Supplementary Table 1, Spacer Sequences Tested in This Study

Cas Effector	Gene Target	Alias	Spacer Sequence	Free Energy, kcal/mol
SpCas9	IL1RN site 1	WT	GCAUCAAGUCAGCCAUCAGC	-0.3
SpCas9	IL1RN site 1	Hp9	GAUGC AACA GCAUCAAGUCAGCCAUCAGC	-6.7
SpCas9	IL1RN site 1	Hp13	GCUUGAUGC AACA GCAUCAAGUCAGCCAUCAGC	-12.4
SpCas9	IL1RN site 1	Hp14	GACUUGAUGC AACA GCAUCAAGUCAGCCAUCAGC	-16.4
SpCas9	IL1RN site 1	Hp15	GGACUUGAUGC AACA GCAUCAAGUCAGCCAUCAGC	-16.1
SpCas9	IL1RN site 1	Hp16	GUGACUUGAUGC AACA GCAUCAAGUCAGCCAUCAGC	-17.4
SpCas9	IL1RN site 1	Hp17	GCUGACUUGAUGC AACA GCAUCAAGUCAGCCAUCAGC	-23.0
SpCas9	IL1RN site 1	Hp21	GAUGGCUGACUUGAUGC AACA GCAUCAAGUCAGCCAUCAGC	-32.8
SpCas9	IL1RN site 1	Ns9	GUAUC AAUA GCAUCAAGUCAGCCAUCAGC	-0.5
SpCas9	IL1RN site 1	Ns13	GUCGAUAUC AAUA GCAUCAAGUCAGCCAUCAGC	-0.7
SpCas9	IL1RN site 1	Ns17	GUCGAUCAGUAUC AAUA GCAUCAAGUCAGCCAUCAGC	-0.9
SpCas9	IL1RN site 1	Ns21	GCAGUUCAGUCAGUAUC AAUA GCAUCAAGUCAGCCAUCAGC	-0.7
SpCas9	HBG1 site 1	WT	GGCUAGGGAUGAAGAAUAAA	0.0
SpCas9	HBG1 site 1	Hp8	GGCC AACA GGCUAGGGAUGAAGAAUAAA	-4.0
SpCas9	HBG1 site 1	Hp10	GUAGCC AACA GGCUAGGGAUGAAGAAUAAA	-6.6
SpCas9	HBG1 site 1	Hp12	GCCUAGCC AACA GGCUAGGGAUGAAGAAUAAA	-11.7
SpCas9	HBG1 site 1	Hp13	GCCCUAGCC AACA GGCUAGGGAUGAAGAAUAAA	-14.4
SpCas9	HBG1 site 1	Hp15	GAUCCCUAGCC AACA GGCUAGGGAUGAAGAAUAAA	-17.4
SpCas9	HBG1 site 1	Hp17	GUCAUCCCUAGCC AACA GGCUAGGGAUGAAGAAUAAA	-21.4
SpCas9	HBG1 site 1	Hp19	GCUUCAUCCCUAGCC AACA GGCUAGGGAUGAAGAAUAAA	-24.3
SpCas9	HBG1 site 1	Hp23	GUAUUCUUCAUCCCUAGCC AACA GGCUAGGGAUGAAGAAUAAA	-29.2
SpCas9	HBG1 site 1	Ns17	GACAAAAGAGACG AAAA GGCUAGGGAUGAAGAAUAAA	0.0
SpCas9	HBG1 site 1	Ns19	GGAACAAAAGAGACG AAAA GGCUAGGGAUGAAGAAUAAA	0.0
SpCas9	HBG1 site 1	Ns23	GAUAAGAAAACAAGAGACG AAAA GGCUAGGGAUGAAGAAUAAA	0.0
SpCas9	IL1B site 1	WT	G AAAAACAGCGAGGGAGAAAC	0.0
SpCas9	IL1B site 1	Hp11	GUGUUUUC AACA AAAAACAGCGAGGGAGAAAC	-3.6
SpCas9	IL1B site 1	Hp12	GCUGUUUUC AACA AAAAACAGCGAGGGAGAAAC	-9.4
SpCas9	IL1B site 1	Hp15	GUCGCUGUUUUC AACA AAAAACAGCGAGGGAGAAAC	-13
SpCas9	IL1B site 1	Hp16	GCUCGCUGUUUUC AACA AAAAACAGCGAGGGAGAAAC	-15.2
SpCas9	IL1B site 1	Hp17	GCCUCGCUGUUUUC AACA AAAAACAGCGAGGGAGAAAC	-18.1
SpCas9	IL1B site 1	Hp19	GUCCCUCGCUGUUUUC AACA AAAAACAGCGAGGGAGAAAC	-22.8
SpCas9	IL1B site 1	Hp23	GUUUCUCCCUCGCUGUUUUC AACA AAAAACAGCGAGGGAGAAAC	-29.7
SpCas9	IL1B site 1	Ns11	GACAUACU AACA AAAAACAGCGAGGGAGAAAC	0.0
SpCas9	IL1B site 1	Ns15	GAUAGACAAAAA AACA AAAAACAGCGAGGGAGAAAC	0.0
SpCas9	IL1B site 1	Ns17	GGGAAAGACAUACU AACA AAAAACAGCGAGGGAGAAAC	0.0
SpCas9	IL1B site 1	Ns19	GACGGAAAGACAUACU AACA AAAAACAGCGAGGGAGAAAC	0.0
SpCas9	IL1B site 1	Ns23	GAAACAGGGAAUCACAUACU AACA AAAAACAGCGAGGGAGAAAC	0.0
SpCas9	EMX1 site 1	WT	GAGUCCGAGCAGAAGAAGAA	0.0
SpCas9	EMX1 site 1	Tru	GUCCGAGCAGAAGAAGAA	0.0
SpCas9	EMX1 site 1	Hp1	GCUCGGACUC UUCG GAGUCCGAGCAGAAGAAGAA	-20.9
SpCas9	EMX1 site 1	Hp2	GGACUC UUCG GAGUCCGAGCAGAAGAAGAA	-11.5
SpCas9	EMX1 site 1	Hp3	GCGG GAGUCCGAGCAGAAGAAGAA	-2.8
SpCas9	EMX1 site 1	Hp4	GUCGG GAGUCCGAGCAGAAGAAGAA	-4.8
SpCas9	EMX1 site 1	Hp5	GCUCGG GAGUCCGAGCAGAAGAAGAA	-10.6
SpCas9	EMX1 site 1	Hp6	GGAC UUCG GUCCGAGCAGAAGAAGAA	-7.5
SpCas9	EMX1 site 1	Hp7	GCGGAC UUCG GUCCGAGCAGAAGAAGAA	-9.1
SpCas9	EMX1 site 1	Ns2	GUAAUG AAUA GAGUCCGAGCAGAAGAAGAA	-0.1
SpCas9	VEGFA site 1	WT	GGUGAGUGAGUGUGUGCGUG	-1.2
SpCas9	VEGFA site 1	Tru	GAGUGAGUGUGUGCGUG	-1.2
SpCas9	VEGFA site 1	Hp1	GACC UUCG GGUGAGUGAGUGUGUGCGUG	-5.8
SpCas9	VEGFA site 1	Hp2	GCACC UUCG GGUGAGUGAGUGUGUGCGUG	-7.6
SpCas9	VEGFA site 1	Hp3	GUCACC UUCG GGUGAGUGAGUGUGUGCGUG	-9.1
SpCas9	VEGFA site 1	Hp4	GCACG UUCG GGUGAGUGAGUGUGUGCGUG	-7.4

SpCas9	VEGFA site 1	Hp5	GUACG UUCG GGUGAGUGAGUGUGUGCGUG	-5.1
SpCas9	VEGFA site 1	Hp6	GCAUG UUCG GGUGAGUGAGUGUGUGCGUG	-5.3
SpCas9	VEGFA site 1	Ns4	GAGGAGUUA GGUGAGUGAGUGUGUGCGUG	-1.2
SpCas9	VEGFA site 2	WT	GGGUGGGGGGAGUUUGCUCC	-3.8
SpCas9	VEGFA site 2	Tru	GUGGGGGGAGUUUGCUCC	-3.4
SpCas9	VEGFA site 2	Hp1	GCCCCCCACCC UUCG GGGUGGGGGGAGUUUGCUCC	-24.0
SpCas9	VEGFA site 2	Hp2	GCCACCC UUCG GGGUGGGGGGAGUUUGCUCC	-15.4
SpCas9	VEGFA site 2	Hp3	GCCCC GGGUGGGGGGAGUUUGCUCC	-8.7
