGATCGCAGTGCCACCTTTCCTGACGCGCTCGGCCCCATATTCGGACGCAATTGTCATTTGTAGCACAATTGGAGCAAATCTGGCGAGGCAGTAGGCTTTTAAGTTGCAAGGCGAGAGAGCAAAGTGGGACGCGGCGTGATTATTGGTATTTACGCGACGGCCCGGCGCGTTAGCGGCCCTTCCCCCAGGCCAGGGACGATTATGTATCAATATTGTTGCGTTCGGGCACTCGTGCGAGGGCTCCTGCGGGCTGGGGAGGGGGATCTGGGAATTGGAGGTACGACCGAGATGGCTTGCTCGGGGGGAGGTTTCCTCGCCGAGCAAGCCAGGGTTAGGTGTTGCGCTCTTGACTCGTTGTGCATTCTAGGACCCCACTGCTACTCACAACAAGCCCATATGGACAAGAAGTACAGCATCGGCCTGGACATCGGCACGAACTCGGTGGGCTGGGCGGTGATCACGGACGAGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGCCACTCGATCAAGAAGAACCTGATCGGCGCCCTGCTGTTCGACTCCGGCGAGACCGCCGAGGCGACGCGCCTGAAGCGCACCGCGCGTCGCCGCTACACGCGTCGCAAGAACCGCATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACTCGTTCTTCCACCGCCTGGAGGAGTCCTTCCTGGTGGAGGAAGACAAGAAGCACGAGCGCCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCCGACGATCTACCACCTGCGCAAGAAGCTGGTGGACAGCACCGACAAGGCGGACCTGCGCCTGATCTACCTGGCCCTGGCGCACATGATCAAGTTCCGCGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACTCGGACGTGGACAAGCTGTTCATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCGATCAACGCCTCCGGCGTGGACGCCAAGGCGATCCTGAGCGCGCGCCTGTCCAAGAGCCGTCGCCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGTTCGGCAACCTGATCGCGCTGTCGCTGGGCCTGACGCCGAACTTCAAGTCCAACTTCGACCTGGCCGAGGACGCGAAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCGGACCTGTTCCTGGCCGCGAAGAACCTGTCGGACGCCATCCTGCTGTCCGACATCCTGCGCGTGAACACCGAGATCACGAAGGCCCCCCTGTCGGCGTCCATGATCAAGCGCTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCGCTGGTGCGCCAGCAGCTGCCGGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCGTCGCAAGAGGAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACGGAGGAGCTGCTGGTGAAGCTGAACCGCGAGGACCTGCTGCGCAAGCAGCGCACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGCACGCCATCCTGCGTCGCCAAGAGGACTTCTACCCGTTCCTGAAGGACAACCGCGAGAAGATCGAGAAGATCCTGACGTTCCGCATCCCCTACTACGTGGGCCCACTTGCTAGAGGAAACTCTCGTTTCGCTTGGATGACCAGAAAGTCTGAGGAGACCATCACCCCTTGGAACTTCGAGGAGGTGAGTCGACGAGGCAGCTGCGCTCCCGGGTGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTTTTTGCAGCGTGCTTGCAGATTTGACTTGCAACGCCCGCATTGTGTCGACGAAGGCTTTTGGCTCCTCTGTCGCTGTCTCAAGCAGCATCTAACCCTGCGTCGCCGTTTCCATTTGCAGGTTGTTGATAAGGGAGCTTCTGCTCAGTCTTTCATCGAGAGAATGACCAACTTCGATAAGAACCTTCCAAACGAGAAGGTTCTTCCAAAGCACTCTCTTCTTTACGAGTACTTCACCGTGTACAACGAGCTGACGAAGGTGAAGTACGTGACCGAGGGCATGCGCAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCGATCGTGGACCTGCTGTTCAAGACCAACCGCAAGGTGACGGTGAAGCAGCTGAAAGAGGACTACTTCAAGAAGATCGAGTGCTTCGACAGCGTGGAGATCTCGGGCGTGGAGGACCGCTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACGCTGTTCGAGGACCGCGAGATGATCGAGGAGCGCCTGAAGACGTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGTCGCCGCTACACCGGCTGGGGCCGCCTGAGCCGCAAGCTGATCAACGGCATCCGCGACAAGCAGTCCGGCAAGACCATCCTGGACTTCCTGAAGAGCGACGGCTTCGCGAACCGCAACTTCATGCAGCTGATCCACGACGACTCGCTGACCTTCAAAGAGGACATCCAGAAGGCCCAGGTGTCGGGCCAGGGCGACTCCCTGCACGAGCACATCGCCAACCTGGCGGGCTCCCCCGCGATCAAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGCCACAAGCCGGAGAACATCGTGATCGAGATGGCCCGCGAGAACCAGACCACGCAGAAGGGCCAGAAGAACAGCCGCGAGCGCATGAAGCGCATCGAGGAAGGCATCAAGGAGCTGGGCTCGCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTACTACCTGCAGAACGGCCGCGACATGTACGTGGACCAGGAGCTGGACATCAACCGCCTGTCCGACTACGACGTGGACCACATCGTGCCCCAGAGCTTCCTGAAGGACGACTCGATCGACAACAAGGTGCTGACCCGCAGCGACAAGAACCGCGGCAAGAGCGACAACGTGCCGTCGGAGGAAGTGGTGAAGAAGATGAAGAACTACTGGCGCCAGCTGCTGAACGCCAAGCTGATCACGCAGCGCAAGTTCGACAACCTGACCAAGGCCGAGCGCGGTGGCCTGTCGGAGCTGGACAAGGCGGGCTTCATCAAGCGCCAGCTGGTGGAGACCCGCCAGATCACGAAGCACGTGGCGCAGATCCTGGACTCCCGCATGAACACGAAGTACGACGAGAACGACAAGCTGATCCGCGAGGTGAAGGTGATCACCCTGAAGTCCAAGCTGGTCAGCGACTTCCGCAAGGACTTCCAGTTCTACAAGGTGCGCGAGATCAACAACTACCACCACGCCCACGACGCGTACCTGAACGCCGTGGTGGGCACCGCGCTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGCAAGATGATCGCCAAGTCGGAGCAGGAGATCGGCAAGGCCACCGCGAAGTACTTCTTCTACTCCAACATCATGAACTTCTTCAAGACCGAGATCACGCTGGCCAACGGCGAGATCCGCAAGCGCCCGCTGATCGAGACCAACGGCGAGACGGGCGAGATCGTGTGGGACAAGGGCCGCGACTTCGCGACCGTGCGCAAGGTGCTGAGCATGCCCCAGGTGAACATCGTGAAGAAGACCGAGGTGCAGACGGGCGGCTTCTCCAAGGAGAGCATCCTGCCGAAGCGCAACTCGGACAAGCTGATCGCCCGCAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACTCCCCGACCGTGGCCTACAGCGTGCTGGTGGTGGCGAAGGTGGAGAAGGGCAAGTCCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGCAGCTCGTTCGAGAAGAACCCCATCGACTTCCTGGAGGCCAAGGGCTACAAAGAGGTGAAGAAGGACCTGATCATCAAGCTGCCGAAGTACTCGCTGTTCGAGCTGGAGAACGGCCGCAAGCGCATGCTGGCCTCCGCGGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCCCAGCAAGTACGTGAACTTCCTGTACCTGGCGTCCCACTACGAGAAGCTGAAGGGCTCGCCGGAGGACAACGAGCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCTCGGAGTTCTCCAAGCGCGTGATCCTGGCCGACGCGAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCGCGACAAGCCCATCCGCGAGCAGGCGGAGAACATCATCCACCTGTTCACCCTGACGAACCTGGGCGCCCCGGCCGCGTTCAAGTACTTCGACACCACGATCGACCGCAAGCGCTACACCTCCACGAAAGAGGTGCTGGACGCGACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGACGCGCATCGACCTGAGCCAGCTGGGCGGCGACTCCCGCGCGGACCCGAAGAAGAAGCGCAAGGTGTAAGAATTCTGGCAGCAGCTGGACCGCCTGTACCATGGAGAAGAGCTTTACTTGCCGGGATGGCCGATTTCGCTGATTGATACGGGATCGGAGCTCGGAGGCTTTCGCGCTAGGGGCTAGGCGAAGGGCAGTGGTGACCAGGGTCGGTGTGGGGTCGGCCCACGGTCAATTAGCCACAGGAGGATCAGGGGGAGGTAGGCACGTCGACTTGGTTTGCGACCCCGCAGTTTTGGCGGACGTGCTGTTGTAGATGTTAGCGTGTGCGTGAGCCAGTGGCCAACGTGCCACACCCATTGAGAAGACCAACCAACTTACTGGCAATATCTGCCAATGCCATACTGCATGTAATGGCCAGGCCATGTGAGAGTTTGCCGTGCCTGCGCGCGCCCCGGGGGCGCAGTTTAGCTGACCAGCCGTGGGATGATGCACGCATTTGCAAGGACAGGGTAATCACAGCAGCAACATGGTGGGCTTAGGACAGCTGTGGGTCAGTGGACGGACGGCAGGGGAGGGACGGCGCAGCTCGGGAGACAGGGGGAGACAGCGTGACTGTGCAATCAAGCTGGCGCGCCGGTACCAAGCTTATCGATACCGTCGACCTCGACAGCTTTTGTTCCCTTTAGTGAGGGTTAATTTCGAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGA

**Fig. S19.** The DNA sequence of the Cas9/intron-sgRNA gene targeting the *FKB12* gene.

CGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCTAAATTGTAAGCGTTAATATTTTGTTAAAATTCGCGTTAAATTTTTGTTAAATCAGCTCATTTTTTAACCAATAGGCCGAAATCGGCAAAATCCCTTATAAATCAAAAGAATAGACCGAGATAGGGTTGAGTGTTGTTCCAGTTTGGAACAAGAGTCCACTATTAAAGAACGTGGACTCCAACGTCAAAGGGCGAAAAACCGTCTATCAGGGCGATGGCCCACTACGTGAACCATCACCCTAATCAAGTTTTTTGGGGTCGAGGTGCCGTAAAGCACTAAATCGGAACCCTAAAGGGAGCCCCCGATTTAGAGCTTGACGGGGAAAGCCGGCGAACGTGGCGAGAAAGGAAGGGAAGAAAGCGAAAGGAGCGGGCGCTAGGGCGCTGGCAAGTGTAGCGGTCACGCTGCGCGTAACCACCACACCCGCCGCGCTTAATGCGCCGCTACAGGGCGCGTCCCATTCGCCATTCAGGCTGCGCAACTGTTGGGAAGGGCGATCGGTGCGGGCCTCTTCGCTATTACGCCAGCTGGCGAAAGGGGGATGTGCTGCAAGGCGATTAAGTTGGGTAACGCCAGGGTTTTCCCAGTCACGACGTTGTAAAACGACGGCCAGTGAATTGTAATACGACTCACTATAGGGCGAATTGGAGCTCCACCGCGGTGGCGGCCGCTCTAGAACTAGTGGATCCCACACACCTGCCCGTCTGCCTGACAGGAAGTGAACGCATGTCGAGGGAGGCCTCACCAATCGTCACACGAGCCCTCGTCAGAAACACGTCTCCGCCACGCTCTCCCTCTCACGGCCGACCCCGCAGCCCTTTTGCCCTTTCCTAGGCCACCGACAGGACCCAGGCGCTCTCAGCATGCCTCAACAACCCGTACTCGTGCCAGCGGTGCCCTTGTGCTGGTGATCGCTTGGAAGCGCATGCGAAGACGAAGGGGCGGAGCAGGCGGCCTGGCTGTTCGAAGGGCTCGCCGCCAGTTCGGGTGCCTTTCTCCACGCGCGCCTCCACACCTACCGATGCGTGAAGGCAGGCAAATGCTCATGTTTGCCCGAACTCGGAGTCCTTAAAAAGCCGCTTCTTGTCGTCGTTCCGAGACATGTTAGCAGATCGCAGTGCCACCTTTCCTGACGCGCTCGGCCCCATATTCGGACGCAATTGTCATTTGTAGCACAATTGGAGCAAATCTGGCGAGGCAGTAGGCTTTTAAGTTGCAAGGCGAGAGAGCAAAGTGGGACGCGGCGTGATTATTGGTATTTACGCGACGGCCCGGCGCGTTAGCGGCCCTTCCCCCAGGCCAGGGACGATTATGTATCAATATTGTTGCGTTCGGGCACTCGTGCGAGGGCTCCTGCGGGCTGGGGAGGGGGATCTGGGAATTGGAGGTACGACCGAGATGGCTTGCTCGGGGGGAGGTTTCCTCGCCGAGCAAGCCAGGGTTAGGTGTTGCGCTCTTGACTCGTTGTGCATTCTAGGACCCCACTGCTACTCACAACAAGCCCATATGGACAAGAAGTACAGCATCGGCCTGGACATCGGCACGAACTCGGTGGGCTGGGCGGTGATCACGGACGAGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGCCACTCGATCAAGAAGAACCTGATCGGCGCCCTGCTGTTCGACTCCGGCGAGACCGCCGAGGCGACGCGCCTGAAGCGCACCGCGCGTCGCCGCTACACGCGTCGCAAGAACCGCATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACTCGTTCTTCCACCGCCTGGAGGAGTCCTTCCTGGTGGAGGAAGACAAGAAGCACGAGCGCCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCCGACGATCTACCACCTGCGCAAGAAGCTGGTGGACAGCACCGACAAGGCGGACCTGCGCCTGATCTACCTGGCCCTGGCGCACATGATCAAGTTCCGCGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACTCGGACGTGGACAAGCTGTTCATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCGATCAACGCCTCCGGCGTGGACGCCAAGGCGATCCTGAGCGCGCGCCTGTCCAAGAGCCGTCGCCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGTTCGGCAACCTGATCGCGCTGTCGCTGGGCCTGACGCCGAACTTCAAGTCCAACTTCGACCTGGCCGAGGACGCGAAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCGGACCTGTTCCTGGCCGCGAAGAACCTGTCGGACGCCATCCTGCTGTCCGACATCCTGCGCGTGAACACCGAGATCACGAAGGCCCCCCTGTCGGCGTCCATGATCAAGCGCTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCGCTGGTGCGCCAGCAGCTGCCGGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCGTCGCAAGAGGAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACGGAGGAGCTGCTGGTGAAGCTGAACCGCGAGGACCTGCTGCGCAAGCAGCGCACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGCACGCCATCCTGCGTCGCCAAGAGGACTTCTACCCGTTCCTGAAGGACAACCGCGAGAAGATCGAGAAGATCCTGACGTTCCGCATCCCCTACTACGTGGGCCCACTTGCTAGAGGAAACTCTCGTTTCGCTTGGATGACCAGAAAGTCTGAGGAGACCATCACCCCTTGGAACTTCGAGGAGGTGAGTCGACGAGCAAGCCCGGCGGATCAGGACCGTGTTTGTGCACTACAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTTTTTGCAGCGTGCTTGCAGATTTGACTTGCAACGCCCGCATTGTGTCGACGAAGGCTTTTGGCTCCTCTGTCGCTGTCTCAAGCAGCATCTAACCCTGCGTCGCCGTTTCCATTTGCAGGTTGTTGATAAGGGAGCTTCTGCTCAGTCTTTCATCGAGAGAATGACCAACTTCGATAAGAACCTTCCAAACGAGAAGGTTCTTCCAAAGCACTCTCTTCTTTACGAGTACTTCACCGTGTACAACGAGCTGACGAAGGTGAAGTACGTGACCGAGGGCATGCGCAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCGATCGTGGACCTGCTGTTCAAGACCAACCGCAAGGTGACGGTGAAGCAGCTGAAAGAGGACTACTTCAAGAAGATCGAGTGCTTCGACAGCGTGGAGATCTCGGGCGTGGAGGACCGCTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACGCTGTTCGAGGACCGCGAGATGATCGAGGAGCGCCTGAAGACGTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGTCGCCGCTACACCGGCTGGGGCCGCCTGAGCCGCAAGCTGATCAACGGCATCCGCGACAAGCAGTCCGGCAAGACCATCCTGGACTTCCTGAAGAGCGACGGCTTCGCGAACCGCAACTTCATGCAGCTGATCCACGACGACTCGCTGACCTTCAAAGAGGACATCCAGAAGGCCCAGGTGTCGGGCCAGGGCGACTCCCTGCACGAGCACATCGCCAACCTGGCGGGCTCCCCCGCGATCAAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGCCACAAGCCGGAGAACATCGTGATCGAGATGGCCCGCGAGAACCAGACCACGCAGAAGGGCCAGAAGAACAGCCGCGAGCGCATGAAGCGCATCGAGGAAGGCATCAAGGAGCTGGGCTCGCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTACTACCTGCAGAACGGCCGCGACATGTACGTGGACCAGGAGCTGGACATCAACCGCCTGTCCGACTACGACGTGGACCACATCGTGCCCCAGAGCTTCCTGAAGGACGACTCGATCGACAACAAGGTGCTGACCCGCAGCGACAAGAACCGCGGCAAGAGCGACAACGTGCCGTCGGAGGAAGTGGTGAAGAAGATGAAGAACTACTGGCGCCAGCTGCTGAACGCCAAGCTGATCACGCAGCGCAAGTTCGACAACCTGACCAAGGCCGAGCGCGGTGGCCTGTCGGAGCTGGACAAGGCGGGCTTCATCAAGCGCCAGCTGGTGGAGACCCGCCAGATCACGAAGCACGTGGCGCAGATCCTGGACTCCCGCATGAACACGAAGTACGACGAGAACGACAAGCTGATCCGCGAGGTGAAGGTGATCACCCTGAAGTCCAAGCTGGTCAGCGACTTCCGCAAGGACTTCCAGTTCTACAAGGTGCGCGAGATCAACAACTACCACCACGCCCACGACGCGTACCTGAACGCCGTGGTGGGCACCGCGCTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGCAAGATGATCGCCAAGTCGGAGCAGGAGATCGGCAAGGCCACCGCGAAGTACTTCTTCTACTCCAACATCATGAACTTCTTCAAGACCGAGATCACGCTGGCCAACGGCGAGATCCGCAAGCGCCCGCTGATCGAGACCAACGGCGAGACGGGCGAGATCGTGTGGGACAAGGGCCGCGACTTCGCGACCGTGCGCAAGGTGCTGAGCATGCCCCAGGTGAACATCGTGAAGAAGACCGAGGTGCAGACGGGCGGCTTCTCCAAGGAGAGCATCCTGCCGAAGCGCAACTCGGACAAGCTGATCGCCCGCAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACTCCCCGACCGTGGCCTACAGCGTGCTGGTGGTGGCGAAGGTGGAGAAGGGCAAGTCCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGCAGCTCGTTCGAGAAGAACCCCATCGACTTCCTGGAGGCCAAGGGCTACAAAGAGGTGAAGAAGGACCTGATCATCAAGCTGCCGAAGTACTCGCTGTTCGAGCTGGAGAACGGCCGCAAGCGCATGCTGGCCTCCGCGGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCCCAGCAAGTACGTGAACTTCCTGTACCTGGCGTCCCACTACGAGAAGCTGAAGGGCTCGCCGGAGGACAACGAGCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCTCGGAGTTCTCCAAGCGCGTGATCCTGGCCGACGCGAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCGCGACAAGCCCATCCGCGAGCAGGCGGAGAACATCATCCACCTGTTCACCCTGACGAACCTGGGCGCCCCGGCCGCGTTCAAGTACTTCGACACCACGATCGACCGCAAGCGCTACACCTCCACGAAAGAGGTGCTGGACGCGACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGACGCGCATCGACCTGAGCCAGCTGGGCGGCGACTCCCGCGCGGACCCGAAGAAGAAGCGCAAGGTGTAAGAATTCTGGCAGCAGCTGGACCGCCTGTACCATGGAGAAGAGCTTTACTTGCCGGGATGGCCGATTTCGCTGATTGATACGGGATCGGAGCTCGGAGGCTTTCGCGCTAGGGGCTAGGCGAAGGGCAGTGGTGACCAGGGTCGGTGTGGGGTCGGCCCACGGTCAATTAGCCACAGGAGGATCAGGGGGAGGTAGGCACGTCGACTTGGTTTGCGACCCCGCAGTTTTGGCGGACGTGCTGTTGTAGATGTTAGCGTGTGCGTGAGCCAGTGGCCAACGTGCCACACCCATTGAGAAGACCAACCAACTTACTGGCAATATCTGCCAATGCCATACTGCATGTAATGGCCAGGCCATGTGAGAGTTTGCCGTGCCTGCGCGCGCCCCGGGGGCGCAGTTTAGCTGACCAGCCGTGGGATGATGCACGCATTTGCAAGGACAGGGTAATCACAGCAGCAACATGGTGGGCTTAGGACAGCTGTGGGTCAGTGGACGGACGGCAGGGGAGGGACGGCGCAGCTCGGGAGACAGGGGGAGACAGCGTGACTGTGCAATCAAGCTTATCGATACCGTCGACCTCGACAGCTTTTGTTCCCTTTAGTGAGGGTTAATTTCGAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGA

**Fig. S20.** Complete DNA sequences for the Cas9/intron-sgRNA gene targeting the *ARG* gene.

CGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCTAAATTGTAAGCGTTAATATTTTGTTAAAATTCGCGTTAAATTTTTGTTAAATCAGCTCATTTTTTAACCAATAGGCCGAAATCGGCAAAATCCCTTATAAATCAAAAGAATAGACCGAGATAGGGTTGAGTGTTGTTCCAGTTTGGAACAAGAGTCCACTATTAAAGAACGTGGACTCCAACGTCAAAGGGCGAAAAACCGTCTATCAGGGCGATGGCCCACTACGTGAACCATCACCCTAATCAAGTTTTTTGGGGTCGAGGTGCCGTAAAGCACTAAATCGGAACCCTAAAGGGAGCCCCCGATTTAGAGCTTGACGGGGAAAGCCGGCGAACGTGGCGAGAAAGGAAGGGAAGAAAGCGAAAGGAGCGGGCGCTAGGGCGCTGGCAAGTGTAGCGGTCACGCTGCGCGTAACCACCACACCCGCCGCGCTTAATGCGCCGCTACAGGGCGCGTCCCATTCGCCATTCAGGCTGCGCAACTGTTGGGAAGGGCGATCGGTGCGGGCCTCTTCGCTATTACGCCAGCTGGCGAAAGGGGGATGTGCTGCAAGGCGATTAAGTTGGGTAACGCCAGGGTTTTCCCAGTCACGACGTTGTAAAACGACGGCCAGTGAATTGTAATACGACTCACTATAGGGCGAATTGGAGCTCCACCGCGGTGGCGGCCGCTCTAGAACTAGTGGATCCCACACACCTGCCCGTCTGCCTGACAGGAAGTGAACGCATGTCGAGGGAGGCCTCACCAATCGTCACACGAGCCCTCGTCAGAAACACGTCTCCGCCACGCTCTCCCTCTCACGGCCGACCCCGCAGCCCTTTTGCCCTTTCCTAGGCCACCGACAGGACCCAGGCGCTCTCAGCATGCCTCAACAACCCGTACTCGTGCCAGCGGTGCCCTTGTGCTGGTGATCGCTTGGAAGCGCATGCGAAGACGAAGGGGCGGAGCAGGCGGCCTGGCTGTTCGAAGGGCTCGCCGCCAGTTCGGGTGCCTTTCTCCACGCGCGCCTCCACACCTACCGATGCGTGAAGGCAGGCAAATGCTCATGTTTGCCCGAACTCGGAGTCCTTAAAAAGCCGCTTCTTGTCGTCGTTCCGAGACATGTTAGCAGATCGCAGTGCCACCTTTCCTGACGCGCTCGGCCCCATATTCGGACGCAATTGTCATTTGTAGCACAATTGGAGCAAATCTGGCGAGGCAGTAGGCTTTTAAGTTGCAAGGCGAGAGAGCAAAGTGGGACGCGGCGTGATTATTGGTATTTACGCGACGGCCCGGCGCGTTAGCGGCCCTTCCCCCAGGCCAGGGACGATTATGTATCAATATTGTTGCGTTCGGGCACTCGTGCGAGGGCTCCTGCGGGCTGGGGAGGGGGATCTGGGAATTGGAGGTACGACCGAGATGGCTTGCTCGGGGGGAGGTTTCCTCGCCGAGCAAGCCAGGGTTAGGTGTTGCGCTCTTGACTCGTTGTGCATTCTAGGACCCCACTGCTACTCACAACAAGCCCATATGGACAAGAAGTACAGCATCGGCCTGGACATCGGCACGAACTCGGTGGGCTGGGCGGTGATCACGGACGAGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGCCACTCGATCAAGAAGAACCTGATCGGCGCCCTGCTGTTCGACTCCGGCGAGACCGCCGAGGCGACGCGCCTGAAGCGCACCGCGCGTCGCCGCTACACGCGTCGCAAGAACCGCATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACTCGTTCTTCCACCGCCTGGAGGAGTCCTTCCTGGTGGAGGAAGACAAGAAGCACGAGCGCCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCCGACGATCTACCACCTGCGCAAGAAGCTGGTGGACAGCACCGACAAGGCGGACCTGCGCCTGATCTACCTGGCCCTGGCGCACATGATCAAGTTCCGCGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACTCGGACGTGGACAAGCTGTTCATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCGATCAACGCCTCCGGCGTGGACGCCAAGGCGATCCTGAGCGCGCGCCTGTCCAAGAGCCGTCGCCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGTTCGGCAACCTGATCGCGCTGTCGCTGGGCCTGACGCCGAACTTCAAGTCCAACTTCGACCTGGCCGAGGACGCGAAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCGGACCTGTTCCTGGCCGCGAAGAACCTGTCGGACGCCATCCTGCTGTCCGACATCCTGCGCGTGAACACCGAGATCACGAAGGCCCCCCTGTCGGCGTCCATGATCAAGCGCTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCGCTGGTGCGCCAGCAGCTGCCGGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCGTCGCAAGAGGAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACGGAGGAGCTGCTGGTGAAGCTGAACCGCGAGGACCTGCTGCGCAAGCAGCGCACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGCACGCCATCCTGCGTCGCCAAGAGGACTTCTACCCGTTCCTGAAGGACAACCGCGAGAAGATCGAGAAGATCCTGACGTTCCGCATCCCCTACTACGTGGGCCCACTTGCTAGAGGAAACTCTCGTTTCGCTTGGATGACCAGAAAGTCTGAGGAGACCATCACCCCTTGGAACTTCGAGGAGGTGAGTCGACGAGGGCATGAGCGAGGAGCTGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTTTTTGCAGCGTGCTTGCAGATTTGACTTGCAACGCCCGCATTGTGTCGACGAAGGCTTTTGGCTCCTCTGTCGCTGTCTCAAGCAGCATCTAACCCTGCGTCGCCGTTTCCATTTGCAGGTTGTTGATAAGGGAGCTTCTGCTCAGTCTTTCATCGAGAGAATGACCAACTTCGATAAGAACCTTCCAAACGAGAAGGTTCTTCCAAAGCACTCTCTTCTTTACGAGTACTTCACCGTGTACAACGAGCTGACGAAGGTGAAGTACGTGACCGAGGGCATGCGCAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCGATCGTGGACCTGCTGTTCAAGACCAACCGCAAGGTGACGGTGAAGCAGCTGAAAGAGGACTACTTCAAGAAGATCGAGTGCTTCGACAGCGTGGAGATCTCGGGCGTGGAGGACCGCTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACGCTGTTCGAGGACCGCGAGATGATCGAGGAGCGCCTGAAGACGTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGTCGCCGCTACACCGGCTGGGGCCGCCTGAGCCGCAAGCTGATCAACGGCATCCGCGACAAGCAGTCCGGCAAGACCATCCTGGACTTCCTGAAGAGCGACGGCTTCGCGAACCGCAACTTCATGCAGCTGATCCACGACGACTCGCTGACCTTCAAAGAGGACATCCAGAAGGCCCAGGTGTCGGGCCAGGGCGACTCCCTGCACGAGCACATCGCCAACCTGGCGGGCTCCCCCGCGATCAAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGCCACAAGCCGGAGAACATCGTGATCGAGATGGCCCGCGAGAACCAGACCACGCAGAAGGGCCAGAAGAACAGCCGCGAGCGCATGAAGCGCATCGAGGAAGGCATCAAGGAGCTGGGCTCGCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTACTACCTGCAGAACGGCCGCGACATGTACGTGGACCAGGAGCTGGACATCAACCGCCTGTCCGACTACGACGTGGACCACATCGTGCCCCAGAGCTTCCTGAAGGACGACTCGATCGACAACAAGGTGCTGACCCGCAGCGACAAGAACCGCGGCAAGAGCGACAACGTGCCGTCGGAGGAAGTGGTGAAGAAGATGAAGAACTACTGGCGCCAGCTGCTGAACGCCAAGCTGATCACGCAGCGCAAGTTCGACAACCTGACCAAGGCCGAGCGCGGTGGCCTGTCGGAGCTGGACAAGGCGGGCTTCATCAAGCGCCAGCTGGTGGAGACCCGCCAGATCACGAAGCACGTGGCGCAGATCCTGGACTCCCGCATGAACACGAAGTACGACGAGAACGACAAGCTGATCCGCGAGGTGAAGGTGATCACCCTGAAGTCCAAGCTGGTCAGCGACTTCCGCAAGGACTTCCAGTTCTACAAGGTGCGCGAGATCAACAACTACCACCACGCCCACGACGCGTACCTGAACGCCGTGGTGGGCACCGCGCTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGCAAGATGATCGCCAAGTCGGAGCAGGAGATCGGCAAGGCCACCGCGAAGTACTTCTTCTACTCCAACATCATGAACTTCTTCAAGACCGAGATCACGCTGGCCAACGGCGAGATCCGCAAGCGCCCGCTGATCGAGACCAACGGCGAGACGGGCGAGATCGTGTGGGACAAGGGCCGCGACTTCGCGACCGTGCGCAAGGTGCTGAGCATGCCCCAGGTGAACATCGTGAAGAAGACCGAGGTGCAGACGGGCGGCTTCTCCAAGGAGAGCATCCTGCCGAAGCGCAACTCGGACAAGCTGATCGCCCGCAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACTCCCCGACCGTGGCCTACAGCGTGCTGGTGGTGGCGAAGGTGGAGAAGGGCAAGTCCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGCAGCTCGTTCGAGAAGAACCCCATCGACTTCCTGGAGGCCAAGGGCTACAAAGAGGTGAAGAAGGACCTGATCATCAAGCTGCCGAAGTACTCGCTGTTCGAGCTGGAGAACGGCCGCAAGCGCATGCTGGCCTCCGCGGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCCCAGCAAGTACGTGAACTTCCTGTACCTGGCGTCCCACTACGAGAAGCTGAAGGGCTCGCCGGAGGACAACGAGCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCTCGGAGTTCTCCAAGCGCGTGATCCTGGCCGACGCGAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCGCGACAAGCCCATCCGCGAGCAGGCGGAGAACATCATCCACCTGTTCACCCTGACGAACCTGGGCGCCCCGGCCGCGTTCAAGTACTTCGACACCACGATCGACCGCAAGCGCTACACCTCCACGAAAGAGGTGCTGGACGCGACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGACGCGCATCGACCTGAGCCAGCTGGGCGGCGACTCCCGCGCGGACCCGAAGAAGAAGCGCAAGGTGTAAGAATTCTGGCAGCAGCTGGACCGCCTGTACCATGGAGAAGAGCTTTACTTGCCGGGATGGCCGATTTCGCTGATTGATACGGGATCGGAGCTCGGAGGCTTTCGCGCTAGGGGCTAGGCGAAGGGCAGTGGTGACCAGGGTCGGTGTGGGGTCGGCCCACGGTCAATTAGCCACAGGAGGATCAGGGGGAGGTAGGCACGTCGACTTGGTTTGCGACCCCGCAGTTTTGGCGGACGTGCTGTTGTAGATGTTAGCGTGTGCGTGAGCCAGTGGCCAACGTGCCACACCCATTGAGAAGACCAACCAACTTACTGGCAATATCTGCCAATGCCATACTGCATGTAATGGCCAGGCCATGTGAGAGTTTGCCGTGCCTGCGCGCGCCCCGGGGGCGCAGTTTAGCTGACCAGCCGTGGGATGATGCACGCATTTGCAAGGACAGGGTAATCACAGCAGCAACATGGTGGGCTTAGGACAGCTGTGGGTCAGTGGACGGACGGCAGGGGAGGGACGGCGCAGCTCGGGAGACAGGGGGAGACAGCGTGACTGTGCAATCAAGCTGGCGCGCCGGTACCAAGCTTATCGATACCGTCGACCTCGACAGCTTTTGTTCCCTTTAGTGAGGGTTAATTTCGAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGA