

Supplementary Table 1.

A. Single Cpf1 crRNAs and SpCas9 gRNAs

Name	Spacer Sequence with Cpf1 PAM	Genomic coordinates
HBB_1 crRNA (H1)	TTTG TACTGATGGTATGGGCCAA	Chr11: 5248505 - 5248528
HBB_2 crRNA (H2)	TTTGAAGTC CAACTCCTAAGCCAG	Chr11: 5248452 - 5248475
HBB_3 crRNA (H3)	TTTG CAAGTGTATTACGTAAATAT	Chr11: 5248550 - 5248573
AR_1 crRNA (A1)	TTTG GAGAGTCTGGATGAGAAATGC	ChrX: 66763209 - 66763232
AR_2 crRNA (A2)	TTTCT ACCCTCTTCTCTGCCTTTC	ChrX: 66763260 - 66763283
AR_3 crRNA (A3)	TTTG CTCTAGGAACCCCTCAGCCCC	ChrX: 66763299 - 66763322
NPY1R_1 crRNA (N1)	TTTC AAGCCTCGGGAAACTGCCCT	Chr4: 164254005 - 164254028
NPY1R_2 crRNA (N2)	TTTCT TTTGTTCAGGTCAGTGC	Chr4: 164254048 - 164254071
NPY1R_3 crRNA (N3)	TTTGG GCTGGCGCTCGAGCTCTCC	Chr4: 164254099 - 164254122
CD22_1_crRNA	TTTC CTCCTCAATATCTATGTGCT	Chr19: 35819609 -35819632
CD22_2_crRNA	TTTC CATCATAGGCATAATGGTGG	Chr19: 35819677- 35819700
CD22_3_crRNA	TTTAT GCCATGATGAAAAGAGTG	Chr19: 35819683 -35819706
CD22_4_crRNA	TTTAG TGACACCATCCAGTTATT	Chr19: 35819714- 35819737
CD22_5_crRNA	TTTGT AGTTAGTGAACACCATCCA	Chr19: 35819721- 35819744
CD22_6_crRNA	TTTC AGCGGGCTGCAGTTCTCCTG	Chr19: 35819769 -35819792
CD22_7_crRNA	TTTC CTGAGAGCTGGTAGAGGGG	Chr19: 35819813- 35819836
CD22_8_crRNA	TTTC CAGAACGGCTCCTCCACAAC	Chr19: 35819839- 35819862
CD22_9_crRNA	TTTGA ATATCAGATCAGTTTCAG	Chr19: 35819857- 35819880
CD22_10_crRNA	TTTC CGTGTATGGTTGCAATAT	Chr19: 35819871-35819894
CD22_11_crRNA	TTTCCC CACTCCCCAGATCACGGT	Chr19: 35819965- 35819988
CD22_12_crRNA	TTTCCC CTCCATGGCCACACCCCC	Chr19: 3582002- 35820046
CD22_13_crRNA	TTTGT CTCTAGATGCTGCCAGGGT	Chr19: 3582008- 35820104
CD22_14_crRNA	TTTCC CGCGTGTCTCCCTTTCAG	Chr19: 35820107- 35820130
CD22_15_crRNA	TTTA CCTGTTCCCGGTGTCCTCC	Chr19: 35820115-35820138
CD22_16_crRNA	TTTGC ATTCAACAAGCAAGTTATT	Chr19: 35820156- 35820179
CD5_1_crRNA	TTTCC CATGTTGTGTGTTGTGATT	Chr11: 60869058- 60869081
CD5_2_crRNA	TTTCT GTGTTGTGTGATCTCCA	Chr11: 60869176-60869199
CD5_3_crRNA	TTTG CTAGCAAGTACAAGAGATGG	Chr11: 60869454- 60869477
CD5_4_crRNA	TTTG AGCTGACTTCCACAGGTGG	Chr11: 60869481- 60869504
CD5_5_crRNA	TTTGT GAGGGATGAGGTGGAAGT	Chr11: 60869504 -60869527
CD5_6_crRNA	TTTGG CTTCACTGGAGTCTGCAA	Chr11: 60869548 -60869571
CD5_7_crRNA	TTTC ACTGGAGTCTGCAACAAGAA	Chr11: 60869554- 60869577
CD5_8_crRNA	TTTCCC GCCTCTCCCCACCCAGAC	Chr11: 60869596 - 60869619
CD5_9_crRNA	TTTGA ATGGCAGCCCTGGCCTCTG	Chr11: 60869804- 60869827
CD5_10_crRNA	TTTGA AGTTGAACGTCAACTTCC	Chr11: 60869852- 60869875
CD5_11_crRNA	TTTGC CAGGAGGAAGTTGACAGTT	Chr11: 60869842- 60869865
CD5_12_crRNA	TTTAC CCAAGGCTGACTCTGGGAT	Chr11: 60870156 -60870179

CD5_13_crRNA	TTTGGGCCACTGGGATCCCTGCC	Chr11: 6087021- 60870235
CD5_14_crRNA	TTTACCCCTCCAGTGCAAGAGAGA	Chr11: 60870331 60870354
CD5_15_crRNA	TTTGATGGGGCCCAGACAACCTGA	Chr11: 60870373 60870396
CD5_16_crRNA	TTTAGCAGAGCATTCAAGGCCTCCC	Chr11: 60870416 60870439

Name	Spacer Sequence with SpCas9 PAM	Genomic coordinates
VEGFA_1	GTGTGCAGACGGCAGTCAGTAGG	Chr6: 43737352 - 43737374
VEGFA_2	GAGCAGCGTCTCGAGAGTGAGG	Chr6: 43737414 - 43737436
VEGFA_3	GGTAGAGTGAGTGTGCGTGTGG	Chr6: 43737454- 43737476

B. Multiplex Cpf1 crRNAs targeting a single promoter

Name	Pair #	Oligonucleotides sequences to be ordered	Orientation
HBB_MST	Pair1	AGATTACTGATGGTATGGGCCAAA	Top
		TAGTAGAAATTTGGCCCCATACCATCAGTA	Bottom
	Pair 2	ATTCTACTAAGTGTAGATAAGTCCAACCTCTA AGCCAGAATTCTACTAA	Top
		ATCTACACTTAGTAGAAATTCTGGCTTAGGAG TTGGACTTATCTACACT	Bottom
	Pair 3	GTTAGATCAAGTGTATTTACGTAATATAATT CTACTAAGTGTAGATTTTTTTA	Top
		AGCTTAAAAAAATCTACACTTAGTAGAAATT TATTACGTAATACACTTG	Bottom
AR_MST	Pair1	AGATAGAGTCTGGATGAGAAATGCA	Top
		TAGTAGAAATTGCATTCTCATCCAGACTCT	Bottom
	Pair 2	ATTCTACTAAGTGTAGATTACCCTCTTCTG CCTTCAATTCTACTAA	Top
		ATCTACACTTAGTAGAAATTGAAAGGCAGAGA AGAGGGTAATCTACACT	Bottom
	Pair 3	GTTAGATCTCTAGGAACCCCTCAGCCCCAATT TCTACTAAGTGTAGATTTTTTTA	Top
		AGCTTAAAAAAATCTACACTTAGTAGAAATTG GGGCTGAGGGTTCTAGAG	Bottom
NPY1R_MST	Pair1	AGATAAGCCTCGGAAACTGCCCTA	Top
		TAGTAGAAATTAGGGCAGTTCCGAGGCTT	Bottom

	Pair 2	ATTTCTACTAAGTGTAGATTTGTTGCAGGTC AGTGCCAATTCTACTAA	Top
		ATCTACACTTAGTAGAAATTGGCACTGACCTG CAAACAAAATCTACACT	Bottom
	Pair 3	GTGTAGATGGCTGGCGCTCGAGCTCTCCAAT TTCTACTAAGTGTAGATTTTTTA	Top
		AGCTTAAAAAAATCTACACTTAGTAGAAATTG GAGAGCTCGAGCGCCAGCC	Bottom

C. Multiplex Cpf1 crRNAs targeting multiple promoters

Name	Pair #	Oligonucleotides sequences to be ordered	Orientation
HBB_AR_NPY1R_MST	Pair1	AGATTACTGATGGTATGGGGCCAAA	Top
		TAGTAGAAATTGGCCCCATACCATCAGTA	Bottom
	Pair 2	ATTTCTACTAAGTGTAGATCTCTAGGAACCCTC AGCCCCAATTCTACTAA	Top
		ATCTACACTTAGTAGAAATTGGGCTGAGGGT TCCTAGAGATCTACACT	Bottom
	Pair 3	GTGTAGATAAGCCTCGGGAACTGCCCTAATT TCTACTAAGTGTAGATTTTTTA	Top
		AGCTTAAAAAAATCTACACTTAGTAGAAATTA GGCAGTTCCCGAGGCTT	Bottom

Supplementary Table 2.

Primer name	Sequence	Orientation	Target Gene	Purpose
oET_173	ATGGTGAGCAGAGTGCCTATC	Forward	NPY1R	RT-qPCR
oET_174	ATGGTCCCTGGCAGTCTCCAAA	Reverse		
oET_175	CCATCGGACTCTCATAGGTTGTC	Forward		
oET_176	GACCTGTACTTATTGTCTCTCATC	Reverse		
oET_225	GCACGTGGATCCTGAGAACT	Forward		
oET_226	ATTGGACAGCAAGAAAGCGAG	Reverse		

qPCR condition	Number of Cycle	Temperature(°C)	Time(sec)
Denaturation	1	95	20
Amplification	45	95	3
		60	30

Supplementary Note 1

Initial characterization of dLbCpf1- and dAsCpf1-based activators

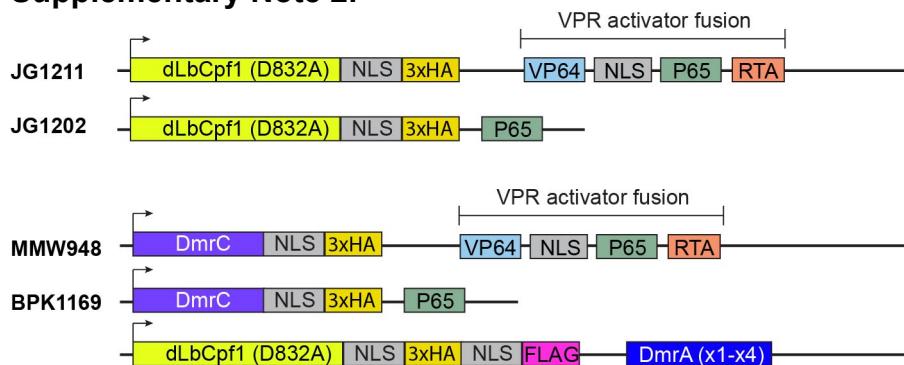
Initial GFP reporter-based assay experiments showed that a “dead” Cpf1 from *Lachnospiraceae bacterium* (**dLbCpf1**)-VPR fusion induced higher levels of gene activation than a “dead” *Acidaminococcus* sp. *BV3L6* Cpf1 (**dAsCpf1**)-VPR fusion (**Supplementary Figs. 1a – 1c**). This difference is consistent with previous reports from our group showing that LbCpf1 generally exhibits higher genome-editing activities than AsCpf1 in human cells¹. Western blots performed with these fusions showed only modestly lower expression of the dAsCpf1-VPR compared with dLbCpf1-VPR (**Supplementary Fig. 1d**). Based on these results, we chose to use the dLbCpf1 protein for building activators.

Attempts to optimize MST crRNA-mediated transcriptional activation

We attempted to optimize the activities of MST crRNAs relative to single individually expressed crRNAs and focused on dLbCpf1-VPR because as a single protein system (as opposed to the two-protein drug-inducible systems) it has fewer parameters to vary. We altered the relative and absolute amounts of plasmids encoding crRNAs and dLbCpf1-VPR protein and also tested more extended post-transfection time points but did not observe any substantial improvements relative to our initial experimental conditions (compare **Supplementary Fig. 4** to **Fig. 2d**). For example, for the MST crRNA targeted to the *NPY1R* gene, the level of activation consistently remained between ~45% and 80% of that observed with the individually expressed crRNA across all biological replicates. For the *HBB* and *AR* genes, matched single individually

expressed and MST crRNAs still showed comparable activation levels across the different optimization conditions. We conclude from these results that differences observed between single and MST crRNAs are likely target site-dependent and that further optimization will be required to achieve consistently equivalent activities (e.g., changes to MST crRNA transcript architecture or other alterations to the activators).

Supplementary Note 2.



	Name	Addgene #	Description
1	MMW1578	TBD	pCAG-human dLbCpf1(D832A)-NLS-3xHA
2	BPK1169	TBD	pCAG-DmrC-NLS-FLAG-P65
3	MMW948	TBD	pCAG-DmrC-NLS-FLAG-VPR
4	JG1202	TBD	pCAG-human dLbCpf1(D832A)-NLS-3xHA-p65
5	JG1211	TBD	pCAG-human dLbCpf1(D832A)-NLS-3xHA-VPR
6	JG674	TBD	pCAG-human dLbCpf1(D832A)-NLS-3xHA-DmrA(X1)
7	JG676	TBD	pCAG-human dLbCpf1(D832A)-NLS-3xHA-DmrA(X2)
8	JG693	TBD	pCAG-human dLbCpf1(D832A)-NLS-3xHA-DmrA(X3)
9	YET1000	TBD	pCAG-human dLbCpf1(D832A)-NLS-3xHA-DmrA(X4)
10	BPK3082	78742	pU6-LbCpf1-crRNA-BsmBI cassette
11	BPK617	TBD	pCAG-NLS-human-dSpCas9(D10A/H840)-NLS(SV40)-3xFLAG-VP64
12	BPK1160	TBD	pCAG-NLS-human-dSpCas9(D10A/H840)-NLS(SV40)-3xFLAG-p65
13	BPK278	TBD	pCAG-VP64-human-dSpCas9(D10A/H840)-NLS(SV40)-3xFLAG
14	BPK1163	TBD	pCAG-p65-human-dSpCas9(D10A/H840)-NLS(SV40)-3xFLAG