SpCas9	VEGFA site 2	Hp4	GCCC GGGUGGGGGGAGUUUGCUCC	-7.1
SpCas9	VEGFA site 2	Hp5	GCAUCC UUCG GUGUGGGGGGAGUUUGCUCC	-8.5
SpCas9	VEGFA site 2	Ns4	GUGC GUGUGGGGGGAGUUUGCUCC	-3.5
SaCas9	EMX1 site 2	WT	GGGCCUCCCCAAAGCCUGGCCA	-6.6
SaCas9	EMX1 site 2	Tru 20 nt	GGCCUCCCCAAAGCCUGGCCA	-6.6
SaCas9	EMX1 site 2	Tru 19 nt	GCCUCCCCAAAGCCUGGCCA	-2.8
SaCas9	EMX1 site 2	Tru 18 nt	GCUCCCCAAAGCCUGGCCA	-2.0
SaCas9	EMX1 site 2	Hp1	GCC UUCG GGCCUCCCCAAAGCCUGGCCA	-7.6
SaCas9	EMX1 site 2	Hp2	GGCC UUCG GGCCUCCCCAAAGCCUGGCCA	-11.4
SaCas9	EMX1 site 2	Hp3	GGGCC UUCG GGCCUCCCCAAAGCCUGGCCA	-11.4
SaCas9	EMX1 site 2	Hp4	GAGGCC UUCG GGCCUCCCCAAAGCCUGGCCA	-14.2
SaCas9	EMX1 site 2	Ns4	GACCAU AAUA GGCCUCCCCAAAGCCUGGCCA	-6.8
SaCas9-KKH	EMX1 site 3	WT	GUGUGGUUCCAGAACCGGAGGA	-3.5
SaCas9-KKH	EMX1 site 3	Tru 21 nt	GGUGGUUCCAGAACCGGAGGA	-3.5
SaCas9-KKH	EMX1 site 3	Tru 20 nt	GUGGUUCCAGAACCGGAGGA	-3.5
SaCas9-KKH	EMX1 site 3	Tru 19 nt	GGGUUCCAGAACCGGAGGA	-3.5
SaCas9-KKH	EMX1 site 3	Hp1	GCACAC UUCG GUGUGGUUCCAGAACCGGAGGA	-11.3
SaCas9-KKH	EMX1 site 3	Hp2	GCCACAC UUCG GUGUGGUUCCAGAACCGGAGGA	-13.3
SaCas9-KKH	EMX1 site 3	Hp3	GACCACAC UUCG GUGUGGUUCCAGAACCGGAGGA	-15.0
SaCas9-KKH	EMX1 site 3	Hp4	GAACCACAC UUCG GUGUGGUUCCAGAACCGGAGGA	-15.7
SaCas9-KKH	EMX1 site 3	Hp5	GGAACCACAC UUCG GUGUGGUUCCAGAACCGGAGGA	-19.5
SaCas9-KKH	EMX1 site 3	Ns	GUAAUGUG AAGC GUGUGGUUCCAGAACCGGAGGA	-4.7
SaCas9-KKH	EMX1 site 4	WT	GCUCAGCCUGAGUGUUGAGGC	-6.0
SaCas9-KKH	EMX1 site 4	Tru 20 nt	GUCAGCCUGAGUGUUGAGGC	-4.3
SaCas9-KKH	EMX1 site 4	Tru 19 nt	GCAGCCUGAGUGUUGAGGC	-4.3
SaCas9-KKH	EMX1 site 4	Tru 18 nt	GAGCCUGAGUGUUGAGGC	-4.3
SaCas9-KKH	EMX1 site 4	Hp1	GAGC AACA GCUCAGCCUGAGUGUUGAGGC	-9.7
SaCas9-KKH	EMX1 site 4	Hp2	GUGAGC AACA GCUCAGCCUGAGUGUUGAGGC	-10
SaCas9-KKH	EMX1 site 4	Hp3	GCUGAGC AACA GCUCAGCCUGAGUGUUGAGGC	-11.6
SaCas9-KKH	EMX1 site 4	Hp4	GGCUGAGC AACA GCUCAGCCUGAGUGUUGAGGC	-14.9
SaCas9-KKH	EMX1 site 4	Ns	GAUA AACA GCUCAGCCUGAGUGUUGAGGC	-6.0
SaCas9-KKH	EMX1 site 5	WT	GCAACCACAAACCCACGAGGG	-2.8
