

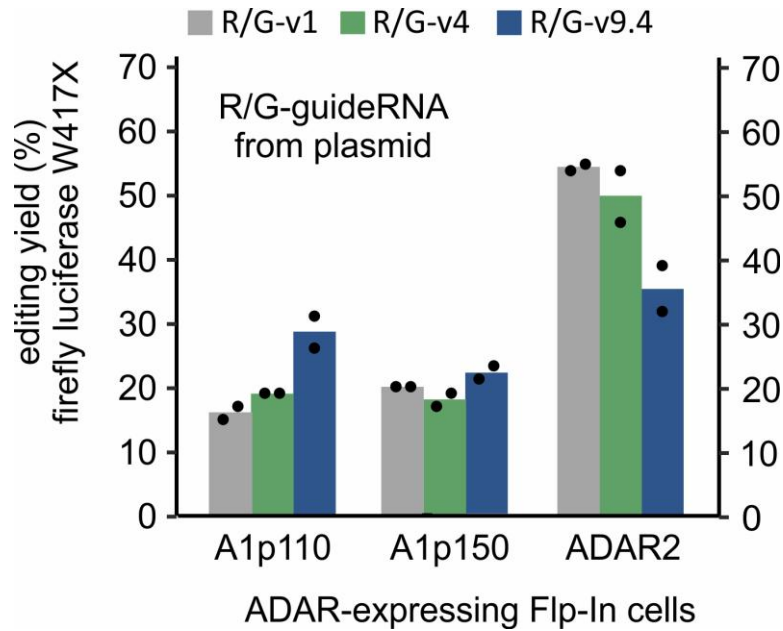
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Precise RNA editing by recruiting endogenous ADARs with antisense oligonucleotides

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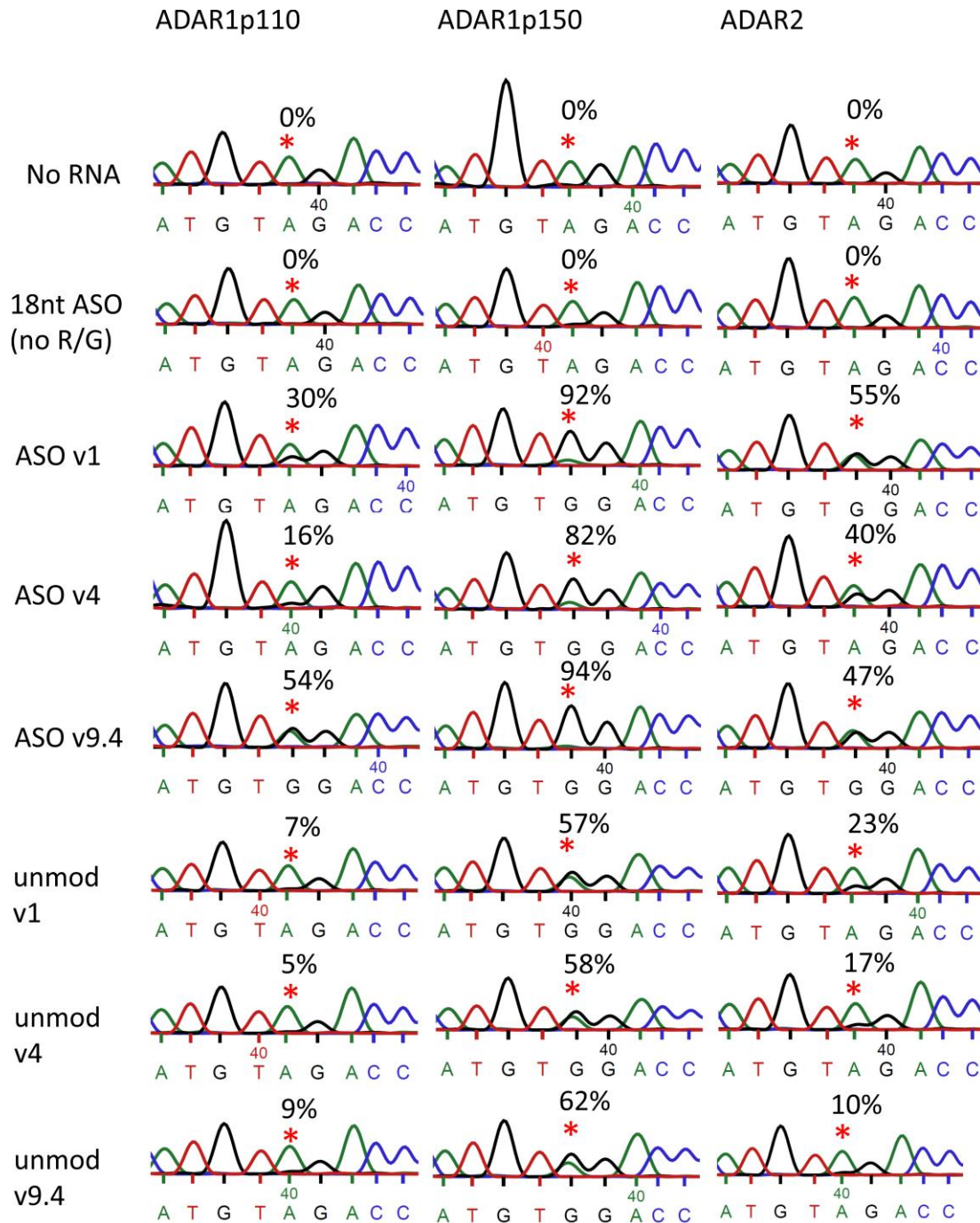
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Supplementary Figure 1

Screening to improve the ADAR-recruiting domain

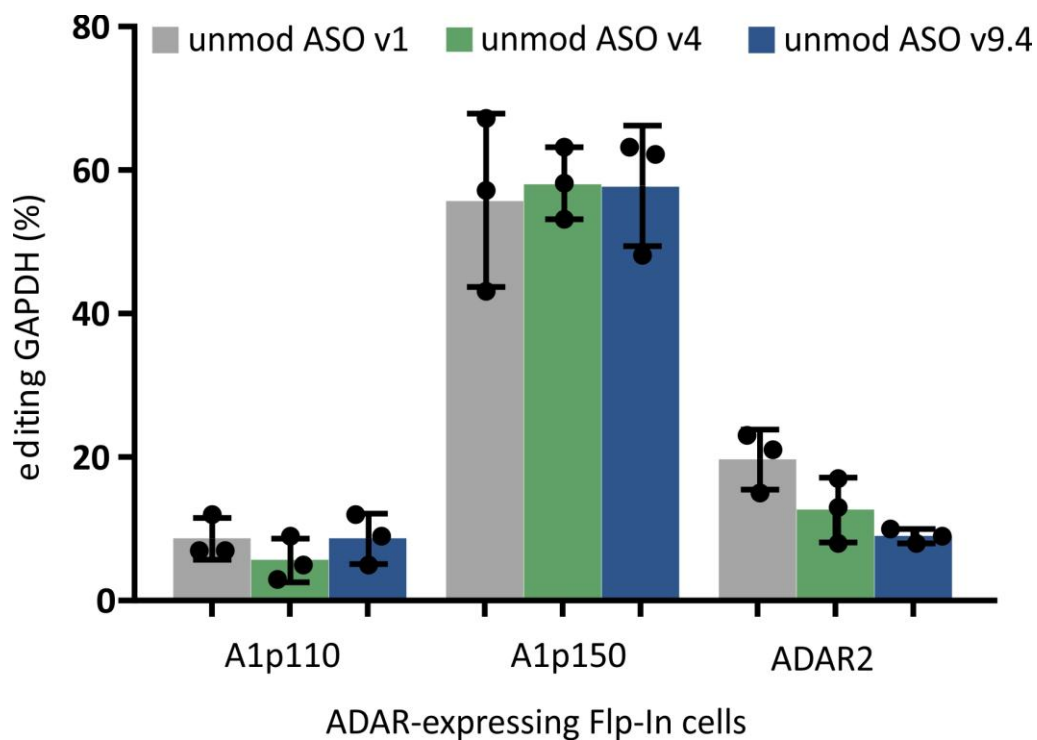
A plasmid borne screening assay was applied to screen for improved ADAR-recruiting domains. For this, plasmids expressing the respective ASO as a chemically unmodified guideRNA from a U6 promotor were prepared. The guide RNA plasmids were co-overexpressed together with a reporter construct (firefly luciferase) in 293 Flp-In T-REx cells expressing a specific ADAR isoform (A1p110 = ADAR1p110; A1p150 = ADAR1p150). Editing yields were determined by Sanger sequencing. Data are shown as the mean $\pm$ SD, N=2 independent experiments



Supplementary Figure 2

Sequencing traces for editing of a 5' UAG site in the 3' UTR of GAPDH in 293 Flp-In T-REx ADAR cells

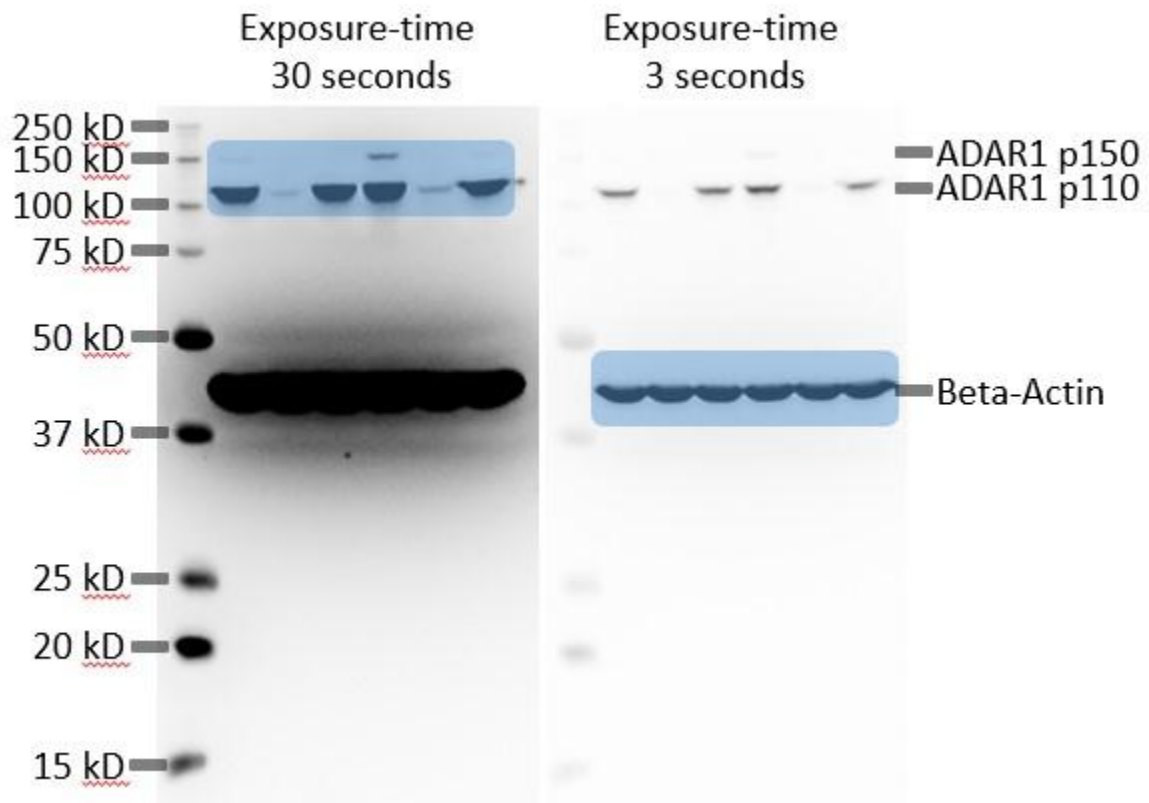
Exemplary editing traces for the editings shown in Figure 1C in the manuscript, but including additional controls ("No RNA" = empty transfection; "18nt ASO no R/G" = ASO lacking the ADAR-recruiting domain; "unmod" means chemically unmodified, *in-vitro* transcribed ASOs of the indicated design v1, v4 or v9.4. Red asterisks indicate the editing sites.



