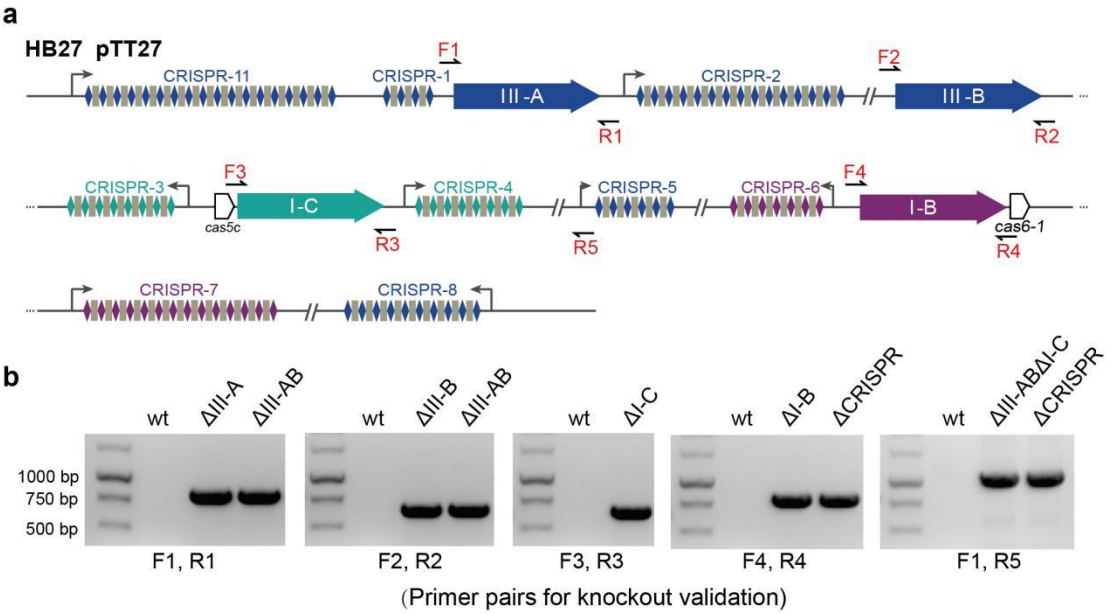
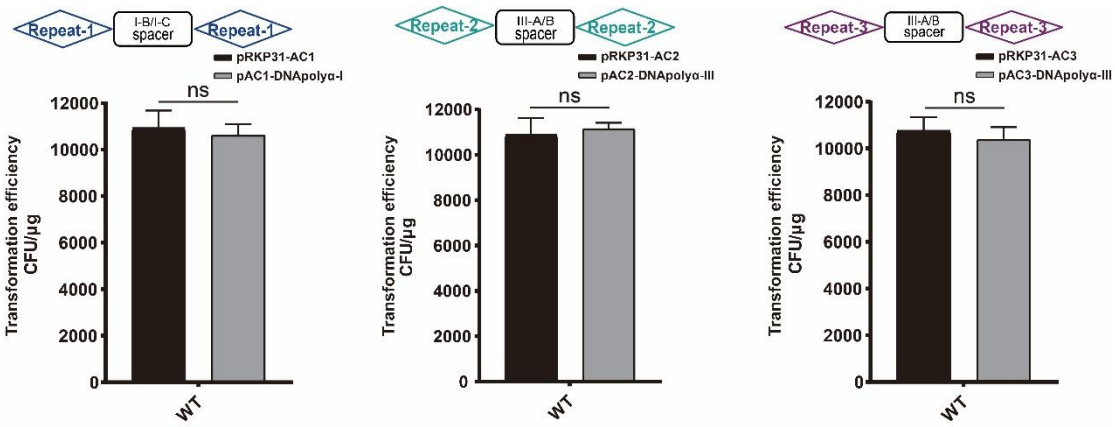
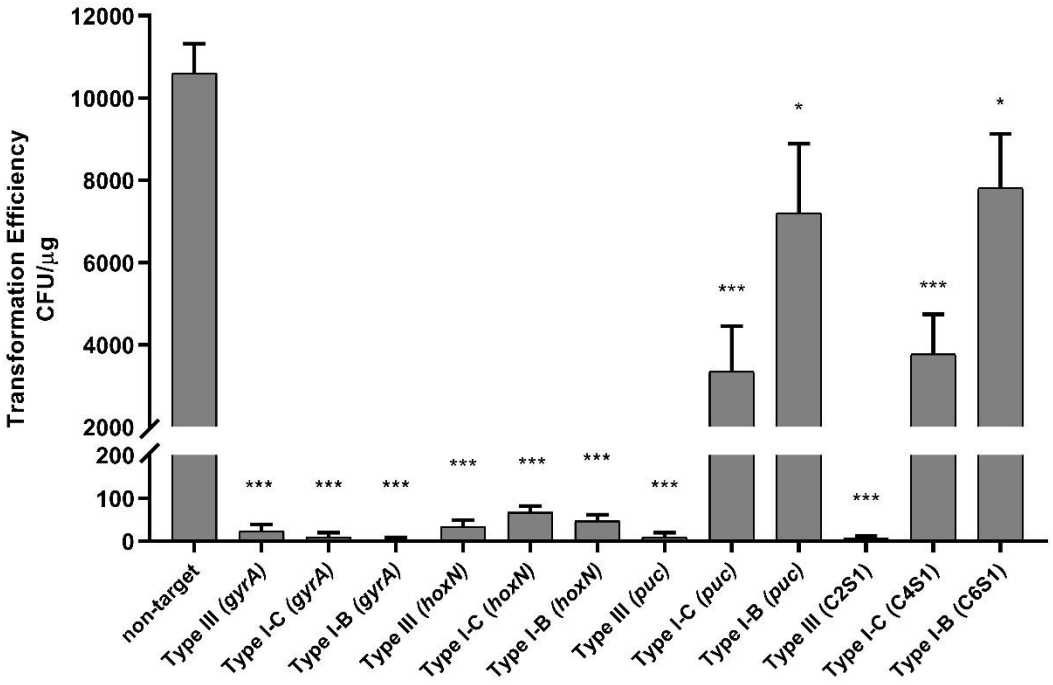