15	BPK1019	TBD	pCAG-NLS-human-dSpCas9(D10A/H840)-NLS(SV40)-3xFLAG-DmrA
16	BPK1033	TBD	pCAG-NLS-human-dSpCas9(D10A/H840)-NLS(SV40)-3xFLAG-DmrA(x2)
17	BPK1040	TBD	pCAG-NLS-human-dSpCas9(D10A/H840)-NLS(SV40)-3xFLAG-DmrA(x3)
18	BPK1179	TBD	pCAG-NLS-human-dSpCas9(D10A/H840)-NLS(SV40)-3xFLAG-DmrA(x4)
19	BPK975	TBD	pCAG-DmrA-NLS-human-dSpCas9(D10A/H840)-NLS(SV40)-3xFLAG
20	BPK976	TBD	pCAG-DmrA(x2)-NLS-human-dSpCas9(D10A/H840)-NLS(SV40)-3xFLAG
21	BPK1143	TBD	pCAG-DmrA(x3)-NLS-human-dSpCas9(D10A/H840)-NLS(SV40)-3xFLAG
22	BPK1147	TBD	pCAG-DmrA(x4)-NLS-human-dSpCas9(D10A/H840)-NLS(SV40)-3xFLAG
23	JKNp44	TBD	pHR-SFFV-HA-NLS-dSpCas9(D10A/H840)-VPR-2PA-BFP
24	JKNp47	TBD	pHR-SFFV-HA-NLS-dLbCpf1(D832A)-VPR-2PA-BFP
25	JKNp49	TBD	pHR-SFFV-HA-NLS-dAsCpf1(D908A/E993A)-VPR-2PA-BFP

1. MMW1578: CAG-human dLbCpf1(D832A)-NLS-3xHA

Human codon optimized dLbCpf1: **bold**, NLS: *italic*, 3xHA: lower case

ATGAGCAAGCTGGAGAAGTTACAAACTGCTACTCCCTGTCTAACGACCCTGAGGGT
 TCAAGGCCATCCCTGTGGGCAAGACCCAGGAGAACATCGACAATAAGCGGCTGC
 TGGTGGAGGACGAGAAGAGAGCCGAGGATTATAAGGGCGTGAAGAAGCTGCTG
 GATCGCTACTATCTGTCTTTATCAACGACGTGCTGCACAGCATCAAGCTGAAGA
 ATCTGAACAATTACATCAGCCTGTCGGAAAGAAAACCAGAACCGAGAAGGAGA
 ATAAGGAGCTGGAGAACCTGGAGATCAATCTGCGGAAGGAGATCGCCAAGGCCT
 TCAAGGGCAACGAGGGCTACAAGTCCCTGTTAAGAAGGATATCATCGAGACAA
 TCCTGCCAGAGTTCCCTGGACGATAAGGACGAGATGCCCTGGTAACAGCTTCA
 ATGGCTTACACAGCCTCACCGGCTTCTTGATAAACAGAGAGAATATGTTTCC
 GAGGAGGCCAAGAGCACATCCATGCCCTCAGGTGTATCAACGAGAACATGACC
 CGCTACATCTTAATATGGACATCTCGAGAAGGTGGACGCCATCTTGATAAGC
 ACGAGGTGCAGGAGATCAAGGAGAACATCTGAACAGCGACTATGATGTGGAGG
 ATTCCTTGAGGGCGAGTTCTTAACTTGTGCTGACACAGGAGGGCATCGACGT
 GTATAACGCCATCATGGCGCTCGTGACCGAGAGCGGGCGAGAACATCAAGGG
 CCTGAACGAGTACATCAACCTGTATAATCAGAAAACCAAGCAGAACAGCTGCCTAA
 GTTTAAGCCACTGTATAAGCAGGTGCTGAGCGATCGGGAGTCTCTGAGCTTCTAC
 GGCGAGGGCTATACATCCGATGAGGGAGGTGCTGGAGGTGTTAGAAACACCCCTG
 AACAAAGAACAGCGAGATCTTCAGCTCCATCAAGAACGCTGGAGAACAGCTGTTCAAG
 AATTTCGACGAGTACTCTAGCGCCGGCATTTGTGAAGAACGGCCCCCATCA
 GCACAATCTCCAAGGATATCTCGGCCAGTGGAACGTGATCCGGGACAAGTGG
 ATGCCGAGTATGACGATATCCACCTGAAGAACAGGCCGTGGTACCGAGAAC
 ACGAGGACGATCGGAGAAAGCCTCAAGAACAGATCGGCTCCTTCTGGAGCA
 GCTGCAGGAGTACGCCGACGCCGATCTGTCTGGTGGAGAACAGCTGAAGGAGAT
 CATCATCCAGAACGGTGGATGAGATCTACAAGGTGTATGGCTCCTCTGAGAACAGCTG
 TTCGACGCCGATTTGTGCTGGAGAACAGCCTGAAGAACAGCAGGCCGTGGTG
 GCCATCATGAAGGACCTGCTGGATTCTGTGAAGAGCTTCGAGAACATTACATCAAGG
 CCTTCTTGGCGAGGGCAAGGAGACAAACAGGGACGAGTCCTCTATGGCGATT
 TGTGCTGGCCTACGACATCCTGCTGAAGGTGGACCACATCTACGATGCCATCCGC
 AATTATGTGACCCAGAACGCCACTCTAACGGATAAGTTCAAGCTGTATTTCAGAA

