

A comprehensive survey of 3' animal miRNA modification events and a possible role for 3' adenylation in modulating miRNA targeting effectiveness

A. Maxwell Burroughs^{*^1}, Yoshinari Ando^{^1}, Michiel L. de Hoon¹, Yasuhiro Tomaru¹, Takahiro Nishibu², Ryo Ukekawa², Taku Funakoshi², Tsutomu Kurokawa², Harukazu Suzuki¹, Yoshihide Hayashizaki¹, Carsten O. Daub¹

Supplementary Material

¹-RIKEN Omics Science Center (OSC), RIKEN Yokohama Institute, 1-7-22, Suehiro-cho, Tsurumi-ku, Yokohama-shi, 230-0045, Kanagawa, Japan

²- Wako Pure Chemical Industries, Ltd., 1-2, Doshomachi 3-Chome, Chuo-ku, Osaka 540-8605 Japan

^{*}These authors contributed equally to this work

[^]corresponding authors

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****Due to their size, Supplementary Data S1-S3 are provided as separate files.**

I. Supplementary Discussion

Expression levels of miRNA targets following PAPD4 knockdown

In Fig. 3e, expression levels of miRNA-targeted mRNA transcripts are assessed using qRT-PCR. While we observed a general decrease in mRNA transcripts, the increase in *SMAD1* expression is puzzling, particularly in light of the more direct evidence indicating a decrease in expression in Figure 3d. However, there is considerable potential for conflicting results in this analysis stemming from counteracting downstream effects. For example, if expression of the mRNA of a factor repressing the transcription of *SMAD1* mRNA is reduced through a PAPD4 knockdown-mediated loss of adenine addition to a targeting miRNA this could affect the expression of *SMAD1* in an unanticipated manner. Despite this, we feel Figure 3e does hint at a general trend in reduction of known targets and is therefore of interest. Ideally, a larger sample size of mRNA targets would be tested but in collecting potential targets for testing we are substantially hampered by the lack of experimentally demonstrated targets in which both the miRNA and mRNA are expressed in THP-1 and the fact that the miRNA must belong to the list of miRNA demonstrated to be significantly affected by PAPD4 in THP-1.

To bypass these downstream effects, we directly tested the relationship between PAPD4 knockdown and target expression through a luciferase reporter assay in Figure 3f. These experiments showed a small but consistent decrease in luciferase activity in the PAPD4 condition relative to the normal condition, again suggesting that PAPD4 is involved in modulating the effectiveness of miRNA targeting.

In a related vein, it can be pointed out that target expression in Figure 3e (particularly *CHORDC1* expression) drops much more than would be expected based on the transfection experiments in Figure 3b-d. Again, this is likely related to the observation that a PAPD4 knockdown will affect many miRNA loci at the same time as we have demonstrated in the text. *CHORDC1*, for example, in addition to having three predicted sites for mir-26a binding, has a predicted 7mer targeting site for mir-16 which also displays significantly reduced adenine addition following PAPD4 knockdown. This may indicate that the surprising drops in expression results from the culmination of adenine addition across several miRNA loci.

II. Supplementary Methods

Primer sequences

For quantitative reverse transcription-PCR (qRT-PCR), primer sequences were as follows.

PAPD4-sense 5'-GGAGGACACCTGACCAAAG-3'

PAPD4-antisense 5'-TGATTTGGAGTGAAGGGTGG-3'

PAPD5-sense 5'-TCATGCAATGGAAATGGTGT-3'

PAPD5-antisense 5'-TGGACTGTGTGGCAGAAGAG-3'

PAPD7-sense 5'-CCCACCACTTCCAGAACACT-3'

PAPD7-antisense 5'-GCTTTCAAAGACGCGATTCC-3'

GAPDH-sense 5'-GAAGGTGAAGGTCGGAGT-3'

GAPDH-antisense 5'-GAAGATGGTGATGGGATTTC-3'

ZBTB10-sense 5'-GCTCAGTAATGCAGCCACCT-3'
ZBTB10-antisense 5'-GAAGTACCAGCATCACCTCCA-3'
SMAD1-sense 5'-CTTTCCAGATGCCAGCTGAT-3'
SMAD1-antisense 5'-GCACCAGTGTTTTGGTTCCT-3'
CHORDC1-sense 5'-GTGTTCCGGTCTTTCACGAT-3'
CHORDC1-antisense 5'-AGGTTTGACTGGCTCAGGTG-3'
PER2-sense 5'-TTTGCAGCCCACCCCTGCAC
PER2-antisense 5'-GGTGCTCGTGGGACCCGTTG
CNDP2-sense 5'-TACGGGGGCTCGGTGCATGA
CNDP2-antisense 5'-GCGGCCACGGCCTCGTTAAT
HMGA1-sense 5'-CCTGCCCCTGGGTCGCTCTT
HMGA1-antisense 5'-CCCCGGCTCGGAGTCCCAAT

Sequences of insert regions for CHORDC1 luciferase reporter assay

CHORDC1-miR-26a target site #1: sense 5'-GCTCGCTAGCCTCGAATTCCATAGTTGTGTCCTATACTTGAAGAG-3' and antisense 5'-CGACTCTAGACTCGACTCTTCAAGTATAGGACACAACATATG-3'
CHORDC1-miR-26a target site #2: sense 5'-GCTCGCTAGCCTCGAATTGGAATTTGTTACAACACTACTTGAATTT-3' and antisense 5'-CGACTCTAGACTCGAAAATTCAAGTAGTTGTAAACAAATTC-3'

Phylogenetic Analysis of TRF family

Sequences for the TRF family were identified by searching the non-redundant (nr) database of protein sequences housed at the National Center for Biotechnology Information (NCBI). Iterative sequence profile searches were conducted using the PSI-BLAST program (Altschul et al. 1997) with an inclusion threshold (e-value) of 0.01. The BLASTCLUST (<ftp://ftp.ncbi.nih.gov/blast/documents/blastclust.html>) program was employed for preliminary clustering of the TRF family, using a range of bit score density cutoffs (1–0.4) and length ratios (0.8–0.6). This established the cores of potential TRF subfamilies which were then used to trace their maximum phyletic depth. Multiple sequence alignments of the family were constructed using the MUSCLE program (Edgar 2004). Higher-order relationships between families were determined with through phylogenetic tree-building using neighbor-joining and minimum evolution-based methods with gamma-distributed rates and the JTT substitution matrix as implemented in the MEGA4 software package (Tamura et al. 2007). The shape parameter α was empirically determined through experimental trials. Maximum likelihood trees were also obtained with the least-square method implemented in the FITCH program of the PHYLIP software package (Felsenstein 1996) with subsequent local rearrangement using the PROTML program of the MOLPHY package (Adachi and Hasegawa 1996).

III. Supplementary Figure Legends

Supplementary Figure S1. Comparison of rates of addition with raw expression within a cell type. (a) Complete scatterplots for all cell types, with raw counts plotted on the x-axis and percent addition plotted on the y-axis. (b) Spearman and Pearson correlations and accompanying p-values for

scatterplots in (a). (c) Same scatterplots as in (a), but only containing tag counts under 3000 to provide a detailed picture of the area on the plot where most of the points are located.

Supplementary Figure S2. Stylized phylogenetic tree depicting relationships between subfamilies of the TRF family of non-canonical RNA nucleotidyltransferases. Clades shown are conserved across all methods of phylogenetic tree-building (Supplementary Methods). Sizes of the branches are roughly proportional to the total number of sequences obtained for each subfamily. Newly-discovered families are denoted with a star. Nodes with bootstrap values greater than 70% as calculated by the minimum evolution method in the MEGA4 software package are shown with a yellow circle at the root of the clade.

Supplementary Figures S3-S8. Pairwise plots depicting conservation of unambiguous addition types across control and different nucleotidyltransferase knockdown libraries. Lower left panels plot the percentage of adenine addition at specific loci between libraries, which are labeled on the diagonal panels. Loci with less than fifty sequence tags are excluded. Upper right panels give the correlation coefficient value R between two libraries.

Supplementary Figures S9-S14. Pairwise plots depicting conservation of ambiguous addition types across control and different nucleotidyltransferase knockdown libraries. Lower left panels plot the percentage of adenine addition at specific loci between libraries, which are labeled on the diagonal panels. Loci with less than fifty sequence tags are excluded. Upper right panels give the correlation coefficient value R between two libraries.

Supplementary Figure S15. miRNA expression is unaffected by nucleotidyltransferase knock down. Total sequence tag counts mapping to all miRNA loci compared across control and PAPD4, PAPD5, and PAPD7 knockdown short RNA libraries. Lower left panels compare the total counts between libraries, which are labeled on the diagonal panels. Tag counts are normalized into tags per million (tpm) and $\log_2$ -transformed. Upper right panels give the correlation coefficient value R between two libraries.

Supplementary Figure S16. Luciferase activity of reporter assay with two wildtype 3' UTR miRNA target sequences from *CHORDC1* (see Supplementary Methods above for sequences). Expression is normalized to luciferase activity observed in negative control (see Methods) and tested in normal and PAPD4 knockdown conditions. *P=0.0075, **P=0.013 in normal condition and ***P=0.013 and ****P=0.011 in the PAPD4 knockdown condition (n=5).

Supplementary Figure S17. Check for systematic presence of exonuclease activity in deep sequenced AGO-IP libraries. (a) We counted the number of primary miRNA isomir sequences in each library and also the number of sequences exactly matching the primary sequence but lacking the 3' terminal residue ("minus one" isomir). If exonuclease activity is systematically affecting the AGO-IP libraries, we would expect to see increases in the "minus one" isomir count at the expense of the primary isomir count. Differences in the ratio of the two isomir types are minute, in fact, in two of the libraries the ratio actually decreases very slightly. (b) Comparison of the total tag counts in each library at distinct

nucleotide lengths. All libraries display increase and decrease in a similar manner across different lengths. (c) Percent change in tag counts at specific nucleotide lengths in AGO-IP libraries relative to control library. While modest total expression differences exist in lengths of tags in the AGO-IP libraries relative to the control library, there is no evidence of systematic reduction that would be characteristic of exonuclease activity.

Supplementary Figure S18. Unambiguous addition at the 3' end of precursor miRNA from the FANTOM4 deep-sequenced 42-82bp RNA library. (a) Barplot depicting total number of precursor miRNA loci with at least one tag found in the library alongside total number of precursor miRNA with unambiguous adenine and uridine addition. Raw numbers of loci are given above bars. Loci with addition are listed to the right of the chart. (b) Representative alignment of tags mapping to hsa-mir-223. Despite the lack of counts, 3' addition is still observed.

Supplementary Figure S19. (a) Expression of miRNA loci for compared subsets across multiple human cell lines. "A addition" and "U addition" refers to the subset of miRNA loci identified in Figure 1 with significant amounts of adenine or uridine addition in three of the four human cell lines and mouse ES cells while "lacks A addition" and "lacks U addition" refers to the subset of miRNA loci lacking significant amounts of adenine or uridine addition in three of the four human cell lines and mouse ES cells (see Methods). There is a general trend for the miRNA loci in the former subset to be greater in abundance than miRNA loci in the latter subset. To investigate whether level of abundance could confound the relationship between pairing probability in the 19th position and adenine addition depicted in Figure 6, we probed the relationship between abundance and pairing probability. (The lack of a relationship between adenine addition and abundance is addressed in Supplementary Figure S1). (b) Plotting the pairing probabilities at the 19th position on a dotchart for all miRNA loci reveals two distinct classes of values, those clustered around a value of 1.0 and those clustered around a value of 0.0. This distinction is an intuitive one, as pairing in a duplex structure can be thought of as a largely a binary value (either there is binding or there is no binding) with partial predicted binding occurring much less frequently. (c) Comparison of miRNA expression values for the two classes of pairing probability values indicated no difference in expression values between the two populations, with the p-value from a Wilcoxon rank-sum test across the two classes given in the upper-left hand corner of the boxplot. Expression values were calculated by summing expression across all human tissue types for the miRNA loci in the two classes. A single locus is not shown in the second column (*miR-21-5p*) due to its high expression (893850 tpm). While analysis displayed in Figure 6 compares higher abundance versus lower abundance miRNA loci, we can infer from (c) that pairing probability at the 19th position is not affected by expression. This suggests that in addition to abundance and addition rates, abundance and pairing probability are not influencing each other and the relationship observed between the presence of addition at a loci and pairing probability is likely independent of abundance.

Supplementary Figure S20. No stable interaction observed between PAPD4 and AGO proteins. THP-1 cells were immunoprecipitated with anti-human EIF2C1, anti-human EIF2C2 and anti-human EIF2C3 antibodies. Immunoprecipitated proteins prepared from 3×10^6 cells with each antibody were loaded onto a NuPAGE 4-12% Bis-Tris gel (Invitrogen). On the input (IP) lanes, 5% of the amount of cell lysate

used for IP was loaded. On the flowthrough (FT) lanes, 5% of the amount of flow-through fraction in each IP was loaded. Proteins were analyzed by western blotting with anti-human PAPD4 antibody, and PAPD4 can be observed in the flowthrough lanes. The position of PAPD4 is marked with an arrow on the left-hand side of the figure. The band marked with the asterisk corresponds to the IgG protein.

Supplementary Figure S21. Characterization of immunoprecipitates with anti-EIF2C1, anti-EIF2C2, and anti- EIF2C3 antibodies. THP-1 cells were immunoprecipitated with anti-human EIF2C1, anti-human EIF2C2 and anti-human EIF2C3 antibodies, respectively. Immunoprecipitated proteins prepared from 2×10^6 cells with each antibody were loaded onto a NuPAGE 4-12% Bis-Tris gel (Invitrogen). On the input (IP) lane, 5% of the amount of cell lysate used for IP was loaded. On the flowthrough (FT) lane, 5% of the amount of flow-through fraction in each IP was loaded. Proteins were analyzed by western blotting with each antibody which was different from antibodies used for IP.

IV. Supplementary References

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Table S1. miRNA loci with tissue-shared and tissue-specific significant addition.

shared across all human cell lines, A addition	A addition found in three of four human cell lines	shared across all human cell lines, U addition	U addition found in three of four human cell lines
hsa-let-7b	hsa-let-7d	hsa-miR-101	hsa-let-7e
hsa-let-7g	hsa-let-7e	hsa-miR-140-3p	hsa-let-7i
hsa-let-7i	hsa-let-7f	hsa-miR-148b	hsa-miR-103
hsa-miR-140-5p	hsa-miR-101	hsa-miR-151	hsa-miR-106b
hsa-miR-16	hsa-miR-106b	hsa-miR-152	hsa-miR-107
hsa-miR-17	hsa-miR-148b	hsa-miR-221	hsa-miR-125a
hsa-miR-185	hsa-miR-15b	hsa-miR-24	hsa-miR-140-5p
hsa-miR-191	hsa-miR-152	hsa-miR-25	hsa-miR-148a
hsa-miR-20a	hsa-miR-18a	hsa-miR-26a	hsa-miR-15a
hsa-miR-210	hsa-miR-193b	hsa-miR-26b	hsa-miR-196b
hsa-miR-21	hsa-miR-22	hsa-miR-27a	hsa-miR-203
hsa-miR-24	hsa-miR-222	hsa-miR-27b	hsa-miR-320a
hsa-miR-25	hsa-miR-324-3p	hsa-miR-28-3p	hsa-miR-324-3p
hsa-miR-26a	hsa-miR-339-5p	hsa-miR-342-3p	hsa-miR-484
hsa-miR-26b	hsa-miR-361-5p	hsa-miR-345-5p	hsa-miR-577
hsa-miR-27a	hsa-miR-361-3p	hsa-miR-423-3p	hsa-miR-92b
hsa-miR-28-5p	hsa-miR-378	hsa-miR-425-5p	
hsa-miR-28-3p	hsa-miR-744	hsa-miR-652	
hsa-miR-374a		hsa-miR-99b	
hsa-miR-374b			
hsa-miR-92a			
hsa-miR-93			
hsa-miR-98			
hsa-miR-99b			

A addition mouse-ES	U addition mouse-ES
mmu-miR-101a	mmu-miR-101a
mmu-miR-101b	mmu-miR-101b
mmu-miR-106a	mmu-miR-103
mmu-miR-126-3p	mmu-miR-106a
mmu-miR-127	mmu-miR-106b
mmu-miR-130a	mmu-miR-124
mmu-miR-130b	mmu-miR-126-5p
mmu-miR-140	mmu-miR-126-3p
mmu-miR-142	mmu-miR-127
mmu-miR-15a	mmu-miR-130a
mmu-miR-15b	mmu-miR-130b
mmu-miR-16	mmu-miR-140
mmu-miR-17	mmu-miR-140*
mmu-miR-182	mmu-miR-142-3p
mmu-miR-183	mmu-miR-143
mmu-miR-185	mmu-miR-148a
mmu-miR-186	mmu-miR-148b
mmu-miR-191	mmu-miR-150
mmu-miR-193	mmu-miR-152
mmu-miR-195	mmu-miR-15a
mmu-miR-19a	mmu-miR-181d
mmu-miR-19b	mmu-miR-182
mmu-miR-200b	mmu-miR-183
mmu-miR-205	mmu-miR-18a
mmu-miR-20a	mmu-miR-191
mmu-miR-20b	mmu-miR-200a
mmu-miR-210	mmu-miR-200b
mmu-miR-21	mmu-miR-23b
mmu-miR-22	mmu-miR-24
mmu-miR-23b	mmu-miR-25
mmu-miR-24	mmu-miR-26a
mmu-miR-25	mmu-miR-26b
mmu-miR-26a	mmu-miR-27a
mmu-miR-26b	mmu-miR-27b
mmu-miR-27a	mmu-miR-291a-3p
mmu-miR-290	mmu-miR-292-3p
mmu-miR-291a-5p	mmu-miR-292-5p
mmu-miR-291a-3p	mmu-miR-293
mmu-miR-292-3p	mmu-miR-295
mmu-miR-292-5p	mmu-miR-295*
mmu-miR-293	mmu-miR-298
mmu-miR-294	mmu-miR-300
mmu-miR-295	mmu-miR-302b
mmu-miR-295*	mmu-miR-302c
mmu-miR-296-3p	mmu-miR-30a
mmu-miR-298	mmu-miR-30b
mmu-miR-300	mmu-miR-30c
mmu-miR-30b	mmu-miR-30e
mmu-miR-30c	mmu-miR-322
mmu-miR-322	mmu-miR-324-3p
mmu-miR-33	mmu-miR-331
mmu-miR-34a	mmu-miR-342-3p
mmu-miR-361	mmu-miR-345-3p
mmu-miR-374	mmu-miR-363
mmu-miR-376b	mmu-miR-484
mmu-miR-495	mmu-miR-495
mmu-miR-503	mmu-miR-542
mmu-miR-665	mmu-miR-652
mmu-miR-708	mmu-miR-665
mmu-miR-744	mmu-miR-674
mmu-miR-7a	mmu-miR-708
mmu-miR-805	mmu-miR-708*
mmu-miR-92a	mmu-miR-744
mmu-miR-93	mmu-miR-92b
mmu-miR-96	mmu-miR-99b

A addition chicken-embryo	U addition chicken-embryo
gga-let-7a	gga-let-7f
gga-let-7b	gga-let-7i
gga-let-7c	gga-miR-100
gga-let-7d	gga-miR-101
gga-let-7f	gga-miR-103
gga-let-7g	gga-miR-106
gga-let-7i	gga-miR-106*
gga-let-7j	gga-miR-10a*
gga-let-7k	gga-miR-124a
gga-miR-100	gga-miR-125b*
gga-miR-101	gga-miR-126
gga-miR-10a	gga-miR-126*
gga-miR-122	gga-miR-1306
gga-miR-125b	gga-miR-130b
gga-miR-125b*	gga-miR-135a-1*
gga-miR-126	gga-miR-135a-2*
gga-miR-126*	gga-miR-140
gga-miR-128	gga-miR-140*
gga-miR-130a	gga-miR-1416
gga-miR-130b	gga-miR-144
gga-miR-140	gga-miR-1456
gga-miR-140*	gga-miR-146b
gga-miR-144	gga-miR-1550
gga-miR-1451	gga-miR-1552*
gga-miR-1456	gga-miR-1553
gga-miR-15b	gga-miR-1560
gga-miR-15c	gga-miR-15a
gga-miR-1677	gga-miR-1712
gga-miR-16c	gga-miR-17*
gga-miR-181b-1*	gga-miR-184
gga-miR-184	gga-miR-187
gga-miR-199	gga-miR-187*
gga-miR-200a	gga-miR-196
gga-miR-200b	gga-miR-199
gga-miR-205a	gga-miR-203
gga-miR-206	gga-miR-20b
gga-miR-20a	gga-miR-218
gga-miR-20b	gga-miR-221
gga-miR-21	gga-miR-223
gga-miR-218	gga-miR-24
gga-miR-221	gga-miR-26a
gga-miR-222	gga-miR-30d
gga-miR-222*	gga-miR-30e
gga-miR-23b	gga-miR-375
gga-miR-26a	gga-miR-429
gga-miR-30a*	gga-miR-456
gga-miR-30e*	gga-miR-551
gga-miR-31	gga-miR-9-1*
gga-miR-33	gga-miR-9-2*
gga-miR-375	
gga-miR-449	
gga-miR-455-3p	
gga-miR-460	
gga-miR-499	
gga-miR-9	
gga-miR-92	
gga-miR-99a	

A addition drosophila-head	U addition drosophila-head
dme-bantam	dme-let-7
dme-miR-1	dme-miR-1
dme-miR-100	dme-miR-10
dme-miR-1006	dme-miR-1000
dme-miR-11	dme-miR-1004
dme-miR-125	dme-miR-1006
dme-miR-13a	dme-miR-1012
dme-miR-184	dme-miR-1016
dme-miR-210	dme-miR-11
dme-miR-252	dme-miR-12
dme-miR-263a	dme-miR-133
dme-miR-276a	dme-miR-14
dme-miR-276a*	dme-miR-210
dme-miR-276b*	dme-miR-263a
dme-miR-277	dme-miR-274
dme-miR-278	dme-miR-275*
dme-miR-284	dme-miR-278
dme-miR-285	dme-miR-279
dme-miR-2b	dme-miR-282
dme-miR-304	dme-miR-2b
dme-miR-307	dme-miR-305
dme-miR-316	dme-miR-307
dme-miR-31a	dme-miR-314
dme-miR-33	dme-miR-317
dme-miR-34	dme-miR-31a
dme-miR-34*	dme-miR-34
dme-miR-7	dme-miR-8
dme-miR-8	dme-miR-929*
dme-miR-87	dme-miR-932
dme-miR-8*	dme-miR-957
dme-miR-927*	dme-miR-965
dme-miR-929	dme-miR-970
dme-miR-929*	dme-miR-980
dme-miR-932	dme-miR-986
dme-miR-957	dme-miR-995
dme-miR-971	dme-miR-996
dme-miR-980	dme-miR-999
dme-miR-981	dme-miR-9a
dme-miR-986	
dme-miR-998	
dme-miR-9a	

Table S2. Comparison of percent addition and total counts for miRNA loci in multiple cell lines and organisms.

miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA locus				miRNA 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hsa-miR-27a*	0	429	hsa-miR-21*	0.002683	1118	hsa-miR-29a	0.092404	8939.033	hsa-miR-199a-3p	0.114498	3568.643	mmu-miR-291b-3p	0	279.9827	gga-miR-181b-1*	0.050913	544.6157	dme-miR-927*	0.116564	326
hsa-miR-27b	0	2266.779	hsa-miR-21	0.074289	138714.9	hsa-miR-29a*	0.044444	67.5	hsa-miR-199a-1-5p	0	842.7262	mmu-miR-291b-5p	0.039369	127.0048	gga-miR-181b	0.007474	57172.72	dme-miR-927	0.00033	3033
hsa-miR-28-3p	0.192786	1140.777	hsa-miR-221	0.016964	1296.839	hsa-miR-29b	0.027226	6701	hsa-miR-199a-2-5p	0	844.7262	mmu-miR-292-3p	0.002011	41282.97	gga-miR-181b-2*	0.015625	64	dme-miR-929	0.019712	2080
hsa-miR-28-5p	0.142719	1085.626	hsa-miR-222	0.009379	1705.981	hsa-miR-29c	0.088784	1205.167	hsa-miR-199b-3p	0.114498	1757.571	mmu-miR-292-5p	0.035894	33933.53	gga-miR-184	0.055723	6981	dme-miR-929*	0.253899	1154
hsa-miR-29a	0	2975.5	hsa-miR-22	0.023469	13208.96	hsa-miR-301a	0	4623.563	hsa-miR-19a	0.009339	3426.667	mmu-miR-293	0.003351	56405.78	gga-miR-187	0.005906	508	dme-miR-92a*	0.017094	117
hsa-miR-29a*	0	98	hsa-miR-224*	0	213	hsa-miR-301b	0	115	hsa-miR-19b	0.014585	7125.178	mmu-miR-293*	0.001729	10991.81	gga-miR-187*	0.049536	323	dme-miR-92b	0	52
hsa-miR-29b	0.018748	1338.991	hsa-miR-224	0.028414	1267	hsa-miR-19b-1*	0.015534	1287.5	hsa-miR-200c	0.002345	102779.8	mmu-miR-294	0.002345	102779.8	gga-miR-18a*	0.04918	61	dme-miR-932*	0	94
hsa-miR-29c	0.085932	125.2341	hsa-miR-22*	0	102	hsa-miR-30c	0.007844	892.6	hsa-miR-200c	0.076923	182	mmu-miR-294*	0	2735	gga-miR-18a	0.01039	385	dme-miR-932	0.009938	2415
hsa-miR-301a	0	504.9734	hsa-miR-23a	0.000104	9648.912	hsa-miR-30d	0.012398	2016.5	hsa-miR-203	0	168	mmu-miR-295	0.001487	176863.7	gga-miR-18b*	0	219	dme-miR-956	0	201
hsa-miR-301b	0	172	hsa-miR-23b	0.001703	7046.036	hsa-miR-30e*	0.088816	101.3333	hsa-miR-204	0	52	mmu-miR-295*	0.005359	4664.982	gga-miR-18b	0	1958	dme-miR-957	0.059658	2045
hsa-miR-30a	0.001475	251.9491	hsa-miR-24	0.049228	64745.97	hsa-miR-30e	0.00458	655	hsa-miR-20a*	0	103	mmu-miR-296-3p	0.043213	485.9697	gga-miR-193a	0.014344	488	dme-miR-958	0	457
hsa-miR-30b	0.028226	4464	hsa-miR-24-1*	0	148	hsa-miR-320a	0	1865.5	hsa-miR-20a	0.07814	5912.5	mmu-miR-296-5p	0.007813	767.9835	gga-miR-193a*	0.006221	643	dme-miR-965	0	2174
hsa-miR-30c*	0.081145	73.93726	hsa-miR-24-2*	0.0084	475.9583	hsa-miR-320b	0.028641	199.5143	hsa-miR-210	0.064253	1182.833	mmu-miR-298*	0	69	gga-miR-193b	0.046296	108	dme-miR-965*	0.019417	103
hsa-miR-30c	0.006076	97280.96	hsa-miR-25	0.033532	1848.997	hsa-miR-320b-2*	0.02838	201.3476	hsa-miR-21*	0.023128	908	mmu-miR-298	0.059199	404.9056	gga-miR-196	0.002894	7558.899	dme-miR-969	0	81
hsa-miR-30d	0.005005	28568.01	hsa-miR-26a	0.022785	12950.88	hsa-miR-320c	0.044684	262.1	hsa-miR-214	0.014388	69.5	mmu-miR-299	0.045417	66.05392	gga-miR-199*	0.018758	391931.5	dme-miR-970	0	3501.996
hsa-miR-30e*	0	100.9864	hsa-miR-26b	0.022098	9412.638	hsa-miR-320d	0.002483	131.9135	hsa-miR-214*	0	134	mmu-miR-299	0.018474	378.9203	gga-miR-199	0.006933	6059	dme-miR-971	0.969454	358.9649
hsa-miR-30e	0.003514	390423.8	hsa-miR-27a	0.023652	34625.15	hsa-miR-32*	0	65	hsa-miR-21	0.10272	495212	mmu-miR-29b	0.016204	449.8394	gga-miR-19a	0.010055	596.472	dme-miR-971*	0	54
hsa-miR-320a	0	4809.793	hsa-miR-27a*	0.003521	284	hsa-miR-324-3p	0.215455	102.1095	hsa-miR-218	0	396.6667	mmu-miR-29c	0.018987	158	gga-miR-19a*	0.017857	56	dme-miR-980	0.027457	692
hsa-miR-324-3p	0.120799	173.7853	hsa-miR-27b	0	12335.61	hsa-miR-324-5p	0	451	hsa-miR-219-5p	0	58	mmu-miR-300	0.112756	283.7975	gga-miR-19b	0.008856	10613.77	dme-miR-981	0.061988	3662
hsa-miR-324-5p	0	54	hsa-miR-27b*	0	144	hsa-miR-32	0	1457.361	hsa-miR-221	0.00011	9091.875	mmu-miR-301a	0	3105.747	gga-miR-1a	0.002865	708502.9	dme-miR-986	0.016858	1305
hsa-miR-32	0	1744.905	hsa-miR-28-3p	0.112875	645.5842	hsa-miR-331-3p	0.158491	530	hsa-miR-221*	0	131.2	mmu-miR-301b	0	952.9152	gga-miR-1b	0.003642	18945.75	dme-miR-987	0.001259	7149
hsa-miR-326	0.116804	136.9819	hsa-miR-28-5p	0.086734	1358.378	hsa-miR-335*	0	106.5	hsa-miR-222	0.003872	14202.83	mmu-miR-302a	0	92	gga-miR-200a	0.034601	2919	dme-miR-988	0.007143	280
hsa-miR-328	0.057693	51.99973	hsa-miR-296-3p	0.043956	91	hsa-miR-335	0	512.5	hsa-miR-22	0.008244	22926.67	mmu-miR-302b	0	240	gga-miR-200b	0.035762	2265	dme-miR-988*	0	253
hsa-miR-330-3p	0.023806	167.5068	hsa-miR-296-5p	0	138.9979	hsa-miR-338-5p	0.341463	82	hsa-miR-22*	0.066282	347	mmu-miR-302c	0.035714	56	gga-miR-200b*	0.036616	81.93124	dme-miR-990	0.020548	146
hsa-miR-335	0	204.9305	hsa-miR-29a	0	8059.981	hsa-miR-339-3p	0.030581	327	hsa-miR-23a	0.000145	6892.719	mmu-miR-302d	0	389	gga-miR-202	0.028169	70.99942	dme-miR-993	0	974
hsa-miR-338-3p	0	275.555	hsa-miR-29a*	0.004855	205.9569	hsa-miR-339-5p	0.036972	121.7143	hsa-miR-23b	0.029193	1918.25	mmu-miR-30a	0.016612	601.9728	gga-miR-202*	0.00891	448.9327	dme-miR-993*	0	110
hsa-miR-338-5p	0	52	hsa-miR-29b	0.011382	7499.807	hsa-miR-33a	0.147494	433.9167	hsa-miR-24	0.032787	37758.92	mmu-miR-30b	0.017226	1044.95	gga-miR-203	0	12298	dme-miR-995	0.006008	1498
hsa-miR-339-3p	0.049296	1420	hsa-miR-29c	0	456.4933	hsa-miR-33b	0	426.4762	hsa-miR-24*	0	60	mmu-miR-30c	0.028556	1890.484	gga-miR-204*	0.059259	134.9995	dme-miR-996	0	4988
hsa-miR-339-5p	0.071568	697.1634	hsa-miR-29c*	0	52	hsa-miR-340	0.0125	1520	hsa-miR-24*	0.006098	164	mmu-miR-30c-2*	0	58	gga-miR-204	0.002885	2950.067	dme-miR-996*	0	232
hsa-miR-33a	0	1493.718	hsa-miR-301a	0	2297.798	hsa-miR-342-3p	0.00489	11861	hsa-miR-25	0.032514	4152	mmu-miR-30b	0.021146	472.8968	gga-miR-205a*	0	172	dme-miR-998	0.023602	805
hsa-miR-33b	0	90.91568	hsa-miR-301b	0	372.875	hsa-miR-342-5p	0.034483	377	hsa-miR-26a	0.014581	31138.23	mmu-miR-30e	0.002333	1285.953	gga-miR-205a	0.034682	865	dme-miR-998*	0.022222	90
hsa-miR-340*	0	86	hsa-miR-30a*	0.025109	915.9998	hsa-miR-345	0.06849	1708.272	hsa-miR-26b	0.034979	13965.44	mmu-miR-320	0	273	gga-miR-205b	0.00431	232	dme-miR-999	0.000693	21648
hsa-miR-340	0.024884	642.9428	hsa-miR-30a	0.000581	10320.66	hsa-miR-34a	0.022761	900.6667	hsa-miR-27a	0.004761	19847.39	mmu-miR-322*	0.148148	54	gga-miR-206	0.021029	198437	dme-miR-999*	0	129
hsa-miR-342-3p	0.000321	6239	hsa-miR-30b	0.005412	1662.964	hsa-miR-361-5p	0.070777	1003.15	hsa-miR-27a*	0	204	mmu-miR-322	0.064565	1083.965	gga-miR-20a	0.025987	2078	dme-miR-9a*	0	1290
hsa-miR-342-5p	0.020409	881.9847	hsa-miR-30c	0.0105	4952.568	hsa-miR-362-3p	0	88	hsa-miR-27b	0	12950.86	mmu-miR-32*	0	115	gga-miR-20b*	0.029289	239	dme-miR-9a	0.025533	6854
hsa-miR-345	0.083117	769.9977	hsa-miR-30c-2*	0	77	hsa-miR-362-5p	0	80	hsa-miR-27b*	0	94	mmu-miR-324-3p	0.044616	111.8735	gga-miR-20b	0.02338	7869.982	dme-miR-9b	0.002327	1719
hsa-miR-34a	0.012048	83	hsa-miR-30d	0.002939	2721.646	hsa-miR-365	0.022404	3303	hsa-miR-28-3p	0.048503	371.1111	mmu-miR-324-5p	0	169	gga-miR-211	0.002867	5052.933	dme-miR-9c	0	1375
hsa-miR-34c-5p	0.00829	4945.999	hsa-miR-30e*	0.017741	112.7323	hsa-miR-374a*	0.018913	211.5	hsa-miR-28-5p	0.023482	1078.833	mmu-miR-32	0	816.8743	gga-miR-21*	0	423			
hsa-miR-361-3p	0.018692	107	hsa-miR-30e	0.000433	2312	hsa-miR-374a	0.00715	2097.833	hsa-miR-296-3p	0.021739	138	mmu-miR-329	0.00813	123	gga-miR-214*	0	443.3141			
hsa-miR-361-5p	0.077219	918.8631	hsa-miR-31*	0.018036	499	hsa-miR-374b*	0	99	hsa-miR-296-5p	0	138	mmu-miR-329*	0.037736	53	gga-miR-21	0.076557	35085			
hsa-miR-362-5p	0	66	hsa-miR-31	0.01147	348.7404	hsa-miR-374b	0.00883	3227.667	hsa-miR-29a	0.0574	17543.43	mmu-miR-331-3p	0.113636	88	gga-miR-216*	0.067797	59			
hsa-miR-363	0	192.9999	hsa-miR-320a	0.000554	5253.865	hsa-miR-37a	0.049563	418.5	hsa-miR-29a*	0.021505	418.5	mmu-miR-332*	0.002115	472.8966	gga-miR-216	0	193			
hsa-miR-374a*	0.024073	996.9724	hsa-miR-320c	0.005622	68.82264	hsa-miR-421	0.136129	484.8333	hsa-miR-29b	0.04434	12879.92	mmu-miR-335-5p	0	370	gga-miR-216b	0.012285	1627.947			
hsa-miR-374a	0.131013	396.8897	hsa-miR-324-3p	0.074564	428.5165	hsa-miR-423-3p	0.017699	452	hsa-miR-29c	0.055111	1125	mmu-miR-33	0.130131	1705.972	gga-miR-217	0.013347	4720			
hsa-miR-374b	0.08557	782.986	hsa-miR-324-5p	0	816	hsa-miR-423-5p	0.014706	136	hsa-miR-301a	0	9722.5	mmu-miR-337-3p	0.021505	93	gga-miR-218	0.080372	1545.013			
hsa-miR-378	0.153304	9312.424	hsa-miR-32	0.044269	496.9658	hsa-miR-424	0.000157	6352.298	hsa-miR-301b	0.071017	57	mmu-miR-339-5p	0.075014	159.9704	gga-miR-219*	0.001552	7731			
hsa-miR-421	0.10003	59.98188	hsa-miR-331-3p	0	767.9913	hsa-miR-425*	0.031915	94	hsa-miR-30a*	0.070175	57	mmu-miR-340-5p	0.001642	608.9237	gga-miR-221	0.014617	46796			
hsa-miR-423-3p	0.059015	7693	hsa-miR-331-5p	0.057785	51.91635	hsa-miR-425	0.00539	3154.033	hsa-miR-30a	0	504	mmu-miR-342-3p	0.005025	199	gga-miR-221*	0.011331	706			
hsa-miR-423-5p	0.062109	9740.988	hsa-miR-335*	0	174.8573	hsa-miR-429	0.00741	1169.667	hsa-miR-30b	0.007592	922	mmu-miR-342-3p	0.013158	76	gga-miR-222	0.021518	3973.5			
hsa-miR-424	0	843.66	hsa-miR-335	0.00356	842.787	hsa-miR-454	0.016916													

hsa-miR-582-5p	0	781.8819
hsa-miR-589	0.019048	105
hsa-miR-590-3p	0.015296	522.9971
hsa-miR-590-5p	0.033856	738.4194
hsa-miR-615-3p	0.006211	160.9952
hsa-miR-627	0.026674	74.97839
hsa-miR-629	0.11402	420.9787
hsa-miR-652	0.009183	108.8965
hsa-miR-654-3p	0.032787	61
hsa-miR-660	0.005102	196
hsa-miR-671-5p	0.016067	248.9582
hsa-miR-7*	0	79.81071
hsa-miR-7	0.002273	870.9775
hsa-miR-720	0	71.8151
hsa-miR-744	0.060701	411.8573
hsa-miR-767-5p	0	56.92846
hsa-miR-873	0	102
hsa-miR-886-3p	0.014916	203.4936
hsa-miR-886-5p	0.017677	309.7606
hsa-miR-889	0	80
hsa-miR-923*	0	115.6531
hsa-miR-92a	0.033893	11723.96
hsa-miR-92a-1*	0	83
hsa-miR-92b	0.042823	1587.929
hsa-miR-92b*	0.0125	80
hsa-miR-93*	0.016393	61
hsa-miR-93	0.070289	5890
hsa-miR-95	0.087687	136.8501
hsa-miR-96	0.004222	1657.316
hsa-miR-98	0.075984	2263.626
hsa-miR-99a*	0	70
hsa-miR-99a	0.29528	5946.883
hsa-miR-99b	0.08026	1332.986

hsa-miR-519a-1*	0	56.83333
hsa-miR-519a-2*	0	90.5
hsa-miR-519b-3p	0	64.28571
hsa-miR-520b*	0	90.5
hsa-miR-521	0.011538	260
hsa-miR-522	0.105992	415.125
hsa-miR-532-3p	0	69
hsa-miR-532-5p	0.02439	246
hsa-miR-545*	0	73
hsa-miR-548e	0.095694	104.5
hsa-miR-548j	0	117
hsa-miR-548k	0.011905	168
hsa-miR-551b	0	85
hsa-miR-570	0	152.1333
hsa-miR-574-3p	0.031478	285.9167
hsa-miR-576-5p	0	89.11111
hsa-miR-577	0	178
hsa-miR-584	0.015355	130.25
hsa-miR-589*	0.031579	95
hsa-miR-589	0.015625	192
hsa-miR-590-3p	0.008222	1337.95
hsa-miR-590-5p	0.017402	1896.333
hsa-miR-592	0	100
hsa-miR-615-3p	0.010303	291.1667
hsa-miR-618	0	62
hsa-miR-625*	0.010582	94.5
hsa-miR-625	0.010811	92.5
hsa-miR-629	0.014252	421
hsa-miR-641	0	51
hsa-miR-651	0.027397	73
hsa-miR-652	0.067298	237.75
hsa-miR-660	0	327
hsa-miR-671-5p	0.014684	136.2
hsa-miR-708*	0.112676	71
hsa-miR-708	0.045579	2121.914
hsa-miR-7*	0.020942	95.5
hsa-miR-7	0.010972	33419.79
hsa-miR-744	0.052935	1553.783
hsa-miR-767-5p	0.031477	413
hsa-miR-769-3p	0	52
hsa-miR-873	0	90
hsa-miR-9*	0	147.5
hsa-miR-9	0.012642	1258.76
hsa-miR-9*	0	147.5
hsa-miR-92a	0.020661	4223.333
hsa-miR-92a-1*	0	63
hsa-miR-92b	0.015224	656.875
hsa-miR-92b*	0	67
hsa-miR-9*	0	135
hsa-miR-93*	0.051282	117
hsa-miR-935	0.043956	91
hsa-miR-93	0.036209	11185
hsa-miR-942	0.191348	60.1
hsa-miR-95	0.102128	107.7083
hsa-miR-96	0.002705	1848.25
hsa-miR-98	0.057762	2198.667
hsa-miR-99a	0.301587	567
hsa-miR-99b*	0.113703	114.3333
hsa-miR-99b	0.049172	1952.333

mmu-miR-669c	0.032654	60.99162
mmu-miR-672	0.027624	362
mmu-miR-674*	0.039216	51
mmu-miR-674	0	113.9888
mmu-miR-700*	0	77
mmu-miR-708*	0	148
mmu-miR-708	0.07396	1525.222
mmu-miR-741	0.125111	55.95023
mmu-miR-744	0.093759	351.966
mmu-miR-7a	0.035072	3675.836
mmu-miR-805	0.036845	621.6945
mmu-miR-871*	0	55
mmu-miR-872*	0	135
mmu-miR-872	0	543
mmu-miR-880	0	61
mmu-miR-881	0	59
mmu-miR-9-1*	0	99.37505
mmu-miR-9	0.014205	703.9993
mmu-miR-9-2*	0	99.37505
mmu-miR-92a	0.029052	5834.548
mmu-miR-92a-1*	0.007194	278
mmu-miR-92b	0.071429	196
mmu-miR-9-3*	0	52.42551
mmu-miR-93*	0.068966	58
mmu-miR-93	0.044043	4926.956
mmu-miR-96	0.006486	8017.707
mmu-miR-99b	0.041667	144

gga-miR-92	0.042689	44110
gga-miR-92*	0.004808	416
gga-miR-99a*	0.031311	511
gga-miR-99a	0.053079	28768.58

Table S3. Percentage of addition in miRNA loci with significant addition across human cell lines.

A additon

miRNA locus	THP-1	HeLa	MCF-7	U2OS
hsa-let-7b	0.131349	0.056391	0.108852	0.038192
hsa-let-7g	0.091767	0.02624	0.046702	0.035792
hsa-let-7i	0.039265	0.18528	0.202379	0.077317
hsa-miR-140-5p	0.023836	0.125	0.166359	0.08841
hsa-miR-16	0.048694	0.015985	0.069695	0.017076
hsa-miR-17	0.084522	0.069245	0.066674	0.038753
hsa-miR-185	0.047022	0.09753	0.103077	0.071489
hsa-miR-191	0.082332	0.033176	0.022246	0.033232
hsa-miR-20a	0.06824	0.135278	0.066423	0.07814
hsa-miR-210	0.070402	0.075581	0.068602	0.064253
hsa-miR-21	0.064119	0.074289	0.018834	0.10272
hsa-miR-24	0.091996	0.049228	0.082477	0.032787
hsa-miR-25	0.050729	0.033532	0.035219	0.032514
hsa-miR-26a	0.059037	0.022785	0.035955	0.014581
hsa-miR-26b	0.026133	0.022098	0.052716	0.034979
hsa-miR-27a	0.025057	0.023652	0.041077	0.004761
hsa-miR-28-3p	0.192786	0.112875	0.072823	0.048503
hsa-miR-28-5p	0.142719	0.086734	0.039385	0.023482
hsa-miR-374a	0.131013	0.046193	0.00715	0.048051
hsa-miR-374b	0.08557	0.160916	0.00883	0.130293
hsa-miR-92a	0.150768	0.033893	0.055793	0.020661
hsa-miR-93	0.058325	0.070289	0.06062	0.036209
hsa-miR-98	0.039506	0.075984	0.053824	0.057762
hsa-miR-99b	0.083694	0.08026	0.105867	0.049172

U addition

miRNA locus	THP-1	HeLa	mcf7	U2OS
hsa-miR-101	0.036761	0.059175	0.010245	0.036464
hsa-miR-140-3p	0.014592	0.043388	0.053672	0.057093
hsa-miR-148b	0.34079	0.275015	0.201629	0.239298
hsa-miR-151-3p	0.164914	0.087858	0.037629	0.081338
hsa-miR-152	0.081717	0.163417	0.056532	0.112603
hsa-miR-221	0.10816	0.054749	0.031201	0.076882
hsa-miR-24	0.461514	0.517206	0.249389	0.30775
hsa-miR-25	0.038316	0.036234	0.011608	0.025289
hsa-miR-26a	0.070906	0.057929	0.058047	0.05504
hsa-miR-26b	0.045154	0.023585	0.028609	0.040051
hsa-miR-27a	0.061913	0.204773	0.068516	0.166617
hsa-miR-27b	0.014392	0.092091	0.048406	0.047264
hsa-miR-28-3p	0.054348	0.06041	0.068476	0.088922
hsa-miR-342-3p	0.090079	0.123944	0.01096	0.099291
hsa-miR-345	0.116883	0.028619	0.059124	0.044448
hsa-miR-423-3p	0.036787	0.033419	0.033186	0.02107
hsa-miR-425	0.00359	0.02306	0.006605	0.013362
hsa-miR-652	0.274264	0.246992	0.403475	0.520505
hsa-miR-99b	0.046898	0.091524	0.071464	0.095441

Table S4. miRNA loci with significant addition, above estimated sequencing error rate

	addition type	human-THP-1	human-Hela	human-MCF-7	human-U2OS	mouse-ES	chicken-embryo	drosophila-head	total
unambiguous addition	A	73	59	67	73	65	57	41	435
	U	55	61	42	70	67	49	38	382
	G	13	1	8	1	2	0	1	26
	C	7	5	2	2	0	4	3	23
	AA	32	23	25	30	17	45	11	183
	UA	6	10	9	8	5	3	6	47
	CA	1	0	0	0	0	2	2	5
	GA	4	2	2	0	1	0	2	11
	AU	26	18	14	19	11	8	4	100
	UU	14	11	11	17	11	13	11	88
	CU	1	2	0	0	0	1	3	7
	GU	7	2	1	1	3	0	2	16
	AC	4	2	0	0	0	1	0	7
	UC	0	0	0	0	0	1	0	1
	CC	0	1	0	0	0	1	0	2
	GC	1	0	0	0	0	0	0	1
	AG	14	3	5	0	3	2	0	27
	UG	0	1	0	0	0	0	1	2
	CG	0	0	0	0	0	0	2	2
	GG	0	0	0	0	1	0	0	1
total		258	201	186	221	186	187	127	
ambiguous + unambiguous addition	AA	9	10	7	7	7	9	8	57
	UA	14	5	3	2	3	2	3	32
	CA	3	5	6	4	1	2	0	21
	GA	6	3	9	4	4	4	5	35
	AU	7	11	7	10	8	5	6	54
	UU	13	8	2	13	6	3	2	47
	CU	2	4	5	4	1	1	1	18
	GU	2	5	7	6	2	4	6	32
	AC	1	0	0	0	0	0	3	4
	UC	1	0	0	0	0	0	0	1
	CC	0	1	1	2	1	2	0	7
	GC	1	0	0	0	1	2	2	6
	AG	1	3	2	1	0	0	3	10
	UG	2	0	0	0	0	0	0	2
	CG	2	0	2	0	0	0	0	4
	GG	1	0	0	0	0	0	1	2
total		65	55	51	53	34	34	40	
ambiguous addition	A	35	37	29	26	35	23	23	208
	U	40	61	37	57	35	44	27	301
	G	14	16	20	18	12	11	15	106
	C	16	18	31	15	9	14	4	107
	AA	2	4	3	3	2	4	4	22
	UA	0	2	1	1	0	1	0	5
	CA	2	2	2	1	1	2	0	10
	GA	4	1	3	2	2	3	1	16
	AU	3	6	3	7	4	5	5	33
	UU	2	12	7	8	1	2	6	38
	CU	1	2	5	3	2	2	1	16
	GU	8	5	7	9	3	3	2	37
	AC	1	0	1	0	1	0	0	3
	UC	1	0	0	0	0	0	0	1
	CC	0	2	1	0	0	1	0	4
	GC	1	2	2	3	0	0	0	8
	AG	2	7	3	2	3	2	5	24
	UG	4	0	0	0	0	2	4	10
	CG	0	3	2	1	1	2	1	10
	GG	0	3	3	3	1	2	3	15
total		136	183	160	159	112	123	101	

Table S5. Natural classification of the TRF family of nucleotidyltransferases.

Subfamily	Phyletic distribution	Prominent members^	Known functions	Comments
TRF4 classic	all eukaryotes	TRF4 (<i>Scer</i>), TRF5 (<i>Scer</i>), cid14 (<i>Spom</i>), DmTRF4-1 (<i>Dmel</i>), DmTRF4-2 (<i>Dmel</i>), GLD-4 (<i>Cele</i>)	snRNA polyadenylation ⁶ , U14 snoRNA, U5 snRNA, pre-ribosomal rRNA degradation ⁷ , intergenic transcript degradation ⁸ , hypomodified tRNA degradation ^{9 10}	POL5-like and PAPD5-like assemblages formed via gene duplication event occurring in TRF4 during chordate evolution; <i>Scer</i> TRF4 and TRF5, meanwhile, result from an <i>Scer</i> -specific gene duplication event
**POL5-like	jawed vertebrates	POL5/TRF4-1/LAK1/POLK/TRF4 (<i>Hsap</i>)	-	
**PAPD5-like	jawed vertebrates and <i>Xenopus</i>	PAPD5/TRF4-2(<i>Hsap</i>)	-	
GLD-2/PAPD4	animals	GLD-2 (<i>Cele</i>), PAPD4/Hs1 (<i>Hsap</i>), XGLD-2 (<i>Xlae</i>)	Cytoplasmic mRNA polyadenylation ^{11, 12 13} , miRNA adenylation ¹⁴	
TUT1	animals	TUT1/PAPD2/TUTase/U6-TUTase/STAR-PAP/Hs5 (<i>Hsap</i>)	Regulation of selected mRNAs ¹⁵ , U6 snRNA uridylyl transferase ¹⁶	TUT1 & MTPAP subfamilies form a monophyletic higher-order assemblage
MTPAP	animals	MTPAP/PAPD1/Hs4 (<i>Hsap</i>)	mt-mRNA polyA tail extension ^{17 18}	
ZCCHC6/ZCCHC11 repeat 2 subfamily	crown group eukaryotes	ZCCHC6/PAPD6/Hs2 (<i>Hsap</i>), ZCCHC11/PAPD3 (<i>Hsap</i>), cid-1(<i>Cele</i>), pup-2 (<i>Cele</i>), cid11 (<i>Spom</i>), cid13 (<i>Spom</i>)	checkpoint control ^{19, 20} , RNA polyuridylation ²¹ , targets ribonucleotide reductase mRNA ²²	Subfamily 2 likely emerged via gene duplication of subfamily before divergence of nematodes. cid11, cid13 are closely related to the exclusion of other sequences, suggesting late gene duplication event in <i>S. pombe</i>
ZCCHC6/ZCCHC11 repeat 1 subfamily	chordates, <i>Strongylocentrotus</i> , <i>C. elegans</i>	ZCCHC6/PAPD6/Hs2 (<i>Hsap</i>), ZCCHC11/PAPD3 (<i>Hsap</i>), cid-1 (<i>Cele</i>)	-	
RET1-like	kinetoplastids	RET1 (<i>Ltar</i>), RET2 (<i>Ltar</i>), TbTUT3(<i>Tbru</i>), TbTUT4 (<i>Tbru</i>)	mRNA, gRNA uridylation, mitochondrial mRNA editing ^{23 24 25 26 27}	Monophyletic kinetoplastid-specific expansion
MEE44-like ^{%, \$}	plants	MEE44 (<i>Atha</i>)	-	Deletion linked to embryonic arrest ²⁸
MUT68-like	plants	MUT68 (<i>Crei</i>)	adenylation of RISC-cleaved	

			mRNA fragments ²⁹	
AT3G56320-like ^{%,§}	plants, <i>Toxoplasma</i>	AT3G56320 (<i>Atha</i>)	-	
monkey king	insects	mkg (<i>Dmel</i>), mkg-p(<i>Dmel</i>)	-	monkey king has been previously discussed in detail ³⁰ and it forms a monophyletic higher-order assemblage with the CG1091-like proteins
CG1091-like [%]	insects	CG1091 (<i>Dmel</i>)	-	
PFD1045c-like [%]	apicomplexa	PFD1045c (<i>Pfal</i>)	-	PFD1045c was identified as an erythrocyte membrane-associated antigen ³¹
<i>Paramecium</i> expansion [%]	<i>Paramecium</i>	--	-	<i>Paramecium</i> lineage-specific expansion

Footnotes:

^ Several well-studied members of the TRF4/TRF5 family in *S. pombe* failed to reliably fall within a clear, monophyletic assemblage. These included cid12, and cid16, cid1 (*Spom*). Additional members with described functional roles not reliably found to cluster within a monophyletic assemblage included mut-2 (*C. elegans*), linked to transposon silencing³² and RNAi^{33, 34}.

[%]Indicates newly-identified subfamily

[§]Candidate for miRNA adenylating enzyme in plants

Table S6. Detailed phyletic distribution of TRF family members present in humans.

		**Met	Hsap	Ptro	Mmus	Rnor	Drer	Tnig	Spur	Cint	Bflo	Dmel	Agam	Amel	Tcas	Cele	Bmal	Tadh	Nvec	Mbre	**E&D	Ehis	Ddis	**Asco	Afum	Cgla	Dhan	Gzea	Klac	Ncra	Scer	Spom	Ylip	**Basid	Cneo	Umay	**Micro	Ecun	**Plants	Crei	Otau	Atha	Ppat	
confirmed presence of miRNA*			x	x	x	x	x	x?	?	x	x	x	x	x	x?	x	?	o	x	o		?	o		o	o?	o?	o?	o?	o	o?	o?	o?		o?	o?		o?			x	?	x	x
TRF subfamily	GLD-2/PAPD4		1	3	1	1	1	1		1	2	2	2	1	1	1	1		1									1			1				2	1								
	PAPD5^		1		1	1	1	1																																				
	PAPD7^		1		1	1	1	2																																				
	TRF^								1	1	2	2	1	1		1	1	1	1					1	2	2	1	1	1	2	1	1		2	1				2	1	1	2		
	TUT1		1	1			1	1		1	2								1	1																2								
	ZCCHC6_ZCCHC11_repeat_1		2	3	2	1	2	1	1		1																																	
	ZCCHC6_ZCCHC11_repeat_2		2	4	2	2	2	1	1	1							1	1	1	1			2		1			1			2													
	mtPAP		1	1	1		1	1	1			2	1	1	1	1																												

*x, confirmed presence via experimental methods; o, absence of miRNA despite experimental attempts to identify miRNA; x?, computational prediction of miRNA; o?, direct testing not performed, but likely absent due to presence in closely related lineages; ?, unknown

^PAPD5 and POLS result from a gene duplication event in the TRF family that occurred in the jawed vertebrates

Abbreviations:

- **Asco: ascomycetes
- Afum: Aspergillus fumigatus
- Cgla: Candida glabrata
- Dhan: Debaryomyces hansenii
- Gzea: Gibberella zeae
- Klac: Kluyveromyces lactis
- Ncra: Neurospora crassa
- Scer: Saccharomyces cerevisiae
- Spom: Schizosaccharomyces pombe
- Ylip: Yarrowia lipolytica
- **Basid: basidiomycetes
- Cneo: Cryptococcus neoformans
- Umay: Ustilago maydis
- **Micro: microsporidia
- Ecun: Encephalitozoon cuniculi
- **Met: metazoa
- Agam: Anopheles gambiae
- Amel: Apis mellifera
- Bflo: Branchiostoma floridae
- Cele: Caenorhabditis elegans
- Cint: Ciona intestinalis
- Drer: Danio rerio
- Dmel: Drosophila melanogaster
- Hsap: Homo sapiens
- Mmus: Mus musculus
- Ptro: Pan troglodytes
- Rnor: Rattus norvegicus
- Spur: Strongylocentrotus purpuratus
- Tnig: Tetraodon nigroviridis
- Tcas: Tribolium castaneum
- Mbre: Monosiga brevicollis

Nvec: Nematostella vectensis
Bmal: Brugia malayi
Tadh: Trichoplax adhaerens
**E&D: Entamoeba and Dictyostelium
Ehis: Entamoeba histolytica
Ddis: Dictyostelium discoideum
**Plants:
Crei: Chlamydomonas reinhardtii
Otau: Ostreococcus tauri
Atha: Arabidopsis thaliana
Ppat: Physcomitrella patens

References: 35,36,37,38,39,40,41,42,43,44,45.

Table S7. Proportion unambiguous addition at miRNA loci across nucleotidyltransferase knockdown libraries. (**significant decreases highlighted in yellow)

	proportion unambiguous A addition				proportion unambiguous U addition				proportion unambiguous AA addition				proportion unambiguous UU addition				proportion unambiguous AU addition				proportion unambiguous G addition				proportion unambiguous GA addition				
miRNA locus	control	PAPD4 KD	PAPD5 KD	PAPD7 KD	control	PAPD4 KD	PAPD5 KD	PAPD7 KD	control	PAPD4 KD	PAPD5 KD	PAPD7 KD	control	PAPD4 KD	PAPD5 KD	PAPD7 KD	control	PAPD4 KD	PAPD5 KD	PAPD7 KD	control	PAPD4 KD	PAPD5 KD	PAPD7 KD	control	PAPD4 KD	PAPD5 KD	PAPD7 KD	
hsa-let-7a	0.033836	0.028255	0.046511	0.050579	0	0	0	0	0.000535	0.000553	0.000981	0.000893	0	0	0	0	0.001401	0.000812	0.001199	0.001357	0.002297	0.003012	0.002928	0.003435	5.22E-05	5.01E-05	0.000116	0.000104	
hsa-let-7a-3*	0.031146	0.007236	0	0.019773	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
hsa-let-7b*	0.054329	0.007096	0.098328	0.09445	0.659716	0.702466	0.430186	0.602121	0	0	0	0.011806	0.015523	0.021287	0.012291	0.023613	0	0	0	0	0.007762	0	0	0	0	0	0	0	
hsa-let-7b	0.085236	0.031522	0.13084	0.116395	0	0	0	0	0.030062	0.007347	0.044521	0.037206	0	0	0	0	0.033441	0.017253	0.033744	0.030889	0.005403	0.002223	0.006256	0.006734	0.00227	0.000706	0.00292	0.003043	
hsa-let-7c	0	0	0	1.25E-08	0.000879	0.00144	0.000377	0.000331	0	0	0	0	5.02E-05	7.70E-05	1.48E-05	1.53E-05	0	0	0	0	4.49E-05	2.26E-05	3.06E-05	2.87E-05	0.000229	0.000132	0.000178	0.000165	
hsa-let-7d*	0	0.008264	0.008696	0.011364	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.005348	0	0.008696	0	0	0	0	0	
hsa-let-7d	0.068851	0.024979	0.065455	0.063719	0	0	0	0	0.016167	0.002647	0.012923	0.013567	0	0	0	0	0.003066	0.00182	0.003378	0.00407	0.005575	0.003474	0.006759	0.006977	0.001394	0.000331	0.001779	0.00155	
hsa-let-7e	0.041812	0.026969	0.053509	0.048179	0.0054	0.003404	0.002879	0.003897	0.009767	0.004511	0.010015	0.003447	5.10E-05	7.18E-06	1.56E-05	4.06E-05	0.001097	0.001126	0.000466	0.003591	0	0	0	0	0	0	0	0	
hsa-let-7f	0.031914	0.027474	0.035488	0.042872	0.001677	0.001395	0.001444	0.001863	0.002383	0.001768	0.001509	0.002306	4.48E-06	7.40E-06	6.06E-06	7.93E-06	0.000645	0.000344	0.000408	0.00059	0	0	0	0	0	0	0	0	
hsa-let-7g	0.039623	0.037436	0.084158	0.091767	0	0	0	0	0.005174	0.002845	0.007121	0.00986	0	0	0	0	0.00265	0.001353	0.002636	0.003087	0.0029	0.00548	0.008456	0.010803	0.000505	0.000173	0.000393	0.00063	
hsa-let-7i	0.049959	0.033938	0.046285	0.05074	0.000311	0.000567	0.000292	8.31E-05	0.038907	0.029851	0.038003	0.052404	0	0.000114	0	0	0.003113	0.002043	0.001949	0.002828	0.000311	0.001135	0.000877	0.000665	0.000156	0.000227	0.000682	0.000582	
hsa-miR-101	0.003868	0.001225	0.00334	0.003231	0.072422	0.064332	0.048933	0.064207	9.28E-06	1.02E-06	1.05E-05	7.95E-06	0.000866	0.000935	0.00056	0.000873	7.91E-06	1.02E-06	6.31E-06	9.52E-06	0.000102	5.85E-05	0	5.82E-05	0	5.85E-05	0	5.82E-05	
hsa-miR-103	0	0	0	0	0.003643	0.006512	0.005852	0.004422	0	0	0	0	0.000192	0.000237	2.37E-05	0.000108	0	0	0	0	0.001726	0.000686	0.002298	0.001798	9.59E-05	2.64E-05	9.48E-05	3.59E-05	
hsa-miR-106a	0.086168	0.016168	0.067574	0.082679	0.002286	0.00423	0.002896	0.005058	8.31E-05	0	0.012125	0.005125	0	0	0	0	0	0	0	0	0	0.003975	4.50E-05	0.003537	0	0	0	0	0
hsa-miR-106b*	0.087901	0.034241	0.098691	0.095031	0.174766	0.201931	0.164149	0.170008	0.003102	0.007024	0.011078	0.007847	0.001034	0	0	0	0.001034	0	0.001007	0	0.001034	0.001756	0	0.000872	0.001034	0	0	0	0
hsa-miR-106b	0.00286	0.002284	0.002263	0.003762	0.001107	0.001246	0.000792	0.001075	0.000461	0.000519	0.000453	0.000322	9.23E-05	0.000104	0	0.000107	9.23E-05	0.000311	0	0.000107	0	0	0	0	0	0	0	0	
hsa-miR-10a	0.025	0.025126	0.026738	0.034749	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-miR-125a-5p	0.003365	0.001068	0.004567	0.001074	0.000673	0	0	0.001074	0	0	0	0	0	0	0	0	0.000673	0	0	0.003223	0	0	0	0	0	0	0	0	0
hsa-miR-126	0.017176	0.015444	0.014702	0.020413	0.015721	0.016168	0.010466	0.016853	0	0	0	0	0.000291	0.000483	0	0.000237	0	0	0	0	0.000291	0.000483	0.000249	0	0	0	0	0	0
hsa-miR-126*	0.013861	0.007921	0.01002	0.011194	0.075248	0.041584	0.052104	0.05597	0	0.00198	0	0	0	0	0	0.003731	0	0	0	0	0.00396	0.007921	0.004008	0.001866	0	0	0	0	0
hsa-miR-1274b	0.00131	0	0	0	0.000682	0	0.000917	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.000629	0	0.000642	0	0	0
hsa-miR-128	0.01221	0.007563	0.039245	0.060838	0	0	0	0	0.016275	0	0.020928	0.021286	0	0	0	0	0.005275	0	0.011613	0.012015	0.036631	0.013236	0.073258	0.073006	0.083412	0.013231	0.073249	0.097307	
hsa-miR-1292	0	0	0	0.010753	0.055556	0.026087	0.040404	0.086022	0.018519	0	0	0	0	0	0	0	0	0	0	0.010753	0	0	0	0	0	0	0	0	0
hsa-miR-1304*	0.008223	0	0.004646	0.007548	0	0	0	0	0	0	0	0	0	0	0	0	0.003295	0	0.002326	0	0	0	0.002326	0.002519	0	0	0	0	0
hsa-miR-1307																													

hsa-miR-191	0.162472	0.035358	0.086993	0.115416	0	0	0	0	0.002961	0.000426	0.001369	0.002215	0	0	0	0	0.000722	0.000153	0.00044	0.000587	0.001535	0.000546	0.000554	0.000665	7.22E-05	0	0	6.65E-05
hsa-miR-192	0.064936	0.032389	0.085586	0.081566	0.005772	0.002699	0.002252	0.011419	0.007215	0	0	0.001631	0	0.001349	0	0	0	0	0	0	0.001443	0	0.002252	0	0	0	0	0
hsa-miR-193a-5p	0.03207	0.039106	0.041209	0.052786	0.049563	0.044693	0.035714	0.052786	0.014577	0.00838	0.005495	0.005865	0.011662	0.005587	0.002747	0.002933	0.008746	0.00838	0.008242	0.014663	0	0	0	0	0	0	0	0
hsa-miR-194	0.009926	0	0.012512	0.016021	0	0	0	0	0.00031	0	0	0	0	0	0	0.013546	0.005022	0	0.00706	0.004403	0	0	0	0	0	0	0	0
hsa-miR-196a	0.016004	0.009415	0.012182	0.017941	0.038696	0.065559	0.025833	0.044985	0.000327	0.000215	0.000259	0.000395	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-miR-196b	0	0	0	0	0.120066	0.114488	0.103064	0.118565	0	0	0	0	0.003717	0.003842	0.003348	0.003463	0	0	0	0	0.002456	0.002277	0.001282	0.001539	0	0.000142	0	0
hsa-miR-197	0	0	0	0	0.003263	0.001445	0.003656	0.005155	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.001631	0	0	0	0
hsa-miR-199a-3p	0	0	0	0	0.037567	0.064374	0.033494	0.039539	0	0	0	0	0.001342	0	0	0	0	0	0	0	0.001345	0.001216	0	0	0	0	0	0
hsa-miR-199b-3p	0	0	0	0	0.037567	0.064374	0.033501	0.039539	0	0	0	0	0.001342	0	0	0	0	0	0	0	0.001345	0.001216	0	0	0	0	0	0
hsa-miR-199b-5p	0	0	0	0	0.076592	0.082667	0.046569	0.039387	0	0	0	0	0	0.002667	0	0	0	0	0	0	0.006565	0.005333	0	0.006565	0	0	0	0
hsa-miR-19a	0	0.000398	0	0	0	0	0	0	0.00036	0	0.000542	0	0	0	0	0	0	0	0	0	0.007137	0.002387	0.005923	0.011123	0.001439	0	0.000542	0.000329
hsa-miR-19b	0.000513	0.000558	0.000392	0.001251	0.000214	0.000191	0.000116	0.000273	0	0.00028	0	0	5.44E-05	7.18E-06	0	6.30E-05	0	0	0	0	0.007444	0.001116	0.006279	0.004752	0.00129	0	0.000394	0.000502
hsa-miR-19b*	0.016129	0.011494	0.045455	0.028986	0	0	0	0	0	0	0	0.014493	0	0	0	0	0	0.011494	0	0	0	0	0	0	0	0	0	0
hsa-miR-200a	0.128571	0.045455	0.057143	0.075949	0.042857	0.022727	0.028571	0.025316	0	0	0	0	0	0	0	0	0	0	0	0	0.014286	0	0	0	0	0	0	0
hsa-miR-200b	0.144928	0.147541	0.104478	0.13253	0.188406	0.180328	0.134328	0.253012	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-miR-200c	0.009368	0.013029	0.008696	0.008961	0.014052	0.013029	0.015217	0.017921	0	0	0	0	0.002342	0.001629	0	0	0.002342	0.006515	0.002174	0.003584	0	0	0	0	0	0	0	0
hsa-miR-20a*	0	0	0	0	0.007119	0	0.012521	0	0	0	0	0	0.009503	0	0	0.010421	0	0	0	0	0	0.009256	0	0	0	0	0	0
hsa-miR-20a	0.055003	0.016488	0.049926	0.052421	0	0	0	0	0.002514	0.000591	0.002541	0.002274	0	0	0	0	0.000294	7.88E-05	0.000138	0.0002	0.000505	0.000374	0.000751	0.000882	2.10E-05	9.86E-06	3.76E-05	2.73E-05
hsa-miR-20b	0.098125	0.027459	0.079978	0.092752	0	0	0	0	0.003634	0.000837	0.003037	0.003442	0	0	0	0	0.001211	0.000837	0	0	0	0.002025	0.001721	0	0	0	0	0
hsa-miR-210	0.07728	0.032854	0.054422	0.065399	0	0	0	0	0.057187	0.013005	0.059864	0.04943	0	0	0	0	0.080371	0.045175	0.062585	0.050951	0.015456	0.008214	0.020408	0.022814	0.029366	0.01232	0.043537	0.026616
hsa-miR-21*	0	0	0	0.022936	0	0	0	0	0	0	0	0.004587	0	0	0	0	0	0.006579	0	0	0.014599	0.006579	0.009174	0.004587	0	0	0	0
hsa-miR-215	0	0	0	0	0.02	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-miR-21	0.05159	0.050847	0.014521	0.036272	0	0	0	0	0.000106	0.000105	5.63E-06	2.66E-05	0	0	0	0	1.12E-05	1.97E-05	0	2.13E-05	0.002403	0.002826	0.000979	0.001839	5.59E-06	2.62E-05	0	2.13E-05
hsa-miR-221	0	0	0	0	0.078223	0.121412	0.070206	0.099168	0	0	0	0	0.000889	0.00082	0	0.002774	0	0	0	0	0.062223	0.02379	0.059932	0.049931	0.000889	0	0.000856	0.00208
hsa-miR-221*	0	0.002644	0.003071	0.003216	0.027628	0.016746	0.018431	0.018231	0.001625	0.000881	0	0	0.004873	0.003525	0.00512	0.00107	0.001625	0.001763	0	0.00429	0	0	0	0	0	0	0	0
hsa-miR-222	0.000426	0.000906	0.000692	0.000752	0	0.001511	0.000692	0.001127	0.000852	0	0.000346	0.000752	0	0	0.000346	0	0.000852	0	0	0.000752	0	0.000302	0.000346	0	0	0	0	0
hsa-miR-222*	0.009091	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-miR-223	0.019209	0.00316	0.022341	0.015926	0.035782	0.0625	0.040347	0.0475	0.000753	0	0.001	0.001397	0.001507	0.002809	0.002001	0.003912	0	0	0.000333	0.000279	0.052355	0.015801	0.052018	0.038279	0.01695	0.00316	0.010004	0.013412
hsa-miR-223*	0	0	0.004651	0	0.00369	0.004348	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-miR-22	0.036415	0.013283	0.026403	0.043697	0	0	0	0	0	0	0	0.003361	0	0	0	0	0	0	0	0.005042	0	0	0	0	0	0	0	0
hsa-miR-224	0.050633	0.085714	0.052632	0.047619	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.028571	0	0.02381	0	0	0	0
hsa-miR-23a	0.024818	0.010929	0.027136	0.036032	0.444163	0.422753	0.372404	0.409676	0.002555	0.000497	0.001155	0.002468	0.022628	0.014903	0.01097	0.015301	0.006204	0.000994	0.003464	0.003949	0.027368	0.005464	0.034636	0.036522	0.003285	0.000497	0.001155	0.002468
hsa-miR-23b	0.0232	0.006006	0.025187	0.029915	0.477248	0.510523	0.420984	0.521368	0.006628	0	0	0	0.003314	0.003003	0.007196	0.004274	0.003314	0	0.003598	0	0	0	0	0	0	0	0	0
hsa-miR-24	0.073475	0.037651	0.079275	0.073371	0.483631	0.416825	0.380942	0.423039	0.001823	0.000989	0.001893	0.00151	0.011437	0.00965	0.00928	0.010573	0.001446	0.000674	0.000957	0.000836	0	0	0	0	0	0	0	0
hsa-miR-24-2*	0	0.005797	0.006211	0.002532	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-miR-25	0.025203	0.013572	0.018917	0.024006	0.045604	0.03754	0.042656	0.046722	0.005401	0.00231	0.002226	0.003098	0.0009	0.000866	0.002226	0.001291	0.0039	0.000578	0.00408	0.003356	0.022802	0.007797	0.031157	0.022457	0	0	0.000371	0
hsa-miR-26a	0.053088	0.013531	0.045958	0.049318	0.044732	0.056925	0.041716	0.053467	0.006881	0	0.011312	0.008756	0.005406	0.007932	0.004242	0.003226	0.029981	0.004666	0.031814	0.033643	0	0	0	0	0	0	0	0
hsa-miR-26b	0.021298	0.008955	0.016427	0.021042	0.029412	0.035821	0.01232	0.014203	0.004057	0.000995	0.000684	0.00526	0.003043	0.001493	0.000684	0.000526	0.002028	0.000995	0.002053	0.002104	0	0	0	0	0	0	0	0
hsa-miR-27a	0.013931	0.007338	0.013425	0.01779	0.037161	0.042232	0.026982	0.040359	0.001048	0.000266	0.00053	0.001244	0.000187	0.000384	0.000449	0.00043	0.001484	0.001505	0.00212	0.001452	0.000654	0.000288	0.000672	0.000787	0.000187	9.61E-05	0.000449	0.000286
hsa-miR-27a*	0.001468	0.001792	0	0	0.005874	0.005376	0.002463	0.005277	0	0.001792	0	0	0.001468	0	0	0.002639	0	0	0	0	0	0	0	0	0	0	0	0
hsa-miR-27b	0	0	0	0	0.018956	0.012032	0.013216	0.012582	0	0	0	0	0.000808	0.001216	0	0.001276	0	0	0	0	0.001974	0.000902	0.000645	0.001573	0.001212	0.001216	0.000978	0.000957
hsa-miR-27b*	0	0	0	0	0	0.016304	0	0.007874	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-miR-28-3p	0.062584	0.025959	0.058633	0.057199	0.04092	0.044472	0.024832	0.036891	0.014213	0.004975	0.011507	0.013932	0.001779	0.001779	0.00108	0.001743	0.003192	0.00603	0.001437	0.00377	0	0	0	0	0	0	0	0
hsa-miR-28-5p	0.005112	0.00165	0.001034	0.008069	0	0	0.001035	0.000897	0	0	0	0	0	0.000826	0	0.000897	0.003072	0	0.002069	0.002692	0	0	0	0	0	0	0	0
hsa-miR-29a	0	0	0	0	0.00511	0.003024	0.00385	0.003251	0	0	0	0	0	0.000864	0.00055	0.000464	0	0	0	0	0	0.000864	0	0.000464	0	0	0	0
hsa-miR-29a*	0.010989	0.042857																										

[illegible]

Table S8. Proportion of ambiguous addition at miRNA loci across nucleotidyltransferase knockdown libraries. (**significant decreases highlighted in yellow)

	proportion ambiguous A addition				proportion ambiguous U addition				proportion ambiguous AA addition				proportion ambiguous UU addition				proportion ambiguous AU addition				proportion ambiguous G addition				proportion ambiguous GA addition			
miRNA locus	control	GLD-2 KD	PAPD5 KD	POLS KD	control	GLD-2 KD	PAPD5 KD	POLS KD	control	GLD-2 KD	PAPD5 KD	POLS KD	control	GLD-2 KD	PAPD5 KD	POLS KD	control	GLD-2 KD	PAPD5 KD	POLS KD	control	GLD-2 KD	PAPD5 KD	POLS KD	control	GLD-2 KD	PAPD5 KD	POLS KD
hsa-let-7a	0	0	0	0	0.020531	0.022963	0.017514	0.020296	0	0	0	0	0.001786	0.003681	0.001524	0.001911	0	0	0	0	0	0	0	0	0	0	0	0
hsa-let-7a-3*	0	0	0	0	0.061818	0.078823	0.245731	0.185654	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-let-7b*	0	0	0	0	0.000835	0.001427	0.050321	0.01293	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-let-7b	0	0	0	0	0.09371	0.106198	0.072196	0.071089	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-let-7c	0.0008	0.000428	0.000684	0.000542	1.22E-05	1.55E-05	6.02E-06	5.65E-06	0.003563	0.001747	0.002899	0.002182	0	0	0	0	0	0	0	0	1.15E-06	1.65E-06	7.02E-07	6.59E-07	0	0	0	0
hsa-let-7d*	0	0	0	0	0.005348	0.008264	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
hsa-let-7d	0	0	0	0	0.039025	0.046153	0.039056	0.048214	0	0	0	0	0.000836	0.000495	0.000356	0.000194	0	0	0	0	0	0	0	0	0	0	0	0
hsa-let-7e	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.057768	0.132727	0.116832	0.083432	0.007877	0.012016	0.019472	0.015976
hsa-let-7f	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.010905	0.018879	0.013377	0.014557	0	0	0	0
hsa-let-7g	0	0	0	0	0.074956	0.098638	0.070978	0.090475	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-let-7i	0	0	0	0	0.089964	0.133147	0.097935	0.080272	0	0	0	0	0	0	0	0	0	0	0	0	0.000156	0	0	8.32E-05	0	0	0	0
hsa-mir-101	0.12313	0.107994	0.112479	0.093872	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.00473	0.002896	0.002737	0.004174	0.000472	0.000313	0.000538	0.000906
hsa-mir-103	0.006041	0.005247	0.009501	0.008125	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-106a	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-106b*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-106b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.014762	0.020351	0.018106	0.019561	0	0	0	0
hsa-mir-10a	0	0	0	0	0.028571	0.030151	0.010695	0.023166	0	0	0	0	0	0	0	0	0	0	0	0	0.257143	0.321608	0.326203	0.416988	0	0	0	0
hsa-mir-125a-5p	0.002692	0.001068	0.002283	0.007519	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.000673	0.003205	0.005709	0.002148	0.001346	0.002137	0.002283	0.003223
hsa-mir-126	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-126*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-1274b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-128	0	0	0	0	0.081764	0.105561	0.034839	0.064082	0	0	0	0	0	0.004649	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-1292	0	0.06087	0.121212	0.11828	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.148148	0.252174	0.212121	0.215054	0.222222	0.191304	0.20202	0.150538
hsa-mir-1304*	0	0	0	0	0.011507	0.017586	0.006967	0.020127	0	0	0	0	0.003271	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-1307	0	0	0	0	0.092229	0.107975	0.097665	0.086973	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-1307*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-130b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-130b*	0.006227	0.01634	0.02247	0.019551	0	0	0	0	0	0	0	0	0	0	0	0	0	0.005447	0	0	0	0	0	0	0	0	0	0
hsa-mir-132	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-140-3p	0.009929	0.003751	0.009299	0.012218	0.000108	0	0	8.09E-05	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-140-5p	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.012304	0.008012	0.006744	0.006135	0	0	0	0
hsa-mir-141	0	0	0	0	0	0.026316	0	0.021739	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-142-3p	0.184372	0.173546	0.165508	0.17019	0.00447																							

[illegible]

hsa-mir-342-5p	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.090074	0.085799	0.104286	0.093502	0.104779	0.10355	0.12	0.077655
hsa-mir-345	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.016477	0.007047	0.013187	0.017544	0	0	0	0
hsa-mir-34c-5p	0	0	0	0	0.00027	0	0	0	0	0	0	0	0	0	0	0	0	0	0.00054	0.00122	0	0.000863	0	0	0	0
hsa-mir-361-3p	0	0	0	0	0.005182	0	0.010365	0	0	0	0	0	0	0.010365	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-361-5p	0	0	0	0	0.021903	0.03165	0.01231	0.024897	0	0	0	0	0	0.001266	0	0.001383	0	0	0	0	0	0	0	0	0	0
hsa-mir-362-5p	0	0	0	0	0.003906	0.004149	0	0.004556	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-363	0.084596	0.053706	0.051583	0.060706	0	0	0	0	0.003788	0.002148	0.004689	0.005519	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-374a*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.000233	0	0	0.000276	0	0	0	0
hsa-mir-374a	0	0	0	0	0.151305	0.195743	0.127502	0.162598	0	0	0	0	0	0	0	0.002464	0	0	0	0	0	0	0	0	0	0
hsa-mir-374b	0	0	0	0	0.079828	0.075631	0.055877	0.066378	0	0	0	0	0	0	0	0	0	0	0.001446	0.002796	0	0	0	0	0	0
hsa-mir-378	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-378*	0	0	0	0	0.240002	0.421741	0.312502	0.307694	0	0	0	0	0	0	0	0	0	0	0.02	0.008696	0.013889	0	0	0	0	0
hsa-mir-423-3p	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-423-5p	0	0	0	0	0.225613	0.251071	0.222843	0.234329	0	0	0	0	0	0	6.35E-05	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-424	0.179436	0.304326	0.255963	0.293578	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-425*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-425	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.24753	0.214223	0.228348	0.234282	0	0	0	0
hsa-mir-450b-5p	0.068028	0.117186	0.078435	0.202614	0	0	0	0	0	0	0	0	0	0	0	0	0	0.040827	0.062508	0.009806	0.039221	0	0	0	0	0
hsa-mir-452	0.011766	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-454	0	0	0	0	0.10101	0.168224	0.150442	0.166667	0	0	0	0	0	0.050505	0.102804	0.044248	0.03125	0	0	0	0	0	0	0	0	0
hsa-mir-455-3p	0	0	0	0	0.225267	0.228678	0.209279	0.265091	0	0	0	0	0	0	0	0.029897	0.014727	0	0	0	0	0	0	0	0	0
hsa-mir-484	0.12395	0.0477	0.08557	0.088792	0	0	0	0	0.021008	0.005111	0.021812	0.0131	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-486-3p	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.010718	0	0	0	0	0	0	0
hsa-mir-486-5p	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.000852	0	0	0	0	0	0	0
hsa-mir-500*	0	0	0	0	0.007109	0.022154	0.025293	0.010389	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.003647	0	0.003715	0
hsa-mir-501-3p	0.014917	0.019416	0.01075	0.047042	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.014912	0.019413	0.053747	0.035277	0	0.029115	0.010747	0.011756
hsa-mir-502-3p	0.063903	0.04333	0.020677	0.047218	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-505	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-532-3p	0.306819	0.310078	0.336283	0.326923	0	0	0	0	0.011364	0.007752	0.026549	0.009615	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-532-5p	0	0	0	0	0.011887	0.010801	0.009797	0.007653	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-542-3p	0.095891	0.096086	0.065728	0.076923	0	0	0	0	0.045662	0.053381	0.023474	0.054945	0	0	0	0	0	0	0.054795	0.099644	0.079812	0.065934	0	0	0	0
hsa-mir-548e	0.012345	0.010204	0.014706	0.030303	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-548j	0.005849	0.013247	0.014931	0.012743	0.005848	0.019867	0	0	0	0	0	0	0	0	0	0	0	0.00585	0	0	0	0	0	0	0	0
hsa-mir-577	0.015054	0.008412	0.012592	0.012911	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-580	0	0	0	0	0.090909	0.105263	0.054054	0.022222	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-582-3p	0.008218	0.001661	0.002494	0.009381	0	0	0	0	0	0	0.002494	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-582-5p	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-584	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.139673	0.09633	0.108847	0.125	0	0	0	0
hsa-mir-589	0	0	0	0	0.003086	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-590-3p	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-590-5p	0	0	0	0	0	0	0.009091	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-598	0	0	0	0	0.043847	0.045896	0.039128	0.043384	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-618	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-625*	0	0	0	0	0.083723	0.081872	0.100005	0.065667	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-625	0	0	0	0	0.083317	0.081387	0.099995	0.066656	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-627	0	0	0	0	0.00893	0.002946	0.003312	0.007006	0	0	0	0	0	0	0	0	0	0	0.007441	0.004418	0.009934	0.008757	0	0	0	0
hsa-mir-628-5p	0	0	0	0	0	0	0.010601	0	0	0	0	0	0	0	0	0	0	0	0.031546	0.050677	0.053004	0.043479	0	0	0	0
hsa-mir-629	0	0	0	0	0.376001	0.480892	0.480638	0.398877	0	0	0	0	0.0192	0.017516	0.013667	0.018727	0	0	0	0	0	0	0	0	0	0
hsa-mir-652	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-660	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.019608	0.029126	0.036585	0.042735	0	0	0.012195	0
hsa-mir-664*	0.193898	0.222236	0.150014	0.144157	0.007756	0.006945	0	0	0	0	0	0	0	0	0	0	0	0.007756	0.01389	0.014287	0	0	0	0	0	0
hsa-mir-671-3p	0	0	0	0	0.015625	0.086957	0.08	0.090909	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-671-5p	0	0	0	0	0.007874	0.020867	0.019956	0.016447	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-7	0	0	0	0	0.04909	0.039113	0.036764	0.037199	0	0	0	0	0.004758	0.002411	0.002705	0.003022	0	0	0	0	0	0	0	0	0	0
hsa-mir-720	0.007332	0	0.037877	0	0	0	0	0	0.016924	0	0	0.009743	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-744	0.33576	0.352354	0.333558	0.336713	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-760	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.035717	0.097782	0.064395	0.057704	0	0	0	0
hsa-mir-766	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-769-5p	0	0	0	0	0.169519	0.165403	0.145197	0.175983	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hsa-mir-877	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.029279	0.070272	0.027355	0.017053	0.050215	0.155309	0.059271	0.063567
hsa-mir-886-5p	0	0	0	0	0.111822	0.093079	0.105276	0.099562	0	0	0	0														

Table S9. List of miRNA loci showing significant reduction in unambiguous or ambiguous adenine addition in PAPD4 KD library.

miRNA	A	AA	GA	G	AU
hsa-let-7a	16.2%	--	--	--	--
hsa-let-7b	63.0%	75.6%	68.9%	58.9%	48.4%
hsa-let-7d	63.7%	83.6%	--	--	--
hsa-let-7f	13.7%	--	--	--	--
hsa-let-7i	32.1%	--	--	--	--
hsa-miR-101	12.6%	--	--	--	--
hsa-miR-106b*	61.0%	--	--	--	--
hsa-miR-130b	85.0%	81.8%	--	--	--
hsa-miR-140-3p	62.2%	--	--	55.1%	62.6%
hsa-miR-152	55.6%	--	--	--	--
hsa-miR-16	38.8%	--	--	--	--
hsa-miR-17	64.9%	71.1%	--	--	--
hsa-miR-182	83.4%	--	70.2%	--	--
hsa-miR-183	63.5%	--	--	--	--
hsa-miR-185	69.1%	87.6%	--	--	66.9%
hsa-miR-186	72.5%	--	--	--	--
hsa-miR-18a	53.3%	--	--	--	--
hsa-miR-20b	72.0%	--	--	--	--
hsa-miR-210	57.5%	77.3%	--	--	--
hsa-miR-221	77.1%	--	--	61.8%	--
hsa-miR-223	83.5%	--	80.2%	69.8%	--
hsa-miR-24	48.8%	--	--	--	--
hsa-miR-26a	74.5%	--	--	--	84.5%
hsa-miR-27a	47.3%	--	--	--	--
hsa-miR-28-3p	58.5%	--	--	--	--
hsa-miR-339-3p	85.3%	--	--	--	--
hsa-miR-339-5p	81.5%	--	--	--	--
hsa-miR-345	85.8%	--	--	--	--
hsa-miR-423-3p	80.3%	83.7%	--	--	--
hsa-miR-423-5p	81.3%	85.9%	--	--	--
hsa-miR-484	61.5%	--	--	--	--
hsa-miR-652	49.4%	--	--	--	--
hsa-miR-886	66.0%	--	--	--	--
hsa-miR-92a	71.3%	--	78.7%	79.5%	--
hsa-miR-99b	42.8%	--	--	--	--
hsa-miR-146b	--	64.8%	--	--	72.6%
hsa-miR-20a	--	76.5%	--	--	--
hsa-miR-93	--	74.2%	--	--	--
hsa-miR-155	--	58.7%	--	--	--
hsa-miR-320a	--	--	65.7%	--	26.8%
hsa-miR-128	--	--	84.1%	--	--
hsa-miR-221	--	--	--	61.8%	--
hsa-miR-23a	--	--	--	80.0%	--
hsa-miR-25	--	--	--	65.8%	--
hsa-miR-342	--	--	--	77.2%	--
hsa-miR-378	--	--	--	--	24.2%

Table S10. List of miRNA loci showing significant reduction in PAPD5 KD library

miRNA	A	U	UU
hsa-miR-30d	55.0%	19.9%	38.0%
hsa-miR-196b	26.6%	14.2%	n/a
hsa-miR-140	50.5%	40.6%	n/a
hsa-miR-92a	n/a	21.9%	36.0%
hsa-miR-183	n/a	17.7%	n/a
hsa-miR-20a	n/a	35.3%	n/a
hsa-miR-151	n/a	33.9%	n/a
hsa-miR-23a	n/a	16.2%	n/a
hsa-miR-378	n/a	29.7%	n/a
hsa-let-7a	n/a	14.7%	n/a
hsa-let-7f	n/a	23.7%	n/a
hsa-miR-101	n/a	32.1%	n/a
hsa-miR-30c	n/a	24.0%	n/a
hsa-let-7i	n/a	n/a	27.2%

Table S11. Counts comparison for all tags mapping to a given miRNA locus across control and nucleotidyltransferase knockdown libraries.

miRNA locus	control	PAPD4 KD	PAPD5 KD	PAPD7 KD
hsa-let-7a-1*	30.51	43.17	10.67	34.88
hsa-let-7a	46680.90	515256.40	465184.26	578939.93
hsa-let-7a-3*	79.12	279.52	129.80	158.62
hsa-let-7b*	53.73	182.15	108.11	113.45
hsa-let-7b	32527.98	542941.50	455507.09	395397.45
hsa-let-7c	83.39	211.70	1322.36	1034.74
hsa-let-7d*	91.08	317.94	183.97	132.14
hsa-let-7d	1698.77	7780.78	7155.81	6570.79
hsa-let-7e	217.66	2623.62	2471.25	2507.14
hsa-let-7f	25142.59	171798.74	150255.85	173950.47
hsa-let-7f-2*	3.31	10.34	3.75	3.71
hsa-let-7g*	7.70	34.98	18.46	18.00
hsa-let-7g	3479.33	35423.77	30872.71	37839.43
hsa-let-7i*	13.91	50.00	19.00	43.00
hsa-let-7i	2595.39	9885.59	11348.77	13152.69
hsa-miR-100	4.78	9.99	9.01	11.00
hsa-miR-101	9531.67	22123.86	18525.21	22496.26
hsa-miR-103	4523.40	45846.60	50016.33	32918.44
hsa-miR-103-2*	1.92	7.02	3.66	9.02
hsa-miR-106a	31.53	182.94	209.97	237.07
hsa-miR-106b*	456.28	1441.26	1219.76	1429.98
hsa-miR-106b	5465.22	14400.55	12770.19	13831.17
hsa-miR-107*	0.36	0.99	1.34	3.99
hsa-miR-10a	115.16	230.05	215.07	293.14
hsa-miR-10b	0.02	1.95	0.93	2.86
hsa-miR-1180	7.70	22.00	34.00	30.00
hsa-miR-1201	19.42	48.00	39.98	49.94
hsa-miR-122	7.60	36.57	37.58	32.20
hsa-miR-1246	3.23	13.46	9.22	16.17
hsa-miR-1249	5.50	18.00	17.00	13.00
hsa-miR-1254	18.86	54.44	93.34	74.33
hsa-miR-1259	8.99	31.94	21.15	33.31
hsa-miR-125a-3p	5.87	38.00	21.98	26.04
hsa-miR-125a-5p	1103.59	2306.87	2196.54	2079.67
hsa-miR-126	1657.23	5340.99	5046.95	5337.67
hsa-miR-126*	232.18	670.86	615.10	697.78
hsa-miR-1269*	4.62	5.00	6.00	11.00
hsa-miR-1274a	12.53	28.00	29.05	17.39
hsa-miR-1274b	498.03	1156.89	905.22	1449.11
hsa-miR-1278	5.14	16.00	12.00	21.00
hsa-miR-1280	1.21	1.12	3.24	1.17
hsa-miR-128	212.20	716.95	492.95	396.95
hsa-miR-128-1*	7.70	25.00	21.91	19.00
hsa-miR-1284	3.30	6.00	4.00	3.00
hsa-miR-1285	23.03	28.84	47.92	71.56
hsa-miR-129-5p	26.04	132.00	124.86	146.00
hsa-miR-129-2-3p	1.85	8.91	6.97	8.97

hsa-miR-1292	28.24	163.00	144.92	120.00
hsa-miR-1296	9.47	48.34	21.91	32.74
hsa-miR-1301	22.01	111.86	101.94	79.94
hsa-miR-1303	0.81	7.82	4.60	3.56
hsa-miR-1303*	10.87	23.36	15.66	25.37
hsa-miR-1304*	305.45	645.02	629.01	583.41
hsa-miR-1305	6.19	9.00	19.99	18.99
hsa-miR-1306	4.77	20.00	19.55	23.00
hsa-miR-1306*	5.14	30.00	23.00	24.99
hsa-miR-1307	1507.22	6499.94	6487.82	6430.87
hsa-miR-1307*	765.52	2414.97	2439.99	2903.96
hsa-miR-130b	614.50	2145.97	1645.01	1619.61
hsa-miR-130b*	135.19	223.53	169.25	200.34
hsa-miR-132	38.52	139.00	115.99	114.98
hsa-miR-137	12.47	61.00	56.00	47.00
hsa-miR-138	2.93	9.00	9.00	5.00
hsa-miR-140-3p	10060.98	40154.92	28009.82	35465.43
hsa-miR-140-5p	583.21	1494.88	1161.99	1755.89
hsa-miR-141	48.77	144.98	72.98	116.04
hsa-miR-142-3p	49807.85	130203.11	104681.95	139205.55
hsa-miR-142-5p	2449.18	8450.82	5379.88	8637.23
hsa-miR-143	309.29	653.83	675.69	759.01
hsa-miR-143*	1.83	1.00	1.00	3.00
hsa-miR-144*	16.10	52.00	36.00	53.00
hsa-miR-145*	12.84	24.00	13.98	19.00
hsa-miR-145	26.38	100.85	59.94	60.90
hsa-miR-146a	133.82	332.49	266.35	277.47
hsa-miR-146b-3p	39.98	89.72	81.49	127.88
hsa-miR-146b-5p	28224.59	67451.18	54053.08	78958.80
hsa-miR-147b	2.19	7.00	3.99	3.00
hsa-miR-147b*	2.20	7.00	7.99	5.00
hsa-miR-148a	9998.19	48168.08	45139.11	27715.64
hsa-miR-148a*	329.75	762.94	843.93	1023.94
hsa-miR-148b	3276.18	18237.86	18563.14	12151.06
hsa-miR-148b*	268.87	837.00	813.00	852.97
hsa-miR-149*	1.46	29.02	20.99	11.99
hsa-miR-149	149.65	292.00	237.94	204.95
hsa-miR-151-3p	730.04	2486.60	1908.62	1879.36
hsa-miR-151-5p	28.91	282.37	179.08	144.29
hsa-miR-152	933.69	4988.89	4854.05	3534.80
hsa-miR-152*	11.37	20.90	19.60	26.00
hsa-miR-153	6.22	27.00	11.99	29.95
hsa-miR-155*	5.87	57.00	18.00	33.00
hsa-miR-155	17007.88	54380.84	44001.75	45019.88
hsa-miR-15a*	1.10	11.78	4.00	4.00
hsa-miR-15a	5087.32	13817.51	11725.44	15328.48
hsa-miR-15b*	18.34	58.00	62.92	51.00
hsa-miR-15b	578.23	2050.74	1802.77	1795.79
hsa-miR-16-1*	39.59	163.94	86.00	119.00
hsa-miR-16	5937.12	18108.02	15314.96	18336.86

hsa-miR-16-2*	133.87	459.88	218.96	339.92
hsa-miR-17*	1271.58	5418.82	4309.64	5417.38
hsa-miR-17	12514.75	48538.53	43772.76	53606.58
hsa-miR-181a-1*	13.57	43.00	28.00	45.76
hsa-miR-181a	71.53	266.83	351.08	250.75
hsa-miR-181a-2*	764.07	1729.97	1245.96	1359.00
hsa-miR-181b-1*	564.80	2062.95	2247.10	2197.56
hsa-miR-181b-2*	7.31	15.76	10.00	11.02
hsa-miR-181b	1657.66	8059.16	6664.55	5530.67
hsa-miR-181c*	9.17	27.00	21.00	28.24
hsa-miR-181d	20.14	94.07	51.99	78.06
hsa-miR-182	7872.81	23746.72	17819.91	29794.87
hsa-miR-183*	72.97	210.99	197.95	251.97
hsa-miR-183	3539.03	12367.56	10889.87	12550.08
hsa-miR-184	1.92	13.00	8.00	6.00
hsa-miR-185*	41.27	143.10	107.90	141.86
hsa-miR-185	1756.40	7072.32	6539.77	7169.79
hsa-miR-186*	51.39	103.55	130.20	147.22
hsa-miR-186	10022.33	33256.04	34417.83	30196.78
hsa-miR-187	8.07	40.00	20.00	47.00
hsa-miR-188-5p	68.19	337.79	257.94	253.87
hsa-miR-18a*	219.70	639.92	596.00	616.00
hsa-miR-18a	2365.77	11969.75	10925.72	13032.00
hsa-miR-18b	14.49	41.52	48.35	53.25
hsa-miR-190	79.16	161.91	139.97	169.98
hsa-miR-190b	70.43	181.99	115.97	240.95
hsa-miR-191*	228.50	710.99	598.98	676.65
hsa-miR-191	25097.14	136690.19	143597.94	107192.80
hsa-miR-192	361.84	1107.68	653.91	929.64
hsa-miR-193a-3p	17.96	77.61	54.96	61.97
hsa-miR-193a-5p	159.56	470.98	450.00	427.00
hsa-miR-194-2*	3.67	11.00	8.00	10.00
hsa-miR-196a	76.02	352.24	190.45	339.35
hsa-miR-196b	7137.25	18521.27	18587.50	20537.43
hsa-miR-197	244.16	747.96	584.93	224.92
hsa-miR-199a-3p	300.01	863.09	715.60	708.08
hsa-miR-199b-3p	110.02	372.73	271.21	242.78
hsa-miR-199b-5p	185.96	434.00	464.00	528.00
hsa-miR-19a	1322.68	3363.18	2417.91	3881.14
hsa-miR-19b	1771.32	4553.58	3215.44	5022.33
hsa-miR-19b-1*	38.50	128.95	65.00	123.99
hsa-miR-200a	28.26	52.98	47.02	93.90
hsa-miR-200b	33.67	104.72	93.75	123.76
hsa-miR-200b*	3.30	4.00	7.00	6.00
hsa-miR-200c	196.68	757.28	581.25	690.24
hsa-miR-203	0.61	1.60	1.00	0.67
hsa-miR-20a*	42.27	128.75	87.87	114.39
hsa-miR-20a	37811.06	110707.42	87914.81	118897.13
hsa-miR-20b	327.41	1313.63	1081.20	1262.75
hsa-miR-210	281.28	1926.86	930.87	1603.91

hsa-miR-210*	5.13	12.00	4.00	17.00
hsa-miR-21*	72.59	234.91	180.00	310.00
hsa-miR-215	34.56	88.72	63.01	86.25
hsa-miR-21	83224.68	198312.23	219310.31	237929.33
hsa-miR-216a	12.10	21.00	19.00	14.00
hsa-miR-216b	15.77	18.00	57.74	54.00
hsa-miR-217*	17.97	30.00	41.00	46.00
hsa-miR-219-5p	3.03	8.87	7.95	7.95
hsa-miR-221	1215.61	4147.72	3041.47	3790.34
hsa-miR-221*	363.00	1698.91	1559.03	1416.60
hsa-miR-222	1243.37	4683.68	4181.95	3776.64
hsa-miR-222*	45.12	122.00	73.00	121.99
hsa-miR-223	1507.43	4631.08	4441.82	5448.46
hsa-miR-223*	228.16	768.00	650.00	634.98
hsa-miR-22	143.02	590.95	351.89	652.69
hsa-miR-224	33.75	44.00	65.00	45.96
hsa-miR-22*	8.44	18.00	4.00	18.00
hsa-miR-23a	1823.04	5050.57	3628.02	4025.50
hsa-miR-23a*	3.53	12.74	5.00	6.00
hsa-miR-23b	161.38	526.17	411.11	366.85
hsa-miR-24	17294.78	40934.48	38635.01	49108.11
hsa-miR-24-2*	191.48	581.00	279.00	614.00
hsa-miR-25	1593.24	4601.77	3546.98	4832.59
hsa-miR-25*	12.02	533.99	215.92	109.00
hsa-miR-26a-1*	2.57	5.00	5.00	10.00
hsa-miR-26a	1309.60	3838.57	2637.48	3737.43
hsa-miR-26a-2*	1.47	7.00	1.00	4.00
hsa-miR-26b*	17.58	51.98	41.00	52.00
hsa-miR-26b	900.67	2572.96	1958.14	2425.11
hsa-miR-27a	4481.81	12239.09	10497.57	15995.48
hsa-miR-27a*	347.73	801.98	511.00	993.97
hsa-miR-27b	1204.55	4201.23	3849.51	3989.42
hsa-miR-27b*	44.02	199.00	102.00	133.00
hsa-miR-28-3p	1235.71	3489.92	3414.39	4128.69
hsa-miR-28-5p	389.38	1366.41	1119.05	1216.39
hsa-miR-29a	821.94	2706.79	2112.28	2471.73
hsa-miR-29a*	57.59	148.00	125.00	133.95
hsa-miR-29b	242.85	740.03	559.76	821.48
hsa-miR-29b-1*	63.82	155.00	153.08	182.52
hsa-miR-29b-2*	9.13	27.00	28.00	25.44
hsa-miR-29c	30.13	114.87	73.76	111.82
hsa-miR-29c*	20.54	42.00	41.00	60.00
hsa-miR-301a	48.40	215.84	165.68	198.86
hsa-miR-301b	16.83	58.00	49.94	47.93
hsa-miR-301b*	4.03	12.00	23.00	13.00
hsa-miR-30a	122.52	786.93	554.53	692.12
hsa-miR-30b*	6.97	18.00	11.00	20.00
hsa-miR-30b	570.85	1169.44	591.86	861.04
hsa-miR-30c-1*	115.89	406.45	290.04	315.63
hsa-miR-30c	38735.94	100379.85	79240.50	79243.56

hsa-miR-30c-2*	4.32	20.54	19.53	17.00
hsa-miR-30d*	18.71	52.00	83.00	57.00
hsa-miR-30d	16899.58	40123.73	43039.17	44819.79
hsa-miR-30e*	1261.43	2761.84	2952.57	55204.25
hsa-miR-30e	292886.03	713050.71	577556.49	781893.41
hsa-miR-320a	1782.52	15951.91	16542.09	11123.42
hsa-miR-320b	2.90	10.55	20.30	21.92
hsa-miR-320c	3.92	29.17	14.28	20.64
hsa-miR-320d	0.52	6.17	9.48	7.33
hsa-miR-32*	11.00	32.99	25.83	35.00
hsa-miR-324-3p	58.50	280.04	247.10	213.18
hsa-miR-324-5p	26.34	99.00	98.95	109.00
hsa-miR-32	236.85	763.90	540.21	658.87
hsa-miR-326	17.94	92.63	64.55	51.96
hsa-miR-328	11.00	53.00	22.00	56.96
hsa-miR-330-3p	27.74	175.04	160.90	72.86
hsa-miR-330-5p	30.07	103.97	135.84	134.90
hsa-miR-331-3p	26.04	82.85	67.00	46.00
hsa-miR-331-5p	9.90	34.00	29.00	38.00
hsa-miR-335*	176.04	168.69	387.26	354.94
hsa-miR-335	59.04	240.97	138.87	151.96
hsa-miR-338-3p	66.56	184.71	183.39	214.83
hsa-miR-338-5p	76.12	196.99	187.00	199.94
hsa-miR-339-3p	1382.05	4689.94	3778.96	4826.53
hsa-miR-339-5p	409.78	1330.27	938.32	1559.12
hsa-miR-33a*	223.76	631.08	549.30	715.53
hsa-miR-33a	204.14	384.60	376.56	483.76
hsa-miR-33b*	3.95	39.87	49.76	35.92
hsa-miR-33b	35.96	112.28	108.22	193.52
hsa-miR-340*	70.06	150.00	150.00	158.00
hsa-miR-340	185.54	480.83	572.74	423.76
hsa-miR-342-3p	1900.81	5931.99	4291.00	5243.00
hsa-miR-342-5p	230.72	809.96	833.96	735.00
hsa-miR-345*	5.87	26.99	9.00	21.00
hsa-miR-345	434.22	2147.73	1383.39	1527.82
hsa-miR-34a	19.44	51.99	55.89	56.99
hsa-miR-34b*	13.93	23.00	18.02	28.92
hsa-miR-34c-3p	8.43	14.99	30.99	11.00
hsa-miR-34c-5p	1454.71	3502.97	3751.80	3708.24
hsa-miR-361-3p	104.53	333.93	254.92	312.00
hsa-miR-361-5p	376.97	1131.32	920.81	1024.75
hsa-miR-362-3p	4.03	10.00	8.00	19.00
hsa-miR-362-5p	146.72	633.00	512.98	575.00
hsa-miR-363	325.73	1066.00	966.98	1002.00
hsa-miR-365	1.28	10.00	4.00	7.00
hsa-miR-365	1.28	10.00	4.00	7.00
hsa-miR-365*	17.59	87.96	50.00	47.00
hsa-miR-374a*	1675.73	3935.19	3009.63	3888.12
hsa-miR-374a	235.00	547.76	481.82	537.75
hsa-miR-374b*	16.06	27.04	25.10	25.00

hsa-miR-374b	380.18	1060.89	791.60	1004.91
hsa-miR-378	16496.03	47292.20	36524.16	40412.99
hsa-miR-378*	82.10	247.83	155.90	170.37
hsa-miR-421	17.24	88.63	88.79	74.89
hsa-miR-421*	1.28	2.13	1.58	2.55
hsa-miR-423-3p	4385.93	12288.93	13091.87	13151.54
hsa-miR-423-5p	1644.99	23018.27	19763.09	10916.75
hsa-miR-424	40.27	111.71	97.55	119.82
hsa-miR-425*	580.65	2420.98	1883.95	2257.83
hsa-miR-425	12133.99	42859.89	40799.47	37902.55
hsa-miR-429	16.14	53.00	37.99	68.00
hsa-miR-449a	24.28	81.07	77.08	93.89
hsa-miR-449b	7.26	24.92	18.90	17.96
hsa-miR-450a	17.59	51.99	41.95	52.95
hsa-miR-450b-5p	56.46	140.18	106.80	160.66
hsa-miR-451*	2.93	13.00	9.00	10.00
hsa-miR-452	65.29	103.50	124.98	88.44
hsa-miR-454	95.74	296.00	285.00	276.00
hsa-miR-454*	16.14	70.98	69.00	60.00
hsa-miR-455-3p	37.92	100.55	80.46	90.47
hsa-miR-455-5p	26.74	71.00	43.93	82.00
hsa-miR-484	309.83	1014.64	999.14	1120.73
hsa-miR-486-3p	38.98	73.46	75.22	99.08
hsa-miR-486-5p	75.39	169.27	160.38	166.26
hsa-miR-491-5p	4.40	20.00	11.00	16.00
hsa-miR-497	2.57	13.81	3.00	17.00
hsa-miR-500*	166.15	482.53	407.77	432.50
hsa-miR-500	15.96	70.00	53.48	59.99
hsa-miR-501-3p	42.42	179.08	165.80	141.40
hsa-miR-501-5p	37.05	214.00	171.00	120.00
hsa-miR-502-3p	52.29	175.38	136.43	148.09
hsa-miR-502-5p	8.80	27.00	26.01	33.00
hsa-miR-503*	5.14	16.00	18.00	18.99
hsa-miR-503	31.51	475.44	215.74	169.88
hsa-miR-505	74.83	307.00	230.00	255.00
hsa-miR-505*	4.40	21.00	28.00	14.00
hsa-miR-508-3p	1.83	6.00	2.00	1.00
hsa-miR-509-3p	1.47	7.00	15.00	8.00
hsa-miR-514	0.37	4.00	6.00	7.00
hsa-miR-532-3p	33.74	138.17	120.95	111.98
hsa-miR-532-5p	295.28	1855.91	1596.94	1813.58
hsa-miR-542-3p	132.75	469.54	378.33	477.88
hsa-miR-542-5p	20.54	64.00	52.00	52.00
hsa-miR-548a-3p	10.64	31.35	26.85	46.14
hsa-miR-548a-3-5p	8.99	25.43	21.91	21.90
hsa-miR-548b-3p	4.20	6.00	11.99	13.00
hsa-miR-548d-3p	3.80	20.62	10.44	22.20
hsa-miR-548e	44.20	181.52	214.94	173.48
hsa-miR-548e*	2.15	10.00	9.00	6.00
hsa-miR-548j*	3.28	4.65	7.67	5.61