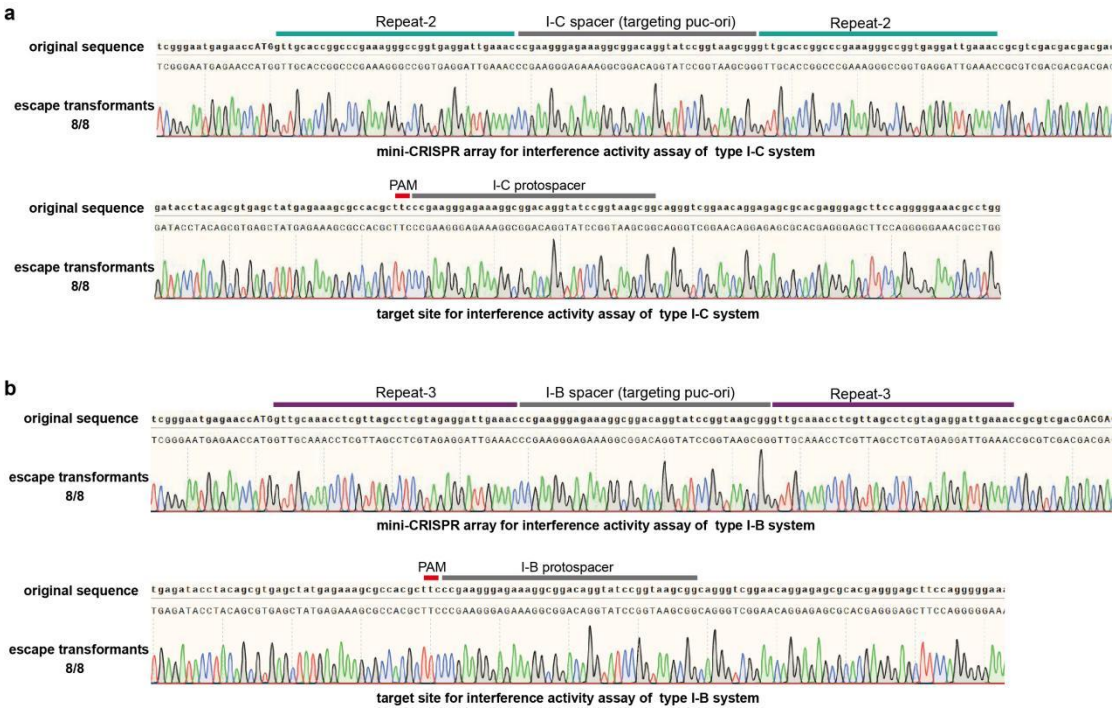
Supplementary Figure S1. Validation of deletion mutant strains of different CRISPR-Cas systems. (A) The location of PCR validation primers is all marked in red. (B) PCR verification of deletion mutants of different endogenous CRISPR-Cas systems. The wild-type strain was not amplified because the target fragment was too long, and only the deletion strain could get the nucleic acid fragment with the expected length.



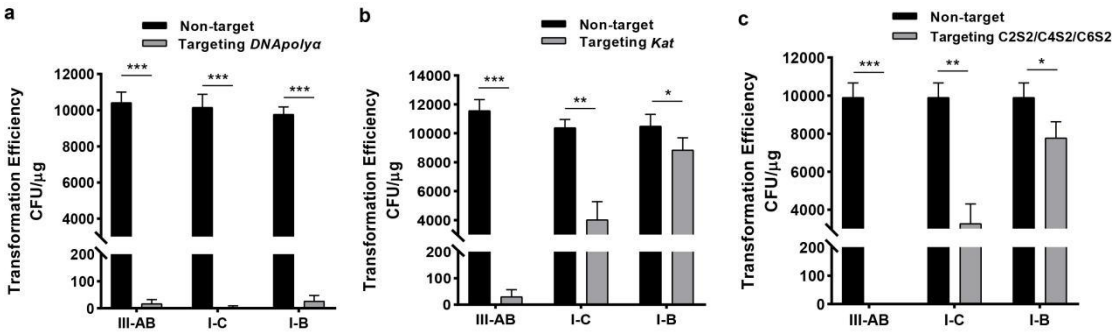
Supplementary Figure S2. Three repeats and two spacers cross-combined mini-CRISPR plasmids showed no interference activity in wild type strain. The spacers in the mini-CRISPR array were designed based on the characteristics of different endogenous systems, targeting the *DNApolyα* gene on the *T. thermophilus* HB27 chromosome. The combination diagram of repeats and spacers is shown in rectangles and diamonds of different colors. The data show means of three replicates. Error bars indicate the standard deviations (SD). Between-group significance was determined using the unpaired two-sample t-test (*$P < 0.05$, **$P < 0.01$, and ***$P < 0.001$). And ns indicates no significance.



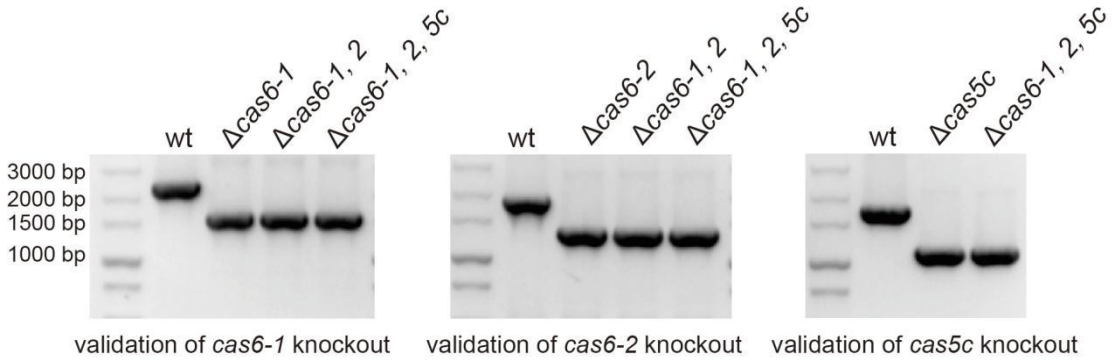
Supplementary Figure S3. The evaluation of defense activity of endogenous CRISPR-Cas systems in HB27 against different targets through the transformation of self-targeting mini-CRISPR plasmids and plasmids containing protospacers. *gyrA*, *hoxN*, and *puc* represent the three target genes located on the chromosome, megaplasmid and exogenous plasmid, respectively. Spacers in the mini-CRISPR plasmid was designed based on the sequences of these three genes. C2S1/C4S1/C6S1 represents the invading plasmids carrying a target sequence of spacer 1 in CRISPR arrays 2, 4 and 6, respectively, which were used to detect the defense activity of III-AB, I-C and I-B CRISPR-Cas systems, respectively. Non-target plasmid was used as a control. Significance values indicate a significant difference from the non-target plasmid group. The data show means of three replicates. Error bars indicate the standard deviations (SD). Between-group significance was determined using the unpaired two-sample t-test (*$P < 0.05$, **$P < 0.01$, and ***$P < 0.001$). And ns indicates no significance.



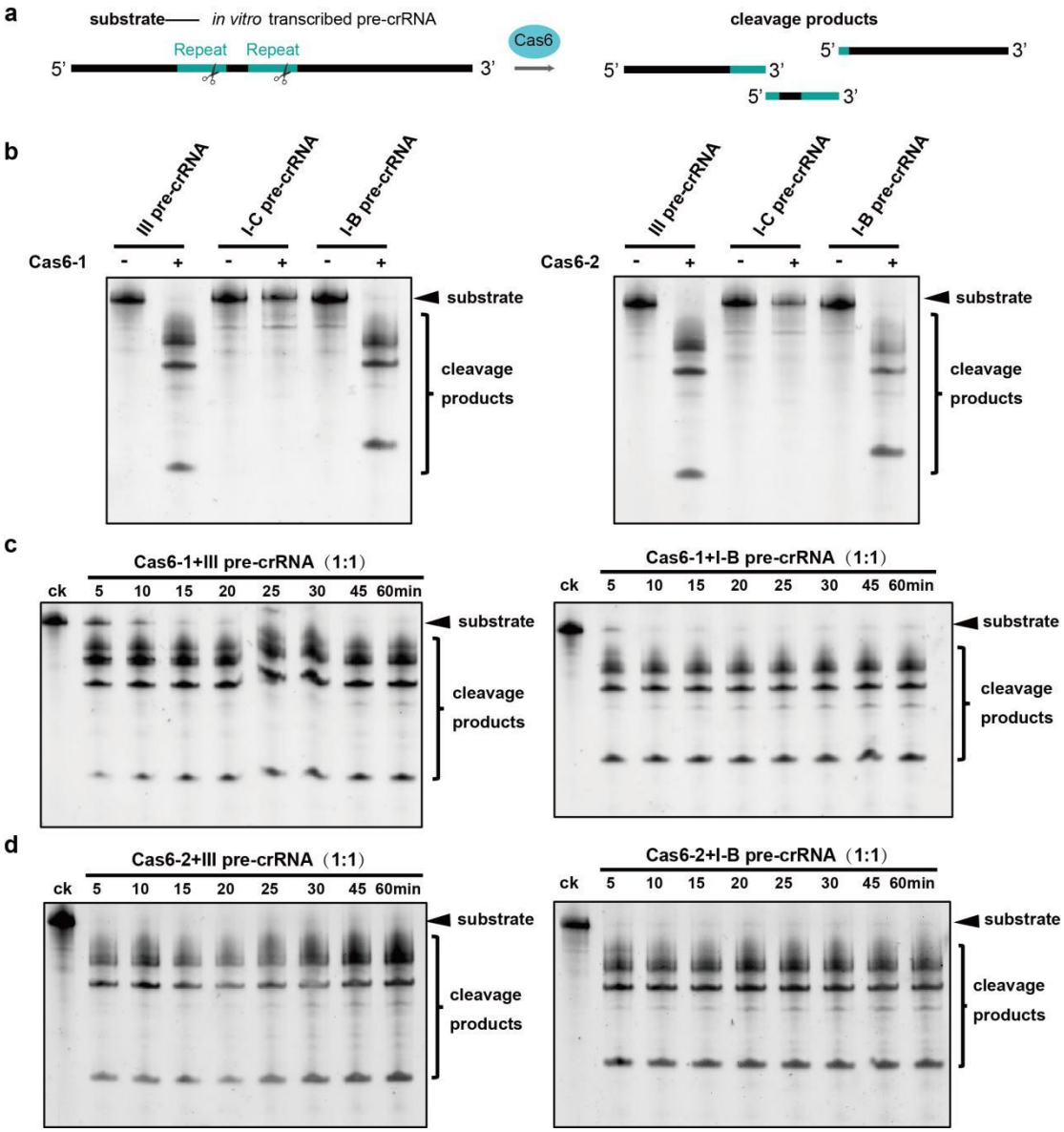
Supplementary Figure S4. Analysis of the mutations in the escape variants when the endogenous type I system interferes with high-copy targets. (**A**) Mutation detection in the mini-CRISPR array and the protospacer sequence of the escape variants for the type I-C system. (B) Mutation detection in the mini-CRISPR array and the protospacer sequence of the escape variants for the type I-B system. For these two systems, both eight escape transformants were randomly selected for mutation detection.



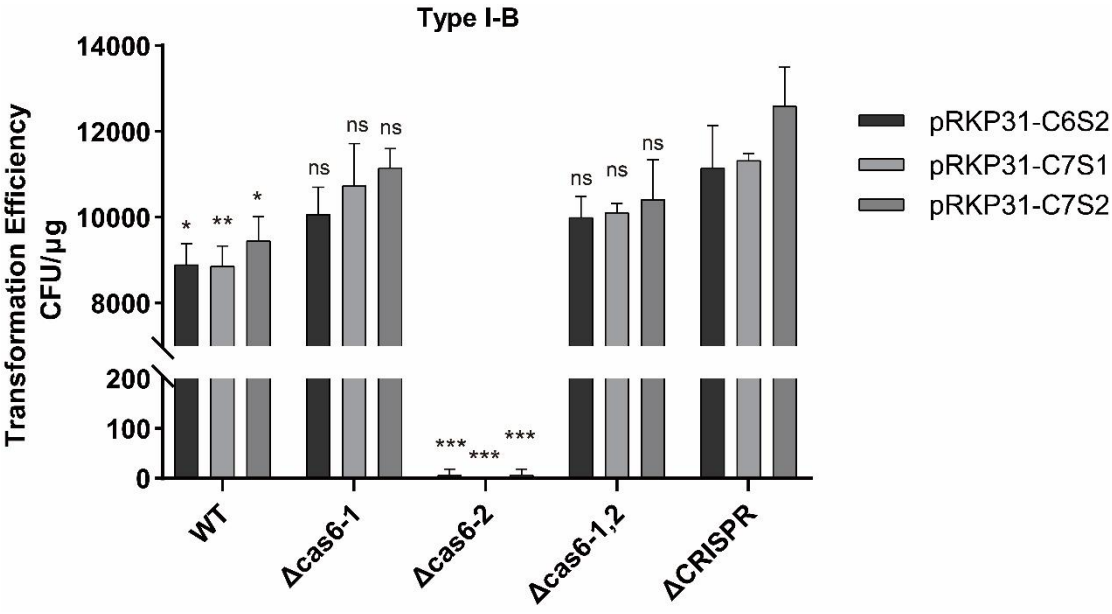
Supplementary Figure S5. The activity differences in interfering with different targets by the endogenous type I and type III systems. (**A**) Three artificial mini-CRISPR plasmids producing a crRNA targeting the *DNApolyα* gene were used to detect the interference activity of III-AB, I-C and I-B CRISPR-Cas systems respectively. Non-target plasmids were used as control. (**B**) Three artificial mini-CRISPR plasmids producing a crRNA targeting the resistance gene *kat* on the same plasmid were used to detect the interference activity of III-AB, I-C and I-B CRISPR-Cas systems respectively. Non-target plasmids were used as control. (**C**) Three invader plasmids carrying a target sequence of spacer 2 in CRISPR arrays 2, 4 and 6 were used to detect the interference activity of III-AB, I-C and I-B CRISPR-Cas systems respectively. Non-target plasmids were used as control. The data show means of three replicates. Error bars indicate the standard deviations (SD). Between-group significance was determined using the unpaired two-sample t-test (*P < 0.05, **P < 0.01, and ***P < 0.001). And ns indicates no significance.



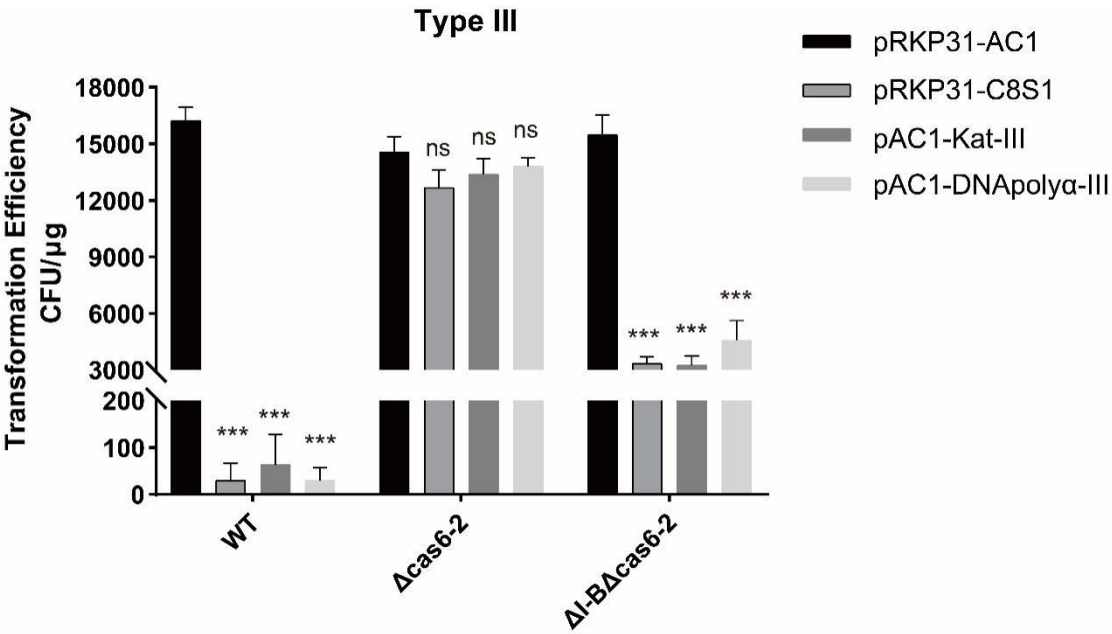
Supplementary Figure S6. PCR verification of *cas6*-1, *cas6*-2 and *cas5c* deletion mutants. The primer pairs used for identification are listed in supplementary table S2.



