

Supplementary Table 1. List of adRNA and gRNA antisense sequences.

Name	adRNA/gRNA antisense sequence (5' to 3')
mOTC [†]	ACAAAC <u>C</u> GAGCGGTGTCTGT
mDMD [†]	GCCATT <u>CC</u> ATTGCTCTTTCA
RAB7A (20, 6)	TGCCGC <u>C</u> AGCTGGATTTC
CCNB1 (20, 6)	CTGTAC <u>C</u> AGCCAGTCAATTA
DAXX (20, 6)	CTTCTC <u>C</u> ACAGCCCGAAGCA
CKDN2 (20, 6)	CTCCTC <u>C</u> ACCCGACCCCGGG
GAPDH (20, 6)	GGGTGC <u>C</u> AAGCAGTTGGTGG
ALDOA (20, 6)	CTTGT <u>C</u> ACCTTGATGCCCA
ARHGAP8 (20, 6)	TTCATC <u>C</u> AATGGCTGGTTAT
CKB (20, 6)	CAAGGC <u>C</u> AAGGGCTCGCCAG
KRAS (20, 6)	TCCAAC <u>C</u> ACCACAAGTTTAT
Cas13b_RAB7A	TACAGAATACTGCCGC <u>C</u> AGCTGGATTTC
Cas13b_mOTC	GAAAAGTTTTACAAAC <u>C</u> GAGCGGTGTCTGTGAGACTTTCATTACACCCA
Cas9_mDMD_1	ATAATTTCTATTATATTACA
Cas9_mDMD_2	ATTTACAGGTAAGCCGAGGTT
RAB7A (20, 10)	ATACTGCCGC <u>C</u> AGCTGGATT
RAB7A (60, 6)	TGCCGC <u>C</u> AGCTGGATTTC
RAB7A (60, 30)	TCTTGTGTCTACTGTACAGAATACTGCCGC <u>C</u> AGCTGGATTTC
RAB7A (100, 6)	TGCCGC <u>C</u> AGCTGGATTTC
RAB7A (100, 50)	TGATAAAAGGCGTACATAATTCTTGTGTCTACTGTACAGAATACTGCCGC <u>C</u> AGC
KRAS (100, 50)	TGAATTAGCTGTATCGTCAAGGCACTCTTGCCACGCCACCAGCTCCAAC <u>C</u> AC
CKB (100, 50)	ATCAAAAAATAAACTCTACCAAGGGTGACGGAAGTCTCTACAGCAAGGC <u>C</u> AA

[†]mOTC and mDMD refer to mouse mRNA targets.

Supplementary Table 2. List of primers for next generation sequencing (NGS) analyses.

Name	Sequence (5' to 3')
mDMD_NGS_F [†]	CTCTCTGTACCTTATCTTAGTGTTACTGA
mDMD_NGS_R [†]	ATTTCTGGCATATTTCTGAAGGTG
mOTC_NGS_F [†]	ACCCTTCCTTTCTTACCACACA
mOTC_spliced_NGS_R [†]	CAGGGTGTCCAGATCTGATTGTT
mOTC_unspliced_NGS_R [†]	CTTCTCTTTTAAACTAACCCATCAGAGTT
CCNB1_NGS_F	CAAGCAGTCAGACCAAATACCTACTG
CCNB1_NGS_R	TCTTAGCATGCTTCGATGTGGCATA
DAXX_NGS_F	CATCAACAAGCCAGGGCCTG
DAXX_NGS_R	GAAGAGGAAATGTCCGTCTCCAC
RAB7A_NGS_F	AGGCCTGTAAGGTGGAGGG
RAB7A_NGS_R	TGAAATAACGGCAATTTATCCATTGCACATAC
CDKN2A_NGS_F	GGGAGCAGCATGGAGCCTT
CDKN2A_NGS_R	TCCGACCGTAACTATTCGGTGC
GAPDH_NGS_F	TGGGTGTGAACCATGAGAAGTAT
GAPDH_NGS_R	TGGCATGGACTGTGGTCATG
CKB_NGS_F	CCTAACTTATTGCCTGGGCAGTG
CKB_NGS_R	GCATCAGCAGTATCTTAGCCATCAA
NGS_KRAS_F	CAGAGGCTCAGCGGCTCC
NGS_KRAS_R	TAGCTGTATCGTCAAGGCACTC
ARHGAP8_NGS_F	CACACCTGTCTGTGCACTTGTA
ARHGAP8_NGS_R	CGGTCCACAGCTCAGGAACC
ALDOA_NGS_F	ACCAGAAGGCGGATGATGGG
ALDOA_NGS_R	CTCAGACAGCCCATCCAACC
KRAS_NGS_R2	TACTACTTGCTTCCTGTAGGAATCCTC
CKB_NGS_F2	AGCCCTGCTGCTTCCTAACTT
CKB_NGS_R2	ACCCTAGTTTATTTTCAGCATCAGCAG