hsa-miR-548j	73.18	179.33	155.42	185.91
hsa-miR-548k	5.87	22.98	44.98	29.99
hsa-miR-548l	4.39	16.98	16.85	6.99
hsa-miR-548n	6.89	11.00	3.00	2.00
hsa-miR-548o	2.47	18.05	15.24	14.48
hsa-miR-550*	15.38	32.33	27.31	25.32
hsa-miR-550	45.05	132.24	96.48	122.31
hsa-miR-550-2*	14.85	32.33	27.31	25.32
hsa-miR-551a	4.00	10.90	9.00	12.00
hsa-miR-570	1.10	4.99	2.00	5.99
hsa-miR-574-3p	12.45	78.84	67.83	39.96
hsa-miR-576-3p	10.18	28.30	24.38	28.51
hsa-miR-576-5p	12.09	19.97	11.33	8.99
hsa-miR-577	449.75	1282.75	1203.42	1116.40
hsa-miR-579	2.57	3.00	5.00	15.00
hsa-miR-579*	3.67	12.00	11.00	18.00
hsa-miR-580	22.01	59.00	40.00	50.00
hsa-miR-582-3p	571.86	1320.86	899.98	1208.14
hsa-miR-582-5p	116.20	284.89	123.90	166.83
hsa-miR-584	79.89	269.62	177.83	265.12
hsa-miR-588	5.50	18.96	6.99	21.99
hsa-miR-589*	13.18	80.00	64.98	85.00
hsa-miR-589	221.54	378.00	437.00	387.97
hsa-miR-590-3p	98.92	233.94	195.93	243.89
hsa-miR-590-5p	60.37	139.58	127.97	169.96
hsa-miR-597*	5.50	11.00	21.00	11.00
hsa-miR-598	672.57	2022.62	1783.69	2251.02
hsa-miR-616	9.73	17.84	27.40	33.12
hsa-miR-616*	2.38	6.00	2.00	3.00
hsa-miR-618	71.88	158.00	167.96	138.99
hsa-miR-624*	8.07	27.00	21.63	31.99
hsa-miR-625*	84.98	222.21	122.41	196.12
hsa-miR-625	83.32	221.49	121.49	185.36
hsa-miR-627	300.08	850.66	752.17	709.73
hsa-miR-628-5p	123.97	321.98	309.78	252.89
hsa-miR-629*	24.03	89.23	42.94	53.45
hsa-miR-629	292.88	763.72	578.92	688.18
hsa-miR-636	0.73	9.00	5.00	2.00
hsa-miR-642*	9.88	18.94	15.89	20.93
hsa-miR-642	2.59	14.06	7.08	14.06
hsa-miR-643	15.77	28.00	49.00	24.00
hsa-miR-651	9.17	30.00	14.00	13.00
hsa-miR-652	488.12	1938.25	1928.56	2079.67
hsa-miR-659*	17.97	25.07	28.95	43.91
hsa-miR-660	56.86	169.95	161.00	192.00
hsa-miR-664	17.24	72.00	45.00	55.00
hsa-miR-664*	52.79	165.94	163.96	130.93
hsa-miR-671-3p	27.80	53.86	31.88	28.97
hsa-miR-671-5p	216.79	987.81	638.88	886.92
hsa-miR-708	3.29	19.76	8.98	7.72

hsa-miR-7	587.93	4056.31	3998.11	2619.60
hsa-miR-720	38.88	140.65	100.80	134.87
hsa-miR-7	294.11	1573.07	1815.48	1511.86
hsa-miR-7	117.97	751.78	821.29	633.56
hsa-miR-744*	12.10	26.50	31.00	15.00
hsa-miR-744	457.02	1768.81	1886.36	1619.95
hsa-miR-760	52.38	306.85	356.88	208.93
hsa-miR-766	26.03	98.62	49.81	83.78
hsa-miR-769-3p	18.34	97.97	52.94	71.00
hsa-miR-769-5p	327.88	1163.01	1012.35	1039.89
hsa-miR-874	14.30	51.07	46.00	44.00
hsa-miR-877	130.02	2115.72	1931.25	910.54
hsa-miR-886-3p	8.59	28.31	41.85	27.56
hsa-miR-886-5p	1554.70	5932.90	7225.49	4452.03
hsa-miR-9-1*	8.62	23.82	20.46	29.16
hsa-miR-9	14068.13	34017.55	23474.83	41437.94
hsa-miR-9-2*	8.66	23.82	20.55	29.16
hsa-miR-92a	33490.55	101846.74	85026.83	96482.09
hsa-miR-92a*	93.17	430.00	326.78	338.95
hsa-miR-92b	654.62	2738.16	2121.26	1912.76
hsa-miR-92b*	8.44	285.27	274.94	128.99
hsa-miR-9-3*	116.60	270.36	247.98	317.67
hsa-miR-93*	30.45	137.96	95.00	204.00
hsa-miR-93	22661.57	72214.80	64491.29	69535.89
hsa-miR-939	4.37	21.39	12.80	29.63
hsa-miR-941	20.18	212.91	180.90	139.01
hsa-miR-941-1*	0.77	4.48	4.24	4.21
hsa-miR-941-2*	6.68	69.83	60.16	45.77
hsa-miR-941-3*	6.70	70.16	60.21	46.08
hsa-miR-942	100.84	244.85	180.87	201.93
hsa-miR-944	4.03	9.00	10.00	10.00
hsa-miR-95	43.43	96.78	91.69	116.15
hsa-miR-96	455.57	1478.83	667.97	1087.95
hsa-miR-98	339.46	1875.59	1592.64	1787.68
hsa-miR-99b*	59.04	213.98	155.97	171.29
hsa-miR-99b	3213.97	9495.97	7788.98	6624.92

Table S12. miRNA loci with significant reduction in addition relative to control, above estimated sequencing error rate
infrequent instances where miRNA loci with significant increase in addition relative to control, above estimated sequencing error rate are also displayed
^denotes a loci with ambiguous addition which may or may not result from 3' nucleotidyltransferase-catalyzed addition
EIF2C1 (AGO1)

miRNA loci	%A reduction	%U reduction	%AA reduction	%UU reduction
let-7a	--	^~25.4%	--	--
let-7f	--	^~21.0%	--	--
let-7g	-24.6%	^~29.8%	-53.0%	--
let-7i	-33.3%	--	--	--
miR-142-3p	5.2%	--	-57.6%	--
miR-148a	--	-32.0%	--	--
miR-148b	--	--	--	-38.6%
miR-152	--	-57.2%	--	--
miR-155	--	--	--	^~32.0%
miR-185	38.3%	--	--	--
miR-186	-73.0%	^~50.6%	--	--
miR-191	16.6%	^~47.9%	--	--
miR-196b	^~26.0%	-30.0%	--	--
miR-16	--	^~38.3%	--	--
miR-17	--	^~39.0%	--	--
miR-20a	-70.2%	^~22.1%	--	--
miR-21	-38.1%	^~39.7%	--	--
miR-222	-55.2%	--	--	--
miR-223	--	-61.2%	--	--
miR-23a	^~24.1%	--	^~48.1%	--
miR-24	38.6%	4.1%	--	--
miR-26b	--	-59.4%	--	--
miR-27a	--	-31.0%	--	--
miR-29a	^~51.9%	--	--	--
miR-30c	-67.8%	^~63.0%	--	--
miR-30d	--	^~39.3%	--	--
miR-30e	--	^~8.7%	--	--
miR-32	^~45.8%	--	--	--
miR-342-3p	^~57.7%	-62.2%	--	--
miR-423-3p	28.6%	--	--	--
miR-378	34.8%	--	--	--
miR-744	^~39.2%	--	--	--
miR-92a	--	^~43.9%	55.2%	--
miR-99b	--	-83.2%	--	--

EIF2C2 (AGO2)

miRNA loci	%A reduction	%U reduction	%AA reduction	%UU reduction
let-7a	-24.2%	^6.9%	-26.2%	--
let-7b	-10.9%	^12.0%	--	--
let-7d	-22.6%	--	--	--
let-7f	-30.5%	--	-39.0%	--
let-7g	--	^30.8%	--	--
miR-101	^~38.4%	--	--	--
miR-106b*	--	57.2%	--	--
miR-125a	^~43.7%	--	--	--
miR-130b	-61.3%	--	--	--
miR-140-3p	-32.3%	--	--	--
miR-140-5p	-75.0%	--	--	--
miR-142-5p	^80.7%	--	--	--
miR-148a	-58.0%	-32.0%	--	--
miR-148b	-53.3%	-19.7%	-62.2%	--
miR-152	--	-58.1%	--	--
miR-155	-40.1%	^~9.2%	46.0%	--
miR-16	-23.1%	^~24.5%	--	--
miR-17	-35.5%	^~32.4%	--	--
miR-183	-50.2%	--	--	--
miR-186	--	^~42.7%	--	--
miR-191	28.4%	^~26.3%	--	--
miR-196b	^~29.5%	--	--	--
miR-20a	-41.1%	--	--	--
miR-21	-50.0%	^~35.9%	--	--
miR-210	--	^37.8%	--	--
miR-221	--	-34.7%	--	--
miR-222	-64.4%	^14.7%	--	--
miR-223	-53.7%	24.3%	--	--
miR-23a	^~57.2%	--	--	--
miR-24	-19.5%	-5.5%	--	-29.2%
miR-25	42.4%	52.3%	--	--
miR-28-3p	-54.9%	--	--	--
miR-29a	^~42.5%	--	--	--
miR-30c	-82.3%	^~81.7%	--	--
miR-30d	-64.3%	^~59.7%	--	--
miR-30e	-40.2%	^~22.8%	--	--
miR-320a	^~17.3%	--	--	--
miR-33a	^~62.5%	--	--	--
miR-342-3p	^~53.7%	-64.8%	--	--
miR-345	-57.9%	-84.6%	--	-96.9%
miR-361	-72.2%	--	--	--
miR-374b	--	^63.0%	--	63.0%
miR-423-3p	-29.7%	--	--	--
miR-425	--	-67.2%	--	--
miR-454	--	^34.3%	--	--
miR-484	--	50.6%	--	--
miR-532-3p	^~76.7%	--	--	--
miR-744	^~45.8%	--	--	--
miR-769	--	^~49.8%	--	--
miR-92a	--	^~14.3%	32.1%	--
miR-93	-28.1%	--	--	--
miR-98	--	^~30.9%	--	--
miR-99b	--	-51.4%	--	--

EIF2C3 (AGO3)

miRNA loci	%A reduction	%U reduction	%AA reduction	%UU reduction
let-7a	-47.7%	^~48.7%	-62.0%	--
let-7b	-21.1%	^~22.1%	-53.3%	--
let-7d	-51.1%	--	--	--
let-7e	-63.3%	--	--	--
let-7f	-55.8%	^~32.1%	-70.4%	--
let-7g	-55.6%	^~32.5%	-79.3%	--
let-7i	-37.1%	^~44.0%	-63.4%	--
miR-103	^~66.7%	--	--	--
miR-125a	^34.8%	--	--	--
miR-126	-62.3%	--	--	--
miR-126*	-82.8%	--	--	--
miR-140-3p	-57.9%	--	--	--
miR-140-5p	-88.2%	--	--	--
miR-142-3p	-25.1%	^37.9%	-60.6%	--
miR-142-5p	^47.4%	--	--	--
miR-152	--	-51.8%	--	--
miR-155	-47.7%	--	--	^~34.8%
miR-16	--	^~42.1%	--	--
miR-17	-42.4%	^~44.2%	--	--
miR-183	-60.4%	--	--	--
miR-186	-64.2%	^~29.6%	--	--
miR-191	-32.5%	^~50.1%	--	--
miR-20a	-55.3%	--	--	--
miR-21	-55.1%	^~20.5%	--	--
miR-222	-63.5%	^17.3%	--	--
miR-223	-69.8%	-62.9%	--	-66.7%
miR-23a	--	--	^36.1%	--
miR-24	-17.7%	--	--	-31.3%
miR-26b	--	-51.7%	--	--
miR-27a	-38.7%	--	--	--
miR-28-3p	-65.3%	--	--	--
miR-29a	^~62.6%	--	--	--
miR-30c	-78.0%	^~59.5%	--	--
miR-30d	--	^~15.3%	--	--
miR-30e	-24.0%	^26.2%	--	--
miR-32	^37.5%	--	--	--
miR-342-3p	^~61.5%	--	--	--
miR-378	--	--	-63.9%	--
miR-423-3p	-62.8%	-68.4%	--	--
miR-532	--	^~91.1%	--	--
miR-92a	-28.5%	^~33.8%	21.4%	--
miR-93	-25.4%	--	--	--
miR-99b	-55.9%	-74.5%	--	--

Table S13. Proportion of adenine addition across control and AGO-IP-generated libraries.

**yellow highlighting indicates significant decrease,
orange highlighting indicates significant increase

miRNA locus	proportion of addition in each library			
	control	EIF2C1	EIF2C2	EIF2C3
hsa-let-7a	0.0669	0.0727	0.0507	0.0350
hsa-let-7b	0.1313	0.1398	0.1171	0.1034
hsa-let-7d	0.1082	0.1113	0.0840	0.0530
hsa-let-7e	0.0801	0.1143	0.0580	0.0294
hsa-let-7f	0.0666	0.0626	0.0463	0.0295
hsa-let-7g	0.0914	0.0690	0.0965	0.0406
hsa-let-7i	0.0392	0.0250	0.0390	0.0219
hsa-miR-106b	0.0110	0.0073	0.0099	0.0082
hsa-miR-106b*	0.1715	0.1538	0.1105	0.0784
hsa-miR-126	0.0312	0.0262	0.0288	0.0118
hsa-miR-126*	0.0262	0.0119	0.0360	0.0045
hsa-miR-128	0.0954	0.0845	0.0000	0.0511
hsa-miR-1307	0.1123	0.1188	0.1010	0.0932
hsa-miR-130b	0.0632	0.0462	0.0245	0.0558
hsa-miR-140-3p	0.0077	0.0123	0.0062	0.0049
hsa-miR-140-5p	0.0238	0.0109	0.0060	0.0028
hsa-miR-142-3p	0.1347	0.1421	0.1312	0.1009
hsa-miR-146a	0.0780	0.0388	0.0630	0.0262
hsa-miR-148a	0.0134	0.0143	0.0056	0.0092
hsa-miR-148b	0.0585	0.0406	0.0273	0.0385
hsa-miR-152	0.0765	0.0952	0.0764	0.0643
hsa-miR-155	0.0249	0.0226	0.0149	0.0138
hsa-miR-15b	0.0347	0.0355	0.0341	0.0221
hsa-miR-16	0.0487	0.0645	0.0375	0.0327
hsa-miR-17	0.0845	0.0728	0.0545	0.0487
hsa-miR-17*	0.1532	0.2005	0.1520	0.1208
hsa-miR-183	0.1084	0.0767	0.0581	0.0449
hsa-miR-185	0.0470	0.0762	0.0411	0.0416
hsa-miR-186	0.0179	0.0062	0.0078	0.0064
hsa-miR-18a	0.0505	0.0325	0.0396	0.0315
hsa-miR-190b	0.1181	0.1429	0.1111	0.1613
hsa-miR-191	0.0823	0.0987	0.1150	0.0556
hsa-miR-20a	0.0682	0.0556	0.0402	0.0305
hsa-miR-20b	0.0650	0.0880	0.0696	0.0375
hsa-miR-21	0.0641	0.0397	0.0320	0.0288
hsa-miR-210	0.0704	0.0822	0.0592	0.0600
hsa-miR-222	0.0532	0.0239	0.0190	0.0194
hsa-miR-223	0.0090	0.0080	0.0043	0.0026
hsa-miR-223_star	0.0630	0.0498	0.0000	0.0217
hsa-miR-24	0.0927	0.1509	0.0745	0.0761
hsa-miR-25	0.0507	0.0860	0.0880	0.0487
hsa-miR-26a	0.0590	0.0702	0.0467	0.0282
hsa-miR-26b	0.0261	0.0212	0.0228	0.0153
hsa-miR-27a	0.0251	0.0265	0.0241	0.0154
hsa-miR-28-5p	0.1427	0.2401	0.1589	0.1586

hsa-miR-28-3p	0.1928	0.1240	0.0869	0.0669
hsa-miR-30b	0.0282	0.0192	0.0109	0.0088
hsa-miR-30c	0.0061	0.0020	0.0011	0.0013
hsa-miR-30d	0.0050	0.0032	0.0018	0.0027
hsa-miR-30e	0.0035	0.0037	0.0021	0.0027
hsa-miR-324	0.1208	0.1818	0.1113	0.0882
hsa-miR-326	0.1168	0.0589	0.1429	0.0263
hsa-miR-339	0.0493	0.0594	0.0308	0.0412
hsa-miR-339_star	0.0716	0.0517	0.0628	0.0393
hsa-miR-342_star	0.0204	0.0228	0.0094	0.0192
hsa-miR-345	0.0831	0.0928	0.0350	0.0319
hsa-miR-34c	0.0083	0.0211	0.0062	0.0107
hsa-miR-361	0.0772	0.0750	0.0215	0.0375
hsa-miR-374a	0.0241	0.0479	0.0365	0.0443
hsa-miR-374a_star	0.1310	0.1226	0.1173	0.1486
hsa-miR-374b	0.0856	0.0345	0.0494	0.0629
hsa-miR-378	0.1533	0.2352	0.1387	0.1273
hsa-miR-423-3p	0.0621	0.0714	0.0436	0.0231
hsa-miR-423-5p	0.0590	0.0827	0.0569	0.0513
hsa-miR-532	0.0739	0.0446	0.0720	0.0257
hsa-miR-652	0.1139	0.1147	0.1223	0.1179
hsa-miR-877	0.0837	0.0000	0.0185	0.0909
hsa-miR-886	0.0456	0.0270	0.0222	0.0230
hsa-miR-9	0.0112	0.0143	0.0166	0.0246
hsa-miR-92a	0.1525	0.1544	0.1510	0.1095
hsa-miR-92b	0.0549	0.0977	0.0493	0.0433
hsa-miR-93	0.0583	0.0742	0.0419	0.0433
hsa-miR-98	0.0395	0.0335	0.0337	0.0149
hsa-miR-99b	0.0837	0.0508	0.0581	0.0369

Table S14. Lists of miRNAs used in Figure 6 analysis.

List of miRNAs with conserved A addition

hsa-miR-101-1
 hsa-miR-140-5p
 hsa-miR-15b
 hsa-miR-16-1
 hsa-miR-16-2
 hsa-miR-17
 hsa-miR-185
 hsa-miR-191
 hsa-miR-20a
 hsa-miR-21
 hsa-miR-22
 hsa-miR-24-2
 hsa-miR-26a-2
 hsa-miR-26b
 hsa-miR-27a
 hsa-miR-361-5p
 hsa-miR-374a
 hsa-miR-92a-1
 hsa-miR-93

List of miRNAs lacking A addition

hsa-miR-125a-3p
 hsa-miR-125a-5p
 hsa-miR-1307
 hsa-miR-142-5p
 hsa-miR-146b-3p
 hsa-miR-148a
 hsa-miR-151-5p
 hsa-miR-193a-5p
 hsa-miR-199b-3p
 hsa-miR-199b-5p
 hsa-miR-27b
 hsa-miR-30e
 hsa-miR-324-5p
 hsa-miR-335
 hsa-miR-338-3p
 hsa-miR-338-5p
 hsa-miR-339-3p
 hsa-miR-340
 hsa-miR-342-3p
 hsa-miR-342-5p
 hsa-miR-361-3p
 hsa-miR-362-3p
 hsa-miR-362-5p
 hsa-miR-425
 hsa-miR-455-3p
 hsa-miR-455-5p
 hsa-miR-486-3p
 hsa-miR-486-5p
 hsa-miR-532-3p
 hsa-miR-532-5p
 hsa-miR-542-3p
 hsa-miR-542-5p
 hsa-miR-582-3p
 hsa-miR-582-5p
 hsa-miR-589
 hsa-miR-590-3p
 hsa-miR-629
 hsa-miR-664
 hsa-miR-671-5p
 hsa-miR-9-1
 hsa-miR-9-2
 hsa-miR-9-3

List of miRNAs with conserved U addition

hsa-miR-101-1
 hsa-miR-106b
 hsa-miR-140-3p
 hsa-miR-140-5p

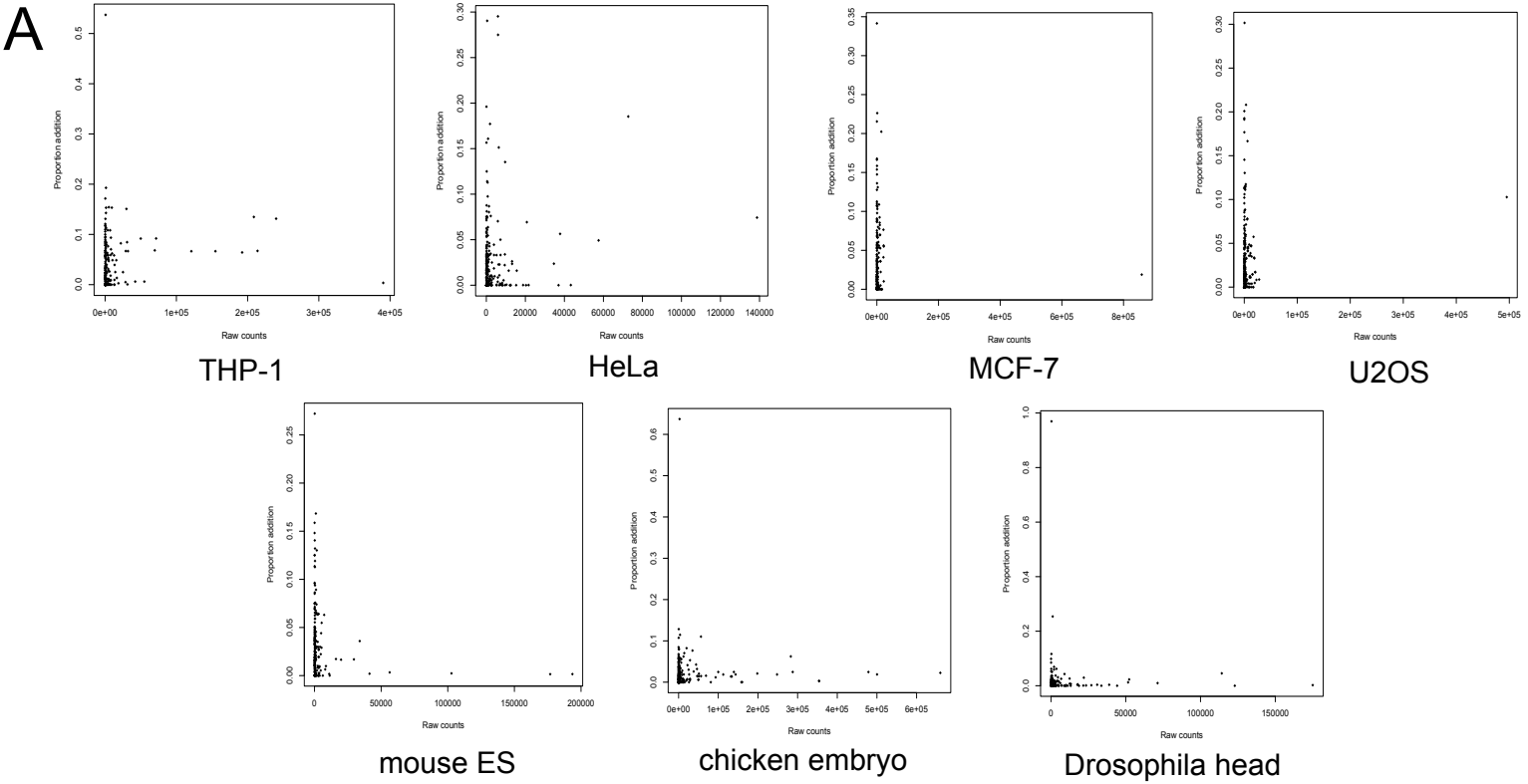
List of miRNAs lacking U addition

hsa-let-7a-1
 hsa-let-7a-3
 hsa-let-7d
 hsa-let-7f-1

hsa-miR-148a
hsa-miR-148b
hsa-miR-24-2
hsa-miR-26a-2
hsa-miR-26b
hsa-miR-27a
hsa-miR-27b
hsa-miR-324-3p
hsa-miR-342-3p
hsa-miR-99b

hsa-let-7g
hsa-miR-125a-3p
hsa-miR-1307
hsa-miR-142-5p
hsa-miR-146b-3p
hsa-miR-151-5p
hsa-miR-15b
hsa-miR-16-1
hsa-miR-16-2
hsa-miR-17
hsa-miR-183
hsa-miR-185
hsa-miR-186
hsa-miR-193a-3p
hsa-miR-193a-5p
hsa-miR-199b-3p
hsa-miR-199b-5p
hsa-miR-19b-1
hsa-miR-20a
hsa-miR-21
hsa-miR-22
hsa-miR-28-5p
hsa-miR-29b-1
hsa-miR-335
hsa-miR-338-3p
hsa-miR-338-5p
hsa-miR-339-3p
hsa-miR-339-5p
hsa-miR-33a
hsa-miR-340
hsa-miR-342-5p
hsa-miR-361-3p
hsa-miR-361-5p
hsa-miR-362-3p
hsa-miR-362-5p
hsa-miR-374a
hsa-miR-423-5p
hsa-miR-455-3p
hsa-miR-455-5p
hsa-miR-486-3p
hsa-miR-486-5p
hsa-miR-532-3p
hsa-miR-532-5p
hsa-miR-542-5p
hsa-miR-582-3p
hsa-miR-582-5p
hsa-miR-589
hsa-miR-590-3p
hsa-miR-590-5p
hsa-miR-629

hsa-miR-664
hsa-miR-671-5p
hsa-miR-9-1
hsa-miR-9-2
hsa-miR-9-3
hsa-miR-92a-1
hsa-miR-93



