

Precise in vivo RNA base editing with a wobble-enhanced circular CLUSTER guide RNA

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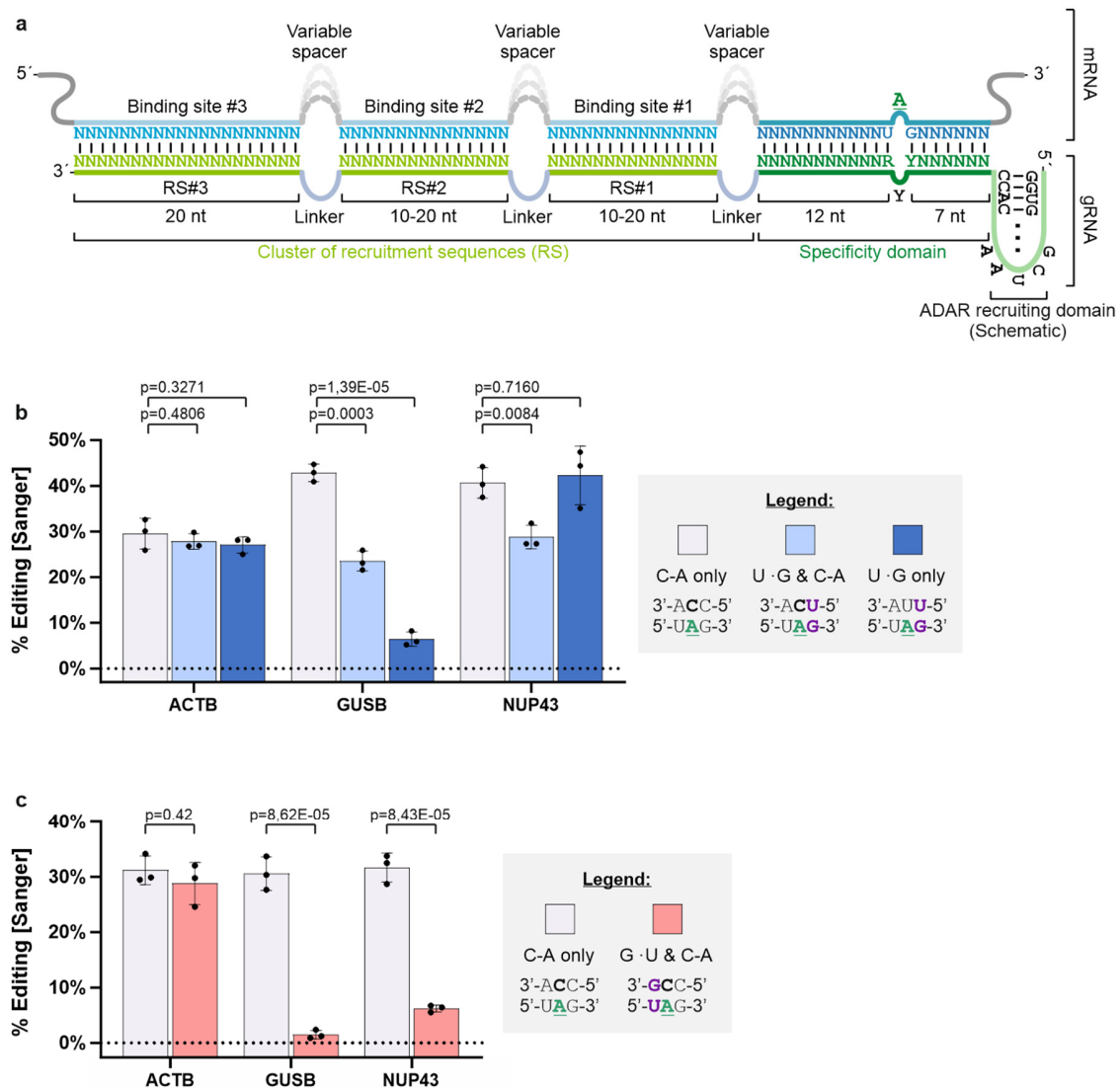
Supplementary Information

Inventory of Supplementary Information

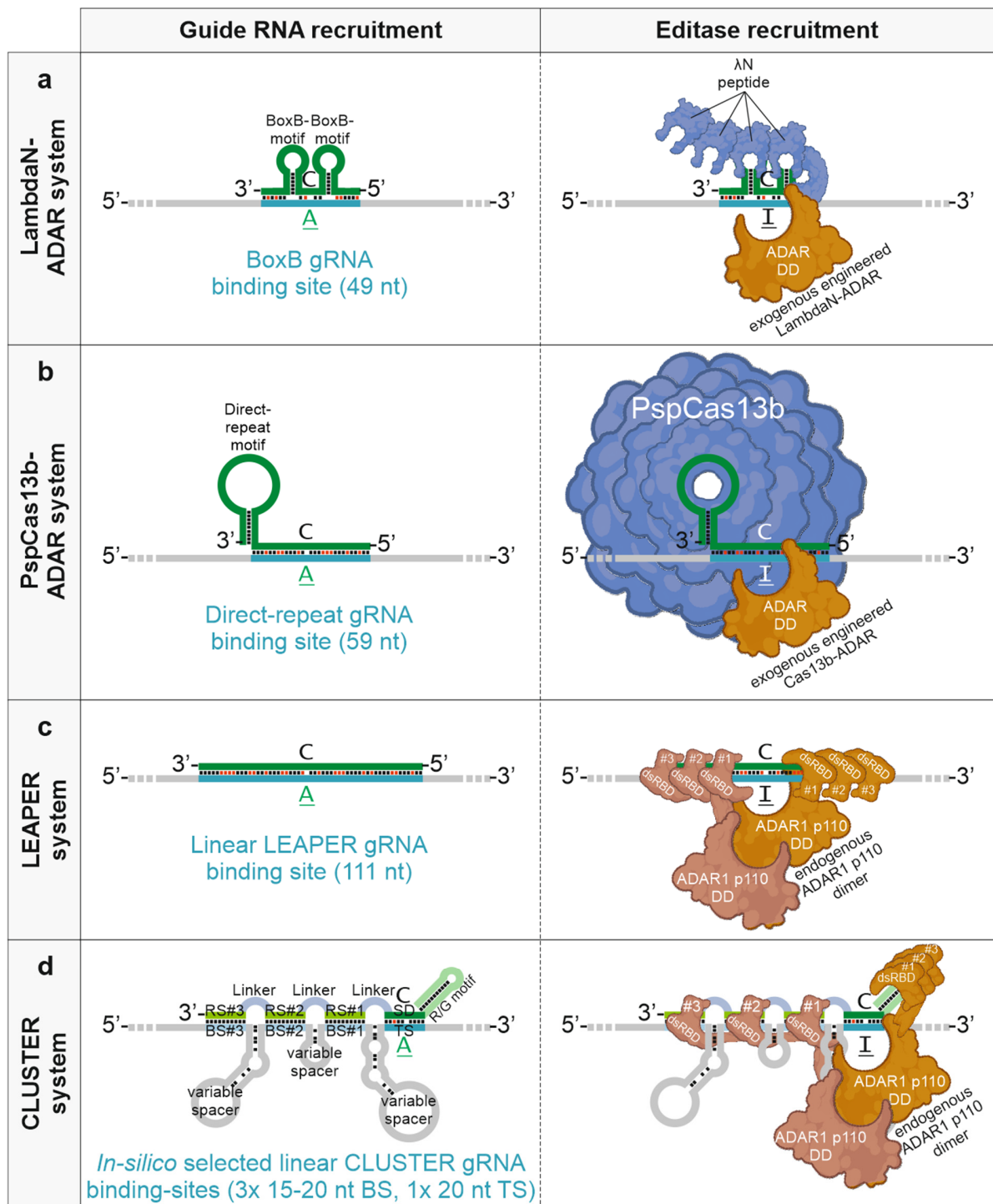
- Supplementary Figures S1-S14
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Supplementary Figure S1. Exemplary sequencing reads related to the dataset from main text Figure 1. Editing of cis-acting reporters in ADAR1 p110 Flp-In T-REx cells, showing the effect of wobble base pairs on target triplets containing Uracil and/or Guanine. The target adenosine is highlighted in green bold and underlined. The sort and position of mismatch/wobble is indicated in the sequencing trace and explained in the legend.



Supplementary Figure S2. Enhancing U-G- and suppressing G-U wobble base pairs in the context of a C-A mismatched target adenosine. **a)** Design of a linear CLUSTER gRNA consisting of three recruitment sequences (RS) connected by triple adenosine linkers, a 20 nt long specificity domain and an ADAR recruitment motif based on the natural R/G motif of the glutamate receptor 2. The guide RNA is displayed bound to its target transcript. The target adenosine is highlighted in green, bold and underlined. The counter base of the target adenosine is a Y (Y = C or U). The counter base of the Guanine at the 3' nearest neighbor position is also a Y, the counterbase at the 5' nearest neighbor position is a R (R = A or G). **b)** Editing yields achieved using linear CLUSTER guide RNAs targeting the endogenous housekeeping genes ACTB, GUSB and NUP43. The designs differ only in the counter bases present at the target adenosine and its 3' nearest neighbor Guanine. **c)** Similar to b), but the designs differ in the counter base present at the 5' nearest neighbor Uracil. Editing in b) and c) was performed in HEK293FT cells using plasmid-borne guide RNAs and endogenous ADAR1. Data in b) and c) are shown as the mean editing percentage $\pm$ s.d. of N = 3 biological replicates. For statistical analysis, a student t-test (two-tailed, parametric) was applied.

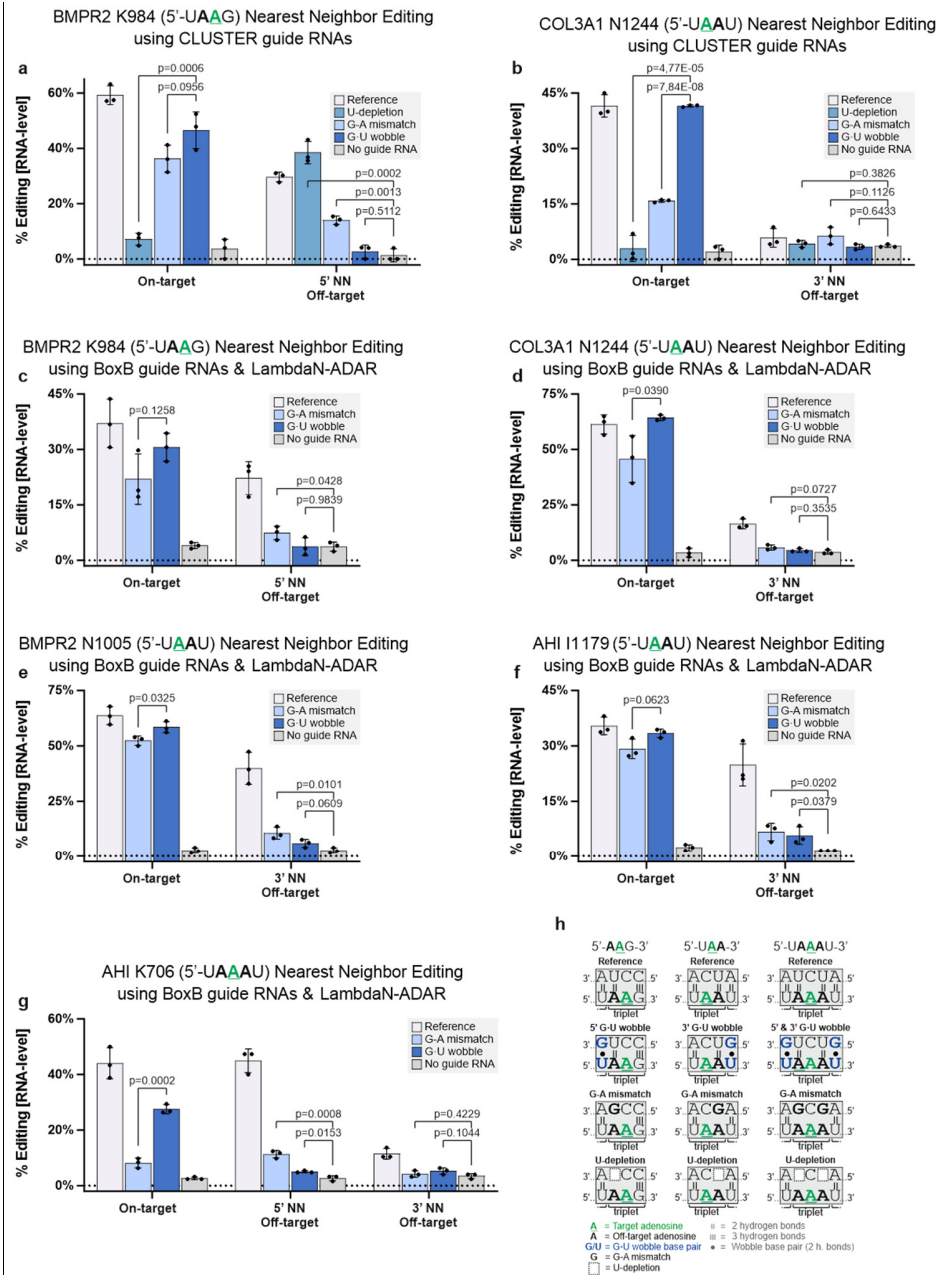


Supplementary Figure S3. Overview of the targeting strategies of the encodable side-directed RNA editing systems that are applied in this study. In all panels the target mRNA is displayed in grey and the guide RNA binding site(s) on it in different shades of blue. Guide RNA elements are displayed in different shades of green. The target adenosine within the target mRNA is displayed bold, underlined, and in green, while its Cytosine counterbase in the guide RNA is displayed in bold and black. Hydrogen bonds are displayed as black or red lines.

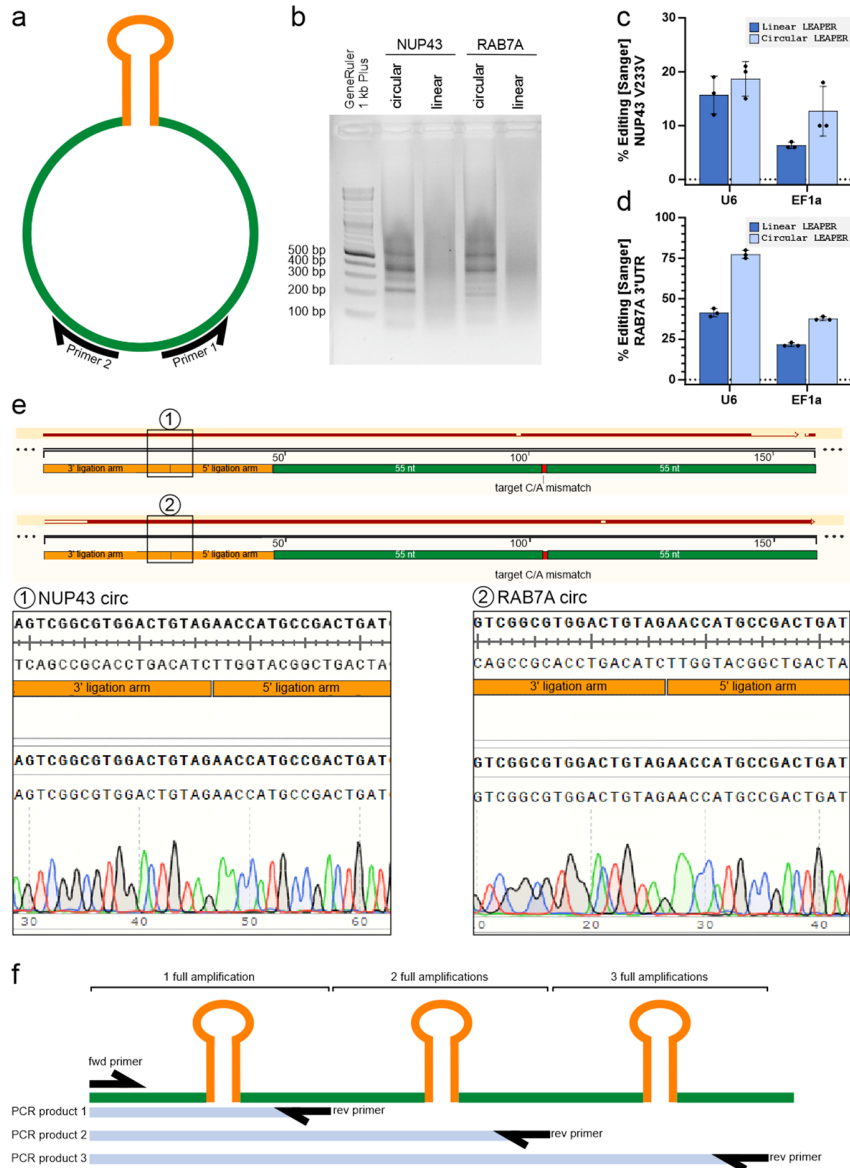
Supplementary Figure S3 continued. Overview of the targeting strategies of the encodable side-directed RNA editing systems that are applied in this study. The abundance of red lines (not their specific positions) illustrates the likelihood of bystander off-target events for the respective system and antisense element. Non-human protein domains/peptides are displayed in dark blue. Human protein domains are displayed in orange. To distinguish two independent human proteins within a homodimer the domains of the first protein are displayed in orange and the domains of the second one in red. **(a)** The targeting strategy of the λ N-ADAR system utilizes phage-derived elements. The nanomolar affinity of the λ N peptide for boxB RNA-hairpin motifs enables efficient recruitment of the editase fusion protein. The latter consists of an ADAR deaminase domain (e.g. hADAR1d, hADAR2d, or hyperactive mutants) and four λ N peptides, while the guide RNA consists of a 49 nt antisense part that is interrupted by two boxB motifs. **(b)** The targeting strategy of the λ N-ADAR system utilizes bacteria-derived elements and is a variation of the λ N-ADAR system. The affinity of the PspCas13b protein for direct-repeat motifs enables recruitment of the editase fusion protein. The latter consists again of an ADAR deaminase domain (e.g. hADAR1d, hADAR2d, or hyperactive mutants) and the PspCas13b protein, while the guide RNA consists of a 59 nt antisense part and a 3'-terminal direct repeat motif. **(c)** The targeting strategy of the LEAPER system utilizes the double-stranded RNA binding domains of endogenous human ADARs. In contrast to the previous two systems the overexpression of an engineered editase is not required. Instead, the 111 nt long LEAPER guide RNA forms a dsRNA substrate with the target mRNA allowing for recruitment of endogenous ADAR enzymes. Due to the length of the duplex this could potentially allow for ADAR homo- and/or heterodimer formation. Exemplary an ADAR1 p110 homodimers is displayed. The unstructured duplex makes the design prone to off-target editing events, if no further off-target solutions like e.g. GA-mismatches are applied. There is also a version of this system that utilizes the Tornado expression system to achieve circularization of the guide RNA. The latter increases its stability and thus guide RNA abundance and consequently improves the editing yields. **(d)** The targeting strategy of the CLUSTER system does also utilize the double-stranded RNA binding domains of endogenous human ADARs. Thus, the overexpression of an engineered editase is again not required. The guide RNA design is however not unstructured but instead highly sophisticated. It consists of several functional elements. The R/G motif is a dsRNA-hairpin based on the natural R/G site of the GRIA2 transcript, that has evolved for efficient ADAR2 binding and was engineered for human ADAR1 p110 recruitment via rational design. It might potentially enable ADAR recruitment even before the antisense parts of the CLUSTER guide RNA have bound their target transcript. In addition, it increases the guide RNA's binding surface for ADAR enzymes without extending its antisense part. The length of the latter is an important factor for the abundance of bystander off-target events. The specificity domain (SD) of the guide RNA binds to the target sequence (TS), which represents the sequence on the target transcript that contains the target adenosine. The SD is the only part of the CLUSTER guide RNA's antisense part that is not fully modular, as its sequence depends on the sequence context around the target adenosine in the TS. In contrast the antisense parts of all other site-directed RNA editing systems are completely defined by their target sequence and do not contain any modular elements. The length of the SD, although flexible, is in most instances set to 20 nt, according to the footprint of the ADAR deaminase domain. A shorter sequence might negatively affect editing, while a longer sequence increases the chance of bystander off-target events caused by this element of the guide RNA. The Cluster of recruitment sequences (RS) is the last and most modular element of the CLUSTER guide RNA design. It consists of between 3 and 9 RS each being 15 to 20 nt long.

Supplementary Figure S3 continued. Overview of the targeting strategies of the encodable side-directed RNA editing systems that are applied in this study. Their corresponding binding sites (BS) on the target transcript can be located thousands of nucleotides distal from each other, although closer proximity is correlated with higher editing yields. The optimal RS number and length was experimentally determined. However, the rationale for the RS number was to provide at least one RS per ADAR dsRBD. The rationale for the RS length was their ability to bind their target transcript independent from the binding power of the remaining RS's at 37°C and at a reasonable GC-content. Each RS binding site is identified by an algorithm that searches for uninterrupted >15 nt sequences that contain adenosines only in the very hard to edit 5'-GAB (B = G, C; U) triplet context or that contain no adenosines at all. This selection process makes sure that bystander off-target events within the binding sites of the cluster of recruitment sequences are virtually impossible. The individual RS are connected to each other via adenosine linkers of 1-5 nt length. The corresponding spacer within the target transcript is variable and can range from zero to thousands of nucleotides, depending on the placement of each RS. The RS selection process depends on the secondary structure within the antisense part of all potential guide RNAs for a certain target transcript. All potential RS that are identified by the algorithm are recombined by our gRNA-Forge tool, folded using the ViennaRNA package, and scored for low secondary structure within the antisense part. The scoring is performed via the DBR (dot-bracket ratio) metric, which gives a higher value the more bases are unpaired in the MFE (mean free energy) structure of the guide RNA. A high DBR score thus means that most of the guide RNAs antisense part is readily available for target transcript binding, instead of engaging in unproductive folding in cis. CLUSTER guide RNAs can be circularized using the Tornado expression system. Circularization increases their stability and thus the guide RNA abundance. Consequently, this improves the editing yields. The engineering of circular CLUSTER guide RNAs is described in further detail in Extended Data Figure 4, S9, and S10. This figure contains elements from BioRender.com.

Supplementary Figure S4 continued. Characterizing the up- and downstream distance of editing suppression after protecting the first (-1, +1), second (-2, +2) or third (-3, +3) nearest neighbor sites by G·U wobble. Editing efficiencies on-target (± 0) and at bystander sites (± 1 , ± 2 , ± 3) are displayed in a heatmap fashion. The exact positioning of the respective wobble or G-A mismatch is indicated by blue and yellow frames, respectively. The design of the cis-acting RNA editing reporter and a detailed description of the evaluated sequence motifs are given below the datasets. The G·U wobble base pairs (5' and 3') enable a more precise control of bystander editing by giving stronger and more focused suppression compared to the G-A mismatches. Thus, the wobble strategy is particularly powerful to suppress bystander editing close to an on-target adenosine in A-rich codons. Data in a) – f) are shown as the mean $\pm$ s.d. of $N = 3$ biological replicates for each position in the heatmap.



Supplementary Figure S5. Individual datasets used for the meta-analysis shown in Extended Data Figure 3e. Suppression of bystander editing at nearest neighbor adenosines via G·U wobbles, G-A mismatches, or uridine-depletion using either trans-acting CLUSTER guide RNAs in **a)** and **b)** or the λN-ADAR approach in **c) – g)**. The target transcript, -amino-acid and sequence context are indicated at each bar chart. The target adenosine is green, underlined and bold. The off-target adenosine(s) is/are black and bold. **h)** Detailed notation of the different base-pairing motifs to target specific sequence motifs. Editing was performed in HeLa cells using plasmid-borne editase (λN-ADAR) and/or guide RNA (2x boxB, CLUSTER). Data in **a) - g)** are shown as the mean editing percentage ± s.d. of N = 3 biological replicates. For statistical analysis, a student t-test (two-tailed, parametric) was applied.



Supplementary Figure S6. Initial characterization of circular LEAPER guide RNAs. a) Schematic view of primer binding sites for verification of guide RNA circularization **b)** Circularization of 111 nt antisense guide RNAs targeting NUP43 and RAB7A was verified by RT-PCR and subsequent agarose gel electrophoresis. Primers were facing outwards from the central cytosine base opposite the target adenosine. Clear bands were only obtained for the circular guide RNAs but not their linear analogs. Multiple bands are visible due to rolling circle amplification during reverse transcription. **c)-d)** Circularization of guide RNAs improved NUP43 (panel c) and RAB7A (panel d) editing compared to their linear analogs up to 2-fold and was achieved both with pol-II (EF1 α) and pol-III (U6) promoters. **e)** Precise circularization between 3' and 5' ligation arm was verified by Sanger sequencing of PCR products from panel b) for both guide RNAs (NUP43 and RAB7A). Editing was performed with plasmid-borne guide RNAs and endogenous NUP43 or RAB7A in HEK293FT cells (endogenous ADAR). Data in c) and d) are shown as the mean editing percentage $\pm$ s.d. of N = 3 biological replicates.

Endogenous RAB7A 3' UTR					
Triplet context	Adenosine pos. from 5'-end (relative to target site)	U6 Linear LEAPER	U6 Circular LEAPER	Ef1α Linear LEAPER	Ef1α Circular LEAPER
GAG	1595 (-55)	2±1	1±0	2±0	1±0
GAA	1602 (-48)	2±1	6±1	1±0	1±0
AAC	1603 (-47)	3±1	25±2	1±0	7±0
GAU	1614 (-36)	1±0	1±0	1±0	1±0
CAG	1619 (-31)	4±1	15±0	2±0	7±1
GAG	1621 (-29)	1±0	2±0	1±0	1±0
UAC	1627 (-23)	26±1	45±2	12±0	17±0
CAG	1631 (-19)	6±1	16±1	2±1	4±0
GAA	1633 (-17)	1±0	4±1	1±0	1±0
AAU	1634 (-16)	7±0	19±2	4±2	5±1
GAA	1640 (-10)	2±0	5±0	1±0	1±0
AAA	1641 (-9)	10±2	34±3	5±1	10±1
AAU	1642 (-8)	6±0	26±1	2±0	8±1
CAG	1646 (-4)	1±0	3±0	2±0	2±0
UAG	1650 (±0)	54±0	68±3	23±2	33±1
CAG	1656 (+6)	2±0	7±1	2±0	3±0
UAU	1659 (+9)	21±1	43±2	11±2	14±1
UAC	1666 (+16)	3±1	42±2	2±0	15±1
CAG	1668 (+18)	1±0	2±0	2±0	2±0
UAG	1671 (+21)	2±0	45±3	2±0	13±1
GAC	1673 (+23)	1±1	0±0	2±0	0±0
CAC	1675 (+25)	1±0	3±1	2±0	2±0
CAA	1677 (+27)	3±1	13±1	3±1	4±0
AAG	1678 (+28)	4±0	25±3	3±1	6±0
GAA	1680 (+30)	1±0	0±0	1±0	0±0
AAU	1681 (+31)	2±1	4±0	2±1	1±0
UAU	1684 (+34)	9±1	31±2	8±0	4±1
UAC	1688 (+38)	3±0	4±2	4±0	4±0
UAU	1697 (+47)	1±0	26±1	1±0	2±0
CAA	1700 (+50)	1±1	1±1	1±1	1±0
AAA	1701 (+51)	2±0	2±1	3±1	3±1
AAG	1702 (+52)	1±0	2±0	1±0	1±0
GAC	1704 (+54)	1±0	0±0	0±0	1±0

Legend:

Av±Sd Target adenosine row

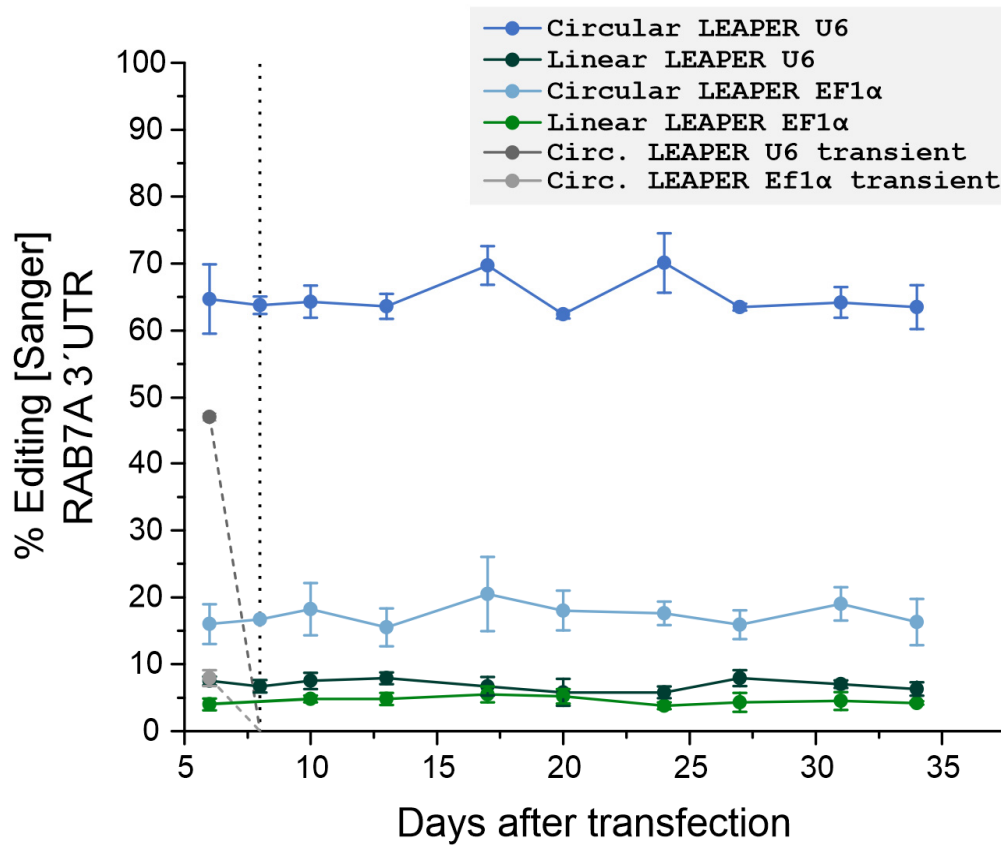
Av±Sd Off-target adenosine row

Zero **Max.** Editing yield for each target mRNA

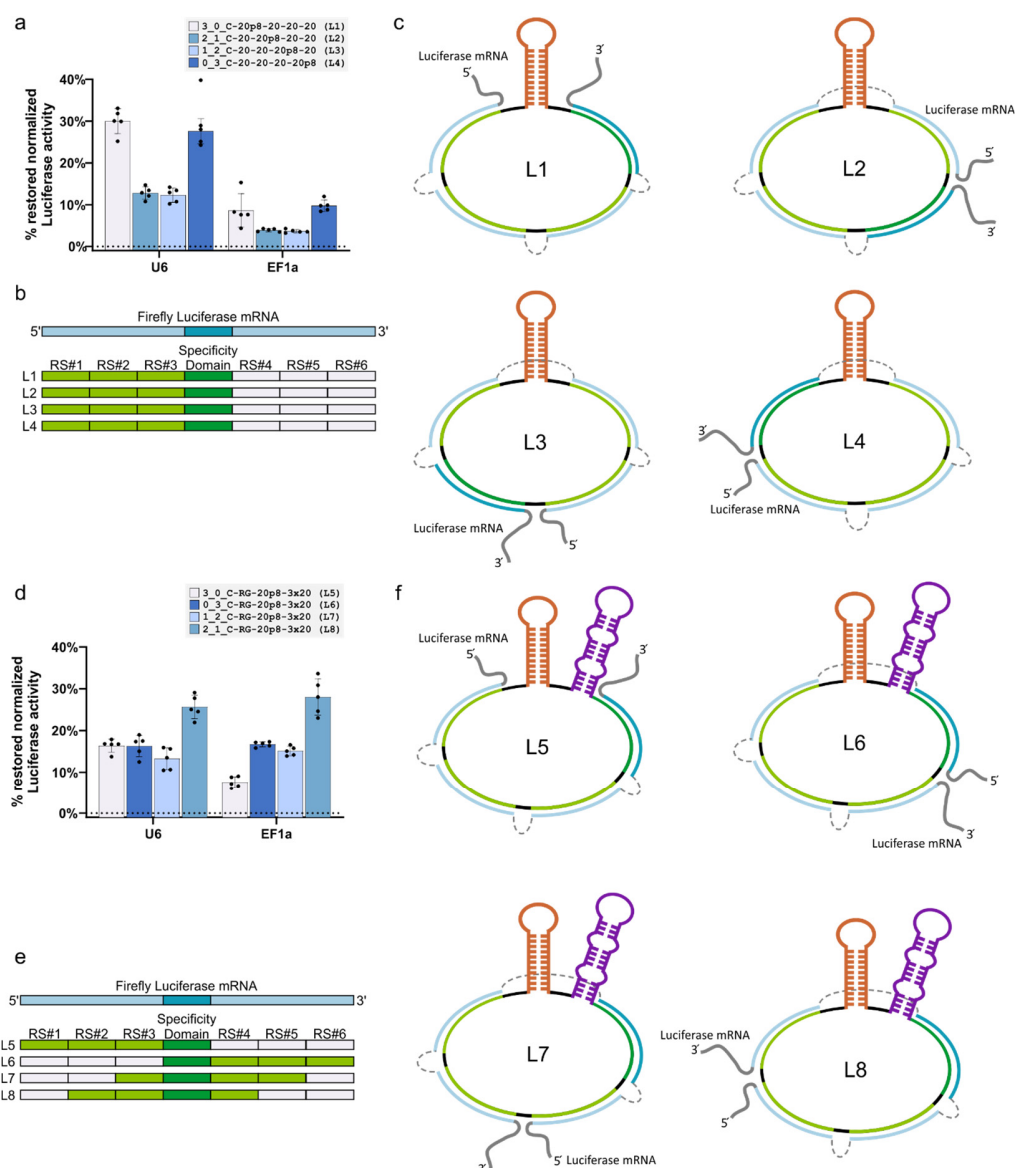
UAG = Target triplet

NAN = Off-target triplet

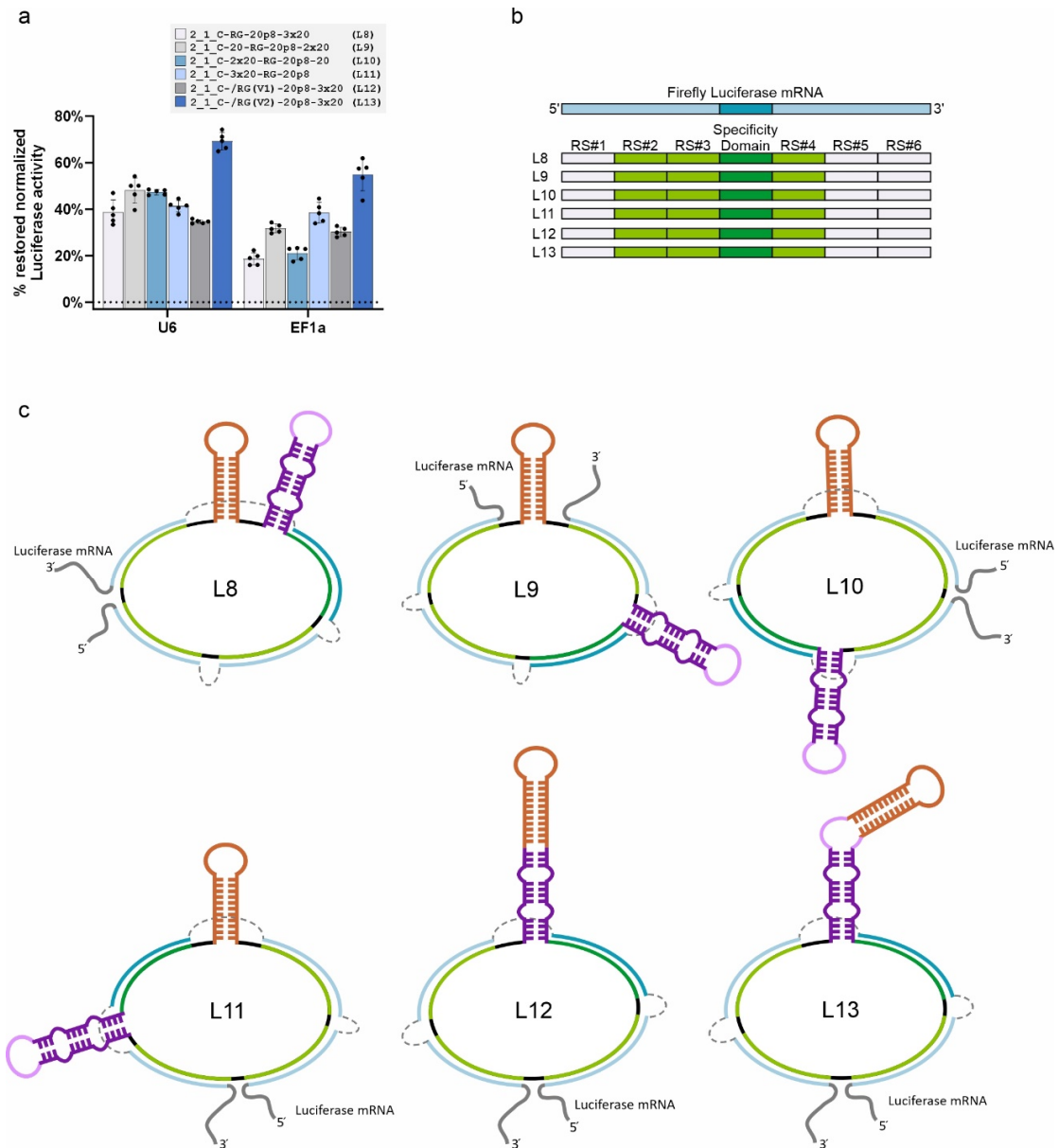
Supplementary Figure S7. Circularization of LEAPER guide RNAs increases both on-target and bystander editing. Editing heat-maps of LEAPER guide RNA binding sites within RAB7A. LEAPER guide RNAs are an unstructured, 111 nt long antisense sequence to the target mRNA with a central C-A mismatch. The triplet context for each listed bystander editing event is given with the edited adenosine highlighted in bold blue. The position of each site is given relative to the target adenosine (±0 position, in bold green and underlined). Editing was performed with plasmid-borne guide RNAs and endogenous RAB7A in HEK293FT cells (endogenous ADAR) after guide RNA expression from U6 (pol-III) or EF1α (pol-II) promoter. Data are shown as the mean editing percentage ± s.d. of N = 3 biological replicates.



