## **Supplementary information**

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## High-throughput continuous evolution of compact Cas9 variants targeting singlenucleotide-pyrimidine PAMs

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**Supplementary Figure 1. High level description of ePACE components. (a)** Photograph of ePACE, consisting of an eVOLVER continuous culture unit with custom vial caps, fluidics unit with a set of slow (~1 ml/m, pink pump heads) and fast (~1 ml/s, black pump heads) pump arrays for vial-to-vial/media pumping and waste pumping respectively, IPP device for chemical inducer pumping (~0.5 ul/s), and a multi-channel pressure regulator for powering IPP devices and pressurizing inducer bottles. (b) Diagram of fluidics for a single ePACE chemostat/lagoon pair. (c) Photograph of custom vials and caps designed for ePACE, labeled for a typical setup. Caps are designed to be used with hypodermic needles, but can also be used with other types of tubing if desired. (d) Diagram of volume levels for each input/output (I/O) port on the caps with different length needles. In ePACE, the efflux needle is set to 31 ml and 9 ml for the chemostat and lagoon, respectively (highlighted in red).



### Supplementary Figure 2. Integrated Peristaltic Pump (IPP) characterization.

(a) Diagram of IPP functionality. Three valves in series are sequentially opened and closed to induce a peristaltic effect on the flow line. A single set of control lines can be used to pump many channels in parallel. (b) Valve geometry effects on achievable flow rates. Error bars represent the standard deviation over three measurements on a single channel of a single device. (c) Three IPP devices, each with three parallel channels with linked control lines, were run continuously for 168 hours at 10 Hz. Every 24 hours, the devices were briefly stopped and flow rate measurements were taken across the device performance range at 10 Hz, 5 Hz, 1 Hz, and 0.1 Hz. Devices were then restarted at 10 Hz immediately after measurements were taken. For **b** and **c**, data are presented as mean $\pm$ SD of *n*=3 independent technical replicates.



**Supplementary Figure 3. eVOLVER pressure regulator characterization. (a)** Diagram and photo of an 8-channel PID controlled pressure regulator. **(b)** Comparison of pressures over 24 hours of PID controlled pressure to a manually set valve, both initial set at 1.5 psi. **(c)** Simplified electrical schematic of eVOLVER pressure regulator. Each proportional valve is controlled via pulse-width modulation (PWM) using a standard eVOLVER PWM board. A single PWM board can control 16 valves simultaneously, enabling control of eight individual pressure lines. Electrical pressure gauge readouts are connected to a standard eVOLVER analog-to-digital (ADC) converter. Both PWM and ADC boards are connected to a SAMD21 Arduino microcontroller which controls valve open/closeness and reads data from the gauges. The microcontroller receives commands from and sends data to the eVOLVER via serial communication protocol. **(d)** Schematic of pressure regulator and standard lab bench vacuum. Inducer bottles receive 1.5 psi. **(e)** Comparison of flow rates between media bottles with varying volumes of media while pressurized and un-pressurized.



**Supplementary Figure 4. ePACE validation on two-hybrid Maltose Binding Protein (MBP) selection. (a)** Diagram of two-hybrid MBP selection. Upon proper folding of MBP, a T7 RNA Polymerase is recruited to transcribe gIII. **(b)** Mutation tables of negative control WT MBP and structurally defective MBP after 120 hours of ePACE. MBP G32+I33S shows converging mutations at residues clustered around the monobody-MBP interaction interface (D32G, A63T, R66L), previously observed in PACE<sup>1</sup>.



**Supplementary Figure 5. Flow rate schedule and titers for ePACE1**. SP containing wildtype, full-length Nme2ABE8e were first diversified in *E.coli* host cells containing pJC175e<sup>2</sup> and MP6<sup>2</sup>, isolated, then seeded into ePACE1 (eight chemostats, one lagoon each targeting each of the eight N<sub>3</sub><u>YTN</u> PAMs). Flow rate stringency for each PAM is shown in the plots, as are resulting titers (measured by qPCR). If lagoons were reseeded with starting phage, the timepoint is highlighted in a green circle. The N<sub>3</sub><u>TTA</u> lagoon failed prematurely due to a pump failure in the ePACE setup. LOD=limit of detection of qPCR titering, as set by the titer corresponding to the C<sub>q</sub> for which the qPCR primers alone had been observed to amplify.



Supplementary Figure 6. Mutation table and representative activity of ePACE1 evolved Nme2Cas9 variants. (a) Genotypes of individually sequenced plaques following ePACE1, with positions varying from wild-type displayed. Clones evolved on different PAMs are delineated by a bold line. (b) Adenine base editing activity of a representative ePACE1 clone (E1-2-ABE8e) at eight N<sub>3</sub>NCN PAM-containing sites and eight N<sub>4</sub>TN PAM-containing sites in HEK293T cells. Mean±SEM are shown and are representative of n=3 independent biological replicates.

**NNNCTN PAMs** 



Supplementary Figure 7. Flow rate schedule and titers for ePACE2. SP previously isolated from ePACE1 lagoons evolved on  $N_3$ <u>TTC</u> and  $N_3$ <u>CTC</u> PAMs were pooled and reseeded into ePACE2 (eight chemostats, two lagoons each targeting each of the eight  $N_3$ <u>YTN</u> PAMs). Flow rate stringency for each PAM is shown in the plots, as are resulting titers (measured by qPCR). LOD=limit of detection of qPCR titering, as set by the titer corresponding to the C<sub>q</sub> for which the qPCR primers alone had been observed to amplify.



**Supplementary Figure 8. Identification of ePACE2 selection cheating. (a)** Representative agarose gel of PCR products amplifying the target insert from individual ePACE2 late timepoint SP plaques. The expected insert size for Nme2ABE8e is ~4.5 kb (left, starting SP), whereas multiple recombinant bands appeared for ePACE2 evolved SP (right). The gels were not repeated (*n*=1). **(b)** Sanger sequencing partially mapping the recombinant bands from (a) onto the gVI coding sequence, the unaligned sequence to the left maps to the gIII-containing AP sequence. **(c)** Nucleotide sequence homology between the coding sequence of gIV (where recombination was seen) and the gIII coding sequence present on the AP, aligned nucleotides highlighted in black.



**Supplementary Figure 9. Source gels for Supplementary Figure 8.** Uncropped gels that were used to generate Supplementary Figure 8a. The two gels were taken at separate times, but contain the same ladder for reference. The right gel wase cropped to remove lanes from unrelated experiments.





get A: A<sub>9</sub> A<sub>6</sub> A<sub>5</sub> A<sub>8</sub> A<sub>9</sub> A<sub>5</sub> A<sub>8</sub> A<sub>6</sub> A<sub>8</sub> A<sub>6</sub> A<sub>8</sub> A<sub>9</sub> A<sub>4</sub> A<sub>4</sub> A<sub>5</sub> A<sub>7</sub> A<sub>7</sub> A<sub>4</sub> Site: ACC-1 CCC-1 TCA-1 GCA-1 CCG-1 GCG-1 CCT-1 GCT-1 CTA-1 GTA-1 CTC-1 ATG-1 GTG-1 CTG-1 ATT-1 TTT-1

N4TN PAMs

а

60

% A•T converted to G•C at maximally edited position 07 05

0 Target A:

(PAM: NNN<u>NYN</u>)

N4CN PAMs

ePACE2, with positions varying from wild-type displayed. Clones evolved on different PAMs are delineated by a bold line. Mutations that had previously appeared in ePACE1 are shown in light pink, while novel mutations are shown in magenta. **(b)** Adenine base editing activity of a representative ePACE2 clone (E2-12-ABE8e) at eight N<sub>4</sub>CN PAM-containing sites and eight N<sub>4</sub>TN PAM-containing sites in HEK293T cells. Mean±SEM are shown and are representative of *n*=3 independent biological replicates.



Supplementary Figure 11. Validation of the split-SAC-PACE selection with different TadABE8e variants. Overnight propagation assay to test the activity of the split-SAC-PACE selection with different TadA8e variants. Each TadA8e variant was fused to the N-terminal half of an intein (gp41-8N) and placed on a complementary plasmid (CP) in host cells. FL-Nme2ABE8e phage contained full-length, active Nme2ABE8e, and OT phage did not contain Nme2Cas9, intein, or TadA8e. Mean±SEM are shown and are representative of n=2 independent biological replicates. Fold-propagation is calculated as the ratio of phage titer after overnight propagation over inoculating titer.



Supplementary Figure 12. Flow rate schedule and titers for ePACE3. SP from ePACE1 sequenced SP from ePACE2 were pooled and recloned into the split-SAC-PACE phage architecture (SP404, Supplementary Table 7), then seeded into ePACE3 (seven chemostats, two lagoons each targeting each of the eight  $N_3$ <u>YTN</u> PAMs;  $N_3$ <u>TTA</u> was excluded due to a cloning error). Flow rate stringency for each PAM is shown in the plots, as are resulting titers (measured by qPCR). The  $N_3$ <u>TTC</u> and  $N_3$ <u>TTT</u> lagoons were started late due to slow initial host cell growth. LOD=limit of detection of qPCR titering, as set by the titer corresponding to the C<sub>q</sub> for which the qPCR primers alone had been observed to amplify.

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Supplementary Figure 13. Mutation table and representative activity of ePACE3 evolved Nme2Cas9 variants. (a) Genotypes of individually sequenced plaques following ePACE3, with positions varying from wild-type displayed. Clones evolved on different PAMs are delineated by a bold line. Mutations that had previously appeared in ePACE1 and ePACE2 are shown in light pink and magenta, respectively, while novel mutations are shown in purple. (b) Adenine base editing activity of a representative ePACE3 clone (E3-18-ABE8e) at eight N<sub>4</sub>TN PAM-containing sites in HEK293T cells. Mean±SEM are shown and are representative of n=3 independent biological replicates. а

Passage		Replic	cate 1 o	dilutior	n table			Replic	ate 2	dilutior	table		Notes
/PAM	ACA	ACG	ACT	TCA	TCG	TCT	ACA	ACG	ACT	TCA	TCG	TCT	
1	20	20		20	20		20	20		20	20		
2	20	20		20	20		20	20		20	20		
3	13	13		13	13		13	13		13	13		Pa2 (1:20) + MP6-diversified Pa1 (1:40)
4	20	20		20	20		20	20		20	20		
5	20	20		20	20		20	20		20	20		
6	20	20		20	20		20	20		20	20		Host strain: 2208+MP6
7	20	20		20	20		20	20		20	20		
8	20	20		20	20		20	20		20	20		Host strain: 2208+MP6
9	20	20		20	20		20	20		20	20		
10	20	20		20	20		20	20		20	20		Host strain: 2208+MP6
11	20	20	20	20	20	20	20	20	20	20	20	20	ACT/TCT PAMs added, 1:20 pooled PAMs
12	20	20	20	20	20	20	20	20	20	20	20	20	
13	20	20	20	20	20	20	20	20	20	20	20	20	
14	20	20	20	20	20	20	20	20	20	20	20	20	
15	20	20	20	100	100	100	20	20	20	100	100	100	
16	20	20	20	100	100	100	20	20	20	100	100	100	
17	20	20	20	600	600	600	20	20	20	600	600	600	
18	20	20	20	600	600	600	20	20	20	600	600	600	
19	20	20	20	6000	6000	6000	20	20	20	6000	6000	6000	ACN PAMs - Host strain 2208+MP6
20	20	20	20	6000	6000	6000	20	20	20	6000	6000	6000	ACN PAMs - spiked 1:600 TCN phage

Passage		Replic	cate 3 d	dilution	table			Replic	cate 4 o	dilution	table		Notes
/PAM	ACA	ACG	ACT	TCA	TCG	TCT	ACA	ACG	ACT	TCA	TCG	TCT	
1	20	20		20	20		20	20		20	20		
2	20	20		20	20		20	20		20	20		
3	13	13		13	13		13	13		13	13		Pa2 (1:20) + MP6-diversified Pa1 (1:40)
4	20	20		20	20		20	20		20	20		
5	20	20		20	20		20	20		20	20		
6	20	20		20	20		20	20		20	20		Host strain: 2208+MP6
7	20	20		20	20		20	20		20	20		
8	20	20		20	20		20	20		20	20		Host strain: 2208+MP6
9	20	20		20	20		20	20		20	20		
10	20	20		20	20		20	20		20	20		Host strain: 2208+MP6
11	20	20	20	20	20	20	20	20	20	20	20	20	ACT/TCT PAMs added, 1:20 pooled PAMs
12	20	20	20	20	20	20	20	20	20	20	20	20	Pa11 (1:40) + Pa6 (1:40)
13	20	20	20	20	20	20	20	20	20	20	20	20	
14	20	20	20	20	20	20	20	20	20	20	20	20	
15	20	20	20	20	20	20	20	20	20	20	20	20	Host strain: 2208+MP6, Pa13 & Pa14
16	20	20	20	20	20	20	20	20	20	20	20	20	
17	20	20	20	20	20	20	20	20	20	20	20	20	
18	20	20	20	20	20	20	20	20	20	20	20	20	
19	20	20	20	20	20	20	20	20	20	20	20	20	ACN PAMs - Host strain 2208+MP6
20	20	20	20	20	20	20	20	20	20	20	20	20	ACN PAMs - spiked 1:600 TCN phage





b		
-	PANCE conditions	
		proC-split-Npu-gIII
	AP	(Target PAMs CTT <u>NCN</u> T, AGG <u>NCN</u> G)
	CP	psp-sd8-TadA8e R26G
	MP	MP6
	SP	Replicate 1 & 2: wild-type split-dNme2Cas9 Replicate 3 & 4: ePACE1 & ePACE2 pool, recloned as split Cas9

**Supplementary Figure 14. PANCE dilution schedule and titers for N1.** SP containing wild-type split-dNme2Cas9 or pooled ePACE1/ePACE2 split-Nme2Cas9 were first diversified in *E.coli* host cells containing pJC175e<sup>2</sup> and MP6<sup>2</sup>, isolated, then seeded into PANCE1 (N1, 6

chemostats of each of six  $N_3$ <u>WTD</u> PAMs, where W=A or T and D=A,G, or T; 4 replicates). (a) Passage stringency schedule and resulting titers (measured by qPCR) for replicates 1 and 2 (top) or replicates 3 and 4 (bottom). Passages were done after 16-24 hr for all passages. For some passages, some conditions were passaged uniquely to others or in a different host cell line, and these changes are listed in the Notes column. Grey coloring represents titers that were not measured or the PAM had not yet been included. All N<sub>3</sub>ACD PAMs were unable to support phage propagation, which retroactively was discovered to be attributable to an AP design error (see **Supplementary Note 6**). LOD=limit of detection of qPCR titering, as set by the titer corresponding to the C<sub>q</sub> for which the qPCR primers alone had been observed to amplify. (b) PANCE conditions used for N1.



Supplementary Figure 15. Flow rate schedule and titers for ePACE4. SP from N1, passage 20, were combined and seeded into corresponding PAMs in ePACE4 (six chemostats, two lagoons each of the three N<sub>3</sub>ACD PAMs, where D=A,G, or T, three lagoons

each of the three  $N_3 \underline{TCD}$  PAMs). N1 replicates 1 and 2 were pooled into "Lagoon 1" lagoons, N1 replicates 3 and 4 were pooled into "Lagoon 2" lagoons, and all N1 replicates were pooled into any "Lagoon 3" lagoons. The  $N_3\underline{ACD}$  PAMs all washed out, which retroactively was discovered to be attributable to an AP design error (see **Supplementary Note 6**). Flow rate stringency for each PAM is shown in the plots, as are resulting titers (measured by qPCR). LOD=limit of detection of qPCR titering, as set by the titer corresponding to the C<sub>q</sub> for which the qPCR primers alone had been observed to amplify.

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Passage		R	eplica	ate 1 d	dilutio	n tab	le			R	eplica	ate 2 d	dilutio	n tab	le			R	eplica	ate 3 o	dilutio	n tab	le	
/PAM	CTA	CTC	CTG	CTT	TTA	TTC	TTG	TTT	СТА	CTC	CTG	CTT	TTA	TTC	TTG	TTT	СТА	CTC	CTG	CTT	TTA	TTC	TTG	TTT
1	20			20	20		20	20	20			20	20		20	20	20			20	20		20	20
2	20			20	20		20	20	20			20	20		20	20	20			20	20		20	20
3	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20
4	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	100	100	100	100	100	100	100	100
5	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	100	100	100	100	100	100	100	100
6	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	500	500	500	500	500	500	500	500
7																	500	500	500	500	500	500	500	500
								_																

6 8 LOD

Log<sub>10</sub> titer (pfu/mL) by qPCR

Passage	Notes
/PAM	
1	
2	
3	missing PAMs added, 1:20 starting phage
4	MP6-diversified Pa3 (1:20)
5	
6	
7	Replicates 1 & 2 stopped

b

PANCE conditions	
۸P	proC-split-Npu-gIII
7.0	(Target PAMs CTT <u>NTN</u> T, AGG <u>NTN</u> G)
CP	psp-sd8-TadA8e R26G
MP	MP6
SP	Replicate 1: wild-type split-dNme2Cas9 Replicate 2: ePACE1 & ePACE2 pool, recloned as split Cas9 Replicate 3: ePACE3 pool, recloned as split Cas9

Supplementary Figure 16. PANCE dilution schedule and titers for N2. SP containing wild-type split-dNme2Cas9, pooled ePACE1/ePACE2 split-Nme2Cas9, or pooled ePACE3 split-Nme2Cas9 were first diversified in *E.coli* host cells containing pJC175e<sup>2</sup> and MP6<sup>2</sup>, isolated, then seeded into PANCE2 (N2, eight chemostats of each of eight N<sub>3</sub>YTN PAMs, where Y=C or T; three replicates). (a) Passage stringency schedule and resulting titers (measured by gPCR) for replicates 1-3. Passages were done after 16-24 hr for all passages. For some passages, some conditions were passaged uniquely to others or in a different host cell line, and these changes are listed in the Notes column. Grey coloring represents titers that were not measured or the PAM had not yet been included. LOD=limit of detection of qPCR titering, as set by the titer corresponding to the C<sub>a</sub> for which the qPCR primers alone had been observed to amplify. (b) PANCE conditions used for N2.



#### Supplementary Figure 17. Flow rate schedule and titers for ePACE5.

SP from N2 replicate 3, passage 7, were combined and seeded into corresponding PAMs in ePACE5 (eight chemostats, two lagoons each of the eight  $N_3$ <u>YTN</u> PAMs, where Y=C or T). Flow rate stringency for each PAM is shown in the plots, as are resulting titers (measured by qPCR). As most lagoons were unable to support consistent phage propagation, the timepoints used for isolating and sequencing phage (**Extended Data Figure 5**) are marked by a black box. LOD=limit of detection of qPCR titering, as set by the titer corresponding to the C<sub>q</sub> for which the qPCR primers alone had been observed to amplify.



Supplementary Figure 18. eNme2-T.1-ABE8e and eNme2-T.2-ABE8e activity at N<sub>4</sub>VN PAM sites. (a) Adenine base editing activity of eNme2-T.1-ABE8e and eNme2-T.2-ABE8e at 22 N<sub>3</sub>NVN PAM sites in HEK293T cells. Mean±SEM is shown and reflects the average activity and standard error of n=3 replicates at the maximally edited position within each genomic site. (b) Adenine base editing activity in (a) pooled by PAM position 5 (N<sub>4</sub>NN) identity, also including pooled N<sub>4</sub>TN sites from **Extended Data Figure 6a**. Each point represents the average editing of n=3 independent biological replicates measured at the maximally edited position within each given genomic site. Mean±SEM is shown and reflects the average the average activity and standard error of the pooled genomic site averages.



	20 nt	protospa	acer (Sp	Cas9)	23 nt protospacer (Nme2Cas9)				
Site	0 MM*	1 MM	2 MM	3 MM	0 MM*	1 MM	2 MM	3 MM	
ACC-1	0	0	3	111	0	0	0	0	
GCT-1	0	0	14	271	0	0	0	6	
CCC-1	4	11	149	1612	0	6	6	70	
CCG-1	0	1	13	168	0	0	0	12	
GCA-1	0	1	25	426	0	0	0	10	
GCG-1	0	0	3	70	0	0	0	1	
Average	0.7	2.2	34.5	443.0	0.0	1.0	1.0	16.5	

Supplementary Figure 19. In silico prediction of off-target sites with  $\leq$  3 mismatches for a 20-nt or 23-nt protospacer. (a) Count of genome-wide (GRCh38) sites with 0, 1, 2, or 3 mismatches to a 20-nt (SpCas9) or 23-nt (Nme2Cas9) protospacer identified with CHOPCHOPv3<sup>3</sup>. Mean±SEM representing identified off-targets at six randomly selected 20-nt or 23-nt protospacers are shown. (b) Table listing the number of identified sites with the corresponding number of mismatches to a 20-nt or 23-nt protospacer at six randomly selected genomic sites (see Supplementary Table 5).

### b



Supplementary Figure 20. High-throughput sequencing validation of GUIDE-seqidentified off-target activity. High-throughput sequencing in HEK293T cells at the top offtarget sites nominated by GUIDE-seq for eNme2-C, eNme2-C.NR, SpRY, or SpRY-HF1 nucleases (**Supplementary Table 3**). Off-target indel formation by Nme2Cas9, eNme2-C.NR, SpRY, or SpRY-HF1 nuclease at nominated off target sites for the sgRNAs targeting Site 3 (a), Site 4 (b), Site 5 (c), or Site 6 (d). Off-target adenine base editing by Nme2-ABE8e, eNme2-C-ABE8e, SpRY-ABE8e, or SpRY-HF1-ABE8e at nominated off-target sites for the sgRNAs targeting Site 3 (d), Site 4 (e), Site 5 (f), or Site 6 (g). Mean±SEM is shown and reflects the average activity and standard error of n=3 independent biological replicates measured at the maximally edited position within each given genomic site. On-target activity is shown at the left-most entry for each site.



Supplementary Figure 21. Off-target adenine base editing at in silico-predicted offtarget sites for SpRY-ABE8e, SpRY-HF1-ABE8e, eNme2-T.1-ABE8e and eNme2-T.2-ABE8e. (a) Off-target adenine base editing by SpRY-ABE8e, SpRY-HF1-ABE8e, eNme2-T.1-ABE8e and eNme2-T.2-ABE8e at (a) 12 computationally determined off-targets of a protospacer-matched sgRNA (Site 7) or (b) 23 computationally determined off-targets of a protospacer matched sgRNA (Site 8). Mean±SEM is shown and reflects the average activity and standard error of the of *n*=3 independent biological replicates measured at the maximally edited position within each given genomic site. On-target activity is shown at the left-most entry for each site.



Supplementary Figure 22. Dose-dependent adenine base editing activity in primary human dermal fibroblasts. Dose titration of mRNA encoding Nme2-ABE8e, eNme2-C-ABE8e, SpRY-ABE8e, or SpRY-HF1-ABE8e electroporated into primary human dermal fibroblasts together with synthetic guide RNA targeting either the GCT-2 or CCG-1 site (Supplementary Table 5). Mean±SEM is shown and reflects the average activity of one biological replicate measured for each dose targeting the two different endogenous genomic sites.



Supplementary Figure 23. Off-target adenine base editing at in silico-predicted offtarget sites for SpCas9-NRCH and eNme2-C sgRNAs targeting the *HBB* sickle-cell disease mutation. (a) Off-target adenine base editing by eNme2-C-ABE8e at nine computationally nominated off-target sites for the sgRNA targeting the *HBB* sickle-cell disease mutation. (b) Off-target adenine base editing by SpCas9-NRCH-ABE8e at 11 computationally nominated off-target sites for the sgRNA targeting the *HBB* sickle-cell disease mutation. Mean±SEM is shown and reflects the average activity and standard error of the of n=3 independent biological replicates measured at the maximally edited position within each given genomic site. On-target activity is shown at the left-most entry for each site.

# Supplementary Table 1. BE-PPA library editing data (See the separately provided Excel file.)

## Supplementary Table 2. CHOPCHOPv3 identified off-target sites of protospacer-matched sgRNAs comparing eNme2-C to SpRY and SpRY-HF1

			PAM	
			(top:	Mismatches
		Protospacer sequence	Nme2Cas9;	(PAM proximal <sup>^</sup> )
Target site or		(5'-3'; top: Nme2Cas9, bottom:	bottom:	(top: Nme2Cas9;
off-target site	Gene	SpRY)	SpRY)	bottom: SpRY)
0:4- 4	00004	GCAGATCCCACAGGCGCCCTGGC	CAGTCG	• /
Site	PDCD1	GATCCCACAGGCGCCCTGGC	CAG	-
		GCA <b>tt</b> TCCCACAGGCGCCCTGGC	GATGCC	2 (0)
Site1-011	Intergenic	<b>tt</b> TCCCACAGGCGCCCTGGC	GAT	2 (0)
		tgAGgTCCCACAGGCcCCCTGGC	GCAGCC	4 (1)
Site 1-012	PLCH2	G <b>g</b> TCCCACAGGC <b>C</b> CCCTGGC	GCA	2 (1)
		tggGcTCCCACAGGCcCCCTGGC	CTCCCC	5 (1)
Site 1-013	Intergenic	G <b>C</b> TCCCACAGGC <b>C</b> CCCTGGC	CTC	2 (1)
	TOFOO	agAGATaCCACAGGCaCCCTGGC	ATGATA	4 (1)
Sile 1-014	10F20	GAT <mark>a</mark> CCACAGGC <mark>a</mark> CCCTGGC	ATG	2 (1)
Site 1 OTE	CVVCE	GC <b>t</b> G <b>c</b> TCCCA <b>g</b> AGGCGCCCTGGC	TCTGCA	3 (0)
Sile 1-015	07700	G <b>C</b> TCCCA <b>g</b> AGGCGCCCTGGC	TCT	2 (0)
Sito 1 OT6*	Intorgonio	<b>ag</b> AGATC <b>a</b> C <b>C</b> AGGCGCCCTGGC	TCATGC	4 (0)
Sile 1-010	Intergenic	GATC <b>a</b> C <b>C</b> AGGCGCCCTGGC	TCA	2 (0)
Sito 1-0T7*	SADCD2DA	<b>tgg</b> GA <b>c</b> CCCACA <b>t</b> GCGCCCTGGC	CGGGAC	5 (0)
Sile 1-017	SAF CDZF4	GA <b>c</b> CCCACA <b>t</b> GCGCCCTGGC	CGG	2 (0)
0:4+ 0	FANOE	GCTGCAGAAGGGATTCCATGAGG	TGCGCG	
Site 2	FANCE	GCAGAAGGGATTCCATGAGG	TGC	-
	0.1.1 (20)	tgTGaAGAAGGGtTTCCATGAGG	AGATAC	4 (0)
Site 2-011	C110rt80	G <b>a</b> AGAAGGG <b>t</b> TTCCATGAGG	AGA	2 (0)
	44/00	GattCtGAAGGGATTCCATGAGG	TCTAAA	3 (0)
Sile 2-012	ANO3	<b>t</b> C <b>t</b> GAAGGGATTCCATGAGG	TCT	2 (0)
		<b>ca</b> TG <b>g</b> AGAAGGGAT <b>c</b> CCATGAGG	ACAAGG	4 (1)
Sile 2-013	MEAN/	G <b>g</b> AGAAGGGAT <b>C</b> CCATGAGG	ACA	2 (1)
	Intergonia	G <b>gTa</b> CAGAAGGG <b>C</b> TTCCATGAGG	CTGGGT	3 (0)
Sile 2-014	Intergenic	<b>a</b> CAGAAGGG <b>C</b> TTCCATGAGG	CTG	2 (0)
Sito 2 OT5	SI C10A1	G <b>ga</b> GCAGAAGG <b>c</b> ATT <b>t</b> CATGAGG	GGTCAA	4 (1)
Sile 2-015	SLUTIAT	GCAGAAGG <b>c</b> ATT <b>t</b> CATGAGG	GGT	2 (1)
Site 2-OT6	100105374492	<b>cag</b> GCAGAA <b>a</b> GGA <b>a</b> TCCATGAGG	ACTCCC	5 (1)
0110 2-010	200100014492	GCAGAA <mark>a</mark> GGA <mark>a</mark> TCCATGAGG	ACT	2 (1)
Site 2-OT7	ΜΔΡΟ	<b>aag</b> GCAGA <b>t</b> GGGATTCC <b>t</b> TGAGG	TCTGGA	5 (1)
	100 (1 0	GCAGA <b>t</b> GGGATTCC <b>t</b> TGAGG	TCT	2 (1)
Site 2-OT8	Intergenic	<b>aag</b> GCAGAAGG <b>a</b> ATTCCATGAG <b>t</b>	TAAAGT	5 (1)
	Intergerne	GCAGAAGG <b>a</b> ATTCCATGAG <b>t</b>	TAA	2 (1)
Site 2-OT9	RIPOR2	ctTGCtGAAGGGATTCaATGAGG	TGCTAC	4 (1)
		GC <b>t</b> GAAGGGATTC <b>a</b> ATGAGG	TGC	2 (1)
Site 2-OT10	Interaenic	GagGCAGgAGGGATTCCcTGAGG	AAGTGA	4 (1)
		GCAG <b>g</b> AGGGATTCC <b>C</b> TGAGG	AAG	2(1)
Site 2-OT11	Interaenic	agaGCgGAAGGGATgCCATGAGG	GATCCG	5(1)
		GC <b>g</b> GAAGGGAT <b>g</b> CCATGAGG	GA'I'	2(1)
Site 2-OT12*	Interaenic	aaaggagaaggaattccatgagg	ATACAA	5(0)
		G <b>g</b> AGAAGG <b>a</b> ATTCCATGAGG	ATA	2(0)

\*site did not sequence well (mixed bases) with HTS primers that were tried, see Supplementary Table 8. These sites were excluded from further analysis. ^PAM proximal defined as positions within 10 bases of the PAM

# Supplementary Table 3. GUIDE-Seq identified off-target sites (See separately attached Excel file.)

## Supplementary Table 4. CHOPCHOPv3 identified off-target sites of protospacermatched sgRNAs comparing eNme2-T.1 and eNme2-T.2 to SpRY and SpRY-HF1

			PAM	
			(top:	Mismatches
		Protospacer sequence	Nme2Cas9;	(PAM proximal <sup>^</sup> )
Target site or		(5'-3'; top: Nme2Cas9, bottom:	bottom:	(top: Nme2Cas9;
off-target site	Gene	SpRY)	SpRY)	bottom: SpRY)
Site 7	GRIN2B	GTGGGCTGTAACAGGAGGGCCAG	GAGATT	_
	Granze	GGCTGTAACAGGAGGGCCAG	GAG	
Site 7 OT1	SHANKD	<b>aa</b> GGGCTG <b>c</b> A <b>g</b> CAGGAGGGCCAG	GTGCTC	4 (0)
	SI IANAZ	GGCTG <b>C</b> A <b>G</b> CAGGAGGGCCAG	GTG	2 (0)
Site 7-OT2		<b>aa</b> GGGCTG <b>c</b> AACAGGAGGG <mark>a</mark> CAG	GGTACC	4 (1)
	11111400	GGCTG <b>C</b> AACAGGAGGG <mark>a</mark> CAG	GGT	2 (1)
Site 7-OT3	ATP11A	G <b>gt</b> GGCTGT <b>g</b> ACAG <b>c</b> AGGGCCAG	GAGCAG	4 (1)
	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	GGCTGT <b>g</b> ACAG <b>c</b> AGGGCCAG	GAG	2 (1)
Site 7-OT4	TMEM63C	<b>aa</b> GGGCTG <b>g</b> AAC <b>t</b> GGAGGGCCAG	AACCAG	4 (0)
		GGCTG <b>g</b> AAC <b>t</b> GGAGGGCCAG	AAC	2 (1)
Site 7-OT5	AQP8		GTGACG	5 (0)
		GGCTCTACCAGGAGGGCCAG	GTG	2 (0)
Site 7-OT6	Intergenic	GgaGGCTGTCACAGCAGGGCCAG	CAGCTC	4 (1)
	<u> </u>			$\sum (1)$
Site 7-OT7	UNC13D		GAGGCA	5 (1)
			JCCJCT	2 (1) 4 (0)
Site 7-OT8	ZNF566		AGCACI	4(0)
				$\frac{2}{4}(0)$
Site 7-OT9	SIX3	GCTGAAACAGGAGGGCGAG	TACAIG	4(1)
			GCAGAG	
Site 7-OT10	Intergenic	GaCTGaAACAGGAGGGCCAG	GCA	(0)
		tgaGcCTGTgACAGGAGGGCCAG	CTGCCA	5 (0)
Site 7-OT11	Intergenic	GCTGTGACAGGAGGGCCAG	CTG	2 (0)
		<b>c</b> TG <b>a</b> GCTGT <b>c</b> ACAGGAGGGCCAG	TGTCAA	3 (0)
Site 7-0112	Intergenic	<b>a</b> GCTGT <b>C</b> ACAGGAGGGCCAG	TGT	2 (0)
0.4. 7.074.0*		<b>c</b> T <b>t</b> GGCTG <b>g</b> AACAGGAGG <b>a</b> CCAG	CCTTCC	4 (1)
Site 7-0113*	SAPCD2P4	GGCTG <mark>g</mark> AACAGGAGG <mark>a</mark> CCAG	CCT	2 (1)
		ATATTGGAGATGAGGGTGGCAAG	GCGCTG	
Site 8	SEC61B	TTGGAGATGAGGGTGGCAAG	GCG	-
		<b>c</b> TATTGG <b>g</b> GATGAGGGTGGCA <b>t</b> G	AGGAGG	3 (1)
Site 8-OT1	PIGR	TTGG <b>q</b> GATGAGGGTGGCA <b>t</b> G	AGG	2 (1)
011 0 070			GGCTTG	5 (1)
Site 8-012	Intergenic	TTGGAGATG <b>G</b> GGTGG <b>G</b> AAG	GGC	2 (1)
		cgcTTGGcGATGAGGGTGGCAtG	GCCAAG	5 (1)
Site 8-013	TCF/L2	TTGG <b>C</b> GATGAGGGTGGCA <b>t</b> G	GCC	2 (1)
Site 9 OT4	100100207100	aTgcTGGAGATGAGGGTGGCAAG	GAGCTG	5 (1)
Sile 0-014	LUC100207109	<b>C</b> TGGAGATGAGGGTGGCAAG	GAG	2 (1)
Site 8-0T5	Intergenic	<b>t</b> T <b>cc</b> TGGAGATGAGGGTGG <mark>g</mark> AAG	GAAGTT	4 (1)
	intergenie	<b>c</b> TGGAGATGAGGGTGG <b>g</b> AAG	GAA	2 (1)
Site 8-OT6	ADAMTS15	<b>gct</b> TTGG <b>t</b> GATGAGGGTGG <b>g</b> AAG	GGCTAA	5 (1)
	, , , , , , , , , , , , , , , , , , , ,	TTGG <b>t</b> GATGAGGGTGG <b>g</b> AAG	GGC	2 (1)
Site 8-OT7	Interaenic	aTgTgGGAGATGAGGGTGGCAgG	AGCGGA	4 (1)
		T <b>G</b> GGAGATGAGGGTGGCA <b>g</b> G	AGC	2 (1)
Site 8-OT8	Intergenic		CAGAAG	5 (1)
	Ŭ Ŭ			$\angle (1)$
Site 8-OT9	FREM2		GAAATA	4 (0)
		I ag Lagaigaggigglagcaag	GAA	_ ∠(∪)

	Internenie	<b>gg</b> A <b>c</b> TGGAGATG <b>g</b> GGGTGGCAAG	CAGGAA	4 (0)
Sile 8-0110	intergenic	<b>c</b> TGGAGATG <b>g</b> GGGTGGCAAG	CAG	2 (0)
	Intergonia	<b>gat</b> TT <b>a</b> GAGATGAGGGTG <b>c</b> CAAG	GCTCAG	5 (1)
	Intergenic	TT <b>a</b> GAGATGAGGGTG <b>C</b> CAAG	GCT	2 (1)
	CMID	<b>c</b> T <b>ga</b> TGGAGATGAGGGTGGCA <b>g</b> G	TCGGAG	4 (1)
Sile 0-0112	CIVIIP	<b>a</b> TGGAGATGAGGGTGGCA <b>g</b> G	TCG	2 (1)
	Intorgonio	<b>gag</b> TTGGAG <b>c</b> TGAGGGTG <b>t</b> CAAG	GAAAGC	5 (1)
Sile 0-0115	Intergenic	TTGGAG <b>c</b> TGAGGGTG <b>t</b> CAAG	GAA	2 (1)
	1.014	gcATTGGAGATGcGGGTGGCAAt	CTTTTT	4 (1)
Sile 6-01 14	LGI4	TTGGAGATG <b>C</b> GGGTGGCAA <b>t</b>	CTT	2 (1)
	Intorgonio	<b>t</b> TATTGGAGAT <b>a</b> AGGGTGG <b>g</b> AAG	AGCTCT	3 (1)
Sile 0-0115	Intergenic	TTGGAGAT <b>a</b> AGGGTGG <mark>g</mark> AAG	AGC	2 (1)
	Intorgonio	<b>ggc</b> T <b>g</b> GGAGA <b>a</b> GAGGGTGGCAAG	GGAGGT	5 (0)
Sile 0-0110	intergenic	T <b>g</b> GGAGA <b>a</b> GAGGGTGGCAAG	GGA	2 (0)
Sito 9 0717*	Contromoro	<b>t</b> T <b>t</b> TTG <b>a</b> AGATGAGGGTGGCA <b>t</b> G	GTCCCA	4 (1)
Sile 0-0117	Centromere	TTG <b>a</b> AGATGAGGGTGGCA <b>t</b> G	GTC	2 (1)
	Intorgonio	tggTTaGAGATGAGGGTGtCAAG	AGGCAC	5 (1)
Sile 0-0110	Intergenic	TT <b>a</b> GAGATGAGGGTG <b>t</b> CAAG	AGG	2 (1)
Site 9 OT10*		<b>ta</b> A <b>a</b> TGGAGATGAGGGTGG <b>a</b> AAG	ATGCAT	4 (1)
Sile 6-0119	GRIAT	<b>a</b> TGGAGATGAGGGTGG <b>a</b> AAG	ATG	2 (1)
Site 8 OT20	NCOAZ	<b>CTCC</b> TGGAGATGAGGGTGGCA <b>a</b> G	GAAGGG	4 (1)
Sile 0-0120	NCOAT	<b>c</b> TGGAGATGAGGGTGGCA <b>a</b> G	GAA	2 (1)
Sito 8 OT21		A <b>ag</b> T <b>g</b> GGAGATGAGGGTGGCAAG	GCTTAC	3 (0)
Sile 0-0121	FDETC	T <b>g</b> GGAGATGAGGGTGGCAAG	GCT	1 (0)
Sito 8 OT22		A <b>ag</b> T <b>g</b> GGAGATG <b>c</b> GGGTGGCAAG	GTGGCG	4 (0)
Sile 0-0122	FDETC	T <b>g</b> GGAGATG <b>C</b> GGGTGGCAAG	GTG	2 (0)
Site 8-OT23	Intergenic	<b>tcc</b> TT <b>t</b> GAGATGAGGGTG <b>c</b> CAAG	GAAATA	5 (1)
Sile 0-0123	Intergenic	TT <b>t</b> GAGATGAGGGTG <b>c</b> CAAG	GAA	2 (1)
Site 8-0T2/*	Intergenic	<b>tac</b> TTGGAGA <b>a</b> GAGGG <mark>a</mark> GGCAAG	AGGTAG	5 (1)
Sile 0-0124	Intergenic	TTGGAGA <b>a</b> GAGGG <mark>a</mark> GGCAAG	AGG	2 (1)
Site 8-OT25		<b>ggcc</b> TGGAGATGAGGGTGGCA <b>g</b> G	CAGGCT	5 (1)
Sile 0-0123	DAFZIF	<b>c</b> TGGAGATGAGGGTGGCA <b>g</b> G	CAG	2 (1)
Site 8-0726*	TTI I 11	A <b>gga</b> TGGAGATGAGG <b>c</b> TGGCAAG	TCTAAT	4 (1)
0//0 0-0120	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	<b>a</b> TGGAGATGAGG <b>C</b> TGGCAAG	TCT	2 (1)
Site 8-OT27	Intergenic	<b>Aa</b> ATTGG <b>CC</b> ATGAGGGTGGCAAG	TCGGTC	4 (0)
	intergenic	TTGG <b>CC</b> ATGAGGGTGGCAAG	TCG	2 (0)

\*site did not sequence well (mixed bases) with HTS primers that were tried, see **Supplementary Table 8**. These sites were excluded from further analysis. ^PAM proximal defined as positions within 10 bases of the PAM

# Supplementary Table 5. List of target sites (See separately attached Excel file.)

## Supplementary Table 6. CHOPCHOPv3-identified off-target sites of sgRNAs targeting the HBB sickle-cell disease mutation

				Mismatches	
Target site or off-		Protospacer sequence		(PAM	Previously
target site	Gene	(5' to 3')	PAM	proximal^)	validated?
HBB-eNme2-C	HBB	AGACTTCTCCACAGGAGTCAGGT	GCACCA	_	
HBB-Nme-OT1	HBB	AGACTTCTCC <b>t</b> CAGGAGTCAG <mark>a</mark> T	GCACCA	2(1)	Overlaps HBB-NRCH-OT2
HBB-Nme-OT2	Intergenic	<b>tt</b> ACTTCTCCACAG <b>c</b> AGTCAGGT	TTTGAT	3 (1)	
HBB-Nme-OT3	CNTN5	A <b>a</b> ACTTCTCCAC <b>t</b> GGAGTCAGG <b>g</b>	CAGGAG	3 (1)	
HBB-Nme-OT4	Intergenic	gagCTTCTtCACAaGAGTCAGGT	AACCTA	5 (1)	
HBB-Nme-OT5	CGNL1	<b>CCCT</b> TTCTCCACAGGAGTCAGG	GAGACA	5 (1)	Overlaps HBB-NRCH-OT3
HBB-Nme-OT6	NUP50	<b>tc</b> ACTTCTCCAGAGG <b>t</b> GTCAGGT	AACTAA	3 (1)	
HBB-Nme-OT7	Intergenic	<b>ctg</b> CTTCTCCA <b>c</b> A <b>a</b> GAGTCAGGT	ATCACT	5(1)	
HBB-Nme-OT8	Intergenic	A <b>agt</b> TTCTCCAGAGGAGTCAGGT	TAGGAG	3(0)	Overlaps HBB-NRCH-OT10
HBB-Nme-OT9	Intergenic	<b>ctt</b> CTTCTCCA <b>t</b> AGGAGTCAG <b>a</b> T	GTGATG	5(1)	Overlaps HBB-NRCH-OT11
HBB-SpCas9-NRCH	HBB	TTCTCCACAGGAGTCAGGTG	CAC	-	
HBB-NRCH-OT1	TET1	T <b>aa</b> TCCACAGGAGTCAGGTG	CAC	2(0)	Y <sup>4</sup>
HBB-NRCH-OT2	HBB	TTCTCC <b>t</b> CAGGAGTCAG <b>a</b> TG	AGA	2(1)	$Y^4$
HBB-NRCH-OT3	CGNL1	TTCTCCACAGGAGTCAGG <mark>a</mark> G	ATA	1(1)	
HBB-NRCH-OT4	PCSK6	TTCTCCA <b>g</b> AGGAGTCAGG <mark>g</mark> G	GGT	2(1)	$Y^4$
HBB-NRCH-OT5	CFDP1	<b>C</b> TC <b>C</b> CCACAGGAGTCAGGTG	CCT	2(0)	Y <sup>4</sup>
HBB-NRCH-OT6	ETFB	TTCTCC <b>t</b> CAGGAGTCAGG <mark>a</mark> G	GGC	2(1)	Y <sup>4</sup>
HBB-NRCH-OT7	Intergenic	TTCTCC <b>C</b> CAGGAG <b>C</b> CAGGTG	GCC	2(1)	Y <sup>4</sup>
	LOC1053				Y <sup>4</sup>
	77396	TTCT <b>g</b> CACAGGAGTCA <b>t</b> GTG	AAG	2(1)	
HBB-NRCH-OT9	LOC1053				$Y^4$
	74898	TTCTCC <b>C</b> GGAGTCAGGTG	CAC	2(0)	
HBB-NRCH-OT10	Intergenic	TTCTCCA <b>g</b> AGGAGTCAGGT	AGG	2(1)	
HBB-NRCH-OT11	Intergenic	TTCTCCA <b>t</b> AGGAGTCAG <b>a</b> TG	TGA	2(1)	Y <sup>4</sup>

## Supplementary Table 7. Plasmids and selection phage (SP) used in this work

Name	Usage (resistance)	Origin	ORF1 (prom [RBS] genes)	ORF2 (prom [RBS] genes)
pTPH353e	AP validation (carb <sup>R</sup> )	SC101	P <sub>psp</sub> <sup>5</sup> [SD8 <sup>6</sup> ] gIII(1-18)-NpuN-32aa	
-			linker-NpuC-gIII(18-425), luxAB	
pTPH353e-d	AP validation (carb <sup>R</sup> )	SC101	P <sub>nsp</sub> <sup>5</sup> [SD8 <sup>6</sup> ] glll(1-18)-NpuN-32aa	
F			linker-NpuC(C1A)-all((18-425), luxAB	
nTPH353e-d stops	AP validation (carb <sup>B</sup> )	SC101	$P_{rm}^{5}$ [SD8 <sup>6</sup> ] dIII(1-18)-NpuN-32aa linker	
	Ai validation (carb )	00101	(double stop codop)-NpuC-all((18-425)	
			(uouble stop couoli)-inpuc-giii(10-425),	
TDI 1404	A D validation (asuk P)			
ртрн401	AP validation (carb'')	COIET	$P_{ProC'}$ [S08°] gill(1-18)-NpuN-64aa	Plac EVO-1 SGRINA
			linker(Evo-1 protospacer, NNNNCC	
			PAM)-NpuC-gIII(18-425), luxAB	
pTPH400	AP validation (carb <sup>R</sup> )	CoIE1	P <sub>ProC</sub> <sup>7</sup> [sd8 <sup>6</sup> ] gIII(1-18)-NpuN-121aa	Plac Evo-1 sgRNA
			linker(Evo-1 protospacer, NNNNCC	
			PAM)-NpuC-gIII(18-425), luxAB	
pTPH397	AP validation (carb <sup>R</sup> )	ColE1	P <sub>ProC</sub> <sup>7</sup> [sd8 <sup>6</sup> ] gIII(1-18)-NpuN-32aa	Plac Evo-1 sgRNA
p			linker(Evo-1 protospacer_NNNNCC	
			PAM)-NpuC-all((18-425) JuxAB	
nTPH307h	AP validation (carb <sup>R</sup> )		$P_{-3}$ [cd96] clll/(1.19) NpuN 22cc	P. Evo 2 og PNA
prensarb	AF Validation (Carb )		PproC' [Suos] gill(1-10)-inpuin-32da	Flac EVO-2 SYNNA
		0 154	Inker(Evo-2 protospacer, NNNNCC	
		COIE1	PAM)-NpuC-gill(18-425), luxAB	
pTPH397c	AP validation (carb <sup>r</sup> )		P <sub>ProC<sup>7</sup></sub> [sd8 <sup>6</sup> ] gIII(1-18)-NpuN-32aa	Plac Evo-3 sgRNA
			linker(Evo-3 protospacer, NNNNCC	
		CoIE1	PAM)-NpuC-gIII(18-425), luxAB	
pTPH405b	AP: ePACE1-2 (carb <sup>R</sup> )		P <sub>ProC</sub> <sup>7</sup> [sd8 <sup>6</sup> ] gIII(1-18)-NpuN-32aa	Plac Evo-2 sgRNA
-			linker(Evo-2 protospacer, varied	
		ColF1	PAMs)-NpuC-gIII(18-425), luxAB	
pTPH405c	AP: ePACE3 (carb <sup>R</sup> )		P <sub>p.o</sub> <sup>7</sup> [sd8 <sup>6</sup> ] dll(1-18 recoded)-NpuN-	P. Evo-2 sgBNA
printeeo			22aa linker/Evo 2 protospasor varied	
		0-154		
		COIET	PAMS)-NPUC-GIII(18-425), IUXAB	
pTPH412 WT sd8	CP validation (kan'')	SC101	P <sub>psp</sub> <sup>o</sup> [sd8 <sup>o</sup> ] TadABE8e-gp41-8N	
pTPH412 WT sd2	CP validation (kan <sup>r</sup> )	SC101	P <sub>psp</sub> <sup>3</sup> [sd2 <sup>o</sup> ] TadABE8e-gp41-8N	
pTPH412 R26G sd8	CP: ePACE3-5 (kan <sup>k</sup> )	SC101	P <sub>psp</sub> <sup>o</sup> [sd8 <sup>o</sup> ] TadABE8e(R26G)-gp41-8N	
pTPH412 R26G sd2	CP validation (kan <sup>R</sup> )	SC101	P <sub>psp</sub> <sup>5</sup> [sd2 <sup>6</sup> ] TadABE8e(R26G)-gp41-8N	
pTPH418b	AP: ePACE4-5 (carb <sup>R</sup> )		P <sub>ProC<sup>7</sup></sub> [sd8 <sup>6</sup> ] gIII(1-18 recoded)-NpuN-	P <sub>lac</sub> Evo-4 sgRNA
			45aa linker(2 x Evo-4 protospacer,	_
		ColE1	varied PAMs)-NpuC-gIII(18-425), luxAB	
pTPH343c	CBE-PPA (spec <sup>R</sup> )	ColE1	PRAD [SD8 <sup>6</sup> ] rAPOBEC1-dSpCas9-UGI	PlacCBE-PPA sqBNA
nTPH342		00121	CBE-PPA protospacer	
p1111342	CBE-PPA library (carb <sup>R</sup> )	SC101	ODE-IT A protospacei	(inactive)
pTDU412		00101	$D_{\text{res}} = [ad4u^{6}] T_{\text{res}} \Delta PE^{9} a dNma^{2}C_{\text{res}} O$	
p1FH413	$ABE BBA (am^{B})$	m15A	PBAD [SU4U ] TAUADE0e-UNITe2Cas9	Flac ADE-FFA SYNNA
TDUADA	ABE-PPA (CM <sup>*</sup> )	p15A	variant	
pTPH424		00404	ABE-PPA protospacer	PPro1 [SD8] SIGFP
	ABE-PPA library (carb <sup>*</sup> )	SC101		(Inactive)
Nme-IV I	IV I template (carb <sup>^</sup> )	pUC	PT7(mutated)° Nme2ABE8e variant	
SpRY-IVT			P <sub>T7(mutated)</sub> ° SpRYABE8e or SpRY-HF1-	
	IVT template (carb <sup>R</sup> )	pUC	ABE8e variant	
Nme sgRNA	Mammalian guide expression (carb <sup>R</sup> )	pUC	Phue Nme2Cas9 sgRNA	
SpRY sgRNA	Mammalian guide expression (carb <sup>R</sup> )	pUC	Phue SpRY/SpRY-HF1 sgRNA	
Nme2ABE8e	Mammalian expression of adenine		PCMV Nme2ABE8e variant	
variants	base editor (carb <sup>R</sup> )	pUC		
SpRYABE8e	Mammalian expression of adenine		PCMV SpRY/SpRY-HF1-ABE8e variant	
variants	base editor (carb <sup>R</sup> )	DUq		
Nme2BE4 variants	Mammalian expression of cytosine		PCMV Nme2BE4 variant	
	base editor (carb <sup>R</sup> )	nUC		
SnRVBE4 variants	Mammalian expression of adenine	100	Powy SpRV/SpRY-HE1-BE4 variant	
	hase editor (carb <sup>R</sup> )	nuc		
Nmo2 nucloaso	Mammalian expression of nuclease	poo	PNmo2Cas0 nuclease variant	
Nillez lluciease			PCMV NITIEZCAS9 HUClease Variant	
		ρυς		
Sprir nuclease	ivianmalian expression of nuclease		PCMV SPRT/SPRT-HFT nuclease variant	
variants	(carb'`)	pUC		
SP391c	ePACE1-2, ∆gIII SP, backbone	1	P <sub>gIII</sub> [SD4 <sup>4</sup> ] TadABE8e-dNme2Cas9	
	recoded <sup>9</sup>	M13 f1	variant	
SP404	ePACE3-5, ∆gIII SP, backbone		Pglll [SD4 <sup>4</sup> ] gp41-C-dNme2Cas9 variant	
	recoded <sup>9</sup>	M13 f1		

## Supplementary Table 8. Primers used in this work

Amplicon	Fw (5'-3')	Rv (5'-3')	Purpose
SP backbone	CACCGTTCATCTGTCCTCTTT	CGACCTGCTCCATGTTACTTAG	qPCR estimation of SP titer
SP insert	TAATGGAAACTTCCTCATGAAAAAGTC	ACAGAGAGAATAACATAAAACAGGG	PCR amplification of SP insert for
	TTTAG	AAGC	Sanger sequencing
BE-PPA library	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	HTS of BE-PPA libraries (both CBE
insert	CCGATCTNNNNCAATACGCAACGCCT	ATCCTTGTCTGTAAGCGGATGC	and ABE-PPE)
	CTC		
CBE-PPA 5N oligo	AGACTGAGCACGUGANNNNTTAAG	ACGTGCTCAGTCUGGGCCATTGCGT	Cloning of 5N library for CBE-PPE
library (1 024	CCAGCCCCGACAC	TGCGCTCACTG	validation
members)			Validation
ABE-PPA pseudo-		CCAGTCGGGAAACCTGTC	KLD cloping of ABE-PPE library
7N oligo library	TGGCCCAGACTGAGCACGTGANNNN		first set of Ns replaced by UMI
(512 members)	NNNTTAAGCCAGCCCCGAC		tag(s) second set of Ns replaced by
	INNI		target PAMs
HTS-1 genomic site			HTS of genomic target site see
The rigenomic site	CCGATCINNNATIGCICITITCICC	TGGAGTTCAGACGTGTGCTCTTCCG	Supplementary Table 5
	GCCCA	ATCTTTCACAAAACAGGGGGGGGGC	cupplementary ruble of
HTS-2 genomic site	ACACTCTTTCCCTACACGACGCTCTT		«»
The 2 generate one	CCGATCTNNNNGCTCAGAAAAAGGG	TGGAGTTCAGACGTGTGCTCTTCCG	
	CCCTGA	ATCTGAGATTCAGTGTGGTGGGGGG	
HTS-3 genomic site	ACACTCTTTCCCTACACGACGCTCTT		4633
	CCGATCTNNNNAACTTTCTATCCGTC	TGGAGTTCAGACGTGTGCTCTTCCG	
	CGCGT	ATCTGGCTGTAGAGGGAGACAAGC	
HTS-4 genomic site	ACACTCTTTCCCTACACGACGCTCTT		4699
5	CCGATCTNNNNGACGTCTTCTCCTGT	TGGAGTTCAGACGTGTGCTCTTCCG	
	GGTGG	ATCTGGGTGTCTGGCTGGAATCTC	
HTS-5 genomic site	ACACTCTTTCCCTACACGACGCTCTT		£233
	CCGATCTNNNNGGGCCTGGAAGTTC	TGGAGTTCAGACGTGTGCTCTTCCG	
	GCTAAT	ATCTTGGATCGCTTTTCCGAGCTT	
HTS-6 genomic site	ACACTCTTTCCCTACACGACGCTCTT		££77
	CCGATCTNNNNGGCTCCCTCTCCCAG	TGGAGTTCAGACGTGTGCTCTTCCG	
	TTACCG	ATCTCACCACCATCCGCTCTGCCC	
HTS-7 genomic site	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	4477
	CCGATCTNNNNGGGACTCAGTTCCAA	ATCTGGCATCCACAAATCACCTGGA	
	CCCAAATGC	GAG	
HTS-8 genomic site	ACACTCTTTCCCTACACGACGCTCTT		2633
	CCGATCTNNNNGAACCCAGGTAGCC	TGGAGTTCAGACGTGTGCTCTTCCG	
	AGAGAC	ATCTTCCTTTCAACCCGAACGGAG	
HIS-9 genomic site	ACACICITICCCTACACGACGCTCTT	IGGAGIICAGACGIGIGCICIICCG	W//
		ATCTCCTAGAAAGGCATGGATGAGA	
		GAAGU	4179
HIS-10 genomic			
site		ATCIGUCACUIGGITTAIGGGATTI	
HTS-11 genomic			""
sito		TGGAGTTCAGACGTGTGCTCTTCCC	
316	TCCAAA	ATCTCTCCTTCTGGGGGCCTTTTTCCC	
HTS-12 genomic	ACACTCTTTCCCTACACGACGCTCTT		""
site	CCGATCTNNNNCCCCCGCACTCCTTC	TGGAGTTCAGACGTGTGCTCTTCCG	
	TTC	ATCTAATCTACCTCCGCGGACCT	
HTS-13 genomic	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	437
site	CCGATCTNNNNGCGCACCTCATGGAA	ATCTCTTGCCTCCACTGGTTGTGCA	
	ТСССТТС	G	
HTS-14 genomic	ACACTCTTTCCCTACACGACGCTCTT		433
site	CCGATCTNNNNGGCACCACTGTAGTT	TGGAGTTCAGACGTGTGCTCTTCCG	
	TAGTGATCCC	ATCTACCCTTGACCCCCTCCACCAG	
HTS-15 genomic	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	6633
site	CCGATCTNNNNCATTCCCTCTTTAGC	ATCTCAGATCTATTGGAATCCTGGA	
	CAGAGCCGG	GTGACC	
HTS-16 genomic	ACACTCTTTCCCTACACGACGCTCTT		"
site		IGGAGTTCAGACGTGTGCTCTTCCG	
	GACAC	ATCTAAGGAGGAACAGGAGAGCCA	- un
HIS-1/ genomic			
site			
UTS 18 genemic			6633
site			
316	GAGCTATCG	G	
L		<b>v</b>	

			<b>433</b>
HIS-19 genomic	ACACICITICCCTACACGACGCICIT		
site	CCGATCTNNNNGCTCCTCTCTGTTTG	TGGAGTTCAGACGTGTGCTCTTCCG	
	GCCTT		
			u
HIS-20 genomic	ACACICITICCCTACACGACGCTCTT	IGGAGIICAGACGIGIGCICIICCG	
site	CCGATCTNNNNCCTCCTGAAAATGCA	ATCTGGTGCATTTTTTAATAGGGCTT	
	CONTENTET	0000	
		6666	
HTS-21 genomic	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	4479
sito	CCGATCTNNNNGGACCTTATCTCCTT	ΑΤΟΤΟΑΤΑΟΤΟΘΟΑΤΘΟΟΤΑΟΟΤΘΟ	
Sile		ATCTCATACTCOCATOOCTACCTOO	
	TCATTGAGCACC	AC	
HTS-22 genomic	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	4679
oito		ATCTCCTTCCCCACCCTACTCATTC	
sile	CCGATCTINININGGGGGCCTCCTGAGT	ATCIGGTIGCCCACCCTAGTCATIG	
	TTCTCATCTG	GAG	
HTS-23 genomic	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	<b>439</b>
site	CCGATCTNNNNGGAATAGCACCAGAA	ATCTGCCTACACTTAAAAACTTGACG	
	TGTTCGAGGC	TGGG	
UTS 24 gonomic		TECACITEACACCTETECTC	£177
TT 3-24 genomic			
site	CCGATCINNNNGGAAAAGAGGIIGIG	ATCTAGAATGCAGGGCTTGTGTACT	
	AGTGGTCCAG	TATAGC	
UTS 25 gonomia			""
H13-25 genomic	ACACICITICCCIACACGACGCICIT		
site	CCGATCTNNNNGGTGGAAGGTCCCT	TGGAGTTCAGACGTGTGCTCTTCCG	
	CCAGA	ATCTCCTTCAACCTGACCTGGGAC	
	A040T0TTT000T404004000T0TT	T0040TT040400T0700T0T000	6679
п I S-26 genomic	ACACTUTTTUUUTACAUGAUGUTUTT	TGGAGTTCAGACGTGTGCTCTTCCG	
site	CCGATCTNNNNGGTAGTGCTTGAGAC	ATCTCCCTCCACTAAGAAGAACCTC	
	CGCCAG	TTTGTG	
			4644
HIS-27 genomic	ACACICIIICCCTACACGACGCTCTT		•••
site	CCGATCTNNNNCACACTCCCAGCTTC	TGGAGTTCAGACGTGTGCTCTTCCG	
0.10			
	AUUTU	ATCTTCGTCCAACTCAGCCTTGTC	
HTS-28 genomic	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	4479
site	CCGATCTNNNNCGCTAGACGGTAGA	ATCTCCCATTGCAACTTCCAGTCCT	
3110	0007101111111000017070001707	A101000A1100A01100A01001	
	GUUTAUTGU	GC	
HTS-29 genomic	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	4479
site		ATCTCCCTACACTTAAAAACTTCACC	
Sile		ATCIGUCIACACITAAAAACITGACG	
	IGIICGAGGC	IGGG	
HTS-30 genomic	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	437 H
oito			
site	CCGATCTINININGCCACACCCTAGGG	ATCTOGGAAAATAGACCAATAGGCA	
	TTG	G	
Site 1-OT1	ACACTCTTTCCCTACACGACGCTCTT		HTS of genomic target site, see
Site 1-OT1	ACACTCTTTCCCTACACGACGCTCTT	TOCACTTOACACOTOTOCTOTOCO	HTS of genomic target site, see
Site 1-OT1 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG	TGGAGTTCAGACGTGTGCTCTTCCG	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA	HTS of genomic target site, see <b>Supplementary Table 2</b> .
Site 1-OT1 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA	HTS of genomic target site, see <b>Supplementary Table 2</b> .
Site 1-OT1 genomic site Site 1-OT2	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA	HTS of genomic target site, see <b>Supplementary Table 2.</b>
Site 1-OT1 genomic site Site 1-OT2 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA TGGAGTTCAGACGTGTGCTCTTCCG	HTS of genomic target site, see <b>Supplementary Table 2</b> .
Site 1-OT1 genomic site Site 1-OT2 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTTT	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGG	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGG	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTTT ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGG	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGG TGGAGTTCAGACGTGTGCTCTTCCG	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGG TGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGC	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCCAACA TGCTA	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGG TGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGC	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGG TGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGC	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACTCCA	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGG TGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGC TGGAGTTCAGACGTGTGCTCTTCCG	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACTCCA CTTTC	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGG TGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGC TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACTCA	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGG TGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGC TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACTCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGG TGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGC TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACTCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGATGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGGTGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGCTGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCCTGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT AATGCT	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACGTGGTGGTGG TGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGC TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC TGGAGTTCAGACGTGTGCTCTTCCG ATCTGCCTCTGTCTGTGTACTCCC	HTS of genomic target site, see Supplementary Table 2. 477 477 477 477 477 477 477 47
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACTCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT AATGCT	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGATGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGGTGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGCTGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCAGGCCTTAACATACCCTGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCAGGCCTTAACATACCC	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT5	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACTCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT AATGCT ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACGTGGATGGTGG TGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGC TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC TGGAGTTCAGACGTGTGCTCTTCCG ATCTGCCTCTGTCTGTGTACTCCC	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT AATGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGATGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGGTGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGCTGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCCTGGAGTTCAGACGTGTGCTCTTCCG ATCTGCCTCTGTCTGTGTACTCCCTGGAGTTCAGACGTGTGCTCTTCCG ATCTGCCTCTGTCTGTGTACTCCCTGGAGTTCAGACGTGTGCTCTTCCG ATCTGCCTCTGTCTGTGTACTCCCTGGAGTTCAGACGTGTGCTCTTCCG ATCTGCCTCTGTCTGTGTACTCCC	HTS of genomic target site, see Supplementary Table 2. 477 477 477 477 477 477 477 47
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACTCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCGCTCTT CCGATCTNNNNCCCAGCGCTCTT CCGATCTNNNNCCCAGCGCTCTT CCGATCTNNNNCTTACGCACGCTCTT CCGATCTNNNNCTTACGTGATCCTC	TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGGGAGAGACGTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGCCTCTGTCTGTGTACTCCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGCCTCTGTCTGTGTGCTCTTCCG         ATCTCCCACACAAGACGTGTGCTCTTCCG	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACTCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT AATGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT	TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGGGAGAGACTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGCCTCTGTCTGTGTGTACTCCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGCCTCTGTCTGTGTGTACTCCC	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site Site 1-OT7	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGGCTGAGT AATGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGGGAGAGACTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGCCTCTGTCTGTGTGTACTCCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGCCTCTGTCTGTGTGTACTCCC	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site Site 1-OT7 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACTCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTAAGGTGATCCTC	TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGGGAGAGACTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGCCTCTGTCTGTGTACTCCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGCCTCTGTCTGTGTGCTCTTCCG         ATCTCCCACACAAGAAGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCACACAAGAAGAGGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site Site 1-OT7 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACTCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCGCTCTT CCGATCTNNNNCCCAGCGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT	TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGGGAGAGACTGGATGGTGGTG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCACAGTCCAGTGGGCCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTGTGCTCTTCCG         ATCTCCACACAAGAAGAAGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCACACAAGAAGAAGAGGAGGGGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCACACAAGAAGAAGAAGAGGAGGGGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGGTGCTGGAGGGCTTGTG	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site Site 1-OT7 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT AATGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTGCCTCTGTCTGTGTACTCCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCACACAAGAAGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCACACAAGAAGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCACACAAGAAGAGGAGGGGG	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site Site 1-OT7 genomic site Site 2-OT1	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGGGAGAGACTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCACAGTCCAGTGTGCTCTTCCG         ATCTCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGCCTCTGTCTGTGTACTCCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCACACAAGAAGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCACACAAGAAGAAGAGGAGGGGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGGTGCTGGAGGGCTTGTG	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site Site 1-OT7 genomic site Site 2-OT1 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACTCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTACCTCCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGACGTGTGCTCTTCCG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCACACAAGAAGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGTGCTGGAGGGCTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGTGCTGGAGGGCTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site Site 1-OT7 genomic site Site 2-OT1 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT AATGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTGGGGC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCACACAAGAAGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCACACAAGAAGAAGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGTGCTGGAGGGCTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGTGCTGGAGGGCTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGTGCTGGAGGGCTTGTG	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site Site 1-OT7 genomic site Site 2-OT1 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACTCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCGCAGT AATGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG	TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGGGAGAGACTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCACAGTCCAGTGTGCTCTTCCG         ATCTCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGCCTCTGTCTGTGTACTCCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCACACAAGAAGAGGAGGGGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGGTGCTGGAGGGCTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGGTGCTGGAGGGCTTGTG	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site Site 1-OT7 genomic site Site 2-OT1 genomic site Site 2-OT2	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCGCCCTT CCGATCTNNNNCCCAGCGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCTGAAGCTGAGGC AGTAGG ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACGTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTACCTCCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCACACAAGAAGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCACACAAGAAGAGGAGGGGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGTGCTGGAGGGCTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCAGACGTGTGCTCTTCCG ATCTCTAGGAGGGGATGCAGACCT	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site Site 1-OT7 genomic site Site 2-OT1 genomic site Site 2-OT2 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACTCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT AATGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCTGAAGCTGAGGC AGTAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCTGAAGCTGAGGC	TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGGGAGAGACTGGATGGTGGTG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCACAGTCCAGTGTGCTCTTCCG         ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCACACAAGAAGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCACACAAGAAGAGGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGGTGCTGGAGGGGTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCGGAGCTGGAGGGGATGCAGACCT         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCTAGGAGGGGATGCAGACCT         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCAGACGTGTGCTCTTCCG	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic siteSite 1-OT2 genomic siteSite 1-OT3 genomic siteSite 1-OT4 genomic siteSite 1-OT5 genomic siteSite 1-OT6 genomic siteSite 1-OT7 genomic siteSite 2-OT1 genomic siteSite 2-OT2 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCTGAAGCTGAGGC AGTAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCTGAAGCTGAGGC	TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGGGAGAGACTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGCCTCTGTCTGTGTACTCCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCACACAAGAAGAGGAGGGGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGGTGCTGGAGGGCTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCAGACGTGTGCTCTTCCG         ATCTCAGACGTGTGCTCTTCCG         ATCTCAGACGTGTGCTCTTCCG         ATCTCTAGACGTGTGCTCTTCCG         ATCTCAGACGTGTGCTCTTCCG         ATCTCAGACGTGTGCTCTTCCG         ATCTCAGACGTGTGCTCTTCCG         ATCTCAGACCTCAAACGGTAAAGTC         CA	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site Site 1-OT7 genomic site Site 2-OT1 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT AATGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCTGAAGCTGAGGC AGTAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG TTCACAT	TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGGGAGAGACTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCACACAAGAAGAGGAGGGGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGGTGCTGGAGGGCTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGGTGCTGGAGGGGCTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGGTGCTGGAGGGGATGCAGACCT         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCTAGGAGGGGATGCAGACCT         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCAGACCTTCAAACGGTAAAGTC         CA	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic siteSite 1-OT2 genomic siteSite 1-OT3 genomic siteSite 1-OT4 genomic siteSite 1-OT5 genomic siteSite 1-OT6 genomic siteSite 1-OT7 genomic siteSite 2-OT1 genomic siteSite 2-OT2 genomic siteSite 2-OT3	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACTCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT AATGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCTGAAGCTGAGGC AGTAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG TTCACAT	TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGGGAGAGACTGGATGGTGGTG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTGTGTGTACTCCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCACACAAGAAGAAGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGGTGCTGGAGGGCTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCGAGACGTGTGCTCTTCCG         ATCTCTAGGAGGGGATGCAGACCT         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCTAGGAGGGGATGCAGACCT         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCTAGGAGGTCAGACGTGTGCTCTTCCG         ATCTAGACCTTCAAACGGTAAAGTC         CA	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site Site 1-OT7 genomic site Site 2-OT1 genomic site Site 2-OT2 genomic site Site 2-OT3 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCC CGGT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCTGAAGCTGAGGC AGTAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCGACTTGAATGTG TTCACAT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG	TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGGGAGAGACTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGCCTCTGTCTGTGTACTCCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCACACAAGAAGAGGAGGGGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGGTGCTGGAGGGCTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCAGACGTGTGCTCTTCCG         ATCTCTAGGAGGGGATGCAGACCT         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCTAGAACGTGTGCTCTTCCG         ATCTAGACCTTCAAACGGTAAAGTC         CA	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic siteSite 1-OT2 genomic siteSite 1-OT3 genomic siteSite 1-OT4 genomic siteSite 1-OT5 genomic siteSite 1-OT6 genomic siteSite 1-OT7 genomic siteSite 2-OT1 genomic siteSite 2-OT2 genomic siteSite 2-OT3 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT AATGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCTGAAGCTGAGGC AGTAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG TTCACAT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACGTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTACCTCCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCACACAAGAAGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCACACAAGAAGAGGAGGGGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGTGCTGGAGGGGATGCAGACCT         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCAGACCTTCAAACGGTAAAGTC CA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGACCTTCAAACGGTAAAGTC CA	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site Site 1-OT7 genomic site Site 2-OT1 genomic site Site 2-OT2 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT AATGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAGGC AGTAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG TTCACAT	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTACGTGTCCTCCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCACACAAGAAGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCACACAAGAAGAGGAGGGGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCTAGGAGGGGATGCAGACCT         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCTAGACCTTCAAACGGTAAAGTC CA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGACCTTCAAACGGTAAAGTC CA	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site Site 1-OT7 genomic site Site 2-OT1 genomic site Site 2-OT2 genomic site Site 2-OT3 genomic site Site 2-OT4	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT AATGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCTGAAGCTGAGGC AGTAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG TTCACAT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG TTCACAT	TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAAAACCCTGTGTGCTCTTCCG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGGGAGAGACTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGCCTCTGTCTGTGTGACTCCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCACACAAGAAGAGGAGGGGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGGTGCTGGAGGGCTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCTAGACGTGTGCTCTTCCG         ATCTCTAGAACGTGTGCCCTTCCG         ATCTCAGACGTGTGCTCTTCCG         ATCTAGACCTTCAAACGGTAAAGTC         CA	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site Site 2-OT1 genomic site Site 2-OT1 genomic site Site 2-OT2 genomic site Site 2-OT3 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCTGAAGCTGAGGC AGTAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG TTCACAT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG TTCACAT	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTGCCTCTGTCTGTGTACTCCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCACACAAGAAGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCGTGCTGGAGGGCTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGTGCTGGAGGGGATGCAGACCT         TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGACCTTCAAACGGTAAAGTC CA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGACCTTCAAACGGTAAAGTC CA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTTGCTGAAACCCAGTGAAGCA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGACCTTCAAACGGTAAAGTC CA	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic siteSite 1-OT2 genomic siteSite 1-OT3 genomic siteSite 1-OT4 genomic siteSite 1-OT5 genomic siteSite 1-OT6 genomic siteSite 1-OT7 genomic siteSite 2-OT1 genomic siteSite 2-OT2 genomic siteSite 2-OT3 genomic siteSite 2-OT4 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGGCTGAGT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCGCCCTT CCGATCTNNNNCCTACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CGGT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCTCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG TTCACAT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG TTCACAT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG TTCACAT	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGGGAGAGACTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTACGTGTCCTCCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCACACAAGAAGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCACACAAGAAGAGGAGGGGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCTAGGAGGGGATGCAGACCT         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCTAGACCTTCAAACGGTAAAGTC CA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTTGCTGAAACCCAGTGAAGCA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTTGCTGAAACCCAGTGAAGCA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTTGCTGAAACCCAGTGAAGCA	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site Site 1-OT7 genomic site Site 2-OT1 genomic site Site 2-OT2 genomic site Site 2-OT3 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT AATGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCTGAAGCTGAGGC AGTAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCTGAAGCTGAGGC AGTAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG TTCACAT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGGGACTTGAATGTG TTCACAT	TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGGGAGAGACTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGCCTCTGTCTGTGTACTCCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCACACAAGAAGAGGAGGGGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGGTGCTGGAGGGCTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCTAGACGTGTGCTCTTCCG         ATCTCTAGAACGTGTGCTCTTCCG         ATCTAGACCTTCAAACGGTAAAGTC         CA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGACCTTCAAACGGTAAAGTC         CA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGACCTTCAAACGGTAAAGTC         CA	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic siteSite 1-OT2 genomic siteSite 1-OT3 genomic siteSite 1-OT4 genomic siteSite 1-OT5 genomic siteSite 1-OT6 genomic siteSite 2-OT1 genomic siteSite 2-OT1 genomic siteSite 2-OT2 genomic siteSite 2-OT3 genomic siteSite 2-OT4 genomic siteSite 2-OT4 Site 2-OT5	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCTGAGT AATGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAGGC AGTAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG TTCACAT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG TTCACAT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG TTCACAT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCAGCTTCCGAGGTCA AGAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCAGCTTCCGAGGTCA AGAGG	TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAAAACCCTGTGTGCTCCTGA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGGGAGAGACTGGATGGTGCTCTTCCG         ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCGTGTGCTCTTCCG         ATCTCGGTGCTGGAGGGGCTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCGGTGCTGGAGGGGCTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCGGTGCTCTCCG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGACCTTCAAACGGTAAAGTC         CA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGACCTTCAAACGGTAAAGTC         CA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGCTGAAACCCAGTGAAGCA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTTGCTGAAACCCAGTGAAGCA	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic site Site 1-OT2 genomic site Site 1-OT3 genomic site Site 1-OT4 genomic site Site 1-OT5 genomic site Site 1-OT6 genomic site Site 2-OT1 genomic site Site 2-OT1 genomic site Site 2-OT2 genomic site Site 2-OT3 genomic site Site 2-OT4 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCAGAGGCTGAGT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCTGAAGCTGAGGC AGTAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG TTCACAT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGACTTGAATGTG TTCACAT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCTCCGAGGTCA AGAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCTCCGAGGTCA AGAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCTTTGGCCTTCCTG ATAGCA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCTTTGGCCTTCCTG ATAGCA	TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAAACCCTGTGTGCTCTTCCG ATCTAGGGAGACGACGGATGGTGGTGGTGGTCTAGGGGAGAGACTGGATGGTGGTGCTCTCCG ATCTCACAGTCCAGTGGGCTCTTCCG ATCTCACAGTCCAGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCCAGGCCTTACGTGTCCTCCCG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCACACAAGAAGAGGAGGGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCCACACAAGAAGAGGAGGGGG         TGGAGTTCAGACGTGTGCTCTTCCG ATCTCTAGGAGGGGATGCAGACCT         TGGAGTTCAGACGTGTGCTCTTCCG ATCTAGACCTTCAAACGGTAAAGTC CA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTTGCTGAAACCCAGTGAAGCA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTTGCTGAAACCCAGTGAAGCA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTTGCTGAAACCCAGTGAAGCA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTTGCTGAAACCCAGTGAAGCA         TGGAGTTCAGACGTGTGCTCTTCCG ATCTTGCTGAAACCCAGTGAAGCA	HTS of genomic target site, see Supplementary Table 2.
Site 1-OT1 genomic siteSite 1-OT2 genomic siteSite 1-OT3 genomic siteSite 1-OT4 genomic siteSite 1-OT5 genomic siteSite 1-OT6 genomic siteSite 1-OT7 genomic siteSite 2-OT1 genomic siteSite 2-OT2 genomic siteSite 2-OT3 genomic siteSite 2-OT4 genomic siteSite 2-OT5 genomic site	ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTCACAAGCTCGGTGG TTCAA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCCCTCAGAGACC CTTTT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCTCAGCCACCCAACA TGCTA ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCCAGCTCCACCCA CTTTC ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCCCAGAGCGCTCTT CCGATCTNNNNGCCCAGAGCGCTCTT CCGATCTNNNNCTTAAGGTGATCCTC CCGCT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTGGGGCTTCCTCCC AGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCTGAAGCTGAGGC AGTAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGCTGAAGCTGAGGC AGTAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGGGACTTGAATGTG TTCACAT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGGGACTTGAATGTG TTCACAT ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGCTTCCGAGGTCA AGAGG ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCTTTGGCCTTCCTG ATAGCA	TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAAAACCCTGTGTGCTCTTCCG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGGGAGAGACTGGATGGTGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCACAGTCCAGTTGAGGAGGC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCCCAGGCCTTAACATACCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGCCTCTGTCTGTGTGTACTCCC         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTCCACACAAGAAGAGGAGGGGG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGGTGCTGGAGGGCTTGTG         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTGGTGCTGGAGGGGATGCAGACCT         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGACCTTCAAACGGTAAAGTC         CA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGACCTTCAAACGGTAAAGTC         CA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTTGCTGAAACCCAGTGAAGCA         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTTGCTGAAACCCAGTGAGCACT	HTS of genomic target site, see Supplementary Table 2.

yenomic sile CCGATCTINNINGTGRAGGGAGCAGTA TGGAGTTCAACGTGTGCTTCCG CCCGATCTINNINGTGGAGGGAGCGTT TGGAGTTCACTTACCTACACGAGGGGCTGT CCGATCTINNINGTCGGCACCGGGA T GGAGTCAACGGTGGCTTTCCGTACCGAGGGCGTT genomic sile CCGATCTINNINGTCGGCACGGCGTCT GGAGTCAACGGTGGCGTCGCG TGGC TGGC	Site 2-OT6			4479
Sile 2017         ACACTETTICCTACCACGAGEGETETT         TGGASTTCAGAGETEGTETTICCE           genomic sile         CCGATCTNNNNACAGEGECETT         TGCAGTCTACCACGAGEGETET           genomic sile         CCGATCTNNNNACCTECTCCCTGGCA         TGCAGTCCACGAGEGETET           Sile 2018         ACACTETTICCCTACCAGGGCETET         TGCAGTCCANNNACCTECTCCCTGCCA           Sile 2019         CGGATCTNNNNTCCTACCTCTCCCTGCA         TGCAGTCCAACGACGTGTCTTCCG           Sile 20110         CGGATCTNNNTTCCTACCTCCCCCTGCGCA         TGGAGTCCAACGACGTGTGCTCTTCCG           Sile 20110         CGGATCTNNNTTCCTACCTCGCCACGCCTTT         TGGAGTCCAACGGTGTGCTCTTCCG           genomic sile         CGGATCTNNNNTCCTCCTCACGACGCTCTT         TGGAGTCCAACGGTGTGCTCTTCCG           genomic sile         CGGATCTNNNNCGTGATCACGGCGCTTT         TGGAGTCCAGGGTGTGCTCTTCCG         ""           genomic sile         CGGATCTNNNNCGTGATCGGCACT         TGGAGTCCAGCGTGTGCCTCTCCG         ""           genomic sile         CGGATCTNNNNCGTGATCACGGCACTT         TGGAGTCCAGCGTGACCTAATACGGACTCT         TGGAGTCCAGCGTGTGCCTTCCG         ""           Transcript for in         CGGACTCGGTACCTAATACGGACTCT         TGGAGTCCAACGGTGGTGCCTTCCG         ""         ""           TGCAGCCGGTACCTAATACGGACTCT         TGGAGTCCACAGAGGTGGTGCTCTTCGG         TGGAGTCCAACGAGGGTGCTT         TGGAGTCCAACGAGGGTGCTT         TGGAGTCCAACGAGGTGGCCTTCGGGAACGCGGGCCTT         TGGAGTCCAACGAGGGGGCCTT <td>genomic site</td> <td>CCGATCTNNNNGTGAAGGCACCAGTA</td> <td>TGGAGTTCAGACGTGTGCTCTTCCG</td> <td></td>	genomic site	CCGATCTNNNNGTGAAGGCACCAGTA	TGGAGTTCAGACGTGTGCTCTTCCG	
Site 2-017         COCATCTINUNCAGENETATION         ATTENDENTIAL CAGAAGAGENETATION           Site 2-018         ACACTETTICCTIALACGAAGAGENETATION         ************************************	Site 2 OTZ			4473
Sile 2018         KACKTCTTTCCTAACGAGAGETCTT         TGGAGTTCAACGAGECTGTT           genomic sile         CCCATCTINNINACCTCCTCCCCCTGGGA         TGGAGTTCAACGCGTGGGAGTGTT           genomic sile         CCCATCTINNINACCTCCTCCCCCTGGGA         """"""""""""""""""""""""""""""""""""	genomic site	CCGATCTNNNNCAAGTGATCCTGCCA	ATCTAACTTAACCAAGAAGGCCAGG	
Side 2-013 genomic site         CCCATCTINUMNACCECCOCCOTOGIGA TGAA         TGAACTICAGACGTOTECTCTCGC TGACTICACCACGACGCGTCTT           Site 2-079 genomic site         ACACTCTTTCCCTACACGACGCGCTCTT CCGATCTCANNITCCTGCCCACGACGCGCTCTT GCGATCTCCCTCACGACGCGCCCTT GCGGTC         """"""""""""""""""""""""""""""""""""	Site 2 OT9		1	££73
Sile 2017         ACCOUNT CONTRACTCACCEACCENCE TO CONTRACT CONTROL CON	genomic site	CCGATCTNNNNACCTCCTCCCTGGGA	TGGAGTTCAGACGTGTGCTCTTCCG	
State 2013         Concent Con	Site 2 OT0		ATCTCGTCAACCGTGGGAATGTTT	6673
CTTBC         TEGASTICAGACGITCATCCG           Site 2-0710         AdACTECTIFICCTACACGACGCCETCTT         TGCTCCCCCTCTACACGACGCGCCTCT           Germanic site         CCGATECTININNICCCTGATCACGACGCCETCTT         TGGAGTTCAGACGACGCCTCCCG           Site 2-0712         ACACTECTIFICCCTAACGACGCCETCTT         TGGAGTTCAGACGACGCCTCCCG           genomic site         CCGATECTNNINACCTGATGCGGAA         TGGAGTTCAGACGACGCCTCCCG           genomic site         CCGATECTNNINACGAGAGACACGCGCCTCT         TGGAGTTCAGACGCCTCCCCCCCCCG           Transcription in         Vito transcription         TGGAGTTCAGACGCCTCTCCG         ""           Transcription in         Vito transcription in         TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	genomic site	CCGATCTNNNNTTCCTACCTCTGCCA		
Site 2-0110         ACACTETTTCCCTACACGACGCTCTT         ALTERCECTION           genomic site         CGATC         CONTINUENTCCTGTCCATACACGACGCTCTT         GGACTTCAGACGTGTGGTCATACCG           genomic site         CCCGATCTNNINAGAGTGACGTGTGGA         TGGAGTTCAGACGCTGTTCCG		CHIGC		
Site 2-0110         CCGATCTINNINTCCTGCTCATACA         ACCTOR           Site 2-0111         CACATCTITTCCCTACACGAGGCTCTT         TGGAGTTCAGAGGGTCTTCCG         "           Site 2-0112         CACATCTITTCCCTACACGAGGCTCTT         TGGAGTTCAGACGAGGTCTTCCG         "           Site 2-0112         CACATCTTTCCCTACACGAGGCTCTT         TGGAGTTCAGACGTGGGTCTTCCG         "           genomic site         CCGATCTNNNNCCTGATGCGGAA         TGGAGTTCAGACGTGGCTCTTCCG         "           genomic site         CCGATCTNNNNCCTGATGCCTGGGAA         TGGAGTTCAGACGTGGTCTTCCG         "           Transcription in         vitro transcription         TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT			ATCTCCCCTTCCTCTCTATGCCA	
genomic site         OCCAT CINNINGCTOC COCCACCONSCITACA         Tested TACACCTETTICS           Site 2-0711         ACACTETTINGCTACAGE ACCETET         TEGAGETTICACTACAGE ACCETETTICS         """"""""""""""""""""""""""""""""""""	Site 2-0110			
Site 2-0711         DOLD/CONTROLOGYTACAGCOGGTCTT         TIGAGTTCAGACCIGGTCATCCG           genomic site         CCCATCTINNINGAGTGACTGGGA         TGGAGTTCAGACCIGGTGCTCTCCG           genomic site         CCCATCTINNINCGTGATGCCTGGGAA         TGGAGTTCAGACCIGTGCTCTCCG           Tanscript for in         Vito transcription         TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	genomic site			
Still 2:0111         CARLETTICCT (ACAGAGECETT)         Testin CASAGET (CETTICC)           Sile 2:0112         CCGATTONNINAGAGETGEGGET         "GGAGETCTINNINAGGEGEGEGETTI         "GGAGETCTINNINAGGEGEGEGEGEGEGEGEGEGEGEGEGEGEGEGEGEGEG			ATCITIGGETGCAGGTCTGAATCAC	4473
getermin: site         Occan_nmmasks/isac_isac_isac_and isac_isac_and isac_isac_and isac_and isac	Site 2-0111			
Sile 2-0112         Code Cart CINTROCCTACACGACGCTCTT CCACT CINNINACTGATGCCTGGGAA         To Cact Cart Cart Cacc Cact Cart Cacc Cacc Cart Cart Cacc Cacc Cacc Cart Cart Cacc Cacc Cacc Cart Cart Cacc Cacc Cacc Cart Cacc Cacc Cacc Cart Cart Cacc Cacc Cacc Cart Cacc Cacc Cart Cart Cacc Cacc Cacc Cart Cart Cacc Cacc Cart Cacc Cacc Cart Cacc Cacc Cart Cacc Cacc Cart Cacc Cacc Cart Cacc Cacc Cart Cart Cacc Cacc Cart Cacc Cacc Cart Cart Cacc Cart Cart Cart Cacc Cart Cart Cacc Cart Cart Cart Cart Cart Cart Cacc Cart Cart Cart Cart Cart Cart Cacc Cart Cart Cart Cacc Cacc Cart Cart Cart Cacc Cart Cart Cacc Cart Cart Cart Cacc Cart Cart Cart Cacc Cart Cart Cart Cart Cart Cart Cart Cart	genomic site			
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genomic site         CCCATCTNNNNCCTAATGCCTGGGAA         TogGAGTCAGAGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG	Site 2-0112		TOCACTTOACACOTOTOCTOTOC	
Transcript for in vitro transcription         GEGAA         ALC IGLATITAGUECTICAUCTICUT         Generate linear PCR product for ITTITITITITITITITITITITITITITITITITITI	genomic site	CCGATCTNININCCTGATGCCTGGGAA		
Hanscription       TGAGGTCGGTACCTAATACGACTCA       HITTITTITTITTITTITTITTITTITTITTITTITTITT	Trene exist for in	GTGAA		Concepta line on DCD and duct for
Name         Information         Information         Information         Information         Information           NR-Site3-0T1         CCAGCTCGGTACCTAATACGACCAA         Information	I ranscript for in			Generate linear PCR product for
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IDSAGDTOSGIACTIANACGACIGA         ITTITTITTITTITTITTITTITTITTITTITTITTITT				
CTATAGGAAATAAGAGAAAGAA GACCA ITTCTTCACTACGACGACGACGACG GACCA NR-Site3-0T1 genomic site CCGATCTNNINAGGTGGCAAATAGGCCCTCT RR-Site3-0T2 genomic site CCGATCTNNINACGCCAGGACGCCCTT TGGAGTCAGACGTGGCCCTCGGACGCCCTCG GAGGC NR-Site3-0T3 genomic site CCGATCTNNINACGCCAGGACGCCCTT TGGAGTCAGACGTGGGCCTCGGGCGCCCCGGCCCCCGGACGCCCCGGCCCCCGGCCCCCGGCCCCCGGCCCCCGGCCCC				
NR-Site3-OT1         ACACTCTTTCCCTACACGACGCTCTT         TGGAGTTCAGACGTGTGCTCTTCCG           genomic site         CCCATCTNNINACGAATAGGCCCTCTT         TGGAGTTCAGACGTGTGCTCTTCCG           genomic site         CCCATCTNNINACGACATAGGCCCTCTT         TGGAGTTCAGACGTGTGCTCTTCCG           genomic site         CCCATCTNNINACGACATAGGCCCTCTT         TGGAGTTCAGACGTGTGCTCTTCCG           genomic site         CCCATCTNNINACTGACCCCTGACGCGCTCTT         TGGAGTTCAGACGTGTGCTCTTCCG           genomic site         CCCATCTNNINACTGACCCCTGACGCGCTCTT         TGGAGTTCAGACGTGTGCTCTTCCG           genomic site         CCCATCTNNINNTCCCCATGGTAGCCTCTT         TGGAGTTCAGACGTGTGCTCTTCCG           genomic site         CCCATCTNNINNTCCCCATGGTAGCCTCTT         TGGAGTTCAGACGTGTGCTCTTCCG           genomic site         CCCATCTNNINNTCCCCAAGGCCTCTT         TGGAGTTCAGACGTGTGCTCTTCCG           genomic site         CCCATCTNNINNTCCCAAGGCCCCTT         TGGAGTTCAGACGTGTGCTCTTCCG           genomic site         CCCATCTNNINNTCCCAAGGCCCCTT         TGGAGTTCAGACGTGGTGCTCTTCCG           genomic site         CCCATCTNNINNTCCTGTGTCTGCAGC         ACCCTCTTCCCTACACGAGCCCCTT           genomic site         CCCATCTNNINNTCCTGTGTGTGCCTT         TGGAGTTCAGACGTGGTGCTCTTCCG           S-Site3-072         ACACTCTTTCCTACACGAGCGCTCTT         TGGAGTTCAGACGTGGGGGGAC           genomic site         CCCATCTNNINNTCGTGTGTGTGTGCCTT         TGGAGTTCAGACGTGG				
NR-Site3-011       ACACTCTITTCCCTACAGGAGGCTCTT       TGGAGTTCAGACGATGGAAATAGGACCTCT         RN-Site3-072       ACACTCTITTCCCTACAGGACGCTCTT       TGGAGTTCAGACGTGGACGTCTTCCG         NR-Site3-073       CGATCTINNNACACTCTGATAATGGG       ATCTTCAGCGCCCTAAGATGCGTGG         genomic site       CCGATCTINNNACCCTCGACGGCGCTCTT       TGGAGTTCAGACGTGTGGCTCTTCCG         genomic site       CCGATCTINNNACCCTCGACGGCGCTCTT       TGGAGTTCAGACGGTGTGGTCTTCCG         genomic site       CCGATCTINNNTCCCCACGGAGGCTCTT       TGGAGTTCAGACGGTGTGCTCTTCCG         genomic site       CCGATCTINNNTCCCCACGGAGGCTCTT       TGGAGTTCAGACGGTGTGCTCTTCCG         genomic site       CCGATCTINNNTCCCCACGGAGGCTCTT       TGGAGTTCAGACGGTGTGCTCTTCCG         genomic site       CCGATCTINNNTCCCCAACGGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTINNNTCCCCAACGGCGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTINNNTCCCCTACACGCGCGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTINNNTCCTGTGTGTGTGCAT       TGGAGTTCAGACCGTGTGCTCTTCCG         s-Site3-072       ACACTCTTTCCCTAACAGAGGCGCTCTT       TGGAGTTCAGACCGTGTGCTCTTCCG         genomic site       CCGATCTNNNNTCCTGTGTGTGTGTCTT       TGGAGTTCAGACCGTGGGCTCTCCG         S-Site3-074       ACACTCTTTCCCTAACAGCAGCGCTCTT       TGGAGTTCAGACGGTGGCTCTTCCG         S-Site3-074		G	AGACCA	
genomic site         CCGATCTINNINCGAAATAGGCCCTCT         ACTGCTTCCTGGAAAGTGCCATG           NR-Site3-0T2         ACACTCTTTCCCTACACGACGCTCTT         TGGAGTTCAGACGTGGCTCTTCCG           genomic site         CCGATCTINNINCCGCACGGCGCTCTT         TGGAGTTCAGACGTGGCCTTCCG         Also used for C-Site3-OT3           NR-Site3-OT1         ACACTCTTTCCCTACACGACGCCTCTT         TGGAGTTCAGACGTGTGCTCTCCG         Also used for C-Site3-OT3           genomic site         CCGATCTINNINTCGCACAGGACGCTCTT         TGGAGTTCAGACGTGTGCTCTCCG         Also used for C-Site3-OT3           genomic site         CCGATCTINNINTCCCCAACGGACGCTCTT         TGGAGTTCAGACGTGTGCTCTTCCG         AcACTCTTTCCCTACACGACGCCCCTT         CA           Genomic site         CCGATCTINNINTTCCCCAACGGACGCTCTT         TGGAGTTCAGACGTGTGCCTTTCCG         ACACTCTTTCCCTACACGACGCCCTTT         TGGAGTTCAGACGTGTGCCTTCCG           S-Site3-OT2         ACACTCTTTCCCTACACGACGCTCTT         TGGAGTTCAGACGGGGGGGGGGGGA         ACCTCTTCCCTACACGACGCCTCTT         TGGAGTTCAGACGTGTGCCTTCCG         Also used for HF-Site3-OT1           genomic site         CCGATCTNNINTGCGTGTGTGCCAT         TGGAGTTCAGACGGGGGGGGGGGGGGGGGGGGGGGGGGG	NR-Site3-OT1	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
NR-Site3-OT2         CGCCC         TGGAGTTCAGACGGTGTGCTCTCCG           genomic site         CCGATCTINNNCACTCTGATAATGGG         ATCTTCAGCGCCCTAAGATGTCG           NR-Site3-OT3         ACACTCTTTCCCTACAGGACGCTCTT         TGGAGTTCAGACGTGTGCTCTCCG         Also used for C-Site3-OT3, C-Site3- OT4, and S-Site-OT1           genomic site         CCGATCTINNNTCGACCCCTGACTT         TGGAGTTCAGACGTGTGCTCTCCG         Also used for C-Site3-OT3, C-Site3- OT4, and S-Site-OT1           C-Site3-OT1         ACACTCTTTCCCTACAGGAGGCTCTT         TGGAGTTCAGACGTGTGCTCTCCG         ACACTCTTTCCCTACAGGAGGCCCTTT           genomic site         CCGATCTNNNNTTCCCCAACGGACGCTCTT         TGGAGTTCAGACGTGTGCTCTTCCG         ACACTCTTCCCTACAGGAGCGCCCTT           genomic site         CCGATCTNNNNTTCCCTACAGGAGGCCCTTT         TGGAGTTCAGACGTGTGCTCTTCCG         ACACTCTTTCCCTACAGGAGGCCCTT           genomic site         CCGATCTNNNNTCCTGTGTGTGTGCCTT         TGGAGTTCAGACGTGTGCTCTTCCG         AcACTCTTTCCCTACAGGAGGCTCTT           genomic site         CCGATCTNNNNTGCTGTGTGTGTGCAT         TGGAGTTCAGACGTGTGCCTTCCG         Also used for HF-Site3-OT1           genomic site         CCGATCTNNNNTCCCTACAGGAGGCTCTT         TGGAGTTCAGACGTGTGCCTTCCG         Also used for HF-Site3-OT1           genomic site         CCGATCTNNNNTGCTGTGTGTGTGCAT         TGGAGTTCAGACGTGTGCCTTCCG         ACACTCTTTCCCTAACAGGAGGCTCTT           Genomic site         CCGATCTNNNNATCCCTGCTCTCCT         TGGAGTTCAGACG	genomic site	CCGATCINNNNCGAAATAGGCCCICI	AICIGCTICCIGGAAGAIGCCAIG	
NR-Site3-012 genomic site       ACACTCTITTCCCTACACGACGCTCTT CGACTOTNINNCCACTCGATATGGG GGAGGC       TGGAGTTCAGACGGTGTCTTCCG ATCTACGCCCCTACACGACGCCTTT TGGAGTTCAGACGGTGGTCCTTCCG ATCTACGCGACGTTNINNCCACTCGACACGCCCTT TGCC       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNINNTTCCCCAGGACGCTCTT TGGAGTTCAGACGTGTGCTCTCCG ATCTACGCACCTCTNNINNTTCCCCAGGACGCTCTT TGGAGTTCAGACGTGTGCCTCCCG genomic site       ACACTCTTTCCCTACACGACGCTCTT CGGATCTNNINNTTCCCCAGGACGCTCTT TGGAGTTCAGACGTGTGCCTCCCG GCACT S-Site3-072       ACACTCTTTCCCTACACGACGCTCTT TGGAGTTCAGACGTGTGCCCCAATG GCACT       TGGAGTTCAGACGTGTGCCTCCCG ATCTACGCCGATCTNNINNTTCCCCAGACGCTCTT TGGAGTTCAGACGTGTGTCCCCATG GCACT         S-Site3-072       ACACTCTTTCCCTACACGACGCTCTT GCACTTNNINNTTCCCTACAGCGCGCTCTT GCACTTNNINNTTCCCTACAGCGCGCTCTT genomic site       TGGAGTTCAGACGTGTGCCTCCCG ATCTCCCCCGAACACTGGTGGCCTTCCG ACCTCTNNINNTTCCTGTGTGTGCCAT GCAC       ACACTCTTTCCCTACACGACGCTCTT GGAGTTCAGACGTGTGTCCCCATG ACCTCTTTCCCTACACGACGCTCTT GGAGTTCAGACGTGTGCCTCCCG ACCGG       Also used for HF-Site3-0T1 ACACTCTTTCCCTACACGACGCTCTT GGAGTTCAGACGTGTGCTCTCCG ACCGG         S-Site3-073       ACACTCTTTCCCTACACGACGCTCTT GGAGTCAGACGTGTGTCCCCCCG GCAC       TGGAGTCAGACGTGTGCCTTCCG ACCGGTCTNNINNAGGTGGCTTCAGAC CCGATCTNNINNAGGTGGCTCTTCG ACCTCTTCCCTACACGACGCCTTT CCGATCTNNINNACCCCGCCCCCCCT CACTC       TGGAGTCAGACGTGTGCCTTCCG ATCTTGCCCGATCTNNINNACCCCGCCCCCCCCCCCCCCCCCCCCCCCCCCCCC		GTCCC		
genomic site         CCGATCTNNINNCACTCTGATAATGGG         ATCTTCAGCTGCCCTAAGAGATGTCG           NR-Site3-013         ACACTCTTTCCCTACACGACGACTTT         TGGAGTTCAGACGTGTGCCTTCCG         Also used for C-Site3-013, C-Site3- 0T4, and S-Site-011           C-Site3-011         ACACTCTTTCCCTACACGACGCCTTT         TGGAGTTCAGACGTGTGCCTTCCG         Also used for C-Site3-013, C-Site3- 0T4, and S-Site-011           C-Site3-011         ACACTCTTTCCCTACACGACGCCTCTT         TGGAGTTCAGACGTGTGCCTTCCG         ACACTCTTTCCCTACACGACGCCTCTT           genomic site         CCGATCTNNINNTTCCCCATGGTGAGCC         ACCTCTTCCCTACACGACGCCTCTT         TGGAGTTCAGACGTGTGCCTTCCG           genomic site         CCGATCTNNINNTTCCCCAAGGCGCTCTT         TGGAGTTCAGACGTGTGCCTTCCG         ACACTCTTTCCCTACACGACGCCTCTT           genomic site         CCGATCTNNINNTCCTGTGTGTCCAAGT         TCTGGAGTTCAGACGTGTGCCTTTCCG         Also used for HF-Site3-0T1           genomic site         CCGATCTNNINNTTCCTGTGTGTGCCTT         TGGAGTTCAGACGTGTGCCTTTCCG         Also used for HF-Site3-0T1           genomic site         CCCGATCTNNINNTGCTGTGTGCCTTT         TGGAGTTCAGACGTGTGCCTTTCCG         Also used for HF-Site3-0T1           genomic site         CCCGATCTNNINNAGGTGGCTTTAGAT         TCTGCAAGCGTGTGCCTTTCCG         ACACTCTTTCCCTACAGACGCCTTT         TGGAGTTCAGACGTGTGCCTTTCCG           S-Site3-0T2         ACACTCTTTCCCTACAGACGCCTCTT         TGGAGTTCAGACGTGTGCCTTTCCG         ACCTCT         TCTGCCCATCAGACGCGCTT	NR-Site3-OT2	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
INP.Site3-0T3         GGAGGC         TGGAGTCTTTCCCTACACGACGCTCTT         TGGAGTCAGACGTGTGCTCTTCCG         Also used for C-Site3-0T3, C-Site3- 0T4, and S-Site-0T1           CCSHE3-0T1         CACACTCTTTCCCTACACGACGCTCTT         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTAGACAGTGCTCTCCG         OT4, and S-Site-0T1           Genomic site         CCCGATCTNNNNTTCCCCACAGGACGCTCTT         TGGAGTTCAGACGTGTGCCTTCCG         ACCTCTTTCCCTACACGACGCTCTT         TGGAGTCAGCCCTACACGACGCCTCTT         TGGAGTCAGACGCTGTGCCTCCCAATG           Genomic site         CCGATCTNNNNTTCACAAAGCCAGGT         ACCACTCTTTCCCTACACGACGCTCTT         TGGAGTTCAGACGCTGTGCCTCTCCG           genomic site         CCGATCTNNNNTTCACAAAGCCAGGT         ACCACTCTTTCCCTACACGACGCTCTT         TGGAGTTCAGACGTGTGCTCTCCG           genomic site         CCGATCTNNNNTTCACAAGCGCGCTTT         TGGAGTTCAGACGTGTGCTCTTCCG         ACCACTCTTTCCCTACACGACGCTCTT           genomic site         CCGATCTNNNNTTGCTGTGTGTGTGTCCT         TGGAGTTCAGACGTGTGCTCTTCCG         Also used for HF-Site3-0T1           genomic site         CCCGATCTNNNNTGCTGTGTGTGTGCTCTT         TGGAGTTCAGACGTGTGCTCTTCCG         ACACTCTTTCCCTACACGACGCTCTT         TGGAGTTCAGACGTGTGCTCTTCCG           genomic site         CCCTGA         ACACTCTTTCCCTACACGACGCTCTT         TGGAGTTCAGACGTGTGCTCTTCCG         ACCTCTTCCCTACACGACGCCTCTT         TGGAGTTCAGACGTGTGCCTTTCCG         ACCTCTTCCCTACACGACGCCTCTT         TGGAGTTCAGACGTGTGCCTTTCCG         ACCTCTTTCCCTACACGACGCCTCTT	genomic site	CCGATCTNNNNCACTCTGATAATGGG	ATCTTCAGCTGCCCTAAGATGTCTG	
NR-Site3-013 genomic site       ACACTCTTTCCCTACACGACGCCTCTT TTCCC       TGGAGTTCAGACGTGTGCTCTTCCG ATCTAAGAGATGCTTGGCTCTTCCG ATCTAAGAGATGCTTGGCTCTTCCG ATCTAAGAGATGCTTGGCGCTGTG C-Site3-012       ACACTCTTTCCCTACACGACGCTCTT TGAGA       TGGAGTTCAGACGTGTGCTCTTCCG ATCTTAGCACGTGTGCTCTTCCG ATCTTAGCGACGTGTGCTCTTCCG ATCTTAGCGACGTGTGCTCTTCCG GCGATCTNNNNTCCCACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG ATCTTAGCGACGTGTGCTCTTCCG GCGATCTNNNNTCGCTGTGCTCTCCAGT GCGATCTNNNNTCGCTGTGTGCACT       TGGAGTTCAGACGTGGCTCTTCCG ATCTTAGGCAGCGCGGGAGGGAA ATCTGCGAACGTGGCCTCTCCG ATCTCCCCGACGTNNNNTGCTGTGTGCAT         S-Site3-013       ACACTCTTTCCCTACACGACGCCTCTT GCGATCTNNNNTGCTGTGTGTGCAT       TGGAGTTCAGACGTGTGCCTTCCG ATCTCCCCGACGTNNNTTGCTGTGTGCAT         S-Site3-013       ACACTCTTTCCCTACACGACGCTCTT GCGATCTNNNNTGCTGTGTGTGCAT       TGGAGTTCAGACGTGGCCTTCCG ATCTTCACACGACGTGGCCCTTCCG ATCTTAACTCCCAAATGCACGGCGGA ATCTTGCCCAATGCACGACGCCTCT       AcACTCTTTCCCTACACGACGCTCTT CGCATCTNNNNAGGTGGCTTTAGAT         S-Site3-014       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNATGCCGCCCCCCCCCCCCCCCCCCCCCCC		GGAGGC		
genomic site       CCGATCTINNNCTGACCCTGACTT       ATCTAAGAGAGGTGGGGCTGGG       OT4, and S-Site-OT1         TCCC       CSite3-OT1       ACACTCTTTCCCTACCACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNTTCCCCATGGTAGCC       TTTCAGCAGTGTGCTCTTCCG         genomic site       CCGATCTNNNNTTCACCAAGCCAGCGT       TGGAGTTCAGACGTGGCTCTTCCG         genomic site       CCGATCTNNNNTCCACAAGCCAGCGT       TGGAGTTCAGACGTGGCTCTTCCG         S-Site3-OT2       ACACTCTTTCCCTACCACGACGCTCTT       TGGAGTTCAGACGTGGGCTCTTCCG         genomic site       CCGATCTNNNNTCCTGTGTCTCCAGT       TGGAGTTCAGACGTGGGGCTCTTCCG         genomic site       CCGATCTNNNNTCCTGTGTGTGCAT       TGGAGTTCAGACGTGGGGGGGGAA         S-Site3-OT3       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGGGGGGGGGAA         genomic site       CCCGATCTNNNNTGCGTGTGTGTGCAT       TGGAGTTCAGACGTGTGCTCTTCCG         S-Site3-OT4       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCCGATCTNNNNATCCCTGCTCTCGTC       TGGAGTTCAGACGTGTGCTCTTCCG         S-Site3-OT5       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCCGATCTNNNNATCCCGCGCCTCTT       TGGAGTTCAGACGTGGTGCTCTTCCG         HF-Site3-OT2       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGGTGCTCTTCCG         genomic site	NR-Site3-OT3	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	Also used for C-Site3-OT3, C-Site3-
C-Site3-OT1 ACACTCITTCCCTACACGACGCTCTT TGGAGTTCAGACGTGTGCTCTTCCG ACACTCTTTCCCTACACGACGCCTCTT TGGAGTTCAGACGTGTGCCTTTCCG GCAGT ACACTCTTTCCCTACACGACGCCGCTCTT TGGAGTTCAGACGTGGTGCTCTTCCG GCAGT ACACTCTTTCCCTACACGACGCCGCTCTT TGGAGTTCAGACGTGGTGCTCTTCCG GCAGT ACACTCTTTCCCTACACGACGCGCTCTT TGGAGTTCAGACGTGGTGCTCTTCCG GCAGT ACACTCTTTCCCTACACGACGCGCTCTT TGGAGTTCAGACGTGGGGGGGGGA GCCTG ACACTCTTCCCTACACGACGCGCTCTT TGGAGTTCAGACGTGGGCTCTTCCG S-Site3-OT3 ACACTCTTTCCCTACACGACGCGCTCTT TGGAGTTCAGACGTGGGCGGGGGGGAA GCCAG ACCCTTTCCCTACACGACGCCCTCT TGGAGTTCAGACGTGGGCGGGGGGGGAA S-Site3-OT4 ACACTCTTTCCCTACCGACGCGCTCTT TGGAGTTCAGACGTGGCGCTCTTCCG genomic site CCGATCTNNNNATGCCTGCGCTGCTCT CCGTGA ACACTCTTTCCCTACCGACGCCCTT TGGAGTTCAGACGTGGCTCTTCCG S-Site3-OT5 ACACTCTTTCCCTACCGACGCCCTT TGGAGTTCAGACGTGGTGCTCTTCCG genomic site CCGATCTNNNNAGGTGGCCACGGCCCTT TGGAGTTCAGACGTGGTGCTCTTCCG HF-Site3-OT3 ACACTCTTTCCCTACCGACGCCCTT TGGAGTTCAGACGTGGTGCTCTTCCG GCAGTCTNNNNAGGTGGCCAGCGCCTT TGGAGTCAGACGTGGTCCTTCCG GCAGTCTNNNNAGGGCCAAGACCG CCGTT TGGAGTTCAGACGTGGTGCTCTTCCG HF-Site3-OT3 ACACTCTTTCCCTACCGACGCCCTT TGGAGTTCAGACGTGTGCTCTTCCG ACACTC CTTTCCCTACCGACGCCCTT TGGAGTCCAGCGCGTGTCCTTCCG ACCTC CATCT CCTTCCCTACCGACGCCCTT TGGAGTCCAGACGTGTGCTCTTCCG ACCTC CAAGAA HF-Site3-OT3 ACACTCTTTCCCTACCGACGCCCTT TGGAGTCCAGACGTGTGCTCTTCCG ACCTC CCTTCCCTACCGCAGCGCCCTT TGGAGTCCATGCATCCCCATC CACTC ACCTCTTCCCTACCGACGCCCTT TGGAGTCCAGACGTGTGCTCTTCCG ACCTC CCGATCTNNNNCCCTGCCCCCCCCCCCCCCCCCCCCCCCC	genomic site	CCGATCTNNNNCTGACCCCTGACTTG	ATCTAAGAGATGCTTGGGCTGTGG	OT4, and S-Site-OT1
C-Site3-OT1 ACACTCTTTCCCTACAGAGAGCGTCTT TGGAGTTCAGAGGTGGCTCTTCCG genomic site CCGATCTNNNNTTCACAGAGCGAGGT GCAGT GCAGTCTNNNNTTCACAGAGCGAGGT GCAGTCTNNNNTTCACAGAGCGAGGT GCAGT S-Site3-OT2 ACACTCTTTCCCTACAGAGAGCGCTCTT TGGAGTTCAGACGTGGTGCTCTTCCG GCAGT S-Site3-OT3 ACACTCTTTCCCTACAGAGGGCGCTCTT TGGAGTTCAGACGTGGTGGCTCTTCCG genomic site CCGATCTNNNNTTCCCTGTGTGTGGCAT GCACC S-Site3-OT3 ACACTCTTTCCCTACAGAGCGCGCTCTT TGGAGTTCAGACGTGGGCGCGGGGGAGGGAA GCAC S-Site3-OT4 ACACTCTTTCCCTACAGCGACGCTCTT TGGAGTTCAGAGCGTGGTGCTCTTCCG genomic site CCGATCTNNNNTGGCTGTGGTGGCAT GCACC S-Site3-OT4 ACACTCTTTCCCTACAGCGACGCTCTT TGGAGTTCAGAGCGTGGGCGCTCTTCCG genomic site CCGATCTNNNNAGGTGGCAGCGCTCTT TGGAGTTCAGAGCGTGGCGCTCTTCCG S-Site3-OT4 ACACTCTTTCCCTACAGCGACGCTCTT TGGAGTTCAGAGCGTGGCGCTCTTCCG genomic site CCGATCTNNNNAGGTGGCCAGAGCGCTCTT TGGAGTTCAGAGCGTGGCGCTCTTCCG ACCTCT HF-Site3-OT2 ACACTCTTTCCCTACAGCGCGCTCTT TGGAGTTCAGAGCGTGGCTCTTCCG HF-Site3-OT3 ACACTCTTTCCCTACCGCACGCGCTCTT TGGAGTTCAGAGCGTGGCTCTTCCG HF-Site3-OT3 ACACTCTTTCCCTACAGCGCGCCTTT TGGAGTTCAGAGCGTGGCTCTTCCG HF-Site3-OT3 ACACTCTTTCCCTACACGACGCGCTCTT TGGAGTTCAGACGTGGTGCTCTTCCG HF-Site3-OT3 ACACTCTTTCCCTACACGACGCGCTCTT TGGAGTTCAGACGTGGTGCTCTTCCG HF-Site3-OT4 ACACTCTTTCCCTACACGACGCGCTCTT TGGAGTTCAGACGTGGTGCTCTTCCG HF-Site3-OT3 ACACTCTTTCCCTACACGACGCGCTCTT TGGAGTTCAGACGTGGTGCTCTTCCG HF-Site3-OT4 ACACTCTTTCCCTACACGACGCGCCTT TGGAGTCCAGACGTGGTGCTCTTCCG HF-Site3-OT4 ACACTCTTTCCCTACACGACGCGCCTT TGGAGTCCAGACGTGTGCTCTTCCG HF-Site3-OT4 ACACTCTTTCCCTACACGACGCGCCTT TGGAGTCCAGACGTGTGCTCTTCCG HF-Site3-OT4 ACACTCTTTCCCTACACGACGCGCCTT TGGAGTCAGACGTGTGCTCTTCCG HF-Site3-OT4 ACACTCTTTCCCTACACGACGCGCCTT TGGAGTCAGACGTGTGCTCTTCCG HF-Site3-OT4 ACACTCTTTCCCTACACGACGCGCCTT TGGAGTCAGACGTGTGCTCTTCCG HF-Site3-OT4 ACACTCTTTCCCTACACGACGCGCCTT TGGAC HF-Site3-OT4 ACACTCTTCCCTACACGACGCGCCTT TGGAGTCAGAGCGTGGTGCTCTTCCG HF-Site3-OT4 ACACTCTTCCCTACACGACGCCCTT TGGAGTCAGACGTGGTGCTCTTCCG HF-Site3-OT4 ACACTCTTTCCCTACACGACGCGCTTT TGGAGTCAGACGTGGTGCTCTTCCG HF-Site3-OT4 ACACTCTTTCCCTACACGACGCCCTT TGGAGTC		TTCCC		
genomic site       CCGATCTINNNNTCCCCATGGTAGCC       ATCTITCACGTATCCGTCCGTCTT         CSite3-0T2       ACACTCTTTCCTACACGACGCCGTCT       TGGAGTTCAGACGCTGGTCCTCTCCG         genomic site       CCGATCTNNNNTTCACAAAGCCAGGT       ATCTAGGCAGCCTGATCCCAATG         S-Site3-0T2       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGGTGGCTCTTCCG         genomic site       CCGATCTNNNNTCGCCAGAGCGCTCTT       TGGAGTTCAGACGGTGGCTCTTCCG         genomic site       CCGATCTNNNNTTGCTGTGTGTGCAT       ATCTGGAAAAGCTGGGGAGGGAA         S-Site3-0T3       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGGTGGCTCTTCCG         genomic site       CCGATCTNNNNTGCTGCTGTGTGTGCAT       TGGAGTTCAGACGGGGGGCCTTCCG         genomic site       CCGATCTNNNNAGGTGGCTTTAGAT       TGGAGTTCAGACGGTGGTCCTTCCG         genomic site       CCGATCTNNNNAGGTGCCTTTAGAT       TGGAGTTCAGACGGTGGTCCTTCCG         genomic site       CCGATCTNNNNATCCCTGCTCCTGCT       TGGAGTTCAGACGGTGGTCCTTCCG         genomic site       CCGATCTNNNAATGCCCAGCGCCTCTT       TGGAGTTCAGACGTGGTGCTCTTCCG         genomic site       CCGATCTNNNAATGCCCAGCGCCTCTT       TGGAGTTCAGACGGTGGTCCTTCCG         HF-Site3-0T2       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTCAGACGTGGTGCTCTTCCG         genomic site       CCGATCTNNNNAAGGTGGCCAAGACCG       ATCTGGCTCATCGGACGGTGGTCCTTCCG         HF-Site3-0T3       ACACTCTTTCCCTACACGACGCGCCTTT	C-Site3-OT1	ACACICITICCCTACACGACGCTCTT	IGGAGIICAGACGIGIGCICIICCG	
C-Site3-OT2 ACACTCTTTCCCTACACGACGCCTCTT TGGAGTTCAGACGTGTGCTCTTCCG genomic site CCGATCTNNNNTTCACAAAGCCAGGT ATCTAGGCAGCCTGATTCCCAATG GCAGT ACACTCTTTCCCTACACGACGCCTCTT TGGAGTTCAGACGTGTGCTCTTCCG genomic site CCGATCTNNNNCTCTGTGTCTCCAGT ATCTCCTCCCGAACACTGGTGAC GCCTG ACACTCTTTCCCTACACGACGCCTCTT TGGAGTTCAGACGTGTGCTCTTCCG Also used for HF-Site3-OT1 genomic site CCGATCTNNNNTTGCTGTGTGTGCAT ATCTGTGAAAAGCTGGGGAGGGAA GCAC S-Site3-OT4 ACACTCTTTCCCTACACGACGCTCTT TGGAGTTCAGACGTGTGCTCTTCCG genomic site CCGATCTNNNNATGCTGTGTGTGCTTT TGGAGTTCAGACGTGTGCTCTTCCG genomic site CCGATCTNNNNAGGTGGCTTTAGAT ATCTTAACTCCCAAATGCACTGCCT CCGCTGA ACACTCTTTCCCTACACGACGCTCTT TGGAGTTCAGACGTGTGCTCTTCCG genomic site CCGATCTNNNNATCCCTGCTCTCCTGCT ATCTTAACTCCCCAAATGCACTGCCT CCGATCTNNNNATCCCTGCTCCTGCT TGGAGTTCAGACGTGTGCTCTTCCG genomic site CCGATCTNNNNATCCCTGCTCCTCCT TGGAGTTCAGACGTGTGCTCTTCCG genomic site CCGATCTNNNNATGCCAGGCGCTCTT TGGAGTTCAGACGTGTGCTCTTCCG HF-Site3-OT5 ACACTCTTTCCCTACACGACGCTCTT TGGAGTTCAGACGTGTGCTCTTCCG Genomic site CCGATCTNNNNATGCCAGACGCCC ATCTGGCTCGTGCTCTTCCG Genomic site CCGATCTNNNNATGCCAGGCGCTCTT TGGAGTTCAGACGTGTGCTCTTCCG HF-Site3-OT3 ACACTCTTTCCCTACACGACGCCTCTT TGGAGTTCAGACGTGTGCTCTTCCG GCGATCTNNNNCCACACCGGACGCCC ATCTGGCTCATTCGCACCCTCCCATC CAAGAA HF-Site3-OT3 ACACTCTTTCCCTACACGACGCTCTT TGGAGTTCAGACGTGTGCTCTTCCG ACCTC HF-Site3-OT4 ACACTCTTTCCCTACACGACGCTCTT TGGAGTTCAGACGTGTGCTCTTCCG ACCTC HF-Site3-OT5 ACACTCTTTCCCTACACGACGCTCTT TGGAGTTCAGACGTGTGCTCTTCCG ACCTC HF-Site3-OT5 ACACTCTTTCCCTACACGACGCTCTT TGGAGTTCAGACGTGTGCTCTTCCG ACCTC HF-Site3-OT5 ACACTCTTTCCCTACACGACGCTCTT TGGAGTTCAGACGTGTGCTCTTCCG ACCTT CCGATCTNNNNCCCTGGCTTGTGGAC CCGATCTNNNNCCCTGGCTTGTGGCC CCGATCTNNNNCCCTGGCTTGTGGCC CCGATCTNNNNCGCACACCCTGGGCTCA HF-Site4-OT1 ACACTCTTTCCCTACACGACGCTCTT TGGAGTTCAGACGTGTGCTCTTCCG ACCTT TGCT NR-Site4-OT1 ACACTCTTTCCTACACGACGCTCTT TGGAGTCGTGCCTCTCCG ATCTG genomic site CCGATCTTNNNGGGTGGATCATGAG ATCATGCACGTGTGCTCTTCCG ATCTGAGGG	genomic site	CCGATCTNNNNTTCCCCATGGTAGCC	ATCTTTCACGTATCCATCCGTCTATT	
C-Site3-012       ACACTCITTCCCTACACGACGCTCTT       IGGAGTCAGACGTGTGCTCTCCG         genomic site       CCGATCTNNNNTCACAAAGCCAGGT       ATCTAGGCAGCCTGATCCCAATG         S-Site3-072       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGAACGTGGTGCTCTTCCG         genomic site       CCGATCTNNNNTCCTGTGTCCCAGT       ATCTAGGCAGCGTGGCTCTTCCG         genomic site       CCGATCTNNNNTTGCTGTGTGTGCAT       AGCACGCTCTT         S-Site3-073       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGGGGGGGGGGGGGAA         genomic site       CCGATCTNNNNTGCTGTGTGTGCAT       ATCTAGGCAGCGTGTGCTCTTCCG         genomic site       CCGATCTNNNAGGTTGGCTTTAGAT       ATCTAGCACGACGGTGTGCTCTTCCG         genomic site       CCGATCTNNNAGGTTGGCTTTAGAT       TGGAGTTCAGACGGTGGTGCTCTTCCG         genomic site       CCGATCTNNNATCCCTGCTCCTGCT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNATCCCTGCTCCTGCT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNATGCCCACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNACCCACCTGACGCAGCCC       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNCCACACCTGAGCGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNCCACACCTGACGCTCTT       TGGAGTTCAGACGTGGCTCTTCCG         genomic site       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGAC	0.0% 0.070	IGAGA		
genomic site         CCGATCTINNINTICACAAAGCCAGGT         ATCLAGGCAGCCIGATTCCCAATG           S-Site3-0T2         ACACTCTTTCCCTACACGACGCTCTT         TGGAGTTCAGACGTGTGCTCTCCG         ATCTCCTCCCTAACACTGGTGAC           genomic site         CCGATCTNNNNCTCTGTGTGTCCCAGT         TGGAGTTCAGACGTGTGGCTTTCCG         Atso used for HF-Site3-OT1           genomic site         CCGATCTNNNNTGCTGTGTGTGCAT         TGGAGTTCAGACGTGTGGCTTTCCG         Atso used for HF-Site3-OT1           genomic site         CCGATCTNNNNTGCTGTGTGTGCAT         TGGAGTTCAGACGTGTGCCTTTCCG         AtCTGTGACAACGTGGGGAGGAAA           S-Site3-OT4         ACACTCTTTCCCTACAGAGGCTCTT         TGGAGTTCAGACGTGTGCCTTTCCG         ACCGTGTTCCCTACCGACGACGCTCTT         TGGAGTTCAGACGTGTGCTTTCCG           genomic site         CCGATCTNNNAGTTGCCTTGCTGCT         TGGAGTTCAGACGTGTGCTCTTCCG         ATCTTGCCCGAAGACGCT           genomic site         CCGATCTNNNNACCCTGGCCCTGCT         TGGAGTTCAGACGTGTGCCTTCCG         ACCACTCTTTCCCTACACGACGCTCTT           genomic site         CCGATCTNNNNACGCCACCGACGCTCTT         TGGAGTTCAGACGTGTGCCTTCCG         ACCACTCTTTCCCTACACGACGCTCTT           genomic site         CCGATCTNNNNCCACACCTGATGGGCT         TGGAGTTCAGACGTGTGCCTTCCG         ACCACTCTTTCCCTACACGACGCTCTT           genomic site         ACACTCTTTCCCTACACGACGCTCTT         TGGAGTTCAGACGTGTGCCTTCCG         ACCACTCTTTCCCTACACGACGCTCTT           HF-Site3-OT4         ACACTCTTTCCCTACACGACGCTCTT	C-Site3-O12	ACACICITICCCTACACGACGCICIT	IGGAGIICAGACGIGIGCICIICCG	
S-Site3-OT2       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTCCG         genomic site       CCGATCTNNNNCTCTGTGTCTCCAGT       ATCTCCTCCCTGAACACTGGTGAC         S-Site3-OT3       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGGTGGCTCTTCCG       Also used for HF-Site3-OT1         genomic site       CCGATCTNNNNTGCTGTGTGTGCAT       TGGAGTTCAGACGGGGGAGGAA       AcACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCCTTCCG         genomic site       CCGATCTNNNNAGGTTGGCTTTAGAT       TGGAGTTCAGACGTGTGCCTTTCCG       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCCTTCCG         s-Site3-OT5       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG       ACCTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNATCCCTGCTCCTGCT       TGGAGTTCAGACGTGTGCTCTTCCG       ACCTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         HF-Site3-OT2       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG       ACCTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCCTTCCG         genomic site       CCGATCTNNNNCCACACCTGATGGCT       TGGAGTTCAGACGTGTGCTCTTCCG       ACCTCTTTCCCTACACGACGCCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG       ACACTCTTTCCCTACACGACGCCTCTT       GGAAGCTCATGACGTGGCTCTTCCG         HF-Site3-OT5       ACACTCTTTCCCTACACGACGCCTCTT       TGGAGTTCAGACGTGTGCCTTTCCG	genomic site	CCGATCINNNNIICACAAAGCCAGGI	AICIAGGCAGCCIGAIICCCAAIG	
S-Site3-012       ACACTCTTTCCCTACACGACGCCTCTT       TGGAGTTCAGACGACGTGTGCC         genomic site       CCGATCTNNNNCTCTGTGTCTCCAGT       ATCTCCTCCCCTACACGACGTGTGCT         genomic site       CCGATCTNNNNGGTGGTGCTT       TGGAGTTCAGACGTGGGCTCTTCCG         genomic site       CCGATCTNNNNGGTGGCTTTAGAT       TGGAGTTCAGACGGGGGGAA         S-Site3-0T4       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTCCG         genomic site       CCGATCTNNNNAGTTGCCTTAGAT       TGGAGTTCAGACGTGTGCTCTCCG         S-Site3-0T5       ACACTCTTTCCCTACACGACGCCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNACCCTGCTCCTGCT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNATCCCTGCCCAGCGCCTTT       TGGAGTTCAGACGTGTGCTCTTCCCG         genomic site       CCGATCTNNNNATGCCTGACGCGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCCG         genomic site       CCGATCTNNNNAATGGCCAAGACCG       ATCTGGTGCTCTTCCCCACC         HF-Site3-0T3       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCCG         genomic site       ACACTCTTTCCCTACACGACGCCTCTT       TGGAGTTCAGACGTGTGCTCTTCCCG         HF-Site3-0T4       ACACTCTTTCCCTACACGACGCCTCTT       TGGAGTTCAGACGTGTGCTCTTCCCG         genomic site       ACACTCTTTCCCTACACGACGCCCTTT       TGGAGTTCAGACGTGTGCTCTTCCCG         HF-Site3-0T4       ACACTCTTTCCCTACACGACGCGCTCTT       TGGA		GCAGI		
genomic site       CCGATCTINNNCTCTGTGTCTCCAGT       ATCTCCTCCCTGAACACTGGTGAC         S-Site3-OT3       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGGCTCTTCCG       Also used for HF-Site3-OT1         genomic site       CCGATCTNNNNTGCTGTGTGTGCAT       TGGAGTTCAGACGAGGGGGGAA       ACACTCTTCCCT         S-Site3-OT4       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG       Also used for HF-Site3-OT1         genomic site       CCCTGA       TGGAGTTCAGACGTGTGCTCTTCCG       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNATCCCTGCTCCTGCT       TGGAGTTCAGACGTGTGCTCTTCCG       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNATGCCCAGCGCCTTT       TGGAGTTCAGACGTGTGCTCTTCCG       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNCCACACCTGATGGCT       TGGAGTTCAGACGTGTGCTCTTCCG       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG       ACACTCTTNNNNCCCACACCTGACGCGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG       GGTAGGCTGAATAATGGCCC         HF-Site3-OT5       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG       ATCT       GGTAGGCTGAATAATGGCCC       ATCT <td>S-Site3-O12</td> <td>ACACICITICCCTACACGACGCTCTT</td> <td>IGGAGIICAGACGIGIGCICIICCG</td> <td></td>	S-Site3-O12	ACACICITICCCTACACGACGCTCTT	IGGAGIICAGACGIGIGCICIICCG	
S-Site3-0T3 genomic site       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNTTGCTGTGTGTGCAT GCAC       TGGAGTTCAGACGTGGCTCTTCCG ACCTCTTTCCCTACACGACGCTCTT genomic site       ACACTCTTTCCCTACACGACGCTCTT CCGTGA       TGGAGTTCAGACGTGGCTCTTCCG ACCTCTACACGACGCGCTCTT TGGAGTTCAGACGTGTGCTCTTCCG       Also used for HF-Site3-OT1         S-Site3-0T4 genomic site       CCGATCTNNNAGGTTGGCTTTAGAT CCCTGA       TGGAGTTCAGACGTGTGCTCTTCCG ATCTTACCCCCAACTGCCCGCCCT       ACACTCTTTCCCTACACGACGCTCTT TGGAGTTCAGACGTGTGCTCTTCCG ATCTTGCCCGAGCGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGTGCTCTGCCCAGCGCCC CATCT         HF-Site3-0T2       ACACTCTTTCCCTACACGACGCCCTTT CCGATCTNNNNAATGGCCAAGACCG CCAGACA       TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGTGCTCTGCCACCCCCCC CAGACA       ACACTCTTTCCCTACACGACGCCCTTT CCGATCTNNNNAATGGCCAAGACCG CAAGAA       TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGCTCATGCCCCCCCCCC	genomic site	CCGATCINNNNCICIGIGICICCAGI	ATCTCCTCCCTGAACACTGGTGAC	
S-Site3-013       ACACTETTICCETACACGACGCTETT       TGGAGTTCAGACGTGTGCTTCCG       ATCTGTGAAAAGCTGGGAGGGAA         genomic site       CCGATCTNNNNTGCTGGTGTGCAT       ATCTGGAAAAGCTGGGAGGGAA       ATCTGGACGCTCTTCCG         genomic site       CCGATCTNNNNAGGTTGGCTTTAGAT       TGGAGTTCAGACGTGTGCTCTCCG       ATCTTAACTCCCAAATGCACTGCCT         S-Site3-0T5       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG       ATCTTGCCGTAGTAATCCCAGCT         genomic site       CCGATCTNNNNATCCCTGCTCCTGCT       TGGAGTTCAGACGTGTGCTCTTCCG       ATCTTGCCGTAGTACCCAGCT         HF-Site3-0T2       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG       ATCTGGTGCTCTGTCATCCCCACC         genomic site       CCGATCTNNNNATGCCCAGCGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG       ATCTGGTGCTCTTCCG         genomic site       CCGATCTNNNNCCACACCGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG       ATCTGGCTCATTGCACC         HF-Site3-0T3       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG       ATCTGGCGCTAATGCCC         genomic site       ACACTCTTTCCTACACGACGCTCTT       CGGACTANNNCCCTGGCTGTGGCAC       ATCT         GGAGTA       ACACTCTTNCCTACCGACGCCCTTT       TGGAGTTCAGACGTGTGCTCTTCCG       ATCT         genomic site       ACACTCTTNCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG       ATCT         genomic site       CCGGTAT       ACACTCTTNCCTACACGACGCGCTCTT				
genomic siteCCGATCTNNNNTGCTGTGTGTGTGTGTGTGTGTGTGTGTGTGTG	S-Site3-O13		IGGAGIICAGACGIGIGCICICCG	Also used for HF-Site3-OT1
S-Site3-OT4       ACACTCTTTCCCTACACGACGCTCTT Genomic site       TGGAGTTCAGACGTGTGCTCTTCCG ACACTCTTNNNAGGTTGGCTTTAGAT         S-Site3-OT5       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNATCCCTGCTCCTGCT       TGGAGTTCAGACGTGTGCTCTTCCG ATCTTGCCCGTAGTAATCCCAGCT         HF-Site3-OT2       ACACTCTTTCCCTACACGACGCTCTT CATCT       TGGAGTTCAGACGTGTGCTCTTCCG ATCTTGCCCGTAGTAATCCCAGCT         HF-Site3-OT2       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNAATGGCCAAGACCG       TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGTGCTCTGTCATCCCCATC         genomic site       CCGATCTNNNNAATGGCCAAGACCG CAAGAA       TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGTGCTCTTCCCG         HF-Site3-OT3       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCACACCTGATGGCT       TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGCTCATTGCATCCTTGACC         genomic site       CCGATCTNNNNCCACACCTGATGGCT CACTC       TGGAGTTCAGACGTGTGCTCTTCCG ATCT       GGTAGGCTGAATAATGGCCCC         HF-Site3-OT4       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCTTGGCTTGTGGAC       TGGAGTTCAGACGTGTGCTCTTCCG ATCT       GGTAGGCTGAATAATGGCCCC         HF-Site3-OT5       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNCGACATCCTGGGTCA       TGGAGTTCAGACGTGTGCTCTTCCG ATCT       TGGAGTTCAGACGTGTGCTCTTCCG         HF-Site3-OT5       ACACTCTTTCCCTACACGACGCTCTT TGCATCTNNNNCGACATCCTGGGTCA       TGGAGTTCAGACGTGTGCTCTTCCG ATCT       TTGCT         ITGCT       CCGATCTNNNNCGACATCCTGGGTCA       TGGAGTTCAGACGTGTGCTCTTCCG ATCT       TGGAGTTCAGACGTGTGCTCTTCCG ATCT <td>genomic site</td> <td></td> <td>ATCTGTGAAAAGCTGGGGGGGGGGAA</td> <td></td>	genomic site		ATCTGTGAAAAGCTGGGGGGGGGGAA	
S-Site3-014       ACACTCTITICCCTACACGACGCTCTT       IGGAGTICAGACGTGTGCTTTCCG         genomic site       CCGATCTNNNNAGGTTGGCTTTAGAT       ATCTTAACTCCCAAATGCACTGCCT         S-Site3-0T5       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNATCCCTGCTCCTGCT       TGGAGTTCAGACGTGTGCTCTTCCG         HF-Site3-0T2       ACACTCTTTCCCTACACGACGCCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNAATGGCCAAGACCG       ATCTGGTGCTCTTCCCG         genomic site       CCGATCTNNNNAATGGCCAAGGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNCCACACCTGATGGCT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNCCACACCTGATGGCT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         Genomic site       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         HF-Site3-OT4       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         GTGCATCTNNNNCCGACACCTGGGTCA       TTGCT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNCGACATCCTGGGTCA       TCT         TGCT       TGGAGTTCAGACGTGGTGCTCTTCCG       ATCT         g		GLAC		
genomic site       CCGATCTINNINAGGTTGGCTTTAGAT       ATCTTAACTCCCAAATGCACTGCCT         S-Site3-OT5       ACACTCTTTCCCTACACGACGCCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNAATGCCCAAGACGC       ATCTGGCCCGTAGTAATCCCAGCT         HF-Site3-OT2       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNAATGGCCAAGACCG       ATCTGGTGCTCTGCATCCCCATC         HF-Site3-OT3       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNCCACACCTGATGGCT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNCGACATCCTGGGTCA       TGGAGTTCAGACGTGTGCTCTTCCG         NR-Site4-OT1       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGGCTCTTCCG         genomic site       CCGATCTNNNNGGGTGGATCATGAG       ATCTGCTCTGCCACCA	S-Site3-014			
S-Site3-OT5 genomic siteACACTCTTTCCCTACACGACGCTCTT CATCTTGGAGTTCAGACGTGTGCTCTTCCG ATCTTGCCCGAGTATCCCAGCTHF-Site3-OT2 genomic siteACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNAATGGCCAAGACCG CAAGAATGGAGTTCAGACGTGTGCTCTTCCG ATCTGGTGCTCTGCATCCCCATCHF-Site3-OT3 genomic siteACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCACACCTGATGGCTTGGAGTTCAGACGTGTGCTCTTCCG ATCTGGTCATGCACCACCG ATCTGGCTCATGCATCCTTGCACCHF-Site3-OT4 genomic siteACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCACACCTGGCTCTTGTGGAC CACTCTGGAGTTCAGACGTGTGCTCTTCCG ATCTGGCTCATGCACCCCHF-Site3-OT4 genomic siteACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCTTGGCTTGTGGAC CAGTATGGAGTTCAGACGTGTGCTCTTCCG ATCT GGTAGGCTGAATAATGGCCCCHF-Site3-OT5 genomic siteACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGACATCCTGGGTCA TTGCTTGGAGTTCAGACGTGTGCTCTTCCG ATCT CTCTCTGACTGGCTGCTTT TGGAGTTCAGACGTGTGCTCTTCCG ATCT CTCTCTGACTGGCTGCTTT CTCTCTGACTGGCTGTCTTCCG ATCT CTCTCTGACTGGCTGTCTTCCG ATCT CTCTCTGACTGGCTGTTCTCCG ATCT CTCTCTGACTGGCTGTCTTCCG ATCT CTCTCTGACTGGCTGTCTTCCG ATCT CTCTCTGACTGGCTGTCTTCCG ATCT CTCTCTGACTGGCTCTTCCG ATCT CTCTCTGACTGGCTCTTCCG ATCT CTCTCTGACTGGCTCTTCCG ATCT CTCTCTGACTGGCTGCTCTTCCG ATCT CCGATCTNNNNCGGTGGATCATGAG ATCTGGTCAGGCTGGCTCTTCCG ATCTGGATCTAGACGTGTGCTCTTCCG ATCTGCTCTCCCACCA	genomic site		ATCTTAACTCCCAAATGCACTGCCT	
S-Site3-015       ACACTCTTTCCCTACACGACGCTCTT CATCT       IGGAGTTCAGACGTGTGTCTTCCCG ATCTTGCCCGAGCAGCACGCTCTT genomic site       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNAATGGCCAAGACCG CAAGAA       TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGTGCTCTGTCATCCCCATC         HF-Site3-0T3       ACACTCTTTCCCTACACGACGCTCTT genomic site       TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGCTCATTGCATCCCCATC         HF-Site3-0T4 genomic site       CCGATCTNNNNCCACACGACGCTCTT CAGTC       TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGCTCATTGCATCCTTGACC         HF-Site3-0T4 genomic site       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCTTGGCTGGCAC CAGTA       TGGAGTTCAGACGTGTGCTCTTCCG ATCT         HF-Site3-0T5       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGACATCCTGGGTCA TTGCT       TGGAGTTCAGACGTGTGCTCTTCCG ATCT         HF-Site4-0T1       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGACATCCTGGGTCA TTGCT       TGGAGTTCAGACGTGTGCTCTTCCG ATCT         NR-Site4-0T1       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGGGTGGATCATGAG GTCAGG       TGGAGTTCAGACGTGTGCTCTTCCG ATCTGATGCTCAGACGTGTGCTCTTCCG ATCTGATGCTCAGCCA	0.0%-0.075		TOCACTTOACACOTOTOCTOTOC	
genomic site       CCGATCTTINNINATCCCTGCTCCTGCTCTGCTGCTGCTGCAGCAGCAGCTGTGCTCTTCCG         HF-Site3-OT2       ACACTCTTTCCCTACACGACGCCAGACCG       ATCTGGTGCTCTGTCATCCCCATC         genomic site       CCGATCTNNNNAATGGCCAAGACCG       ATCTGGTGCTCTGTCATCCCCATC         genomic site       CCGATCTNNNNCCACACCTGATGGCT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNCCACACCTGATGGCT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         HF-Site3-OT4       GGTAGCTGAATAATGGCCCC       ATCT         genomic site       ACACTCTTTCCCTACACGACGCTCTT       GGTAGGCTGAATAATGGCCCC         HF-Site3-OT5       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNCGACATCCTGGGTCA       TGGAGTTCAGACGTGTGCTCTTCCG         NR-Site4-OT1       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNGGGTGGATCATGAG       ATCT         NR-Site4-OT1       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNGGGTGGATCATGAG       ATCTGATGCTCAGACGTGTGCTCTTCCG	S-Site3-015			
HF-Site3-OT2       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNAATGGCCAAGACCG       ATCTGGTGCTCTGTCATCCCCATC         HF-Site3-OT3       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNCCACACCTGATGGCT       TGGAGTTCAGACGTGTGCTCTTCCG         HF-Site3-OT4       CCGATCTNNNNCCACACCGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         HF-Site3-OT4       GGTAGGCTGGAC       GGTAGGCTGAATAATGGCCCC         HF-Site3-OT5       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNCGACATCCTGGGTCA       TGGAGTTCAGACGTGTGCTCTTCCG         NR-Site4-OT1       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNGGGTGGATCATGAG       ATCTGGTGCTCTTCCG         NR-Site4-OT1       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNGGGTGGATCATGAG       ATCTGGTCAGACGTGTGCTCTTCCG	genomic site		ATCTIGUCUGTAGTAATUUUAGUT	
HF-Site3-012       ACACTCTTTCCCTACACGACGCCTCTT       IGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNAATGGCCAAGACCG       ATCTGGTGCTCTGTCATCCCCATC         HF-Site3-0T3       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNCCACACCTGATGGCT       TGGAGTTCAGACGTGTGCTCTTCCG         HF-Site3-0T4       CCGATCTNNNNCCACACGTGTGGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         GGTAGGCTGAATAATGGCCCC       ACACTCTTTCCCTACACGACGCTCTT       GGTAGGCTGAATAATGGCCCC         HF-Site3-0T5       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNCGACATCCTGGGTCA       ATCT         TTGCT       TGGAGTTCAGACGTGTGCTCTTCCG       ATCT         NR-Site4-0T1       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNGGGTGGATCATGAG       ATCTGGTGCTCTTCCG         NR-Site4-0T1       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         GTCAGG       GTCAGG       ATCTGATGCTCAGTCTGTCACCA       ATCTGATGCTCAGTCTGTCACCA			TOCACTTOACACOTOTOCTOTOCO	
genomic site       CCGATCTNNNNAATGGCCAAGACCG       ATCTGGTGCTCTGTCATCCCCATC         HF-Site3-OT3       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNCCACACCTGATGGCT       ATCTGGCTCATTGCATCCTTGACC         HF-Site3-OT4       GGTAGCTCTNCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         HF-Site3-OT5       ACACTCTTTCCCTACACGACGCTCTT       GGTAGGCTGAATAATGGCCCC         genomic site       CCGATCTNNNNCGACATCCTGGGTCA       TGGAGTTCAGACGTGTGCTCTTCCG         MR-Site4-OT1       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNGGGTGGATCATGAG       ATCT         NR-Site4-OT1       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         GTCAGG       GTCAGG       ATCTGATGCTCAGTCAGTCTGTCACCCA	HF-Sile3-012			
HF-Site3-OT3 genomic site       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCACACCTGATGGCT CACTC       TGGAGTTCAGACGTGTGCTCTTCCG ATCTGGCTCATTGCATCCTGACC         HF-Site3-OT4 genomic site       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCTTGGCTTGTGGAC CAGTA       TGGAGTTCAGACGTGTGCTCTTCCG ATCT GGTAGGCTGAATAATGGCCCC         HF-Site3-OT5 genomic site       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGACATCCTGGGTCA TTGCT       TGGAGTTCAGACGTGTGCTCTTCCG ATCT CCGATCTNNNNCGACATCCTGGGTCA TTGCT         NR-Site4-OT1 genomic site       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGGGTGGATCATGAG GTCAGGG       TGGAGTTCAGACGTGTGCTCTTCCG ATCT CTCTCTGACTGGGCTGCTTTCCG	genomic site		ATCIGGIGCICIGICATCCCCATC	
HF-Site3-013       ACACTCTTTCCCTACACGACGCTCTT       IGGAGTTCAGACGTGTGTCTTCCG         HF-Site3-074       ACACTCTTTCCCTACACGACGCTCTT       ATCTGGCTCATGCACGACGTGTGCTCTTCCG         genomic site       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         HF-Site3-075       ACACTCTTTCCCTACACGACGCTCTT       GGTAGGCTGAATAATGGCCCC         genomic site       CCGATCTNNNNCGACATCCTGGGTCA       TGGAGTTCAGACGTGTGCTCTTCCG         NR-Site4-071       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNGGGTGGATCATGAG       ATCT         Order       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG       ATCT         Order       CCGATCTNNNNGGGTGGATCATGAG       ATCTGATGCTCAGTCTGTCACCCA	HE Site? OT?		TOCACTTCACACCTCTCCTCTCTCCC	
genomic site       CCGATCTINNINCCACACCTGATGGCT       ATCTGGCTCATGCATGCTGATGCCT         HF-Site3-OT4 genomic site       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCTTGGCTTGTGGAC CAGTA       TGGAGTTCAGACGTGCTCTTCCG ATCT GGTAGGCTGAATAATGGCCCC         HF-Site3-OT5 genomic site       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGACATCCTGGGTCA TTGCT       TGGAGTTCAGACGTGTGCTCTTCCG ATCT CTCTCTGACTGGGCTGCTTT         NR-Site4-OT1 genomic site       ACACTCTTNCCTACACGACGCTCTT CCGATCTNNNNGGGTGGATCATGAG GTCAGGG       TGGAGTTCAGACGTGTGCTCTTCCG ATCT CTCTCTGACTGGGCTGCTCTTCCG				
HF-Site3-OT4 genomic site       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCTTGGCTTGTGGAC CAGTA       TGGAGTTCAGACGTGTGCTCTTCCG ATCT         HF-Site3-OT5 genomic site       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNCGACATCCTGGGTCA       TGGAGTTCAGACGTGTGCTCTTCCG ATCT         NR-Site4-OT1 genomic site       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGACATCCTGGGTCA       TGGAGTTCAGACGTGTGCTCTTCCG ATCT         NR-Site4-OT1 genomic site       ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGGGTGGATCATGAG       TGGAGTTCAGACGTGTGCTCTTCCG ATCT	genomic site		ATTIGUTUATIGUATUUTIGAUU	
genomic site     ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCCTTGGCTTGTGGAC CAGTA     ATCT GGTAGGCTGAATAATGGCCCC       HF-Site3-OT5 genomic site     ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNCGACATCCTGGGTCA TTGCT     TGGAGTTCAGACGTGTGCTCTTCCG ATCT CTCTCTGACTGGGCTGCTCTT       NR-Site4-OT1 genomic site     ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGGGTGGATCATGAG GTCAGG     TGGAGTTCAGACGTGTGCTCTTCCG ATCT CTCTCGACTGGGCTGCTCTTCCG ATCT CTCTGACTGGGCTGCTCTTCCG ATCTGATGCTCAGCCGACGCTCTT	HF-Site3-OT4		TGGAGTTCAGACGTGTGCTCTTCCC	
genomic site       ACACTCTTNOCCTACACGACGCTCTT       ATCT         GGTAGGCTGAATAATGGCCCC       GGTAGGCTGACTAATGGCCCC         HF-Site3-OT5       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNCGACATCCTGGGTCA       ATCT         TTGCT       CTCTCTGACTGGGCTGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         NR-Site4-OT1       ACACTCTTTCCCTACACGACGCTCTT       TGGAGTTCAGACGTGTGCTCTTCCG         genomic site       CCGATCTNNNNGGGTGGATCATGAG       ATCTGATGCTCAGTCTGTCACCCA	denomic site		ATCT	
CAGTA     CAGTA       HF-Site3-OT5     ACACTCTTTCCCTACACGACGCTCTT     TGGAGTTCAGACGTGTGCTCTTCCG       genomic site     CCGATCTNNNNCGACATCCTGGGTCA     ATCT       NR-Site4-OT1     ACACTCTTTCCCTACACGACGCTCTT     TGGAGTTCAGACGTGTGCTCTTCCG       genomic site     CCGATCTNNNNGGGTGGATCATGAG     ATCTGATGCTCAGCGTGTGCTCTTCCG       GTCAGG     ATCTGATGCTCAGTCTGTCACCCA     GTCAGGG	genomic site		GGTAGGCTGAATAATGGCCCC	
HF-Site3-OT5 genomic site     ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNCGACATCCTGGGTCA TTGCT     TGGAGTTCAGACGTGTGCTCTTCCG ATCT CTCTCTGACTGGGCTGCTTT       NR-Site4-OT1 genomic site     ACACTCTTTCCCTACACGACGCTCTT CCGATCTNNNNGGGTGGATCATGAG GTCAGG     TGGAGTTCAGACGTGTGCTCTTCCG ATCTGATGCTCAGCCGACGCTCTT			GUIAGGUIGAAIAAIGGUUUU	
genomic site     CCGATCTNNNNCGACGCTCCTGGGTCA TTGCT     ATCT CTCTCTGACTGGGCTGCTTT       NR-Site4-OT1     ACACTCTTTCCCTACACGACGCTCTT     TGGAGTTCAGACGTGTGCTCTTCCG ATCTGATGCTCAGCCGTGCTCTTCCG       genomic site     GCGATCTNNNNGGGTGGATCATGAG     ATCTGATGCTCAGTCTGTCACCCA	HF-Site3-OT5		TGGAGTTCAGACGTGTGCTCTTCCC	
genomic site         CCGATCTINININGGAGATOGTOGGATOA         ATCT           TTGCT         CTCTCTGACTGGGCTGCTTT           NR-Site4-OT1         ACACTCTTTCCCTACACGACGCTCTT         TGGAGTTCAGACGTGTGCTCTTCCG           genomic site         CCGATCTNNNNGGGTGGATCATGAG         ATCTGATGCTCAGTCTGTCACCCA           GTCAGG         GTCAGG         ATCTGATGCTCAGTCTGTCACCCA	aenomic site			
NR-Site4-OT1     ACACTCTTTCCCTACACGACGCTCTT     TGGAGTTCAGACGTGTGCTCTTCCG       genomic site     CCGATCTNNNNGGGTGGATCATGAG     ATCTGATGCTCAGTCTGTCACCCA	genomic site	TTGCT		
genomic site CCGATCTNNNNGGGTGGATCATGAG ATCTGATGCTCAGTCTGTCACCCA GTCAGG	NR-Site/LOT1			
GTCAGG	denomic site			
	genomic site	STORIO INNININGOO I GOAT CATGAG	A STORIOUTOROTOROTOROTOR	

NR-Site4-OT2	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CCGATCTNNNNAAGCACAGAGATAAA	ATCTTCCCTCTGGCTTCTTTTAAGTT	
	AGGACAGA	TT	
NR-Site4-OT3	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site			
NR-Site/-OT/			Also used for C-Site4-OT2 and C-
denomic site		TGGAGTTCAGACGTGTGCTCTTCCG	Site4-OT4
genomio site	TCCCA	ATCTAGGGCCGCCATACCATATTG	0104 014
C-Site4-OT1	ACACTCTTTCCCTACACGACGCTCTT		
genomic site	CCGATCTNNNNCAACAAATGATGCTG	TGGAGTTCAGACGTGTGCTCTTCCG	
	GCCGC	ATCTTTGTTTGGAGAGGGGAGTGC	
C-Site4-OT3	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CCGATCTNNNNTCCAATATGGTATGG	ATCTGAGGATCCCACGTTAGTGCC	
	CGGCC		
S-Site4-011			Also used for HF-Site4-OT1
genomic site	CCGATCTINININTGCTCATGGGATAGT	ATCTTTCTCTGCCAGCCCTAGGA	
S-Site4-OT2		TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CCGATCTNNNNAGGCAGGAGAGTAA	ATCTTCCCCTTACACAACACACCTG	
generine ene	CTGGTCT		
S-Site4-OT3	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CCGATCTNNNNCCGAGCCCTTTAGCG	ATCTTTTGCGGCCCAAATCTCCTT	
	CTAAT		
S-Site4-OT4	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CCGATCTNNNNTCTCTGGGATCCTCA	ATCTCCATGTTCTCGCCAAAGCTG	
	GCCIG	100401104040010101010100	
NR-Site5-011			
genomic site		ATCTCACTGTGGCTGGGAATCCTT	
NR-Site5-OT2		TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CCGATCTNNNNTGAGAACAAGCTCAG	ATCTACTCCGTAGCATGGCTGTTC	
3	CCCAG		
C-Site5-OT1	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CCGATCTNNNNGGTGACTCCATTGCC	ATCTTACTCCTCAGGCACTCACCA	
	AAGGA		
C-Site5-OT2	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site		ATCTCCCATGCCCATTCTGCCTAT	
C-Site5-OT3		TEGAGTICAGACGTETECTCTTCCG	
genomic site		ATCTGACAATTCGCTGTCCACGTG	
gonomio olto	TTGA		
C-Site5-OT4	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CCGATCTNNNNACAGAATATTCCACT	ATCTGACACTTTGCTTGCTTCTGTGT	
	GTTGATGAAAA		
S-Site5-OT1	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CCGATCTNNNNGACCCAACCTGAGAC	ATCTACAGAGGCTAGCCAGTACCT	
0.0%+5.070		TOCACTTOACACOTOTOCTOTOC	
S-Sileo-012			
genomic site	AGTAGA	ATCHIGHTIGGGGAAGGAAGGAAGGCTT	
S-Site5-OT3	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CCGATCTNNNNCCAACTCCGAGCTCC	ATCTTGTAGGCTGACAATGGCTGG	
•	TTCTC		
S-Site5-OT4	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CCGATCTNNNNGTGAAGCCAAGGTG	ATCTCAGCCTCAGCAAGACCTCAC	
	AGCAGA		
HF-Site5-011			
		ATCHIGGATCHIGCCTCHIGAGCA	
HE-Site5-OT2		TGGAGTTCAGACGTGTGCTCTTCCG	
	CCGATCTNNNNGGTCACTTCCTGTGT	ATCTATCGGAGCATGAGAGAAGGC	
	TTAATGGC		
NR-Site6-OT1	ACACTCTTTCCCTACACGACGCTCTT		
	CCGATCTNNNNCTGTGAGGCTCAGTT	TGGAGTTCAGACGTGTGCTCTTCCG	
	TCTGA	ATCTTGTGCATCTAGTCACCCTACAC	
NR-Site6-OT2		TOOLOTTOLOGAOOTOTOTOTOTO	Also used for C-Site6-OT3
NR-Site6-OT2		TGGAGTTCAGACGTGTGCTCTTCCC	
	CCGATCTNNNNGCACGATTGACAGGT	ATCTGACTATAAGTGCCTGCCACCA	
	CATGG		

C-Site6-OT1	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
	CCGATCTNNNNCGCACACTCTGTCAA	ATCTTGGGAGCCAGAGAAGGAAAG	
	ATGGC		
C-Site6-OT2	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
	CCGATCTNNNNGGAGGTGCCAGGTT	ATCTACTAGGTGGAGTCCGGATGA	
	CCTTT		
C-Site6-OT4	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
	CCGATCTNNNNGCATTCGCATGGTGC	ATCTTTTCCTTCTGCCACACCCAG	
	AGTAG		
S-Site6-OT1	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
		ATCTAGTTGACAGGGGATTGGCTT	
	TCAGCA		
S Sitos OT2		TECACITEACACCITETECT	
3-51160-012			
		ATCTCCAGCCAGATGACTGACACT	
C CiteC OT2			
3-31160-013		TOOLOTTOLOOLOTOTOTOTOTO	
0.0% 0.074		ATCITGACCCTTTCTGGCTTCAGAC	
S-Site6-014			
	CCGATCINNNNAAGCGATCCACTCAC	IGGAGIICAGACGIGIGCICIICCG	
	CIIGG	AICIICGIGGCCIICIIICIIICCA	
S-Site6-OT5	ACACTCTTTCCCTACACGACGCTCTT		
	CCGATCTNNNNGGCAAAGGGATGGA	IGGAGTTCAGACGTGTGCTCTTCCG	
	TTGGGA	ATCTTAGCTTTGTGGCATCAGGTGA	
HF-Site6-OT1	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
	CCGATCTNNNNCATCATTTGCATGCA	ATCTTTGTTATGGTCAATTATCAGGA	
	GACTTGT	TGGA	
	ACACTCTTTCCCTACACGACGCTCTT		
HBB-NRCH-OT1	CCGATCTNNNNTGGGCTTGTTTGGTA	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CTTCC	ATCTACCATTTGGCAAACACCACA	
0	ACACTCTTTCCCTACACGACGCTCTT		Also used for HBB-Nme-OT1
HBB-NRCH-OT2	CCGATCTNNNNAAACAGCCCAAGGG	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	ACAGAG	ATCTAGCATAAAAGGCAGGGCAGA	
generate			Also used for HBB-Nme-OT5
HBB-NRCH-OT3		TEGAGTTCAGACGTETECTCTTCCG	Also discu foi TIBB-Nille-OTS
aonomio sito	CACCO		
genomic site		ATCTCATCTCTCATCCACCTCCCC	
		TOCACTTOACACOTOTOCTOTTOCO	
genomic site		ATCTAGCCAAGTGGTTGTGAGGAG	
HBB-NRCH-015		IGGAGITCAGACGIGIGCICTICCG	
genomic site	AGIGA	ATCTIGTIGGCACCTGTAGTCCCA	
	ACACICITICCCTACACGACGCTCTT		
HBB-NRCH-OT6	CCGATCTNNNNAGCCACATCTTGCTC	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	TIGCI	ATCTCAGTCTCCTAAGGTGCTGGG	
	ACACTCTTTCCCTACACGACGCTCTT		
HBB-NRCH-OT7	CCGATCTNNNNGTCCCCACTCTGTTG	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	GAAGG	ATCTGAGCACCCCACTCCAGAAAA	
	ACACTCTTTCCCTACACGACGCTCTT		
HBB-NRCH-OT8	CCGATCTNNNNAGGGACTGAAGCCA	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site		ATCTCAGGAGTCACGTGTCAAGGT	
	ACACTCTTTCCCTACACGACGCTCTT		
HBB-NRCH-OT9	CCGATCTNNNNTGCCTCCTTTGAGCC	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	ATTTGA	ATCTGCATGGTGAGTTTAAGGGCC	
	ACACTCTTTCCCTACACGACGCTCTT		Also used for HBB-Nme-OT8
HBB-NRCH-OT10	CCGATCTNNNNACAGGTATGAGCCAC	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	TGTGC	ATCTGCAAGAAAGGGCATGGTGTG	
	ACACTCTTTCCCTACACGACGCTCTT		Also used for HBB-Nme-OT9
HBB-NRCH-OT11	CCGATCTNNNNAACCAGTAAGTCAGG	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CCTGC	ATCTTTGGGCCACAAGGTCTTTCA	
_	ACACTCTTTCCCTACACGACGCTCTT		
HBB-Nme-OT2	CCGATCTNNNNTTGCAATGGAACCAT	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CTTTCTGG	ATCTTGGATGGTTCACATGGCACT	
	ACACTCTTTCCCTACACGACGCTCTT		
HBB-Nme-OT3	CCGATCTNNNNGGTTGTGAGGTAGG	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	GTTGGG	ATCTIGITGTATGGGTGCTGCTGT	
30			
HBB-Nme-OT4	CCGATCTNNNNATCTGAGGTGCCTTG	TGGAGTTCAGACGTGTGCTCTTCCC	
denomic site		ΑΤΟΤΩΟΤΩΔΩΟΟΟΟΙΟΙΟΟΙΟΙΙΟΟΟ	
genomic alle		ATTICTOROCOROCOROTATI	
HBB-Nmo-OT6		TGGAGTTCAGACGTGTGCTCTTCCC	
genomic site	GGAGC		

HPR Nma OT7		TOCACTTOACACOTOTOCTOTOCO	
genomic site		ATCTCAAACAAAAGGGAGCCAGGC	
Site 7 OT1		TOCACTTOACACOTOTOCTOTTOCO	
genomic site		ATCTGCCACCTGCGTGAAAATGTT	
Site 7 OT2		TOCACTTOACACOTOTOCTOTOCO	
Site 7-012			
genomic site	GGAAG	ATCITCCAAGTCAGACTCACGGGA	
011 7 070			
Site 7-013			
genomic site	AGIGI	ATCIGGICACCCGAGAATGGAGAC	
01 7 074			
Site 7-014	CCGATCINNNNGGAGTIGAATCIGAC		
genomic site		ATCTCTCCACTGTGGGCTTCTCAA	
0.1 7 0 7 5	ACACICITICCCTACACGACGCICIT		
Site 7-015	CCGATCINNNNIGAGGIIGIICACIG	IGGAGIICAGACGIGIGCICIICCG	
genomic site	GAICCA	ATCTCAGATGAAGTCAGGGTGAGGC	
0.4 7 0 7 0	ACACICIIICCCIACACGACGCICII		
Site 7-016	CCGATCINNNNICCIGCICAGIICCA	IGGAGIICAGACGIGIGCICIICCG	
genomic site	GIIGC	ATCTTGGCCTCACTTTGTCACACC	
	ACACICITICCCTACACGACGCTCTT		
Site 7-017		IGGAGIICAGACGIGIGCICIICCG	
genomic site	IIIGG	ATCTCTCTACCACATCCCAGCACC	
	ACACTCTTTCCCTACACGACGCTCTT	TGGAGTTCAGACGTGTGCTCTTCCG	
Site 7-OT8	CCGATCTNNNNGGCTGGTAGCTTTTG	ATCTCCATATCTGTCCACAAATGAGT	
genomic site	TACTGGA	CC	
	ACACTCTTTCCCTACACGACGCTCTT		
Site 7-OT9	CCGATCTNNNNCAAGGGGAAAAGGC	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CAGAGG	ATCTTGACTTTGTGGCCAACTTGC	
	ACACTCTTTCCCTACACGACGCTCTT		
Site 7-OT10	CCGATCTNNNNTAGACAAAGGATGTT	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	GGGGCC	ATCTAGCAGGAGACAGACTCAGCA	
	ACACTCTTTCCCTACACGACGCTCTT		
Site 7-OT11	CCGATCTNNNNCCACGACTGGAGCT	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	GAAGAA	ATCTATTCAAGCCTGCTGGGGTG	
	ACACTCTTTCCCTACACGACGCTCTT		
Site 7-OT12	CCGATCTNNNNTTCTTGCCACTCTTG	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	GGGAC	ATCTGGCCCCAAAGAGTTCCTCTC	
	ACACTCTTTCCCTACACGACGCTCTT		
Site 8-OT1	CCGATCTNNNNCCTTCAAGGGACCCA	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	IGAGG	ATCTAATCATGTCGATCCTGGGGGC	
	ACACICITICCCTACACGACGCTCTT		
Site 8-012	CCGATCINNNNGCIGGAAGGGCCCA	IGGAGIICAGACGIGIGCICIICCG	
genomic site		ATCTIGTAAGGCCAGTGTCCAAAGG	
	ACACICITICCCTACACGACGCTCTT		
Site 8-013		IGGAGIICAGACGIGIGCICIICCG	
genomic site			
	ACACICITICCCTACACGACGCTCTT		
Site 8-014			
genomic site			
01 0 0T-		T00407704040670707777777	
Site 8-015			
genomic site	GCCAG	ATCIGCICIGIGAGIGCCIIGCIA	
		10040770404040707070707070	
genomic site			
		TOCACTTOACACOTOTOCTOTOC	
genomic site		ATTIGUCAGGIUTUTGUAGITIUA	
Sito 8 OTO		TECACITCACACOTOTOTOTOTOT	
Sile 0-010			
genomic site		ATCHIGHTACIGIGGACCCCI	
Sito 8 OTO		TECACITCACACOTOTOTOTOTOT	
	CCCCT		
genomic site		ATTACAGGATCCACCATGACACG	
Site 8-OT10		TEGAETTCACACCTETECTOTTCCC	
denomic sito	GAAGTO		
genomic site			
Site 8-OT11		TEGAETTCAEACETETECTCTTCCC	
genomic site	ATGGA	ATCTTTCTGTGGATGTCTGTGGGC	
genomic site	11001		

	ACACTCTTTCCCTACACGACGCTCTT		
Site 8-OT12	CCGATCTNNNNGGGTGGGGAGTTTC	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	AGGAAG	ATCTTCACCCCACACTGGTAGACT	
0	ACACTCTTTCCCTACACGACGCTCTT		
Site 8-OT13	CCGATCTNNNNCTAGCTGTGTCTTGC	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	СТӨСТ	ATCTCTGCTGGTTCTTTTTCGCCC	
Ŭ	ACACTCTTTCCCTACACGACGCTCTT		
Site 8-OT14	CCGATCTNNNNCACCCACTCCCATCA	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	ACACC	ATCTACTCCGGCAGTGGTAGTACT	
	ACACTCTTTCCCTACACGACGCTCTT		
Site 8-OT15	CCGATCTNNNNACCAGCAGTGCAATC	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	TAGACTT	ATCTAACAAGCCTGTTTGAGGATGC	
0	ACACTCTTTCCCTACACGACGCTCTT		
Site 8-OT16	CCGATCTNNNNCCACCACCTCCACAT	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	GGATC	ATCTTGTGAAGCAGAGAGGTCAGC	
0	ACACTCTTTCCCTACACGACGCTCTT		
Site 8-OT17	CCGATCTNNNNAGCTTTCCTAGGGAG	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	GGAGG	ATCTCCCCTTCTAACACCCCTTGC	
	ACACTCTTTCCCTACACGACGCTCTT		
Site 8-OT18	CCGATCTNNNNCTGTCCTGCCATTCC	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CCTAC	ATCTTCACCCAACTCAGCGTTTGA	
	ACACTCTTTCCCTACACGACGCTCTT		
Site 8-OT20	CCGATCTNNNNTCCCCATTTCACACT	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CTCCC	ATCTGCCTGGGTGACAAGAGCAA	
	ACACTCTTTCCCTACACGACGCTCTT		Also used for Site 8-OT22
Site 8-OT21	CCGATCTNNNNAGCCTCAGCCCATAC	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	AGAGA	ATCTCCGATGGCCATCAGGATCAT	
	ACACTCTTTCCCTACACGACGCTCTT		
Site 8-OT23	CCGATCTNNNNGCAGTAAAGTGATGC	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CCCCT	ATCTAAGTTTCGCTAGGGTGCAGT	
	ACACTCTTTCCCTACACGACGCTCTT		
Site 8-OT25	CCGATCTNNNNGAGGCTGTGTCCATG	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	ATGCT	ATCTCTCTTTCAGCTGGGTCAGGG	
	ACACTCTTTCCCTACACGACGCTCTT		
Site 8-OT27	CCGATCTNNNNGATAGTGGTGCTGG	TGGAGTTCAGACGTGTGCTCTTCCG	
genomic site	CTGAGG	ATCTTGGGTTCCCATTCACCAAGG	

## Supplementary Table 9. Chemically-synthesized guide RNAs used for HDFa cells

Site/Guide ID*	Protospacer sequence (5'-3')	sgRNA scaffold (5'-3')
ACC-1/Nme1	CGCAAAGCTGCATCCACCCCCCG	GTTGTAGCTCCCTTTCTCATTTCGGAAACGAAATGAGAACCGTTGCTA
		CAATAAGGCCGTCTGAAAAGATGTGCCGCAACGCTCTGCCCCTTAAAG
		CTTCTGCTTTAAGGGGCATCGTTTATTTT <sup>^</sup>
GCA-1/Nme11	GGGTCCAAAGCAGGATGACAGGCA	GTTGTAGCTCCCTTTCTCATTTCGGAAACGAAATGAGAACCGTTGCTA
		CAATAAGGCCGTCTGAAAAGATGTGCCGCAACGCTCTGCCCCTTAAAG
		CTTCTGCTTTAAGGGGCATCGTTTATTTT
TCA-1/Nme14	TGGCTACAGCAACAGGGTGGTGG	GTTGTAGCTCCCTTTCTCATTTCGGAAACGAAATGAGAACCGTTGCTA
000 1/Nm 10		
CCG-I/INITIETo	GICICCGCITTAACCCCCACCIC	
GCG-1/Nme22	GGTGTGCAGACGGCAGTCACTAG	
		CTTCTGCTTTAAGGGGCATCGTTTATTTT
GCT-1/Nme29	GCACAACCAGTGGAGGCAAGAGG	GTTGTAGCTCCCTTTCTCATTTCGGAAACGAAATGAGAACCGTTGCTA
		CAATAAGGCCGTCTGAAAAGATGTGCCGCAACGCTCTGCCCCTTAAAG
		CTTCTGCTTTAAGGGGCATCGTTTATTTT <sup>^</sup>
GCT-2/Nme30	GAAATGGCACACACATCCCTCGT	GTTGTAGCTCCCTTTCTCATTTCGGAAACGAAATGAGAACCGTTGCTA
		CAATAAGGCCGTCTGAAAAGATGTGCCGCAACGCTCTGCCCCTTAAAG
		CTTCTGCTTTAAGGGGCATCGTTTATTTT
100 1/0 51/1		
ACC-1/SpRY1	GCTGCATCCACCCCCGAGG	SpCas9 sgRNA EZ Kit scatfold from Synthego (with 2'-O-Methyl and 3'
		phosphorothioate bond modifications)
GCA-1/SPR14	AAGCAGGATGACAGGCAGGG	SpCase sgRina EZ Kit scaffold from Synthego (with 2 -O-Methyl and 3
TCA-1/SpRV7		SpCas9 sqRNA EZ Kit scaffold from Synthego (with 2'-O-Methyl and 3'
	000000000000000000000000000000000000000	phosphorothioate bond modifications)
CCG-1/SpRY9	GCTTTAACCCCCACCTCCAG	SpCas9 sqRNA EZ Kit scaffold from Syntheon (with 2'-O-Methyl and 3'
		phosphorothioate bond modifications)
GCG-	CAGACGGCAGTCACTAGGGG	SpCas9 sgRNA EZ Kit scaffold from Synthego (with 2'-O-Methyl and 3'
1/SpRY10		phosphorothioate bond modifications)
GCT-1/SpRY12	CCAGTGGAGGCAAGAGGGCG	SpCas9 sgRNA EZ Kit scaffold from Synthego (with 2'-O-Methyl and 3'
•		phosphorothioate bond modifications)
GCT-2/SpRY13	GCACACACATCCCTCGTGCA	SpCas9 sgRNA EZ Kit scaffold from Synthego (with 2'-O-Methyl and 3'
		phosphorothioate bond modifications)

\*See Supplementary Table 5 for list of target sites ^Nme2Cas9 chemically-synthesized sgRNAs ordered from IDT, including 2'-O-Methyl and 3' phosphorothioate bond modifications, as previously described<sup>10</sup>

### Supplementary Note 1. ePACE pressure regulation

As IPP devices are sensitive to changes in pressure at valves and in connected media bottles, we developed an 8-channel pressure regulator that can be used to regulate these pressures through the eVOLVER framework. The device consists of sets of two proportional valves that can limit air flow from a high-pressure source and a vent at atmospheric pressure. By connecting an electronic pressure gauge to the output of this valve configuration, it is possible to implement proportional-integral-derivative (PID) control over the valves in order to set the output pressure to any desired level between the input and atmospheric pressure. We validated the functionality of this device by regulating pressure at 1.5 psi over 24 hours, and compared the performance of our device with that of a fixed, manually set regulator (PARKER-WATTS R25-02A) connected to the benchtop air supply (Supplementary Figure 3). The average pressure with PID control was 1.498 psi with an RMS error of 0.0086 psi, while the fixed regulator had an average pressure of 1.706 psi with an RMS error of 0.2220 psi. Large pressure deviations (>0.5 psi) that can affect the performance of the devices were observed with the fixed regulator, but were successfully eliminated with our automated pressure regulator scheme. We further characterized the effects of pressure changes at various locations in the system in order to optimize performance of the IPP devices for the course of a PACE experiment (Supplementary Figure 3).

#### Supplementary Note 2. ePACE2 recombination and cheating

During ePACE2, evolving Nme2Cas9 variants on the SP appeared to propagate well in all lagoons on targeted PAMs (each of the eight N<sub>3</sub>YTN PAMs). Phage were sampled from some lagoons, and the insert was amplified via PCR. Following agarose gel electrophoresis, we found that these SP pools appeared to lose the expected Nme2Cas9 insert, as the resulting bands no longer corresponded to the correct insert size (**Supplementary Fig. 8a**). Sanger sequencing of the incorrectly sized band revealed a region of nucleotide homology between the N-terminus of the gIII construct on the AP and gVI in the phage genome (**Supplementary Fig. 8b,c**). This site of homology was likely acting as a recombination site enabling some phage to incorporate the gIII-C half into the SP genome. As gIII-N is constitutively expressed in the original SAC-PACE selection, this enables phage to propagate in a selection genomic siteree manner. For subsequent evolutions, we altered the codon usage of the N-terminus of gIII within the AP, such that the nucleotide homology was no longer present (pTPH412, **Supplementary Table 7**). Following this alteration, recombination was no longer observed.

#### Supplementary Note 3. Validation of the split base editor SAC-PACE selection

To enable control over the expression of active enzyme in the SAC-PACE selection, we split Nme2ABE8e at the linker sequence between TadABE8e and Nme2Cas9. The TadABE8e-half was linked to the N-terminal half of the gp41-8 intein (gp41-8N), and this entire construct (TadABE8e-gp41-8N) was placed on a complementary plasmid (CP) under the control of a psp-promoter and a user-defined ribosome binding sequence. The C-terminal half of the base editor (dNme2Cas9) was linked to the C-terminal half of the gp41-8 intein (gp41-8C), and this construct (gp41-8C-dNme2Cas9) was recloned into the SP architecture (SP404, **Supplementary Table 7**). The split SAC-PACE selection was then validated by overnight propagation using new split-SP and host cells containing both AP and CP.

While testing the split SAC-PACE selection, we wanted to select a TadA variant with the highest Cas-*dependent* activity to limit bottlenecking the selection at the deamination step. In addition to TadABE8e, we tested the TadABE8e-R26G point mutant that had converged in prior evolutions (**Supplementary Fig. 6a, 10a**). TadABE8e-R26G enabled 10-to 20 genomic siteoid stronger propagation compared to wild-type TadABE8e in a Cas-dependent manner, with no propagation in host-cells lacking Nme2Cas9. Moving forward, we chose to use TadABE8e-R26G in split base editor SAC-PACE selections (split SAC-PACE).

## Supplementary Note 4. PAM-specific activity of ePACE4 evolved variants observed in ABE-PPA.

Activity improvements of ePACE4 variants on specific PAMs appeared to be agnostic of the PAM targeted during evolution, with most variants preferring  $N_4CA > N_4CC > N_4CT >$  $N_4CG$ . The exceptions were variants evolved on the  $N_3TCG$  PAM, which exhibited  $N_4CG$ activity comparable to or better than activity on the other three  $N_4CD$  PAMs. This result would suggest that binding of the position 6 G is distinct from binding to the other three nucleobases. In line with this hypothesis, the mutation profiles in the PID are relatively conserved between variants evolved on the  $N_3TCA$  and  $N_3TCT$  APs (S933R, R1033S/G, Q1047R); however, additional mutations outside of the three seen in those variants converged in the  $N_3TCG$  trajectory (D873V, E932K, D961G, N1031D/S, K1044R, E1045A, K1077E) (**Extended Data Fig. 3c**). We note, however, that the difference in activity between the variants was nuanced, as the overall trend reflects general improvements to activity on all N<sub>4</sub>CN PAMs (**Extended Data Fig. 3b**).

#### Supplementary Note 5. Reversion analysis of eNme2-C RuvC/HNH domain mutations.

Simple reversion of the RuvC-inactivating mutation D16A in eNme2-C did not yield a robust nuclease Cas9. Upon reversion of the eight mutations in the RuvC/HNH domains and their associated linker regions to their wild-type residues, the resulting variant eNme2-C.NR had robust nuclease activity across N<sub>4</sub>CN PAM sites. However, reversion of these mutations had a detrimental effect on base editing activity, as the ABE8e version of eNme2-C.NR had a 1.8 genomic siteold reduction in adenine base editing activity relative to eNme2-C-ABE8e (**Extended Data Fig. 7e**). These results would suggest that some or all the mutations in the RuvC/HNH domains are important for Nme2Cas9 activities necessary for base editing, but detrimental to the subsequent activation or catalytic activity of Nme2Cas9 nuclease.

To further explore this idea and to potentially find an optimal dual base editor/nuclease variant, we generated the set of eight single-point reversion variants of mutations in the RuvC/HNH domains of eNme2-C and evaluated them as nucleases and ABEs (**Extended Data Fig. 7e,f**). Only two of the eight single-point reversion variants, eNme2-C V696F and eNme2-C R711G, showed significant rescue of nuclease activity (12.5- and 4.4 genomic siteold improvement over eNme2-C, respectively). Conversely, most of the reversions reduced ABE efficiency relative to eNme2-C-ABE8e. Notably, none of the eight variants outperformed eNme2-C as an ABE or eNme2-C.NR as a nuclease, highlighting the importance of the amino acid identities at these RuvC/HNH positions in differentiating between base editor and nuclease activities of evolved Nme2Cas9.

## Supplementary Note 6. Analysis and limitations of BE-PPA for evaluating Nme2Cas9 PAM compatibility.

All Nme2Cas9 variants (wild-type and evolved) were profiled using ABE-PPA on a single protospacer ("ABE-PPA", see **Supplementary Table 5**) flanked by 512 unique PAMs (pTPH424, see **Supplementary Tables 1 and 7**). The 512 unique PAMs are only a subset of the theoretical PAM space potentially encompassed by Nme2Cas9 (a six base pair region encompasses 4,096 targetable sequences). We designed the library to observe PAM compatibilities primarily at PAM positions 4-7 (NNN<u>NNN</u>, 256 combinations), as we hypothesized that the positions that would most likely alter their nucleotide preference during

evolution are the positions canonically recognized by the wild-type enzyme (PAM positions 5 and 6, ± 1 base). We also included two groups of sequences at PAM positions 1-3 (<u>ACGNNNN or CATNNNN</u>), giving the total 512 PAM sequences, although these positions were pooled during analysis. We limited the library size to 512 members for throughput-purposes, as this number allows for profiling of up to 8 variants on an Illumina MiSeq kit (15 m reads, 1.9 m reads per variant, ~4,000 reads per PAM assuming equal distribution). We note that by limiting the analysis to these positions, it is possible that the PAM compatibility observed is biased by the identity of the bases chosen for positions 1-3, the selected protospacer, or the target adenine position. A larger library may be useful for more comprehensive PAM profiling of final variants. Nevertheless, the subset library used in this work provided a rapid, high-throughput method for quickly filtering evolved variants with desired PAM compatibilities and high efficiencies.

To analyze BE-PPA sequenced files, the demultiplexed fastq files were filtered using the seqkit package/grep function<sup>11</sup> to search for two flank sequences near either end of the amplicon. For ABE-PPA profiled variants, groups of PAMs were UMI-tagged, and the specific UMI tag was used in place of one of the flank sequences. Filtered files were then binned into individual fastq files per PAM using the same function. The resulting PAM-specific fastq files were analyzed using standard CRISPResso2<sup>12</sup> analysis.

## Supplementary Note 7. Design error for the N₄CN trajectory dual PAM split SAC-PACE APs.

When designing the dual PAM split SAC-PACE APs (pTPH418b, see **Supplementary Table 5**), the identity of PAM positions 1-3 were set as CTT and AGG for the two target PAMs, both of which fall on the non-coding strand. The TT nucleotides of the CTT-containing PAM occupy codon positions two and three for an arbitrary codon within the AP linker. Notably, when the target PAM is designed to be 3'-CTT<u>ACN</u>-5', the 3'-TTA-5' nucleotides introduce an additional stop codon in the PAM (5'-TAA-3' on coding strand), preventing proper correction of the AP. As such, none of the dual PAM split SAC-PACE APs containing an A at PAM position 4 were able to support phage propagation, as observed.

### Supplementary Note 8. Evolved Nme2Cas9 amino acid sequences.

### eNme2-C:

MAAFKSNPINYILGLDIGIASVGWAMVEIDEEGNPIRLIDLGVRVFERAEVPKTGDSLAMARRL ARSVRRLTRRRAHRLLRARRLLKREGVLQAADFDENGLITSLPNTPWQLRAAALDRKLTPLE WSAVLLHLIKHRGYLSQRKNEGETAAKELGALLKGVANNAHALQTGDFRTPAELALNKFEKE SGHIRNQRGDYSHTFSRKDLQAELILLFEKQKEFGNPHVSGGLKEGIETLLMTQRPALSGDA VQKMLGHCTLEPTEPKAAKNTYTAERFIWLTKLNNLRILEQGSERPLTDTERSTLMDEPYRK SKLTYAQARKLLGLEDTAFFKGLRYGKDNAEASTLMEMKAYHAISRALEKEGLKDKKSPLNL SSELQDEIGTAFSLFKTDEDITGRLKDRVQPEILEALLKHISFDKFVQISLKALRRIVPLMEQGK RYDEACAEIYGVHYGKKNTEEKIYLPPIPADEIRNPVVLRALSQARKVINGVVRRYGSPARIHI ETAREVGKSFKDRKEIAKRQEENRKDREKAAAKFREYFPNFVGEPKSKDILKLRLYEQQHGK CLYSGKEINLVRLNEKGYVEIDHALPFSRTWDDSFNNKVLVLGSENQNKGNQTPYEYFNGK DNSREWQEFKARVETSRFPSSKKQRILLQKFDEDGFKECNLNDTRYVNRFLCQFVADHILLT GKGKRRVVASNGQITNLLRGFWRLRKVRAENDRHHALDAVVVACSTVAMQQKITRFVRYKE MNAFDGKTVDKETGKVLYQKTHFPQPWEFFAQEVMIRVFGKPDGKPEFEEADTPEKLRTLL AEKLSSRPEAVHEYVTPLFVSRAPNRKMSGAHKDTLRSAKRFVKHNEKISVKRVWLTEIKLA DLENMVNYKNGREIELYEALKARLEAYGGNAKQAFDPKDNPFYKKGGQLVKAVRVEKTQKS **GVLLNKKNAYTIADNGDMVRVDVFCKVDKKGKNQYFIVPIYAWQVAENILPDIDCKGYRIDDS** YTFCFSLHKYDLIAFQKDEKSKVEFAYYINCDSSSGGFYLAWHDKGSREQRFRISTQNLALIQ **KYQVNELGKEIRPCRLKKRPPVR** 

## eNme2-C.NR:

MAAFKPNPINYILGLDIGIASVGWAMVEIDEEENPIRLIDLGVRVFERAEVPKTGDSLAMARRL ARSVRRLTRRRAHRLLRARRLLKREGVLQAADFDENGLITSLPNTPWQLRAAALDRKLTPLE WSAVLLHLIKHRGYLSQRKNEGETAAKELGALLKGVANNAHALQTGDFRTPAELALNKFEKE SGHIRNQRGDYSHTFSRKDLQAELILLFEKQKEFGNPHVSGGLKEGIETLLMTQRPALSGDA VQKMLGHCTLEPTEPKAAKNTYTAERFIWLTKLNNLRILEQGSERPLTDTERSTLMDEPYRK SKLTYAQARKLLGLEDTAFFKGLRYGKDNAEASTLMEMKAYHAISRALEKEGLKDKKSPLNL SSELQDEIGTAFSLFKTDEDITGRLKDRVQPEILEALLKHISFDKFVQISLKALRRIVPLMEQGK RYDEACAEIYGVHYGKKNTEEKIYLPPIPADEIRNPVVLRALSQARKVINGVVRRYGSPARIHI ETAREVGKSFKDRKEIEKRQEENRKDREKAAAKFREYFPNFVGEPKSKDILKLRLYEQQHGK CLYSGKEINLVRLNEKGYVEIDHALPFSRTWDDSFNNKVLVLGSENQNKGNQTPYEYFNGK DNSREWQEFKARVETSRFPRSKKQRILLQKFDEDGFKECNLNDTRYVNRFLCQFVADHILLT GKGKRRVFASNGQITNLLRGFWGLRKVRAENDRHHALDAVVVACSTVAMQQKITRFVRYKE MNAFDGKTIDKETGKVLHQKTHFPQPWEFFAQEVMIRVFGKPDGKPEFEEADTPEKLRTLLA EKLSSRPEAVHEYVTPLFVSRAPNRKMSGAHKDTLRSAKRFVKHNEKISVKRVWLTEIKLAD LENMVNYKNGREIELYEALKARLEAYGGNAKQAFDPKDNPFYKKGGQLVKAVRVEKTQKSG VLLNKKNAYTIADNGDMVRVDVFCKVDKKGKNQYFIVPIYAWQVAENILPDIDCKGYRIDDSY TFCFSLHKYDLIAFQKDEKSKVEFAYYINCDSSSGGFYLAWHDKGSREQRFRISTQNLALIQK YQVNELGKEIRPCRLKKRPPVR

## eNme2-T.1:

MAAFKPNPINYILGLDIGIASVGWAMVEIDEEENPIRLIDLGVRVFKRAEVPKTGDSLAMARRL ARSMRRLTRRRAHRLLRARRLLKREGVLQAADFDENGLIKSLPNTPWQLRAAALDRKLAPL EWSAVLLHLIKHRGYLSQRKNEGETAGKKLGALLKGVANNAHALQTGDFRTPAELALNKFEK ESGHIRNQRGDYSHTFSRKDLQAELILLFEKQKEFGNPHVSGGLKEGIETLLMTQRPALSGD AVQKMLGHCTFEPAEPKAAKNTYTAERFIWLTKLNNLRILEQGSERPLTDTERATLMDEPYR KSKLTYAQARKLLGLEDTAFFKGLRYGKDNAEASTLMEMKAYHAISRALEKEGLKDKKSPLN LSSELQDEIGTAFSLFKTDEDIAGRLKDRVQPEILEALLKNISFDKFVQISLKSLRRIVPLMEQG KRYDEACAEIYGDRYGKKNTEAKIYLPPIPADEIRNPVVLRALSQTRKVINGVVRRYGSPARIH IETAREVGKSFKDRKEIEKRQEENRKDREKAAAKFREYFPNFVGEPKSKDILKLRLYEQQHG KCLYSGKEINLVRLNEKGYVEIDHALPFSRTWDDSFNNKVLVLGSENQNKGNQTPYEYFNG KDNPREWQEFKARVETSRFPRSKKQRILLQKFDEDGFKECNLNDTRYVSRFLCQFVADHILL TGKGKRRVFASNGQITNLLRGFWGLRKVRAENARHHALDAVVVACSTVAMQQKITRFVRYK EMNAFDGKTIDKETGKALYQKTRFPQPWEFFAQEVMIRVFGKPDGKPEFEEADTPEKLRTLL AEKLSSRPEAAHEYVTPLFVSRAPNRKMSGAHKATLRSAKRFVKHNEKVSVKRVLLTEIKLA DLENMVNYKNGREIELYEALKARLEAYGGNAKQAFDPKDNPFYKKGGQLVKAVRVEKTQES GVLLNKKNAYTIADNGDRVRVDVFCKVDKKGKNQYFIVPIYAWQVAENILPDIDCKGYRIDDS YTFCFSLHRYDLIAFQKDEKSKVEFAYYINCNASNGYFYLAWHDKGSKEQQFSISTQNLVLIQ KYQVSELGKEIRPCRLKKRPPVR

eNme2-T.2:

MAAFKPNPINYILGLDIGIASVGWAMVEIDEEENPIRLIDLGVRVFKRAEVPKTGDSLAMARKL ARSMRRLTRRRAHRLLRARRLLKREGVLQAADFDENGLIKSLPNTPWQLRATALDRKLAPLE WSAVLLHLIKHRGYLSQRKNEGETANKKLGALLKGVANNAHALQTGDFRTPAELALNKFEKE SGHIRNQRGDYSHTFSRKDLQAELILLFEKQKDFGNPHVSGGLKEGIETLLMTQRPALSGDA VQKMLGHCTFEPAEPKAAKNTYTAERFIWLTKLNNLRILEQGSERPLTDTERATLMDEPYRK SKLTYAQARKLLGLEDTAFFKGLRYGKDNAEASTLMEMKAYHAISRALEKEGLKDKKSPLNL SSELQDEIGTAFSLFKTDEDIAGRLKDRVQPEILEALLKHISFDKFVQISLKALRRIVPLMEQGK RYDEACAEIYGDRYGKKNTEKKIYLPPIPADEIRNPVVLRALSQARKVINGVVRRYGSPARIHI ETAREVGKSFKDRKEIEKRQEENRKDREKAAAKFREYFPNFVGEPKSKDILKLRLYEQQHGK CLYSGKEINLVRLNEKGYVEIDHALPFSRTWDDSFNNKVLVLGSENQNKGNQTPYEYFNGK DNSREWQEFKARVETSRFPRSKKQRILLQKFDEDGFKECNLNDTRYVSRFLCQFVADHILLT GKGKRRVFASNGQITNLLRGFWGLRKVRAENARHHSLDAVVVACSTVAMQQKITRFVRYKE MNAFDGKTIDKETGKVLHQRTHFPQPWEFFAQEVMIRVFGKPDGKPEFEEADTPEKLRTLL AEKLSIRPEAVHEYVTPLFVSRAPNRKMSGAHKATLRSAKRFVKHNEKISVKRVWLTEIKLAD LENMVNYKNGREIELYEALKARLEAYGGNAKQAFDPKDNPFYKKGGQLVKAVRVEKTQKSG VLLNKRNAYTIADNGDRVRVDVFCKVDKKGKNQYFIVPIYAWQVAENILPDIDCKGYRIDDSY TFCFSLHRYDLIAFQKDEKSKVEFAYYINCNASNGNFYLAWHDKGSKEQQFCISTQNLVLIQK YQVNELGKEIRPCRMKKRPPVR

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