SaCas9-KKH	EMX1 site 5	Tru 20 nt	GAACCACAAACCCACGAGGG	-2.8
SaCas9-KKH	EMX1 site 5	Tru 19 nt	GACCACAAACCCACGAGGG	-2.8
SaCas9-KKH	EMX1 site 5	Tru 18 nt	GCCACAAACCCACGAGGG	-2.8
SaCas9-KKH	EMX1 site 5	Hp1	GUGC AACA GCAACCACAAACCCACGAGGG	-5.5
SaCas9-KKH	EMX1 site 5	Hp2	GUUGC AACA GCAACCACAAACCCACGAGGG	-8.34
SaCas9-KKH	EMX1 site 5	Hp3	GGUUGC AACA GCAACCACAAACCCACGAGGG	-12.1
SaCas9-KKH	EMX1 site 5	Hp4	GUGGUUGU AACA GCAACCACAAACCCACGAGGG	-14.5
SaCas9-KKH	EMX1 site 5	Ns	GAUA AACA GCAACCACAAACCCACGAGGG	-2.8
SaCas9-KKH	FANCF site 1	WT	GCAAGGCCCGGCGCACGGUGG	-3.7
SaCas9-KKH	FANCF site 1	Tru 20 nt	GAAGGCCCGGCGCACGGUGG	-3.7
SaCas9-KKH	FANCF site 1	Tru 19 nt	GAGGCCCGGCGCACGGUGG	-3.7
SaCas9-KKH	FANCF site 1	Tru 18 nt	GGGCCCGGCGCACGGUGG	-3.7
SaCas9-KKH	FANCF site 1	Hp1	GUGC AACA GCAAGGCCCGGCGCACGGUGG	-6.4
SaCas9-KKH	FANCF site 1	Hp2	GUUGC AACA GCAAGGCCCGGCGCACGGUGG	-7.3
SaCas9-KKH	FANCF site 1	Hp3	GCUUGC AACA GCAAGGCCCGGCGCACGGUGG	-9.5
SaCas9-KKH	FANCF site 1	Hp4	GCCUUGC AACA GCAAGGCCCGGCGCACGGUGG	-14.0

SaCas9-KKH	FANCF site 1	Ns	GAUA AACA GCAAGGCCCGGCGCACGGUGG	-3.7
AsCas12a	DNMT site 1	WT	CUGAUGGUCCAUGUCUGUUA	-1.8
AsCas12a	DNMT site 1	Tru 19 nt	CUGAUGGUCCAUGUCUGUU	-1.8
AsCas12a	DNMT site 1	Tru 18 nt	CUGAUGGUCCAUGUCUGU	-1.8
AsCas12a	DNMT site 1	Tru 17 nt	CUGAUGGUCCAUGUCUG	-1.8
AsCas12a	DNMT site 1	Hp1	CUGAUGGUCCAUGUCUGUUA AGAC	-3.0
AsCas12a	DNMT site 1	Hp2	CUGAUGGUCCAUGUCUGUUA AGACAU	-6.0
AsCas12a	DNMT site 1	Hp3	CUGAUGGUCCAUGUCUGUUA AGACAUGG	-10.5
AsCas12a	DNMT site 1	Hp4	CUGAUGGUCCAUGUCUGUUA AGACAUGGAC	-14.8
AsCas12a	DNMT site 1	Ns3	CUGAUGGUCCAUGUCUGUUA CUCUGCUC	-1.8
AsCas12a	DNMT site 1	Ns4	CUGAUGGUCCAUGUCUGUUA CUCUGCUCAA	-1.8
AsCas12a-RVR	RPL32P3 site 1	WT	GGGUGAUCAGACCCAACAGC	-6.1
AsCas12a-RVR	RPL32P3 site 1	Tru 19 nt	GGGUGAUCAGACCCAACAG	-6.1
AsCas12a-RVR	RPL32P3 site 1	Tru 18 nt	GGGUGAUCAGACCCAACA	-6.1
AsCas12a-RVR	RPL32P3 site 1	Tru 17 nt	GGGUGAUCAGACCCAAC	-6.1
AsCas12a-RVR	RPL32P3 site 1	Hp1	GGGUGAUCAGACCCAACAGC UUCG GCUGUUGGGU	-20.2
AsCas12a-RVR	RPL32P3 site 1	Hp2	GGGUGAUCAGACCCAACAGC UUCG GCUGUUGGGUCUGA	-26.5