Supplementary Figure 3

Editing yields for targeting a 5' UAG codon in the 3' UTR of *GAPDH* with chemically unmodified, in vitro transcribed ASOs in 293 Flp-In T-REX ADAR cells

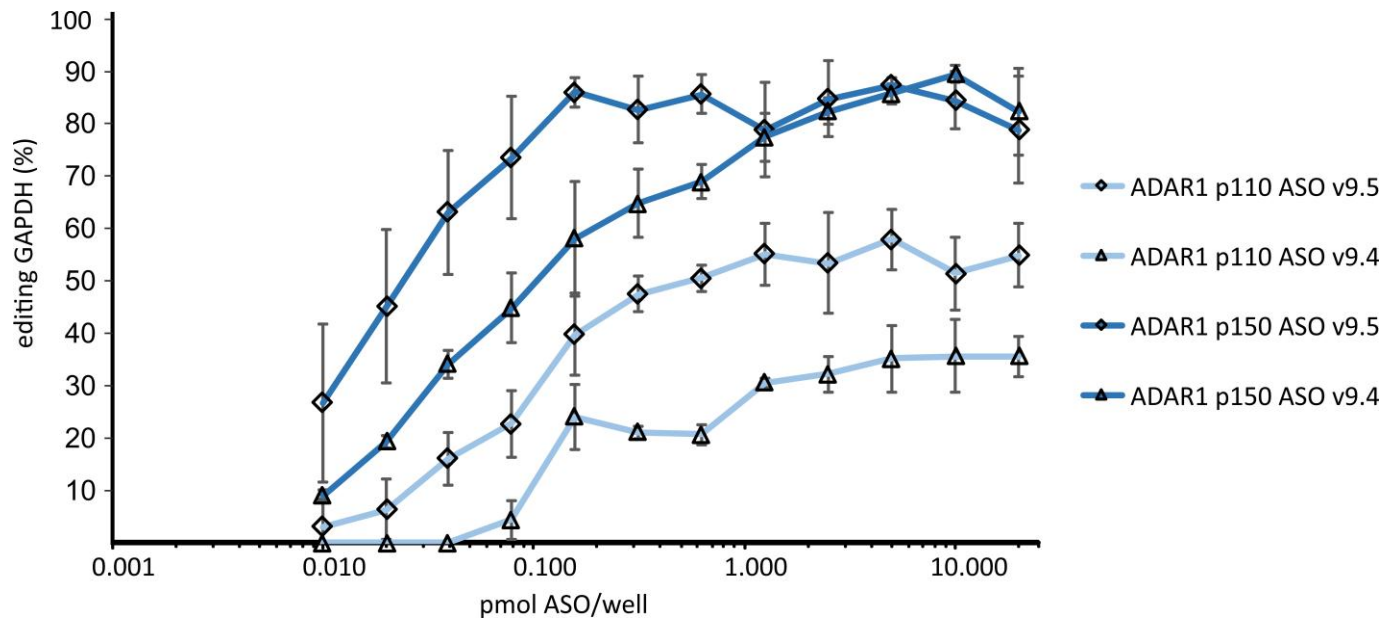
Unmodified *in-vitro* transcribed ASOs v1, v4 and v9.4 (5 pmol / 96well) were transfected into the respective ADAR-expressing Flp-In cell line. Data are shown as the mean $\pm$ SD, N=3 independent experiments. A1p110 = ADAR1p110; A1p150 = ADAR1p150



Supplementary Figure 4

Western blot analysis of ADAR knockdown

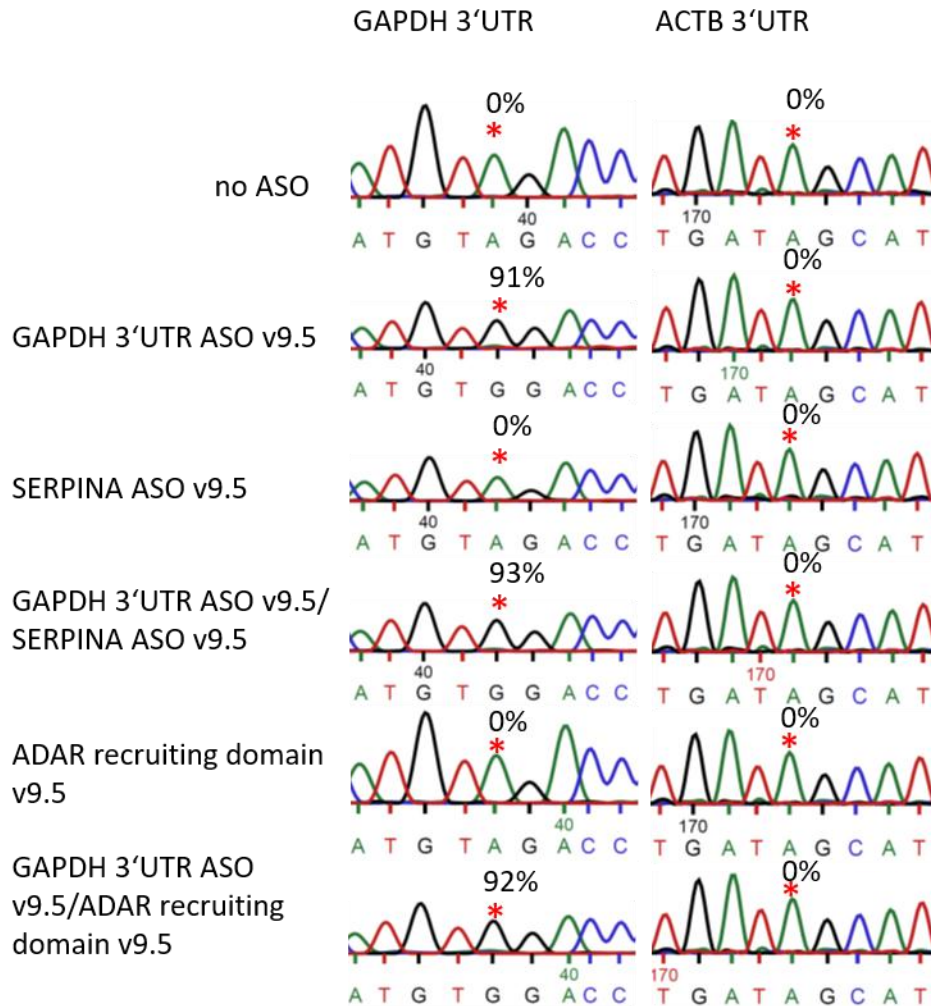
The western blot shown in Figure 2D in the manuscript was merged from images generated with two different exposure times. The part showing the ADAR bands comes from a 30 second exposure. The part showing β -actin from a 3 second exposure. The pictures were captured by the FusionCapt Advance SL4 (16.09b) software installed on the Fusion SL Vilber Lourmat (Vilber) western blot analyzer. No further image processing with respect to contrast or brightness was done. The western blot was done in technical duplicate.



Supplementary Figure 5

Determination of the effective dose (ED_{50}) of the respective ASO for editing *GAPDH* in the respective 293 Flp-In T-REx ADAR cells

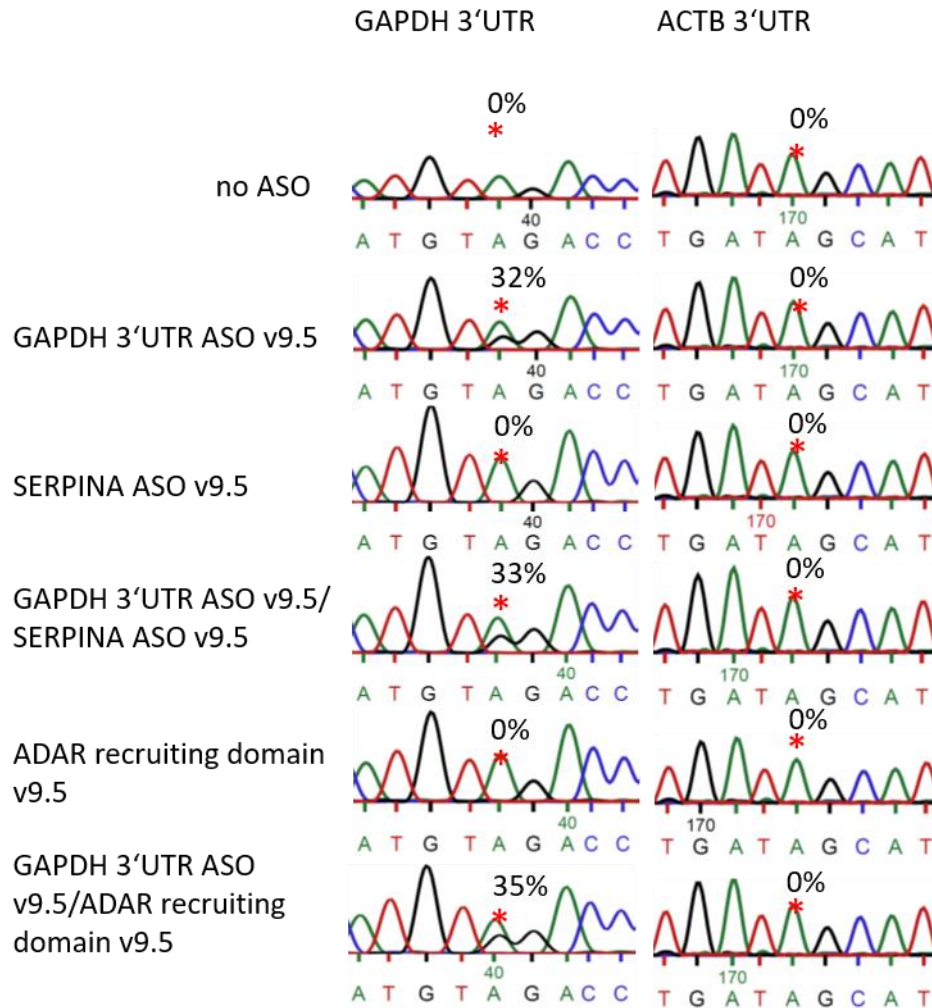
Shown is an experiment completely analog to that shown in the manuscript in Figure 2E, but in the indicated ADAR-expressing 293 Flp-In T-REx cell. Data are shown as the mean $\pm$ SD, N=3 independent experiments.



Supplementary Figure 6

Effect of cotransfection of a nontargeting ASO v9.5 or the chemically stabilized ADAR-recruiting domain v9.5 alone on the *GAPDH* 3'-UTR editing with ASO v9.5 in ADAR1p150-expressing 293 Flp-In T-REx cells

This is an additional control experiment. The on-target is the 5'-UAG codon in the 3'-UTR of *GAPDH*. A surveyed potential off-target is the 5'-UAG site in the 3'-UTR of *ACTB*. *SERPINA* ASO v9.5 acts as a non-targeting control, as the target (*SERPINA1*) is not expressed in this cell line. Another control is the ADAR-recruiting domain v9.5. This is the isolated, chemically stabilized ADAR-recruiting domain lacking any specificity domain. An ASO v9.5 against the on-target was co-transfected with either the non-targeting control or the control lacking a specificity domain. On-target editing requires the presences of the matching ASO. The surveyed potential off-target (*ACTB*) was not edited to detectable level under any condition. The on-target yield was not perturbed by the presence of the non-targeting ASO or the ADAR-recruiting domain alone, suggesting that only the combination of matching specificity and ADAR-recruiting domain enables site-directed RNA editing. It further suggests that the natural editing capacity is not limiting the editing reaction. (5 pmol ASO/96 well have been used)

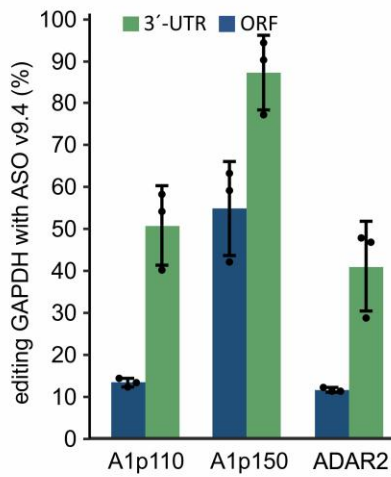


Supplementary Figure 7

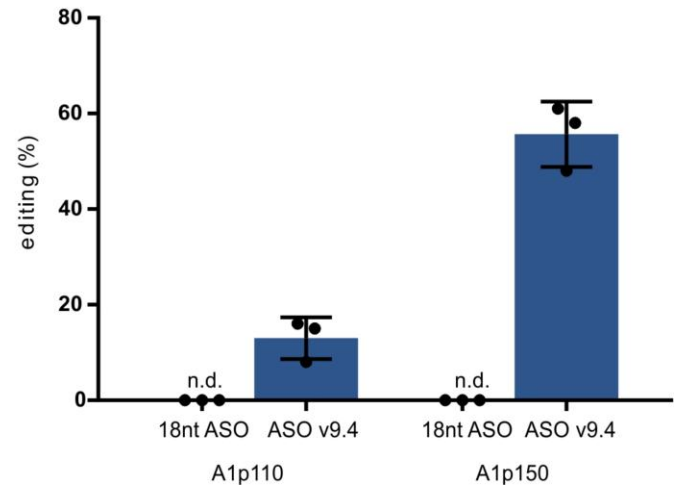
Effect of cotransfection of a nontargeting ASO v9.5 or the chemically stabilized ADAR-recruiting domain v9.5 alone on the *GAPDH* 3'-UTR editing with ASO v9.5, but for the recruitment of endogenous ADAR in HeLa cells without IFN- α .