CCCTCAGTTCATGGCGGCTGGACAAGGATAAGGAGACAGACTATCGGCCAC
CATCCTGAGATACGGCTCCAAGTACTATCTGGCCATCATGGATAAGAAGTACGCC
AACTGCCTGCAGAACGATCGACAAGGACGATGTGAACGGCAATTACGAGAACGATC
AACTATAAGCTGCTGCCGCCCTAATAAGATGCTGCCAAAGGTGTTCTTTCTA
AGAAGTGGATGGCTACTATAACCCCAGCGAGGACATCCAGAACGATCTACAAGA
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CGACTTCTTAAGGATAGCATCTCCCGGTATCCAAAGTGGTCCAATGCCCTACGAT
TTCAACTTTCTGAGACAGAGAACGATATAAGGACATGCCGGCTTTACAGAGAGG
TGGAGGAGCAGGGCTATAAGGTGAGCTCGAGTCTGCCAGCAAGAACGGAGGTG
GATAAGCTGGTGAGGAGGGCAAGCTGTATATGTTCCAGATCTATAACAAGGACT
TTTCCGATAAGTCTCACGGCACACCCATCTGCACACCAGTACTCAAGCTGCT
GTTTGACGAGAACAAATCACGGACAGATCAGGCTGAGCGGAGGAGCAGAGCTGTT
CATGAGGCGCGCCTCCCTGAAGAACGGAGGAGCTGGTGGTGACCCAGCCAACTC
CCCTATCGCCAACAAGAACATCCAGATAATCCCAAGAAAACCACAACCCCTGCCTAC
GACGTGTATAAGGATAAGAGGTTCTGAGGACCGAGTACGAGCTGCACATCCCAA
TCGCCATCAATAAGTCCCCAAGAACATCTTCAGATAATACAGAGGTGCGCGT
GCTGCTGAAGCACGACGATAACCCCTATGTGATCGGCATGCCAGGGCGAGCG
CAATCTGCTGTATATCGTGGTGGACGGCAAGGGCAACATCGTGGAGCAGTA
TTCCCTGAACGAGATCATCAACAACCTCAACGGCATCAGGATCAAGACAGATTAC
CACTCTGCTGGACAAGAACGGAGAGAGGAGGGTCTGAGGCCGCCAGAACTG
GACCTCCATCGAGAATATCAAGGAGCTGAAGGCCGGTATATCTCAGGTGGT
GCACAAAGATCTGCAGCTGGTGGAGAACGATACCGATGCCGTATCGCCCTGGAGGA
CCTGAACCTGGCTTTAAGAACATGCCGCTGAAGGTGGAGAACGAGGTGTATCA
GAAGTTCGAGAACGATGCTGATCGATAAGCTGAACATGGTGGACAAGAACGTC
TAATCCTTGCAACAGCGGCCCTGAAGGGCTATCAGATACCAATAAGTTC
GAGAGCTTAAGTCCATGTCTACCCAGAACGGCTCATCTTACATCCCTGCCTG
GCTGACATCCAAGATCGATCCATCTACCGGCTTGTGAACCTGCTGAAAACCAAG
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ACGTGCCGAGGAGGATCTGTCGAGTTGCCCTGGACTATAAGAACTCTCG
CACAGACGCCGATTACATCAAGAACGTTGAGACTCCTACGGCAACCGGAT
CAGAATCTCCGGAATCCTAAGAACAAACGTGTTGACTGGAGGAGGTGTG
CCTGACCAGCGCTATAAGGAGCTGTTCAACAAAGTACGGCATCAATTACAGCAG
GGCGATATCAGAGCCCTGCTGTGCGAGCAGTCCGACAAGGCCTCTACTCTAGCT
TTATGGCCCTGATGAGCCTGATGCTGAGATGCGGAACAGCATCACAGGCCGCA
CCGACGTGGATTCTGATCAGCCCTGTGAAGAACCTCGACGGCATCTCTACGA
TAGCCGGAACTATGAGGCCAGGAGAACGCTCCATCCTGCCAAAGAACGCCGACGC
CAATGGCGCTATAACATGCCAGAACAGGTGCTGTGGCCATCGGCCAGTTCAA
GAAGGCCGAGGAGCAGAGAACGCTGGATAAGGTGAAGATCGCCATCTTAACAAGGA
GTGGCTGGAGTACGCCAGACCAGCGTGAAGCACAAAAGGCCGGCCACGAA
AAAGGCCGCCAGGCAAAAAAGAAAAAGGGATCCtaccatacgtatccatgtttcc
tacgacgtgcctgattatgcataccatatgtccccgactatgcc TAA