B

	Pearson		Spearman	
cell type	correlation coefficient	p-value	correlation coefficient	p-value
THP-1	0.12	0.070	0.25	0.00012
HeLa	0.15	0.015	0.17	0.0050
MCF-7	-0.02	0.80	0.15	0.028
U2OS	0.11	0.057	0.28	6.1e-7
mouse ES	-0.09	0.14	0.08	0.17
chicken embryo	-0.01	0.93	0.15	0.015
Drosophila head	-0.04	0.60	-0.03	0.73

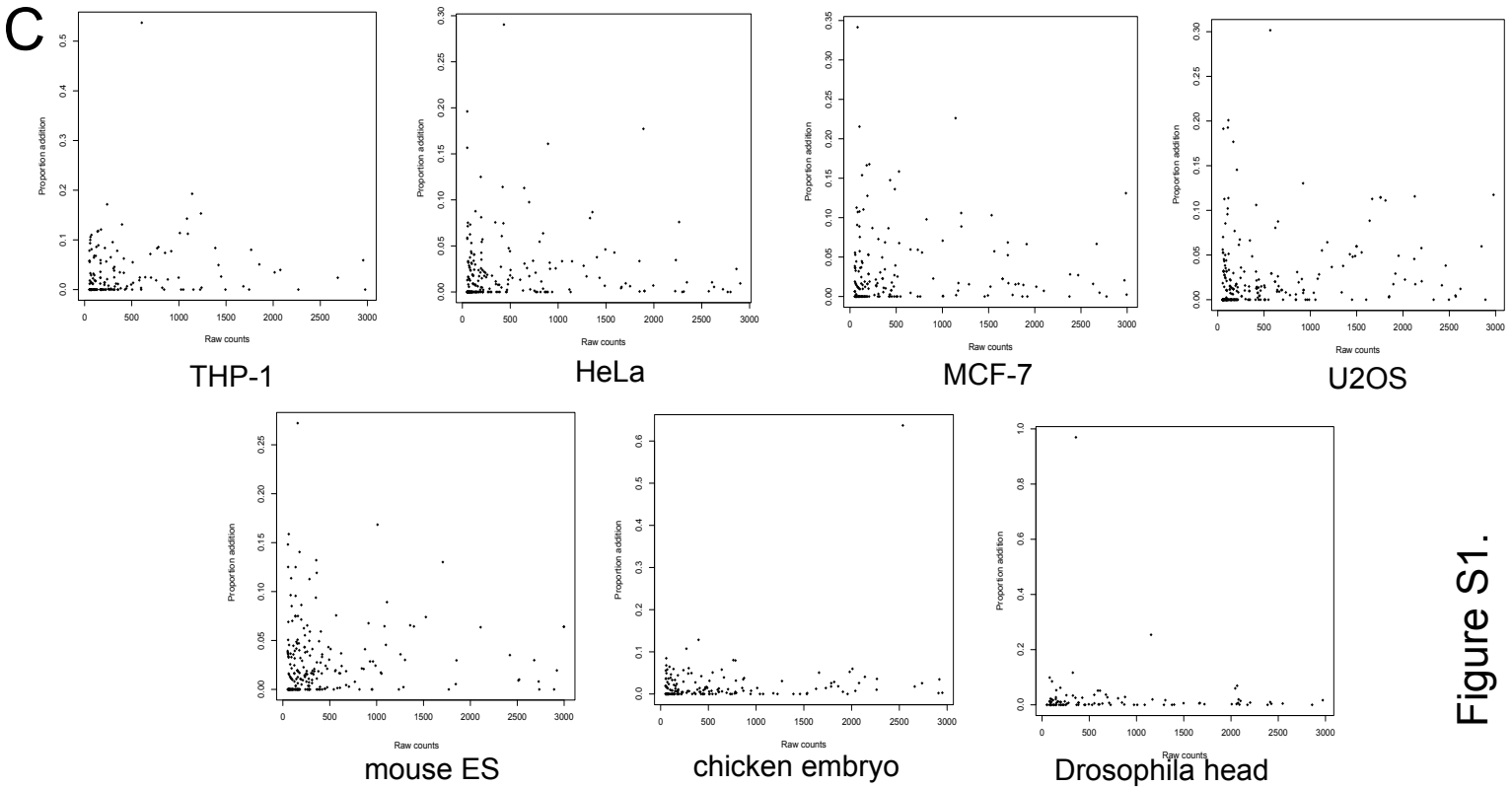


Figure S1.

Figure S2.

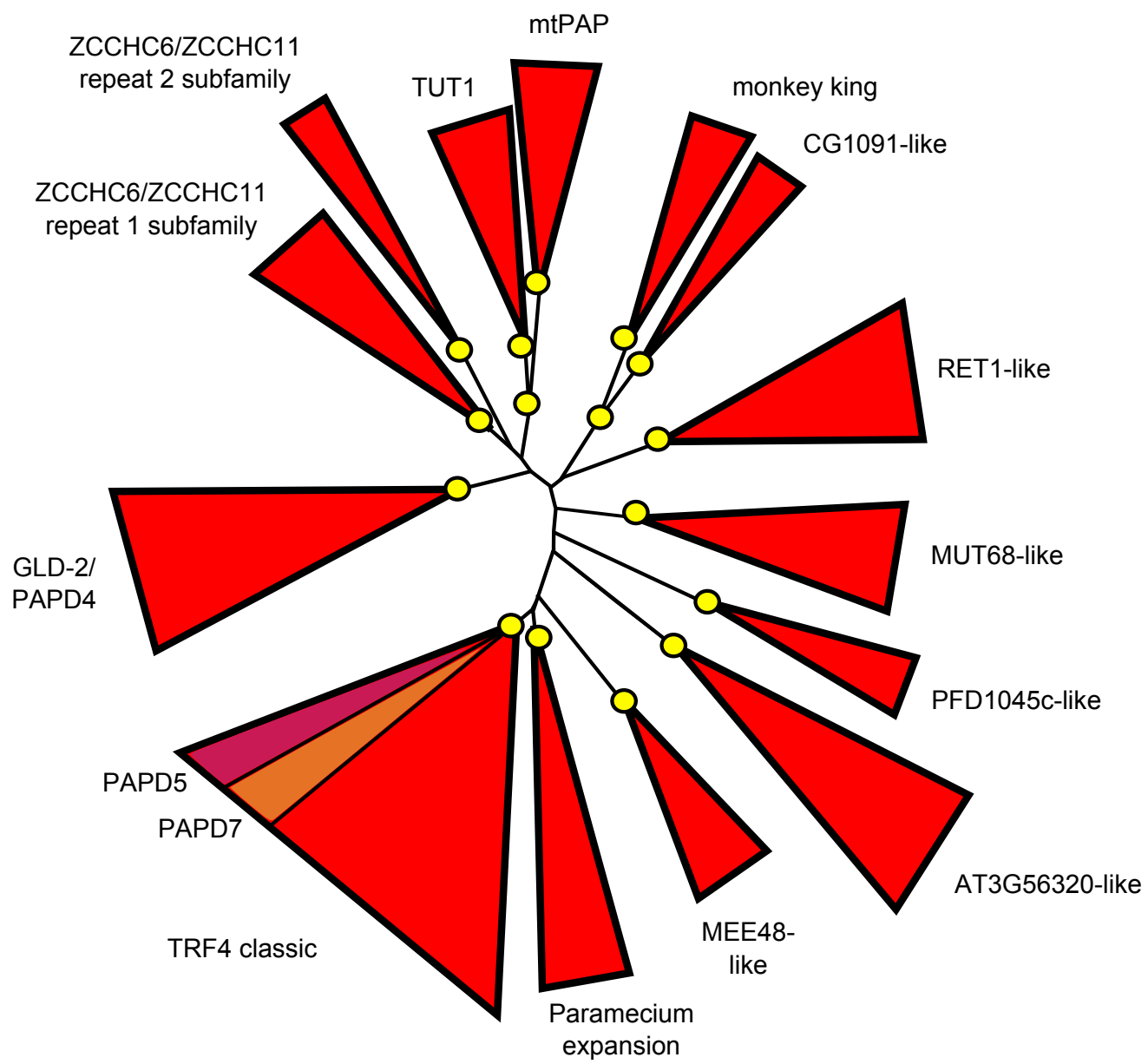


Figure S3.

U unambiguous addition

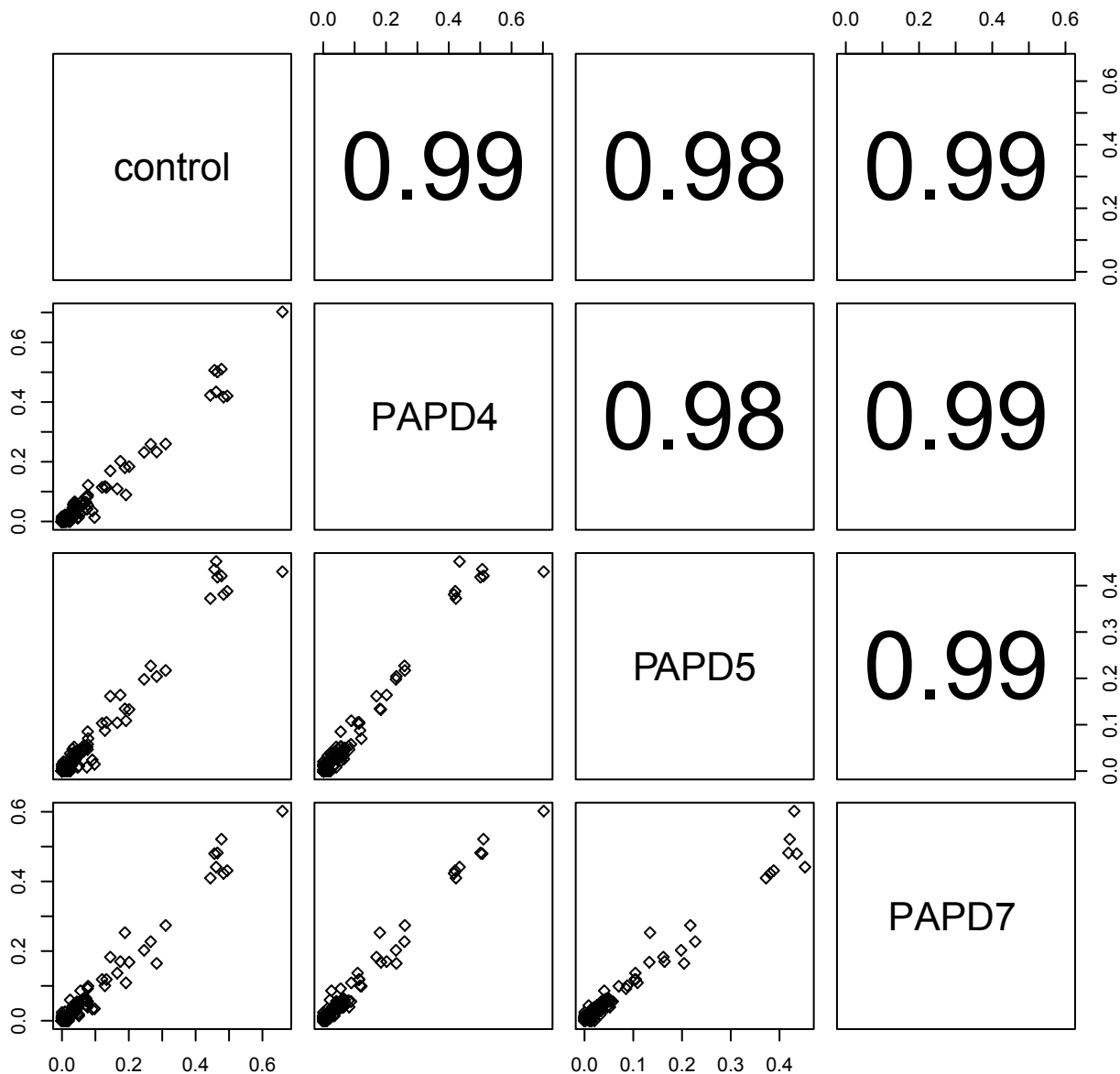


Figure S4.

UU unambiguous addition

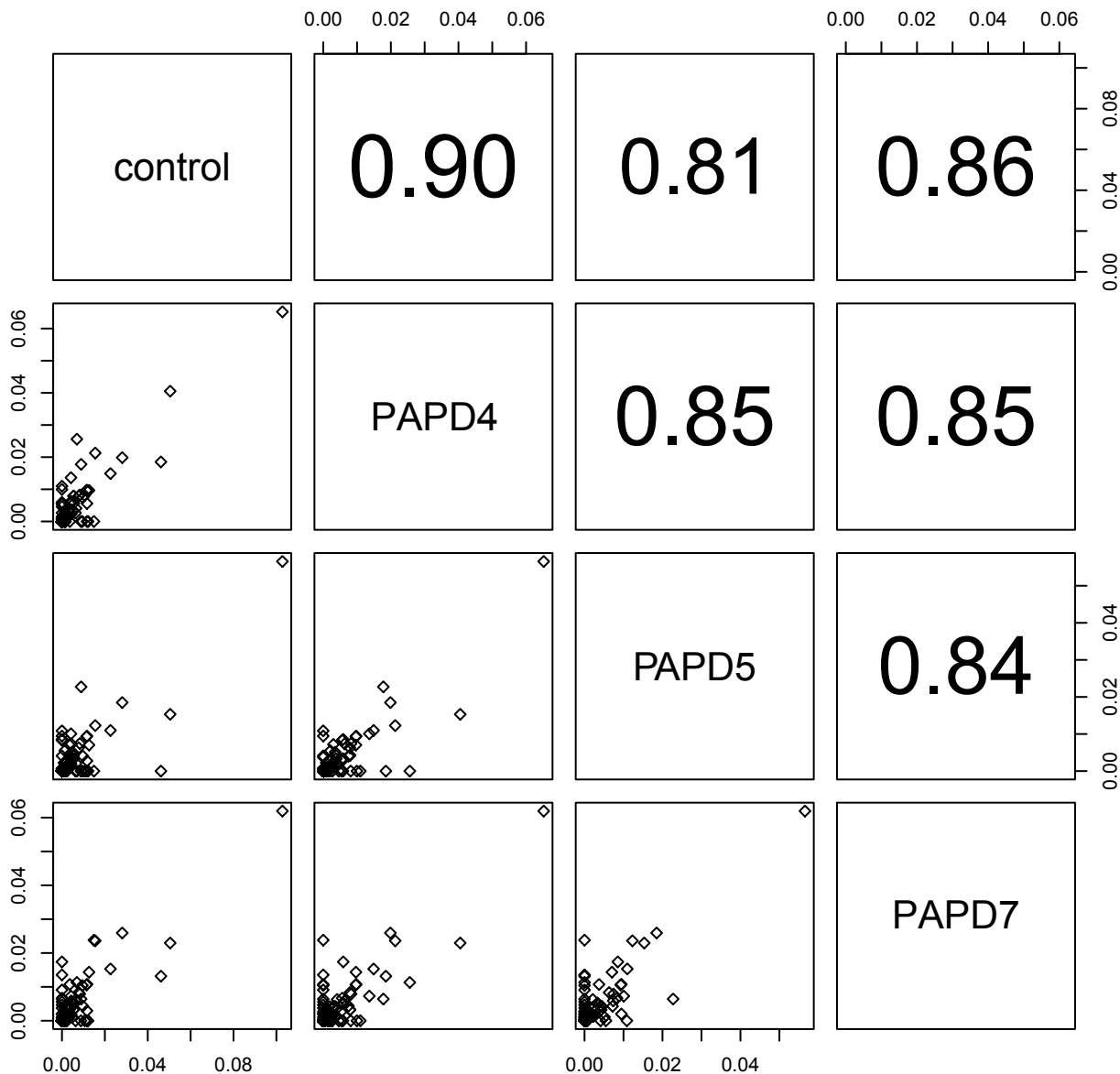


Figure S5.

AA unambiguous addition

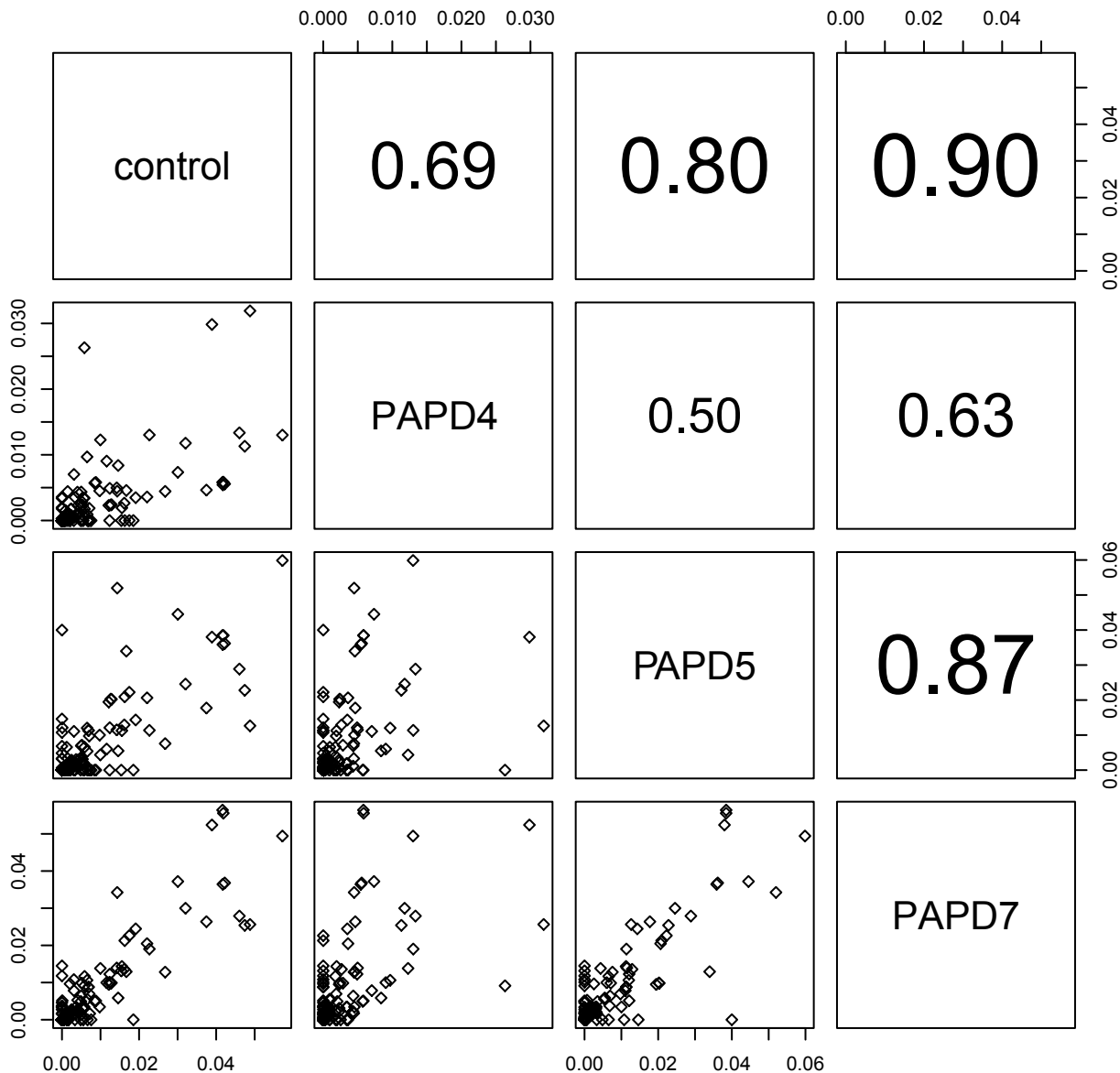


Figure S6.

AU unambiguous addition

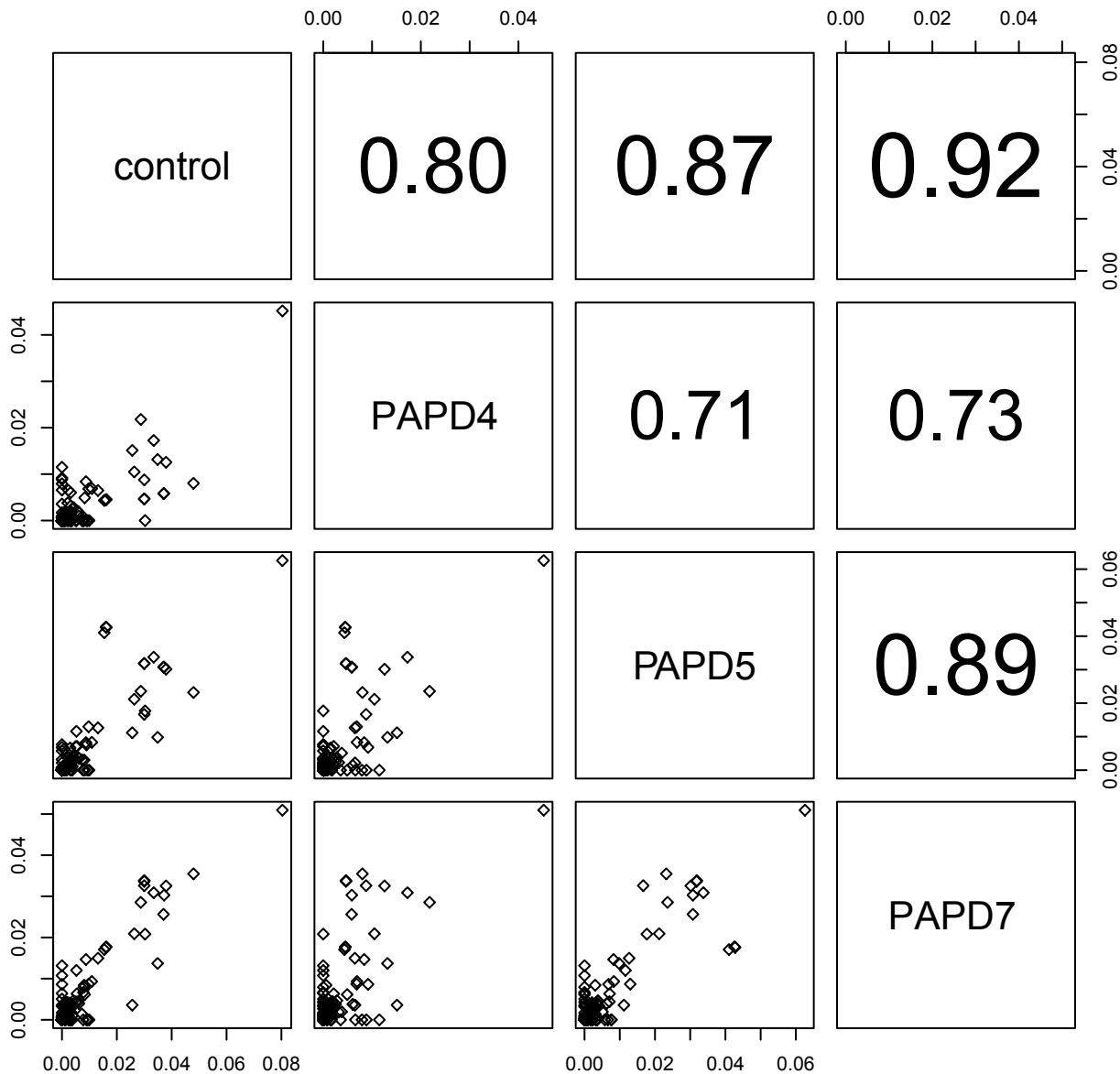


Figure S7.

G unambiguous addition

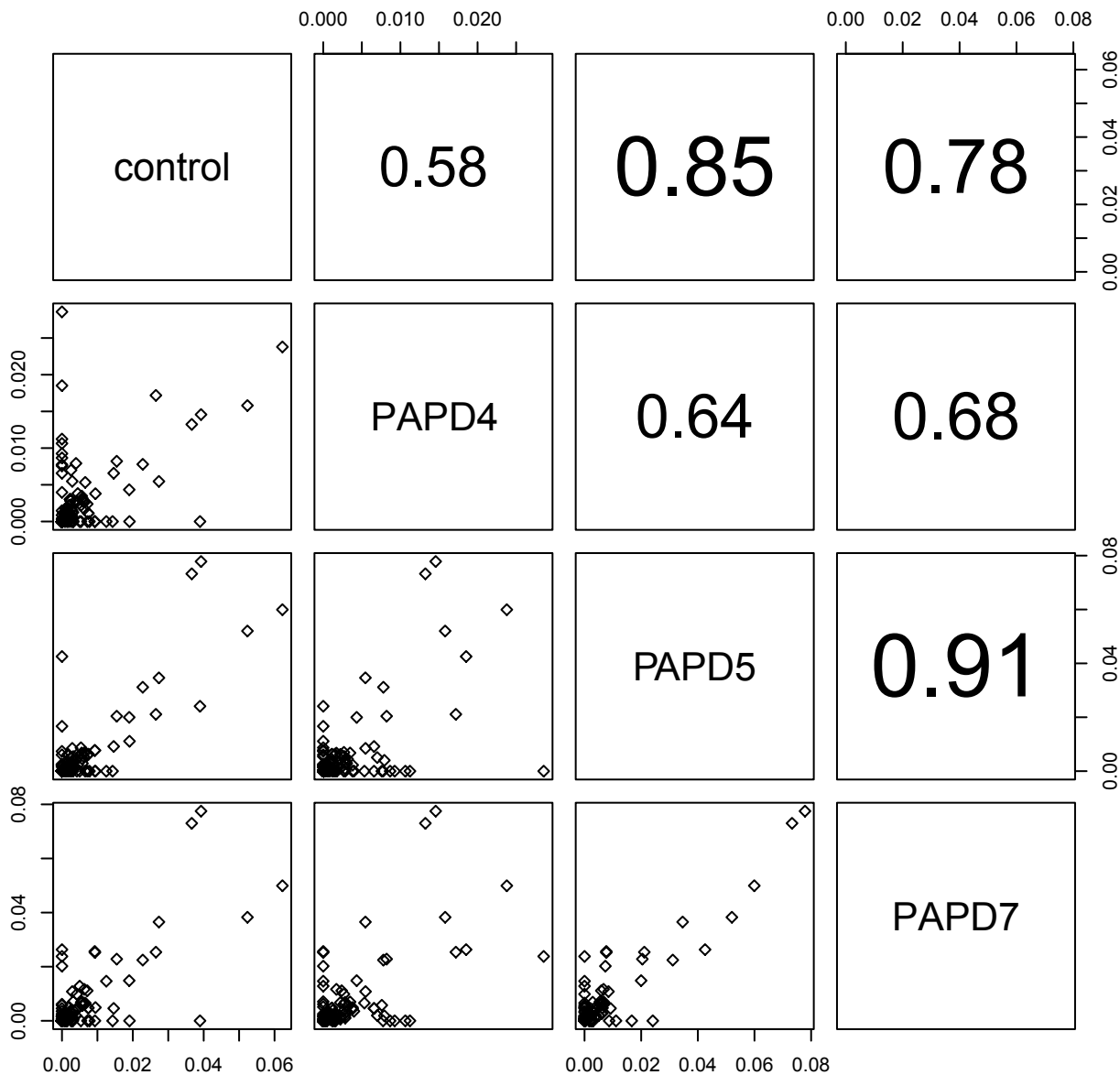


Figure S8. GA unambiguous addition

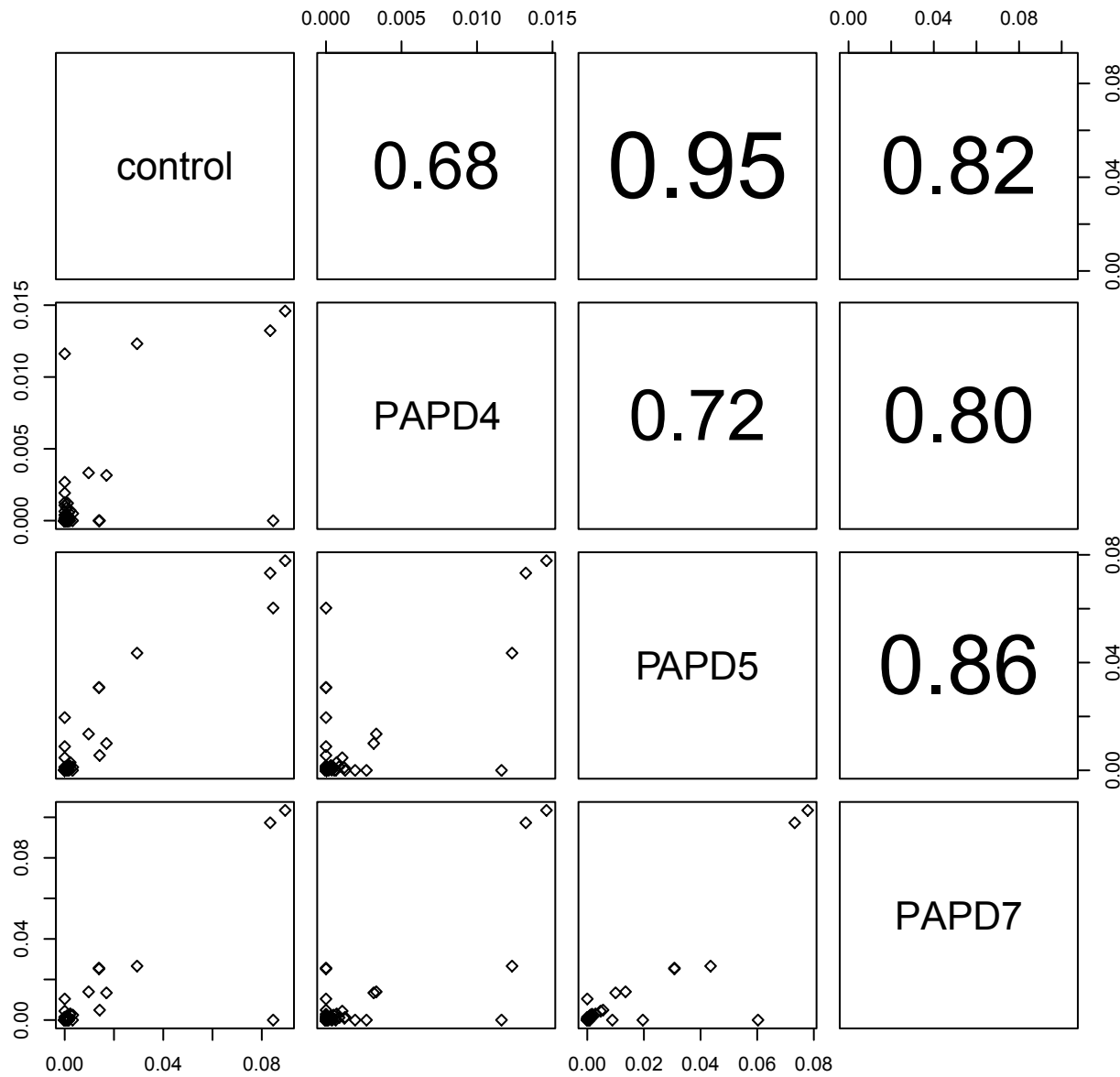


Figure S9.

U ambiguous addition

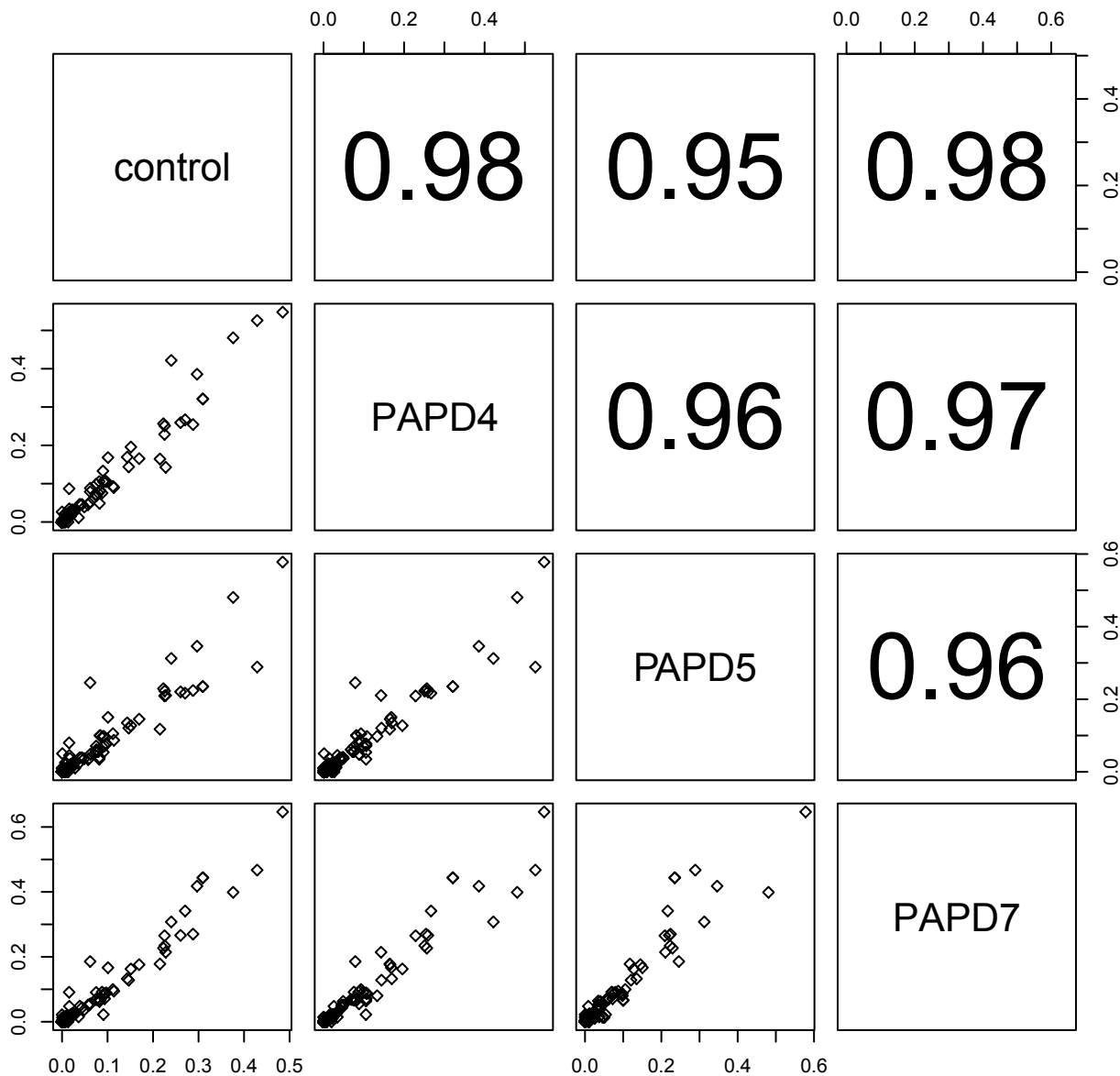


Figure S10.

UU ambiguous addition

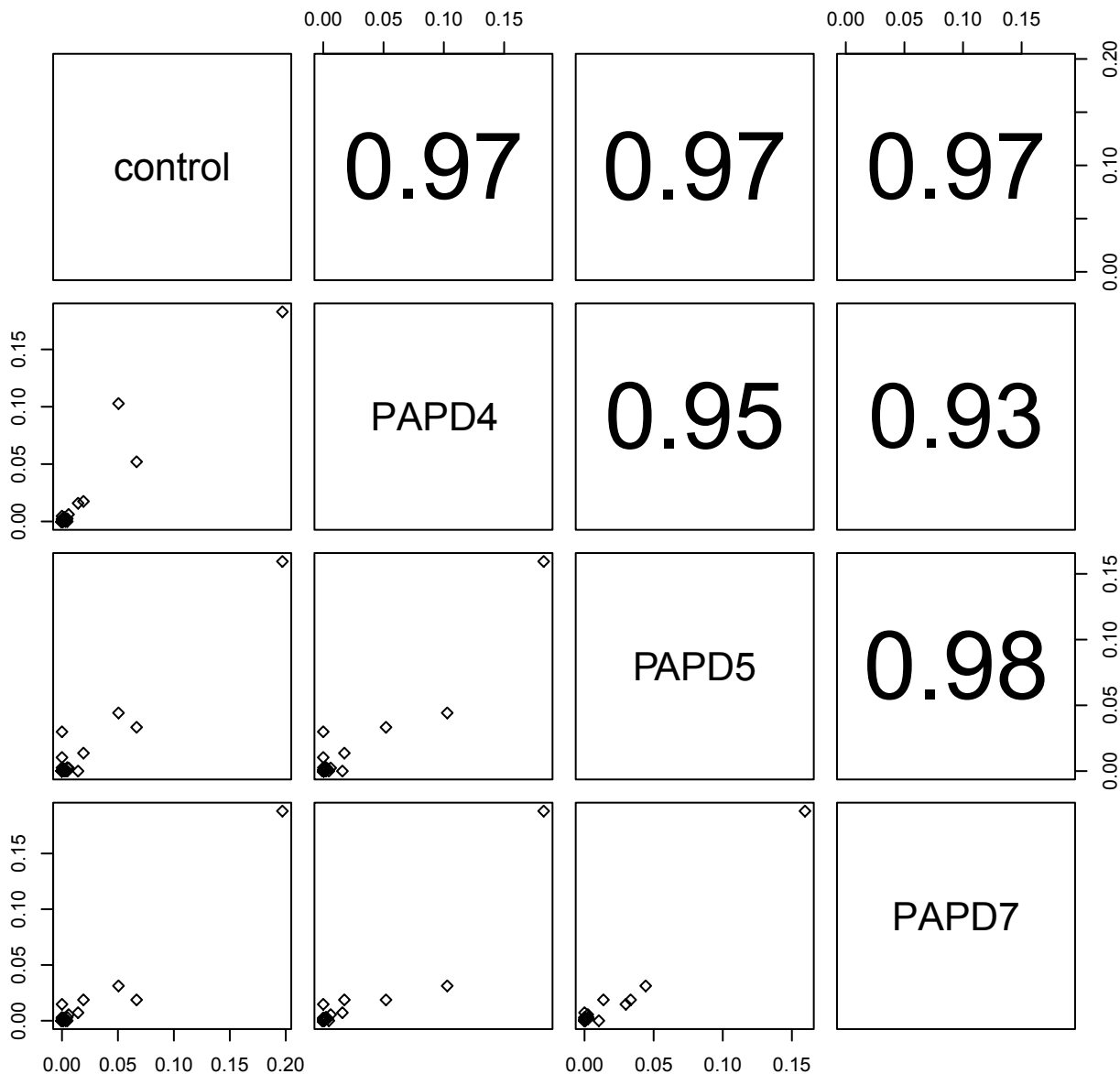


Figure S11.

AA ambiguous addition

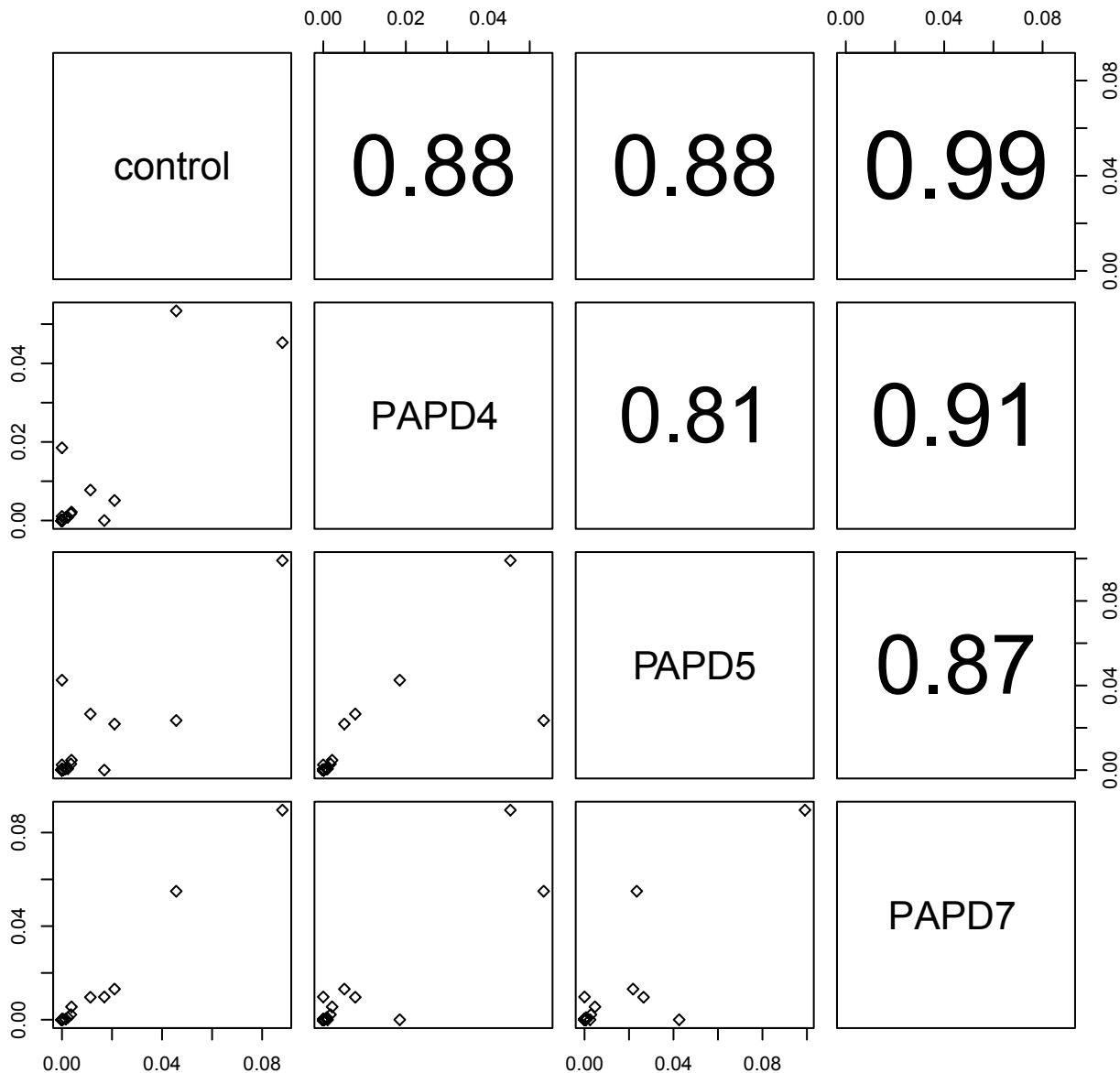


Figure S12.

AU ambiguous addition

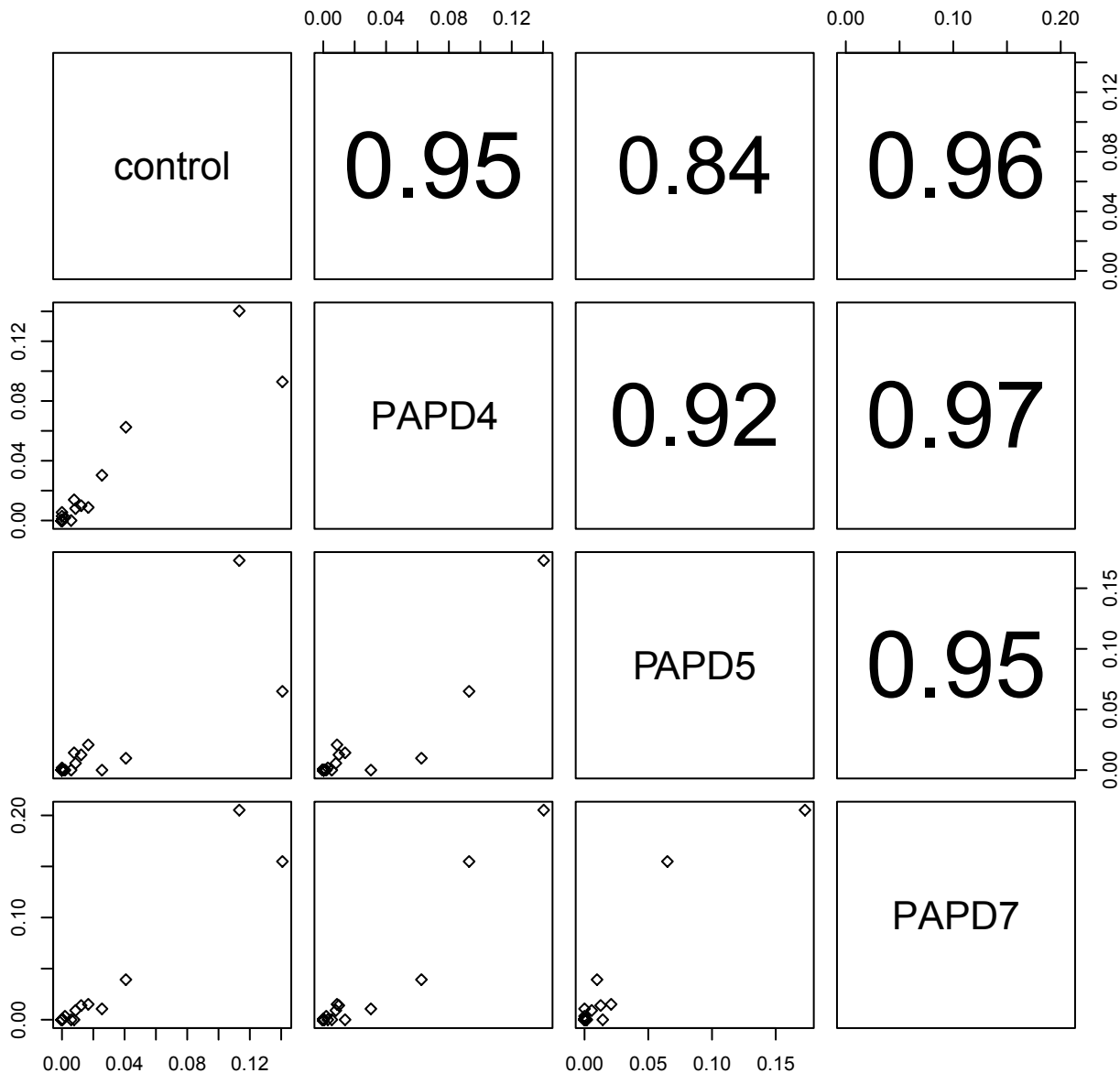


Figure S13.

G ambiguous addition

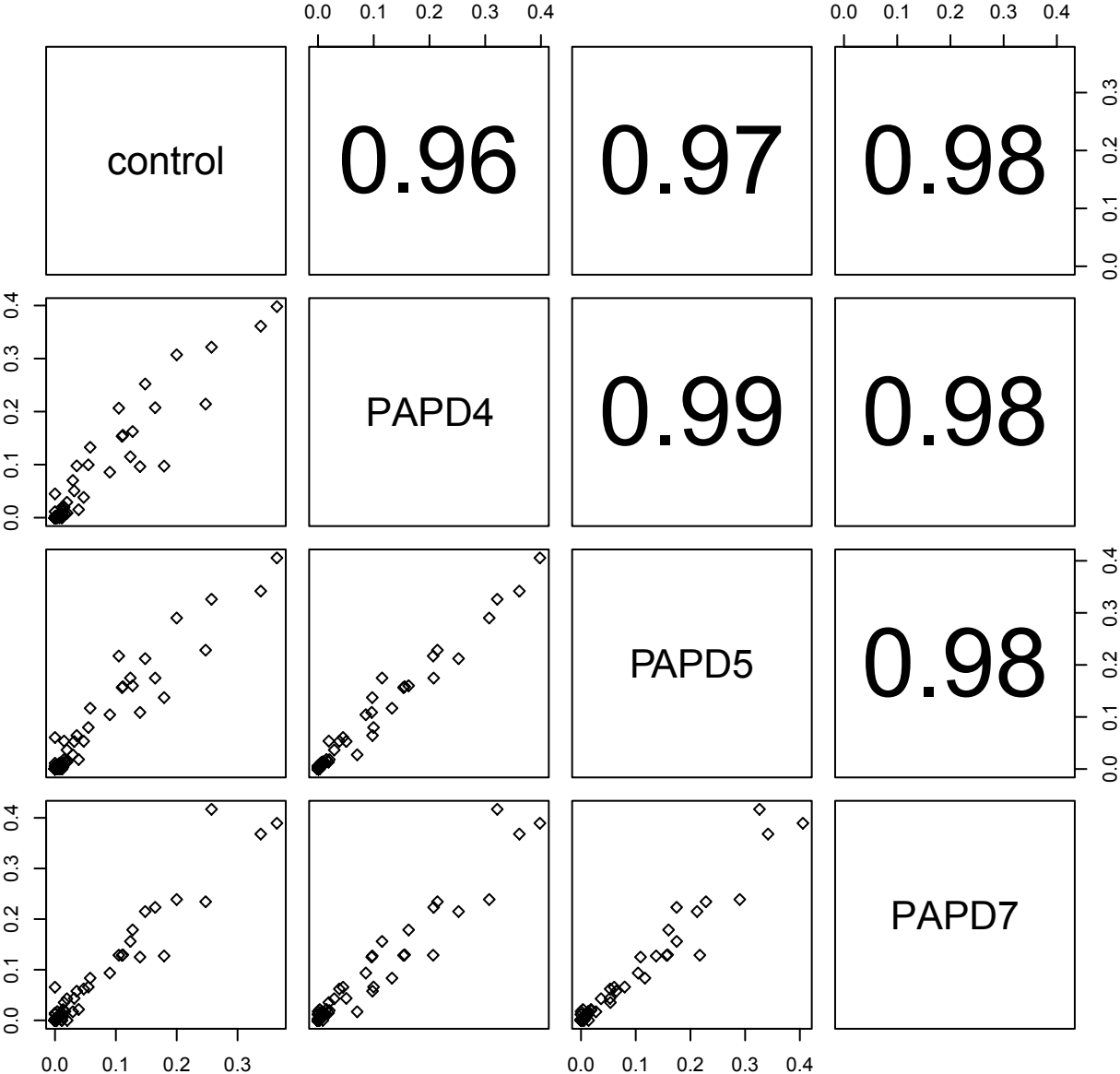


Figure S14.

GA ambiguous addition

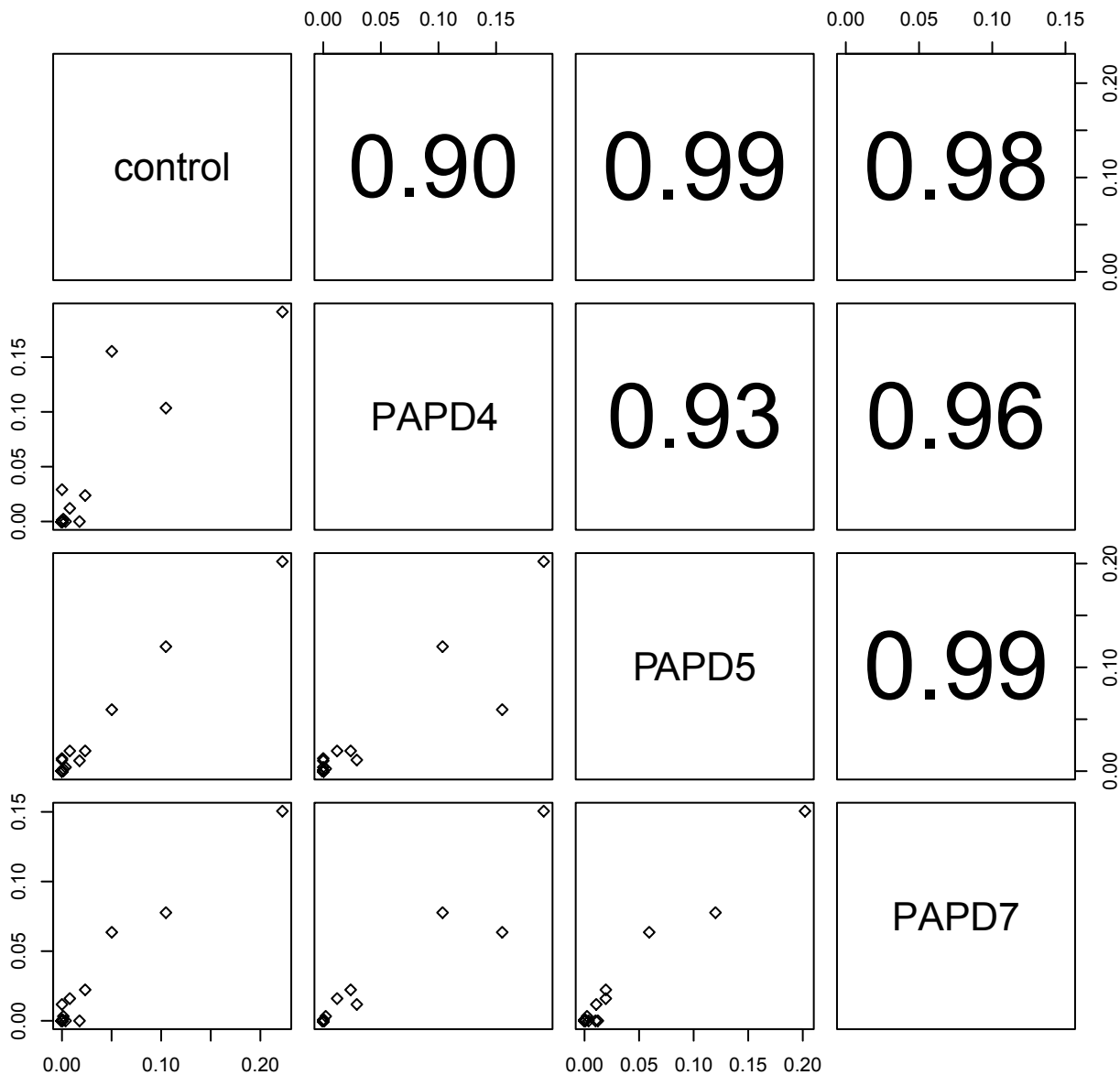


Figure S15.