This control experiment is the exact copy of the experiment shown in the preceding Supplementary Figure but was carried out in HeLa cells, recruiting endogenous ADAR. Exactly the same results have been observed and the same conclusions can be drawn.

A



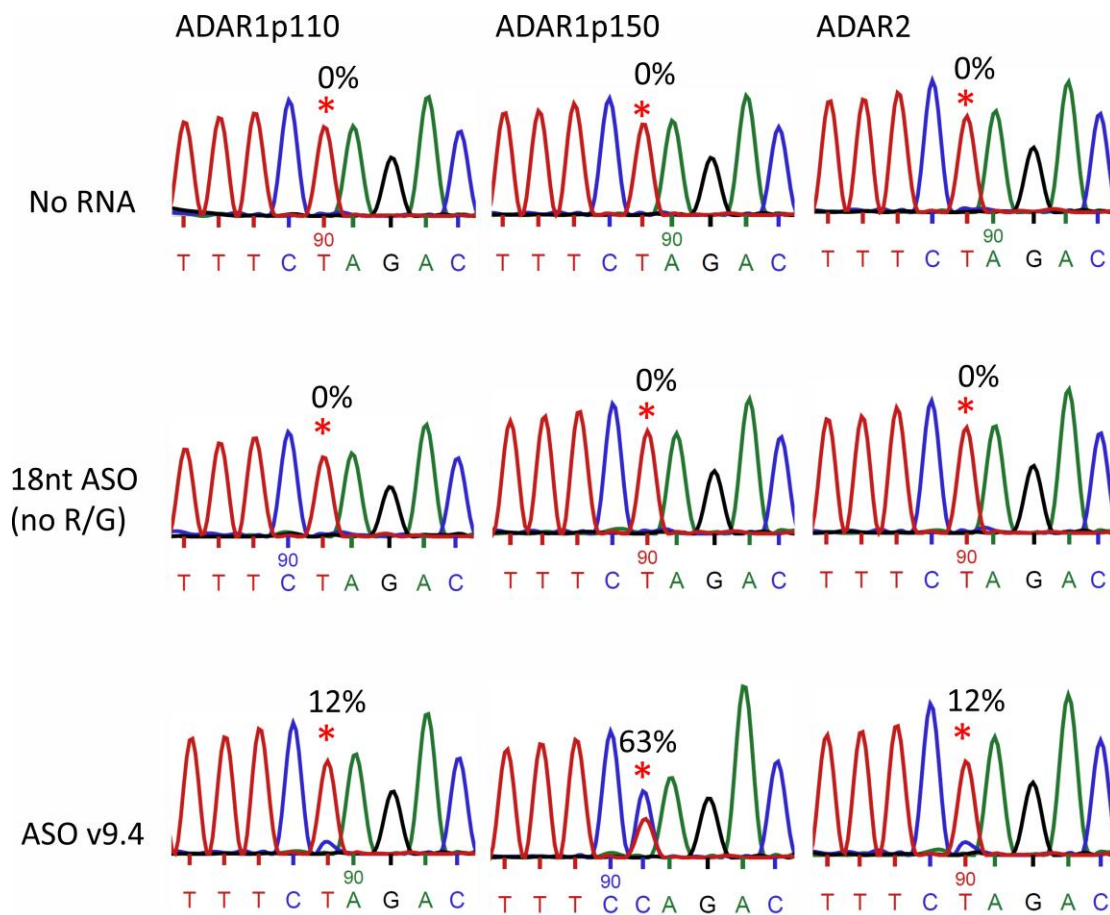
B



Supplementary Figure 8

Editing of 5' UAG codons in the ORF of GAPDH versus 3' UTR in ADAR-expressing 293 Flp-In T-REx cells

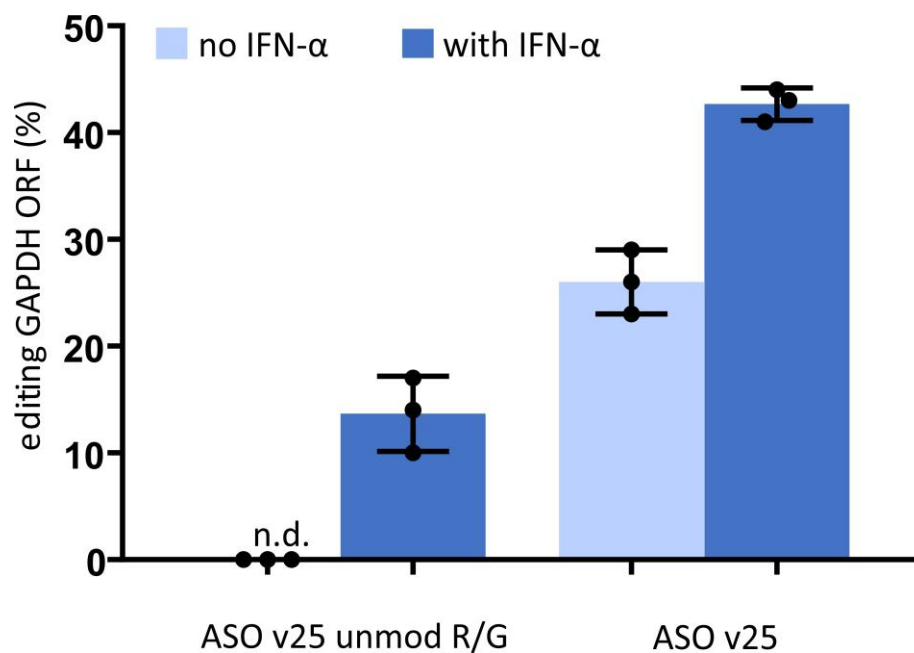
Editing of two different 5'-UAG codons in the ORF of GAPDH in 293 Flp-In T-REx ADAR cells (ORF #1 and #2). A) ORF site #2; here the comparison was made to the editing of the 5'-UAG codon in the 3'-UTR; and all three ADAR-expressing 293 Flp-In T-REx cell lines are included. B) The editing of the ORF site #1 was only tested in ADAR1-expressing Flp-In T-REx cell lines. The results are very similar. Further editing experiments, as shown in Figure 3B, target ORF site #1. Data in A) and B) are shown as the mean $\pm$ SD, N=3 independent experiments. A1p110 = ADAR1p110; A1p150 = ADAR1p150.



Supplementary Figure 9

Sequencing traces for editing of a 5' UAG site (ORF site 2) in the ORF of *GAPDH* in 293 Flp-In T-REx ADAR cells

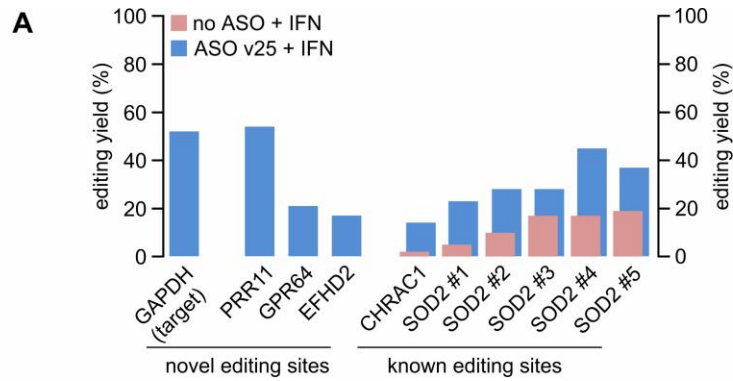
Exemplary editing traces for the editings shown in Supplementary Figure 8A, but including additional controls ("No RNA" = empty transfection; "18nt ASO no R/G" = ASO lacking the ADAR-recruiting domain. Red asterisks indicate the editing sites. A reverse primer was used for sequencing.



Supplementary Figure 10

Editing yields for the editing of a 5' UAG codon in the ORF of *GAPDH* in HeLa cells with ASO v25 containing a chemically unmodified versus modified ADAR-recruiting domain

Here, an ASO v25 with a chemically unmodified ADAR-recruiting domain (unmod R/G), was compared to an ASO of the same sequence with additional chemical modification (all pyrimidine nucleotides in the ADAR-recruiting domain are backbone 2'-O-methylated). ASOs were transfected in HeLa cells. Data are shown as the mean $\pm$ SD, N=3 independent experiments.



B

Edited site	Editing level		Sequence
	ASO v25+IFN	no gRNA+IFN	
GAPDH	53%	0%	CCAACTGCTTAGCACCCCTGGCCAAGGTCATCCATGACAA
PRR11	55%	0%	TGCCAACTCTGCCTCACTCCATGAGATGATCCATACAAATACAGATAAAAAACACCCAGCTGGGTGCAG
GPR64	21%	0%	TGCACCAAGATGTTTGGCTTTTATACCTTGGCCACAGAGAGGGATGAAGTG
EFHD2	17%	0%	GAGACACCGCTGCTTAGCACCCCTCAGCCAGAAACCCCTGAGGGTCTCGGG
CHRC1	14%	2%	ATTTTGTATTTTGTAGACGGGGTTCAACATGTTGGCCAGGCTTGCT
SOD2#1	23%	5%	ATGCTACCATGCCTGGCTACTTTTGTATTTTGGCAGACAGGGTTTCACCATGTTGGCCAGGGTG
SOD2#2	28%	10%	TGGCTCAGCCTCCCAAGTGCTGGGATTACAGGTGTAGCCACTGCACCT
SOD2#3	28%	17%	GGCCAAGGCAGGCCTTGAAGGAGTTCAAGACCAGCTGGCCAACTGGTGAAACCCCTGTCT
SOD2#4	45%	17%	GGCTCAGCCTCCCAAGGTGCTGGGATTACAGGTGTAGCCACTGCACCT
SOD2#5	37%	19%	TGATCCGTCTGGCTCAGCTCCAAAGTGCTGGGATTACAGGTGTAGGCC

