

Supplementary Information

Supplementary Figure 1. The workflow of IDC strategy.

Supplementary Figure 2. Western blot assay of Cas13 and mini-Cas13.

Supplementary Figure 3. Expression and identification of Cas13 proteins.

Supplementary Figure 4. Programmable RNA targeting by RfxCas13d and PspCas13b with their mini variants *in vitro*.

Supplementary Figure 5. The effect of crRNA length and mismatch on RfxCas13d, mini-RfxCas13d and hfRfxCas13d activity.

Supplementary Figure 6. Volcano plot of differential transcript with Cas13d.

Supplementary Figure 7. The overall structure of EsCas13d and mini-EsCas13d.

Supplementary Figure 8. The overall structure of RspCas13d and mini-RspCas13d.

Supplementary Figure 9. Comparison of the HEPN1 and HEPN2 domains of Cas13d.

Supplementary Figure 10. Comparison of the Helical1 and Helical2 domains of Cas13d.

Supplementary Figure 11. Comparison of the HEPN1 and HEPN2 domains of Cas13b.

Supplementary Figure 12. Comparison of the Helical1 and Helical2 domains of Cas13b.

Supplementary Figure 13. Sanger sequencing of mini-Vx and Vx mediated base transversion.

Supplementary Figure 14. Off-target RNA editing effect for Vx and mini-Vx system.

Supplementary Figure 15. The results of mini-RfxCas13d in N2A cells and *in vivo*.

Supplementary Figure 16. Comparison the $\Delta 2$ and N3V7 fragments of RfxCas13d.

Supplementary Figure 17. EsCas13d and PbuCas13b colored by conservation of Cas13ds and Cas13bs.

Supplementary Figure 18. Multiple sequence alignment of Cas13d proteins from different species.

Supplementary Figure 19. Multiple sequence alignment of Cas13b proteins from different species.

Supplementary Tables

Supplementary Table 1. Cas13 protein sequences used in this study.

Supplementary Table 2. Primers used in this study.

Supplementary Table 3. CrRNA spacer sequences for RNA knockdown experiments.

Supplementary Table 4. CrRNA sequences used in this study for RNA editing in mammalian cells.

Supplementary Table 5. CrRNA spacer sequences for *Pcsk9* knockdown experiments.

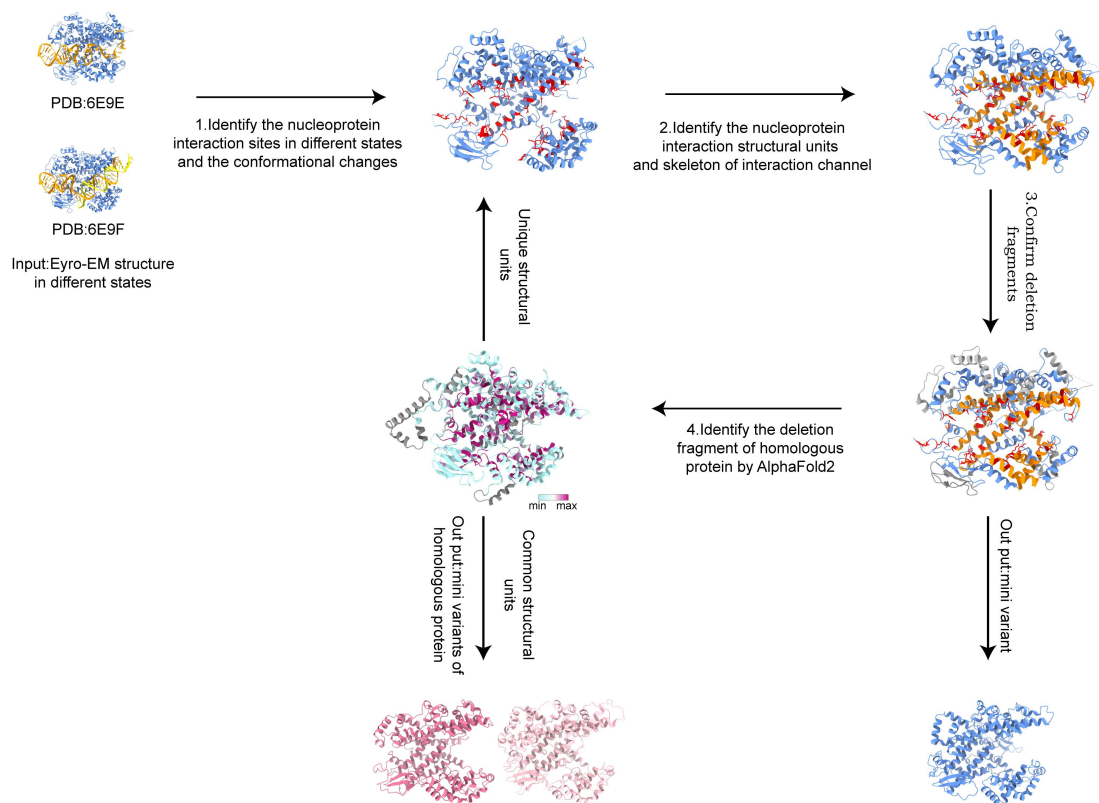


Figure S1. The workflow of IDC strategy.

The interaction sites and the structural units of interaction sites are colored in red and orange.

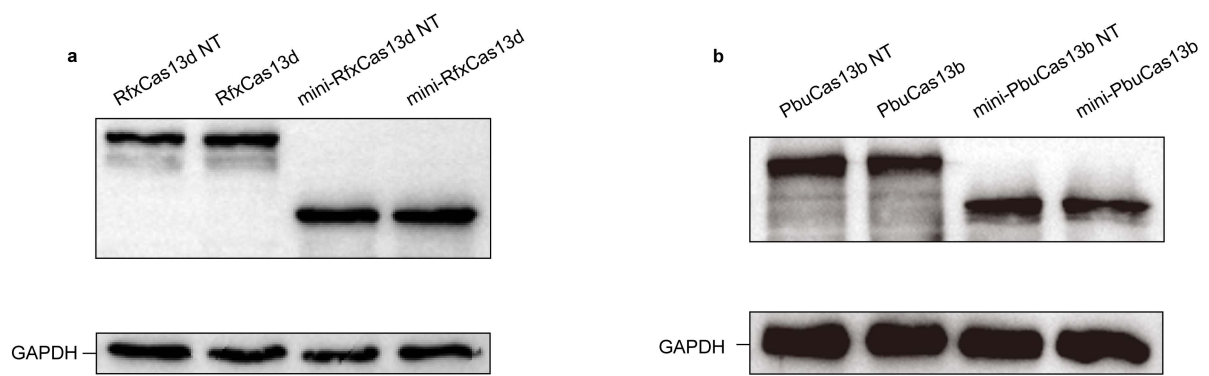


Figure S2. Western blot assay of Cas13 and mini-Cas13.

(a) The protein expression level of RfxCas13d and mini-RfxCas13d. (b) The protein expression level of PbuCas13b and mini-PbuCas13b. (a-b) Source data are provided as a Source Data file.

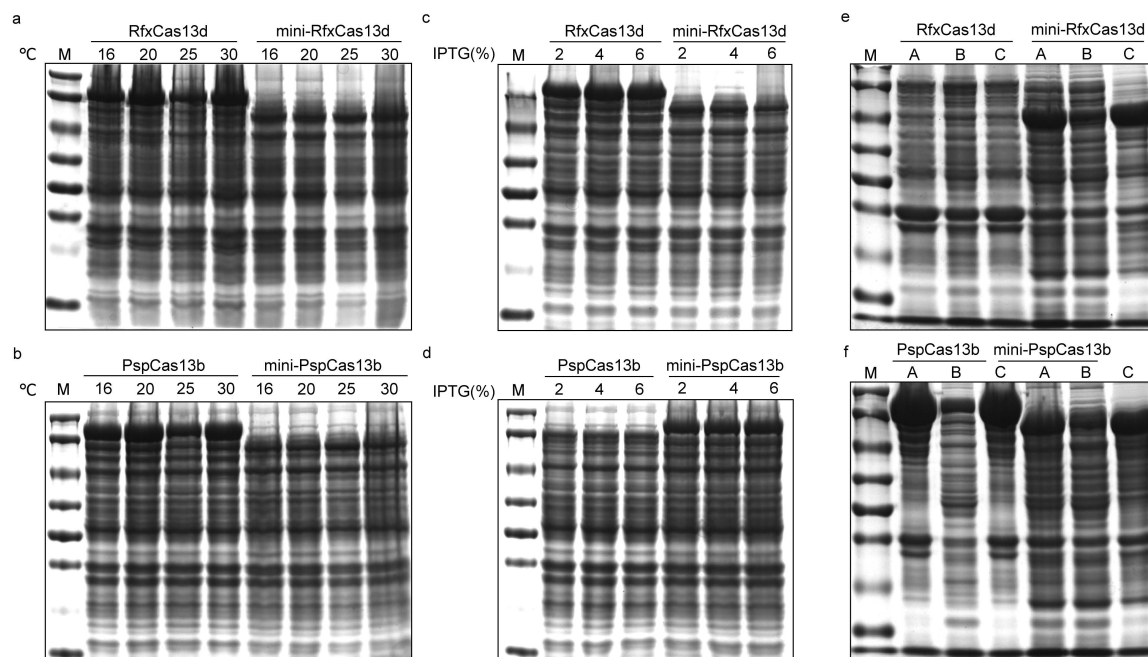


Figure S3. Expression and identification of Cas13 proteins.

(a) Optimal induced temperature range for RfxCas13d, mini-RfxCas13d, PspCas13b, and mini-PspCas13b proteins expression at 2% concentration of IPTG. (b) RfxCas13d, mini-RfxCas13d, PspCas13b, and mini-PspCas13b proteins expression induced at different concentrations of IPTG. (c) Identification of the expression form of RfxCas13d, mini-RfxCas13d, PspCas13b, and mini-PspCas13b proteins. M: Protein Marker; A: Induced recombinant bacteria; B: Induced recombinant bacteria lysed supernatant; C: Induced recombinant bacteria lysed precipitate. (a-c) Source data are provided as a Source Data file.

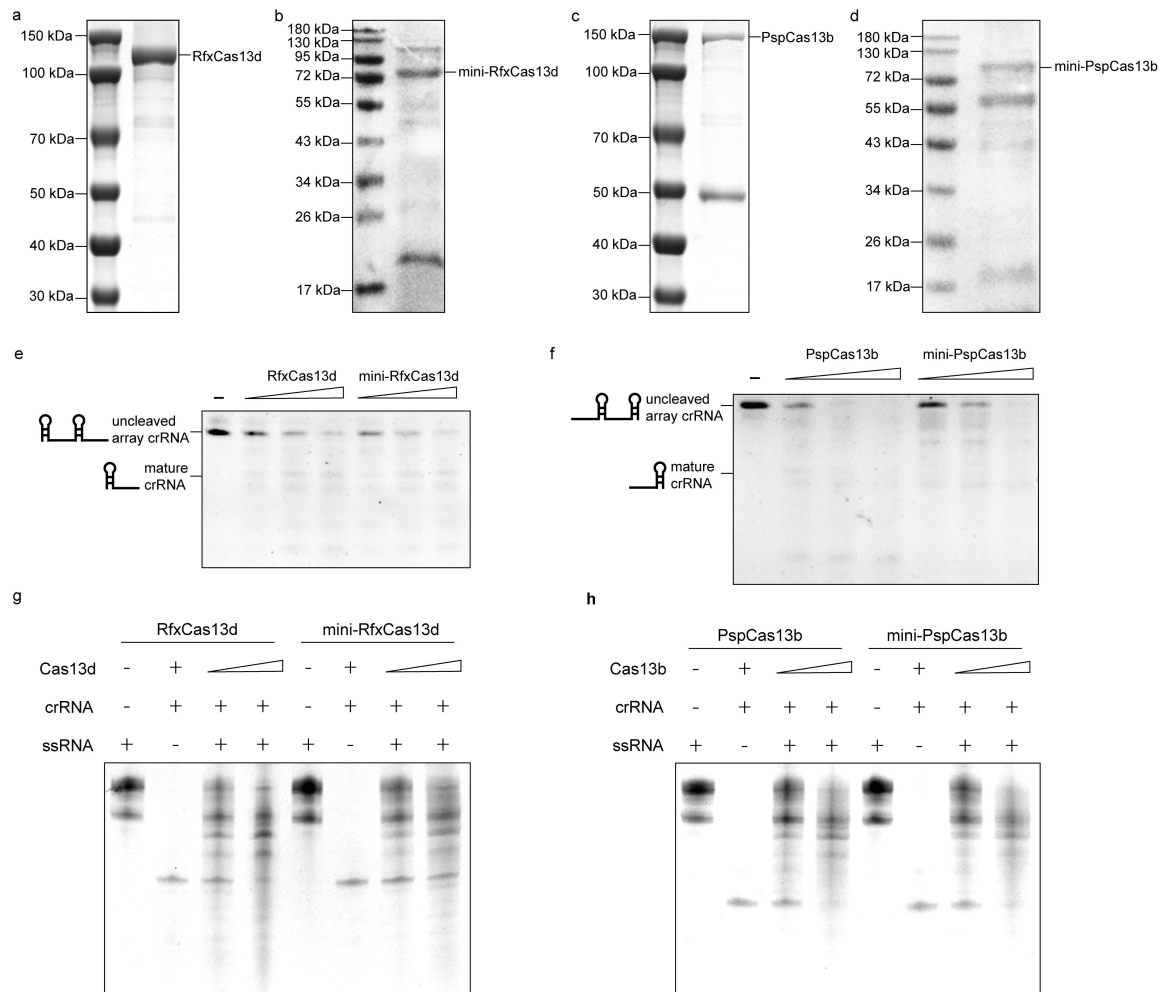


Figure S4. Programmable RNA targeting by RfxCas13d and PspCas13b with their mini variants *in vitro*.

(a-d) Coomassie blue stained polyacrylamide gel of purified recombinant proteins (a)RfxCas13d, (b)mini-RfxCas13d, (c)PspCas13b and (d)mini-PspCas13b respectively, which were used in all biochemical assays.

(e) Representative denaturing gels depicting RfxCas13d and mini-RfxCas13d mediated cleavage of their cognate pre-crRNAs over a dose titration of effector concentration.

(f) Representative denaturing gels depicting PspCas13b and mini-PspCas13b mediated cleavage of their cognate pre-crRNAs over a dose titration of effector concentration.

(g) Representative denaturing gels displaying the targeted RNase activity of RfxCas13d and mini-RfxCas13d effector proteins, with substrate RNA cleavage occurring when the crRNA matches its complementary target ssRNA.

(h) Representative denaturing gels displaying the targeted RNase activity of PspCas13b and mini-PspCas13b effector proteins, with substrate RNA cleavage occurring when the crRNA matches its complementary target ssRNA. (a-h) Source data are provided as a Source Date file.

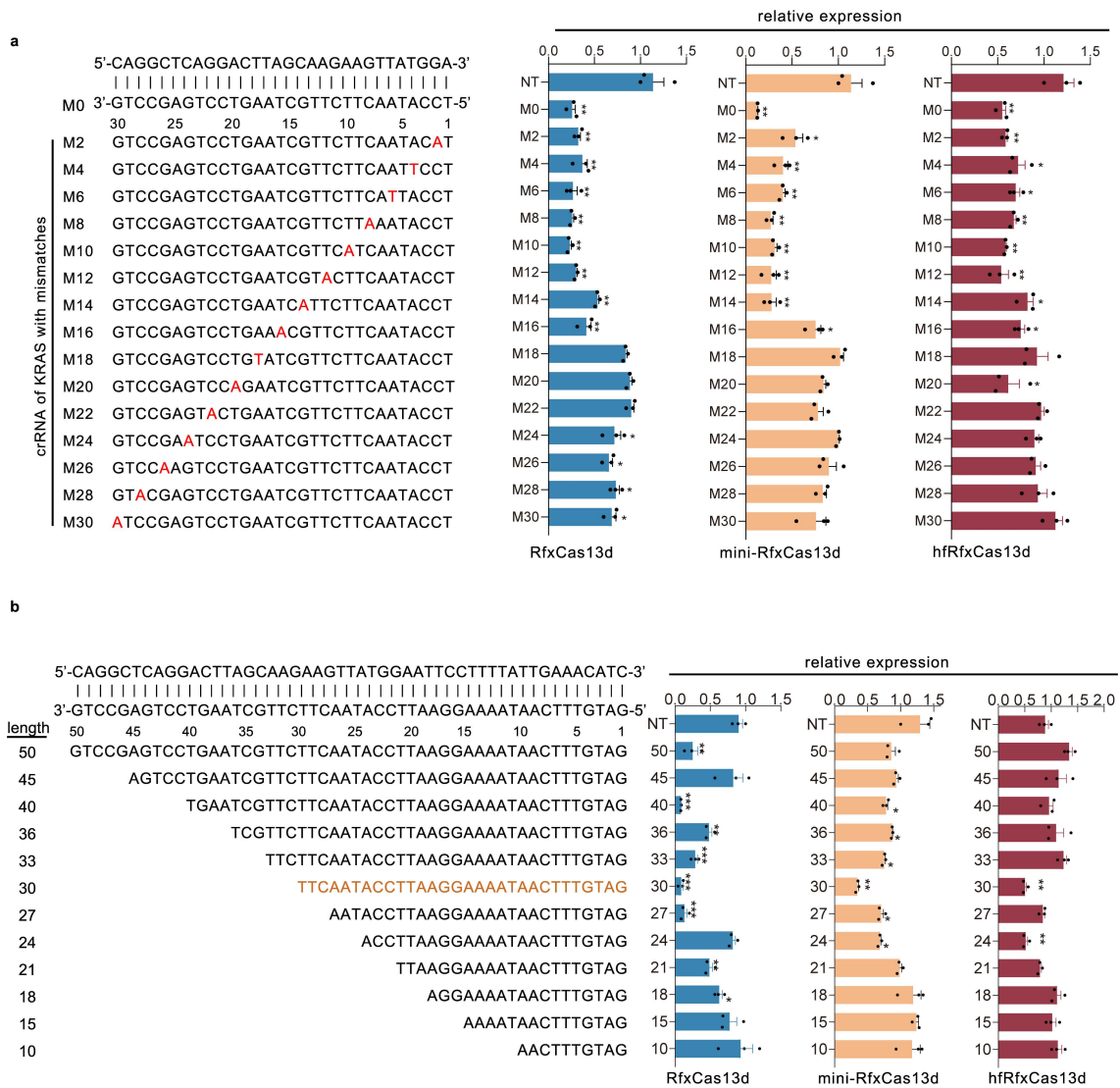


Figure S5. The effect of crRNA length and mismatch on RfxCas13d, mini-RfxCas13d and hfRfxCas13d activity.

(a) Left, *KRAS* crRNAs of different single-nucleotide mismatches; right, relative expression of *KRAS* transcript by co-transfection with RfxCas13d, mini-RfxCas13d, or hfRfxCas13d. (b) Left, *KRAS* crRNAs of different lengths; right, relative expression of *KRAS* transcript by co-transfection of RfxCas13d, mini-RfxCas13d, or hfRfxCas13d. The data are presented as the mean $\pm$ SD. Two-tailed unpaired two-sample t-test. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, ns, not significant. Source data are provided as a Source Data file.

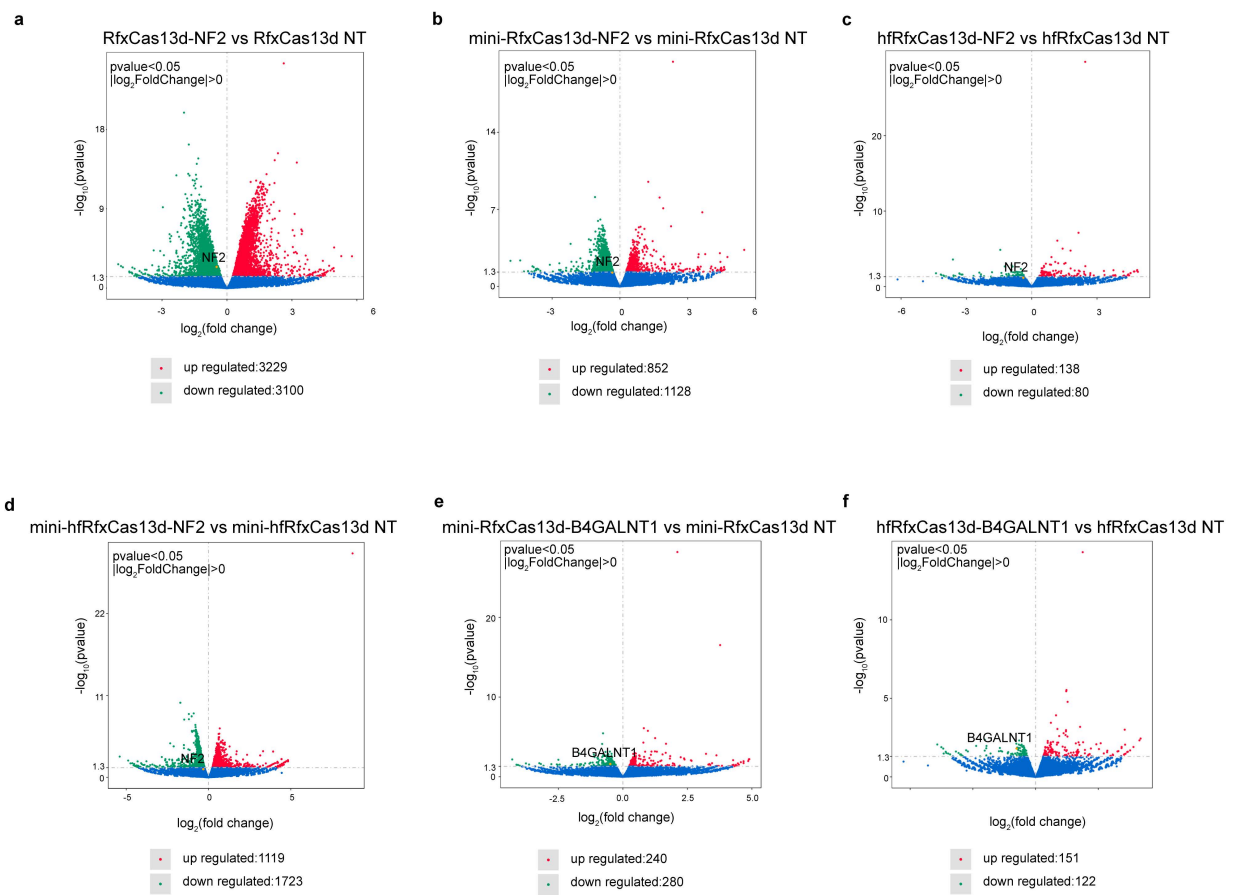


Figure S6. Volcano plot of differential transcript with Cas13d.

(a-d) Volcano plot of differential expression genes between *NF2* targeting and non-targeting (NT) by (a) RfxCas13d, (b) mini-RfxCas13d and (c) hfRfxCas13d (d) mini-hfRfxCas13d ($n = 3$).

(e-f) Volcano plot of differential expression genes between *B4GALNT1* targeting and non-targeting (NT) by (d) mini-RfxCas13d and (e) hfRfxCas13d ($n = 3$).

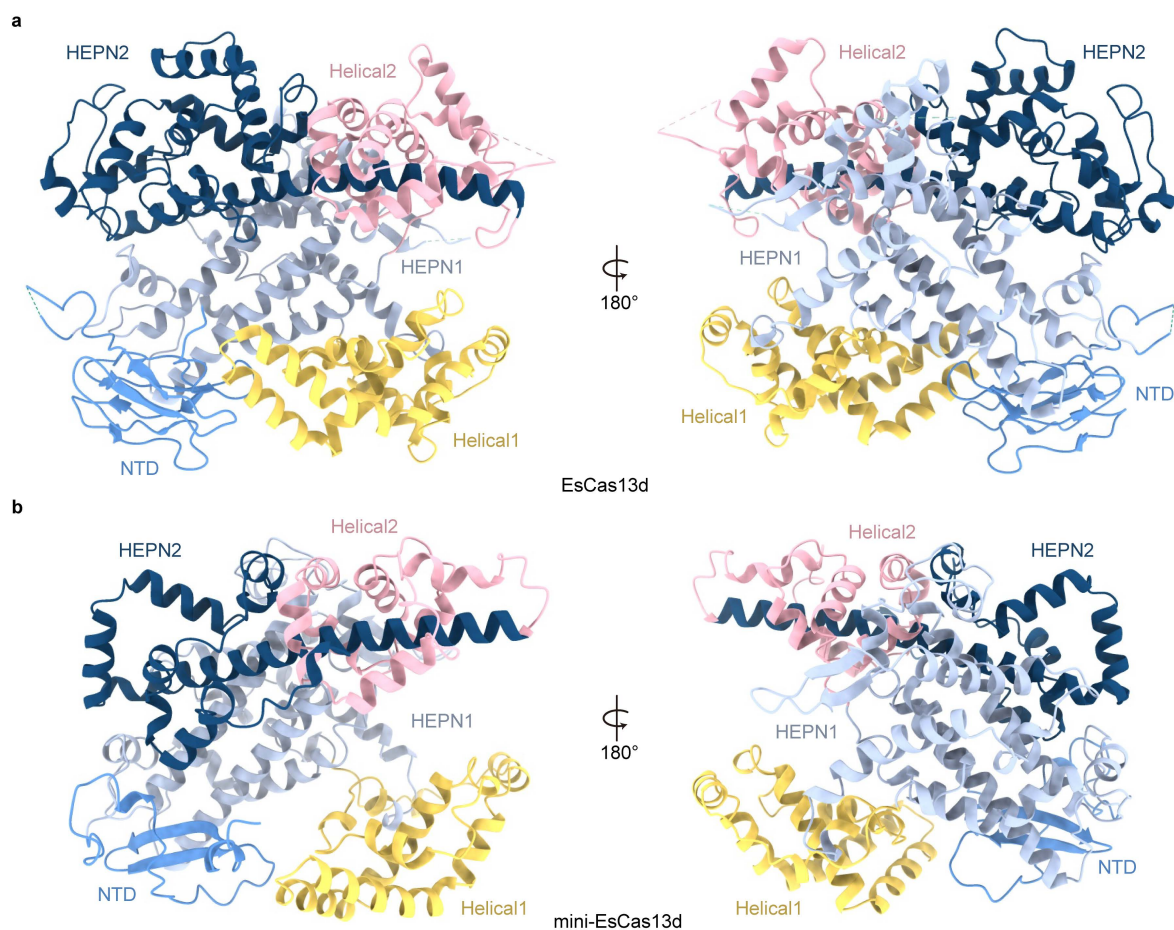


Figure S7. The overall structure of EsCas13d and mini-EsCas13d.

The cryo-electron microscopy structure of (a)EsCas13d (PDB: 6E9E) and predicted overall structure of (b)mini-EsCas13d as indicated by AlphaFold2 are shown in two different orientations and color coded as indicated in Figure 3c.

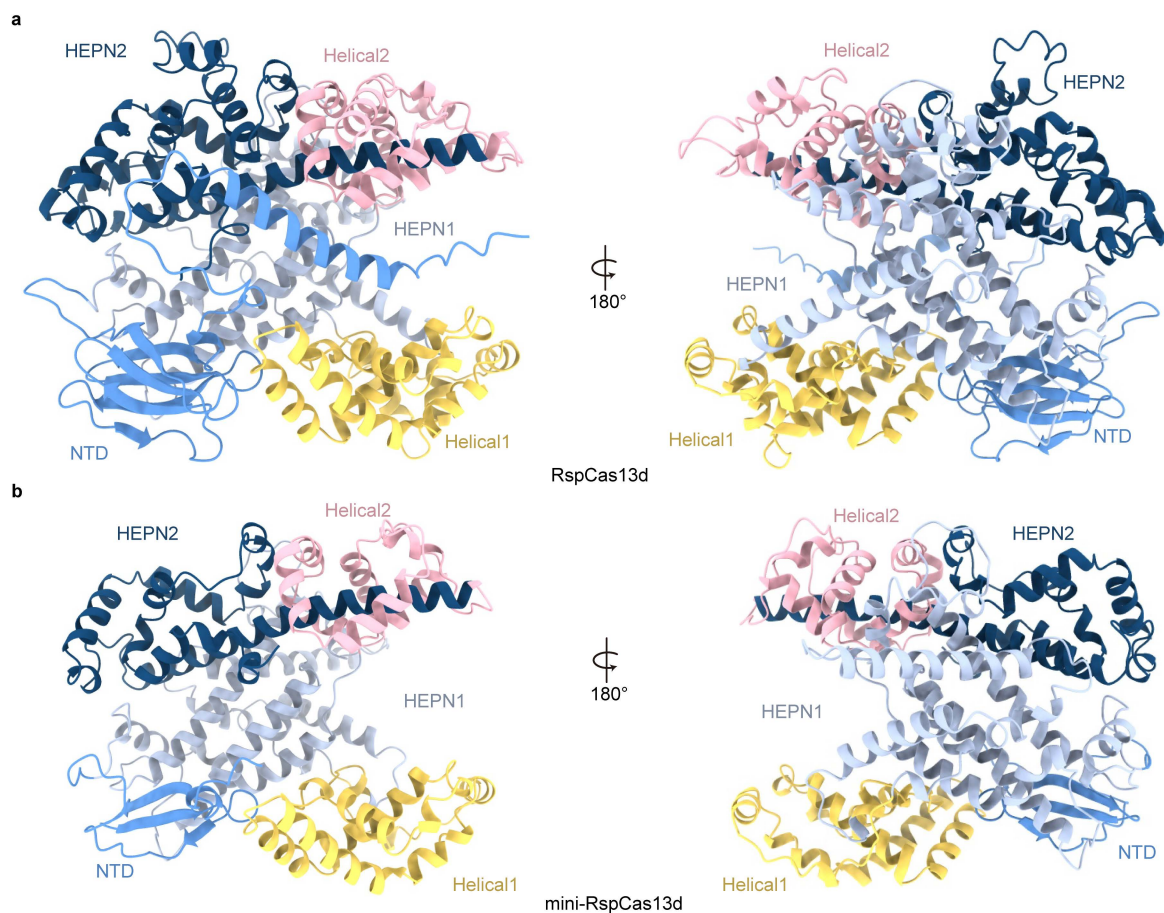


Figure S8. The overall structure of RspCas13d and mini-RspCas13d.

The predicted overall structure of (a)RspCas13d and (b)mini-RspCas13d by AlphaFold2, which is shown in two different orientations and color coded as indicated in Figure 3d.

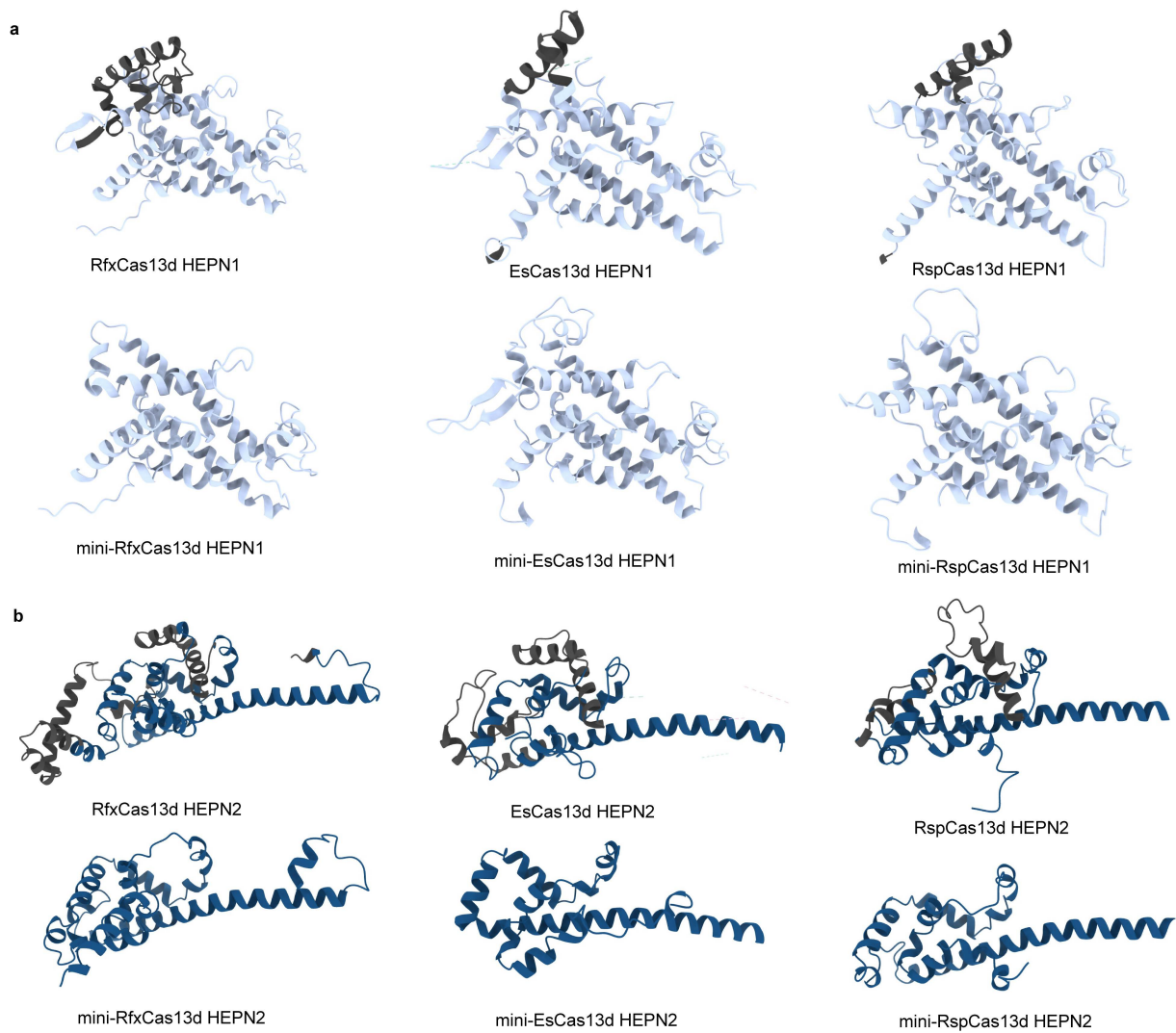


Figure S9. Comparison of the HEPN1 and HEPN2 domains of Cas13d.

(a) The HEPN1 domains of RfxCas13d, mini-RfxCas13d, EsCas13d (6E9E), mini-EsCas13d, RspCas13d and mini-RspCas13d. (b) The HEPN2 domains of RfxCas13d, mini-RfxCas13d, EsCas13d (6E9E), mini-EsCas13d, RspCas13d and mini-RspCas13d. All deletion regions were colored deep gray.

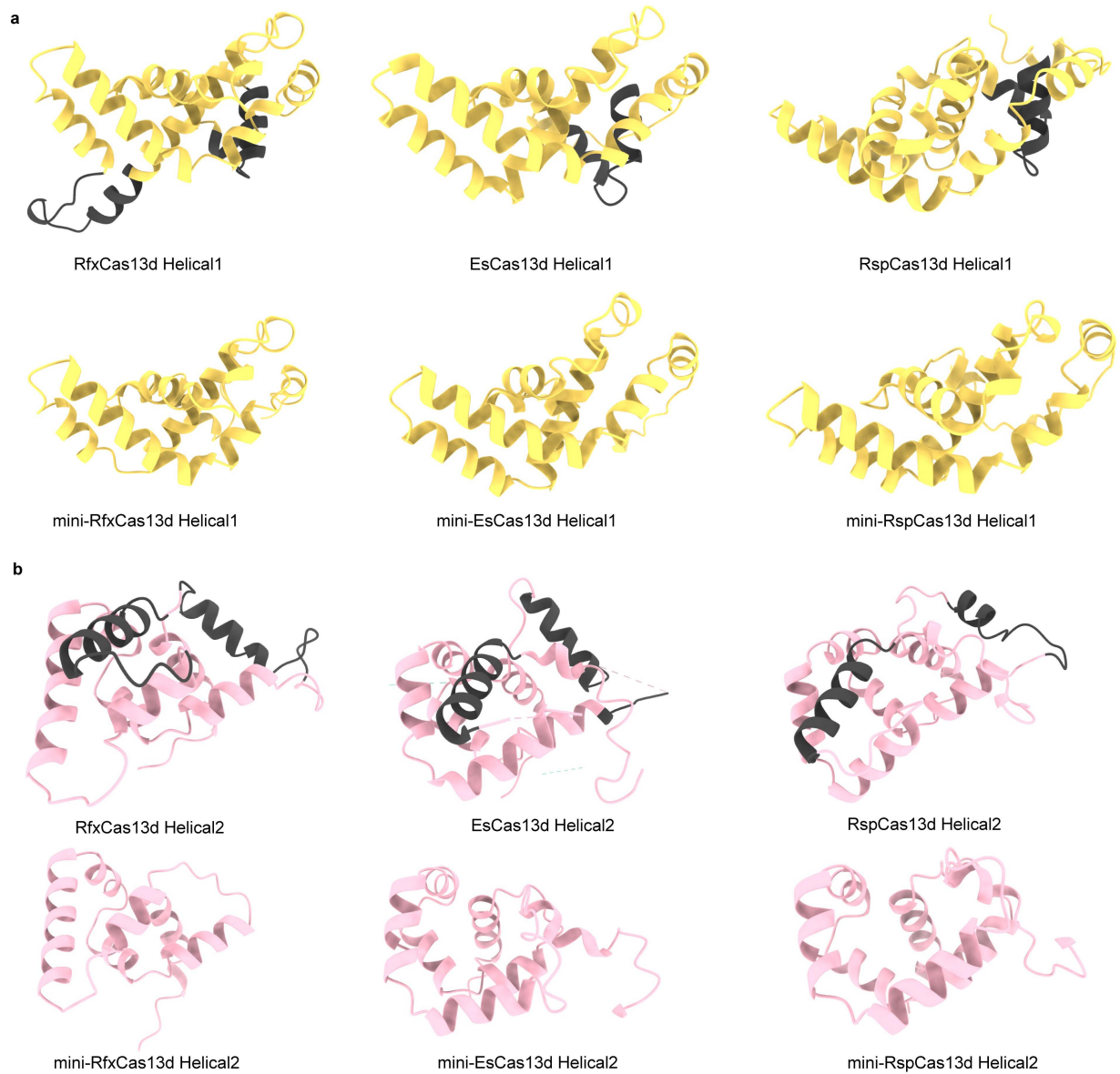


Figure S10. Comparison of the Helical1 and Helical2 domains of Cas13d.