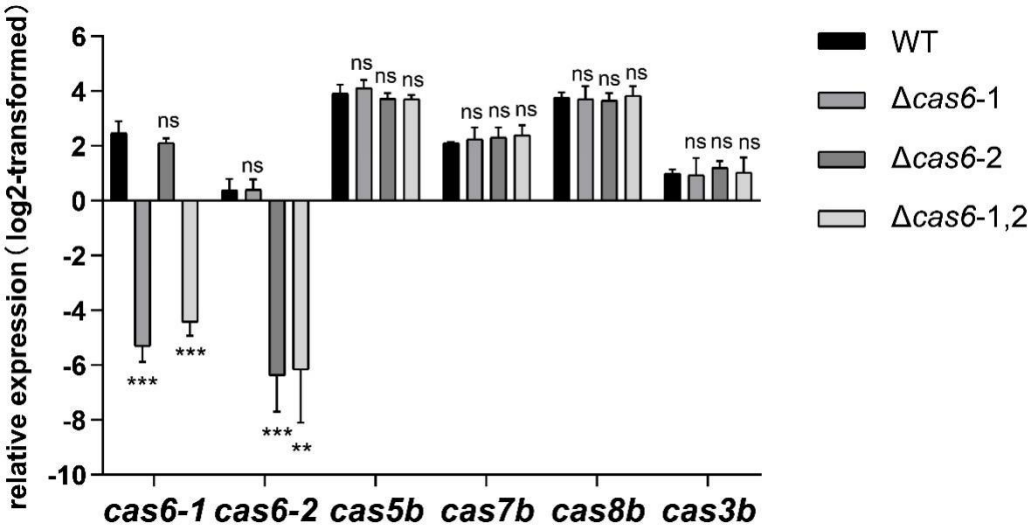
Supplementary Figure S7. The cleavage of Cas6-1 and Cas6-2 on *in vitro* transcribed pre-crRNAs. (**A**) Schematic of *in vitro* transcribed pre-crRNA cleavage assay of Cas6-1 and Cas6-2 proteins. (**B**) The cleavage of Cas6-1 and Cas6-2 on three types of *in vitro* transcribed pre-crRNAs in 60 minutes. (**C**) The cleavage of *in vitro* transcribed type III and I-B pre-crRNAs by Cas6-1 over different time periods. (**D**) The cleavage of *in vitro* transcribed type III and I-B pre-crRNAs by Cas6-2 over different time periods.



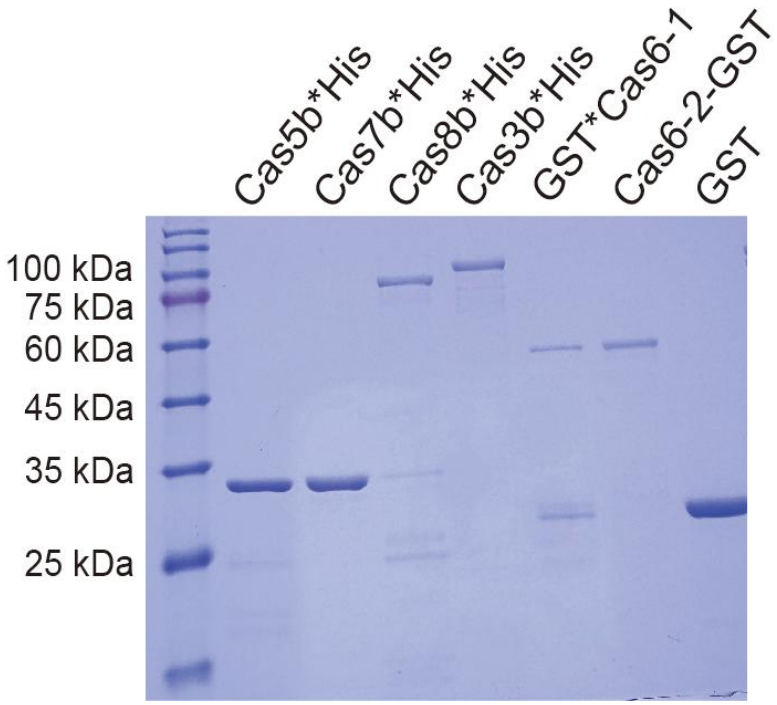
Supplementary Figure S8. The impact of Cas6-1 and Cas6-2 deletions on the interference activity of the type I-B systems. Three invading plasmids carrying different target sequences were both used to detect the interference activity of type I-B CRISPR-Cas systems. pRKP31-C6S2 represents the invading plasmid carrying a target sequence of spacer 2 in CRISPR arrays 6. pRKP31-C7S1 represents the invading plasmid carrying a target sequence of spacer 1 in CRISPR arrays 7. pRKP31-C7S2 represents the invading plasmid carrying a target sequence of spacer 2 in CRISPR arrays 7. Significance values indicate a significant difference from the ΔCRISPR group. The data show means of three replicates. Error bars indicate the standard deviations (SD). Between-group significance was determined using the unpaired two-sample t-test (*$P < 0.05$, **$P < 0.01$, and ***$P < 0.001$). And ns indicates no significance.



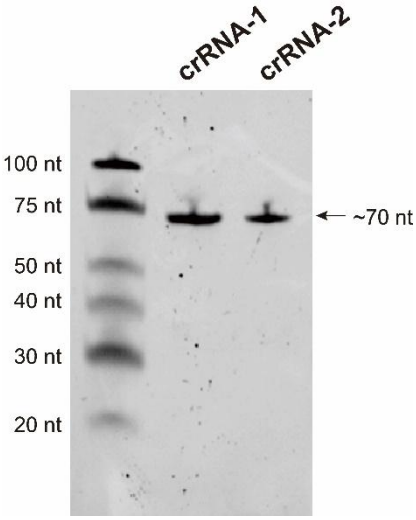
Supplementary Figure S9. The impact of Cas6-2 and I-B system deletion on the interference activity of the type III systems. Two artificial mini-CRISPR plasmids expressing crRNAs targeting the *DNApolyα* gene or the *kat* gene, and one invading plasmid carrying a target sequence of spacer 1 in CRISPR arrays 8, were used to detect the interference activity of type III system. Non-target plasmid was used as control. Significance values indicate a significant difference from the non-target plasmid group. The data show means of three replicates. Error bars indicate the standard deviations (SD). Between-group significance was determined using the unpaired two-sample t-test (*$P < 0.05$, **$P < 0.01$, and ***$P < 0.001$). And ns indicates no significance.



