| Supplementary Table 1 gRNA | | | |
|---|---|---|---|
| Organism | Gene | Location | Sequence |
| *Homo sapiens* | *ASCL1* | -181 | CGGGAGAAAGGAACGGGAGG |
| *Homo sapiens* | *NEUROD1* | -221 | AGGTCCGCGGAGTCTCTAAC |
| *Homo sapiens* | *TTN* | -169 | CCTTGGTGAAGTCTCCTTTG |
| *Homo sapiens* | *HBG* | -100 | CTTGACCAATAGCCTTGACA |
| *Homo sapiens* | *MIAT* | -219 | ATGCGGGAGGCTGAGCGCAC |
| *Homo sapiens* | *TUNAR* | -275 | GGCGGCGTCGGGGTCCCTAC |
| *Homo sapiens* | *CXCR4* | -116 | GCAGACGCGAGGAAGGAGGGCGC |
| *Homo sapiens* | *RHOXF2* | -44 | ACGCGTGCTCTCCCTCATC |
| *Homo sapiens* | *ACTC1* | -229 | TGGCGCCCTGCCCTCTGCTG |
| *Homo sapiens* | *ASCL1* | -442 | TCCAATTTCTAGGGTCACCG |
| *Homo sapiens* | *ASCL1* | -557 | AAGAACTTGAAGCAAAGCGC |
| *Homo sapiens* | *NEUROD1* | -164 | ACCTGCCCATTTGTATGCCG |
| *Homo sapiens* | *NEUROD1* | -33 | AGGGGAGCGGTTGTCGGAGG |
| *Homo sapiens* | *CXCR4* | -162 | CCGACCACCCGCAAACAGCA |
| *Homo sapiens* | *CXCR4* | -193 | GCCTCTGGGAGGTCCTGTCCGGCTC |
| *Drosophila melanogaster* | *wingless* | -337 | GGAAATGGAAAAACTCTGCCCGG |
| *Drosophila melanogaster* | *twist* | -156 | GCATCGGCAGGTATGACGTCAGG |
| *Drosophila melanogaster* | *hindsight* | -180 | ATTTGAAACGAAGAATGAGAAGG |
| *Mus musculus* | *ttn* | -143 | AATTTAGCACTGCCAATCAG |
| *Mus musculus* | *hbb-bh1* | -108 | AGAGAGTCTGGGCAAGACAG |
| *Mus musculus* | *actc1* | -204 | CTCCCAGACCATGTAAGGAA |

| Supplementary Table 2 qPCR | | | |
|---|---|---|---|

| Primers | | | |
|---|---|---|---|
| Organism | Gene | Forward | Reverse |
| *Homo sapiens* | *ACTB* | CATGTACGTTGCTATCCAGGC | CTCCTTAATGTCACGCACGAT |
| *Homo sapiens* | *ASCL1* | CGCGGCCAACAAGAAGATG | CGACGAGTAGGATGAGACCG |
| *Homo sapiens* | *NEUROD 1* | GGATGACGATCAAAAGCCCAA | GCGTCTTAGAATAGCAAGGCA |
| *Homo sapiens* | *TTN* | TGTTGCCACTGGTGCTAAAG | ACAGCAGTCTTCTCCGCTTC |
| *Homo sapiens* | *HBG1* | AGATGCCACAAAGCACCTG | CTGCAGTCACCATCTTCTGC |
| *Homo sapiens* | *MIAT* | TGGCTGGGGTTTGAACCTTT | AGGAAGCTGTTCCAGACTGC |
| *Homo sapiens* | *TUNAR* | AGAACAAGGGGGAAAGCTCG | ATACCCCACCCGCTTTTGAG |
| *Homo sapiens* | *CXCR4* | ACTACACCGAGGAAATGGGCT | CCCACAATGCCAGTTAAGAAGA |
| *Homo sapiens* | *RHOXF2* | GGCAAGAAGCATGAATGTGA | TGTCTCCTCCATTTGGCTCT |
| *Homo sapiens* | *ACTC1* | ATGTGTGACGACGAGGAGAC | CGGACAATTTCACGTTCAGCA |
| *Drosophila melanogaster* | *wingless* | CCAAGTCGAGGGCAAACAGAA | TGGATCGCTGGGTCCATGTA |
| *Drosophila melanogaster* | *twist* | AAGTCCCTGCAGCAGATCAT | CGGCACAGGAAGTCAATGTA |
| *Drosophila melanogaster* | *hindsight* | ACATCCGGTGCCACAATTA | AGGGATGAAGCCGAGGATAGC |
| *Mus musculus* | *ttn* | GACACCACAAGGTGCAAAGTC | CCCACTGTTCTTGACCGTATCT |
| *Mus musculus* | *hbb-bh1* | CTGGGAAGGCTCCTGATTGT | GTTCTTAACCCCCAAGCCCA |
| *Mus musculus* | *actc1* | ATGTGTGACGACGAGGAGAC | CGGACAATTTCACGTTCAGCA |

**Supplementary Note 1. Description of main activators.**

dCas9-VP64 consists of dCas9 with four copies of the VP16 activation domain fused the C-terminus of dCas9. dCas9-VPR consists of dCas9 fused to the activation domains VP64, p65, and rta with each activation domain separated by a short amino acid linker. This results in six activation domains fused to the C-terminus of dCas9. SAM (synergistic activation mediator) consists of dCas9-VP64 with a modified gRNA which recruits the construct, MCP-p65-hsf1. The modified gRNA within the SAM system contains two MS2 hairpins which protrude from the gRNA at the tetraloop and stem loop 2 and are what are used to recruit MCP-p65-hsf1. MCP-p65-hsf1 binds these MS2 hairpin sequences as a dimer, resulting in four sets of the activation domains p65 and hsf1 being recruited. Along with the VP64 component, this means that 12 domains are theoretically recruited within the SAM system. Suntag consists of a dCas9 component with a chain of 10 peptide epitopes called GCN4 fused repetitively to the C-terminus of dCas9. Along with this epitope containing dCas9 protein a single chain antibodies with specificity to the GCN4 epitope fused to VP64 is also expressed in trans. This results in the theoretical recruitment of 10 VP64 molecules or  40 activation domains recruited to one locus. Scaffold consists of a dCas9 component with a modified gRNA similar to the SAM gRNA except only three copies of MCP-VP64 are recruited[14]. The gRNA has one normal MS2 hairpin which recruits a dimer of MCP-VP64 and an F6 aptamer which recruits two MCP-VP64 protein resulting in a theoretical total of sixteen activation domains being recruited by Scaffold. P300 is the catalytic core of the human acetyltransferase p300 protein directly fused to dCas9[18]. VP160 consists of 10 repeats of VP16 fused to the C-terminus of dCas9 instead of the usual four repeats used in dCas9-VP64[19]. VP64-dCas9-BFP-VP64 is dCas9 with VP64 fused to the N-terminus and BFP-VP64 fused to the C-terminus resulting in eight activation domains driving transcription[17].

**Supplementary Note 2: Sequences for original constructs**

**ms2-VPR**

**SV40-NLS + MS2 + VP64 + SV40-NLS + p65 + rta**

**CCTAAGAAAAAGAGGAAGGTGGCGGCCGCTGACTACAAGGATGACGACGATAAATCTA
GAATGGCTTCTAACTTTACTCAGTTCGTTCTCGTCGACAATGGCGGAACTGGCGACGTGA
CTGTCGCCCCAAGCAACTTCGCTAACGGGATCGCTGAATGGATCAGCTCTAACTCGCGT
TCACAGGCTTACAAAGTAACCTGTAGCGTTCGTCAGAGCTCTGCGCAGAATCGCAAATA
CACCATCAAAGTCGAGGTGCCTAAAGGCGCCTGGCGTTCGTACTTAAATATGGAACTAA
CCATTCCAATTTTCGCCACGAATTCCGACTGCGAGCTTATTGTTAAGGCAATGCAAGGTC
TCCTAAAAGATGGAAACCCGATTCCCTCAGCAATCGCAGCAAACTCCGGCATCTACGAG
GCCAGCGAGGCCAGCGGTTCCGGACGGGCTGACGCATTGGACGATTTTGATCTGGATAT
GCTGGGAAGTGACGCCCTCGATGATTTTGACCTTGACATGCTTGGTTCGGATGCCCTTGA
TGACTTTGACCTCGACATGCTCGGCAGTGACGCCCTTGATGATTTCGACCTGGACATGCT
GATTAACTCTAGAAGTTCCGGATCTCCGAAAAAGAAACGCAAAGTTGGTAGCCAGTACC
TGCCCGACACCGACGACCGGCACCGGATCGAGGAAAAGCGGAAGCGGACCTACGAGA
CATTCAAGAGCATCATGAAGAAGTCCCCCTTCAGCGGCCCCACCGACCCTAGACCTCCA
CCTAGAAGAATCGCCGTGCCCAGCAGATCCAGCGCCAGCGTGCCAAAACCTGCCCCCC
AGCCTTACCCCTTCACCAGCAGCCTGAGCACCATCAACTACGACGAGTTCCCTACCATG
GTGTTCCCCAGCGGCCAGATCTCTCAGGCCTCTGCTCTGGCTCCAGCCCCTCCTCAGGT
GCTGCCTCAGGCTCCTGCTCCTGCACCAGCTCCAGCCATGGTGTCTGCACTGGCTCAGG
CACCAGCACCCGTGCCTGTGCTGGCTCCTGGACCTCCACAGGCTGTGGCTCCACCAGCC
CCTAAACCTACACAGGCCGGCGAGGGCACACTGTCTGAAGCTCTGCTGCAGCTGCAGTT**

**CGACGACGAGGATCTGGGAGCCCTGCTGGGAAACAGCACCGATCCTGCCGTGTTCACC
GACCTGGCCAGCGTGGACAACAGCGAGTTCCAGCAGCTGCTGAACCAGGGCATCCCTG
TGGCCCCTCACACCACCGAGCCCATGCTGATGGAATACCCCGAGGCCATCACCCGGCTC
GTGACAGGCGCTCAGAGGCCTCCTGATCCAGCTCCTGCCCCTCTGGGAGCACCAGGCCT
GCCTAATGGACTGCTGTCTGGCGACGAGGACTTCAGCTCTATCGCCGATATGGATTTCTC
AGCCTTGCTGGGCTCTGGCAGCGGCAGCCGGGATTCCAGGGAAGGGATGTTTTTGCCGA
AGCCTGAGGCCGGCTCCGCTATTAGTGACGTGTTTGAGGGCCGCGAGGTGTGCCAGCCA
AAACGAATCCGGCCATTTCATCCTCCAGGAAGTCCATGGGCCAACCGCCCACTCCCCGC
CAGCCTCGCACCAACACCAACCGGTCCAGTACATGAGCCAGTCGGGTCACTGACCCCG
GCACCAGTCCCTCAGCCACTGGATCCAGCGCCCGCAGTGACTCCCGAGGCCAGTCACCT
GTTGGAGGATCCCGATGAAGAGACGAGCCAGGCTGTCAAAGCCCTTCGGGAGATGGCC
GATACTGTGATTCCCCAGAAGGAAGAGGCTGCAATCTGTGGCCAAATGGACCTTTCCCA
TCCGCCCCCAAGGGGCCATCTGGATGAGCTGACAACCACACTTGAGTCCATGACCGAGG
ATCTGAACCTGGACTCACCCCTGACCCCGGAATTGAACGAGATTCTGGATACCTTCCTGA
ACGACGAGTGCCTCTTGCATGCCATGCATATCAGCACAGGACTGTCCATCTTCGACACAT
CTCTGTTT**

All scFv proteins are downstream of an SV40 promoter and upstream of a GB1 sequence and a Rex NLS

**scFv-VPR**

**scFv + sfGFP + VP64 + SV40-NLS + p65 + rta**

**ATGGGCCCCGACATCGTGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCG
ACCGCGTGACCATCACCTGCCGCAGCAGCACCGGCGCCGTGACCACCAGCAACTACGC
CAGCTGGGTGCAGGAGAAGCCCGGCAAGCTGTTCAAGGGCCTGATCGGCGGCACCAAC
AACCGCGCCCCCGGCGTGCCCAGCCGCTTCAGCGGCAGCCTGATCGGCGACAAGGCCA
CCCTGACCATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTTCTGCGCCCTGTGG
TACAGCAACCACTGGGTGTTCGGCCAGGGCACCAAGGTGGAGCTGAAGCGCGGCGGCG
GCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCAGCGGCGGCGGCAGCGAG
GTGAAGCTGCTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAAGCTG
AGCTGCGCCGTGAGCGGCTTCAGCCTGACCGACTACGGCGTGAACTGGGTGCGCCAGG
CCCCCGGCCGCGGCCTGGAGTGGATCGGCGTGATCTGGGGCGACGGCATCACCGACTA
CAACAGCGCCCTGAAGGACCGCTTCATCATCAGCAAGGACAACGGCAAGAACACCGTG
TACCTGCAGATGAGCAAGGTGCGCAGCGACGACACCGCCCTGTACTACTGCGTGACCG
GCCTGTTCGACTACTGGGGCCAGGGCACCCTGGTGACCGTGAGCAGCTACCCATACGAT
GTTCCAGATTACGCTGGTGGAGGCGGAGGTTCTGGGGGAGGAGGTAGTGGCGGTGGTG
GTTCAGGAGGCGGCGGAAGCTTGGATCCAGGTGGAGGTGGAAGCGGTAGCAAAGGAGA
AGAACTTTTCACTGGAGTTGTCCCAATTCTTGTTGAATTAGATGGTGATGTTAATGGGCAC
AAATTTTCTGTCCGTGGAGAGGGTGAAGGTGATGCTACAAACGGAAAACTCACCCTTAA
ATTTATTTGCACTACTGGAAAACTACCTGTTCCGTGGCCAACACTTGTCACTACTCTGACC
TATGGTGTTCAATGCTTTTCCCGTTATCCGGATCACATGAAACGGCATGACTTTTTCAAGA
GTGCCATGCCCGAAGGTTATGTACAGGAACGCACTATATCTTTCAAAGATGACGGGACC
TACAAGACGCGTGCTGAAGTCAAGTTTGAAGGTGATACCCTTGTTAATCGTATCGAGTTA
AAGGGTATTGATTTTAAAGAAGATGGAAACATTCTTGGACACAAACTCGAGTACAACTTT
AACTCACACAATGTATACATCACGGCAGACAAACAAAAGAATGGAATCAAAGCTAACTT**

CAAAATTCGCCACAACGTTGAAGATGGTTCCGTTCAACTAGCAGACCATTATCAACAAAA
TACTCCAATTGGCGATGGCCCTGTCCTTTTACCAGACAACCATTACCTGTCGACACAATC
TGTCCTTTCGAAAGATCCCAACGAAAAGCGTGACCACATGGTCCTTCTTGAGTTTGTAAC
TGCTGCTGGGATTACACATGGCATGGATGAGCTCTACAAAGGTGGAGGTCGGACCGGTG
TTGATGCGTACAAACCGACCAAGTCTGGCTCAGAGGCCAGCGGTTCCGGACGGGCTGA
CGCATTGGACGATTTTGATCTGGATATGCTGGGAAGTGACGCCCTCGATGATTTTGACCT
TGACATGCTTGGTTCGGATGCCCTTGATGACTTTGACCTCGACATGCTCGGCAGTGACGC
CCTTGATGATTTCGACCTGGACATGCTGATTAACTCTAGAAGTTCCGGATCTCCGAAAAA
GAAACGCAAAGTTGGTAGCCAGTACCTGCCCGACACCGACGACCGGCACCGGATCGAG
GAAAAGCGGAAGCGGACCTACGAGACATTCAAGAGCATCATGAAGAAGTCCCCCTTCA
GCGGCCCCACCGACCCTAGACCTCCACCTAGAAGAATCGCCGTGCCCAGCAGATCCAG
CGCCAGCGTGCCAAAACCTGCCCCCCAGCCTTACCCCTTCACCAGCAGCCTGAGCACCA
TCAACTACGACGAGTTCCCTACCATGGTGTTCCCCAGCGGCCAGATCTCTCAGGCCTCTG
CTCTGGCTCCAGCCCCTCCTCAGGTGCTGCCTCAGGCTCCTGCTCCTGCACCAGCTCCA
GCCATGGTGTCTGCACTGGCTCAGGCACCAGCACCCGTGCCTGTGCTGGCTCCTGGACC
TCCACAGGCTGTGGCTCCACCAGCCCCTAAACCTACACAGGCCGGCGAGGGCACACTG
TCTGAAGCTCTGCTGCAGCTGCAGTTCGACGACGAGGATCTGGGAGCCCTGCTGGGAAA
CAGCACCGATCCTGCCGTGTTCACCGACCTGGCCAGCGTGGACAACAGCGAGTTCCAGC
AGCTGCTGAACCAGGGCATCCCTGTGGCCCCTCACACCACCGAGCCCATGCTGATGGAA
TACCCCGAGGCCATCACCCGGCTCGTGACAGGCGCTCAGAGGCCTCCTGATCCAGCTCC
TGCCCCTCTGGGAGCACCAGGCCTGCCTAATGGACTGCTGTCTGGCGACGAGGACTTCA
GCTCTATCGCCGATATGGATTTCTCAGCCTTGCTGGGCTCTGGCAGCGGCAGCCGGGAT
TCCAGGGAAGGGATGTTTTTGCCGAAGCCTGAGGCCGGCTCCGCTATTAGTGACGTGTT
TGAGGGCCGCGAGGTGTGCCAGCCAAAACGAATCCGGCCATTTCATCCTCCAGGAAGTC
CATGGGCCAACCGCCCACTCCCCGCCAGCCTCGCACCAACACCAACCGGTCCAGTACAT
GAGCCAGTCGGGTCACTGACCCCGGCACCAGTCCCTCAGCCACTGGATCCAGCGCCCG
CAGTGACTCCCGAGGCCAGTCACCTGTTGGAGGATCCCGATGAAGAGACGAGCCAGGC
TGTCAAAGCCCTTCGGGAGATGGCCGATACTGTGATTCCCCAGAAGGAAGAGGCTGCAA
TCTGTGGCCAAATGGACCTTTCCCATCCGCCCCCAAGGGGCCATCTGGATGAGCTGACA
ACCACACTTGAGTCCATGACCGAGGATCTGAACCTGGACTCACCCCTGACCCCGGAATT
GAACGAGATTCTGGATACCTTCCTGAACGACGAGTGCCTCTTGCATGCCATGCATATCAG
CACAGGACTGTCCATCTTCGACACATCTCTGTTTGGAGGAGGATCTCGGACCGAA

**scFv-p65-hsf1**

**scFv + sfGFP + p65 + hsf1**

ATGGGCCCCGACATCGTGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCG
ACCGCGTGACCATCACCTGCCGCAGCAGCACCGGCGCCGTGACCACCAGCAACTACGC
CAGCTGGGTGCAGGAGAAGCCCGGCAAGCTGTTCAAGGGCCTGATCGGCGGCACCAAC
AACCGCGCCCCCGGCGTGCCCAGCCGCTTCAGCGGCAGCCTGATCGGCGACAAGGCCA
CCCTGACCATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTTCTGCGCCCTGTGG
TACAGCAACCACTGGGTGTTCGGCCAGGGCACCAAGGTGGAGCTGAAGCGCGGCGGCG
GCGGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCAGCGGCGGCGGCAGCGAG
GTGAAGCTGCTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAAGCTG
AGCTGCGCCGTGAGCGGCTTCAGCCTGACCGACTACGGCGTGAACTGGGTGCGCCAGG

**CCCCCGGCCGCGGCCTGGAGTGGATCGGCGTGATCTGGGGCGACGGCATCACCGACTA
CAACAGCGCCCTGAAGGACCGCTTCATCATCAGCAAGGACAACGGCAAGAACACCGTG
TACCTGCAGATGAGCAAGGTGCGCAGCGACGACACCGCCCTGTACTACTGCGTGACCG
GCCTGTTCGACTACTGGGGCCAGGGCACCCTGGTGACCGTGAGCAGCTACCCATACGAT
GTTCCAGATTACGCTGGTGGAGGCGGAGGTTCTGGGGGAGGAGGTAGTGGCGGTGGTG
GTTCAGGAGGCGGCGGAAGCTTGGATCCAGGTGGAGGTGGAAGCGGTAGCAAAGGAGA
AGAACTTTTCACTGGAGTTGTCCCAATTCTTGTTGAATTAGATGGTGATGTTAATGGGCAC
AAATTTTCTGTCCGTGGAGAGGGTGAAGGTGATGCTACAAACGGAAAACTCACCCTTAA
ATTTATTTGCACTACTGGAAAACTACCTGTTCCGTGGCCAACACTTGTCACTACTCTGACC
TATGGTGTTCAATGCTTTTCCCGTTATCCGGATCACATGAAACGGCATGACTTTTTCAAGA
GTGCCATGCCCGAAGGTTATGTACAGGAACGCACTATATCTTTCAAAGATGACGGGACC
TACAAGACGCGTGCTGAAGTCAAGTTTGAAGGTGATACCCTTGTTAATCGTATCGAGTTA
AAGGGTATTGATTTTAAAGAAGATGGAAACATTCTTGGACACAAACTCGAGTACAACTTT
AACTCACACAATGTATACATCACGGCAGACAAACAAAAGAATGGAATCAAAGCTAACTT
CAAAATTCGCCACAACGTTGAAGATGGTTCCGTTCAACTAGCAGACCATTATCAACAAAA
TACTCCAATTGGCGATGGCCCTGTCCTTTTACCAGACAACCATTACCTGTCGACACAATC
TGTCCTTTCGAAAGATCCCAACGAAAAGCGTGACCACATGGTCCTTCTTGAGTTTGTAAC
TGCTGCTGGGATTACACATGGCATGGATGAGCTCTACAAAGGTGGAGGTCGGACCGGTG
CGGCCGCTGGATCCCCTTCAGGGCAGATCAGCAACCAGGCCCTGGCTCTGGCCCCTAG
CTCCGCTCCAGTGCTGGCCCAGACTATGGTGCCCTCTAGTGCTATGGTGCCTCTGGCCC
AGCCACCTGCTCCAGCCCCTGTGCTGACCCCAGGACCACCCCAGTCACTGAGCGCTCCA
GTGCCCAAGTCTACACAGGCCGGCGAGGGGACTCTGAGTGAAGCTCTGCTGCACCTGC
AGTTCGACGCTGATGAGGACCTGGGAGCTCTGCTGGGGAACAGCACCGATCCCGGAGT
GTTCACAGATCTGGCCTCCGTGGACAACTCTGAGTTTCAGCAGCTGCTGAATCAGGGCG
TGTCCATGTCTCATAGTACAGCCGAACCAATGCTGATGGAGTACCCCGAAGCCATTACC
CGGCTGGTGACCGGCAGCCAGCGGCCCCCCGACCCCGCTCCAACTCCCCTGGGAACCA
GCGGCCTGCCTAATGGGCTGTCCGGAGATGAAGACTTCTCAAGCATCGCTGATATGGAC
TTTAGTGCCCTGCTGTCACAGATTTCCTCTAGTGGGCAGGGAGGAGGTGGAAGCGGCTT
CAGCGTGGACACCAGTGCCCTGCTGGACCTGTTCAGCCCCTCGGTGACCGTGCCCGACA
TGAGCCTGCCTGACCTTGACAGCAGCCTGGCCAGTATCCAAGAGCTCCTGTCTCCCCAG
GAGCCCCCCAGGCCTCCCGAGGCAGAGAACAGCAGCCCGGATTCAGGGAAGCAGCTG
GTGCACTACACAGCGCAGCCGCTGTTCCTGCTGGACCCCGGCTCCGTGGACACCGGGA
GCAACGACCTGCCGGTGCTGTTTGAGCTGGGAGAGGGCTCCTACTTCTCCGAAGGGGAC
GGCTTCGCCGAGGACCCCACCATCTCCCTGCTGACAGGCTCGGAGCCTCCCAAAGCCAA
GGACCCCACTGTCTCCGGTAGT**