(a) The Helical1 domains of RfxCas13d, mini-RfxCas13d, EsCas13d (6E9E), mini-EsCas13d, RspCas13d and mini-RspCas13d. (b) The Helical2 domains of RfxCas13d, mini-RfxCas13d, EsCas13d (6E9E), mini-EsCas13d, RspCas13d and mini-RspCas13d. All deletion regions were colored deep gray.

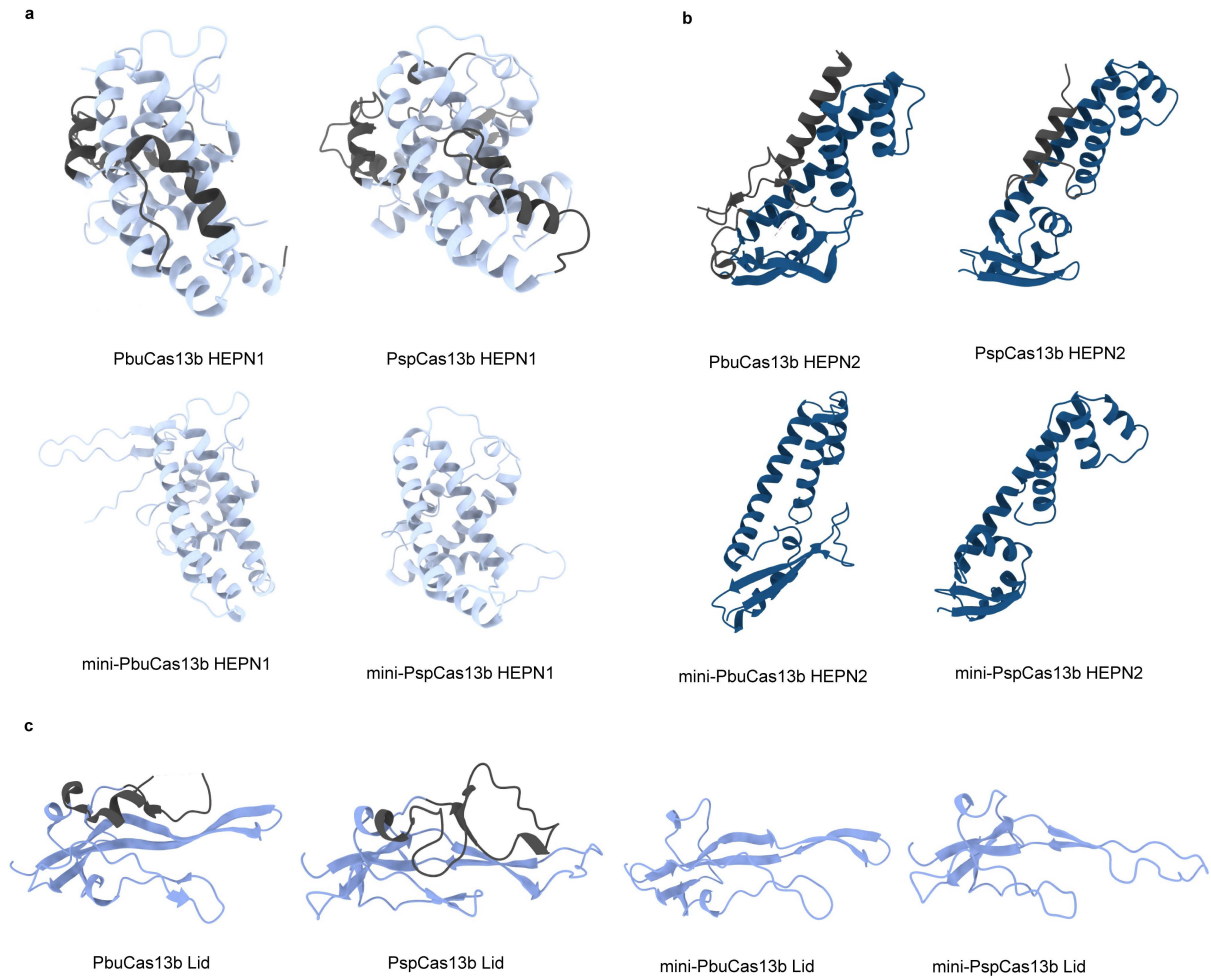


Figure S11. Comparison of the HEPN1 and HEPN2 domains of Cas13b.

(a) The HEPN1 domains of PspCas13b, mini-PspCas13b, PbuCas13b (6DTD), and mini-PbuCas13b. (b) The HEPN2 domains of PspCas13b, mini-PspCas13b, PbuCas13b (6DTD), and mini-PbuCas13b. (c) The Lid domains of PspCas13b, mini-PspCas13b, PbuCas13b (6DTD), and mini-PbuCas13b. All deletion regions were colored deep gray.

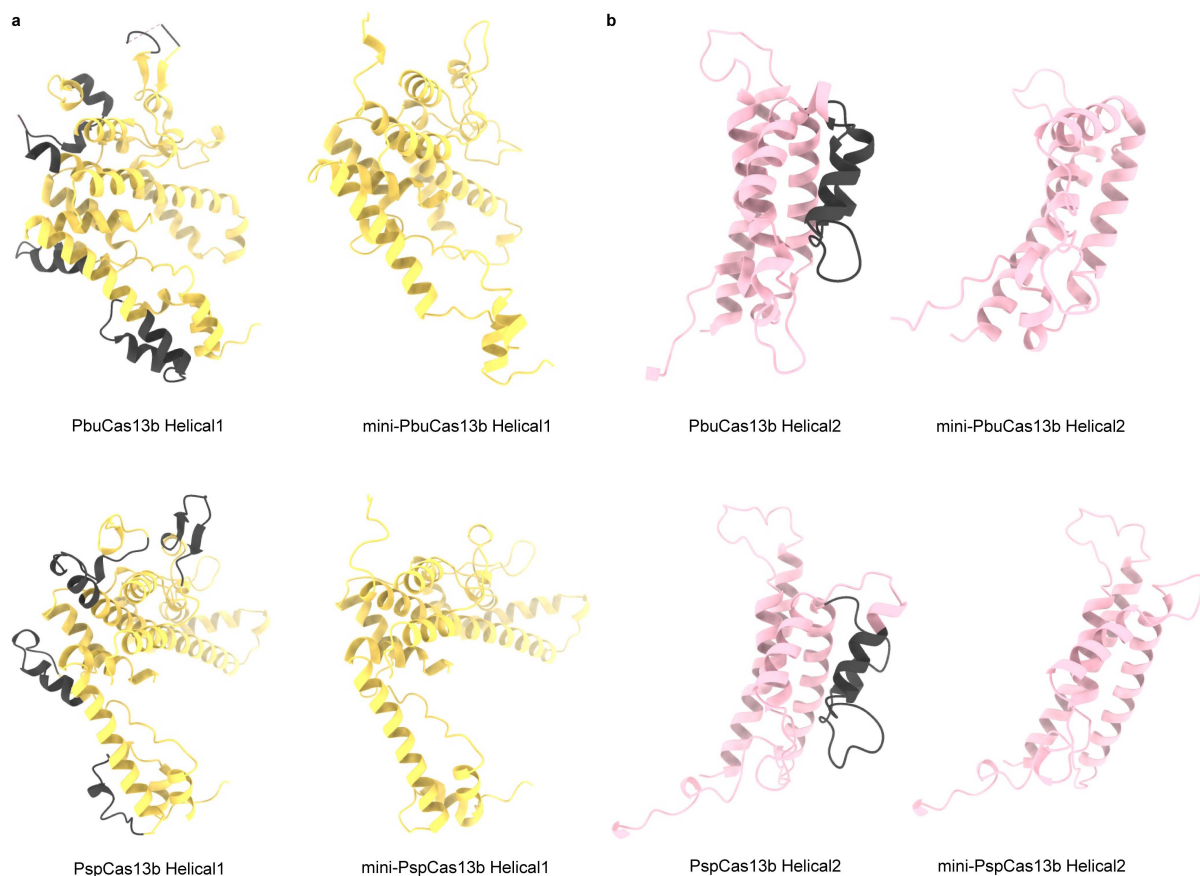


Figure S12. Comparison of the Helical1 and Helical2 domains of Cas13b.

(a) The Helical1 domains of PspCas13b, mini-PspCas13b, PbuCas13b (6DTD), and mini-PbuCas13b. (b) The Helical2 domains of PspCas13b, mini-PspCas13b, PbuCas13b (6DTD), and mini-PbuCas13b. All deletion regions were colored deep gray.

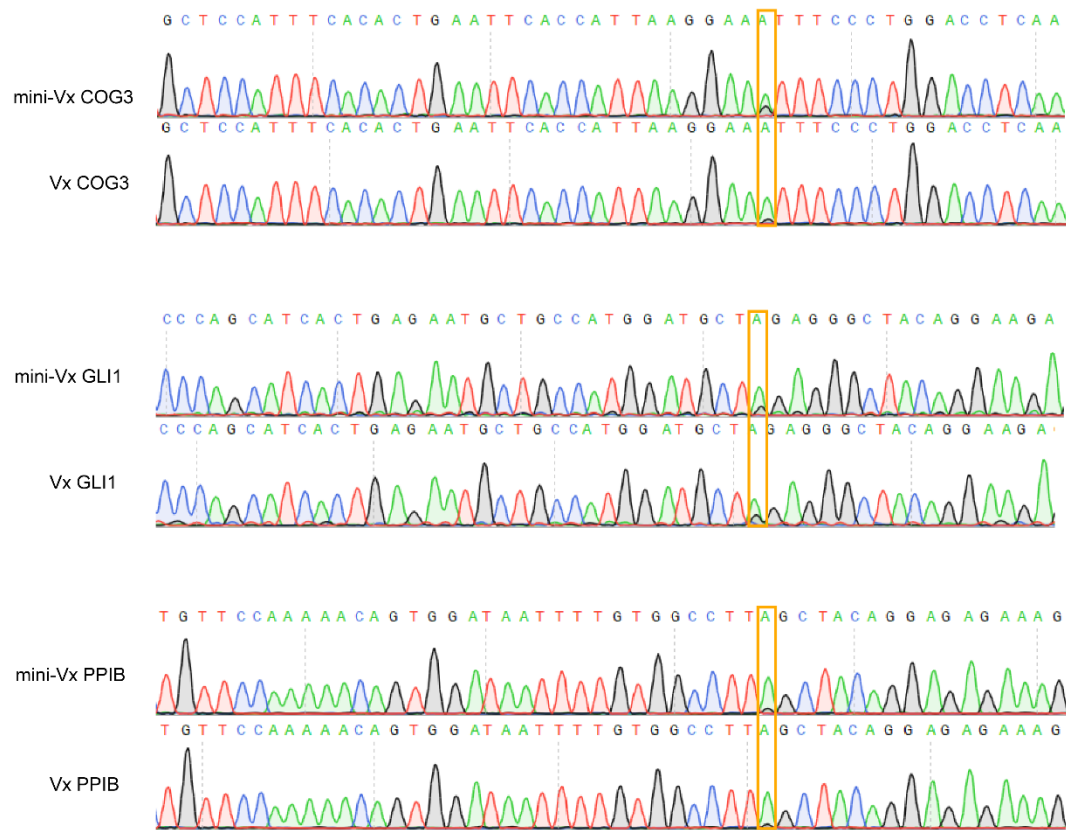


Figure S13. Sanger sequencing of mini-Vx and Vx mediated base transversion. The targeted bases are encompassed by an orange quadrangle. Vx: REPAIRx, mini-Vx: mini-REPAIRx.

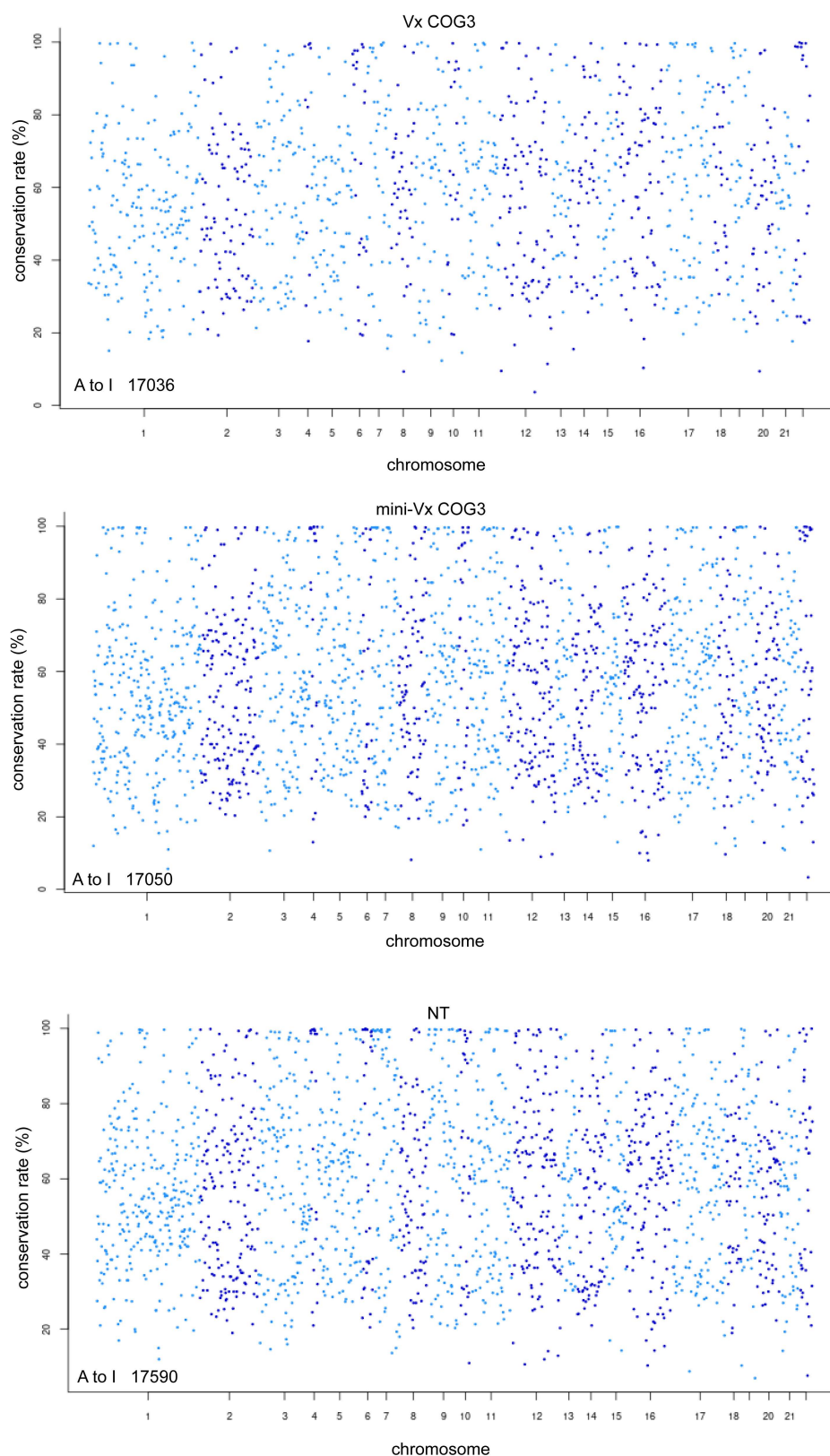


Figure S14. Off-target RNA editing effect for Vx and mini-Vx system. Manhattan plots of transcriptome-wide off-target RNA editing analysis for Vx and mini-Vx with *COG3* targeting guide and non-targeting (NT) guide in HEK293T cells. Vx: REPAIRx, mini-Vx: mini-REPAIRx.

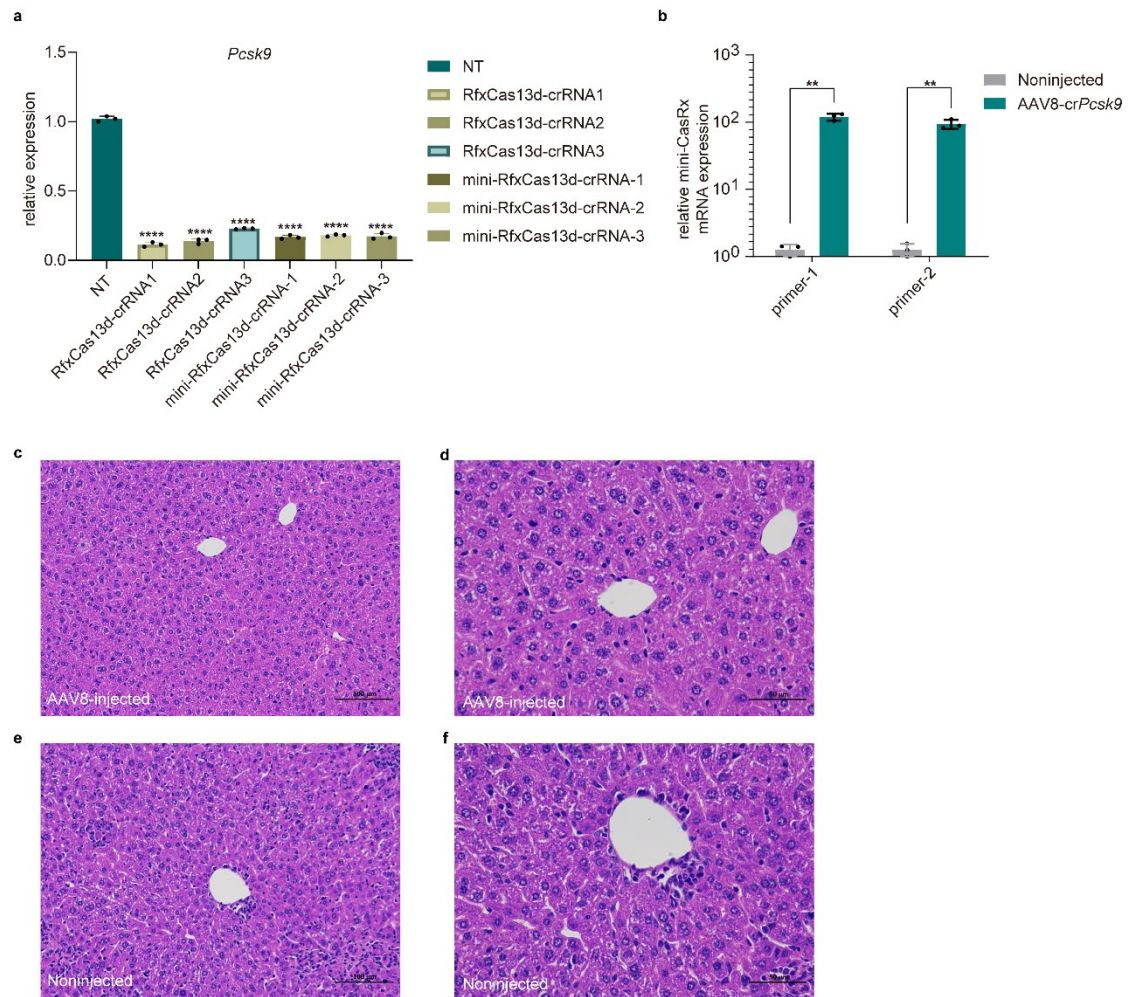


Figure S15. The results of mini-RfxCas13d in N2A cells and *in vivo*.