Supplementary Figure S8. Circularization strongly increases editing yields of stably integrated guide RNAs. Circular or linear 111 nt LEAPER guide RNAs targeting the 3'-UTR of RAB7A were stably integrated into the genome of HeLa cells via the PiggyBac transposon system and puromycin selection for 8 days (spotted vertical line). Stable integration of circular guide RNAs increased the editing yield from both promoters, U6 and EF1α, by 8-fold and 3-fold, respectively. Editing yields stayed constant over ten passages (= 28 days) for the stably integrated circular guide RNA under both promoters. In contrast, editing yields for the linear embodiment and the transiently transfected circular guide RNAs was at the Sanger detection limit after selection. Data are shown as the mean editing percentage $\pm$ s.d. of N = 3 biological replicates per data point.

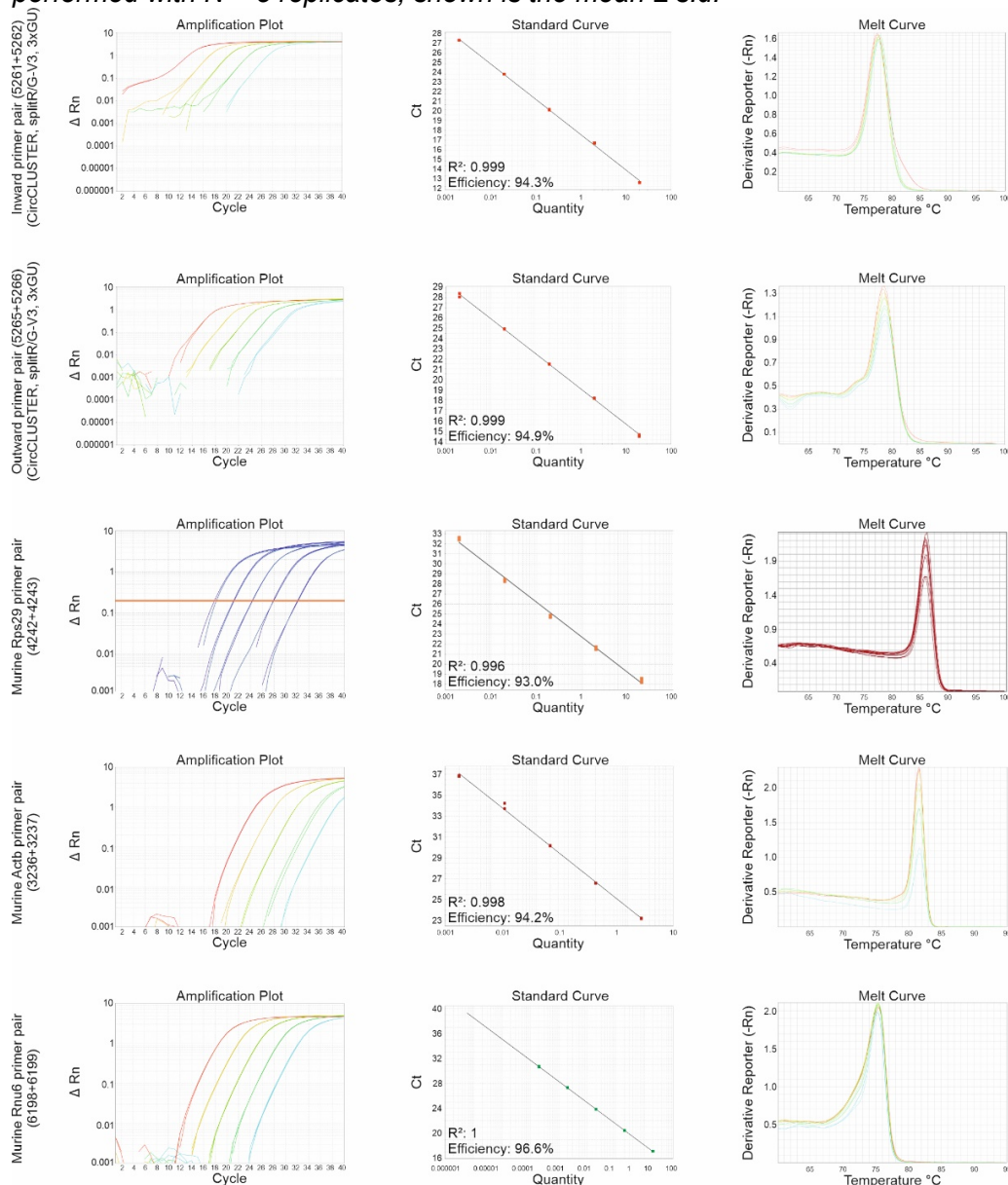


Supplementary Figure S9. First round engineering circular CLUSTER guide RNAs. **a)** Percentage of restored firefly luciferase activity normalized to renilla luciferase activity for circular guide RNAs expressed via U6 or EF1α promoter in HeLa cells. Placement of the specificity domain (see panel **b** and **c**) adjacent to the ligation stem of the Tornado expression system improves restoration of normalized Luciferase activity (L1 and L4). **d)** Introduction of an R/G-motif (see panel **e** and **f**) improves editing for EF1α expressed guide RNAs and can compensate for potential lower expression level compared to U6 expression. Placement of the mRNA exits approximately opposite of the specificity domain resulted in the highest restoration (L8). Panel **b** and **e** give a schematic view of recruitment sequences (light green) and their binding sites (light blue) relative to the target site (dark blue) on the mRNA. Panel **c** and **f** give 2-dimensional representations of guide RNAs with green = specificity domain, light green = recruitment sequence, dark blue = specificity domain binding site, light blue = recruitment sequence binding site, orange = ligation stem, dark purple = R/G-motif. All Dual Luciferase Assays were performed with N = 5 replicates, shown is the mean ± s.d.

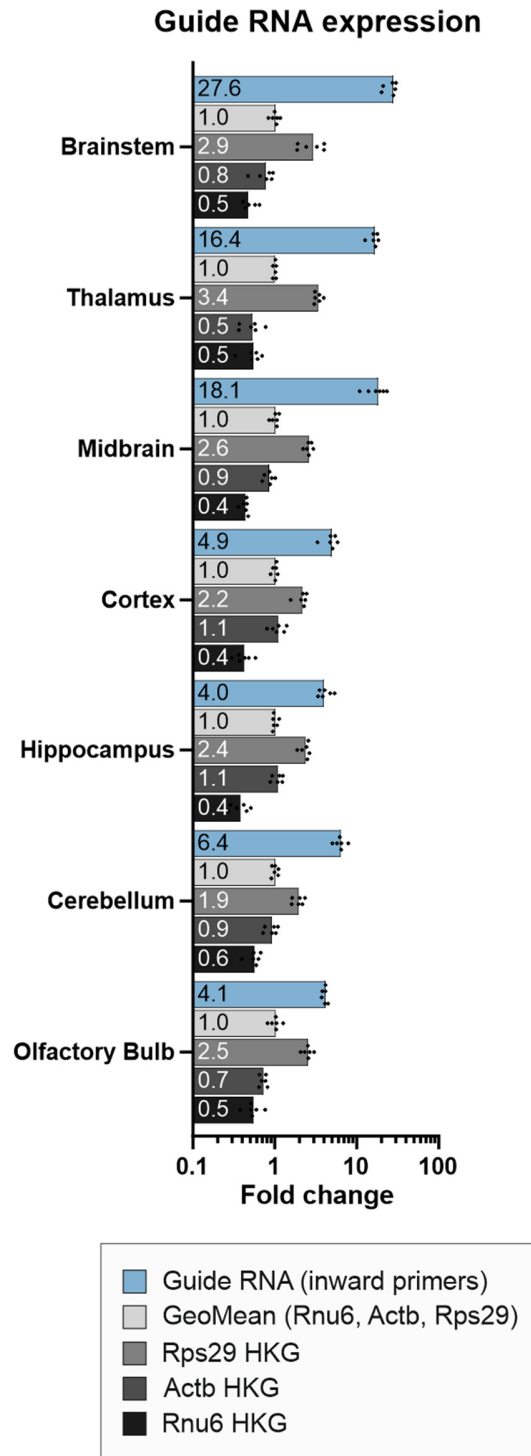


Supplementary Figure S10. Second round engineering circular CLUSTER guide RNAs. a) Percentage of restored Firefly luciferase activity normalized to Renilla luciferase activity for circular gRNAs expressed via U6 or EF1 α promoter in HeLa cells. Position of the R/G-motif and the specificity domain in relation to the ligation stem had only minor influence (L5, L9-L12). In contrast, a flexible split-R/G-motif adjacent to the ligation stem (construct L13) boosted luciferase restoration. **b)** Schematic view of recruitment sequences and their position relative to the target site for the guide RNAs shown in panel a) on the mRNA. **c)** 2-Dimensional representation of guide RNAs from panel a) bound to the target transcript; green = specificity domain, light green = recruitment sequence, dark blue = specificity domain binding site, light blue = recruitment sequence binding site, orange = ligation stem, dark purple = R/G-motif (ADAR recruitment motif), light purple = penta-loop (5 nt bulge). All dual luciferase assays were

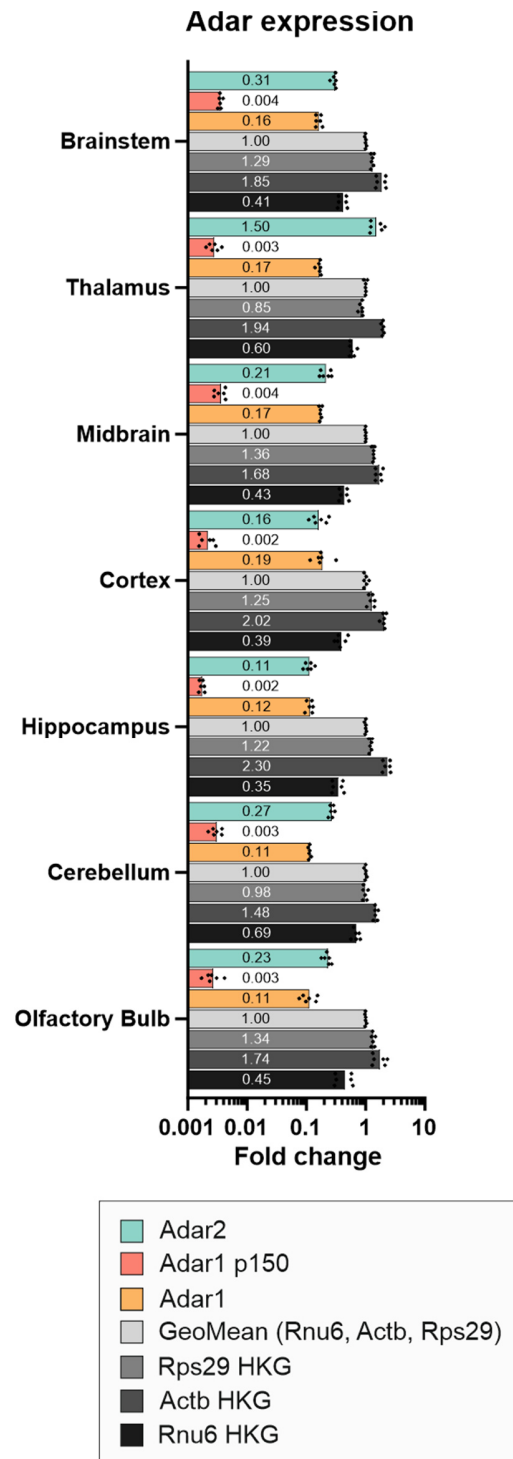
performed with $N = 5$ replicates, shown is the mean $\pm$ s.d.



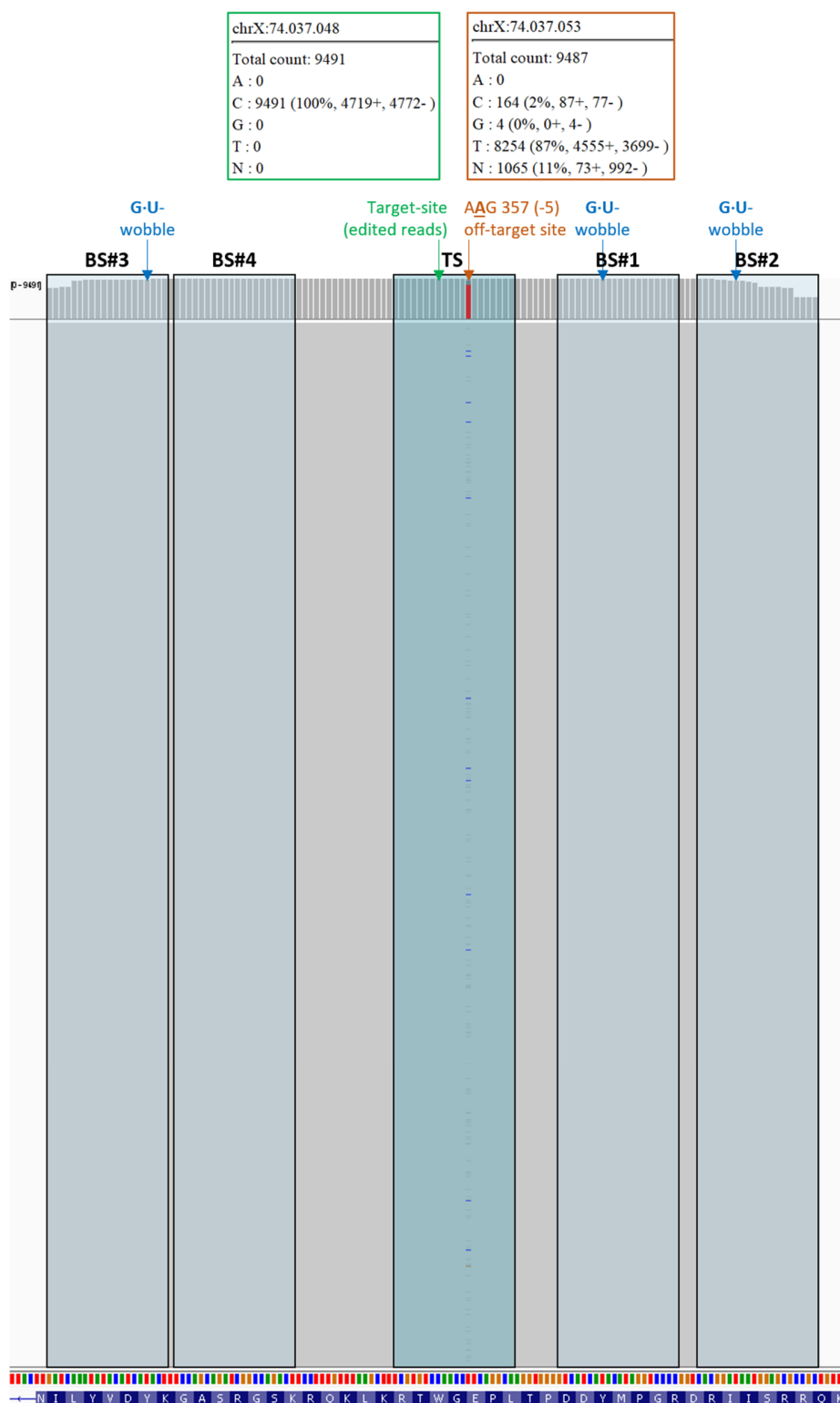
Supplementary Figure S11: Characterization of RT-qPCR primer pairs. All RT-qPCR primer pairs used (see Supplementary Table S2 & S3) were characterized here or previously [1] for their efficiency and were in the acceptable range between 80% and 110%, with good standard curve fits represented by R^2 -values >0.99 . The dilution series (20 ng, 2 ng, 0.2 ng, 0.02 ng, 0.002 ng) resulted in a linear dynamic range up to 0.002 ng cDNA template in the amplification plots, and clean single-transition melting curves. The cDNA template used for the guide RNA primer pair characterization came from HeLa cell total RNA. 0.8×10^5 HeLa cells were transfected with 1000 ng circular CLUSTER gRNA plasmid (pTS2108) and 200 ng mMecp2 W104Amber encoding plasmid per well using a plasmid to Lipofectamine-3000 ratio of 1:1.5. The template for the characterization of the three housekeeping genes murine Actb, Rps29 and Rnu6 came from primary murine brain tissue (cerebellum) of a targeting virus treated animal.



Supplementary Figure S12. Extended in-vivo guide RNA RT-qPCR dataset. In-vivo guide RNA expression in all analysed brain tissues including all used housekeeping genes. Data from $N = 2$ targeting guide RNA treated Rett syndrome animals are shown as the median of three technical replicates each. All fold changes are normalized to the geometric mean of the three murine housekeeping genes *Rnu6*, *Actb*, and *Rps29*.



Supplementary Figure S13. Extended in-vivo Adar RT-qPCR dataset. In-vivo Adar1, Adar1 p150 and Adar2 expression in all analysed brain tissues including all used housekeeping genes. Data from N = 2 targeting guide RNA treated Rett syndrome animals are shown as the median of three technical replicates each. All fold changes are normalized to the geometric mean of the three murine housekeeping genes *Rnu6*, *Actb*, and *Rps29*.



Supplementary Figure S14. Bystander off-target evaluation via amplicon sequencing.
 Excerpt of amplicon sequencing results measured in the thalamus of N = 2 circCLUSTER
 guideRNA-treated *Mecp2* W104Amber mice.

Supplementary Figure S14 continued. Bystander off-target evaluation via amplicon sequencing. The fastq files were pre-processed using Seqtk trimfq. Base-calls with QV<30 were masked as N. The base-call accuracy of the remaining bases was thus 99.9%. The alignment was performed using BWA-mem against the GRCm38/mm10 reference genome. In two successive trimming steps first soft-clippings and then all sequences outside the guide RNA binding region were removed from all reads. Trimming was performed using a custom Python script. In the next step all reads with successful on-target editing were selected by writing reads with a cytosine at index chrX:74.037.048 into a new file individually for each animal. Finally, these two files were merged using Samtools 1.9. The merged file was sorted and indexed using IGV 2.16.2. The reads are displayed in Quick Consensus Mode with the coverage allele-fraction threshold being set to 0.5%. Only one bystander off-target site was detected at the 5'-AAG-triplet at position 357 in the Mecp2 ORF (-5 position relative to the on-target site). Only 1.73% of the on-target edited reads showed bystander off-target events, almost all at the -5 site. The sites protected by G·U-wobbles showed no detectable bystander off-target editing.

Supplementary Table S1: List of applied encoded guide RNAs and ASOs. For the ease of use, the encoded guide RNAs are given as coding DNA sequences including all functional elements like e.g. split-R/G-, boxB- or direct repeat-motifs. Circular guide RNAs are given after ribozyme processing. ASOs are given as modified RNA sequences.

Sequence annotation:

Targeting sequence / Specificity domain

Target sequence (in cis-acting reporters)

Cluster of recruitment sequences

R/G-motif

Split-R/G-motif V1

Split-R/G-motif V2

Split-R/G-motif V3

BoxB-motif

DR-motif

BoxB gRNA, DR gRNA and LEAPER targeting sequence

Ligation stems after ribozyme processing

AC50-linker

mN = 2'O-methyl

* = Phosphorothioate linkage

pTS #	Guide RNA Name	Sequence 5'→3'	Used in Figure
pTS1444	Cis-acting_systematic_GU-evaluation_AAT-TTA	GGTGTGCGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGATTCAACATGCTGTAAAAACAGC ATGTTGAATCTACTG	1, S1
pTS1445	Cis-acting_systematic_GU-evaluation_AAT-TTG	GGTGTGCGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGGTTCAACATGCTGTAAAAACAG CATGTTGAATCTACTG	1, S1
pTS1446	Cis-acting_systematic_GU-evaluation_AAG-TTC	GGTGTGCGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGCTTCAACATGCTGTAAAAACAGC ATGTTGAAGCTACTG	1, S1
pTS1447	Cis-acting_systematic_GU-evaluation_AAG-TTT	GGTGTGCGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGTTTCAACATGCTGTAAAAACAGC ATGTTGAAGCTACTG	1, S1
pTS1448	Cis-acting_systematic_GU-evaluation_TAA-ATT	GGTGTGCGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGTTTCAACATGCTGTAAAAACAGC ATGTTGTAATCTACTG	1, S1
pTS1449	Cis-acting_systematic_GU-evaluation_TAA-GTT	GGTGTGCGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGTTGCAACATGCTGTAAAAACAG CATGTTGTAATCTACTG	1, S1
pTS1450	Cis-acting_systematic_GU-evaluation_TAT-ATA	GGTGTGCGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGATACAACATGCTGTAAAAACAGC ATGTTGTATCTACTG	1, S1
pTS1451	Cis-acting_systematic_GU-evaluation_TAT-GTA	GGTGTGCGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGATGCAACATGCTGTAAAAACAG CATGTTGTATCTACTG	1, S1
pTS1452	Cis-acting_systematic_GU-evaluation_TAT-ATG	GGTGTGCGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGGTACAACATGCTGTAAAAACAG CATGTTGTATCTACTG	1, S1

pTS1453	Cis-acting_systematic_GU-evaluation_TAT-GTG	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGGTGCAACATGCTGTAAAAACAG CATGTTGTATCTACTG	1, S1
pTS1454	Cis-acting_systematic_GU-evaluation_TAG-ATC	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGCTACAACATGCTGTAAAAACAG CATGTTGTAGCTACTG	1, EDF1, S1
pTS1455	Cis-acting_systematic_GU-evaluation_TAG-GTC	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGCTGCAACATGCTGTAAAAACAG CATGTTGTAGCTACTG	1, EDF1, S1
pTS1456	Cis-acting_systematic_GU-evaluation_TAG-ATT	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGTTACAACATGCTGTAAAAACAGC ATGTTGTAGCTACTG	1, EDF1, S1
pTS1457	Cis-acting_systematic_GU-evaluation_TAG-GTT	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGTTGCAACATGCTGTAAAAACAG CATGTTGTAGCTACTG	1, EDF1, S1
pTS1458	Cis-acting_systematic_GU-evaluation_TAC-ATG	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGGTACAACATGCTGTAAAAACAG CATGTTGTACCTACTG	1, S1
pTS1459	Cis-acting_systematic_GU-evaluation_TAC-GTG	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGGTGCAACATGCTGTAAAAACAG CATGTTGTACCTACTG	1, S1
pTS1460	Cis-acting_systematic_GU-evaluation_GAA-CTT	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGTTCCAACATGCTGTAAAAACAGC ATGTTGGAACCTACTG	S1
pTS1461	Cis-acting_systematic_GU-evaluation_GAA-TTT	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGTTTCAACATGCTGTAAAAACAGC ATGTTGGAACCTACTG	S1
pTS1462	Cis-acting_systematic_GU-evaluation_GAT-CTA	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGATCCAACATGCTGTAAAAACAG CATGTTGGATCTACTG	S1
pTS1463	Cis-acting_systematic_GU-evaluation_GAT-TTA	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGATTCAACATGCTGTAAAAACAGC ATGTTGGATCTACTG	S1
pTS1464	Cis-acting_systematic_GU-evaluation_GAT-CTG	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGGTCCAACATGCTGTAAAAACAG CATGTTGGATCTACTG	S1
pTS1465	Cis-acting_systematic_GU-evaluation_GAT-TTG	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGGTTCAACATGCTGTAAAAACAG CATGTTGGATCTACTG	S1
pTS1466	Cis-acting_systematic_GU-evaluation_GAG-CTC	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGCTCCAACATGCTGTAAAAACAG CATGTTGGAGCTACTG	S1
pTS1467	Cis-acting_systematic_GU-evaluation_GAG-TTC	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGCTTCAACATGCTGTAAAAACAGC ATGTTGGAGCTACTG	S1
pTS1468	Cis-acting_systematic_GU-evaluation_GAG-CTT	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGTTCCAACATGCTGTAAAAACAGC ATGTTGGAGCTACTG	S1
pTS1469	Cis-acting_systematic_GU-evaluation_GAG-TTT	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGTTTCAACATGCTGTAAAAACAGC ATGTTGGAGCTACTG	S1
pTS1470	Cis-acting_systematic_GU-evaluation_GAC-CTG	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGGTCCAACATGCTGTAAAAACAG CATGTTGGACCTACTG	S1
pTS1471	Cis-acting_systematic_GU-evaluation_GAC-TTG	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGGTTCAACATGCTGTAAAAACAG CATGTTGGACCTACTG	S1
pTS1472	Cis-acting_systematic_GU-evaluation_CAT-GTA	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGATGCAACATGCTGTAAAAACAG CATGTTGCATCTACTG	S1
pTS1473	Cis-acting_systematic_GU-evaluation_CAT-GTG	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGGTGCAACATGCTGTAAAAACAG CATGTTGCATCTACTG	S1
pTS1474	Cis-acting_systematic_GU-evaluation_CAG-GTC	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGCTGCAACATGCTGTAAAAACAG CATGTTGCAGCTACTG	1, S1
pTS1475	Cis-acting_systematic_GU-evaluation_CAG-GTT	GGTGTGCGAGAAGAGGAGGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGTTGCAACATGCTGTAAAAACAG CATGTTGCAGCTACTG	1, S1

pTS1484	Cis-acting_systematic_GU-evaluation_AAT-TGA	GGTGTCTGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGAGTCAACATGCTGTAAAAACAG CATGTTGAATCTACTG	1, S1
pTS1485	Cis-acting_systematic_GU-evaluation_AAG-TGC	GGTGTCTGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGCGTCAACATGCTGTAAAAACAG CATGTTGAAGCTACTG	S1
pTS1486	Cis-acting_systematic_GU-evaluation_TAA-AGT	GGTGTCTGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGTGACAACATGCTGTAAAAACAG CATGTTGTAACCTACTG	1, S1
pTS1487	Cis-acting_systematic_GU-evaluation_TAT-AGA	GGTGTCTGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGAGACAACATGCTGTAAAAACAG CATGTTGTATCTACTG	1, S1
pTS1488	Cis-acting_systematic_GU-evaluation_TAG-AGC	GGTGTCTGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGCGACAACATGCTGTAAAAACAG CATGTTGTAGCTACTG	1, EDF1, S1
pTS1489	Cis-acting_systematic_GU-evaluation_TAC-AGG	GGTGTCTGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGGGACAACATGCTGTAAAAACAG CATGTTGTACCTACTG	1, S1
pTS1490	Cis-acting_systematic_GU-evaluation_GAA-CGT	GGTGTCTGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGTGCCAACATGCTGTAAAAACAG CATGTTGGAACCTACTG	S1
pTS1491	Cis-acting_systematic_GU-evaluation_GAT-CGA	GGTGTCTGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGAGCCAACATGCTGTAAAAACAG CATGTTGGATCTACTG	S1
pTS1492	Cis-acting_systematic_GU-evaluation_GAG-CGC	GGTGTCTGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGCGCCAACATGCTGTAAAAACAG CATGTTGGAGCTACTG	S1
pTS1493	Cis-acting_systematic_GU-evaluation_GAC-CGG	GGTGTCTGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGGGCCAACATGCTGTAAAAACAG CATGTTGGACCTACTG	S1
pTS1494	Cis-acting_systematic_GU-evaluation_CAT-GGA	GGTGTCTGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGAGGCAACATGCTGTAAAAACAG CATGTTGCATCTACTG	S1
pTS1495	Cis-acting_systematic_GU-evaluation_CAG-GGC	GGTGTCTGAGAAGAGGAGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACCAGTAGCGCAACATGCTGTAAAAACAG CATGTTGCAGCTACTG	S1
pTS1909	Cis-acting_NN_ttaAgtt-aatCcaa	CCATATATATTAAGTTATCGGGTGTCTGAGAAGAGGAGAGAACAAT ATGCTAAATGTTGTTCTCGTCTCCTCGACACCAGATAACCTAA TATATATGG	EDF3, S4
pTS1910	Cis-acting_NN_ttaAgtt-aGtCcaa	CCATATATATTAAGTTATCGGGTGTCTGAGAAGAGGAGAGAACAAT ATGCTAAATGTTGTTCTCGTCTCCTCGACACCAGATAACCTGA TATATATGG	EDF3, S4
pTS1911	Cis-acting_NN_ttaAgtt-GatCcaa	CCATATATATTAAGTTATCGGGTGTCTGAGAAGAGGAGAGAACAAT ATGCTAAATGTTGTTCTCGTCTCCTCGACACCAGATAACCTAG TATATATGG	S4
pTS1912	Cis-acting_NN_ttaAgtt-aaGCcaa	CCATATATATTAAGTTATCGGGTGTCTGAGAAGAGGAGAGAACAAT ATGCTAAATGTTGTTCTCGTCTCCTCGACACCAGATAACCGAA TATATATGG	EDF3, S4
pTS1913	Cis-acting_NN_tttAatt-aaaCtaa	CCATATATATTTAATTATCGGGTGTCTGAGAAGAGGAGAGAACAAT ATGCTAAATGTTGTTCTCGTCTCCTCGACACCAGATAATCAAA TATATATGG	EDF3, S4
pTS1914	Cis-acting_NN_tttAatt-aaaCtGa	CCATATATATTTAATTATCGGGTGTCTGAGAAGAGGAGAGAACAAT ATGCTAAATGTTGTTCTCGTCTCCTCGACACCAGATAGTCAAA TATATATGG	EDF3, S4
pTS1915	Cis-acting_NN_tttAatt-aaaCtaG	CCATATATATTTAATTATCGGGTGTCTGAGAAGAGGAGAGAACAAT ATGCTAAATGTTGTTCTCGTCTCCTCGACACCAGATGATCAAA TATATATGG	S4
pTS1916	Cis-acting_NN_tttAatt-aaaCGaa	CCATATATATTTAATTATCGGGTGTCTGAGAAGAGGAGAGAACAAT ATGCTAAATGTTGTTCTCGTCTCCTCGACACCAGATAAGCAAA TATATATGG	EDF3, S4
pTS1917	Cis-acting_2nd-NN_tatAaat-ataCtta	CCATATATATATAAATATCGGGTGTCTGAGAAGAGGAGAGAACAAT ATGCTAAATGTTGTTCTCGTCTCCTCGACACCAGATATTCATA TATATATGG	S4
pTS1918	Cis-acting_2nd-NN_tatAaat-ataCttG	CCATATATATATAAATATCGGGTGTCTGAGAAGAGGAGAGAACAAT ATGCTAAATGTTGTTCTCGTCTCCTCGACACCAGATGTTTATA TATATATGG	S4
pTS1919	Cis-acting_2nd-NN_tatAaat-ataCtGa	CCATATATATATAAATATCGGGTGTCTGAGAAGAGGAGAGAACAAT ATGCTAAATGTTGTTCTCGTCTCCTCGACACCAGATAGTCATA TATATATGG	S4

pTS1920	Cis-acting_2nd- NN_taaAgat-attCcta	CCATATATATAAAGATATCGGGTGTCTGAGAAGAGGAGAACAA TATGCTAAATGTTGTTCTCGTCTCCTCGACACC CGATATCCTT ATATATATGG	S4
pTS1921	Cis-acting_2nd- NN_taaAgat-GttCcta	CCATATATATAAAGATATCGGGTGTCTGAGAAGAGGAGAACAA TATGCTAAATGTTGTTCTCGTCTCCTCGACACC CGATATCCTT GTATATATGG	S4
pTS1922	Cis-acting_2nd- NN_taaAgat-aGtCcta	CCATATATATAAAGATATCGGGTGTCTGAGAAGAGGAGAACAA TATGCTAAATGTTGTTCTCGTCTCCTCGACACC CGATATCCTG ATATATATGG	S4
pTS1923	Cis-acting_3nd- NN_taatAaaat-attaCtta	CCATATATATAAAGATATCGGGTGTCTGAGAAGAGGAGAACAA ATGCTAAATGTTGTTCTCGTCTCCTCGACACC CGAATTCATT AATATATGG	S4
pTS1924	Cis-acting_3nd- NN_taatAaaat-attaCtttG	CCATATATATAAAGATATCGGGTGTCTGAGAAGAGGAGAACAA ATGCTAAATGTTGTTCTCGTCTCCTCGACACC CGAGTTTCATT AATATATGG	S4
pTS1925	Cis-acting_3nd- NN_taatAaaat-attaCttGa	CCATATATATAAAGATATCGGGTGTCTGAGAAGAGGAGAACAA ATGCTAAATGTTGTTCTCGTCTCCTCGACACC CGAAGTTTCATT AATATATGG	S4
pTS1926	Cis-acting_3nd- NN_taaaAgaat-atttCctta	CCATATATATAAAGATATCGGGTGTCTGAGAAGAGGAGAACAA TATGCTAAATGTTGTTCTCGTCTCCTCGACACC CGAATTCCTT TAATATATGG	S4
pTS1927	Cis-acting_3nd- NN_taaaAgaat-GtttCctta	CCATATATATAAAGATATCGGGTGTCTGAGAAGAGGAGAACAA TATGCTAAATGTTGTTCTCGTCTCCTCGACACC CGAATTCCTT TGATATATGG	S4
pTS1928	Cis-acting_3nd- NN_taaaAgaat- aGttCctta	CCATATATATAAAGATATCGGGTGTCTGAGAAGAGGAGAACAA TATGCTAAATGTTGTTCTCGTCTCCTCGACACC CGAATTCCTT GAATATATGG	S4
pTS1717	AHI1_LEAPER_gRNA	GTGAACGTCAAACGTCTCGGACCAATATGGCAGAATCTTCTCT CATCTCAACTTTCCATATCCGATCATGGAATCATAGCATCCT GTAACACTAGCTCTCTTACAGCTGG	2
pTS1758	AHI1_LEAPER_GU_at GU_amenable_sites_gR NA	GTGAACGTCAAACGTCTCGGACCAATGTGGCAGAATCTTCTCT CATCTCAACTTTCCATGTCCGTGTCTGGAATCATGGCATCCT GTGACTGCTGGCTCTCTTGCAGCTGG	2
pTS1791	AHI1_LEAPER_GA_at GU_amenable_sites_gR NA	GTGAACGTCAAACGTCTCGGACCAAGAGGGCAGAATCTTCTCT CATCTCAACTTTCCAGATCCGATCATGGAATCAGAGCATCCT GGAACGACGAGCTCTCTGACAGCTGG	2
pTS1757	AHI1_LEAPER_GA_at_ all_off- target_sites_gRNA	GTGAACGTCAAACGTCTCGGACCAAGAGGGCAGAATCGTCGC GCATCGCAACGGTCCAGATCCGATCATGGAATCAGAGCATC CGGGAACGACGAGCTCTCTGACAGCTGG	2
pTS1818	AHI1_LEAPER_GU&GA _at_all_off- target_sites_gRNA	GTGAACGTCAAACGTCTCGGACCAATGTGGCAGAATCGTCGCG CATCTCAGCTTTCCATGTCCGTGTCTGGAATCATGGCATCC GGTGACTGCTGGCTCTCTGTCAGCTGG	2
pTS1718	BMPR2_LEAPER_gRN A	GTGAAGATAAGCCAGTCTCTAGTAACAGAATGAGCAAGACG GCAAGAGCTTACCCAGTCACCTTGTGTGGAGACTTAAATACCTG CATAAAGATCCATTGGGATAGTACTC	2
pTS1752	BMPR2_LEAPER_GU_ at_GU_amenable_sites_ gRNA	GTGAAGATAAGCCAGTCTCTGGTGACAGAATGAGCAAGACG GCAAGAGCTTGCCAGTCACCTTGTGTGGAGACTTGAATGCTT GCATGAAGATCCGTTGGGATGGTGCTC	2
pTS1753	BMPR2_LEAPER_GA_ at_GU_amenable_sites_ gRNA	GTGAAGATAAGCCAGTCTCTGAGGAACAGAATGAGCAAGACG GCAAGAGCTGACCCAGTCACCTTGTGTGGAGACTGAAAGACTT GCAGAAAGATCCAGTGGGAGAGGACTC	2
pTS1751	BMPR2_LEAPER_GA_ at_all_off- target_sites_gRNA	GTGAAGATAAGCCAGTCTCTGGTGACAGAATGAGCAAGACG GCAAGAGCGGACCCAGTCACGGGTGTGGAGACGGAAAGACG GGCAGAAAGATCCAGTGGGAGAGGACTC	2
pTS1827	BMPR2_LEAPER_GU& GA_at_all_off- target_sites_gRNA	GTGAAGATAAGCCAGTCTCTGGTGACAGAATGAGCAAGACG GCAAGAGCGGACCCAGTCACGGGTGTGGAGACGTGAATGCG GGCATGAAGATCCGTTGGGATGGTGCTC	2
pTS1760	COL3A1_LEAPER_gRN A	CATATTACAGAATACCTTGATAGCATCCAATTTGCATCCTTGG TTAGGGTCAACCCAGTATTCTCCACTCTTGAGTTCAGGATGG CAGAATTTCAAGTCTCTGCAGTTTCT	2
pTS1821	COL3A1_LEAPER_GU_ at_GU_amenable_sites_ gRNA	CATATTACAGAATACCTTGATAGCATCCAGTTTGCATCCTTGG TTAGGGTCAACCCAGTATTCTCCACTCTTGAGTTCAGGGTGG CAGAGTTTCAGGTCTCTGCAGTTTCT	2
pTS1822	COL3A1_LEAPER_GA_ at_GU_amenable_sites_ gRNA	CATATTACAGAATACCTTGAGAGCATCCAAGTTGCATCCTTGG TTAGGGTCAACCCAGGAGTCTCCACTCTTGAGTTCAGGAGGG CAGAAGTTTCAGGTCTCTGCAGTTTCT	2
pTS1823	COL3A1_LEAPER_GA_ at_all_off- target_sites_gRNA	CATATTACAGAATACCTTGAGAGCATCCAAGGTGCATCCTTGG TTAGGGTCAACCCAGGAGTCTCCACTCGTGAGTTCAGGAGGG CAGAAGGTTCAGGTCTCTGGCAGGTTCT	2