C

GAPDH CCAACTGCTTAGCACCCCTGGCCAAGGTCATCCATGACAA

PRR11 TGCCAACTCTGCCTCACTCCATGAGATGATCCATACAAATACAGATAAAAAACACCCAGCTGGGTGCAG

GAPDH CCAACTGCTTAGCAC----CCCTGGCCAAGGTCATCCATG-ACAA

GPR64 TGCACCAAGATGTTTGGCTTTTATACCTTGGCCACAGAGAGGGATGAAGTG

GAPDH CCAACTGCTTAGCACCCCTGGCCAAGGTCATCCATGACAA

EFHD2 GAGACACCGCTGCTTAGCACCCCTCAGCC-AGAACACC-TGAGGGTCTCGGG

GAPDH CCAACTGCTTAG-----CACCC--CTGGCCAAGGTCATCCATGACAA

CHRC1 ATTTTGTATTTTGTAGACGGGGTTCAACATGTTGGCCAGGCTTGCT

GAPDH CCAACTGC--TTAGCACCCCTGGCCAAG-----GTATCCATGACAA

SOD2#1 ATGCTACCATGCCTGGCTACTTTTGTATTTTGGCAGACAGGGTTTCACCATGTTGGCCAGGGTG

GAPDH CCAACTGCTTAGCACCC-----TGGCCAAGGTCATCCATGACAA

SOD2#2 TGGCTCAGCCTCCCAAGTGCTGGGATTACAGGTGTAGCCACTGCACCT

GAPDH CCA-----ACT-----GCTTAGCACC--CTGGCCAAGGTCAT-----CCATGACAA

SOD2#3 GGCCAAGGCAGGCCTTGAAGGAGTTCAAGACCAGCTGGCCAACGTGGTGAAACCCCTGTCT

GAPDH CCAACTGCTTAGCACCC-----TGGCCAAGGTCATCCATGACAA

SOD2#4 GGCTCAGCCTCCCAAGGTGCTGGGATTACAGGTGTAGCCACTGCACCT

GAPDH CCAACTGCTTAGCACCCCTGGCCAAGGT-----CATCCATGACAA

SOD2#5 TGATCCGTCTGGCTCAGCTCCAAAGTGCTGGGATTACAGGTGTAGGCC

D

GAPDH CCAA-----CTGCTTAGCACCC-----

SOD2 nt2100f . AGGAACTCAAGATTCTCCTTTATTTCTGTGCTTGTGGGAATCCCTTGGCACACCCAAAGAGGGG

GAPDH -----TGGCCAAG-GTCATCCATGACAA

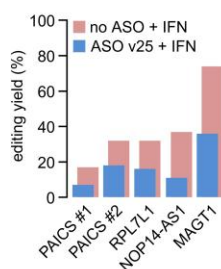
SOD2 nt2100f . TCCCTGCTCCGTCTCACAGGGATCTTTTGTATATTTGGCTTAGCATCATACA-----

Supplementary Figure 11

Analysis of off-target editing sites with increased editing yield upon ASO treatment

A) Besides the targeted site in GAPDH, 9 off-target editing sites were identified in ASO + IFN- α -treated cells compared to the control (no ASO + IFN- α). Six of them (CHARC1, SOD2 #1-#5) were known editing sites and found to be already edited in the control, N=2 independent experiments. **B)** and **C)** The regions around the off-target sites were aligned to the ASO-interacting region (40 nt) of the GAPDH transcript using MUSCLE (ebi.ac.uk/tools/msa/muscle/). The red A indicates the edited site and nucleotides matching to the target sequence of the ASO in GAPDH are highlighted in turquoise. The sequence alignment suggests that the editing at the three novel editing sites (PRR11, GPR64, EFHD2) is clearly induced by misguiding through the ASO. Notably, the strongest off-target (PRR11) might be controllable by further chemical modification of the specificity domain of the ASO. Four of the nine off-target sites (SOD2 #2-5) lack any strong homology to target region, also the edited codon is different from 5'-UAG. This makes it very unlikely that the off-target editing at such sites was induced by the ASO via direct binding to the off-target site, also because those sites all reside in secondary RNA structure (Alu elements). However, we found a potential ASO binding site in the 3'-UTR of SOD2 (panel **D)**) around nt 2100ff. (referring to NM_000636.3) that resides around 300 nt 5' to the first Alu element (nt 2380-2670) and around 1300 nt 5' to the second Alu element (nt 3400-3525). Since all SOD2 off-target sites reside in the two Alu elements one could imagine an ASO-dependent induction of the editing by either increase of the local ADAR concentration or by assisting the formation of an editable RNA secondary structure in the Alu element.

A



B

Edited site	Editing level		Sequence
	ASO v25+IFN	no ASO+IFN	
GAPDH	53%	0%	CCAACTGCTTGCACCCCTGGCCAAGGTCATCCATGACAA
PAICS#1	7%	17%	TAGCTGGGCACAGTGGCTCACACCTTCGATCACAACACTTGGGAGGCTGAAGCAAGCAGATC
PAICS#2	18%	32%	TGACAGGCACCTGTAATCCAGCTACTCGGAGGCTGAGGCATGAGATTGAA
RPL7L1	16%	32%	AGAAATGCTTGAACCCAGGAGGCAGAGGTTGCAGTGAGCCGAGATCACCATTGCACTCCCTTGGGCAACAAAG
NOP14-AS1	11%	37%	ACCAAGCCTGGGCACACAGGAAGACCCCTCTCTACCAGAAAAACATAAAATAGCCAAGTGTGGTGGCAC
MAGT1	36%	74%	GAGGCCAGGAGTTAGAGACCAAGCCTGGCCAAACAGGCAGAACCCCGTCTCTACTAAATATGAAATTAGCTGG

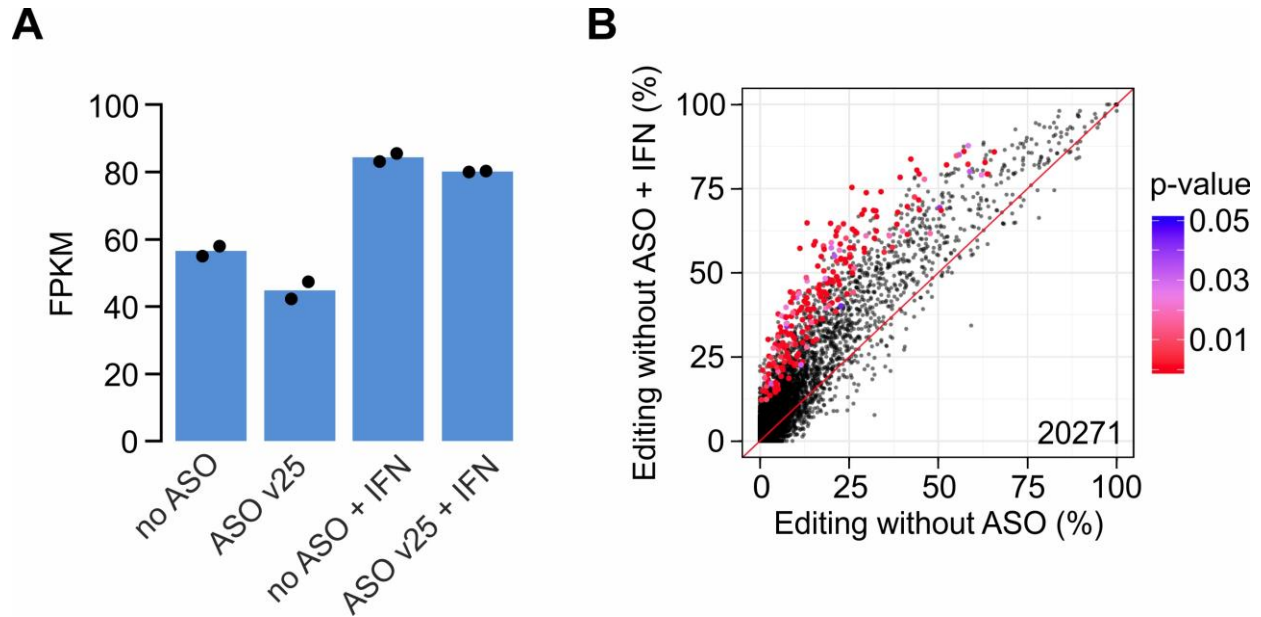
C

GAPDH	CCAACTGCTTGCACCCCTGGCCAAGGTCATCCATGACAA
PAICS#1	TAGCTGGGCACAGTGGCTCACACCTTCGATCACAACACTTGGGAGGCTGAAGCAAGCAGATC
GAPDH	CCAACTGCTTGCACCCCTGGCCAAGGTCATCCATGACAA
PAICS#2	TGACAGGCACCTGTAATCCAGCTACTCGGAGGCTGAGGCATGAGATTGAA
GAPDH	CCAACTGCTTGCACCCCTGGCCAAGGTCATCCATGACAA
RPL7L1	AGAAATGCTTGAACCCAGGAGGCAGAGGTTGCAGTGAGCCGAGATCACCATTGCACTCCCTTGGGCAACAAAG
GAPDH	CCAACTGCTTGCACCCCTGGCCAAGGTCATCCATGACAA
NOP14-AS1	ACCAAGCCTGGGCACACAGGAAGACCCCTCTCTACCAGAAAAACATAAAATAGCCAAGTGTGGTGGCAC
GAPDH	CCAACTGCTTGCACCCCTGGCCAAGGTCATCCATGACAA
MAGT1	GAGGCCAGGAGTTAGAGACCAAGCCTGGCCAAACAGGCAGAACCCCGTCTCTACTAAATATGAAATTAGCTGG

Supplementary Figure 12

Analysis of off-target editing sites with attenuated editing upon ASO treatment

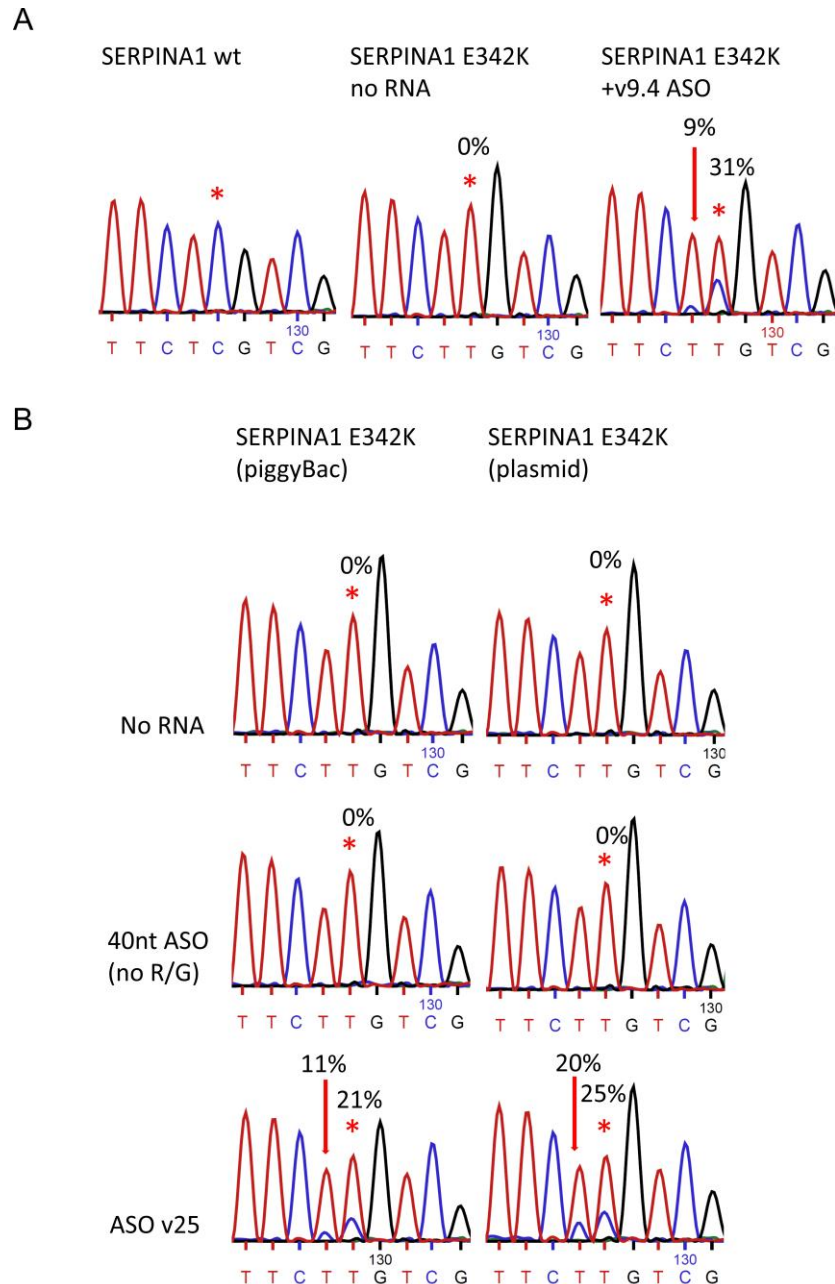
A) Five editing sites, all located in Alu sequences, were found to be significantly less edited in ASO-transfected, IFN- α -treated cells compared to the control lacking ASO transfection (but treated with IFN- α), N=2 independent experiments. **B)** and **C)** The regions around the off-target sites were aligned to the ASO-interacting region (40 nt) of the GAPDH transcript using MUSCLE (ebi.ac.uk/tools/msa/muscle/). The red A indicates the respective edited site and nucleotides matching with the ASO target sequence on GAPDH are highlighted in turquoise. For the most strongly affected site (MAGT1), but also for the other four sites, the ASO seems to be able to bind tightly in proximity to the respective editing sites and therefore interrupt the dsRNA secondary structure of the Alu repeat, which is required for editing. This suggests that the attenuated editing found at those sites is caused by direct interaction of the ASO with the off-target transcript and is not due to a global sequestering of the ADAR enzyme by the ASO.