2. BPK1169: CAG-DmrC-NLS-FLAG-P65

DmrC: **bold**, NLS-Flag: *italic*, P65: lower case

ATGGGATCCAGAACATCCTCTGGCATGAGATGTGGCATGAAGGCCCTGGAAGAGGCA
TCTCGTTGTACTTGAGAACGATGCCAAAGGACGATGAAAGGCATGTTGAGGTGCTGGAGC
CCTTGCTATGATGGAACGGGGACCCAGACTCTGAAGGAAACATCCTTAA
TCAGGCCTATGGTCGAGATTAAATGGAGGCCAAGAGTGGTGCAGGAAGTACAT

GAAATCAGGGAATGTCAAGGACCTCCCAAGCCTGGACCTCTATTATCATGTG
TTCCGACGAATCTCAAAGGGCGGATCCCCAAGAAGAAGAGGAAAGTCTGA
GCGACTACAAAGACCATGACGGTGATTATAAGATCATGACATCGATTACAAGGAT
GACGATGACAAGGCTGCAGGAGGCGGTGGAAGCGGGatggagttccagtagccagataca
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ccaggcctggccctggcccccggccctcccaagtcctgcccaggtccagccctgccccgtccagccatggatc
agctctggcccaggccccagccctgtccctgagccctccatggctgtggcccccacctgccccaaagc
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ggcaacagcacagacccagctgttacagacccatccgtcgataactccgagttcagcagctgctgaaccaggg
catacgtggccccccacacaactgagccatgctgatggagtaccctgaggctataactccctagtgacaggggccc
agaggccccccgacccagctctgtccactggggccccggctcccaatggctcattcaggagatgaagacttc
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3. MMW948: CAG-DmrC-NLS-FLAG-VPR

DmrC: **bold**, NLS-Flag: *italic*, VP64: **red**, NLS: italic and underline, p65: **blue**, Rta: **orange**

ATGGGATCCAGAATCCTCTGGCATGAGATGTGGCATGAAGGCCTGGAAGAGGCA
TCTCGTTGTACTTGGGAAAGGAACGTGAAAGGCATGTTGAGGTGCTGGAGC
CCTTGCATGCTATGATGGAACGGGGACCCCAGACTCTGAAGGAAACATCCTTAA
TCAGGCCTATGGTCGAGATTAAATGGAGGCCAAGAGTGGTGCAGGAAGTACAT
GAAATCAGGGAATGTCAAGGACCTCCCAAGCCTGGACCTCTATTATCATGTG
TTCCGACGAATCTCAAAGGGCGGATCCCCAAGAAGAAGAGGAAAGTCTGA
GCGACTACAAAGACCATGACGGTGATTATAAGATCATGACATCGATTACAAGGAT
GACGATGACAAGGCTGCAGGAGGCGGTGGAAGCGGGTGGAGGCCAGCGGTTCC
GGACGGGCT**GACGCATTGGACGATTTGATCTGGATATGCTGGGAAGTGACGCC**
TCGATGATTTGACCTTGACATGCTGGTCTGGATGCCCTGATGACTTGACCTCG
ACATGCTCGGAGTGCACGCCCTGATATTGACCTGGACATGCTGATTAACCT
AGAAGTTCCGGATCTCGAAAAAGAAACGCAAAGTTGGTAGCCAGTACCTGCCGA
CACCGACCGGGACCGGATCGAGGAAAAGCGGAAGCGGACCTACGAGACATT
CAAGAGCATCATGAAGAAGTCCCCCTTCAGCGGCCCCACCGACCCCTAGACCTCCA
CCTAGAAGAATCGCCGTGCCAGCAGATCCAGCGCCAGCGTGCCAAAACCTGCC
CCCAGCCTACCCCTTACCCAGCAGCCAGCTGAGCACCATCAACTACGACGAGTCCCT
ACCATGGTGTCCCCAGCGGCCAGATCTCTCAGGCCTCTGCTCTGGCTCCAGGCC
CTCCTCAGGTGCTGCCTCAGGCTCCTGCTCAGCACCAGCTCCAGGCCATGGTGT
TGCACTGGCTCAGGCACCAGCACCCGTGCCTGTGCTGGCTCCTGGACCTCCACAG
GCTGTGGCTCACCAGCCCCCTAAAAGCTCTGCTGCAGCTGAGGACGAGGATCTGGAGGCC
AAGCTCTGCTGCAGCTGAGGACGAGGATCTGGAGGCC
CAGCACCGATCCTGCCGTGTTCACCGACCTGGCCAGCGTGGACAACAGCGAGTTC
CAGCAGCTGCTGAACCAGGGATCCCTGTGGCCCTCACACCACCGAGGCCATGC
TGATGGAATACCCCGAGGCCATCACCCGGCTCGTACAGGCCTGCTCAGAGGCC
TGATCCAGCTCCTGCCCTCTGGAGGCACCAGGCCTGCCATATGGACTGCTGTCT
GGCGACGAGGACTTCAGCTATGCCGATATGGATTCTCAGCCTGCTGGCTCCTGGACCTCCACAG
TGGCAGCGGCAGC**CAGGATTCCAGGGAGGGATGTTTGCCGAAGCCTGAGGC**
CGGCTCCGCTATTAGTGACGTGTTGAGGGCCCGAGGGTGTGCCAGC
AAAACGAA