pTS1824	COL3A1_LEAPER_GU & GA_at_all_off-target_sites_gRNA	CATATTACAGAATACCTTGGTAGCATCCAGTGTGCATCCTTGGTTAGGGTCAACCCAGTGTCTCCACTCGTGAGTTCAGGGTGGCAGAGTGTCTAGGTCTCTGCAGGTTCT	2
pTS1193	RAB7A_LEAPER_gRNA	GTCTTTGATAAAAGGCGTACATAATTCTTGTGTCTACTGTACAGAATACTGCCGCCAGCTGGATTTCCCAATTCTGAGTAACACTCTGCAATCCAAACAGGGTTCAACCCT	EDF2
pTS1801	RAB7A_LEAPER_GU_at GU amenable sites_gRNA	GTCTTTGATAAAAGGCGTGCCTAGTTCTTGTGTCTGCTGTGCAGAATGCTGCCGCCAGCTGGGTTTCCAGTTCTGAGTGACACTCTGCAATCCAAACAGGGTTCAACCCT	EDF2
pTS1802	RAB7A LEAPER GA_at GU amenable_sites_gRNA	GTCTTTGAGAAAAGGCGGACAGAAGTCTTGTGTGCGACTGGACAGAAGACTGCCGCCAGCTGGAGTTCCCAAGTCTGAGGAACA CTCTGCAATCCAAACAGGGTTCAACCCT	EDF2
pTS1216	RAB7A_LEAPER_GA_at_all_off-target_sites_gRNA	GTCTTTGAGAAAAGGCGGACAGAAGTCTGGTGTGACGGGACAGAAGACGGCCGCCAGCTGGAGGGCCCAAGGCGGAGGAACTCGGCAATCCAAACAGGGGGCAACCCT	EDF2
pTS1803	RAB7A_LEAPER_GU& GA_at_all_off-target_sites_gRNA	GTCTTTGATAAAAGGCGTGCCTAGTTCTGGGTGTCTGCTGTGCAGAATGCCGCCGCCAGCTGGGTGCCCGAGTGCGGAGTGACACGCGGCAATCCAAACAGGGGGCAACCCT	EDF2
pTS1964	mMecp2_LEAPER_Linear_gRNA	TACATCATACTTTCCAGCAGATCGGCCAGACTTCCTTTGTTTAACTTTCTGTCTCAACCTTCAGGCAAGGTGGGGTCATCATACATAGGTCCCCGGTCACGGATAATGGA	EDF5
pTS2031	mMecp2_LEAPER_Circular_gRNA	AACCATGCCGACTGATGGCAGTACATCATACTTTCCAGCAGATCGGCCAGACTTCCTTTGTTTAAAGCTTTCTGTCTCAACCTTCAGGCAAGGTGGGGTCATCATACATAGGTCCCCGGTCACGGATAATGGACTGCCATCAGTCGGCGTGGACTGTAG	5, EDF5
pTS2529	mMecp2_LEAPER_Circular_gRNA_GA_at_GU_ amenable_sites	AACCATGCCGACTGATGGCAGTACATCATACTTTCCAGCAGATCGGCCAGACTTCCTTTGTTTAAAGCTTTCTGTCTCAACCTTCAGGCAAGGTGGGGTCATCAgACAgAGGTCCCCGGTCACGGAAATGGAATGGACTGCCATCAGTCGGCGTGGACTGTAG	5, EDF5
pTS2530	mMecp2_LEAPER_Circular_gRNA_Uridine-depletion_at_GU_ amenable_sites	AACCATGCCGACTGATGGCAGTACATCATACTTTCCAGCAGATCGGCCAGACTTCCTTTGTTTAAAGCTTTCTGTCTCAACCTTCAGGCAAGGTGGGGTCATCAACAAGGTCCCCGGTCACGGAAATGGAATGGACTGCCATCAGTCGGCGTGGACTGTAG	5, EDF5
pTS2033	mMecp2_LEAPER_Circular_GA_at_all_off-target_sites_gRNA	AACCATGCCGACTGATGGCAGTACATCATACTTTCCAGCAGATCGGCCAGACTTCCTTTGTTTAAAGCTTTCTGTCTCAACCTTCAGGCAAGGTGGGGTCATCAGACAGAGGTCCCCGGTCACGGAAATGGAATGGACTGCCATCAGTCGGCGTGGACTGTAG	5, EDF5
pTS2034	mMecp2_LEAPER_Circular_U-depletion_gRNA	AACCATGCCGACTGATGGCAGTACATCATACTTTCCAGCAGATCGGCCAGACTTCCTTTGTTTAAAGCTTTCTGTCTCAACCTTCAGGCAAGGTGGGGTCATCAACAAGGTCCCCGGTCACGGAAATGGAATGGACTGCCATCAGTCGGCGTGGACTGTAG	5, EDF5
pTS2035	mMecp2_LEAPER_Circular_GU-only_gRNA	AACCATGCCGACTGATGGCAGTACATCATACTTTCCAGCAGATCGGCCAGACTTCCTTTGTTTAAAGCTTTCTGTCTCAACCTTCAGGCAAGGTGGGGTCATCATgCATgGGTCCCCGGTCACGGATgATGGAATGGACTGCCATCAGTCGGCGTGGACTGTAG	5, EDF5
pTS2037	mMecp2_LEAPER_Circular_GU&U-depletion_gRNA	AACCATGCCGACTGATGGCAGTACATCATACTTTCCAGCAGATCGGCCAGACTTCCTTTGTTTAAAGCTTTCTGTCTCAACCTTCAGGCAAGGTGGGGTCATCATgCATgGGTCCCCGGTCACGGATgATGGAATGGACTGCCATCAGTCGGCGTGGACTGTAG	5, EDF5
pTS2036	mMecp2_LEAPER_Circular_GU&GA_at_all_off-target_sites_gRNA	AACCATGCCGACTGATGGCAGTACATCATACTTTCCAGCAGATCGGCCAGACTTCCTTTGTTTAAAGCTTTCTGTCTCAACCTTCAGGCAAGGTGGGGTCATCATGCATGGGTCCCCGGTCACGGATGATGGAATGGACTGCCATCAGTCGGCGTGGACTGTAG	5, EDF5
pTS2043	mMecp2_W104Amber_Linear_3x20-20p8_RG-V21 (V45 mMecp2 gRNA)	GGTGTGCGAGAAGAGGAGAACAATATCTTTCTATGTTGTTCTCTCTCTCGACACCTCGTGTCCAACCTTCAGGCAAAAGTCATCATATAGGTCCCCAAACACGGATAATGGAGCGCCGCAAATTGGGGAAGCCGAGGCTTC	EDF5
pTS2058	mMecp2_W104Amber_Linear_3x20-20p8_RG-V21 GU-wobbles (V45.2 mMecp2 gRNA)	GGTGTGCGAGAAGAGGAGAACAATATGCTAAATGTTGTTCTCTCTCTCGACACCTCGTGTCCAACCTTCAGGCAAAAGTCATCATATAGGTCCCCAAACACGGATGATGGAGCGCCGCAAATTGGGGAAGCCGAGGCTTC	EDF5
pTS2023	mMecp2_W104Amber_Circular_6x20-20p8_NoRG (V37 mMecp2 gRNA)	AACCATGCCGACTGATGGCAGAAAAATCAAAATCATTAGGGTCCAAAAATCAAAGTATGCAATCAATTAATCCAGCAGATCGGCCAGACTAAAATCGTGTCCAACCTTCAGGCAAAAGTCATCATATAGGTCCCCAAACACGGATAATGGAGCGCCGCAAATTGGGGAAGCCGAGGCTTCAAAACTGCCATCAGTCGGCGTGGACTGTAG	EDF5
pTS2055	mMecp2_W104Amber_Circular_6x20-	AACCATGCCGACTGATGGCAGAAAAATCAAAATCATTAGGGTCCAAAAATCAAAGTGTGCAATCAATTAATCCAGCAGATCGG	EDF5

	20p8_NoRG_GU-wobbles (V37.2 mMecp2 gRNA)	CCAGACTAAA TCGTGTCCAACCTTCAGGCA AAAAGTCATCATAC ATAGGTCCCCAAACACGGATGATGGAGCGCCGCAAATTGGG GGAAGCCGAGGCTTCAAAAA CTGCCATCAGTCGGCGTGGAC TGTAG	
pTS2228	mMecp2_W104Amber_Linear_4x20-20p8_Split-RG-V3_GU-wobbles (Linear V27.2.4 mMecp2 gRNA)	G CATGTTGTTCTCGTCTCCTCGACACC TCGTGTCCAACCTTCA GGCA AAAAGTCATCATGCATAGGTCCCCAAACACGGATGATG GAGCGCCGCAAAGATCAAATATACATCGTACTAAATCCAGCA GATCGGCCAGACTAAAA GGTGTGCGAGAAGAGGAGAACAATA TCCTT	EDF5-6
pTS2013	mMecp2_W104Amber_Circular_4x20-20p8_Split-RG-V2 (V27 mMecp2 gRNA)	AACCATGCCGACTGATGGCAG AATGTTGTTCTCGTCTCCTCG ACACC TCGTGTCCAACCTTCAGGCA AAAAGTCATCATACATAG GTCCCCAAACACGGATAATGGAGCGCCGCAAAGATCAAATAT ACATCATACTAAATCCAGCAGATCGGCCAGACTAAAA GGTG TCGAGAAGAGGAGAACAATATGCTA CTGCCATCAGTCGGCGT GGACTGTAG	EDF5
pTS2336	mMecp2_W104Amber_Circular_4x20-20p8_Split-RG-V3_gRNA-V1 (Previous Filter)	AACCATGCCGACTGATGGCAG CATGTTGTTCTCGTCTCCTCG ACACC TCGTGTCCAACCTTCAGGCA AAAATCCTCCAGTCTCTC CTCCTCAAACCTCCGCTCGGCGCGGCGGCAAACCTCTCTCG GTCACGGGCGAAATCCTCAGAGCTCTCAGGCTCAAAA GGTG TCGAGAAGAGGAGAACAATATCTTT CTGCCATCAGTCGGCGT GGACTGTAG	4
pTS2337	mMecp2_W104Amber_Circular_4x20-20p8_Split-RG-V3_gRNA-V2 (Previous Filter)	AACCATGCCGACTGATGGCAG CATGTTGTTCTCGTCTCCTCG ACACC TCGTGTCCAACCTTCAGGCA AAAATCCTCCCTCGCC TCCTCCAAACCTCCGCTCGGCGCGGCGGCAAATCCTCAGAG CTCTCAGGCTCAAAGGAGGGGCTCCCTCTCCAGAAAA GGT GTCGAGAAGAGGAGAACAATATCTTT CTGCCATCAGTCGGCG TGGACTGTAG	4
pTS2051	mMecp2_W104Amber_Circular_4x20-20p8_Split-RG-V3_gRNA-V3 (Latest Filter)	AACCATGCCGACTGATGGCAG CATGTTGTTCTCGTCTCCTCG ACACC TCGTGTCCAACCTTCAGGCA AAAAGTCATCATACATAG GTCCCCAAACACGGATAATGGAGCGCCGCAAAGATCAAATAT ACATCATACTAAATCCAGCAGATCGGCCAGACTAAAA GGTG TCGAGAAGAGGAGAACAATATCTTT CTGCCATCAGTCGGCGT GGACTGTAG	4, 5, EDF5
pTS2082	mMecp2_W104Amber_Circular_4x20-20p8_Split-RG-V3_2xGU-wobbles (V27.2.2 mMecp2 gRNA)	AACCATGCCGACTGATGGCAG CATGTTGTTCTCGTCTCCTCG ACACC TCGTGTCCAACCTTCAGGCA AAAAGTCATCATgCATAG GTCCCCAAACACGGATgATGGAGCGCCGCAAAGATCAAATAT ACATCATACTAAATCCAGCAGATCGGCCAGACTAAAA GGTG TCGAGAAGAGGAGAACAATATCTTT CTGCCATCAGTCGGCGT GGACTGTAG	EDF5
pTS2108 / Targeting virus	mMecp2_W104Amber_Circular_4x20-20p8_Split-RG-V3_3xGU-wobbles (V27.2.4 mMecp2 gRNA)	AACCATGCCGACTGATGGCAG CATGTTGTTCTCGTCTCCTCG ACACC TCGTGTCCAACCTTCAGGCA AAAAGTCATCATGCATA GGTCCCCAAACACGGATGATGGAGCGCCGCAAAGATCAAATA TACATCGTACTAAATCCAGCAGATCGGCCAGACTAAAA GGT GTCGAGAAGAGGAGAACAATATCTTT CTGCCATCAGTCGGCG TGGACTGTAG	5, 6, EDF5-9, S11-14
pTS2191 / Non-targeting virus	Scrambled_mMecp2_W104Amber_Circular_4x20-20p8_Split-RG-V3 (Scrambled V27.2.4 mMecp2 gRNA)	AACCATGCCGACTGATGGCAG CATGTTGTTCTCGTCTCCTCG ACACC GGGCTTATACCCGACCTACT AAAAGGACTGTCTCGAC CTCTACAAAAGGGCGACCCCGATGACAGGTAAGTTAACATA CTCCTAGATAAAAAGCGACACCGCTGCTGACATAAAAA GGT GTCGAGAAGAGGAGAACAATATCTTT CTGCCATCAGTCGGCG TGGACTGTAG	6, EDF7-8
pTS2109	mMecp2_W104Amber_Circular_4x20-20p8_Split-RG-V3_3xGU-wobbles (V27.2.5 mMecp2 gRNA)	AACCATGCCGACTGATGGCAG CATGTTGTTCTCGTCTCCTCG ACACC TCGTGTCCAACCTTCAGGCA AAAAGTCATCATgCATAG GTCCCCAAACACGGATgATGGAGCGCCGCAAAGATCAAATAT ACATCATgCTAAATCCAGCAGATCGGCCAGACTAAAA GGTGT CGAGAAGAGGAGAACAATATCTTT CTGCCATCAGTCGGCGTG GA CTGTAG	EDF5
pTS2521	mMecp2_W104Amber_Circular_4x20-20p8_Split-RG-V3_3xGU-wobbles_1xGA-mismatch (V27.2.6 mMecp2 gRNA)	AACCATGCCGACTGATGGCAG CATGTTGTTCTCGTCTCCTCG ACACC TCGTGTCCAACCGTCAGGCA AAAAGTCATCATGCATA GGTCCCCAAACACGGATGATGGAGCGCCGCAAAGATCAAATA TACATCGTACTAAATCCAGCAGATCGGCCAGACTAAAA GGT GTCGAGAAGAGGAGAACAATATCTTT CTGCCATCAGTCGGCG TGGACTGTAG	5, EDF5
pTS2522	mMecp2_W104Amber_Circular_4x20-20p8_Split-RG-V3_3xGU-wobbles_1xUridine-	AACCATGCCGACTGATGGCAG CATGTTGTTCTCGTCTCCTCG ACACC TCGTGTCCAACCTTCAGGCA AAAAGTCATCATGCATAG GTCCCCAAACACGGATGATGGAGCGCCGCAAAGATCAAATAT ACATCGTACTAAATCCAGCAGATCGGCCAGACTAAAA GGTG	5, EDF5

	depletion (V27.2.7 mMecp2 gRNA)	TCGAGAAGAGGAGAACAATATCTTTCTGCCATCAGTCGGCGT GGACTGTAG	
pTS1885	AHI1_2xBoxB_10(3)-29p15-(3)10_gRNA	GCAGAATCTTGGCCCTGAAAAAGGGCCTCATCTCAACTTTCC ATATCCGTATCATGGCCCTGAAAAAGGGCCTCATAGCATC	3
pTS1969	AHI1_2xBoxB_10(3)-29p15-(3)10_GU_at_GU_amenable_sites_gRNA	GCAGAATCTTGGCCCTGAAAAAGGGCCTCATCTCAACTTTCC ATGTCCGTGTCATGGCCCTGAAAAAGGGCCTCATAGCATC	3
pTS1968	AHI1_2xBoxB_10(3)-29p15-(3)10_GA_at_GU_amenable_sites_gRNA	GCAGAATCTTGGCCCTGAAAAAGGGCCTCATCTCAACTTTCC AGATCCGGATCATGGCCCTGAAAAAGGGCCTCATAGCATC	3
pTS1967	AHI1_2xBoxB_10(3)-29p15-(3)10_GA_at_all_off-target_sites_gRNA	GCAGAATCTTGGCCCTGAAAAAGGGCCTCATCGCAACGGTCC AGATCCGGATCATGGCCCTGAAAAAGGGCCTCATAGCATC	3
pTS1970	AHI1_2xBoxB_10(3)-29p15-(3)10_GU&GA_at_all_off-target_sites_gRNA	GCAGAATCTTGGCCCTGAAAAAGGGCCTCATCGCAACGGTCC ATGTCCGTGTCATGGCCCTGAAAAAGGGCCTCATAGCATC	3
pTS1973	AHI1_DR_gRNA	CTCTCATCTCAACTTTCCATATCCGTATCATGGAATCATAGCA TCCTGTAA GTTGGAAGGTCCAGTTTGAGGGGCTATTACA AC	3
pTS1976	AHI1_DR_GU_at_GU_amenable_sites_gRNA	CTCTCATCTCAACTTTCCATGTCCGTGTCATGGAATCATAGCA TCCTGTAA GTTGGAAGGTCCAGTTTGAGGGGCTATTACA AC	3
pTS1975	AHI1_DR_GA_at_GU_amenable_sites_gRNA	CTCTCATCTCAACTTTCCAGATCCGGATCATGGAATCATAGCA TCCTGTAA GTTGGAAGGTCCAGTTTGAGGGGCTATTACA AC	3
pTS1974	AHI1_DR_GA_at_all_off-target_sites_gRNA	CTCTCATCTCAACGGTCCAGATCCGGATCATGGAATCATAGC ATCCTGTAA GTTGGAAGGTCCAGTTTGAGGGGCTATTAC AAC	3
pTS1977	AHI1_DR_GU&GA_at_all_off-target_sites_gRNA	CTCTCATCTCAACGGTCCATGTCCGTGTCATGGAATCATAGCA TCCTGTAA GTTGGAAGGTCCAGTTTGAGGGGCTATTACA AC	3
pTS1997	BMPR2_K983_3x20-20p8_RG-V21_Reference	GGTGTGCGAGAAGAGGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACC CCACCGCTAAGAGAATAGGAAATGCTGC CATCCAGGACATTTAAACTGAAAGATCCAGAGAATTAAGAA CACCCTGTGCAAGAACA	EDF3, S5
pTS2000	BMPR2_K983_3x20-20p8_RG-V21_GU	GGTGTGCGAGAAGAGGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACC CCACCGCTGAGAGAATAGGAAATGCTGC CATCCAGGACATTTAAACTGAAAGATCCAGAGAATTAAGAA CACCCTGTGCAAGAACA	EDF3, S5
pTS1998	BMPR2_K983_3x20-20p8_RG-V21_GA	GGTGTGCGAGAAGAGGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACC CCACCGCCGAAGAGAATAGGAAATGCTGC CATCCAGGACATTTAAACTGAAAGATCCAGAGAATTAAGAA CACCCTGTGCAAGAACA	EDF3, S5
pTS1999	BMPR2_K983_3x20-19p8_RG-V21_U-depletion	GGTGTGCGAGAAGAGGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACC CCACCGCCAAGAGAATAGGAAATGCTGCC ATCCAGGACATTTAAACTGAAAGATCCAGAGAATTAAGAA ACCCTGTGCAAGAACA	EDF3, S5
pTS2002	COL3A1_N1244_3x20-20p8_RG-V21_Reference	GGTGTGCGAGAAGAGGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACC TGTCCATCAACAGACTTGAG AAAACGGGG CAAACCGCCAGCTAAATCACCTCCAATCCCAGCAATAAACTC CAACACCACACAGCAA	EDF3, S5
pTS2005	COL3A1_N1244_3x20-20p8_RG-V21_GU	GGTGTGCGAGAAGAGGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACC TGTCCGTCAACAGACTTGAG AAAACGGGG CAAACCGCCAGCTAAATCACCTCCAATCCCAGCAATAAACTC CAACACCACACAGCAA	EDF3, S5
pTS2003	COL3A1_N1244_3x20-20p8_RG-V21_GA	GGTGTGCGAGAAGAGGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACC TGTCCAGCAACAGACTTGAG AAAACGGGG CAAACCGCCAGCTAAATCACCTCCAATCCCAGCAATAAACTC CAACACCACACAGCAA	EDF3, S5
pTS2004	COL3A1_N1244_3x20-20p8_RG-V21_U-depletion	GGTGTGCGAGAAGAGGAGAACAATATGCTAAATGTTGTTCTCG TCTCCTCGACACC TGTCCACAACAGACTTGAG AAAACGGGG AAAACCGCCAGCTAAATCACCTCCAATCCCAGCAATAAACTC AACACCACACAGCAA	EDF3, S5
pTS1764	NUP43_V233V_3x20-20p8_RG-V25_CA-only	GGTGTGCGAGAAGAGGAGAACAATATCTTTCATGTTGTTCTCCT CTCCTCGACACC CAGTAGCCACAACATGCTGT AAAGGCACTC	S2

		GGTCACCAGTCAGAAAAAACCTCCATCAGAGTCCAAAAAGG CAGCGGTCGCCAGCGGG	
pTS1766	NUP43_V233V_3x20- 20p8_RG-V25_UG&CA	GGTGTGCGAGAAGAGGAGAACAATATCTTTTCATGTTGTTCTCCT CTCCTCGACACCAGTAGTTCACAACATGCTGTAAAGGCACTC GGTCACCAGTCAGAAAAAACCTCCATCAGAGTCCAAAAAGG CAGCGGTCGCCAGCGGG	S2
pTS1805	NUP43_V233V_3x20- 20p8_RG-V25_UG-only	GGTGTGCGAGAAGAGGAGAACAATATCTTTTCATGTTGTTCTCCT CTCCTCGACACCAGTAGTTACAACATGCTGTAAAGGCACTC GGTCACCAGTCAGAAAAAACCTCCATCAGAGTCCAAAAAGG CAGCGGTCGCCAGCGGG	S2
pTS2531	NUP43_V233V_3x20- 20p8_RG-V25_CA&GU	GGTGTGCGAGAAGAGGAGAACAATATCTTTTCATGTTGTTCTCCT CTCCTCGACACCAGTAGCAGCAACATGCTGTAAAGGCACTC GGTCACCAGTCAGAAAAAACCTCCATCAGAGTCCAAAAAGG CAGCGGTCGCCAGCGGG	S2
pTS1702	GUSB_L456L_3x20- 20p8_RG-V25_CA-only	GGTGTGCGAGAAGAGGAGAACAATATCTTTTCATGTTGTTCTCCT CTCCTCGACACCAGATTTCAGGTGGGACGCAAAAGCCACA GACCACATCACGACAAACACGCCGGGACACTCATCGAAAAGC ACCAAGCCAGCGAAGCAG	S2
pTS1770	GUSB_L456L_3x20- 20p8_RG-V25_UG&CA	GGTGTGCGAGAAGAGGAGAACAATATCTTTTCATGTTGTTCTCCT CTCCTCGACACCAGATTTCAGGTGGGACGCAAAAGCCACAG ACCACATCACGACAAACACGCCGGGACACTCATCGAAAAGCA CCAAGCCAGCGAAGCAG	S2
pTS1769	GUSB_L456L_3x20- 20p8_RG-V25_UG-only	GGTGTGCGAGAAGAGGAGAACAATATCTTTTCATGTTGTTCTCCT CTCCTCGACACCAGATTTCAGGTGGGACGCAAAAGCCACAG ACCACATCACGACAAACACGCCGGGACACTCATCGAAAAGCA CCAAGCCAGCGAAGCAG	S2
pTS2532	GUSB_L456L_3x20- 20p8_RG-V25_CA&GU	GGTGTGCGAGAAGAGGAGAACAATATCTTTTCATGTTGTTCTCCT CTCCTCGACACCAGATTTCAGGTGGGACGCAAAAGCCACAG ACCACATCACGACAAACACGCCGGGACACTCATCGAAAAGCA CCAAGCCAGCGAAGCAG	S2
pTS1705	ACTB_3'-UTR_3x20- 20p8_RG-V25_CA-only	GGTGTGCGAGAAGAGGAGAACAATATCTTTTCATGTTGTTCTCCT CTCCTCGACACCACGCAACCAAGTCATAGTCCAAAAGCCGCC GATCCACACGGAGAAACCTCAGGGCAGCGGAACCGCAAAGC TCGAAGTCCAGGGCGACG	S2
pTS1774	ACTB_3'-UTR_3x20- 20p8_RG-V25_UG&CA	GGTGTGCGAGAAGAGGAGAACAATATCTTTTCATGTTGTTCTCCT CTCCTCGACACCACGCAATCAAGTCATAGTCCAAAAGCCGCC GATCCACACGGAGAAACCTCAGGGCAGCGGAACCGCAAAGC TCGAAGTCCAGGGCGACG	S2
pTS1773	ACTB_3'-UTR_3x20- 20p8_RG-V25_UG-only	GGTGTGCGAGAAGAGGAGAACAATATCTTTTCATGTTGTTCTCCT CTCCTCGACACCACGCAATTAAGTCATAGTCCAAAAGCCGCC GATCCACACGGAGAAACCTCAGGGCAGCGGAACCGCAAAGC TCGAAGTCCAGGGCGACG	S2
pTS2533	ACTB_3'-UTR_3x20- 20p8_RG-V25_CA&GU	GGTGTGCGAGAAGAGGAGAACAATATCTTTTCATGTTGTTCTCCT CTCCTCGACACCACGCAACcGAGTCATAGTCCAAAAGCCGCC GATCCACACGGAGAAACCTCAGGGCAGCGGAACCGCAAAGC TCGAAGTCCAGGGCGACG	S2
pTS2087	AHI1_K706_2xBoxB_10 (3)-29p15-(3)10_5'- _and_3' NN_reference	ACTAGCTCTCAGCCCTGAAAAAGGGCCAGCTGGATGGAATC TAGCCGTGTAAACAAGCCCTGAAAAAGGGCCGAAGGATGAG	EDF3, S5
pTS2111	AHI1_K706_2xBoxB_10 (3)-29p15-(3)10_5'- _and_3' NN_GA- mismatch	ACTAGCTCTCAGCCCTGAAAAAGGGCCAGCTGGATGGAAG CGAGCCGTGTAAACAAGCCCTGAAAAAGGGCCGAAGGATGA G	EDF3, S5
pTS2117	AHI1_K706_2xBoxB_10 (3)-29p15-(3)10_5'- _and_3' NN_GU-wobble	ACTAGCTCTCAGCCCTGAAAAAGGGCCAGCTGGATGGAGT CTGGCCGTGTAAACAAGCCCTGAAAAAGGGCCGAAGGATGA G	EDF3, S5
pTS2088	BMPR2_K984_2xBoxB_10 (3)-29p15-(3)10_5' NN_reference	ATGACCCAGGAGCCCTGAAAAAGGGCCAGGGGCGCCACCG CCTAAGAGAATAGGGAAGCCCTGAAAAAGGGCCATCACACGT T	EDF3, S5
pTS2114	BMPR2_K984_2xBoxB_10 (3)-29p15-(3)10_5' NN_GA-mismatch	ATGACCCAGGAGCCCTGAAAAAGGGCCAGGGGCGCCACCG CCGAAGAGAATAGGGAAGCCCTGAAAAAGGGCCATCACACG TT	EDF3, S5
pTS2120	BMPR2_K984_2xBoxB_10 (3)-29p15-(3)10_5' NN_GU-wobble	ATGACCCAGGAGCCCTGAAAAAGGGCCAGGGGCGCCACCG CCTGAGAGAATAGGGAAGCCCTGAAAAAGGGCCATCACACG TT	EDF3, S5
pTS2086	AHI1_11179_2xBoxB_10 (3)-29p15-(3)10_3' NN_reference	GCTTGTCTTCAGCCCTGAAAAAGGGCCATCCGTGTATCCAT CATGTGTCCTTGGTCAAGCCCTGAAAAAGGGCCATGGCTCTGT	EDF3, S5

pTS1870	0_3 20p8-3x20 Luci circ + RG EF1α	AACCATGCCGACTGATGGCAGAAAAAGTGTCGAGAAGAGG AGAACAATATGCTAAATGTTGTTCTCGTCTCCTCGACACCGTG CAGCCAGCCGTCCTTGTAAAAGCTCGCCGGCATCGTCGTCAA ACCCCGGCGTCGAAGATGTTAAAGTGCTCGTCCTCGTCCAG TAAAAACTGCCATCAGTCGGCGTGGACTGTAG	S9
pTS1872	Z-20p8-20-20-20 Luci circ U6	AACCATGCCGACTGATGGCAGAAAAAGTGCGAGCCAGCCGTC CTTGTAAACGTAGCCGCTCATGATCATGAAACACGGACGCAC AGCTCGCCGAAACCGGTGTCCAAGTCCACCACAAAACTGCC ATCAGTCGGCGTGGACTGTAG	S9
pTS1873	Z-20-20p8-20-20 Luci circ U6	AACCATGCCGACTGATGGCAGAAAAACCGGTGTCCAAGTCCA CCACAAAAGTGCGAGCCAGCCGTCCTTGTAAACGTAGCCGCTCA TGATCATGAAACACGGACGCACAGCTCGCCGCTGCCATCAGT CGGCGTGGACTGTAG	S9
pTS1874	Z-20-20-20p8-20 Luci circ U6	AACCATGCCGACTGATGGCAGAAAAACACGGACGCACAGCTC GCCGAAACCGGTGTCCAAGTCCACCACAAAGTGCGAGCCAGC CGTCCTTGTAAACGTAGCCGCTCATGATCATAAAACTGCC ATCAGTCGGCGTGGACTGTAG	S9
pTS1875	Z-20-20-20-20p8 Luci circ U6	AACCATGCCGACTGATGGCAGAAAAACGTAGCCGCTCATGAT CATGAAACACGGACGCACAGCTCGCCGAAACCGGTGTCCAA GTCCACCACAAAGTGCGAGCCAGCCGTCCTTGTAAAACTGCC ATCAGTCGGCGTGGACTGTAG	S9
pTS1877	Z-20p8-20-20-20 Luci circ EF1α	AACCATGCCGACTGATGGCAGAAAAAGTGCGAGCCAGCCGTC CTTGTAAACGTAGCCGCTCATGATCATGAAACACGGACGCAC AGCTCGCCGAAACCGGTGTCCAAGTCCACCACAAAACTGCC ATCAGTCGGCGTGGACTGTAG	S9
pTS1878	Z-20-20p8-20-20 Luci circ EF1α	AACCATGCCGACTGATGGCAGAAAAACCGGTGTCCAAGTCCA CCACAAAAGTGCGAGCCAGCCGTCCTTGTAAACGTAGCCGCTCA TGATCATGAAACACGGACGCACAGCTCGCCGCTGCCATCAGT CGGCGTGGACTGTAG	S9
pTS1879	Z-20-20-20p8-20 Luci circ EF1α	AACCATGCCGACTGATGGCAGAAAAACACGGACGCACAGCTC GCCGAAACCGGTGTCCAAGTCCACCACAAAGTGCGAGCCAGC CGTCCTTGTAAACGTAGCCGCTCATGATCATAAAACTGCC ATCAGTCGGCGTGGACTGTAG	S9
pTS1880	Z-20-20-20-20p8 Luci circ EF1α	AACCATGCCGACTGATGGCAGAAAAACGTAGCCGCTCATGAT CATGAAACACGGACGCACAGCTCGCCGAAACCGGTGTCCAA GTCCACCACAAAGTGCGAGCCAGCCGTCCTTGTAAAACTGCC ATCAGTCGGCGTGGACTGTAG	S9
pTS1931	2-1-circ_3x_RC_20-20_20p8-RG-20_Luci_gRNA EF1α	AACCATGCCGACTGATGGCAGAAAAAGTGCTCGTCCTCGTCC CAGTAAAGGTGTGCGAGAAGAGGAGAACAATATGCTAAATGTT GTTCTCGTCTCCTCGACACCCTGCGAGCCAGCCGTCCTTGTAA ACGTAGCCGCTCATGATCATGAAACACGGACGCACAGCTCGC CGAAAACTGCCATCAGTCGGCGTGGACTGTAG	S10
pTS1932	2-1-circ_3x_RC_20_20p8-RG-20-20_Luci_gRNA EF1α	AACCATGCCGACTGATGGCAGAAAAACACGGACGCACAGCTC GCCGAAAGTGCTCGTCCTCGTCCAGTAAAGTGTCGAGAAG AGGAGAACAATATGCTAAATGTTGTTCTCGTCTCCTCGACACC GTGCGAGCCAGCCGTCCTTGTAAACGTAGCCGCTCATGATCAT GAAAACTGCCATCAGTCGGCGTGGACTGTAG	S10
pTS1933	2-1-circ_3x_RC_20p8-RG-20-20_Luci_gRNA EF1α	AACCATGCCGACTGATGGCAGAAAAACGTAGCCGCTCATGAT CATGAAACACGGACGCACAGCTCGCCGAAAGTGCTCGTCCTC GTCCAGTAAAGGTGTGCGAGAAGAGGAGAACAATATGCTAAAT GTTGTTCTCGTCTCCTCGACACCCTGCGAGCCAGCCGTCCTT GTAAAACTGCCATCAGTCGGCGTGGACTGTAG	S10
pTS1938	2-1-circ_3x_RC_20-20_20p8-RG-20_Luci_gRNA U6	AACCATGCCGACTGATGGCAGAAAAAGTGCTCGTCCTCGTCC CAGTAAAGGTGTGCGAGAAGAGGAGAACAATATGCTAAATGTT GTTCTCGTCTCCTCGACACCCTGCGAGCCAGCCGTCCTTGTAA ACGTAGCCGCTCATGATCATGAAACACGGACGCACAGCTCGC CGAAAACTGCCATCAGTCGGCGTGGACTGTAG	S10
pTS1939	2-1-circ_3x_RC_20_20p8-RG-20-20_Luci_gRNA U6	AACCATGCCGACTGATGGCAGAAAAACACGGACGCACAGCTC GCCGAAAGTGCTCGTCCTCGTCCAGTAAAGGTGTGCGAGAAG AGGAGAACAATATGCTAAATGTTGTTCTCGTCTCCTCGACACC GTGCGAGCCAGCCGTCCTTGTAAACGTAGCCGCTCATGATCAT GAAAACTGCCATCAGTCGGCGTGGACTGTAG	S10
pTS1940	2-1-circ_3x_RC_20p8-RG-20-20_Luci_gRNA U6	AACCATGCCGACTGATGGCAGAAAAACGTAGCCGCTCATGAT CATGAAACACGGACGCACAGCTCGCCGAAAGTGCTCGTCCTC GTCCAGTAAAGGTGTGCGAGAAGAGGAGAACAATATGCTAAAT GTTGTTCTCGTCTCCTCGACACCCTGCGAGCCAGCCGTCCTT GTAAAACTGCCATCAGTCGGCGTGGACTGTAG	S10