Supplementary Figure 13

Effect of IFN- α and ASO treatment on ADAR1 expression and the natural editing homeostasis

A) FPKM values describing overall ADAR1 (p110+p150) expression following IFN- α treatment and ASO administration. IFN- α treatment induced ADAR1 expression in HeLa cells in a similar manner independent of ASO transfection. N=2 independent experiments. **B)** Analysis of significantly differently edited sites after IFN- α treatment in HeLa cells (no ASO transfection). Editing appears globally increased following IFN- α treatment. Significance of 20271 edited sites was tested using Fisher's exact test (two-sided, $p < 0.01$, $N \geq 50$); 116 sites were detected as significantly differently edited. The NGS experiment was done in independent duplicate.

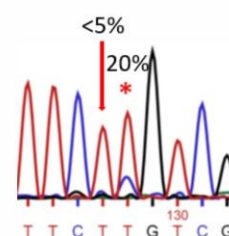
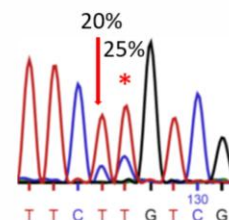
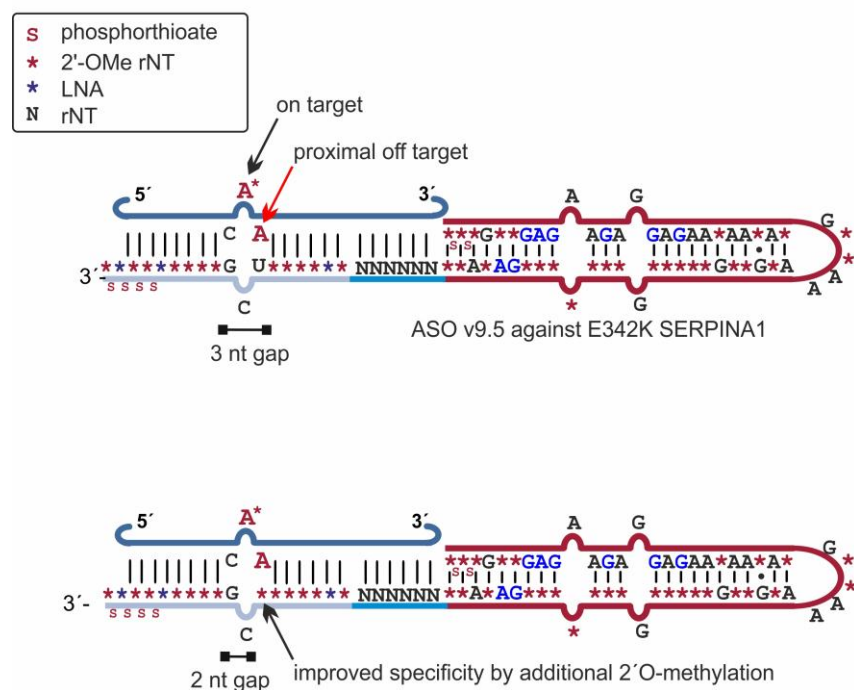


Supplementary Figure 14

Sequencing traces of editing the PiZZ mutation in *SERPINA1*, showing on- and off-target editing in the A-rich 5' CAA codon

Exemplary sequencing traces of the 3 experimental conditions shown in Figure 3E of the manuscript. Red arrows indicate off-target, red asterisks indicate on-target editing sites, a reverse primer was used for sequencing. Shown are additional controls for empty transfection, and for transfecting an ASO lacking the ADAR-recruiting domain (no R/G). A) Editing in ADAR1p150-expressing 293 Flp-In T-REx cells; B) Editing of *SERPINA1* PiZZ in HeLa cells expressing *SERPINA1* PiZZ either genomically integrated (piggyBac) or transiently overexpressed (plasmid). In particular ASO v25 gave substantial off-target editing with the proximal adenosine in the targeted 5'-CAA codon.

editing result



Supplementary Figure 15

Improvement of editing specificity in the ASO:mRNA hybrid

Editing of the 5'-CAA codon to restore the E342K mutation in SERPINA1 (a reverse primer was used here!) comes along with off target editing at the nearest neighboring adenosine (see also preceding Supplementary Figure, panel B). To reduce proximal off-target editing, the 3 nt gap in the modification pattern of the ASO was reduced to a 2 nt gap by putting an additional chemical modification (2'-O-methyl uridine) opposite the off-target nucleotide. Two representative sequencing traces were selected from three very similar replicates which show that the additional chemical modification strongly reduces the proximal off-target edit while only modestly influencing the on target editing. (editing was performed in HeLa cells with SERPINA1 PiZZ cDNA overexpressed from a plasmid, 5 pmol/96 well ASO was transfected)

Supplementary Notes and Tables

Supplementary Table 1: List of guideRNAs, ASOs and further oligonucleotides used in this study.

(N)=RNA base, [N]=2'-OMe RNA base, *=Phosphorothioate linkage, {N}=LNA base.

R/G guide RNAs expressed from plasmid	5'-3' sequence	Figure
Luciferase R/G-v1	(GUGGAAUAGUAUAACAAUAGCUAAAUGUUGUUAUAGUAUCCACGUGCAGC CAGCCGUCCUCUAGAGGGCCUGAAGAGGGCCC)	SI1
Luciferase R/G-v4	(GUGGAAGAGGAGAACAAUAGCUAAAUGUUGUUCUCGUCUCCACGUGCAGC CAGCCGUCCUCUAGAGGGCCUGAAGAGGGCCC)	SI1
Luciferase R/G-v9.4	(GUGGUCGAGAAGAGGAGAACAAUAGCUAAAUGUUGUUCUCGUCUCCUCGAC CACGUGCAGCCAGCCGUCUCUAGAGGGCCUGAAGAGGGCCC)	SI1
Chemically synthesized ASOs	5'-3' sequence	Figure
ACTB 3'UTR 18nt	[GC AAU G] (CCA) [UC AC] [C*][U*][C*][C*][C] Propandiol	2A
ACTB 3'UTR ASO v1	(GGUGA AUAGUAUAC AAUAGCUAA AUGUUGUUAU AGUAUCCACC) [GC AAU G] (CCA) [UC AC] [C*][U*][C*][C*][C] Propandiol	1C,2A
ACTB 3'UTR ASO v4	(GGUGAAG AGGAGAACAA UAUGCUAAA GUUGUUCUCG UCUCACC)[GC AAU G](CCA) [UC AC][C*][U*][C*][C*][C] Propandiol	1C,2A
ACTB 3'UTR ASO v9.4	(GGU GUC GAG AAG AGG AGA AC AAU AUG CUA AAU GUU GUU CUCGUC UCC UCG ACA CC) [GC AAU G] (CCA) [UC AC] [C*][U*][C*][C*][C] Propandiol	1C,2A
GAPDH 3'UTR 18nt	[AG GGG U] (CCA) [CA UG] [G*][C*][A*][A*][C] Propandiol	2A, SI2
GAPDH 3'UTR ASO v1	(GGUGA AUAGUAUAC AAUAGCUAA AUGUUGUUAU AGUAUCCACC) [AG GGG U] (CCA) [CA UG] [G*][C*][A*][A*][C] Propandiol	1C,2A, SI2
GAPDH 3'UTR ASO v4	(GGUGAAG AGGAGAACAA UAUGCUAAA GUUGUUCUCG UCUCACC)[AG GGG U](CCA)[CA UG][G*][C*][A*][A*][C] Propandiol	1C,2A, SI2
GAPDH 3'UTR ASO v9.4	(GGU GUC GAG AAG AGG AGA AC AAU AUG CUA AAU GUU GUU CUCGUC UCC UCG ACA CC) [AG GGG U] (CCA) [CA UG] [G*][C*][A*][A*][C] Propandiol	1C,2A,2B, SI2, SI5
GAPDH 3'UTR ASO v9.5	[G*][G*][U] (G)[U][C] (GAG AAG AGG AGA A)[C] (AA)[U] (A)[U](G) [C][U](A AA)[U] (G)[UU](G)[UUCUC](G)[UCUCCUC](G A)[C](A) [CCAGGGGU] (CCA) [CAUG][G*][C*][A*] [A*][C]	2B, 2C, 2E, 2F, 2G, 2H, SI5, SI6, SI7, SI8A
GAPDH ORF1 ASO 18nt	[GGG GUG] (CCA) [AG CA] [G*][U*][U*][G*][G] Propandiol	SI8B
GAPDH ORF1 ASO v9.4	(GGU GUC GAG AAG AGG AGA AC AAU AUG CUA AAU GUU GUU CUCGUC UCC UCG ACA CC)[GGG GUG](CCA)[AG CA] [G*][U*][U*][G*][G] Propandiol	SI8B
GAPDH ORF2 ASO 18nt	[GGG GUG](CCA)[AG CA] [G*][U*][U*][G*][G] Propandiol	SI9
GAPDH ORF2 ASO v9.4	(GGU GUC GAG AAG AGG AGA AC AAU AUG CUA AAU GUU GUU CUCGUC UCC UCG ACA CC)[GU UUU U] (CCA) [GA CG] [G*][C*][A*][G*][G] Propandiol	SI8A, SI9
GAPDH ORF1 ASO v25	[G*][G*][U] (G)[U][C] (GAG AAG AGG AGA A)[C] (AA) [U] (A)[U](G) [C][U](A AA)[U] (G)[U][U] (G)[U][U] [C][U][C](G)[U][C] [U][C][C] [U][C](G A)[C](A) [C][C] (UUGUCAUGGAUGACCUU GGCCA) [G] {G} [GG UG] (CCA) [AGCA] {G*}[U*][U*]{G*}[G] Aminolinker	3B,3C, SI10-13
GAPDH ORF1 ASO R/G unmod v25	[G*][G*][U] (GUCGAG AAG AGG AGA ACAAUAGCUA AAUGUUGUUCUCGUCUCCUCG ACACC UUGUCAUGGAUGACCUU GGCCA) [G] {G} [GG UG] (CCA) [AGCA] {G*}[U*][U*]{G*}[G] Aminolinker	SI10
SERPINA ASO v9.4	(GGU GUC GAG AAG AGG AGA AC AAU AUG CUA AAU GUU GUU CUCGUC UCC UCG ACA CC) [CCU UUC] (UCG) [UCG A] [U*][G*][G*][U*][C] Propandiol	3E, SI6, SI7, SI14A
SERPINA ASO 40nt	(CAUGGCCCCAGCAGCUUCAGUC) [C] {C}[UUUC] (UCG) [UCGA]{T*}[G*] [G*] {T*} [C] Aminolinker	SI14B
SERPINA ASO v25	[G*] [G*] [U] (G)[U][C] (GAG AAG AGG AGA A)[C] (AA) [U] (A)[U](G) [C][U](A AA)[U] (G)[U][U] (G)[U][U] [C][U][C](G)[U][C] [U][C][C] [U][C](G A C A C C CAUGGCCCCAGCAGCUUCAGUC) [C] {C}[UUUC] (UCG) [UCGA]{T*}[G*] [G*] {T*} [C] Aminolinker	3E, SI14B, SI15
STAT1 ASO v25	[G*] [G*] [U] (G)[U][C] (GAG AAG AGG AGA A)[C] (AA) [U] (A)[U](G) [C][U](A AA)[U] (G)[U][U] (G)[U][U] [C][U][C](G)[U][C] [U][C][C] [U][C](G A C A C C CAUGGCCCCAGCAGCUUCAGUC) [C] {T} [UGAU] (ACA) [UCCA] {G*} [U*] [U*] {C*}[C] Aminolinker	3D
GAPDH 3'UTR unmod ASO v1	(GGUGA AUAGUAUAC AAUAGCUAA AUGUUGUUAU AGUAUCCACC AG GGG UCCACA UG GCAAC)	SI2, SI3
GAPDH 3'UTR unmod ASO v4	(GGUGAAG AGGAGAACAA UAUGCUAAA GUUGUUCUCG UCUCACCAG GGG UCCACA UGGCAAC)	SI2, SI3
GAPDH 3'UTR unmod ASO v9.4	(GGU GUC GAG AAG AGG AGA AC AAU AUG CUA AAU GUU GUU CUCGUC UCC UCG ACA CCAG GGG U CCACA UGGCAAC)	SI2, SI3
SERPINA ASO v25 2nt gap also called ASO v25.1 in Fig. 3E	[G*] [G*] [U] (G)[U][C] (GAG AAG AGG AGA A)[C] (AA) [U] (A)[U](G) [C][U](A AA)[U] (G)[U][U] (G)[U][U] [C][U][C](G)[U][C] [U][C][C] [U][C](G A C A C C CAUGGCCCCAGCAGCUUCAGUC) [C] {C}[UUUCU] (CG) [UCGA]{T*}[G*] [G*] {T*} [C] Aminolinker	3E, SI15
Sense guideRNAs for RT PCR	5'-3' sequence	Figure
GAPDH sense	(GGACCAACUGCUUGGCACCCUGGCCAAGGUCAUCCAUGACAACUUUGGUAUCUGGAAGGACC)	3B, 3C