ATCCGGCCATTCATCCTCCAGGAAGTCCATGGGCCAACGCCCACTCCCCGCCA
GCCTCGCACCAACACCAACCAGGTCCAGTACATGAGCCAGTCGGGCACTGACCCC
GGCACCAAGTCCCTCAGCCACTGGATCCAGCGCCCGAGTGAACCTGGAGGCCAGT
CACCTGTTGGAGGATCCGATGAAGAGACGAGCCAGGCTGTCAAAGCCCTCGGG
AGATGGCCGATACTGTGATTCCCCAGAAGGAAGAGGCTGCAATCTGTGGCCAAAT
GGACCTTCCATCCGCCCCAAGGGCCATCTGGATGAGCTGACAACCACACTT
GAGTCATGACCGAGGATCTAACCTGGACTCACCCCTGACCCCGGAATTGAACG
AGATTCTGGATACCTCCTGAACGACGAGTCCTGCATGCCATGCATATCAGC
ACAGGACTGTCCATCTCGACACATCTCTGTT

4. JG1202: CAG-human dLbCpf1(D832A)-NLS-3xHA-P65

Human codon optimized dLbCpf1: **bold**, NLS: italic, 3xHA: lower case, P65: lower case and **bold**

ATGAGCAAGCTGGAGAAGTTACAAACTGCTACTCCCTGTCTAAAGACCTGAGGT
TCAAGGCCATCCCTGTGGCAAGACCCAGGAGAACATCGACAATAAGCGGCTGC
TGGTGGAGGACGAGAAGAGAGCCGAGGATTATAAGGGCGTGAAGAAGCTGCTG
GATCGCTACTATCTGCTTTATCAACGACGTGCTGCACAGCATCAAGCTGAAGA
ATCTGAACAATTACATCAGCCTGTTCCGGAAGAAAACCAAGAACCGAGAAGGAGA
ATAAGGAGCTGGAGAACCTGGAGATCAATCTCGGAAGGAGATGCCAAGGCCT
TCAAGGGCAACGAGGGCTACAAGTCCCTGTTAAGAAGGATATCATCGAGACAA
TCCTGCCAGAGTTCCTGGACGATAAGGACGAGATGCCCTGGTAACAGCAGCTTCA
ATGGCTTACACAGCCTCACCGGCTTCTTGATAACAGAGAGAATATGTTTCC
GAGGAGGCCAAGAGCACATCATGCCCTCAGGTGTATCAACGAGAACAGCTGACC
CGCTACATCTAATATGGACATCTCGAGAACAGGAGCTGACAGGAGGGATCGACG
ACGAGGTGCAGGAGATCAAGGAGAACGATCTGAACAGCGACTATGATGTGGAGG
ATTTCTTGAGGGCGAGTTCTTAACTTGTGCTGACACAGGAGGGATCGACGT
GTATAACGCCATCATGGCGGCTCGTGACCGAGAGCGCGAGAACAGATCAAGGG
CCTGAACGAGTACATCAACCTGTATAATCAGAAAACCAAGCAGAACAGCTGCC
GTTTAAGCCACTGTATAAGCAGGTGCTGAGCGATCGGAGTCTGAGCTTCTAC
GGCGAGGGCTATACATCCGATGAGGAGGTGCTGGAGGTGTTAGAACACCCCTG
AACAAAGAACAGCGAGATCTTCAGCTCCATCAAGAACGCTGGAGAACAGCTTCAAG
AATTTGACGAGTACTCTAGGCCGGCATTTGTGAAGAACGGCCCCGCCATCA
GCACAATCTCAAGGATATCTCGGCCAGTGGAACGTGATCCGGGACAAGTGG
ATGCCAGTATGACGATATCCACCTGAAGAACAGGCGTGGACCGAGAACG
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GCTGCAGGAGTACGCCGACGCCGATCTGTCTGGTGGAGAACAGCTGAAGGAGA
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AATTATGTGACCCAGAACAGCCACTCTAACGGATAAGTCAAGCTGTATTTCAAG
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CATCCTGAGATACGGCTCCAAGTACTATCTGGCCATCATGGATAAGAACG
AACTGCCTGCAGAACAGATCGACAAGGACGATGTGAACGGCAATTACGAGAAC
AACTATAAGCTGCTGCCGGCCCTAATAAGATGCTGCCAAAGGTGTTCTTCTA

