

Supplementary Table 1. Sequence similarity between top-ranked off-targets (TMX3 and AAGAB) and the target site in β -actin (ACTB) reveals sequence similarity as the cause of guideRNA-dependent off-target editing.

mRNA	sequence bound by gRNA ^a
ACTB	5'-GGGAGGUGAU AG CAUUGCU-3'
TMX3	5'- A GGAGGUGAU AG CAUU UUG -3'
AAGAB	5'- CC AGG U UGAU AG CAUU UG -3'

^a edited adenosines are highlighted in bold and not matching nucleotides in red.

Supplementary Table 2. Comparison SNAP-ADAR and dCas13b-ADAR system (Cox et al. Science 2017)

	SNAP-ADAR (SA) system	dCas13b-ADAR system
Targeting System	SNAP-tag – gRNA covalent bond SNAP-tag: human, < 200 aa gRNA: ca. 22 nt, chemically stabilized	guideRNA / dCAS13b RNP assembly ^{a)} Cas13: bacterial >1000 aa gRNA: ~85 nt, genetically encoded
Deaminase tested	4 enzymes fully tested: ADAR1 and ADAR2 each wildtype and E488Q	1 enzyme strongly tested: ADAR2 E488Q (REPAIRv1) 1 enzyme briefly tested: ADAR2 E488Q/T375G (REPAIRv2)
Delivery	SNAP-ADAR: single genomic copy, inducible gRNA: lipofection of chemically stabilized gRNA (22 nt)	dCas-ADAR: massive overexpression via plasmid lipofection guideRNA: massive overexpression via plasmid lipofection
Editing of endogenous targets	ACTB, GAPDH, GUSB, SA, KRAS, STAT1	KRAS and PPIB
Concurrent editing	3 sites or 4 endogenous house keeping transcripts, no loss in efficiency 2 sites or 2 endogenous signaling transcripts (KRAS, STAT1), no loss in efficiency	Nothing shown
Editing range for the best editable codon (UAG) on endogenous targets	wild-type SA: 15 - 90%, (12 sites on 6 targets, ORF & UTRs) SAQ variants: 46 - 90%, (13 sites on 6 targets, ORF & UTRs)	REPAIRv2: 7-25%, (5 sites on 2 targets, only ORF) REPAIRv1: 15-40%, (5 sites on 2 targets, only ORF)
Codon scope	all 16 codons tested on an endogenous target with SA1Q and SA2Q	all 16 codons tested, but on an overexpressed reporter transcript with overexpressed Cas-ADAR. The co-overexpression together with the low editing yields suggest that the shallow codon specificity observed could be an overexpression artefact. Codon scope was only tested for REPAIRv1, not for version 2
Applications in the manuscript	Manipulation of signaling transcripts, KRAS and STAT1, recoding of phosphorylation switch Tyr701 in STAT1	Manipulation of the signaling transcript KRAS, but not at a phosphorylation site. The claimed editing of 34 “ <i>release-relevant transcripts</i> ” (Figure 4) is somewhat misleading. ^{b)}
Editing duration	stable over several days	Nothing shown
Off-targets in gRNA/substrate duplex	the guideRNA/mRNA duplex is small (19 bp), chemical modification of guideRNA blocks off-target editing almost entirely even in A-rich codons	General: the guideRNA/mRNA duplex is large (50 bp) REPAIRv1: massive problem, several sites, high yields REPAIRv2: better, but present, too little data is shown yet
Global off-target editing	Wild-type SA: almost absent SAQ variants: moderate (~1000 sites, might be further decreased by lowering SAQ expression)	REPAIRv2: almost absent (but the 125x coverage/deep sequencing analysis (Figure 6D) was done with 15fold less Cas13-ADAR plasmid (10 ng instead of 150 ng) than used in the relevant editing reactions on KRAS and PPIB (Figure 6F & Figure 5). It is unclear if KRAS/PPIB editing would be effective with 15fold less CAS13-ADAR plasmid. ^{c)} REPAIRv1: extremely high (>18 000 sites, even though 15fold less Cas13-ADAR was transfected then in almost all other experiments)
Unique property	1) Chemically stabilized guideRNAs enable perfect specificity inside gRNA/mRNA duplex 2) low expression of editase enables high editing yields with reduced global off-target editing	1) Fashionable there are at least two other RNA editing systems that apply encodable guideRNAs which encounter the same specificity problems as Cas13-ADAR does (local off-target editing in the guideRNA/mRNA duplex, global off-target editing due to

	2) clearly proven, covalent RNA targeting 3) very short guideRNA/mRNA duplex, unlikely to interfere with endogenous ADARs or translation 4) simple co-transfection of guideRNAs enables concurrent editing	overexpression, in particular with hyperactive ADAR deaminases, low editing yields with wildtype or less active ADAR domains like version2)
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a) It remains to be determined to which extent the RNA-targeting via the 35 nt DR-helix in the Cas13-guideRNAs and dCas13b interaction contributes to Cas13-ADAR editing, in particular under overexpression conditions on reporter constructs. From previous control experiments we know that under overexpression conditions editing can be obtained even in absence of any RNA targeting mechanism by self-targeting of the ADAR, in particular for long RNA duplexes (like >30 bp). When carefully reading the Cox et al. paper, the evidence is lacking that the dCAS13/guideRNA RNP assembly is strictly required for editing; the respective important control for this (Figure S8 in the Cox et al. paper) is flawed: it shows that overexpression of the ADAR2 deaminase lacking Cas13 doesn't give editing, but the guideRNA is missing too. There is also no proof that the ADAR deaminase domain they express is giving stable, catalytically functional protein. On one hand, they claim that the free-floating deaminase is giving rise to off-target editing. On the other hand, their control ADAR deaminase alone (ADAR2DD) gives much less off-targets compared to REPAIRv1 (Figure S8, C) indicating that the truncation is less functional per se. The proper control would have been to mutate the guideRNA (at the DR domain or leave the DR domain away). We tested the Cas13 guideRNAs and found them similarly active (editing yields around 25%) when overexpressing them together with either wildtype ADAR2 or SNAP-ADAR2Q, independent of the DR domain (see Supplementary Figure 11, and further Supplementary Notes 1 and 2 below). This shows that any overexpressed highly active ADAR fusion can edit 50 bp guideRNA/mRNA duplexes independent of a targeting mechanism to similar yields under the conditions reported by Cox et al. (their Figure 2-4).

b) Cox et al. suggest that 34 disease-relevant editings have been achieved (Figure 4E). This is somewhat misleading, in particular the suggestive Figure 4G that pretends that the data from the codon screen can be transferred to thousands of clinical variants. As the 34 disease-relevant transcripts are only small pieces of cDNA (ca. 200 bp) that have been overexpressed within a reporter cassette it is unlikely that one will be able to edit the respective real transcripts with the suggested editing yields in a relevant cell with the current Cas-ADAR versions (in particular version2) and the current delivery methods. It is also unclear if any of the mutations (all selected for simple-to-edit 5'-UAG codons) is really relevant for human disease (incidence, penetrance), and what editing yield might be required for therapy. Anyway, only hyperactive, off-target-prone REPAIRv1 has been used, the more precise REPAIRv2, which has a lower editing activity (similar or lower than wildtype ADAR2, see Supplementary Fig. 10), has not been characterized in this respect. Similar experiments with disease-relevant, and overexpressed cDNAs like CFTR, and PINK1 have anyway already been described before by others, however, additionally including a relevant phenotypic change.

c) Cox et al. use very high amounts of plasmids (150 ng/96 well Cas-ADAR, 300 ng/96 well guideRNA plasmid) for the editings. However, for the deep sequencing analysis they transfect only 10 ng/96 well Cas-ADAR plasmid (if understood correctly from their manuscript). One can expect that 15fold less plasmid will strongly reduce the transfection efficiency, thus the background of many untransfected cells will clearly reduce global off-target editing, while editing on a co-transfected reporter transcript (Cluc) is less affected by lowering Cas-ADAR (Cox et al. Fig S15). Nevertheless, one can expect that editing of an endogenous target (like KRAS, PPIB) will strongly suffer if less cells are transfected. If we understand the paper correctly, the editing on endogenous targets was not shown with low plasmid transfection. For the SNAP-ADAR system, however, we can much better and more homogeneously control the enzyme expression levels (by doxycycline induction) and we did show to what extent the reduction of SNAP-ADAR does change the editing at endogenous targets and at selected off-targets (see our Supplementary Figure 9).

Supplementary Table 3. Comparison SNAP-ADAR and 4λN-DD / BoxB system (Vallecillo-Viejo et al. RNA Biol 2018 & Sinnamon et al. PNAS 2017)^{a)}

	SNAP-ADAR (SA) system	4λN-DD / BoxB system
Targeting System	SNAP-tag – gRNA covalent bond SNAP-tag: human, < 200 aa gRNA: ca. 22 nt, chemically stabilized	λN / BoxB RNA peptide interaction λN (typically 4 copies): bacteriophage, ca. 100 aa optional 3x NLS: ca. 30 aa gRNA: ~84 nt, genetically encoded
Deaminase tested	4 enzymes fully tested: ADAR1 and ADAR2 each wildtype and E488Q	several versions, all based on ADAR2 deaminase domain, either wt or E488Q in combination with 1-4 copies λN peptide, with and without NLS 4 copies λN increase efficiency; 3xNLS can reduce off-target editing by ca. 50%
Delivery	SNAP-ADAR: single genomic copy, inducible gRNA: lipofection of chemically stabilized gRNA (22 nt)	Enzyme: currently massive overexpression via plasmid lipofection (or AAV) guideRNA: massive overexpression via plasmid lipofection (or AAV)
Editing of endogenous targets	ACTB, GAPDH, GUSB, SA, KRAS, STAT1	This system has mainly been characterized with reporter constructs, in particular GFP and CFTR; to my knowledge only a single example of an endogenous target has been described (MeCP2); the targeting of endogenous transcripts has not yet been tested systematically
Concurrent editing	3 sites or 4 endogenous housekeeping transcripts, no loss in efficiency 2 sites or 2 endogenous signaling transcripts (KRAS, STAT1), no loss in efficiency	Not shown; it is unclear if several different guideRNAs can ever be co-expressed as very high amounts of U6-guideRNA plasmids are currently used already for a single target (like 4- 15fold more than the editase plasmid)
Editing range for the best editable codon (UAG) on endogenous targets	wild-type SA: 15 - 90%, (12 sites on 6 targets, ORF & UTRs) SAQ variants: 46 - 90%, (13 sites on 6 targets, ORF & UTRs)	With the E488Q variant editing levels of 70-80% have been observed on reporter transcripts GFP and CFTR; with the wildtype enzyme editing levels typically stay below (more like 40-60%); so far only a few preferred codons have been targeted, mostly UAG and mostly in reporter transcripts
Codon scope	all 16 codons tested on an endogenous target with SA1Q and SA2Q	There is no systematic test on the full codon scope published
Applications in the manuscript	Manipulation of signaling transcripts, KRAS and STAT1, recoding of phosphorylation switch Tyr701 in STAT1	The system has been explored for the repair of CFTR (cDNA) and endogenous MeCP2
Editing duration	stable over several days	Nothing shown yet
Off-targets in gRNA/substrate duplex	the guideRNA/mRNA duplex is small (19 bp), chemical modification of guideRNA blocks off- target editing almost entirely even in A-rich codons	General: the guideRNA/mRNA duplex is large (50 bp, twice interrupted by the two 17 nt BoxB hairpins) The system suffers from major off-target editing inside the gRNA/mRNA duplex (e.g. PNAS 2017), even though endogenous MeCP2 was repaired in primary cells to ca. 75% yield, this came along with 5 off-target editings in the duplex (10-50% yield). The system also elicits strong guideRNA dependent off-target editing in the target transcript but outside the gRNA/mRNA duplex due to a proximity effect; e.g. RNA Biol 2018, depending on the enzyme 5-14 off-target editings (10-55%) have been found along the CFTR transcript

Global off-target editing	Wild-type SA: almost absent SAQ variants: moderate (≈ 1000 sites, decreased by lowering SAQ expression)	The E488Q version of Vallecillo-Viejo et al. was also tested by Cox et al. (Supporting Figure S9 in their paper) and showed massive global off-editing at rates very similar to Cas13-ADAR repairV1. We performed a re-analysis of Vallecillo-Viejo et al.'s NGS analysis with our pipeline (see Supplementary Figure 8). The wildtype enzymes elicit several hundred-fold more off-target edits compared to the wt SA. The wt Vallecillo-Viejo et al. enzymes are even more off-target-prone than our hyperactive SA1Q/SA2Q mutants. The hyperactive Vallecillo-Viejo et al. enzymes seem extremely off-target-prone.
Unique property	<ol style="list-style-type: none"> 1) Chemically stabilized guideRNAs enable proper specificity inside gRNA/mRNA duplex 2) low expression of editase enables high editing yields with reduced global off-target editing 2) clearly proven, covalent RNA targeting 3) very short guideRNA/mRNA duplex, unlikely to interfere with endogenous ADARs or translation 4) simple co-transfection of guideRNAs enables concurrent editing 	<ol style="list-style-type: none"> 1) the system is fully genetically encoded 2) the entire system (editase + 6 copies guideRNA) has been delivered as a single AAV

a) This system has already undergone several rounds of refinement. We focused on the results reported in the two most recent papers.

Supplementary Table 4. Sequences of gRNAs applied in this study. BG-conjugated gRNAs were synthesized and PAGE-purified from commercially acquired oligonucleotides containing a 5'-amino-C6 linker (BioSpring, Germany) as described by Hanswillemenke et al. (*J. Am. Chem. Soc.* **2015**, *137*, 15875-15881). Nucleotides highlighted in bold are unmodified and are placed opposite the triplet with the target adenosine in the middle. Nucleotides highlighted in italic are modified with 2'-O-methylation, those highlighted in red are 2'-fluorinated nucleotides. The backbone contains terminal phosphorothioate linkages as indicated by "s". The first three nucleotides at the 5'-end are not complementary to the mRNA substrate, but serve as linker sequence between gRNA and SNAP-tag.

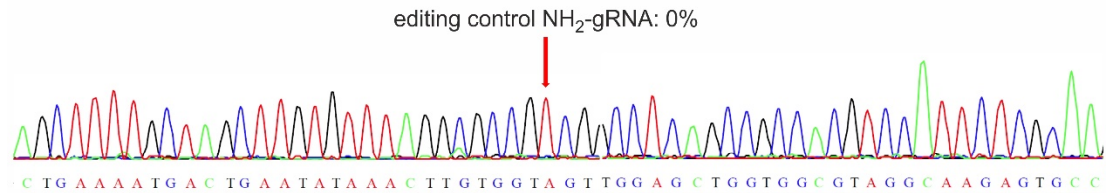
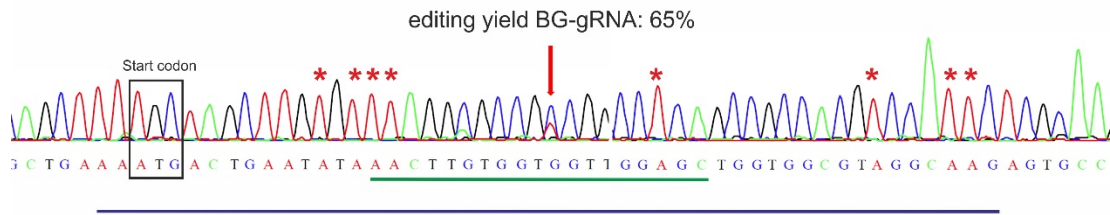
target	gRNA sequence	applied gRNA amount ^{a)}
editing of various endogenous transcripts		
5'-UTR SNAP-ADAR	5'-UsCsAUUAAACG CCA GAGUCsCsGsGsA-3'	5 pmol
5'-UTR GAPDH isoform 2	5'-UsCsUGAAUAAU CCA GGAAAsAsGsCsA-3'	5 pmol
ORF #1 GAPDH	5'-UsAsUAGGGGUG CCA AGCAGsUsUsGsG-3'	5 pmol
ORF #2 GAPDH ^{b)}	5'-UsAsUGGUUUUU CCA GACGGsCsAsGsG-3'	5 pmol
ORF #1 GUSB	5'-GsGsUGCAGAUU CCA GGUGGsGsAsCsG-3'	5 pmol
ORF #2 GUSB	5'-AsCsAGACUUGG CCA CUGAGsUsGsGsG-3'	5 pmol
3'-UTR SNAP-ADAR	5'-UsAsUGUGUCGG CCA CGGAAAsCsAsGsG-3'	5 pmol
3'-UTR GAPDH ^{c)}	5'-AsAsUAAGGGGU CCA CAUGGsCsAsA-3'	5 pmol
3'-UTR ACTB	5'-UsCsGAGCAAUG CCA UACCsUsCsCsC-3'	5 pmol
3'-UTR GUSB	5'-UsAsUUUCCUG CCA GAAUsGsAsUsG-3'	5 pmol
KRAS target A/1	5'-GsAsUGCUCCAA CCA CCACAsAsGsUsU-3'	SA1: 40 pmol , SA1Q: 10 pmol
KRAS target 2	5'-CsGsUCUCUUGC CCA CGCCAsCsCsAsG-3'	20 pmol
STAT1 Y701	5'-GsUsCUCUUGAU ACA UCCAGsUsUsCsC-3'	20 pmol
editing of all 16 adenosine-containing triplets in GAPDH isoform 1		
5'-GAA	5'-CsAsCAUGGGAU UCC CAUUGsAsUsGsA-3'	5 pmol
5'-GAU	5'-UsAsUCGACCAA ACC CGUUGsAsCsUsC-3'	5 pmol
5'-GAC	5'-CsAsCGUCAUGA GCC CUUCCsAsCsGsA-3'	5 pmol
5'-GAG	5'-AsAsCGAGGGAU CCC GCUCCsUsGsGsA-3'	5 pmol
5'-CAA	5'-GsAsAGAGGCUG UCG UCAUAsCsUsUsC-3'	5 pmol
5'-CAU	5'-CsAsAGAGGUCA ACG AAGGsGsUsCsA-3'	5 pmol
5'-CAC	5'-AsAsCGCCAGGG GCG CUAAGsCsAsGsU-3'	5 pmol
5'-CAG	5'-UsAsCGCAUGGA CCG UGGUCsAsUsGsA-3'	5 pmol
5'-AAA	5'-UsAsCAUGACCC UCU UGGCUsCsCsCsC-3'	5 pmol
5'-AAU	5'-GsAsCUAGCCAA ACU CGUUGsUsCsAsU-3'	5 pmol
5'-AAC	5'-AsGsUCGCCACA GCU UCCCCGsGsAsGsG-3'	5 pmol
5'-AAG	5'-UsGsUAUAUCCA CCU UACCAAsGsAsGsU-3'	5 pmol
5'-UAA	5'-AsGsGAGGGGUC UCA CUCCUsUsGsGsA-3'	5 pmol
5'-UAU	5'-CsUsAGGCAACA ACA UCCACsUsUsUsA-3'	5 pmol
5'-UAC	5'-CsCsGAGCGCCA GCA GAGGCsAsGsGsG-3'	5 pmol
5'-UAG	5'-UsAsUGGUUUUU CCA GACGGsCsAsGsG-3'	5 pmol
avoiding off-target editing of neighboring adenosine		
5'-CAA methoxy	5'-GsAsAGAGGCUGU CG UCAUAsCsUsUsC-3'	5 pmol
5'-CAA fluoro	5'-GsAsAGAGGCUGU CG UCAUAsCsUsUsC-3'	5 pmol
5'-AAA methoxy	5'-UsAsCAUGACCCU CU UGGCUsCsCsCsC-3'	5 pmol
5'-AAA fluoro	5'-UsAsCAUGACCCU CU UGGCUsCsCsCsC-3'	5 pmol
5'-AAC methoxy	5'-AsGsUCGCCACA GC UCCCCGsGsAsGsG-3'	5 pmol
5'-AAC fluoro	5'-AsGsUCGCCACA GC UCCCCGsGsAsGsG-3'	5 pmol
5'-UAA methoxy	5'-AsGsGAGGGGUCU CA CUCCUsUsGsGsA-3'	5 pmol
5'-UAA fluoro	5'-AsGsGAGGGGUCU CA CUCCUsUsGsGsA-3'	5 pmol

- The indicated gRNA amounts were used for single and concurrent editings.
- This gRNA was additionally applied to test the dose dependency of RNA editing (Fig. 1c)
- This gRNA was additionally applied to test the time dependency of RNA editing (Fig. 1b)

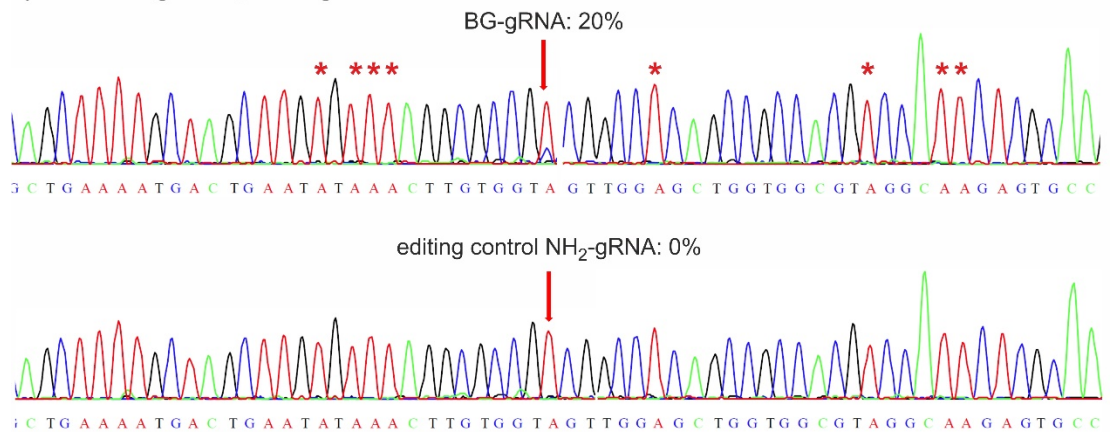
Editing of two sites in endogenous KRAS as previously reported by Cox et al. with Cas13b-ADAR

a) KRAS Target 1/A, editing with SA1Q

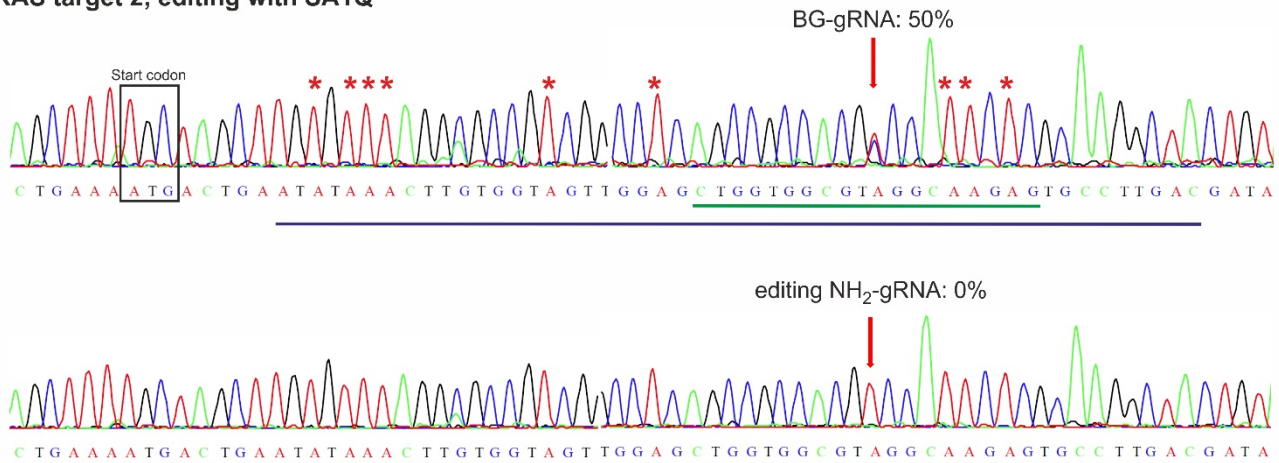
mRNA/gRNA duplex of the BG guideRNA (19 bp)
mRNA/gRNA duplex of the Cas13 guideRNA (50 bp)
* off-target sites for Cas13-ADAR



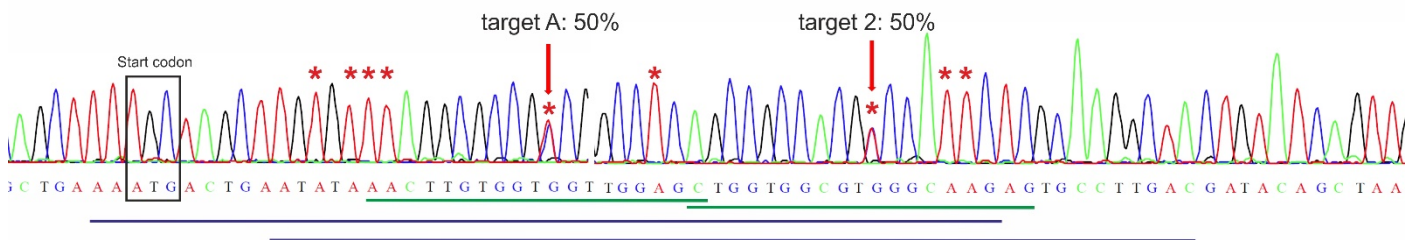
b) KRAS Target 1/A, editing with wt SA1



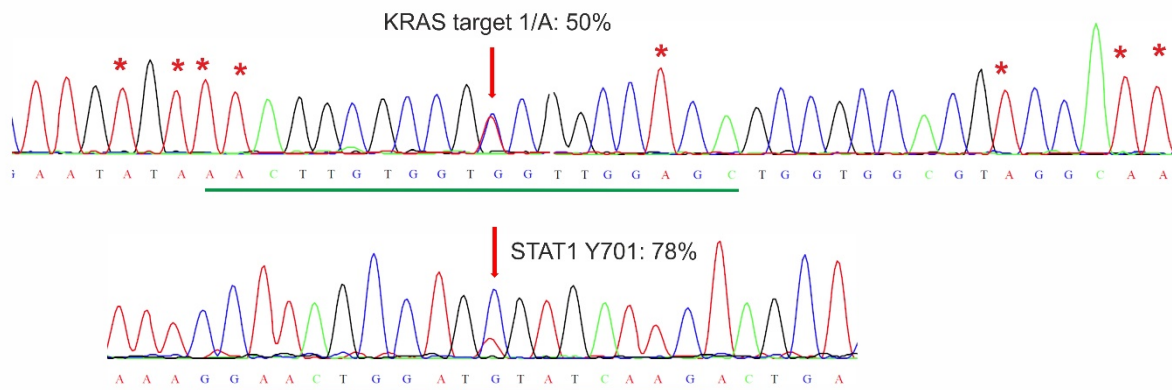
c) KRAS target 2, editing with SA1Q



d) KRAS concurrent editing target1/A and target 2 with SA1Q / BG-guideRNAs



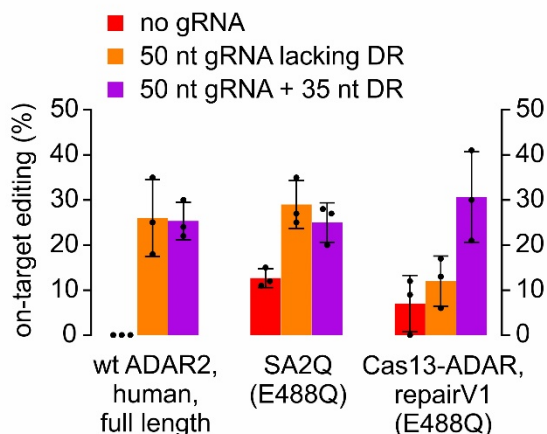
e) Concurrent editing KRAS target 1/A and STAT1 Tyr701 with SA1Q



Supplementary Note 1. Editing of KRAS target #1, #2, and STAT1 with SNAP-ADARs. Editing of KRAS target #1/A gives very high yields with SA1Q and absolutely no off-target editing at the sites reported for Cas13b-ADAR (*). Note also the large mRNA/gRNA duplexes applied for Cas13b-ADAR guideRNAs (50 bp, blue lines) versus the short ones applied for SNAP-ADAR (green lines). For target #1/A, the long Cas13 guideRNA even overlaps with the translation start site (boxed ATG) of the KRAS transcript (translation inhibition?). Also note the strong dependency of the SNAP-ADAR on the targeting mechanism. The same guideRNA lacking the BG modification (NH₂-guideRNA) cannot form the covalent bond with the deaminase and is incapable of editing the target at all (a-c). Panel a), the editing yield is significantly larger (50-65%) compared to off-target prone Cas13b-ADAR version 1 (ca. 25%). The precise wildtype SA1 edits target #1/A better than the precise Cas13-ADAR version 2 (20% versus ca. 12%). Target #2 (panel c) is also better edited by SA1Q than Cas13b version 1 (50% compared to 32%). Finally, we show efficient concurrent editing of KRAS site #1 + site #2, with yields of 50% both (d). And we show concurrent editing of KRAS site #1 with the most important phosphorylation site of STAT1 (Y701) with very good yields (50% and 78%, panel e). a-e) N=3 independent experiments were performed with similar results.

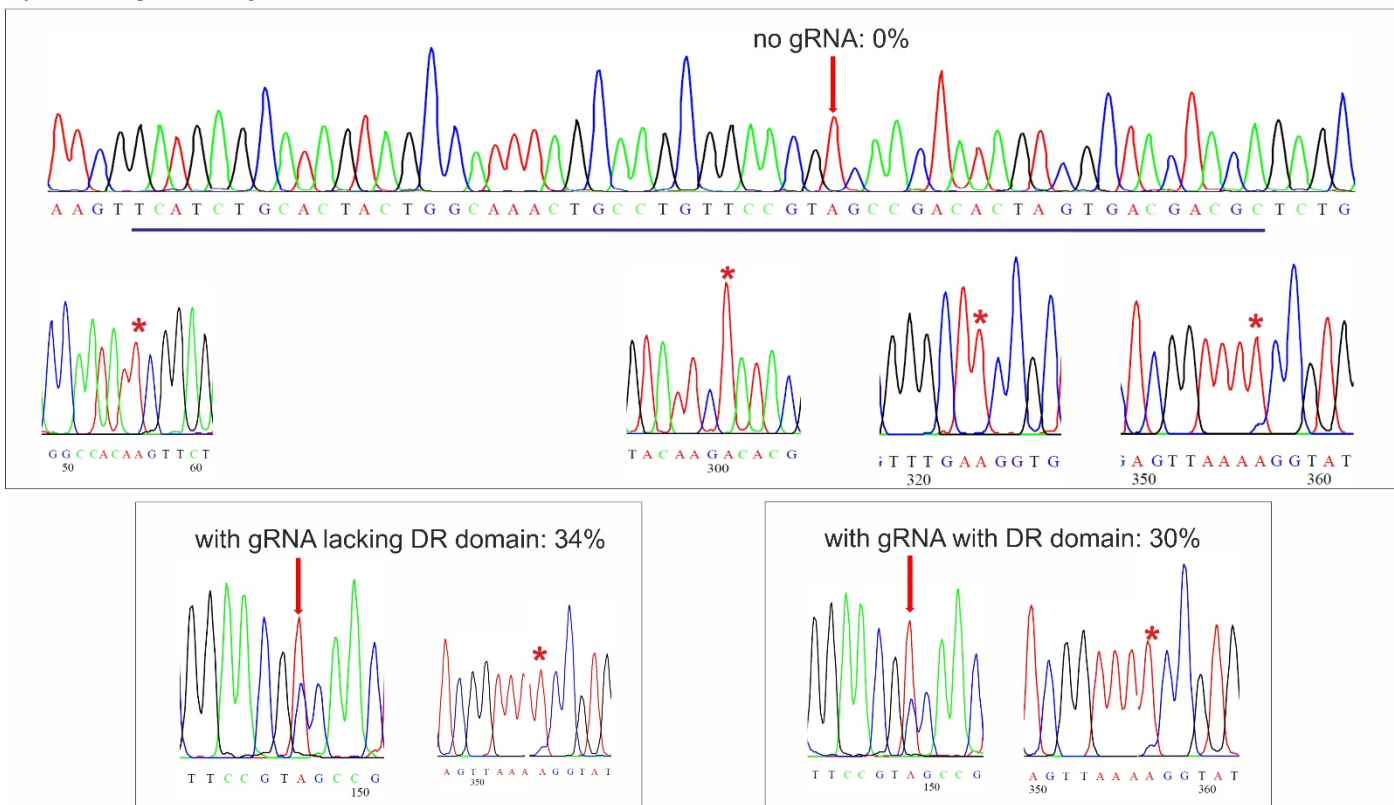
Editing of overexpressed GFP reporter W58X with co-overexpressed Cas13-guideRNAs and co-overexpressed, different ADAR fusions (SA2Q, human full length ADAR2, and Cas13-ADAR version1) following exactly the protocol given by Cox et al.

a) Overview of n=3 experiments

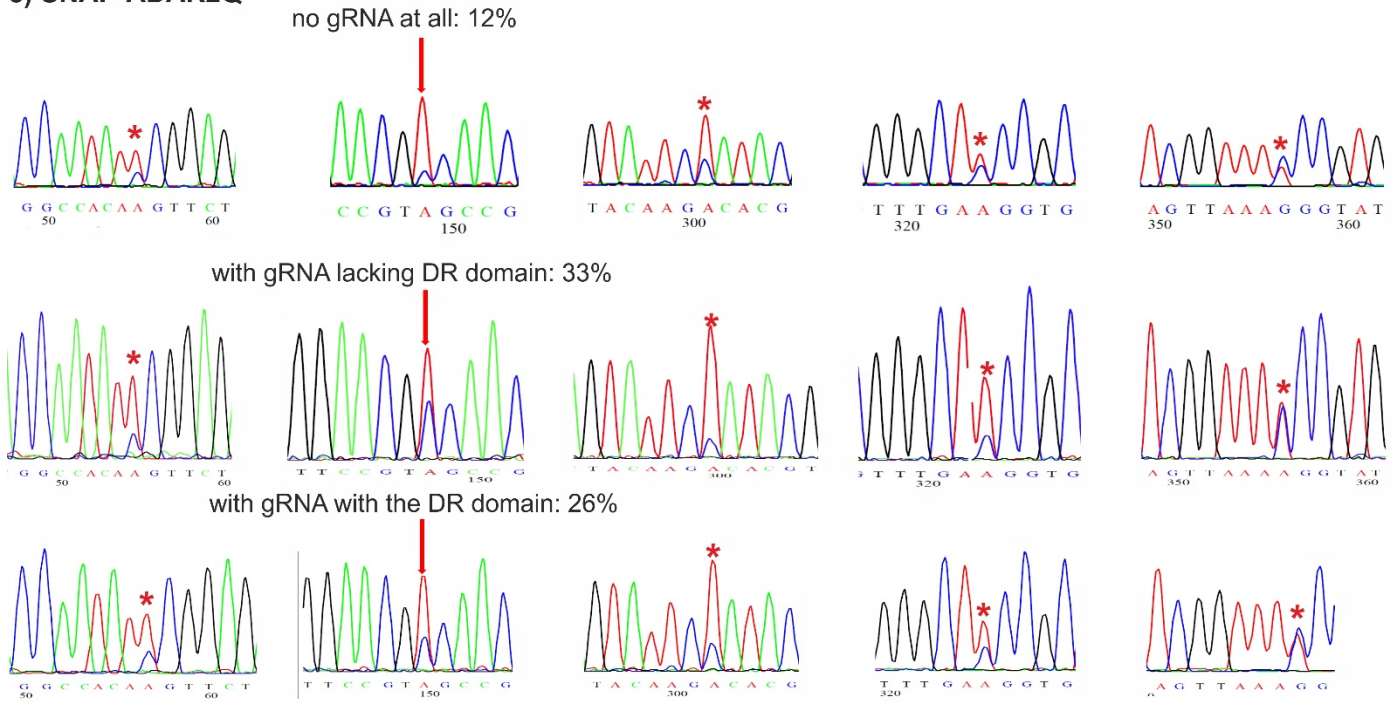


Selected Sanger sequencing traces (selected was always the trace with the highest on-target yield out of 3 experiments)

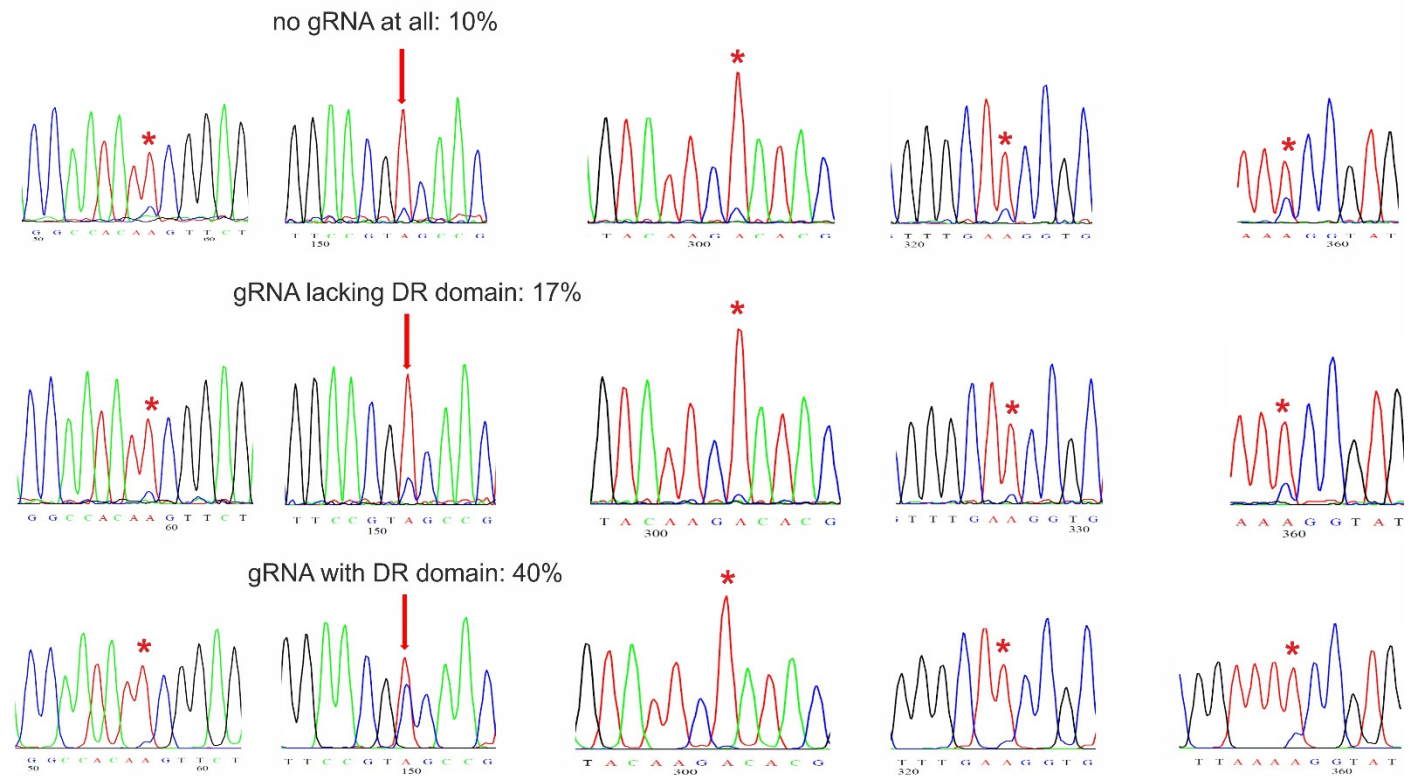
b) full length wildtype human ADAR2



c) SNAP-ADAR2Q



d) Cas-ADAR13, repairV1



Supplementary Note 2. Lacking specificity of overexpressed Cas13-guideRNAs. Cox et al. repeatedly claim a unique Cas-dependent targeting mechanism which is the reason for the claimed higher effectiveness of “repair” compared to other editing systems, the reason for the lacking codon preference they find, and the reason for the lack of a PFS dependency. However, all those claims are built on co-overexpression experiments of Cas-ADAR together with a guideRNA and reporter constructs. Here, we show that the Cas13-guideRNAs, they apply, are able to elicit editing with ADAR2 but also with SNAP-ADAR2Q in yields comparable to Cas-ADAR repair1, demonstrating that the applied guideRNAs under the applied conditions are not specific for Cas-ADAR and that many of the findings, in particular under overexpression / reporter conditions could be partly flawed by self-targeting of the deaminase (domain) itself. Unfortunately, Cox et al.

did not properly address this question in their paper (e.g. control experiments with guideRNAs lacking the DR domain are completely missing).