(a) Quantification of *Pcsk9* mRNA levels in N2a cells. Source data are provided as a Source Date file. (b) Quantification of the mini-RfxCas13d transcript in the liver. NT, non-target crRNA. The data are presented as the mean $\pm$ SD. Two-tailed unpaired two-sample t-test. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, **** $P < 0.0001$. (n = 3 biological replicates, each with an average of 3 technical replicates). CasRx: RfxCas13d. Source data are provided as a Source Date file. (c) Morphology of liver slices 21 days after AAV8 injection in mice. The scale bar represents 100 μm in length. (d) A close-up view of (c). The scale bar represents 50 μm in length. (e) Morphology of liver slices from noninjected mice at 21 days. The scale bar represents 100 μm in length. (f) A close-up view of (e). The scale bar represents 50 μm in length.

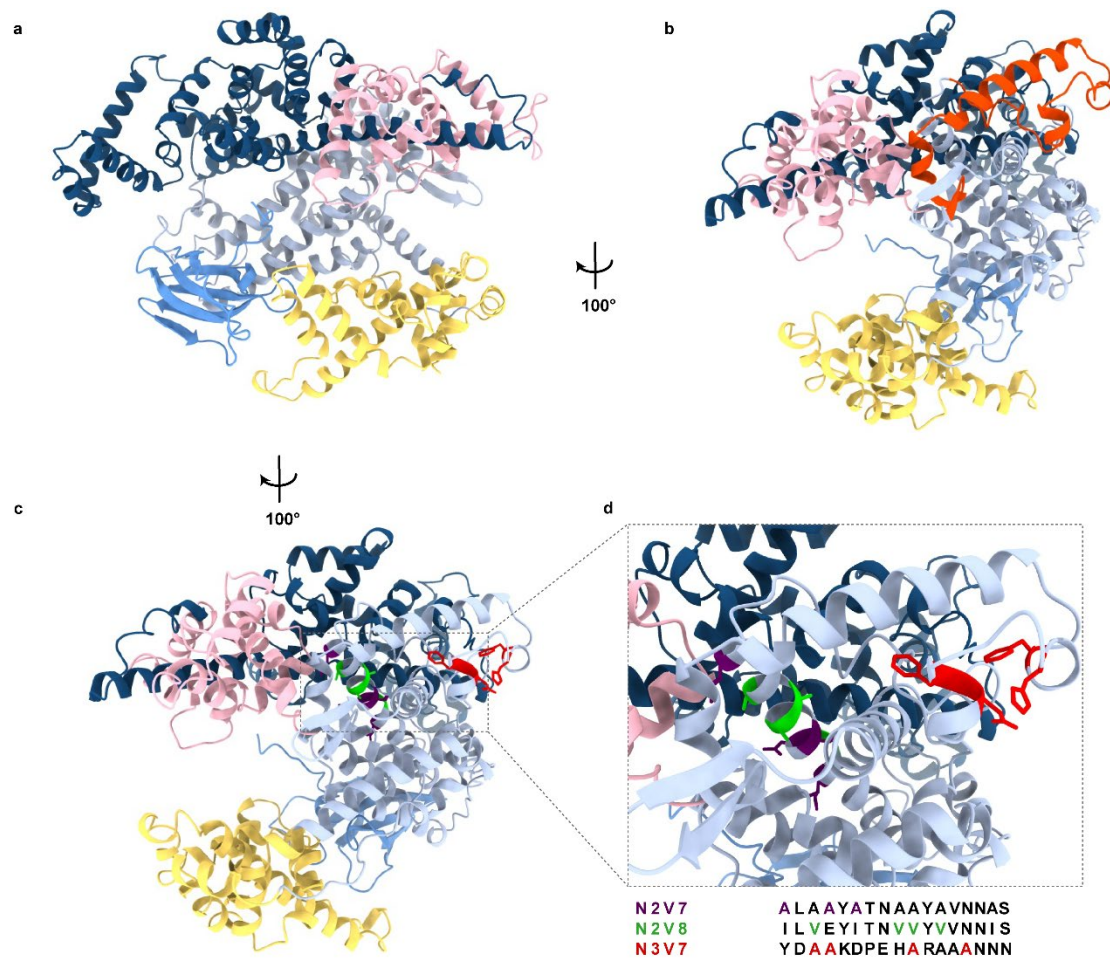


Figure S16. Comparison the $\Delta 2$ and N3V7 fragments of RfxCas13d. (a) The predicted structure of RfxCas13d by AlphaFold2 is shown. (b) Positions of $\Delta 2$ (orange) in RfxCas13d. (c) Positions of N2V7 (purple), N2V8 (green), and N3V7 (red) in RfxCas13d. (d) A close-up view of the N2V7 (purple), N2V8 (green), and N3V7 (red) sequence (red) of RfxCas13d.

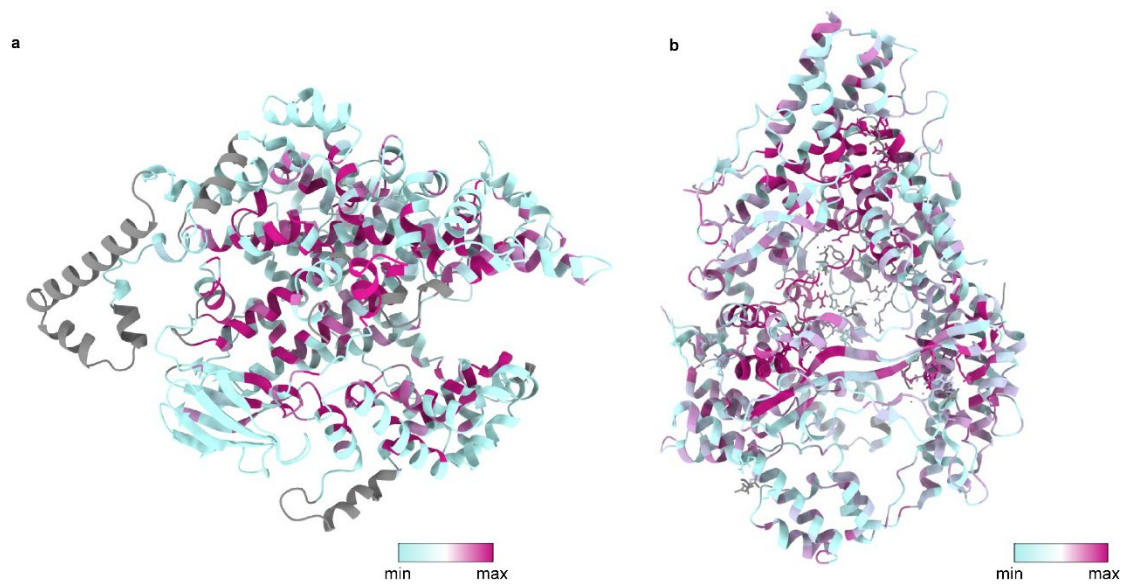


Figure S17. EsCas13d and PbuCas13b colored by conservation of Cas13ds and Cas13bs.

(a) Schematic representation of EsCas13d colored based on conserved sequence percentage. No-value fragments are gray. Regions with a high degree of conservation are concentrated in the RNA-binding cleft and the HEPN active site. Related to Figure S18.

(b) Schematic representation of PbuCas13b colored based on conserved sequence percentage. No-value fragments are gray. Regions with a high degree of conservation are concentrated in the RNA-binding cleft and the HEPN active site. Related to Figure S19.

RSP 1 .MAKKNNMKPRELREAQKKARQLKAAEINN...NAAPAIAAMPAAEVIAPVAEKKK...
UR 1 .MAKKNNMKPRELREAQKKARQLKAAEINN...NAAPAIAAMPAAEVIAPAAEKKK...
RFF 1 ..MKKKMSLREKREAEKQAKKAAYSAAASKNTDSKPAEKKAEETPKPAEII SDNSRNK...
RA 1 ..MKKKMSLREKREAEKQAKKAAYSAAASKNTDSKPAEKKAEETPKPAEII SDNSRNK...
PIE0 1MEREVKKPPKK...
ES 1 ..MGKKIHARDLREQRKTDRTKEFADQNKKREAERAVPKKDAAVSVKSVSSVSSKKDNVT
RFX 1MIEKKK...
ADM 1MNNKKK...

RSP 53 .SVKKAAGMKSILVS...KNKMYITTSFGKGN SAVLEYEVNNDYNQTOISSKGSSNTEILR
UR 53 .SVKKAAGMKSILVS...ENKMYITTSFGKGN SAVLEYEVNNDYNQTOISSKDNNSNIQLG
RFF 55 .TAVKKAAGLKSTIIIS...GDKLYMTSFGKGNAAVIEQKIDINDYSFSAMKDTPS...LEVVD
RA 55 .TAVKKAAGLKSTIIIS...GDKLYMTSFGKGNAAVIEQKIDINDYSFSAMKDTPS...LEVVD
PIE0 12 .SLAKAAGLKSTFVISPOEKE LAMTA FGGRNDALLQKRIVDG...VVRDVAGEKQQFQ
ES 59 KSMAKAAGVKS VFAVG...NTVYMTSFGGRND AVLEQKIVDTTSHEPLNIDDPAY...QLN
RFX 7 .SFAKGMGVKSTLVSG...SKVYMTTFAGESDARLEKIVEGDSIRSVMNEGEAFS...AEMA
ADM 7 .TKAKAAGLKSVFEDQ...KQAVLITTFAGKGNNSQIEKKVNS EVKDLRPPAFDLELKEK

RSP 109 GVNEVN.....ITFSSKHGFESGVEINTSN PTHRSGESS..PVRG...DMLGLK
UR 109 GVNEVN.....ITFSSKHGFESGVEINTSN PTHRSGESS..PVRG...DMLGLK
RFF 109 KAESKE.....ISFSSHHPFVKNDRLT TYNPLYGGKDNPEKPVGR...DMLGLK
RA 109 KAESKE.....ISFSSHHPFVKNDRLT TYNPLYGGKDNPEKPVGR...DMLGLK
PIE0 66 VQRQDE.....SRFRLQNSRLADRTVTADDPLHRAETPRRQPLGAGMDOTRRK
ES 113 VVTMNG.....YSVTGHGETVSAVT DNPLRRFNGRKKDEPEQSVPTDMLGLK
RFX 61 DKNAGY.....KIGNAKFSHPKGYAVVANNPLYTG.....PVQQDMLGLK
ADM 63 TFYISGKNNINTSRENPLASASLELSKRQIRARERIKRAREENRPYHNVKRVGEDDLRAK

RSP 153 SELEKREFGKTFD...DNIHQIQLIYNILDI EKILAVYV TNIVYALNNMLSIKDS.ESYDDF
UR 153 SELEKREFGKTFD...DNIHQIQLIYNILDI EKILAVYV TNIVYALNNMLGVKGS.ESHDDF
RFF 155 DKLEERYFGCTFN...DNLHQIQLIYNILDI EKILAVHSANIT T ALDHMVDEDEDEKYLNSDY
RA 155 DKLEERYFGCTFN...DNLHQIQLIYNILDI EKILAVHSANIT T ALDHMVDEDEDEKYLNSDY
PIE0 114 AILEQKYFCRTFD...DNIHQIQLIYNILDI HKMLAVPANHIVHTLNLLGG...YGETDF
ES 161 PTEKKEFGKEFD...DNIHQIQLIYNILDI EKILAVYS TNAIYALNNMSADEN..IENSDF
RFX 101 ETLEKRYFGESADGNDNICIQVTHNILDI EKILAEYITNAAYAVNNISGLDKDIIIGFGKF
ADM 123 ADLEKH YFGKEYS...DNLKIQIYNILDI NKITISPYINDIVYSMNNLARNDEYIDGKIDV

RSP 210 MGYLSARNTYEVFTHPD.KSNLSDKAKGNTIKKSFTSTFNDLTKTKRLG.....YFGLE
UR 210 IGYLSTNNIYDVFIDPD.NSSLSDDKKANVRKSLSKFNALLKTKRLG.....YFGLE
RFF 213 IGYMNTINTYDVFMDPSKNSLSPKDRKNIDNSRAKFELLSSTKRLG.....YFGFD
RA 213 IGYMNTINTYDVFMDPSKNSLSPKDRKNIDNSRAKFELLSSTKRLG.....YFGFD
PIE0 167 VGMPLPAGLPYDKLRVVKKNNGD TVDIKADIA.AYAKRPQLAYLGAAF.....YDVT
ES 217 FMKRITTDDET FDDFEKKKES TNSREKADFDAFEKFIGNYRLAYFADAF.....YVNKK
RFX 161 S.TVYTYDEFKDPDEHHRAAFNNNDKLINAIKAQYDEFDNFLDNPRLG.....YFG.Q
ADM 181 IGSLSSTTDYSSFMSPNKDLKKEKFSFHR ENYKKFVEASKPYMRYYGKVFIRDVKSKSL

RSP 261 EPK.TKDTRVSQAYKKRVYHMLAIVGQIRQSVFHDKS...SKLDEDLYSFIDIDSEYRE
UR 261 EPK.TKDNRVSQAYKKRVYHMLAIVGQIRQCVFHDKS...GAKRFDLYSFINNIDPEYRD
RFF 265 YDANGDKKKKNEEIKKRLYHLTAFAAGQLRQWSFHSAG...NYPRTWLY.KLDSLDKEYLD
RA 265 YDANGDKKKKNEEIKKRLYHLTAFAAGQLRQWSFHSAG...NYPRTWLY.KLDSLDKEYLD
PIE0 218 GKSKRDAARGRVKREQDVYAII LSLMSL LRQFCAHDSVRIWGQNTTAAALYHLQALPQDMKD
ES 269 NPKGKAKNVLRE...DKELYSVLTLLIGKLRHWCVHSEE...GRAEFWLYKLDLKDDEFKN
RFX 211 AFFSKEGRNYIINYGNECYDILALLSGLRHWVHNNEEESRISRTWLYNLDKNLDNEYIS
ADM 241 STGKGKIEVMYRSDEELFTIFQLLSYVRQSIMHNDIG...NKSILALTEKYPAREVG

RSP 317 TLDYLVDERFDSINKGFIQGN.KVNIISLLIDMMKGYEADD...IIRLYYDFIVLKSKQKN
UR 317 TLDYLVVEERLKSINKDFIEDN.KVNIISLLIDMMKGYEADD...IIRLYYDFIVLKSKQKN
RFF 321 TLDHYFDKRFENDINDDFVTKN.ATNLYILKEVFPEANFKD...IADLYYDFIVIKSKKN
RA 321 TLDHYFDKRFENDINDDFVTKN.ATNLYILKEVFPEANFKD...IADLYYDFIVIKSKKN
PIE0 278 LLDGWRRALGGVNDHFLDTN.KVNLLTLFEYYGAETKQARV.ALTQDFYRFVVLKKEQKN
ES 323 VLDVVYNRPVVEEINNRFIENN.KVNIQILGSVYKNTDIAE...LVRSYEFELITKKYKN
RFX 271 TLDNYLYDRITNELTNSFSKNS.AANVNYIAETLGINPAEF...AEQYFRFSIMKEQKN
ADM 296 FLSDLLKTKTNDVNRMFIDNNSQITNEFWLFI FGLQDHTSGADKICRNLYYDFIVIKADSKN


```

RSP 707 QQA.KGR.ENV.AKERA.KAVIG.LYLTVMY.LLVKNLVNVNARYVIAIHCLERD.FG.LYKEI.IPE.L
UR 707 QQA.KGR.ENV.AKERA.KAVIG.LYLTVMY.LLVKNLVNVNARYVIAIHCLERD.FG.LYKEI.IPE.L
RFF 715 QSA.K.ENME.KERF.KAVIG.LYLTVMY.RVVKNLV.DVNSRYIMAFHSLERDS......QL
RA 715 QSA.K.ENME.KERF.KAVIG.LYLTVMY.RVVKNLV.DVNSRYIMAFHSLERDS......QL
P1E0 688 QRG.RG.DNPK.KERY.KALIG.LYLTVMY.YLAVKNM.VNCA.NARYVIAFYCRDRD.TAL.YQK....EV
ES 724 VTS.RTSE.AEI.KRKN.QAI.IR.LYLTVMY.YIMLKNLVNVNARYVIAFHCV.ERD.TK.LYAESGLE.V
RFX 688 IED.TGR.ENAE.REKF.KKI.IS.LYLTVMY.YHILKNIVNINARYVIGFHC.VERD.AQ.LYKEKGYD.I
ADM 734 VRPG.TN.ESIE.KEKK.KALVGL.CLTI.QY.LVYKNLVNINARYTTAFYCLERD.SK.LKGF.G...V

```

```

RSP 767 ASKN.LKNDYRI.LSQTLCELCDKSP......
UR 767 ASKN.LKNDYRI.LSQTLCELCDKSP......
RFF 765 YNVS.VDNDYLA.LTDTLVKEGDNSR......
RA 765 YNVS.VDNDYLA.LTDTLVKEGDNSR......
P1E0 744 CWYD.LEEDKKS.GKQ.RQVEDYTALT......
ES 784 GNIE.KNKTNLT.MAVMGVKLENGII......
RFX 748 NLKK.LEEKGFSS.SVTKLCAGIDETAPDKRKDVEKEMAERAKESIDSLESANPKLYANYIKY
ADM 791 DVWR.DFESYTA.LTNHFIKEG......