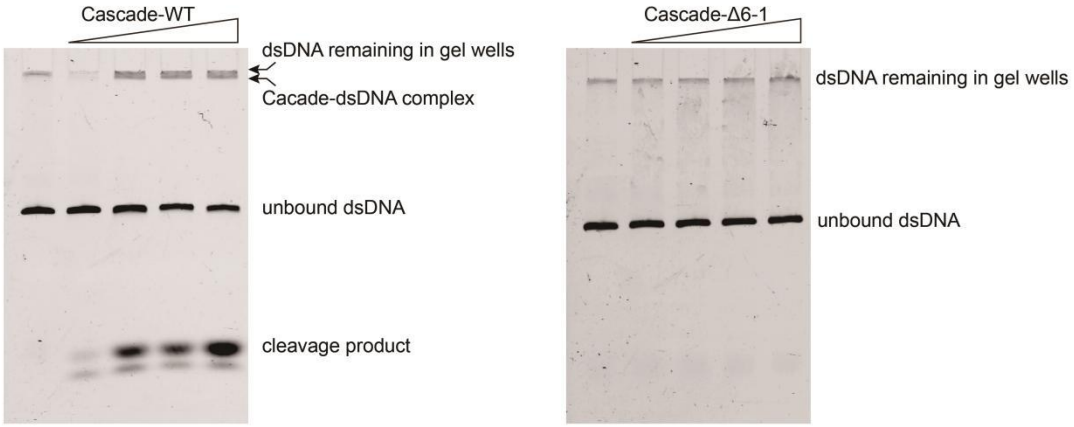
Supplementary Figure S10. The impact of Cas6-1 and Cas6-2 deletions on the transcriptional levels of the type I-B Cas proteins. Significance was determined by comparing the deletion strains with the wild-type strain. The data show means of three replicates. Error bars indicate the standard deviations (SD). Between-group significance was determined using the unpaired two-sample t-test (*$P < 0.05$, **$P < 0.01$, and ***$P < 0.001$). And ns indicates no significance.



Supplementary Figure S11. SDS-PAGE analysis of purified Cas5b*His, Cas7b*His, Cas8b*His, Cas3b*His, GST-Cas6-1, Cas6-2-GST and GST proteins expressed in *E. coli*.



Supplementary Figure S12. Size analysis of crRNAs from Cascade complexes derived from the wild-type strain and the Δ*cas6-1* strain. The crRNA samples were separated on denaturing 7 M urea 12.5% polyacrylamide gels. Gels were first stained with SYBR Green II, and then visualized using a gel imaging system. crRNA-1 represents the crRNA sample extracted from the Cascade-WT. crRNA-2 represents the crRNA sample extracted from the Cascade-Δ6-1.



Supplementary Figure S13. The binding affinities of Cascade-WT and Cascade-Δ6-1 to 5' FAM-labeled dsDNA substrates.

Supplementary Table S1. Strains and plasmids used in this study.

Strains/plasmid	Description	Source
Strains		
E. coli DH5α	host for plasmid construction	Lab storage
E. coli BL21(DE3)	host for protein expression	Lab storage
T. thermophilus HB27	wild-type *T. thermophilus* HB27 strain	Lab storage
ΔIII-A	HB27 with the type III-A CRISPR-Cas system deleted	This study
ΔIII-B	HB27 with the type III-B CRISPR-Cas system deleted	This study
ΔI-C	HB27 with the type I-C CRISPR-Cas system deleted	This study
ΔI-B	HB27 with the type I-B CRISPR-Cas system deleted	This study
ΔIII-AB	HB27 with the type III-A and III-B CRISPR-Cas systems deleted	This study
ΔIII-ABΔI-C	HB27 with the type III-A, III-B and I-C CRISPR-Cas systems deleted	This study
ΔCRISPR	HB27 with all endogenous CRISPR-Cas systems deleted	This study
Δ*cas6-1*	HB27 with *cas6-1* gene deleted	This study
Δ*cas6-2*	HB27 with *cas6-2* gene deleted	This study
Δ*cas5c*	HB27 with *cas5c* gene deleted	This study
Δ*cas6-1,2*	HB27 with *cas6-1* and *cas6-2* genes deleted	This study
Δ*cas6-1,2,5c*	HB27 with *cas6-1*, *cas6-2* and *cas5c* genes deleted	This study
Plasmids		
pRKP31	*E. coli* - *T. thermophilus* shuttle vector with P31 promoter.	Lab storage
pRKP31-AC1	pRKP31 plasmid carrying a mini-CRISPR array composed of Repeat-1.	Lab storage
pRKP31-AC2	pRKP31 plasmid carrying a mini-CRISPR array composed of Repeat-2.	Lab storage
pRKP31-AC3	pRKP31 plasmid carrying a mini-CRISPR array composed of Repeat-3.	Lab storage
pAC1-DNApolyα-III	The pRKP31-AC1 plasmid carries a III-A/B spacer with characteristics of the type III system that targets *DNApolyα*.	This study
pAC1-DNApolyα-I	The pRKP31-AC1 plasmid carries a I-B/I-C spacer with characteristics of the type I system that targets *DNApolyα*.	This study

pAC2-DNApolyα-III	The pRKP31-AC2 plasmid carries a III-A/B spacer with characteristics of the type III system that targets *DNApolyα*.	This study
pAC2-DNApolyα-I	The pRKP31-AC2 plasmid carries a I-B/I-C spacer with characteristics of the type I system that targets *DNApolyα*.	This study
pAC3-DNApolyα-III	The pRKP31-AC3 plasmid carries a III-A/B spacer with characteristics of the type III system that targets *DNApolyα*.	This study
pAC3-DNApolyα-I	The pRKP31-AC3 plasmid carries a I-B/I-C spacer with characteristics of the type I system that targets *DNApolyα*.	This study
pRKP31-IIIA-Sp2-LR	Editing plasmid for the type III-A CRISPR-Cas system deletion.	This study
pRKP31-IIIB-Sp2-LR	Editing plasmid for the type III-B CRISPR-Cas system deletion.	This study
pRKP31-IC-Sp2-LR	Editing plasmid for the type I-C CRISPR-Cas system deletion.	This study
pRKP31-IB-Sp2-LR	Editing plasmid for the type I-B CRISPR-Cas system deletion.	This study
pRKP31-cas6-1-Sp2-LR	Editing plasmid for cas6-1 gene deletion.	This study
pRKP31-cas6-2-Sp2-LR	Editing plasmid for cas6-2 gene deletion.	This study
pRKP31-cas5c-Sp2-LR	Editing plasmid for cas5c gene deletion.	This study
pAC1-gyrA-III	pRKP31-AC1 plasmid with a type III mini-CRISPR array targeting the *gyrA* gene.	This study
pAC2-gyrA-I	pRKP31-AC2 plasmid with a type I-C mini-CRISPR array targeting the *gyrA* gene.	This study
pAC3-gyrA-I	pRKP31-AC3 plasmid with a type I-B mini-CRISPR array targeting the *gyrA* gene.	This study
pAC1-hoxN-III	pRKP31-AC1 plasmid with a type III mini-CRISPR array targeting the *hoxN* gene.	This study
pAC2-hoxN-I	pRKP31-AC2 plasmid with a type I-C mini-CRISPR array targeting the *hoxN* gene.	This study
pAC3-hoxN-I	pRKP31-AC3 plasmid with a type I-B mini-CRISPR array targeting the *hoxN* gene.	This study
pAC1-puc-III	pRKP31-AC1 plasmid with a type III mini-CRISPR array targeting the *puc-ori*.	This study
pAC2-puc-I	pRKP31-AC2 plasmid with a type I-C mini-CRISPR array targeting the *puc-ori*.	This study
pAC3-puc-I	pRKP31-AC3 plasmid with a type I-B mini-CRISPR array targeting the *puc-ori*.	This study
pRKP31-C2S1	pRKP31 plasmid with a protospacer designed based on the first spacer of CRISPR-2.	This study