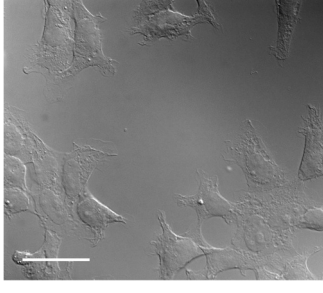
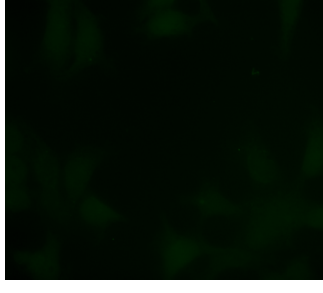
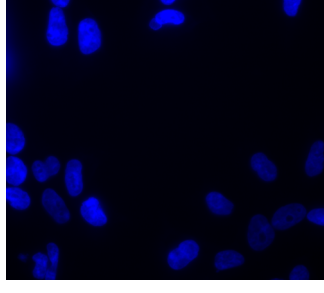
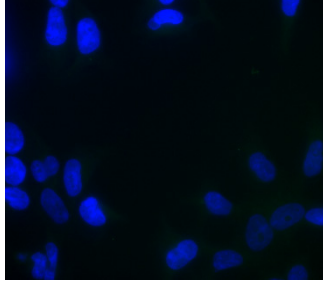
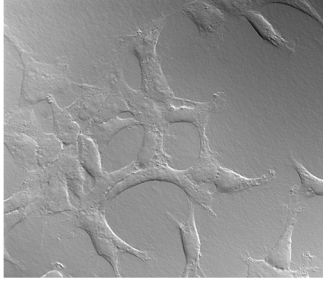
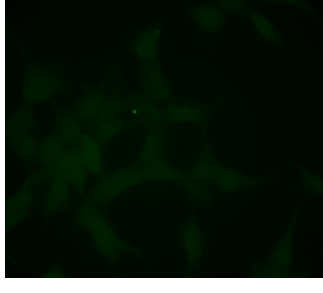
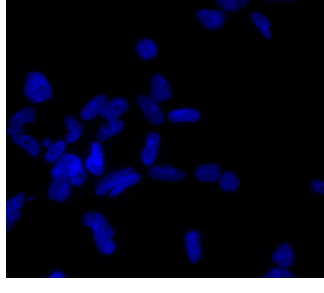
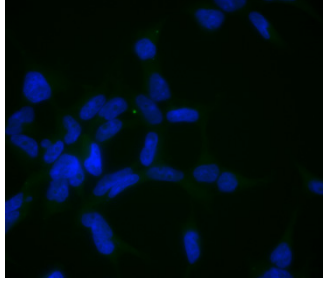
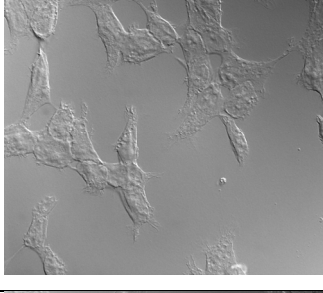

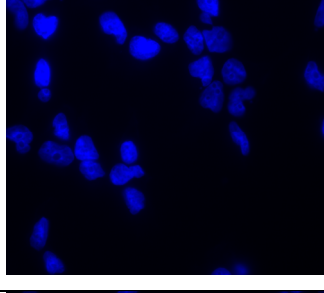
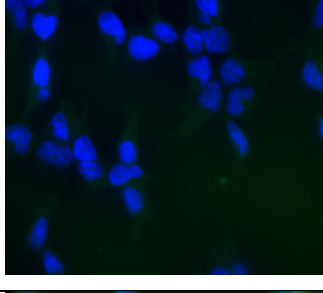
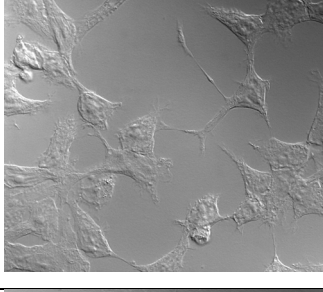
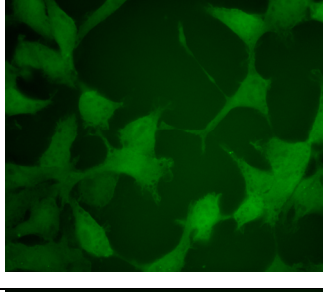
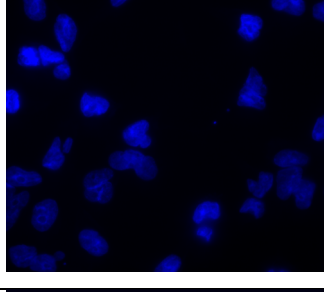
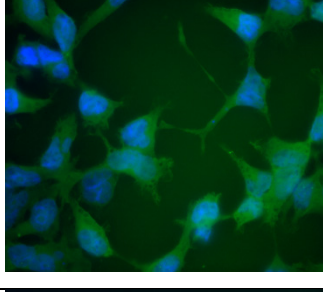
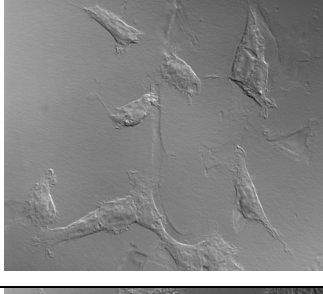
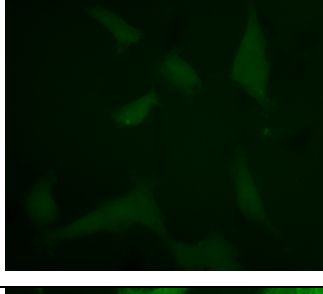
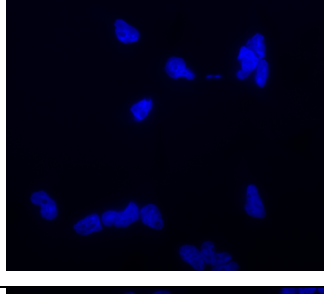
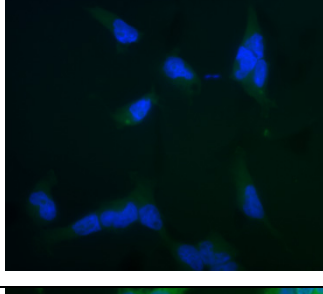
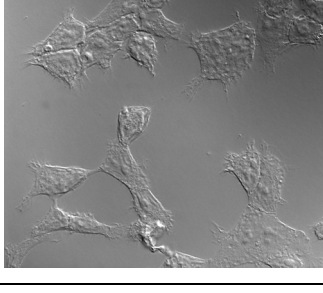
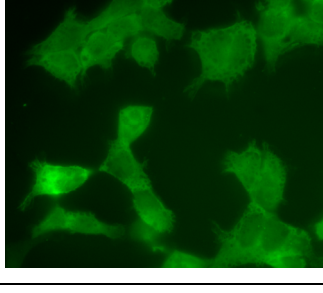
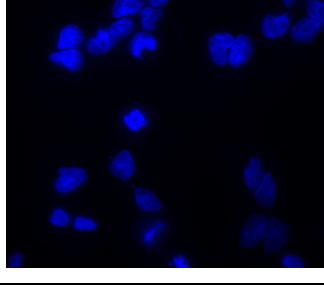
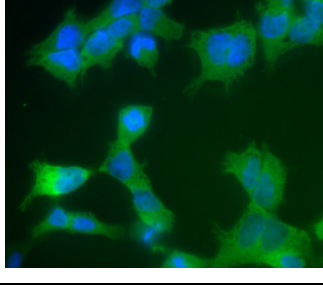
For this, we designed a Cas13 guideRNA according to Cox et al. containing a 50 nt part antisense to our GFP reporter (W58amber), putting the targeted A into mismatch with C. Mismatch position was 34. We constructed guideRNAs with the 3'-terminal DR hairpin for Cas-targeting but also lacking the DR motif (the DR motif is a 34 nt hairpin that has the function to recruit Cas13). The guideRNAs were expressed from a U6 promotor (pSilencer plasmid), as applied by Cox et al. Co-transfection was carried out as described by Cox et al.: 150 ng editing enzyme, 300 ng guideRNA vector, 40 ng GFP reporter plasmid in a coated 96 well into 293T cells. As enzymes, we co-transfected either full length human ADAR2 (wildtype), or the respective hyperactive SNAP-ADAR2Q, or Cas13-ADAR repairV1 (containing the same mutated deaminase domain of ADAR2 E488Q as SA2Q). guideRNA (antisense part: capital letters; DR domain: small letters):GCGTCACTAGTGTCGGCCACGGAACAGGCAGTTTGCCAGTAGTGAGtggtggaaggtccagtttgaggggctattacaac. In panel b), the position and length of the gRNA is indicated as a blue line under the sequence, the on-target site is marked by a red arrow, main off-target sites are marked by red asterisks.

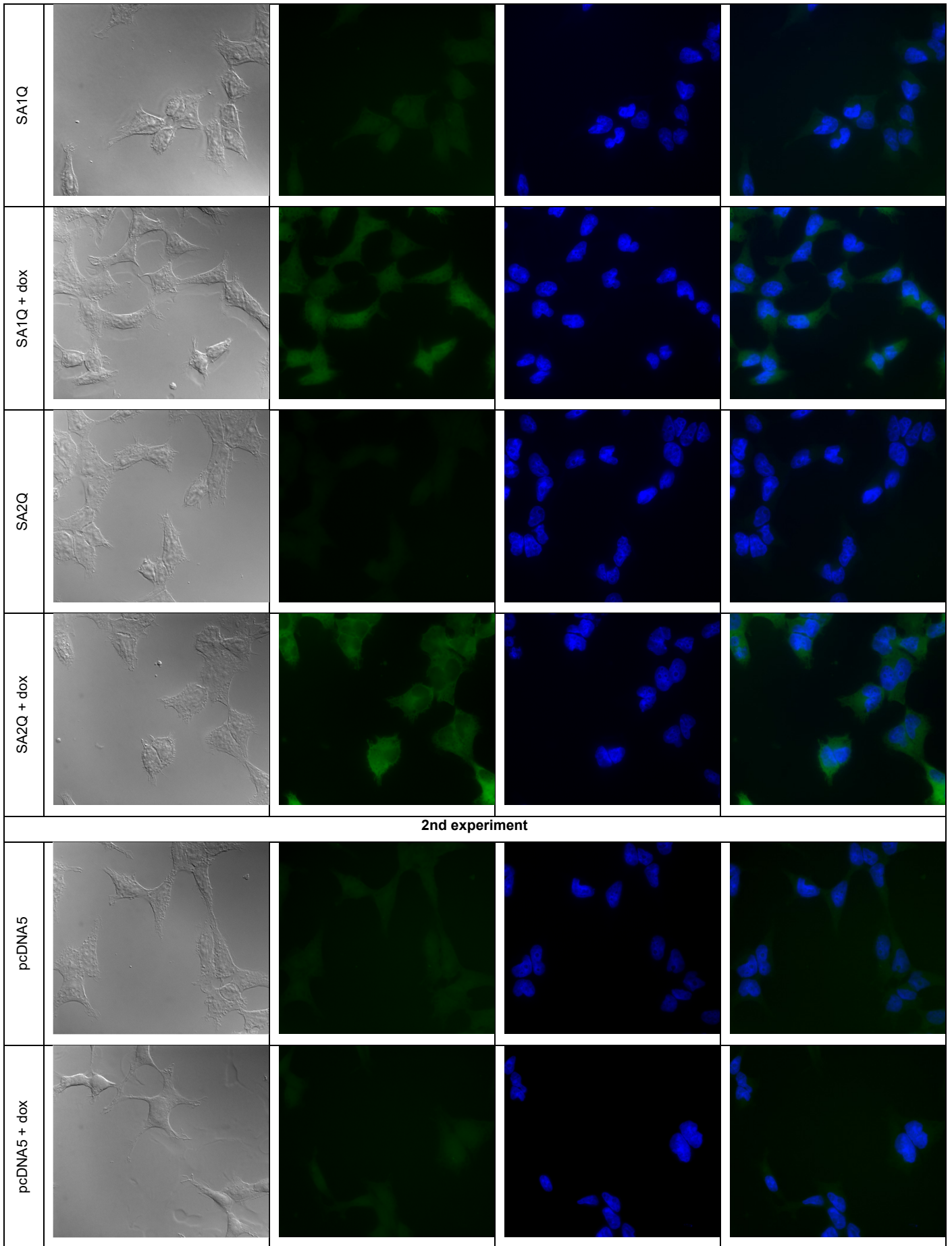
a) shows that the Cas13-guideRNA can also recruit human ADAR2 or SNAP-ADAR2Q to elicit editing yields similar to Cas13-ADAR. The average editing levels (25-30%) are very similar to those described by Cox et al. for various similar overexpression / reporter experiments in their Figures 2-4 (15-30%). As expected the recruitment of ADAR2 and SNAP-ADAR2Q is independent of the DR motif. In contrast, we have shown in the past that short chemically stabilized (BG)-guideRNAs (as we apply) are unable to recruit ADAR2 (see NAR 2016, gkw911, Figure S9A); and as we have shown repeatedly in our manuscript that SNAP-ADARs are only recruited by short chemically stabilized guideRNAs when the BG moiety is present, clearly demonstrating the SNAP-tag-dependent targeting mechanism. The editing control with Cas13-ADAR shows several interesting things. First, editing is to some extent depending on the DR motif, but second, editing also occurs without a guideRNA and also with a guideRNA lacking the DR motif, even though with reduced editing yields; this indicates that the editing yields reported by Cox et al. are composed of an unknown Cas-dependent and an unknown Cas-independent (self-targeting) part, probably differing for each respective target and condition; third, the editing yield with Cas13-ADAR with the ideal guideRNA (30%) was not notably better than that with other deaminases (25-30%); d) the off-target editing of Cas13-ADAR was higher than that of ADAR2 but lower than that of SA2Q. Finally, we want to mention that editing yields are strongly varying under co-overexpression conditions as seen in the error bars of N=3 independent experiments (Data are shown with the mean±SD, black dots represent individual data points). This is in agreement with our earlier experience.