```

```

RSP 791 .....NLF.LKKNERL.RKCEVDIN......NADSSMTRK.YRNC.IAHL.TVV
UR 791 .....NLF.LKKNERL.RKCEVDIN......NADSSMTRK.YRNC.IAHL.TVV
RFF 789 .....SRY.LGNKRL.RDCVKQDIDN.....AKKW.FVSDKYN.SITK.YRNN.VAHL.TAV
RA 789 .....SRY.LGNKRL.RDCVKQDIDN.....AKKW.FVSDKYN.SITK.YRNN.VAHL.TAV
P1E0 768 .....RYF.VSQGYLN.RHACGYLRSN.....MN.....GISNSLLTA.YRNA.VDHLNAI
ES 808 .....KTE.FDKSFAEN.AANRYLRNARWYKLILDNLKKSERAVVNE.FRNT.VCHLNAI
RFX 808 SDEKKAEEFTRQ.INREKAKTALNAYLRNTKWNVI.IREDDL.LRIDNK.CTL.FRNK.AVHLEVA
ADM 811 .....YLP.VRKAEIL.RANLKHLDCE.DG.....FKY.YRNQ.VTHLNAI

```

```

RSP 830 REL.KEYI.GDI.RTVDSY.ESIYHYVMQ.RCITKRENDTKQ...EEKIKYEDD.LLKN.HGYTK.KDF
UR 830 REL.KEYI.GDI.CTVDSY.ESIYHYVMQ.RCITKRENDTKQ...EEKIKYEDD.LLKN.HGYTK.KDF
RFF 835 RNCAE.FI.GDI.TKIDSY.EALYHYLIQ.RQLAKGLDHERSGF.DRNYPQYAP.LFKW.HTYV.KDV
RA 835 RNCAE.FI.GDI.TKIDSY.EALYHYLIQ.RQLAKGLDHERSGF.DRNYPQYAP.LFKW.HTYV.KDV
P1E0 810 PPLGSLCR.DIGR.VDSY.EALYHYAVQ.YLLNGRYRKT.P...REQELFAAM.QAHR.TWCSD.DL
ES 859 RNININ.IK.EIKEVENY.EALYHYLIQ.KHLENR.FADKKVE.RDTGDFISK.LEE.HKT.YCK.DF
RFX 868 RYV.HAYI.NDIAE.VNSY.QLYHYIMQ.RIIMNERYEKSS...GKVSEYFDA.VNDE.KKYND.RDL
ADM 847 R.VA.YK.YI.NE.IKS.VHSY.EALYHYIMQ.RHLYDSLQAKAKDSSGFVIDALKKS.FEH.KI.YS.KDL

```

```

RSP 887 VKAL.NS.PFGYNI.PREKNLS.IEQLFDR...NEYLTEK.....
UR 887 VKAL.NS.PFGYNI.PREKNLS.IEQLFDR...NEYLTEK.....
RFF 894 VKAL.NA.PFGYNI.PREKNLS.IDALFDR...NEIKKNDGEKKSD.D.
RA 894 VKAL.NA.PFGYNI.PREKNLS.IDALFDR...NEIKKNDGEKKSD.D.
P1E0 866 VKAL.NT.PFGYNL.ARYKNLS.IDGLFDR.REGDHVVREDGEKPAE..
ES 917 VKAY.CT.PFGYNL.VRYKNLT.IDGLFDR.KNYPGKDDSD.EQK....
RFX 925 LKLL.CV.PFGYCI.PREKNLS.IEALFDR.NEAAKFDKEKKK.VSGNS
ADM 907 LHVL.HS.PFGYNT.ARYKNLS.IEALFDR.KNESRPEVNPLSTND...

```

Figure S18. Multiple sequence alignment of Cas13d proteins from different species.

Sequence alignment of RspCas13d, UrCas13d, RffCas13d, RaCas13d, P1E0, EsCas13d, RfxCas13d, and ADM was performed using Clustal Omega, and the figure was prepared with ESPript (<http://esprict.ibcp.fr>). Related to Figure S17a.

PBU 223IIDSPNFHYHFADKEGNMTIA[•]GLLFVVS[•]LF[•]DKKDAIWMQK[•]KLK[•]GF[•]K
PGU 212HNDNPSFKHHFVDGEGMVTEA[•]GLLFVVS[•]LF[•]EKKRDAIWMQK[•]KIR[•]GF[•]K
PAU 188GQFKYSFAD..NEGN[•]ITES[•]GLLFVVS[•]LF[•]EKKDAIWMQK[•]KLNG[•]GF[•]K
PRE 195EDFNLYFTDKDNKGKITKN[•]GLLFVVS[•]LF[•]EKKDAIWMQK[•]KFR[•]GF[•]K
PIN 187EEEFNYFTKDNEGNITES[•]GLLFVVS[•]LF[•]EKKDAIWMQK[•]KLNG[•]GF[•]K
RAN 202DNPDFNRYRFEKDGFTES[•]GLLF[•]FTN[•]LF[•]DKRDAYWMLK[•]KVSG[•]GF[•]K
PGI 181EQLISVADGKE...CLTVS[•]GFAFF[•]IC[•]LF[•]LDREQASGLMS[•]RIR[•]GF[•]K
BP 187DNKKFFAIGGNEGILKDNALIF[•]IC[•]LF[•]LDREAFKFLSRAT[•]GF[•]K
CCA 253 VWELCSKSSSKYTEKSPNRENDKHCLEVPISQK[•]GIVFL[•]LS[•]FT[•]NKGEIYALTSN[•]IK[•]GF[•]K
BZ 236LKESSKAKYNTKSDPQQEEGDLKIPISKN[•]GIVFL[•]LS[•]FT[•]NKQEIYALTSN[•]IK[•]GF[•]K
MOD 235 ...KETVVAKGADAYFEKNHHKSNDDFALNISEK[•]GIVYL[•]LS[•]FT[•]NKEMDSLKANLT[•]GF[•]K
PXI 186YRPRSLANSPDHENTVAFVTC[•]LF[•]TERKYAF[•]PFLS[•]RLD[•]GF[•]K
PSP 207FFLSLQDYNGDTQKKLHLSGV[•]GIAL[•]IC[•]LF[•]LDKQYINIFLS[•]RLP[•]IES
Alistipes 158WNEGERKYEILRD[•]GLIF[•]FCC[•]LF[•]TERKGAERFLNEL[•]RE[•]GF[•]K
FBR 205INNEHNILNIEKGKYLTFE[•]AMLF[•]LIT[•]IF[•]YKN[•]EANHLLP[•]KLY[•]DE[•]K

PBU 270 DGRNLRRE.....QMTNE[•]VF[•]CRSRISLP[•]KL[•]KL[•]EN[•]VQT.....
PGU 259 GGTETYQ.....QMTNE[•]VF[•]CRSRISLP[•]KL[•]KL[•]ESLRT.....
PAU 231 DNLENKK.....KMTHE[•]VF[•]CRSRILMP[•]KL[•]RL[•]ESTQT.....
PRE 240 DNRGNKE.....KMTHE[•]VF[•]CRSRMLLP[•]KIR[•]LESTQT.....
PIN 232 DNRENKK.....KMTNE[•]VF[•]CRSRMLLP[•]KL[•]RL[•]ESTQT.....
RAN 247 ASHKQRE.....KMTTE[•]VF[•]CRSRILLP[•]KL[•]RL[•]ESRYD.....
PGI 223 RTDENWA.....RAVHET[•]FC[•]DL[•]CIRHP[•]HD[•]RL[•]ESSNT.....
BP 232 STKEKGF.....LAVRE[•]TF[•]CALCCRP[•]HER[•]LLSVNP.....
CCA 313 AKITKEE.....PVYDKNISRYMA[•]ATH[•]MF[•]SFLAYKGL[•]KR[•]KIR[•]ISEINYNEDG...QASST
BZ 291 ATVIDEATVSEATVSHGKNSICFMA[•]THE[•]IF[•]SHLAYKKL[•]KR[•]KV[•]RTAEINYGAE[•]NAE[•]QLSV
MOD 293 GKVDRES.....GNSIKYMATQR[•]IY[•]SFHTYRGL[•]KQ[•]KIR[•]TSEE.....
PXI 226 STNDAAE.....GDPLIRK[•]ASHEC[•]YTMFCCRLP[•]QP[•]KL[•]E.....
PSP 254 SYNAQSE.....ERR[•]IIIR[•]SFGINSIKLP[•]KD[•]RIH[•]SEKS.....
Alistipes 197 RTDEEGR.....IKRT[•]IF[•]TKYCTRES[•]HK[•]HI[•]GIEEQ.....
FBR 250 NNKSKQE.....L[•]TF[•]FSKKFT[•]SQ[•]DI[•]DAEEG.....

PBU 301 ..KDW[•]MQLDMLNEL[•]VR[•]CP[•]KS[•]LYER[•]LREKDRES[•]FKVPFDIFSDDYNA[•]E.....
PGU 290 ..DDW[•]MQLDMLNEL[•]VR[•]CP[•]KPL[•]YDR[•]LREDDRAC[•]FRV[•]VPDILPEDDT[•]DGGG.....
PAU 262 ..QDW[•]ILLDMLNEL[•]IR[•]CP[•]KS[•]LYER[•]LQDDREK[•]FKVPFDPADEYNA[•]E.....
PRE 271 ..QDW[•]ILLDMLNEL[•]IR[•]CP[•]KS[•]LYER[•]LQAYREK[•]FKVPFDSIDEDYDA[•]E.....
PIN 263 ..QDW[•]ILLDMLNEL[•]IR[•]CP[•]KS[•]LYER[•]LREEDREK[•]FRV[•]PIEIADEYDA[•]E.....
RAN 278 ..HNQ[•]MQLDMLSEL[•]SR[•]CP[•]KL[•]LYEK[•]LSEENKKH[•]FQVEADGFLDETEE[•]E.....
PGI 254 ..KEA[•]LLDMLNELN[•]RC[•]PR[•]IL[•]YDML[•]PEEERAQ[•]FLPALDENSMNNLS[•]ENS[•]LD[•]EES[•]RLLWDG
BP 263 ..REA[•]LLDMLNELN[•]RC[•]PR[•]IL[•]YDML[•]PEEERAQ[•]FLPALDENSMNNLS[•]ENS[•]LD[•]EES[•]RLLWDG
CCA 366 YEKET[•]LMLQMLDEL[•]NKV[•]PD[•]VYQ[•]NLSEDVQKT[•]FIEDWNEYLK[•]NNNG[•]DVG[•]TME.....
BZ 351 YAKET[•]LMMQMLDEL[•]SKV[•]PD[•]VYQ[•]NLSEDVQKT[•]FIEDWNEYLK[•]NNNG[•]DVG[•]TME.....
MOD 330 GVKET[•]LLMQMIDEL[•]SKV[•]PN[•]VYQ[•]HLSTTQONS[•]FIEDWNEYK[•]DYED[•]DVETDDL.....
PXI 259 ..SSD[•]ILLDMVNEL[•]GR[•]CP[•]SAL[•]YNLL[•]SEEDQAR[•]FHIKREEITGFEED[•]PD.....
PSP 287 ..NKS[•]VAMDMLNEVK[•]RC[•]PD[•]EL[•]FTT[•]LSA[•]EKQSR[•]FRIISDDHN.....
Alistipes 227 ..DFL[•]IFQDIIGDLN[•]RV[•]PKV[•]CDGV[•]VDLSKENERY[•]IKNRETSNESDEN.....
FBR 276 ..HLI[•]KFRDMIQYLN[•]HY[•]PTA[•]WNND[•]LKLESENKN[•]NKIMTKLIDSIIE[•]FELNSN.....

PBU 346 ...EEPFKNTLV[•]RH[•]QDR[•]FP[•]YFVLRY[•]FDLNEI[•]FE[•]QLRF[•]Q[•]IDL[•]GYHFSIYN[•]KRIGDE.DE
PGU 338 ...EDPFKNTLV[•]RH[•]QDR[•]FP[•]YFALRY[•]FDLKKV[•]FT[•]SLRF[•]Q[•]IDL[•]GYHFAIYK[•]KMIGE.Q.PE
PAU 307 ...QEPFKNTLV[•]RH[•]QDR[•]FP[•]YFVLRY[•]FDYNEI[•]FK[•]NLRF[•]Q[•]IDL[•]GYHFSIYK[•]KLIGGQ.KE
PRE 316 ...QEPFRNTLV[•]RH[•]QDR[•]FP[•]YFALRY[•]FDYNEI[•]FK[•]NLRF[•]Q[•]IDL[•]GYHFSIYK[•]KLIGGQ.KE
PIN 308 ...QEPFKNTLV[•]RH[•]QDR[•]FP[•]YFALRY[•]FDYNEI[•]FT[•]NLRF[•]Q[•]IDL[•]GYHFSIYK[•]KQIGDY.KE
RAN 323 ...QNPFKDTLV[•]RH[•]QDR[•]FP[•]YFALRY[•]FDLNEI[•]FK[•]SIRF[•]Q[•]VDL[•]GYHFSIYK[•]KIGDE.QE
PGI 312 SSDWAEALTKRI[•]RH[•]QDR[•]FP[•]YLMRL[•]FE[•]EMDL[•]LK[•]GIRF[•]VDL[•]GYHFSIYK[•]KVGRNGEY
BP 321 PFEMIASLSKRV[•]RYK[•]NRF[•]PYLMRL[•]YIE[•]EKNLL[•]PF[•]IRF[•]IDL[•]GYHFSIYK[•]KVGRNGEY
CCA 419 ...EQVIHPVIRK[•]RYE[•]DKFN[•]YFAIR[•]FL[•]DEFAQ[•]FP[•]TLRF[•]Q[•]VH[•]LG[•]NYLCKDR[•]TKMIGEDTTT
BZ 404 ...EQVIHPVIRK[•]RYE[•]DKFN[•]YFAIR[•]FL[•]DEFAQ[•]FP[•]TLRF[•]Q[•]VH[•]LG[•]NYLCKDR[•]TKMIGEDTTT
MOD 383 ...SRVIHPVIRK[•]RYE[•]DKFN[•]YFAIR[•]FL[•]DEFFD[•]FP[•]TLRF[•]Q[•]VH[•]LG[•]DYVHDDR[•]TKQLGKVES
PXI 305 ...EELEQEIVLK[•]RHS[•]DRF[•]FP[•]YFALRY[•]DDTEA[•]FQ[•]TLRF[•]Q[•]VH[•]LG[•]RWRTKPVY[•]KRIYQGQER
PSP 326EVL[•]LMK[•]RSS[•]DRF[•]VP[•]LLQY[•]IDY[•]GKL[•]FD[•]HIRF[•]HVNM[•]GKLRYLLKAD[•]KTICIDGQTR
Alistipes 272KARYRLLI[•]REK[•]DKF[•]PYYLMRY[•]IVDFGV[•]LPC[•]ITF[•]KONDY[•]STKEGRGQF[•]HYQDAAVAQ
FBR 326 ...YPSFATDIQF[•]KKEA[•]KAF[•]LFAS[•]NKK[•]RNQTS[•]FS[•]NKS[•]YNEE[•]IR[•]HNP[•]HIKQY[•]RD[•]EIASALTP

PBU 401 VR[•]HL[•]THH[•]YGF[•]ARIQD[•]FAPQNPQPEEWRKLVKDLDHF[•]ETSQEPYISK[•]TA[•]PH[•]YHLENEKIGI
PGU 393 DR[•]HL[•]TRNLYG[•]FRIQD[•]FAEEHRPPEEWRKLVKDLDYF[•]ETGDKPYISQTS[•]PH[•]YHIEKKGIGL
PAU 362 DR[•]HL[•]THKLYG[•]FRIQD[•]FAKQNRPDQWKAIVKDLDYF[•]ETSNKRYISQTS[•]PH[•]YHLENQKIGI
PRE 371 DR[•]HL[•]THKLYG[•]FRIQD[•]FTKQNRPDQWKAIVKDLDYF[•]ETSNERYISQTS[•]PH[•]YHLENQKIGI
PIN 363 SH[•]HL[•]THKLYG[•]FRIQD[•]FTKQNRPDQWKAIVKDLDYF[•]ETSKPEYIPETT[•]PH[•]YHLENQKIGI
RAN 378 DR[•]HL[•]TRTLLS[•]FRLQD[•]FTEINRPQEWKALTKDLDYF[•]ETSNQPPFISKTT[•]PH[•]YHITDNKIGF
PGI 371 DR[•]IT[•]TDHALA[•]FGLSD[•]FQNEEE.....VSRMISGEASYPVRFSLFAP[•]RYAIYDNKIGY
BP 380 ER[•]SV[•]TDHAMA[•]FGLTD[•]FHNEDA.....VLQQITKGIT[•]DEVRFSLYAP[•]RYAIYDNKIGY
CCA 475 ER[•]VKK[•]ITV[•]FRLSE[•]LENKKAIFLN...EREE...IKG...WEVFPN[•]PSYDFPNKISV
BZ 458 DR[•]RIKEK[•]ITV[•]FRLSE[•]LEHKKALFIK...NTET...NE[•]DREHYWEIFPN[•]PNYDFPNKISV
MOD 439 DR[•]RIKEK[•]ITV[•]FRLSD[•]INSASASYFH...SLEEQDK[•]EELDNKWTLPN[•]PSYDFPNKISV
PXI 362 DR[•]VL[•]TQSI[•]IRT[•]FRLSR[•]LLPIYENVKHDVQRNEEDGKLVNPDVTSQFHKS[•]WIQIESDDRA
PSP 379 VR[•]IEQPLNG[•]FRLSE[•]AETMRKQENGTFGNSGIRIR[•]DFENMKRDDAN[•]PANYPIYDVTYTH
Alistipes 328 EERCYNF[•]VVRNG[•]NYYS.....YMPQAQ[•]NVVR[•]ISELQGT[•]ISVEELRNMMVYAS
FBR 384 IS[•]FN[•]VKE[•]D[•]KFKI[•]FVKK[•]HVLEEYFPNSIGYKFLYND[•]FTEKEKEDFGL[•]KLY[•]SNPKNTKLI

PBU 461 KFCSAHNNLFP SLQTDKTCNGRSKFNLGTQFTAEAFLSVHEILPMMFYYLLLT KDYSRK.
PGU 453 RFMP EGQHLPSP EVGTTTRTGRSKYAQDKRLTAEAFLSVHEILPMMFYYLLLR EKYSEE.
PAU 422 RFRNGNKEIWPSLKTNDENNEKSKYKLDKQYQAEAFLSVHEILPMMFYYLLLKKEKPNND
PRE 431 RFRNDNDIWP SLKTNGEKNEKSKYNLDKPYQAEAFLSVHEILPMMFYYLLLKMENTDND
PIN 423 RFRNDNDKIWP SLKTNSEKNEKSKYKLDKSFQAEAFLSVHEILPMMFYYLLLTENTDND
RAN 438 RLG.TSKELYPSLEIKDGANRIAKYPYNSGFVAHAFISVHEILPLMFYQHLTG.....
PGI 424 CHTSDPVYPKSKTGEKR.....ALSNPQSMGFI SVHDLRKLLLMELLCEGFSFRMQ
BP 433 VRTSGSDKISFPTLKKKGEGHCVAYTLQNTKSF GFISIVYDLRKILLLSFLDKDKAKNIV
CCA 526 NYKDFPIVGSILDREKQPVSNKIGIRVKIAD ELQREIDKATKEKKLRNPKNRKANQDEK
BZ 513 NDKDFPIAGSILDREKQPVAGKIGIKVKLLNQYVSEVDKAVKAHQLKQKASKPSIQN.
MOD 494LQHQQEQKNAGKIGIYVKLRDTQYK...EKAAL EEARKSLNPKERSATKA
PXI 422 FLSDRIEHFSPHYNFGDQVIGLKFINPDRYAAIQNVFPKLPGEKKDKDAKL VNETADAI
PSP 439 YILENNKVEMFINDKEDSAPLLPVIEDDRYVVKTI PSCRMSTLEIPAMAFHMF LFGSKK.
Alistipes 375 INGKDVNKSVEQYLYHLHLLEYKILTISGQTIKEGRVDVEDYRPLLDKLLLRPASNGEE.
FBR 444 ERIDNHKLKLVKSHGRNQDRFMDFSMRFLAENNYFGKDAFFKCYKFPYDTQEQDEFLOQSNENN