pTS1934	2-1-circ_3x_RC_split-RG(V2)_Luci_gRNA EF1α	AACCATGCCGACTGATGGCAGAATGTTGTTCTCGTCTCCTCG ACACC GTGCAGCCAGCCGTCCTTGT AAACGTAGCCGCTCATG ATCATGAAACACGGACGCACAGCTCGCCGAAAGTGCTCGTCC TCGTCCCAAGTAAAAAGGTGTCGAGAAGAGGAGAACAATATGC TACTGCCATCAGTCGGCGTGGACTGTAG	S10
pTS1941	2-1-circ_3x_RC_split-RG(V2)_Luci_gRNA U6	AACCATGCCGACTGATGGCAGAATGTTGTTCTCGTCTCCTCG ACACC GTGCAGCCAGCCGTCCTTGT AAACGTAGCCGCTCATG ATCATGAAACACGGACGCACAGCTCGCCGAAAGTGCTCGTCC TCGTCCCAAGTAAAAAGGTGTCGAGAAGAGGAGAACAATATGC TACTGCCATCAGTCGGCGTGGACTGTAG	S10
pTS1989	2-1-circ_3x_RC_split-RG(V1)_Luci_gRNA EF1α	AACCATGCCGACTGATGGCAGATGTTGTTCTCGTCTCCTCGA CACC GTGCAGCCAGCCGTCCTTGT AAACGTAGCCGCTCATGA TCATGAAACACGGACGCACAGCTCGCCGAAAGTGCTCGTCC CGTCCCAAGTAAAAAGGTGTCGAGAAGAGGAGAACAATAT CTG CCATCAGTCGGCGTGGACTGTAG	S10
pTS1992	2-1-circ_3x_RC_split-RG(V1)_Luci_gRNA U6	AACCATGCCGACTGATGGCAGATGTTGTTCTCGTCTCCTCGA CACC GTGCAGCCAGCCGTCCTTGT AAACGTAGCCGCTCATGA TCATGAAACACGGACGCACAGCTCGCCGAAAGTGCTCGTCC CGTCCCAAGTAAAAAGGTGTCGAGAAGAGGAGAACAATAT CTG CCATCAGTCGGCGTGGACTGTAG	S10
pTS1594	NUP43 V233V 111 nt Circular EF1α	AACCATGCCGACTGATGGCAGTAGTACCTTGTCTAACATCCC AAATACTCAACATTCCATCTTGCCACCAGTAGCCACAACATG CTGTTGGTTGGGATGTCTATCAACACAGTGGAGTGGCACTCG GTCAC CTGCCATCAGTCGGCGTGGACTGTAG	S6
pTS1722	NUP43 V233V 111 nt Linear EF1α	TAGTACCTTGTCTAACATCCCAATACTCAACATTCCATCTTG GCCACCAGTAGCCACAACATGCTGTTGGTTGGGATGTCTATC AACACAGTGGAGTGGCACTCGGTCAC	S6
pTS1643	RAB7A 3'UTR 111 nt Circular EF1α	AACCATGCCGACTGATGGCAGGTCTTTGATAAAAGGCGTACA TAATTCTTGTGTCTACTGTACAGAATACTGCCGCCAGCTGGAT TTCCCAATTCTGAGTAACACTCTGCAATCCAAACAGGGTTCAA CCCT CTGCCATCAGTCGGCGTGGACTGTAG	S6-8
pTS1724	RAB7A 3'UTR 111 nt Linear EF1α	GTCTTTGATAAAAGGCGTACATAATTCTTGTGTCTACTGTACA GAATACTGCCGCCAGCTGGATTTCCCAATTCTGAGTAACACT CTGCAATCCAAACAGGGTTCAACCCT	S6-7
pTS1810	NUP43 V233V 111 nt Circular U6	AACCATGCCGACTGATGGCAGTAGTACCTTGTCTAACATCCC AAATACTCAACATTCCATCTTGCCACCAGTAGCCACAACATG CTGTTGGTTGGGATGTCTATCAACACAGTGGAGTGGCACTCG GTCAC CTGCCATCAGTCGGCGTGGACTGTAG	S6
pTS1811	NUP43 V233V LEAPER U6	TAGTACCTTGTCTAACATCCCAATACTCAACATTCCATCTTG GCCACCAGTAGCCACAACATGCTGTTGGTTGGGATGTCTATC AACACAGTGGAGTGGCACTCGGTCAC	S6
pTS1812	RAB7A 3'UTR 111 nt Circular U6	AACCATGCCGACTGATGGCAGGTCTTTGATAAAAGGCGTACA TAATTCTTGTGTCTACTGTACAGAATACTGCCGCCAGCTGGAT TTCCCAATTCTGAGTAACACTCTGCAATCCAAACAGGGTTCAA CCCT CTGCCATCAGTCGGCGTGGACTGTAG	S6-8
pTS1813	RAB7A 3'UTR LEAPER U6	GTCTTTGATAAAAGGCGTACATAATTCTTGTGTCTACTGTACA GAATACTGCCGCCAGCTGGATTTCCCAATTCTGAGTAACACT CTGCAATCCAAACAGGGTTCAACCCT	S6-7
pTS1896	RAB7A 3'UTR 111 nt Circular U6 stable integration	AACCATGCCGACTGATGGCAGGTCTTTGATAAAAGGCGTACA TAATTCTTGTGTCTACTGTACAGAATACTGCCGCCAGCTGGAT TTCCCAATTCTGAGTAACACTCTGCAATCCAAACAGGGTTCAA CCCT CTGCCATCAGTCGGCGTGGACTGTAG	S8
pTS1897	RAB7A 3'UTR 111 nt Linear U6 stable integration	GTCTTTGATAAAAGGCGTACATAATTCTTGTGTCTACTGTACA GAATACTGCCGCCAGCTGGATTTCCCAATTCTGAGTAACACT CTGCAATCCAAACAGGGTTCAACCCT	S8
pTS1899	RAB7A 3'UTR 111 nt Circular EF1α stable integration	AACCATGCCGACTGATGGCAGGTCTTTGATAAAAGGCGTACA TAATTCTTGTGTCTACTGTACAGAATACTGCCGCCAGCTGGAT TTCCCAATTCTGAGTAACACTCTGCAATCCAAACAGGGTTCAA CCCT CTGCCATCAGTCGGCGTGGACTGTAG	S8
pTS1900	RAB7A 3'UTR 111 nt Linear EF1α stable integration	GTCTTTGATAAAAGGCGTACATAATTCTTGTGTCTACTGTACA GAATACTGCCGCCAGCTGGATTTCCCAATTCTGAGTAACACT CTGCAATCCAAACAGGGTTCAACCCT	S8
pTS2515	NUP43_UTR_CircLEAP ER_151p76_AC50	AACCATGCCGACTGATGGCAGAAAAACAAAAACAAAAA CAAAAAACCAAAAAACAAAAACACAAGAGCAAACTCCA TCTCAAAAAATATATATATTTATTAGGACAGAAAAGCAAAACCT TACCATAATTCCATAACCATGATTATTGGAATTACAAAGTAAT GAACACTTCAATTGTCTAATAGCAGTGATTGTCTAATAGGTC TCAGGTAAAAACAAAAACAAAAACAAAAACAAAAACAAAA AAAAACAAAAACACA CTGCCATCAGTCGGCGTGGACTGTAG	EDF2

pTS2560	NUP43_UTR_CircLEAP ER_151p76_AC50_GU_ at_GU-amenable-sites	AACCATGCCGACTGATGGCAGAAAAACAAAAACAAAAAA CAAAAAAAAAACCAAAAAAAAAACAAACACAAGAGCAAACTCCA TCTCAAAAAGTATATATgTTTgTTAGGACAGAAAAGCAAAACCT TgCCATggTTCCgTAACCATGATTgTTGGAATTgCAAAGTgAATG AACACTTCAgTTGTCTgATgGCAGTGATTTGTCgTTgAGGTCTC AGGTAAAAACAAAAACAAAAAAACAAAAAAACCAAAAA AACAAAAACACACTGCCATCAGTCGGCGTGGACTGTAG	EDF2
pTS2561	NUP43_UTR_CircLEAP ER_151p76_AC50_GA_ at_GU-amenable-sites	AACCATGCCGACTGATGGCAGAAAAACAAAAACAAAAAA CAAAAAAAAAACCAAAAAAAAAACAAACACAAGAGCAAACTCCA TCTCAAAAAGTATATgATTgATTAGGACAGAAAAGCAAAACCT gACCAgAAgTCCAgAACCATGATgATTGGAATgACAAAGgAAAT GAACACTTCAAgTGTcGAAgAGCAGTGATTTGTCAggAAGGTCT CAGGTAAAAACAAAAACAAAAAAACAAAAAAACCAAAAA AAACAAAAACACACTGCCATCAGTCGGCGTGGACTGTAG	EDF2
pTS2562	NUP43_UTR_CircLEAP ER_151p76_AC50_GA_ at_all_off-target_sites	AACCATGCCGACTGATGGCAGAAAAACAAAAACAAAAAA CAAAAAAAAAACCAAAAAAAAAACAAACACAAGAGCAAACTCCA TCTCAAAAAGTATATgATggATTAGGACAGAAAAGCAAAACCT gACCAgAAgTCCAgAACCATGATgATTGGAATgACAAAGgAAAT GAACACgTCAAgTGTcGAAgAGCAGTGATgTGTCaggAAGGTCT CAGGTAAAAACAAAAACAAAAAAACAAAAAAACCAAAAA AAACAAAAACACACTGCCATCAGTCGGCGTGGACTGTAG	EDF2
pTS2563	NUP43_UTR_CircLEAP ER_151p76_AC50_GU+ GA	AACCATGCCGACTGATGGCAGAAAAACAAAAACAAAAAA CAAAAAAAAAACCAAAAAAAAAACAAACACAAGAGCAAACTCCA TCTCAAAAAGTATATATgTgTgTTAGGACAGAAAAGCAAAACCT gCCATggTTCCgTAACCATGATTgTTGGAATTgCAAAGTgAATGA ACACgTCAgTTGTCTgATgGCAGTGATgTGTCgTTgAGGTCTCA GGTAAAAACAAAAACAAAAAAACAAAAAAACCAAAAA ACAAAAACACACTGCCATCAGTCGGCGTGGACTGTAG	EDF2

Supplementary Table S2: Primer list

Primer #	Primer Name	Sequence 5'→3'
	+91 Mecp2 E1 Rev	ggaagctttgtcagagccctacc
	-14 Mecp2 E1 Fwd	aaccggtccggaatggcc
	Mecp2 E1 743 Rev	ccaggcgatgcttggaagg
	Mecp2G311A Fwd (genotyping)	cccacctgcctgaagggtg
	Mecp2G311A Rev (genotyping)	cctagccttctaccacctg
	Sex Fwd	acctaagaacaagccaataca
	Sex Rev	ggctgtcctgaaaacatttg
	TM766 Rev	tgtacaagaaagctgggtcg
	TM764 Fwd	ctttgcaagtgtaacct
	TM768 Rev	ttccaggcggaccatacaac
	TM764 Fwd	ctttgcaagtgtaacct
	AAV2_ITR_fw	ggaacccctagtgatggagt
	AAV2_ITR_bw	cggcctcagtgaagcga
121	GFP_fw	gcggatccaccatggctagcaaggagaagaactc
144	BGH_bw	ctagaaggcacagtcgaggc
551	BGH_long_bw	gctggcaactagaaggcacagtcgaggc
566	GFP_seq_fw	gacacgtgctgaagtcaagttgaagggtg
1032	ACTB_fw	cagcagatgtggatcagcaagcaggag
1033	ACTB_bw	ggaagggggggcacgaaggctcatc
2443	Bsal_SV40_PolyA_bw	tatgtgtctctggcctaagatacattgatgagttggacaaac
2901	AHI1_W725Amber_fw	gccgtatcccaacaacacacc
2902	AHI1_W725Amber_bw	ccaacaacaatcacccctgt
2903	BMPR2_W298Amber_fw	ccttggatgagcgtccagtt
2905	COL3A1_W1278Amber_fw	tgctgggattggagggtgaaaa
2919	GUSB_L456L_fw	caacaagcatgaggatgcgg
2920	GUSB_L456L_bw	gtgccgtagtcgtgatacc
2933	NUP43_V233V_fw	tgtgtgcaacaaccagaaat
2934	NUP43_V233V_bw	gtactgtctctcctcctgtgtg
2939	RAB7A_3'UTR_fw	gccccattacaggctcacac
2940	RAB7A_3'UTR_bw	ttgaagtgtggagcaggggg
3041	RAB7A_Exon5_fw	ccagacgattgcacggaatg
3107	Murine_Adar1_fw	tcccgccattaccctgtctt
3108	Murine_Adar1_bw	catggtacggagttcttcccc
3109	Murine_Adar1p150_fw	ctgccggcactatgtctca
3110	Murine_Adar1p150_bw	ctgccgggtatctccactgc
3134	RAB7A_3'UTR_Sense-Oligo	ggttgaaccctgtttggattgcagagtggtactcagaattgggaaatccagctggcggcagttattctgtacagtagacacaagaattatgtacgcctttatcaaaagtga
3236	Murine_Actb fw	gagcgcaagtactctgtgtg
3237	Murine_Actb_bw	aaacgcagctcagtaacagtc
3241	mMecp2_fw	aaccttcagcccaccattct
3243	GUSB_L456L_Meta-Sense-Oligo	gggcttcgactggccgctgctggtgttttctcgtctcgtggtggtgcctttttcagatgagtgctccggcgtggcctggcgtgcgcgttttcccgcggtcgtgatgtggtctgtggcctttttgcgtccacctcgaatgcc
3244	NUP43_V233V_Meta-Sense-Oligo	gttgagaggatggtcgatttttctcctgagattctttttctgactggtgaccgagtgcccttttacagatgtgtcgtagcc

3454	NUP43_5'UTR_fw	ctgctgcggccgcgttctg
3569	ACTB_3'UTR_Sense-Oligo	cgtcgccctggacttcgagctttgcggtccgctgccctgaggtttccggtggtatcggcggctttt ggactatgacttcgttggca
4242	Murine_Rps29_fw	tgaaggcaagatgggtcac
4243	Murine_Rps29_bw	gcacatgttcagcccgtatt
4247	Murine_Adar2_fw	ttgccctgaaggagttttg
4248	Murine_Adar2_bw	gagggcttctgactggc
4964	mMecp2_65°C_bw	acaacaagttcccagggtcttctcc
4965	mMecp2_65°C_fw	ctagcgctaccggactcagatctcg
5058	Mlul_U6_fw	gggcacgcgtgagggcctatttcccatgattcc
5059	BglII_BamHI_KpnI_SV40_bw	aaaagatctggatccaaaggtacctaagatacattgatgagttggacaaacc
5062	KpnI_Circ-guideRNA_fw	aaaggaccacgcgtgctcgcttcggcagc
5122	Mlul_Universal_Stuffer_fw	agaacgcgtgctaccatggaccatcctg
5123	Mlul_2827nt_Stuffer_bw	aaaacgcgtgtatactgctgccatccag
5261	V27.2.4_inwards_qPCR_fw	cataggtcccaaacacgga
5262	V27.2.4_inwards_qPCR_bw	ggccgatctgctggatttagt
5265	V27.2.4_outwards_qPCR_fw	ggagcgccgcaaagatcaa
5266	V27.2.4_outwards_qPCR_bw	ttttgcctgaaggttggacac
6109	NUP43_3' UTR_fw	agctgaaagttgccaaactgg
6110	NUP43_3' UTR_bw	cctgcaacccttgaaagacac
6198	Murine_Rnu6_fw	gcttcggcagcacatatactaaaat
6199	Murine_Rnu6_bw	cgcttcacgaatttcgtgtcat

Supplementary Table S3: Primer pair list

Target	Primer Pair	Sense Oligo	Sequencing Primer
ACTB 3'UTR	1032+1033	3569	1032
AHI1 K706, I1179 & W725Amber	2901+144	None	2901 (K706), 2902 (W725Amber), or 144 (I1179)
BMPR2 K983 & W298Amber	2903+144	None	144
circCLUSTER gRNA V27.2.4 inward (qPCR)	5261+5262	None	None
circCLUSTER gRNA V27.2.4 outward (qPCR)	5265+5266	None	None
COL3A1 N1244	2905+144	None	2905
COL3A1 W1278Amber	2905+144	None	144
eGFP cis-acting guide RNA reporter	551+121	None	566
GUSB L456L	2919+2920	3243	2919
Murine Mecp2 W104Amber (in vitro)	4964+4965	None	3241
Murine Mecp2 W104Amber (in vivo, editing)	-14 Mecp2 E1 Fwd & +91 Mecp2 E1 Rev	None	Mecp2 E1 743 Rev
Murine Mecp2 W104Amber (in vivo, genotyping)	Mecp2G311A Fwd & Rev2934+3454	3244	2933
NUP43 V233V	2934+3454	3244	2933
PEX1 G843D set A	TM766 Rev & TM764 Fwd	None	None
PEX1 G843D set B (nested PCR)	TM768 Rev & TM764 Fwd	None	TM768 Rev
RAB7A 3'UTR	3041+2940	3134	2939
Rett mice genotyping (MeCPp2 W104Amber)	Mecp2G311A Fwd & Mecp2G311A Rev	None	None
Murine Atcb qPCR	3236+3237	None	None
Murine Rnu6 qPCR	6198+6199	None	None
Murine Rps29 qPCR	4242+4243	None	None
Murine Adar1 qPCR	3107+3108	None	None
Murine Adar1p150 qPCR	3109+3110	None	None
Murine Adar2 qPCR	4247+4248	None	None
NUP43 3' UTR	6109+6110	None	6109
AAV ITR	fw+bw	None	None

Supplementary Table S4: Antibody list

Antibody	Target Protein	Produced in	Immuno-globulin Class	Dilution used	Supplier	Order #	Against	Validation
MeCP2 (D4F3) XP Rabbit mAb	α -MeCP2	Rabbit	Monoclonal IgG	1:500	Cell Signaling Technology	3456	Carboxyl end of human MeCP2	Commonly used commercial antibody validated in KO mouse tissue sections previously in our lab. RRID: AB_2143849 PMID: 35939700
Donkey α Rabbit AlexaFluor 488	α -rabbit IgG	Donkey	Polyclonal IgG	1:750	Invitrogen	A21206	Whole molecule rabbit IgG	Commonly used commercial antibody with 135 IHC-IF citations as of Jan. 2024. RRID: AB_2535792 Recent publications: PMID: 36865524 PMID: 36321664 PMID: 38017073

Supplementary Notes:

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 - pAAV-GFP (Cell Biolabs)
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 - circ-mMecp2-V27.2.4_gRNA_pAAV_no-stuffer (pTS2123)
 - BMPR2_W298X_cDNA_pcDNA3.1 (pTS1160)
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 - Tornado OHA vector U6 (pTS1790)
 - Transposon U6 circ RAB7A LEAPER gRNA vector (pTS1896):
 - Transposon U6 linear RAB7A LEAPER gRNA vector (pTS1897):
 - Transposon EF1α circ RAB7A LEAPER gRNA vector (pTS1899):
 - Transposon EF1α linear RAB7A LEAPER gRNA vector (pTS1900):
 - Plasmid-map and sequence of the CircLEAPER AC50 cloning vector (pTS2508):

1. Cloning strategy for cis-acting editing reporters

Two types of cis-acting editing reporters were generated. In both versions the hybrid oligonucleotide inserts were cloned into the 3' UTR of an **eGFP** construct (pTS58) via **Apal** and **AgeI**. To make sure that the reporter would not be unfolded due to ribosomal activity an additional **Ochre (5'-TAA) stop codon** and an additional **linker (20 nt in version #1 and 21 nt in version #2)** were placed between the primary **Amber (5'-TAG) stop codon** and the start of the cis-acting guide RNA. The first version is shown in main Figure 1b. In this design, the ADAR recruiting domain and the cis-acting specificity domain are two separate duplexes, separated by a **5x Adenosine linker**. In Supplementary Table S1 the cis-acting guide RNAs of design version #1 are displayed from the 5'-end of the **R/G motif V21** to the 3'-end of the **cis-representation of the target sequence**. The second version is shown in Extended Data Figure 3. In this design the ADAR recruiting domain and the cis-acting specificity domain are part of one continuous duplex. In Supplementary Table S1 the cis-acting guide RNAs of design version #2 are displayed from the 5'-end of the **cis-representation of the target sequence** to the 3'-end of the **cis-representation of the specificity domain**. In both cases a bGH poly(A) signal serves as termination signal.

Version #1:

```
1      ATGGCTAGCA AAGGAGAAGA ACTCTTCACT GGAGTTGTCC CAATTCTTGT TGAATTAGAT
61     GGTGATGTTA ACGGCCACAA GTTCTCTGTC AGTGGAGAGG GTGAAGGTGA TGCAACATAC
121    GGAAAACTTA CCCTGAAGTT CATCTGCACT ACTGGCAAAC TGCCTGTTCC GTGGCCGACA
181    CTAGTGACGA CGCTCTGCTA TGGCGTCCAG TGCTTTTCAA GATACCCGGA TCACATGAAA
241    CGGCATGACT TTTTCAAGAG TGCCATGCCC GAAGGTTATG TACAGGAAAG GACCATCTTC
301    TTCAAAGATG ACGGCAACTA CAAGACACGT GCTGAAGTCA AGTTTGAAGG TGATACCCTT
361    GTTAATAGAA TCGAGTTAAA AGGTATTGAC TTCAAGGAAG ATGGCAACAT TCTGGGACAC
421    AAATTGGAAT ACAACTATAA CTCACACAAT GTATACATCA TGGCAGACAA ACAAAGAAT
481    GGAATCAAAG TGAAGTTCAA GACCCGCCAC AACATTGAAG ATGGAAGCGT TCAACTAGCA
541    GACCATTATC AACAAAATAC TCCAATTGGC GATGGCCCTG TCCTTTTACC AGACAACCAT
601    TACCTGTCCA CACAATCTGC CCTTTCGAAA GATCCCAACG AAAAGAGAGA CCACATGGTC
661    CTTCTTGAGT TTGTAACAGC TGCTGGGATT ACACATGGCA TGGATGAACT ATACAAATCC
721    GGCTCTAGA GGGCCCTAGTA AGTGGAAAGG ACGCGGGATC CGGTGTGAG AAGAGGAGAA
781    CAATATGCTA AATGTTGTTC TCGTCTCCTC GACACCAGT ACNKNCAACA TGCTGTAAAA
841    ACAGCATGT TGNANCTACT GTTTACCGGT CATCATCACC ATCACCATTG AGTTTAAACC
901    CGCTGATCAG CCTCGACTGT GCCTTCTAGT TGCCAGCCAT CTGTTGTTTG CCCCTCCCCC
961    GTGCCTTCCT TGACCCTGGA AGGTGCCACT CCCACTGTCC TTCCTAATA AAATGAGGAA
1021   ATTGCATCGC ATTGTCTGAG TAGGTGTCAT TCTATTCTGG GGGGTGGGGT GGGGCAGGAC
1081   AGCAAGGGGG AGGATTGGGA AGACAATAGC AGGCATGCTG GGGATGCGGT GGGCTCTATG
1141   G
```

Version #2:

```
1      ATGGCTAGCA AAGGAGAAGA ACTCTTCACT GGAGTTGTCC CAATTCTTGT TGAATTAGAT
61     GGTGATGTTA ACGGCCACAA GTTCTCTGTC AGTGGAGAGG GTGAAGGTGA TGCAACATAC
121    GGAAAACTTA CCCTGAAGTT CATCTGCACT ACTGGCAAAC TGCCTGTTCC GTGGCCGACA
181    CTAGTGACGA CGCTCTGCTA TGGCGTCCAG TGCTTTTCAA GATACCCGGA TCACATGAAA
241    CGGCATGACT TTTTCAAGAG TGCCATGCCC GAAGGTTATG TACAGGAAAAG GACCATCTTC
301    TTCAAAGATG ACGGCAACTA CAAGACACGT GCTGAAGTCA AGTTTGAAGG TGATACCCCTT
361    GTTAATAGAA TCGAGTTAAA AGGTATTGAC TTCAAGGAAG ATGGCAACAT TCTGGGACAC
421    AAATTGGAAT ACAACTATAA CTCACACAAT GTATACATCA TGGCAGACAA AAAAAAGAAT
481    GGAATCAAAG TGAAGTTCAA GACCCGCCAC AACATTGAAG ATGGAAGCGT TCAACTAGCA
541    GACCATTATC AACAAAATAC TCCAATTGGC GATGGCCCTG TCCTTTTACC AGACAACCAT
601    TACCTGTCCA CACAATCTGC CCTTTCGAAA GATCCCAACG AAAAGAGAGA CCACATGGTC
661    CTTCTTGAGT TTGTAACAGC TGCTGGGATT ACACATGGCA TGGATGAACT ATACAAATCC
721    GGCTCTAGA G GGGCC TAGTA AGTGGAAGG ACGCGGGATC CGCCATATAT WWWWARWWWWT
781    CCGGTGTCGA GAAGAGGAGA ACAATATGCT AAATGTTGTT CTCGTCTCCT CGACACC CGW
841    WWWYCWWWWA TATATGGCGG CCGGTCATCA TCACCATCAC CATTGAGTTT AAACCCGCTG
901    ATCAGCCTCG ACTGTGCCTT CTAGTTGCCA GCCATCTGTT GTTGCCCCCT CCCCCGTGCC
961    TTCCTTGACC CTGGAAGGTG CCACTCCCAC TGTCTTTTCC TAATAAAATG AGGAAATTGC
1021   ATCGCATTGT CTGAGTAGGT GTCATTCTAT TCTGGGGGGT GGGGTGGGGC AGGACAGCAA
1081   GGGGGAGGAT TGGGAAGACA ATAGCAGGCA TGCTGGGGAT GCGGTGGGCT CTATGG
```

2. Cloning strategy for circular CLUSTER or LEAPER guide RNAs in the pEdit1.2 backbone

Sequence of the complete expression cassette in our **circular gRNA cloning vector (pTS1541, Tornado OHA vector U6)** that is based on our in-house pEdit1.2 backbone (see editing vector in [2]). The construct contains two twister ribozymes (**P3 twister U2A ribozyme**, **P1 twister ribozyme**) and adjacent **ligation** sequences to enable autocatalytic cleavage followed by processing by the endogenous ligase RtcB resulting in circularization. By using two **Bbs-I** sites the guide RNA sequence can be seamlessly added between the ligation sequences. The inserted sequence can either be an unstructured LEAPER guide RNA or a CLUSTER guide RNA containing a split-R/G motif, a specificity domain and a cluster of recruitment sequences. The circular guide RNA sequences listed in Supplementary Table S1 show the guide RNA ligation sequences after ribozyme processing. The guide RNAs are under control of an **U6 promoter**. A **7xT-stretch** within the **SV40 Poly(A) signal** serves as pol3 termination signal.

```

1      GAGGGCCTAT TTCCCATGAT TCCTTCATAT TTGCATATAC GATACAAGGC TGTTAGAGAG
61     ATAATTAGAA TTAATTTGAC TGTAACACA AAGATATTAG TACAAAATAC GTGACGTAGA
121    AAGTAATAAT TTCTTGGGTA GTTTCAGTT TTAAAATTAT GTTTTAAAAAT GGACTATCAT
181    ATGCTTACCG TAACTTGAAA GTATTTGAT TTCTTGCTT TATATATCTT GTGGAAAGGA
241    CGAAACACCG TGCTCGCTTC GGCAGCACAT ATACTAGTCG ACGGCATCAG TCGCCGGTCC
301    CAAGCCCCGA TAAAAATGGGA GGGGGCGGGA AACCGGCTAA CCATGCCGAC TGATGGCAGT
361    AGTCTTCACT GGTACCGAGC TCGGATCCAC TGGAATTCGC CATGCATCTA GGGCCCTAGA
421    AGACTACTGC CATCAGTCGG CGTGGACTGT AGAACACTGC CAATGCCGGT CCCAAGCCCG
481    GATAAAAGTG GAGGGTACAG TCCACGCTCT AGAGCGGACT TCGGTCCGCT TTTTACTAGG
541    ACCTGCAGGC ATGCAAGCTT GACGTCGGT ACCGATATCC ATATGGCGGC CGCATCGATC
601    TCGAGCCGCG GACTAGTAAC TTGTTTATTG CAGCTTATAA TGTTTACAAA TAAAGCAATA
661    GCATCACAAA TTTCACAAAT AAAGCATTTTT TTTCACTGCA TTCTAGTTGT GGTGTGTCCA
721    AACTCATCAA TGTATCTTA

```

3. Cloning strategy for circular CLUSTER guide RNAs in the pAAV-GFP backbone

For AAV production the circular V27.2.4 splitR/G CLUSTER guide RNA was PCR-cloned into the pAAV-GFP backbone (Cell Biolabs) using the primer pair 5058+5059 on pTS2108 and the MluI and BglII restriction sites. The primers 5122-5123, the PCR template pTS1160 and the restriction site MluI were used to insert stuffer sequences adjusting the distance from the start of the first ITR to the end of the second ITR of each construct to ~4500 bp including the ITRs.

4. ORF & amino acid sequences:

ORF & amino acid sequence of the **murine_Mecp2_W104Amber-eGFP (pTS1034)** construct in the context of the pEGFP-N3 vector (Clontech), under control of the CMV promoter and the SV40 polyA signal:

```

          10          20          30          40          50          60
1 gaattccaccATGGCCGCCGCTGCCGCCACCGCCGCCGCCGCCGCCGCCGAGCGGAGGAGGAGGAGGA
1 EcoRI      M  A  A  A  A  A  T  A  A  A  A  A  A  P  S  G  G  G  G  G

          70          80          90          100         110         120
61      GGCGAGGAGGAGAGACTGGAGGAAAAGTCAGAAGACCAGGATCTCCAGGGCCTCAGAGAC
21      G  E  E  E  R  L  E  E  K  S  E  D  Q  D  L  Q  G  L  R  D

          130         140         150         160         170         180
121     AAGCCACTGAAGTTTAAGAAGGCGAAGAAAGACAAGAAGGAGGACAAAGAAGGCAAGCAT
41      K  P  L  K  F  K  K  A  K  K  D  K  K  E  D  K  E  G  K  H

          190         200         210         220         230         240
181     GAGCCACTACAACCTTCAGCCCACCATTCTGCAGAGCCAGCAGAGGCAGGCAAAGCAGAA
61      E  P  L  Q  P  S  A  H  H  S  A  E  P  A  E  A  G  K  A  E

          250         260         270         280         290         300
241     ACATCAGAAAGCTCAGGCTCTGCCCCAGCAGTGCCAGAAGCCTCGGCTTCCCCCAAACAG
81      T  S  E  S  S  G  S  A  P  A  V  P  E  A  S  A  S  P  K  Q

          310         320         330         340         350         360
301     CGGCGCTCCATTATCCGTGACCGGGGACCTATGTATGATGACCCACCTTGCCTGAAGGT
101     R  R  S  I  I  R  D  R  G  P  M  Y  D  D  P  T  L  P  E  G

          370         380         390         400         410         420
361     TAGACACGAAAGCTTAAACAAAGGAAGTCTGGCCGATCTGCTGGAAAGTATGATGTATAT
121     *  T  R  K  L  K  Q  R  K  S  G  R  S  A  G  K  Y  D  V  Y
```

	430	440	450	460	470	480
421	TTGATCAATCCCCAGGGAAAAGCTTTTCGCTCTAAAGTAGAATTGATTGCATACTTTGAA					
141	L I N P Q G K A F R S K V E L I A Y F E					
	490	500	510	520	530	540
481	AAGGTGGGAGACACCTCCTTGGACCCTAATGATTTTGA CTTCACGGTAACTGGGAGAGGG					
161	K V G D T S L D P N D F D F T V T G R G					
	550	560	570	580	590	600
541	AGCCCCTCCAGGAGAGAGCAGAAACCACCTAAGAAGCCCAAATCTCCCAAAGCTCCAGGA					
181	S P S R R E Q K P P K K P K S P K A P G					
	610	620	630	640	650	660
601	ACTGGCAGGGGTCGGGGACGCCCCAAAGGGAGCGGCACTGGGAGACCAAAGGCAGCAGCA					
201	T G R G R G R P K G S G T G R P K A A A					
	670	680	690	700	710	720
661	TCAGAAGGTGTTTCAGGTGAAAAGGGTCCTGGAGAAGAGCCCTGGGAAACTTGTTGTCAAG					
221	S E G V Q V K R V L E K S P G K L V V K					
	730	740	750	760	770	780
721	ATGCCTTTCCAAGCATCGCCTGGGGGTAAGGGTGAGGGAGGTGGGGCTACCACATCTGCC					
241	M P F Q A S P G G K G E G G G A T T S A					
	790	800	810	820	830	840
781	CAGGTCATGGTGATCAAACGCCCTGGCAGAAAGCGAAAAGCTGAAGCTGACCCCCAGGCC					
261	Q V M V I K R P G R K R K A E A D P Q A					
	850	860	870	880	890	900
841	ATTCTTAAGAAACGGGGTAGAAAGCCTGGGAGTGTGGTGGCAGCTGCTGCAGCTGAGGCC					
281	I P K K R G R K P G S V V A A A A A E A					

	910	920	930	940	950	960
901	AAAAAGAAAGCCGTGAAGGAGTCTTCCATACGGTCTGTGCATGAGACTGTGCTCCCCATC					
301	K K K A V K E S S I R S V H E T V L P I					
	970	980	990	1000	1010	1020
961	AAGAAGCGCAAGACCCGGGAGACGGTCAGCATCGAGGTCAAGGAAGTGGTGAAGCCCCTG					
321	K K R K T R E T V S I E V K E V V K P L					
	1030	1040	1050	1060	1070	1080
1021	CTGGTGTCCACCCTTGGTGAGAAAAGCGGGAAGGGACTGAAGACCTGCAAGAGCCCTGGG					
341	L V S T L G E K S G K G L K T C K S P G					
	1090	1100	1110	1120	1130	1140
1081	CGTAAAAGCAAGGAGAGCAGCCCCAAGGGGCGCAGCAGCAGTGCCTCCTCCCCACCTAAG					
361	R K S K E S S P K G R S S S A S S P P K					
	1150	1160	1170	1180	1190	1200
1141	AAGGAGCACCATCATCACCACCATCACTCAGAGTCCACAAAGGCCCCCATGCCACTGCTC					
381	K E H H H H H H H S E S T K A P M P L L					
	1210	1220	1230	1240	1250	1260
1201	CCATCCCCACCCCCACCTGAGCCTGAGAGCTCTGAGGACCCCATCAGCCCCCCTGAGCCT					
401	P S P P P P E P E S S E D P I S P P E P					
	1270	1280	1290	1300	1310	1320
1261	CAGGACTTGAGCAGCAGCATCTGCAAAGAAGAGAAGATGCCCCGAGGAGGCTCACTGGAA					
421	Q D L S S S I C K E E K M P R G G S L E					
	1330	1340	1350	1360	1370	1380
1321	AGCGATGGCTGCCCCAAGGAGCCAGCTAAGACTCAGCCTATGGTCGCCACCACTACCACA					
441	S D G C P K E P A K T Q P M V A T T T T					

	1390	1400	1410	1420	1430	1440
1381	GTTGCAGAAAAGTACAAACACCGAGGGGAGGGAGAGCGCAAAGACATTGTTTCATCTTCC					
461	V A E K Y K H R G E G E R K D I V S S S					
	1450	1460	1470	1480	1490	1500
1441	ATGCCAAGGCCAAACAGAGAGGAGCCTGTGGACAGCCGACGCCCGTGACCGAGAGAGTT					
481	M P R P N R E E P V D S R T P V T E R V					
	1510	1520	1530	1540	1550	1560
1501	AGC <u>GGTACC</u> GCGGGCCCCGGGATCCATCGCCACC <u>ATG</u> GTGAGCAAGGGCGAGGAGCTGTTC					
	KpnI	Linker	start eGFP			
501	S G T A G P G S I A T M V S K G E E L F					
	1570	1580	1590	1600	1610	1620
1561	ACCGGGGTGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAACGGCCACAAGTTCAGC					
521	T G V V P I L V E L D G D V N G H K F S					
	1630	1640	1650	1660	1670	1680
1621	GTGTCCGGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGAAGTTCATCTGC					
541	V S G E G E G D A T Y G K L T L K F I C					
	1690	1700	1710	1720	1730	1740
1681	ACCACCGGCAAGCTGCCCCGTGCCCTGGCCACCCCTCGTGACCACCCCTGACCTACGGCGTG					
561	T T G K L P V P W P T L V T T L T Y G V					
	1750	1760	1770	1780	1790	1800
1741	CAGTGCTTCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCAAGTCCGCCATG					
581	Q C F S R Y P D H M K Q H D F F K S A M					
	1810	1820	1830	1840	1850	1860
1801	CCCGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGACGGCAACTACAAGACC					

601 P E G Y V Q E R T I F F K D D G N Y K T

 1870 1880 1890 1900 1910 1920
 1861 CGCGCCGAGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGCTGAAGGGCATC
 621 R A E V K F E G D T L V N R I E L K G I

 1930 1940 1950 1960 1970 1980
 1921 GACTTCAAGGAGGACGGCAACATCCTGGGGCACAAGCTGGAGTACAACAGCCAC
 641 D F K E D G N I L G H K L E Y N Y N S H

 1990 2000 2010 2020 2030 2040
 1981 AACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAAGGTGAACTTCAAGATCCGC
 661 N V Y I M A D K Q K N G I K V N F K I R

 2050 2060 2070 2080 2090 2100
 2041 CACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGAACACCCCCATC
 681 H N I E D G S V Q L A D H Y Q Q N T P I

 2110 2120 2130 2140 2150 2160
 2101 GGCGACGGCCCCGTGCTGCTGCCCCGACAACCACTACCTGAGCACCCAGTCCGCCCTGAGC
 701 G D G P V L L P D N H Y L S T Q S A L S

 2170 2180 2190 2200 2210 2220
 2161 AAAGACCCCAACGAGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTGACCGCCGCCGGG
 721 K D P N E K R D H M V L L E F V T A A G

 2230 2240 2250
 2221 ATCACTCTCGGCATGGACGAGCTGTACAAGTAA
 741 I T L G M D E L Y K *

ORF & amino acid sequence of the **human_PEX1_G843D** construct under control of the EF-1 α promoter and the EF-1 α polyA signal:

	10	20	30	40	50	60
1	<u>ATG TGGGGCAGCGATCGCCTGGCGGGTGCTGGGGGAGGCGGGCGGCAGTGACTGTGGCC</u>					
1	M	W	G	S	D	R
	L	A	G	A	G	G
	G	G	A	A	V	T
	V	A				
	70	80	90	100	110	120
61	TTCACCAACGCTCGCGACTGCTTCCTCCACCTGCCGCGCGTCTCGTGGCCCAGCTGCAT					
21	F	T	N	A	R	D
	C	F	L	H	L	P
	R	R	L	V	A	Q
	L	H				
	130	140	150	160	170	180
121	CTGCTGCAGAATCAAGCTATAGAAGTGGTCTGGAGTCACCAGCCTGCATTCTTGAGCTGG					
41	L	L	Q	N	Q	A
	I	E	V	V	W	S
	H	Q	P	A	F	L
	S	W				
	190	200	210	220	230	240
181	GTGGAAGGCAGGCATTTTAGTGATCAAGGTGAAAATGTGGCTGAAATTAACAGACAAGTT					
61	V	E	G	R	H	F
	S	D	Q	G	E	N
	V	A	E	I	N	R
	Q	V				
	250	260	270	280	290	300
241	GGTCAAAACTTGGACTCTCAAATGGGGGACAGGTATTTCTCAAGCCATGTTCCCATGTG					
81	G	Q	K	L	G	L
	S	N	G	G	Q	V
	F	L	K	P	C	S
	H	V				
	310	320	330	340	350	360
301	GTATCTTGTCAACAAGTTGAGGTGGAACCCCTCTCAGCAGATGATTGGGAGATACTGGAG					
101	V	S	C	Q	Q	V
	E	V	E	P	L	S
	A	D	D	W	E	I
	L	E				
	370	380	390	400	410	420
361	CTGCATGCTGTTTCCCTTGAACAACATCTTCTAGATCAAATTCGAATAGTTTTTCCAAAA					
121	L	H	A	V	S	L
	E	Q	H	L	L	D
	Q	I	R	I	V	F
	P	K				
	430	440	450	460	470	480

421 GCCATTTTCTGTTTGGGTTGATCAACAAACGTACATATTTATCCAAATTGTTGCACTA
 141 A I F P V W V D Q Q T Y I F I Q I V A L
 490 500 510 520 530 540
 481 ATACCAGCTGCCTCTTATGGAAGGCTGGAACTGACACCAAACCTCCTTATTCAGCCAAAG
 161 I P A A S Y G R L E T D T K L L I Q P K
 550 560 570 580 590 600
 541 ACACGCCGAGCCAAAGAGAATACATTTTCAAAGCTGATGCTGAATATAAAAACTTCAT
 181 T R R A K E N T F S K A D A E Y K K L H
 610 620 630 640 650 660
 601 AGTTATGGAAGAGACCAGAAAGGAATGATGAAAGAACTTCAAACCAAGCAACTTCAGTCA
 201 S Y G R D Q K G M M K E L Q T K Q L Q S
 670 680 690 700 710 720
 661 AATACTGTGGAATCACTGAATCTAATGAAAACGAGTCAGAGATTCCAGTTGACTCATCA
 221 N T V G I T E S N E N E S E I P V D S S
 730 740 750 760 770 780
 721 TCAGTAGCAAGTTTATGGACTATGATAGGAAGCATTTTTTCCTTTCAATCTGAGAAGAAA
 241 S V A S L W T M I G S I F S F Q S E K K
 790 800 810 820 830 840
 781 CAAGAGACATCTTGGGGTTTAACTGAAATCAATGCATTCAAAAATATGCAGTCAAAGGTT
 261 Q E T S W G L T E I N A F K N M Q S K V
 850 860 870 880 890 900
 841 GTTCCTCTAGACAATATTTTCAGAGTATGCAAATCTCAACCTCCTAGTATATATAACGCG
 281 V P L D N I F R V C K S Q P P S I Y N A
 910 920 930 940 950 960

901 TCAGCAACCTCTGTTTTTCATAAACACTGTGCCATTCATGTATTTCCATGGGACCAGGAA
 301 S A T S V F H K H C A I H V F P W D Q E
 970 980 990 1000 1010 1020
 961 TATTTTGATGTAGAGCCCAGCTTTACTGTGACATATGGAAAGCTAGTTAAGCTACTTTCT
 321 Y F D V E P S F T V T Y G K L V K L L S
 1030 1040 1050 1060 1070 1080
 1021 CCAAAGCAACAGCAAAGTAAAACAAAACAAAATGTGTTATCACCTGAAAAAGAGAAGCAG
 341 P K Q Q Q S K T K Q N V L S P E K E K Q
 1090 1100 1110 1120 1130 1140
 1081 ATGTCAGAGCCACTAGATCAAAAAAAAAATTAGGTCAGATCATAATGAAGAAGATGAGAAG
 361 M S E P L D Q K K I R S D H N E E D E K
 1150 1160 1170 1180 1190 1200
 1141 GCCTGTGTGCTACAAGTAGTCTGGAATGGACTTGAAGAATTGAACAATGCCATCAAATAT
 381 A C V L Q V V W N G L E E L N N A I K Y
 1210 1220 1230 1240 1250 1260
 1201 ACCAAAAATGTAGAAGTTCTCCATCTTGGGAAAGTCTGGATTCCAGATGACCTGAGGAAG
 401 T K N V E V L H L G K V W I P D D L R K
 1270 1280 1290 1300 1310 1320
 1261 AGACTAAATATAGAAATGCATGCCGTAGTCAGGATAACTCCAGTGAAGTTACCCCTAAA
 421 R L N I E M H A V V R I T P V E V T P K
 1330 1340 1350 1360 1370 1380
 1321 ATTCCAAGATCTCTAAAGTTACAACCTAGAGAGAATTTACCTAAAGACATAAGTGAAGAA
 441 I P R S L K L Q P R E N L P K D I S E E
 1390 1400 1410 1420 1430 1440

1381 GACATAAAAACTGTATTTTATTCATGGCTACAGCAGTCTACTACCACCATGCTTCCTTTG
 461 D I K T V F Y S W L Q Q S T T T M L P L
 1450 1460 1470 1480 1490 1500
 1441 GTAATATCAGAGGAAGAATTTATTAAGCTGGAACTAAAGATGGACTGAAGGAATTTTCT
 481 V I S E E E F I K L E T K D G L K E F S
 1510 1520 1530 1540 1550 1560
 1501 CTGAGTATAGTTCATTCTTGGGAAAAAGAAAAAGATAAAAAATATTTTCTGTTGAGTCCC
 501 L S I V H S W E K E K D K N I F L L S P
 1570 1580 1590 1600 1610 1620
 1561 AATTTGCTGCAGAAGACTACAATACAAGTCCTTCTAGATCCTATGGTAAAAGAAGAAAAC
 521 N L L Q K T T I Q V L L D P M V K E E N
 1630 1640 1650 1660 1670 1680
 1621 AGTGAGGAAATTGACTTTATTCTTCCTTTTTTAAAGCTGAGCTCTTTGGGAGGAGTGAAT
 541 S E E I D F I L P F L K L S S L G G V N
 1690 1700 1710 1720 1730 1740
 1681 TCCTTAGGCGTATCCTCCTTGGAGCACATCACTCACAGCCTCCTGGGACGCCCTTTGTCT
 561 S L G V S S L E H I T H S L L G R P L S
 1750 1760 1770 1780 1790 1800
 1741 CGGCAGCTGATGTCTCTTGTTGCAGGACTTAGGAATGGAGCTCTTTTACTCACAGGAGGA
 581 R Q L M S L V A G L R N G A L L L T G G
 1810 1820 1830 1840 1850 1860
 1801 AAGGGAAGTGGAAAATCAACTTTAGCCAAAGCAATCTGTAAAGAAGCATTTGACAAACTG
 601 K G S G K S T L A K A I C K E A F D K L
 1870 1880 1890 1900 1910 1920

1861 GATGCCCATGTGGAGAGAGTTGACTGTAAAGCTTTACGAGGAAAAAGGCTTGAAAACATA
621 D A H V E R V D C K A L R G K R L E N I

1930 1940 1950 1960 1970 1980
1921 CAAAAAACCTAGAGGTGGCTTTCTCAGAGGCAGTGTGGATGCAGCCATCTGTTGTCCTG
641 Q K T L E V A F S E A V W M Q P S V V L

1990 2000 2010 2020 2030 2040
1981 CTGGATGACCTTGACCTCATTGCTGGACTGCCTGCTGTCCCGGAACATGAGCACAGTCCT
661 L D D L D L I A G L P A V P E H E H S P

2050 2060 2070 2080 2090 2100
2041 GATGCGGTGCAGAGCCAGCGGCTTGCTCATGCTTTGAATGATATGATAAAAGAGTTTATC
681 D A V Q S Q R L A H A L N D M I K E F I

2110 2120 2130 2140 2150 2160
2101 TCCATGGGAAGTTTGGTTGCACTGATTGCCACAAGTCAGTCTCAGCAATCTCTACATCCT
701 S M G S L V A L I A T S Q S Q Q S L H P

2170 2180 2190 2200 2210 2220
2161 TTACTTGTCTTGCTCAAGGAGTTCACATATTTAGTGCCTCCACACATTCAGCCTCCT
721 L L V S A Q G V H I F Q C V Q H I Q P P

2230 2240 2250 2260 2270 2280
2221 AATCAGGAACAAAGATGTGAAATTCTGTGTAATGTAATAAAAAATAAATTGGACTGTGAT
741 N Q E Q R C E I L C N V I K N K L D C D

2290 2300 2310 2320 2330 2340
2281 ATAAACAAGTTCACCGATCTTGACCTGCAGCATGTAGCTAAAGAACTGGAGGGTTTGTG
761 I N K F T D L D L Q H V A K E T G G F V

2350 2360 2370 2380 2390 2400

2341 GCTAGAGATTTTACAGTACTTGTGGATCGAGCCATACATTCTCGACTCTCTCGTCAGAGT
 781 A R D F T V L V D R A I H S R L S R Q S

 2410 2420 2430 2440 2450 2460
 2401 ATATCCACCAGAGAAAAATTAGTTTTAACAACATTGGACTTCCAAAAGGCTCTCCGCGGA
 801 I S T R E K L V L T T L D F Q K A L R G

 2470 2480 2490 2500 2510 2520
 2461 TTTCTTCCTGCGTCTTTGCGAAGTGTCAACCTGCATAAACCTAGAGACCTGGGTTGGGAC
 821 F L P A S L R S V N L H K P R D L G W D

 2530 2540 2550 2560 2570 2580
 2521 AAGATTGATGGGTTACATGAAGTTAGGCAGATACTCATGGATACTATCCAGTTACCTGCC
 841 K I D G L H E V R Q I L M D T I Q L P A

 2590 2600 2610 2620 2630 2640
 2581 AAGTATCCAGAATTATTTGCAAACCTTGCCCATACGACAAAGAACAGGAATACTGTTGTAT
 861 K Y P E L F A N L P I R Q R T G I L L Y

 2650 2660 2670 2680 2690 2700
 2641 GGTCCGCCTGGAACAGGAAAAACCTTACTAGCTGGGGTAATTGCACGAGAGAGTAGAATG
 881 G P P G T G K T L L A G V I A R E S R M

 2710 2720 2730 2740 2750 2760
 2701 AATTTTATAAGTGTCAAGGGGCCAGAGTTACTCAGCAAATACATTGGAGCAAGTGAACAA
 901 N F I S V K G P E L L S K Y I G A S E Q

 2770 2780 2790 2800 2810 2820
 2761 GCTGTTCCGGGATATTTTTATTAGAGCACAGGCTGCAAAGCCCTGCATTCTTTCTTTGAT
 921 A V R D I F I R A Q A A K P C I L F F D

 2830 2840 2850 2860 2870 2880

2821 GAATTTGAATCCATTGCTCCTCGGCGGGGTCATGATAATACAGGAGTTACAGACCGAGTA
941 E F E S I A P R R G H D N T G V T D R V

2890 2900 2910 2920 2930 2940
2881 GTTAACCAGTTGCTGACTCAGTTGGATGGAGTAGAAGGCTTACAGGGTGTTTATGTATTG
961 V N Q L L T Q L D G V E G L Q G V Y V L

2950 2960 2970 2980 2990 3000
2941 GCTGCTACTAGTCGCCCTGACTTGATTGACCCTGCCCTGCTTAGGCCTGGTCGACTAGAT
981 A A T S R P D L I D P A L L R P G R L D

3010 3020 3030 3040 3050 3060
3001 AAATGTGTATACTGTCTCCTCCTGATCAGGTGTCACGTCTTGAAATTTTAAATGTCTCTC
1001 K C V Y C P P P D Q V S R L E I L N V L

3070 3080 3090 3100 3110 3120
3061 AGTGACTCTCTACCTCTGGCAGATGATGTTGACCTTCAGCATGTAGCATCAGTAACTGAC
1021 S D S L P L A D D V D L Q H V A S V T D

3130 3140 3150 3160 3170 3180
3121 TCCTTTACTGGAGCTGATCTGAAAGCTTTACTTTACAATGCCCAATTGGAGGCCCTTACAT
1041 S F T G A D L K A L L Y N A Q L E A L H

3190 3200 3210 3220 3230 3240
3181 GGAATGCTGCTCTCGAGTGGACTCCAGGATGGAAGTTCCAGCTCTGATAGTGACCTAAGT
1061 G M L L S S G L Q D G S S S S D S D L S

3250 3260 3270 3280 3290 3300
3241 CTGTCTTCAATGGTCTTTCTTAACCATAGCAGTGGCTCTGACGATTGAGCTGGAGATGGA
1081 L S S M V F L N H S S G S D D S A G D G

3310 3320 3330 3340 3350 3360

3301	GAATGTGGCTTAGATCAGTCCCTTGTTTCTTTAGAGATGTCCGAGATCCTTCCAGATGAA
1101	E C G L D Q S L V S L E M S E I L P D E
	3370 3380 3390 3400 3410 3420
3361	TCAAAATTCAATATGTACCGGCTCTACTTTGGAAGCTCTTATGAATCAGAACTTGAAAT
1121	S K F N M Y R L Y F G S S Y E S E L G N
	3430 3440 3450 3460 3470 3480
3421	GGAACCTCTTCTGATTTGAGCTCACAATGTCTCTCTGCACCAAGCTCCATGACTCAGGAT
1141	G T S S D L S S Q C L S A P S S M T Q D
	3490 3500 3510 3520 3530 3540
3481	TTGCCTGGAGTTCCTGGGAAAGACCAGTTGTTTTACAGCCTCCAGTGTTAAGGACAGCT
1161	L P G V P G K D Q L F S Q P P V L R T A
	3550 3560 3570 3580 3590 3600
3541	TCACAAGAGGGTTGCCAAGAACTTACACAAGAACAAAGAGATCAACTGAGGGCAGATATC
1181	S Q E G C Q E L T Q E Q R D Q L R A D I
	3610 3620 3630 3640 3650 3660
3601	AGTATTATCAAAGGCAGATACCGGAGCCAAAGTGGAGAGGACGAATCCATGAACCAACCA
1201	S I I K G R Y R S Q S G E D E S M N Q P
	3670 3680 3690 3700 3710 3720
3661	GGACCAATCAAAACCAGACTGGCTATTAGTCAGTCACATTTAATGACTGCACTTGGTCAC
1221	G P I K T R L A I S Q S H L M T A L G H
	3730 3740 3750 3760 3770 3780
3721	ACAAGACCATCCATTAGTGAAGATGACTGGAAGAATTTTGCTGAGCTATATGAAAGCTTT
1241	T R P S I S E D D W K N F A E L Y E S F
	3790 3800 3810 3820 3830 3840

3781 CAAAATCCAAAGAGGAGAAAAAATCAAAGTGGACAATGTTTCGACCTGGACAGAAAGTA
 1261 Q N P K R R K N Q S G T M F R P G Q K V

 3850 3860 3870 3880 3890
 3841 ACTTTAGCAGAAAACCTGTATTTTCAGGGACACCATCACCATCACCATTAA
 1281 T L A E N L Y F Q G H H H H H H H *

ORF & amino acid sequence of the **dPspCas13b_ADAR2DD_E488Q** construct under control of the CMV promoter and the bGH poly(A) signal:

	10	20	30	40	50	60
1	ATG AACATCCCCGCTCTGGTGGAAAACCAGAAGAAGTACTTTGGCACCTACAGCGTGATG					
1	M	N	I	P	A	L
	V	E	N	Q	K	K
	Y	F	G	T	Y	S
	V	M				
	70	80	90	100	110	120
61	GCCATGCTGAACGCTCAGACCGTGCTGGACCACATCCAGAAGGTGGCCGATATTGAGGGC					
21	A	M	L	N	A	Q
	T	V	L	D	H	I
	Q	K	V	A	D	I
	E	G				
	130	140	150	160	170	180
121	GAGCAGAACGAGAACAACGAGAATCTGTGGTTTCACCCCGTGATGAGCCACCTGTACAAC					
41	E	Q	N	E	N	N
	E	N	L	W	F	H
	P	V	M	S	H	L
	Y	N				
	190	200	210	220	230	240
181	GCCAAGAACGGCTACGACAAGCAGCCCCGAGAAAACCATGTTTCATCATCGAGCGGCTGCAG					
61	A	K	N	G	Y	D
	K	Q	P	E	K	T
	M	F	I	I	E	R
	L	Q				
	250	260	270	280	290	300
241	AGCTACTTCCCATTCTGAAGATCATGGCCGAGAACCAGAGAGAGTACAGCAACGGCAAG					
81	S	Y	F	P	F	L
	K	I	M	A	E	N
	Q	R	E	Y	S	N
	G	K				
	310	320	330	340	350	360
301	TACAAGCAGAACCGCGTGGAAGTGAACAGCAACGACATCTTCGAGGTGCTGAAGCGCGCC					
101	Y	K	Q	N	R	V
	E	V	N	S	N	D
	I	F	E	V	L	K
	R	A				
	370	380	390	400	410	420
361	TTCGGCGTGCTGAAGATGTACAGGGACCTGACCAACGCATACAAGACCTACGAGGAAAAG					
121	F	G	V	L	K	M
	Y	R	D	L	T	N
	A	Y	K	T	Y	E
	E	K				
	430	440	450	460	470	480
421	CTGAACGACGGCTGCGAGTTCCTGACCAGCACAGAGCAACCTCTGAGCGGCATGATCAAC					

141 L N D G C E F L T S T E Q P L S G M I N

 490 500 510 520 530 540
 481 AACTACTACACAGTGGCCCTGCGGAACATGAACGAGAGATACGGCTACAAGACAGAGGAC
 161 N Y Y T V A L R N M N E R Y G Y K T E D

 550 560 570 580 590 600
 541 CTGGCCTTCATCCAGGACAAGCGGTTCAAGTTCGTGAAGGACGCCTACGGCAAGAAAAAG
 181 L A F I Q D K R F K F V K D A Y G K K K

 610 620 630 640 650 660
 601 TCCCAAGTGAATACCGGATTCTTCCTGAGCCTGCAGGACTACAACGGCGACACACAGAAG
 201 S Q V N T G F F L S L Q D Y N G D T Q K

 670 680 690 700 710 720
 661 AAGCTGCACCTGAGCGGAGTGGGAATCGCCCTGCTGATCTGCCTGTTCTGACAAAGCAG
 221 K L H L S G V G I A L L I C L F L D K Q

 730 740 750 760 770 780
 721 TACATCAACATCTTTCTGAGCAGGCTGCCCATCTTCTCCAGCTACAATGCCCAGAGCGAG
 241 Y I N I F L S R L P I F S S Y N A Q S E

 790 800 810 820 830 840
 781 GAACGGCGGATCATCATCAGATCCTTCGGCATCAACAGCATCAAGCTGCCCCAAGGACCGG
 261 E R R I I I R S F G I N S I K L P K D R

 850 860 870 880 890 900
 841 ATCCACAGCGAGAAGTCCAACAAGAGCGTGGCCATGGATATGCTCAACGAAGTGAAGCGG
 281 I H S E K S N K S V A M D M L N E V K R

 910 920 930 940 950 960
 901 TGCCCCGACGAGCTGTTCAACAACACTGTCTGCCGAGAAGCAGTCCCGGTTTCAGAATCATC

301	C P D E L F T T L S A E K Q S R F R I I
	970 980 990 1000 1010 1020
961	AGCGACGACCACAATGAAGTGCTGATGAAGCGGAGCAGCGACAGATTCGTGCCTCTGCTG
321	S D D H N E V L M K R S S D R F V P L L
	1030 1040 1050 1060 1070 1080
1021	CTGCAGTATATCGATTACGGCAAGCTGTTTCGACCACATCAGGTTCCACGTGAACATGGGC
341	L Q Y I D Y G K L F D H I R F H V N M G
	1090 1100 1110 1120 1130 1140
1081	AAGCTGAGATACCTGCTGAAGGCCGACAAGACCTGCATCGACGGCCAGACCAGAGTCAGA
361	K L R Y L L K A D K T C I D G Q T R V R
	1150 1160 1170 1180 1190 1200
1141	GTGATCGAGCAGCCCCTGAACGGCTTCGGCAGACTGGAAGAGGCCGAGACAATGCGGAAG
381	V I E Q P L N G F G R L E E A E T M R K
	1210 1220 1230 1240 1250 1260
1201	CAAGAGAACGGCACCTTCGGCAACAGCGGCATCCGGATCAGAGACTTCGAGAACATGAAG
401	Q E N G T F G N S G I R I R D F E N M K
	1270 1280 1290 1300 1310 1320
1261	CGGGACGACGCCAATCCTGCCAACTATCCCTACATCGTGGACACCTACACACACTACATC
421	R D D A N P A N Y P Y I V D T Y T H Y I
	1330 1340 1350 1360 1370 1380
1321	CTGGAAAACAACAAGGTCGAGATGTTTATCAACGACAAAAGAGGACAGCGCCCCACTGCTG
441	L E N N K V E M F I N D K E D S A P L L
	1390 1400 1410 1420 1430 1440
1381	CCCGTGATCGAGGATGATAGATACGTGGTCAAGACAATCCCCAGCTGCCGGATGAGCACC

461 P V I E D D R Y V V K T I P S C R M S T

 1450 1460 1470 1480 1490 1500
 1441 CTGGA AATTCCAGCCATGGCCTTCCACATGTTTCTGTTCCGGCAGCAAGAAAACCGAGAAG
 481 L E I P A M A F H M F L F G S K K T E K

 1510 1520 1530 1540 1550 1560
 1501 CTGATCGTGGACGTGCACAACCGGTACAAGAGACTGTTCCAGGCCATGCAGAAAGAAGAA
 501 L I V D V H N R Y K R L F Q A M Q K E E

 1570 1580 1590 1600 1610 1620
 1561 GTGACCGCCGAGAATATCGCCAGCTTCGGAATCGCCGAGAGCGACCTGCCTCAGAAGATC
 521 V T A E N I A S F G I A E S D L P Q K I

 1630 1640 1650 1660 1670 1680
 1621 CTGGATCTGATCAGCGGCAATGCCCACGGCAAGGATGTGGACGCCTTCATCAGACTGACC
 541 L D L I S G N A H G K D V D A F I R L T

 1690 1700 1710 1720 1730 1740
 1681 GTGGACGACATGCTGACCGACACCGAGCGGAGAATCAAGAGATTCAAGGACGACCGGAAG
 561 V D D M L T D T E R R I K R F K D D R K

 1750 1760 1770 1780 1790 1800
 1741 TCCATTTCGGAGCGCCGACAACAAGATGGGAAAGAGAGGCTTCAAGCAGATCTCCACAGGC
 581 S I R S A D N K M G K R G F K Q I S T G

 1810 1820 1830 1840 1850 1860
 1801 AAGCTGGCCGACTTCCTGGCCAAGGACATCGTGCTGTTTCAGCCCAGCGTGAACGATGGC
 601 K L A D F L A K D I V L F Q P S V N D G

 1870 1880 1890 1900 1910 1920
 1861 GAGAACAAGATCACCGGCCTGAACTACCGGATCATGCAGAGCGCCATTGCCGTGTACGAT

621	E N K I T G L N Y R I M Q S A I A V Y D
	1930 1940 1950 1960 1970 1980
1921	AGCGGCGACGATTACGAGGCCAAGCAGCAGTTCAAGCTGATGTTTCGAGAAGGCCCGGCTG
641	S G D D Y E A K Q Q F K L M F E K A R L
	1990 2000 2010 2020 2030 2040
1981	ATCGGCAAGGGCACAACAGAGCCTCATCCATTTCTGTACAAGGTGTTTCGCCCCGAGCATC
661	I G K G T T E P H P F L Y K V F A R S I
	2050 2060 2070 2080 2090 2100
2041	CCCGCCAATGCCGTCGAGTTCTACGAGCGCTACCTGATCGAGCGGAAGTTCTACCTGACC
681	P A N A V E F Y E R Y L I E R K F Y L T
	2110 2120 2130 2140 2150 2160
2101	GGCCTGTCCAACGAGATCAAGAAAGGCAACAGAGTGGATGTGCCCTTCATCCGGCGGGAC
701	G L S N E I K K G N R V D V P F I R R D
	2170 2180 2190 2200 2210 2220
2161	CAGAACAAGTGGAACACCCGCCATGAAGACCCTGGGCAGAATCTACAGCGAGGATCTG
721	Q N K W K T P A M K T L G R I Y S E D L
	2230 2240 2250 2260 2270 2280
2221	CCCGTGGAAGTGGCCAGACAGATGTTTCGACAATGAGATCAAGTCCCACCTGAAGTCCCTG
741	P V E L P R Q M F D N E I K S H L K S L
	2290 2300 2310 2320 2330 2340
2281	CCACAGATGGAAGGCATCGACTTCAACAATGCCAACGTGACCTATCTGATCGCCGAGTAC
761	P Q M E G I D F N N A N V T Y L I A E Y
	2350 2360 2370 2380 2390 2400
2341	ATGAAGAGAGTGCTGGACGACGACTTCCAGACCTTCTACCAGTGGAAACCGCAACTACCGG

781 M K R V L D D D F Q T F Y Q W N R N Y R

 2410 2420 2430 2440 2450 2460
 2401 TACATGGACATGCTTAAGGGCGAGTACGACAGAAAGGGCTCCCTGCAGCACTGCTTCACC
 801 Y M D M L K G E Y D R K G S L Q H C F T

 2470 2480 2490 2500 2510 2520
 2461 AGCGTGGAAGAGAGAGAAGGCCTCTGGAAAGAGCGGGCCTCCAGAACAGAGCGGTACAGA
 821 S V E E R E G L W K E R A S R T E R Y R

 2530 2540 2550 2560 2570 2580
 2521 AAGCAGGCCAGCAACAAGATCCGCAGCAACCGGCAGATGAGAAACGCCAGCAGCGAAGAG
 841 K Q A S N K I R S N R Q M R N A S S E E

 2590 2600 2610 2620 2630 2640
 2581 ATCGAGACAATCCTGGATAAGCGGCTGAGCAACAGCCGGAACGAGTACCAGAAAAGCGAG
 861 I E T I L D K R L S N S R N E Y Q K S E

 2650 2660 2670 2680 2690 2700
 2641 AAAGTGATCCGGCGCTACAGAGTGCAGGATGCCCTGCTGTTTCTGCTGGCCAAAAAGACC
 881 K V I R R Y R V Q D A L L F L L A K K T

 2710 2720 2730 2740 2750 2760
 2701 CTGACCGAACTGGCCGATTTTCGACGGCGAGAGGTTCAAACCTGAAAGAAATCATGCCCGAC
 901 L T E L A D F D G E R F K L K E I M P D

 2770 2780 2790 2800 2810 2820
 2761 GCCGAGAAGGGAATCCTGAGCGAGATCATGCCCATGAGCTTCACCTTCGAGAAAGGCGGC
 921 A E K G I L S E I M P M S F T F E K G G

 2830 2840 2850 2860 2870 2880
 2821 AAGAAGTACACCATCACCAGCGAGGGCATGAAGCTGAAGAACTACGGCGACTTCTTTGTG

941 K K Y T I T S E G M K L K N Y G D F F V

 2890 2900 2910 2920 2930 2940
 2881 CTGGCTAGCGACAAGAGGATCGGCAACCTGCTGGAACTCGTGGGCAGCGACATCGTGTCC
 961 L A S D K R I G N L L E L V G S D I V S

 2950 2960 2970 2980 2990 3000
 2941 AAAGAGGATATCATGGAAGAGTTCAACAAATACGACCAGTGCAGGCCCCGAGATCAGCTCC
 981 K E D I M E E F N K Y D Q C R P E I S S

 3010 3020 3030 3040 3050 3060
 3001 ATCGTGTTC AACCTGGAAAAGTGGGCCTTCGACACATACCCCGAGCTGTCTGCCAGAGTG
 1001 I V F N L E K W A F D T Y P E L S A R V

 3070 3080 3090 3100 3110 3120
 3061 GACCGGGAAGAGAAGGTGGA CTTC AAGAGCATCCTGAAAA TCCTGCTGAACAACAAGAAC
 1021 D R E E K V D F K S I L K I L L N N K N

 3130 3140 3150 3160 3170 3180
 3121 ATCAACAAAGAGCAGAGCGACATCCTGCGGAAGATCCGGAACGCCTTCGATGCAACAAT
 1041 I N K E Q S D I L R K I R N A F D A N N

 3190 3200 3210 3220 3230 3240
 3181 TACCCCGACAAAGGCGTG GTTGGAAATCAAGGCCCTGCCTGAGATCGCCATGAGCATCAAG
 1061 Y P D K G V V E I K A L P E I A M S I K

 3250 3260 3270 3280 3290 3300
 3241 AAGGCCTTTGGGGAGTACGCCATCATGAAGGGAAGCCTGCAGCTGCCTCCACTTGAAAGA
 1081 K A F G E Y A I M K G S L Q L P P L E R

 3310 3320 3330 3340 3350 3360
 3301 CTGACACTGGGATCCCAGCTGCATTTACCGCAGGTTTTAGCTGACGCTGTCTCACGCCTG

1101	L T L G S Q L H L P Q V L A D A V S R L
	3370 3380 3390 3400 3410 3420
3361	GTCCTGGGTAAGTTTGGTGACCTGACCGACAACCTTCTCCTCCCCTCACGCTCGCAGAAAA
1121	V L G K F G D L T D N F S S P H A R R K
	3430 3440 3450 3460 3470 3480
3421	GTGCTGGCTGGAGTCGTCATGACAACAGGCACAGATGTTAAAGATGCCAAGGTGATAAGT
1141	V L A G V V M T T G T D V K D A K V I S
	3490 3500 3510 3520 3530 3540
3481	GTTTCTACAGGAACAAAATGTATTAATGGTGAATACATGAGTGATCGTGGCCTTGCAATTA
1161	V S T G T K C I N G E Y M S D R G L A L
	3550 3560 3570 3580 3590 3600
3541	AATGACTGCCATGCAGAAATAATATCTCGGAGATCCTTGCTCAGATTTCTTTATACACAA
1181	N D C H A E I I S R R S L L R F L Y T Q
	3610 3620 3630 3640 3650 3660
3601	CTTGAGCTTTACTTAAATAACAAAGATGATCAAAAAAGATCCATCTTTCAGAAATCAGAG
1201	L E L Y L N N K D D Q K R S I F Q K S E
	3670 3680 3690 3700 3710 3720
3661	CGAGGGGGGTTTAGGCTGAAGGAGAATGTCCAGTTTCATCTGTACATCAGCACCTCTCCC
1221	R G G F R L K E N V Q F H L Y I S T S P
	3730 3740 3750 3760 3770 3780
3721	TGTGGAGATGCCAGAATCTTCTCACCACATGAGCCAATCCTGGAAGAACCAGCAGATAGA
1241	C G D A R I F S P H E P I L E E P A D R
	3790 3800 3810 3820 3830 3840
3781	CACCCAAATCGTAAAGCAAGAGGACAGCTACGGACCAAAATAGAGTCTGGTCAGGGGACG

1261 H P N R K A R G Q L R T K I E S G Q G T

 3850 3860 3870 3880 3890 3900
 3841 ATTCCAGTGCCTCCAATGCGAGCATCCAAACGTGGGACGGGGTGCTGCAAGGGGAGCGG
 1281 I P V R S N A S I Q T W D G V L Q G E R

 3910 3920 3930 3940 3950 3960
 3901 CTGCTCACCATGTCCTGCAGTGACAAGATTGCACGCTGGAACGTGGTGGGCATCCAGGGA
 1301 L L T M S C S D K I A R W N V V G I Q G

 3970 3980 3990 4000 4010 4020
 3961 TCACTGCTCAGCATTTTCGTGGAGCCCATTACTTCTCGAGCATCATCCTGGGCAGCCTT
 1321 S L L S I F V E P I Y F S S I I L G S L

 4030 4040 4050 4060 4070 4080
 4021 TACCACGGGGACCACCTTTCCAGGGCCATGTACCAGCGGATCTCCAACATAGAGGACCTG
 1341 Y H G D H L S R A M Y Q R I S N I E D L

 4090 4100 4110 4120 4130 4140
 4081 CCACCTCTCTACACCCTCAACAAGCCTTTGCTCAGTGGCATCAGCAATGCAGAAGCACGG
 1361 P P L Y T L N K P L L S G I S N A E A R

 4150 4160 4170 4180 4190 4200
 4141 CAGCCAGGGAAGGCCCCCAACTTCAGTGTCAACTGGACGGTAGGCGACTCCGCTATTGAG
 1381 Q P G K A P N F S V N W T V G D S A I E

 4210 4220 4230 4240 4250 4260
 4201 GTCATCAACGCCACGACTGGGAAGGATGAGCTGGGCCGCGCTCCCGCCTGTGTAAGCAC
 1401 V I N A T T G K D E L G R A S R L C K H

 4270 4280 4290 4300 4310 4320
 4261 GCGTTGTACTGTGCTGGATGCGTGTGCACGGCAAGGTTCCCTCCCACTTACTACGCTCC

ORF & amino acid sequence of the **4λN_ADAR2DD_E488Q** construct under control of the CMV promoter and the bGH poly(A) signal:

	10	20	30	40	50	60
1	ATG GACTACAAGGACGACGATGACAACTAGTAAATGCCCGTACGCGCCGGCGCGAACGG					
1	M	D	Y	K	D	D
	D	D	K	L	V	N
	A	R	T	R	R	R
	E	R				
	70	80	90	100	110	120
61	CGAGCAGAAAAGCAGGCACAGTGGAAGGCAGCTAATGGCGGAGGGGAAGCGGGGGCGGT					
21	R	A	E	K	Q	A
	Q	W	K	A	A	N
	G	G	G	G	S	G
	G					
	130	140	150	160	170	180
121	GGAAGTGGGGGTGGAGGCAGCAATGCGCGGACCCGCCGACGTGAACGGCGAGCAGAAAAA					
41	G	S	G	G	G	S
	N	A	R	T	R	R
	R	R	R	E	R	R
	A	E	K			
	190	200	210	220	230	240
181	CAGGCGCAATGGAAAGCAGCCAACGGCGGCGGTGGAAGTGGAGGTGGTGGAAAGCGGAGGC					
61	Q	A	Q	W	K	A
	A	A	N	G	G	G
	G	G	G	G	S	G
	G	G	G	G	S	G
	G					
	250	260	270	280	290	300
241	GGTGGTAGTAACGCCAGAACCCGACGCAGAGAGAGGGCAGAGAAACAGGCCCAGTGG					
81	G	G	S	N	A	R
	T	R	R	R	E	R
	R	A	E	K	Q	A
	Q	W				
	310	320	330	340	350	360
301	AAAGCCGCTAACGGAGGAGGGGATCCGGTGGAGGCGGCAGTGGAGGCGGGGATCTAAC					
101	K	A	A	N	G	G
	G	G	G	S	G	G
	G	G	G	G	S	G
	G	G	G	G	S	N
	370	380	390	400	410	420
361	GCACGAACACGACGACGTGAGCGTCGCGCTGAGAAACAAGCTCAATGGAAAGCTGCAAAC					
121	A	R	T	R	R	R
	E	R	R	A	E	K
	Q	A	Q	W	K	A
	A	N				
	430	440	450	460	470	480
421	TTGCACTTGGATCAGACGCCATCTCGCCAGCCTATTCAGTGAGGGTCTTCAGCTGCAT					

141	L H L D Q T P S R Q P I P S E G L Q L H
	490 500 510 520 530 540
481	TTACCGCAGGTTTTAGCTGACGCTGTCTCACGCCTGGTCCTGGGTAAGTTTGGTGACCTG
161	L P Q V L A D A V S R L V L G K F G D L
	550 560 570 580 590 600
541	ACCGACAACCTTCTCCTCCCCTCACGCTCGCAGAAAAGTGCTGGCTGGAGTCGTCATGACA
181	T D N F S S P H A R R K V L A G V V M T
	610 620 630 640 650 660
601	ACAGGCACAGATGTTAAAGATGCCAAGGTGATAAGTGTTTCTACAGGAACAAAATGTATT
201	T G T D V K D A K V I S V S T G T K C I
	670 680 690 700 710 720
661	AATGGTGAATACATGAGTGATCGTGGCCTTGCAATTAATGACTGCCATGCAGAAATAATA
221	N G E Y M S D R G L A L N D C H A E I I
	730 740 750 760 770 780
721	TCTCGGAGATCCTTGCTCAGATTTCTTTATACACAACCTTGAGCTTTACTTAAATAACAAA
241	S R R S L L R F L Y T Q L E L Y L N N K
	790 800 810 820 830 840
781	GATGATCAAAAAAGATCCATCTTTTCAGAAATCAGAGCGAGGGGGGTTTAGGCTGAAGGAG
261	D D Q K R S I F Q K S E R G G F R L K E
	850 860 870 880 890 900
841	AATGTCCAGTTTCATCTGTACATCAGCACCTCTCCCTGTGGAGATGCCAGAATCTTCTCA
281	N V Q F H L Y I S T S P C G D A R I F S
	910 920 930 940 950 960
901	CCACATGAGCCAATCCTGGAAGAACCAGCAGATAGACACCCAAATCGTAAAGCAAGAGGA