[†]mOTC and mDMD refer to mouse mRNA targets.

Supplementary Table 3. Tallies of RNA-seq reads from high-throughput sequencing experiments. Tallies of RNA-seq reads from high-throughput sequencing experiments. The given counts represent read mates, not read pairs, from paired end sequencing. Columns are: **sn**, sample name; **nt**, total number of raw reads after demultiplexing; **nu**, number of reads in pairs uniquely aligned to the reference genome; **nd**, number of reads in duplicated pairs; **nr**, number of remaining reads; **df**, down-sampling fraction (see **Methods**). Samples named “293T”, “293T L2”, “293T L8”, and “293T L4” were taken from the same control library but were sequenced on different lanes of the Illumina instrument.

sn	nt	nu	nd	nr	df
293T L1 (0)	108434072	86792552	21376362	65416190	0.474401
293T (1)	107737550	86652062	21362310	65289752	0.47532
MCP-ADAR1 DD-NES -adRNA (2)	75469304	57715184	11907804	45807380	0.677479
MCP-ADAR1 DD-NES +adRNA (3)	76113978	55714058	11591434	44122624	0.703347
MCP-ADAR1 DD-NLS -adRNA (4)	96485146	79023222	17911404	61111818	0.507815
MCP-ADAR1 DD-NLS +adRNA (5)	70684382	56425658	8656076	47769582	0.64965
MCP-ADAR1 DD (E1008Q)-NES -adRNA (6)	73073334	54369950	10484274	43885676	0.707145
MCP-ADAR1 DD (E1008Q)-NES +adRNA (7)	95946852	71154174	18408668	52745506	0.588363
MCP-ADAR1 DD (E1008Q)-NLS -adRNA (8)	54654264	43441234	6314734	37126500	0.835886
MCP-ADAR1 DD (E1008Q)-NLS +adRNA (9)	78346400	59725272	11074654	48650618	0.637886
MCP-ADAR2 DD-NES -adRNA (10)	89534306	74166552	14629650	59536902	0.521249
MCP-ADAR2 DD-NES +adRNA (11)	80859886	66904932	12911706	53993226	0.574767
MCP-ADAR2 DD (E488Q)-NES -adRNA (12)	79769278	65570598	11792520	53778078	0.577066
MCP-ADAR2 DD (E488Q)-NES +adRNA (13)	98084994	80214200	20639602	59574598	0.520919
MCP-ADAR2 DD-NLS -adRNA (14)	75862216	60748320	14040780	46707540	0.664422
MCP-ADAR2 DD-NLS +adRNA (15)	80473694	66106146	12359830	53746316	0.577407
MCP-ADAR2 DD (E488Q)-NLS -adRNA (16)	48576248	40372732	6032488	34340244	0.903707
MCP-ADAR2 DD (E488Q)-NLS +adRNA (17)	72617598	58732422	12388120	46344302	0.66963
293T L8 (18)	68191034	54705760	10254952	44450808	0.698154
293T+GFP (19)	88146982	64109834	15072908	49036926	0.63286
ADAR2 -adRNA (20)	86641852	69462198	18251916	51210282	0.606002
ADAR2 +adRNA (21)	74048950	59010378	16071512	42938866	0.722737
ADAR2 (E488Q) -adRNA (22)	81927154	65842936	16273572	49569364	0.626063
ADAR2 (E488Q) +adRNA (23)	74616248	56997066	17856714	39140352	0.792878
Cas13b-ADAR2 DD (E488Q) -gRNA (24)	72072754	54678392	12500074	42178318	0.73577
Cas13b-ADAR2 DD (E488Q) +gRNA (25)	116274658	91188024	29488244	61699780	0.502976
293T L4 (26)	70234868	56894104	11595590	45298514	0.685089
MS2 adRNA (27)	78457766	51176442	19161354	32015088	0.969341
GluR2 adRNA (28)	65855024	41791326	10757802	31033524	1
gRNA (29)	89132098	59288978	19226242	40062736	0.774623
min	48576248	40372732	6032488	31033524	0.474401
max	116274658	91188024	29488244	65416190	1
total	2588377968	2005961258	481864884	1524096374	21.68535