Human codon optimized dLbCpf1: **bold**, NLS: italic, 3xHA: lower case, VP64: **red**, NLS: italic and underline, p65: **blue**, Rta: **orange**

ATGAGCAAGCTGGAGAAGTTACAAACTGCTACTCCCTGTCTAAGACCCTGAGGT
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ATCTGAACAAATTACATCAGCCTGTCGGAGATCAATCTGCGGAAGGAGATCGCCAAGGCCT
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GCTGCAGGAGTACGCCGACGCCGATCTGTCTGGAGAACAGCTGAAGGAGAAC
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GTTTGACGAGAACAAATCACGGACAGATCAGGCTGAGCGGAGGAGCAGAGCTGTT
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6. JG674: CAG-human dLbCpf1(D832A)-NLS-3xHA-DmrA(X1)

Human codon optimized dLbCpf1: **bold**, NLS: *italic*, 3xHA: lower case, DmrA: lowercase and **bold**

ATGAGCAAGCTGGAGAAGTTACAAACTGCTACTCCCTGTCTAACAGACCCTGAGGT
TCAAGGCCATCCCTGTGGCAAGACCCAGGAGAACATCGACAATAAGCGGCTGC
TGGTGGAGGACGAGAAGAGAGCCGAGGATTATAAGGGCGTGAAGAAGCTGCTG
GATCGCTACTATCTGTCTTTATCAACGACGTGCTGCACAGCATCAAGCTGAAGA
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TCAAGGGCAACGAGGGCTACAAGTCCCTGTTAAGAAGGATATCATCGAGACAA
TCCTGCCAGAGTTCTGGACGATAAGGACGAGATGCCCTGGTGAACAGCTTCA
ATGGCTTACACAGCCTCACCGGCTTCTTGATAAACAGAGAGAACATGTTTCC
GAGGAGGCCAAGAGCACATCCATGCCCTCAGGTGTATCAACGAGAACATGACC
CGCTACATCTCTAATATGGACATCTCGAGAAGGTGGACGCCATCTTGATAAGC
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7. JG676: CAG-human dLbCpf1(D832A)-NLS-3xHA-DmrA(X2)

Human codon optimized dLbCpf1: **bold**, NLS: *italic*, 3xHA: lower case, DmrA: lowercase and **bold**

ATGAGCAAGCTGGAGAACAGTTACAAACTGCTACTCCCTGTCTAACGACCCGTGAGGT
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TGGTGGAGGACGAGAACAGAGAGGCCAGGATTATAAGGGCGTGAAGAACAGCTGCTG
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8. JG693: CAG-human dLbCpf1(D832A)-NLS-3xHA-DmrA(X3)

Human codon optimized dLbCpf1: **bold**, NLS: *italic*, 3xHA: lower case, DmrA: lowercase and **bold**

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9. YET1000: CAG-human dLbCpf1(D832A)-NLS-3xHA-DmrA(X4)

Human codon optimized dLbCpf1: **bold**, NLS: *italic*, 3xHA: lower case, DmrA: lowercase and **bold**

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tgccactctcgatgtggagctctaaaactggaaGGATAA

10. BPK3082: U6-Lb-crRNA-BsmBI cassette

U6 promoter: **bold**, Lb crRNA: *italic*, BsmBI sites: lower case, U6 terminator: *italic* and **bold**

TGTACAAAAAAGCAGGCTTAAAGGAACCAATT~~CAGTCGACTGGATCCGGTACCA~~
~~AGGTGGGCAGGAAGAGGGCCTATTCCATGATTCCCTCATATTGCATATACG~~
~~ATACAAGGCTGTTAGAGAGATAATTAGAATTAATTGACTGTAAACACAAAGATAT~~
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~~TTCTGGCTTATATCTGTGGAAAGGACGAAACACCGAATTCTACTAAGTGT~~
GATGagacgATTAATGcgctc~~CTTTTTT~~

REFERENCES

1. Kleinstiver, B.P. et al. Genome-wide specificities of CRISPR-Cas Cpf1 nucleases in human cells. *Nature biotechnology* **34**, 869-874 (2016).