

**Sequence 1.** CRISPR-*CLONInG*: Partial sequence of final FLE<sub>x</sub> vector with partial 3'UTR, FRT-PGK-Neo-FRT, tdTomato, and IRES sequences

3'UTR (gray highlight); FRT-PGK-Neo-FRT, inverted sequence (yellow highlight), tdTomato, inverted sequence (red highlight), IRES (blue highlight)

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CNTCANAGTNGACTCNTAATAAGCTTGATATCGAATTCCGAAGTTCCTATTCTCTAGAAAGTATAGG
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CGCGTCGTGCAGGACGTGACAAATGGAAGTAGCACGTCTCACTAGTCTCGTGCAGATGGACAGCACCCG
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CAGCTGTGCTCGACGTTGTCACTGAAGCGGGAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGGCAG
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GACGAGTTCTTCTGAGGGGATCAATTCTCTAGAGCTCGCTGATCAGCCTCGACTGTGCCTTCTAGTTGC
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CGGGGATGTCGGCGGGGTGCTTACGTACGCCTTGGAGCCGTACATGAACTGGGGGGACAGGATGTCC
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GCCCTCGCCCTCGCCCTCGATCTCGAACTCGTGGCCGTTTCATGGAGCCCTCCATGCGCACCTTGAAGCG  
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TGCTTCTTACGACATTCAACAGACCTTGCATTCTTTGGCGAGAGGGGAAAGACCCCTAGGAATGC  
TCGTCAAGAAGACAGGGCCAGGTTTCCGGGCCCTCACATTGCCAAAAGACGGCAATATGGTGGAAAAT  
AACATATAGACAAACGCACACCGGCCTTATTCCAAGCGGCTTCGGCCAGTAACGTTAGGGGGGGGGGA  
GGGAGAGGGG

**Sequence 2.** CRISPR-*CLONInG*: Partial FLEx vector sequence showing CRISPR-Cas9 allows precise excision of Luciferase gene from its adjacent 3'UTR and IRES sequences, with only 1 nt deviation

3'UTR (gray highlight), luciferase gene, inverted sequence (green highlight), IRES (blue highlight), PAM NGG (bold), CRISPR target site (underlined), slash (Cas9 cleavage site), gRNA Luc-A (red); partial sequence changed to maintain research confidentiality; gRNA Luc-B (violet)

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GCCAGGTTTCCGGGCCCTCACATTGCCAAAAGACGGCAATATGGTGGAAAATAACATATAGACAAACG  
CACACCGGCCTTATTCCAAGCGGCTTCGGCCAGTAACGTTAGGGGGGGGGGAGGGAGAGGGG

**Sequence 3.** CRISPR-*CLONInG*: Sequence of assembled custom AAV-v2, comprising sgRNA-W, sgRNA-X, and mutant exon10 of Psen1.

ITR (gray highlight), U6 promoter (green highlight), spacer sequence for W and X (yellow highlight), Tracr RNA (underlined), HA (italics), three amino acid replaced (red, green, and blue)

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CCTGCAGGCAGCTGCGGCTCGCTCGCTCACTGAGGCCGCCCGGGCAAAGCCCCGGGCGTCGGGCGA
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CCTGATAAATGCTTCAATAATATTGAAAAAGGAAGAGTATGAGTATTCAACATTTCCGTGTCGCCCTTA
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TCACATGT

**Sequence 4.** CRISPR-*CLIP*: Sequence of IssDNA donor source template (dsDNA) for Psen1-CKI allele.

EcoRV (gray highlight), Lox66 (green highlight), Exon 10 (yellow highlight), Exon 10 with three amino acid KI (blue highlight), Lox71 (pink highlight), three amino acid replaced—inverted orientation (red, green, and blue), Cas9n site (underlined; PAM bolded)

**GATATC**ACGAGAGTCTCCTAGAGAAACAGGCTCTCCCTAGTAAGTACACGTAGGACTATTCACGGA  
GCTGAAATCCCCCCCCCACACACACACACTGTGAGTTCAAGACTAACCTGACTGTGTGGGGA  
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