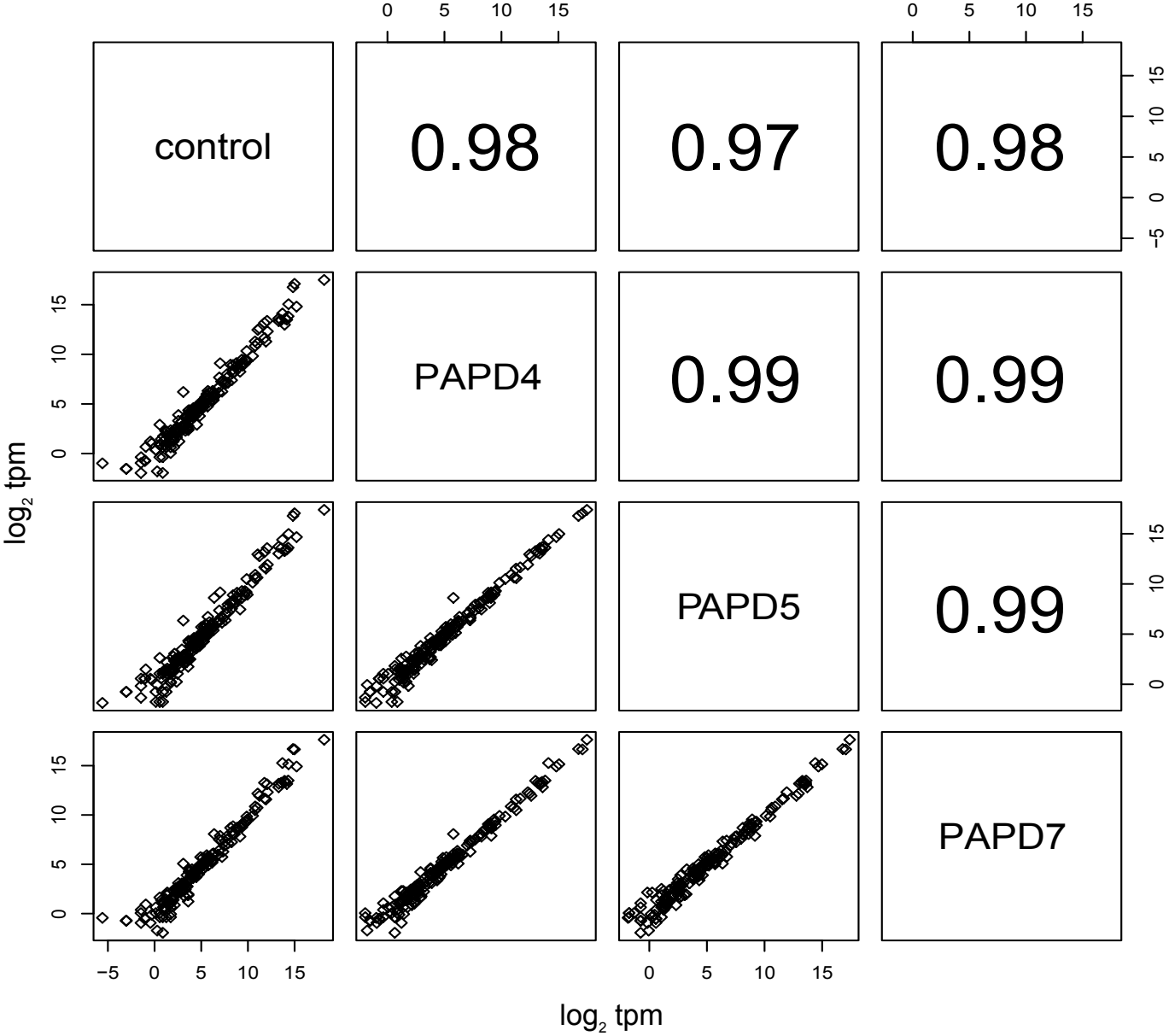


Figure S16.

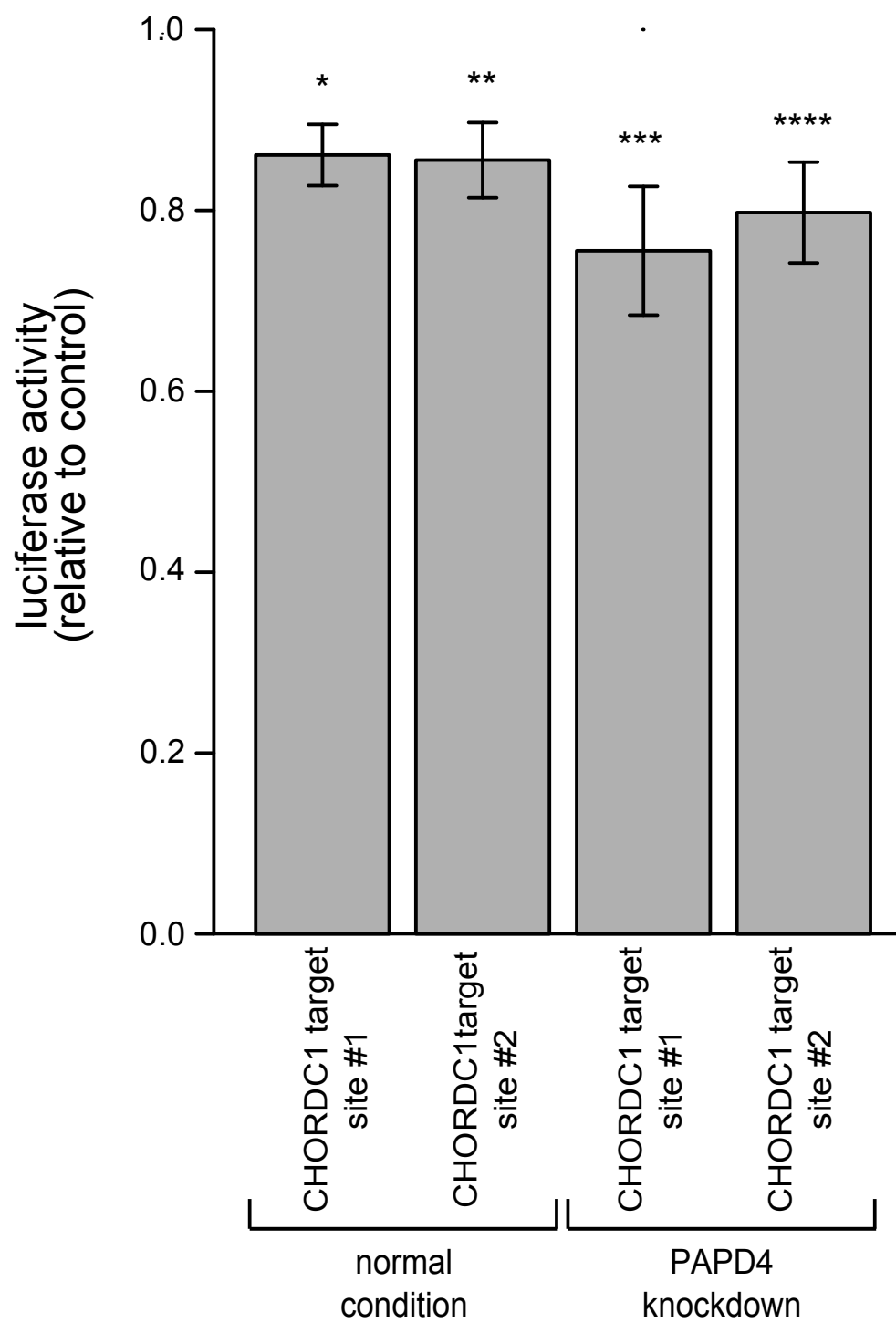


Figure S17.

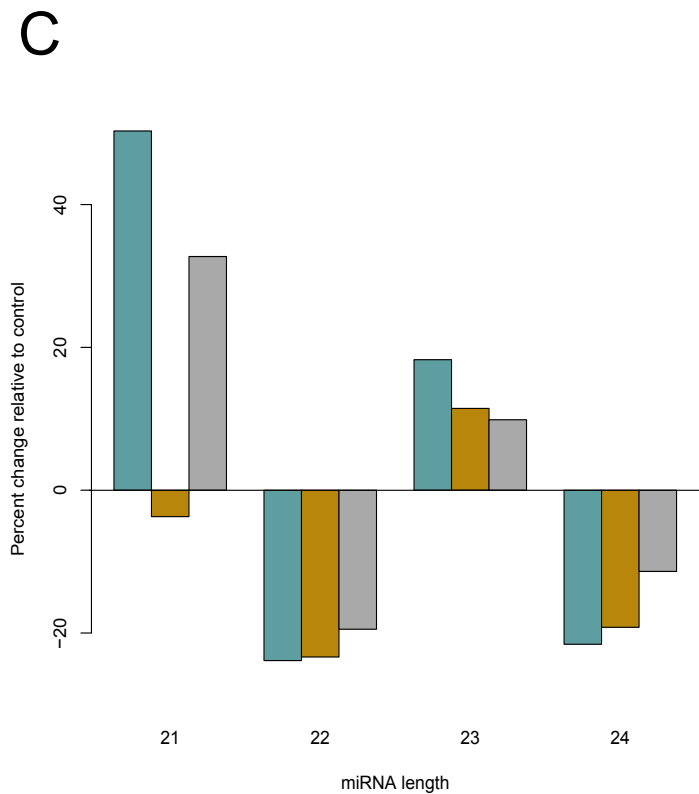
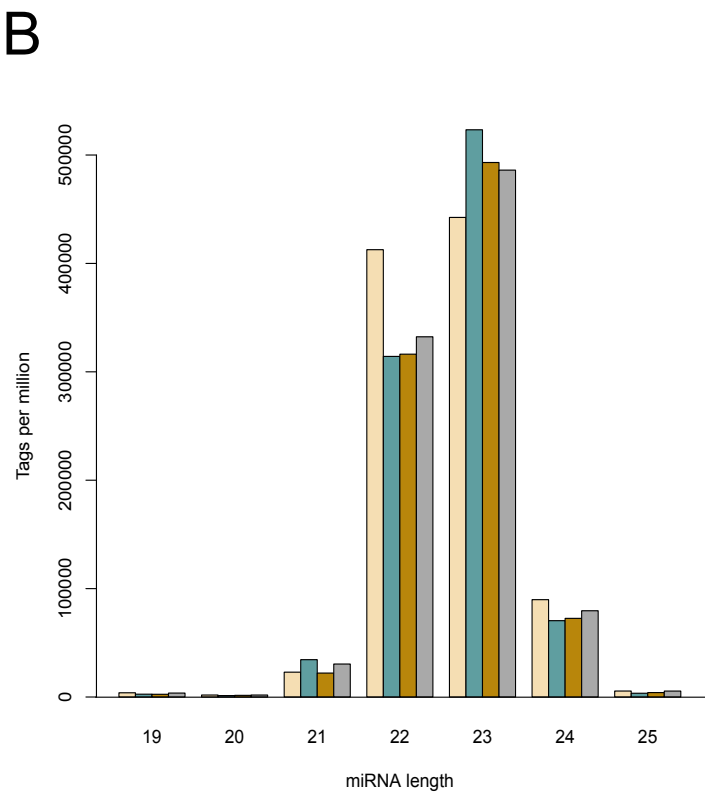
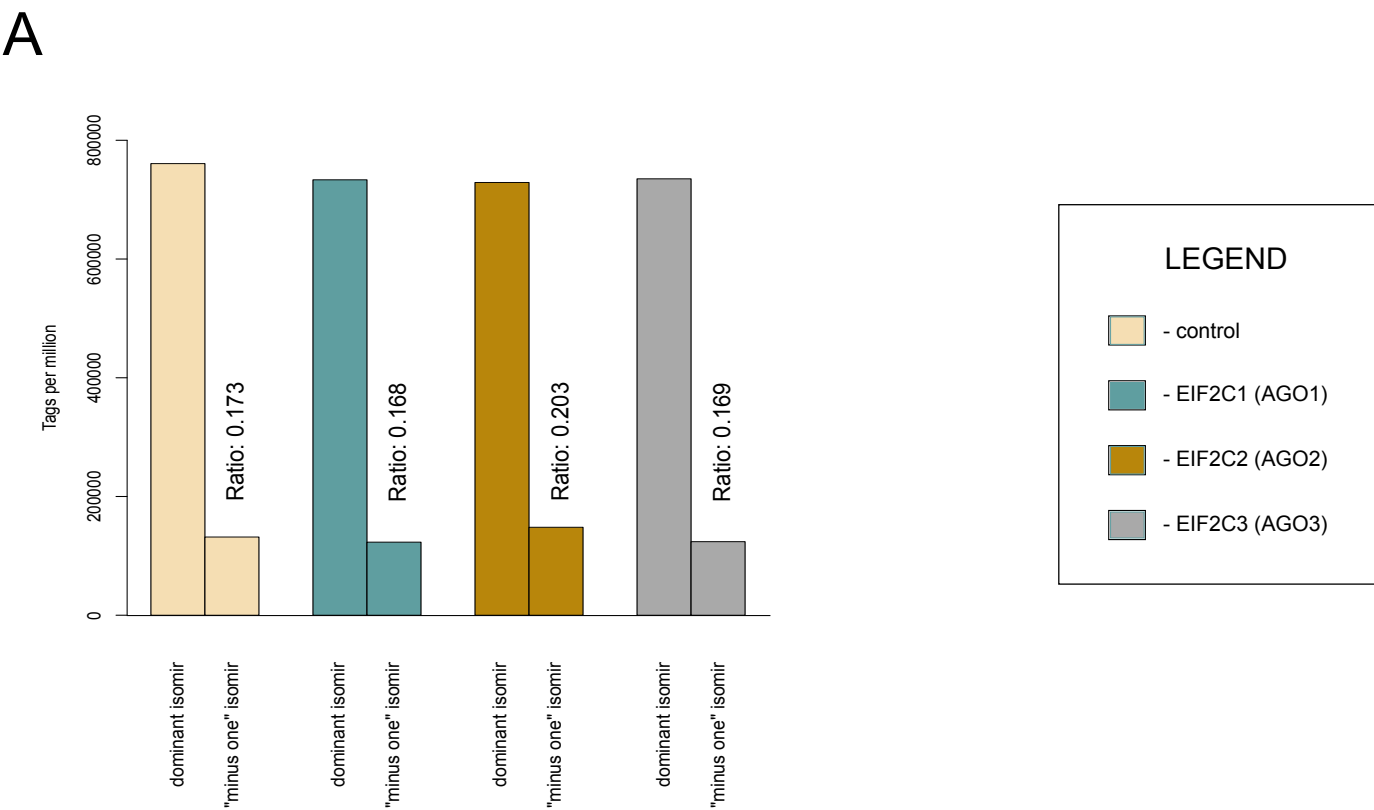
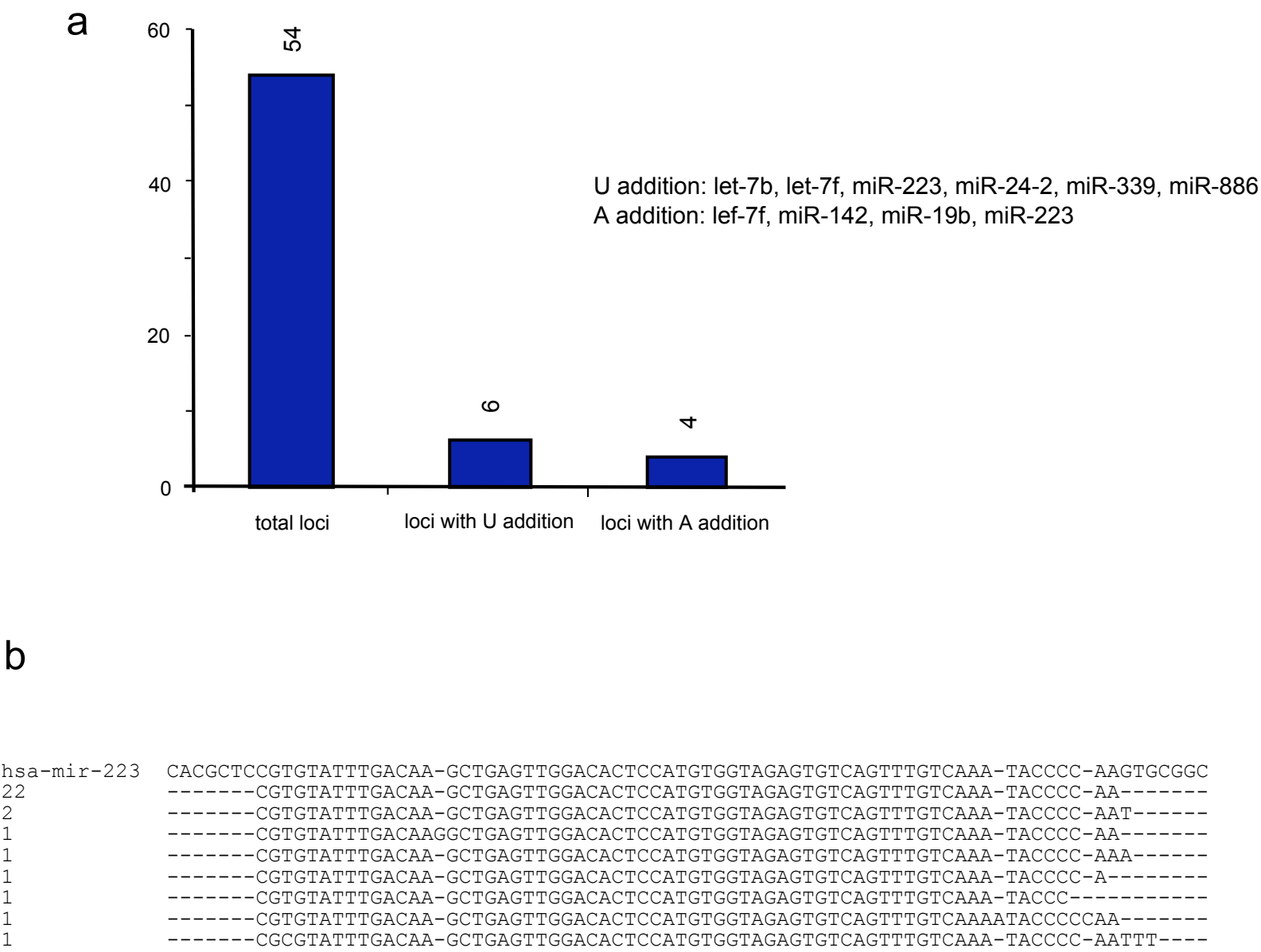
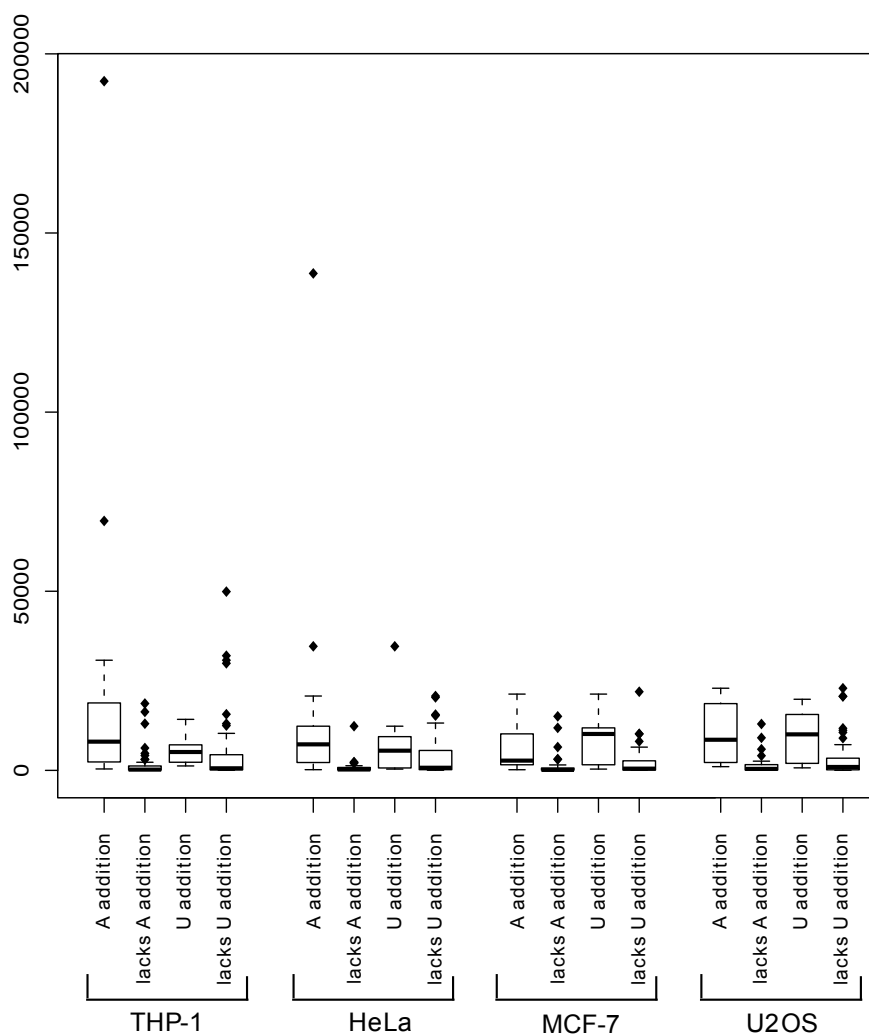


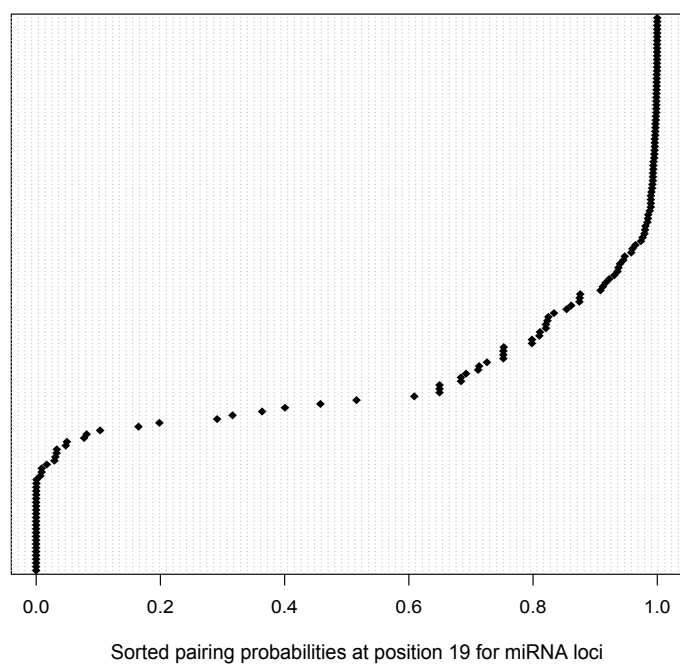
Figure S18.



A



B



C

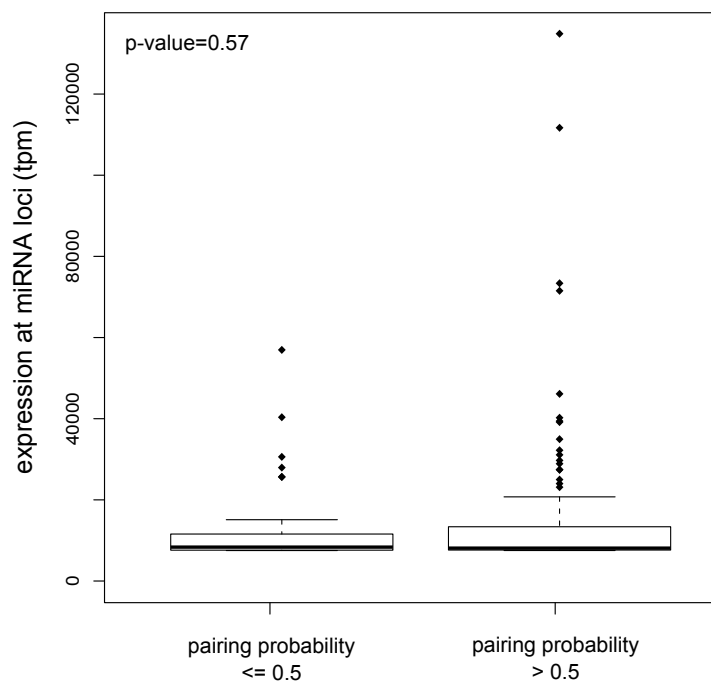


Figure S20.

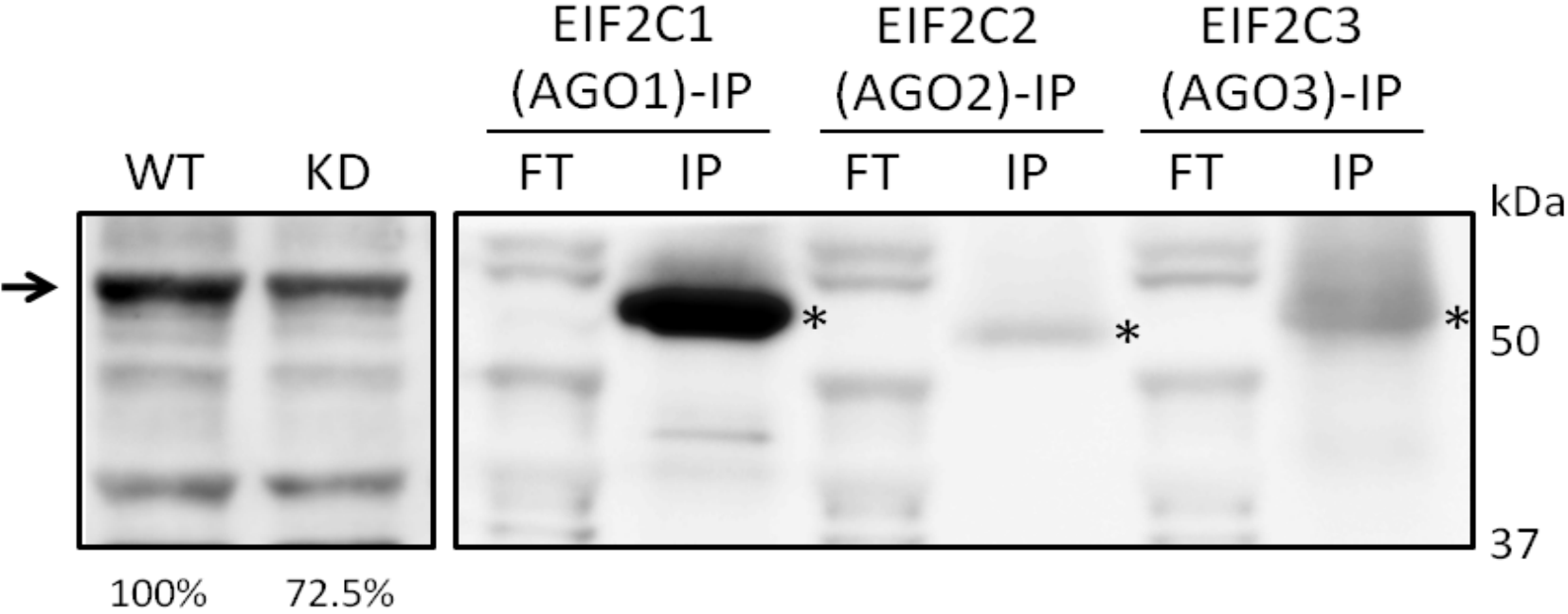


Figure S21.