STAT1 sense	(GGGAACUGGAUCUAUCAAGACUGAGUUGAUUUCUGUGUCUGAAGUGUAAGUGAACACAGAA)	3D
SERPINA1 sense	(GGACCATCGACGAGAAAGGGACTGAAGCTGCTGGGGCCATGTTTTAGAGGCCATACCCAT)	3E,SI14B, SI15

Supplementary Table 2: List of the antibodies used to generate the western blot illustrated in figure 2D.

Antibody	Target Protein	Produced in	Immunoglobulin Class	Dilution used	Supplier	Order #	Against	Validation
ADAR1 antibody	α -ADAR1	Mouse	monoclonal IgG	1:1000	Santa Cruz	sc-73408	amino acids 440-826 corresponding to the middle region of ADAR1 of human origin	Validated in our lab via siRNA KO and Western Blot PMID: # 28669490 PMID: # 28278381 PMID: # 27573237
ADAR2 antibody	α -ADAR2	Mouse	monoclonal IgG	1:1000	Santa Cruz	sc-73409	N-terminal region corresponding to amino acids 2-179 of ADAR2 of human origin	Validated in our lab via overexpression and Western Blot PMID: # 26601943 PMID: # 24345557 PMID: # 27907896
Clone AC-15	α -Beta-Actin	Mouse	monoclonal IgG	1:40.000	Sigma Aldrich	A5441	Actin N-terminal peptide, Ac-Asp-Asp-Asp-Ile-Ala-Ala-Leu-Val-Ile-Asp-Asn-Gly-Ser-Gly-Lys	PMID: # 15809369 PMID: # 15048076 PMID: # 21217779

Supplementary Note 1. List of gene sequences and target sequences

Sequence of dual Luciferase Renilla 2A Firefly W417X reporter cDNA with chosen editing site (Firefly-Luciferase W417X, yellow).

	10	20	30	40	50	60
1	ATGACTTCGAAAGTTTATGATCCAGAACAAAGGAAACGGATGATAACTGGTCCGCAGTGG					
1	M T S K V Y D P E Q R K R M I T G P Q W					
	70	80	90	100	110	120
61	TGGGCCAGATGTAAACAAATGAATGTTCTTGATTCAATTTATTAATTATTATGATTCAGAA					
21	W A R C K Q M N V L D S F I N Y Y D S E					
	130	140	150	160	170	180
121	AAACATGCAGAAAATGCTGTTATTTTTTACATGGTAACGCGGCCTCTTCTTATTTATGG					
41	K H A E N A V I F L H G N A A S S Y L W					
	190	200	210	220	230	240
181	CGACATGTTGTGCCACATATTGAGCCAGTAGCGCGGTGTATTATACCAGACCTTATTGGT					
61	R H V V P H I E P V A R C I I P D L I G					
	250	260	270	280	290	300
241	ATGGGCAAATCAGGCAAATCTGGTAATGGTTCTTATAGGTTACTTGATCATTACAAATAT					
81	M G K S G K S G N G S Y R L L D H Y K Y					
	310	320	330	340	350	360
301	CTTACTGCATGGTTTGAACCTTCTTAATTTACCAAAGAAGATCATTTTTGTGCGCCATGAT					
101	L T A W F E L L N L P K K I I F V G H D					
	370	380	390	400	410	420
361	TGGGGTGCTTGTTGGCATTTCATTATAGCTATGAGCATCAAGATAAGATCAAAGCAATA					
121	W G A C L A F H Y S Y E H Q D K I K A I					
	430	440	450	460	470	480
421	GTTACAGCTGAAAGTGAGTAGATGTGATTGAATCATGGGATGAATGGCCTGATATTGAA					
141	V H A E S V V D V I E S W D E W P D I E					
	490	500	510	520	530	540
481	GAAGATATTGCGTTGATCAAATCTGAAGAAGGAGAAAAAATGGTTTTGGAGAATAACTTC					
161	E D I A L I K S E E G E K M V L E N N F					
	550	560	570	580	590	600
541	TTCGTGGAACCATGTTGCCATCAAAAATCATGAGAAAGTTAGAACCAGAAGAATTTGCA					
181	F V E T M L P S K I M R K L E P E E F A					
	610	620	630	640	650	660
601	GCATATCTTGAACCATTCAAAGAGAAAGGTGAAGTTCGTCGTCACATTATCATGCGCCT					
201	A Y L E P F K E K G E V R R P T L S W P					
	670	680	690	700	710	720
661	CGTGAAATCCCGTTAGTAAAAGGTGGTAAACCTGACGTTGTACAAATTGTTAGGAATTAT					
221	R E I P L V K G G K P D V V Q I V R N Y					
	730	740	750	760	770	780
721	AATGCTTATCTACGTGCAAGTGATGATTTACCAAAAATGTTTATTGAATCGGACCCAGGA					
241	N A Y L R A S D D L P K M F I E S D P G					
	790	800	810	820	830	840
781	TTCTTTTCCAATGCTATTGTTGAAGGTGCCAAGAAGTTTCTAATACTGAATTTGTCAAA					
261	F F S N A I V E G A K K F P N T E F V K					
	850	860	870	880	890	900
841	GTAAAAGGTCTTCATTTTTTCGAAGAAGATGCACCTGATGAAATGGGAAAATATATCAAA					
281	V K G L H F S Q E D A P D E M G K Y I K					
	910	920	930	940	950	960
901	TCGTTCTGTTGAGCGAGTTCTCAAAAATGAACAAGGAAGCGGAGCTACTAATTCAGCCTG					
301	S F V E R V L K N E Q G S G A T N F S L					
	970	980	990	1000	1010	1020
961	CTGAAGCAGGCTGGAGACGTGGAGGAGAACCCTGGACCTATGGAAGATGCCAAAAACATT					

321	L K Q A G D V E E N P G P M E D A K N I
	1030 1040 1050 1060 1070 1080
1021	AAGAAGGGCCAGCGCCATTCTACCCACTCGAAGACGGGACCGCCGGCGAGCAGCTGCAC
341	K K G P A P F Y P L E D G T A G E Q L H
	1090 1100 1110 1120 1130 1140
1081	AAAGCCATGAAGCGCTACGCCCTGGTGCCCGGCACCATCGCCTTTACCGACGCACATATC
361	K A M K R Y A L V P G T I A F T D A H I
	1150 1160 1170 1180 1190 1200
1141	GAGGTGGACATTACCTACGCCGAGTACTTCGAGATGAGCGTTCGGCTGGCAGAAGCTATG
381	E V D I T Y A E Y F E M S V R L A E A M
	1210 1220 1230 1240 1250 1260
1201	AAGCGCTATGGGCTGAATACAAACCATCGGATCGTGGTGTGCAGCGAGAATAGCTTGCAG
401	K R Y G L N T N H R I V V C S E N S L Q
	1270 1280 1290 1300 1310 1320
1261	TTCTTCATGCCCGTGTGGGTGCCCTGTTTCATCGGTGTGGCTGTGGCCCCAGCTAACGAC
421	F F M P V L G A L F I G V A V A P A N D
	1330 1340 1350 1360 1370 1380
1321	ATCTACAACGAGCGCGAGCTGCTGAACAGCATGGGCATCAGCCAGCCCACCGTCGTATTC
441	I Y N E R E L L N S M G I S Q P T V V F
	1390 1400 1410 1420 1430 1440
1381	GTGAGCAAGAAAGGGCTGCAAAAGATCCTCAACGTGCAAAAGAAAGCTACCGATCATACAA
461	V S K K G L Q K I L N V Q K K L P I I Q
	1450 1460 1470 1480 1490 1500
1441	AAGATCATCATGATAGCAAGACCGACTACCAGGGCTTCCAAAGCATGTACACCTTC
481	K I I I M D S K T D Y Q G F Q S M Y T F
	1510 1520 1530 1540 1550 1560
1501	GTGACTTCCCATTTGCCACCCGGCTTCAACGAGTACGACTTCGTGCCCGAGAGCTTCGAC
501	V T S H L P P G F N E Y D F V P E S F D
	1570 1580 1590 1600 1610 1620
1561	CGGGACAAAACCATCGCCTGATCATGAACAGTAGTGGCAGTACCGGATTGCCCAAGGGC
521	R D K T I A L I M N S S G S T G L P K G
	1630 1640 1650 1660 1670 1680
1621	GTAGCCCTACCGACCGCACCCTTGTGTCCGATTAGTCATGCCCGGACCCCATCTTC
541	V A L P H R T A C V R F S H A R D P I F
	1690 1700 1710 1720 1730 1740
1681	GGCAACCAGATCATCCCCGACACCGCTATCCTCAGCGTGGTGCCATTTACCACGGCTTC
561	G N Q I I P D T A I L S V V P F H H G F
	1750 1760 1770 1780 1790 1800
1741	GGCATGTTACACGCTGGGCTACTTGATCTGCGGCTTTGCGGTGCTCATGTACCGC
581	G M F T T L G Y L I C G F R V V L M Y R
	1810 1820 1830 1840 1850 1860
1801	TTCGAGGAGGAGCTATTCTTGCGCAGCTTGCAAGACTATAAGATTCAATCTGCCCTGCTG
601	F E E E L F L R S L Q D Y K I Q S A L L
	1870 1880 1890 1900 1910 1920
1861	GTGCCCACACTATTTAGCTTCTTCGCTAAGAGCACTCTCATCGACAAGTACGACCTAAGC
621	V P T L F S F F A K S T L I D K Y D L S
	1930 1940 1950 1960 1970 1980
1921	AACTTGACGAGATCGCCAGCGGGCGGCGCTCAGCAAGGAGGTAGGTGAGGCCGTG
641	N L H E I A S G G A P L S K E V G E A V
	1990 2000 2010 2020 2030 2040
1981	GCCAAACGCTTCCACCTACCAGGCATCGGCCAGGGCTACGGCTGACAGAAACAACCAGC
661	A K R F H L P G I R Q G Y G L T E T T S
	2050 2060 2070 2080 2090 2100
2041	GCCATTCTGATCACCCCGAAGGGGACGACAAGCCTGGCGCAGTAGGCAAGGTGGTGCCC
681	A I L I T P E G D D K P G A V G K V V P