PBU 520ESADKVEGIIIRKEISNIYAIYDAFANNEINSIADLT
PGU 512VSAEKVQGRIKRVIEDVYAIYDAFARDEINTL KELD
PAU 482 EIN.....ASIVEGFIKREIRNIFKLYDAFANGEINNIDDL E
PRE 491 KEDNEVGTKKKGNKNNK.....QEKHKIEEIIENKIKDIYALYDAFTNGEINSIDELA
PIN 483 NEIETK...KKENKNDK.....QEKHKIEEIIENKITEIYALYDTFANGEIKSIDELE
RAN 490KSEDL LKETVRHIQRIYKDFEERINTIEDLE
PGI 475 SDFLRKANRILDETAEG.....KLQFSALFP EMRRHFIPPONPKSKDRRKEATLTLEKYK
BP 493 SGLLEQCEKHWDLSENLFD AIRELQKEFPVPLIRYTLPRSGGKLVSSKLADKQEKYE
CCA 585 QKE.....RLVNEIVSTNSNEQGE.PVVF IGQPTAYLSMNDIHS
BZ 572IIEEIVPINESNPKE.AIVFGGQPTAYLSMNDIHS
MOD 541 SKY.....DIITQII EANDNVKSEKPLVFTGQPIAYLSMNDIHS
PXI 482 ISTHEIR.....SLFLYHYLSKKPISAGDERRFIQVDTETFIKQYIDITKLFF
PSP 498TEKLIVDVHNRYKRLFQAMQKEEVT AENIAS
Alistipes 434LRRELRLKLLPKRVCDL LSNRFDCS
FBR 504 DD.....VKFHKGVTTYIKYEEHLKNYSYWD CPFVEENNSMS

PBU 556 RRLQNTNILQGHLPKQMISILKGRQKDMGKEAERKIGEMTDDTQRRLLD LCKQTNQKI.R
PGU 548 ACLADKGIRRGHLPKQMIAILS QEHKDMEEKIRKKLOEMTADTDHRLDMLDRQTRDKI.R
PAU 519 KYCADKGIPKRRHLPKQMVAILYDEHKDMVKEAKRKQKEMVKDTKKLLATLEKQTQKE.E
PRE 544 EQREGKDIEIGHLPKQLIVILKNKSKDMAEKANRKQKEMIKDTKKRLATLDKQVKEI.E
PIN 533 EYCKGKDIEIGHLPKQMIAILKDEHKVMATEAERKQKEMLVDVQKSLES LDNQINEEI.E
RAN 522 KANQGR.LPLGAFPKQMLGLLQNKQPD LSEKAKIKIEKLTAETKLLSHRLNTKLKSSP.K
PGI 530 QEIKGRKDKLNSQLLSAFMDQRLPSRLLD EWMNIRPASHSVKLRTYVQQLNEDCRL.R
BP 553 SEFERRKEKLT.EILSEKDFDLSQIPRRMID EWLNVLPTRSREKKLKG VVETLKLDCRE.R
CCA 623 VLYEFFLINKIS.....GEALETKIVEKITETQIKQIIGKDATT KILK.P
BZ 606 ILYEFFDKWEKKKEKLEKKGEKELRKEIGKELEKKIVGKIQAQIQI IDKDTNAKILK.P
MOD 580 MLFSLLT DN AELKKT.....EEVEAKLIDQIGKQINEILSKD TDTKILK.K
PXI 530 EDIKSGELQPIADPPNYQKNEPLPYVRGDKEKTQEERAOYRERQKEIKERRKELNTLL.Q
PSP 529 FGLAESDLPQKILDLISGNAHGKD VDAFIRLTVDMDLTDTERRIKRFDKDRKSIR SADNK
Alistipes 458 EGVSAVEKRLKAILLRHEQLLSQN PALHIDKIKSVIDYLYLFFSDDEKFRQQPT EKAHR
FBR 542 VKISIGSEEKILKIQRNLMIFYLENALYNENVENQGYKLVN NNYRELKKDVEESIASLDL

PBU 615 IGKRNAGLLKSGK IADWL VNDMMRFQPVQKDQNNIPINNSKANSTEYR.....
PGU 607 IGRKNAGLPKSGV IADWLVRDMMRFQPVAKDTS GKPLNNSKANSTEYR.....
PAU 578 DDGRNVKLLKSGE IARWL VNDMMRFQPVQKDNEGKPLNNSKANSTEYQ.....
PRE 603 DGRNIRLLKSGE IARWL VNDMMRFQPVQKDNEGKPLNNSKANSTEYQ.....
PIN 592 NVERKNSSLKSGK IASWL VNDMMRFQPVQKDNEGKPLNNSKANSTEYQ.....
RAN 580 LGKRREKLIK TGVLADWL VKDFMRFPVAYDAQNP I KSSKANSTEFW.....
PGI 589 LRFRKRDGDGKARAIPLV GEMATFLSQDIVRMI I SEETKKLITSAYYN.....
BP 611 LRVEFKREKGEHPLPPRI GEMATDLAKDIIRMVIDQGVKQRITSAYYS.....
CCA 665 YTNANSNSINREKLLRLDLEQEQQILKTLLEEQQQREKDKDKKSK.....
BZ 665 YQDGNST AIDKEKLIKDLKQEQNLQKLKDEQTVREKEYNDFIAYQDKNREINKVRDRNH
MOD 626 YKDNLDKETD TDKITRD LARDEKEIEKLILEQKQRAD DYNYSSTKFN.....
PXI 589 NRYGLSIQYIPSR LREYLLGYKKVPY EKLALQKLRAQRKEVKRKIKDIEKMR.....
PSP 589 MGKRGFKQISTGKLADFLAKDIVLFPQSVNDGENKITGLNRYIMQSAI.....
Alistipes 518 GLKDEEFQMYHYLVGDYDSHPLALWKELEASGR LKPEMRKLT SATSLHG.....
FBR 602 IKSNPDFKSKYKKILPKRL LHNYAPAKQDKAPENAFETLLKKADFREEQ.....

PBU 663MLQRLALALFGSENFR..LKAYFNQMNLVGNDNPHFFLAETQWEHQ T
PGU 655MLQRLALALFGGEKKR..LTPYFRQMNLTGGNNPHFFLHETR WESHT
PAU 626MLQRLALALYNNEEK...PTRYFRQVNLIESNNPHFFLKWTWEECN
PRE 651MLQRLALALYNKEEK...PTRYFRQVNLIKSSNPHFFL EDITKWEECY
PIN 640LQRTLAFFGSEHER..LAPYFKQTKLIESNPHFFLKDT EWEKCN
RAN 628FIRRALALYGG EKNR..LEGYFKQTNLIGNTNPHFFLKNKFHWKACR
PGI 637EMQRLALQYAGEENRRQFRAIVAELRLLD PSSGHPFLSATMET AHR
BP 659EIQRC LAQYAGDNNRRHLD SIIRELRLKDTKNHGFFLGKVL RPLGL
CCA 710RKHEL YPSEKKGK VAVWLANDIKRFPMPKAFKEQWRGYHSSLLQK
BZ 725 KQY LKDNLKKRYPEAPARKEVLYYREKKGK VAVWLANDIKRFPMTDFKNEWKGEQHSLLQK
MOD 674IDKSRRKHL LFNAEKKGKIGVWLANDIKRFPFKESKSKWKGYQHTELQK
PXI 641TPRVGEQATWLAEDIVFLT PPKMHTPERKTTKHPOKLNN DQFRIMQS
PSP 637AVYDSGDDYEAQQQFKLMFEKARLIGKGTTEPHPF LYKVFARSIPA
Alistipes 567LYMLCLKGTVEWCRKQLMSIGKGTAKV EAIADRVGLKLYDKLKEY
FBR 651YKKLLKKAHEHKNKEDFVKRNKKGQFKLHFTRKACQMMYFKEKYNTLKE


```

PBU      909  LRDIDTNTANEES.....NNILNRIMPMKLPVKTYETDNKGNILKERP..
PGU      955  LKDIRPNVQEQQS.....LNVLNRVPMRLPVVVYRADSRGHVHKEEAP..
PAU      896  KLRLNNIDTDTAK.....KEKNNILNRVPMELPVTVYEIDDSHKIVKDKP..
PRE      914  KLRLKDDIDDTAK.....KEKNNILNRVPMRLPVTVYEIDKSFNIVKDKP..
PIN      882  LKNINTNTTKKEKNTEEKNGEEKNIKEKNNILNRIMPMRLPIKVYGRENFSSKNKKKKIRR
RAN      876  LENLAVNVQEADAK.....LNPLNQTLPMVLPVKVYPATAFGEVQYHKTP..
PGI      891  TDREEDILP.....GLKNIDSILDEENQFSLAVHAKVLEKEGEGGDN
BP       915  DWKEAQLD.....LDKIDNMLGEPVSVSQVQIQLGEGQPD.....
CCA      974  QERNLNGILNQPKD.....IKIQG.KITVKGVKLKDIGNFRKYEIDQRVNTFLDYEP
BZ       1005  GERNTNYIWNKTVD.....LKLCDGKITVENVKLKNVGDFFIKYEYDQRVQAFLLKYEN
MOD      943  QERNKNIWNKVVD.....LQLCEGLVRIDKVKLKDIGNFRKYENDSRVKEFLTYQSD
PXI      915  AEDRALWLMIQERQ.....KQKAEHEEIAFQDLDLKNITKILTESIDARL
PSP      899  KTLTELADFGER.....FKLKEHMPDAEKGILSEIMPMSFTFEKGGK..
Alistipes 788  IPR.....KHILAFKEYLDN.....
FBR      927  YKISVPFNKLERYT.....EMIAIKNQNLKARFLIDLPLYLSKNKIKKGKDS

```

```

PBU      952  ..LATFYIEETETKVLKQGNFKALVKDRRLNGLFSFAETT.DLNLEEHPISKLSVDLELI
PGU      999  ..LATVYIEERDTKLLKQGNFKSFVKDRRLNGLFSFVDTG.GLAMEQYPISKLRVEYELA
PAU      942  ..LHTIYIEEAETKLLKQGNFKALVKDRRLNGLFSFVKTNSEAESKRNPISKLREVEYELG
PRE      960  ..LHTVYIEETGTKLLKQGNFKALVKDRRLNGLFSFVKTSSEAESKSKPISKLREVEYELG
PIN      942  NTFFTVYIEEKGTKLLKQGNFKALERDRRLGGLFSFVKTPSKAESKSNISKLREVEYELG
RAN      921  ..IRTVYIEEHTKALKMGNFKALVKDRRLNGLFSFIKEE..NDTQKHIPSQRLRRLELE
PGI      933  SLSLVPATIEIKSKRKDWKSYIRYRDRRVGLMSHFPEH.....KATLDEVKTLGL
BP       949  .....AVIKAECKLKDVSKLMRYCYDGRVKGMLPYFANH.....BATQEQVMEELR
CCA      1026  KEWMAYLPNDWKEKEKQQLPPNNVI DRQISKEYETVRSKILLKDVQELEKIIISDEIKEEH
BZ       1058  IEWQAFLLIKESKEENYP.....YVVREIEEQYKVRREELLKEVHLIEEYILEKVEYDKE
MOD      996  IVWSGYLSNEVDSN.....KLYVIERQLDNYESIRSKELLKEVQEIECIVYNQVANKE
PXI      960  RIPDTKVDITDKLPLRRYGDLRRVAKDRRLVNLASYHVHAG.....LSEIPYDLVKKELE
PSP      942  ....KYTITSEGMKLKNYGDFFVLASDKRIGNLLELVGSD.....IVSKEDIMEEFN
Alistipes 803  ...RVKQKLCEECRNVRKEDLCTCCSPRYSNLTSWLKEN.....HSESSIEREATMM
FBR      975  AGYEIIIKNDLEIEDINTINNKIINDSVKFTFVLMELEKYFILKDKCILSKNYIDNSETIP

```

```

PBU      1009  KYQTT RISIFEMTLGL EKKLITDKYSTLP..TDSFR.....NMLERWLQ..CKANRPELKN
PGU      1056  KYQTA RVCVFELTLRL EESLLTRYPHLP..DESFR.....KMLESWSDP..LLAKWPELHG
PAU      1000  EYQEA RIEIIQDMLALE EKLINIKYKDL..TNKFS.....EMLNSWLEGKDEADKARFQN
PRE      1018  AYQKA RIDIIKDMLELEKT LINDENLP..TNKFS.....DMLKSWLKGKGEANKARLQN
PIN      1002  EYQKA RIEIIKDMLELEKT LIDKYNLSD..TDNFN.....KMLTDWLELKGEPDKASFQN
RAN      977  IYQSL RVDAFKETLSLE EKLNLNKHITSLSSLENEFR.....ALLEEWKKEYAASS..MVTDE
PGI      985  EYDRC RIKIFDWAFAL EGAIMSDRDLKPYLHESSSRREGKSGEHSTLVKMLVEKKGCLTPD
BP       995  HYEDH RRRVFNWVFAL EKSVLKNEKLRRFYEES.....QGGCEHRRCIDALRKASLVSEE
CCA      1086  RHDLK QGKYNFYKYYI LNLGLLRQLKNENVENYKVF..LNTNPEKVNITGLKQEAATDLEQ
BZ       1113  ..ILK KGDNQNFYKYYI LNLGLLRQLKNEDVESYKVF..LNTNPEKVNINQLKQEAATDLEQ
MOD      1049  ..SLK QSGNENFKQYV LQGLLPRG..TDVREMLILS..TDVFKFKEEIMQLGQVR..EVEQ
PXI      1015  EYDRR RVAFFFEHVYQFE EKEVYDRYAAELRNENPKGESTYFSHWYVAVAVKHSADTHFNE
PSP      990  KYDQC RPEISSIVFNLEK WAFDTYPELSARVDREE.....KVDFKSILKILLNNKNINK
Alistipes 854  LLDVE RKLKLSFLLDERRKA IIEYGKFIP.....FSALVKECR
FBR      1035  SLKQF SKVWIKENENE IINRYRNIACHFHLPLLETDFDNLNVEQKFIKEELQNVSTINDL

```

```

PBU      1060  YV..NS LIAVRNAF SHNQYPMYDATLFAEVKKFT.....LFPSVDTKKI
PGU      1108  KV..RL LIAVRNAF SHNQYPMYDEAVFSSIRKYDP.....SSPDAIBERM
PAU      1053  DV..DF LIAVRNAF SHNQYPMHNKIEFANIKPFS.....LYTANNSEEK
PRE      1071  DV..GL LIAVRNAF SHNQYPMYNSEVFKGMKLLS.....LSSDIP..EKE
PIN      1055  DV..DL LIAVRNAF SHNQYPMNRNIAFANINPFS.....LSSANTSEEK
RAN      1031  HI..AF LIAVRNAF SHNQYPFYKEALHAPIPLFT.....VAQPTTEEKD
PGI      1045  ES..QY LILIRNKAAENQFP CAEAEMPLIYRDVSAKVGSIEGSSAKDLPEGSSLVDSLWKK
BP       1050  EY..EF LVHIRNKSAHNQFP DLEIGKLPNVTSG.....FCECIWSK
CCA      1144  KA..FV LTYIRNKFAHNQLP KKEFFWDYCQEKYK.....IEK
BZ       1169  KA..FV LTYIRNKFAHNQLP KKEFFWDYCQEKYK.....IEK
MOD      1102  DL..YS LTYIRNKFAHNQLP KKEFFDFCENNYRP.....ISD
PXI      1075  LFK.EKVMQLRNKFH HNEFFPYFDWLLPEVEKASA.....
PSP      1044  EQS.DI LRKIRNAFDENNYP DKGVVEIKALPEIA.....
Alistipes 891  LAD.AG LCGIRNDVLE DNVISYDAIGKLSAYFP.....KEASE
FBR      1095  SKPQEY LILLFILKFKHNFFY LNLFNKNESKTIKN.....DK

```

```

PBU      1102  ELNIAPQLLEIVGKAIKEIEKSENKN.....
PGU      1151  GLNIAHRLSEEVKQAKETVERIIQV.....
PAU      1095  GLGIAANQLKDKTKETTDKIKKIEKPIETKE...
PRE      1112  GLGIAKQLKDKIKETIERIIEIEKEIRN....
PIN      1097  GLGIAANQLKDKTKHTIEKIIIEKPIETKE...
RAN      1073  GLGIAEALLKVLREYCEIVKSQI.....
PGI      1103  YEMIIRKILPILDPENRFFGKLLNMSQPINDL
BP       1090  YKAIICRIIPFIDPERRFFGKLLQK.....
CCA      1179  EKTYAEYFAEVFKREKEALIK.....
BZ       1204  EKTYAEYFAEVFKREKEALIK.....
MOD      1137  NEYYAEYYMEIFRSIKEKYAS.....
PXI      1108  .ALYADRVEDVAEGYQKMRKLMRQ.....
PSP      1077  .MSIKKAFGEYAIMK.....
Alistipes 929  AVEYIIRRTKEVREQRREELMANSSQ.....
FBR      1131  EVKKNRVLQKFINQVILKKK.....

```

Figure S19. Multiple sequence alignment of Cas13b proteins from different species.

Sequence alignment of PguCas13b, PauCas13b, PreCas13b, PinCas13b, RanCas13b, PgiCas13b, BpCas13b, CcaCas13b, BzoCas13b, ModCas13b, PxiCas13b, PspCas13b, Alistipes, and Fbr was

performed using Clustal Omega, and the figure was prepared with ESPrpt (<http://esprpt.ibcp.fr>).

Related to **Figure S17b**.

Supplementary Table 1. Cas13 protein sequences used in this study.