Scaffold Variants
All Scaffold variants start after guide sequence and end before the terminator

**SAM gRNA + Scaffold Tail with point mutations disabling the second half of the tail
GTTTTAGAGCTAGGCCAACATGAGGATCACCCATGTCTGCAGGGCCTAGCAAGTTAAAA
TAAGGCTAGTCCGTTATCAACTTGGCCAACATGAGGATCACCCATGTCTGCAGGGCCAA
GTGGCACCGAGTCGGTGCGGGAGCACATGAGGATCACCCATGTGCGACTCCGAGAGTA
ACTGGGGAGTCTTCCC**

**SAM gRNA + Scaffold Tail with point mutations disabling the first half of the tail**
**GTTTTAGAGCTAGGCCAACATGAGGATCACCCATGTCTGCAGGGCCTAGCAAGTTAAAA TAAGGCTAGTCCGTTATCAACTTGGCCAACATGAGGATCACCCATGTCTGCAGGGCCAA GTGGCACCGAGTCGGTGCGGGAGCACATCATAATCAGCCATGTGCGACTCCCACAGTCA CTGGGGAGTCTTCCC**

**SAM gRNA + Scaffold Tail**
**GTTTTAGAGCTAGGCCAACATGAGGATCACCCATGTCTGCAGGGCCTAGCAAGTTAAAA TAAGGCTAGTCCGTTATCAACTTGGCCAACATGAGGATCACCCATGTCTGCAGGGCCAA GTGGCACCGAGTCGGTGCGGGAGCACATGAGGATCACCCATGTGCGACTCCCACAGTC ACTGGGGAGTCTTCCC**

**SAM gRNA with first ms2 hairpin extension deleted + Scaffold Tail**
**GTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGGCCAACA TGAGGATCACCCATGTCTGCAGGGCCAAGTGGCACCGAGTCGGTGCGGGAGCACATGA GGATCACCCATGTGCGACTCCCACAGTCACTGGGGAGTCTTCCC**

**SAM gRNA with second ms2 hairpin extension deleted + Scaffold Tail**
**GTTTTAGAGCTAGGCCAACATGAGGATCACCCATGTCTGCAGGGCCTAGCAAGTTAAAA TAAGGCTAGTCCGTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCGGGAGCACATGA GGATCACCCATGTGCGACTCCCACAGTCACTGGGGAGTCTTCCC**

**Supplementary References:**

41. Nishimasu, H. *et al.* Crystal structure of Cas9 in complex with guide RNA and target DNA. *Cell* **156,** 935–949 (2014).