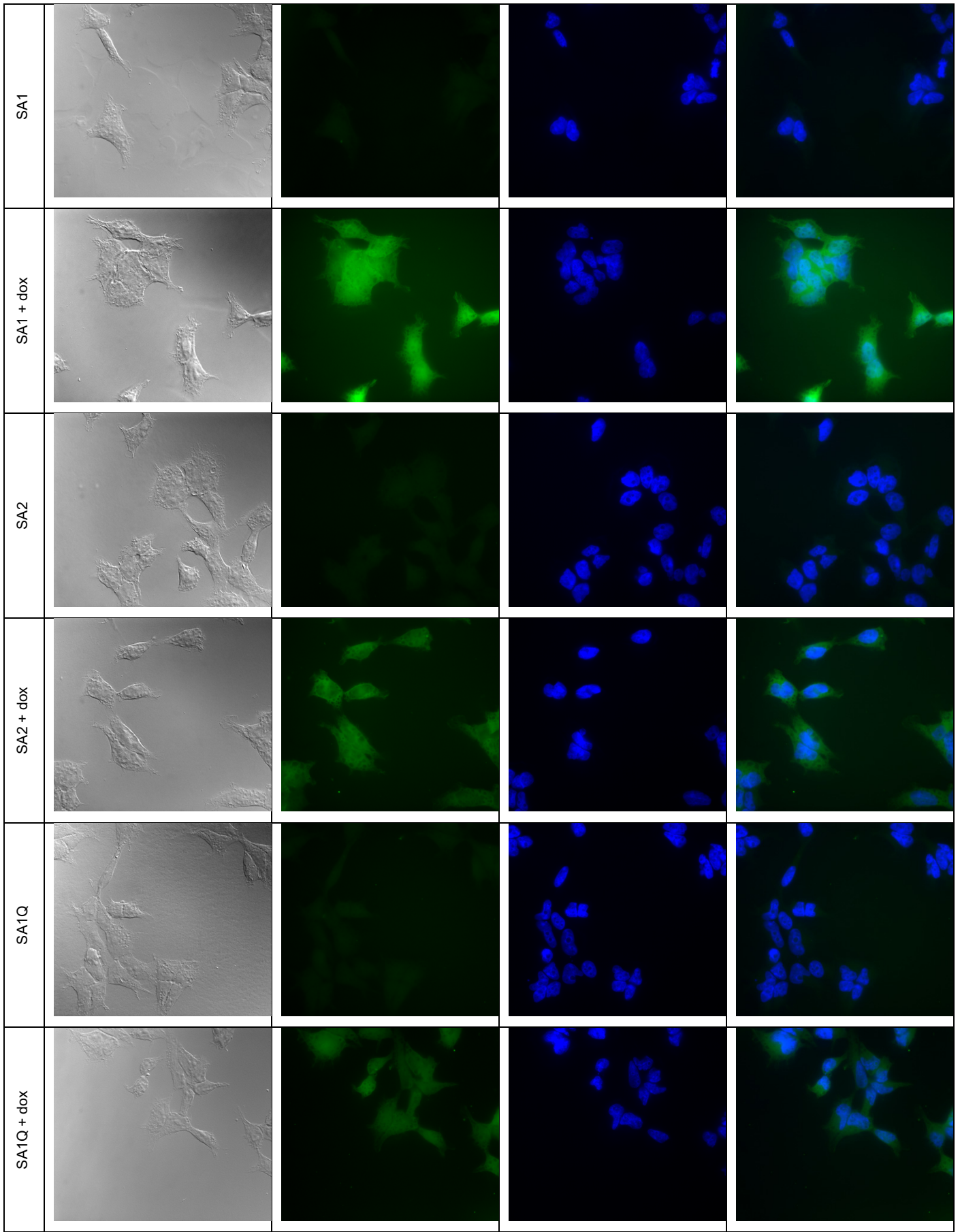
b-d) show selected Sanger sequencing traces (always the trace with the highest on-target editing yield was chosen) to give an idea of off-target editing. While ADAR2 (**b**) gives decent on-target editing (25%) there was only very little off-target editing seen and on-target editing was fully dependent on the presence of the guideRNA, even though not on the DR motif in the guideRNA. The respective single off-target editing site was described before by us (NAR 2017). Co-transfection with hyperactive SA2Q (**c**) largely shows the misery of overexpressing hyperactive deaminases (like Cas13-ADAR repairV1 too): even in absence of the guideRNA, there is massive off-target editing all over the transcript (only few sites are picked here). On-target editing was achieved with 10% yield if though no gRNA was transfected. With the Cas13-guideRNA, on-target editing increased to 25%, independent of the DR-motif. With respect to off-target editing, the experiment with Cas13-ADAR overexpression (**d**) shows results similar to the overexpression of SA2Q, which contains the same ADAR deaminase mutant (E488Q). Off-target editing is found all over the transcript, on-target editing is already found prior to the expression of the guideRNA. However, such off-target yields are roughly half that strong as found for SA1Q, which might be due to lower expression levels. After adding the guideRNA, editing levels increase and there is a targeting effect, however, there is also a notable increase in editing yield with the guideRNA lacking the DR domain. N=3 independent experiments were performed with similar results.

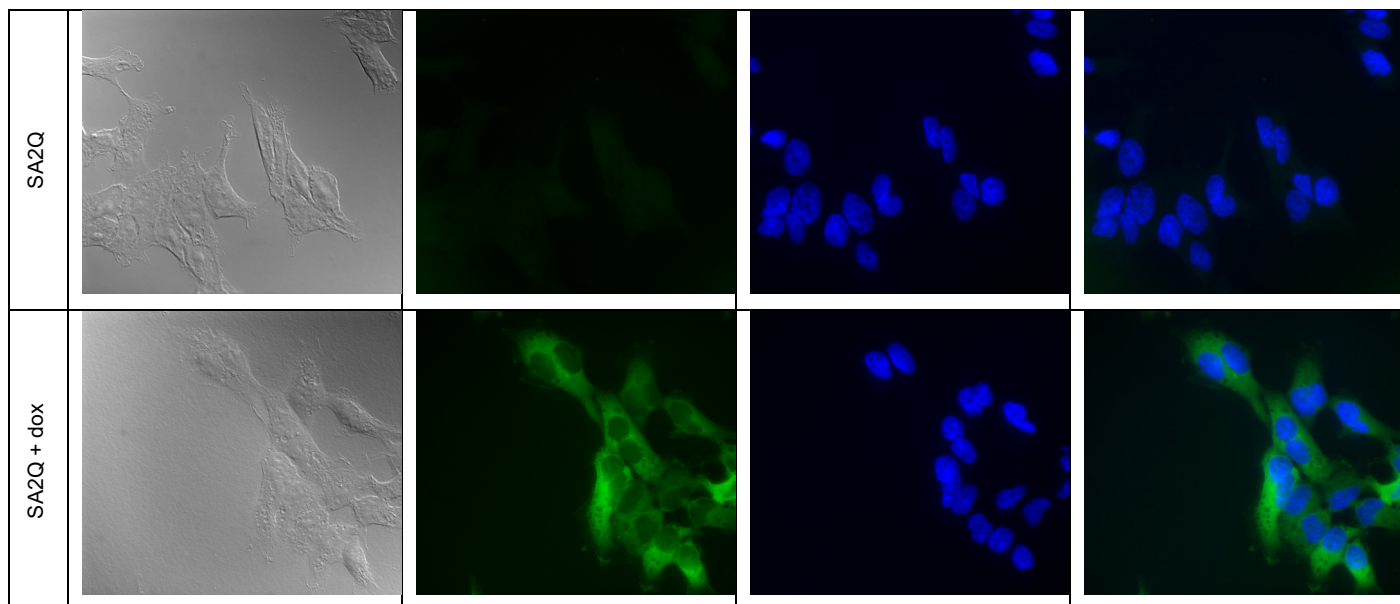
Together, panels **a-d**) suggest that the conditions (overexpression & reporters) under which Cas13-ADAR has mostly been characterized today are not sufficient to support the general claims made by Cox et al.

Determination of intracellular SNAP-ADAR localization by fluorescence microscopy

	DIC (63×)	FITC (F)	Hoechst (H)	F + H
1st experiment				
pcDNA5				
pcDNA5 + dox				
SA1				
SA1 + dox				
SA2				
SA2 + dox				



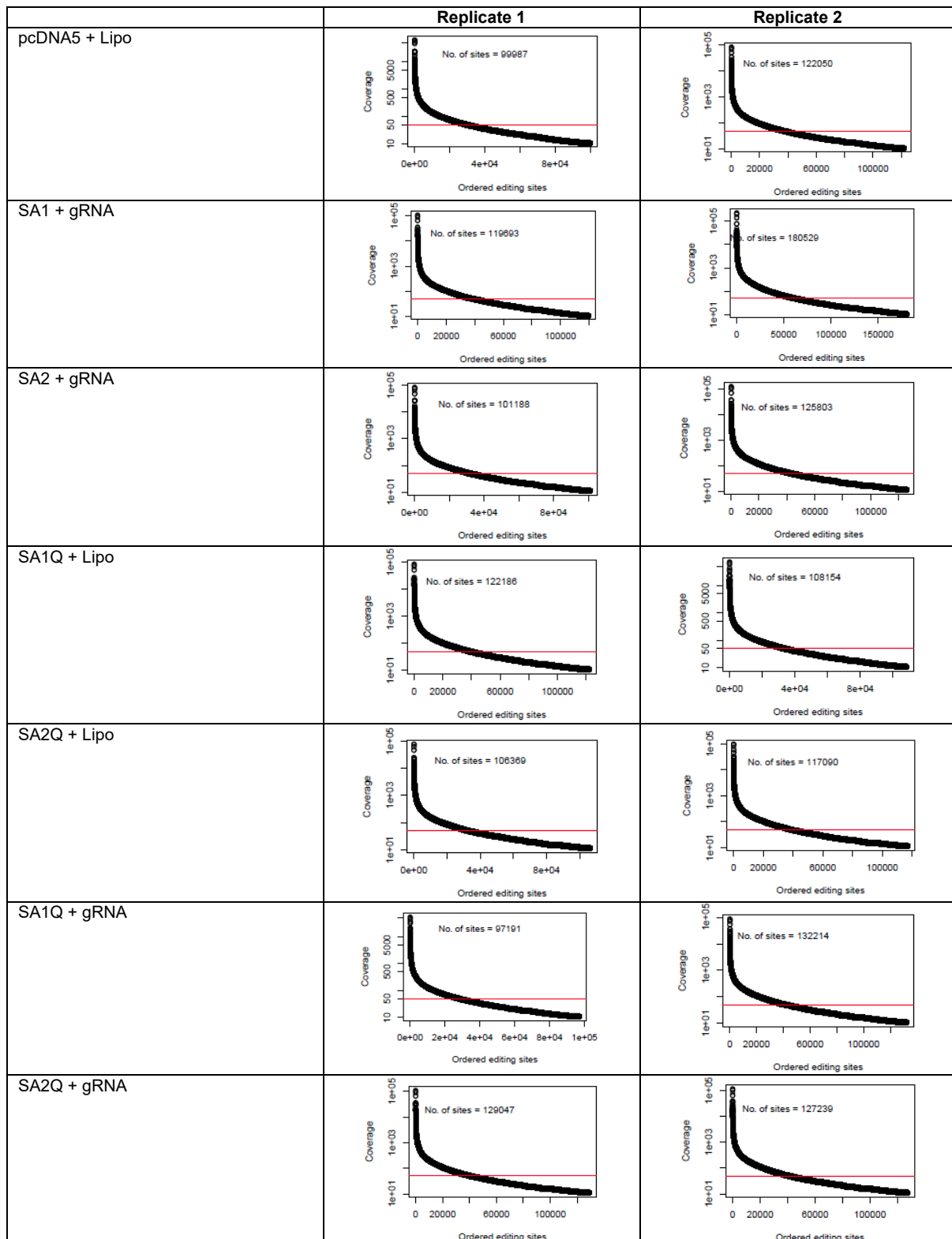




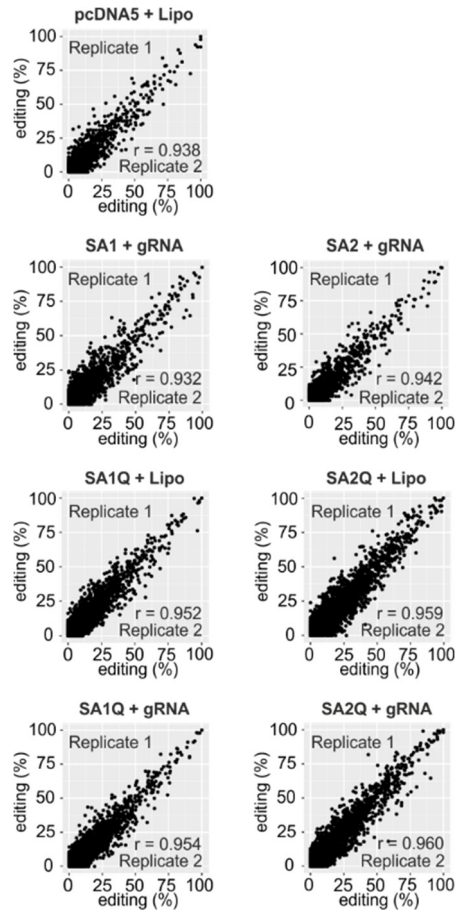
Supplementary Note 3. Protein expression was induced by doxycycline (dox) for 24 h. Cells were incubated with BG-FITC to stain SNAP-ADARs (green) and with Hoechst 33342 to stain nuclei (blue). Microscopy was performed with a Zeiss CellObserverZ1 under 630x total magnification. The scale bar represents 40 μm . FITC-BG/SNAP-tag labeling was done as described before (Vogel et al., ACS Synth. Biol. 2017, doi: 10.1021/acssynbio.7b00113). N=3 independent experiments were performed with similar results.

Appendix (NGS quality data, SNAP-ADAR gene sequences, target sites on endogenous transcripts)

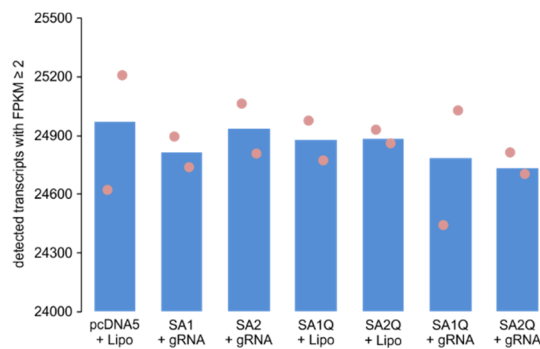
Additional NGS quality data



Detected editing sites ranked by coverage for each experiment. For testing significant editing differences, a coverage cut-off of 50 (red line) for the sum of each experiment with its replicate was applied. This typically yielded around 50.000 sites / experiment to be analyzed.



Scatter plots of editing levels of all called editing sites of replicate 1 against replicate 2 for the indicated editing experiments show good replicability with correlation ranging from 0.932-0.960.



Number of transcript covered in RNA sequencing was performed with two replicates of each sample. Shown are number of detected transcripts with a FPKM value ≥ 2 for both replicates combined (light blue bars) or separated (pink dots).