Name	Protein sequence
RfxCas13d	MIEKKKSFAKGMGVKSTLVSGSKVYMTTFAEGSDARLEKIVEGDSIRSVNEGEAFSAE MADKNAGYKIGNAKFSHPKGYAVVANPLYTGPVQQDMLGLKETLEKRYFGESADG NDNICIQVIHNILDIEKILAEYITNAAYAVNNISGLDKDIIIGFGKFSTVYTYDEFKDPEHH RAAFNNNDKLINAIKAQYDEFDNFLDNPRLGYFGQAFFSKEGRNYIINYGNECYDILAL LSGLRHWV VHNNEEESRISRTWLYNLDKNLDNEYISTLNYLYDRITNELTNSFSKNSA ANVNYIAETLGINPAEFAEQYFRFSIMKEQKNLGFNITKLREVMLDRKDMSEIRKNHK VFDSIRTKVYTMMDFVIYRYIEEDAKVAAANKSLPDNEKSLSEKDIFVINLRGSFNDD QKDALLYDEANRIWRKLENIMHNIKEFRGNKTREYKKKDAPRLPRILPAGRDVSAFSK LMYALTMFLDGKEINDLLTTLINKFDNIQSFLKVMPLIGVNAKFVEEYAFFKDSAKIAD ELRLIKSFARMGEPIADARRAMYIDAIRILGTNLSYDELKALADTFSLDENGKLLKKGK HGMRNFIINNVISNKRHFHYLRYGDP AHLHEIAKNEAVVKFVLGRIADIQKKQGQNGK NQIDRYYETCIGKDKGKSVSEKVDALTKIITGMNYDQFDKKRSVIEDTGRENAEREKF KKIISLYLTVIYHILKNIVNINARYVIGFHCVERDAQLYKEKGYDINLKKLEEKGFSSVT KLCAGIDETAPDKRKDVEKEMAERAKESIDSLESANPKLYANYIKYSDEKKAEEFTRQ INREKAKTALNAYLRNTKWNVIREDLLRIDNKTCTLFRNKAVHLEVARYVHAYINDI AEVNSYFQLYHYIMQRIIMNERYEKSSGKVSEYFDAVNDEKKYNDRLCLKLCPFGY CIPRFKNLSIEALFDRNEAAKFDKEKKKVSGNS*
EsCas13d	MGKKIHARDLREQRKTDRTEKFADQNKKREAERAVPKKDAAVSVKSVSSVSSKKDN VTKSMAKAAGVKS VFAVGNTVYMTSFGRGNDVLEQKIVDTSHEPLNIDDPAYQLN VVTMNGYSVTGHRGETVSAVTDNPLRRFNGRKKDEPEQSVPTDMLCLKPTLEKKFFG KEFDDNIHQIYINILDEKILAVYSTNAIYALNNMSADENIENSDFFMKRTTDETFDDFE KKKESTNSREKADFDAFEKFIGNYRLAYFADAFYVNKKNPKGKAKNVLREDKELYSV LTLIGKLRHWC VHSEEGRAEFWLYKLDELKDDFKNVLDVVYNRPVEEINNRFIENNK VNIQILGSVYKNTDIAELVRSYYEFLITKKYKNMGFSIKKLRESMLEGKGYADKEYDS VRNKLYQMTDFILYTGYINEDSDRADDLVNTRLSSLKEDDKTTVYCKEADYLWKKY RESIREVADALDGDNIKKLSKSNIIEQEDKLKRCFISYADSVSEFTKLIYLLTRFLSGKEI NDLVTTLINKFDNIRSFLEIMDELGLDRTFTA EYSFFEGSTKYLAELVELNSFVKSCSFDI NAKRTMYRDALDILGIESDKTEEDIEKMIDNILQIDANGDKLKKNNGLRNFIASNVID SNRFKYL VRYGNPKKIRETAKCKPAVR FVLNEIPDAQIERYYEACCPKNTALCSANKR REKLADMIAEIKFENFSDAGNYQKANVTSRTSEAEIKRKNQAIIRLYLTVMYIMLKNLV NVNARYVIAFHCVERDTKLYAESGLEVGNIENKNTNLTMAVMGVKLENGIIKTEFDK SFAENAA NRYLRNARWYKLILDNLKKSERAVVNEFRNTVCHLNAIRNININIKEIKEVE NYFALYHYLIQKHLENRFADKKVERDTGDFISKLEEHKTYCKDFVKAYCTPFGYNLV RYKNLTIDGLFDKNYPGKDDSDSEQK*

RspCas13d	MAKKNMKPRELREAQKKARQLKAAEINNNAAPAIAAMPAAEVIAPVAEKKKSSVK AAGMKSILVSKNKMYSFSGKGN SAVLEYEVDNNDYNQTQLSSKGSSNIELRGVNEV NITFSSKHGFESGVEINTSNPTHRSGESSPVRGDMGLGLKSELEKRFFGKTFDDNIHQLIY NILDIEKILAVYVTNIVYALNNMLSIKDSESYDDFMGYLSARNTYEVFTHPKDNLSDK AKGNIKKSFSTFNDLLKTKRLGYFGLEPKTKDTRVVSQAYKKRVYHMLAIVGQIRQSV FHDKSSKLDEDLYSFIDIIDSEYRETLDYLVDERFDSINKGFIQGNKVNISLLIDMMKGY EADDIIRLYYDFIVLKSQKNLGF SIKKLREKMLDEYGFRFKDKQYDSVRSKMYKLMDF LLFCNYYRNDVVAGEALVRKLRFSMTDDEKEGIYADEASKLWGKFRNDFENIADHM NGDVIKELGKADMDFDEKILDSEKKNASDLLYFSKMIYMLTYFLDGKEINDLLTTLISK FDNIKEFLKIMKSSAVDVECELTAGYKLFNDSQRITNELFIVKNIASMRKPASSAKLTM FRDAL TILGIDDNITDDRISEILKLKEKGKGIHGLRNFITNNVIESSRFVYLIKYANAQKIR KVAKNEKVVMFVLGGIPDTQIERYYKSCVEFPDMNSSLEVKRSELARMIKNISFDDFK NVKQQA KGRENVAKERAKAVIGLYLTVMYLLVKNLVNVNARYVIAIHCLERDFGLY KEIPELASKNLKNDYRILSQTLC ELC DKSPNLF LKKNERLRKCVEVDINNADSSMTRK YRNCIAHLTVVRELKEYIGDIRTVDSYFSIYHYVMQRCITKRENDTKQEEKIKYEDDLL KNHGYTKDFVKALNSPFGYNIPRFKNLSIEQLFDRNEYLTEK*
mini- RfxCas13d	MIEKKKSFAKGMGVKSTLVSGSKVYMTTFAEGSDAFSHPKGYAVVANNPLYTGPVQ QDMLGLKETLEKRYFGESADGNDNICIQVIHNILDIEKILAEYITNAAYAVNNISGLDEG RNYIINYGNECYDILALLSGLRHWVVHNNEEESRISRTWLYNLDKNLDNEYISTLNYL YDRITNELTNSFSKNSAEQYFRFSIMKEQKNLGFNITKLREVM LDRKDMSEIRKNHKV FDSIRTKVYTMMDFVIYRYYYIEEEKDIFVINLRGSFNDDQKDALYDEANRIWRKLENI MHNIKEFRGNKTREYKKKDAPRLPRILPAGRDVSAFSKLMYALTMFLDGKEINDLLTT LINKFDNIQSFLKVMPLIGVNAKFVEEYAFFKDSAKIADELRLIKSFARMGEPIADARRA MYIDAIRILGTKLKKKGKHGMRNFIINNVISNKR FHYLR YGDP AHLHEIAKNEAVVKFV LGRIADIQKKQGQNGKNQIDRYYETCIQFDKKRSVIEDTGRENAEREKFKKIISLYLTVI YHILKNIVNINARYVIGFHCVERDAQLYKEKGYDINLKKLEEQINREKAKTALNAYLR NTKWNVIREDLLRIDNKTCTLFRNKAVHLEVARYVHAYINDINDEKKYNDRLLKLLC VPFGYCIPRFKNLSIEALFDRNEAAKFDKEKKKVSGNS*
mini- EsCas13d	MGKKSMAKAAGVKS VFAVGNTVYMTSFGRGNDRGETVSAVTDNPLRRFN GRKKDE PEQSVPTDMLCLKPTLEKKFFGKEFDDNIHQLIYNILDIEKILAVYSTNAIYALNNMSA DENIENSDFFMKRTTDETFDDYRLAYFADAFYVNKKNPKGKAKNVLREDKELYSVLT LIGKLRHWC V HSEEGRAEFWLYKLDELKDDFKNVLDVVYNRPVEEINNRFIENSYYEF LITKKYKNMGFSIKKLRESMLEGKGYADKEYDSVRNKLYQMTDFILYTGYNEDSDR ADDLVNTLRSSLKEDDKTTVYCKEADYLWKKYRESIREVADALDGDNIKKLSKSNIEI QEDKLRKCFISYADSVSEFTKLIYLLTRFLSGKEINDLVTTLINKFDNIRSFLEIMDELGL DRTFTA EYSFFEGSTKYLAELVELNSFVKSCSFDINAKRTMYRDALDILGIESDKLRNFI ASNVIDSNRFKYLVR YGNPKKIRETAKCKPAVRFVLNEIPDAQIERYYEACCPKNTALC KFENFSDAGNYQKANVTSRTSEAEIKRKNQAIIRLYLTVMYIMLKNLVNVNARYVIAF HCNRYLRNARWYKLILDNLKKSERAVVNEFRNTVCHLNAIRNININIKEIKEVETYCK DFVKAYCTPFGYNLVRYKNLTIDGLFDKNYPGKDDSD EQK*

mini-RspCas13d	MAKKSSVKAAGMKSILVSKNKMYSFSGKGN SGFESGVEINTSNP THRSGESSPVRGD MLGLKSELEKRFFGKTFDDNIHQLIYNIL DIEKILAVYVTNIVYALNNMLS IKDSESYD DFMGYLSARNTKRLGYFGLEEPKTKDTRVSQAYKKRVYHMLAIVGQIRQSVFHDKSS KLDEDLYSFIDIIDSEYRETLDYLVDERFDSINKGFIQGNYYDFIVLKSQKNLGFSIKKLR EKMLDEYGF RFKDKQYDSVRSKMYKLMDFLFCNYYRNDVVAGEALVRKLRFSMT DDEKEGIYADEASKLWGKFRNDFENIADHMNGDVIKELGKADMDFDEKILDSEKKNA SDLLYFSKMIYMLTYFLDGKEINDLLTTLISKFDNIKEFLKIMKSSAVDVECELTAGYK LFNDSQRITNELFIVKNIASMRKPASSAKLTMFRDAL TILGIDDNITIHGLRNFITNNVIES SRFVYLIKYANAQKIRKVAKNEKVVMFVLGGIPDTQIERYYKSCVEFPDMNSSFDDFK NVKQQAAGRENVAKERAKAVIGLYLTVMYLLVKNLVNVNARYVIAIHCLERDFGLY KEIIPKSPNLFLKKNERLRKCVEVDINNADSSMTRKYRNCIAHLTVVRELKEYIGDIRT VDSYTKDFVKALNSPFGYNIPRFKNLSIEQLFDRNEYLTEK*
PbuCas13b	MQKQDKLFVDRKKNAIFAFPKYITIMENKEKPEPIYYELTDKHFWA AFLNLARHNVYT TVNHINKLLEIAELKNDEDVLNIKDSWNKQAEKLDKKVRLRDLIMKYFPFLEAAAYEI TNSKSPNNKEQREKEQSEALSLNNLKNVLFIFLEKLQVLRNYYSHYKYSEFPKPIFETS LLKNMYKVFDANVRLVKRDYMHENIDMQRDFTHLNRKKQVGRTKNIIDSPNFHYH FADKEGNMTIAGLLFFVSLFLDKKDAIWMQKKLKGFKDGRNLREQMTNEVFCRSRIS LPKLKMETVQTREWMQLDMLNELIRCPKSLYERLREEDRESFKVPFDIFSDDYNAEEE PFKNTLVRHQDRFPYFVLR YFDLNEIFEQLRFQIDLGT YHFSIYNKLIGDEDEVRLTHH LYGFARIQDFAPQNQP EEWKLVKDLDHFETSQKPYISKTTPHYHLENEKIGIKFCSAH NNLFPSLQTDKTCNGRSKFNLGTQFTA EAFLSVHELLPMMFY YLLLTKDYSRKESADK VEGIIRKEISNIYAIYDAFANGEINSIADLTRRLQNTN ILQGHLPKQMISILEGRQKDMEK KAERKIGEMIDDTQRRLDSLCKQTNQKIRIGKR NAGLLKSGKIADWL VNDMMRFQPV QKDQNNIPINNSKANSTEYRMLQHALALFGSESSRLKAYFRQMNLVGNANPHPFLAET QWEHQTNILSFYRNYLEARKKYLKGLKPQNRKQYQHFLILKVQKTNRNTLVTGWKN SFNLPRGIFTQPIREWFEKHNN SKRIYDQILSFDRVGFVAKAIPLYFAE EYKDNVQPFYD YPFNIGNKLKPQKGQFLDKKERV ELWQKNKELFKNYPSEKKKTDLAYLDFLSWKKFE RELRLIKNQDIVTWLMFKELFKTTTVEGLKIGEIH LRDIDTNTANEE SNNILNRIMPMKL PVKTYETDNKGNILKERPLATFYIEETETKVLKQGNFKVLAKDRRLNGLLSFAETTDID LEKNPITKLSVDHELIKYQTTRISIFEMTLGLEKKLIDKYSTLPTDSFRNMLERWLQCKA NRPELKNYVNSLIAVRNAFSHNQYPMYDATLFAEVKKFTLFP SVDTKKIELNIAPQLLE IVGKAIKEIEKSENKN*

PspCas13b	MNIPALVENQKKYFGTYSVMAMLNAQTVLDHIQKVADIEGEQNENNENLWFHPVMS HLYNAKNGYDKQPEKTMFIERLQSYFPFLKIMAKNQREYSNGKYKQNRVEVNSNDIF EVLKRAFGVLKMYRDLTNHYKTYEEKLNDGCEFLTSTEQPLSGMINNYTVALRNM NERYGYKTEDLAFIQDKRFKFKDAYGKKKSQVNTGFFLSLQDYNGDTQKKLHLSG VGIALLICLFLDKQYISIFLSRLPIFSSYNAQSEERRIIIRSFGINSIKLPKDRIHSEKSNKSV AMDMLNEVKRCPDELFTTLSAEKQSRFRIISDDHNEVLMKRSSDRFVPLLLQYIDYGK LFDHIRFHVNMGKLRYLLKADKTCIDGQTRVRVIEQPLNGFGRLEEAETMRKQENGTF GNSGIRIRDFENMKRDDANPANYPYIVDTYTHYLENNKVEMFINDKEDSAPLLPVIED DRYVVKTIPSCRMSTLEIPAMAFHMFLLFGSKKTEKLIVDVHNRYKRLFQAMQKEEVT AENIASFGIAESDLPQKILDLSIGNAHGKDVDADFIRLTVDMLTDTERRIKRFKDDRKSI RSADNKMGRGFKQISTGKLADFLAKDIVLFQPSVNDGENKITGLNYRIMQSAIAVYD SGDDYEAKQQFKLMFEKARLIGKGTTEPHPFYKVFARSIPANAVEFYERYLIERKFYL TGLSNEIKKGNRVDVPFIRRDQNKWKTPAMKTLGRIYSEDLPVELPRQMFNEIKSHL KSLPQMEGIDFNANVTYLIAEYMKRVLDDDFQTFYQWNRNYRYMDMLKGEYDRK GSLQHCFTSVEEREGLWKERASRTERYRKQASNKIRSNRQMRNASSEIEITILDKRLSN SRNEYQKSEKVIRRYRVQDALLFLLAKKTLTELADFDGERFKLKEIMPDAEKGILSEIM PMSFTFEKGGKKYTITSEGMLKKNYGDFVFLASDKRIGNLLELVGSDIVSKEDIMEEFN KYDQCRPEISSIVFNLEKWAFDTYPELSARVDREEKVDFKSILKILLNNKNINKEQSDIL RKIRNAFDHNNYPDKGVVEIKALPEIAMSIKKAFGEYAIMK*
mini-PbuCas13b	MQKQDKLFVDRKKNAIFAFPKYITIMENKEKPEPIYYELTDKHFWA AFLNLARHNVYT TINHINRRLEQAKKLDKKVRLRDLIMKHFPFLEAAAYEMTNKEQREKEQSEALSNNL KNVLFIFLEKLQVLRNYYSHYKYSEESPKPIFETSLLKNMYKVFDANVRLVKRDYMH HENIDMQRDFTHFADKEGNMTIAGLLFFVSLFLDKCRSRISLPKLKLENVQTKDWMQL DMLNELVRCPSLYERLREKDRESFKVPFKNTLV RHQDRFPYFVLRYFDLNEIFEQLRF QIDLGTYHFSIYNKRIGDEDEVRLTHHLYGFARIQDFTAPHYHLENEKIGIKFCSAHN NLFPSLQTDKTCNGRSKFNLGTQFTA EAFLSVHELLPMMFYLLLLTKDYSRKESADKV EGIIRKEISNIILQGHLPKQMISILKGRQKDMGKEAERKIGEMIDDTQRRLDLLCKQTNQ KIRIGKRNAGLLKSGKIADWL VNDMMRFQPVQKDQNNIPINNSKANSTEYRMLQRAL ALFGSEILSFYRNYLEARKKYLKGLKPQNWKQYQHFLILKVQKTNRNTLVTGWKNSF NLPRGIFTQILSFDRVGFVAKAIPLYFAEEYKDNVQPFYDYPFNIGNRLKPKKRQFLDK KERVERLWQKNKELFKNYPSEKKKTDLAYLDFLSWKKFERELRLIKNQDIVTWLMFKE SNNILNRIMPMLKLPVKTYETDNKGNILKERPLATFYIEETETKVLKQGNFKALVKDRR LNGLFSFAISKLSVDLELIKYQTTRISIFEMTLGLEKKLIDKYSTLPTDSFRNMLERWLQ CKANRPELKNYVNSLIAVRNAFSHNQYP*

mini-PspCas13b	MENQKKYFGTYSVMAMLNAQTVLDHIQKVADIEGEQPEKTMFIERLQSYFPFLKIMA KNQREYSNGKYKQNRVEVNSNDIFEVLKRAFGVLKMYRDLTNHYKTYEEKLNDGCE FLTSTEQPLSGMINNYTVALRNMNERYGYKTEDLAFIQDKLQDYNGDTQKKLHLSG VGIALLICLFLDKGINSIKLPKDRIHSEKSNKSVAMDMLNEVKRCPDELFTTLSAEKQSR SSDRFVPLLLQYIDYGKLFDFHIRFHVNMGKLRLLKADKTCIDGQTRVRVIEQPLNGF GRLEEAYTHYLENNKVEMFINDKEDSAPLLPVIEDDRYVVKTIPSCRMSTLEIPAMAF HMFLFGSKKTEKLIVDVHNRYKRLFQAMQKEESDLPQKILDLISGNAHGKDVDADFIRL TVDDMLTDTERRIKRFKDDRKSIRSADNKMKGKRGFKQISTGKLADFLAKDIVLFQPSV NDGENKITGLNYRIMQSAIAVYDSGDDYEAKAVEFYERYLIERKFYLTGLSNEIKKGN RVDVPFIRRDQNKWKTPAMKTLGRIYSEDLPVELPRQMFDNNANVTYLIAEYMKRV LDDDFQTFYQWNRNYRYMDMLKGEYDRKGSQHCFTSVEEREGLWKERASRTERY RKQASNKIRSNRQMRNASSEIEITILDKRLSNSRNEYQKSEKVIIRYRVQDALLFLLAK DAEKGILSEIMPSFTFEKGGKKYTTITSEGMKLKNYGDFVFLASDKRIGNLLELVGSDI VSKEDIMEEFNKYDQCRPEISSIVFNLEKWAFTYPELSARVDREEKVDFKSILKILLNN KNINKEQSDILRKIRNAFDHNNYP*
REPAIRVx	MIEKKKSFAKGMGVKSTLVSGSKVYMTTFAEGSDARLEKIVEGDSIRSVNEGEAFSAE MADKNAGYKIGNAKFSHPKGYAVVANPLYTGPVQQDMLGLKETLEKRYFGESADG NDNICIQVIHNILDIEKILAEYITNAAYAVNNISGLDKDIIGFGKFSTVYTYDEFKDPHH RAAFNNNDKLINAIKAQYDEFDNFLDNPRLGYFGQAFFSKEGRNYIINYGNECYDILAL LSGLAHWVVANNEESRISRTWLYNLDKNLDNEYISTLNYLYDRITNELTNSFSKNSA ANVNIAETLGINPAEFAEQYFRFSIMKEQKNLGFNITKLREVMLDRKDMSEIRKNHK VFDSIRTKVYTMMDFVIYRYIEEDAKVAAANKSLPDNEKSLSEKDIFVINLRGSFNDD QKDALYYDEANRIWRKLENIMHNIKEFRGNKTREYKKKDAPRLPRILPAGRDVSAFSK LMYALTMFLDGKEINDLLTTLINKFDNIQSFLKVMPLIGVNAKFVEEYAFFKDSAKIAD ELRLIKSFARMGEPIADARRAMYIDAIRILGTNGSKRTADGSEFESPKKKRKVGSQLHL PQVLADAVSRLVLGKFGDLTDNFSSPHARRKVLAVVMTTGTVDKDAKVISVSTGTK CINGEYMSDRGLALNDCHAEIISRRSLLRFLYTQLELYLNNKDDQKRSIFQKSERGGFR LKENVQFHLYISTSPCGDARIFSPHEPILEEPADRHPNRKARGQLRTKIESGQGTIPVRSN ASIQTWDGVLQGERLLTMSCSDKIARWNVVGIQGSLLSIFVEPIYFSSIILGSLYHGDHL SRAMYQRISNIEDLPPLYTLNKPLLSGISNAEARQPGKAPNFSVNWTVGDSAIEVINATT GKDELGRASRLCKHALYCRWMRVHGKVPShLLRSKITKPNVYHESKLAAKEYQAAK ARLFTAFIKAGLGAWVEKPTEQDQFSLTGSKRTADGSEFESPKKKRKVGSMRNFIINN VISNKRHFHYLIRYGDPAHLHEIAKNEAVVKFVLGRIADIQKKQGQNGKNQIDRYYETCI GKDKGKSVSEKVDALTKIITGMNYDQFDKKRSVIEDTGRENAEREKFKKIISLYLTVIY HILKNIVNINARYVIGFHCVERDAQLYKEKGYDINLKKLEEKGFSSVTKLCAGIDETAP DKRKDVEKEMAERAKESIDSLESANPKLYANYIKYSDEKKAEEFTRQINREKAKTALN AYLRNTKWNVIREDLLRIDNKTCTLFANKAVALEVARYVHAYINDIAEVNSYFQLYH YIMQRIIMNERYEKSSGKVSEYFDAVNDEKKYNDRLCLKLLCVPFGYCI PRFKNLSIEAL FDRNEAAKFDKEKKKVSGNS*