2101	2110	2120	2130	2140	2150	2160
701	TTCTTCGAGGCTAAGGTGGTGGACTTGGACACCGGTAAGACACTGGGTGTGAACCAGCGC					
	F F E A K V V D L D T G K T L G V N Q R					
2161	2170	2180	2190	2200	2210	2220
721	GGCGAGCTGTGCGTCCGTGGCCCATGATCATGAGCGGCTACGTTAACAACCCGAGGCT					
	G E L C V R G P M I M S G Y V N N P E A					
2221	2230	2240	2250	2260	2270	2280
741	ACAAACGCTCTCATCGACAAGGACGGCTAGCTGCACAGCGGCGACATCGCCTACTGGGAC					
	T N A L I D K D G * L H S G D I A Y W D					
2281	2290	2300	2310	2320	2330	2340
761	GAGGACGAGCACTTCTTCATCGTGGACCGGCTGAAGAGCCTGATCAAATACAAGGGCTAC					
	E D E H F F I V D R L K S L I K Y K G Y					
2341	2350	2360	2370	2380	2390	2400
781	CAGGTAGCCCCAGCCGAAGTGGAGAGCATCCTGCTGCAACACCCCAACATCTTCGACGCC					
	Q V A P A E L E S I L L Q H P N I F D A					
2401	2410	2420	2430	2440	2450	2460
801	GGGGTCGCCGGCTGCCGACGACGATGCCGGCGAGCTGCCGCGCAGTCGTCGTGCTG					
	G V A G L P D D D A G E L P A A V V V L					
2461	2470	2480	2490	2500	2510	2520
821	GAACACGGTAAACCATGACCGAGAAGGAGATCGTGGACTATGTGGCCAGCCAGGTCACA					
	E H G K T M T E K E I V D Y V A S Q V T					
2521	2530	2540	2550	2560	2570	2580
841	ACGCCAAGAAGCTGCGGGTGGTGTGTGTTGTCGTGGACGAGGTGCCTAAAGGACTGACC					
	T A K K L R G G V V F V D E V P K G L T					
2581	2590	2600	2610	2620	2630	2640
861	GGCAAGTTGGACGCCCGCAAGATCCGCGAGATTCTCATTAAAGCCAAGAAGGGCGGCAAG					
	G K L D A R K I R E I L I K A K K G G K					
2641	2650					
881	ATCGCCGTGTAA					
	I A V *					

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

1	10	20	30	40	50	60
1	GCCTCAAGACCTTGGGCTGGGACTGGCTGAGCCTGGCGGGAGGCGGGGTCGAGTACCG					
61	70	80	90	100	110	120
20	CCTGCCGCCGCGCCCCGGTTTCTATAAATTGAGCCGCGAGCCTCCCGCTTCGCTCTCTG					
121	130	140	150	160	170	180
40	CTCCTCTGTTCGACAGTCAGCCGCATCTTCTTTTGCCTCGCCAGCCGAGCCACATCGCT					
181	190	200	210	220	230	240
60	CAGACACCATGGGGAAGGTGAAGGTCGGAGTCAACGGATTTGGTCGTATTGGGCGCCTGG					
	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	TCACCAGGCTGCTTTTAACCTGTTAAAGTGGATATTGTTGCCATCAATGACCCCTTCA					
	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	TTGACCTCAACTACATGGTTTACATGTTCCAATATGATTCCACCCATGGCAAATCCATG					
	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	GCACCGTCAAGGCTGAGAACGGGAAGCTTGTCAATGGAATCCCATCACCATCTTCC					
	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	AGGAGCGAGATCCCTCCAAAATCAAGTGGGGCGATGCTGGCGCTGAGTACGTCGTGGAGT					
	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	CCACTGGCGTCTTCACCACCATGGAGAAGGCTGGGGCTCATTTGCAGGGGGGAGCCAAAA					
	S T G V F T T M E K A G A H L Q G G A K					


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541      550      560      570      580      590      600
180      GGGTCATCATCTCTGCCCCCTCTGCTGATGCCCCCATGTTTCGTCATGGGTGTGAACCATG
      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      ORF site #1
200      AGAAGTATGACAACAGCCTCAAGATCATCAGCAATGCCTCCTGCACCACCAACTGCTTAG
      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      CACCCCTGGCCAAGGTATCCATGACAACCTTTGGTATCGTGAAGGACTCATGACCACAG
      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      ATGGCCGCGGGGCTCTCCAGAACATCATCCCTGCCTCTACTGGCGCTGCCAAGGCTGTGG
      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      GCAAGGTATCCCTGAGCTGAACGGGAAGCTCACTGGCATGGCCTTCCGTGTCCCACTG
      G K V I P E L N G K L T G M A F R V P T
901      910      920      930 ORF site #2      960
300      CCAACGTGTCACTGGTGGACCTGACCTGCCGTCTAGAAAAACCTGCCAAATATGATGACA
      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      TCAAGAAAGTGGTGAAGCGGTGCGAGGGCCCCCTCAAGGGCATCCTGGGCTACACTG
      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      AGCACCAGGTGGTCTCCTCTGACTTCAACAGCGACACCCACTCCTCCACCTTTGACGCTG
      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      CCTGGACCACCAGCCCCAGCAAGAGCACAAGAGGAAGAGAGACCTCACTGCTGGGGA
      1270      1280      1290      1300      1310      3'-UTR site
1261      GTCCCTGCCACACTCAGTCCCCACCACTGAATCTCCCCTCCTCACAGTTGCCATGTA
420
1321      1330      1340      1350      1360      1370      1380
440      GACCCCTTGAAGAGGGGAGGGGCGCTAGGGAGCCGCACCTTGTATGTACCATCAATAAAG
1381      1390      1400      1410      1420
TACCCTGTGCTCAACCAGTTAAAAAAAAAAAAAAAAAAAAA

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Sequence of β -actin mRNA (NM_001101.3) with chosen editing site (yellow).

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1      10      20      30      40      50      60
1      ACCGCCGAGACCGCGTCCGCCCCGCGAGCACAGAGCCTCGCCTTTGCCGATCCGCCGCC
1      T A E T A S A P R A Q S L A F A D P P P
61      70      80      90      100      110      120
21      GTCCACACCCGCCGCCAGCTCACCATGGATGATGATATCGCCGCGCTCGTCGTCGACAAC
      V H T R R Q L T M D D D I A A L V V D N
121      130      140      150      160      170      180
41      GGCTCCGGCATGTGCAAGGCCGGCTTCGCGGGCGACGATGCCCCCGGGCCGTCTTCCC
      G S G M C K A G F A G D D A P R A V F P
181      190      200      210      220      230      240
61      TCCATCGTGGGGCGCCCCAGGCACAGGGCGTGATGGTGGGCATGGGTGAGAAGGATTCC
      S I V G R P R H Q G V M V G M G Q K D S
241      250      260      270      280      290      300
81      TATGTGGGCGACGAGGCCAGAGCAAGAGAGGCATCCTCACCTGAAGTACCCCATCGAG
      Y V G D E A Q S K R G I L T L K Y P I E
301      310      320      330      340      350      360
101      CACGGCATCGTACCAACTGGGACGACATGGAGAAAATCTGGCACCACACCTTCTACAAT
      H G I V T N W D D M E K I W H H T F Y N
361      370      380      390      400      410      420
121      GAGCTGCGTGTGGTCCCCGAGGAGCACCCCGTGCTGCTGACCGAGGCCCCCTGAACCCC
      E L R V A P E E H P V L L T E A P L N P

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421 430 440 450 460 470 480
 AAGGCCAACGCGAGAAGATGACCCAGATCATGTTTGAGACCTTCAACACCCAGCCATG
 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 TACGTTGCTATCCAGGCTGTGCTATCCCTGTACGCCCTTGCCGTACCACTGGCATCGTG
 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 ATGGACTCCGGTGACGGGGTCACCCACACTGTGCCCATCTACGAGGGGTATGCCCTCCCC
 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 CTCACCGAGCGCGGTACAGCTTCACCACCACGGCCGAGCGGGAAATCGTGCCTGACATT
 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 AAGGAGAAGCTGTGCTACGTCGCCCTGGACTTCGAGCAAGAGATGGCCACGGCTGCTTCC
 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 AGCTCCTCCCTGGAGAAGAGCTACGAGCTGCCTGACGGCCAGGTATCACCATTGGCAAT
 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 GAGCGGTTCCGCTGCCCTGAGGCACTTTCCAGCCTTCTTCTGGGCATGGAGTCCTGT
 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 GGCATCCACGAAACTACCTTCAACTCCATCATGAAGTGTGACGTGGACATCCGCAAGAC
 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 CTGTACGCCAACACAGTGTGTCTGGCGGCACCACCATGTACCCTGGCATTGCCGACAGG
 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 ATGCAGAAGGAGATCACTGCCCTGGCACCCAGCACAAATGAAGATCAAGATCATTGCTCCT
 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 CCTGAGCGCAAGTACTCCGTGTGGATCGGCGGCTCCATCCTGGCCTCGTGTCCACCTTC
 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 CAGCAGATGTGGATCAGCAAGCAGGAGTATGACGAGTCCGGCCCCCTCCATCGTCCACCGC
 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 AAATGCTTCTAGGCGGACTATGACTTAGTTGCGTTACACCTTTTCTTGACAAAACCTAAC
 401 K C F *
 1270 1280 1290 1300 1310 1320
 1261 TTGCGCAGAAAACAAGATGAGATTGGCATGGCTTTATTTGTTTTTTTGTGTTTGTGTTGG
 421
 1330 1340 1350 1360 1370 1380
 1321 TTTTTTTTTTTTTTTGGCTTGACTCAGGATTTAAAACTGGAACGGTGAAGGTGACAGC
 441
 1390 1400 1410 1420 1430 1440
 1381 AGTCGGTTGGAGCGAGCATCCCCAAAGTTCACAATGTGGCCGAGGACTTTGATTGCACA
 461
 1450 1460 1470 1480 1490 1500
 1441 TTGTTGTTTTTTTAAATAGTCATTCCAAATATGAGATGCGTTGTACAGGAAGTCCCTTGC
 481 C
 1510 1520 1530 1540 1550 1560
 1501 CATCCTAAAAGCCACCCCACTTCTCTAAGGAGAATGGCCAGTCCTCTCCCAAGTCCA
 501
 1570 3'-UTR site 1600 1610 1620
 1561 CACAGGGGAGGTGATAGCATTGCTTTTCGTGTAATTATGTAATGCAAAATTTTTTAATC
 521
 1630 1640 1650 1660 1670 1680
 1621 TTCGCCTTAATACTTTTTTATTTTGTGTTTATTTTGAATGATGAGCCTTCGTGCCCCCCT
 541 P
 1690 1700 1710 1720 1730 1740
 1681 TCCCCCTTTTTTGTCCCCCAACTTGAGATGTATGAAGGCTTTTGGTCTCCCTGGGAGTGG
 561
 1750 1760 1770 1780 1790 1800
 1741 GTGGAGGCAGCCAGGGCTTACCTGTACACTGACTTGAGACCAGTTGAATAAAAGTGCACA
 581
 1810 1820 1830 1840 1850
 1801 CCTTAAAAATGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
 601

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

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1      10      20      30      40      50      60
1      GCTGAGCGCGGAGCCGCCCGGTGATTGGTGGGGGCGGAAGGGGGCCGGGCGCCAGCGCTG