301 P H E P I L E E P A D R H P N R K A R G
 970 980 990 1000 1010 1020
 961 CAGCTACGGACCAAAATAGAGTCTGGTCAGGGGACGATTCCAGTGCGCTCCAATGCGAGC
 321 Q L R T K I E S G Q G T I P V R S N A S
 1030 1040 1050 1060 1070 1080
 1021 ATCCAAACGTGGGACGGGGTGCTGCAAGGGGAGCGGCTGCTCACCATGTCCTGCAGTGAC
 341 I Q T W D G V L Q G E R L L T M S C S D
 1090 1100 1110 1120 1130 1140
 1081 AAGATTGCACGCTGGAACGTGGTGGGCATCCAGGGATCCCTGCTCAGCATTTTCGTGGAG
 361 K I A R W N V V G I Q G S L L S I F V E
 1150 1160 1170 1180 1190 1200
 1141 CCCATTTACTTCTCGAGCATCATCCTGGGCAGCCTTTACCACGGGGACCACCTTTCCAGG
 381 P I Y F S S I I L G S L Y H G D H L S R
 1210 1220 1230 1240 1250 1260
 1201 GCCATGTACCAGCGGATCTCCAACATAGAGGACCTGCCACCTCTCTACACCCTCAACAAG
 401 A M Y Q R I S N I E D L P P L Y T L N K
 1270 1280 1290 1300 1310 1320
 1261 CCTTTGCTCAGTGGCATCAGCAATGCAGAAGCACGGCAGCCAGGGAAGGCCCCCAACTTC
 421 P L L S G I S N A E A R Q P G K A P N F
 1330 1340 1350 1360 1370 1380
 1321 AGTGTCAACTGGACGGTAGGCGACTCCGCTATTGAGGTCATCAACGCCACGACTGGGAAG
 441 S V N W T V G D S A I E V I N A T T G K
 1390 1400 1410 1420 1430 1440
 1381 GATGAGCTGGGCCGCGCGTCCCGCCTGTGTAAGCACGCGTTGTACTGTCGCTGGATGCGT

461 D E L G R A S R L C K H A L Y C R W M R

 1450 1460 1470 1480 1490 1500
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 481 V H G K V P S H L L R S K I T K P N V Y

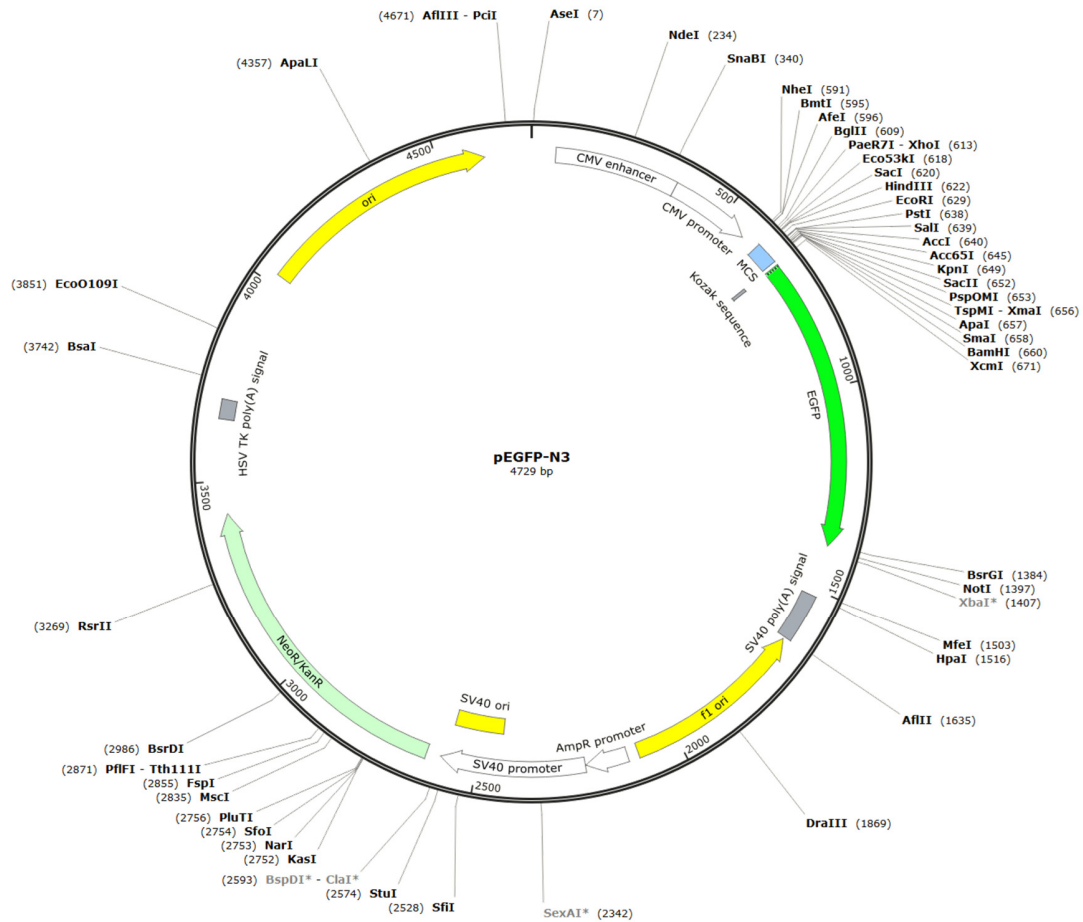
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 501 H E S K L A A K E Y Q A A K A R L F T A

 1570 1580 1590 1600 1610 1620
 1561 TTCATCAAGGCGGGGCTGGGGGCCTGGGTGGAGAAGCCCACCGAGCAGGACCAGTTCTCA
 521 F I K A G L G A W V E K P T E Q D Q F S

 1630 1640 1650
 1621 CTCACGCCACTAGTCCACCATCACCATCACCAT**TGA**
 541 L T P L V H H H H H H *

5. Plasmid-maps & sequences:

Plasmid-map and sequence of the pEGFP-N3 vector (Clontech):



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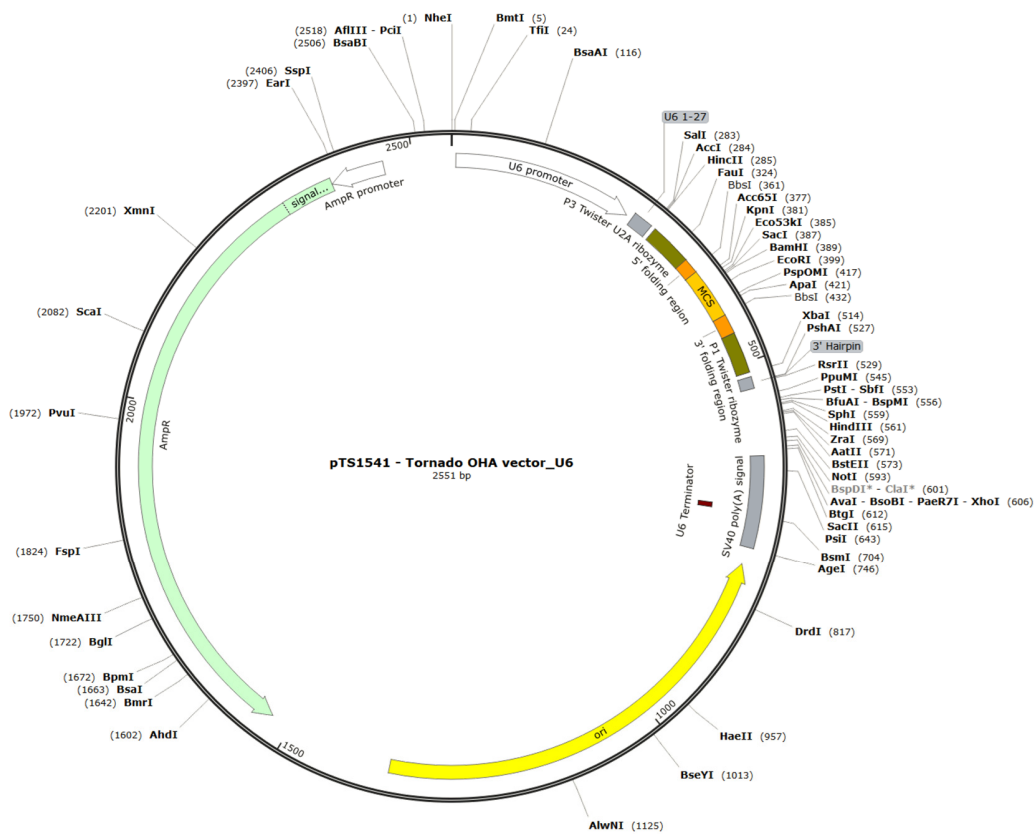
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61     CGTTACATAA CTTACGGTAA ATGGCCCGCC TGGCTGACCG CCCAACGACC CCCGCCCATT
121    GACGTCAATA ATGACGTATG TTCCCATAGT AACGCCAATA GGGACTTTCC ATTGACGTCA
181    ATGGGTGGAG TATTTACGGT AAAC TGCCCA CTTGGCAGTA CATCAAGTGT ATCATATGCC
241    AAGTACGCC CCTATTGACG TCAATGACGG TAAATGGCCC GCCTGGCATT ATGCCAGTA
301    CATGACCTTA TGGGACTTTC CTACTTGGCA GTACATCTAC GTATTAGTCA TCGCTATTAC
361    CATGGTGATG CGGTTTTGGC AGTACATCAA TGGGCGTGGA TAGCGTTTG ACTCACGGGG
421    ATTTCCAAGT CTCCACCCCA TTGACGTCAA TGGGAGTTTG TTTTGGCACC AAAATCAACG
481    GGA CTTTCCA AAATGTCGTA ACAACTCCGC CCCATTGACG CAAATGGGCG GTAGGCGTGT
541    ACGGTGGGAG GTCTATATAA GCAGAGCTGG TTTAGTGAAC CGTCAGATCC GCTAGCGCTA
601    CCGGACTCAG ATCTCGAGCT CAAGCTTCGA ATTCTGCAGT CGACGGTACC GCGGGCCCGG
661    GATCCATCGC CACCATGGTG AGCAAGGGCG AGGAGCTGTT CACCGGGGTG GTGCCCATCC
721    TGGTCGAGCT GGACGGCGAC GTAAACGGCC ACAAGTTCAG CGTGTCCGGC GAGGGCGAGG
781    GCGATGCCAC CTACGGCAAG CTGACCCTGA AGTTCATCTG CACCACCGGC AAGCTGCCCG
841    TGCCCTGGCC CACCCTCGTG ACCACCCTGA CCTACGGCGT GCAGTGCTTC AGCCGCTACC
901    CCGACCACAT GAAGCAGCAC GACTTCTTCA AGTCCGCCAT GCCCGAAGGC TACGTCCAGG
961    AGCGCACCAT CTTCTTCAAG GACGACGGCA ACTACAAGAC CCGCGCCGAG GTGAAGTTCC

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1081	ACATCCTGGG	GCACAAGCTG	GAGTACAAC	ACAACAGCCA	CAACGTCTAT	ATCATGGCCG
1141	ACAAGCAGAA	GAACGGCATC	AAGGTGAAC	TCAAGATCCG	CCACAACATC	GAGGACGGCA
1201	GCGTGCAGCT	CGCCGACCAC	TACCAGCAGA	ACACCCCAT	CGGCGACGGC	CCCGTGCTGC
1261	TGCCCCGACAA	CCACTACCTG	AGCACCCAGT	CCGCCCTGAG	CAAAGACCCC	AACGAGAAGC
1321	GCGATCACAT	GGTCCTGCTG	GAGTTCGTGA	CCGCCGCCGG	GATCACTCTC	GGCATGGACG
1381	AGCTGTACAA	GTAAGCGGC	CGCGACTCTA	GATCATAATC	AGCCATACCA	CATTTGTAGA
1441	GGTTTTACTT	GCTTTAAAAA	ACCTCCACA	CCTCCCCCTG	AACCTGAAAC	ATAAAATGAA
1501	TGCAATTGTT	GTTGTAACT	TGTTTATTGC	AGCTTATAAT	GGTTACAAAT	AAAGCAATAG
1561	CATCACAAAT	TTCACAAATA	AAGCATTTTT	TTCACTGCAT	TCTAGTTGTG	GTTTGTCCAA
1621	ACTCATCAAT	GTATCTTAAG	GCGTAAATTG	TAAGCGTTAA	TATTTTGTTA	AAATTCGCGT
1681	TAAATTTTTG	TTAAATCAGC	TCATTTTTTA	ACCAATAGGC	CGAAATCGGC	AAAATCCCTT
1741	ATAAATCAAA	AGAATAGACC	GAGATAGGGT	TGAGTGTGT	TCCAGTTTGG	AACAAGAGTC
1801	CACTATTAAA	GAACGTGGAC	TCCAACGTCA	AAGGGCGAAA	AACCGTCTAT	CAGGGCGATG
1861	GCCCACTACG	TGAACCATCA	CCCTAATCAA	GTTTTTTGGG	GTCGAGGTGC	CGTAAAGCAC
1921	TAAATCGGAA	CCCTAAAGGG	AGCCCCGAT	TTAGAGCTTG	ACGGGGAAAG	CCGCGAACG
1981	TGGCGAGAAA	GGAAGGGAAG	AAAGCGAAAG	GAGCGGGCGC	TAGGGCGCTG	GCAAGGTAG
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2101	CAGGTGGCAC	TTTTTCGGGA	AATGTGCGCG	GAACCCCTAT	TTGTTTATTT	TTCTAAATAC
2161	ATTCAAATAT	GTATCCGCTC	ATGAGACAAT	AACCCTGATA	AATGCTTCAA	TAATATTGAA
2221	AAAGGAAGAG	TCCTGAGGCG	GAAAGAACCA	GCTGTGGAAT	GTGTGTCAGT	TAGGGTGTGG
2281	AAAGTCCCCA	GGCTCCCCAG	CAGGCAGAAG	TATGCAAAGC	ATGCATCTCA	ATTAGTCAGC
2341	AACCAGGTGT	GGAAAGTCCC	CAGGCTCCCC	AGCAGGCAGA	AGTATGCAAA	GCATGCATCT
2401	CAATTAGTCA	GCAACCATAG	TCCCCGCCCT	AACTCCGCCC	ATCCCCGCCC	TAACTCCGCC
2461	CAGTTCCGCC	CATTCTCCGC	CCCATGGCTG	ACTAATTTTT	TTTATTTATG	CAGAGGCCGA
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2641	GATTGCACGC	AGGTTCTCCG	CCCGCTTGGG	TGGAGAGGCT	ATTCGGCTAT	GAGCTGGCAC
2701	AACAGACAAT	CGGCTGCTCT	GATGCCGCCG	TGTTCCGGCT	GTCAAGCGCAG	GGGCGCCCGG
2761	TTCTTTTTGT	CAAGACCGAC	CTGTCCGGTG	CCCTGAATGA	ACTGCAAGAC	GAGGCAGCGC
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2881	AAGCGGGAAG	GGACTGGCTG	CTATTGGGCG	AAGTGCCGGG	GCAGGATCTC	CTGTCATCTC
2941	ACCTTGCTCC	TGCCGAGAAA	GTATCCATCA	TGGCTGATGC	AATGCGGCGG	CTGCATACGC
3001	TTGATCCGGC	TACCTGCCCA	TTCGACCACC	AAGCGAAACA	TCGCATCGAG	CGAGCACGTA
3061	CTCGGATGGA	AGCCGGTCTT	GTCGATCAGG	ATGATCTGGA	CGAAGAGCAT	CAGGGGCTCG
3121	CGCCAGCCGA	ACTGTTTCGCC	AGGCTCAAGG	CGAGCATGCC	CGACGGCGAG	GATCTCGTCG
3181	TGACCCATGG	CGATGCCTGC	TTGCCGAATA	TCATGGTGGA	AAATGGCCGC	TTTTCTGGAT
3241	TCATCGACTG	TGGCCGGCTG	GGTGTGGCGG	ACCGCTATCA	GGACATAGCG	TTGGCTACCC
3301	GTGATATTGC	TGAAGAGCTT	GGCGGCGAAT	GGGCTGACCG	CTTCTCGTG	CTTTACGGTA
3361	TCGCCGCTCC	CGATTTCGAG	CGCATCGCCT	TCTATCGCCT	TCTTGACGAG	TTCTTCTGAG
3421	CGGGACTCTG	GGGTTTCGAAA	TGACCGACCA	AGCGACGCC	AACCTGCCAT	CACGAGATTT
3481	CGATTCCACC	GCCGCCTTCT	ATGAAAGGTT	GGGCTTCGGA	ATCGTTTTCC	GGGACGCCGG
3541	CTGGATGATC	CTCCAGCGCG	GGGATCTCAT	GCTGGAGTTC	TTGCCCCACC	CTAGGGGGAG
3601	GCTAACTGAA	ACACGGAAGG	AGACAATACC	GGAAGGAACC	CGCGCTATGA	CGGCAATAAA
3661	AAGACAGAAT	AAAACGCACG	GTGTTGGGTC	GTTTGTTCAT	AAACGCGGGG	TTCGGTCCCA
3721	GGGCTGGCAC	TCTGTTCGATA	CCCCACCGAG	ACCCATTGG	GGCCAATACG	CCCGCTTTC
3781	TTCTTTTTCC	CCACCCACC	CCCCAAGTTC	GGGTGAAGGC	CCAGGGCTCG	CAGCCAACGT
3841	CGGGGCGGCA	GGCCCTGCCA	TAGCCTCAGG	TTACTCATAT	ATACTTTAGA	TTGATTTAAA
3901	ACTTCATTTT	TAATTTAAAA	GGATCTAGGT	GAAGATCCTT	TTTGATAATC	TCATGACCAA
3961	AATCCCTTAA	CGTGAGTTTT	CGTTCCACTG	AGCGTCAGAC	CCCGTAGAAA	AGATCAAAGG
4021	ATCTTCTTGA	GATCCTTTTT	TTCTGCGCTG	AATCTGCTGC	TTGCAAACAA	AAAAACCACC
4081	GCTACCAGCG	GTGGTTTGTT	TGCCGAGCTA	AGAGCTACCA	ACTCTTTTTC	CGAAGGTAAC
4141	TGGCTTCAGC	AGAGCGCAGA	TACCAAATAC	TGTCCTTCTA	GTGTAGCCGT	GTGTAGGCCA
4201	CCACTTCAAG	AACTCTGTAG	CACCGCCTAC	ATACCTCGCT	CTGCTAATCC	TGTTACCAGT
4261	GGCTGCTGCC	AGTGGCGATA	AGTCGTGTCT	TACCGGGTTG	GACTCAAGAC	GATAGTTACC
4321	GGATAAGGCG	CAGCGGTCGG	GCTGAACGGG	GGGTTCGTGC	ACACAGCCCA	GCTTGGAGCG
4381	AACGACCTAC	ACCGAACTGA	GATACCTACA	GCGTGAGCTA	TGAGAAAGCG	CCACGCTTCC

4441	CGAAGGGAGA	AAGGCGGACA	GGTATCCGGT	AAGCGGCAGG	GTCGGAACAG	GAGAGCGCAC
4501	GAGGGAGCTT	CCAGGGGGAA	ACGCCTGGTA	TCTTTATAGT	CCTGTCGGGT	TTCGCCACCT
4561	CTGACTTGAG	CGTCGATTTT	TGTGATGCTC	GTCAGGGGGG	CGGAGCCTAT	GGAAAAACGC
4621	CAGCAACGCG	GCCTTTTTTAC	GGTTCCTGGC	CTTTTGCTGG	CCTTTTGCTC	ACATGTTCTT
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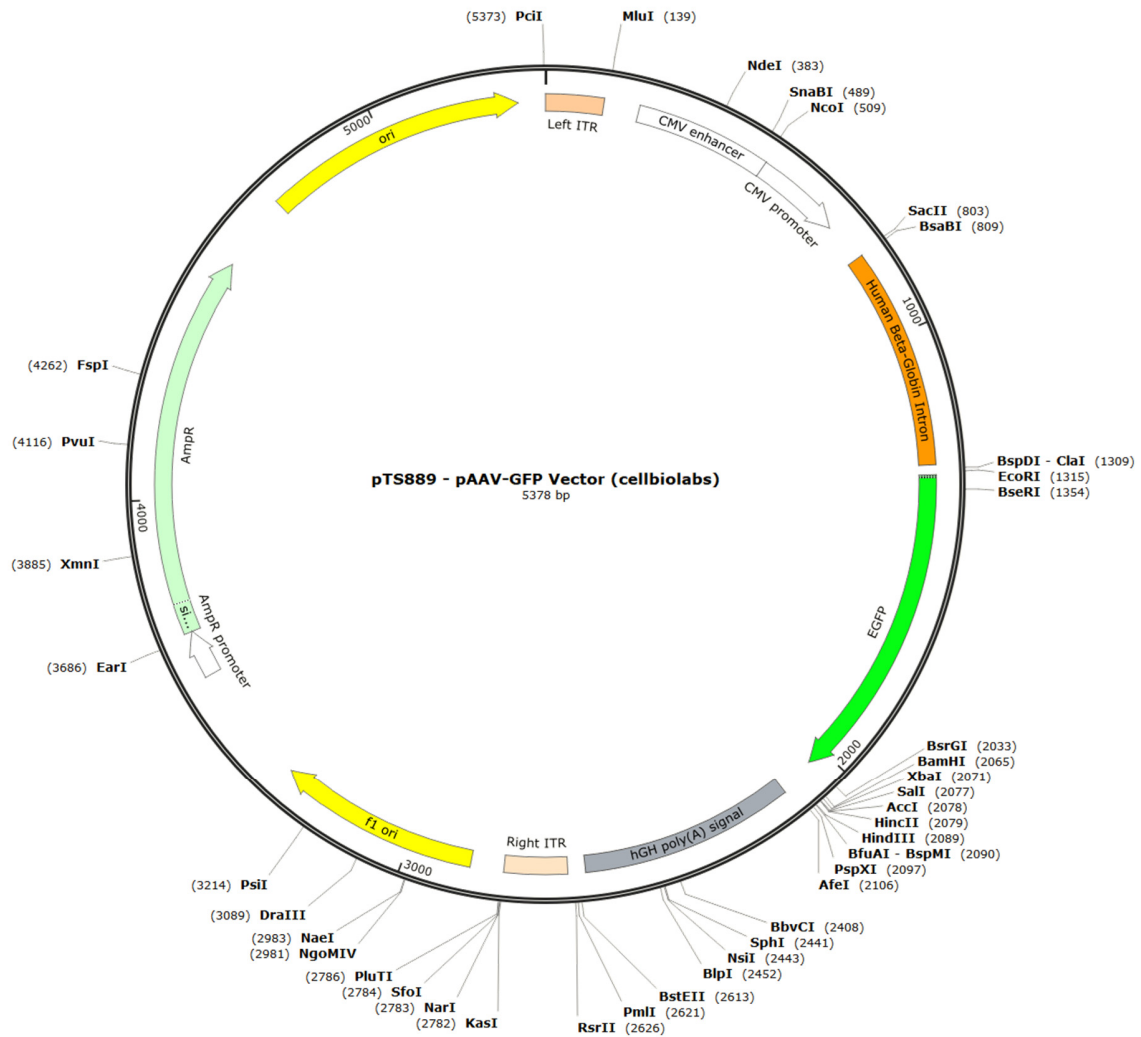
Plasmid-map and sequence of the **Tornado OHA vector U6 (pTS1541)**:



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121	CGTAGAAAGT	AATAATTTCT	TGGGTAGTTT	GCAGTTTTTA	AATTATGTTT	TAAAATGGAC
181	TATCATATGC	TTACCGTAAC	TTGAAAGTAT	TTCGATTTCT	TGGCTTTATA	TATCTTGTGG
241	AAAGGACGAA	ACACCGTGCT	CGCTTCGGCA	GCACATATAC	TAGTCGACGC	CATCAGTCGC
301	CGGTCCCAAG	CCCGGATAAA	ATGGGAGGGG	GCGGGAAACC	GCCTAACCAT	GCCGACTGAT
361	GGCAGTAGTC	TTCACTGGTA	CCGAGCTCGG	ATCCACTGGA	ATTGCGCCATG	CATCTAGGGC
421	CCTAGAAGAC	TACTGCCATC	AGTCGGCGTG	GACTGTAGAA	CACTGCCCAAT	GCCGGTCCCA
481	AGCCCGGATA	AAAGTGGAGG	GTACAGTCCA	CGCTCTAGAG	CGGACTTCGG	TCCGCTTTTT
541	ACTAGGACCT	CGAGGCATGC	AAGCTTGACG	TCGGTTACCG	ATATCCATAT	GGCGGCCGCA
601	TCGATCTCGA	GCCGCGGACT	AGTAACTTGT	TTATTGCAGC	TTATAATGGT	TACAAATAAA
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781	TCCGCCCCCC	TGACGAGCAT	CACAAAATC	GACGCTCAAG	TCAGAGGTGG	CGAAACCCGA
841	CAGGACTATA	AAGATAACCAG	GCGTTTCCCC	CTGGAAGCTC	CCTCGTGCGC	TCTCCTGTTT
901	CGACCCTGCC	GCTTACCGGA	TACCTGTCCG	CCTTTCTCCC	TTCGGGAAGC	GTGGCGCTTT
961	CTCATAGCTC	ACGCTGTAGG	TATCTCAGTT	CGGTGTAGGT	CGTTGCTCC	AAGCTGGGCT
1021	GTGTGCACGA	ACCCCCGTT	CAGCCCGACC	GCTGCGCCTT	ATCCGGTAAC	TATCGTCTTG
1081	AGTCCAACCC	GGTAAGACAC	GACTTATCGC	CAC TGGCATT	AGCCACTGGT	AACAGGATTA
1141	GCAGAGCGAG	GATGTAGGCG	GGTGCTACAG	AGTTCTTGAA	GTGGTGGCCT	AACTACGGCT
1201	ACACTAGAAG	AACAGTATTT	GGTATCTGCG	CTCTGCTGAA	GCCAGTTACC	TTCGGA AAAA
1261	GAGTTGGTAG	CTCTTGATCC	GGCAAACAAA	CCACCGCTGG	TAGCGGTGGT	TTTTTTGTTT

1321	GCAAGCAGCA	GATTACGCGC	AGAAAAAAG	GATCTCAAGA	AGATCCTTTG	ATCTTTTCTA
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1561	CAGCGATCTG	TCTATTTTCGT	TCATCCATAG	TTGCCTGACT	CCCCGTCTG	TAGATAACTA
1621	CGATACGGGA	GGGCTTACCA	TCTGGCCCCA	GTGCTGCAAT	GATACCGCGA	GACCCACGCT
1681	CACCGGCTCC	AGATTTTATCA	GCAATAAACC	AGCCAGCCGG	AAGGGCCGAG	CGCAGAAGTG
1741	GTCTGCAAC	TTTATCCGCC	TCCATCCAGT	CTATTAATTG	TTGCCGGGAA	GCTAGAGTAA
1801	GTAGTTCGCC	AGTTAATAGT	TTGCGCAACG	TTGTTGCCAT	TGCTACAGGC	ATCGTGGTGT
1861	CACGCTCGTC	GTTTGGTATG	GCTTCATTCA	GCTCCGGTTC	CCAACGATCA	AGGCGAGTTA
1921	CATGATCCCC	CATGTTGTGC	AAAAAAGCGG	TTAGCTCCTT	CGGTCCTCCG	ATCGTTGTCA
1981	GAAGTAAGTT	GGCCGCAGTG	TTATCACTCA	TGGTTATGGC	AGCACTGCAT	AATTCTCTTA
2041	CTGTCATGCC	ATCCGTAAGA	TGCTTTTCTG	TGACTGGTGA	GTAACAACC	AAGTCATTCT
2101	GAGAATAGTG	TATGCGGCGA	CCGAGTTGCT	CTTGCCCCGC	GTCAATACGG	GATAATACCG
2161	CGCCACATAG	CAGAACTTTA	AAAGTGCTCA	TCATTGGAAA	ACGTTCTTCG	GGGCGAAAAC
2221	TCTCAAGGAT	CTTACCGCTG	TTGAGATCCA	GTTTCGATGTA	ACCACTCGT	GCACCAACT
2281	GATCTTCAGC	ATCTTTTACT	TTCACCAGCG	TTTCTGGGTG	AGCAAAAACA	GGAAGGCAAA
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2401	TTCAATATTA	TTGAAGCATT	TATCAGGGTT	ATTGTCTCAT	GAGCGGATAC	ATATTTGAAC
2461	GGCCGATTTT	CTTGTCACGC	TTTGATGCAT	CGTTGGTGGT	TGATGGATAT	CTGACGAACA
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Plasmid-map and sequence of the **pAAV-GFP vector (Cell Biolabs)**:



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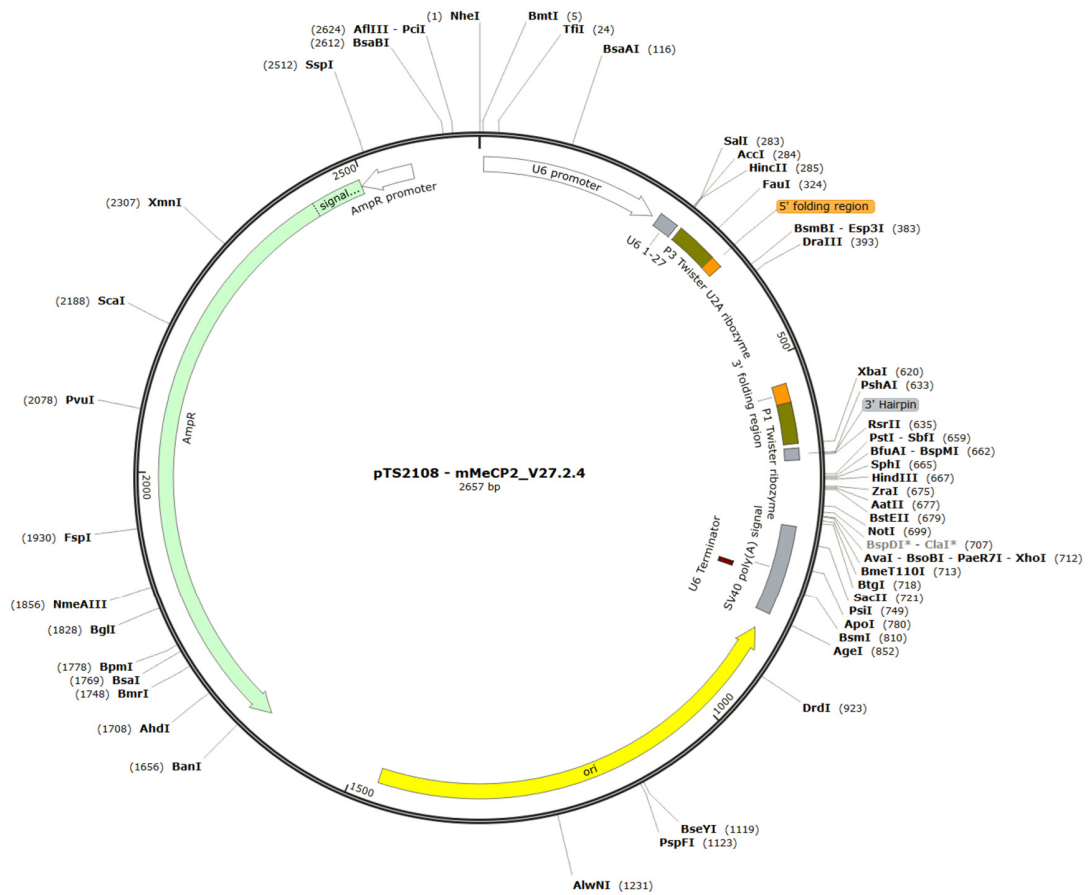
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121    AGGGGTTCCT GCGGCCGCAC GCGTGGAGCT AGTTATTAAAT AGTAATCAAT TACGGGGTCA
181    TTAGTTCATA GCCCATATAT GGAGTTCGCG GTTACATAAC TTACGGTAAA TGGCCCGCCT
241    GGCTGACCGC CCAACGACCC CCGCCCATTG ACGTCAATAA TGACGTATGT TCCCATAGTA
301    ACGTCAATAG GGACTTTCCA TTGACGTCAA TGGGTGGAGT ATTTACGGTA AACTGCCCAC
361    TTGGCAGTAC ATCAAGTGTA TCATATGCCA AGTACGCCCC CTATTGACGT CAATGACGGT
421    AAATGGCCCG CCTGGCATTG TGCCAGTAC ATGACCTTAT GGGACTTTCC TACTTGGCAG
481    TACATCTACG TATTAGTCAT CGCTATTACC ATGGTGATGC GGTTTGGCA GTACATCAAT
541    GGGCGTGGAT AGCGGTTTGA CTCACGGGGA TTTCCAAGTC TCCACCCCAT TGACGTCAAT
601    GGGAGTTTGT TTTGCACCAA AATCAACGGG ACTTTCCAAA ATGTCGTAAC AACTCCGCCC
661    CATTGACGCA AATGGGCGGT AGGCGTGTAC GGTGGGAGGT CTATATAAGC AGAGCTCGTT
721    TAGTGAACCG TCAGATCGCC TGGAGACGCG ATCCACGCTG TTTTGACCTC CATAGAAGAC
781    ACCGGGACCG ATCCAGCCTC CGCGGATTCC AATCCCGGCC GGAACGGTG CATTGGAACG
841    CGGATTCCCC GTGCCAAGAG TGACGTAAGT ACCGCCTATA GAGTCTATAG GCCCAAAAA
901    AATGCTTTCT TCTTTTAATA TACTTTTTTG TTTATCTTAT TTCTAATACT TTCCCTAATC
961    TCTTTCTTTC AGGGCAATAA TGATACAATG TATCATGCCT CTTTGCACCA TTCTAAAGAA
1021   TAACAGTGAT AATTTCTGGG TTAAGGCAAT AGCAATATTT CTGCATATAA ATATTTCTGC

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1081	ATATAAATTG	TAAGTATGT	AAGAGGTTTC	ATATTGCTAA	TAGCAGCTAC	AATCCAGCTA
1141	CCATTCTGCT	TTTATTTTAT	GGTTGGGATA	AGGCTGGATT	ATTCTGAGTC	CAAGCTAGGC
1201	CCTTTTGCTA	ATCATGTTCA	TACCTCTTAT	CTTCCTCCCA	CAGCTCCTGG	GCAACGTGCT
1261	GGTCTGTGTG	CTGGCCCATC	ACTTTGGCAA	AGAATTGGGA	TTCGAACATC	GATTGAATTC
1321	TGAATGGTGA	GCAAGGGCGA	GGAGCTGTTT	ACCGGGGTGG	TGCCCATCCT	GGTCGAGCTG
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1441	TACGGCAAGC	TGACCCTGAA	GTTTCATCTG	ACCACCGGCA	AGCTGCCCCG	GCCCTGGCCC
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1561	AAGCAGCACG	ACTTCTTCAA	GTCCGCCATG	CCCGAAGGCT	ACGTCCAGGA	GCGCACCATC
1621	TTCTTCAAGG	ACGACGGCAA	CTACAAGACC	CGCGCCGAGG	TGAAGTTCGA	GGGCGACACC
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1861	GCCGACCACT	ACCAGCAGAA	CACCCCCATC	GGCGACGGCC	CCGTGCTGCT	GCCCCACAAC
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1981	GTCTCTGCTG	AGTTCGTGAC	CGCCGCCGGG	ATCACTCTCG	GCATGGACGA	GCTGTACAAG
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2101	AGCAGCGCTG	CTCGAGAGAT	CTACGGGTGG	CATCCCTGTG	ACCCCTCCCC	AGTGCCTCTC
2161	CTGGCCCTGG	AAGTTGCCAC	TCCAGTGCCC	ACCAGCCTTG	TCCTAATAAA	ATTAAGTTGC
2221	ATCATTTTGT	CTGACTAGGT	GTCCTTCTAT	AATATTATGG	GGTGGAGGGG	GGTGGTATGG
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2761	GAGCGCGCAG	CTGCCTGCAG	GGGCGCCTGA	TGCGGTATTT	TCTCCTTAGC	CATCTGTGCG
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3361	GCCCCGACAC	CCGCCAACAC	CCGCTGACGC	GCCCTGACGG	GCTTGTCTGC	TCCCGGCATC
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3541	CATGATAATA	ATGGTTTCTT	AGACGTCAGG	TGGCACTTTT	CGGGGAAATG	TGCGCGGAAC
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3661	CTGATAAATG	CTTCAATAAT	ATTGAAAAAG	GAAGAGTATG	AGTATTCAAC	ATTTCCGTGT
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3781	GGTGAAAGTA	AAAGATGCTG	AAGATCAGTT	GGGTGCACGA	GTGGGTTACA	TCGAAGTGGG
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3961	ACTCGGTGCG	CGCATACACT	ATTCTCAGAA	TGACTTGGTT	GAGTACTCAC	CAGTCACAGA
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Plasmid-map and sequence of **circ-mMecp2-V27.2.4_gRNA_pEdit_no-stuffer (pTS2108)**:



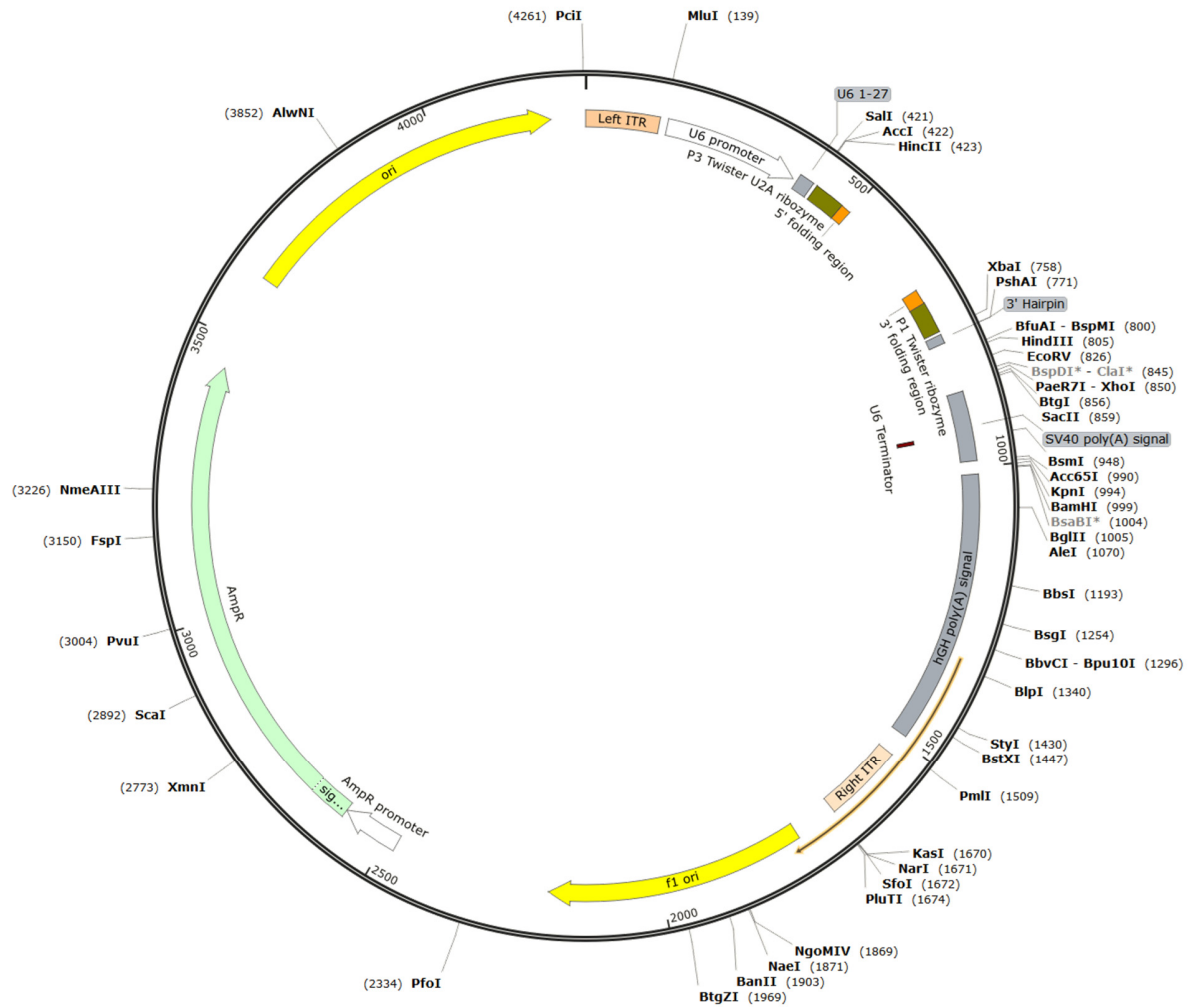
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2281	ACTTTAAAAG	TGCTCATCAT	TGGAAAACGT	TCTTCGGGGC	GAAAACCTCTC	AAGGATCTTA
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2521	AGCATTTATC	AGGGTTATTG	TCTCATGAGC	GGATACATAT	TTGAACGGCC	GGATTTCTTG
2581	TCACGCTTTG	ATGCATCGTT	GGTGGTTGAT	GGATATCTGA	CGAACATGTG	CACAGTGGTA
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Plasmid-map and sequence of **circ-mMecp2-V27.2.4_gRNA_pAAV_no-stuffer (pTS2123)**:



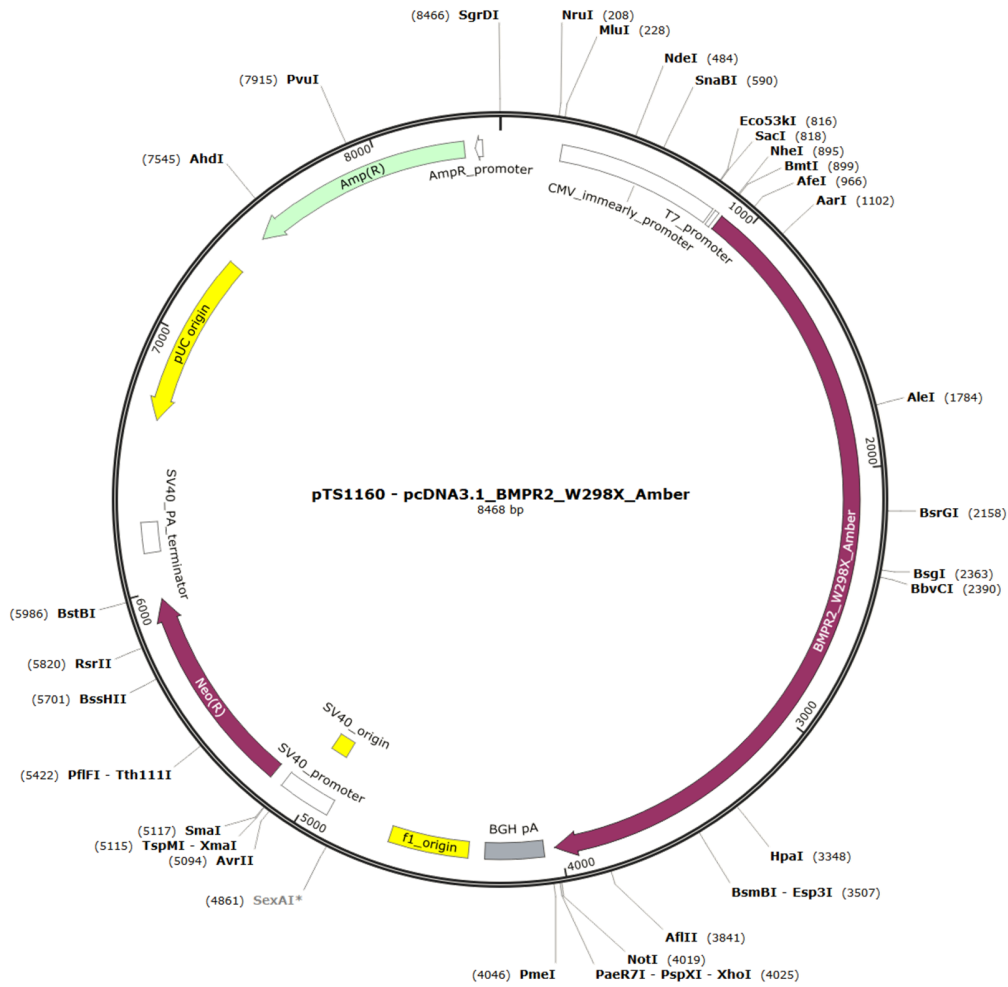
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421    GTCGACGCCA TCAGTCGCCG GTCCCAAGCC CGGATAAAAT GGGAGGGGGC GGGAAACCGC
481    CTAACCATGC CGACTGATGG CAGCATGTTG TTCTCGTCTC CTCGACACCT CGTGTCCAAC
541    CTTCAGGCAA AAAGTCATCA TGCATAGGTC CCCAAACACG GATGATGGAG CGCCGCAAAG
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781    TTTTACTAGG ACCTGCAGGC ATGCAAGCTT GACGTCGGTT ACCGATATCC ATATGGCGGC
841    CGCATCGATC TCGAGCCGCG GACTAGTAAC TTGTTTATTG CAGCTTATAA TGGTTACAAA
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1021   TCCCTGTGAC CCCTCCCCAG TGCCTCTCCT GGCCCTGGAA GTTGCCACTC CAGTGCCAC
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Plasmid-map and sequence of **BMPR2_W298X_cDNA_pcDNA3.1 (pTS1160)**:



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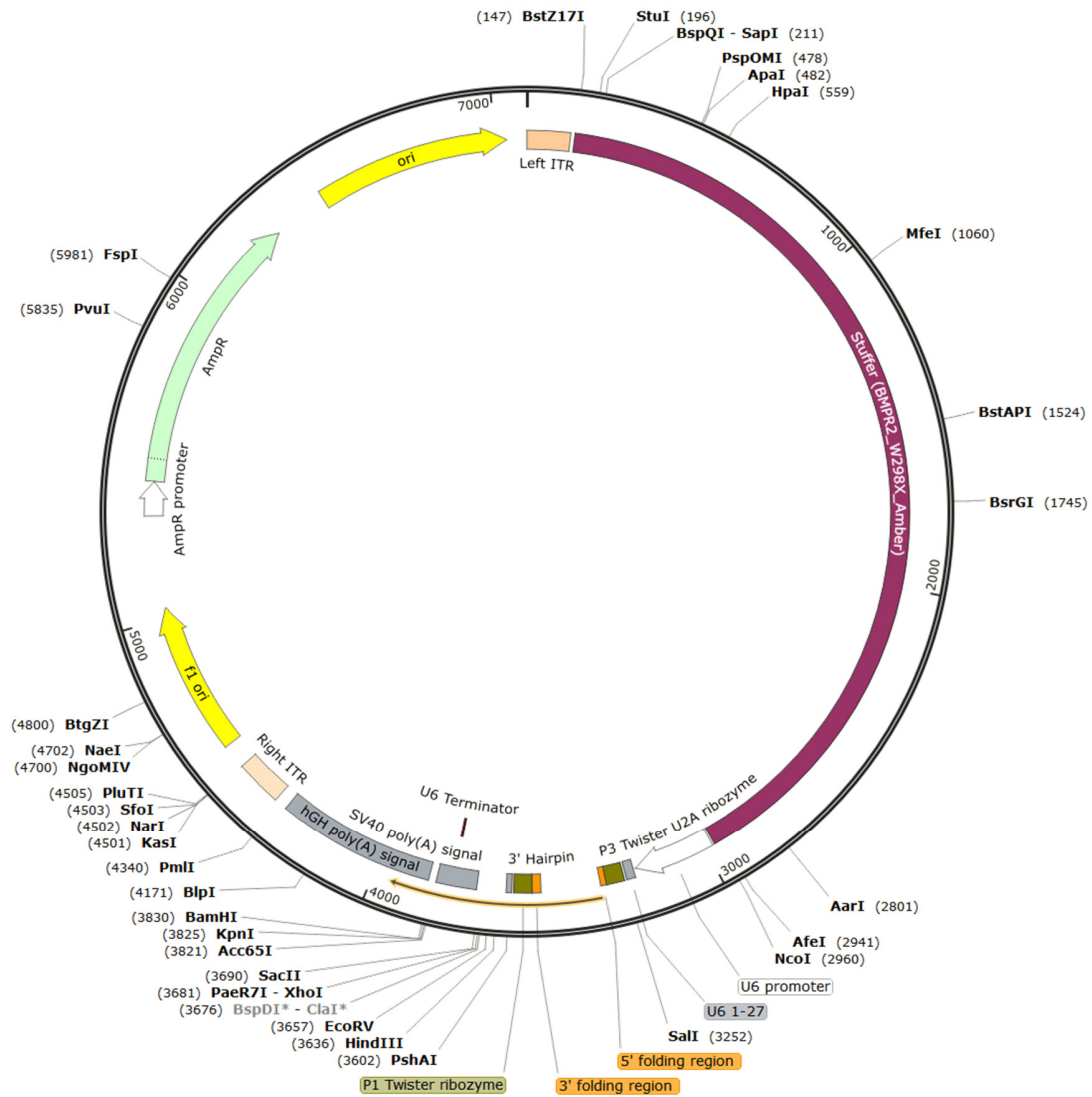
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3601	AATTCCAATA	ACAACAACAG	CAATCCATGT	TCAGAACAAG	ATGTTCTTGC	ACAGGGTGTT
3661	CCAAGCACAG	CAGCAGATCC	TGGGCCATCA	AAGCCCAGAA	GAGCACAGAG	GCCTAATTCT
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Plasmid-map and sequence of **circ-mMecp2-V27.2.4_gRNA_pAAV_stuffer (pTS2154)**:



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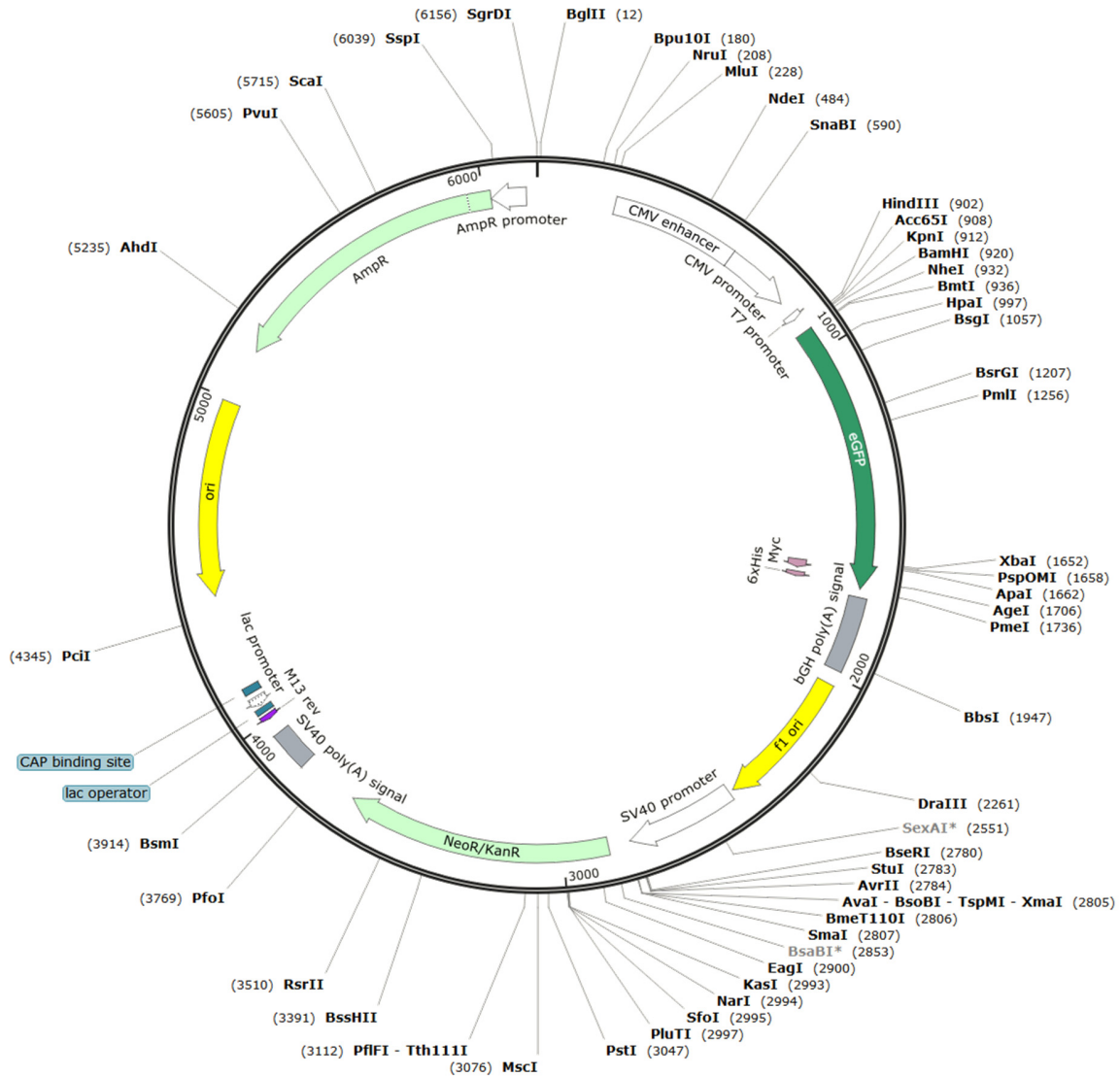
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Plasmid-map and sequence of the **pcDNA3.1 eGFP vector (pTS58)**:



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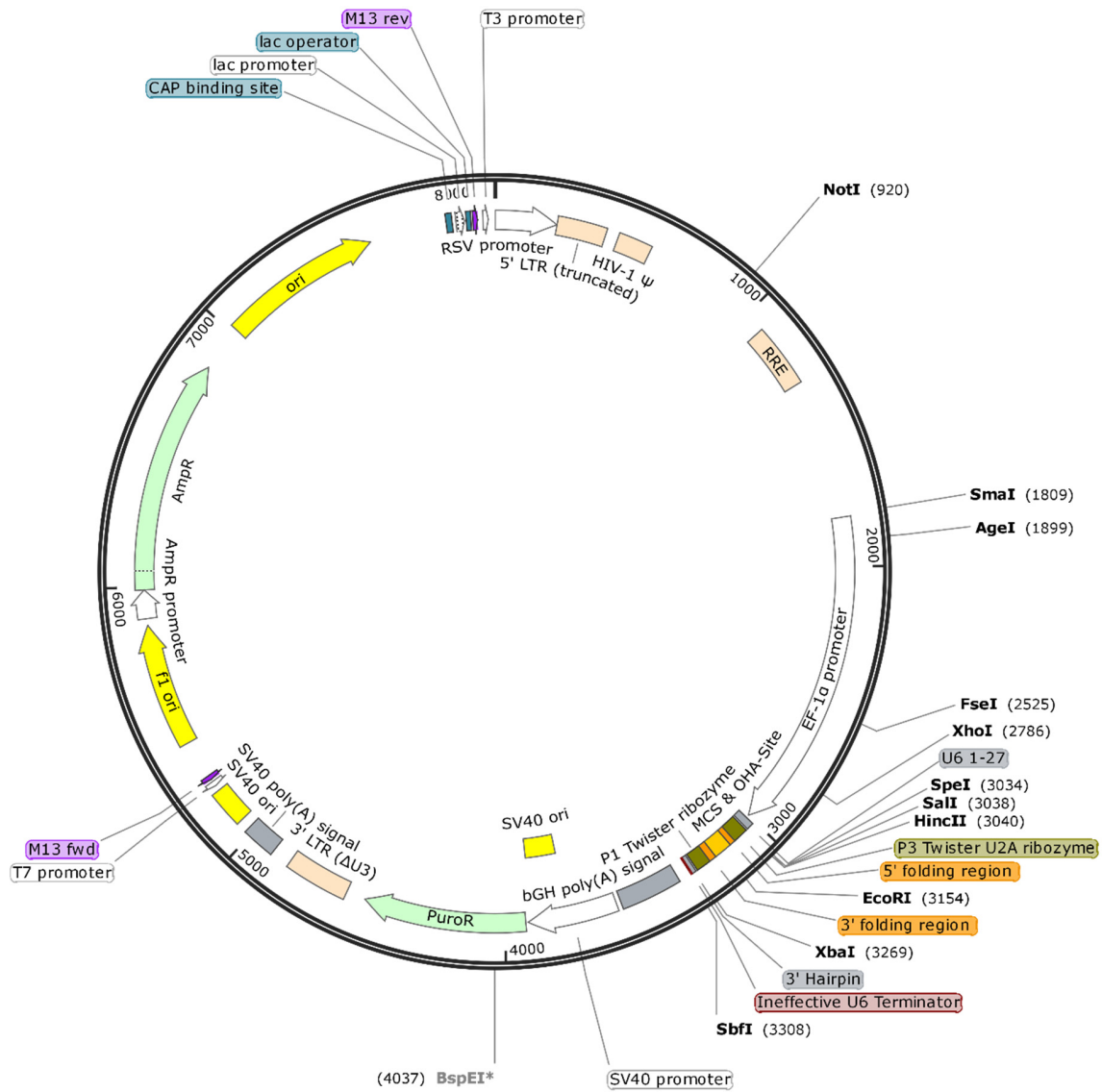
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901	TAAGCTTGGT	ACCGAGCTCG	GATCCACCAT	GGCTAGCAAA	GGAGAAGAAC	TCTTCACTGG
961	AGTTGTCCCA	ATTCTTGTTG	AATTAGATGG	TGATGTTAAC	GGCCACAAGT	TCTCTGTCAG
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1141	CTTTTCAAGA	TACCCGGATC	ACATGAAACG	GCATGACTTT	TTCAAGAGTG	CCATGCCCCG
1201	AGGTTATGTA	CAGGAAAGGA	CCATCTTCTT	CAAAGATGAC	GGCAACTACA	AGACACGTGC
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Plasmid-map and sequence of the **Tornado OHA vector EF1 α (pTS1593)**:



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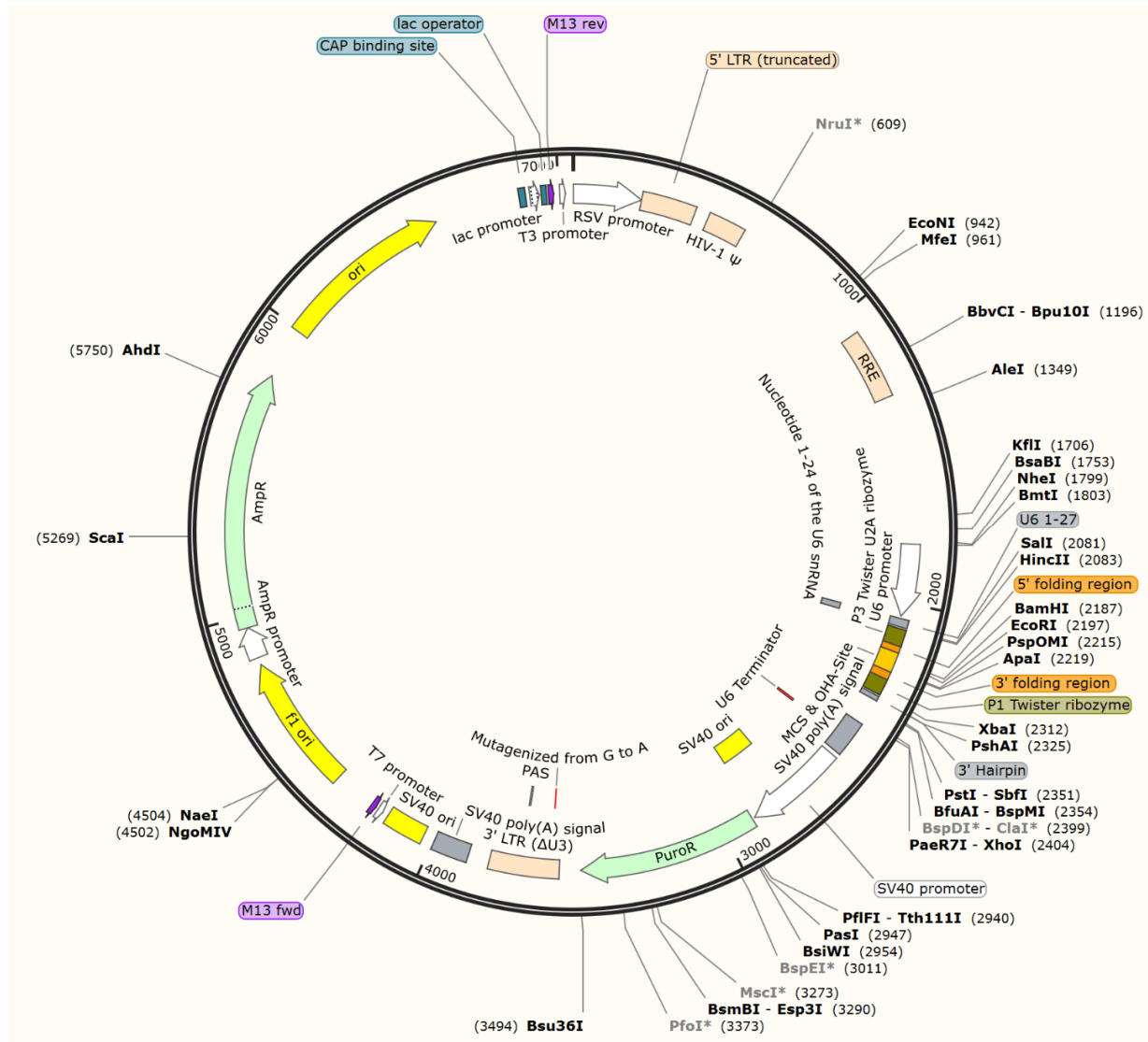
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2821	GGGAGGGGTT	TTATGCGATG	GAGTTTCCCC	ACACTGAGTG	GGTGGAGACT	GAAGTTAGGC
2881	CAGCTTGGA	CTTGATGTAA	TTCTCCTTGG	AATTTGCCCT	TTTTGAGTTT	GGATCTTGGT
2941	TCATTCTCAA	GCCTCAGACA	GTGGTTCAAA	GTTTTTTTCT	TCCATTTTCA	GTGTCGTGAG
3001	GTCTAGCACC	GTGCTCGCTT	CGGCAGCACA	TATACTAGTC	GACGCCATCA	GTCGCCGGTC
3061	CCAAGCCCCG	ATAAAATGGG	AGGGGGCGGG	AAACCGCCTA	ACCATGCCGA	CTGATGCCAG
3121	TAGTCTTCAC	TGGTACCGAG	CTCGGATCCA	CTGGAATTCTG	CCATGCATCT	AGGGCCCTAG
3181	AAGACTACTG	CCATCAGTCG	GCGTGGACTG	TAGAACACTG	CCAATGCCGG	TCCCAAGCCC
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3301	GACCTGCAGG	CATGCTCGAC	AGAGCTCGCT	GATCAGCCTC	GACTGTGCCT	TCTAGTTGCC
3361	AGCCATCTGT	TGTTTTGCCCC	TCCCCCGTGC	CTTCCTTGAC	CCTGGAAGGT	GCCACTCCCA
3421	CTGTCCTTTC	CTAATAAAAT	GAGGAAATTG	CATCGCATTG	TCTGAGTAGG	TGTCATTCTA
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4021	CGCGCCACAC	CGTCGATCCG	GACCGCCACA	TCGAGCGGGT	CACCGAGCTG	CAAGAATCTT
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5881	GTGCGCGGAA	CCCCTATTTG	TTTTATTTTTC	TAAATACATT	CAAATATGTA	TCCGCTCATG
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6781	CAGGCAACTA	TGGATGAACG	AAATAGACAG	ATCGCTGAGA	TAGGTGCCTC	ACTGATTAAG
6841	CATTGGTAAC	TGTCAGACCA	AGTTTACTCA	TATATACTTT	AGATTGATTT	AAAACCTCAT
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7321	GCGCAGCGGT	CGGGCTGAAC	GGGGGGTTCG	TGCACACAGC	CCAGCTTGGA	GCGAACGACC
7381	TACACCGAAC	TGAGATACCT	ACAGCGTGAG	CTATGAGAAA	GCGCCACGCT	TCCCGAAGGG
7441	AGAAAGGCGG	ACAGGTATCC	GGTAAGCGGC	AGGGTCGGAA	CAGGAGAGCG	CACGAGGGAG
7501	CTTCCAGGGG	GAAACGCCTG	GTATCTTTAT	AGTCCTGTCT	GGTTTCGCCA	CCTCTGACTT

7561	GAGCGTCGAT	TTTTGTGATG	CTCGTCAGGG	GGGCGGAGCC	TATGGAAAAA	CGCCAGCAAC
7621	GCGGCCTTTT	TACGGTTCCT	GGCCTTTTGC	TGGCCTTTTG	CTCACATGTT	CTTTCCTGCG
7681	TTATCCCCTG	ATTCTGTGGA	TAACCGTATT	ACCGCCTTTG	AGTGAGCTGA	TACCGCTCGC
7741	CGCAGCCGAA	CGACCGAGCG	CAGCGAGTCA	GTGAGCGAGG	AAGCGGAAGA	GCGCCCAATA
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7921	GCACCCCAGG	CTTTACACTT	TATGCTTCCG	GCTCGTATGT	TGTGTGGAAT	TGTGAGCGGA
7981	TAACAATTTT	ACACAGGAAA	CAGCTATGAC	CATGATTACG	CCAAGCGCGC	AATTAACCCT
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Plasmid-map and sequence of the **Tornado OHA vector U6 (pTS1790)**:



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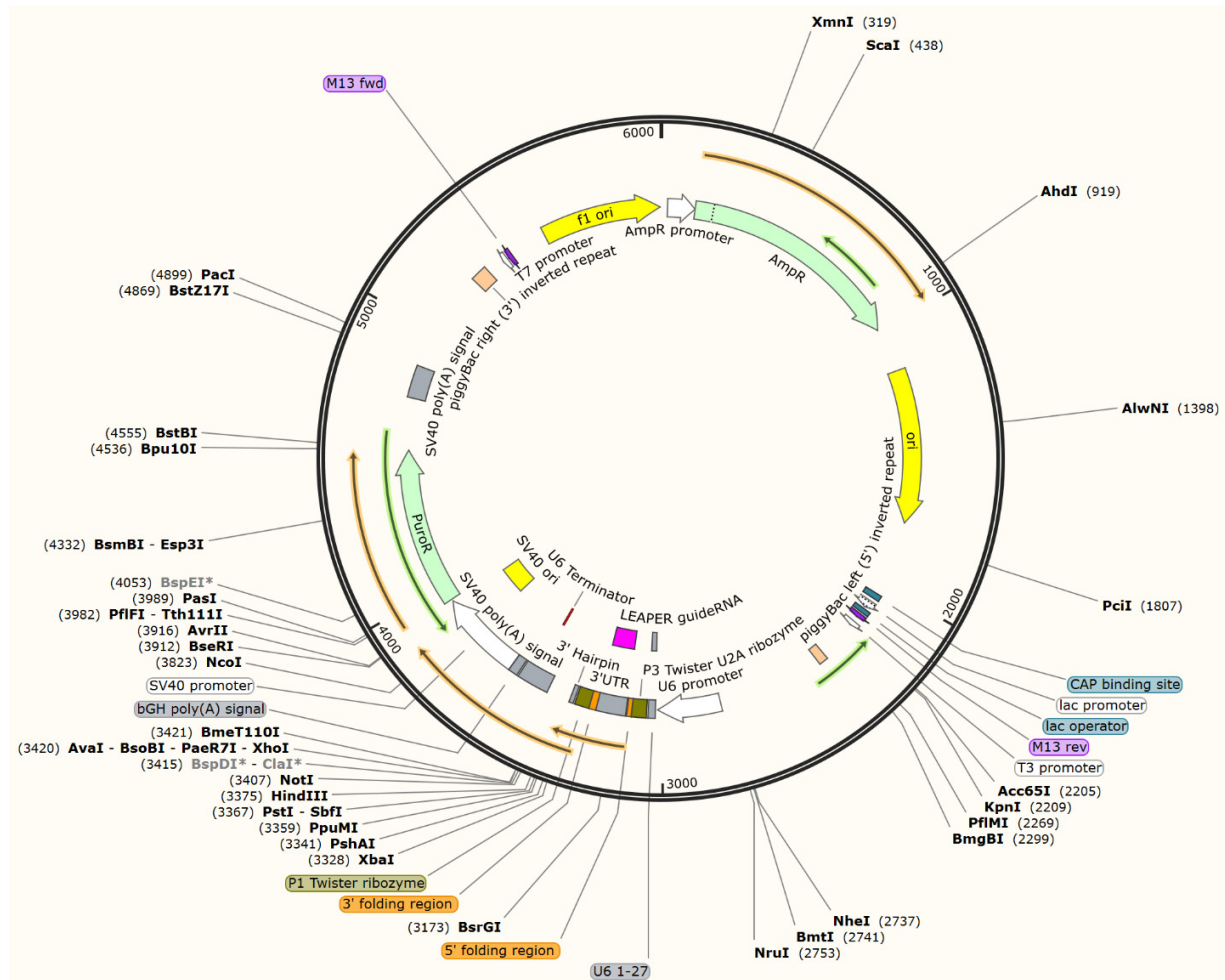
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241    GTTAGACCAG ATCTGAGCCT GGGAGCTCTC TGGCTAACTA GGAACCCAC TGCTTAAGCC
301    TCAATAAAGC TTGCCTTGAG TGCTTCAAGT AGTGTGTGCC CGTCTGTTGT GTGACTCTGG
361    TAACTAGAGA TCCCTCAGAC CCTTTTAGTC AGTGTGGAAG ATCTCTAGCA GTGGCGCCCG
421    AACAGGGACT TGAAAGCGAA AGGGAACCA GAGGAGCTCT CTCGACGCAG GACTCGGCTT
481    GCTGAAGCGC GCACGGCAAG AGGCGAGGGG CGGCGACTGG TGAGTACGCC AAAAATTTTG
541    ACTAGCGGAG GCTAGAAGGA GAGAGATGGG TGCAGAGCGC TCAGTATTAA GCGGGGGAGA
601    ATTAGATCGC GATGGGAAAA AATTCGGTTA AGGCCAGGGG GAAAGAAAAA ATATAAATTA
661    AAACATATAG TATGGGCAAG CAGGGAGCTA GAACGATTCG CAGTTAATCC TGGCCTGTTA
721    GAAACATCAG AAGGCTGTAG ACAAATACTG GGACAGCTAC AACCATCCCT TCAGACAGGA
781    TCAGAAGAAC TTAGATCATT ATATAATACA GTAGCAACCC TCTATTGTGT GCATCAAAGG
841    ATAGAGATAA AAGACACCAA GGAAGCTTTA GACAAGATAG AGGAAGAGCA AAACAAAAGT

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961	CAATTGGAGA	AGTGAATTAT	ATAAATATAA	AGTAGTAAAA	ATTGAACCAT	TAGGAGTAGC
1021	ACCCACCAAG	GCAAAGAGAA	GAGTGGTGCA	GAGAGAAAAA	AGAGCAGTGG	GAATAGGAGC
1081	TTTGTTCCCT	GGGTTCTTGG	GAGCAGCAGG	AAGCACTATG	GGCGCAGCGT	CAATGACGCT
1141	GACGGTACAG	GCCAGACAAT	TATTGTCTGG	TATAGTGCAG	CAGCAGAACA	ATTTGCTGAG
1201	GGCTATTGAG	GCGCAACAGC	ATCTGTTGCA	ACTCACAGTC	TGGGGCATCA	AGCAGCTCCA
1261	GGCAAGAATC	CTGGCTGTGG	AAAGATACCT	AAAGGATCAA	CAGCTCCTGG	GGATTTGGGG
1321	TTGCTCTGGA	AAACTCATTT	GCACCACTGC	TGTGCCTTGG	AATGCTAGTT	GGAGTAATAA
1381	ATCTCTGGAA	CAGATTTGGA	ATCACACGAC	CTGGATGGAG	TGGGACAGAG	AAATTAACAA
1441	TTACACAAGC	TTAATACACT	CCTTAATTGA	AGAATCGCAA	AACCAGCAAG	AAAAGAATGA
1501	ACAAGAATTA	TTGGAATTAG	ATAAATGGGC	AAGTTTGTGG	AATTGGTTTA	ACATAACAAA
1561	TTGGCTGTGG	TATATAAAAT	TATTCATAAT	GATAGTAGGA	GGCTTGGTAG	GTTTAAGAAT
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1681	TCAGACCCAC	CTCCCAACCC	CGAGGGGACC	CGGATTTCTT	GTCACGCTTT	GATGCATCGT
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1861	AGAGATAAAT	AGAATTAATT	TGACTGTAAA	CACAAAGATA	TTAGTACAAA	ATACGTGACG
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1981	TCATATGCTT	ACCGTAACTT	GAAAGTATTT	CGATTTCTTG	GCTTTATATA	TCTTGTGGAA
2041	AGGACGAAAC	ACCGTGCTCG	CTTCGGCAGC	ACATATACTA	GTCGACGCCA	TCAGTCGCCG
2101	GTCCCAAGCC	CGGATAAAAT	GGGAGGGGGC	GGGAAACCGC	CTAACCATGC	CGACTGATGG
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2761	GTTCCGCCCA	TTCTCCGCCC	CATGGCTGAC	TAATTTTTTTT	TATTTATGCA	GAGGCCGAGG
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2881	TTTGCAAAAA	GCTTACCATG	ACCGAGTACA	AGCCCACGGT	GCGCCTCGCC	ACCCGCGACG
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3421	GCTTCACCGT	CACCGCCGAC	GTCGAGGTGC	CCGAAGGACC	GCGCACCTGG	TGCATGACCC
3481	GCAAGCCCGG	TGCCTGAGGT	ACCTTTAAGA	CCAATGACTT	ACAAGGCAGC	TGTAGATCTT
3541	AGCCACTTTT	TAAAAGAAAA	GGGGGGACTG	GAAGGGCTAA	TTCACTCCCA	ACGAAAACAA
3601	GATCTGCTTT	TTGCTTGTAC	TGGGTCTCTC	TGGTTAGACC	AGATCTGAGC	CTGGGAGCTC
3661	TCTGGCTAAC	TAGGGAACCC	ACTGCTTAAG	CCTCAATAAA	GCTTGCCCTG	AGTGCTTCAA
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Plasmid-map and sequence of the **Transposon U6 circ RAB7A LEAPER gRNA vector (pTS1896)**:



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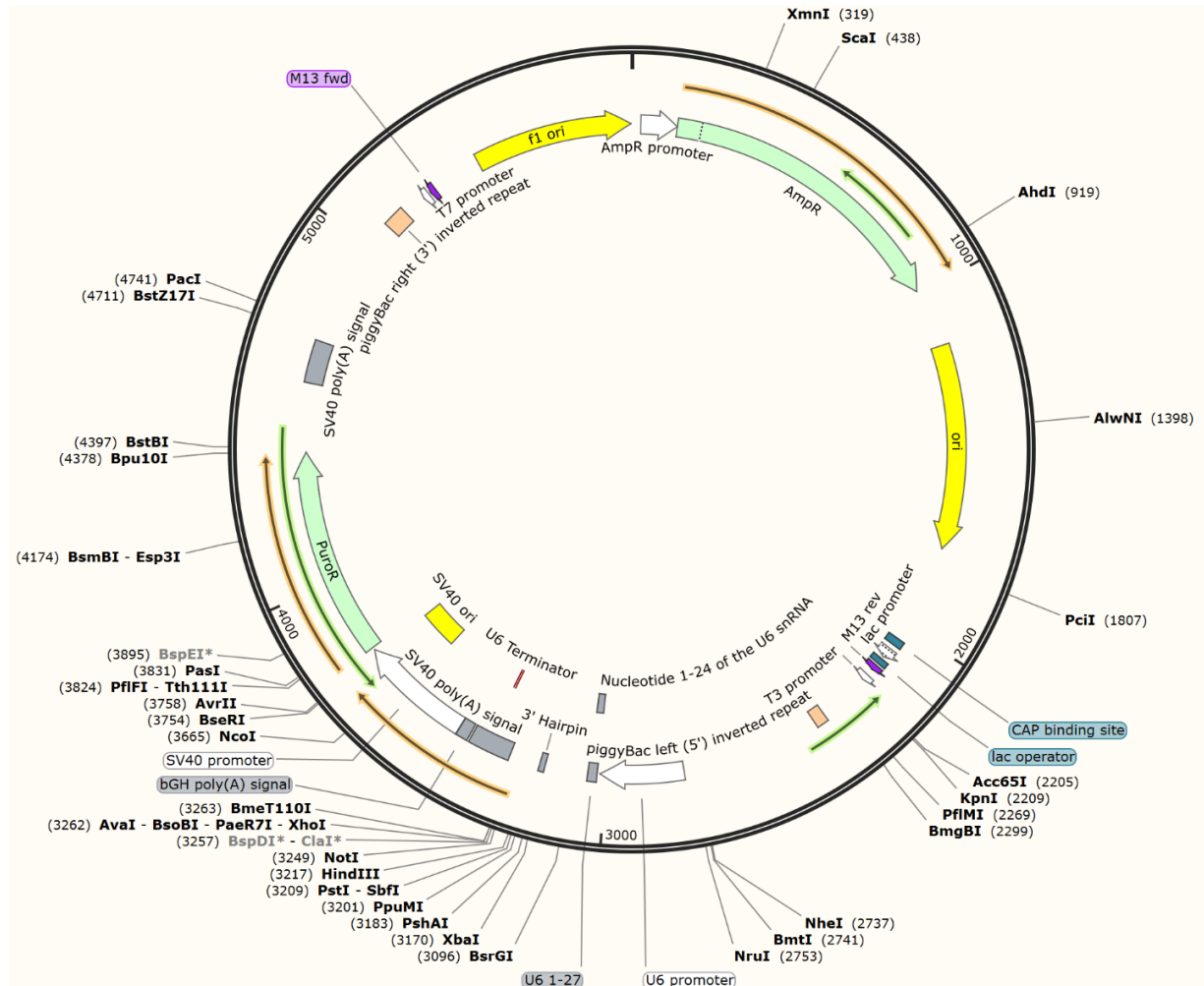
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721    TTACTCTAGC TTCCCGGCAA CAATTAATAG ACTGGATGGA GGCGGATAAA GTTGAGGAC
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841    AGCGTGGGTC TCGCGGTATC ATTGCAGCAC TGGGGCCAGA TGTAAGCCC TCCCGTATCG
901    TAGTTATCTA CACGACGGGG AGTCAGGCAA CTATGGATGA ACGAAATAGA CATACGCTG
961    AGATAGGTGC CTCACTGATT AAGCATTGGT AACTGTCAGA CCAAGTTTAC TCATATATAC
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1261	TTTTTCCGAA	GGTAACTGGC	TTCAGCAGAG	CGCAGATACC	AAATACTGTC	CTTCTAGTGT
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Plasmid-map and sequence of the **Transposon U6 linear RAB7A LEAPER gRNA vector (pTS1897)**:



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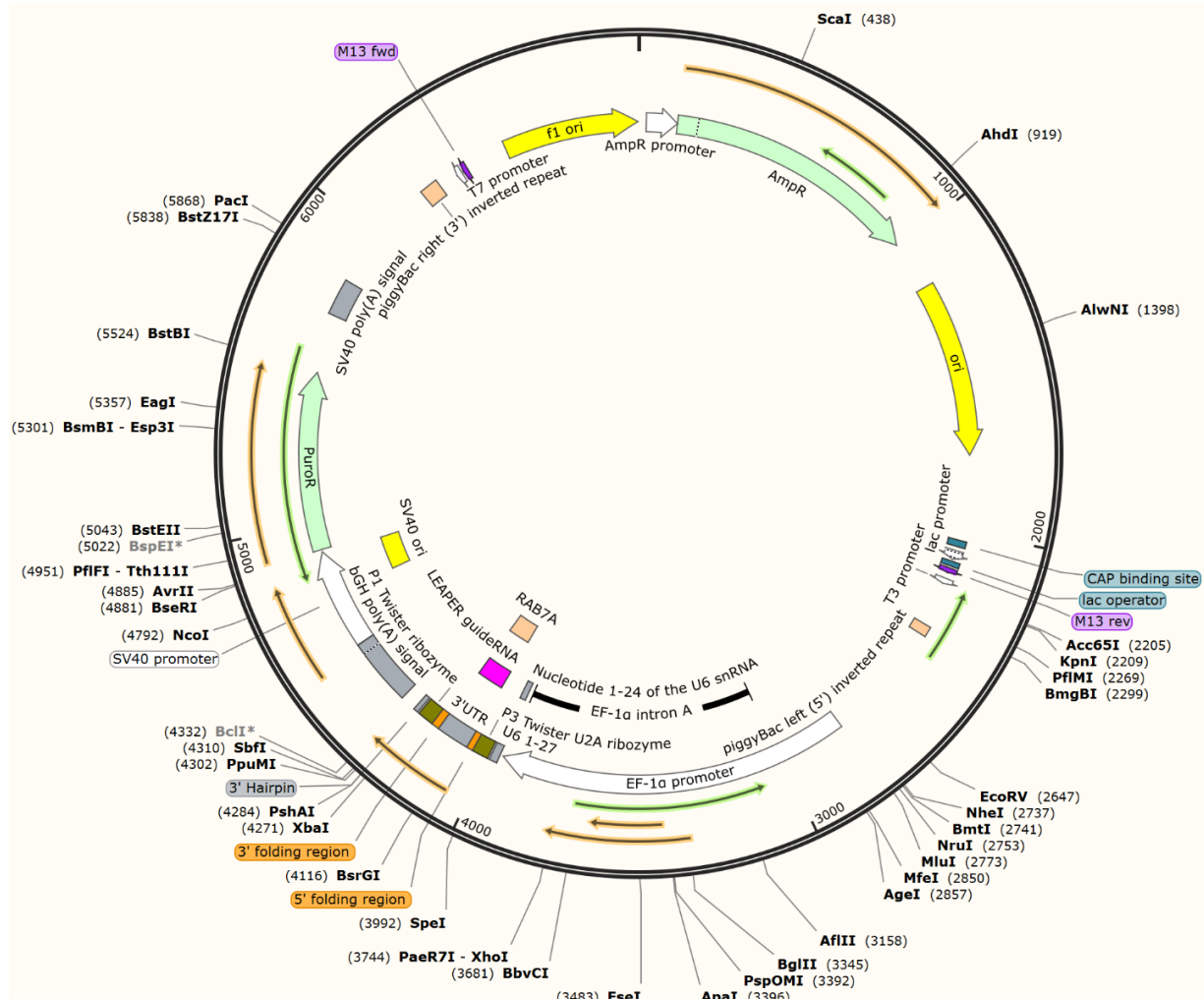
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3661	CGCCCCATGG	CTGACTAATT	TTTTTTATTT	ATGCAGAGGC	CGAGGCCGCC	TCTGCCTCTG
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3781	CATGACCGAG	TACAAGCCCA	CGGTGCGCCT	CGCCACCCGC	GACGACGTCC	CCAGGGCCGT
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Plasmid-map and sequence of the **Transposon EF1 α circ RAB7A LEAPER gRNA vector (pTS1899)**:



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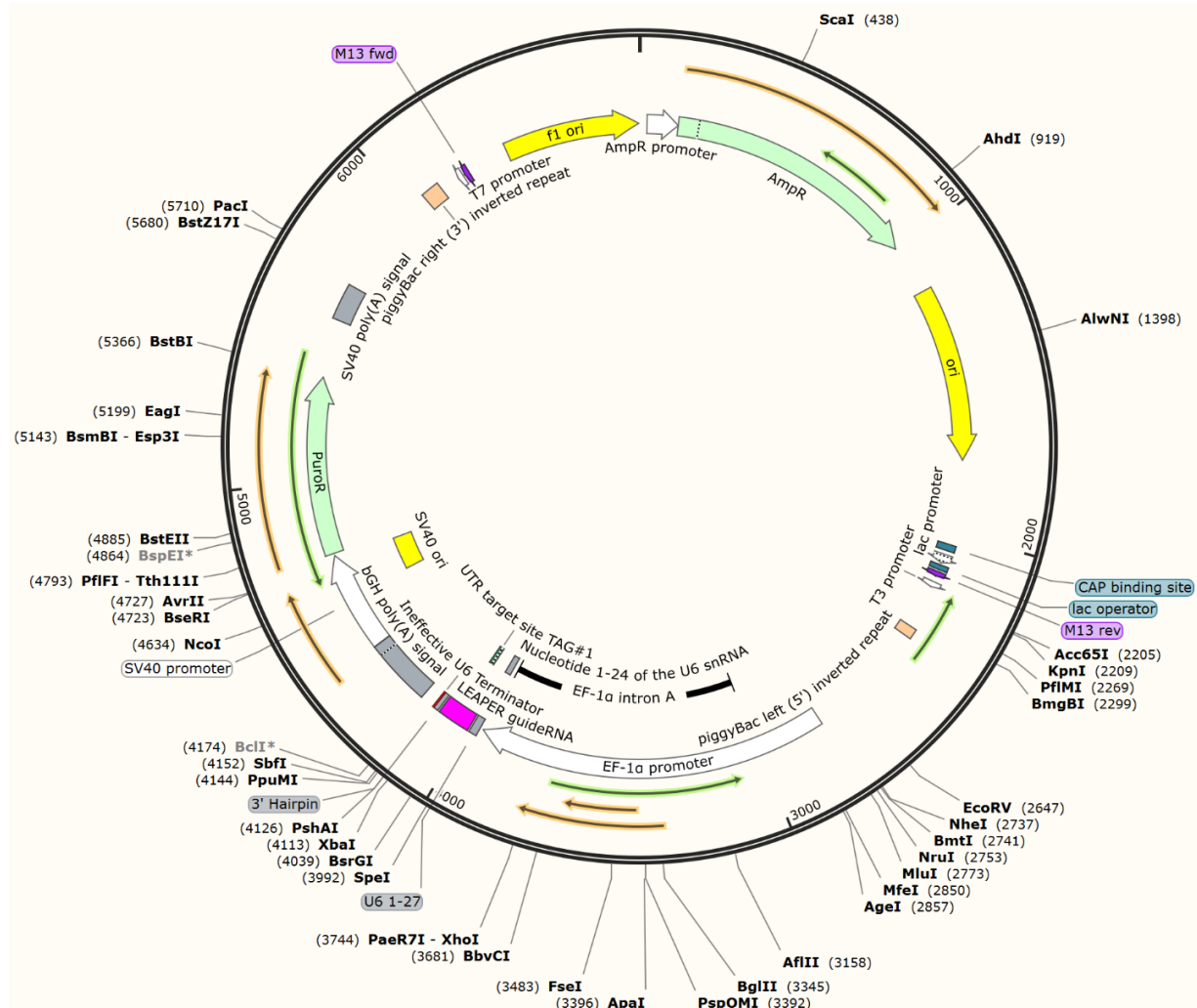
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541    TGACAACGAT  CGGAGGACCG  AAGGAGCTAA  CCGCTTTTTT  GCACAACATG  GGGGATCATG
601    TAACTCGCCT  TGATCGTTGG  GAACCGGAGC  TGAATGAAGC  CATAACCAAC  GACGAGCGTG
661    ACACCACGAT  GCCTGTAGCA  ATGGCAACAA  CGTTGCGCAA  ACTATTAACT  GGCGAACTAC
721    TTACTIONAG  TTCCCGGCAA  CAATTAATAG  ACTGGATGGA  GGCGGATAAA  GTTGAGGAC
781    CACTTCTGCG  CTCGGCCCTT  CCGGCTGGCT  GGTTTATTGC  TGATAAATCT  GGAGCCGGTG
841    AGCGTGGGTC  TCGCGGTATC  ATTGCAGCAC  TGGGGCCAGA  TGGTAAGCCC  TCCCGTATCG
901    TAGTTATCTA  CACGACGGGG  AGTCAGGCAA  CTATGGATGA  ACGAAATAGA  CAGATCGCTG
961    AGATAGGTGC  CTCCTGATT  AAGCATTGGT  AACTGTCAGA  CCAAGTTTAC  TCATATATAC

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1141	TAGAAAAGAT	CAAAGGATCT	TCTTGAGATC	CTTTTTTTCT	GCGCGTAATC	TGCTGCTTGC
1201	AAACAAAAAA	ACCACCGCTA	CCAGCGGTGG	TTTGTTTGCC	GGATCAAGAG	CTACCAACTC
1261	TTTTTCCGAA	GGTAACTGGC	TTCAGCAGAG	CGCAGATACC	AAATACTGTC	CTTCTAGTGT
1321	AGCCGTAGTT	AGGCCACCAC	TTCAAGAACT	CTGTAGCACC	GCCTACATAC	CTCGCTCTGC
1381	TAATCCTGTT	ACCAGTGGCT	GCTGCCAGTG	GCGATAAGTC	GTGTCTTACC	GGGTTGGACT
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1621	GAACAGGAGA	GCGCACGAGG	GAGCTTCCAG	GGGAAACGC	CTGGTATCTT	TATAGTCTCTG
1681	TCGGGTTTTG	CCACCTCTGA	CTTGAGCGTC	GATTTTTGTG	ATGCTCGTCA	GGGGGGCGGA
1741	GCCTATGGAA	AAACGCCAGC	AACGCGGCCT	TTTTACGGTT	CCTGGCCTTT	TGCTGGCCTT
1801	TTGCTCACAT	GTTCTTTCCT	GCGTTATCCC	CTGATTCTGT	GGATAACCGT	ATTACCGCCT
1861	TTGAGTGAGC	TGATACCGCT	CGCCGCAGCC	GAACGACCGA	GCGCAGCGAG	TCAGTGAGCG
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2041	ATGTGAGTTA	GCTCACTCAT	TAGGCACCCC	AGGCTTTACA	CTTTATGCTT	CCGGCTCGTA
2101	TGTTGTGTGG	AATTGTGAGC	GGATAACAAT	TTCACACAGG	AAACAGCTAT	GACCATGATT
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3421	GCGAGGCGGG	GCCTGCGAGC	GCGGCCACCG	AGAATCGGAC	GGGGGTAGTC	TCAAGCTGGC
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3721	CCGTCCAGGC	ACCTCGATTA	GTTCTCGAGC	TTTTTGAGTA	CGTCGTCTTT	AGGTTGGGGG
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4261	CAGTCCACGC	TCTAGAGCGG	ACTTCGGTCC	GCTTTTTACT	AGGACCTGCA	GGCATGCTCG
4321	ACAGAGCTCG	CTGATCAGCC	TCGACTGTGC	CTTCTAGTTG	CCAGCCATCT	GTTGTTTGCC
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4441	ATGAGGAAAT	TGCATCGCAT	TGTCTGAGTA	GGTGTCAATC	TATTCTGGGG	GGTGGGGTGG
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4561	GCTCTATGGC	GTGTGTCAGT	TAGGGTGTGG	AAAGTCCCCA	GGCTCCCCAG	CAGGCAGAAG
4621	TATGCAAAGC	ATGCATCTCA	ATTAGTCAGC	AACCAGGTGT	GGAAAGTCCC	CAGGCTCCCC
4681	AGCAGGCAGA	AGTATGCAAA	GCATGCATCT	CAATTAGTCA	GCAACCATAG	TCCCGCCCCT
4741	AACTCCGCCC	ATCCCGCCCC	TAACTCCGCC	CAGTTCGGCC	CATTCTCCGC	CCCATGGCTG
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5041	CGGGTCACCG	AGCTGCAAGA	ACTCTTCCTC	ACGCGCGTCG	GGCTCGACAT	CGGCAAGGTG
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5461	CCCGAAGGAC	CGCGCACCTG	GTGCATGACC	CGCAAGCCCG	GTGCCTGAGC	GGGACTCTGG
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5701	ACCCCAACTT	GTTTATTGCA	GCTTATAATG	GTTACAAATA	AAGCAATAGC	ATCACAAATT
5761	TCACAAATAA	AGCATTTTTT	TCACTGCATT	CTAGTTGTGG	TTTGTCCAAA	CTCATCAATG
5821	TATCTTATCA	TGTCTGTATA	CCGTCGACCT	CTAGCTAGTC	GAGTTAATTA	ACGAGAGCAT
5881	AATATTGATA	TGTGCCAAAG	TTGTTTCTGA	CTGACTAATA	AGTATAATTT	GTTTCTATTA
5941	TGTATAGGTT	AAGCTAATTA	CTTATTTTAT	AATACAACAT	GACTGTTTTT	AAAGTACAAA
6001	ATAAGTTTAT	TTTTGTAAAA	GAGAGAATGT	TTAAAAGTTT	TGTTACTTTA	TAGAAGAAAT
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6181	ACCTCGATAT	ACAGACCGAT	AAAACACATG	CGTCAATTTT	ACGCATGATT	ATCTTTAACG
6241	TACGTCACAA	TATGATTATC	TTTCTAGGGT	TAAATAATAG	TTTCTAATTT	TTTTATTATT
6301	CAGCCTGCTG	TCGTGAATAC	CGAGCTCCAA	TTCGCCCTAT	AGTGAGTCGT	ATTACAATTC
6361	ACTGGCCGTC	GTTTTACAAC	GTCGTGACTG	GGAAAACCCT	GGCGTTACCC	AACTTAATCG
6421	CCTTGACAGC	CATCCCCCTT	TCGCCAGCTG	GCGTAATAGC	GAAGAGGCCC	GCACCGATCG
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6841	AACAACACTC	AACCCTATCT	CGGTCTATTC	TTTTGATTTA	TAAGGGATTT	TGCCGATTTC
6901	GGCCTATTGG	TTAAAAAATG	AGCTGATTTA	ACAAAAATTT	AACGCGAATT	TTAACAAAAAT
6961	ATTAACGTTT	ACAATTTCC				

Plasmid-map and sequence of the **Transposon EF1 α linear RAB7A LEAPER gRNA vector (pTS1900)**:



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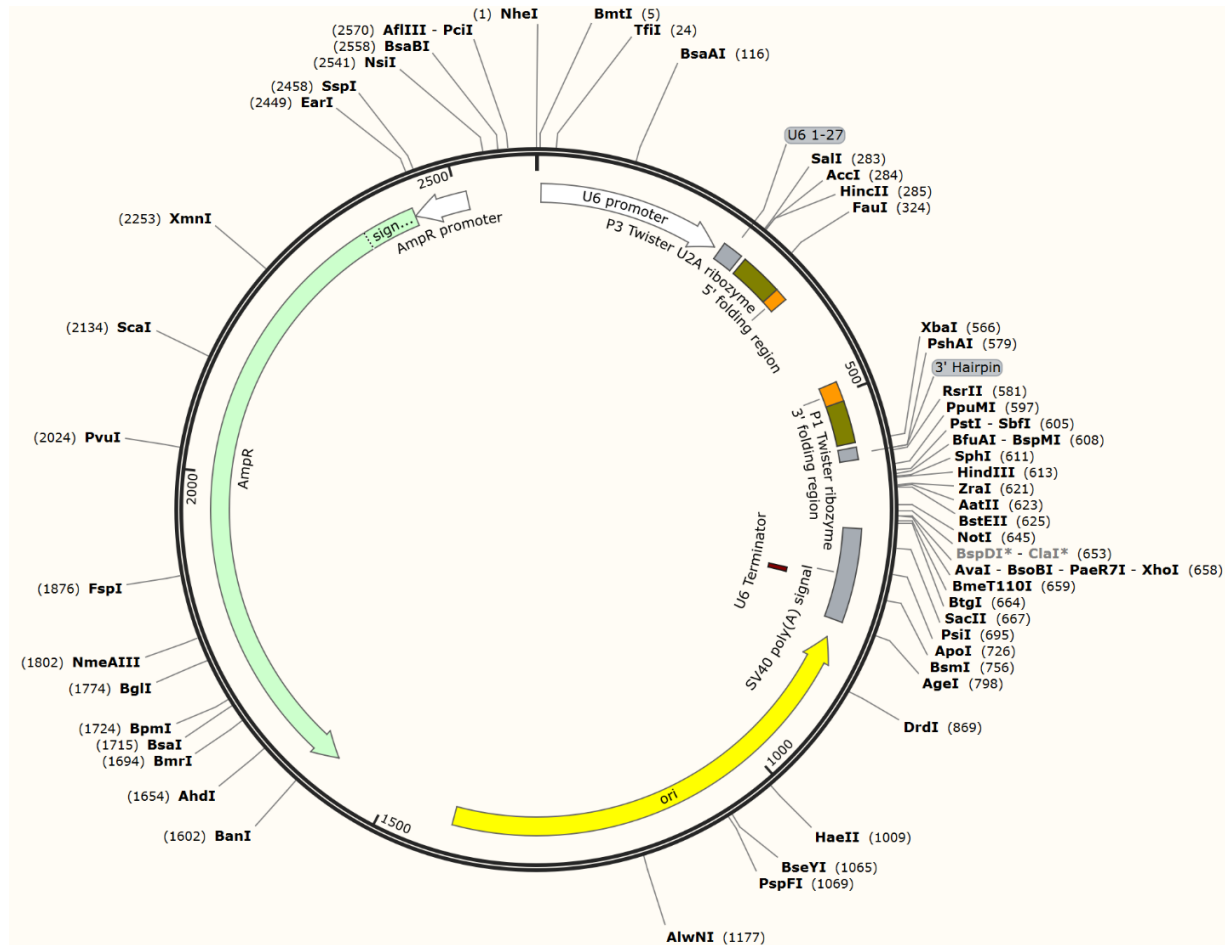
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181    TTTGCCTTCC  TGTTTTTGCT  CACCCAGAAA  CGCTGGTGAA  AGTAAAAGAT  GCTGAAGATC
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361    CGGTATTATC  CCGTATTGAC  GCCGGGCAAG  AGCAACTCGG  TCGCCGCATA  CACTATTCTC
421    AGAATGACTT  GGTTGAGTAC  TCACCAGTCA  CAGAAAAGCA  TCTTACGGAT  GGCATGACAG
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661    ACACCAGAT  GCCTGTAGCA  ATGGCAACAA  CGTTGCGCAA  ACTATTAAC  GGCGAATAC
721    TTACTCTAGC  TTCCCGGCAA  ACTGGATGGA  ACTGGATGGA  GGCGGATAAA  GTTGCAGGAC
781    CACTTCTGCG  CTCGGCCCTT  CCGGCTGGCT  GGTTTATTGC  TGATAAATCT  GGAGCCGGTG
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901    TAGTTATCTA  CACGACGGGG  AGTCAGGCAA  CTATGGATGA  ACGAAATAGA  CAGATCGCTG
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1141	TAGAAAAGAT	CAAAGGATCT	TCTTGAGATC	CTTTTTTTCT	GCGCGTAATC	TGCTGCTTGC
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5641	GGTTTGTCCA	AACTCATCAA	TGTATCTTAT	CATGTCTGTA	TACCGTCGAC	CTCTAGCTAG
5701	TCGAGTTAAT	TAACGAGAGC	ATAATATTGA	TATGTGCCAA	AGTTGTTTCT	GACTGACTAA
5761	TAAGTATAAT	TTGTTTCTAT	TATGTATAGG	TTAAGCTAAT	TACTTATTTT	ATAATACAAC
5821	ATGACTGTTT	TTAAAGTACA	AAATAAGTTT	ATTTTTGTAA	AAGAGAGAAT	GTTTAAAGT
5881	TTTGTTACTT	TATAGAAGAA	ATTTTGAGTT	TTTGTTTTTT	TTTAATAAAT	AAATAAACAT
5941	AAATAAATTG	TTTGTTGAAT	TTATTATTAG	TATGTAAGTG	TAAATATAAT	AAAACCTAAT
6001	ATCTATTCAA	ATTAATAAAT	AAACCTCGAT	ATACAGACCG	ATAAAACACA	TGCGTCAATT
6061	TTACGCATGA	TTATCTTTAA	CGTACGTCAC	AATATGATTA	TCTTTCTAGG	GTTAAATAAT
6121	AGTTTCTAAT	TTTTTTATTA	TTCAGCCTGC	TGTCGTGAAT	ACCGAGCTCC	AATTCGCCCT
6181	ATAGTGAGTC	GTATTACAA	TCACTGGCCG	TCGTTTTTACA	ACGTCGTGAC	TGGGAAAACC
6241	CTGGCGTTAC	CCAACTTAAT	CGCCTTGACG	CACATCCCCC	TTTCGCCCAGC	TGGCGTAATA
6301	GCGAAGAGGC	CCGCACCGAT	CGCCCTTCCC	AACAGTTGCG	CAGCCTGAAT	GGCGAATGGC
6361	GCGACGCGCC	CTGTAGCGGC	GCATTAAGCG	CGGCGGGTGT	GGTGGTTACG	CGCAGCGTGA
6421	CCGCTACACT	TGCCAGCGCC	CTAGCGCCCG	CTCCTTTCGC	TTTCTTCCCT	TCCTTTCTCG
6481	CCACGTTTCG	CGGCTTTCCC	CGTCAAGCTC	TAAATCGGGG	GCTCCCTTTA	GGGTTCCGAT
6541	TTAGTGCTTT	ACGGCACCTC	GACCCCAAAA	AACTTGATTA	GGGTGATGGT	TCACGTAGTG
6601	GGCCATCGCC	CTGATAGACG	GTTTTTCGCC	CTTTGACGTT	GGAGTCCACG	TTCTTTAATA
6661	GTGGACTCTT	GTTCCAAACT	GGAACAACAC	TCAACCCTAT	CTCGGTCTAT	TCTTTTGATT
6721	TATAAGGGAT	TTTGCCGATT	TCGGCCTATT	GGTTAAAAAA	TGAGCTGATT	TAACAAAAAT
6781	TTAACGCGAA	TTTTAACAAA	ATATTAACTG	TTACAATTTT	C	

Plasmid-map and sequence of the **CircLEAPER AC50 cloning vector (pTS2508)**:



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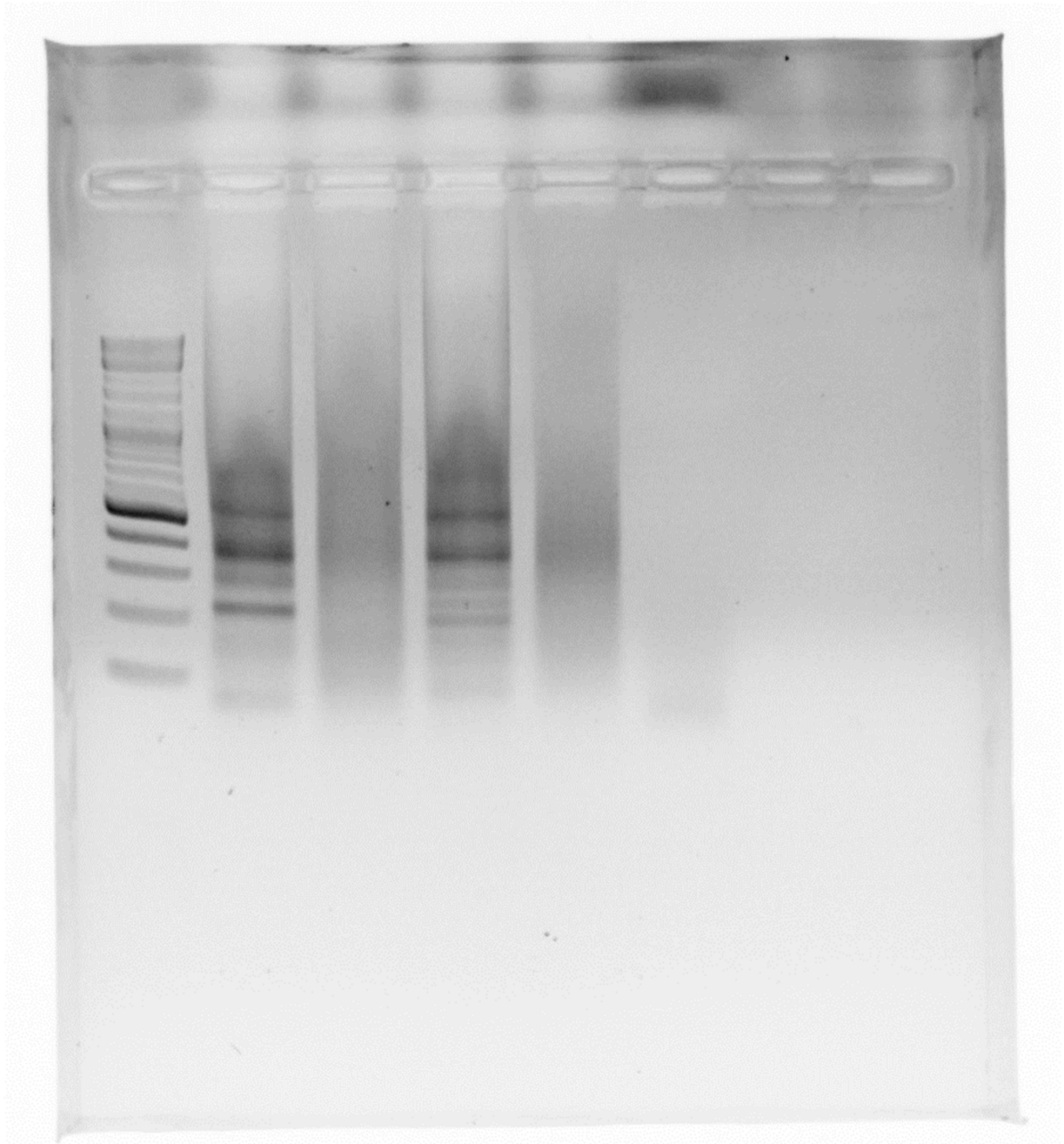
1      GCTAGCGAGG GCCTATTTCC CATGATTCCT TCATATTTGC ATATACGATA CAAGGCTGTT
61     AGAGAGATAA TTAGAATTAA TTTGACTGTA AACACAAAGA TATTAGTACA AAATACGTGA
121    CGTAGAAAGT AATAATTTCT TGGGTAGTTT GCAGTTTTAA AATTATGTTT TAAAATGGAC
181    TATCATATGC TTACCGTAAC TTGAAAGTAT TTCGATTTCT TGGCTTTTAA TATCTTGTGG
241    AAAGGACGAA ACACCGTGCT CGCTTCGGCA GCACATATAC TAGTCGACGC CATCAGTCGC
301    CGGTCCCAAG CCCGATAAAA ATGGGAGGGG GCGGGAAACC GCCTAACCAT GCCGACTGAT
361    GGCAGAAAAA CAAAAACAAA AAAAAACAAA AAAAAACCA AAAAAACAAA ACACATGGTC
421    TTCGTGGAAG ACTTAAAAAC AAAAAACAAA AAAAAACAAA AAAAAACAAA AAAAAACAAA
481    CACACTGCCA TCAGTCGGCG TGGACTGTAG AACACTGCCA ATGCCGGTCC CAAGCCCGGA
541    TAAAAGTGGA GGGTACAGTC CACGCTCTAG AGCGGACTTC GGTCGGCTTT TTACTAGGAC
601    CTGCAGGCAT GCAAGCTTGA CGTCGGTTAC CGATATCCAT ATGGCGGCCG CATCGATCTC
661    GAGCCGCGGA CTAGTAACTT GTTTATTGCA GCTTATAATG GTTACAAATA AAGCAATAGC
721    ATCACAAATG TCACAAATAA AGCATTTTTTC TACTGCAATT CTAGTTGTAG TTTGTCCAAA
781    CTCATCAATG TATCTTAACC GGTGGCCGCG TTGCTGGCGT TTTTCCATAG GCTCCGCCCC
841    CCTGACGAGC ATCACAAAAA TCGACGCTCA AGTCAGAGGT GGCGAAACCC GACGAGACTA
901    TAAAGATACC AGGCGTTTCC CCCTGGAAGC TCCCTCGTGC GCTCTCCTGT TCCGACCCTG
961    CCGCTTACCG GATACCTGTC CGCCTTTCTC CTTTCGGGAA GCGTGGCGCT TTCTCATAGC
1021   TCACGCTGTA GGTATCTCAG TTCGGTGTAG GTCGTTTCGT CCAAGCTGGG CTGTGTGCAC
1081   GAACCCCCCG TTCAGCCCGA CCGCTGCGCC TTATCCGGTA ACTATCGTCT TGAGTCCAAC
1141   CCGGTAAGAC ACGACTTATC GCCACTGGCA GCAGCCACTG GTAACAGGAT TAGCAGAGCG
1201   AGGTATGTAG GCGGTGCTAC AGAGTTCTTG AAGTGGTGGC CTAACACGG CTACACTAGA

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1261	AGAACAGTAT	TTGGTATCTG	CGCTCTGCTG	AAGCCAGTTA	CCTTCGGAAA	AAGAGTTGGT
1321	AGCTCTTGAT	CCGGCAAACA	AACCACCGCT	GGTAGCGGTG	GTTTTTTTGT	TTGCAAGCAG
1381	CAGATTACGC	GCAGAAAAAA	AGGATCTCAA	GAAGATCCTT	TGATCTTTTC	TACGGGGTCT
1441	GACGCTCAGT	GGAACGAAAA	CTCACGTTAA	GGGATTTTGG	TCATGAGATT	ATCAAAAAGG
1501	ATCTTCACCT	AGATCCTTTT	AAATTAAAAA	TGAAGTTTTA	AATCAATCTA	AAGTATATAT
1561	GAGTAAACTT	GGTCTGACAG	TTACCAATGC	TTAATCAGTG	AGGCACCTAT	CTCAGCGATC
1621	TGTCTATTTT	GTTTCATCCAT	AGTTGCCTGA	CTCCCCGTCG	TGTAGATAAC	TACGATACGG
1681	GAGGGCTTAC	CATCTGGCCC	CAGTGCTGCA	ATGATACCGC	GAGACCCACG	CTCACCGGCT
1741	CCAGATTTAT	CAGCAATAAA	CCAGCCAGCC	GGAAGGGCCG	AGCGCAGAAG	TGGTCCTGCA
1801	ACTTTATCCG	CCTCCATCCA	GTCTATTAAT	TGTTGCCGGG	AAGCTAGAGT	AAGTAGTTCG
1861	CCAGTTAATA	GTTTGCGCAA	CGTTGTTGCC	ATTGCTACAG	GCATCGTGTT	GTCACGCTCG
1921	TCGTTTGGTA	TGGCTTCATT	CAGCTCCGGT	TCCCAACGAT	CAAGGCGAGT	TACATGATCC
1981	CCCATGTTGT	GCAAAAAAGC	GGTTAGCTCC	TTCGGTCCTC	CGATCGTTGT	CAGAAGTAAG
2041	TTGGCCGCAG	TGTTATCACT	CATGGTTATG	GCAGCACTGC	ATAATTCTCT	TACTGTCATG
2101	CCATCCGTAA	GATGCTTTTC	TGTGACTGGT	GAGTACTCAA	CCAAGTCATT	CTGAGAATAG
2161	TGTATGCGGC	GACCGAGTTG	CTCTTGCCCG	GCGTCAATAC	GGGATAATAC	CGCGCCACAT
2221	AGCAGAACTT	TAAAAGTGCT	CATCATTGGA	AAACGTTCTT	CGGGGCGAAA	ACTCTCAAGG
2281	ATCTTACCGC	TGTTGAGATC	CAGTTCGATG	TAACCCACTC	GTGCACCCAA	CTGATCTTCA
2341	GCATCTTTTA	CTTTCACCAG	CGTTTCTGGG	TGAGCAAAAA	CAGGAAGGCA	AAATGCCGCA
2401	AAAAAGGGAA	TAAGGGCGAC	ACGGAAATGT	TGAATACTCA	TACTCTTCCT	TTTTCAATAT
2461	TATTGAAGCA	TTTATCAGGG	TTATTGTCTC	ATGAGCGGAT	ACATATTTGA	ACGGCCGGAT
2521	TTCTTGTCAC	GCTTTGATGC	ATCGTTGGTG	GTTGATGGAT	ATCTGACGAA	CATGTGCACA
2581	GTGGTACAAG	GTATTCTCTG	TTG			

References:

1. Reautschnig, P., et al., *CLUSTER guide RNAs enable precise and efficient RNA editing with endogenous ADAR enzymes in vivo*. Nat Biotechnol, 2022. **40**(5): p. 759-768.
2. Wettengel, J., et al., *Harnessing human ADAR2 for RNA repair - Recoding a PINK1 mutation rescues mitophagy*. Nucleic Acids Res, 2017. **45**(5): p. 2797-2808.



Uncropped blot used for Figure S6b. The ladder used in the left most lane is the 1 kb Plus DNA Ladder (#N3200, NEB).