pRKP31-C4S1	pRKP31 plasmid with a protospacer designed based on the first spacer of CRISPR-4.	This study
pRKP31-C6S1	pRKP31 plasmid with a protospacer designed based on the first spacer of CRISPR-6.	This study
pRKP31-C2S2	pRKP31 plasmid with a protospacer designed based on the second spacer of CRISPR-2.	This study
pRKP31-C4S2	pRKP31 plasmid with a protospacer designed based on the second spacer of CRISPR-4.	This study
pRKP31-C6S2	pRKP31 plasmid with a protospacer designed based on the second spacer of CRISPR-6.	This study
pRKP31-C7S1	pRKP31 plasmid with a protospacer designed based on the first spacer of CRISPR-7.	This study
pRKP31-C8S1	pRKP31 plasmid with a protospacer designed based on the first spacer of CRISPR-8.	
pRKP31-C7S2	pRKP31 plasmid with a protospacer designed based on the second spacer of CRISPR-7.	This study
pAC1-Kat-III	pRKP31-AC1 plasmid with a type III mini-CRISPR array targeting the kanamycin resistance gene.	This study
pAC2-Kat-I	pRKP31-AC2 plasmid with a type I-C mini-CRISPR array targeting the kanamycin resistance gene	This study
pAC3-Kat-I	pRKP31-AC3 plasmid with a type I-B mini-CRISPR array targeting the kanamycin resistance gene.	This study
pRKP31-C8S1-OE6-1	pRKP31-C8S1 plasmid carrying an expression cassette for Cas6-1.	This study
pRKP31-C8S1-OE6-2	pRKP31-C8S1 plasmid carrying an expression cassette for Cas6-2.	This study
pRKP31-C7S1-OE6-1	pRKP31-C7S1 plasmid carrying an expression cassette for Cas6-1.	This study
pRKP31-C7S1-OE6-2	pRKP31-C7S1 plasmid carrying an expression cassette for Cas6-2.	This study
pAC1-Kat-III-OE6-1	pAC1-Kat-III plasmid carrying an expression cassette for Cas6-1.	
pAC1-Kat-III-OE6-2	pAC1-Kat-III plasmid carrying an expression cassette for Cas6-2.	
pAC3-Kat-I-OE6-1	pAC3-Kat-I plasmid carrying an expression cassette for Cas6-1.	
pAC3-Kat-I-OE6-2	pAC3-Kat-I plasmid carrying an expression cassette for Cas6-2.	
pAC1-DNApolyα-III-OE6-1	pAC1-DNApolyα-III plasmid carrying an expression cassette for Cas6-1.	

pAC1-DNApolyα-III-OE6-2	pAC1-DNApolyα-III plasmid carrying an expression cassette for Cas6-2.	
pAC3-DNApolyα-I-OE6-1	pAC3-DNApolyα-I plasmid carrying an expression cassette for Cas6-1.	
pAC3-DNApolyα-I-OE6-2	pAC3-DNApolyα-I plasmid carrying an expression cassette for Cas6-2.	
pET28a-HRV3C	Expression plasmid for expressing recombinant proteins carrying a 6xHis tag in *E. coli.*	Lab storage
pET28a-Cas6-1	Expression plasmid for expressing Cas6-1 protein with a 6xHis tag at the C-terminus in *E. coli.*	This study
pET28a-Cas6-2	Expression plasmid for expressing Cas6-2 protein with a 6xHis tag at the C-terminus in *E. coli.*	This study
pET28a-Cas5c	Expression plasmid for expressing Cas5c protein with a 6xHis tag at the C-terminus in *E. coli.*	This study
pET28a-Cas5b	Expression plasmid for expressing Cas5b protein with a 6xHis tag at the C-terminus in *E. coli.*	This study
pET28a-Cas7b	Expression plasmid for expressing Cas7b protein with a 6xHis tag at the C-terminus in *E. coli.*	This study
pET28a-Cas8b	Expression plasmid for expressing Cas8b protein with a 6xHis tag at the C-terminus in *E. coli.*	This study
pET28a-Cas3b	Expression plasmid for expressing Cas3b protein with a 6xHis tag at the C-terminus in *E. coli.*	This study
pGEX-6p-1	Expression plasmid for expressing recombinant proteins carrying a GST tag in *E. coli*.	Lab storage
pGEX-Cas6-1	Expression plasmid for expressing Cas6-1 protein with a GST tag at the N-terminus in *E. coli*.	This study
pGEX-Cas6-2	Expression plasmid for expressing Cas6-2 protein with a GST tag at the C-terminus in *E. coli*.	This study
pAC3-PEDV-Cas8His	Plasmid for the endogenous purification of the I-B Cascade complex.	This study

Supplementary Table S2. Primes used in this study.

Primer name	Sequence (5′→3′)
Primers used for the construction of gene-editing plasmids	
IIIA-sp2-F	aaacatcccccgcctgggcggaaacgccaacccccgcaccacggaa
IIIA-sp2-R	caacttccgtggtgcgggggttggcgtttccgcccaggcgggggat
IIIA-L-F	cggtgaggattgaaaccgcgccatctcgggggtgaacttc
IIIA-L-R	agagcggtccgggcctcgaggcgggcgcgggaatagag
IIIA-R-F	agctctattcccgcgcccgcctcgaggcccggaccgctct
IIIA-R-R	gatggtgatggtgatggtgggggtgtgggaagtgcctcggg
IIIB-sp2-F	aaaccgccaggcccgccccgggggggaccccagaagcccgggccgc
IIIB-sp2-R	caacgcggcccgggcttctggggtcccccccggggcgggcctggcg
IIIB-L-F	cggtgaggattgaaaccgcggcctcctcctttgtctcggg
IIIB-L-R	gaagcccaccgctcccccagggcgatagcgagaag
IIIB-R-F	cgctatcgccctgggggagcggtgggcttccaa
IIIB-R-R	gatggtgatggtgatggtggctcccctcgttcggaaacacc
IC-sp2-F	aaactccgcaccgcctacctcggcacccccccctccccatgcccttt
IC-sp2-R	caacaaagggcatggggaggggggtgccgaggtaggcggtgcgga
IC-L-F	cggtgaggattgaaaccgcgatggaccccaaagcccacac
IC-L-R	gtccagctcaaagagaggcgaagagggtcccctg
IC-R-F	ggaccctcttcgcctctctttgagctggaccgctcg
IC-R-R	gatggtgatggtgatggtggcgtcggcccggcccacta
IB-sp2-F	aaacctggcaagccttcctcggctcggggcgggaaaccccaaaggg
IB-sp2-R	caacccctttggggtttcccgccccgagccgaggaaggcttgccag
IB-L-F	cggtgaggattgaaaccgcgtgagcggcaagctgcacg
IB-L-R	cttttccggggcgtaggcaggcggctttccatagattg
IB-R-F	ggaaagccgcctgcctacgccccggaaaaggacgc
IB-R-R	gatggtgatggtgatggtgggtgagcctgccacttgtccag
cas6-1-sp2-F	aaactaagccgggtgggcgcacccgctacactcccttgcccgaccc
cas6-1-sp2-R	caacgggtcgggcaagggagtgtagcgggtgcgcccacccggctta
cas6-1-L-F	cggtgaggattgaaaccgcgcggagggctacttggaact
cas6-1-L-R	taggggtcttagccccccacgagctcgagga
cas6-1-R-F	tcgagctcgtgggggggctaagacccctacggcat
cas6-1-R-R	gatggtgatggtgatggtgggaggtcctcaccgcgctga
cas6-2-sp2-F	aaacaggggcctccttcccgggacctcgccctgcgcttcgccagcc
cas6-2-sp2-R	caacggctggcgaagcgcagggcgaggtcccgggaaggaggcccct
cas6-2-L-F	cggtgaggattgaaaccgcggagtggggattcaagagggg
cas6-2-L-R	gaagcggcctagggcggaaagaggccgtagaagaagcccc
cas6-2-R-F	ggggcttcttctacggcctctttccgccctaggccgcttc
cas6-2-R-R	gatggtgatggtgatggtggttcttcgccgtatccatcgcc
cas5c-sp2-F	aaacgttgaggatgcgcgccagcagcggacaagcctcgtccttaag
cas5c-sp2-R	caaccttaaggacgaggcttgtccgctgctggcgcgcatcctcaac
cas5c-L-F	cggtgaggattgaaaccgcgcaaaaccgacaaggggatcca
cas5c-L-R	tacttttcggcgggaccccaaacctttaccttgagcc
cas5c-R-F	ggtaaaggtttggggtcccgccgaaaagtaccagg