AsCas12a-RVR	RPL32P3 site 1	Hp3	GGGUGAUCAGACCCAACAGC UUCG GCUGUUGGGUCUGAUCAC	-33.0
AsCas12a-RVR	RPL32P3 site 1	Ns3	GGGUGAUCAGACCCAACAGC UUAC AGACAACCCAGACUAGUG	-6.1
LbCas12a	DNMT site 1	WT	CUGAUGGUCCAUGUCUGUUA	-1.8
LbCas12a	DNMT site 1	Tru 17 nt	CUGAUGGUCCAUGUCUG	-1.8
LbCas12a	DNMT site 1	Hp1	CUGAUGGUCCAUGUCUGUUA AGACAUGGACCA	-19.8
LbCas12a	DNMT site 1	Hp2	CUGAUGGUCCAUGUCUGUUA AGACAUGGACCAUC	-22.7
LbCas12a	POLQ site 1	WT	GGCAUGAAUUAUAAUGCUGU	-4.0
LbCas12a	POLQ site 1	Tru 19 nt	GGCAUGAAUUAUAAUGCUG	-4.0
LbCas12a	POLQ site 1	Tru 18 nt	GGCAUGAAUUAUAAUGCU	-4.0
LbCas12a	POLQ site 1	Tru 17 nt	GGCAUGAAUUAUAAUGC	-2.8
LbCas12a	POLQ site 1	Hp1	GGCAUGAAUUAUAAUGCUGU AACA ACAGC	-5.1
LbCas12a	POLQ site 1	Hp2	GGCAUGAAUUAUAAUGCUGU AACA ACAGCAUUAU	-10.9
LbCas12a	POLQ site 1	Hp3	GGCAUGAAUUAUAAUGCUGU AACA ACAGCAUUAUAAUUC	-16.8
LbCas12a	POLQ site 1	Hp4	GGCAUGAAUUAUAAUGCUGU AACA ACAGCAUUAUAAUUCA	-18.9
LbCas12a	POLQ site 1	Hp5	GGCAUGAAUUAUAAUGCUGU AACA ACAGCAUUAUAAUUCAUG	-21.5
LbCas12a	POLQ site 1	Hp6	GGCAUGAAUUAUAAUGCUGU AACA ACAGCAUUAUAAUUCAUGCC	-27.6
LbCas12a	POLQ site 1	Ns6	GGCAUGAAUUAUAAUGCUGU AACA AUUAUCAAUAUUAAGCUAUG	-4.0
LbCas12a	IL12A-AS site 1	WT	GGAUGCCACUAAAAGGGAAA	-1.2
LbCas12a	IL12A-AS site 1	Tru 19 nt	GGAUGCCACUAAAAGGGAA	-1.2
LbCas12a	IL12A-AS site 1	Tru 18 nt	GGAUGCCACUAAAAGGGA	-1.2
LbCas12a	IL12A-AS site 1	Tru 17 nt	GGAUGCCACUAAAAGGG	-0.8
LbCas12a	IL12A-AS site 1	Tru 16 nt	GGAUGCCACUAAAAGG	-0.5
LbCas12a	IL12A-AS site 1	Hp1	GGAUGCCACUAAAAGGGAAA AACA UUUCC	-3.4
LbCas12a	IL12A-AS site 1	Hp2	GGAUGCCACUAAAAGGGAAA AACA UUUCCCUUUUA	-11.9
LbCas12a	IL12A-AS site 1	Hp3	GGAUGCCACUAAAAGGGAAA AACA UUUCCCUUUUAGUGG	-20.0
LbCas12a	IL12A-AS site 1	Hp4	GGAUGCCACUAAAAGGGAAA AACA UUUCCCUUUUAGUGGC	-23.2
LbCas12a	IL12A-AS site 1	Hp5	GGAUGCCACUAAAAGGGAAA AACA UUUCCCUUUUAGUGGCAU	-26.3
LbCas12a	IL12A-AS site 1	Hp6	GGAUGCCACUAAAAGGGAAA AACA UUUCCCUUUUAGUGGCAUCC	-31.1
LbCas12a	IL12A-AS site 1	Ns5	GGAUGCCACUAAAAGGGAAA AACA AACAUAGAAUAACACACAUA	-1.2