Supplementary Table 4. Results of A->G editing yield quantification from aligned RNA-seq reads. Results of A->G editing yield quantification from aligned RNA-seq reads. Columns are: sample name; total sites, the total number of reference sites with a significant change in A->G editing yield in at least one comparison between treatment and control sample; changed sites, the number of reference A-sites found to have a significant change in A->G editing yield when comparing the treatment to the control sample, which is the first sample in **Supplementary Table 3**; on-target editing yield, the editing yield observed at the intended target A-site within the RAB7A mRNA; median editing yield, the median yield at all sites considered except the target site.

Sample name	Total sites	Changed sites	On-target editing yield	Median editing yield
293T L2	382978	0	0	
293T + GFP	382978	6	0	0.295913155
gRNA	382978	32	0.013333333	0.142102619
Cas13b-ADAR2 DD (E488Q) - gRNA	382978	112853	0.025316456	0.105263158
Cas13b-ADAR2 DD (E488Q) + gRNA	382978	49432	0.11637931	0.092205807
GluR2 adRNA	382978	23	0	0.144542773
ADAR2 - adRNA	382978	5769	0	0.157894737
ADAR2 + adRNA	382978	18573	0.27638191	0.14
ADAR2 (E488Q) - adRNA	382978	25732	0	0.131578947
ADAR2 (E488Q) + adRNA	382978	125409	0.268398268	0.150943396
MS2 adRNA	382978	19	0.006666667	0.169230769
MCP-ADAR1 DD-NLS - adRNA	382978	20481	0.006849315	0.079069767
MCP-ADAR1 DD-NLS + adRNA	382978	28537	0.159763314	0.084745763
MCP-ADAR1 DD (E1008Q)-NLS - adRNA	382978	90182	0	0.112
MCP-ADAR1 DD (E1008Q)-NLS + adRNA	382978	110565	0.261627907	0.118081181
MCP-ADAR1 DD-NES - adRNA	382978	116165	0.017142857	0.097222222
MCP-ADAR1 DD-NES + adRNA	382978	101183	0.366459627	0.096618357
MCP-ADAR1 DD (E1008Q)-NES - adRNA	382978	226634	0.010416667	0.123076923
MCP-ADAR1 DD (E1008Q)-NES + adRNA	382978	195533	0.418604651	0.12244898
MCP-ADAR2 DD-NLS - adRNA	382978	3760	0.006756757	0.056173674
MCP-ADAR2 DD-NLS + adRNA	382978	4740	0.07	0.076555024
MCP-ADAR2 DD (E488Q)-NLS - adRNA	382978	28028	0.014778325	0.095238095
MCP-ADAR2 DD (E488Q)-NLS + adRNA	382978	38087	0.113122172	0.098591549
MCP-ADAR2 DD-NES - adRNA	382978	9489	0.021276596	0.09375
MCP-ADAR2 DD-NES + adRNA	382978	20249	0.416216216	0.102564103
MCP-ADAR2 DD (E488Q)-NES - adRNA	382978	35287	0.004672897	0.09929078
MCP-ADAR2 DD (E488Q)-NES + adRNA	382978	42715	0.278350515	0.101351351