Sequences of editing enzymes and editing targets

```

10      20      30      40      50      60
1      ATGGGGAAGGTGAAGGTCGGAGTCAACGGATTTGGTCGTATTGGGCGCCTGGTCACCAGG
1      M G K V K V G V N G F G R I G R L V T R
70      80      90      100     110     120
61     GCTGCTTTTAACTCTGGTAAAAGTGGTATATTGTTGCCATCAATGACCCCTCATTGACCTC
21     A A F N S G K V D I V A I N D P F I D L
130     140     150     160     170     180
121    AACTACATGGTTTACATGTTCCAATATGATTCCACCCATGGCAAATCCATGGCACCGTC
41     N Y M V Y M F Q Y D S T H G K F H G T V
190     200     210     220     230     240
181    AAGGCTGAGAACGGGAAGCTTGTCAATGGAAATCCCATCACCATCTCCAGGAGCGA
61     K A E N G K L V I N G N P I T I F Q E R
250     260     270     280     290     300
241    GATCCCTCCAAAATCAAGTGGGGCGATGCTGGCGCTGAGTACGTCGTGGAGTCCACTGGC
81     D P S K I K W G D A G A E Y V V E S T G
310     320     330     340     350     360
301    GTCTTCACCACCATGGAGAAGGCTGGGGCTCATTGTCAGGGGGGAGCCAAAGGGTCATC
101    V F T T M E K A G A H L Q G G A K R V I
370     380     390     400     410     420
361    ATCTCTGCCCCCTCTGCTGATGCCCCATGTTCTGTCATGGGTGTGAACCATGAGAAGTAT
121    I S A P S A D A P M F V M G V N H E K Y
430     440     450     460     470     480
421    GACAACAGCCTCAAGATCATCAGCAATGCCTCCTGCACCACCAACTGCTTAGCACCCCTG
141    D N S L K I I S N A S C T T N C L A P L
490     500     510     520     530     540
481    GCCAAGGTTCATCCATGACAACCTTTGGTATCGTGGAAGACTCATGACCACAGTCCATGCC
161    A K V I H D N F G I V E G L M T T V H A
550     560     570     580     590     600
541    ATCACTGCCACCCAGAAGACTGTGGATGGCCCCCTCCGGGAAAACTGTGGCGTGATGGCCCGC
181    I T A T Q K T V D G P S G K L W R D G R
610     620     630     640     650     660
601    GGGGCTCTCCAGAACATCATCCCTGCCTCTACTGGCGCTGCCAAGGCTGTGGGCAAGGTC
201    G A L Q N I I P A S T G A A K A V G K V
670     680     690     700     710     720
661    ATCCCTGAGCTGAACGGGAAGCTCACTGGCATGGCCTTCCCGTGTCCCCACTGCCAACGTG
221    I P E L N G K L T G M A F R V P T A N V
730     740     750     760     770     780
721    TCAGTGGTGGACCTGACCTGCCGTCTAGAAAAACCTGCCAAATATGATGACATCAAGAAG
241    S V V D L T C R L E K P A K Y D D I K K
790     800     810     820     830     840
781    GTGGTGAAGCAGGCGTCGGAGGGCCCCCTCAAGGCATCCTGGGCTACACTGAGCACCAG
261    V V K Q A S E G P L K G I L G Y T E H Q
850     860     870     880     890     900
841    GTGGTCTCCTCTGACTTCAACAGCGACACCCACTCCTCCACCTTTGACGCTGGGGCTGGC
281    V V S S D F N S D T H S S T F D A G A G
910     920     930     940     950     960
901    ATTGCCCTCAACGACCACCTTGTCAAGCTCATTTCCTGGTATGACAACGAATTTGGCTAC
301    I A L N D H F V K L I S W Y D N E F G Y
970     980     990     1000
961    AGCAACAGGGTGGTGGACCTCATGGCCACATGGCCTCCAAGGACTAA
321    S N R V V D L M A H M A S K E *

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Open reading frame of GAPDH transcript isoform 1 (NM_002046.5). All 16 adenosine-containing triplets (yellow and cyan) were tested for editing. Most of the triplets (yellow), sites could be chosen with no resulting amino acid change. Only for 4 triplets (cyan), editing of the corresponding site lead to amino acid change. However, these changes happen in the variable region of the protein and thus, are supposed not to disturb protein activity.

1 10 20 30 40 50 60
1 GGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAAGACACCGGGACCGATCCAGCCTCC
1
61 70 80 90 100 110 120
GGACTCTAGCGTTTAACTTAAGCTTGGTACCGAGCTCGGATCCACCATGGACAAAGACT
20 M D K D
121 130 140 150 160 170 180
GCGAAATGAAGCGCACCACCTGGATAGCCCTCTGGGCAAGCTGGAAGTGTCTGGGTGCG
40 C E M K R T T L D S P L G K L E L S G C
181 190 200 210 220 230 240
AACAGGGCTGCACCGTATCATCTTCTGGGCAAGGAACATCTGCCGCCGACGCCGTGG
60 E Q G L H R I I F L G K G T S A A D A V
241 250 260 270 280 290 300
AAGTGCCTGCCCCAGCCGCGTGTGGGCGGACCAGAGCCACTGATGCAGGCCACCGCCT
80 E V P A P A A V L G G P E P L M Q A T A
301 310 320 330 340 350 360
GGCTCAACGCCTACTTTCCACGACCTGAGGCCATCGAGGAGTTCCCTGTGCCAGCCCTGC
100 W L N A Y F H Q P E A I E E F P V P A L
361 370 380 390 400 410 420
ACCACCCAGTGTTCACGAGGAGAGCTTTACCCGCCAGGTGCTGTGGAAACTGCTGAAAG
120 H H P V F Q Q E S F T R Q V L W K L L K
421 430 440 450 460 470 480
TGGTGAAGTTCGAGAGGTCATCAGCTACAGCCACCTGGCCGCCCTGGCCGGCAATCCCG
140 V V K F G E V I S Y S H L A A L A G N P
481 490 500 510 520 530 540
CCGCCACCGCCGCGTGA AAAACCGCCCTGAGCGGAAATCCCGTGCCCATCTGATCCCCCT
160 A A T A A V K T A L S G N P V P I L I P
541 550 560 570 580 590 600
GCCACCGGGTGGTGCAGGCGCACCTGGACGTGGGGGGCTACGAGGGCGGGCTCGCCGTGA
180 C H R V V Q G D L D V G G Y E G G L A V
601 610 620 630 640 650 660
AAGAGTGGCTGCTGGCCACGAGGGCCACAGACTGGGCAAGCCTGGGCTGGGTCTGCGAG
200 K E W L L A H E G H R L G K P G L G P A
661 670 680 690 700 710 720
GCGGAGGCGCCAGGGTCTGGCGGGCAGTAAGGCAGAACGCATGGGTTTCACAGAGG
220 G G G A P G S G G S K A E R M G F T E
721 730 740 750 760 770 780
TAACCCAGTGACAGGGGCCAGTCTCAGAAACTATGCTCCTCCTCAAGTCCCCAG
240 V T P V T G A S L R R T M L L L S R S P
781 790 800 810 820 830 840
AAGCACAGCCAAAGACACTCCCTCTCACTGGCAGCACCTTCCATGACCAGATAGCCATGC
260 E A Q P K T L P L T G S T F H D Q I A M
841 850 860 870 880 890 900
TGAGCCACCGGTGCTTCAACTCTGACTAACAGCTTCCAGCCCTCCTTGTCTCGCCGCA
280 L S H R C F N T L T N S F Q P S L L G R
901 910 920 930 940 950 960
AGATTCTGGCCGCATCATTATGAAAAAGACTCTGAGGACATGGGTGTCTGTCGTGAGCT
300 K I L A A I I M K K D S E D M G V V V S
961 970 980 990 1000 1010 1020
TGGGAACAGGGAATCGCTGTGTA AAAAGGAGATTCTCTCAGCCTAAAAGGAGAAACTGTCA
320 L G T G N R C V K G D S L S L K G E T V
1021 1030 1040 1050 1060 1070 1080
ATGACTGCCATGCAGAAATAATCTCCCGGAGAGGCTTCATCAGGTTTCTCTACAGTGAGT
340 N D C H A E I I S R R G F I R F L Y S E
1081 1090 1100 1110 1120 1130 1140
TAATGAAATACAACCTCCAGACTGCGAAGGATAGTATATTTGAACCTGCTAAGGAGAGG
360 L M K Y N S Q T A K D S I F E P A K G G
1141 1150 1160 1170 1180 1190 1200
AAAAGCTCCAAATAAAAAAGACTGTGTCTATCCATCTGTATATCAGCACTGCTCCGTGTG
380 E K L Q I K K T V S F H L Y I S T A P C
1201 1210 1220 1230 1240 1250 1260
GAGATGGCGCCCTCTTTGACAAGTCTGCAGCGACCGTGTATGGAAAGCACAGAATCCC
400 G D G A L F D K S C S D R A M E S T E S
1261 1270 1280 1290 1300 1310 1320
GCCACTACCCTGTCTTCGAGAATCCCAAACAAGGAAAGCTCCGCACCAAGGTGGAGAACG
420 R H Y P V F E N P K Q G K L R T K V E N
1321 1330 1340 1350 1360 1370 1380
GAGAAGGCACAATCCCTGTGGAATCCAGTGACATGTGCTACGTGGGATGGCATTCGGC
440 G E G T I P V E S S D I V P T W D G I R
1381 1390 1400 1410 1420 1430 1440
TCGGGGAGAGACTCCGTACCATGTCTGTAGTGACAAAATCCTACGCTGGAACGTGCTGG
460 L G E R L R T M S C S D K I L R W N V L
1441 1450 1460 1470 1480 1490 1500
GCCTGCAAGGGGCACTGTTGACCCACTTCTGCAGCCATTTATCTCAAATCTGTACAT
480 G L Q G A L L T H F L Q P I Y L K S V T
1501 1510 1520 1530 1540 1550 1560
TGGGTTACCTTTTCAGCCAAGGGCATCTGACCCGTGCTATTTGCTGTCTGTGACAAGAG
500 L G Y L F S Q G H L T R A I C C R V T R
1561 1570 1580 1590 1600 1610 1620
ATGGGAGTGCATTTGAGGATGGACTACGACATCCCTTTATTGTCAACCCCAAGTTG
520 D G S A F E D G L R H P F I V N H P K V
1630 1640 1650 1660 1670 1680

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1621 GCAGAGTCAGCATATATGATTCCAAAAGGCAATCCGGGAAGACTAAGGAGACAAGCGTCA
540 G R V S I Y D S K R Q S G K T K E T S V
      1690 1700 1710 1720 1730 1740
1681 ACTGGTGTCTGGCTGATGGCTATGACCTGGAGATCCTGGACGGTACCAGAGGCACTGTGG
560 N W C L A D G Y D L E I L D G T R G T V
      1750 1760 1770 1780 1790 1800
1741 ATGGGCCACGGAATGAATTGTCCCGGGTCTCCAAAAGAACATTTTCTTCTATTTAAGA
580 D G P R N E L S R V S K K N I F L L F K
      1810 1820 1830 1840 1850 1860
1801 AGCTCTGCTCCTCCGTTACCGCAGGGATCTACTGAGACTCTCCTATGGTGAGGCCAAGA
600 K L C S F R Y R R D L L R L S Y G E A K
      1870 1880 1890 1900 1910 1920
1861 AAGCTGCCCGTGACTACGAGACGGCCAAGAAGTACTTCAAAAAGGCCTGAAGGATATGG
620 K A A R D Y E T A K N Y F K K G L K D M
      1930 1940 1950 1960 1970 1980
1921 GCTATGGGAACTGGATTAGCAAACCCAGGAGGAAAAGAACTTTTATCTCTGCCAGTAT
640 G Y G N W I S K P Q E E K N F Y L C P V
      1990 2000 2010 2020 2030 2040
1981 CTAGATGACTGCCTGTTCCGTAGCCGACACGGGCCCGTTTAAACCCGCTGATCAGCCTCG
660 S R *
      2050 2060 2070 2080 2090 2100
2041 ACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCTCCCCCGTGCCTTCCTTGACC
680

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Sequence of SNAP-ADAR1 as expressed from the 293 genome with chosen editing sites (yellow).

10 20 30 40 50 60
1 GGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAAGACACCGGGACCGATCCAGCCTCC
1
70 80 90 100 110 120
61 GGACTCTAGCGTTTTAACTTAAGCTTGGTACCGAGCTCGGATCCACCATGGACAAAGACT
20 M D K D
130 140 150 160 170 180
121 GCGAAATGAAGCGCACCACCTGGATAGCCCTCTGGGCAAGCTGGAAGTGTCTGGGTGCG
40 C E M K R T T L D S P L G K L E L S G C
190 200 210 220 230 240
181 AACAGGGCTGCACCGTATCATCTTCTGGGCAAAGGAACATCTGCCGCCGACGCCGTGG
60 E Q G L H R I I F L G K G T S A A D A V
250 260 270 280 290 300
241 AAGTGCCTGCCCCAGCCGCCGTGTGGGCGGACCAGAGCCACTGATGCAGGCCACCGCCT
80 E V P A P A A V L G G P E P L M Q A T A
310 320 330 340 350 360
301 GGCTCAACGCCTACTTTTACCAGCCTGAGGCCATCGAGGAGTTCCCTGTGCCAGCCCTGC
100 W L N A Y F H Q P E A I E E F P V P A L
370 380 390 400 410 420
361 ACCACCCAGTGTTCACGAGGAGAGCTTTACCCGCCAGGTGTGTGGAAACTGTGAAAG
120 H H P V F Q Q E S F T R Q V L W K L L K
430 440 450 460 470 480
421 TGGTGAAGTTCGAGAGGTCATCAGCTACAGCCACCTGGCCGCCCTGGCCGGCAATCCCG
140 V V K F G E V I S Y S H L A A L A G N P
490 500 510 520 530 540
481 CCGCCACCGCCCGCTGAAAACCGCCCTGAGCGGAAATCCCGTGCCCATCTGTATCCCT
160 A A T A A V K T A L S G N P V P I L I P
550 560 570 580 590 600
541 GCCACCGGGTGGTGCAGGCGCACCTGGACGTGGGGGGCTACGAGGGCGGGCTCGCCGTGA
180 C H R V V Q G D L D V G G Y E G G L A V
610 620 630 640 650 660
601 AAGAGTGGCTGCTGGCCACGAGGGCCACAGACTGGGCAAGCCTGGGCTGGGTCTCGCAG
200 K E W L L A H E G H R L G K P G L G P A
670 680 690 700 710 720
661 GCGGAGGCGCCAGGGTCTGGCGGGCAGTAAGAAGCTTGCCAAGGCCCGGGCTGCGC
220 G G G A P G S G G S K K L A K A R A A
730 740 750 760 770 780
721 AGTCTGCCCTGGCCGCAATTTTTAACTTGCACTGGATCAGACGCCATCTCGCCAGCCTA
240 Q S A L A A I F N L H L D Q T P S R Q P
790 800 810 820 830 840
781 TTCCAGTGAGGGTCTTCAGCTGCATTTACCGCAGGTTTTAGCTGACGCTGTCTCAGCC
260 I P S E G L Q L H L P Q V L A D A V S R
850 860 870 880 890 900
841 TGGTCTGGGTAAGTTTGGTGACCTGACCGACAACCTTCTCCTCCCTCACGCTCGCAGAA
280 L V L G K F G D L T D N F S S P H A R R
910 920 930 940 950 960
901 AAGTGTGGCTGGAGTCTGATGACAACAGGCACAGATGTTAAAGATGCCAAGGTGATAA
300 K V L A G V M T T G T D V K D A K V I
970 980 990 1000 1010 1020
961 GTGTTTCTACAGGAACAAATGTATTAATGGTGAATACATGAGTATCGTGGCCCTGCAT
320 S V S T G T K C I N G E Y M S D R G L A
1030 1040 1050 1060 1070 1080
1021 TAAATGACTGCCATGCAGAAATAATATCTCGGAGATCCTTGCTCAGATTTCTTTATACAC
340 L N D C H A E I I S R R S L L R F L Y T
1090 1100 1110 1120 1130 1140
1081 AACTTGAGCTTTACTTAAATAACAAGATGATCAAAAAAGATCCATTTTCAGAAATCAG
360 Q L E L Y L N N K D D Q K R S I F Q K S
1150 1160 1170 1180 1190 1200
1141 AGCGAGGGGGTTTAGGCTGAAGGAGAATGTCCAGTTTCATCTGTACATCAGCACCTCTC
380 E R G G F R L K E N V Q F H L Y I S T S
1210 1220 1230 1240 1250 1260
1201 CCTGTGGAGATGCCAGAATCTTCTCACCACATGAGCCAATCCTGGAAGAACCAGCAGATA
400 P C G D A R I F S P H E P I L E E P A D
1270 1280 1290 1300 1310 1320
1261 GACACCCAAATCGTAAAGCAAGAGGACAGCTACGGACCAAAATAGAGTCTGGTGAGGGGA
420 R H P N R K A R G Q L R T K I E S G E G
1330 1340 1350 1360 1370 1380
1321 CGATTCCAGTGCCTCCAAATGCGAGCATCCAACGTGGGACGGGTGCTGCAAGGGGAGC
440 T I P V R S N A S I Q T W D G V L Q G E
1390 1400 1410 1420 1430 1440
1381 GGCTGCTCACCATGCTCTGCAGTACAAGATTGCACGCTGGAACGTGGTGGGCATCCAGG
460 R L L T M S C S D K I A R W N V V G I Q
1450 1460 1470 1480 1490 1500
1441 GATCCCTGCTCAGCATTTTCGTGGAGCCCATTTACTTCTCGAGCATCATCCTGGGCAGCC
480 G S L L S I F V E P I Y F S S I I L G S
1510 1520 1530 1540 1550 1560
1501 TTTACCACGGGGACCACCTTTCCAGGGCCATGTACCAGCGGATCTCCAACATAGAGGACC
500 L Y H G D H L S R A M Y Q R I S N I E D
1570 1580 1590 1600 1610 1620
1561 TGCCACCTCTACACCCTCAACAAGCCTTTGCTCAGTGGCATCAGCAATGCAGAAGCAC
520 L P P L Y T L N K P L L S G I S N A E A
1630 1640 1650 1660 1670 1680

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1621 GGCAGCCAGGGAAGGCCCAACTTCAGTGTCAACTGGACGGTAGGCGACTCCGCTATTG
540 R Q P G K A P N F S V N W T V G D S A I
      1690      1700      1710      1720      1730      1740
1681 AGGTCATCAACGCCACGACTGGGAAGGATGAGCTGGGCCGCGCTCCCGCCTGTGTAAGC
560 E V I N A T T G K D E L G R A S R L C K
      1750      1760      1770      1780      1790      1800
1741 ACGCGTTGTACTGTGCTGGATGCGTGTGCACGGCAAGGTTCCCTCCCCTTACTACGCT
580 H A L Y C R W M R V H G K V P S H L L R
      1810      1820      1830      1840      1850      1860
1801 CCAAGATTACCAAGCCCAACGTGTACCATGAGTCCAAGCTGGCGGCAAAGGAGTACCAGG
600 S K I T K P N V Y H E S K L A A K E Y Q
      1870      1880      1890      1900      1910      1920
1861 CCGCCAAGGCGCTCTGTTCACAGCCTTCATCAAGCGGGGCTGGGGGCTGGGTGGAGA
620 A A K A R L F T A F I K A G L G A W V E
      1930      1940      1950      1960      1970      1980
1921 AGCCACCGAGCAGGACCAGTTCTCACTCACGCCCTCTAGATGACTGCCTGTTCCGTAGC
640 K P T E Q D Q F S L T P S R *
      1990      2000      2010      2020      2030      2040
1981 CGACACGGGCCCGTTTAAACCCGCTGATCAGCCTCGACTGTGCCTTCTAGTTGCCAGCCA
660

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Sequence of SNAP-ADAR2 as expressed from the 293 genome with chosen editing sites (yellow).

1 10 20 30 40 50 60
1 GGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAAGACACCGGGACCGATCCAGCCTCC
1
61 70 80 90 100 110 120
GGACTCTAGCGTTTAACTTAAGCTTGGTACCGAGCTCGGATCCACCATGGACAAAGACT
20 M D K D
121 130 140 150 160 170 180
GCGAAATGAAGCGCACCACCTGGATAGCCCTCTGGGCAAGCTGGAAGTGTCTGGGTGCG
40 C E M K R T T L D S P L G K L E L S G C
181 190 200 210 220 230 240
AACAGGGCTGCACCGTATCATCTTCTGGGCAAGGAACATCTGCCGCCGACGCCGTGG
60 E Q G L H R I I F L G K G T S A A D A V
241 250 260 270 280 290 300
AAGTGCCTGCCCCAGCCGCGTGTGGGCGGACCAGAGCCACTGATGCAGGCCACCGCCT
80 E V P A P A A V L G G P E P L M Q A T A
301 310 320 330 340 350 360
GGTCAACGCCTACTTTCCACGCTGAGGCCATCGAGGAGTTCCCTGTGCCAGCCCTGC
100 W L N A Y F H Q P E A I E E F P V P A L
361 370 380 390 400 410 420
ACCACCCAGTGTTCACGAGGAGGCTTTACCCGCCAGGTGCTGTGGAAACTGTGAAAG
120 H H P V F Q Q E S F T R Q V L W K L L K
421 430 440 450 460 470 480
TGGTGAAGTTCGAGAGGTCATCAGCTACAGCCACCTGGCCGCCCTGGCCGGCAATCCCG
140 V V K F G E V I S Y S H L A A L A G N P
481 490 500 510 520 530 540
CCGCCACCGCCGCGTGA AAAACCGCCCTGAGCGGAAATCCCGTGCCCATCTGATCCCCCT
160 A A T A A V K T A L S G N P V P I L I P
541 550 560 570 580 590 600
GCCACCGGGTGGTGCAGGCGCACCTGGACGTGGGGGGCTACGAGGGCGGGCTCGCCGTGA
180 C H R V V Q G D L D V G G Y E G G L A V
601 610 620 630 640 650 660
AAGAGTGGCTGCTGGCCACGAGGGCCACAGACTGGGCAAGCCTGGGCTGGGTCTGCGAG
200 K E W L L A H E G H R L G K P G L G P A
661 670 680 690 700 710 720
GCGGAGGCGCCAGGGTCTGGCGGGCAGTAAGGCAGAACGCATGGGTTTCACAGAGG
220 G G G A P G S G G S K A E R M G F T E
721 730 740 750 760 770 780
TAACCCAGTGACAGGGGCCAGTCTCAGAAACTATGCTCCTCCTCAAGGTCCCCAG
240 V T P V T G A S L R R T M L L L S R S P
781 790 800 810 820 830 840
AAGCACAGCCAAAGACACTCCCTCTCACTGGCAGCACCTTCCATGACCAGATAGCCATGC