mini- REPAIRV _x	MIEKKKSFAKGMGVKSTLVSGSKVYMTTFAEGSDAFSHPKGYAVVANNPPLYTGVPVQ QDMLGLKETLEKRYFGESADGNDNICIQVIHNILDIEKILAEYITNAAYAVNNISGLDEG RNYIINYGNECYDILALLSGLAHWVVANNEEESRISRTWLYNLDKNLDNEYISTLNYL YDRITNELTNSFSKNSAEQYFRFSIMKEQKNLGFNITKLREVMMLDRKDMSEIRKNHKV FDSIRTKVYTMMDFVIYRYYYIEEEKDIFVINLRGSFNDDQKDALLYDEANRIWRKLENI MHNIKEFRGNKTREYKKK DAPRLPRILPAGRDVSAFSKLMYALTMFLDGKEINDLLTT LINKFDNIQSFLKVMPLIGVNAKFVEEYAFFKDSAKIADELRLIKSFARMGEPADARRA MYIDAIRILGTGSKRTADGSEFESP KKKR KVGSQ LHPQVLADAVSRLVLGKFGDLTD NFSSPHARRKVL AGVVM TGT DVKDAKVISVSTGTKCINGEYMSDRGLALNDCHAEII SRRSLLRFLYTQLELYLNNKDDQKRSIFQKSERGGFRLKENVQFHLYISTSPCGDARIFS PHEPILEEPADRHPNRKARGQLRTKIESGQGTIPVRSNASIQTW DGV LQGERLLTMSCS DKIARWNVVGIQGSLLSIFVEPIYFSSIILGSLYHGDHLSRAMYQRISNIEDLPPLYTLNK PLLSGISNAEARQPGKAPNFSVNWTVGDSAIEVINATTGKDELGRASRLCKHALYCRW MRVHKGKVP SHLLRSKITKPNVYHESKLA AKEYQAAKARLFTAFIKAGLGAWVEKPTE QDQFSLTGSKRTADGSEFESP KKKR KVGS MRNFIINNVISNKR FHYLIRYGDPAHLHEI AKNEAVVKFVLGRIADIQKKQGQNGKNQIDRYYETCIQFDKKRSVIEDTGRENAEREK FKKIISLYLTVIYHILKNIVNINARYVIGFHCVERDAQLYKEKGYDINLKKLEEQINREK AKTALNAYLRNTKWNVIREDLLRIDNKTCTLFANKA VALEVAR YVHAYINDINDEK KYNDRLLKLLCVPFGYCI PRFKNLSIEALFDRNEAAKFDKEKKKVSGNS*
-------------------------------	---

Supplementary Table 2. Primers used in this study.

Primers for cloning Δ1, Δ2, Δ3 RfxCas13d expression plasmids

Name	Sequence
Δ1 RfxCas13d	Frament-F:gaaggcagcgacgccttcagccatcctaagggct
	Frament-R:cgtatcgtagttatctacacgacgggg
	Vector-F:gataactacgatacgggagggcctt
	Vector-R:ggcgtcgctgccttcg
Δ2 RfxCas13d	Frament-F:atctccggcctggatgagggcagaaattacatcatcaattacggcaacga
	Frament-R:cgtatcgtagttatctacacgacgggg
	Vector-F:gataactacgatacgggagggcctt
	Vector-R:atccaggccggagatattgttgac
Δ3 RfxCas13d	Frament-F:ttctccaagaactccgccgaacaatatttcagattcagc
	Frament-R:cctgtagcaatggcaacaacggtgcgc
	Vector-F:tgccattgctacaggcatcgt
	Vector-R:ggagttcttgagaaggagttggt

Primers for cloning mammalian expression plasmids

Name	Sequence
EsCas13d	Frament-F:cttaagcttgccaccatgaaaatcgaagaaggtaaaggtcacc
	Frament-R:gactcgagcggccgcttatttctgctcgctatcatctttaccgg
	Vector-F:gcggccgctcgagtc
	Vector-R:ggtggcaagcttaagtttaaacgct
RspCas13d	Frament-F:cttaagcttgccaccatgaaaatcgaagaaggtaaaggtcacc
	Frament-R:gactcgagcggccgcttattttccgtcagatattcattacgatcaaacagctgctcg
	Vector-F:gcggccgctcgagtc
	Vector-R:ggtggcaagcttaagtttaaacgct
PspCas13b	Frament-F:cttaagcttgccaccatgaacatccccg
	Frament-R:gactcgagcggccgccttcgatggcgctactcccc
	Vector-F:gcggccgctcgagtc
	Vector-R:ggtggcaagcttaagtttaaacgct

QPCR primers used in the study

STAT6 -qPCR-F	GAGGATCCAGATTTGGAAACGG
STAT6 -qPCR-R	AATGTCCACCAGGCTTTCAC
NRAS -qPCR-F	CACTGACAATCCAGCTAATCCA
NRAS -qPCR-R	TCTGCTCCCTGTAGAGGTTAATA
LMNA -qPCR-F	CTCCTTGGGCACAGAACC
LMNA -qPCR-R	TGGGCTGTCTAGGACTCAG
EGFR -qPCR-F	AAGTGTGATCCAAGCTGTCC

<i>EGFR</i> -qPCR-R	TGCTGGGCACAGATGATTT
<i>KRAS</i> -qPCR-F	GCCTTCTAGAACAGTAGACACAA
<i>KRAS</i> -qPCR-R	TCCACTCTCTGTCTTGTCTTTG
<i>MATAL1</i> -qPCR-F	AACTTGTA GACTGGAGAAGATAGG
<i>MATAL1</i> -qPCR-R	GAGATCAGCTTCCGCTAAGAT
<i>HRAS</i> -qPCR-F	GGAAGCAGGTGGTCATTGAT
<i>HRAS</i> -qPCR-R	GGAAGCAGGTGGTCATTGAT
<i>NF2</i> -qPCR-F	AAGATCTACTGCCCTCCTGA
<i>NF2</i> -qPCR-R	GGGTCGTAGTCACCATACTTG
<i>STAT1</i> -qPCR-F	GGAATCTGTCCTTCTTCCTGAC
<i>STAT1</i> -qPCR-R	GGTCCACATTGAGACCTCTTT
<i>STAT1</i> -2-qPCR-F	TCTCAATGTGGACCAGCTGAACA
<i>STAT1</i> -2-qPCR-R	GGTCCACATTGAGACCTCTTT
<i>RAF1</i> -qPCR-F	GGCTCAGGGAATGGACTATTT
<i>RAF1</i> -qPCR-R	GAGTAGACATCCGACTGGAAAC
<i>TRAF7</i> -qPCR-F	TCTGGTGGCAGCGTCTA
<i>TRAF7</i> -qPCR-R	TTGGACTCAATGTCCCACAC
<i>PPARG</i> -qPCR-F	GTCGGTTTCAGAAATGCCTTG
<i>PPARG</i> -qPCR-R	ATCTCCGCCAACAGCTTC
<i>XYL2</i> -qPCR-F	AACTTCGAGCAGGTGATTGT
<i>XYL2</i> -qPCR-R	CAATTAGGCAGCCCTCATCA
<i>RPASP58</i> -qPCR-F	CCCTGCTGATGTCAGTGTTAT
<i>RPASP58</i> -qPCR-R	GTGAAGGTTCCAGGAGTGAAG
<i>NFKB1</i> -qPCR-F	GCTACTCTGGCGCAGAAATTA
<i>NFKB1</i> -qPCR-R	CAGAGACCTCATAGTTGTCCATAAG
<i>PPIB</i> -qPCR-F	GAGATGGCACAGGAGGAAAG
<i>PPIB</i> -qPCR-R	ACTGTCGTGATGAAGAACTGG
<i>B4GALNT1</i> -qPCR-F	GACCAGCTGCTCATAGCC
<i>B4GALNT1</i> -qPCR-R	GACCAGAAGCTGCCTGAA

Primers for RNA editing

<i>COG3</i> -F	CAGATGCATAGATAGGGCAGTGTTCCAAGGA
<i>COG3</i> -R	ACCTTTGTCATGAACTCCTCCAGCTGTTC
<i>GLI2</i> -F	CAGAACTTTGATCCTTACCTC
<i>GLI2</i> -R	CCCATATCCCAGAGTATCAGTAGGTGG
<i>PPIB</i> -F	CTGCTGCCGGGACCTTCTG
<i>PPIB</i> -R	CTCCGCCCTGGATCATGAAGT

Primers for Deep sequence of RNA editing

<i>COG3</i> -F	GGAGTGAGTACGGTGTGCGGGCAGTGTTCCAAGGATTA
----------------	--

<i>COG3</i> -R	GAGTTGGATGCTGGATGGGACAGTCATAGGGTTCAGGATTT
<i>GLI2</i> -F	GGAGTGAGTACGGTGTGCAGCTAGAGTCCAGAGGTTCA
<i>GLI2</i> -R	GAGTTGGATGCTGGATGGAGAGTATCAGTAGGTGGGAAGT

Primers for *Pcsk9* mRNA knockdown

<i>Pcsk9</i> -qPCR-F	ACAGGCGAGCAAGTGTG
<i>Pcsk9</i> -qPCR-R	CTGTGCCCTTCCCTTGAC

Primers for Detecting mini-RfxCas13d expression

mini-RfxCas13d-primer1-F	CTGGCTCTACAACCTCGATAAG
mini-RfxCas13d-primer1-R	GGGCGTCCTTCTTCTTATACTC
mini-RfxCas13d-primer2-F	GGATCGCTGACATCCAGAAA
mini-RfxCas13d-primer2-R	TTGGCCTTCTCCCTGTTAATC

Supplementary Table 3. CrRNA spacer sequences for RNA knockdown experiments.

Name	Spacer sequence	DR sequence	Interference Mechanism	First figure
<i>STAT6</i>	ACACCTCTCCTGGAGTGGGGCCA	AACCCC TACCAA CTGGTC GGGGTT TGAAAC	RfxCas13d	Fig 2b
<i>NRAS</i>	GAAGGCTTCCTCTGTGTATTTGC			Fig 2b
<i>LMNA</i>	ACCGTGACACTGGAGGCAGAAGA			Fig 2b
<i>EGFR</i>	GGGGTGCAGGAGAGGAGAACTGCCAGAAAC			Fig 2b,2c
<i>KRAS</i>	CAGGCTCAGGACTTAGCAAGAAGTTATGGA			Fig 2c
<i>MATAL1</i>	CTGATCTCCAATGCTCTTCAGTA			Fig 2c
<i>HRAS</i>	GTCCGAGTCCTTCACCCGTTTGATCTGCTCC			Fig 2c
<i>NF2</i>	TAGTCACCATACTTGGCCTGGACGGCGTAA			Fig 2c
<i>STAT1</i>	GCGGAACCCAGGAATCTGTCCTT			Fig 2c
<i>STAT1-2</i>	TCTCAATGTGGACCAGCTGAACATGTTGGG			Fig 2c
<i>RAF1</i>	GGACAGCAGGATGATTGAGGATGCAATTTCG			Fig 2c
<i>TRAF7</i>	ACAGCAATGGAGTAGACGCTGCC			Fig 2c
<i>PPARG</i>	AATGCCTTGCAGTGGGGATGTCTCATAATG			Fig 2c
<i>XYL2</i>	GGAGCCGGCACTGATGAGGGCTGCCTAATT			Fig 2c
<i>RPASP58</i>	CCAGTATTCCTGGAGGATATAAC			Fig 2c
<i>NFKB1</i>	ACTTATGGACAACATGAGGTCTCTGGGGG	CACCCG TGCAAA ATTGCA GGGGTC TAAAC	EsCas13d	Fig 2c
<i>EGFR</i>	GGGGTGCAGGAGAGGAGAACTGCCAGAAAC			Fig 3e
<i>KRAS</i>	CAGGCTCAGGACTTAGCAAGAAGTTATGGA			Fig 3e
<i>MATAL1</i>	CTGATCTCCAATGCTCTTCAGTAGGGTCAT			Fig 3e
<i>PPIB</i>	CAAACCTGAAGCACTACGGGCCTGGCTGGGT			Fig 3e
<i>NRAS</i>	CTCAGCCAAGACCAGACAGGGTGTTGAAGA			Fig 3e
<i>PPARG</i>	AATGCCTTGCAGTGGGGATGTCTCATAATG	CACTGG TGCAAA TTTGCA CTAGTC TAAAC	RspCas13d	Fig 3e
<i>EGFR</i>	GGGGTGCAGGAGAGGAGAACTGCCAGAAAC			Fig 3f
<i>KRAS</i>	CAGGCTCAGGACTTAGCAAGAAGTTATGGA			Fig 3f
<i>MATAL1</i>	CTGATCTCCAATGCTCTTCAGTAGGGTCAT			Fig 3f
<i>PPIB</i>	CAAACCTGAAGCACTACGGGCCTGGCTGGGT			Fig 3f
<i>NRAS</i>	CTCAGCCAAGACCAGACAGGGTGTTGAAGA			Fig 3f
<i>PPARG</i>	AATGCCTTGCAGTGGGGATGTCTCATAATG	GTTGCA TCTGCC TTCTTT TTGAAA GGTAAA AACAAC	PbuCas13b	Fig 3f
<i>EGFR</i>	GGGGTGCAGGAGAGGAGAACTGCCAGAAAC			Fig 5e
<i>KRAS</i>	CAGGCTCAGGACTTAGCAAGAAGTTATGGA			Fig 5e
<i>MATAL1</i>	CTGATCTCCAATGCTCTTCAGTAGGGTCAT			Fig 5e
<i>PPIB</i>	CAAACCTGAAGCACTACGGGCCTGGCTGGGT			Fig 5e
<i>NRAS</i>	CTCAGCCAAGACCAGACAGGGTGTTGAAGA			Fig 5e
<i>PPARG</i>	AATGCCTTGCAGTGGGGATGTCTCATAATG			Fig 5e
<i>HRAS</i>	GGAGCAGATCAAACGGGTGAAGGACTCGGA			Fig 5e
<i>B4GALNT1</i>	TGAGCCTTCAGGCAGCTTCTGGTCAGGAGG	GTTGTG GAAGGT CCAGTT TTGAGG GGCTAT TACAAC	PspCas13b	Fig 5e
<i>EGFR</i>	GGGGTGCAGGAGAGGAGAACTGCCAGAAAC			Fig 5f
<i>KRAS</i>	CAGGCTCAGGACTTAGCAAGAAGTTATGGA			Fig 5f
<i>MATAL1</i>	CTGATCTCCAATGCTCTTCAGTAGGGTCAT			Fig 5f
<i>PPIB</i>	CAAACCTGAAGCACTACGGGCCTGGCTGGGT			Fig 5f
<i>NRAS</i>	CTCAGCCAAGACCAGACAGGGTGTTGAAGA			Fig 5f
<i>PPARG</i>	AATGCCTTGCAGTGGGGATGTCTCATAATG			Fig 5f
<i>HRAS</i>	GGAGCAGATCAAACGGGTGAAGGACTCGGA			Fig 5f
<i>B4GALNT1</i>	TGAGCCTTCAGGCAGCTTCTGGTCAGGAGG			Fig 5f

Supplementary Table 4. CrRNA sequences used in this study for RNA editing in mammalian cells.

Editing site	Spacer sequence	Mismatch distance	Editing system	First figure
<i>COG3</i>	GCTCCATTTCACTGAATTCACCATTAAGGAAATTC CCTGGACCTCAA	17/50	REPAIRV _x	Fig 6b
<i>GLI2</i>	CCCAGCATCACTGAGAATGCTGCCATGGATGCTAGAG GGCTACAGGAAGA	17/50		Fig 6b
<i>PPIB</i>	GTATTTTGACCTACGAATTGGAGATGAAGATGTAGGCC GGGTGATCTTTG	17/50		Fig 6b
<i>COG3</i>	GCTCCATTTCACTGAATTCACCATTAAGGAAATTC CCTGGACCTCAA	17/50	mini- REPAIRV _x	Fig 6b
<i>GLI2</i>	CCCAGCATCACTGAGAATGCTGCCATGGATGCTAGAG GGCTACAGGAAGA	17/50		Fig 6b
<i>PPIB</i>	GTATTTTGACCTACGAATTGGAGATGAAGATGTAGGCC GGGTGATCTTTG	17/50		Fig 6b

Supplementary Table5.CrRNA spacer sequences for *Pcsk9* knockdown experiments.

Name	Spacer sequence	Interference Mechanism	First figure
<i>Pcsk9</i> -1	CTTCAACAGCGTGCCGGAGGAGGATGGGAC	RfxCas13d	Fig S15a
<i>Pcsk9</i> -2	GCGAGCAAGTGTGACAGCCACGGCACCCAC		Fig S15a
<i>Pcsk9</i> -3	TGGCAGGTGTGGTCAGCGGCCGGGATGCTG		Fig S15a
<i>Pcsk9</i> -1	CTTCAACAGCGTGCCGGAGGAGGATGGGAC	mini-RfxCas13d	Fig S15a
<i>Pcsk9</i> -2	GCGAGCAAGTGTGACAGCCACGGCACCCAC		Fig S15a
<i>Pcsk9</i> -3	TGGCAGGTGTGGTCAGCGGCCGGGATGCTG		Fig S15a