61      70      80      90      100     110     120
21     CCTTTTCTCCTGCCGGGTAGTTTCGCTTTCTCGCGCAGAGTCTGCGGAGGGGCTCGGCTG

121     130     140     150     160     170     180
41     CACCGGGGGGATCGCGCCTGGCAGACCCAGACCGAGCAGAGGCGACCCAGCGCGCTCGG

181     190     200     210     220     230     240
61     GAGAGGCTGCACCGCCGCGCCCCGCCTAGCCCTTCCGGATCCTGCGCGCAGAAAAGTTT

241     250     260     270     280     290     300
81     CATTTGCTGTATGCCATCCTCGAGAGCTGTCTAGGTTAACGTTTCGCACTCTGTGTATATA

301     310     320     330     340     350     360
101    ACCTCGACAGTCTTGGCACCTAACGTGCTGTGCGTAGCTGCTCCTTTGGTTGAATCCCCA

361     370     380     390     400     410     420
121    GGCCCTTGTGGGGCACAAGGTGGCAGGATGTCTCAGTGGTACGAACTTCAGCAGCTTGA
        M S Q W Y E L Q Q L D

421     430     440     450     460     470     480
141    CTCAAAATTCCTGGAGCAGGTTACCAAGCTTTATGATGACAGTTTTCCCATGGAAATCAG
        S K F L E Q V H Q L Y D D S F P M E I R

481     490     500     510     520     530     540
161    ACAGTACCTGGCAGAGTGGTTAGAAAAGCAAGACTGGGAGCACGCTGCCAATGATGTTTC
        Q Y L A Q W L E K Q D W E H A A N D V S

541     550     560     570     580     590     600
181    ATTTGCCACCATCCGTTTTTCATGACCTCCTGTCACAGCTGGATGATCAATATAGTCGCTT
        F A T I R F H D L L S Q L D D Q Y S R F

601     610     620     630     640     650     660
201    TTCTTTGGAGAATAACTTCTTGCTACAGCATAACATAAGGAAAAGCAAGCGTAATCTTCA
        S L E N N F L L Q H N I R K S K R N L Q

661     670     680     690     700     710     720
221    GGATAATTTTCAGGAAGACCCCAATCCAGATGTCTATGATCATTACAGCTGTCTGAAGGA
        D N F Q E D P I Q M S M I I Y S C L K E

721     730     740     750     760     770     780
241    AGAAAGGAAAAATTCTGGAACGCGCCAGAGATTTAATCAGGCTCAGTCGGGGAATATTCA
        E R K I L E N A Q R F N Q A Q S G N I Q

781     790     800     810     820     830     840
261    GAGCACAGTGATGTTAGACAACAGAAAGAGCTTGACAGTAAAGTCAGAAATGTGAAGGA
        S T V M L D K Q K E L D S K V R N V K D

841     850     860     870     880     890     900
281    CAAGGTTATGTGTATAGAGCATGAAATCAAGAGCCTGGAAGATTTACAAGATGAATATGA
        K V M C I E H E I K S L E D L Q D E Y D

901     910     920     930     940     950     960
301    CTTCAAATGCAAAACCTTGCAGAACAGAGAACACGAGACCAATGGTGTGGCAAAGAGTGA
        F K C K T L Q N R E H E T N G V A K S D

961     970     980     990     1000    1010    1020
321    TCAGAAACAAGAACAGCTGTTACTCAAGAAGATGTATTTAATGCTTGACAATAAGAGAAA
        Q K Q E Q L L L K K M Y L M L D N K R K

1021    1030    1040    1050    1060    1070    1080
341    GGAAGTAGTTTCAAAAATAATAGAGTTGCTGAATGTCACTGAACTTACCCAGAATGCCCT
        E V V H K I I E L L N V T E L T Q N A L

1081    1090    1100    1110    1120    1130    1140
361    GATTAATGATGAAGTGTGAGTGGAGCGGAGACAGCAGAGCGCCTGTATTGGGGGGCC
        I N D E L V E W K R R Q Q S A C I G G P

1141    1150    1160    1170    1180    1190    1200
381    GCCCAATGCTTGTGATCAGCTGCAGAACTGGTTCACTATAGTTGCGGAGAGTCTGCA
        P N A C L D Q L Q N W F T I V A E S L Q

1201    1210    1220    1230    1240    1250    1260
        GCAAGTTCGGCAGCAGCTTAAAAAGTTGGAGGAATTGGAACAGAAATACACCTACGAACA

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401 Q V R Q Q L K K L E E L E Q K Y T Y E H
 1261 1270 1280 1290 1300 1310 1320
 TGACCCCTATCACAAAAACAACAAGTGTATGGGACCGCACCTTCAGTCTTTTCCAGCA
 421 D P I T K N K Q V L W D R T F S L F Q Q
 1330 1340 1350 1360 1370 1380
 1321 GCTCATTGAGCTCGTTTGTGGTGGAAAGACAGCCTGCATGCCAACGCACCCTCAGAG
 441 L I Q S S F V V E R Q P C M P T H P Q R
 1390 1400 1410 1420 1430 1440
 1381 GCCGCTGGTCTTGAAGACAGGGGTCCAGTTCAGTGTGAAGTTGAGACTGTTGGTGAAATT
 461 P L V L K T G V Q F T V K L R L L V K L
 1450 1460 1470 1480 1490 1500
 1441 GCAAGAGCTGAATTATAATTTGAAAGTCAAAGTCTTATTTGATAAAGATGTGAATGAGAG
 481 Q E L N Y N L K V K V L F D K D V N E R
 1510 1520 1530 1540 1550 1560
 1501 AAATACAGTAAAAGGATTTAGGAAGTTCAACATTTTGGGCACGCACACAAAAGTGATGAA
 501 N T V K G F R K F N I L G T H T K V M N
 1570 1580 1590 1600 1610 1620
 1561 CATGGAGGAGTCCACCAATGGCAGTCTGGCGGCTGAATTTGGGCACCTGCAATTGAAAGA
 521 M E E S T N G S L 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 CTCCCTTAGTTTTGAAACCAATTGTGCCAGCCTGGTTTGGTAATTGACCTCGAGACGAC
 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 CTCTCTGCGGTTGTGGTGATCTCCAACGTACGCCAGCTCCCGAGCGGTTGGGCTCCAT
 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 CCTTTGGTACAACATGCTGGTGGCGGAACCCAGGAATCTGTCCTTCTCTGACTCCACC
 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 ATGTGCACGATGGGCTCAGCTTTTCAGAAGTGCTGAGTTGGCAGTTTTCTTCTGTACCAA
 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 AAGAGGTCTCAATGTGGACAGCTGAACATGTTGGGAGAGAAGCTTCTTGGTCTTAACGC
 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 TTTTCCCTTCTGGCTTTGGATTGAAAGCATCCTAGAACTCATTAAAAAACCTGCTCCC
 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 TCTCTGGAATGATGGGTGCATCATGGGCTTCATCAGCAAGGAGCGAGAGCGTGCCCTGTT
 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 GAAGGACAGCAGCGGGGACCTTCTGCTGCGGTTCAAGTGAGAGCTCCCGGGAAGGGGC
 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 TGAACCTACACGAAGAAAGAACTTTCTGCTGTTACTTTCCCTGACATCATTCGCAATTA
 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 TGACAAAGACCATGCCTTTGGAAGTATTACTCCAGGCCAAAGGAAGCACCAGAGCCAAT
 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 GGAACCTGATGGCCCTAAAGGAAGTGGATATCAAGACTGAGTTGATTTCTGTGTCTGA
 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 AGTTACACCTTCTAGACTTCAGACCACAGACAACCTGCTCCCATGTCTCCTGAGGAGTT
 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 TGACGAGGTGTCTCGGATAGTGGGCTCTGTAGAATTCGACAGTATGATGAACACAGTATA
 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 GAGCATGAATTTTTTTCATCTTCTGCGACAGTTTTCTTCTCATCTGTGATTCCTC
 881

Sequence SERPINA1 mature peptide cDNA (NM_001127707.1) with chosen editing site (PiZZ E342K, yellow).

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      10      20      30      40      50      60
1  GAGGATCCCCAGGGAGATGCTGCCCAGAAAGACAGATACATCCCACCATGATCAGGATCAC
1  E D P Q G D A A Q K T D T S H H D Q D H

      70      80      90     100     110     120
61 CCAACCTTCAACAAGATCACCCCAACCTGGCTGAGTTGCGCTTCAGCCTATACGCCAG
21 P T F N K I T P N L A E F A F S L Y R Q

      130     140     150     160     170     180
121 CTGGCACACCACTCCAACAGCACCAATATCTTCTTCTCCCCAGTGAGCATCGCTACAGCC
41 L A H Q S N S T N I F F S P V S I A T A

      190     200     210     220     230     240
181 TTTGCAATGCTCTCCCTGGGGACCAAGGCTGACACTCACGATGAAATCCTGGAGGGCCTG
61 F A M L S L G T K A D T H D E I L E G L

      250     260     270     280     290     300
241 AATTTCAACCTCACGGAGATTCCGGAGGCTCAGATCCATGAAGGCTTCAGGAACCTCTC
81 N F N L T E I P E A Q I H E G F Q E L L

      310     320     330     340     350     360
301 CGTACCCCTCAACCAGCCAGACAGCCAGCTCCAGCTGACCACCGGCAATGGCCTGTTCTCTC
101 R T L N Q P D S Q L Q L T T G N G L F L

      370     380     390     400     410     420
361 AGCGAGGGCCTGAAGCTAGTGGATAAGTTTTTGGAGGATGTTAAAAAGTTGTACCACTCA
121 S E G L K L V D K F L E D V K K L Y H S

      430     440     450     460     470     480
421 GAAGCCTTCACTGTCAACTTCGGGGACACCGAAGAGGCCAAGAAACAGATCAACGATTAC
141 E A F T V N F G D T E E A K K Q I N D Y

      490     500     510     520     530     540
481 GTGGAGAAGGGTACTCAAGGGAAAATTGTGGATTTGGTCAAGGAGCTTGACAGAGACACA
161 V E K G T Q G K I V D L V K E L D R D T

      550     560     570     580     590     600
541 GTTTTTGCTCTGGTGAATTACATCTTCTTTAAAGGCAAATGGGAGAGACCCTTTGAAGTC
181 V F A L V N Y I F F K G K W E R P F E V

      610     620     630     640     650     660
601 AAGGACACCGAGGAAGAGGACTTCCACGTGGACCAGGTGACCACCGTGAAGGTGCCTATG
201 K D T E E E D F H V D Q V T T V K V P M

      670     680     690     700     710     720
661 ATGAAGCGTTTAGGCATGTTTAACATCCAGCACTGTAAGAAGCTGTCCAGCTGGGTGCTG
221 M K R L G M F N I Q H C K K L S S W V L

      730     740     750     760     770     780
721 CTGATGAAATACCTGGGCAATGCCACCGCCATCTTCTTCTGCCTGATGAGGGGAAACTA
241 L M K Y L G N A T A I F F L P D E G K L

      790     800     810     820     830     840
781 CAGCACCTGGAAAATGAACTCACCCACGATATCATACCAAGTTCTGGAAAATGAAGAC
261 Q H L E N E L T H D I I T K F L E N E D

      850     860     870     880     890     900
841 AGAAGGTCTGCCAGCTTACATTTACCCAAACTGTCCATTACTGGAACCTATGATCTGAAG
281 R R S A S L H L P K L S I T G T Y D L K

      910     920     930     940     950     960
901 AGCGTCTCTGGGTCAACTGGGCATCACTAAGGTCTTCAGCAATGGGGCTGACCTCTCCGGG
301 S V L G Q L G I T K V F S N G A D L S G
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	970	980	990	1000	1010	1020
961	GTCACAGAGGAGGCACCCCTGAAGCTCTCCAAGGCCGTGCATAAGGCTGTGCTGACCATC					
321	V T E E A P L K L S K A V H K A V L T I					
	1030	1040	1050	1060	1070	1080
1021	GACAAAGAAAGGGACTGAAGCTGCTGGGGCCATGTTTTTAGAGGCCATACCCATGTCTATC					
341	D K K G T E A A G A M F L E A I P M S I					
	1090	1100	1110	1120	1130	1140
1081	CCCCCGAGGTCAAGTTCAACAAACCCTTTGTCTTCTTAATGATTGAACAAAATACCAAG					
361	P P E V K F N K P F V F L M I E Q N T K					
	1150	1160	1170	1180		
1141	TCTCCCTCTTCATGGGAAAAGTGGTGAATCCACCCAAAAATAA					
381	S P L F M G K V V N P T Q K *					