260 E A Q P K T L P L T G S T F H D Q I A M
841 850 860 870 880 890 900
TGAGCCACCGGTGCTTCAACTCTGACTAACAGCTTCCAGCCCTCCTTGTCTCGCCGCA
280 L S H R C F N T L T N S F Q P S L L G R
901 910 920 930 940 950 960
AGATTCTGGCCGCATCATTATGAAAAAGACTCTGAGGACATGGGTGTCTGTCGTCAGCT
300 K I L A A I I M K K D S E D M G V V V S
961 970 980 990 1000 1010 1020
TGGGAACAGGGAATCGCTGTGTA AAAAGGAGATTCTCTCAGCCTAAAAGGAGAAACTGTCA
320 L G T G N R C V K G D S L S L K G E T V
1021 1030 1040 1050 1060 1070 1080
ATGACTGCCATGCAGAAATAATCTCCCGGAGAGGCTTCATCAGGTTTCTCTACAGTGAGT
340 N D C H A E I I S R R G F I R F L Y S E
1081 1090 1100 1110 1120 1130 1140
TAATGAAATACAACCTCCAGACTGCGAAGGATAGTATATTTGAACCTGCTAAGGGAGAG
360 L M K Y N S Q T A K D S I F E P A K G G
1141 1150 1160 1170 1180 1190 1200
AAAAGCTCCAAATAAAAAAGACTGTGTCTATCCATCTGTATATCAGCACTGCTCCGTGTG
380 E K L Q I K K T V S F H L Y I S T A P C
1201 1210 1220 1230 1240 1250 1260
GAGATGGCGCCCTCTTTGACAAGTCTGCAGCGACCGTGTATGGAAAGCACAGAATCCC
400 G D G A L F D K S C S D R A M E S T E S
1261 1270 1280 1290 1300 1310 1320
GCCACTACCCTGTCTTCGAGAATCCCAAACAAGGAAAGCTCCGCACCAAGGTGGAGAACG
420 R H Y P V F E N P K Q G K L R T K V E N
1321 1330 1340 1350 1360 1370 1380
GACAAGGCACAATCCCTGTGGAATCCAGTGACATGTGCTACGTGGGATGGCATTCGGC
440 G Q G T I P V E S S D I V P T W D G I R
1381 1390 1400 1410 1420 1430 1440
TCGGGGAGAGACTCCGTACCATGTCTGTAGTGACAAAATCCTACGCTGGAACGTGCTGG
460 L G E R L R T M S C S D K I L R W N V L
1441 1450 1460 1470 1480 1490 1500
GCCTGCAAGGGGCACTGTTGACCCACTTCTGCAGCCCATTTATCTCAAATCTGTACAT
480 G L Q G A L L T H F L Q P I Y L K S V T
1501 1510 1520 1530 1540 1550 1560
TGGGTTACCTTTTCAGCCAAGGGCATCTGACCCGTGCTATTTGCTGTCTGTGACAAGAG
500 L G Y L F S Q G H L T R A I C C R V T R
1561 1570 1580 1590 1600 1610 1620
ATGGGAGTGCATTTGAGGATGGACTACGACATCCCTTTATTGTCAACCCCAAGTTG
520 D G S A F E D G L R H P F I V N H P K V
1630 1640 1650 1660 1670 1680

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1621 GCAGAGTCAGCATATATGATTCCAAAAGGCAATCCGGGAAGACTAAGGAGACAAGCGTCA
540 G R V S I Y D S K R Q S G K T K E T S V
      1690 1700 1710 1720 1730 1740
1681 ACTGGTGTCTGGCTGATGGCTATGACCTGGAGATCCTGGACGGTACCAGAGGCACTGTGG
560 N W C L A D G Y D L E I L D G T R G T V
      1750 1760 1770 1780 1790 1800
1741 ATGGGCCACGGAATGAATTGTCCCGGGTCTC AAAAAGAACATTTTCTTCTATTTAAGA
580 D G P R N E L S R V S K K N I F L L F K
      1810 1820 1830 1840 1850 1860
1801 AGCTCTGCTCCTCCGTTACCGCAGGGATCTACTGAGACTCTCCTATGGTGAGGCCAAGA
600 K L C S F R Y R R D L L R L S Y G E A K
      1870 1880 1890 1900 1910 1920
1861 AAGCTGCCCGTGACTACGAGACGGCCAAGA AACTACTTCAAAAAGGCCTGAAGGATATGG
620 K A A R D Y E T A K N Y F K K G L K D M
      1930 1940 1950 1960 1970 1980
1921 GCTATGGGAACTGGATTAGCAAACCCCA GAGGAAAAGAACTTTTATCTCTGCCCAGTAT
640 G Y G N W I S K P Q E E K N F Y L C P V
      1990 2000 2010 2020 2030 2040
1981 CTAGATGACTGCCTGTTCCGTAG CCGACACGGGCCCGTTTAAACCCGCTGATCAGCCTCG
660 S R *
      2050 2060 2070 2080 2090 2100
2041 ACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCTCCCGTGCCTTCCTTGACC
680

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Sequence of SNAP-ADAR1Q as expressed from the 293 genome with chosen editing sites (yellow). E/Q site is highlighted in cyan.

10 20 30 40 50 60
1 GGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAAGACACCGGGACCGATCCAGCCTCC
1
70 80 90 100 110 120
61 GGACTCTAGCGTTTAACTTAAGCTTGGTACCGAGCTCGGATCCACCATGGACAAAGACT
20 M D K D
130 140 150 160 170 180
121 GCGAAATGAAGCGCACCACCTGGATAGCCCTCTGGGCAAGCTGGAAGTGTCTGGGTGCG
40 C E M K R T T L D S P L G K L E L S G C
190 200 210 220 230 240
181 AACAGGCCTGCACCGTATCATCTTCTGGGCAAAGGAACATCTGCCGCCGACGCCGTGG
60 E Q G L H R I I F L G K G T S A A D A V
250 260 270 280 290 300
241 AAGTGCCTGCCCCAGCCGCCGTGTGGGCGGACCAGAGCCACTGATGCAGGCCACCGCCT
80 E V P A P A A V L G G P E P L M Q A T A
310 320 330 340 350 360
301 GGCTCAACGCCTACTTTCCACGCTGAGGCCATCGAGGAGTTCCCTGTGCCAGCCCTGC
100 W L N A Y F H Q P E A I E E F P V P A L
370 380 390 400 410 420
361 ACCACCCAGTGTTCACGAGGAGAGCTTTACCCGCCAGGTGTGTGGAAACTGTGAAAG
120 H H P V F Q Q E S F T R Q V L W K L L K
430 440 450 460 470 480
421 TGGTGAAGTTCGAGAGGTCATCAGCTACAGCCACCTGGCCGCCCTGGCCGGCAATCCCG
140 V V K F G E V I S Y S H L A A L A G N P
490 500 510 520 530 540
481 CCGCCACCGCCCGCTGAAAACCGCCCTGAGCGGAAATCCCGTGCCCATTTCTGATCCCT
160 A A T A A V K T A L S G N P V P I L I P
550 560 570 580 590 600
541 GCCACCGGTTGGTGCAGGCGCACCTGGACGTGGGGGGCTACGAGGGCGGGCTCGCCGTGA
180 C H R V V Q G D L D V G G Y E G G L A V
610 620 630 640 650 660
601 AAGAGTGGCTGCTGGCCACGAGGGCCACAGACTGGGCAAGCCTGGGCTGGGTCTCGCAG
200 K E W L L A H E G H R L G K P G L G P A
670 680 690 700 710 720
661 GCGGAGGCGCCAGGGTCTGGCGGGCAGTAAGAAGCTTGCCAAGGCCCGGGCTGCGC
220 G G G A P G S G G G S K K L A K A R A A
730 740 750 760 770 780
721 AGTCTGCCCTGGCCGCAATTTTTAACTTGCACTGGATCAGACGCCATCTCGCCAGCCTA
240 Q S A L A A I F N L H L D Q T P S R Q P
790 800 810 820 830 840
781 TTCCAGTGAGGGTCTTCAGCTGCATTTACCGCAGGTTTTAGCTGACGCTGTCTCAGGCC
260 I P S E G L Q L H L P Q V L A D A V S R
850 860 870 880 890 900
841 TGGTCTGGGTAAGTTTGGTGACCTGACCGACAACCTTCTCCTCCCTCAGCTCGCAGAA
280 L V L G K F G D L T D N F S S P H A R R
910 920 930 940 950 960
901 AAGTGTGGCTGGAGTCGTATGACAACAGGCACAGATGTTAAAGATGCCAAGGTGATAA
300 K V L A G V M T T G T D V K D A K V I
970 980 990 1000 1010 1020
961 GTGTTTCTACAGGAACAAATGTATTAATGGTGAATACATGAGTATCGTGGCCTTGCA
320 S V S T G T K C I N G E Y M S D R G L A
1030 1040 1050 1060 1070 1080
1021 TAAATGACTGCCATGCAGAAATAATATCTCGGAGATCCTTGCTCAGATTTCTTTATAC
340 L N D C H A E I I S R R S L L R F L Y T
1090 1100 1110 1120 1130 1140
1081 AACTTGAGCTTTACTTAAATAACAAGATGATCAAAAAAGATCCATTTTCAGAAATCAG
360 Q L E L Y L N N K D D Q K R S I F Q K S
1150 1160 1170 1180 1190 1200
1141 AGCGAGGGGGTTTAGGCTGAAGGAGAATGTCCAGTTTCATCTGTACATCAGCACCTCTC
380 E R G G F R L K E N V Q F H L Y I S T S
1210 1220 1230 1240 1250 1260
1201 CCTGTGGAGATGCCAGAATCTTCTCACCACATGAGCCAATCCTGGAAGAACCAGCAGATA
400 P C G D A R I F S P H E P I L E E P A D
1270 1280 1290 1300 1310 1320
1261 GACACCCAAATCGTAAAGCAAGAGGACAGCTACGGACCAAAATAGAGTCTGGTCAGGGGA
420 R H P N R K A R G Q L R T K I E S G Q G
1330 1340 1350 1360 1370 1380
1321 CGATTCCAGTGCCTCCAAATGCGAGCATCCAACGTGGGACGGGGTGTGCAAGGGGAGC
440 T I P V R S N A S I Q T W D G V L Q G E
1390 1400 1410 1420 1430 1440
1381 GGCTGCTCACCATGTCCTGCAGTGACAAGATTGCACGCTGGAACGTGGTGGGCATCCAGG
460 R L L T M S C S D K I A R W N V V G I Q
1450 1460 1470 1480 1490 1500
1441 GATCCCTGCTCAGCATTTTCGTGGAGCCCATTTACTTCTCGAGCATCATCCTGGGCAGCC
480 G S L L S I F V E P I Y F S S I I L G S
1510 1520 1530 1540 1550 1560
1501 TTTACCACGGGGACCACCTTTCCAGGGCCATGTACCAGCGGATCTCCAACATAGAGGACC
500 L Y H G D H L S R A M Y Q R I S N I E D
1570 1580 1590 1600 1610 1620
1561 TGCCACCTCTACACCCTCAACAAGCCTTTGCTCAGTGGCATCAGCAATGCAGAAGCAC
520 L P P L Y T L N K P L L S G I S N A E A
1630 1640 1650 1660 1670 1680

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1621   GGCAGCCAGGGAAGGCCCACTTCAGTGTCAACTGGACGGTAGGCGACTCCGCTATTG
540     R  Q  P  G  K  A  P  N  F  S  V  N  W  T  V  G  D  S  A  I
        1690      1700      1710      1720      1730      1740
1681   AGGTCATCAACGCCACGACTGGGAAGGATGAGCTGGGCCGCGCTCCCGCCTGTGTAAGC
560     E  V  I  N  A  T  T  G  K  D  E  L  G  R  A  S  R  L  C  K
        1750      1760      1770      1780      1790      1800
1741   ACGCGTTGTACTGTGCTGGATGCGTGTGCACGGCAAGGTTCCCTCCCCTTACTACGCT
580     H  A  L  Y  C  R  W  M  R  V  H  G  K  V  P  S  H  L  L  R
        1810      1820      1830      1840      1850      1860
1801   CCAAGATTACCAAGCCCAACGTGTACCATGAGTCCAAGCTGGCGGCAAAGGAGTACCAGG
600     S  K  I  T  K  P  N  V  Y  H  E  S  K  L  A  A  K  E  Y  Q
        1870      1880      1890      1900      1910      1920
1861   CCGCCAAGGCGCGTCTGTTCACAGCCTTCATCAAGCGGGGCTGGGGCCTGGGTGGAGA
620     A  A  K  A  R  L  F  T  A  F  I  K  A  G  L  G  A  W  V  E
        1930      1940      1950      1960      1970      1980
1921   AGCCACCGAGCAGGACCAGTTCTCACTCACGCCCTCTAGATGACTGCCTGTTCCGTAGC
640     K  P  T  E  Q  D  Q  F  S  L  T  P  S  R  *
        1990      2000      2010      2020      2030      2040
1981   CGACACGGGCCCGTTTAAACCCGCTGATCAGCCTCGACTGTGCCTTCTAGTTGCCAGCCA
660

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Sequence of SNAP-ADAR2Q as expressed from the 293 genome with chosen editing sites (yellow). E/Q site is highlighted in cyan.

10 20 30 40 50 60
1 GGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAAGACACCGGGACCGATCCAGCCTCC
1
70 80 90 100 110 120
61 GGACTCTAGCGTTTTAACTTAAGCTTGGTACCGAGCTCGGATCCACCATGGACAAAGACT
20 M D K D
130 140 150 160 170 180
121 GCGAAATGAAGCGCACCACCTGGATAGCCCTCTGGGCAAGCTGGAAGTGTCTGGGTGCG
40 C E M K R T T L D S P L G K L E L S G C
190 200 210 220 230 240
181 AACAGGGCTGCACCGTATCATCTTCTGGGCAAAGGAACATCTGCCGCCGACGCCGTGG
60 E Q G L H R I I F L G K G T S A A D A V
250 260 270 280 290 300
241 AAGTGCCTGCCCCAGCCGCCGTGTGGGCGGACCAGAGCCACTGATGCAGGCCACCGCCT
80 E V P A P A A V L G G P E P L M Q A T A
310 320 330 340 350 360
301 GGCTCAACGCCTACTTTCCACGCTGAGGCCATCGAGGAGTTCCCTGTGCCAGCCCTGC
100 W L N A Y F H Q P E A I E E F P V P A L
370 380 390 400 410 420
361 ACCACCCAGTGTTCACGAGGAGAGCTTTACCCGCCAGGTGTGTGGAAACTGTGAAAG
120 H H P V F Q Q E S F T R Q V L W K L L K
430 440 450 460 470 480
421 TGGTGAAGTTCGAGAGGTCATCAGCTACAGCCACCTGGCCGCCCTGGCCGGCAATCCCG
140 V V K F G E V I S Y S H L A A L A G N P
490 500 510 520 530 540
481 CCGCCACCGCCCGCTGAAAACCGCCCTGAGCGGAAATCCCGTGCCCATCTGATCCCCCT
160 A A T A A V K T A L S G N P V P I L I P
550 560 570 580 590 600
541 GCCACCGGGTGGTGCAGGCGCACCTGGACGTGGGGGGCTACGAGGGCGGGCTCGCCGTGA
180 C H R V V Q G D L D V G G Y E G G L A V
610 620 630 640 650 660
601 AAGAGTGGCTGCTGGCCACGAGGGCCACAGACTGGGCAAGCCTGGGCTGGGTCTCGCAG
200 K E W L L A H E G H R L G K P G L G P A
670 680 690 700 710 720
661 GCGGAGGCGCCAGGGTCTGGCGGGCAGTAAGAAGCTTGCCAAGGCCCGGGCTGCGC
220 G G G A P G S G G G S K K L A K A R A A
730 740 750 760 770 780
721 AGTCTGCCCTGGCCGCAATTTTTAACTTGCACTGGATCAGACGCCATCTCGCCAGCCTA
240 Q S A L A A I F N L H L D Q T P S R Q P
790 800 810 820 830 840
781 TTCCAGTGAGGGTCTTCAGCTGCATTTACCGCAGGTTTTAGCTGACGCTGTCTCACGCC
260 I P S E G L Q L H L P Q V L A D A V S R
850 860 870 880 890 900
841 TGGTCTGGGTAAGTTTGGTGACCTGACCGACAACCTTCTCCTCCCTCACGCTCGCAGAA
280 L V L G K F G D L T D N F S S P H A R R
910 920 930 940 950 960
901 AAGTGCTGGCTGGAGTCGTATGACAACAGGCACAGATGTTAAAGATGCCAAGGTGATAA
300 K V L A G V V M T T G T D V K D A K V I
970 980 990 1000 1010 1020
961 GTGTTTCTACAGGAGGCAAAATGTATTAATGGTGAATACATGAGTGATCGTGGCCCTGCAT
320 S V S T G G K C I N G E Y M S D R G L A
1030 1040 1050 1060 1070 1080
1021 TAAATGACTGCCATGCAGAAATAATATCTCGGAGATCCTTGCTCAGATTTCTTTATACAC
340 L N D C H A E I I S R R S L L R F L Y T
1090 1100 1110 1120 1130 1140
1081 AACTTGAGCTTTACTTAAATAACAAGATGATCAAAAAAGATCCATCTTCAGAAATCAG
360 Q L E L Y L N N K D D Q K R S I F Q K S
1150 1160 1170 1180 1190 1200
1141 AGCGAGGGGGTTTAGGCTGAAGGAGAATGTCCAGTTTCATCTGTACATCAGCACCTCTC
380 E R G G F R L K E N V Q F H L Y I S T S
1210 1220 1230 1240 1250 1260
1201 CCTGTGGAGATGCCAGAATCTTCTCACCACATGAGCCAATCCTGGAAGAACCAGCAGATA
400 P C G D A R I F S P H E P I L E E P A D
1270 1280 1290 1300 1310 1320
1261 GACACCCAAATCGTAAAGCAAGAGGACAGCTACGGACCAAAATAGAGTCTGGTCAGGGGA
420 R H P N R K A R G Q L R T K I E S G Q G
1330 1340 1350 1360 1370 1380
1321 CGATTCCAGTGCCTCCAAATGCGAGCATCCAACGTGGGACGGGGTGCTGCAAGGGGAGC
440 T I P V R S N A S I Q T W D G V L Q G E
1390 1400 1410 1420 1430 1440
1381 GGCTGCTCACCATGTCCTGCAGTGACAAGATTGCACGCTGGAACGTGGTGGGCATCCAGG
460 R L L T M S C S D K I A R W N V V G I Q
1450 1460 1470 1480 1490 1500
1441 GATCCCTGCTCAGCATTTTCGTGGAGCCCATTTACTTCTCGAGCATCATCCTGGGCAGCC
480 G S L L S I F V E P I Y F S S I I L G S
1510 1520 1530 1540 1550 1560
1501 TTTACCACGGGGACCACCTTTCCAGGGCCATGTACCAGCGGATCTCCAACATAGAGGACC
500 L Y H G D H L S R A M Y Q R I S N I E D
1570 1580 1590 1600 1610 1620
1561 TGCCACCTCTACACCCTCAACAAGCCTTTGCTCAGTGGCATCAGCAATGCAGAAGCAC
520 L P P L Y T L N K P L L S G I S N A E A
1630 1640 1650 1660 1670 1680

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1621 GGCAGCCAGGGAAGGCCCACTTCAGTGTCAACTGGACGGTAGGCGACTCCGCTATTG
540 R Q P G K A P N F S V N W T V G D S A I
      1690 1700 1710 1720 1730 1740
1681 AGGTCATCAACGCCACGACTGGGAAGGATGAGCTGGGCCGCGCTCCCGCCTGTGTAAGC
560 E V I N A T T G K D E L G R A S R L C K
      1750 1760 1770 1780 1790 1800
1741 ACGCGTTGTACTGTGCTGGATGCGTGTGCACGGCAAGGTTCCCTCCCCTTACTACGCT
580 H A L Y C R W M R V H G K V P S H L L R
      1810 1820 1830 1840 1850 1860
1801 CCAAGATTACCAAGCCCAACGTGTACCATGAGTCCAAGCTGGCGGCAAAGGAGTACCAGG
600 S K I T K P N V Y H E S K L A A K E Y Q
      1870 1880 1890 1900 1910 1920
1861 CCGCCAAGGCGCTCTGTTCACAGCCTTCATCAAGCGGGGCTGGGGCCTGGGTGGAGA
620 A A K A R L F T A F I K A G L G A W V E
      1930 1940 1950 1960 1970 1980
1921 AGCCACCGAGCAGGACCAGTTCTCACTCACGCCCTCTAGATGACTGCCTGTTCCGTAGC
640 K P T E Q D Q F S L T P S R *
      1990 2000 2010 2020 2030 2040
1981 CGACACGGGCCGTTTAAACCCGCTGATCAGCCTCGACTGTGCCTTCTAGTTGCCAGCCA
660

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Sequence of SNAP-ADAR2QG as expressed from the 293 genome with chosen editing sites (yellow). E/Q and T/G sites are highlighted in cyan.

10 20 30 40 50 60
 1 GGCACCGCAGGCCCGGGATGCTAGTGCGCAGCGGGTGCATCCCTGTCCGGATGCTGCGC
 70 80 90 100 110 120
 61 CTGCGGTAGAGCGGCCCGCATGTTGCAACCGGGAAGGAAATGAATGGGCAGCCGTTAGGA
 130 140 150 160 170 180
 121 AAGCTGCCGGTGACTAACCCCTGCGCTCCTGCCTCGATGGGTGGAGTCGCGTGTGGCGGG
 190 200 210 220 230 240
 181 GAAGTCAGGTGGAGCGAGGCTAGCTGGCCCGATTCTCTCCGGGTGATGCTTTTCC **TAG**
 250 260 270 280 290 300
 241 ATTATTCTCTGATTGGTTCGTATTGGGCGCCTGGTCACCAGGGCTGCTTTTAACTCTGGT
 310 320 330 340 350 360
 301 AAAGTGGATATTGTTGCCATCAATGACCCCTTCATTGACCTCAACTACATGGTTTACATG
 M V Y M
 370 380 390 400 410 420
 361 TTCCAATATGATTCCACCCATGGCAAATTCATGGCACCGTCAAGGCTGAGAACGGGAAG
 121 F Q Y D S T H G K F H G T V K A E N G K
 430 440 450 460 470 480
 421 CTTGTCAATGAAATCCCATCACCATCTCCAGGAGCGAGATCCCTCCAAAATCAAG
 141 L V I N G N P I T I F Q E R D P S K I K
 490 500 510 520 530 540
 481 TGGGGCGATGCTGGCGCTGAGTACGTCGTTGGAGTCCACTGGCGTCTTCACCACCATGGAG
 161 W G D A G A E Y V V E S T G V F T T M E
 550 560 570 580 590 600
 541 AAGGCTGGGGCTCATTTGCAGGGGGAGCCAAAAGGGTCATCATCTGCCCCCTCTGCT
 181 K A G A H L Q G G A K R V I I S A P S A
 610 620 630 640 650 660
 601 GATGCCCCATGTTTCGTTCATGGGTGTGAACCATGAGAAGTATGACAACAGCCCTCAAGATC
 201 D A P M F V M G V N H E K Y D N S L K I
 670 680 690 #1 700 710 720
 661 ATCAGCAATGCCTCTGCACCACCAACTGCT **TAG** CACCCTGGCCAAGGTCATCCATGAC
 221 I S N A S C T T N C L A P L A K V I H D
 730 740 750 760 770 780
 721 AACTTTGGTATCGTGAAGGACTCATGACCACAGTCCATGCCATCACTGCCACCCAGAAG
 241 N F G I V E G L M T T V H A I T A T Q K
 790 800 810 820 830 840
 781 ACTGTGGATGGCCCTCCGGAAACTGTGGCGTATGGCCGGGGGCTCTCCAGAACATC
 261 T V D G P S G K L W R D G R G A L Q N I
 850 860 870 880 890 900
 841 ATCCCTGCCCTCTACTGGCGCTGCCAAGGCTGTGGGCAAGGTCATCCCTGAGCTGAACGGG