cas5c-R-R	gatggtgatggtgatggtgggaggtggcgagcccaaaag
Primers used for validating gene deletions	
F1	gaggtccaggtgctgtgaggc
R1	accccggcccaaatggaagag
F2	ccggcgtcccacccagtag
R2	cggacggaggccctttggaa
F3	ccggggtttctgcgcgca
R3	ccgcaccgtcatctcgcc
F4	tccgggcctcgatccctct
R4	cggtgtccataacgccttcc
R5	cctccgggcggcgaggca
exam-cas6-1KO-F	gcctacgtggtgggggaaaccta
exam-cas6-1KO-R	ccccatggctacttggtcacg
exam-cas6-2KO-F	cggtgaggattgaaaccgcggagtggggattcaagagggg
exam-cas6-2KO-R	gaaggccctccgcttcatcg
exam-cas5c KO-F	ccgggtgggcgtggaaaag
exam-cas5c KO-R	cccagaaccaccacttccctg
Primers used for the construction of interference activity assessment plasmids	
R1-III-polyα-Sp-F	CGACagggtgaggtggaagtagcccccgtctaggccctttcccc
R1-III-polyα-Sp-R	CAACggggaaagggcctagacgggggctacttccacctcaccct
R2/3-I-polyα-Sp-F	aaacacggggtaccagaacctggtgcgcctggcgagccggg
R2/3-I-polyα-Sp-R	caaccccggctcgccaggcgcaccaggttctggtaccccgt
R1-I-polyα-Sp-F	CGACacggggtaccagaacctggtgcgcctggcgagccggg
R1-I-polyα-Sp-R	CAACcccggctcgccaggcgcaccaggttctggtaccccgt
R2/3-III-polyα-Sp-F	AAACagggtgaggtggaagtagcccccgtctaggccctttcccc
R2/3-III-polyα-Sp-R	CAACggggaaagggcctagacgggggctacttccacctcaccct
gyrA-sp1-F	CGACcggagaggttgtggggcgggaggctcgtggccatgcccac
gyrA-sp1-R	CAACgtgggcatggccacgagcctcccgccccacaacctctccg
gyrA-sp2/3-F	AAACcgccccaactacgacggctccctcaaggagcccgagg
gyrA-sp2/3-R	CAACcctcgggctccttgagggagccgtcgtagttggggcg
hoxN-sp1-F	CGACccgcccttcgggagtccttggccaggttctgcagacggct
hoxN-sp1-R	CAACagccgtctgcagaacctggccaaggactcccgaagggcgg
hoxN-sp2/3-F	AAACaccctggggatgctcctcgtggacggggtggacgggc
hoxN-sp2/3-R	CAACgcccgtccaccccgtccacgaggagcatccccagggt
puc-sp1-F	CGACctcccttcgggaagcgtggcgctttctcatagctcacgct
puc-sp1-R	CAACagcgtgagctatgagaaagcgccacgcttcccgaagggag
puc-sp2/3-F	AAACccgaagggagaaaggcggacaggtatccggtaagcgg
puc-sp2/3-R	CAACccgcttaccggatacctgtccgcctttctcccttcgg
kat-sp1-F	cgacCACTTTCTCTAAGTATCCACCTGAATCATAAATCGGCAAA
kat-sp1-R	caacTTTGCCGATTTATGATTCAGGTGGATACTTAGAGAAAGTG
kat-sp2/3-F	AAACGTGTGCAAGGACCGACAACATTTCTACCATCCTTGAC
kat-sp2/3-R	caacGTCAAGGATGGTAGAAATGTTGTCGGTCCTTGCACAC
III-CR2SP1-F	TCGAagacctgtcaagaataccggggataaagaggatataccccaAGATGCTG
III-CR2SP1-R	CTAGCAGCATCTtggggtatatcctctttatccccggtattcttgacaggtct

IC-CR4SP1-F	tcgaTTCcccgcgcacccctccacggggcatagcaggtcatgttgcat
IC-CR4SP1-R	ctagatgcaacatgacctgctatgccccgtggaggggtgcgcgggGAA
IB-CR6SP1-F	tcgaTTCCTTCTCCAGCACCCGCCGCAGAGCTGTGGTATACTGA
IB-CR6SP1-R	ctagTCAGTATACCACAGCTCTGCGGCGGGTGCTGGAGAAGGAA
IB-CR7SP1-F	tcgaTTCTCCGGCTCGTGAACGGCGAGATTCAGATCATTCCCG
IB-CR7SP1-R	ctagCGGGAATGATCTGAATCTCGCCGTTCACGAGCCGGAGAA
III-CR2SP2-F	TCGAtcgtcgctttcgcttgcctcaagtacgattttgtgaaAGATGCTG
III-CR2SP2-R	CTAGCAGCATCTttcacaaaatcgtacttgaggcaagcgaaagcgacga
III-CR8SP1-F	tcgaTAAGCCCCAAGGAAGGGAGTTTGCGTGGATCCTGaaagagagatgctg
III-CR8SP1-R	ctagcagcatctCTCTTTCAGGATCCACGCAAACTCCCTTCCTTggggctta
IC-CR4SP2-F	tcgaTTCggggcgggccgccatatctgtacccgctctagagcaactggagttgcat
IC-CR4SP2-R	ctagatgcaactccagttgctctagagcgggtacagatatggcggcccgccccGAA
IB-CR6SP2-F	tcgattcGTGTCGGAGAAGTTCCAGAGGCGGAAGACGAGATAGG
IB-CR6SP2-R	ctagCCTATCTCGTCTTCCGCCTCTGGAACTTCTCCGACACgaa
IB-CR7SP2-F	tcgaTTCCATCACCTCGGCCCGGGCCAGGACCACCCCCACCC
IB-CR7SP2-R	ctagGGGTGGGGGTGGTCCTGGCCCGGGCCGAGGTGATGGAA
OEcas6-1-F	ttaacgtgagttttcgttccccccgcgctcctgccgag
(P01289) cas6-1-F	aggaggaaatgaagtatgcctcaggccgtggtcc
(cas6-1) P01289-R	cacggcctgaggcatacttcatttcctcctaagatttcccgc
OEcas6-1-R	tacggggtctgacgctcagtCTAgagggggactgccaggcc
OEcas6-2-F	ttaacgtgagttttcgttccccccgcgctcctgccgag
(P01289) cas6-2-F	aggaggaaatgaagtgtggtcctcgccgccttgg
(cas6-2) P01289-R	ggcggcgaggaccacacttcatttcctcctaagatttcccgc
OEcas6-2-R	tacggggtctgacgctcagtCTAggcactttccgcccgggc
Primers used for qPCR experiments	
Q-CR1-F	TTCCTGGCCTGCGGCTTC
Q-CR1-R	CGTTTCACTCGGCGCCCTG
Q-CR2-F	AGGACGGGGTTCTTTGGGGG
Q-CR2-R	CAGACCTGTCAAGAATACCGGGG
Q-CR3-F	CTGCCCATCAGGAGGGCTAC
Q-CR3-R	CCCTCTAAGACGGCCTTCTCAC
Q-CR4-F	CTGCCCATCAGGAGGGCTAC
Q-CR4-R	ATGCAACATGACCTGCTATGCC
Q-CR5-F	GGGACGGGGTTCTTAGGGGG
Q-CR5-R	GCAACCCAGAAGGAGACCG
Q-CR6-F	CCTAAAGACCCCCCGCCTG
Q-CR6-R	GTATACCACAGCTCTGCGGC
Q-CR7-F	CCTCAAGACCCCCCGCCTG
Q-CR7-R	CCGGGAATGATCTGAATCTCGC
Q-CR8-F	GGGACGGGGTTCTTTGGGG
Q-CR8-R	CCAAGGAAGGGAGTTTGCGTG
Q-CR9-F	GTCCGGGACGGGGTTCTTTG
Q-CR9-R	CCAAGGAAGGGAGTTTGCGTG
Q-CR10-F	GTCCGGGACGGGGTTCTTAG

Q-CR10-R	AAGTGGACGGGTTGACTCGC
Q-CR11-F	GTCCAGGACGGGGTTCTTTGG
Q-CR11-R	CTAGAGGCGCAACTAGCGG
Q-IB-Cas6-1-F	CCACGGTCTTCGCCACTTC
Q-IB-Cas6-1-R	TGTGAGCCTGCCACTTGTCC
Q-IB-Cas8-F	GCCTGATGCGGTATGCG
Q-IB-Cas8-R	ACGTCCCGGAAGCGTTG
Q-IB-Cas7-F	GGGAGCGAGCGGGTTTA
Q-IB-Cas7-R	TTCAGGAGGTCGGTGAGGTAA
Q-IB-Cas5-F	AGTCCGGTCATAGGGTACGAGG
Q-IB-Cas5-R	CCACCAGATCCCAAGCGAAA
Q-IB-Cas3-F	TGCGGTTGTGGCAGAGG
Q-IB-Cas3-R	GGGTGGAAGTAGACCAGGAAGT
Q-Cas6-2-F	TCTTCTACGGCCTCCTTCGG
Q-Cas6-2-R	GGGCGTAAAGCTCCTCCACA
eno-F	CAACGCCATCCTGGTCAAG
eno-R	ATGAAGCTGTCCTCCGTCTC
Primers used for the construction of protein expression plasmids	
28a-cas6-1-F	actttaagaaggagatataccatgcctcaggccgtggtcc
28a-cas6-1-R	agtggtggtggtggtggtgctcgagggggactgccaggcc
28a-cas6-2-F	actttaagaaggagatataccgtggtcctcgccgccttgg
28a-cas6-2-R	agtggtggtggtggtggtgctcggcactttccgcccgggc
28a-cas5c-F	actttaagaaggagatataccatggcgaggctcaaggtaaagg
28a-cas5c-R	agtggtggtggtggtggtgctcagctcccttagcatggccttc
28a-cas5b-F	actttaagaaggagatataccatgcacgccatcgccctc
28a-cas5b-R	agtggtggtggtggtggtgctcggaagaagaccctcccgatgcc
28a-cas7b-F	actttaagaaggagatataccatggcgagcggactcaccc
28a-cas7b-R	agtggtggtggtggtggtgctcggaagcggaagccagagcc
28a-cas8b-F	actttaagaaggagatataccatggagcgggcgatggtac
28a-cas8b-R	agtggtggtggtggtggtgctcaccctccttttccatccggatg
28a-cas3b-F	actttaagaaggagatataccatgggcgagggcatcgggag
28a-cas3b-R	agtggtggtggtggtggtgctcgtccccctcttcttcctcttcctcg
GST-cas6-1-F	TCTGTTCCAGGGGCCCCTGGGAatgcctcaggccgtggtcc
GST-cas6-1-R	TCACGATGCGGCCGCTCGAGtcagaggggggactgccaggccc
pGEX-linear-F	ATGTCCCCTATACTAGGTTATTGG
pGEX-linear-R	GAATACTGTTTCCTGTGTGAAATTG
C-GST-Cas6-2-F	TCACACAGGAAACAGTATTCAtggtcctcgccgccttgg
C-GST-Cas6-2-R	TAACCTAGTATAGGGGACATggcactttccgcccgggcg
PEDV-Sp3-F	aaacATTTGACTGGTTTCTGTTCTTGGACTGGTTACGAGAC
PEDV-Sp3-R	caacGTCTCGTAACCAGTCCAAGAACAGAAACCAGTCAAAT
SalI-P01289-F	cgtagaggattgaaaccgcgccccgcgctcctgccgag
P01289-R	acttcatttcctcctaagatttcccgc
(P01289) Cas8b-F	atcttaggaggaaatgaagtatggagcgggcgatggtac
(P01289) Cas8b-R	TAGTGGTGATGGTGATGGTGaccctccttttccatccggatg

pRKP-F	actgagcgtcagaccccgtag
pRKP-R	ggaacgaaaactcacgttaaggg
Primers for other uses	
T7-repeat-F	GATACTTGGCtaatacgactcactataGgggtgagcttcaaggcgggg
T7-repeat-R	gagattatcaaaaaggatcttcacctag
IB-PEDV-protoSp-F	tcgaTTCATTTGACTGGTTTCTGTTCTTGGACTGGTTACGAGAC
IB-PEDV-protoSp-R	ctagGTCTCGTAACCAGTCCAAGAACAGAAACCAGTCAAATGAA
IB-target-F	gccgagggaccgggcctac
IB-target-R	ggtctgCTAGTGGTGATGG

Supplementary Table S3. Fluorescently labeled oligonucleotides used in this study.

RNA oligonucleotides	**Sequence (5′→3′)**
Repeat-1 (5’-FAM)	guugcaagggauugagccccguaaggggauugcgac
Repeat-2 (5’-FAM)	guugcaccggcccgaaagggccggugaggauugaaac
Repeat-3 (5’-FAM)	guugcaaaccucguuagccucgtagaggauugaaac
DNA oligonucleotides	**Sequence (5′→3′)**
IB-target-F (5’-FAM)	gccgagggaccgggcctac
IB-target-R (5’-FAM)	ggtctgCTAGTGGTGATGGT
12nt-Ladder	ggtctgCTAGgg
30nt-Ladder	ggtctgCTAGTGGTGATGGTTGTGTTGGTG
40nt-Ladder	ggtctgCTAGTGGTGATGGTTGTGTTGGTGggtggatgtg
50nt-Ladder	ggtctgCTAGTGGTGATGGTTGTGTTGGTGggtggatgtgttggcttggg