 281 I P A S T G A A K A V G K V I P E L N G
 910 920 930 940 950 960
 901 AAGCTCACTGGCATGGCCTTCCGTTGCCACTGCCAACGTGTCAGTGGTGGACCTGACC
 301 K L T G M A F R V P T A N V S V V D L T
 #2 980 990 1000 1010 1020
 961 TGCCGTC **TAG** AAAAACTGCCAAATATGATGACATCAAGAAGGTGGTGAAGCAGGCGTCG
 321 C R L E K P A K Y D D I K K V V K Q A S
 1030 1040 1050 1060 1070 1080
 1021 GAGGGCCCCCTCAAGGGCATCCTGGGCTACACTGAGCACCAGGTGGTCTCCTCTGACTTC
 341 E G P L K G I L G Y T E H Q V V S S D F
 1090 1100 1110 1120 1130 1140
 1081 AACAGCGACACCCACTCCTCCACCTTTGACGCTGGGGCTGGCATGCCCCCAACGACCAC
 361 N S D T H S S T F D A G A G I A L N D H
 1150 1160 1170 1180 1190 1200
 1141 TTTGTCAAGCTCATTTCCCTGGTATGACAACGAATTTGGCTACAGCAACAGGGTGGTGGAC
 381 F V K L I S W Y D N E F G Y S N R V V D
 1210 1220 1230 1240 1250 1260
 1201 CTCATGGCCACATGGCCTCCAAGGAGTAAGACCCTGGACCACCAGCCCCAGCAAGAGC
 401 L M A H M A S K E *
 1270 1280 1290 1300 1310 1320
 1261 ACAAGAGGAAGAGAGAGACCCTCACTGCTGGGGAGTCCCTGCCACACTCAGTCCCCCACC
 421
 1330 1340 1350 1360 1370 1380
 1321 ACACTGAATCTCCCTCCTCACAGTTGCCATG **TAG** ACCCCTTGAAGAGGGGAGGGCCTA
 441
 1390 1400 1410 1420 1430 1440
 1381 GGGAGCCGCACCTTGTCATGTACCATCAATAAAGTACCCTGTGCTCAACCAGTTAAAAAA
 461
 1450
 1441 AAAAAAAAAAAAAAAAAA
 481

Sequence of GAPDH mRNA isoform 2 (NM_001256799.2) with chosen editing sites (yellow).

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1      10      20      30      40      50      60
1      GCCTCAAGACCTTGGGCTGGGACTGGCTGAGCCTGGCGGGAGGCGGGGTCCGAGTCACCG
1
61     70      80      90      100     110     120
20     CCTGCCCGCGCCCCCGGTTTCTATAAAATTGAGCCCGCAGCCTCCCGCTTCGCTCTCTG
121    130     140     150     160     170     180
40     CTCTCTCTGTTTCGACAGTCAGCCGCATCTTCTTTTGGCTGCCAGCCGAGCCACATCGCT
181    190     200     210     220     230     240
60     CAGACACCATGGGGAAGGTGAAGTTCGGAGTCAACGGATTGGTTCGTATTGGGCGCCTGG
      M G K V K V G V N G F G R I G R L
241    250     260     270     280     290     300
80     TCACCAGGGCTGCTTTTAACTCTGGTAAAGTGGATATTGTTGCCATCAATGACCCCTTCA
      V T R A A F N S G K V D I V A I N D P F
301    310     320     330     340     350     360
100    TTGACCTCAACTACATGGTTTACATGTTCCAATATGATTCCACCCATGGCAAATTCCATG
      I D L N Y M V Y M F Q Y D S T H G K F H
361    370     380     390     400     410     420
120    GCACCGTCAAGGCTGAGAACGGGAAGCTTGTCAATCAATGGAAATCCCATCACCATCTTCC
      G T V K A E N G K L V I N G N P I T I F
421    430     440     450     460     470     480
140    AGGAGCGAGATCCCTCCAAAATCAAGTGGGCGATGCTGGCGCTGAGTACGTCGTGGAGT
      Q E R D P S K I K W G D A G A E Y V V E
481    490     500     510     520     530     540
160    CCACTGGCGTCTTACCACCATGGAGAAGGCTGGGGCTCATTTGCAGGGGGAGCCAAAA
      S T G V F T T M E K A G A H L Q G G A K
541    550     560     570     580     590     600
180    GGGTCATCATCTCTGCCCTCTGCTGATGCCCCATGTTTCGTCATGGGTGTAACCATG
      R V I I S A P S A D A P M F V M G V N H
601    610     620     630     640     650     #1
200    AGAAGTATGACAACAGCCTCAAGATCATCAGCAATGCCTCTGCACCACCAACTGCTTAG
      E K Y D N S L K I I S N A S C T T N C L
661    670     680     690     700     710     720
220    CACCCCTGGCCAAGGTCAATCCATGACAACCTTGGTATCGTGAAGGACTCATGACCACAG
      A P L A K V I H D N F G I V E G L M T T
721    730     740     750     760     770     780
240    TCCATGCCATCACTGCCACCCAGAAGACTGTGGATGGCCCTCCGGGAAACTGTGGCGTG
      V H A I T A T Q K T V D G P S G K L W R
781    790     800     810     820     830     840
260    ATGGCCGCGGGCTCTCCAGAACATCATCCCTGCCTCTACTGGCGCTGCCAAGGCTGTGG
      D G R G A L Q N I I P A S T G A A K A V
841    850     860     870     880     890     900
280    GCAAGGTCACTCCCTGAGCTGAACGGGAAGCTCACTGGCATGGCCTTCCGTGCCCACTG
      G K V I P E L N G K L T G M A F R V P T
901    910     920     930     #2 940     950     960
300    CCAACGTGTCAAGTGGTGGACCTGACCTGCCGCTTAGAAAAACCTGCCAAATATGATGACA
      A N V S V V D L T C R L E K P A K Y D D
961    970     980     990     1000    1010    1020
320    TCAAGAAGGTGGTGAAGCAGGCGTCGGAGGGCCCCCTCAAGGGCATCCTGGGCTACACTG
      I K K V V K Q A S E G P L K G I L G Y T
1021  1030    1040    1050    1060    1070    1080
340    AGCACCAGGTGGTCTCCTCTGACTTCAACAGCGACCCCACTCCTCCACCTTTGACGCTG
      E H Q V V S S D F N S D T H S S T F D A
1081  1090    1100    1110    1120    1130    1140
360    GGGCTGGCATTGCCCTCAACGACCACTTTGTCAAGCTCATTTCTGGTATGACAACGAAT
      G A G I A L N D H F V K L I S W Y D N E
1141  1150    1160    1170    1180    1190    1200
380    TTGGCTACAGCAACAGGGTGGTGGACCTCATGGCCACATGGCCTCCAAGGAGTAAGACC
      F G Y S N R V V D L M A H M A S K E *
1201  1210    1220    1230    1240    1250    1260
400    CCTGGACCACCAGCCCCAGCAAGAGCACAAAGAGGAGAGACCCCTCACTGCTGGGGA
1261  1270    1280    1290    1300    1310    1320
420    GTCCCTGCCACACTCAGTCCCCACCACACTGAATCTCCCTCCTCACAGTTGCCATGTAG
1321  1330    1340    1350    1360    1370    1380
440    GACCCCTTGAAGAGGGGAGGGCCCTAGGGAGCCGACCTTGTTCATGTACCATCAATAAAG
1381  1390    1400    1410    1420
460    TACCCTGTCTCAACCAGTTAAAAAAAAAAAAAAAAAAAAA

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Sequence of GAPDH mRNA isoform 1 (NM_002046.5) with chosen editing sites (yellow).

10 20 30 40 50 60
1 ACCGCCGAGACCGCGTCCGCCCGCAGACAGAGCCTCGCCTTTGCCGATCCGCCGCC
1 T A E T A S A P R A Q S L A F A D P P P
70 80 90 100 110 120
61 GTCCACACCCGCCCGCAGCTCACCATGGATGATGATATCGCCGCGCTCGTCGTCGACAAC
21 V H T R R Q L T M D D D I A A L V V D N
130 140 150 160 170 180
121 GGCTCCGGCATGTGCAAGGCCGGCTTCGCGGGCGACGATGCCCCCGGGCCGTCTTCCCC
41 G S G M C K A G F A G D D A P R A V F P
190 200 210 220 230 240
181 TCCATCGTGGGGCGCCCGAGCACCAGGCGGTGATGGTGGGCATGGTCAGAAGGATTCC
61 S I V G R P R H Q G V M V G M G Q K D S
250 260 270 280 290 300
241 TATGTGGGCGACGAGGCCAGAGCAAGAGAGGCATCCTCACCCCTGAAGTACCCCATCGAG
81 Y V G D E A Q S K R G I L T L K Y P I E
310 320 330 340 350 360
301 CACGGCATCGTCACCAACTGGGACGACATGGAGAAAATCTGGCACCACACCTTCTACAAT
101 H G I V T N W D D M E K I W H H T F Y N
370 380 390 400 410 420
361 GAGCTGCGTGTGGCTCCCGAGGAGCACCCCGTGTGCTGCTGACCGAGGCCCCCTGAACCCC
121 E L R V A P E E H P V L L T E A P L N P
430 440 450 460 470 480
421 AAGGCCAACCGCGAGAAGATGACCCAGATCATGTTTGAGACCTTCAACACCCCGCCATG
141 K A N R E K M T Q I M F E T F N T P A M
490 500 510 520 530 540
481 TACGTTGCTATCCAGGCTGTGCTATCCCTGTACGCTTCTGGCCGTACCACTGGCATCGTG
161 Y V A I Q A V L S L Y A S G R T T G I V
550 560 570 580 590 600
541 ATGGACTCCGGTGACGGGGTCAACCACACTGTGCCCATCTACGAGGGTATGCCCTCCCC
181 M D S G D G V T H T V P I Y E G Y A L P
610 620 630 640 650 660
601 CATGCCATCCTGCGTCTGGACCTGGCTGGCCGGGACCTGACTGACTACCTCATGAAGATC
201 H A I L R L D L A G R D L T D Y L M K I
670 680 690 700 710 720
661 CTCACCGAGCGCGCTACAGCTTACCACACGGCCGAGCGGGAATCGTGCCTGACATT
221 L T E R G Y S F T T T A E R E I V R D I
730 740 750 760 770 780
721 AAGGAGAAGCTGTGCTACGCTCGCCCTGGACTTCGAGCAAGAGATGGCCACGGCTGCTTCC
241 K E K L C Y V A L D F E Q E M A T A A S
790 800 810 820 830 840
781 AGCTCCTCCCTGGAGAAGAGCTACGAGCTGCCTGACGGCCAGGTCATCACCATTGGCAAT
261 S S S L E K S Y E L P D G Q V I T I G N
850 860 870 880 890 900
841 GAGCGTTCCGCTGCCCTGAGGCACTTCCAGCCTTCCTTCCTGGGCATGGAGTCCCTGT
281 E R F R C P E A L F Q P S F L G M E S C
910 920 930 940 950 960
901 GGCATCCACGAAACTACCTTCAACTCCATCATGAAGTGTGACGTGGACATCCGCAAAGAC
301 G I H E T T F N S I M K C D V D I R K D
970 980 990 1000 1010 1020
961 CTGTACGCCAACACAGTGTGCTGTGCGCGCACCACCATGTACCCTGGCATTGCCGACAGG
321 L Y A N T V L S G G T T M Y P G I A D R
1030 1040 1050 1060 1070 1080
1021 ATGCAGAAGGAGATCACTGCCCTGGCACCAGCACAATGAAGATCAAGATCATTTGCTCCT
341 M Q K E I T A L A P S T M K I K I I A P
1090 1100 1110 1120 1130 1140
1081 CCTGAGCGCAAGTACTCCGTGTGGATCGGCGGCTCCATCCTGGCCTCGCTGTCCACCTC
361 P E R K Y S V W I G G S I L A S L S T F
1150 1160 1170 1180 1190 1200
1141 CAGCAGATGTGGATCAGCAAGCAGGAGTATGACGAGTCCGGCCCTCCATCGTCCACCGC
381 Q Q M W I S K Q E Y D E S G P S I V H R
1210 1220 1230 1240 1250 1260
1201 AAATGCTTCTAGGCGGACTATGACTTAGTTCGCTTACACCCCTTTCTTGACAAAACCTAAC
401 K C F *
1270 1280 1290 1300 1310 1320
1261 TTGCGCAGAAAACAAGATGAGATTGGCATGGCTTTATTTGTTTTTTTTTTGTTTTTGG
421
1330 1340 1350 1360 1370 1380
1321 TTTTTTTTTTTTTTTTGGCTTACTCAGGATTTAAAAACTGGAACGGTGAAGGTGACAGC
441
1390 1400 1410 1420 1430 1440
1381 AGTCGGTTGGAGCGAGCATCCCCAAAGTTCACAATGTGGCCGAGGACTTTGATTGCACA
461
1450 1460 1470 1480 1490 1500
1441 TTGTTGTTTTTTTAAATAGTCATTCCAAATATGAGATGCGTTGTTACAGGAAGTCCCTTGC
481 C
1510 1520 1530 1540 1550 1560
1501 CATCCTAAAAGCCACCCACTTCTCTCTAAGGAGAATGGCCAGTCTCTCCCAAGTCCA
501
1570 1580 1590 1600 1610 1620
1561 CACAGGGAGGTGATAGCATTGCTTTCGTGTAATTTATGTAATGCAAAATTTTTTAATC
521
1630 1640 1650 1660 1670 1680

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1621   TTCGCCTTAATACTTTTTTATTTTGTGTTTTATTTTGAATGATGAGCCTTCGTGCCCCCCT
541                                     P
          1690      1700      1710      1720      1730      1740
1681   TCCCCCTTTTTTGTCCCCCAACTTGAGATGTATGAAGGCTTTTGGTCTCCCTGGGAGTGG
561
          1750      1760      1770      1780      1790      1800
1741   GTGGAGGCAGCCAGGGCTTACCTGTACACTGACTTGAGACCAGTTGAATAAAAAGTGCACA
581
          1810      1820      1830      1840      1850
1801   CCTTAAAAATGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
601

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Sequence of ACTB mRNA (NM_001101.3) with chosen editing site (yellow).

10 20 30 40 50 60
1 GTCCCTCAACCAAGATGGCGCGGATGGCTTCAGGCGCATCACGACACCCGGCGCGTCACGCG
1
70 80 90 100 110 120
61 ACCCGCCCTACGGGCACCTCCCGGCTTTTCTTAGCGCCGAGACGGTGGCCGAGCGGGG
20
130 140 150 160 170 180
121 GACCGGGAAGCATGGCCCCGGGGTTCGGCGGTTGCCTGGGCGGCGCTCGGGCCGTTGTTGT
40 M A R G S A V A W A A L G P L L
190 200 210 220 230 240
181 GGGGCTGCGCGCTGGGGCTGAGGGCGGGATGCTGTACCCCGAGGAGCCCGTGGCGGG
60 W G C A L G L Q G G M L Y P Q E S P S R
250 260 270 280 290 300
241 AGTGCAAGGAGCTGGACGGCCTCTGGAGCTTCCGCGCCGACTTCTCTGACAACCGACGCC
80 E C K E L D G L W S F R A D F S D N R R
310 320 330 340 350 360
301 GGGGCTTCGAGGAGCAGTGGTACCAGGCGCGGCTGTGGGAGTACAGCCCCACCGTGGACA
100 R G F E E Q W Y R R P L W E S G P T V D
370 380 390 400 410 420
361 TGCCAGTTCCCTCCAGCTTCAATGACATCAGCCAGGACTGGCGTCTGCGGCATTTTGTGCG
120 M P V P S S F N D I S Q D W R L R H F V
430 440 450 460 470 480
421 GCTGGGTGTGGTACGAACGGGAGTGATCCTGCCGGAGCGATGGACCCAGGACCTGGCGCA
140 G W V W Y E R E V I L P E R W T Q D L R
490 500 510 520 530 540
481 CAAGAGTGGTGTGAGGATTGGCAGTGGCCATTCTATGCCATCGTGTGGGTGAATGGGG
160 T R V V L R I G S A H S Y A I V W V N G
550 560 570 580 590 600
541 TCGACACGCTAGAGCATGAGGGGGCTACCTCCCCTTCGAGGCCGACATCAGCAACCTGG
180 V D T L E H E G G Y L P F E A D I S N L
610 620 630 640 650 660
601 TCCAGTGGGGCCCTGCCCTCCCGGCTCCGAATCACTATCGCCATCAACAACACTCA
200 V Q V G P L P S R L R I T I A I N N T L
670 680 690 700 710 720
661 CCCCCACCCTGCCACGGGACCATCCAATACCTGACTGACACCTCCAAGTATCCCA
220 T P T T L P P G T I Q Y L T D T S K Y P
730 740 750 760 770 780
721 AGGGTTACTTTGTCCAGAACACATATTTGACTTTTCAACTACGCTGGACTGCAGCGGT
240 K G Y F V Q N T Y F D F F N Y A G L Q R
790 800 810 820 830 840
781 CTGTACTTCTGTACACGACCCACCACCTACATCGATGACATCACCGTACCACCAGCG
260 S V L L Y T T P T T Y I D D I T V T T S
850 860 870 880 890 900
841 TGGAGCAAGACAGTGGGCTGGTGAATTACCAGATCTCTGTCAAGGGCAGTAACCTGTTCA
280 V E Q D S G L V N Y Q I S V K G S N L F
910 920 930 940 950 960
901 AGTTGGAAGTGCCTTTTTGGATGCAGAAAACAAAGTCTGGCGAATGGGACTGGGACCC
300 K L E V R L L D A E N K V V A N G T G T
970 980 990 1000 1010 1020
961 AGGGCCAACCTTAAGGTGCCAGGTGTCAGCCTCTGGTGGCCGTACCTGATGCACGAACGCC
320 Q G Q L K V P G V S L W W P Y L M H E R
1030 1040 1050 1060 1070 1080
1021 CTGCCTATCTGTATTTCATTTGGAGGTGCAGCTGACTGCACAGACGCTACTGGGCGCTGTGT
340 P A Y L Y S L E V Q L T A Q T S L G P V
1090 1100 1110 1120 1130 1140
1081 CTGACTTCTACACTCCCTGTGGGATCCGCACTGTGGCTGTCAACAGAGCCAGTTCC
360 S D F Y T L P V G I R T V A V T K S Q F
1150 1160 1170 1180 1190 1200
1141 TCATCAATGGGAACCTTTCTATTTCCACGGTGTCAACAAGCATGAGGATGGGCACATCC
380 L I N G K P F Y F H G V N K H E D A D I
1210 1220 1230 1240 1250 1260
1201 GAGGGAAGGGCTTCGACTGGCCGCTGCTGGTGAAGGACTTCAACCTGCTTCGCTGGCTTG
400 R G K G F D W P L L V K D F N L L R W L
1270 1280 1290 1300 1310 1320
1261 GTGCCAACGCTTTCCGTACCAGCCACTACCCCTATGCAGAGGAAGTATGCAGATGTGTG
420 G A N A F R T S H Y P Y A E E V M Q M C
1330 1340 1350 1360 1370 1380
1321 ACCGCTATGGGATTTGTGGTCATCGATGAGTGTCCCGGCGTGGGCCTGGCGCTGCCGAGT
440 D R Y G I V V I D E C P G V G L A L P Q
1390 1400 1410 1420 1430 1440
1381 TCTTCAACAACGTTTCTCTGCATCACCACATGCAGGTGATGGAAGAAGTGGTGGCTAGGG
460 F F N N V S L H H H M Q V M E E V V R R
1450 1460 1470 1480 1490 #1
1441 ACAAGAACCACCCCGGCTGCTGATGTGGTCTGTGGCCAACGAGCCTGCGTCCCACC TAG
480 D K N H P A V V M W S V A N E P A S H L
1510 1520 1530 1540 1550 1560
1501 AATCTGCTGGCTACTACTGAAGATGGTGTGCTCACACCAAATCCTTGGACCCCTCCC
500 E S A G Y Y L K M V I A H T K S L D P S
1570 1580 1590 1600 1610 1620
1561 GGCCTGTGACCTTTGTGAGCAACTTAACATATGCAGCAGACAAGGGGCTCCGTATGTGG
520 R P V T F V S N S N Y A A D K G A P Y V
1630 1640 1650 1660 1670 1680

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1621 ATGTGATCTGTTTGAACAGCTACTACTCTTGGTATCAGACTACGGGCACCTGGAGTTGA
540 D V I C L N S Y Y S W Y H D Y G H L E L
      1690      1700      1710      1720      1730      1740
1681 TTCAGCTGCAGCTGGCCACCCAGTTTGAGAACTGGTATAAGAAGTATCAGAAGCCCATTA
560 I Q L Q L A T Q F E N W Y K K Y Q K P I
      1750      1760      1770      1780      1790      1800
1741 TTCAGAGCGAGTATGGAGCAGAAACGATTGCAGGGTTTCACCAGGATCCACCTCTGATGT
580 I Q S E Y G A E T I A G F H Q D P P L M
      1810      1820      1830      1840      1850      1860
1801 TCACTGAAGAGTACCAGAAAAAGTCTGCTAGAGCAGTACCATCTGGGTCTGGATCAAAAAC
600 F T E E Y Q K S L L E Q Y H L G L D Q K
      1870      1880      1890      1900      1910      1920
1861 GCAGAAAAATCGTGGTTGGAGAGCTCATTGGAATTTTGCCGATTCATGACTGAACAGT
620 R R K Y V V G E L I W N F A D F M T E Q
      1930      1940      1950      1960      1970      1980
1921 CACCGACGAGAGTCTGGGGAATAAAAAAGGGGATCTTCACTCGGCAGAGACAACCAAAAA
640 S P T R V L G N K K G I F T R Q R Q P K
      1990      2000      2010      2020      2030      2040
1981 GTGCAGCGTTCCTTTTGGCAGAGAGATACTGGAAGATTGCCAATGAAACCAGGTATCCCC
660 S A A F L L R E R Y W K I A N E T R Y P
      #2      2060      2070      2080      2090      2100
2041 ACTCAGTAGCCAAGTCACAATGTTTGGAAAAACAGCCTGTTTACTTGAGCAAGACTGATAC
680 H S V A K S Q C L E N S L F T *
      2110      2120      2130      2140      2150      2160
2101 CACCTGCGTGTCCCTTCCTCCCCGAGTCAGGGCGACTTCCACAGCAGCAGAACAAGTGCC
700
      2170      2180      2190      2200      2210      2220
2161 TCCTGGACTGTTTACGGCAGACCAGAACGTTTCTGGCCTGGGTTTGTGGTCATCTATTC
720
      2230      2240      2250      2260      2270      2280
2221 TAGCAGGGAACACTAAAGGTGGAATAAAAAGATTTTCTATTATGGAATAAAGAGTTGGC
740
      2290      2300      2310      2320
2281 ATGAAAGTGGCTACTGAAAAAAAAAAAAAAAAAAAAAAAAAAAA
760

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Sequence of GUSB mRNA (NM_000181.3) with chosen editing sites (yellow).

```

10      20      30      40      50      60
1      TCCTAGGCGGGCCGCGCGCGGGAGGCGAGCAGCGGGCGCGGCAGTGGCGGGCGGCAAG
1
70      80      90      100     110     120
61     GTGGCGGGGGCTCGGCCAGTACTCCCGGCCCGCCATTTTCGGACTGGGAGCGAGCGGG
21
130     140     150     160     170     180
121    CGCAGGCACTGAAGGCGGGCGGGGCCAGAGGCTCAGCGGCTCCAGGTGCGGGAGAGA
41
190     200     210     target A/1     target 2
181    GGCCTGCTGAAAATGACTGAATATAAACTTGTGGTAGTTGGAGCTGGTGGCGTAGGCAAG
61          M T E Y K L V V V G A G G V G K
250     260     270     280     290     300
241    AGTGCCTTGACGATACAGCTAATTCAGAATCATTGTGGACGAATATGATCCAACAATA
81      S A L T I Q L I Q N H F V D E Y D P T I
310     320     330     340     350     360
301    GAGGATTCCTACAGGAAGCAAGTAGTAATTGATGGAGAAACCTGTCTCTTGATATTCTC
101     E D S Y R K Q V V I D G E T C L L D I L
370     380     390     400     410     420
361    GACACAGCAGGTCAAGAGGAGTACAGTGC AATGAGGGACCAAGTACATGAGGACTGGGGAG
121     D T A G Q E E Y S A M R D Q Y M R T G E
430     440     450     460     470     480
421    GGCTTTCTTTGTGTATTTGCCATAATAATACTAAATCATTGGAAGATATTCACCATTAT
141     G F L C V F A I N N T K S F E D I H H Y
490     500     510     520     530     540
481    AGAGAACAATTAAGAGGTTAAGGACTCTGAAGATGTACCTATGGTCCCTAGTAGGAAAT
161     R E Q I K R V K D S E D V P M V L V G N
550     560     570     580     590     600
541    AAATGTGATTTGCCTTCTAGAACAGTAGACACAAAACAGGCTCAGGACTTAGCAAGAAGT
181     K C D L P S R T V D T K Q A Q D L A R S
610     620     630     640     650     660
601    TATGGAATTCCTTTTATTGAAACATCAGCAAAGACAAGACAGGGTGTGATGATGCCTTC
201     Y G I P F I E T S A K T R Q G V D D A F
670     680     690     700     710     720
661    TATACATTAGTTCGAGAAATTCGAAAACATAAAGAAAAGATGAGCAAAGATGGTAAAAAG
221     Y T L V R E I R K H K E K M S K D G K K
730     740     750     760     770     780
721    AAGAAAAAGAAGTCAAAGACAAAGTGTGTAATTATGTAATAACAATTTGTACTTTTTTCT
241     K K K K S K T K C V I M *
790     800     810     820     830     840
781    TAAGGCATACTAGTACAAGTGGTAATTTTGTACATTACACTAAATTATTAGCATTGT
261

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Sequence of KRAS mRNA (NM_004985.4) with chosen editing sites (yellow).

10 20 30 40 50 60
1 GCTGAGCGCGGAGCCGCCCGGTGATTGGTGGGGGCGGAAGGGGGCCGGCGCCAGCGCTG
1
70 80 90 100 110 120
61 CCTTTTCTCCTGCCGGTAGTTTCGCTTTCCTGCGCAGAGTCTGCGGAGGGGCTCGGCTG
21
130 140 150 160 170 180
121 CACCGGGGGGATCGCGCCTGGCAGACCCAGACCGAGCAGAGGCGACCCAGCGCTCGG
41
190 200 210 220 230 240
181 GAGAGGCTGCACCGCCGCGCCCCGCCTAGCCCTTCCGGATCCTGCGCGCAGAAAAGTTT
61
250 260 270 280 290 300
241 CATTTGCTGTATGCCATCCTCGAGAGCTGTCTAGGTTAACGTTTCGCACTCTGTGTATATA
81
310 320 330 340 350 360
301 ACCTCGACAGTCTTGGCACCTAACGTGCTGTGCGTAGCTGCTCCTTTGGTTGAATCCCCA
101
370 380 390 400 410 420
361 GGCCCTTGTGGGGCACAAGGTGGCAGGATGTCTCAGTGGTACGAACTTCAGCAGCTTGA
121 M S Q W Y E L Q Q L D
421 CTCAAAATTCCTGGAGCAGGTTCCACCAGCTTTATGATGACAGTTCATGGAATCAG
141 S K F L E Q V H Q L Y D D S F P M E I R
481 ACAGTACCTGGCAGAGTGGTTAGAAAAGCAAGACTGGGAGCAGCTGCCAATGATGTTTC
161 Q Y L A Q W L E K Q D W E H A A N D V S
541 ATTTGCCACCATCCGTTTTTCATGACCTCCTGTACAGCTGGATGATCAATATAGTCGCTT
181 F A T I R F H D L L S Q L D D Q Y S R F
601 TTCTTTGGAGAATAAATTCTTGCTACAGCATAACATAAGGAAAAGCAAGCGTAATCTTCA
201 S L E N N F L L Q H N I R K S K R N L Q
661 GGATAATTTTCAGGAAGACCCCAATCCAGATGTCTATGATCATTACAGCTGTCTGAAGGA
221 D N F Q E D P I Q M S M I I Y S C L K E
721 AGAAAGGAAAATTCGAAAACGCCAGAGATTTAATCAGGCTCAGTCGGGGAATATTCA
241 E R K I L E N A Q R F N Q A Q S G N I Q
781 GAGCACAGTGTGTAGACAAAACAGAAAGAGCTTGACAGTAAAGTCAGAAATGTGAAGGA
261 S T V M L D K Q K E L D S K V R N V K D
841 CAAGGTTATGTGTATAGAGCATGAAATCAAGAGCCTGGAAGATTTACAAGATGAATATGA
281 K V M C I E H E I K S L E D L Q D E Y D
901 CTTCAAATGCAAAACCTTGAGAACAGAGAACACGAGACCAATGGTGTGGCAAAGAGTGA
301 F K C K T L Q N R E H E T N G V A K S D
961 TCAGAAAACAAGAAGCAGCTGTACTCAAGAAGATGATTTAATGCTTGACAATAAGAGAAA
321 Q K Q E Q L L L K K M Y L M L D N K R K
1021 GGAAGTAGTTCACAAAATAATAGAGTTGCTGAATGTCACTGAACTTACCCAGAATGCCCT
341 E V V H K I I E L L N V T E L T Q N A L
1081 GATTAATGATGAAGTAGTGGAGTGAAGCGGAGACAGCAGAGCGCTGTATTGGGGGCC
361 I N D E L V E W K R R Q Q S A C I G G P
1141 GCCCAATGCTTGCTTGGATCAGCTGCAGAACTGGTTCACTATAGTTGCGGAGAGTCTGCA
381 P N A C L D Q L Q N W F T I V A E S L Q
1201 GCAAGTTCGGCAGCAGCTTAAAAAGTTGGAGGAATTGGAACAGAAATACACCTACGAACA
401 Q V R Q Q L K K L E E L E Q K Y T Y E H
1261 TGACCCTATCACAAAAACAACAAGTGTATGGGACCGCACCTTCAGTCTTTCCAGCA
421 D P I T K N K Q V L W D R T F S L F Q Q
1321 GCTCATTACAGAGCTCGTTTGGTGGAAAGACAGCCCTGCATGCCAACGCACCCTCAGAG
441 L I Q S S F V V E R Q P C M P T H P Q R
1381 GCCGCTGGTCTTGAAGACAGGGTCCAGTTCAGTGAAGTTGAGACTGTGGTGAATTT
461 P L V L K T G V Q F T V K L R L L V K L
1441 GCAAGAGCTGAATATAATTTGAAAGTCAAAGTCTTATTGATAAAGATGTGAATGAGAG
481 Q E L N Y N L K V K V L F D K D V N E R
1501 AAATACAGTAAAAGGATTTAGGAAGTTCACATTTTGGGCACGCACACAAAAGTATGAA
501 N T V K G F R K F N I L G T H T K V M N
1561 CATGGAGGAGTCCACCAATGGCAGTCTGGCGGCTGAATTCGGCACCTGCAATTGAAAGA
521 M E E S T N G S L A A E F R H L Q L K E
1630 1640 1650 1660 1670 1680

1621 ACAGAAAAATGCTGGCACCAGAACGAATGAGGGTCTCTCATCGTTACTGAAGAGCTTCA
541 Q K N A G T R T N E G P L I V T E E L H
1690 1700 1710 1720 1730 1740
1681 CTCCTTAGTTTTGAAACCAATTGTGCCAGCCTGGTTTGGTAATTGACCTCGAGACGAC
561 S L S F E T Q L C Q P G L V I D L E T T
1750 1760 1770 1780 1790 1800
1741 CTCTCTGCCCGTTGTGGTGATCTCCAACGTCAGCCAGCTCCCGAGCGGTTGGCCTCCAT
581 S L P V V V I S N V S Q L P S G W A S I
1810 1820 1830 1840 1850 1860
1801 CCTTTGGTACAACATGCTGGTGGCGGAACCCAGGAATCTGTCCTTCTTCCCTGACTCCACC
601 L W Y N M L V A E P R N L S F F L T P P
1870 1880 1890 1900 1910 1920
1861 ATGTGCACGATGGGCTCAGCTTTCAGAAGTGCTGAGTTGGCAGTTTTCTTCTGTCCACAA
621 C A R W A Q L S E V L S W Q F S S V T K
1930 1940 1950 1960 1970 1980
1921 AAGAGGTCTCAATGTGGACCAGCTGAACATGTTGGGAGAGAAGCTTCTTGGTCCTAACGC
641 R G L N V D Q L N M L G E K L L G P N A
1990 2000 2010 2020 2030 2040
1981 CAGCCCCGATGGTCTCATTCCGTGGACGAGGTTTTGTAAGGAAAATATAAATGATAAAAA
661 S P D G L I P W T R F C K E N I N D K N
2050 2060 2070 2080 2090 2100
2041 TTTTCCCTTCTGGCTTTGGATTGAAAGCATCCTAGAACTCATTAAAAAACACCTGCTCCC
681 F P F W L W I E S I L E L I K K H L L P
2110 2120 2130 2140 2150 2160
2101 TCTCTGGAATGATGGGTGCATCATGGGCTTCATCAGCAAGGAGCGAGAGCGTGCCTGT
701 L W N D G C I M G F I S K E R E R A L L
2170 2180 2190 2200 2210 2220
2161 GAAGGACCAGCAGCCGGGACCTTCTGCTGCGGTTCAGTGAGAGCTCCCGGGAAGGGGC
721 K D Q Q P G T F L L R F S E S S R E G A
2230 2240 2250 2260 2270 2280
2221 CATCACATTACATGGGTGGAGCGGTCCCAGAACGGAGGCGAACCTGACTTCCATGCGGT
741 I T F T W V E R S Q N G G E P D F H A V
2290 2300 2310 2320 2330 2340
2281 TGAACCTACACGAAGAAGAACTTTCTGCTGTTACTTTCCCTGACATCATTGCAATTA
761 E P Y T K K E L S A V T F P D I I R N Y
2350 2360 2370 2380 2390 2400
2341 CAAAGTCATGGCTGCTGAGAATATTCCTGAGAATCCCCTGAAGTATCTGTATCCAAATAT
781 K V M A A E N I P E N P L K Y L Y P N I
2410 2420 2430 2440 2450 2460
2401 TGACAAAGACCATGCCTTTGGAAAGTATTACTCCAGGCCAAAGGAAGCACCAGAGCCAAT
801 D K D H A F G K Y Y S R P K E A P E P M
2470 2480 2490 2500 2510 2520
2461 GGAACCTGATGGCCCTAAAGGAACGGAATATCAAGACTGAGTTGATTTCTGTGTCTGA
821 E L D G P K G T G Y I K T E L I S V S E
2530 2540 2550 2560 2570 2580
2521 AGTTCACCCTTCTAGACTTCAGACCACAGACAACCTGCTCCCCATGTCTCCTGAGGAGTT
841 V H P S R L Q T T D N L L P M S P E E F
2590 2600 2610 2620 2630 2640
2581 TGACGAGGTGCTCGGATAGTGGGCTCTGTAGAATTCGACAGTATGATGAACACAGTATA
861 D E V S R I V G S V E F D S M M N T V *
2650 2660 2670 2680 2690 2700
2641 GAGCATGAATTTTTTTCATCTTCTCTGGCGACAGTTTTTCTTCTCATCTGTGATTCCCTC
881

Sequence of STAT1 mRNA (NM_007315.3) with chosen editing site Y701 (yellow).